NEW CATALYTIC METHODS FOR THE PREPARATION OF TRYPTOPHANS AND PYRROLOINDOLINES: TOTAL SYNTHESIS OF (+)-NASESEAZINES A AND B AND (–)-ASPERGILAZINE A

Thesis by

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ABSTRACT

Tryptophan and unnatural tryptophan derivatives are important building blocks for the total synthesis of natural products, as well as the development of new drugs, biological probes, and chiral small molecule catalysts. This thesis describes various catalytic methods for the preparation of tryptophan derivatives as well as their functionalization and use in natural product total synthesis.

Herein, the tandem Friedel–Crafts conjugate addition/asymmetric protonation reaction between 2-substituted indoles and methyl 2-acetamidoacrylate to provide enantioenriched trytophans is reported. This method inspired further work in the area of transition metal catalyzed arylation reactions. We report the development of the copper-catalyzed arylation of tryptamine and tryptophan derivatives. The utility of these transformations is highlighted in the five-step syntheses of the natural products (+)-naseseazine A and B. Further work on the development of a mild and general Larock indolization protocol to access unnatural tryptophans is also discussed.

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LIST OF ABBREVIATIONS

$[a]_D$	angle of optical rotation of plane-polarized light
Å	angstrom(s)
p-ABSA	*para*-acetamidobenzenesulfonyl azide
Ac	acetyl
APCI	atmospheric pressure chemical ionization
app	apparent
aq	aqueous
Ar	aryl group
At	benztriazolyl
atm	atmosphere(s)
BHT	2,6-di-*tert*-butyl-4-methylphenol ("butylated hydroxytoluene")
Bn	benzyl
Boc	*tert*-butoxycarbonyl
bp	boiling point
br	broad
Bu	butyl
i-Bu	*iso*-butyl
n-Bu	butyl or *norm*-butyl
t-Bu	*tert*-butyl
Bz	benzoyl
C	cytosine

c	concentration of sample for measurement of optical rotation
^{13}C	carbon-13 isotope
^{14}C	carbon-14 isotope
/C	supported on activated carbon charcoal
°C	degrees Celcius
calc'd	calculated
CAN	ceric ammonium nitrate
Cbz	benzyloxycarbonyl
CCDC	Cambridge Crystallographic Data Centre
CDI	1,1'-carbonyldiimidazole
cf.	consult or compare to (Latin: *confer*)
cm^{-1}	wavenumber(s)
cod	1,5-cyclooctadiene
comp	complex
conc.	concentrated
Cy	cyclohexyl
CSA	camphor sulfonic acid
d	doublet
d	dextrorotatory
D	deuterium
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane

de	diastereomeric excess
DIAD	diisopropyl azodicarboxylate
DMAD	dimethyl acetylenedicarboxylate
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DMTS	dimethylthexylsilyl
DNA	deoxyribonucleic acid
DPPA	diphenylphosphorylazide
dppp	1,3-bis(diphenylphosphino)propane
dr	diastereomeric ratio
DTT	dithiothreitol
ee	enantiomeric excess
E	methyl carboxylate (CO_2CH_3)
E^+	electrophile
E	trans (entgegen) olefin geometry
EC_{50}	median effective concentration (50%)
e.g.	for example (Latin: *exempli gratia*)
EI	electron impact
eq	equation
ESI	electrospray ionization
Et	ethyl

et al.	and others (Latin: *et alii*)
FAB	fast atom bombardment
Fmoc	fluorenylmethyloxycarbonyl
g	gram(s)
G	guanine
h	hour(s)
^{1}H	proton
^{2}H	deuterium
^{3}H	tritium
[H]	reduction
HATU	2-(7-aza-1*H*-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
HMDS	hexamethyldisilamide or hexamethyldisilazide
HMPT	hexamethylphosphoramide
hn	light
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
IC_{50}	half maximal inhibitory concentration (50%)
i.e.	that is (Latin: *id est*)
IR	infrared spectroscopy
J	coupling constant
k	rate constant
kcal	kilocalorie(s)

kg	kilogram(s)
L	liter or neutral ligand
l	levorotatory
LA	Lewis acid
LD_{50}	median lethal dose (50%)
LDA	lithium diisopropylamide
LTMP	lithium 2,2,6,6-tetramethylpiperidide
m	multiplet or meter(s)
M	molar or molecular ion
m	meta
m	micro
m-CPBA	*meta*-chloroperbenzoic acid
Me	methyl
mg	milligram(s)
MHz	megahertz
MIC	minimum inhibitory concentration
min	minute(s)
mL	milliliter(s)
MM	mixed method
mol	mole(s)
MOM	methoxymethyl
mp	melting point
Ms	methanesulfonyl (mesyl)

MS	molecular seives
m/z	mass-to-charge ratio
N	normal or molar
NBS	*N*-bromosuccinimide
nm	nanometer(s)
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	nuclear Overhauser enhancement spectroscopy
Nu^-	nucleophile
o	ortho
[O]	oxidation
t-Oct	*tert*-octyl (1,1,3,3-tetramethylbutyl)
p	para
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Ph	phenyl
pH	hydrogen ion concentration in aqueous solution
pK_a	acid dissociation constant
PMB	*para*-methoxybenzyl
ppm	parts per million
PPTS	pyridinium *para*-toluenesulfonate
Pr	propyl
i-Pr	isopropyl

n-Pr	propyl or *norm*-propyl
psi	pounds per square inch
py	pyridine
q	quartet
R	alkyl group
R	rectus
REDAL	sodium bis(2-methoxyethoxy)aluminum hydride
ref	reference
R_f	retention factor
RNA	ribonucleic acid
s	singlet or seconds
S	sinister
sat.	saturated
SEM	2-(trimethylsilyl)ethoxymethyl
SOD	superoxide dismutase
Su	succinimide
t	triplet
T	thymine
TBAF	tetra-*n*-butylammonium fluoride
TBAT	tetra-*n*-butylammonium difluorotriphenylsilicate
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl
TCA	trichloroacetic acid

temp	temperature
TES	triethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TFE	2,2,2-trifluoroethanol
THF	tetrahydrofuran
THIQ	tetrahydroisoquinoline
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMEDA	*N*,*N*,*N'*,*N'*-tetramethylethylenediamine
TMS	trimethylsilyl
TOF	time-of-flight
tol	tolyl
Troc	2,2,2-trichloroethoxycarbonyl
Ts	*para*-toluenesulfonyl (tosyl)
UV	ultraviolet
w/v	weight per volume
v/v	volume per volume
X	anionic ligand or halide
Z	cis (zusammen) olefin geometry

Chapter 1

An Introduction to Tryptophan

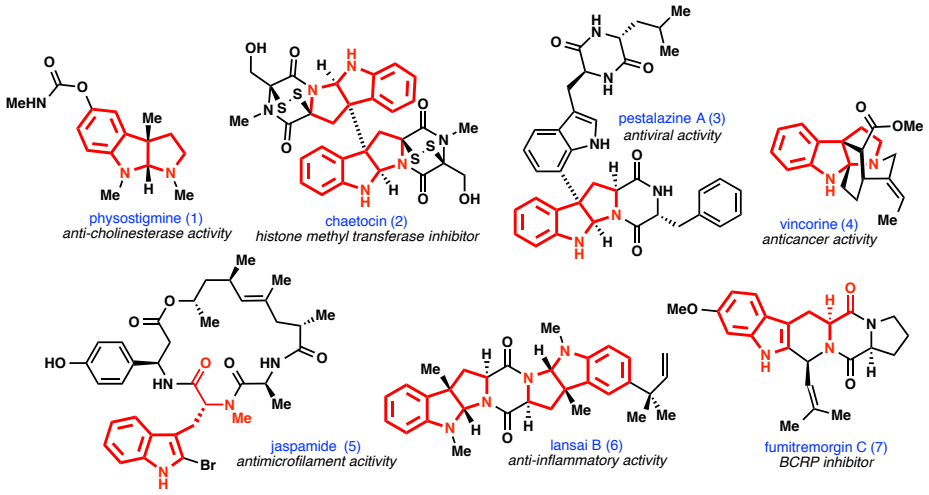
1.1 INTRODUCTION

Tryptophan and unnatural tryptophan derivatives are important building blocks in the total synthesis of natural products, as well as for the development of new drugs,[1] biological probes,[2] and chiral small molecule catalysts.[3] The central tryptophan motif can be found within numerous biologically active natural products, either explicitly or implicitly, some of which are shown in **Figure 1.1**. Furthermore, the utilization of functionalized tryptophans for the study of complex biological systems has served as an important strategy for studying protein conformational dynamics as well as elucidating key protein interactions, such as the identification of a critical cation–π interaction of the nicotinic acetylcholine receptor.[2c]

Biosynthetically, these key amino acids serve as the basis for another fascinating class of natural products, the pyrroloindoline alkaloids.[4] This family comprises a large class of compounds characterized by their unique indoline fused pyrrolidine core (**Figure**

1.1). These compounds have been shown to exhibit a broad array of biological activity across a range of cell lines that is intricately related to their broad structural diversity. Given their promising medicinal relevance, these products have inspired innovative work on new synthetic methodologies to access the central pyrroloindoline framework that have culminated in the total synthesis of a number of these challenging natural products.[5]

Figure 1.1. *Trytophan and cyclotryptophan natural products*



Together, these molecules have served as topics of intense interest from synthetic chemists and chemical biologists alike. The following introductory chapter serves to briefly summarize and highlight modern synthetic strategies and tactics to access unnatural tryptophan derivatives as well as pyrroloindoline alkaloids with selected examples in total synthesis.

1.2 SYNTHESIS OF TRYPTOPHAN DERIVATIVES

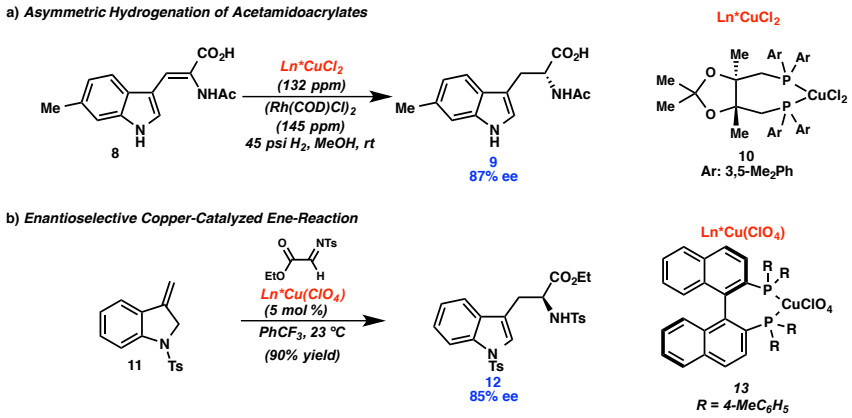
Due to their pervasiveness across many fields, the development of new methods to access enantioenriched tryptophan derivatives represents an important endeavor in synthetic chemistry.[1,2,3] This is particularly true due the inherent challenges associated

with selective backbone functionalization of the indole nucleus, making simple derivatization of natural (*L*)-tryptophan largely untenable. As a result, a range of methods for the preparation of enantioenriched unnatural tryptophans, including auxiliary controlled, enantiospecific, and enantioselective methods, have been reported.[6]

Surprisingly, to date, there exist relatively few convergent and enantioselective syntheses of tryptophan derivatives lacking β-substitution. Perhaps the most common method to access unnatural amino acids is through the asymmetric hydrogenation of dehydroamino acids. In 1980, Townsend and co-workers demonstrated that subjection of 6-methyl dehydrotryptophan to $[Rh(COD)Cl]_2$, copper-phosphine complex **10**, and 45 psi of hydrogen gas gave 6-methyl tryptophan (**9**) in high enantiomeric excess (**Scheme 1.1**, **a**).[7] Subsequent work on asymmetric hydrogenation has further streamlined this process to provide excellent ee's at low Rh-catalyst loadings, making it an efficient choice in many instances. Still, the preparation of the dehydroamino acids, often from the corresponding carboxyaldehyde, can sometimes require a laborious synthetic undertaking.

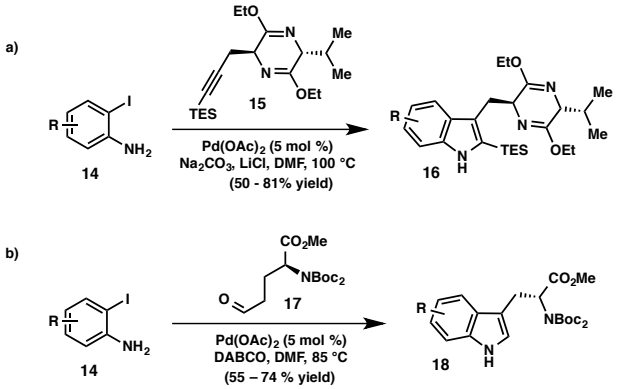
An alternative enantioselective method was described by Leckta and co-workers in 1998. By employing 5 mol % of copper-BINAP catalyst **13,** tosylindoline **11** can undergo an enantioselective imino-ene reaction to furnish tosyl tryptophan derivative **12** in 90% yield and 85% ee (**Scheme 1.1**, **b**).[8] While this method offers access to enantioenriched products, strict substrate requirements limit the generality of this approach and thus this method has largely not been broadly adopted for tryptophan synthesis.

Scheme 1.1. *Enantioselective methods for the synthesis of unnatural tryptophans*



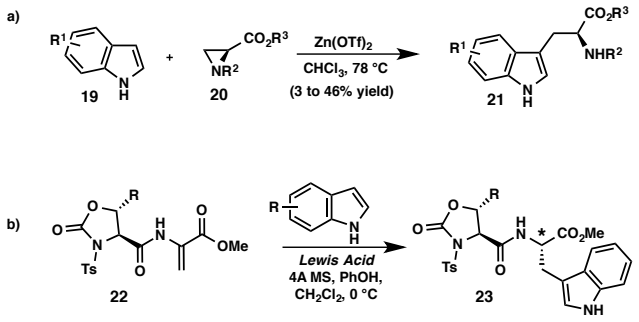
Given the dearth of catalytic, enantioselective methods reported to date, alternative strategies are also commonly employed, including enantiospecific and auxiliary-controlled methods. One such enantiospecific approach utilizes *ortho*-iodoanlines (**14**) in conjunction with an amino-acid derived coupling partner (**Scheme 1.2**, **a**).[9] In 1999, Cook and co-workers reported the Pd(0)-catalyzed heteroannulation (Larock indole synthesis) of *o*-iodoaniline with Schöllkpf-auxiliary derived triethylsilyl alkyne **15**. Utilizing Larock's originally reported conditions, functionalized indoles containing the amino acid moiety masked as a bis-imidate are efficiently synthesized (**16**). These products can be readily advanced to the parent amino acid through sequential acid-mediated hydrolysis followed by saponification. A complementary approach to the Larock indole synthesis was reported by Jia and Zhu in 2005, utilizing an aldehyde coupling partner (**17**) in place of a disubstituted alkyne (**Scheme 1.2**, **b**).[10] Operating through the intermediacy of the aldimine, Pd-mediated heteroannulation affords 2-unsubstituted tryptophans in moderate to good yield. Importantly, this method requires the formation of reactive aliphatic aldehyde intermediates and therefore necessitates protection of the amine as an imide.

Scheme 1.2. *Enantiospecific methods for the synthesis of unnatural tryptophans*



Lewis-acid mediated coupling strategies have also been employed for tryptophan synthesis from enantiopure starting materials. In 1989, Sato and Kozikowski reported a $Zn(OTf)_2$-mediated stereospecific opening of enantiopure aziridines to directly provide functionalized tryptophans, albeit in modest yields (**Scheme 1.3**, **a**). Subsequent work by Bennani[11] and Isobe[12] have illustrated that improved yields of this process may be achieved by utilizing scandium-based Lewis acids. An alternative, auxiliary-based approach has also been developed by Gentilucci and coworkers, employing oxazolidinone-based acetamidoacrylates with a variety of Lewis-acids to effect 1,4-addition of an indole nucleophile (**Scheme 1.3**, **b**).[13] Using this approach, moderate diastereoselectivities are achieved depending on the indole nucleophile and Lewis acid employed.

Scheme 1.3. *Enantiospecific and auxiliary based approaches for the synthesis of unnatural tryptophans*



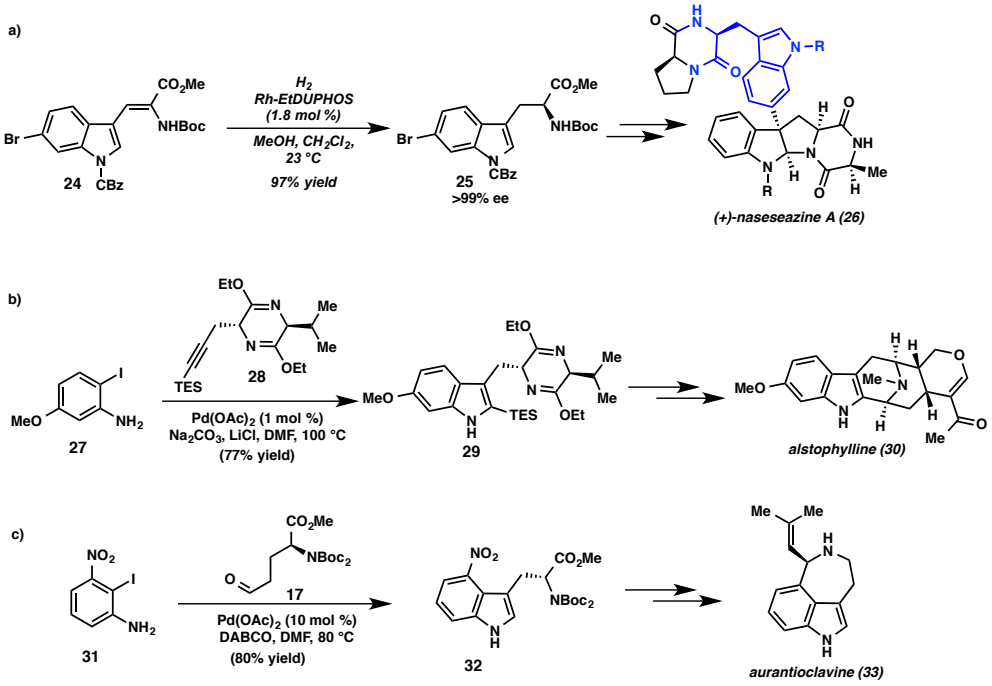
1.3 TRYPTOPHAN DERIVATIVES IN TOTAL SYNTHESIS

As highlighted above, the tryptophan motif is prevalent in many natural product scaffolds and it is therefore unsurprising that the methods outlined previously have been widely adopted in total synthesis. In most instances, the assembly of a requisite tryptophan moiety occurs at an early stage of the synthesis, and is subsequently functionalized or appended to more complex fragments in order to complete the total synthesis. Far fewer examples exist in the literature of late-stage tryptophan synthesis, a likely consequence of limitations in the existing methodology in functional group tolerance.

For example, **Scheme 1.4** illustrates the preparation of three unnatural tryptophans. In their synthesis of the (+)-naseseazines, Movassaghi and Kim utilize a highly selective Rh-EtDUPHOS catalyzed asymmetric hydrogenation in order to prepare 6-bromotryptophan **25** for elaboration to the northern diketopiperazine of (+)-naseseazine A (**26**).[14] This hydrogenation is not only high yielding and enantioselective, it occurs in the presence of other potentially reactive groups such as a CBz protecting group and the

aryl bromide. Cook and co-workers have also utilized their methodology in their total synthesis of the complex polycyclic alkaloid alstophylline (**Scheme 1.4**, **b**). Employing a Larock indole synthesis on 300-gram scale with only 1 mol % $Pd(OAc)_2$, aniline **27** is readily advanced to 6-methoxytryptophan *en route* to the natural product.[15] Similarly, Jia and co-workers have utilized their Pd-catalyzed aldehyde-aniline coupling to synthesize 4-nitrotrytophan derivative **32**, which is then advanced to the natural product aurantioclavine (**33**).[16]

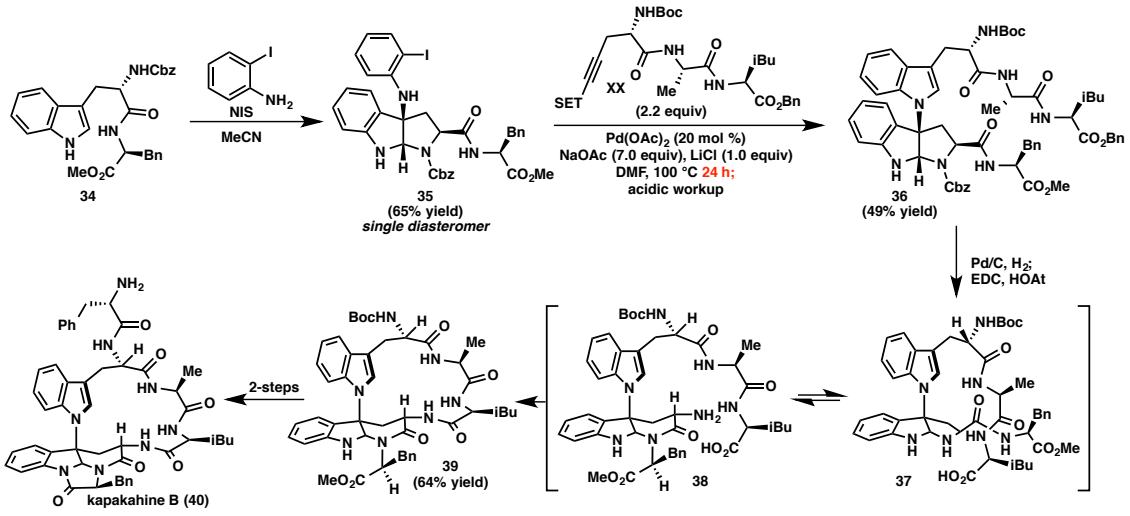
Scheme 1.4. *Tryptophan in total synthesis*



Although early-stage tryptophan synthesis is the most common, several remarkable examples of late-stage tryptophan assembly via Larock indolization have been reported in the literature. In 2009 Baran and co-workers reported the total synthesis of kapakahine B, utilizing a Larock indole synthesis to assemble the key tryptophan motif.[17] Beginning with tryptophan-derived peptide **24**, subjection to *o*-iodoaniline and NIS provided pyrroloindoline **35** as a single diastereomer. Under palladium catalysis,

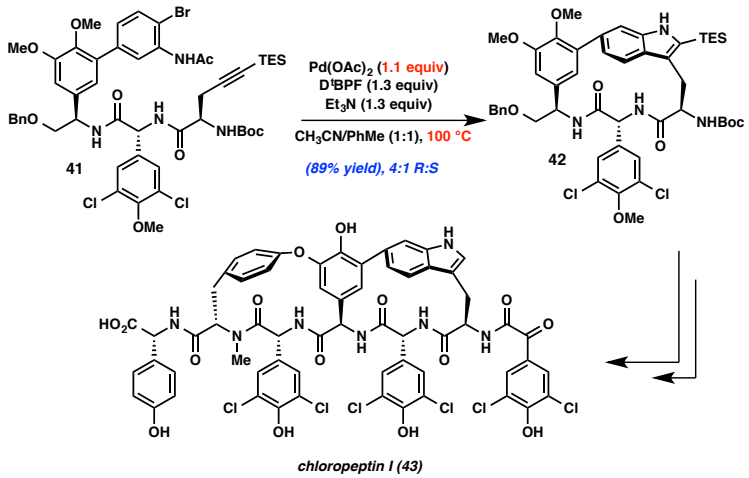
iodoaniline **35** underwent a Larock indole synthesis with a serine-derived derived alkyne in a moderate 49% yield. Debenzylation and concomitant Cbz deprotection furnished pyrroloindoline **37**, which existed in equilibrium with α-carboline **38**. Addition of EDC and HOAt resulted in facile and selective macrocycle formation from α-carboline **38**, providing the product in 64% yield. The synthesis of kapakahine B was completed in a further two-steps. This elegant synthesis, which assembles the key tryptophan moiety in an exceptionally complex setting, illustrates both the power of the Larock indole synthesis, but also its limitations – the key step requires upwards of 20 mol % catalyst for prolonged reaction times (24 h) in order to achieve two productive turnovers.

Scheme 1.5. *Baran's synthesis of kapakahine B*



An equally impressive Larock indole synthesis was used as the key step in Boger's fabulous synthesis of the chloropeptins (**Scheme 1.6**).[18] Utilizing an intramolecular macrocyclization strategy, treatment with 1.1 equiv $Pd(OAc)_2$ in the presence of 1,1'-di-tertbutylphosphinoferrocene in a mixed solvent system provided 89% yield of indolization product **42** in favor of the desired atropisomer.

Scheme 1.6. *Boger's late stage tryptophan synthesis*

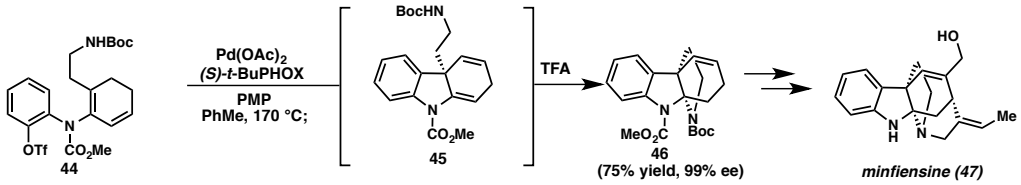


1.4 STRATEGIES FOR THE SYNTHESIS OF PYRROLOINDOLINES

The abundance of pyrroloindoline natural products and the breadth of structural diversity, coupled intricately with their biological activities, has sparked a tremendous interest from the synthetic community, both in methodology develop and in total synthesis.[5] Due to intense interest in this area of research, the structure, activity, and synthesis of pyrroloindolines has been reviewed in detail.[19]

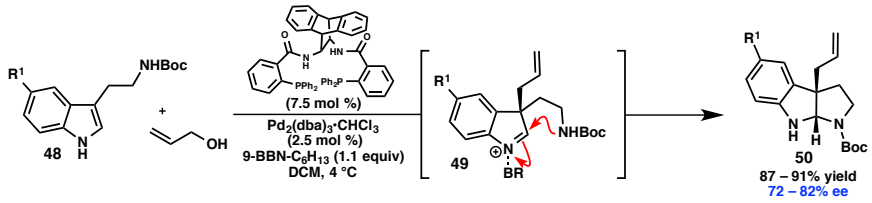
From a strategic standpoint, there are numerous disconnections to arrive at the pyrroloindoline motif. Instrumental in enabling the enantioselective synthesis of pyrroloindolines, however, has been the adoption of chiral transition metal complexes. One such approach is exemplified in work by Overman and co-workers on the enantioselective, intramolecular Heck cyclization (**Scheme 1.7**).[20] Treatment of aryl triflate **44** in the presence $Pd(OAc)_2$, (*S*)-^{t}BuPHOX, and pentamethylpiperidine as base resulted in clean Heck cyclization to provide 1,3-cyclohexadiene intermediate **45**. Immediate quenching with TFA then effected cyclization of the pendant amine, thereby providing the pyrroloindoline framework (**46**) in 75% overall yield and 99% ee.

Scheme 1.7. *Overman's Heck strategy to access pyrroloindolines*



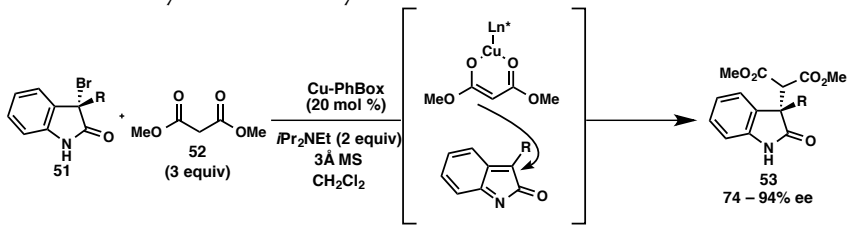
A mechanistically distinct approach using a Pd-catalyst was reported by Trost in 2006, utilizing allyl alcohols in conjunction with trialkylborates to effect C3-allylation in high yields and good enantioselectivities (**Scheme 1.8**).[21] The reaction is presumed to occur *via* an electrophilic, chiral Pd-π-allyl complex, thus providing high enantiofacial bias of the prochiral electrophile. This reaction, which provides the pyrroloindoline directly from a corresponding tryptamine, follows up previous work from the Trost lab on the asymmetric allylic alkylation of oxindole nucleophiles, the products of which can also be elaborated to the pyrroloindoline motif *via* reductive functionalization.[22]

Scheme 1.8. *Trost's transition metal strategy to access pyrroloindolines*



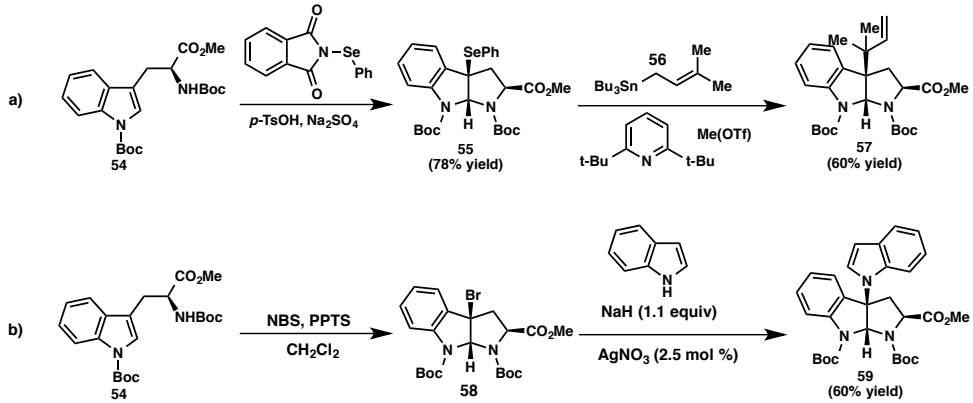
The application of a chiral Pd-π-allyl complex constitutes a chiral electrophile strategy to access pyrroloindolines. Alternatively, a chiral nucleophile strategy can be employed as reported by Stoltz in 2009.[23] Utilizing a CuPhBOX complex in the presence of excess base, dimethylmalonate **52** can be efficiently alkylated in excellent yields and enantioselectivities to afford functionalized oxindole products (**Scheme 1.9**). Reductive elaboration of these oxindole products affords the pyrroloindoline scaffolds in high ee.

Scheme 1.9. *Stoltz's asymmetric alkylation of oxindoles*



Perhaps one of the most widely adopted strategies to date is that of C3-oxidative functionalization *via* an electrophilic heteroatom. This versatile approach has been utilized extensively on tryptamine and tryptophan scaffolds, and occurs through direct C3-functionalization followed by cyclization of a pendant nucleophile onto the resulting iminium ion. The C3-substituent can often act as a leaving group, enabling subsequent functionalization in a highly selective manner. Two such examples are illustrated in **Scheme 1.10**. An early report by Danishefsky and co-workers illustrated the ability of electrophilic selenation to enable the highly diastereoselective selenocyclization of Boc-tryptophan derivative **54** in 78% yield.[24] Subsequent activation with MeOTf in the presence of a prenylstannane reagent provides reverse prenylated pyrroloindoline **57** in 60% yield.

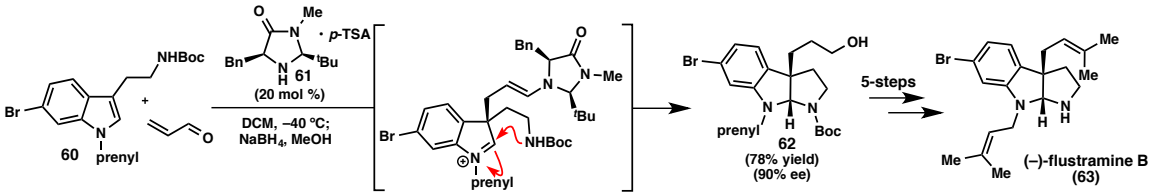
Scheme 1.10. *C3-functionalization/cyclization to access pyrroloindolines*



This strategy is applicable with a range of electrophiles. As shown in scheme **1.10**, addition of *N*-bromosuccinimide and pyridinium *p*-toluensulfonate to tryptophan **54** results in clean formation of bromopyrroloindoline **58**. Subsequent treatment with excess base and catalytic $AgNO_3$ results in stereoretentive substitution by an indole nucleophile. Extension of this strategy to other electrophilic atom sources as well as a range of enantioselective variants have been reported.[25]

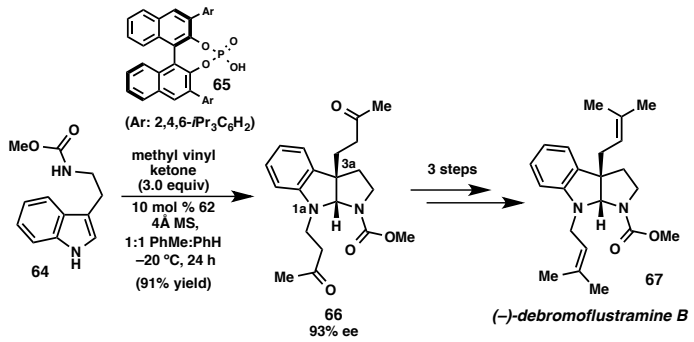
In contrast to heteroatom based electrophiles, carbon-based electrophiles can also be utilized with great success. In 2004, MacMillan and coworkers illustrated the success of this strategy *via* iminium activation. Utilizing imidazolinone catalyst **61** with acrolein as an electrophile, a highly enantioselective preparation of C3-alkylated pyrroloindolines was achieved (**Scheme 1.11**).[26]

Scheme 1.11. *MacMillan's organocatalyzed pyrroloindoline synthesis*



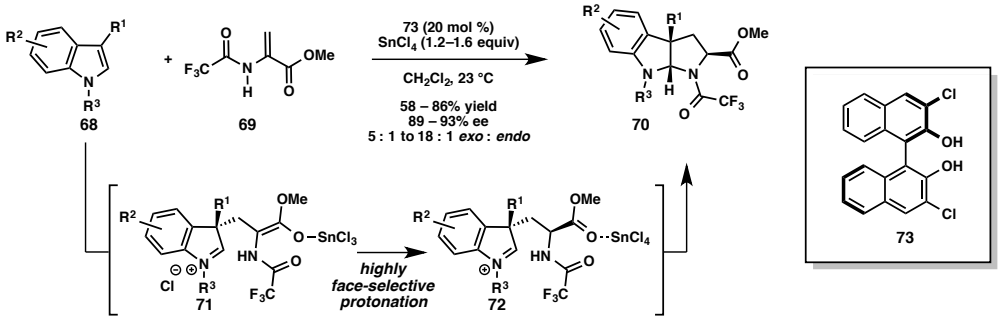
Activation of Michael acceptors can also be realized utilizing chiral Brønsted acids, such as *(R)*-TRIP (**Scheme 1.12**). As demonstrated by Antilla and co-workers, addition of catalytic *(R)*-TRIP phosphoric acid **65** to an excess of methyl vinyl ketone resulted in a highly enantioselective, double conjugate addition to provide pyrroloindoline **66**, which was readily advanced to the natural product (–)-debromoflustramine B in an additional three steps.[27]

Scheme 1.12. *Antilla's organocatalyzed pyrroloindoline synthesis*



Distinct from the two reactions shown above, Reisman and co-workers reported a highly enantioselective, formal (3 + 2) cycloaddition reaction between 3-substituted indoles and acetamidoacrylates (**Scheme 1.13**).[28] Employing stoichiometric $SnCl_4$ and catalytic (*R*)-BINOL, which together presumably generate a Lewis-acid assisted Brønsted acid, pyrroloindolines **70** are convergently synthesized in a single step from simple starting materials. It is proposed that this reaction proceeds *via* a highly face-selective protonation reaction, which resolves two diastereomeric conjugate addition complexes (**71**–**72**). From a synthetic standpoint, a key distinction of this method compared to others is that the pendant amine nucleophile resides on the electrophilic coupling partner, rather than on the nucleophile.

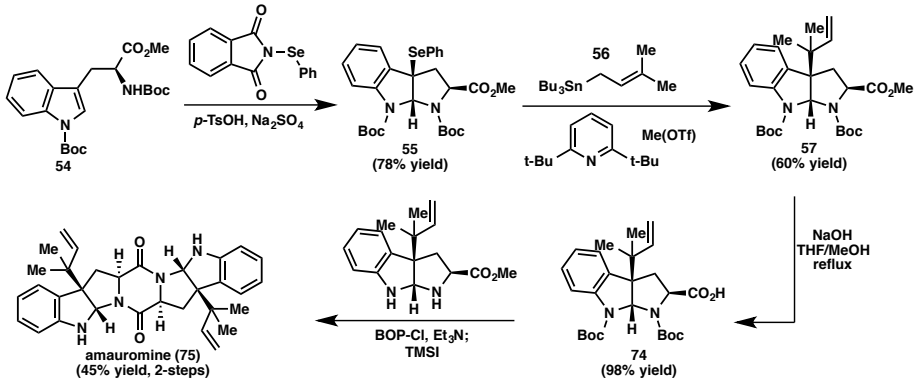
Scheme 1.13. *Reisman's formal (3+2) cycloaddition to access pyrroloindlines*



1.5 PYRROLOINDOLINES IN TOTAL SYNTHESIS

Given the enormous body of research dedicated to the total synthesis of pyrroloindolines, only a small sampling of total syntheses will be presented in the section below. One of the first successful examples employing a diastereoselective pyrroloindoline synthesis comes from the Danishefsky lab (**Scheme 1.14**).[24] Beginning with Boc protected tryptophan **54**, they were able to effect a selenation/cyclization sequence to furnish *exo*-pyrroloindoline **55** as a 9:1 diastereomeric mixture. Activation of the phenyl selenide with MeOTf and exposure to prenyl stannane **56**, provided the reverse prenyl adduct in 60% yield. Saponification of the methyl ester, peptide coupling with the free amine, and successive diketopiperazine formation provided amauromine in only four-steps from tryptophan **54**.

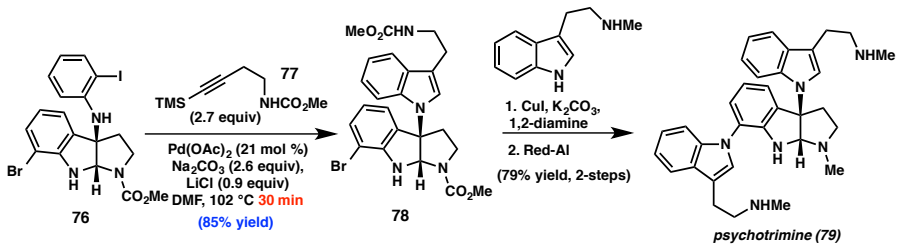
Scheme 1.14. *Danishefsky's synthesis of amauromine*



In 2008, Baran and co-workers demonstrated the diastereoselective cyclization of tryptamines with nitrogen-based electrophiles.[29] Beginning with tryptamine, treatment with the unique combination of *N*-iodosuccinimide, 2-iodoaniline, and Et_3N at –45°C results in an electrophilic, C3-amination of the tryptamine to afford pyrroloindoline **76**. Under palladium catalysis, iodoaniline **76** underwent a Larock indole synthesis with

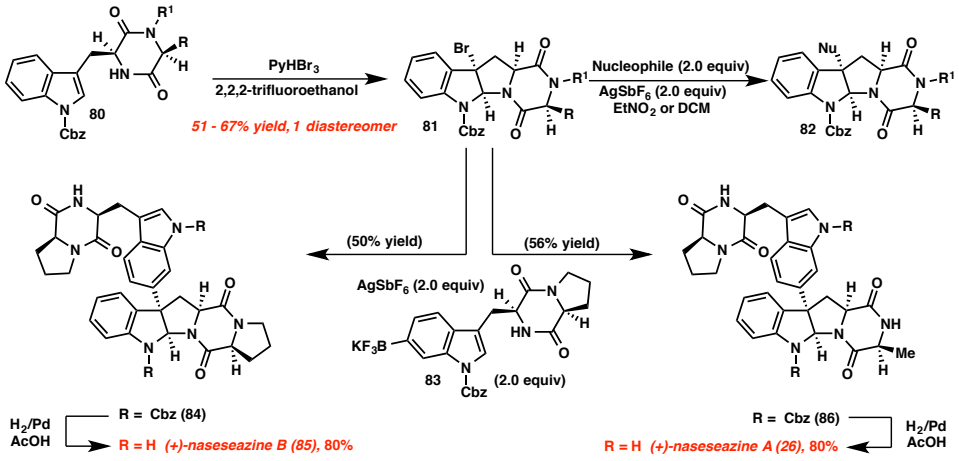
alkyne **77** in excellent yield. C–N bond formation, followed by treatment with Red-Al provided the natural product psychotrimine (**79**) in excellent overall yield.

Scheme 1.15. *Baran's synthesis of psychotrimine*



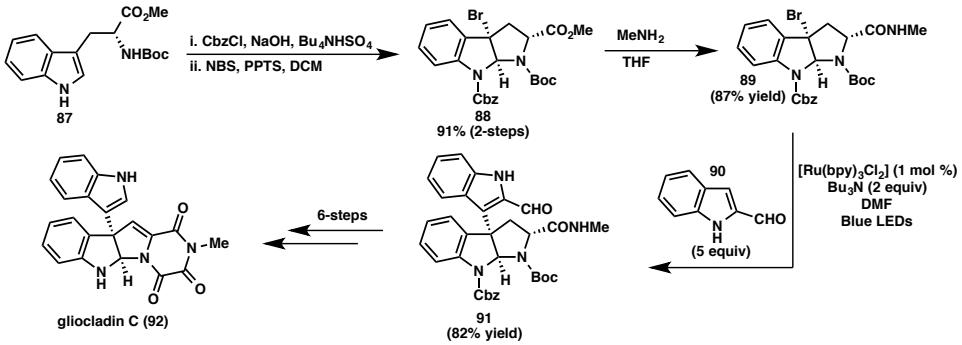
In 2011, Movassaghi and Kim reported a general strategy for the synthesis of 3-arylpyrroloindolines *via* a two-step bromocyclization/Friedel-Crafts sequence of tryptophan-derived diketopiperazines (**Scheme 1.16**).[14] Treatment of protected diketopiperazine **80** with $PyHBr_3$ in 2,2,2-trifluoroethanol effected an oxidative cyclization to form C3-bromopyrrolodinoline **81** in moderate yield and as a single diastereomer. In a subsequent step, addition of superstoichiometric silver salts resulted in halide abstraction to form a benzylic cation, which is then readily trapped in a stereoretentive fashion with excess nucleophile (**82**). Using this strategy, a variety of C3-substituted pyrroloindolines are readily prepared, accomodating C3-allyl, aryl, and hetereoaryl substitution. Although a number of arenes react to form a mixture of positional isomers during the Friedel-Crafts step in this reaction, the corresponding potassium trifluoroborate salts can be used to adequately restore regioselectivity. Using this method, the authors advanced bromotetracycle **81** to 3-arylpyrroloindolines **84** and **86** in 50 and 56% yield, respectively, utilizing an excess of functionalized potassium trifluoroborate salt **83**, derived from 6-bromotryptophan. Subsequent global deprotection provided (+)-naseseazines A and B in 80% yield and 9-steps longest linear sequence.

Scheme 1.16. *Movassaghi's synthesis of (+)-naseseazines A and B*



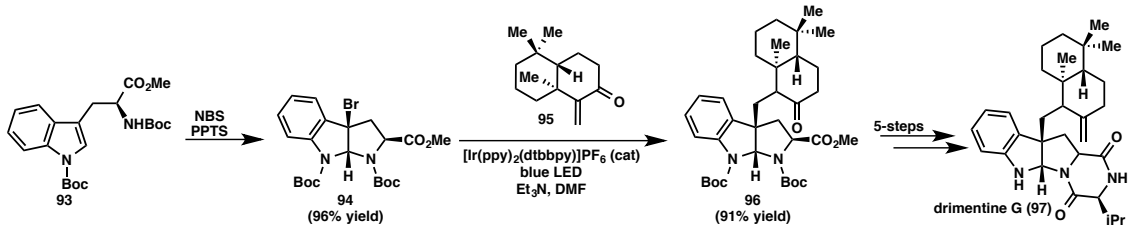
A similar approach was adopted by Stephenson and co-workers in their synthesis of gliocladin C using photoredox catalysis.[30] Following an oxidative cyclization of protected tryptophan **87**, the bromopyrroloindoline underwent amidation to furnish carboximide **89**. Subsequent exposure to $[Ru(bpy)_3Cl_2]$ and visible light generated a tertiary benzylic radical, which was trapped with five equivalents of indole **90** to form the desired C3–C3' aryl linkage. Notably, C2 substitution of the indole nucleophile is imperative to achieve the desired regioselectivity in the transformation. Additional elaboration to the natural product was accomplished in six-steps.

Scheme 1.17. *Stephenson's synthesis of gliocladin C*



An intermediate bromopyrroloindoline **94**, formed *via* the oxidative bromocyclization of tryptophan, was also utilized in Li's synthesis of drimentine G.[31] Employing a photoredox strategy similar to Stephenson's, generation of a tertiary benzylic radical followed by conjugate addition into enone **95** provided complex pyrroloindoine **96** in excellent yield. An additional five-steps is subsequently required to construct the diketopiperazine moiety and effect deoxygenation to provide the natural product.

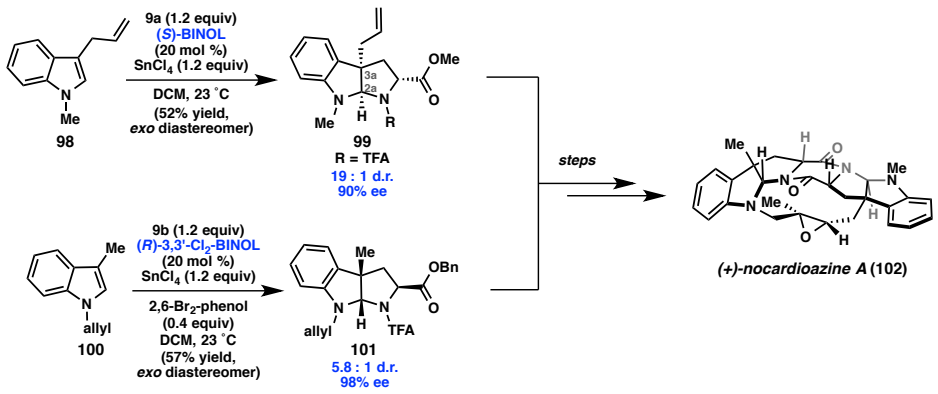
Scheme 1.18. *Li's synthesis of drimentine G*



In 2014, Reisman and co-workers reported a concise total synthesis of the complex macrocyclic bispyrroloindoline (+)-nocardioazine A (**102**) utilizing their previously reported $SnCl_4$•BINOL catalyzed formal (3 + 2) cycloaddition.[32] Importantly, this complex natural product contains two pyrroloindoline units, each of *opposite stereochemical configuration* at the 5/5-ring junction, making an excellent case for convergent asymmetric synthesis. To this end, 3-allyl-*N*-methylindole (**98**) was subjected to the previously optimized reaction conditions to afford pyrroloindoline **99** in 52% yield, 19:1 dr, and 90% ee. Simultaneously, treatment of 3-methyl-*N*-allylindole (**100**) under newly optimized conditions provided pyrroloindoline **101** in 57% yield, 5.8 : 1 dr, and 98% ee. Subsequent functionalization of each fragment followed by coupling and

cyclocondensation to prepare the diketopiperazine assembles the natural product in short order.

Scheme 1.19. *Reisman's synthesis of nocardioazine A*



1.6 CONCLUSIONS

These interesting scaffolds still serve as fascinating motivations for new synthetic methodologies and the basis for novel chemistry in total synthesis. Although much work has been done, the implementation and actualization of new synthetic strategies to meet unmet challenges will clearly be of interest in the coming times.

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Chapter 2

Enantioselective Synthesis of Tryptophan Derivatives by a Tandem Friedel–Crafts Conjugate Addition/Asymmetric Protonation Reaction[†]

2.1 INTRODUCTION

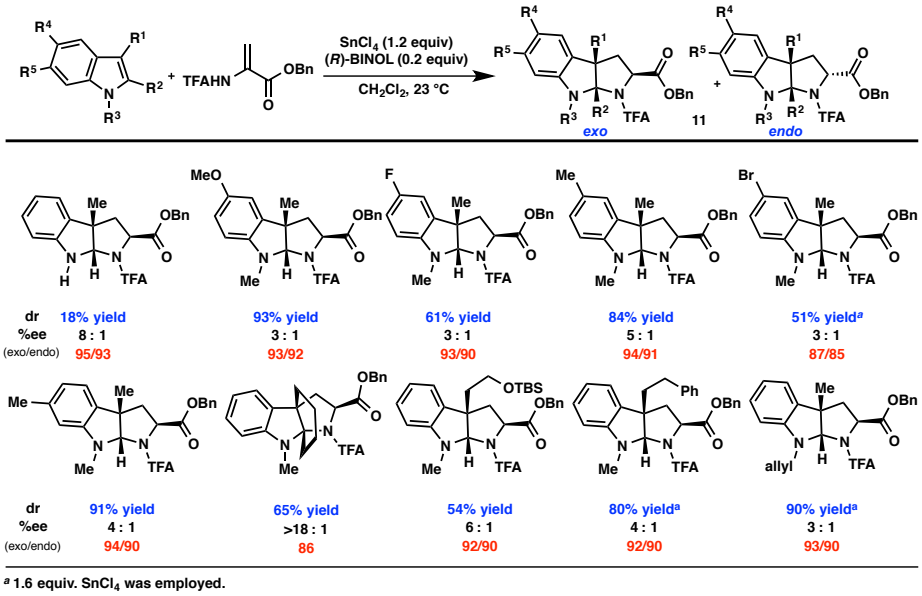
The biological importance of tryptophan as discussed in **Chapter 1** has inspired a variety of racemic, enzymatic, auxiliary-controlled, and enantiospecific methodologies.[1] There are, however, very few reported catalytic asymmetric methods for the preparation of tryptophan derivatives containing no β-stereocenter.[2,3,4]

In 2010, our laboratory reported a highly enantioselective formal (3 + 2) cycloaddition reaction utilizing catalytic (*R*)-BINOL and superstoichiometric $SnCl_4$ (**Table 2.1**).[5,6,7] By exploiting the intrinsic nucleophilicity of 3-substituted indoles and the electrophilicity of 2-amidoacrylates, functionalized pyrroloindoline scaffolds can be convergently synthesized in a single step. Both the enantio- and diastereoselectivity of

[†] Portions of this chapter have been reproduced from published studies (Kieffer, M. E.; Repka, L. M.; Reisman, S. E. *J. Am. Chem. Soc.* **2012**, *134*, 5131) and the supporting information found therein. Work was conducted in collaboration with Dr. Lindsay M. Repka.

this transformation were found to be highly dependent on the protecting groups of the acrylate, with benzyl 2-trifluoroacetamidoacrylate providing the best results for a variety of indole nucleophiles (**Table 2.1**).

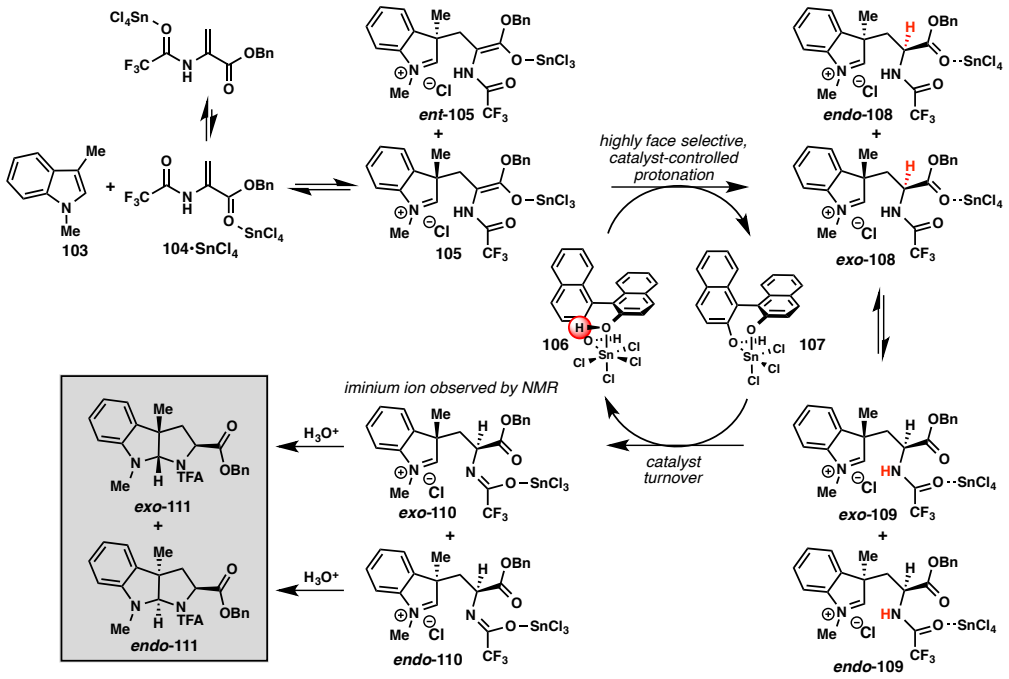
Table 2.1. *Substrate scope of formal (3+2) cycloaddition reaction*



Interestingly, a series of epimerization studies revealed that the reaction produced *endo/exo*-diastereomers of opposite enantiomeric series. In accord with preliminary mechanistic data, one limiting scenario that could explain this finding is if the initial conjugate addition proceeds reversibly to provide an enantiomeric mixture of enolate intermediates **105** and ***ent*-105**. A face-selective, catalyst controlled protonation would serve to irreversibly resolve the enantiomers, providing diastereomers **endo-** and **exo-108**. Subsequent cyclization of the amide onto the iminium ion provides the product in moderate diastereoselectivity and high enantioselectivity. Importantly, under this mechanistic scenario, the diastereomeric ratio is dependent upon the relative rates of protonation of **105** and ***ent*-105**. Following the precedence of Yamamoto and co-workers,

it is anticipated that (*R*)-BINOL•$SnCl_4$ serves as the asymmetric proton source in this reaction *via* a Lewis acid-assisted Brønsted acid (LBA).

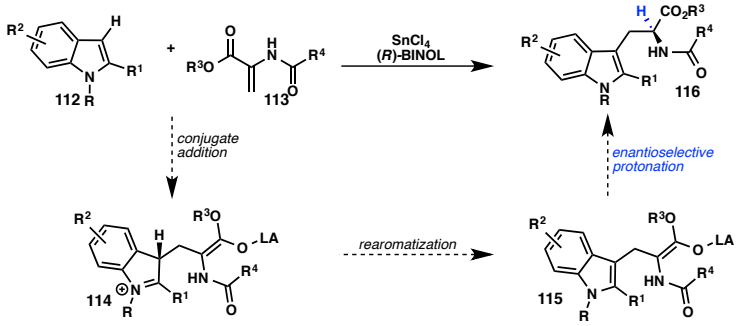
Scheme 2.1. *Proposed mechanism of formal (3+2) cycloaddition reaction*



Given this mechanistic insight, we reasoned that the related Friedel–Crafts alkylation of 3-*un*substituted indoles would further probe the role of such an enantioselective protonation, instead providing functionalized tryptophan products rather than pyrroloindolines. Mechanistically, this reaction would occur through initial conjugate addition of an indole into a Lewis-acid activated acrylate (**Scheme 2.2**). Rearomatization, followed by catalyst-controlled protonation of the resultant enolate was expected to provide alkylation product **116**. Successful implementation of this strategy would not only be mechanistically useful, but would also allow direct access to enantioenriched tryptophan derivatives from simple indole starting materials. This chapter describes our efforts towards the synthesis of enantioenriched tryptophan

derivatives through a tandem Friedel–Crafts conjugate addition/asymmetric protonation reaction.

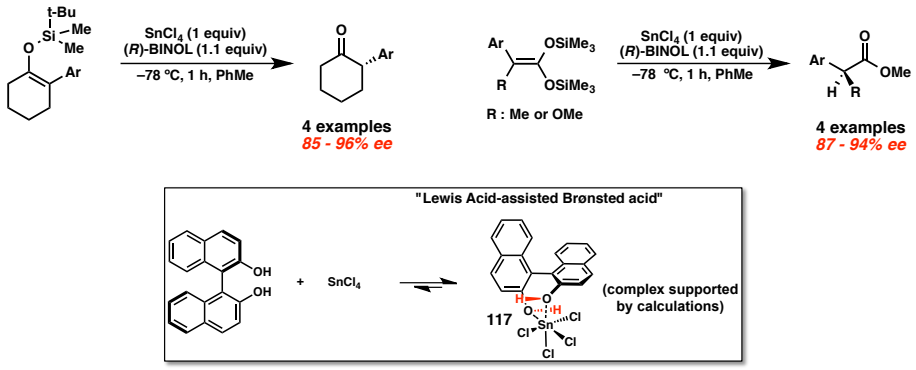
Scheme 2.2. *Proposed mechanism for the formation of enantioenriched tryptophan*



2.1.1 Precedence for Asymmetric Protonation

Our hypothesis that the Friedel–Crafts conjugate addition might undergo a selective protonation is consistent with work published by Yamamoto and co-workers, in which they report that $SnCl_4$•(*R*)-BINOL acts as an asymmetric proton source.[8] Upon subjection to stoichiometric $SnCl_4$ and (*R*)-BINOL, silyl enol ethers were cleanly converted to α-arylated ketones and esters in good yields and in excellent enantioselectivities (**Scheme 2.3**). Yamamoto proposes complex **117** acts as a Lewis acid-assisted Brønsted acid (LBA), in which complexation of (*R*)-BINOL to $SnCl_4$ greatly acidifies the alcohols, providing a selective proton source. Although subsequent reports were able to render this reaction catalytic through the addition of stoichiometric phenol derivatives, these complexes have never previously been applied to tandem conjugate addition/asymmetric protonation reactions.

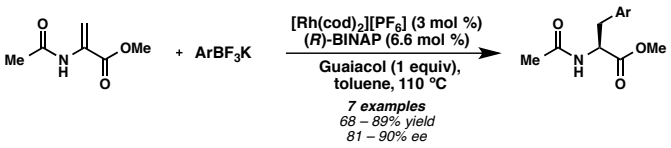
Scheme 2.3. *Yamamoto's enantioselective protonation*



2.1.2 Previous Conjugate Addition/Asymmetric Protonation Reactions

The synthesis of enantioenriched compounds employing conjugate addition/asymmetric protonation reactions has gained considerable momentum within the last decade, and a variety of nucleophiles and electrophiles have been found to be competent coupling partners.[9] One particularly relevant example comes from the labs of Genet and Darses, where they were able to construct enantioenriched phenylalanine derivatives using this approach (**Scheme 2.4**).[10]

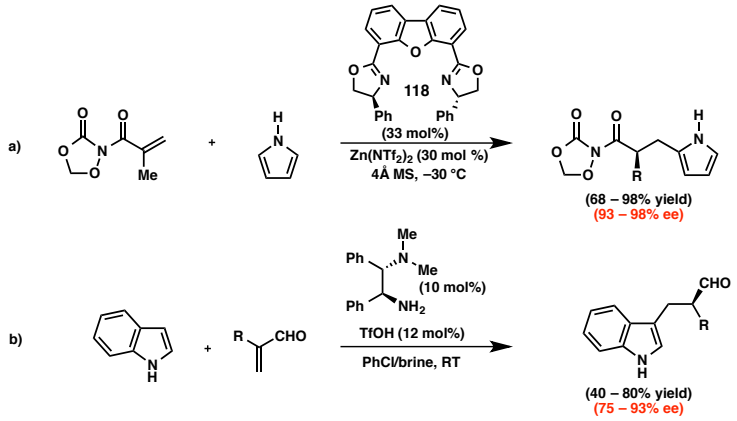
Scheme 2.4. *Tandem conjugate addition/asymmetric protonation*



Despite the prevalence of conjugate addition/asymmetric protonation reactions in the literature, the first report of a *Friedel–Crafts* conjugate addition/asymmetric protonation reaction was not disclosed until 2008. In their publication, Sibi and co-workers reveal the use of a novel isoxazolidinone auxiliary, which provides high levels of rotamer control of the enolate (**Scheme 2.5**).[11] When used in conjunction with $Zn(NTf_2)_2$

and chiral ligand **118**, they observe enantioenriched pyrrole products (**Scheme 2.5**, **a**). Concomitant to our work in this field, the Luo lab developed a chiral diamine catalyzed Friedel–Crafts conjugate addition/asymmetric protonation reaction that proceeds through an enamine intermediate.[12] They found this reaction was general for a range of α-substituted acroleins and indoles, providing products in good yield and moderate to high enantioselectivity (**Scheme 2.5**, **b**). Notably, there are no examples of Friedel–Crafts conjugate addition/asymmetric protonation reactions using indole-based nucleophiles to give tryptophan derivatives.

Scheme 2.5. *Tandem Friedel–Crafts conjugate addition/asymmetric protonation*



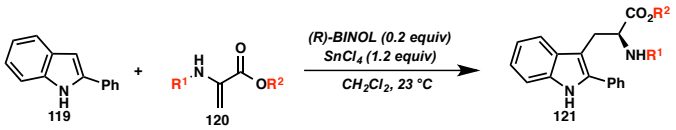
2.2 SCREENING AND OPTIMIZATION

2.2.1 Initial Screening of Acrylate and Additives

Our efforts to effect a tandem Friedel–Crafts conjugate addition/asymmetric protonation reaction began with model substrate 2-phenyl indole (**119**), which we subjected to the conditions optimized for pyrroloindoline formation. After two hours, we were disappointed to see only 12% yield of the desired product in low enantiomeric excess (**Table 2.2**, **entry 1**). As tuning of the acrylate was found to greatly affect the enantioselectivity in the pyrroloindoline methodology, a screen of 2-amido acrylates was

conducted. Gratifyingly, the use of commercially available methyl-2-acetamido acrylate provided the product in 73% yield and 78% ee (**entry 3**). Control experiments confirmed that while $SnCl_4$ alone catalyzes a background reaction, a substantial rate increase is observed upon addition of (*R*)-BINOL. No reaction was observed in the absence of $SnCl_4$ (**entry 7**).

Table 2.2. *Optimization of acrylate*



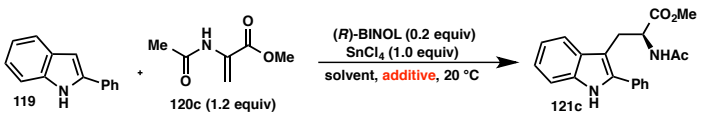
entry	R^1	R^2	time (h)	yield (%)[b]	ee (%)[c]	pdt
1	TFA	Bn	2	12	35	121a
2	TFA	Me	2	12	42	121b
3	Ac	Me	5	73	78	121c
4	CO_2Me	Me	13	nd	39	121d
5	Ts	Me	13	0	–	121e
6[d]	Ac	Me	2	13	–	121c
7[e]	Ac	Me	2	0	–	121c

[a] Reaction conducted under inert atmosphere on 0.2 mmol scale. [b] Isolated yield. [c] Determined by chiral stationary phase SFC. [d] No (*R*)-BINOL was employed. [e] No $SnCl_4$ was employed.

As the screening process progressed, we began to observe inconsistencies in the selectivity of the reaction. For example, a freshly opened bottle of $SnCl_4$ provided acetamido ester **121c** in 80% ee (**Table 2.3**, **entry 1**). However, switching to older sources of $SnCl_4$ decreased enantioenrichment to 76% (**entry 2**). Similarly, we noted a marked decrease in ee as the reaction progressed (**entries 3–7**) and suspected that HCl formed by the reaction of adventitious water with $SnCl_4$ was serving as a non-selective proton source. To this end, we investigated additives known to scavenge water or neutralize HCl. While insoluble bases such as K_2CO_3 appeared to have no effect on the reaction (**entry 9**), coordinating bases such as 2,6-lutidine completely shut down reactivity (**entry 10**). Instead, the use of activated 4Å molecular sieves increased both the yield and selectivity of the reaction, furnishing tryptophan **121c** in 86% yield and 81% ee

(**entry 11**). A small solvent screen confirmed that dichloromethane was indeed the optimal solvent for this transformation (**entries 11–13**).

Table 2.3. *Tandem Friedel–Crafts conjugate addition/asymmetric protonation*



entry	solvent	time (h)	additive	yield (%)[b]	ee (%)[c]
1	CH_2Cl_2	2	–	nd	80[d]
2	CH_2Cl_2	2	–	nd	76[e]
3	CH_2Cl_2	0.25	–	nd	84
4	CH_2Cl_2	0.5	–	nd	84
5	CH_2Cl_2	1	–	nd	82
6	CH_2Cl_2	2	–	nd	80
7	CH_2Cl_2	7	–	nd	80
8	CH_2Cl_2	2	–	73	78
9	CH_2Cl_2	2	K_2CO_3	73	78
10	CH_2Cl_2	2	2,6-lutidine	0	–
11	CH_2Cl_2	2	4Å MS	86	81
12	DCE	2	4Å MS	87	79
13	$CHCl_3$	2	4Å MS	80	72

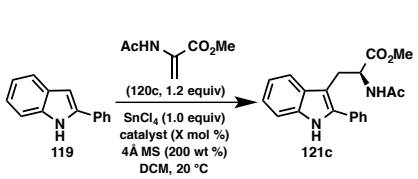
[a] Reactions conducted under inert atmosphere on 0.2 mmol scale. [b] Isolated yield. [c] Determined by chiral stationary phase SFC. [d] Reaction conducted using freshly opened $SnCl_4$. [e] Reaction conducted using previously opened $SnCl_4$.

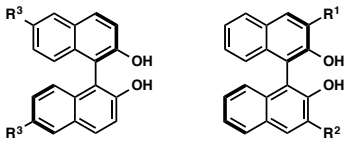
2.2.2 Screening of Chiral Ligands

With an optimal acrylate, solvent, and additive in hand, we next turned to the optimization of the catalyst structure (**Table 2.4**). Although there appeared to be no profound effect on selectivity when altering the electronics of the BINOL backbone (**entries 1–3**), we were pleased to find that modifications to the steric profile of the ligand exhibited a clearer trend. Dimethyl catalyst **122e** provided tryptophan **121c** in improved selectivities and comparable yields. Further augmentation of the steric bulk of the catalyst by substitution with phenyl groups lowered reactivity and selectivity (**entry 6**). Interestingly, dimethoxy catalyst **122g** delivered acetamido ester **121c** in low yield and as a racemate. This is likely due to its ability to participate in alternate binding modes,

resulting in a less reactive and selective catalyst. Gratifyingly, 3,3'-disubstitution with halides furnished the highest selectivities, with (*R*)-3,3'-dibromo-BINOL providing the best results (**entries 8–10**).[13] Although we found that catalyst loading could be decreased to 5 mol % while still observing 88% ee, we chose to employ 20 mol % loading as it gave reliably higher enantioselectivites for more functionalized substrates.

Table 2.4. *Optimization of a chiral ligand*





122a: R^3 = OMe 122b: R^3 = Me 122c: R^3 = Br 122d: R^1 = R^2 = H 122e: R^1 = R^2 = Me 122f: R^1 = R^2 = Ph 122g: R^1 = R^2 = OMe 122h: R^1 = R^2 = Cl 122i: R^1 = R^2 = Br 122j: R^1 = H, R^2 = Cl

entry	catalyst	loading (mol %)	yield (%)	ee (%)	entry	catalyst	loading (mol %)	yield (%)	ee (%)
1	122a	20	86	54	8	122h	20	85	90
2	122b	20	88	78	9	122i	20	76	93
3	122c	20	82	78	10	122j	20	76	84
4	122d	20	86	81	11	122i	5	72	88
5	122e	20	83	87	12	122i	10	75	92
6	122f	20	17	37	13	122i	15	77	93
7	122g	20	7	1	14	122i	40	76	93

[a] Reactions conducted under inert atmosphere on 0.2 mmol scale for 2 h. [b] Isolated yield. [c] Determined by chiral stationary phase SFC.

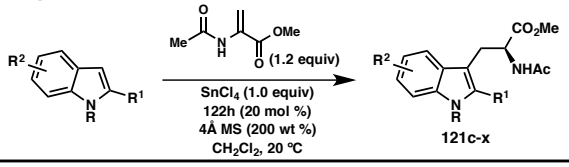
2.3 SUBSTRATE SCOPE

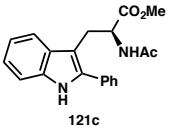
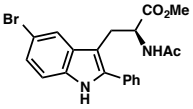
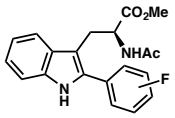
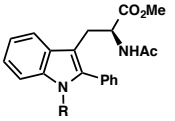
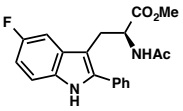
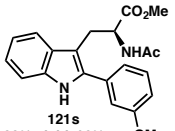
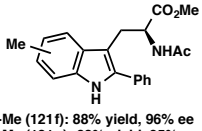
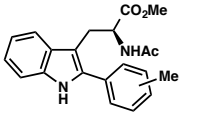
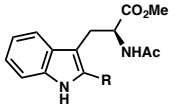
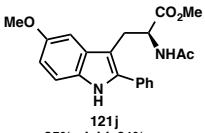
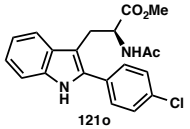
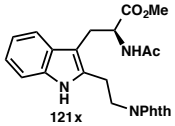
2.3.1 Friedel–Crafts/asymmetric protonation of substituted indoles

With optimal conditions in hand, an exploration of substrate scope was conducted (**Table 2.5**). In contrast to the findings from the formal (3+2) cycloaddition, we observed optimal results using *N*-protio indoles; however, methylated and allylated substrates were accommodated in slightly reduced selectivities. Substitution of the 4–7 positions of the indole backbone provided acetamido ester **121f–121i** in uniformly high yield and ee. Although both electron-rich and electron-poor indoles furnished tryptophans in high ee,

electron-deficient substrates display markedly decreased reaction rates, a finding consistent with a Friedel–Crafts type mechanism.

Table 2.5. *Substrate Scope*



entry	entry	entry
 121c 1) 76% yield, 93% ee	 121k 9)[b] 60% yield, 93% ee	 14) 4-F (121p): 78% yield, 93% ee 15) 3-F (121q): 76% yield, 92% ee 16) 2-F (121r): 35% yield, 92% ee
 2) R = Me (121d) 63% yield, 85% ee 3) R = allyl (121e) 68% yield, 85% ee	 121l 10)[b] 63% yield, 92% ee	 121s 17) 88% yield, 92% ee
 4) 4-Me (121f): 88% yield, 96% ee 5) 5-Me (121g): 83% yield, 95% ee 6) 6-Me (121h): 80% yield, 89% ee 7) 7-Me (121i): 94% yield, 94% ee	 11) 4-Me (121m): 86% yield, 94% ee 12) 2-Me (121n): 26% yield, 87% ee	 18) R = Me (121t): 61% yield, 85% ee 19) R = *n*-Bu (121u): 72% yield, 91% ee 20) R = *i*-Pr (121v): 66% yield, 92% ee 21) R = *t*-Bu (121w): 29% yield, 84% ee
 121j 8) 85% yield, 91% ee	 121o 13) 75% yield, 93% ee	 121x 22) 80% yield, 90% ee

[a] Reactions conducted under inert atmosphere on 0.1 or 0.2 mmol scale for 2 h. Isolated yields are reported. Enantiomeric excess was determined by chiral stationary phase SFC. [b] 1.6 equiv $SnCl_4$ were employed.

We found that the reaction was amenable to substrates with both alkyl and aryl substitution at the 2-position of the indole. 2-Aryl indoles bearing both electron donating and electron withdrawing substituents at the *para* and *meta* positions were tolerated (**121o**–**121s**). Unfortunately, even small functionality at the *ortho* position, such as fluoro, resulted in diminished reactivity (**121r**); a slightly larger methyl group further attenuated both yield and ee (**121n**). For 2-alkyl indoles, the ee improved when moving from a methyl group to bulkier *n*-butyl and *i*-propyl; however, a drastic decrease in yield

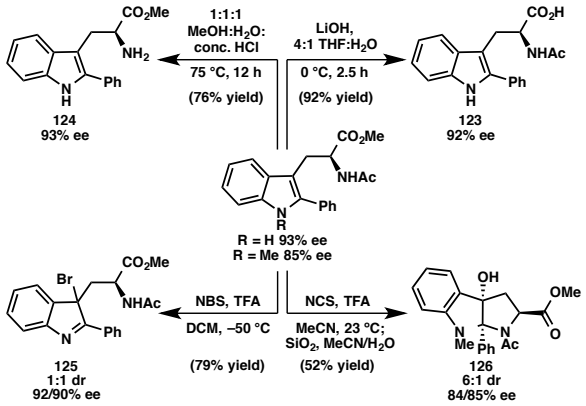
and ee is observed with the introduction of a *t*-butyl substituent (**121t**–**121w**). Remarkably, a phthalimide-containing indole proceeds in 80% yield and 90% ee (**121x**).

2.3.2 Scale-up and derivatization

Although optimization and substrate exploration were run in the glove box to streamline the screening protocol, this reaction has been reproduced on the bench top using standard Schlenk technique. Using 2-phenyl indole on 5 mmol scale, acetamido ester **121c** was isolated in 77% yield and 93% ee. Furthermore, we have shown that the methyl ester of **121c** can be selectively hydrolyzed upon subjection to aqueous LiOH in THF at 0°C (**Scheme 2.6**). Alternatively, orthogonal acetamide deprotection proceeds in methanolic HCl at 75 °C to afford free amine **124** in 76% yield with no erosion of ee.

Further functionalization of tryptophan **121c** was explored by subjection to NBS and TFA, common conditions for the oxidative cyclization of tryptophan derivatives to pyrroloindolines. Surprisingly, uncyclized imine **125** is remarkably stable, and was isolated in 79% yield as a 1:1 mixture of diasteromers. Instead, successful cyclization was achieved through exposure to NCS and TFA to initially form the 2-phenyl-3-chloro pyrroloindoline (detected by HRMS). Subsequent silica gel promoted hydrolysis delivers 2-phenyl-3-hydroxy pyrroloindoline **126** in 52% yield as a 6:1 mixture of diastereomers, constituting a new class of pyrroloindolines.

Scheme 2.6. *Derivatization of tryptophan products*



2.4 MECHANISTIC STUDIES

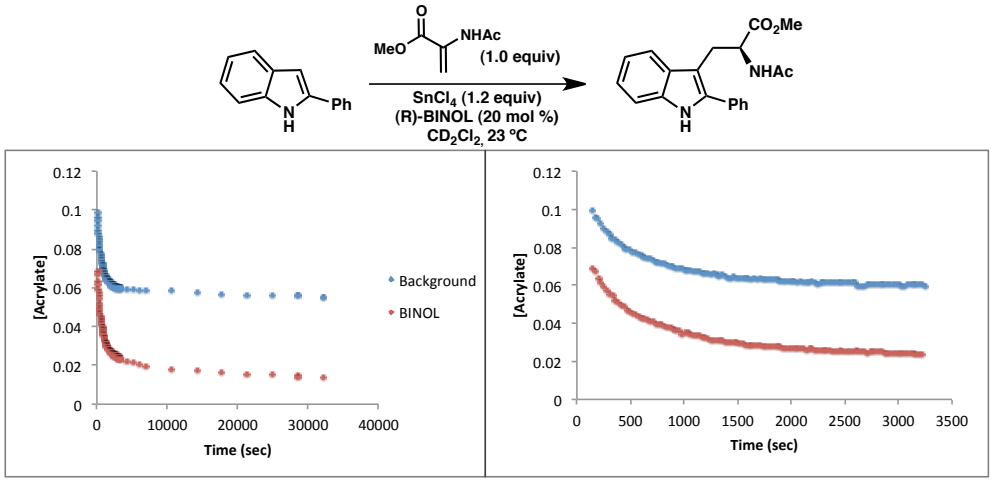
2.4.1 ^{1}H NMR Studies

As was seen in the pyrroloindoline methodology, the Friedel–Crafts conjugate addition/asymmetric protonation reaction exhibits excellent enantioselectivity, even in the presence of stoichiometric $SnCl_4$. Therefore, to better understand the mechanism of this reaction, a variety of ^{1}H NMR and deuterium labeling experiments were carried out.

We first set out to understand the relative rate of the background reaction compared to that of the $SnCl_4$•(*R*)-BINOL catalyzed reaction. A ^{1}H NMR experiment was designed in which the consumption of acrylate was monitored over time. As can be seen in **Figure 2.1**, the background reaction employing only $SnCl_4$ proceeded quickly (blue line); within thirty minutes (2000 seconds), the reaction reached 50% conversion. However, addition of catalytic (*R*)-BINOL (red line) pushed the reaction to greater than 80% conversion in the same time period. Closer examination of the first 3000 seconds of the reaction revealed that the rate of acrylate consumption is actually quite comparable for both the background and $SnCl_4$•(*R*)-BINOL catalyzed reactions. This suggests that the (*R*)-BINOL promoted rate acceleration might occur in the first two minutes of the

reaction, before ^{1}H NMR data is available. Attempts to slow the reaction through dilution and decreased catalyst loading in order to facilitate enhanced monitoring by ^{1}H NMR proved unfruitful.

Figure 2.1. *^{1}H NMR studies*

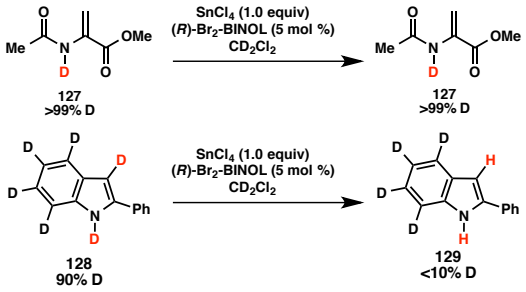


2.4.2 Deuterium labeling studies

To better understand the asymmetric protonation, we sought to find the stoichiometric proton source, which likely serves to turn over the chiral diol. Excluding adventitious water, there are three exchangeable protons: (i) the N-H of the acrylate, (ii) the N-H of the indole, or (iii) the C3 proton of the indole (which is lost in rearomatization). Therefore, *N*-deutero acrylate **127** and perdeutero indole **128** were prepared. Control reactions were carried out on each to determine if exchange occurred under the reaction conditions. Molecular sieves were omitted to prevent undesired deuterium/proton exchange between the substrates and sieves. Additionally, solutions of each substrate in dry CD_2Cl_2 were prepared in the glovebox in order to minimize exposure to moisture. Upon addition of $SnCl_4$ and (*R*)-Br_2-BINOL, each substrate was

monitored by ^{1}H NMR analysis. Although deutero acrylate **127** exhibited no deuterium-proton scrambling, perdeutero indole **128** underwent rapid exchange. In only a few minutes the substrate exhibited less than 10% deuterium incorporation. Unfortunately, the facile exchange of deuterium under the reaction conditions renders these labeling studies inconclusive. Furthermore, despite efforts to rigorously exclude moisture from these experiments, adventitious water cannot be ruled out as the stoichiometric proton source.

Scheme 2.7. *Deuterium labeling studies*

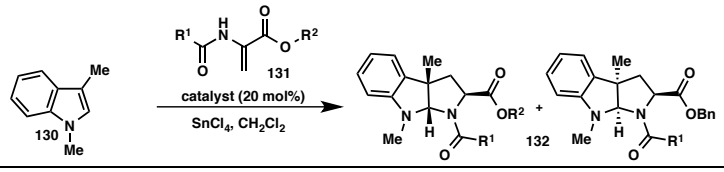


2.4.3 Comparison studies

Due to the apparent mechanistic similarities of the formal (3+2) cycloaddition and the Friedel–Crafts, we wondered if our newly optimized conditions for the Friedel–Crafts could be applied to the synthesis of pyrroloindolines to enhance selectivity. Using methyl-2-acetamido acrylate, indole **130** was subjected to optimal Friedel–Crafts conditions (**entry 2**). While there was a discernible increase in the selectivity of the product mixture compared to the originally reported conditions for acrylate **131** (**entry 1**), better results were still achieved using benzyl-2-trifluoroacetamido acrylate (**entry 3**). Interestingly, use of acrylate **131**, with optimal Friedel–Crafts conditions delivered the product in good dr and excellent enantioselectivity (**entry 4**). Unfortunately, use of (*R*)-3,3'-Br_2-BINOL and 4Å molecular sieves also mitigates the reactivity of the transformation, returning an inadmissibly low yield of product. Thus, appropriate

matching of catalyst and acrylate is necessary to synthesize either tryptophan derivatives (**121**) or pyrroloindolines (**132**) in both high yield and ee.

Table 2.6. *Comparison studies*



entry	conditions	R^1, R^2	yield (%)[a]	dr[b]	ee (%)[c]
1	(*R*)-BINOL	Me, Me	70	5:1	65/80
2	(*R*)-Br_2-BINOL, 4Å MS	Me, Me	58	8:1	87/85
3	(*R*)-BINOL	CF_3, Bn	86	4:1	94/91
4	(*R*)-Br_2-BINOL, 4Å MS	CF_3, Bn	39	7:1	98/95

[a] Isolated yield. [b] Determined by ^{1}H NMR analysis of crude reaction mixture. [c] Determined by chiral stationary phase SFC. [d] Reaction run with 1.0 equiv acrylate, 1.2 equiv $SnCl_4$. [e] Reaction run with 1.2 equiv acrylate, 1.0 equiv $SnCl_4$.

2.5 CONCLUSION

In summary, this report describes the development of a $SnCl_4$•(*R*)-Br_2-BINOL catalyzed tandem Friedel–Crafts conjugate addition/asymmetric protonation reaction. Utilizing a wide range of 2-substituted indoles and methyl-2-acetamido acrylate, we are able to access non-canonical tryptophan derivatives in a convergent manner. We have demonstrated that the acetamide and methylester functionality can be orthogonally deprotected and that acetamido ester **121c** can be advanced to more functionalized compounds. Moreover, experiments directed towards elucidation of the mechanism have been carried out. While the rapid rate of this reaction as well as deuterium scrambling under the reaction conditions has complicated analysis, data suggest that catalytically generated **122i**•$SnCl_4$ is serving as a chiral Lewis-acid assisted Brønsted acid to protonate an intermediate Sn-enolate. Future work is directed towards further expansion of substrate scope to include C2 unsubstituted indoles.

2.6 EXPERIMENTAL SECTION

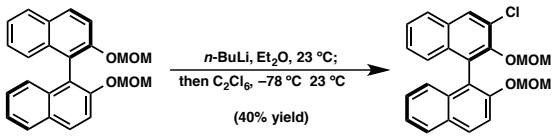
2.6.1 Materials and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Methylene chloride, deuterated methylene chloride, dioxane, ether, tetrahydrofuran, and toluene were dried by passing through activated alumina. Dichloroethane and chloroform were distilled over calcium hydride. Powdered 4Å molecular sieves were flame-dried under vacuum immediately prior to use. Potassium carbonate was dried for 12 h at 130 °C under vacuum and 2,6-lutidine was distilled over $AlCl_3$. All other commercially obtained reagents were used as received unless specifically indicated. (*R*)–BINOL, 2-phenylindole and 2-methylindole were purchased from Alfa Aesar, *N*-methyl-2-phenylindole was obtained from Sigma-Aldrich, and 1 M $SnCl_4$ in CH_2Cl_2 was purchased from Acros Organics. (*R*)- 3,3'-diphenyl-BINOL, (*R*)-3,3'-dimethyl-BINOL, (*R*)-3,3'-dichloro- BINOL, (*R*)-3,3'-dibromo-BINOL, (*R*)-3,3'-dimethoxy-BINOL, (*R*)-6,6'-dimethyl-BINOL, (*R*)-6,6'-dibromo-BINOL, (*R*)-2'-methoxy-[1,1'-binaphthalen]-2-ol, (*R*)-2'-isopropoxy-[1,1'-binaphthalen]-2-ol, (*R*)-3,3'-difluoro-BINOL, (*R*)-3-phenyl-BINOL, (*R*)- 5,5',6,6',7,7',8,8'-octahydro-BINOL, (*R*)-2'-benzoyl-[1,1'-binaphthalen]-2-ol, (*R*)-3-bromo-BINOL and (*R*)-3-iodo-BINOL, TADDOL, Napthyl-TADDOL, and 2-(trimethylsilyl)indole, were prepared according to literature procedures. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm). Silica gel column chromatography was performed either as described by Still et al. (W.C. Still, M. Kahn, A. Mitra, *J. Org. Chem*. **1978**, *43*, 2923.) using silica gel (particle size 0.032-0.063)

purchased from Silicycle or using pre-packaged RediSep®Rf columns on a CombiSilica gel Rf system (Teledyne ISCO Inc.). ^{1}H and ^{13}C NMR were recorded on a Varian Inova 500 (at 500 MHz and 125 MHz respectively) or a Varian Inova 600 (at 600 MHz and 150 MHz respectively, and are reported relative to internal chloroform (^{1}H, δ = 7.26, ^{13}C, δ = 77.0) or internal acetonitrile (^{1}H, δ = 1.94, ^{13}C, δ = 1.32). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system with Chiralcel AD-H, OD-H, AS-H, and OB-H columns (4.6 mm x 25 cm). Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. HRMS were acquired using either an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI) or mixed (MM) ionization mode.

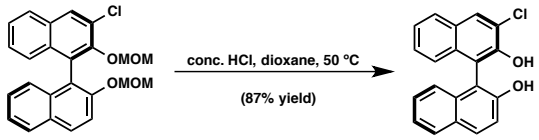
2.6.2 Catalyst and substrate preparation

Preparation of (*R*)-3-chloro-BINOL (122h)



To a flame-dried 100 mL flask containing MOM–protected (*R*)-BINOL **S1** (748 mg, 2.00 mmol, 1.00 equiv) was added Et_2O (45 mL), followed by dropwise addition of *n*-BuLi as a solution in hexanes (2.5 M, 960 μL, 2.40 mmol, 1.20 equiv) at room

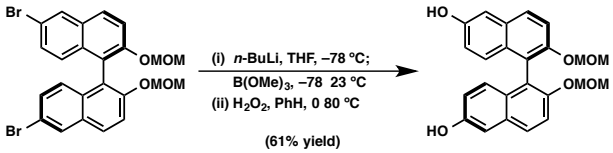
temperature. The mixture was then stirred at room temperature for 3 h and subsequently cooled to –78 ºC, followed by addition of C_2Cl_6 (569 mg, 2.40 mmol, 1.20 equiv) in one portion. The reaction mixture was allowed to warm to room temperature over 3 h, then diluted with EtOAc (15 mL) and washed with saturated aqueous NH_4Cl (50 mL). The aqueous layer was extracted with EtOAc (45 mL) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The crude yellow oil was purified by silica gel chromatography (0:100 to 12:88 EtOAc:hexanes) to yield 328 mg (40% yield) of **SI-1** as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.59 (d, *J* = 9.1 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.37 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.28 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.24 (ddd, *J* = 8.5, 6.7, 1.3 Hz, 1H), 7.18 (dddd, *J* = 8.6, 1.3, 0.7, 0.7 Hz, 1H), 7.16 (ddd, *J* = 8.5, 1.8, 0.8 Hz, 1H), 5.15 (d, *J* = 7.0 Hz, 1H), 5.04 (d, *J* = 7.0 Hz, 1H), 4.80 (d, *J* = 5.6 Hz, 1H), 4.75 (d, *J* = 5.6 Hz, 1H), 3.19 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.9, 148.9, 133.8, 132.6, 131.1, 130.0, 129.5, 128.8, 128.0, 127.9, 127.8, 127.0, 126.7, 126.4, 126.1, 125.8, 125.5, 124.2, 119.9, 116.3, 98.8, 94.9, 56.5, 55.9; IR (NaCl/thin film): 2955, 2902, 1594, 1508, 1354, 1241, 1159, 1149, 1034, 1014, 961, 922 cm^{-1}; $[\alpha]_D^{25}$ = +69.1 (*c* = 0.90, $CHCl_3$). HRMS (FAB+) calc'd for M^+ 408.1128, found 408.1128.



A 10 mL flask was charged with **SI-1** (305 mg, 0.75 mmol, 1.00 equiv), dioxane (3.7 mL) and aqueous HCl (12 M, 130 μL, 1.58 mmol, 2.10 equiv), then heated to 50 ºC for 2 h. The mixture was cooled to room temperature, then diluted with H_2O (30 mL) and

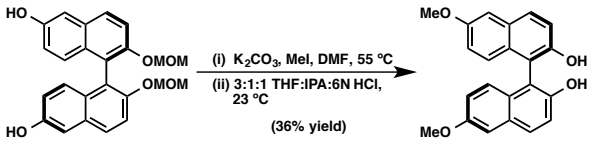
extracted with EtOAc (6 x 20 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (0:100 to 20:80 EtOAc:hexanes) to yield 210 mg (87% yield) of (*R*)-3-chloro-BINOL (**122j**) as a white foam, which was dried over P_2O_5 under vacuum. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.97 (d, *J* = 8.9 Hz, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.45 – 7.35 (m, 3H), 7.34 – 7.28 (m, 2H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 8.4 Hz, 1H), 5.60 (s, 1H), 4.94 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 148.3, 133.1, 132.4, 131.3, 129.7, 129.32, 129.26, 128.4, 127.7, 127.5, 127.3, 125.1, 124.6, 124.1, 123.9, 122.4, 117.7, 113.6, 111.7; IR (NaCl/thin film): 3503, 3057, 1620, 1596, 1502, 1451, 1379, 1265, 1212, 1184, 1146, 828 cm^{-1}; $[\alpha]_D^{25}$ = +55.4 (*c* = 1.01, $CHCl_3$). HRMS (MM) calc'd for $[M-H]^-$ 319.0531, found 319.0549.

Preparation of (*R*)-6,6'-dimethoxy-BINOL



(*R*)-6,6'-dimethoxy-BINOL was prepared following a procedure adapted from a reported synthesis of (*R*)-3,3'-dimethoxy-BINOL. To a 25 mL flask containing MOM–protected (*R*)-6,6'-dibromo-BINOL (1.10 g, 2.07 mmol, 1.00 equiv) was added THF (6.3 mL). The flask was cooled to –78 ºC, followed by dropwise addition of *n*-BuLi as a solution in hexanes (2.5 M, 2.50 mL, 6.20 mmol, 3.00 equiv). After stirring 1 hour at –78 ºC, $B(OMe)_3$ (645 mg, 6.20 mmol, 3.00 equiv) was added and the reaction was allowed to warm to room temperature. After 14 hours, the reaction mixture was concentrated to give the crude borate intermediate, which was suspended in benzene (7.2 mL) and cooled to 0 ºC, followed by dropwise addition of aqueous hydrogen peroxide

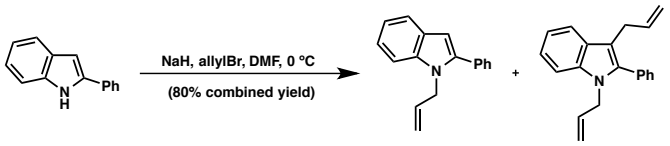
(30 wt %, 0.61 mL, 5.98 mmol, 2.89 equiv). The suspension was heated to reflux for 4 hours, then cooled to room temperature, poured into ice-cold saturated aqueous $NaSO_3$ (20 mL), and extracted with EtOAc (3 x 15 mL). The combined organics were washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography (0:100 to 50:50 EtOAc:hexanes) to yield 512 mg (61% yield) of the product as a light yellow foam. ^{1}H NMR (500 MHz, CD_3CN) δ 7.80 (ddd, *J* = 9.1, 0.8, 0.4 Hz, 2H), 7.51 (d, *J* = 9.1 Hz, 2H), 7.20 (ddd, *J* = 2.5, 0.5, 0.5 Hz, 2H), 7.09 (br s, 2H), 6.93 (ddd, *J* = 9.1, 0.7, 0.7 Hz, 2H), 6.87 (dd, *J* = 9.1, 2.5 Hz, 2H), 5.02 (d, *J* = 6.7 Hz, 2H), 4.94 (d, *J* = 6.7 Hz, 2H), 3.11 (s, 6H) ; ^{13}C NMR (125 MHz, CD_3CN) δ 154.4, 151.6, 132.1, 129.6, 128.4, 127.8, 122.1, 119.6, 118.7, 110.1, 96.0, 56.1; IR (NaCl/thin film): 3368, 2914, 1624, 1599, 1511, 1240, 1196, 1148, 1023 cm^{-1}; $[\alpha]_D^{25}$ = +87.1 (*c* = 1.00, MeCN). HRMS (MM) calc'd for $[M-H]^-$ 405.1344, found 405.1350.



A 15 mL flask was charged with (R)-MOM-hydroxy-BINOL (200 mg, 0.493 mmol, 1.00 equiv) and K_2CO_3 (177 mg, 1.28 mmol, 2.60 equiv). DMF (2 mL) was added, followed by MeI (123 μL, 1.97 mmol, 4.00 equiv) dropwise. The reaction was then heated to 55 °C for 22 hours, then cooled to room temperature and quenched with saturated aqueous NH_4Cl (2 mL) and Et_3N (3 drops). The mixture was stirred at room temperature for 6 hours, then diluted with H_2O (15 mL) and extracted with EtOAc (3 x 10 mL). The combined organics were washed with brine (15 mL), dried (Na_2SO_4), and concentrated. THF (28 mL) and IPA (9.5 mL) were added to the crude residue, followed

by dropwise addition of aqueous HCl (6.0 M, 9.4 mL). The reaction was stirred at room temperature for 3 hours, then diluted with H_2O (70 mL) and extracted with EtOAc (3 x 30 mL). The combined organics were washed with saturated aqueous $NaHCO_3$ (2 x 45 mL) and brine (45 mL), then dried (Na_2SO_4), filtered, and concentrated. The crude oil was purified by silica gel chromatography (0:100 to 30:70 EtOAc:hexanes) to yield 62 mg (36% yield) of (*R*)-6,6'-dimethoxy-BINOL as a light brown solid, which was dried over P_2O_5 under hi-vacuum. Spectral data are in agreement with the literature.

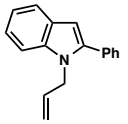
Preparation of 1-allyl-2-phenylindole



To a 50 mL flask was added NaH (620 mg, 15.5 mmol, 3.00 equiv) and DMF (8 mL) and the suspension was cooled to 0 ºC in an ice bath. A solution of 2-phenylindole (1.00 g, 5.18 mmol, 1.00 equiv) in DMF (3 mL) was added slowly to the suspension over 15 minutes and the reaction mixture was further stirred at 0 ºC for 20 minutes, followed by dropwise addition of allyl bromide (670 μL, 7.77 mmol, 1.50 equiv). The ice bath was then removed and the mixture was stirred for 15 minutes, then quenched by addition of saturated aqueous NH_4Cl (5 mL) and Et_3N (5 drops). After 2 hours, the reaction was diluted with H_2O (40 mL) and extracted with EtOAc (3 x 30 mL). The combined organics were washed with brine (120 mL), dried (Na_2SO_4), filtered, and concentrated. The crude was then purified by reverse phase preparatory HPLC (55:45 to 95:5 MeCN:H_2O) using an Agilent 1200 Series HPLC with an Agilent XDB-C18 5 μM column (9.4 x 250 mm and 21.2 x 150 mm) to yield 687 mg (57% yield) of 1-allyl-2-

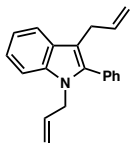
phenylindole as a yellow solid and 331 mg (23% yield) of 1,3-diallyl-2-phenylindole as a yellow oil.

1-allyl-2-phenylindole :



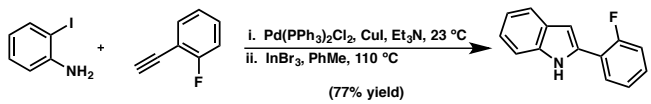
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (ddd, *J* = 7.8, 1.2, 0.8 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.48 – 7.43 (m, 2H), 7.42 – 7.38 (m, 1H), 7.33 (br d, *J* = 8.2 Hz, 1H), 7.22 (ddd, *J* = 7.0, 7.0, 1.3 Hz, 1H), 7.15 (ddd, *J* = 7.0, 7.0, 1.0 Hz, 1H), 6.60 (br s, 1H), 6.02 (ddt, *J* = 17.2, 10.5, 4.4 Hz, 1H), 5.22 (dtd, *J* = 10.5, 1.8, 1.1 Hz, 1H), 5.00 (dtd, *J* = 17.1, 2.0, 1.2 Hz, 1H), 4.74 (dt, *J* = 4.2, 1.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.5, 137.8, 133.8, 132.7, 129.1, 128.5, 128.1, 128.0, 121.7, 120.5, 120.0, 116.5, 110.3, 102.0, 46.5; IR (NaCl/thin film): 3055, 2917, 1602, 1462, 1443, 1392, 1345, 1317, 1162 cm^{-1}; HRMS (APCI) calc'd for $[M+H]^+$ = 234.1277, found 234.1284.

1,3-diallyl-2-phenylindole:



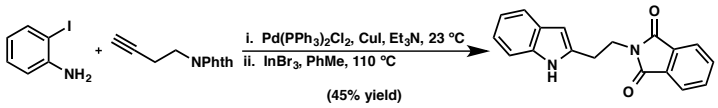
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (ddd, *J* = 7.8, 1.2, 0.7 Hz, 1H), 7.50 – 7.40 (m, 5H), 7.33 (ddd, *J* = 8.1, 0.9, 0.9 Hz, 1H), 7.24 (ddd, *J* = 7.0, 7.0, 1.2 Hz, 1H), 7.16 (ddd, *J* = 7.0, 7.0, 1.1 Hz, 1H), 6.05 (ddt, *J* = 17.0, 10.1, 5.9 Hz, 1H), 5.91 (ddt, *J* = 17.1, 10.4, 4.7 Hz, 1H), 5.14 (dtd, *J* = 10.4, 1.8, 1.2 Hz, 1H), 5.08 – 5.02 (m, 2H), 4.92 (dtd, *J* = 17.1, 1.9, 1.3 Hz, 1H), 4.62 (dt, *J* = 4.6, 1.9 Hz, 2H), 3.46 (dt, *J* = 6.0, 1.7 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.0, 137.9, 136.7, 133.9, 131.8, 130.4, 128.3, 128.2, 128.1, 128.0, 121.7, 119.34, 119.30, 116.2, 114.6, 110.9, 110.1, 46.4, 29.2; IR (NaCl/thin film): 3056, 2915, 1637, 1463, 1443, 1408, 1360, 1340, 1191 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ = 274.1590, found 274.1591.

Preparation of 2-(2-fluorophenyl)indole:



2-(2-fluorophenyl)indole was prepared by an analogous procedure to that reported by Sakai et. al. A flame-dried flask was charged with 2-iodoaniline (200 mg, 0.90 mmol, 1.00 equiv), ethynyl-2-fluorobenzene (133 mg, 1.10 mmol, 1.20 equiv), $Pd(PPh_3)_2Cl_2$ (13 mg, 0.02 mmol, 0.02 equiv), copper (I) iodide (2.0 mg, 0.025 mmol, 0.01 equiv) and Et_3N (4 mL). The mixture was stirred overnight at room temperature, then filtered through a plug of silica, concentrated and redissolved in PhMe (5 mL). $InBr_3$ (16 mg, 0.05 mmol, 0.05 equiv) was added in one portion and the mixture was heated to 110 ºC for 5 h, then cooled to room temperature, filtered through celite, and concentrated. The crude residue was purified by silica gel chromatography (10:90 EtOAc:hexanes) to yield 148 mg (77% yield) of 2-(2-fluorophenyl)indole as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.89 (br s, 1H), 7.80 (ddd, *J* = 7.8, 7.8, 1.8 Hz, 1H), 7.66 (dddd, *J* = 2.5, 1.3, 0.8, 0.8 Hz, 1H), 7.43 (ddd, *J* = 8.1, 1.5, 0.8 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.26 – 7.16 (m, 3H), 7.14 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.97 (d, *J* = 1.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3 (d, $J_{C\text{-}F}$= 246.4 Hz), 134.6 (d, $J_{C\text{-}F}$ = 501.8 Hz), 128.8 (d, $J_{C\text{-}F}$ = 8.8 Hz), 128.1, 128.0 (d, $J_{C\text{-}F}$ = 4.1 Hz), 124.8 (d, $J_{C\text{-}F}$ = 3.2 Hz), 122.7, 120.6, 120.2, 119.9 (d, $J_{C\text{-}F}$ = 11.0 Hz), 116.6, 116.4, 111.0, 101.6 (d, $J_{C\text{-}F}$ = 3.0 Hz); IR (NaCl/thin film): 3469, 3042, 2918, 2848, 1577, 1472, 1460, 1212, 1178, 1109, 928 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 212.0870, found 212.0869.

Preparation of 2-(ethylphthalimide)indole:



2-(ethylphthalimide)indole was prepared by an analogous procedure to that reported by Sakai et. al. A flame-dried flask was charged with 2-iodoaniline (500 mg, 2.30 mmol,

1.00 equiv), 2-(but-3-yn-1-yl)isoindoline-1,3-dione (550 mg, 2.75 mmol, 1.20 equiv), $Pd(PPh_3)_2Cl_2$ (32 mg, 0.05 mmol, 0.02 equiv), copper (I) iodide (4.5 mg, 0.025 mmol, 0.01 equiv) and Et_3N (8 mL). The mixture was stirred overnight at room temperature, then filtered through a plug of silica, concentrated and redissolved in PhMe (10 mL). $InBr_3$ (40 mg, 0.1 mmol, 0.05 equiv) was added in one portion and the mixture was heated to 110 ºC for 5 h, then cooled to room temperature, filtered through celite and concentrated. The crude residue was purified by silica gel chromatography (60:40 EtOAc:hexanes) to yield 302 mg (45% yield) of 2-(ethylphthalimide)indole as a light yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26 (br s, 1H), 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.51 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 8.1 Hz, 1H), 7.13 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 7.06 (ddd, J = 7.5, 7.5, 1.0 Hz, 1H), 6.33 (d, J = 1.2 Hz, 1H), 4.06 (t, *J* = 7.5 Hz, 2H), 3.21 (t, J = 7.4 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 136.1, 134.9, 134.1, 131.9, 128.6, 123.4, 121.4, 120.0, 119.7, 110.6, 101.1, 37.1, 27.4.; IR (NaCl/thin film): 3366, 1772, 1707, 1653, 1617, 1466, 1395, 1363, 1293 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 291.1128, found 291.1138.

2.6.3 Optimization of Reaction Parameters

2.6.3.1 General Procedure 1

An oven-dried vial was charged with 2-phenylindole (0.20 mmol, 1.00 equiv), the acrylate (0.24 mmol, 1.20 equiv) and an (*R*)-BINOL derivative and pumped into a glove box. The vial was charged with solvent to an indole concentration of 0.12 M, and $SnCl_4$ (1.00 equiv, as a 1.0 M solution in CH_2Cl_2) was added. The reaction was stirred at 20 °C for 2 hours, after which time it was removed from the glove box and quenched by

dilution with 1 M HCl (5 mL) and MeCN (1 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography.

Additive screens. Reactions were performed following General Procedure 1 using 0.20 equiv (*R*)-BINOL. After the vial was pumped into the glove box, one of the following additives was added:

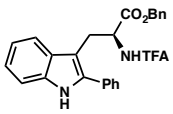
- flame-dried powdered 4Å molecular sieves (200 wt % relative to indole)
- K_2CO_3 (1.00 equiv)
- 2,6-lutidine (1.00 equiv)

Upon addition of the additive, DCM was added to an indole concentration of 0.12 M and the reaction was further conducted as described above.

Catalyst screens. Reactions were performed following General Procedure 1 using flame-dried powdered 4Å molecular sieves (200 wt % relative to indole) as an additive and DCM as a solvent.

2.6.3.2 Characterization Data

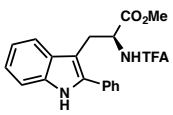
(*S*)-N_α-Trifluoroacetyl-2-phenyltryptophan benzyl ester (121a)



Prepared from benzyl 2-trifluoroacetamidoacrylate (65.5 mg, 0.24 mmol) following General Procedure 1. The crude residue was purified by silica gel chromatography (30:70 to 70:30 DCM:hexanes) to yield 11.1 mg (12% yield) of **121a** as a yellow solid. The enantiomeric excess was determined to be 35% by chiral SFC analysis (OB-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R(major) = 11.0 min,

t_R(minor) = 12.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 7.57 (ddd, *J* = 7.9, 1.8, 0.7 Hz, 1H), 7.54 – 7.50 (m, 2H), 7.50 – 7.45 (m, 2H), 7.42 – 7.36 (m, 2H), 7.34 – 7.29 (m, 3H), 7.24 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 7.16 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 7.11 – 7.07 (m, 2H), 6.67 (br d, *J* = 7.6 Hz, 1H), 4.95 (d, *J* = 12.2 Hz, 1H), 4.88 (dt, *J* = 7.8, 6.0 Hz, 1H), 4.53 (d, *J* = 12.2 Hz, 1H), 3.65 – 3.56 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 156.6 (q, J_{C-F} = 37.8 Hz), 136.3, 135.6, 134.6, 132.4, 129.2, 128.9, 128.5, 128.44, 128.38, 128.2, 128.1, 122.8, 120.3, 118.6, 115.3 (q, J_{C-F} = 287.9 Hz), 111.0, 105.6, 67.5, 53.3, 26.7; IR (NaCl/thin film): 3391, 3061, 2924, 1714, 1542, 1457, 1210, 1173 cm^{-1}; $[\alpha]_D^{25}$ = +3.5 (*c* = 0.44, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 467.1577, found 467.1580.

(*S*)-N_α-Trifluoroacetyl-2-phenyltryptophan methyl ester (121b)



Prepared from methyl 2-trifluoroacetamidoacrylate (47.3 mg, 0.24 mmol) following General Procedure 1. The crude residue was purified by silica gel chromatography (0:100 to 5:95 EtOAc:toluene, then 0:100 to 20:80 EtOAc:hexanes) to yield 9.0 mg (12% yield) of **121b** as a yellow solid. The enantiomeric excess was determined to be 42% by chiral SFC analysis (AS-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 8.7 min, t_R(minor) = 7.7 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (br s, 1H), 7.58 – 7.52 (m, 3H), 7.52 – 7.47 (m, 2H), 7.43 – 7.39 (m, 1H), 7.38 (ddd, *J* = 8.1, 0.9, 0.9 Hz, 1H), 7.23 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.16 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 6.65 (br d, *J* = 7.3 Hz, 1H), 4.83 (dt, *J* = 7.8, 5.6 Hz, 1H), 3.66 – 3.56 (m, 2H), 3.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 156.6 (q, J_{C-F} = 37.7 Hz), 136.3, 135.6, 132.5, 129.2, 129.0, 128.4, 128.2, 122.8, 120.3, 118.5, 115.3 (q, J_{C-F}= 287.7 Hz), 111.0, 105.5, 53.2, 52.5, 26.4; IR (NaCl/thin film): 3391, 3057, 2917, 2849, 1718, 1542, 1458,

1449, 1211, 1170 cm^{-1} ; $[\alpha]_D^{25}$ = +22.3 (*c* = 0.39, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 391.1264, found 391.1267.

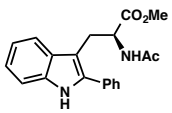
2.6.4 Optimized Conjugate Addition/Asymmetric Protonation

2.6.4.1 General Procedure 2

An oven-dried vial was charged with the indole (1.00 equiv), methyl 2-acetamidoacrylate (1.20 equiv) and (*R*)-3,3'-dibromo-BINOL (0.20 equiv) and pumped into a glove box. To the vial was added flame-dried powdered 4Å molecular sieves (200 wt % relative to indole). The vial was charged with DCM to an indole concentration of 0.12 M, and $SnCl_4$ (1.00 equiv unless specifically indicated, as a 1 M solution in DCM) was added. The reaction was stirred at 20 °C for 2 hours, after which time it was removed from the glove box and quenched by dilution with 1 M HCl (5 mL) and MeCN (1 mL). The aqueous layer was extracted with EtOAc (2 x 5 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography.

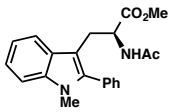
2.6.4.2 Characterization Data

(*S*)-*N*α-Acetyl-2-phenyltryptophan methyl ester (121c)



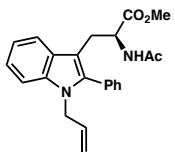
Prepared from 2-phenylindole (19.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 25.6 mg (76% yield) of **121c** as a white foam. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm). t_R(major) = 5.7 min, t_R(minor) = 6.9 min. $[\alpha]_D^{25}$ = +37.7 (*c* = 0.94, $CHCl_3$). Spectral data matches that reported in the literature.

(*S*)-N_α-Acetyl-1-methyl-2-phenyltryptophan methyl ester (121d)



Prepared from 1-methyl-2-phenylindole (41.4 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (0:100 to 55:45 EtOAc:hexanes) to yield 43.4 mg (63% yield) of **121d** as a yellow solid. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 4.6 min, t_R(minor) = 3.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (ddd, *J* = 7.9, 1.2, 0.7 Hz, 1H), 7.56 – 7.49 (m, 2H), 7.48 – 7.44 (m, 1H), 7.42 – 7.38 (m, 2H), 7.34 (ddd, *J* = 8.2, 0.9, 0.9 Hz, 1H), 7.26 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.17 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 5.72 (br d, *J* = 7.8 Hz, 1H), 4.74 (dt, *J* = 8.0, 5.6 Hz, 1H), 3.57 (s, 3H), 3.39 (s, 3H), 3.41 (dd, *J* = 14.7, 5.7 Hz, 1H), 3.34 (dd, *J*=14.8, 5.6 Hz, 1H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 139.2, 136.9, 131.6, 130.7, 128.7, 128.4, 127.9, 122.0, 119.7, 118.7, 109.5, 106.7, 52.8, 52.0, 30.8, 26.6, 23.0.; IR (NaCl/thin film): 3288, 3055, 2950, 1743, 1657, 1539, 1469, 1441, 1368, 1238, 1212 cm^{-1}; $[\alpha]_D^{25}$ = +21.3 (*c* = 0.91, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1708.

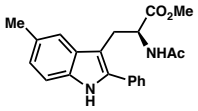
(*S*)-N_α-Acetyl-1-allyl-2-phenyltryptophan methyl ester (121e)



Prepared from 1-allyl-2-phenylindole (46.6 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (0:100 to 55:45 EtOAc:hexanes) to yield 51.3 mg (68% yield) of **121e** as a yellow foam. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AS-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 2.9 min, t_R(minor) = 2.4 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (ddd, *J* = 7.8, 1.0, 1.0 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.47 – 7.42 (m, 1H), 7.42 – 7.37 (m, 2H), 7.30 (ddd, *J* = 8.1,

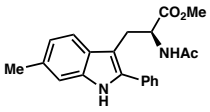
0.9, 0.9 Hz, 1H), 7.23 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.17 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 5.85 (ddt, *J* = 17.1, 10.3, 4.7 Hz, 1H), 5.76 (br d, *J* = 7.9 Hz, 1H), 5.11 (dtd, *J* = 10.4, 1.7, 1.2 Hz, 1H), 4.82 (dtd, *J* = 17.1, 1.9, 1.3 Hz, 1H), 4.76 (dt, *J* = 8.0, 5.8 Hz, 1H), 4.56 (dt, *J* = 4.7, 1.8 Hz, 2H), 3.39 (s, 3H), 3.36 (dd, *J* = 14.7, 5.7 Hz, 1H), 3.29 (dd, *J* = 14.7, 5.9 Hz, 1H), 1.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 139.0, 136.3, 133.5, 131.5, 130.5, 128.7, 128.5, 128.1, 122.0, 119.8, 118.8, 116.3, 110.2, 107.2, 52.8, 52.0, 46.3, 26.8, 23.0; IR (NaCl/thin film): 3435, 3287, 3056, 2950, 2926, 2851, 1744, 1658, 1538, 1500, 1408, 1367, 1219, 1196, 1134; $[\alpha]_D^{25}$ = +13.8 (*c* = 2.96, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 377.1860, found 377.1865.

(*S*)-N_α-Acetyl-4-methyl-2-phenyltryptophan methyl ester (121f)



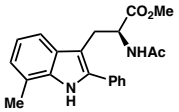
Prepared from 4-methyl-2-phenylindole (21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 30.8 mg (88% yield) of **121f** as a white foam. The enantiomeric excess was determined to be 96% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 9.9 min, t_R(minor) = 8.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (br s, 1H), 7.55 – 7.45 (m, 4H), 7.44 – 7.37 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.08 (m, 1H), 6.91 (m, 1H), 5.44 (br d, J = 7.6 Hz, 1H), 4.63 (td, *J* = 8.2, 5.0 Hz, 1H), 3.69 – 3.45 (m, 2H), 3.44 (s, 3H), 2.78 (s, 3H), 1.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 169.7, 136.3, 136.1, 133.1, 130.5, 129.2, 128.9, 128.3, 126.9, 122.5, 122.3, 109.0, 107.6, 54.2, 52.1, 27.6, 22.8, 20.5; IR (NaCl/thin film): 3295, 3052, 2952, 1741, 1659, 1602, 1547, 1514, 1492, 1449, 1372, 1218; $[\alpha]_D^{25}$ = -29.0 (*c* = 0.63, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1698.

(*S*)-N_α-Acetyl-6-methyl-2-phenyltryptophan methyl ester (121g)



Prepared from 6-methyl-2-phenylindole (21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 27.9 mg (80% yield) of **121g** as a colorless oil. The enantiomeric excesses was determined to be 89% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 9.1 min, t_R(minor) = 10.1 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (br s, 1H), 7.55 (ddd, *J* = 5.8, 4.0, 2.1 Hz, 2H), 7.48 – 7.44 (m, 3H), 7.39 – 7.33 (m, 1H), 7.14 (s, 1H), 6.97 (dd, *J* = 8.3, 1.5 Hz, 1H), 5.78 (br d, *J* = 7.8 Hz, 1H), 4.83 (dt, *J* = 8.0, 5.4 Hz, 1H), 3.55 – 3.49 (m, 2H), 3.30 (s, 3H), 2.47 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) 172.1, 169.6, 136.1, 135.2, 133.3, 132.4, 129.1, 128.2, 127.9, 127.3, 121.8, 118.5, 110.9, 106.5, 52.7, 52.0, 26.6, 22.9, 21.7; IR (NaCl/thin film): 3292, 3052, 2958, 2908, 1741, 1658, 1545, 1530, 1511, 1446, 1375, 1216; $[\alpha]_D^{25}$ = +39.3 (*c* = 0.38, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1698.

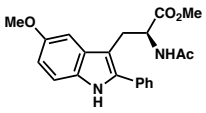
(*S*)-N_α-Acetyl-7-methyl-2-phenyltryptophan methyl ester (121h)



Prepared from 7-methyl-2-phenylindole (21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (30:70 to 100:0 EtOAc:hexanes) to yield 33.0 mg (94% yield) of **121h** as a white foam. The enantiomeric excess was determined to be 94% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 5.6 min, t_R(minor) = 5.0 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (br s, 1H), 7.61 – 7.54 (m, 2H), 7.51 – 7.45 (m, 2H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.40 – 7.35 (m, 1H), 7.11 – 7.04 (m, 1H), 7.03 – 6.97 (m, 1H), 5.79 (br d, *J* = 8.1 Hz, 1H), 4.82 (dt, *J* = 8.1, 5.7 Hz, 1H), 2.55 (dd,

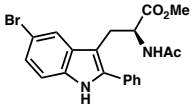
J = 12.5, 3.1 Hz, 1H), 3.51 (dd, *J* = 12.5, 3.1 Hz, 1H), 3.30 (s, 3H), 2.50 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.6, 135.8, 135.3, 133.3, 129.1, 128.9, 128.4, 128.0, 123.1, 120.20, 120.18, 116.5, 107.1, 52.7, 51.9, 26.6, 22.8, 16.6; IR (NaCl/thin film): 3283, 3053, 2950, 1736, 1659, 1518, 1438, 1372, 1306, 1266, 1219, 1137, 1043; $[\alpha]_D^{25}$ = +26.5 (*c* = 0.20, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1708.

(*S*)-*N*$_\alpha$-Acetyl-5-methoxy-2-phenyltryptophan methyl ester (121i)



Prepared from 5-methoxy-2-phenylindole (45.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 62.0 mg (85% yield) of **121i** as a colorless oil. The enantiomeric excess was determined to be 91% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 4.7 min, t_R(minor) = 6.5 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (br s, 1H), 7.58 – 7.49 (m, 2H), 7.50 – 7.41 (m, 2H), 7.36 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.24 (d, J = 8.7 Hz, 1H), 7.05 (d, J = 2.3 Hz, 1H), 6.90 – 6.80 (m, 1H), 5.82 (br d, J = 7.9 Hz, 1H), 4.82 (td, J = 7.9, 5.4 Hz, 1H), 3.87 (s, 3H), 3.49 (m, 2H), 3.29 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.6, 154.4, 136.7, 133.2, 130.8, 129.8, 129.1, 128.2, 128.0, 112.7, 111.7, 106.5, 100.5, 55.9, 52.7, 52.0, 26.6, 22.9; IR (NaCl/thin film): 3291, 3057, 2926, 1739, 1652, 1558, 1539, 1520, 1483, 1455, 1374, 1218, 1178; $[\alpha]_D^{25}$ = +32.6 (*c* = 0.93, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1658.

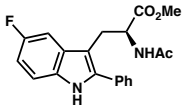
(*S*)-*N*$_\alpha$-Acetyl-5-bromo-2-phenyltryptophan methyl ester (121j)



Prepared from 5-bromo-2-phenylindole (54.0 mg, 0.20 mmol) with 1.6

equiv $SnCl_4$ following General Procedure 2. The crude residue was purified by silica gel chromatography (30:70 to 100:0 EtOAc:hexanes) to yield 49.5 mg (60% yield) of **121j** as a white foam. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 5.3 min, t_R(minor) = 7.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (br s, 1H), 7.66 (d, *J* = 2.0 Hz, 1H), 7.56 – 7.50 (m, 2H), 7.49 – 7.43 (m, 2H), 7.42 – 7.34 (m, 1H), 7.28 – 7.24 (m, 1H), 7.22 – 7.18 (m, 1H), 5.75 (br d, *J* = 8.1 Hz, 1H), 4.82 (dt, *J* = 8.1, 5.7 Hz, 1H), 3.53 (dd, J = 14.9, 5.5 Hz, 1H), 3.46 (dd, J = 14.9, 4.8 Hz, 1H), 3.36 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 169.6, 137.2, 134.2, 132.6, 131.1, 129.2, 128.3, 128.2, 125.2, 121.6, 113.1, 112.4, 106.4, 52.6, 52.1, 26.5, 22.8; IR (NaCl/thin film): 3417, 3369, 3282, 1734, 1654, 1521, 1466, 1437, 1374, 1215; $[\alpha]_D^{25}$ = +47.2 (*c* = 1.04, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 415.0652, found 415.0653.

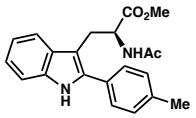
(*S*)-N_α-Acetyl-5-fluoro-2-phenyltryptophan methyl ester (121k)



Prepared from 5-fluoro-2-phenylindole (42.0 mg, 0.20 mmol) with 1.6 equiv $SnCl_4$ following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 44.7 mg (63% yield) of **121k** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 3.8 min, t_R(minor) = 5.2 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (br s, 1H), 7.60 – 7.52 (m, 2H), 7.50 – 7.43 (m, 2H), 7.42 – 7.34 (m, 1H), 7.27 – 7.24 (m, 1H), 7.21 (dd, *J* = 9.8, 2.6 Hz, 1H), 6.94 (ddd, *J* = 9.0, 9.0, 2.6 Hz, 1H), 5.77 (br d, *J* = 7.8 Hz, 1H), 4.82 (dt, *J* = 8.1, 5.4 Hz, 1H), 3.53 (dd, J = 14.9, 5.6 Hz, 1H), 3.47 (dd, J = 14.9, 5.0 Hz, 1H), 3.35 (s, 3H), 1.64 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 169.8, 168.3,

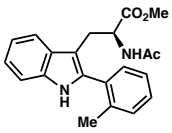
135.6, 134.2, 132.5, 131.9, 128.6, 123.5, 121.8, 119.7, 118.2, 110.8, 107.4, 52.9, 52.4, 37.0, 27.0, 25.3, 23.1; IR (NaCl/thin film): 3275, 3062, 2952, 1733, 1652, 1584, 1558, 1539, 1520, 1486, 1456, 1436, 1374, 1266, 1217, 1180; $[\alpha]_D^{25}$ = +49.9 (*c* = 1.25, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1455.

(*S*)-*N*α-Acetyl-2-(4-methylphenyl)tryptophan methyl ester (121l)



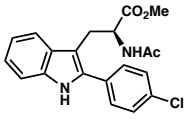
Prepared from 2-(4-methylphenyl)indole (41.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 60.1 mg (86% yield) of **121l** as a white foam. The enantiomeric excess was determined to be 94% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm). t_R(major) = 6.6 min, t_R(minor) = 8.8 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20 (br s, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 8.1, 2H), 7.34 (d, *J* = 8.1, 1H), 7.28 (d, *J* = 8.1, 2H), 7.19 (ddd, *J* = 7.8, 7.1, 1.2 Hz, 1H), 7.15 – 7.09 (m, 1H), 5.77 (br d, *J* = 8.1, 1H), 4.82 (dt, *J* = 7.8, 5.5 Hz, 1H), 3.54 (dd, J = 13.1, 4.0 Hz, 1H), 3.50 (dd, J = 13.1, 3.7 Hz, 1H), 3.33 (s, 3H), 2.40 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.6, 138.0, 136.1, 135.6, 130.2, 129.8, 129.4, 128.1, 122.3, 119.9, 118.7, 110.9, 106.4, 52.8, 52.0, 26.6, 22.8, 21.2; IR (NaCl/thin film): 3365, 3271, 3052, 2951, 1737, 1657, 1519, 1460, 1439, 1375, 1305, 1217 cm^{-1}; $[\alpha]_D^{25}$ = 43.2 (*c* = 0.74, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1700.

(*S*)-N_α-Acetyl-2-(2-methylphenyl)tryptophan methyl ester (121m)



Prepared from 2-(2-methylphenyl)indole (21.0 mg, 0.1 mmol) following General Procedure 2. The crude residue was purified by flash chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 9.2 mg (26% yield) of **121m**. The enantiomeric excess was determined to be 87% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 4.3 min, t_R(minor) = 4.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.62 – 7.55 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.38 – 7.32 (m, 4H), 7.31 – 7.27 (m, 1H), 7.22 (ddd, J = 8.1, 5.6, 2.1 Hz, 1H), 7.16 (ddd, J = 7.1, 5.6, 1.1 Hz, 1H), 5.71 (br d, J = 7.9 Hz, 1H), 4.82 – 4.68 (dt, *J* = 7.9, 5.4 Hz, 1H), 3.38 – 3.29 (m, 4H), 3.28 – 3.16 (m, 1H), 2.28 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.6, 137.3, 135.8, 135.5, 132.1, 130.9, 130.8, 128.9, 128.7, 126.0, 122.3, 119.9, 118.8, 110.8, 107.6, 52.8, 52.0, 26.6, 23.0, 20.0; IR (NaCl/thin film): 3385, 3271, 3062, 2924, 2853, 1734, 1653, 1559, 1539, 1521, 1457, 1437, 1374; $[\alpha]_D^{25}$ = +21.5 (*c* = 0.29, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 351.1703, found 351.1709.

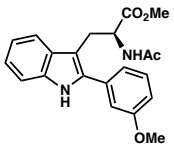
(*S*)-*N*α-Acetyl-2-(4-chlorophenyl)tryptophan methyl ester (121n)



Prepared from 2-(4-chlorophenyl)indole (45.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 55.2 mg (75% yield) of **121n** as a colorless oil. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 6.1 min, t_R(minor) = 7.0 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (br s, 1H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.43 – 7.37 (m, 2H), 7.33 (ddd, *J* = 8.1, 8.1, 1.0 Hz, 1H), 7.23 – 7.18 (m, 1H), 7.14 (ddd, *J* = 8.0, 7.1, 1.1 Hz, 1H), 5.85 (br d, *J* = 8.1 Hz, 1H), 4.83 (dt,

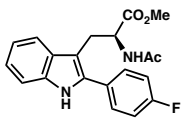
J = 8.1, 5.5 Hz, 1H), 3.55 – 3.38 (m, 2H), 3.34 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.6, 135.8, 134.6, 133.9, 131.5, 129.4, 129.3, 122.7, 120.1, 118.9, 111.1, 107.1, 52.8, 52.1, 29.6, 26.7, 22.9; IR (NaCl/thin film): 3280, 3058, 2948, 1737, 1657, 1519, 1487, 1458, 1439, 1373, 1310, 1216, 1093 cm^{-1}; $[\alpha]_D^{25}$ = +40.8 (*c* = 0.96, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 371.1157, found 371.1158.

(*S*)-N_α-Acetyl-2-(3-methoxyphenyl)tryptophan methyl ester (121o)



Prepared from 2-(3-methoxyphenyl)indole (45.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (30:70 to 100:0 EtOAc:hexanes) to yield 65.0 mg (88% yield) of **121o** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 5.9 min, t_R(minor) = 7.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (br s, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.40 – 7.31 (m, 2H), 7.19 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.16 – 7.10 (m, 2H), 7.08 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.91 (ddd, *J* = 8.3, 2.6, 0.8 Hz, 1H), 5.82 (br d, *J* = 7.8 Hz, 1H), 4.83 (dt, *J* = 7.8, 5.5 Hz, 1H), 3.85 (s, 3H), 3.57 – 3.49 (m, 2H), 3.35 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.6, 160.0, 135.8, 135.6, 134.4, 130.2, 129.3, 122.5, 120.6, 119.9, 118.8, 113.8, 113.5, 111.0, 106.7, 55.4, 52.8, 52.0, 26.6, 22.8; IR (NaCl/thin film): 3282, 3058, 2951, 1738, 1658, 1603, 1520, 1462, 1439, 1373, 1218, 1040; $[\alpha]_D^{25}$ = +40.3 (*c* = 1.16, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1656.

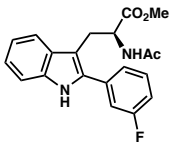
(*S*)-N_α-Acetyl-2-(4-fluorophenyl)tryptophan methyl ester (121p)



Prepared from 2-(4-fluorophenyl)indole (42.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica

gel chromatography (40:60 to 100:0 EtOAc/hexanes) to yield 55.6 mg (78% yield) of **121p** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 6.1 min, t_R(minor) = 6.9 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 47.9 Hz, 1H), 7.57 (dd, *J* = 7.9, 1.1 Hz, 1 H), 7.54 – 7.51 (m, 2H), 7.36 (ddd, *J* = 8.1, 8.1, 0.9 Hz, 1H), 7.23 – 7.10 (m, 4H), 5.82 (d, J = 8.1 Hz, 1H), 4.83 (dt, J = 8.1, 5.5 Hz, 1H), 3.55 – 3.40 (m, 2H), 3.34 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 135.6, 135.0, 130.1, 130.1, 129.4, 122.7, 120.2, 118.9, 116.2, 116.1, 110.9, 106.9, 52.8, 52.0, 26.7, 22.9.; IR (NaCl/thin film): 3364, 3271, 3061, 2925, 2853, 1738, 1661, 1553, 1505, 1460, 1440, 1373, 1221, 1158; $[\alpha]_D^{25}$ = +38.2 (*c* = 0.65, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1460.

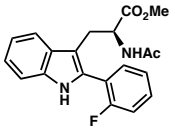
(*S*)-*N*α-Acetyl-2-(3-fluorophenyl)tryptophan methyl ester (121q)



Prepared from 2-(3-fluorophenyl)indole (42.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 ethyl acetate/hexanes) to yield 50.6 mg (76% yield) of **121q** as a white foam. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 3.8 min, t_R(minor) = 4.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (br s, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.33-7.31 (m, 2H), 7.27-7.24 (m, 1H), 7.19 (ddd, *J* = 8.2, 7.0, 1.0 Hz, 1H), 7.13 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 7.07 – 7.03 (m, 1H), 5.89 (br d, *J* = 8.1 Hz, 1H), 4.84 (dt, *J* = 8.1, 5.5 Hz, 1H), 3.53 (dd, J = 13.6, 4.7 Hz, 1H), 3.49 (dd, J = 13.6, 4.2 Hz, 1H), 3.34 (s, 3H), 1.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.1, 169.7, 162.9 (d, J_{C-F} = 246.3 Hz), 135.8, 135.2 (d, J_{C-F} = 7.5 Hz), 134.5 (d, J_{C-F} = 2.5 Hz),

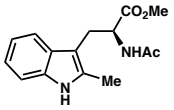
130.6 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.2, 123.9 (d, $J_{C\text{-}F}$ = 3.8 Hz), 122.8, 120.0, 118.9, 115.1 (d, $J_{C\text{-}F}$ = 21.2 Hz), 114.7 (d, $J_{C\text{-}F}$ = 21.2 Hz), 111.1, 107.3, 52.8, 52.0, 26.7, 22.8; IR (NaCl/thin film): 3370, 3275, 3060, 2952, 1735, 1655, 1614, 1585, 1522, 1438, 1374, 1266, 1200, 1155 cm^{-1}; $[\alpha]_D^{25}$ = +37.6 (*c* = 1.21, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1450.

(*S*)-N_α-Acetyl-2-(2-fluorophenyl)tryptophan methyl ester (121r)



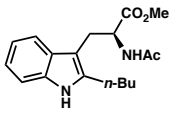
Prepared from 2-(2-fluorophenyl)indole (21.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 12.4 mg (35% yield) of **121r**. The enantiomeric excesses was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 9.5 min, t_R(minor) = 8.4 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.55 (ddd, J = 7.5, 7.5, 1.8 Hz, 1H), 7.45 – 7.35 (m, 2H), 7.29 (ddd, J = 7.5, 7.5, 1.2 Hz, 1H), 7.25 – 7.20 (m, 1H), 7.19 – 7.10 (m, 1H), 5.83 (br d, J = 7.6 Hz, 1H), 4.85 (dt, J = 7.9, 5.5 Hz, 1H), 3.55 – 3.39 (m, 2H), 3.36 (s, 2H), 1.73 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 169.5, 159.8 (d, $J_{C\text{-}F}$ = 246.3 Hz), 135.9, 131.4 (d, $J_{C\text{-}F}$ = 3.8 Hz) 130.2 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.73, 128.65, 124.8 (d, $J_{C\text{-}F}$ = 3.8 Hz), 122.84, 120.6 (d, $J_{C\text{-}F}$ = 15.0 Hz), 120.0, 119.0, 116.4 (d, $J_{C\text{-}F}$ = 21.3 Hz), 111.0, 108.8, 52.5, 52.0, 26.8, 26.8, 22.9; IR (NaCl/thin film): 3275, 3058, 2925, 2853, 1734, 1653, 1523, 1490, 1457, 1437, 1374, 1245, 1216, 1130, 1104; $[\alpha]_D^{25}$ = +39.8 (*c* = 0.41, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1463.

(*S*)-*N*α-Acetyl-2-methyltryptophan methyl ester (121s)



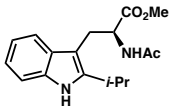
Prepared from 2-methylindole (26.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (50:50 to 100:0 EtOAc:hexanes) to yield 31.0 mg (61% yield) of **121s** as a white foam. The enantiomeric excess was determined to be 85% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 3.9 min, t_R(minor) = 2.7 min. $[\alpha]_D^{25}$ = +25.9 (*c* = 0.99, $CHCl_3$). Spectral data matches that reported in the literature.

(*S*)-N_α-Acetyl-2-butyltryptophan methyl ester (121t)



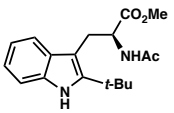
Prepared from 2-butylindole (35.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 45.8 mg (72% yield) of **121t** as a colorless oil. The enantiomeric excess was determined to be 91% by chiral SFC analysis (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 5.1 min, t_R(minor) = 4.2 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.46 – 7.40 (m, 1H), 7.31 – 7.24 (m, 1H), 7.15 – 6.99 (m, 2H), 6.00 (br d, *J* = 7.8 Hz, 1H), 4.88 (dt, *J* = 8.1, 5.7 Hz, 1H), 3.65 (s, 3H), 3.26 (dd, *J* = 5.7, 0.9 Hz, 2H), 2.69 (td, *J* = 7.8 2.2 Hz, 2H), 1.93 (s, 3H), 1.66 – 1.57 (m, 2H), 1.45 – 1.31 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 169.6, 137.4, 135.2, 128.8, 121.3, 119.5, 117.9, 110.4, 105.26, 105.29, 53.0, 52.3, 31.8, 26.8, 25.7, 23.2, 22.6, 13.9; IR (NaCl/thin film): 3296, 3058, 2955, 2871, 1737, 1658, 1562, 1530, 1463, 1439, 1376, 1217, 1129; $[\alpha]_D^{25}$ = +16.3 (*c* = 0.83, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 317.1860, found 317.1855.

(*S*)-*N*α-Acetyl-2-isopropyltryptophan methyl ester (121u)



Prepared from 2-isopropylindole (32.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 39.6 mg (66% yield) of **121u** as a colorless oil. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AD-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm). t_R(major) = 6.4 min, t_R(minor) = 5.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (br s, 1H), 7.48 – 7.41 (m, 1H), 7.30 – 7.27 (m, 1H), 7.15 – 7.02 (m, 2H), 6.04 (br d, *J* = 8.0 Hz, 1H), 4.89 (dt, *J* = 8.1, 5.7 Hz, 1H), 3.66 (s, 3H), 3.29 (dd, J = 12.7, 4.0 Hz, 1H), 3.26 (dd, J = 12.7, 3.4 Hz, 1H), 3.18 (m, 1H), 1.93 (s, 3H1.31 (d, J = 3.3 Hz, 3H), 1.30 (d, J = 3.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 169.7, 142.7, 135.2, 128.7, 121.3, 119.5, 117.9, 110.6, 103.6, 53.0, 52.3, 26.7, 25.3, 23.2, 23.0; IR (NaCl/thin film): 3305, 2962, 1734, 1700, 1653, 1559, 1539, 1506, 1457, 1436, 1374, 1299, 1217 cm^{-1}; $[\alpha]_D^{25}$ = +22.2 (*c* = 0.35, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 303.1703, found 303.1709.

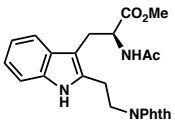
(*S*)-*N*$_\alpha$-Acetyl-2-(tert-butyl)tryptophan methyl ester (121v)



Prepared from 2-(tert-butyl)indole (35.0 mg, 0.20 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 18.1 mg (29% yield) of **121v** as a yellow oil. The enantiomeric excess was determined to be 84% by chiral SFC analysis (OD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(major) = 12.8 min, t_R(minor) = 14.2 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 7.47 (dd, J = 14.0, 7.1 Hz, 1H), 7.27 (dd, J = 5.8, 4.8 Hz, 1H), 7.15 – 7.03 (m, 2H), 6.06 (br d, J = 7.4 Hz,

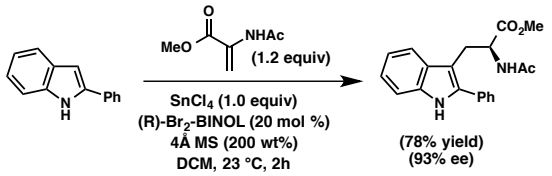
1H), 4.84 (m, 1H), 3.54 (s, 3H), 3.38 – 3.29 (m, 2H), 1.86 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 169.6, 143.4, 133.9, 129.8, 121.3, 119.4, 117.7, 110.4, 104.3, 53.7, 52.2, 33.2, 30.7, 28.6, 23.0; IR (NaCl/thin film): 3326, 3047, 2961, 2918, 2868, 1734, 1653, 1539, 1457, 1436, 1374, 1303, 1254, 1211, 1128; $[\alpha]_D^{25}$ = +12.4 (*c* = 0.36, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 317.1860, found 317.1856.

(*S*)-N_α-Acetyl-2-(ethylphthalimide)tryptophan methyl ester (121w)

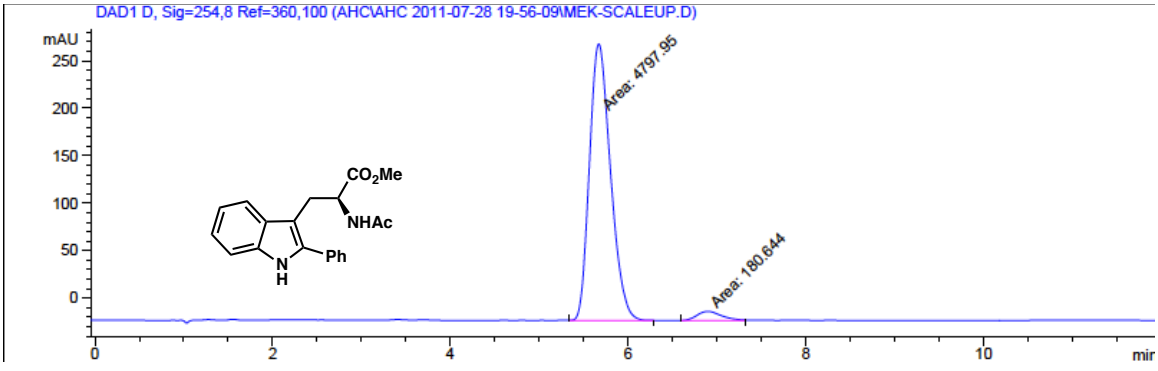


Prepared from 2-(ethylphthalimide)indole (29.0 mg, 0.10 mmol) following General Procedure 2. The crude residue was purified by silica gel chromatography (70:30 to 100:0 EtOAc:hexanes) to yield 34.6 mg (80% yield) of **121w** as a yellow foam. The enantiomeric excess was determined to be 90% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 7.3 min, t_R(minor) = 6.3 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (br s, 1H), 7.83 (dd, *J* = 5.4, 2.9 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.31 (ddd, *J* = 8.1, 8.1, 1.0 Hz, 1H), 7.13 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.07 (ddd, *J* = 10.5, 5.8, 2.2 Hz, 1H), 6.13 (br d, *J* = 8.1 Hz, 1H), 4.92 (dt, *J* = 8.2, 6.0 Hz, 1H), 4.05 – 3.89 (m, 2H), 3.66 (s, 3H), 3.33 – 2.98 (m, 4H), 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 169.8, 168.3, 135.6, 134.2, 132.5, 131.9, 128.6, 123.5, 121.8, 119.7, 118.2, 110.8, 107.4, 52.9, 52.4, 37.0, 27.0, 25.3, 23.1; IR (NaCl/thin film): 3369, 3280, 3052, 2948, 1770, 1738, 1711, 1659, 1530, 1438, 1397, 1371; $[\alpha]_D^{25}$ = +14.8 (*c* = 0.96, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 355.1452, found 355.1455.

2.6.5 Scale-up Procedure



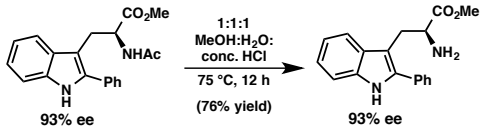
To a flame-dried flask under nitrogen containing freshly activated powdered 4Å molecular sieves (200 wt %) was added 2-phenylindole (1.00 g, 5.20 mmol, 1.00 equiv), methyl 2-acetamidoacrylate (890 mg, 6.20 mmol, 1.20 equiv), and (*R*)-3,3'-dibromo-BINOL (457 mg, 1.00 mmol, 0.20 equiv). The flask was charged with DCM (40 mL) and $SnCl_4$ (1 M in DCM, 5.20 mL, 5.20 mmol, 1.00 equiv) was added. The reaction was stirred at room temperature for 2 hours, then quenched by addition of 1 M HCl (50 mL). The aqueous layer was extracted with EtOAc (2 x 50 mL) and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (50 mL), dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (40:60 to 100:0 EtOAc:hexanes) to yield 1.33 g (77% yield) of **121c** as a pale yellow foam. The enantiomeric excess was determined to be 93% by chiral SFC analysis (AD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R(major) = 5.7 min, t_R(minor) = 6.9 min.



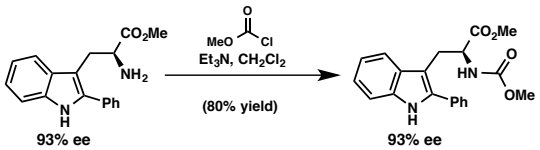
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.670	MM	0.2746	4797.95020	291.18689	96.3716
2	6.889	MM	0.3168	180.64430	9.50427	3.6284

2.6.6 Functionalization of Tryptophan 121c

2.6.6.1 Acetamide Hydrolysis of 121c

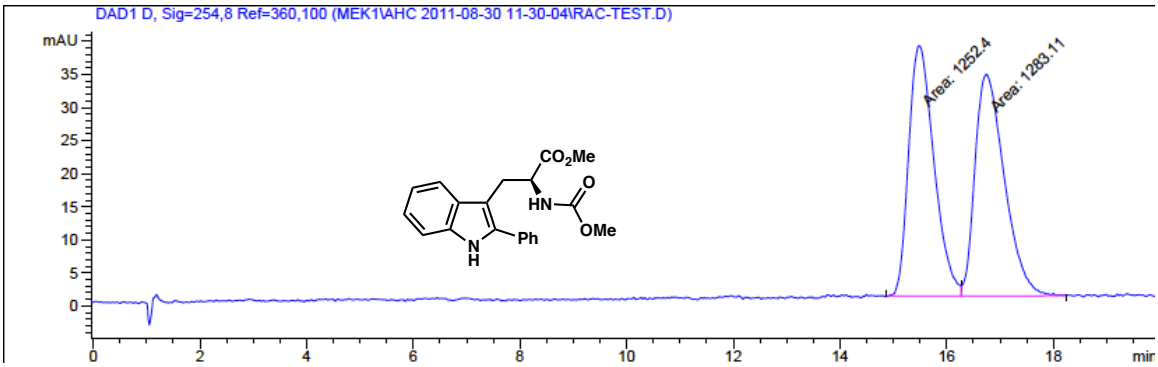


A vial was charged with (*S*)-*N*α-acetyl-2-phenyltryptophan methyl ester (**121c**, 30.0 mg, 0.09 mmol), MeOH (1 mL), H_2O (1 mL) and aqueous HCl (12 M, 1 mL). The reaction was heated to 75 °C for 12 hours, then concentrated, redissolved in DCM (10 mL) and washed with saturated aqueous $NaHCO_3$ (3 X 5 mL). The aqueous layers were combined and extracted with DCM (4 X 5 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (99:1 CH_2Cl_2:MeOH) to yield 20.0 mg (76% yield) of **124** as a light yellow oil. The enantiomeric excess was determined by chiral SFC analysis of the corresponding methylcarbamate (see below). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (br s, 1H), 7.67 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.62 – 7.60 (m, 2H), 7.50 – 7.43 (m, 2H), 7.41 – 7.34 (m, 2H), 7.22 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H), 7.15 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 3.89 (dd, J = 8.4, 5.0 Hz, 1H), 3.56 (s, 3H), 3.47 – 3.38 (m, 1H), 3.27 – 3.14 (m, 1H), 1.69 (br s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 136.1, 135.8, 132.9, 129.1, 129.0, 128.3, 128.0, 122.5, 119.9, 119.2, 110.9, 108.2, 55.2, 51.9, 30.2; IR (NaCl/thin film): 3367, 3062, 2948, 1732, 1603, 1489, 1457, 1207; $[\alpha]_D^{25}$ = -12.4 (*c* = 0.85, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 295.1441, found 295.1446.



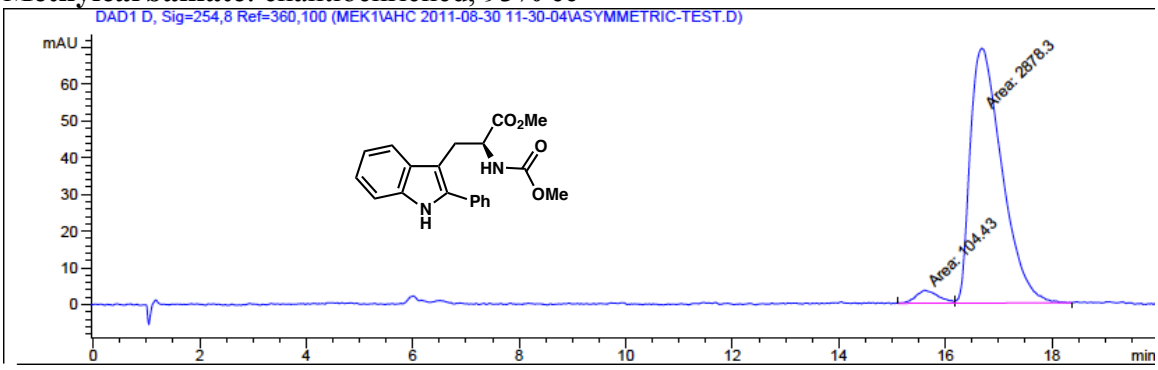
A flame-dried flask was charged with free amine **124** (19.5 mg, 0.70 mmol, 1.00 equiv), Et_3N (19 µL, 0.13 mmol, 2.0 equiv) and DCM (5 mL). Methylchloroformate (6.0 µL, 0.73 mmol, 1.10 equiv) was added and the solution was stirred at room temperature for 3 hours, then quenched with saturated aqueous NH_4Cl (5 mL) and extracted with EtOAc (2 X 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The crude residue was purified by silica gel chromatography (25:75 EtOAc:hexanes) to yield 18.5 mg (80% yield) of methylcarbamate as a colorless oil. The enantiomeric excess was determined to be 93% by chiral SFC analysis (OD-H, 2.5 mL/min, 15% IPA in CO_2, λ = 254 nm): t_R(major) = 16.7 min, t_R(minor) = 15.6 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (br s, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.48 – 7.45 (m, 2H), 7.40 – 7.35 (m, 2H), 7.25 – 7.19 (m, 1H), 7.16 (m, 1H), 5.06 (br d, J = 7.7 Hz, 1H), 4.63 – 4.59 (m, 1H), 3.54 (s, 3H), 3.50 (m, 2H), 3.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 156.1, 136.2, 135.7, 132.9, 129.2, 129.0, 128.3, 128.0, 122.5, 120.0, 118.9, 110.9, 106.7, 54.5, 52.12, 52.07, 27.1; IR (NaCl/thin film) 3338, 2953, 2923, 2852, 1718, 1701, 1507, 1457, 1363, 1213, 1072 cm^{-1}; $[\alpha]_D^{25}$ = +22.6 (*c* = 0.10, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 353.1496, found 353.1497.

Methylcarbamate: racemic



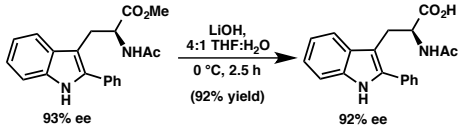
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.480	MF	0.5516	1252.40308	37.84099	49.3945
2	16.749	FM	0.6385	1283.11060	33.49063	50.6055

Methylcarbamate: enantioenriched, 93% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.610	MF	0.4860	104.43002	3.58131	3.5012
2	16.684	FM	0.6913	2878.30273	69.39832	96.4988

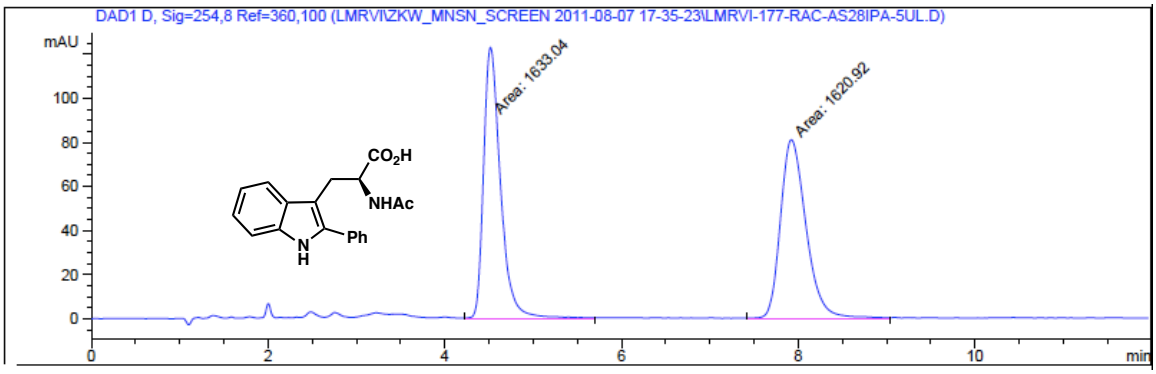
2.6.6.2 Methyl Ester Hydrolysis of 121c



A 10 mL flask was charged with (*S*)-*N*α-acetyl-2-phenyltryptophan methyl ester **121c** (67.2 mg, 0.20 mmol, 1.00 equiv) and THF (0.9 mL) then cooled to 0 ºC, followed by dropwise addition of aqueous LiOH (1.75 M, 230 μL, 0.40 mmol, 2.00 equiv). The reaction was vigorously stirred at 0 ºC for 2 hours, then diluted with H_2O (15 mL) and extracted with EtOAc (2 x 10 mL). The aqueous layer was acidified to pH = 1.5 and extracted with EtOAc (5 x 15 mL). The combined organic layers from the acidic aqueous extraction were dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by silica gel chromatography (0:99:1 to 15:84:1 MeOH:DCM:AcOH) to yield 59.2 mg (92% yield) of carboxylic acid **123** as a pale yellow foam. The enantiomeric excess was determined to be 92% by chiral SFC analysis (AS-H, 2.5 mL/min, 28% IPA

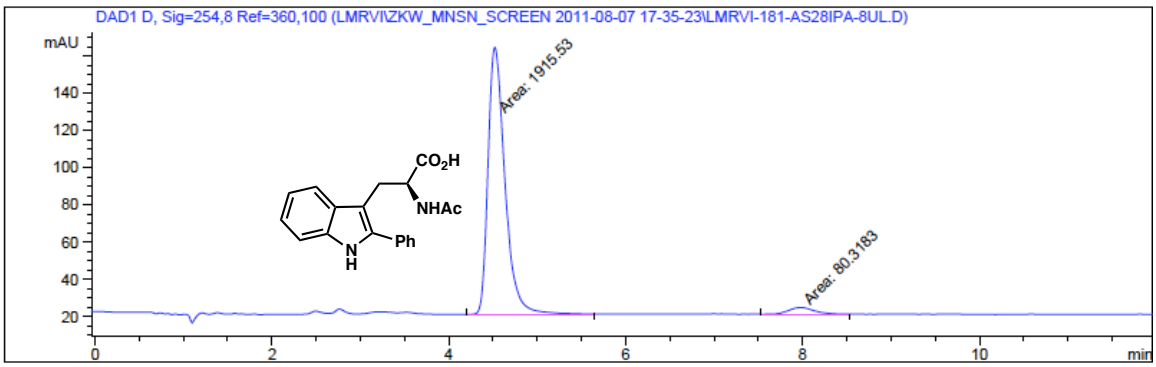
in CO_2, λ = 254 nm): t_R(major) = 4.5 min, t_R(minor) = 8.0 min. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.47 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.40 (m, 1H), 7.37 (ddd, *J* = 8.0, 0.8, 0.8 Hz, 1H), 7.21 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 7.14 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 5.72 (br d, *J* = 7.4 Hz, 1H), 4.73 (td, *J* = 7.1, 5.4 Hz, 1H), 3.56 (dd, *J* = 14.9, 5.2 Hz, 1H), 3.49 (dd, *J*=15.0, 6.9 Hz, 1H), 1.62 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7, 170.9, 136.2, 135.7, 132.9, 129.13, 129.05, 128.3, 128.2, 122.6, 120.1, 118.8, 111.0, 106.8, 53.1, 26.2, 22.6; IR (NaCl/thin film): 3391, 3306, 3055, 3011, 2921, 2850, 1717, 1615, 1527, 1457, 1448, 1215 cm^{-1}; $[\alpha]_D^{25}$ = +9.2 (*c* = 1.05, MeCN). HRMS (MM) calc'd for $[M+H]^+$ 323.1390, found 323.1390.

Racemic



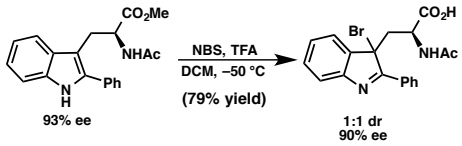
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.517	MM	0.2216	1633.03918	122.81268	50.1863
2	7.923	MM	0.3341	1620.91711	80.86505	49.8137

Enantioenriched, 92% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.521	MM	0.2225	1915.53430	143.46094	95.9757
2	7.970	MM	0.3592	80.31825	3.72675	4.0243

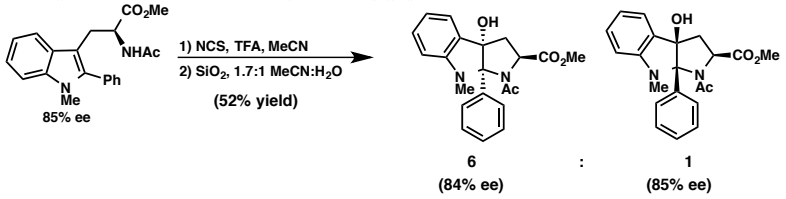
2.6.6.3 Preparation of bromo-dehydroindoline 125



A solution of (*S*)-*N*α-acetyl-2-phenyltryptophan methyl ester **121c** (101 mg, 0.30 mmol, 1.00 equiv) in DCM (8.4 mL) was cooled to –50 °C in an acetonitrile/dry ice bath. NBS (53.4 mg, 0.30 mmol, 1.00 equiv) was then added, followed by TFA (900 µL). The reaction was stirred in the dark at –50 °C for 3 hours, then poured onto ice, quenched with aqueous ammonia (1.5 mL) and extracted with DCM (3 x 25 mL). The combined organics were washed (40 mL H_2O, then 40 mL brine), dried (Na_2SO_4), filtered, and concentrated. The product **125** was formed in a 1:1 ratio of diastereomers (determined by ^{1}H NMR analysis of the crude reaction mixture) and was purified by silica gel chromatography (30:70 to 70:30 EtOAc:hexanes) to yield 98 mg (79% yield) of the combined diastereomers as a bright yellow foam. The enantiomeric excesses of the two diastereomers were determined to be 92% and 90% by chiral SFC analysis (AS-H, 2.5

mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 3.8 min, t_R(minor) = 4.1 min; t_R(major) = 4.6 min, t_R(minor) = 6.0 min. Spectral data and optical rotation are reported for the mixture of diastereomers. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 – 8.32 (m, 4H), 7.70 – 7.64 (m, 2H), 7.57 – 7.49 (m, 8H), 7.47 – 7.40 (m, 2H), 7.39 – 7.30 (m, 2H), 5.37 (br d, *J* = 7.4 Hz, 1H), 5.05 (br d, *J* = 8.5 Hz, 1H), 4.33 (dt, *J* = 7.5, 5.5 Hz, 1H), 3.95 (td, *J* = 8.9, 4.0 Hz, 1H), 3.56 (dd, *J* = 14.8, 5.2 Hz, 1H), 3.47 – 3.41 (m, 4H), 3.38 – 3.32 (m, 4H), 3.23 (dd, *J* = 14.6, 9.3 Hz, 1H), 1.45 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.6, 174.8, 170.7, 170.0, 169.4, 169.2, 151.82, 151.76, 139.8, 139.6, 131.6, 131.4, 131.3, 130.5, 130.4, 128.81, 128.80, 128.71, 128.70, 127.2, 126.6, 123.2, 122.5, 121.9, 121.7, 59.16, 59.14, 52.5, 52.3, 50.3, 49.8, 41.6, 41.4, 22.3, 22.0; IR (NaCl/thin film): 3271, 3062, 2952, 2924, 2853, 1747, 1661, 1525, 1444, 1372, 1264, 1216 cm^{-1}; $[\alpha]D^{25}$ = +17.1 (*c* = 0.50, $CHCl_3$). HRMS (MM) calc'd for M^+ 415.0652, found 415.0652.

2.6.6.4 Preparation of 3-hydroxypyrroloindoline 126



A 15 mL flask containing (*S*)-*N*α-acetyl-1-methyl-2-phenyltryptophan methyl ester **121d** (52.5 mg, 0.150 mmol, 1.00 equiv) was flushed with argon and then charged with MeCN (3.3 mL). TFA was added as a solution in MeCN (1.3 M, 125 μL, 0.150 mmol, 1.00 equiv), followed by NCS as a solution in MeCN (0.2 M, 0.75 mL, 0.150 mmol, 1.00 equiv). The flask was then sealed under argon and the solution was stirred in the dark at room temperature. After 3 hours, the reaction was quenched with aqueous ammonia (1.5

mL), poured onto ice, and extracted with DCM (3 x 15 mL). The combined organics were washed (20 mL H_2O, then 20 mL brine), dried (Na_2SO_4), filtered, and concentrated to give the crude mixture of 3-chloropyrroloindoline diastereomers (detected by HRMS direct injection (MM) calc'd for $[M+H]^+$ 385.1313, found 385.1320). The crude residue was redissolved in MeCN (2 mL), then H_2O (1.2 mL) and SiO_2 (2.5 mL) were added. The mixture was vigorously stirred open to air at room temperature for 30 minutes, then filtered through a 1.5 mL silica plug with EtOAc (50 mL), dried (Na_2SO_4), filtered and concentrated. The 3-hydroxypyrroloindoline **126** existed in a 6:1 ratio of diastereomers, favoring the *endo* diastereomer (determined by ^1H NMR analysis of the crude reaction mixture) and was purified by silica gel chromatography (0:100 to 10:90 EtOAc:hexanes) to yield 30.8 mg (contains 18 wt % $CHCl_3$, 46% corrected yield) of the *endo* diastereomer as a yellow oil. The *exo* diastereomer, obtained post chromatography in a mixture with (*S*)-*N*α-acetyl-1-methyl-2- phenyltryptophan methyl ester **XX**, was subjected to reverse phase preparatory HPLC (30:70 to 90:10 MeCN:H_2O) using an Agilent 1200 Series HPLC with an Agilent XDB-C18 5 μM column (9.4 x 250 mm) to yield 3.5 mg (6% yield) of the *exo* diastereomer as a yellow oil.

Endo diastereomer:

The enantiomeric excess was determined to be 84% by chiral SFC analysis (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 254 nm): t_R(major) = 7.4 min, t_R(minor) = 4.7 min. The relative stereochemistry was assigned by 2D NMR analysis. ^1H NMR (500 MHz, CD_3CN; compound exists as a 15:1 mixture of rotamers, the major rotamer is reported) δ 7.40 – 7.35 (m, 2H), 7.34 – 7.26 (m, 3H), 7.20 (ddd, *J* = 7.9, 7.5, 1.3 Hz, 1H), 7.12 (ddd, *J* = 7.2, 1.3, 0.5 Hz, 1H), 6.66 (ddd, *J* = 7.3, 7.3, 1.0 Hz, 1H), 6.51 (d, *J* = 7.9 Hz, 1H),

4.79 (d, J = 8.8 Hz, 1H), 3.19 (s, 3H), 2.97 (s, 3H), 2.90 (br s, 1H), 2.82 (d, J = 12.7 Hz, 1H), 2.59 (ddd, J = 12.7, 8.8, 1.1 Hz, 1H), 1.95 (s, 3H); ^{13}C NMR (125 MHz, CD_3CN; compound exists as a 15:1 mixture of rotamers, the major rotamer is reported) δ 172.0, 171.3, 153.1, 138.0, 131.6, 128.9, 128.6, 128.3, 125.2, 118.0, 107.1, 95.3, 88.3, 61.3, 52.7, 39.0, 32.7, 23.6; IR (NaCl/thin film): 3292, 3010, 2948, 1735, 1653, 1648, 1610, 1491, 1448, 1388, 1313, 1220 cm^{-1}; $[\alpha]D^{25}$ = +264.0 (c = 1.35, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1650.

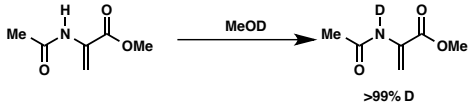
Exo diastereomer:

The enantiomeric excess was determined to be 85% by chiral SFC analysis (OD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 254 nm): t_R(major) = 6.2 min, t_R(minor) = 4.0 min. The relative stereochemistry was assigned by 2D NMR analysis. ^{1}H NMR (500 MHz, CD_3CN; compound exists as a 1.5:1 mixture of rotamers, the major rotamer isdenoted by *, the minor rotamer by§) δ 7.60 – 7.22 (m, 6H*, 7H§), 7.17 (ddd, J = 7.3, 0.6, 0.6 Hz, 1H*), 6.79 (dd, J = 7.5, 7.5 Hz, 1H§), 6.70 (dd, J = 7.5, 7.5 Hz, 1H*), 6.65 (d, J = 7.9 Hz, 1H§), 6.54 (d, J = 7.9 Hz, 1H*), 4.49 (dd, J = 8.0, 6.7 Hz, 1H*), 4.07 (dd, J = 10.0, 6.9 Hz, 1H§), 3.81 (s, 3H*), 3.71 (s, 3H§), 3.34 (s, 1H§), 3.01 (s, 1H*), 2.963 (s, 3H*), 2.958 (s, 3H§)**,** 2.71 (dd, J = 13.0, 8.1 Hz, 1H*), 2.68 (dd, J = 12.6, 7.0 Hz, 1H§)**,** 2.34 (dd, J = 12.9, 6.7 Hz, 1H*), 2.07 (dd, J = 12.7, 10.0 Hz, 1H§), 1.89 (s, 3H*), 1.80 (s, 3H§); ^{13}C NMR (125 MHz, CD_3CN) δ 174.1, 173.6, 172.3, 171.8, 151.2, 151.1, 136.3, 136.2, 131.6, 131.3, 130.3, 129.60, 129.57, 129.4, 128.7, 128.6, 124.4, 123.9, 119.3, 118.2, 108.0, 106.4, 98.8, 96.1, 90.1, 88.5, 61.2, 60.3, 53.3, 52.6, 40.9, 37.2, 33.4, 32.4, 24.6, 23.8; IR (NaCl/thin film): 3305, 2924, 1747, 1646, 1610, 1491, 1448, 1381, 1311, 1207

cm^{-1}; $[\alpha]D^{25}$ = -138.2 (*c* = 0.33, $CHCl_3$). HRMS (MM) calc'd for $[M+H]^+$ 367.1652, found 367.1655.

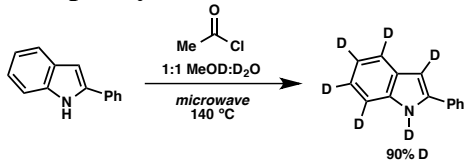
2.6.7 Deuterium Labeling Studies

Preparation of *N*-deuteroacrylate (XX)



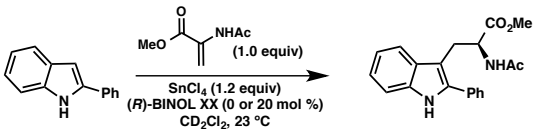
Acrylate **120c** was dissolved in MeOD (1 mL) under nitrogen. After stirring for 1 minute, the solution was concentrated under high vacuum. This procedure was repeated three times to give >99% deuterium incorporation.

Preparation of per-deutero-2-phenylindole



To MeOD (1 mL) in a microwave vial was added acetyl chloride (100 μL), followed by 2-phenylindole (6a, 50 mg) and D_2O (1 mL). The vial was sealed and heated in a microwave to 140 °C for 1 hour. Upon cooling, the heterogenous solution was diluted with DCM. The phases were separated and the aqueous was extracted with DCM (2 x 5 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated to give per-deutero-2-phenylindole with 90% deuterium incorporation.

2.6.7 ^{1}H NMR Kinetics Studies



An oven-dried vial was charged with 2-phenylindole (19.0 mg, 0.10 mmol, 1.00 equiv), methyl 2-acetamidoacrylate (14.0 mg, 0.10 mmol, 1.00 equiv), (*R*)-BINOL if necessary (6.0 mg, 0.02 mmol, 0.20 equiv) and 1,4-diethylbenzene (4.7 μL, 0.03 mmol, 0.30 equiv) as the internal standard. The vial was pumped into a glove box and charged with CD_2Cl_2 (0.75 mL, to an indole concentration of 0.12 M), then transferred to a screw-cap NMR tube. A ^{1}H NMR spectrum (1 scan) was taken to determine the inital ratio of acrylate and 1,4-diethylbenzene. $SnCl_4$ (1 M in CD_2Cl_2, 120 μL, 0.12 mmol, 1.20 equiv) was then added through the septum of the screw-cap and the NMR tube was inverted once and quickly inserted into the spectrometer. The concentration of acrylate was monitored by ^{1}H NMR over 9 hours and was determined by integration of its resonance at 3.83 ppm relative to 1,4-diethylbenzene's resonance at 2.74 ppm.

2.7 NOTES AND REFERENCES

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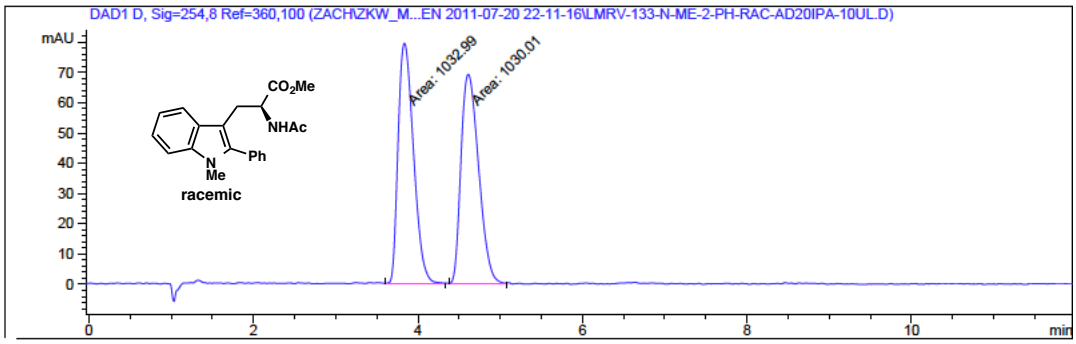
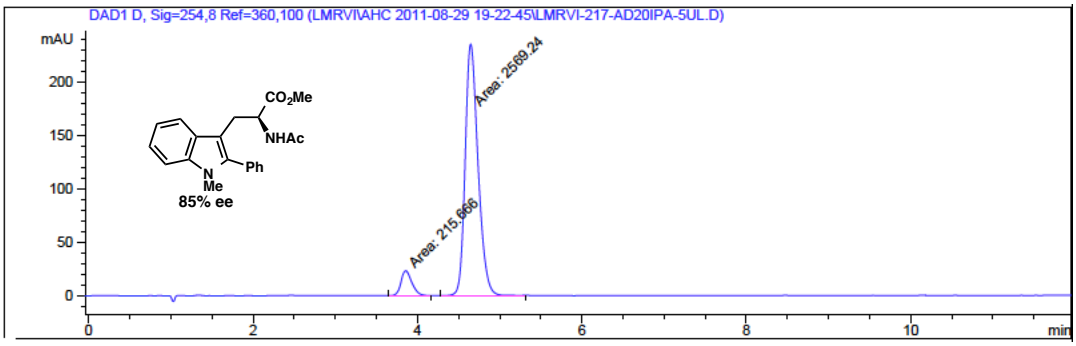
Appendix 1

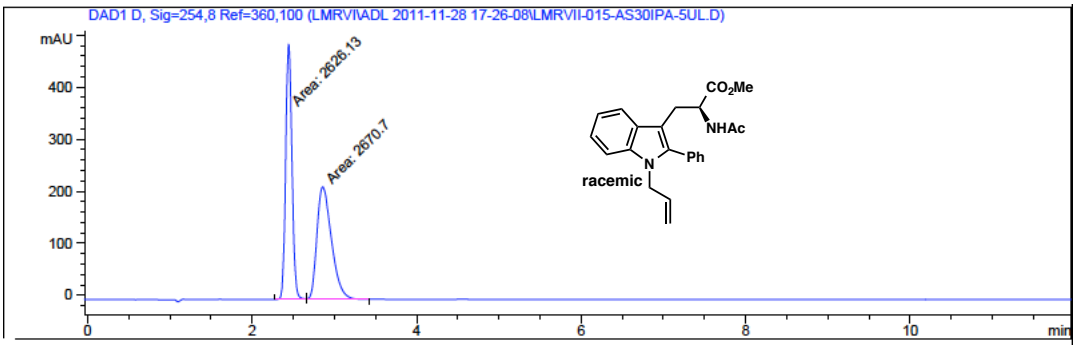
Spectra Relevant to Chapter 2:Enantioselective Synthesis of Tryptophan Derivatives by a Tandem Friedel–Crafts Conjugate Addition/Asymmetric Protonation Reaction



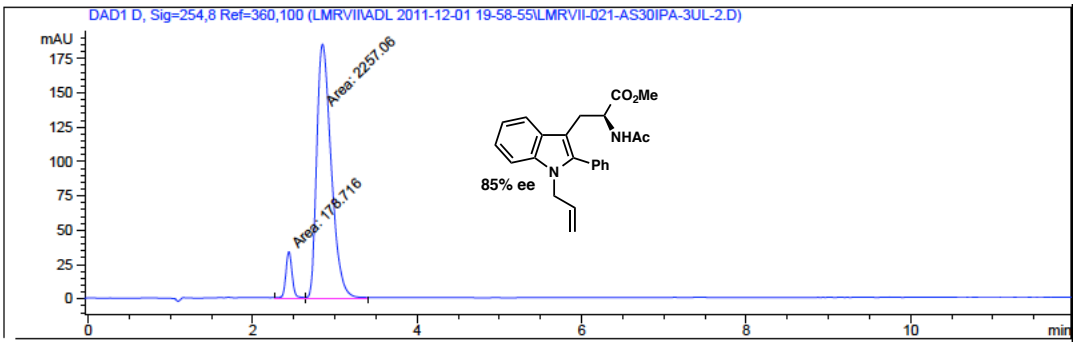
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.836	MM	0.2168	1032.99182	79.40057	50.0722
2	4.612	MM	0.2483	1030.01440	69.12988	49.9278



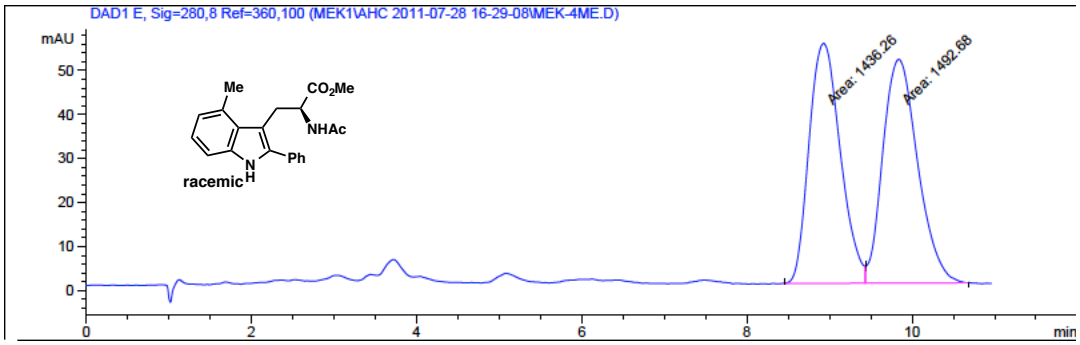
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.857	MM	0.1536	215.66585	23.40283	7.7441
2	4.648	MM	0.1816	2569.23853	235.83917	92.2559



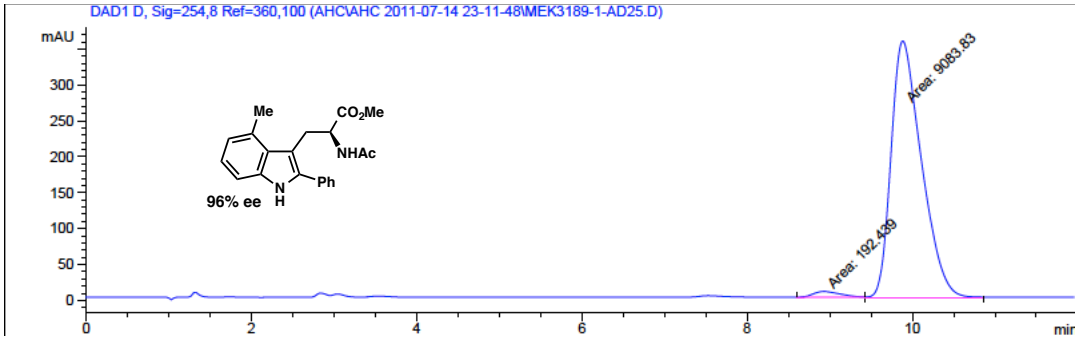
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.445	MM	0.0885	2626.12964	494.64706	49.5793
2	2.860	MM	0.2054	2670.69971	216.69223	50.4207



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.440	MM	0.0877	178.71585	33.96154	7.3371
2	2.850	MM	0.2033	2257.05518	185.04457	92.6629



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.929	MF	0.4389	1436.26184	54.54070	49.0370
2	9.840	FM	0.4892	1492.67529	50.85297	50.9630



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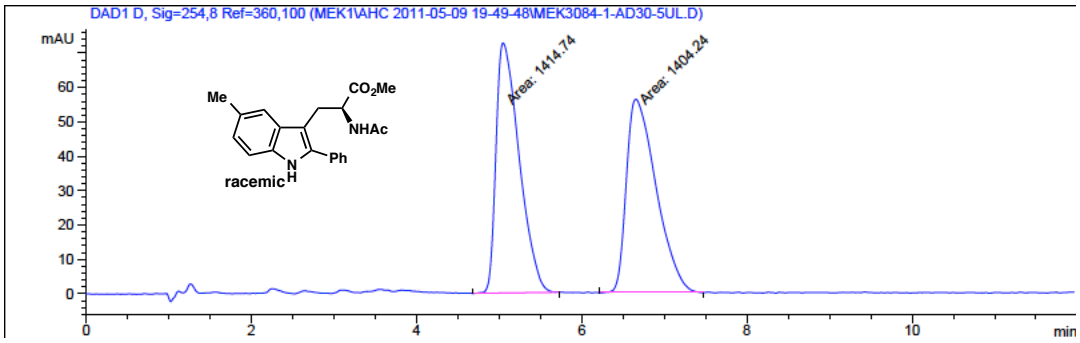
1	8.934	MF	0.3836	192.43893	8.36206	2.0745
2	9.884	FM	0.4243	9083.83105	356.81247	97.9255



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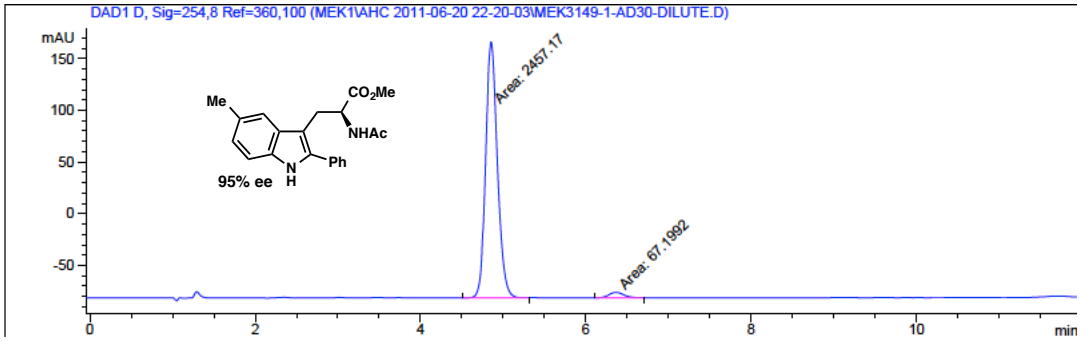
1	5.050	MM	0.3239	1414.74487	72.79134	50.1863
2	6.656	MM	0.4167	1404.24048	56.16964	49.8137



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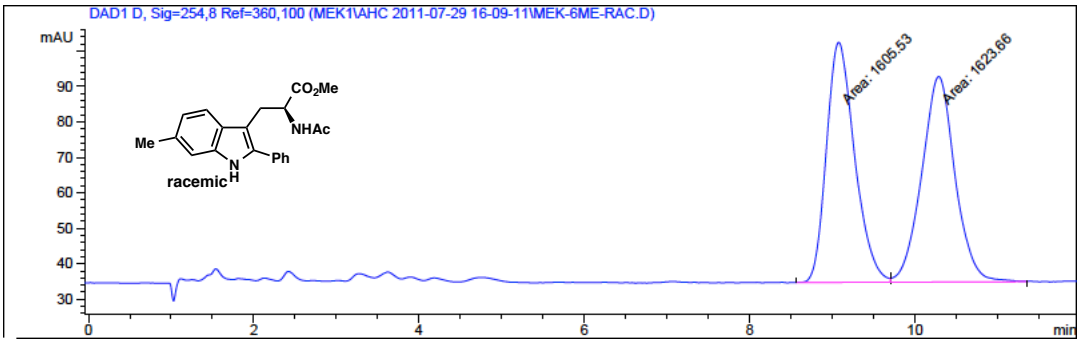
2	6.363	MM	0.2091	67.19923	5.35534	2.6620



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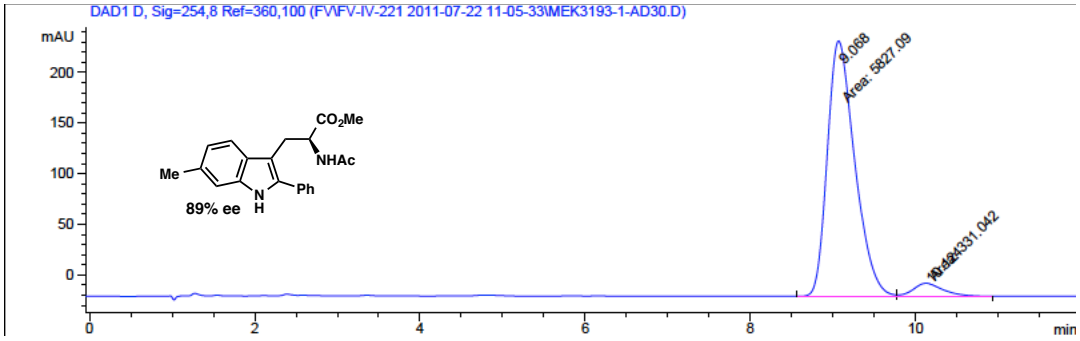
2	10.287	FM	0.4674	1623.65698	57.89628	50.2806



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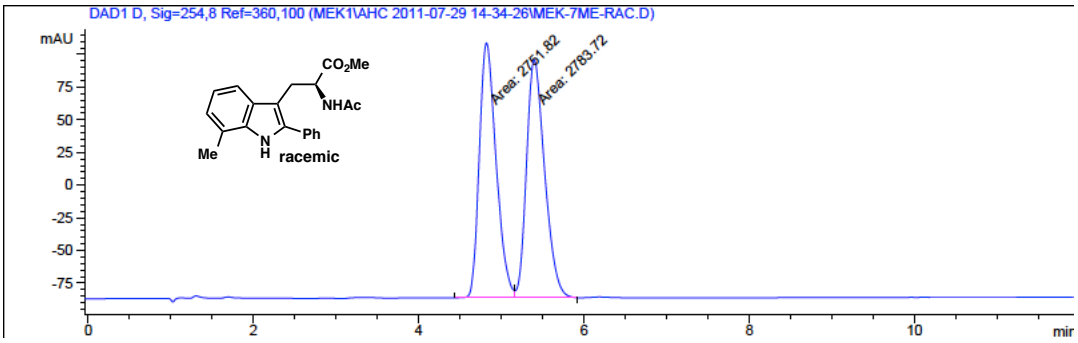

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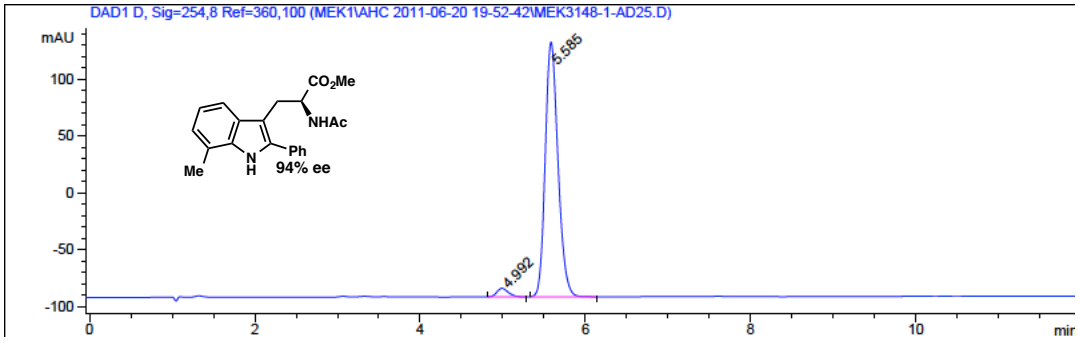

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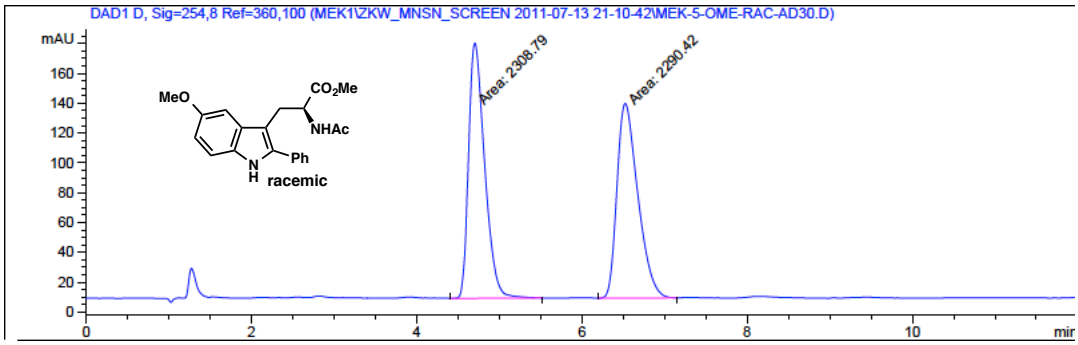

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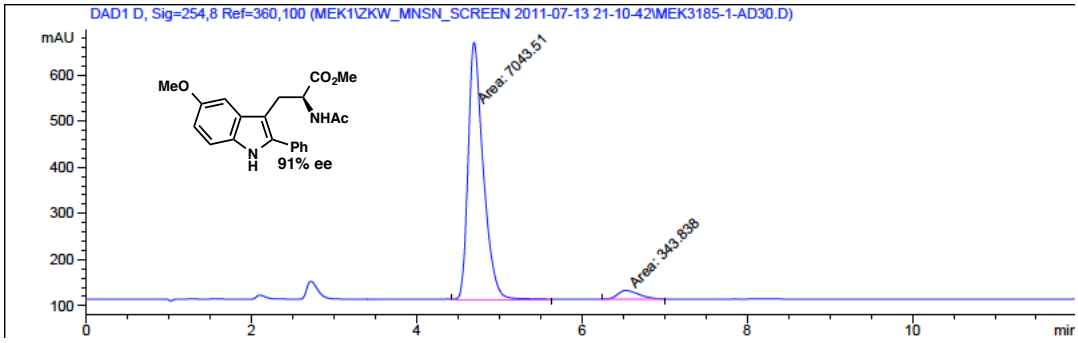
1	4.705	MM	0.2251	2308.79272	170.98026	50.1998
2	6.524	MM	0.2925	2290.41650	130.51103	49.8002



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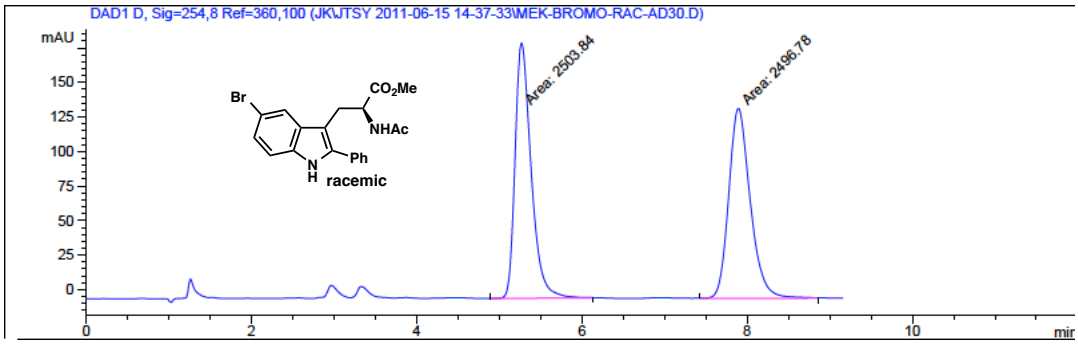
1	4.696	MM	0.2109	7043.50879	556.51990	95.3456
2	6.537	MM	0.3008	343.83807	19.05145	4.6544



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1	5.271	MM	0.2255	2503.83789	185.02051	50.0705
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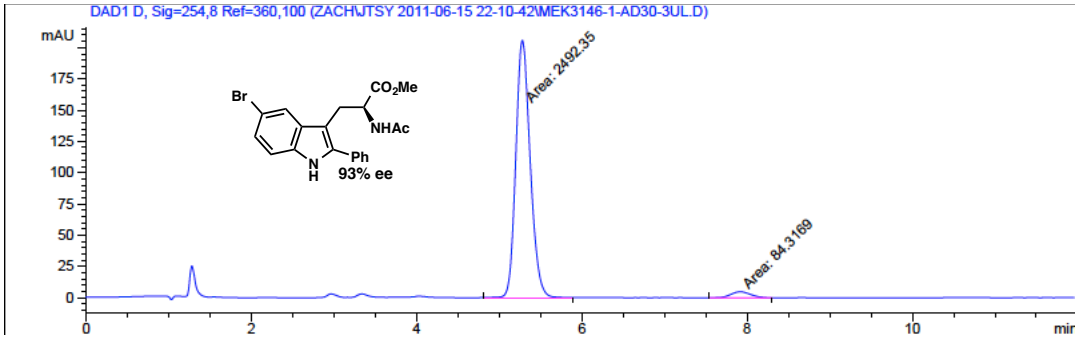

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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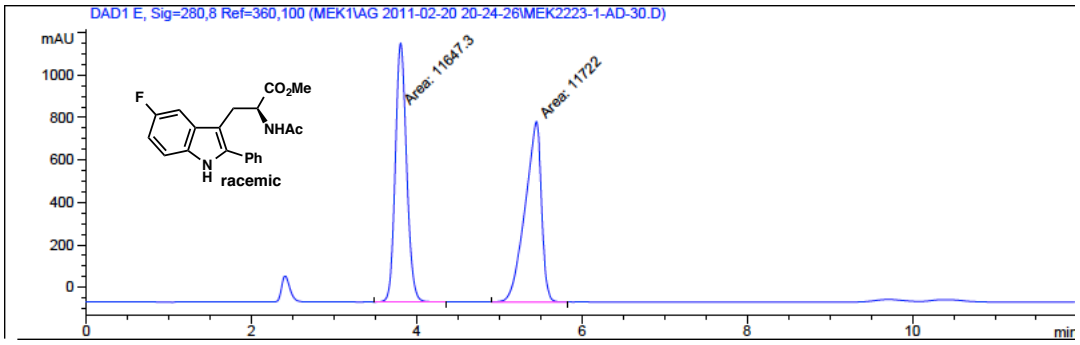
2	7.908	MM	0.2847	84.31690	4.93608	3.2723



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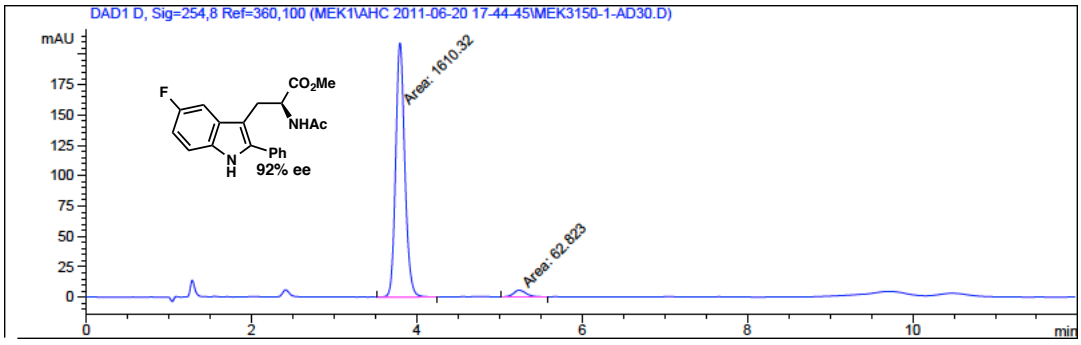

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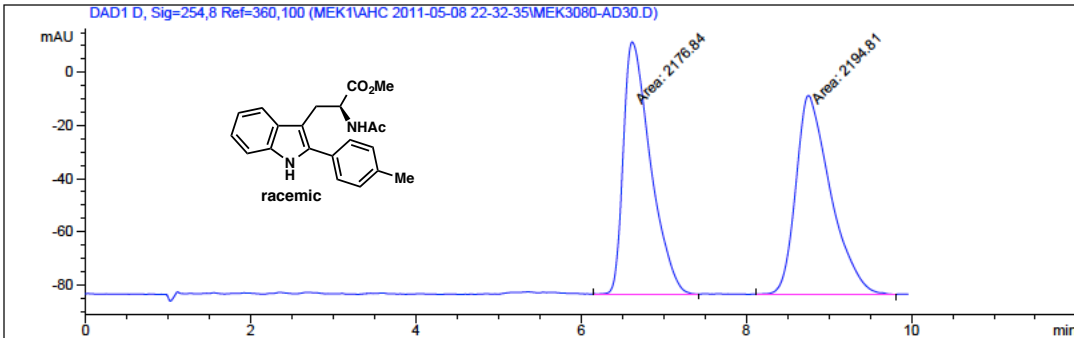
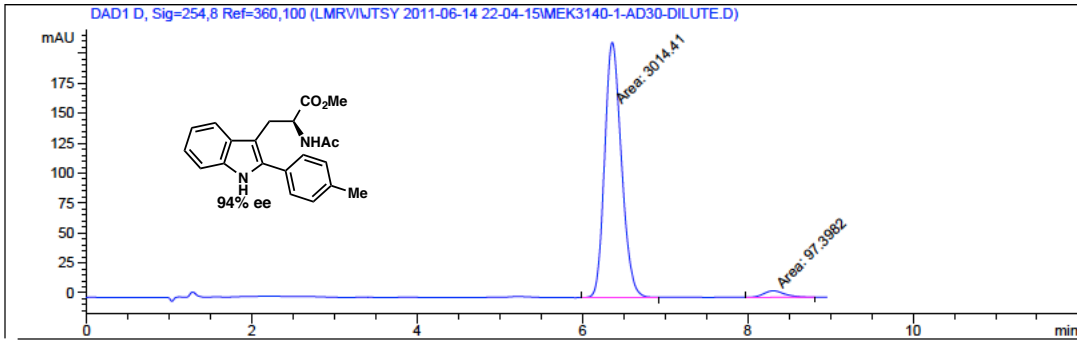
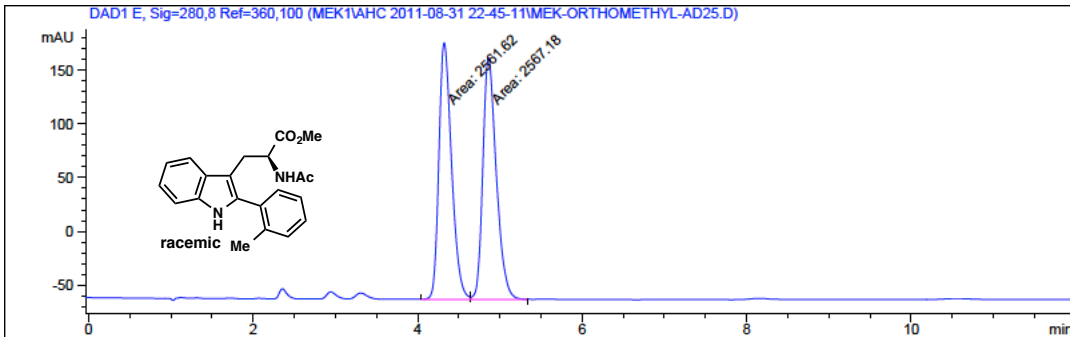
2	5.237	MM	0.1839	62.82299	5.69236	3.7548



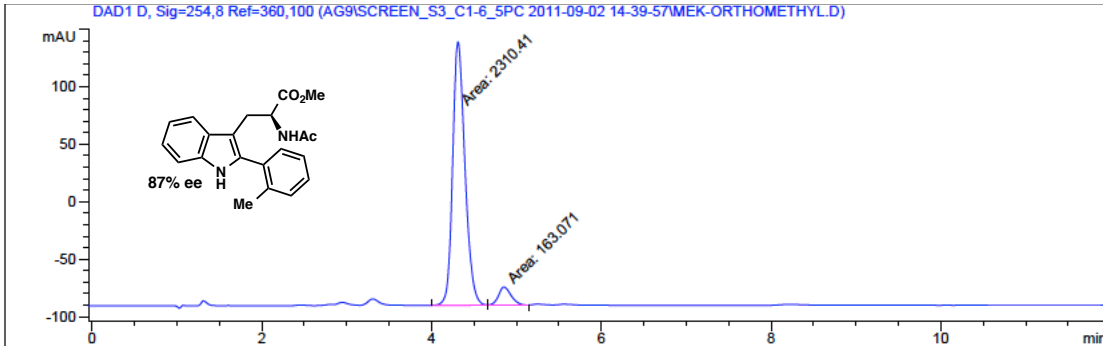
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.621	MM	0.3814	2176.84033	95.11774	49.7945
2	8.753	MM	0.4879	2194.80835	74.98085	50.2055



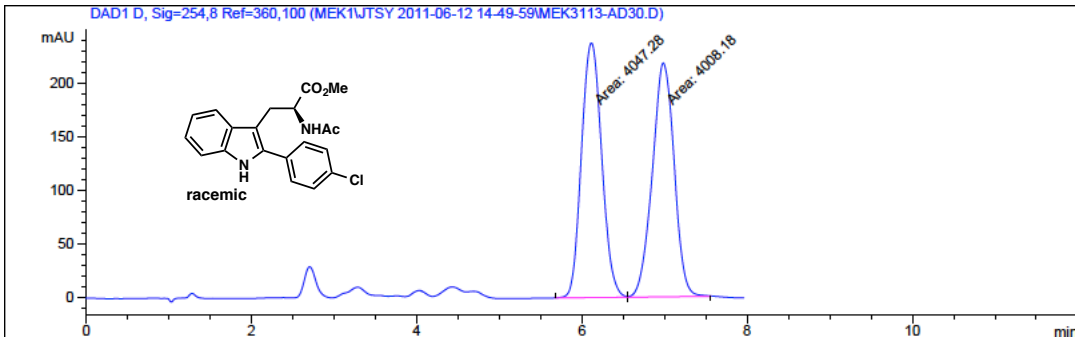
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.362	MM	0.2356	3014.40527	213.28644	96.8700
2	8.308	MM	0.2940	97.39824	5.52150	3.1300



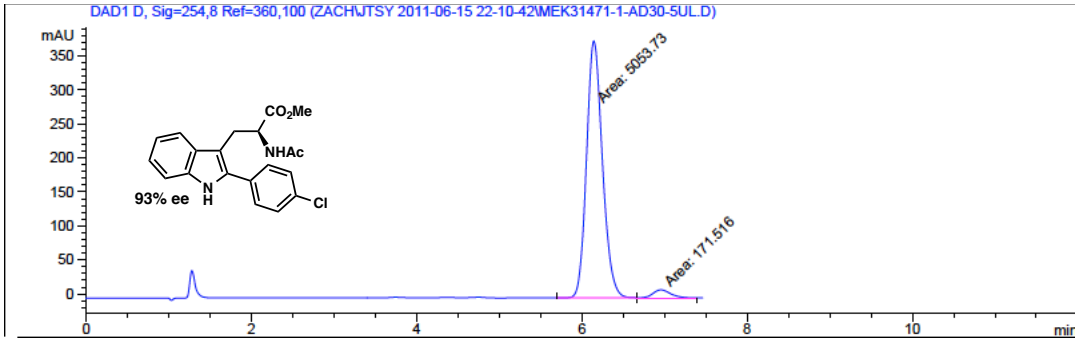
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.324	MF	0.1781	2561.61523	239.71214	49.9458
2	4.862	FM	0.1897	2567.17676	225.56844	50.0542



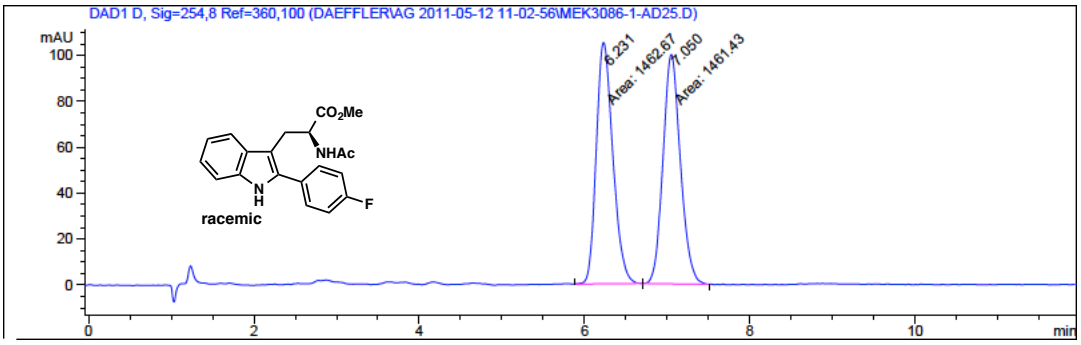
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.312	MF	0.1680	2310.40869	229.23323	93.4072
2	4.854	FM	0.1724	163.07098	15.76543	6.5928



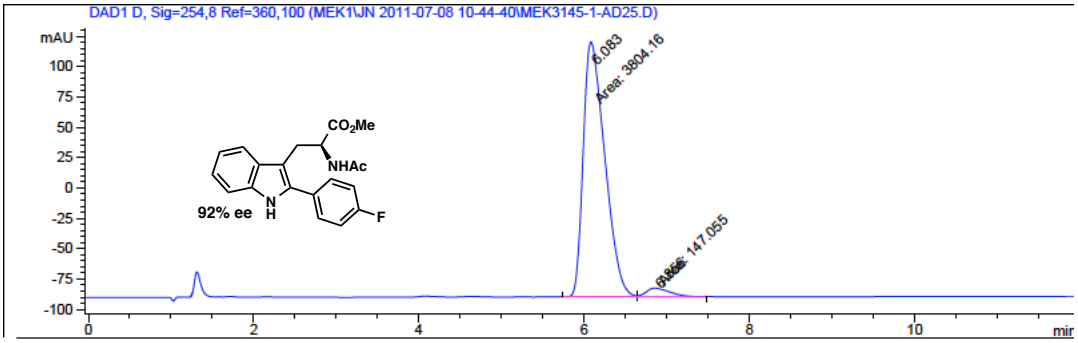
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.115	MF	0.2839	4047.27661	237.58223	50.2427
2	6.986	FM	0.3061	4008.18091	218.21001	49.7573



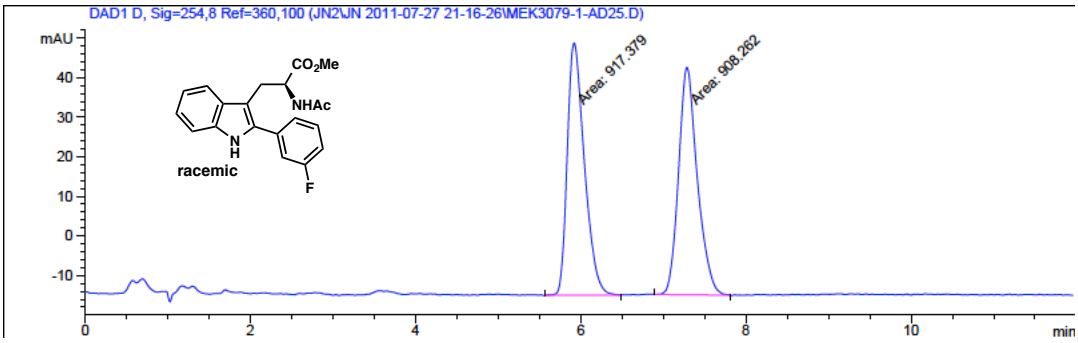
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.146	MF	0.2229	5053.73291	377.91241	96.7176
2	6.960	FM	0.2433	171.51614	11.74924	3.2824



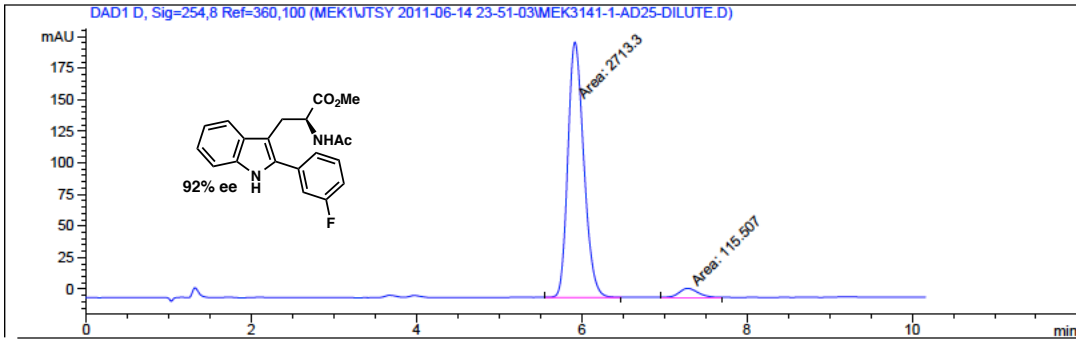
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.231	MM	0.2319	1462.67285	105.12125	50.0213
2	7.050	MM	0.2437	1461.42761	99.94221	49.9787



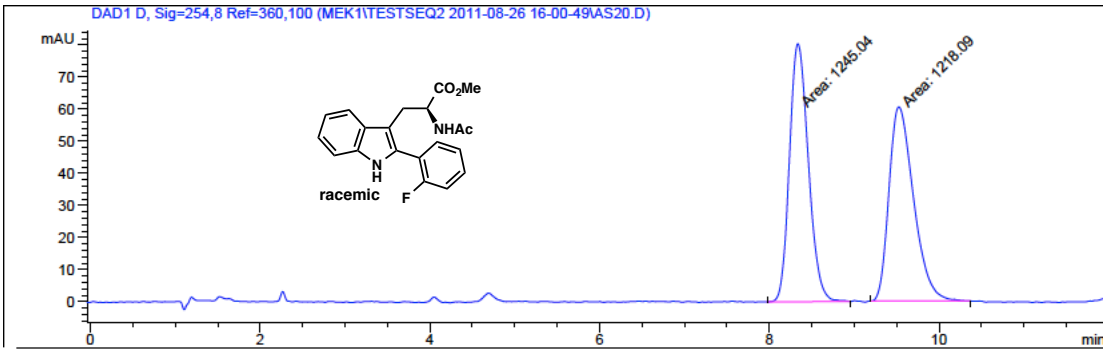
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.083	MF	0.3018	3804.16431	210.09053	96.2782
2	6.856	FM	0.3379	147.05510	7.25396	3.7218



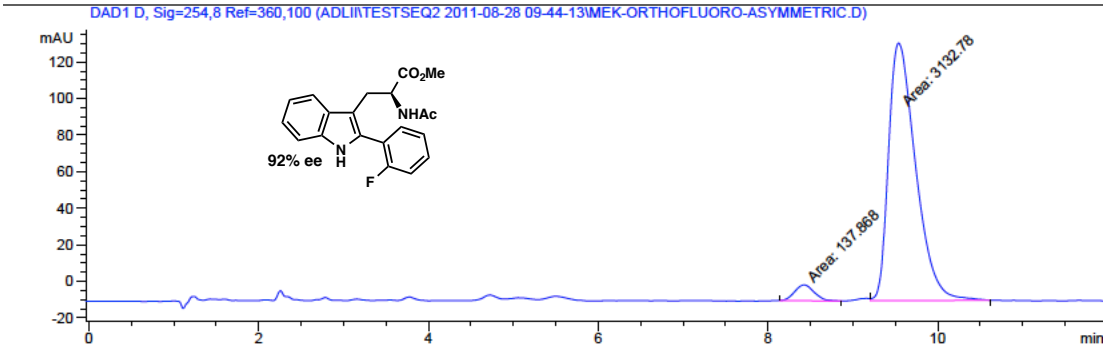
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.921	MM	0.2396	917.37872	63.80575	50.2497
2	7.287	MM	0.2632	908.26233	57.51292	49.7503



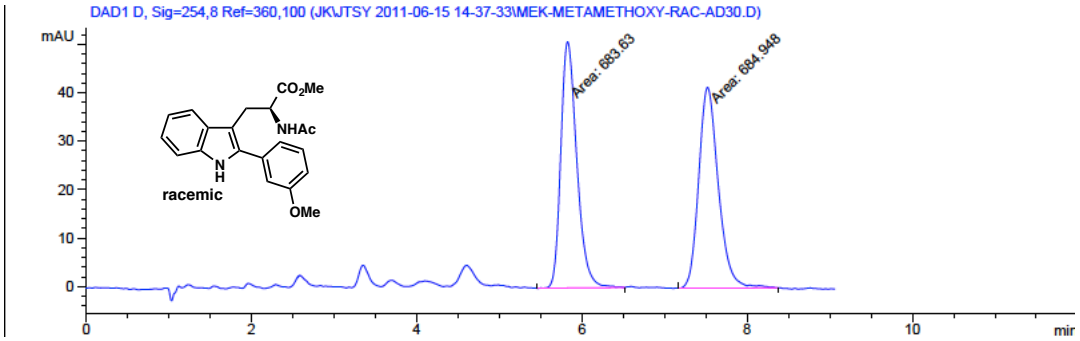
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.919	MM	0.2233	2713.30493	202.51631	95.9167
2	7.288	MM	0.2660	115.50748	7.23739	4.0833



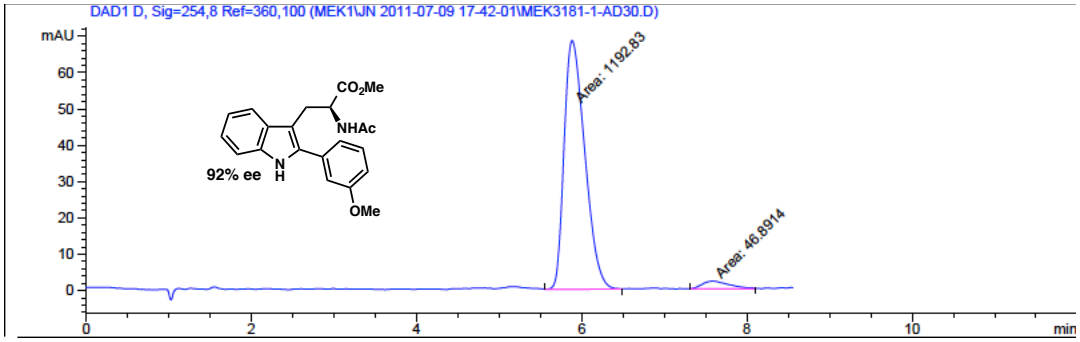
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.337	MM	0.2581	1245.03833	80.40385	50.5471
2	9.527	MM	0.3356	1218.08643	60.50121	49.4529



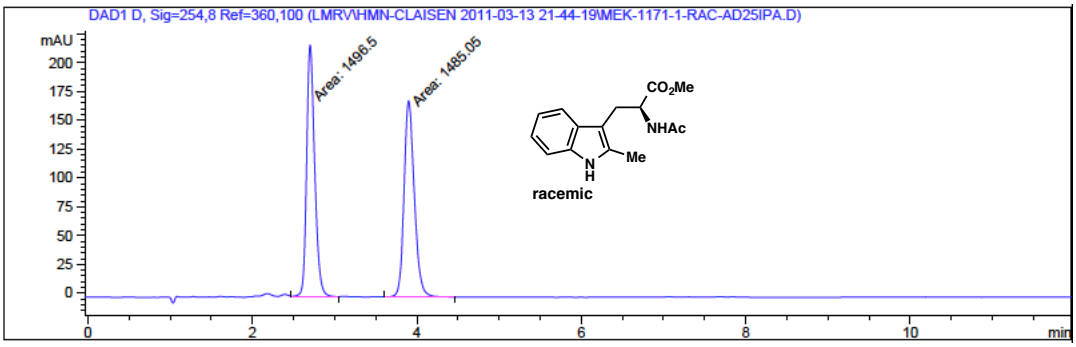
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.424	MM	0.2645	137.86769	8.68627	4.2153
2	9.540	MM	0.3705	3132.78320	140.94464	95.7847



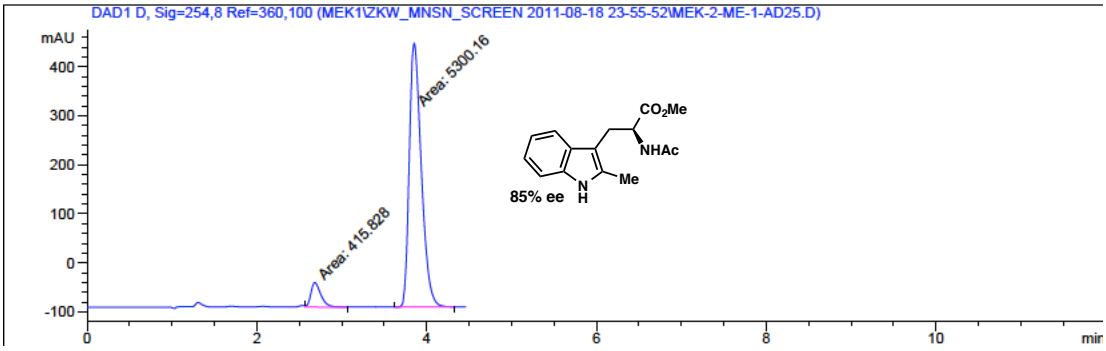
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.829	MM	0.2242	683.62952	50.82516	49.9518
2	7.521	MM	0.2756	684.94781	41.42142	50.0482



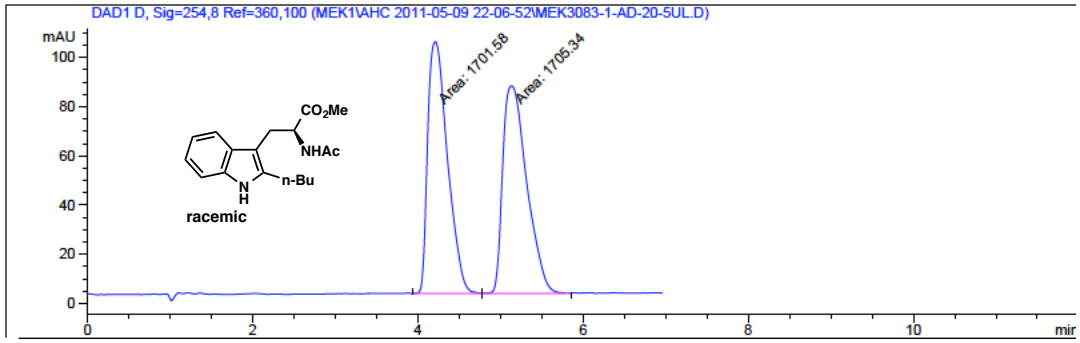
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.885	MM	0.2902	1192.82666	68.51757	96.2176
2	7.580	MM	0.3706	46.89137	2.10879	3.7824



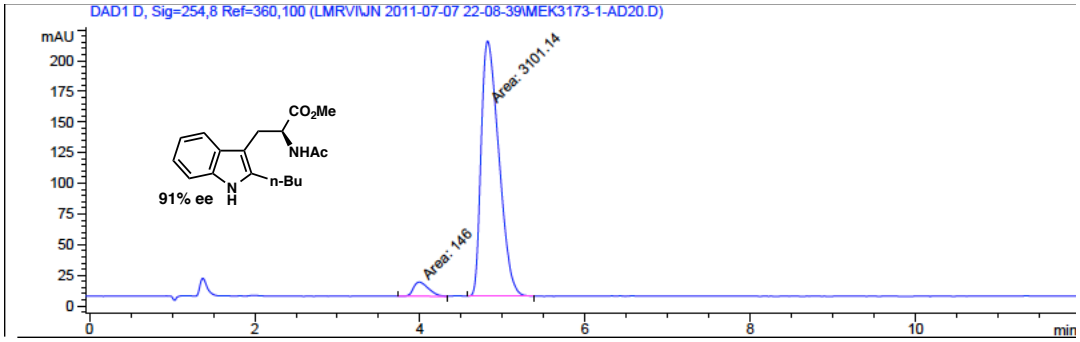
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.704	MM	0.1135	1496.50342	219.75923	50.1920
2	3.902	MM	0.1449	1485.05188	170.80902	49.8080



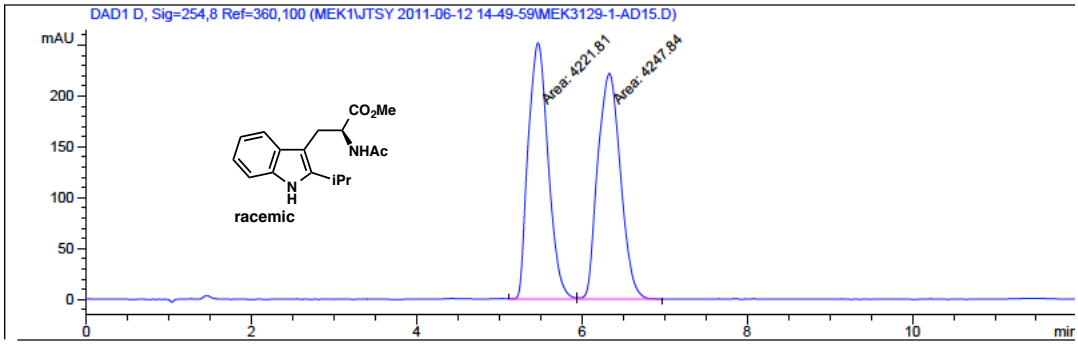
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.683	MM	0.1386	415.82819	49.99455	7.2748
2	3.853	MM	0.1639	5300.16357	538.95465	92.7252



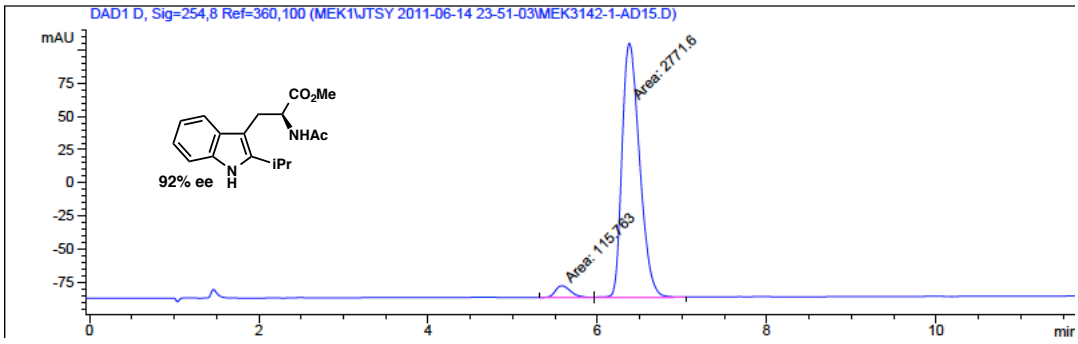
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.212	MM	0.2768	1700.02417	102.35526	50.0010
2	5.137	MM	0.3361	1699.95459	84.29318	49.9990



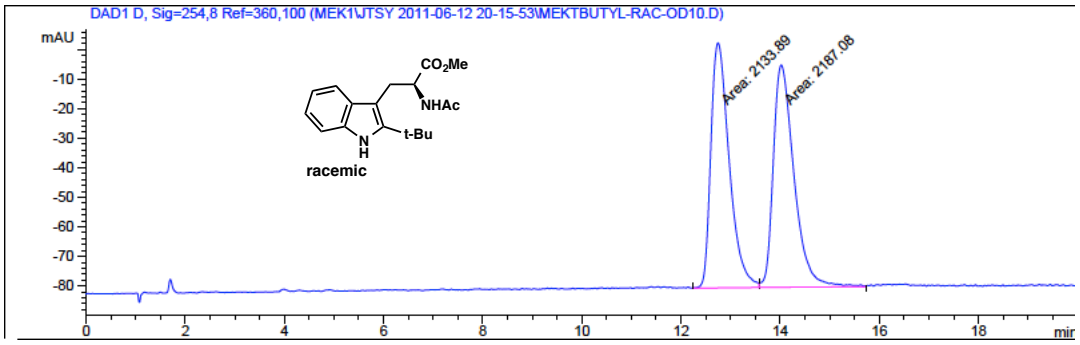
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.989	MM	0.2108	145.99951	11.54476	4.4962
2	4.820	MM	0.2481	3101.14380	208.34941	95.5038



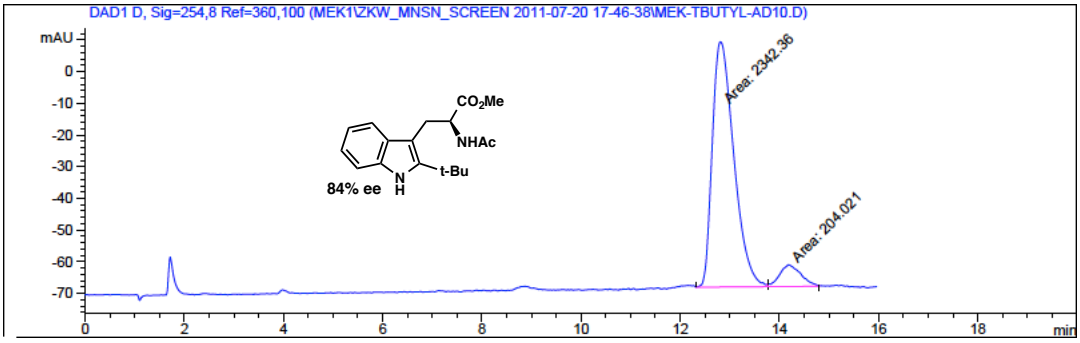
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.470	MF	0.2791	4221.81055	252.11853	49.8463
2	6.333	FM	0.3188	4247.84424	222.08144	50.1537



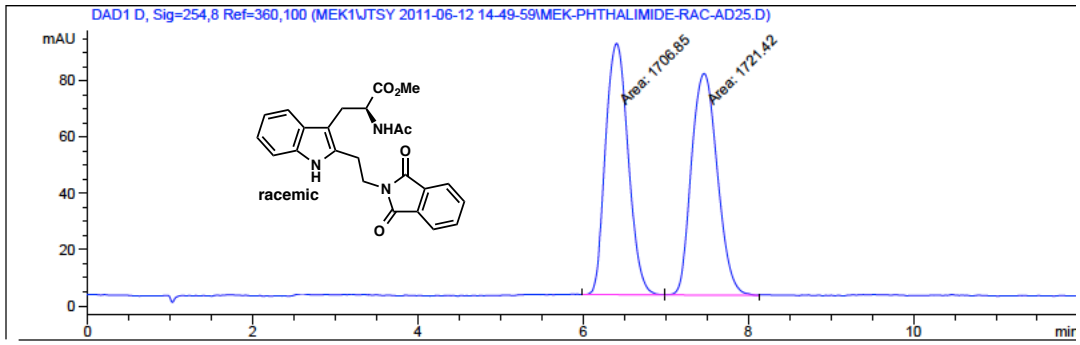
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.579	MF	0.2157	115.76347	8.94554	4.0093
2	6.378	FM	0.2407	2771.60327	191.88481	95.9907



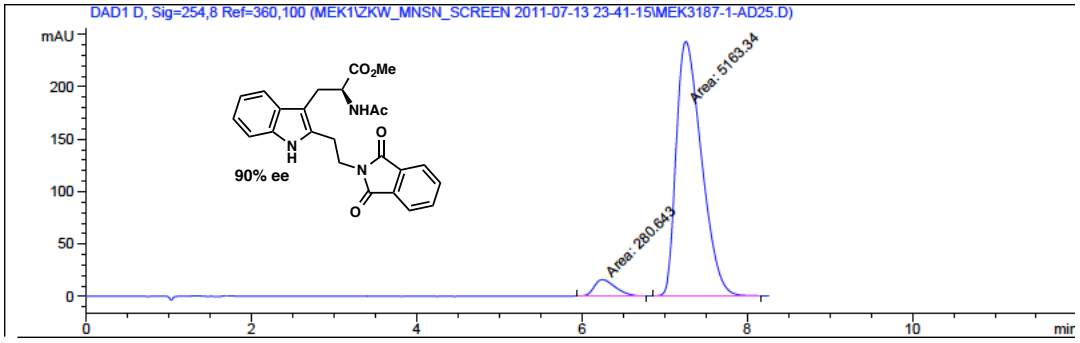
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.747	MF	0.4289	2133.88867	82.91142	49.3845
2	14.022	FM	0.4846	2187.08203	75.22533	50.6155



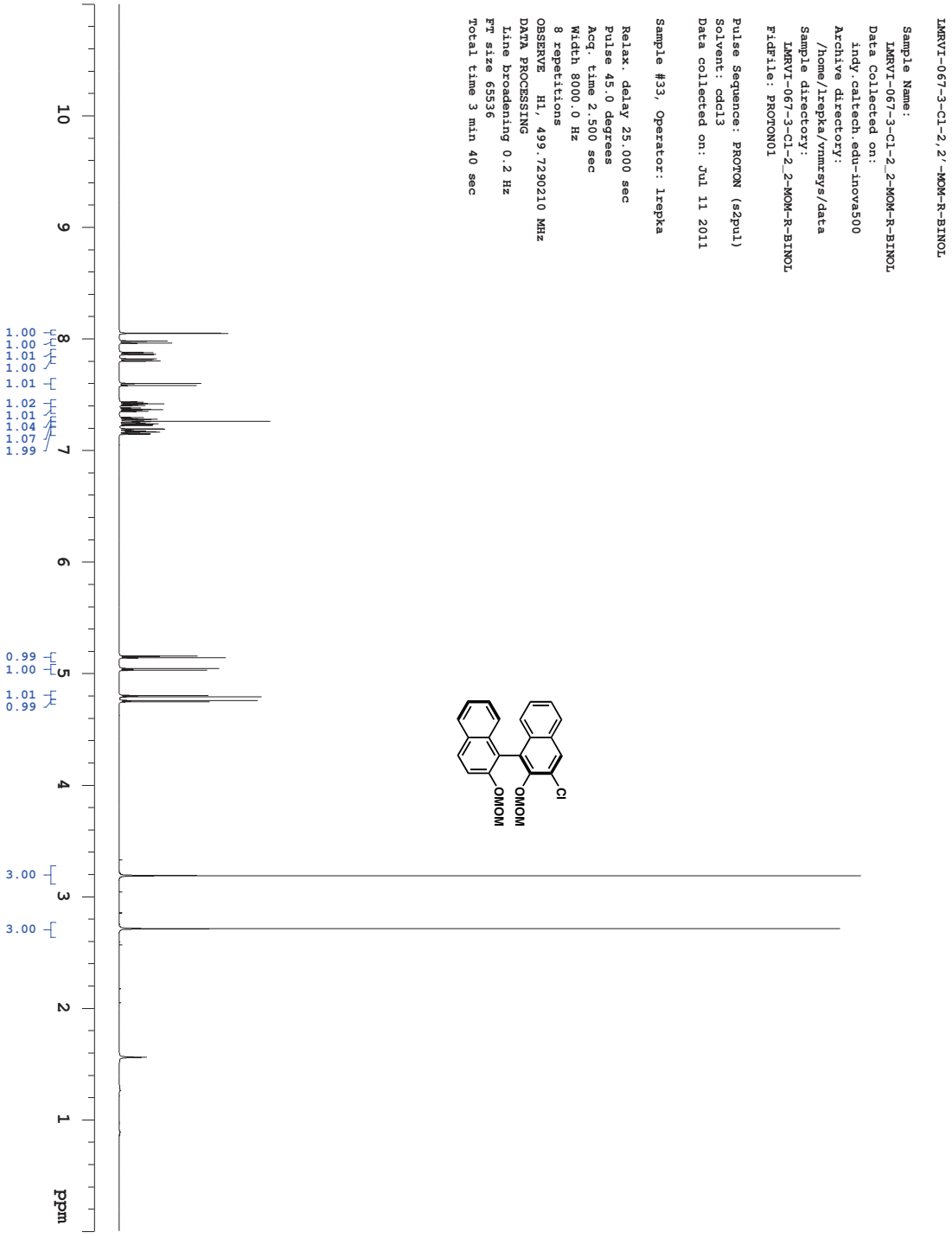
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.811	MF	0.5042	2342.36499	77.42957	91.9878
2	14.185	FM	0.4960	204.02127	6.85510	8.0122



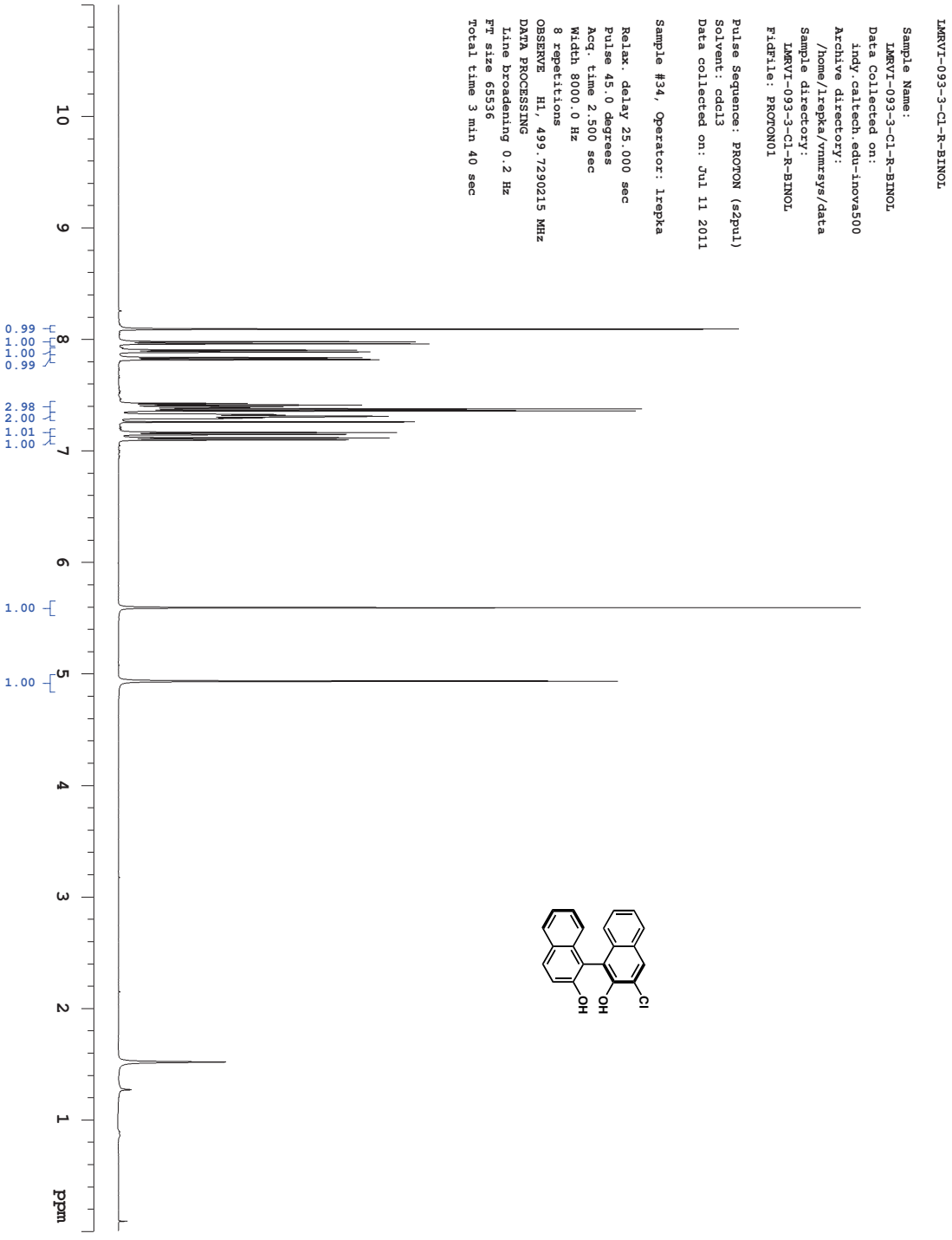
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.408	MF	0.3187	1706.84790	89.26434	49.7874
2	7.465	FM	0.3642	1721.42261	78.76897	50.2126

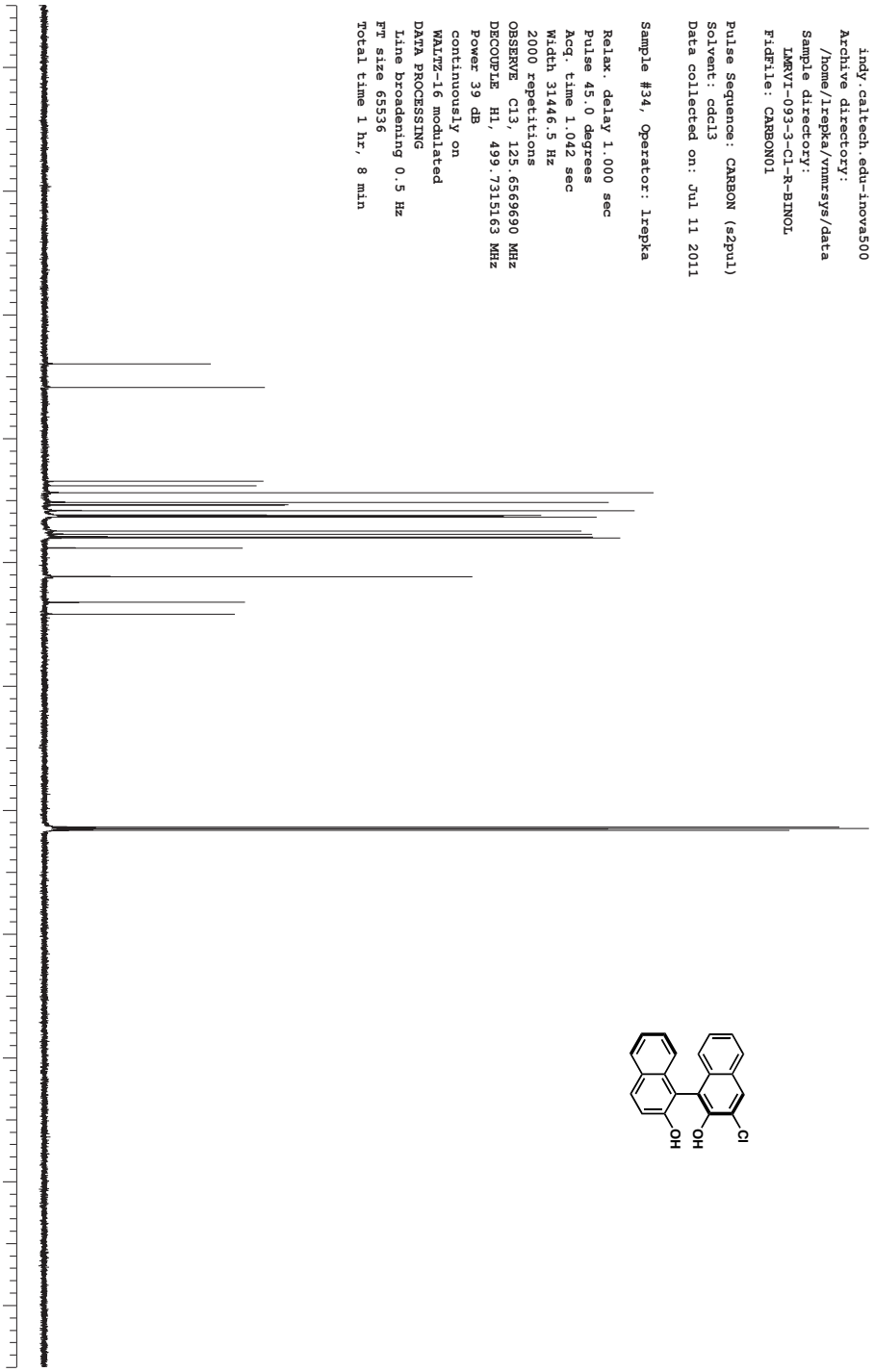


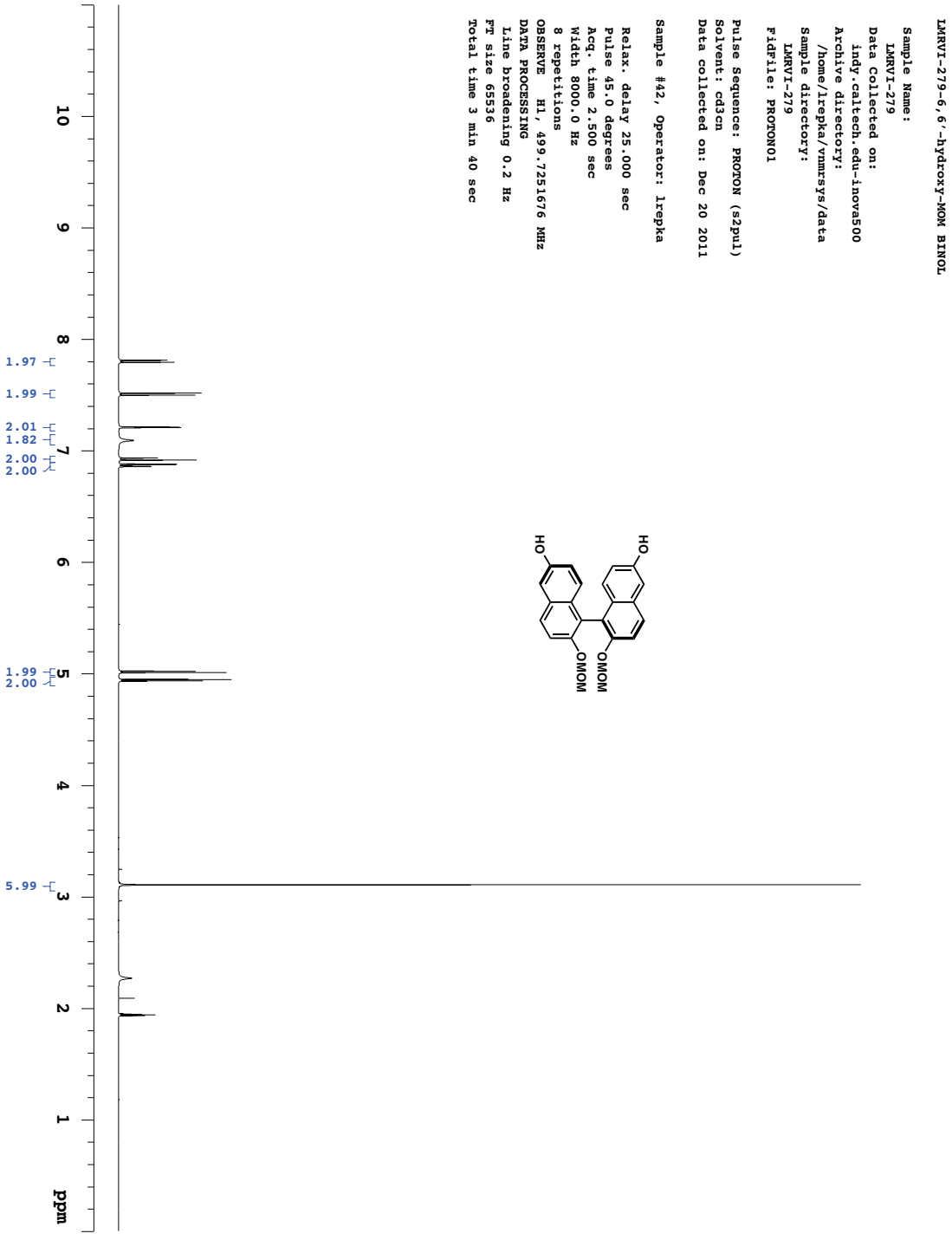
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.251	MM	0.2975	280.64285	15.72261	5.1551
2	7.260	MM	0.3544	5163.33643	242.81979	94.8449

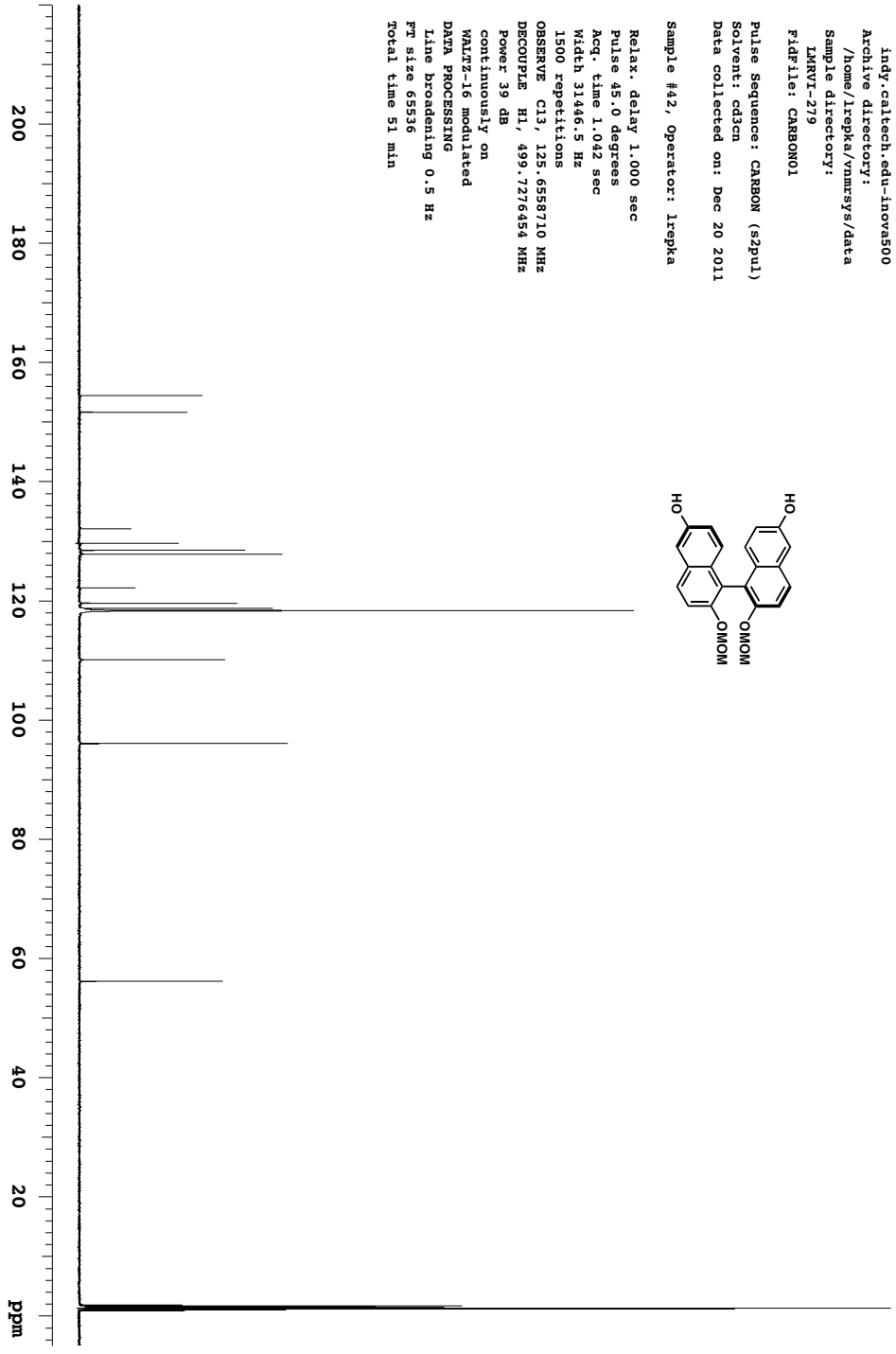

LMRVI-067-3-Cl-2,2'-MOM-R-BINOL
Sample Name:
LMRVI-067-3-Cl-2_2-MOM-R-BINOL
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-067-3-Cl-2_2-MOM-R-BINOL
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 11 2011
Sample #33, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7290210 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
OMOM
OMOM
Cl
1.00
1.00
1.01
1.00
1.01
1.02
1.01
1.04
1.07
1.99
0.99
1.00
1.01
0.99
3.00
3.00
10
9
8
7
6
5
4
3
2
1
ppm

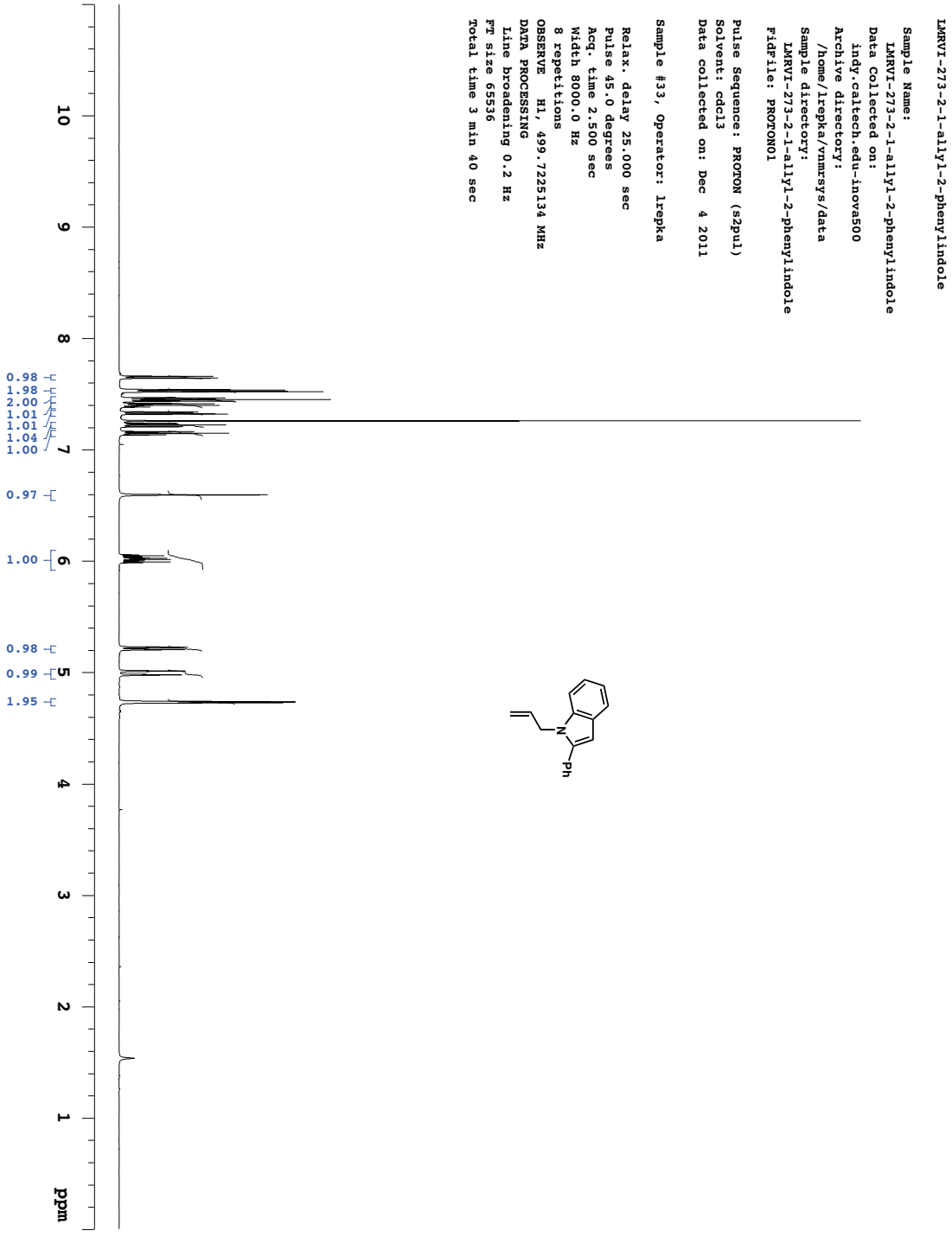
LMRVI-067-3-Cl-2,2'-MOM-R-BINOL
Sample Name:
LMRVI-067-3-Cl-2_2-MOM-R-BINOL
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-067-3-Cl-2_2-MOM-R-BINOL
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 11 2011
Sample #33, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1590 repetitions
OBSERVE C13, 125.6569667 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
Cl
OMOM
OMOM
200
180
160
140
120
100
80
60
40
20
ppm

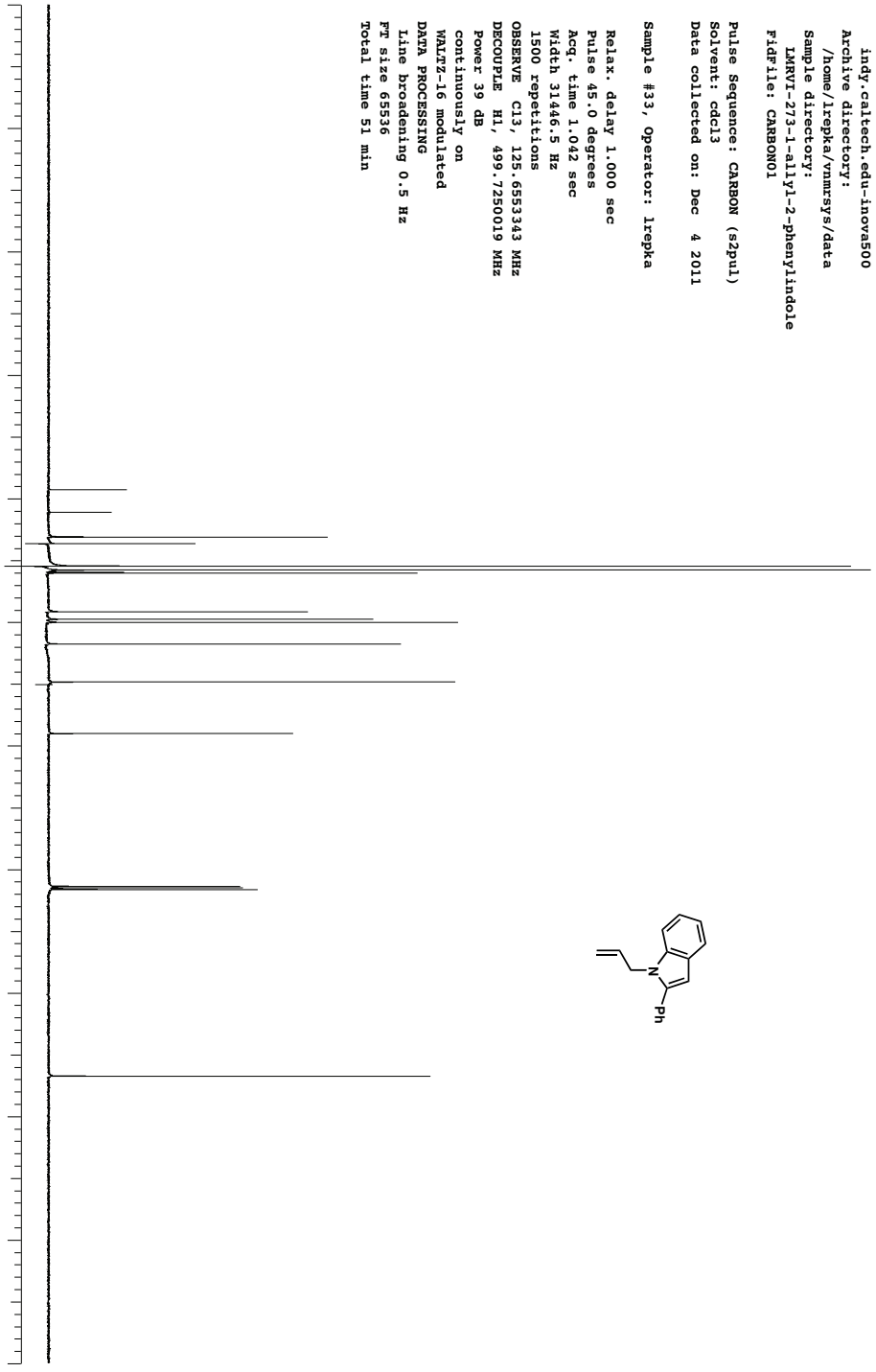

LMRVI-093-3-Cl-R-BINOL
Sample Name:
LMRVI-093-3-Cl-R-BINOL
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-093-3-Cl-R-BINOL
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 11 2011
Sample #34, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7290215 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
0.99
1.00
1.00
0.99
2.98
2.00
1.01
1.00
1.00
1.00
10
9
8
7
6
5
4
3
2
1
ppm
OH
OH
Cl

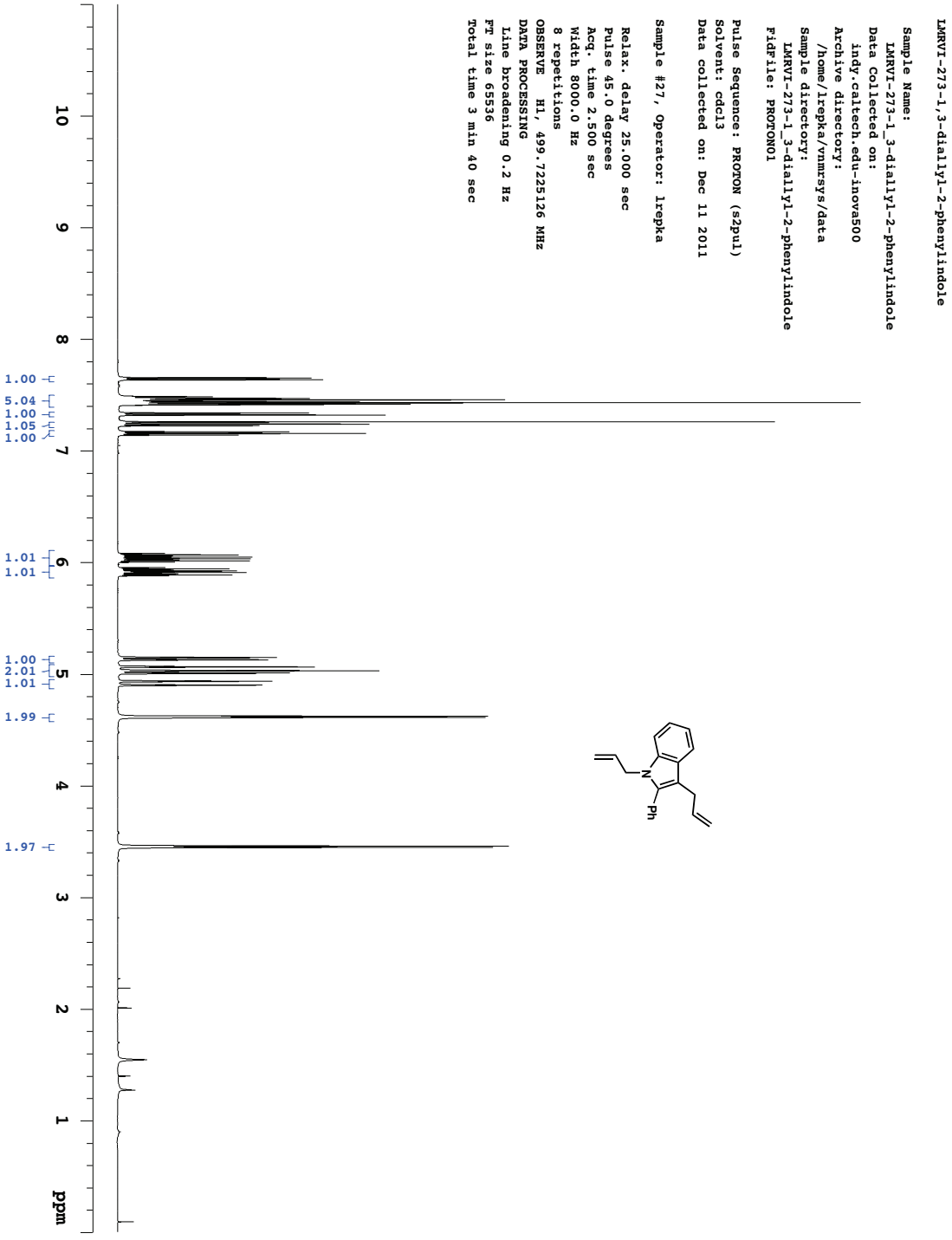

LMRVI-093-3-Cl-R-BINOL
Sample Name:
LMRVI-093-3-Cl-R-BINOL
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-093-3-Cl-R-BINOL
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 11 2011
Sample #34, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6569690 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
OH
OH
Cl
200
180
160
140
120
100
80
60
40
20
ppm

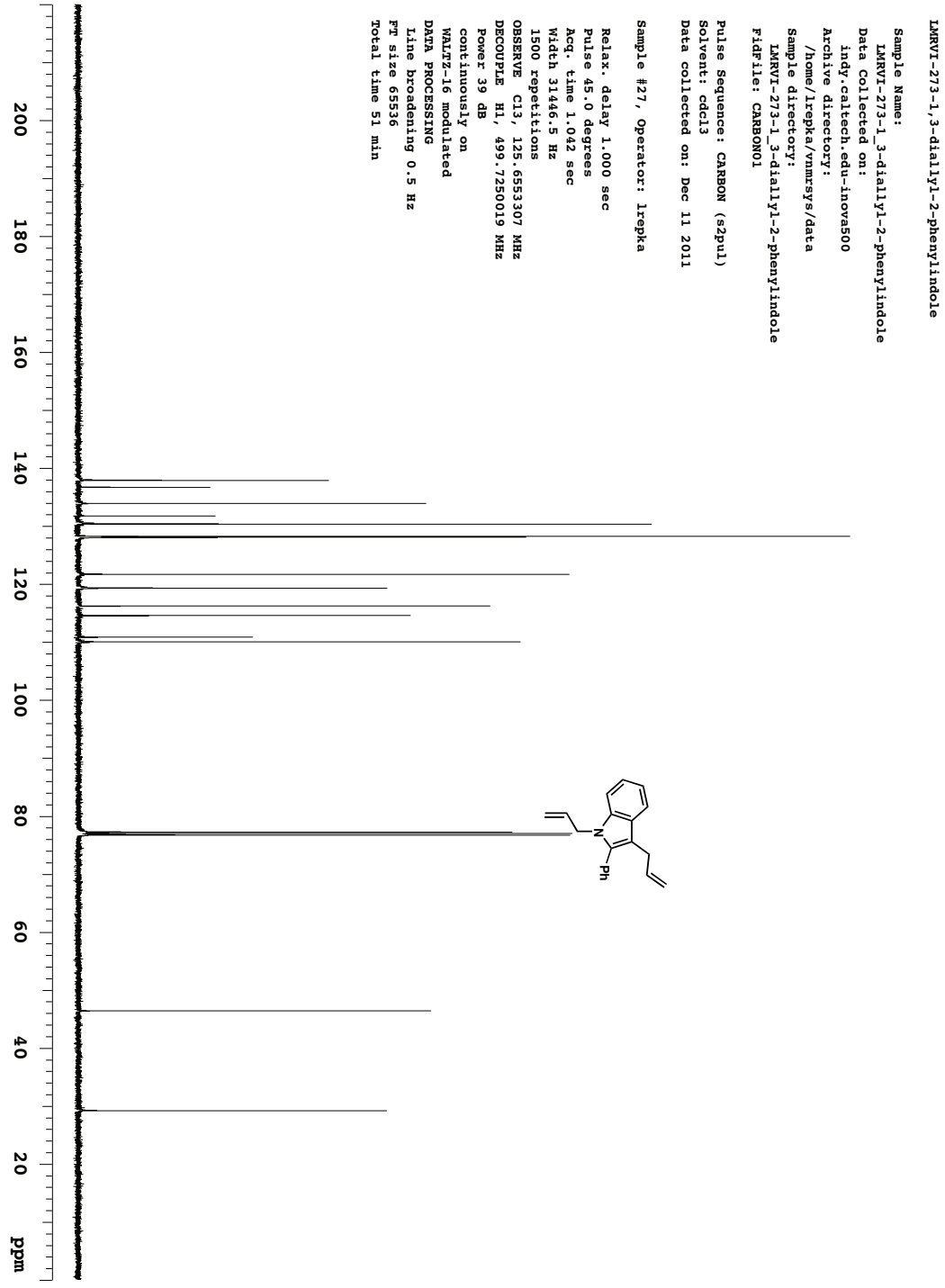

LMRVI-279-6,6'-hydroxy-MOM BINOL
Sample Name:
LMRVI-279
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-279
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Dec 20 2011
Sample #42, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7251676 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
HO
OMOM
OMOM
HO
1.97
1.99
2.01
1.82
2.00
2.00
1.99
2.00
5.99
10
9
8
7
6
5
4
3
2
1
ppm

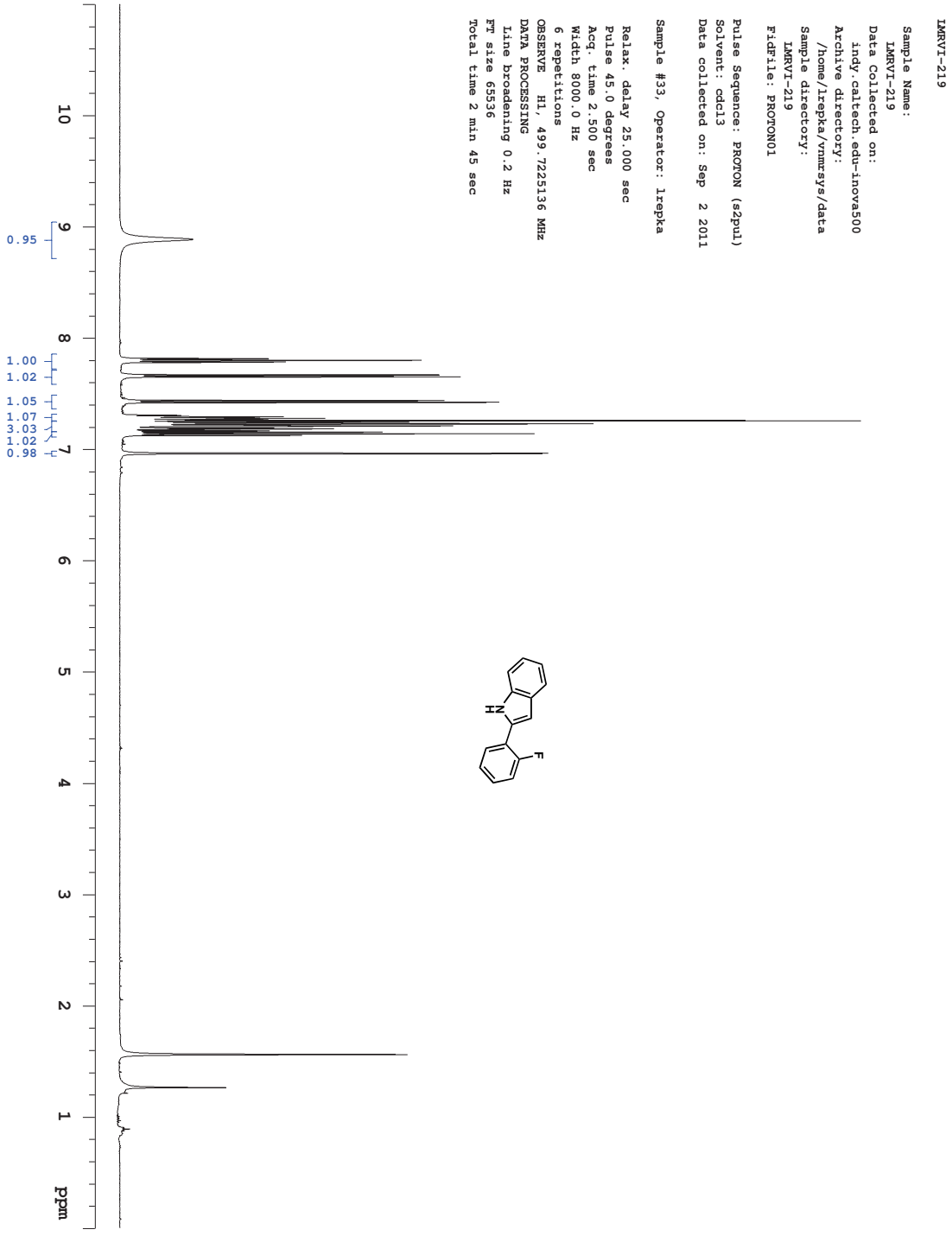

LMRVI-279-6,6'-hydroxy-MOM BINOL
Sample Name:
LMRVI-279
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-279
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Dec 20 2011
Sample #42, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6558710 MHz
DECOUPLE H1, 499.7276454 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
HO
HO
OMOM
OMOM
200
180
160
140
120
100
80
60
40
20
ppm

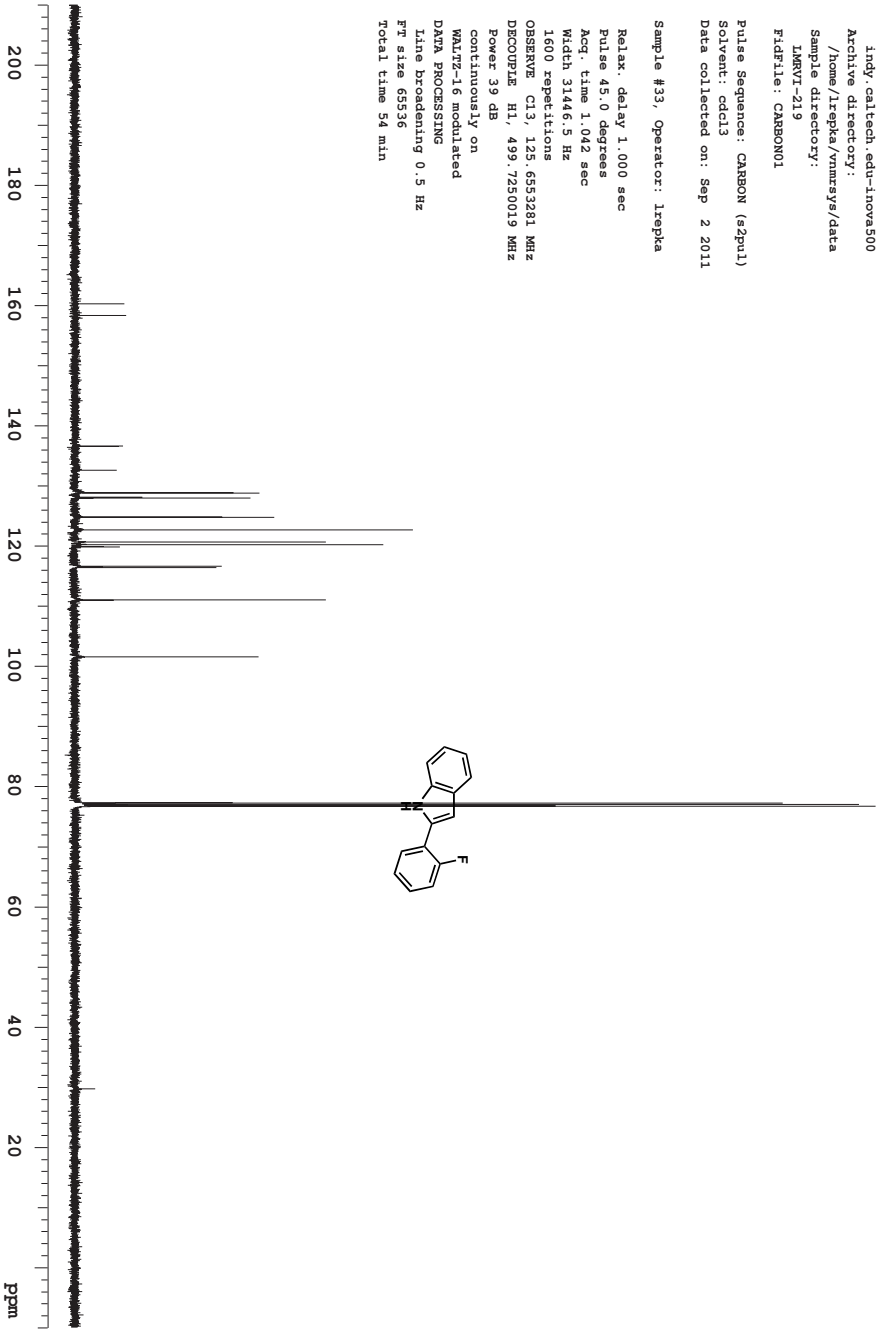

LMRVI-273-2-1-allyl-2-phenylindole
Sample Name:
LMRVI-273-2-1-allyl-2-phenylindole
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-273-2-1-allyl-2-phenylindole
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 4 2011
Sample #33, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225134 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
0.98
1.98
2.00
1.01
1.01
1.04
1.00
0.97
1.00
0.98
0.99
1.95
N
Ph
10
9
8
7
6
5
4
3
2
1
ppm

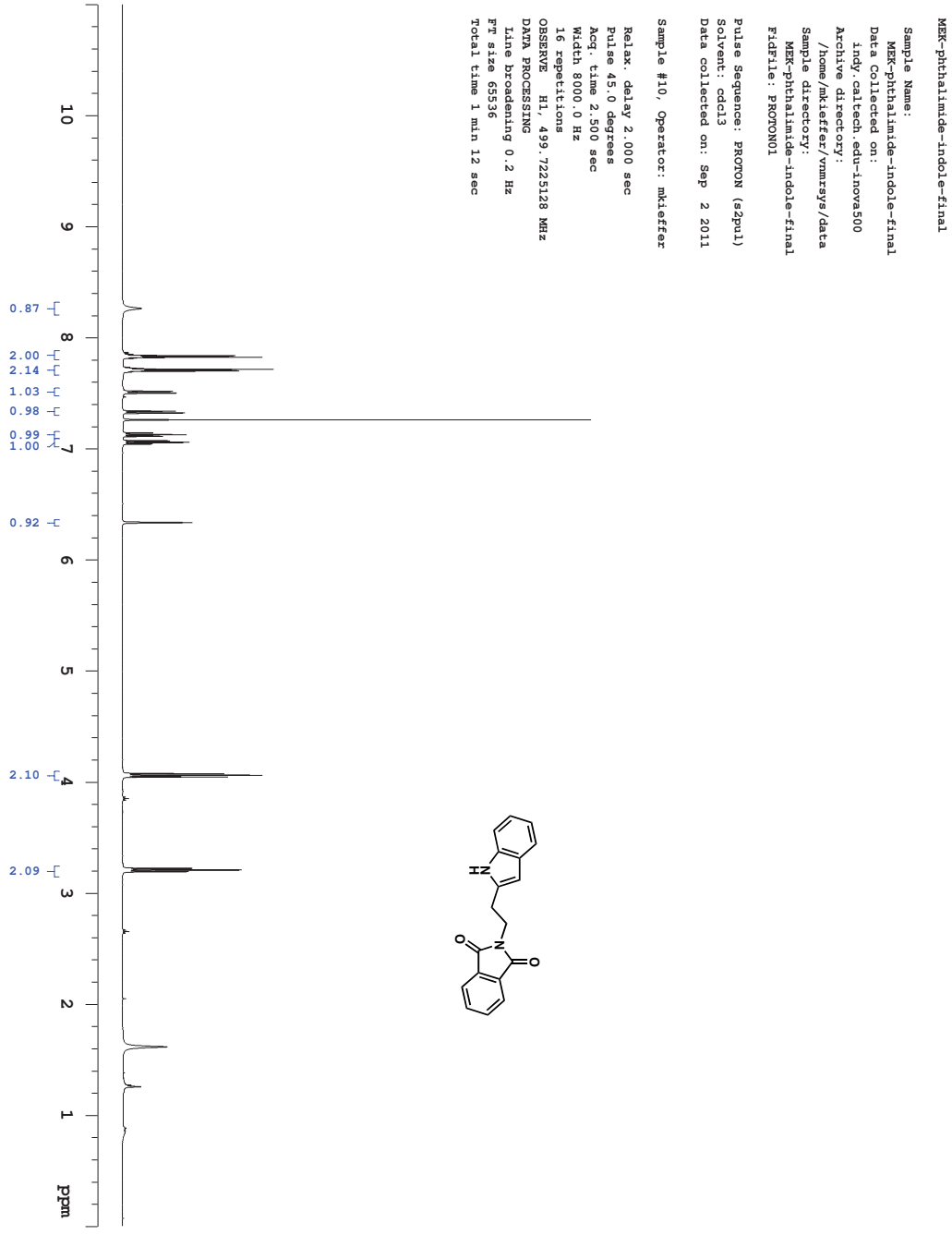

LMRVI-273-1-allyl-2-phenylindole
Sample Name:
LMRVI-273-1-allyl-2-phenylindole
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-273-1-allyl-2-phenylindole
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 4 2011
Sample #33, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.655343 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
N
Ph
200
180
160
140
120
100
80
60
40
20
ppm

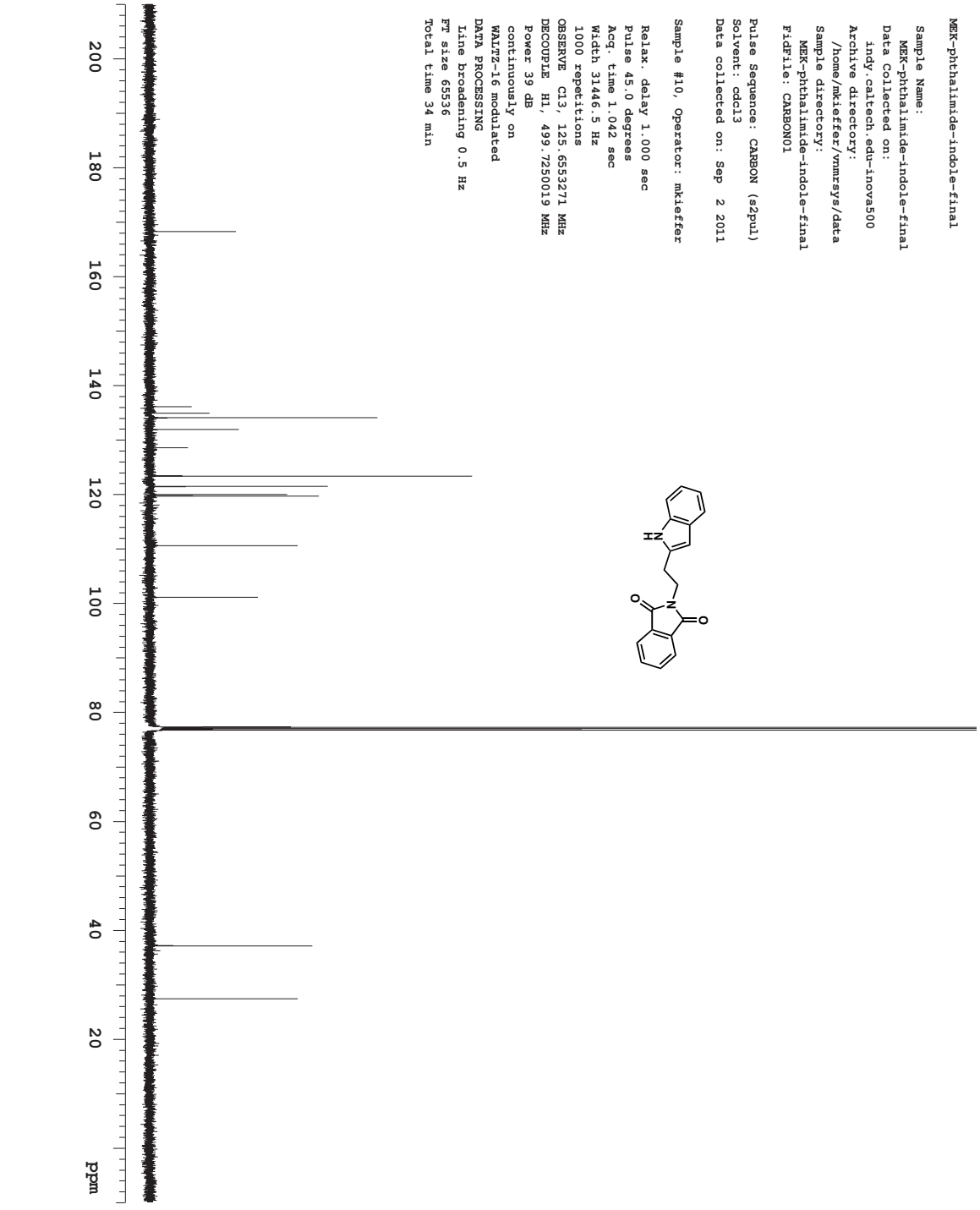

LMRVI-273-1,3-diallyl-2-phenylindole
Sample Name:
LMRVI-273-1_3-diallyl-2-phenylindole
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-273-1_3-diallyl-2-phenylindole
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 11 2011
Sample #27, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225126 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
1.00
5.04
1.00
1.05
1.00
1.01
1.01
1.00
2.01
1.01
1.99
1.97
N
Ph
10
9
8
7
6
5
4
3
2
1
ppm

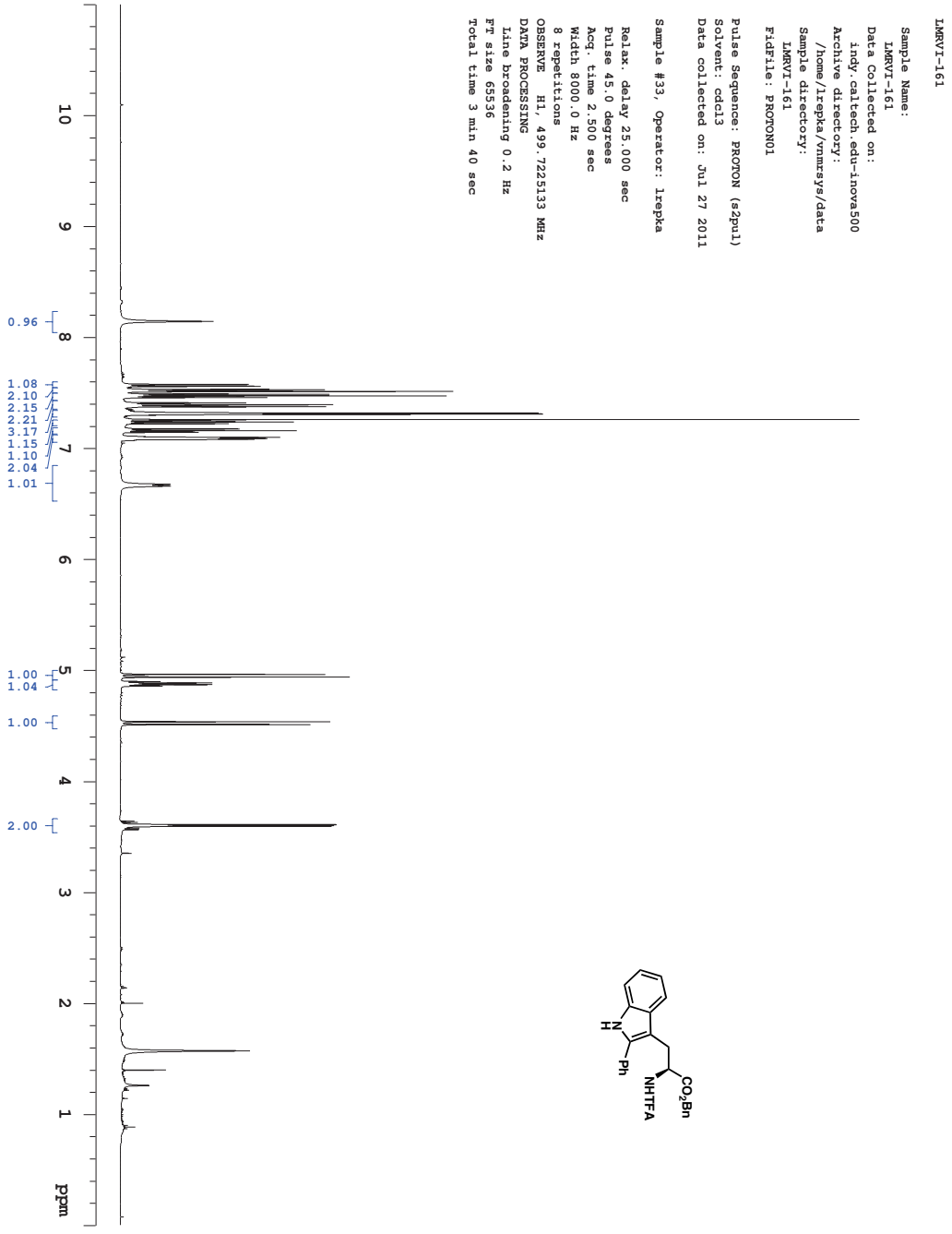

LMRVI-273-1,3-diallyl-2-phenylindole
Sample Name:
LMRVI-273-1_3-diallyl-2-phenylindole
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-273-1_3-diallyl-2-phenylindole
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 11 2011
Sample #27, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.655307 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
N
Ph
200
180
160
140
120
100
80
60
40
20
ppm

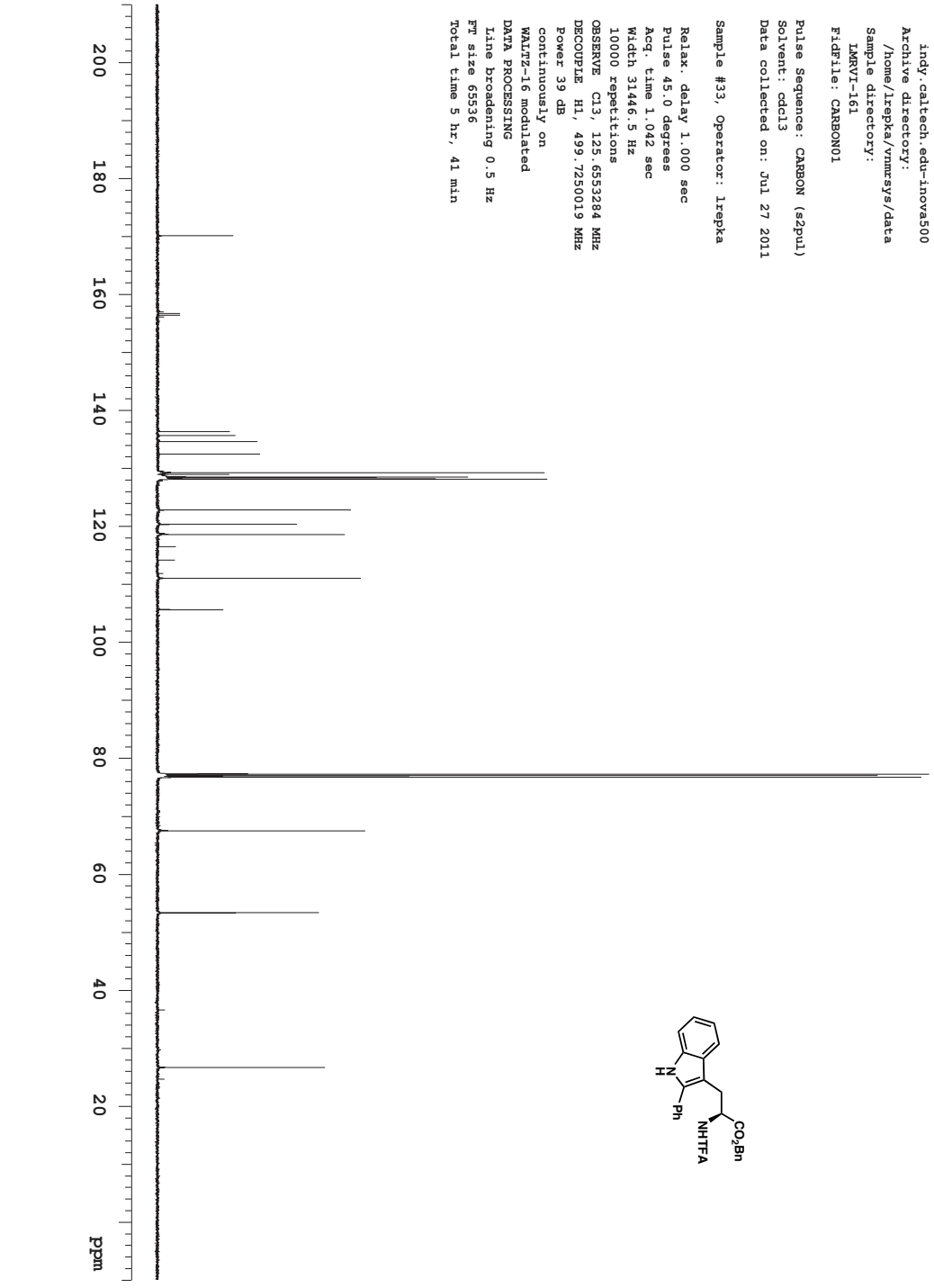

IMRVI-219
Sample Name:
IMRVI-219
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
IMRVI-219
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2011
Sample #33, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
6 repetitions
OBSERVE H1, 499.7225136 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 45 sec
0.95
1.00
1.02
1.05
1.07
3.03
1.02
0.98
10
9
8
7
6
5
4
3
2
1
ppm
H
N
F

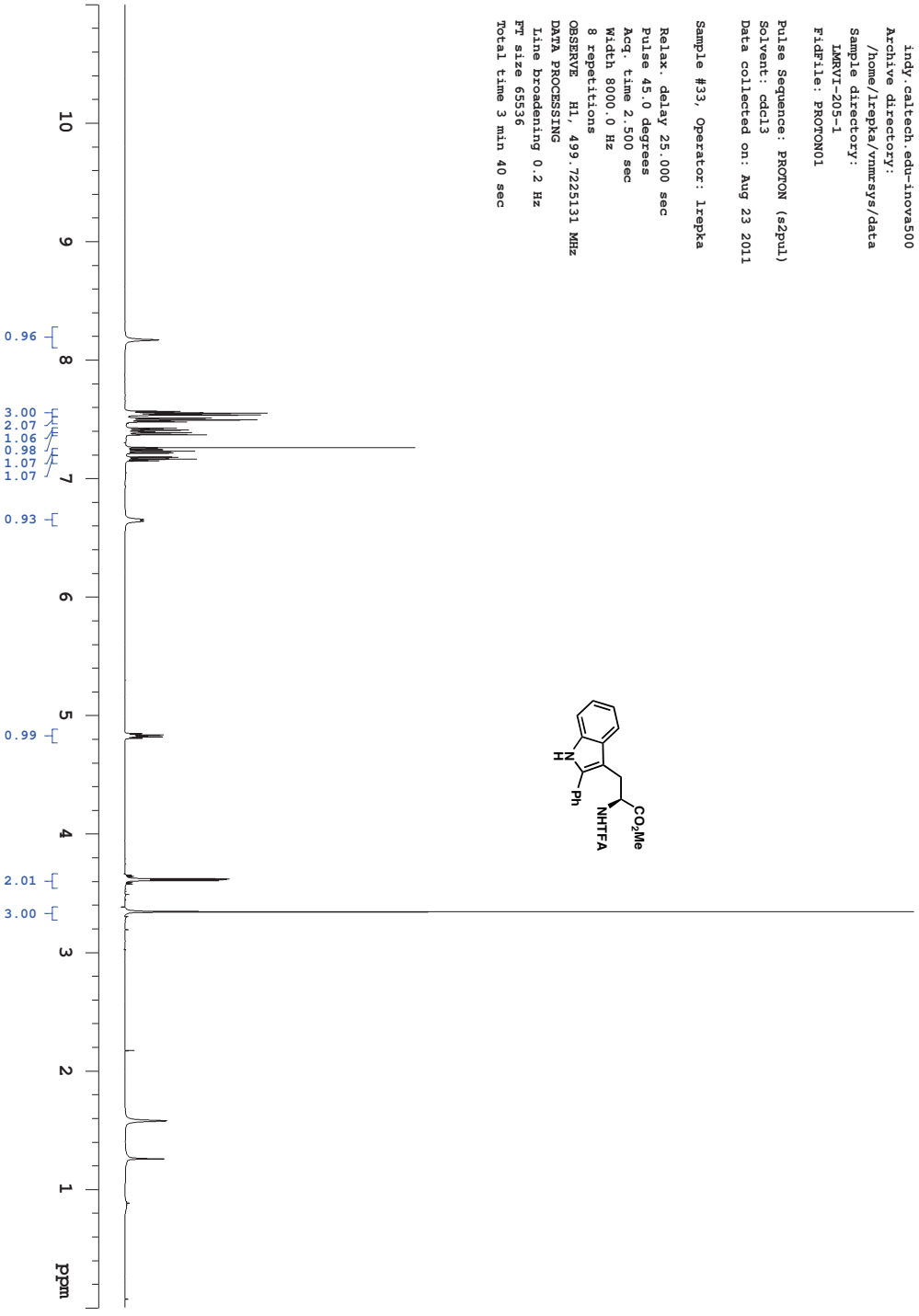

LMRVI-219
Sample Name:
LMRVI-219
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-219
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2011
Sample #33, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6553281 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
F
200
180
160
140
120
100
80
60
40
20
ppm

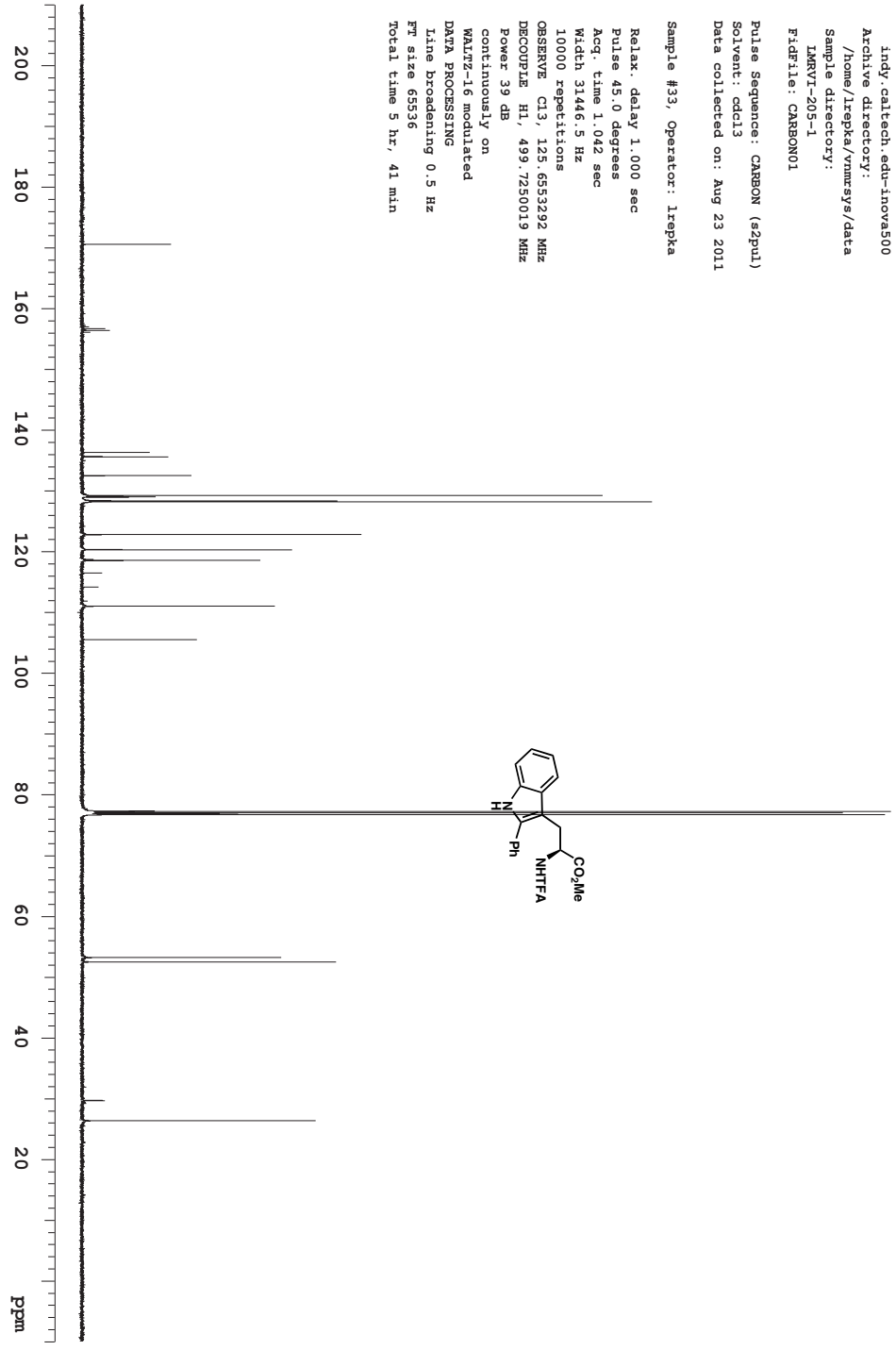

MEK-phthalimide-indole-final
Sample Name:
MEK-phthalimide-indole-final
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-phthalimide-indole-final
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2011
Sample #10, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min 12 sec
0.87
2.00
2.14
1.03
0.98
0.99
1.00
0.92
2.10
2.09
10
9
8
7
6
5
4
3
2
1
ppm
H
N
O
N
O

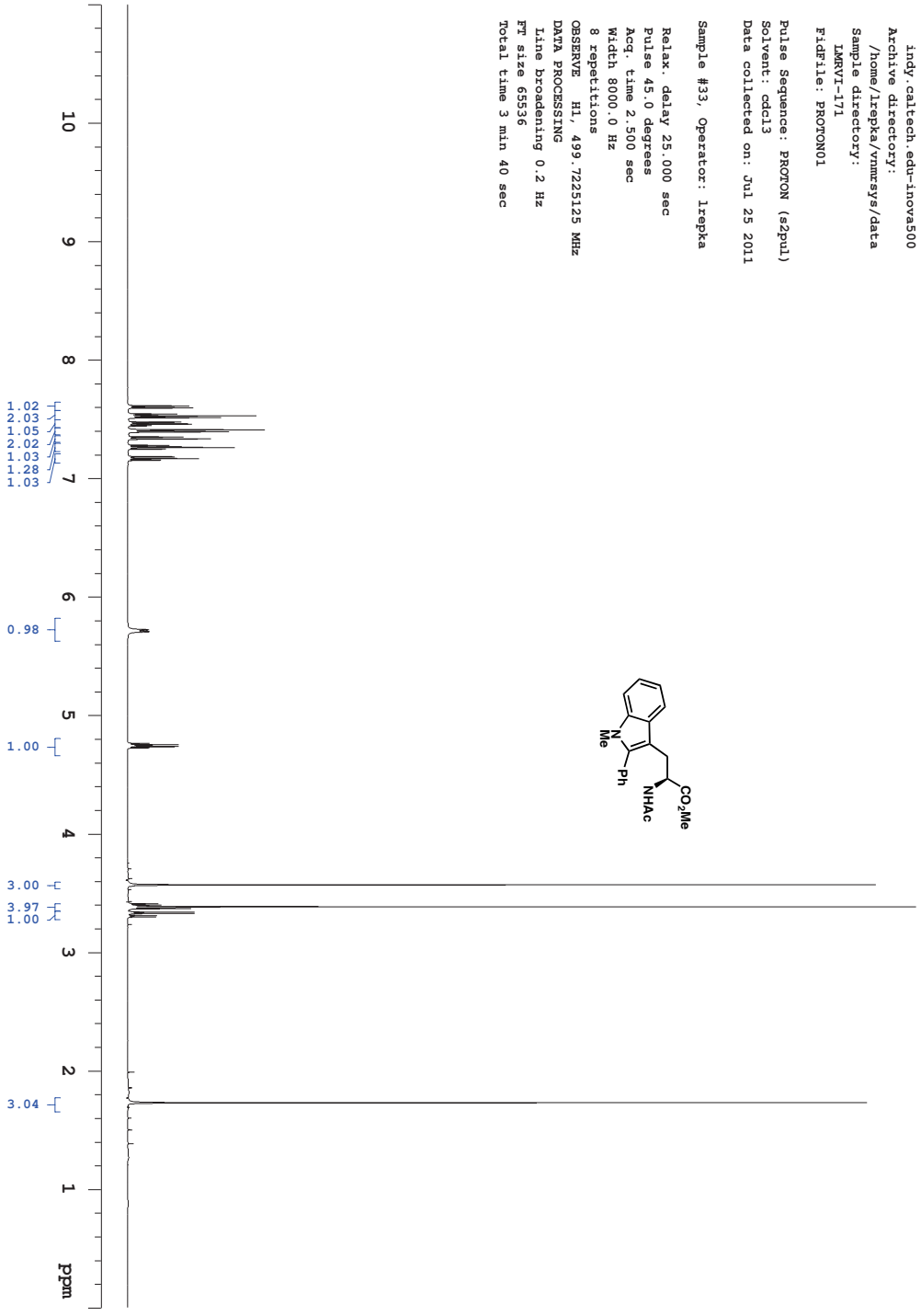

MEK-phthalimide-indole-final
Sample Name:
MEK-phthalimide-indole-final
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-phthalimide-indole-final
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2011
Sample #10, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
H
N
O
N
O
200
180
160
140
120
100
80
60
40
20
ppm

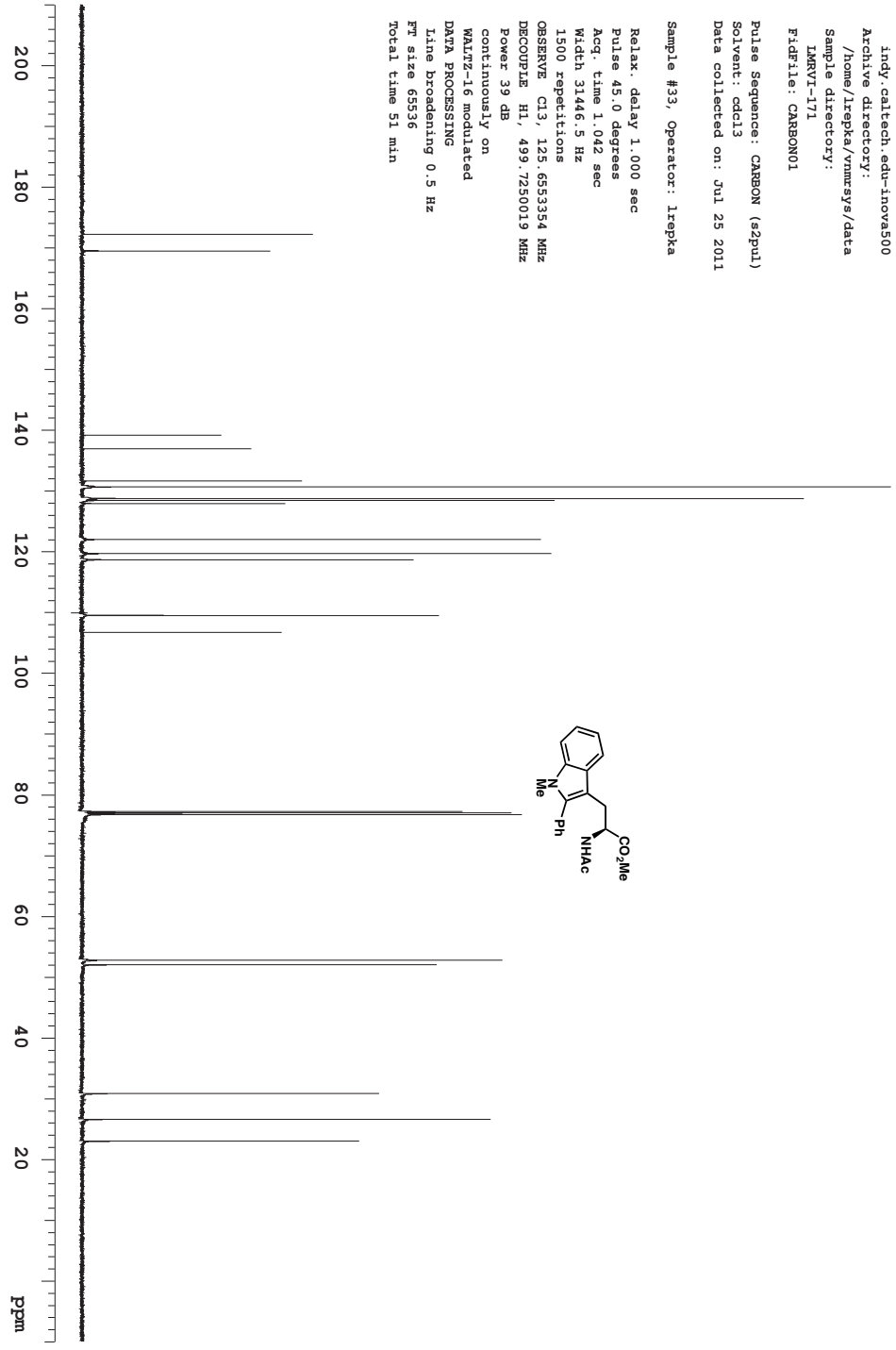

LMRVI-161
Sample Name:
LMRVI-161
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-161
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2011
Sample #33, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225133 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
0.96
1.08
2.10
2.15
2.21
3.17
1.15
1.10
2.04
1.01
1.00
1.04
1.00
2.00
10
9
8
7
6
5
4
3
2
1
ppm
Ph
NHTFA
CO2Bn

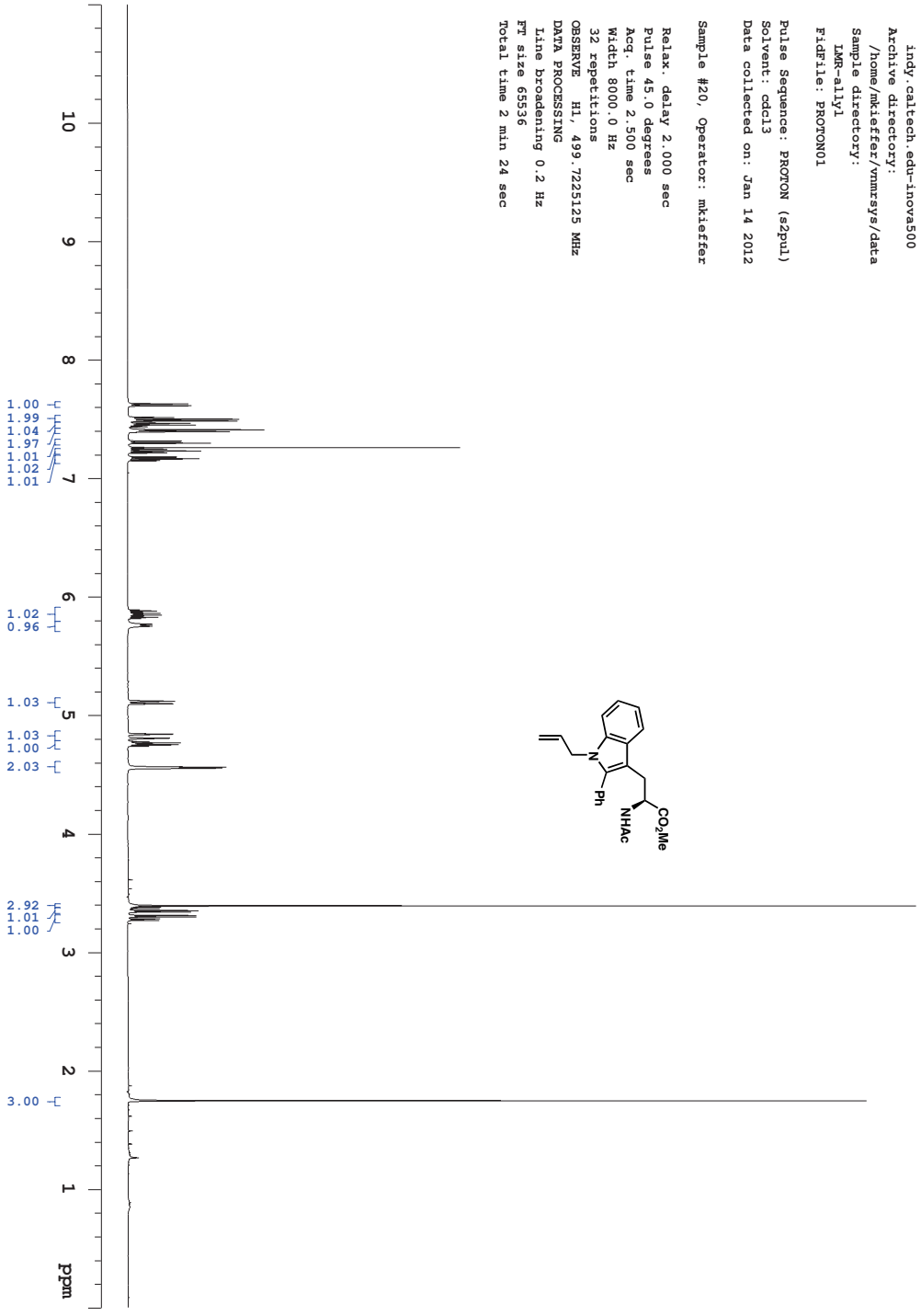

LMRVI-161
Sample Name:
LMRVI-161
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-161
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 27 2011
Sample #33, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
10000 repetitions
OBSERVE C13, 125.6553284 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 5 hr, 41 min
200
180
160
140
120
100
80
60
40
20
ppm
N
H
Ph
NHTFA
CO2Bn

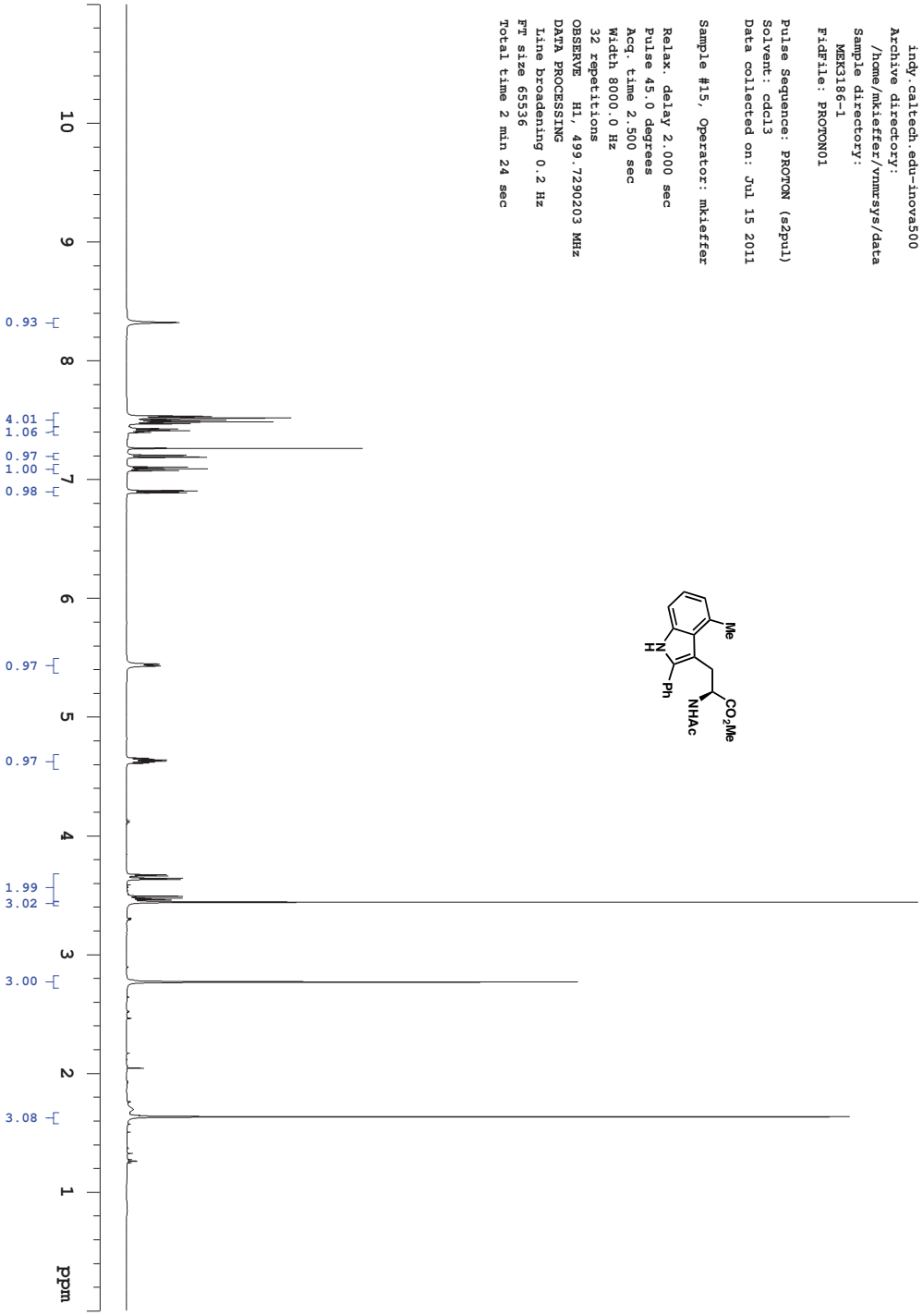

IMRVI-205-1
Sample Name:
IMRVI-205-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
IMRVI-205-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 23 2011
Sample #33, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225131 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
0.96
3.00
2.07
1.06
0.98
1.07
1.07
0.93
0.99
2.01
3.00
10
9
8
7
6
5
4
3
2
1
ppm
NH
Ph
NHTFA
CO2Me

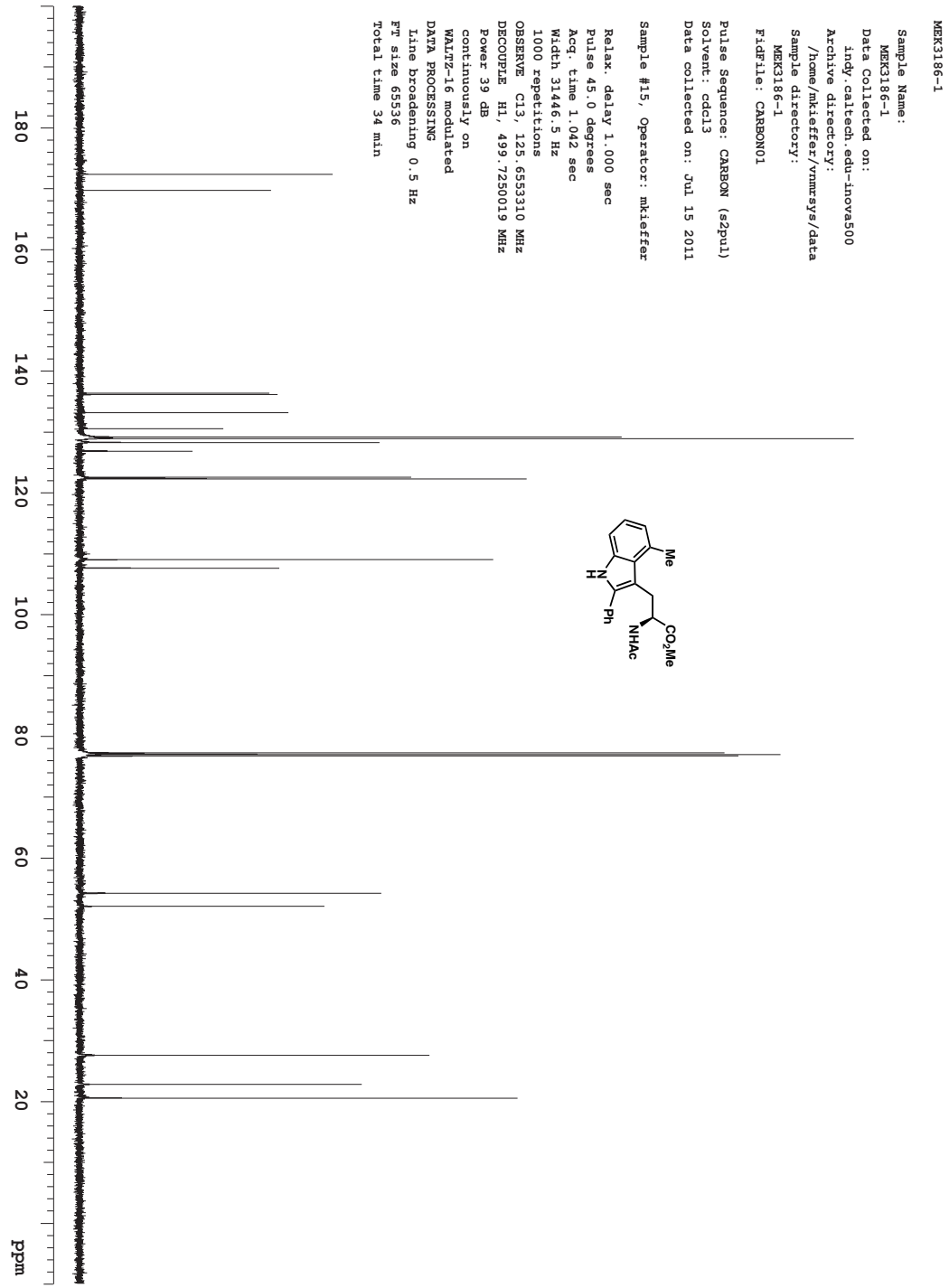

IMRVI-205-1
Sample Name:
IMRVI-205-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
IMRVI-205-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 23 2011
Sample #33, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
10000 repetitions
OBSERVE C13, 125.6553292 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 5 hr, 41 min
HN
Ph
NHTFA
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

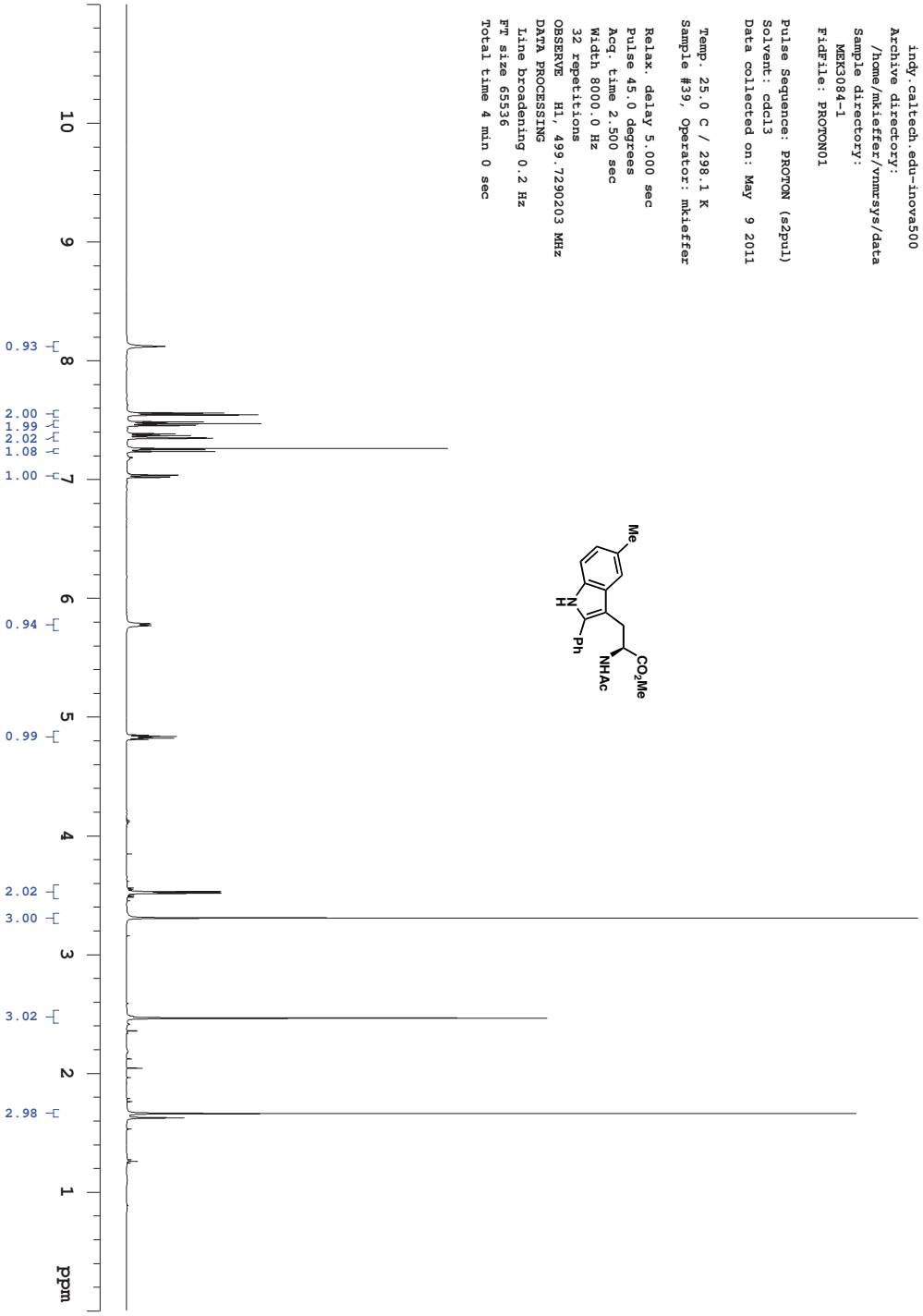

IMRVI-171
Sample Name:
IMRVI-171
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
IMRVI-171
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 25 2011
Sample #33, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225125 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
1.02
2.03
1.05
2.02
1.03
1.28
1.03
0.98
1.00
3.00
3.97
1.00
3.04
10
9
8
7
6
5
4
3
2
1
ppm
N
Me
Ph
NHAc
CO2Me

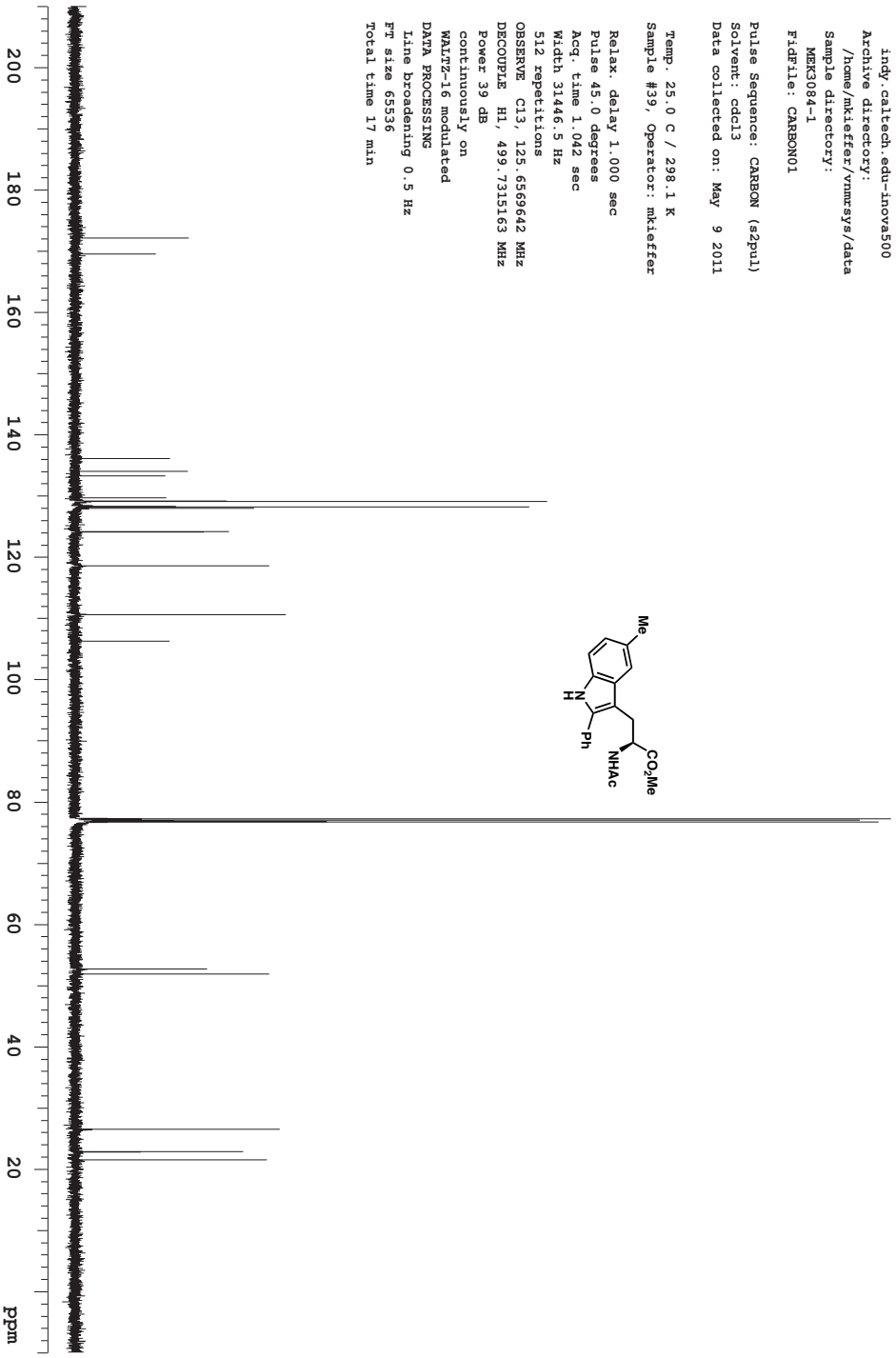

LMRVI-171
Sample Name:
LMRVI-171
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-171
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 25 2011
Sample #33, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6553354 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
N
Me
Ph
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

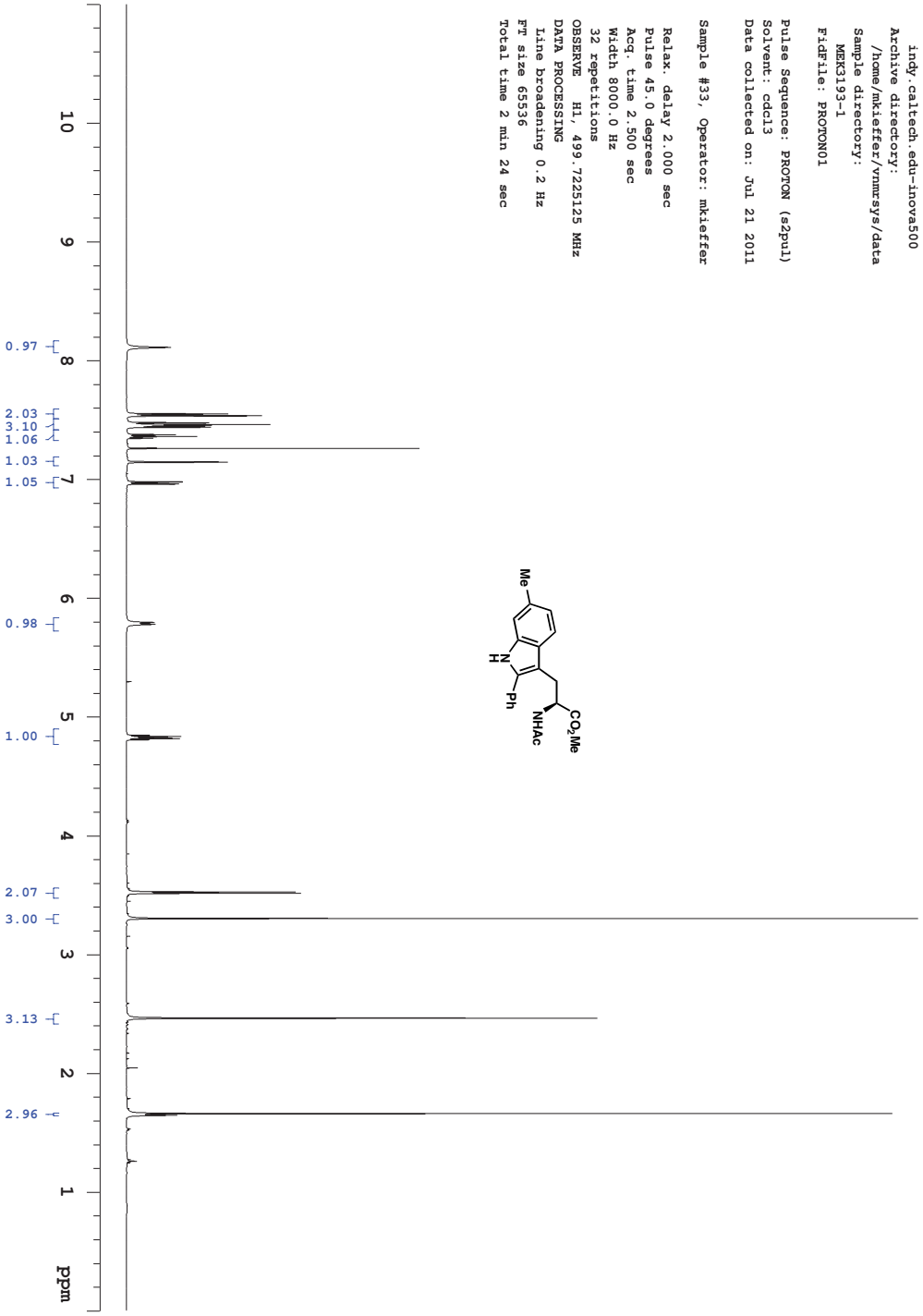

Sample Name:
LMR-allyl
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
LMR-allyl
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 14 2012
Sample #20, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7225125 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
1.00
1.99
1.04
1.97
1.01
1.02
1.01
1.02
0.96
1.03
1.03
1.00
2.03
2.92
1.01
1.00
3.00
10
9
8
7
6
5
4
3
2
1
ppm
N
Ph
NHAc
CO2Me

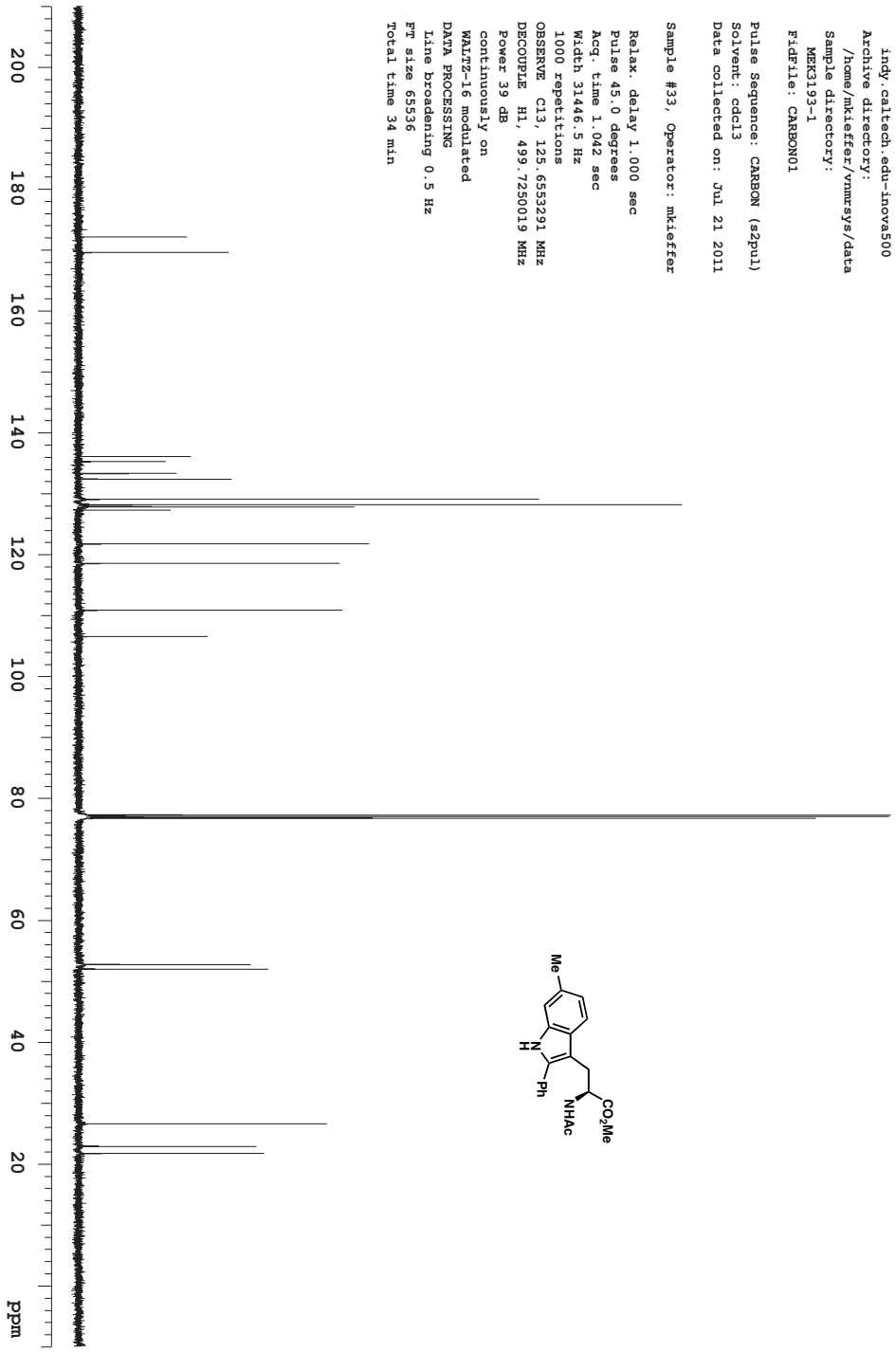

MEK3186-1
Sample Name:
MEK3186-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3186-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 15 2011
Sample #15, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
Me
N
H
Ph
NHAc
CO2Me
0.93
4.01
1.06
0.97
1.00
0.98
0.97
0.97
1.99
3.02
3.00
3.08
10
9
8
7
6
5
4
3
2
1
ppm

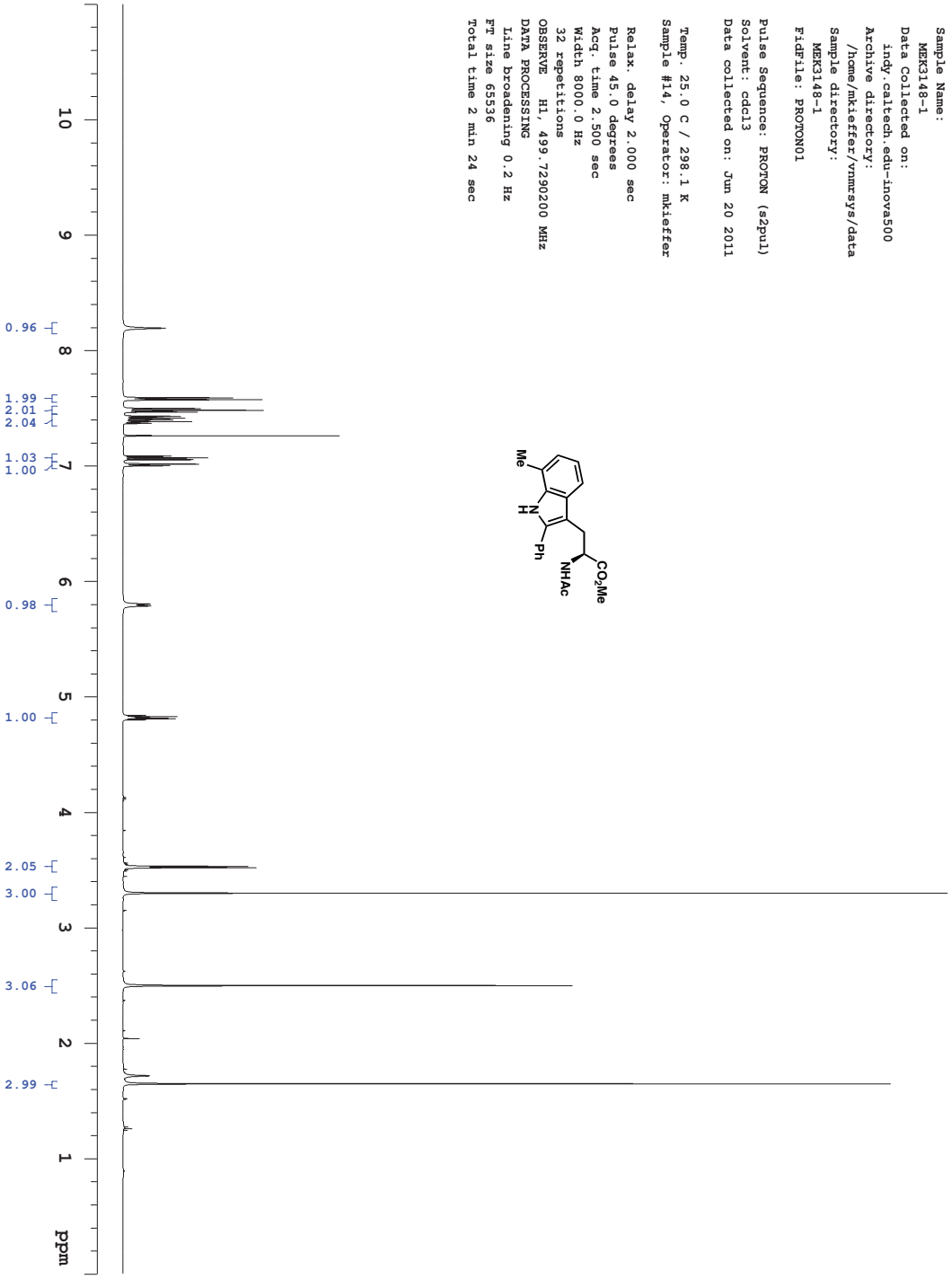

MEK3186-1
Sample Name:
MEK3186-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3186-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 15 2011
Sample #15, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553310 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
N
H
Ph
NHAc
CO2Me
180
160
140
120
100
80
60
40
20
ppm


MEK3084-1
Sample Name:
MEK3084-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3084-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 9 2011
Temp. 25.0 C / 298.1 K
Sample #39, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
N
H
Ph
NHAc
CO2Me
0.93
2.00
1.99
2.02
1.08
1.00
0.94
0.99
2.02
3.00
3.02
2.98
10
9
8
7
6
5
4
3
2
1
ppm

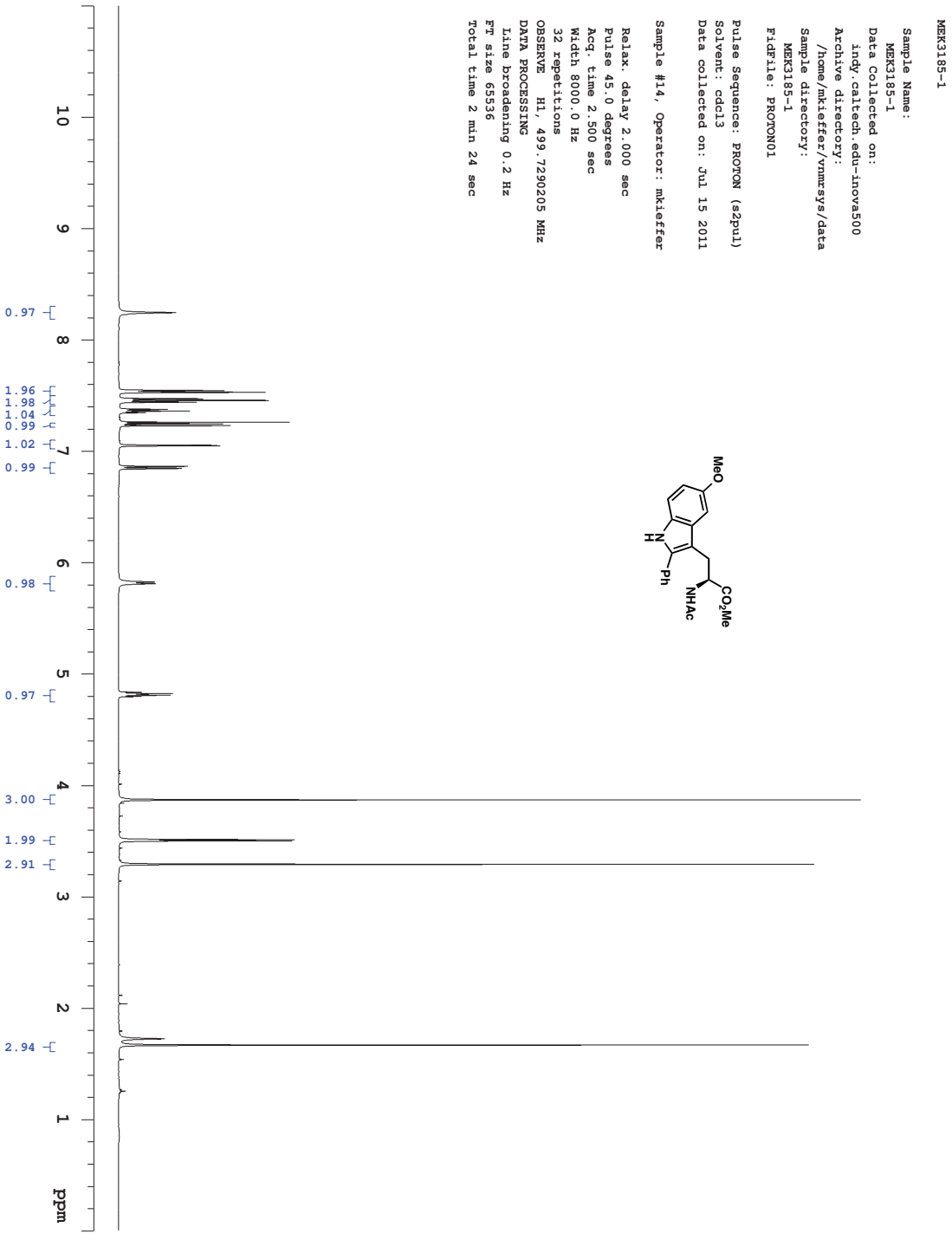

MEK3084-1
Sample Name:
MEK3084-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3084-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 9 2011
Temp. 25.0 C / 298.1 K
Sample #39, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6569642 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
N
H
Ph
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

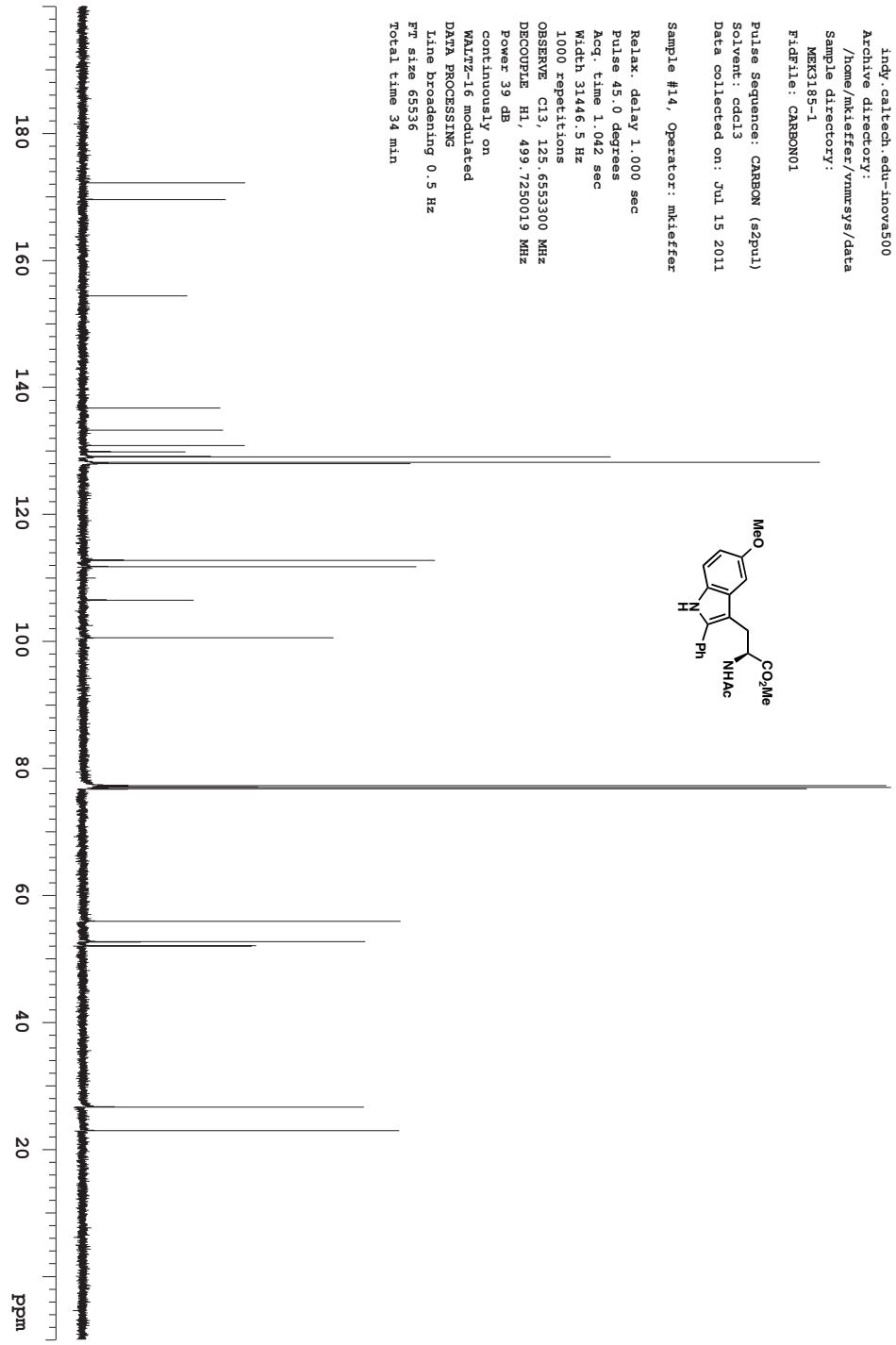

MEK3193-1
Sample Name:
MEK3193-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3193-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 21 2011
Sample #33, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7225125 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
Me
N
H
Ph
NHAc
CO2Me
0.97
2.03
3.10
1.06
1.03
1.05
0.98
1.00
2.07
3.00
3.13
2.96
10
9
8
7
6
5
4
3
2
1
ppm

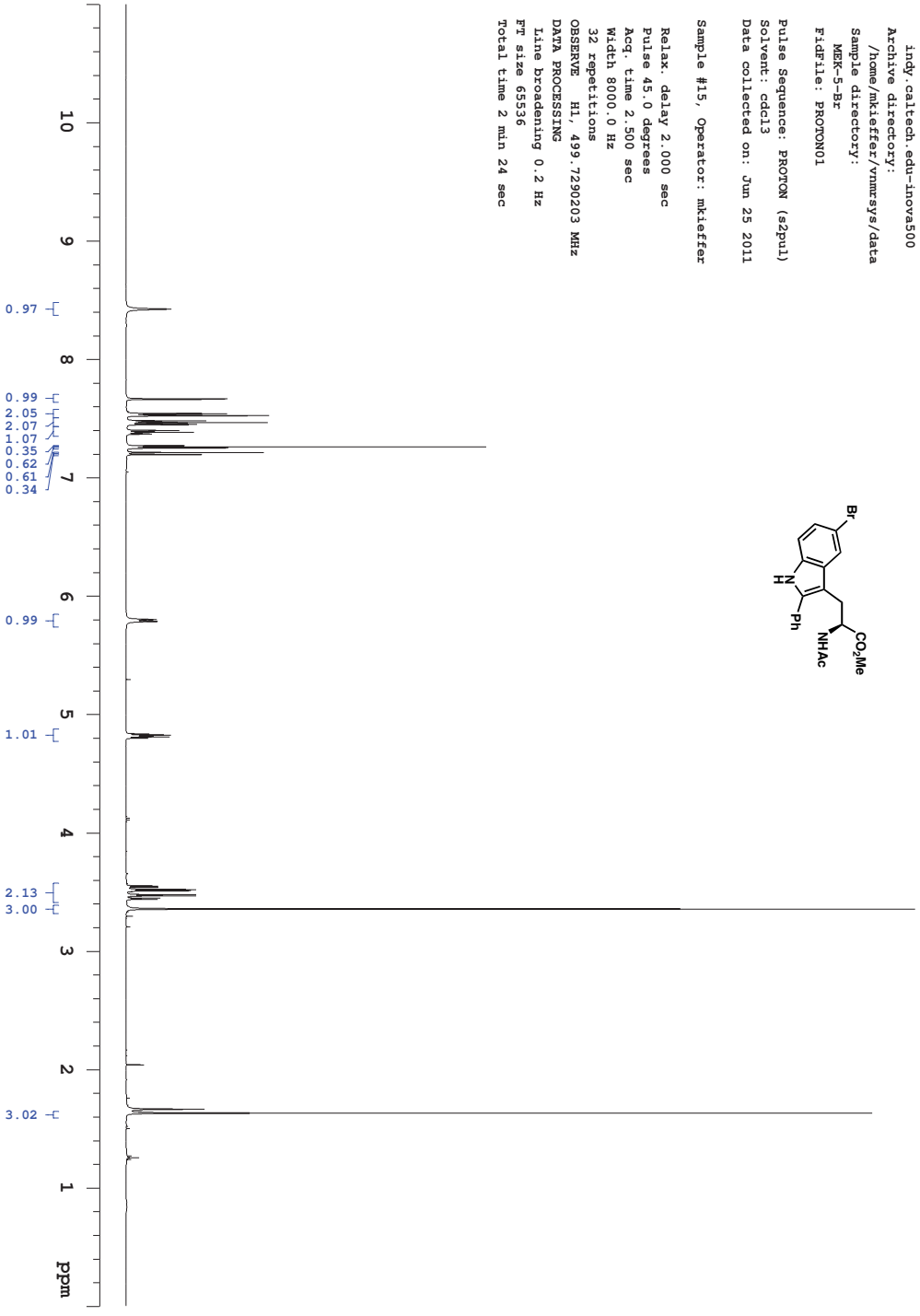

MEK3193-1
Sample Name:
MEK3193-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3193-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 21 2011
Sample #33, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553291 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
H
N
Ph
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

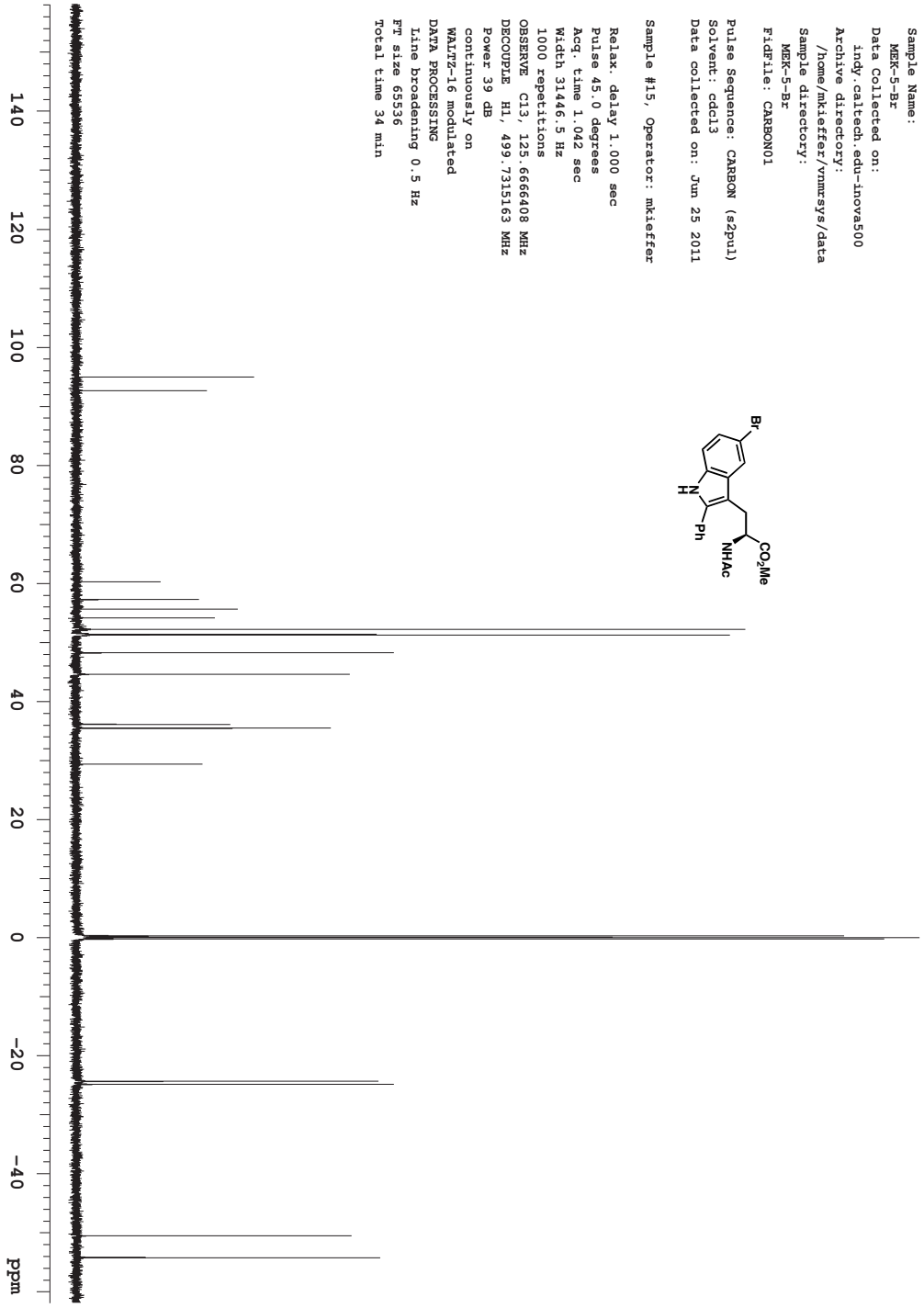

MEK3148-1
Sample Name:
MEK3148-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3148-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 20 2011
Temp. 25.0 C / 298.1 K
Sample #14, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
Me
N
H
Ph
NHAc
CO2Me
0.96
1.99
2.01
2.04
1.03
1.00
0.98
1.00
2.05
3.00
3.06
2.99
10
9
8
7
6
5
4
3
2
1
ppm

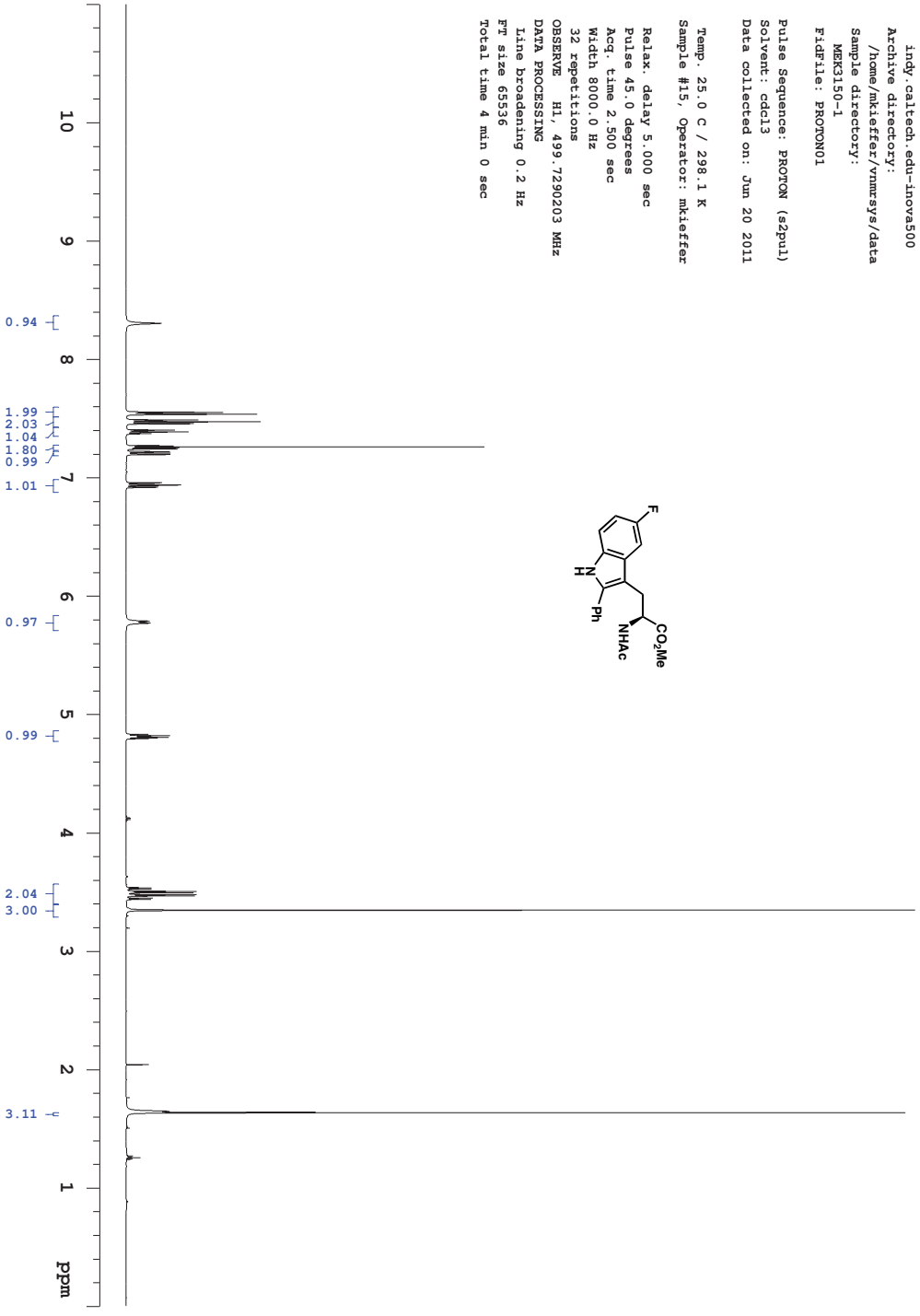

MEK3130-1
Sample Name:
MEK3130-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3130-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 7 2011
Temp. 25.0 C / 298.1 K
Sample #15, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6569681 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 26 min
Me
N
H
Ph
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

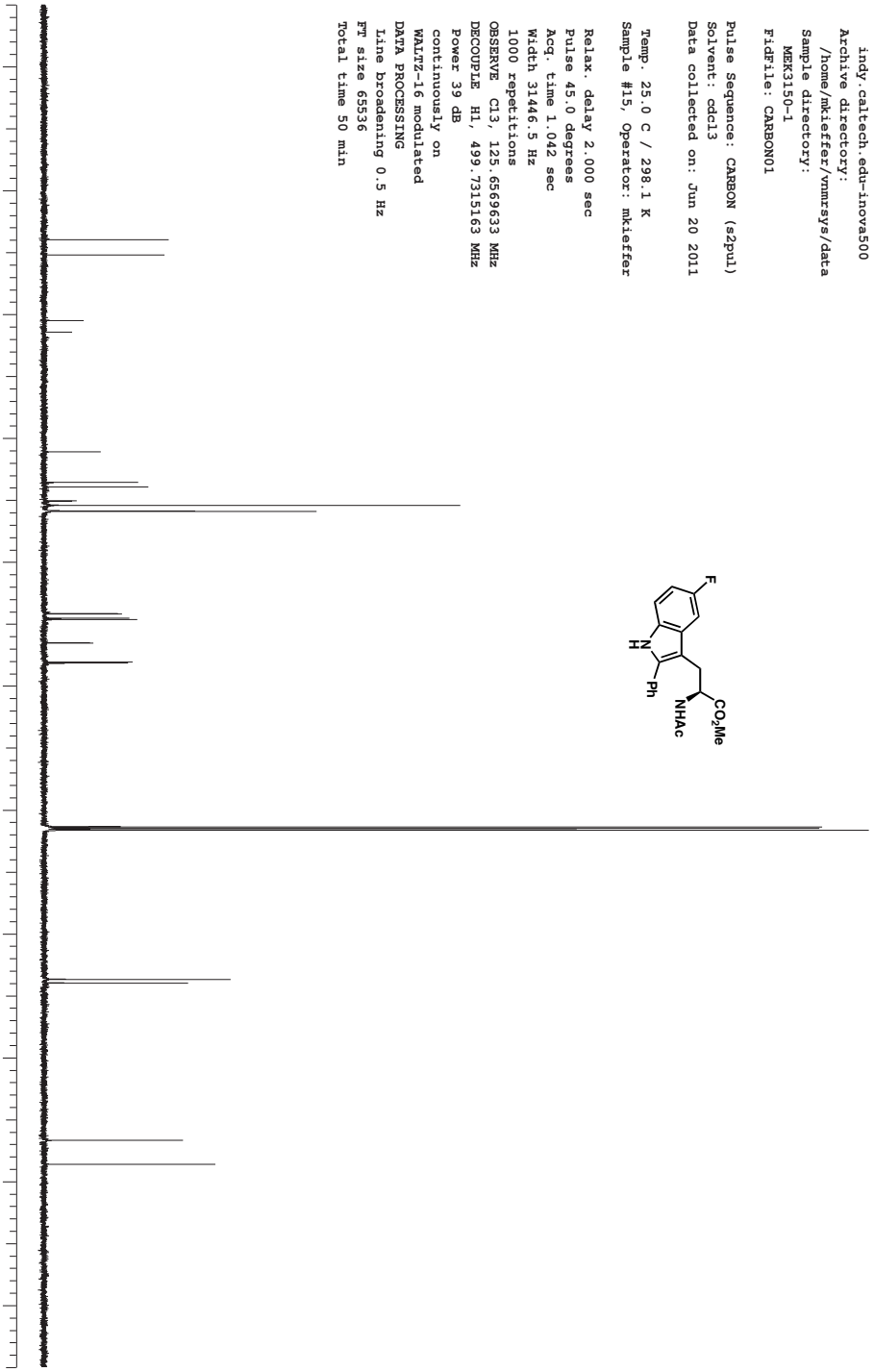

MEK3185-1
Sample Name:
MEK3185-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3185-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jul 15 2011
Sample #14, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290205 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
MeO
N
H
Ph
NHAc
CO2Me
0.97
1.96
1.98
1.04
0.99
1.02
0.99
0.98
0.97
3.00
1.99
2.91
2.94
10
9
8
7
6
5
4
3
2
1
ppm

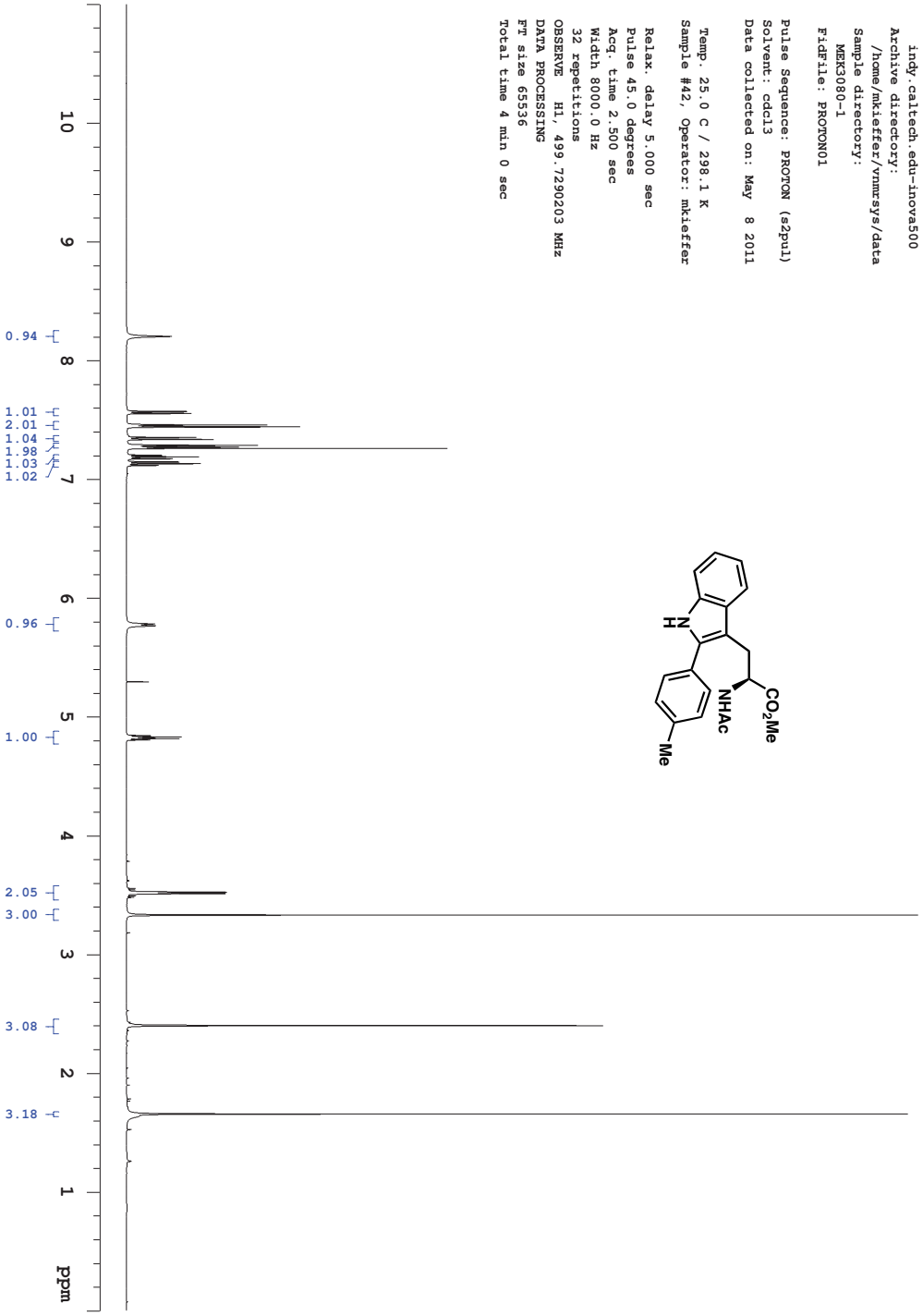

MEK3185-1
Sample Name:
MEK3185-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3185-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jul 15 2011
Sample #14, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553300 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
MeO
H
N
Ph
NHAc
CO2Me
180
160
140
120
100
80
60
40
20
ppm

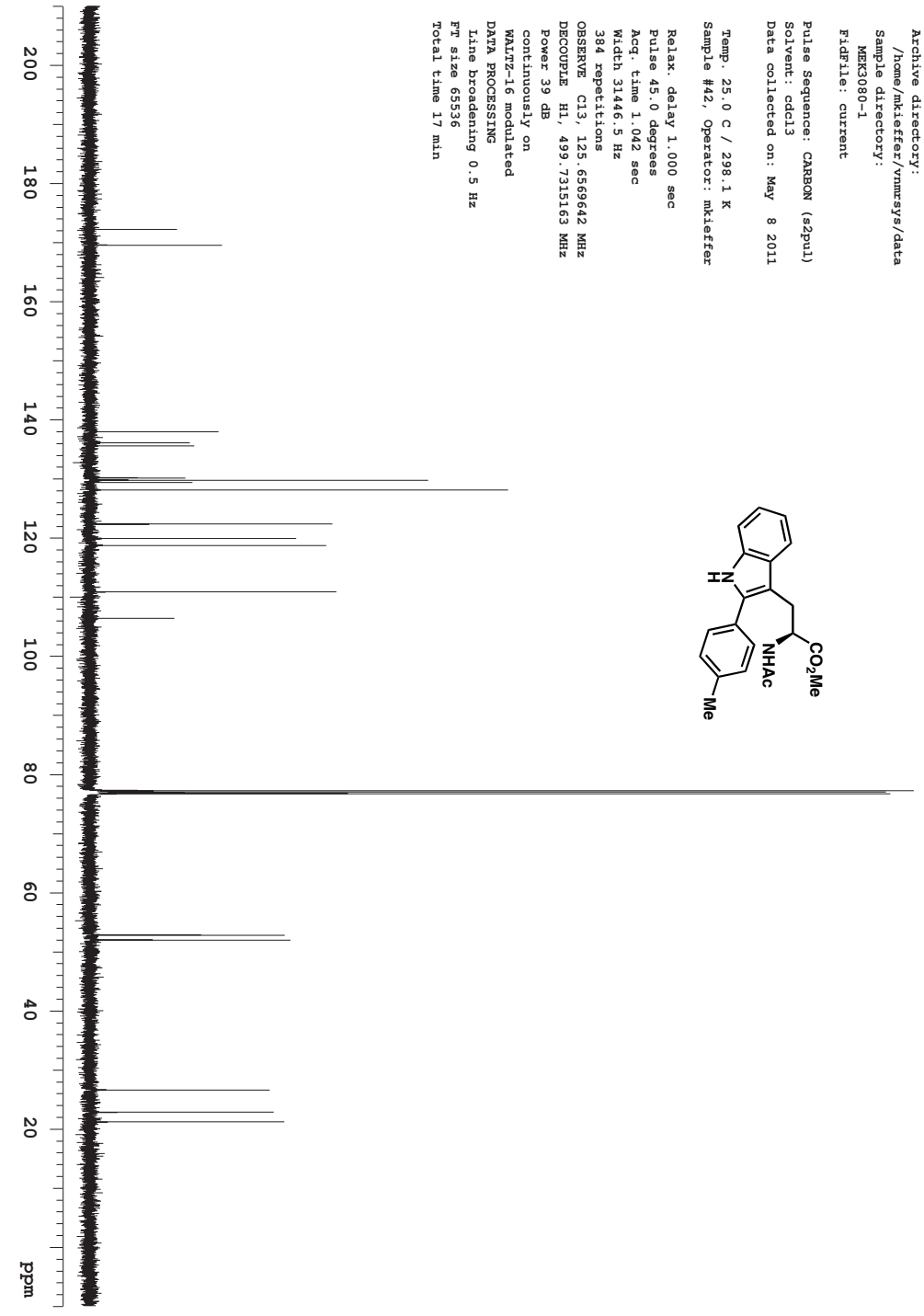

MEK-5-Br
Sample Name:
MEK-5-Br
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-5-Br
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2011
Sample #15, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
Br
N
H
Ph
NHAc
CO2Me
0.97
0.99
2.05
2.07
1.07
0.35
0.62
0.61
0.34
0.99
1.01
2.13
3.00
3.02
10
9
8
7
6
5
4
3
2
1
ppm

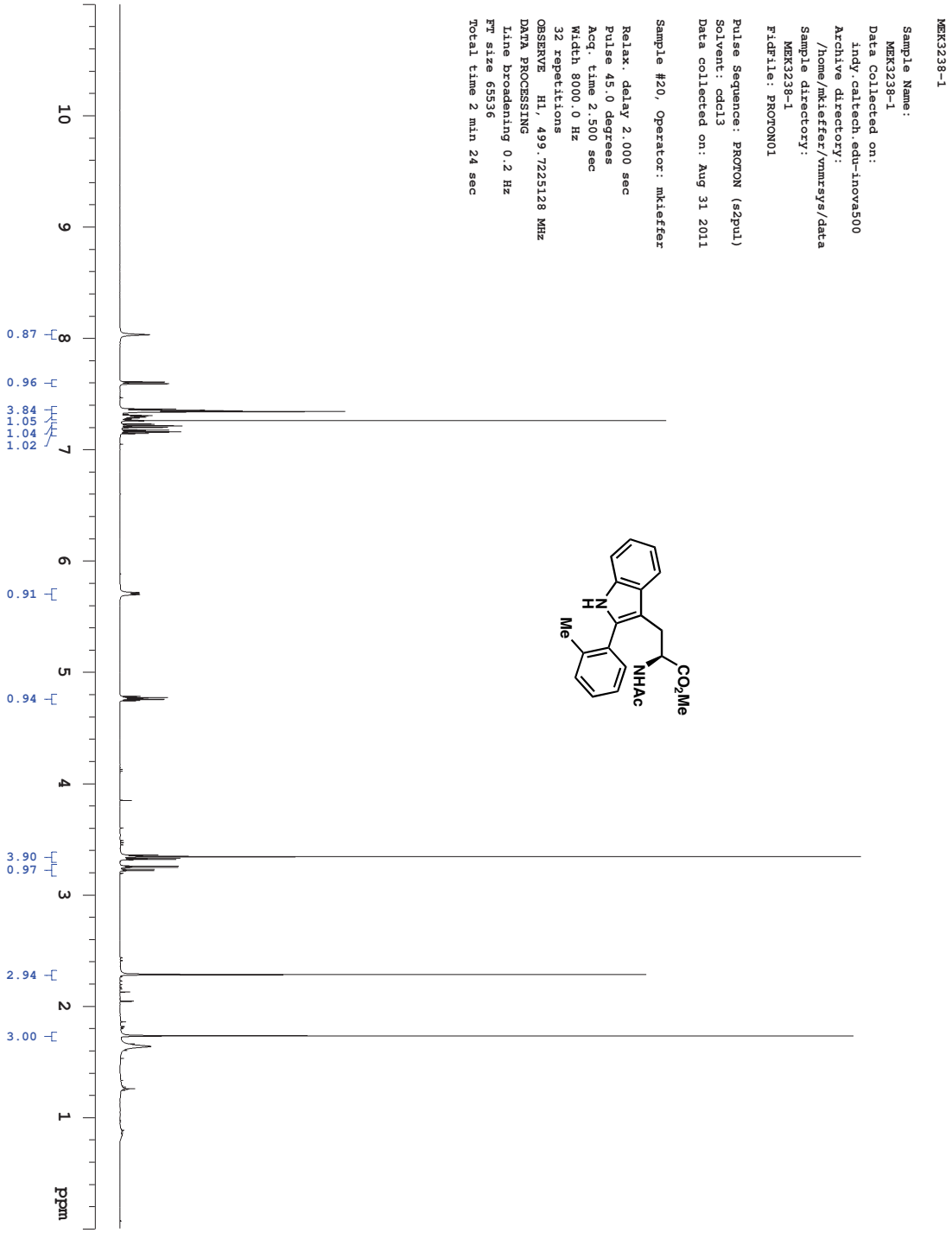

MEK-5-Br
Sample Name:
MEK-5-Br
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-5-Br
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2011
Sample #15, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6666408 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Br
N
H
Ph
NHAc
CO2Me
140
120
100
80
60
40
20
0
-20
-40
ppm

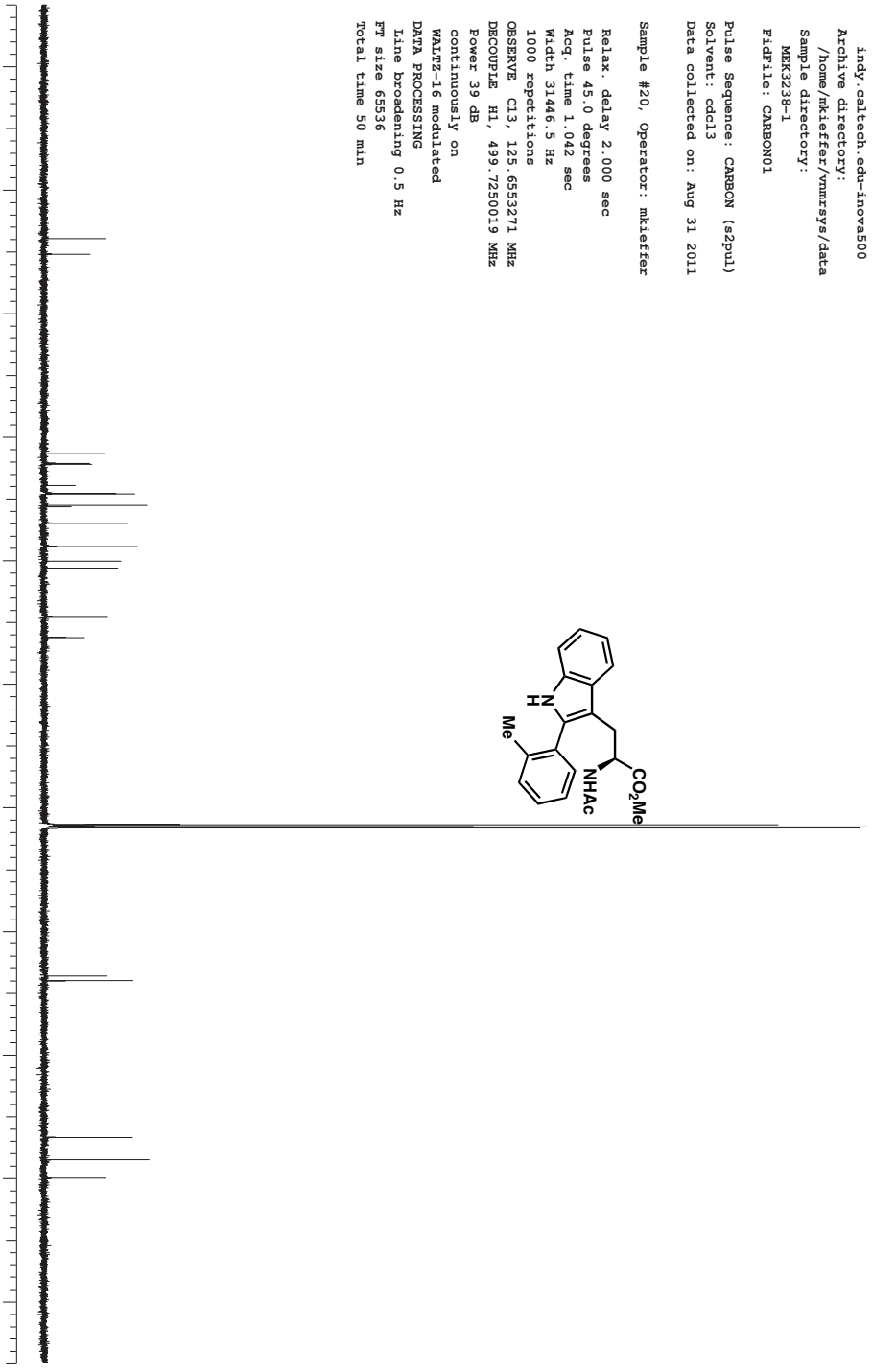

MEK3150-1
Sample Name:
MEK3150-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3150-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 20 2011
Temp. 25.0 C / 298.1 K
Sample #15, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
0.94
1.99
2.03
1.04
1.80
0.99
1.01
0.97
0.99
2.04
3.00
3.11
F
N
H
Ph
NHAc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm

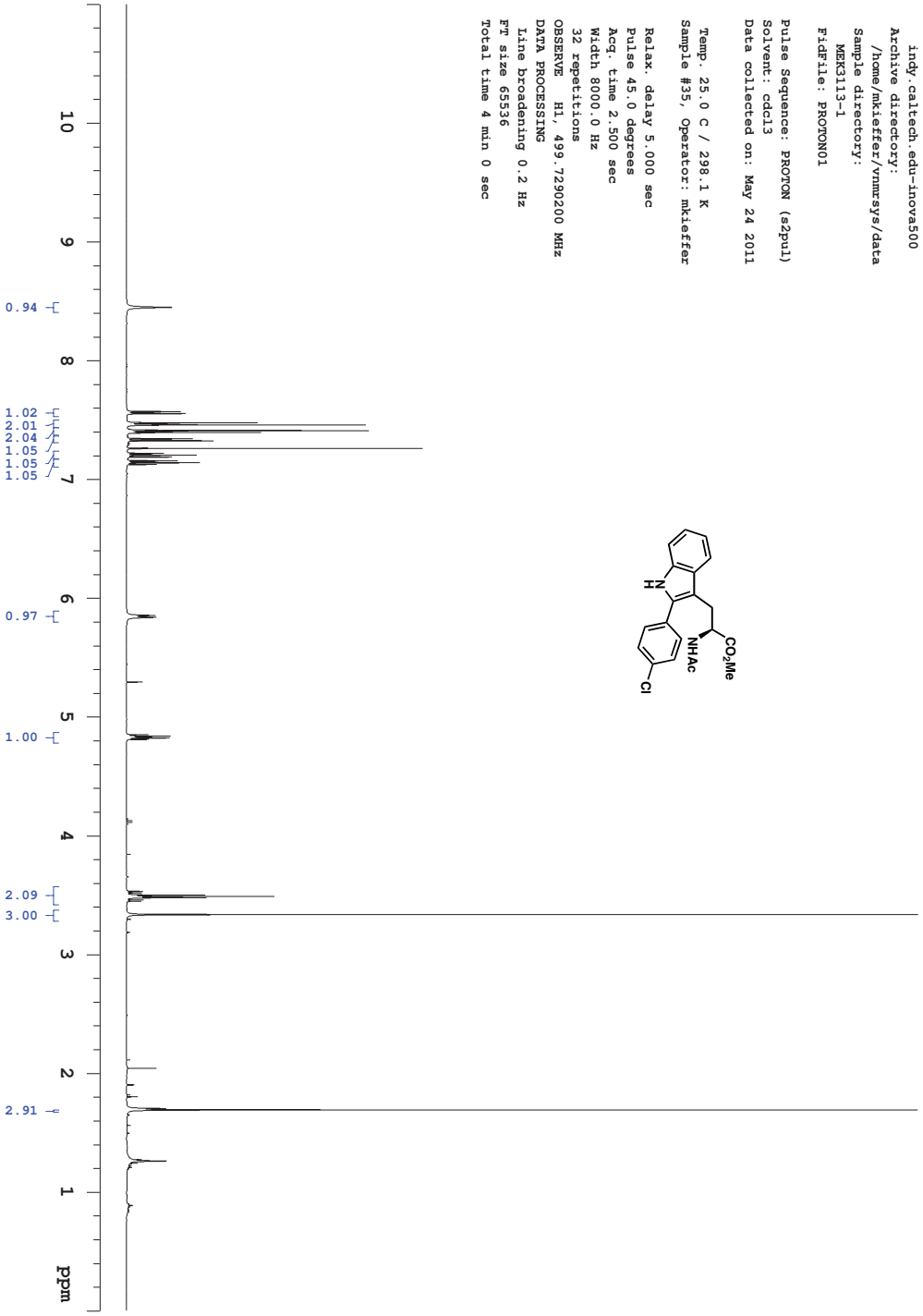

MEK3150-1
Sample Name:
MEK3150-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3150-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 20 2011
Temp. 25.0 C / 298.1 K
Sample #15, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6569633 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 50 min
F
N
H
Ph
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

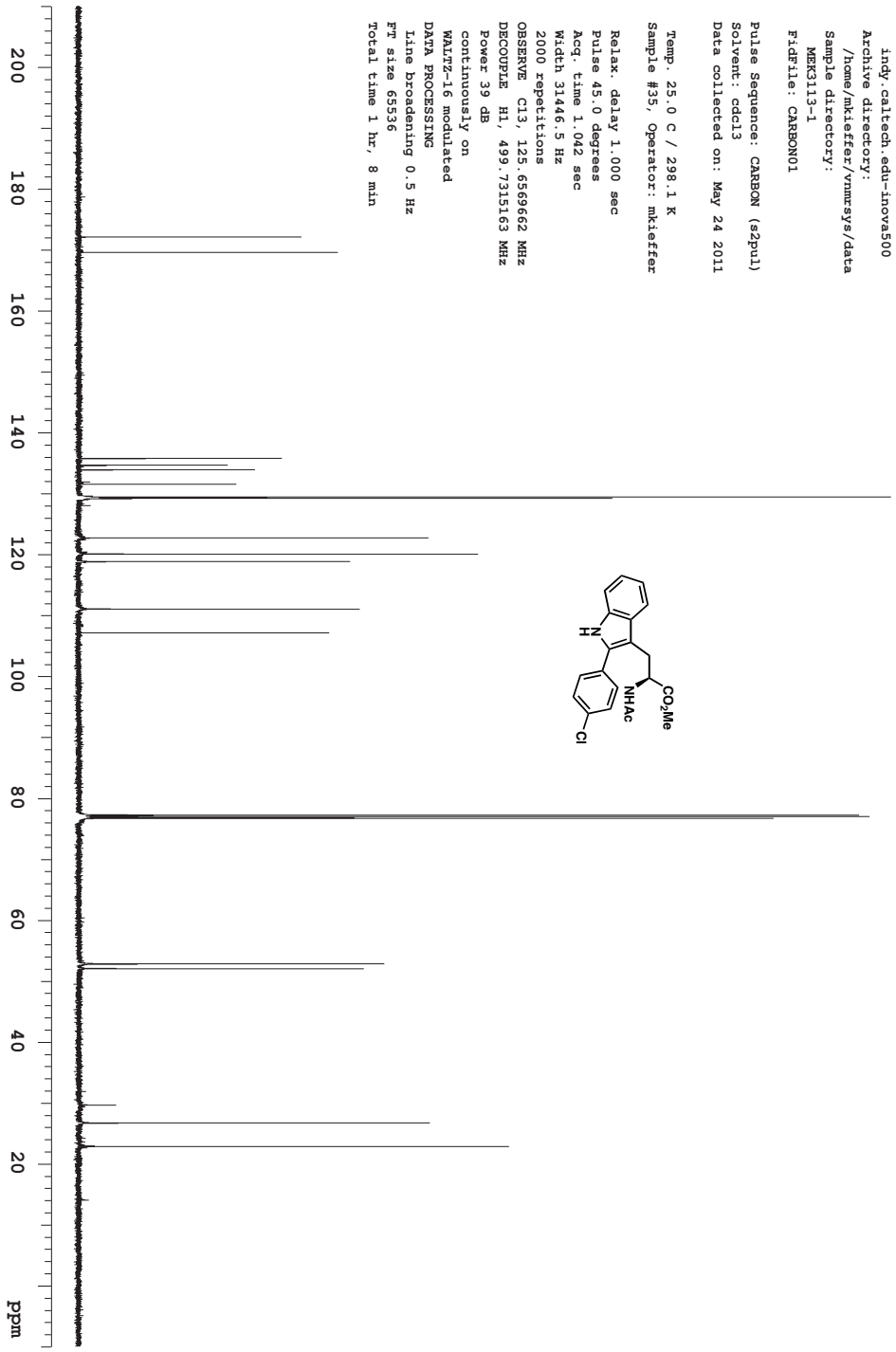

MEK3080-1
Sample Name:
MEK3080-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3080-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2011
Temp. 25.0 C / 298.1 K
Sample #42, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
0.94
1.01
2.01
1.04
1.98
1.03
1.02
0.96
1.00
2.05
3.00
3.08
3.18
10
9
8
7
6
5
4
3
2
1
ppm
H
N
NHAc
CO2Me
Me

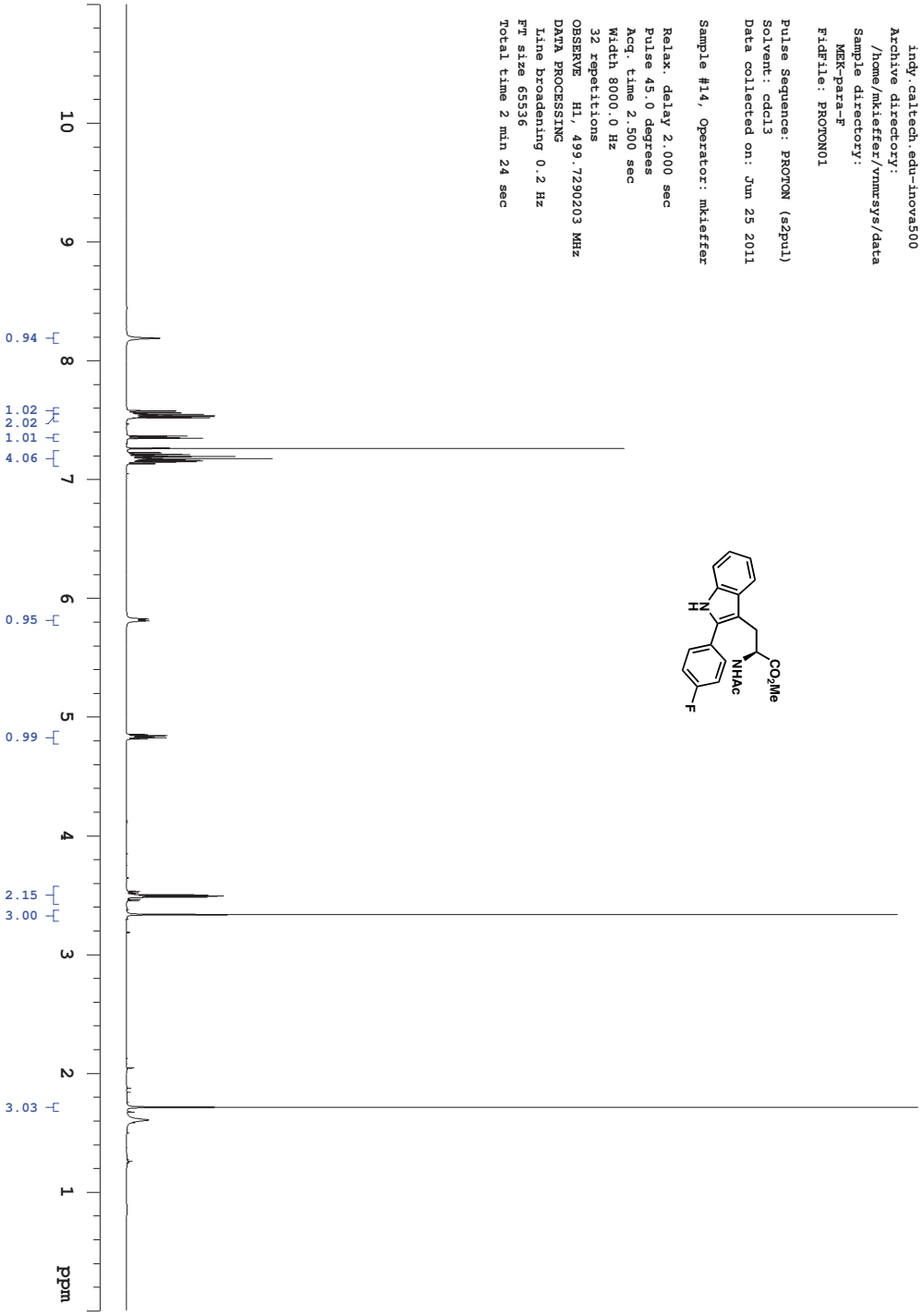

MEK3080-1
Sample Name:
MEK3080-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3080-1
FidFile: current
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2011
Temp. 25.0 C / 298.1 K
Sample #42, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
384 repetitions
OBSERVE C13, 125.6569642 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
H
NHAc
CO2Me
Me
200
180
160
140
120
100
80
60
40
20
ppm

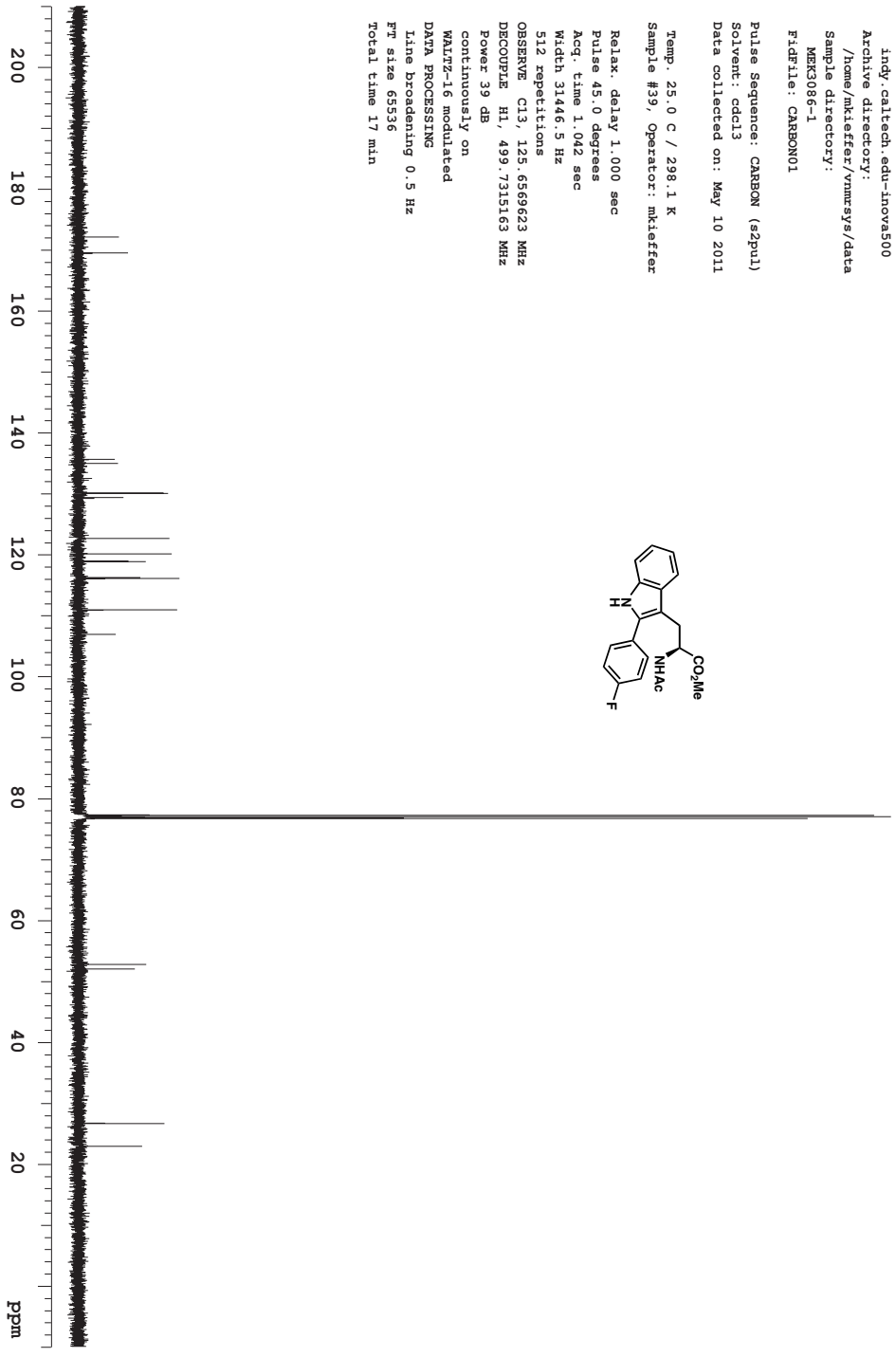

MEK3238-1
Sample Name:
MEK3238-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3238-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 31 2011
Sample #20, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
0.87
0.96
3.84
1.05
1.04
1.02
0.91
0.94
3.90
0.97
2.94
3.00
Me
N
H
NHAc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm

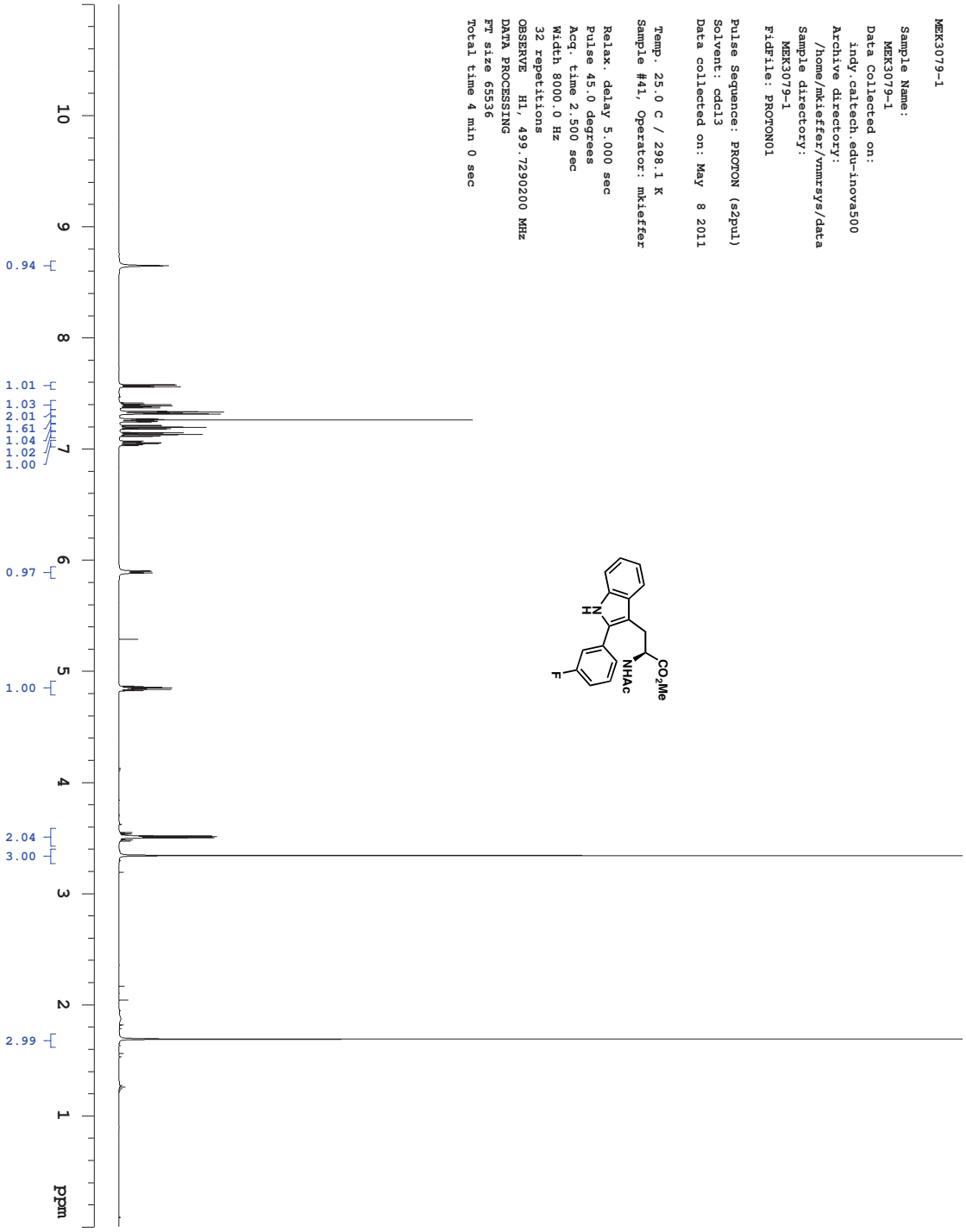

MEK3238-1
Sample Name:
MEK3238-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3238-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 31 2011
Sample #20, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 50 min
N
H
Me
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

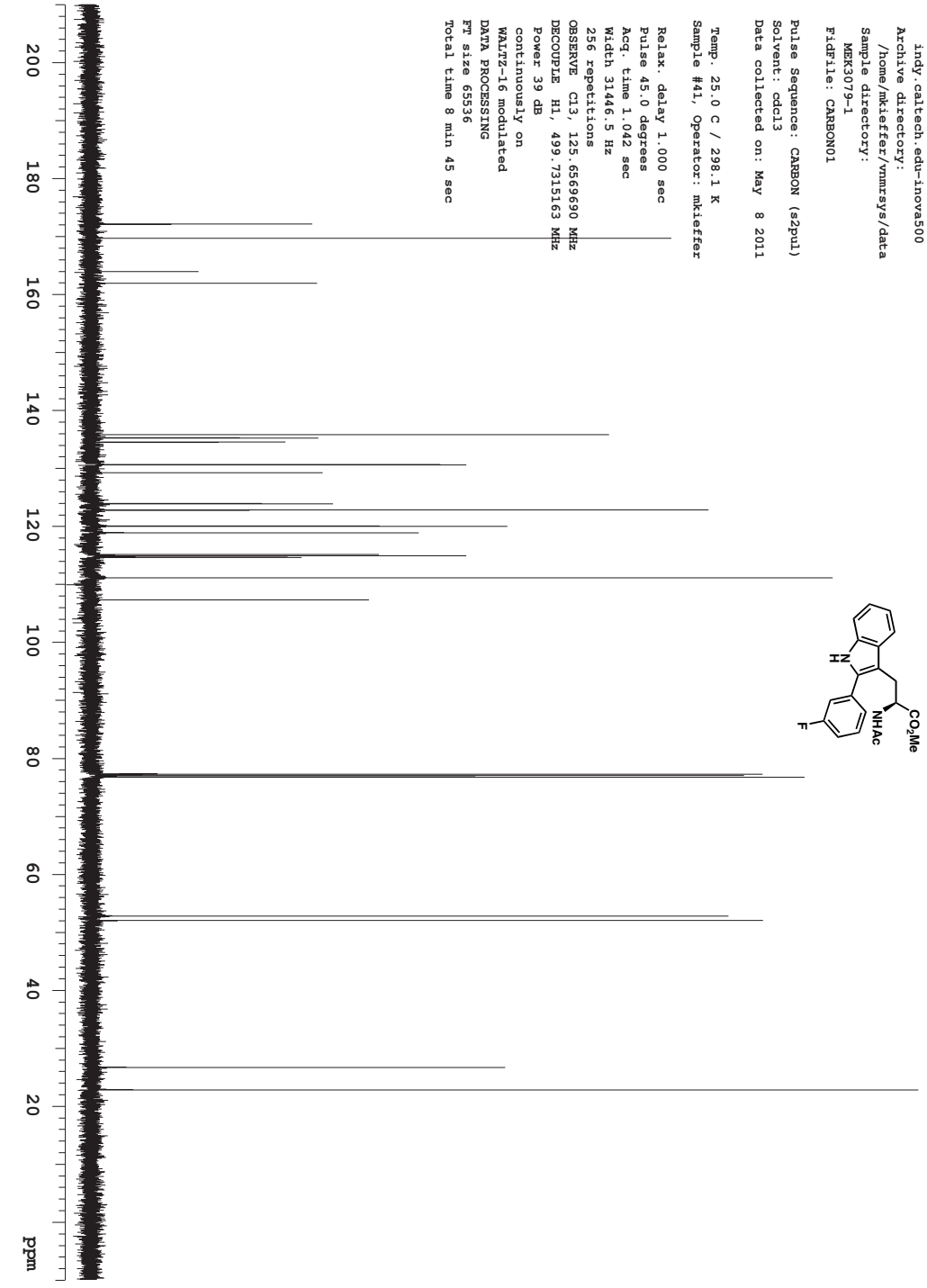

MEK3113-1
Sample Name:
MEK3113-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3113-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 24 2011
Temp. 25.0 C / 298.1 K
Sample #35, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
0.94
1.02
2.01
2.04
1.05
1.05
1.05
0.97
1.00
2.09
3.00
2.91
NHAc
CO2Me
Cl
10
9
8
7
6
5
4
3
2
1
ppm

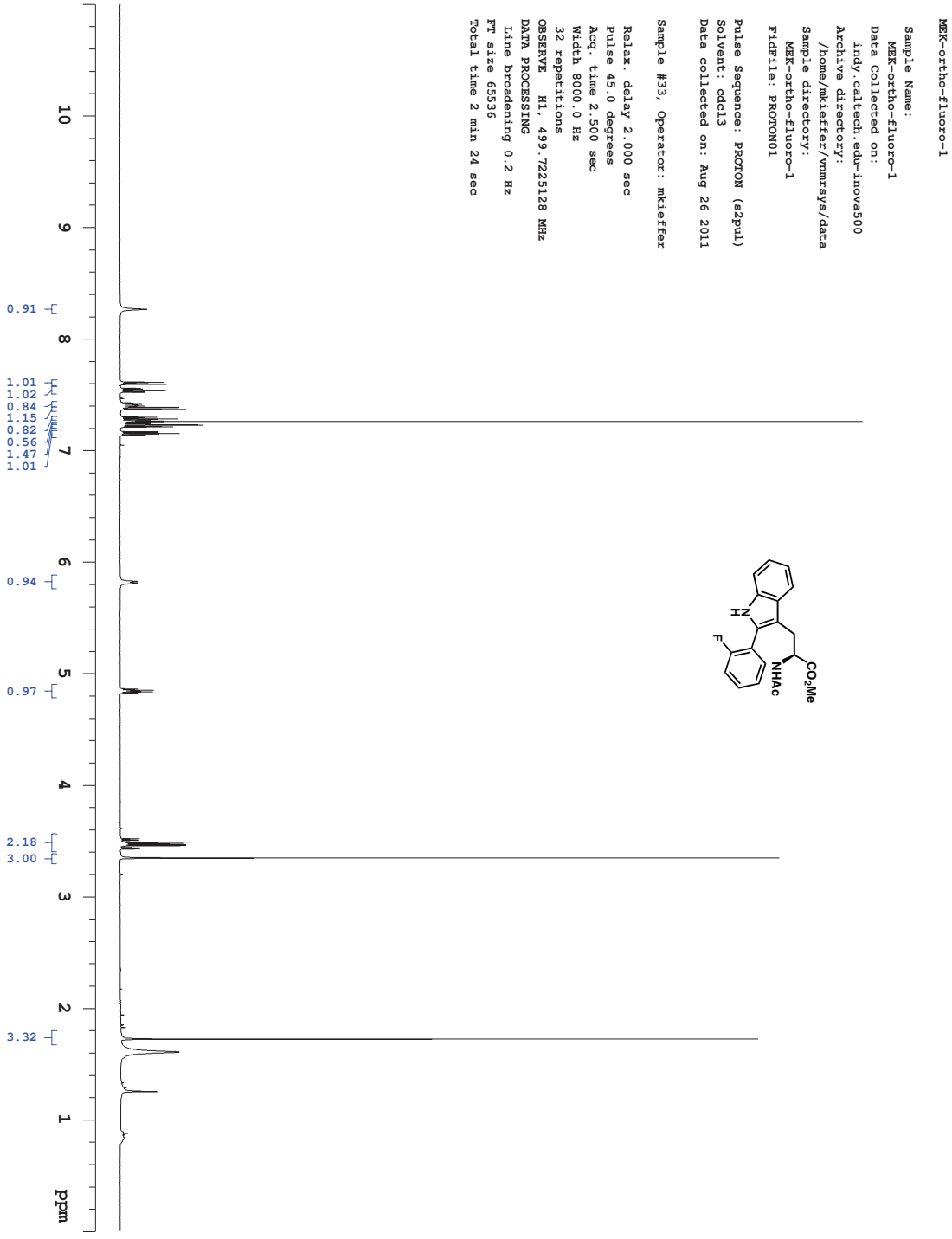

MEK3113-1
Sample Name:
MEK3113-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3113-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 24 2011
Temp. 25.0 C / 298.1 K
Sample #35, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6569662 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
NH
NHAc
CO2Me
Cl
200
180
160
140
120
100
80
60
40
20
ppm

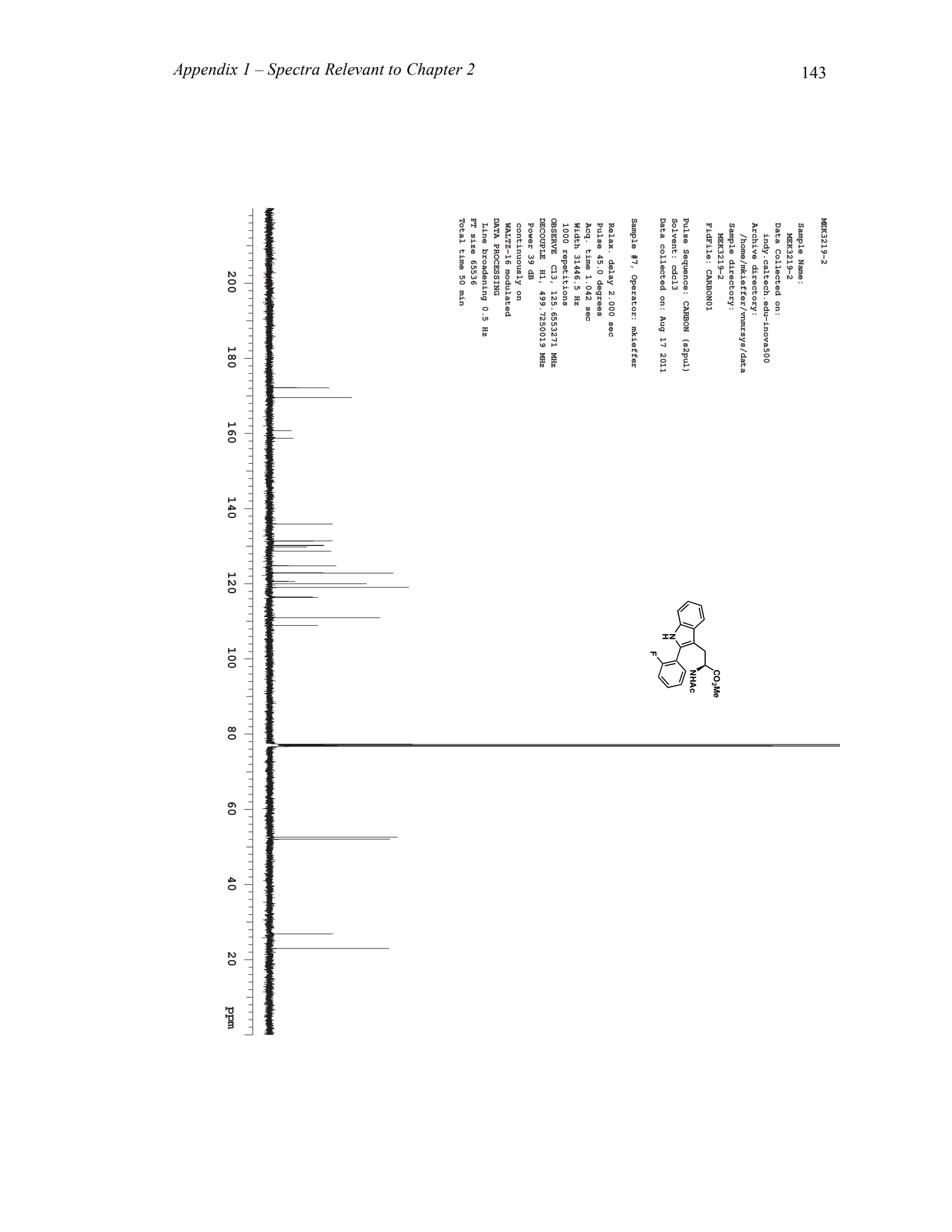

MEK-para-F
Sample Name:
MEK-para-F
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-para-F
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2011
Sample #14, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
0.94
1.02
2.02
1.01
4.06
0.95
0.99
2.15
3.00
3.03
NHAc
CO2Me
F
ppm

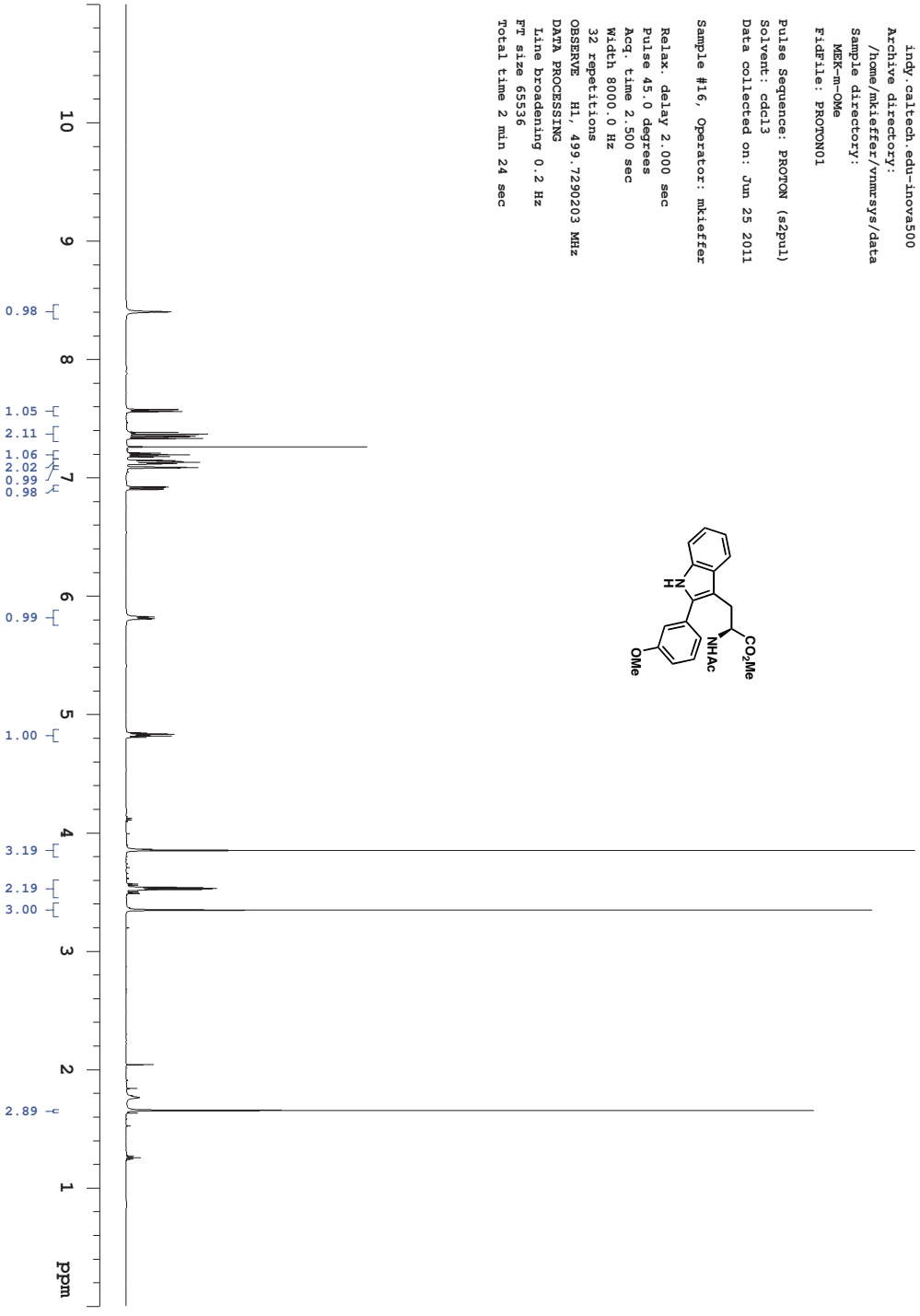

MEK3086-1
Sample Name:
MEK3086-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3086-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2011
Temp. 25.0 C / 298.1 K
Sample #39, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6569623 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
NH
NHAc
CO2Me
F
200
180
160
140
120
100
80
60
40
20
ppm

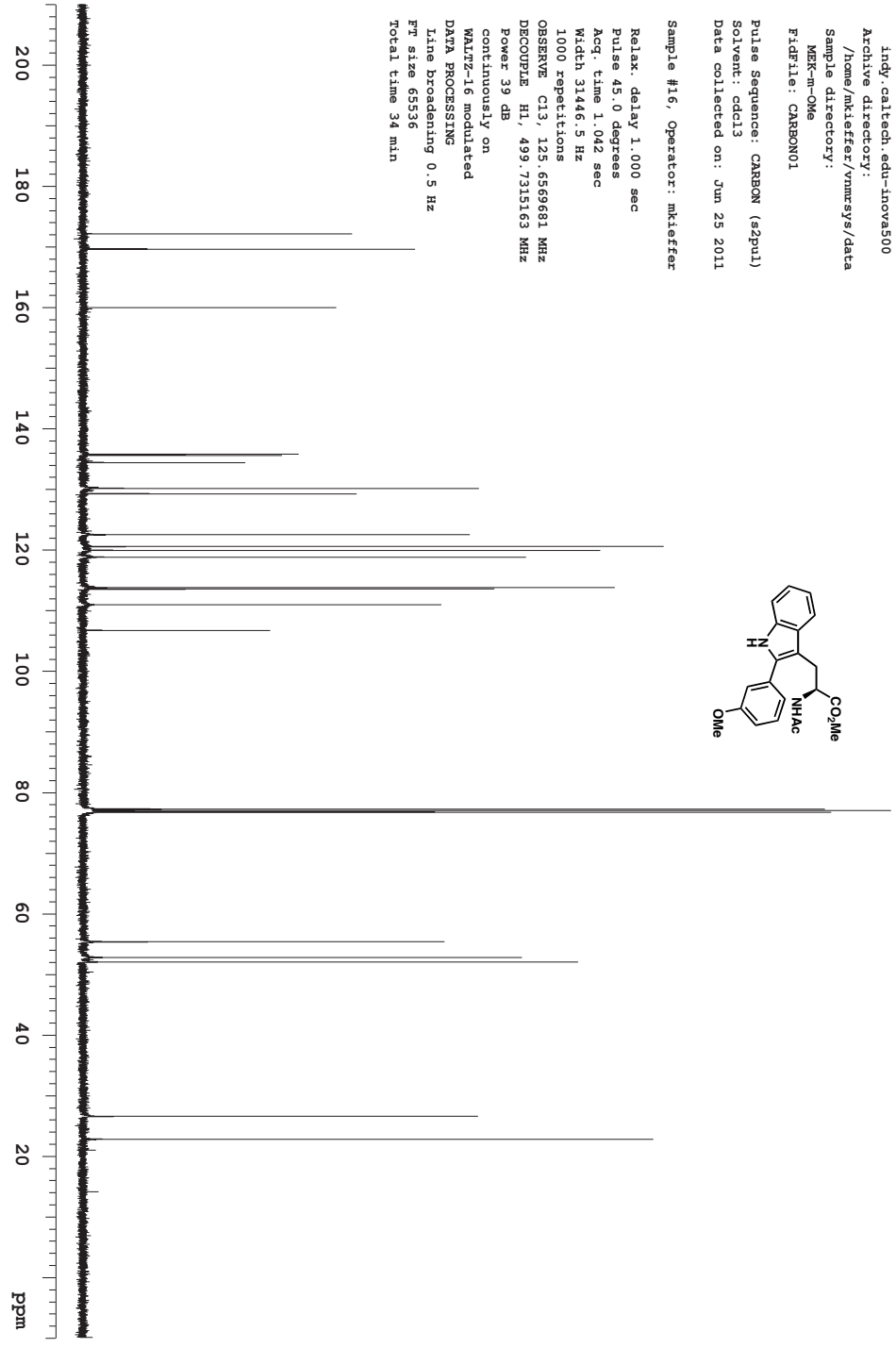

MEK3079-1
Sample Name:
MEK3079-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3079-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2011
Temp. 25.0 C / 298.1 K
Sample #41, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
0.94
1.01
1.03
2.01
1.61
1.04
1.02
1.00
0.97
1.00
2.04
3.00
2.99
10
9
8
7
6
5
4
3
2
1
ppm
H
N
F
NHAc
CO2Me

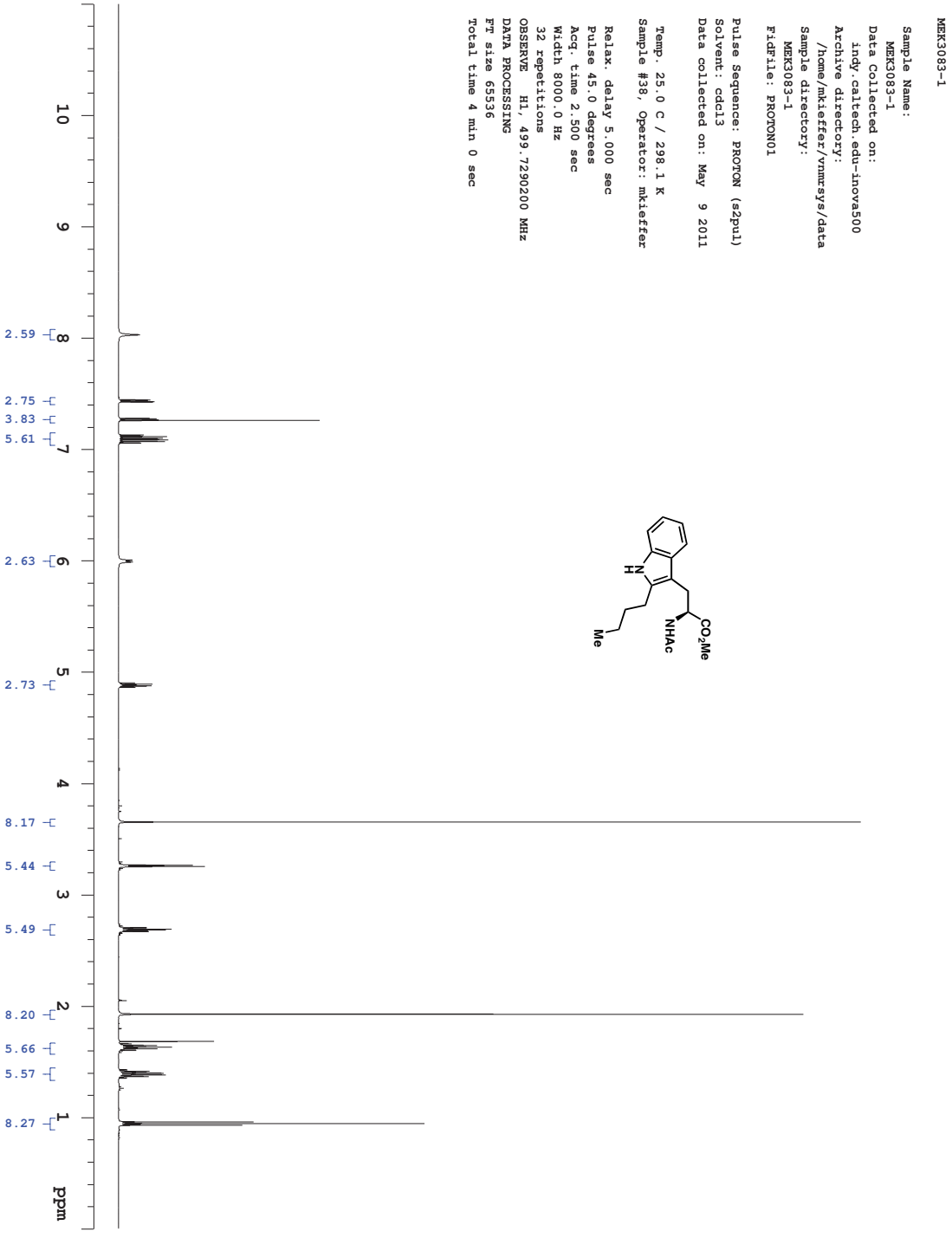

MEK3079-1
Sample Name:
MEK3079-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3079-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2011
Temp. 25.0 C / 298.1 K
Sample #41, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6569690 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
FT size 65536
Total time 8 min 45 sec
NH
F
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

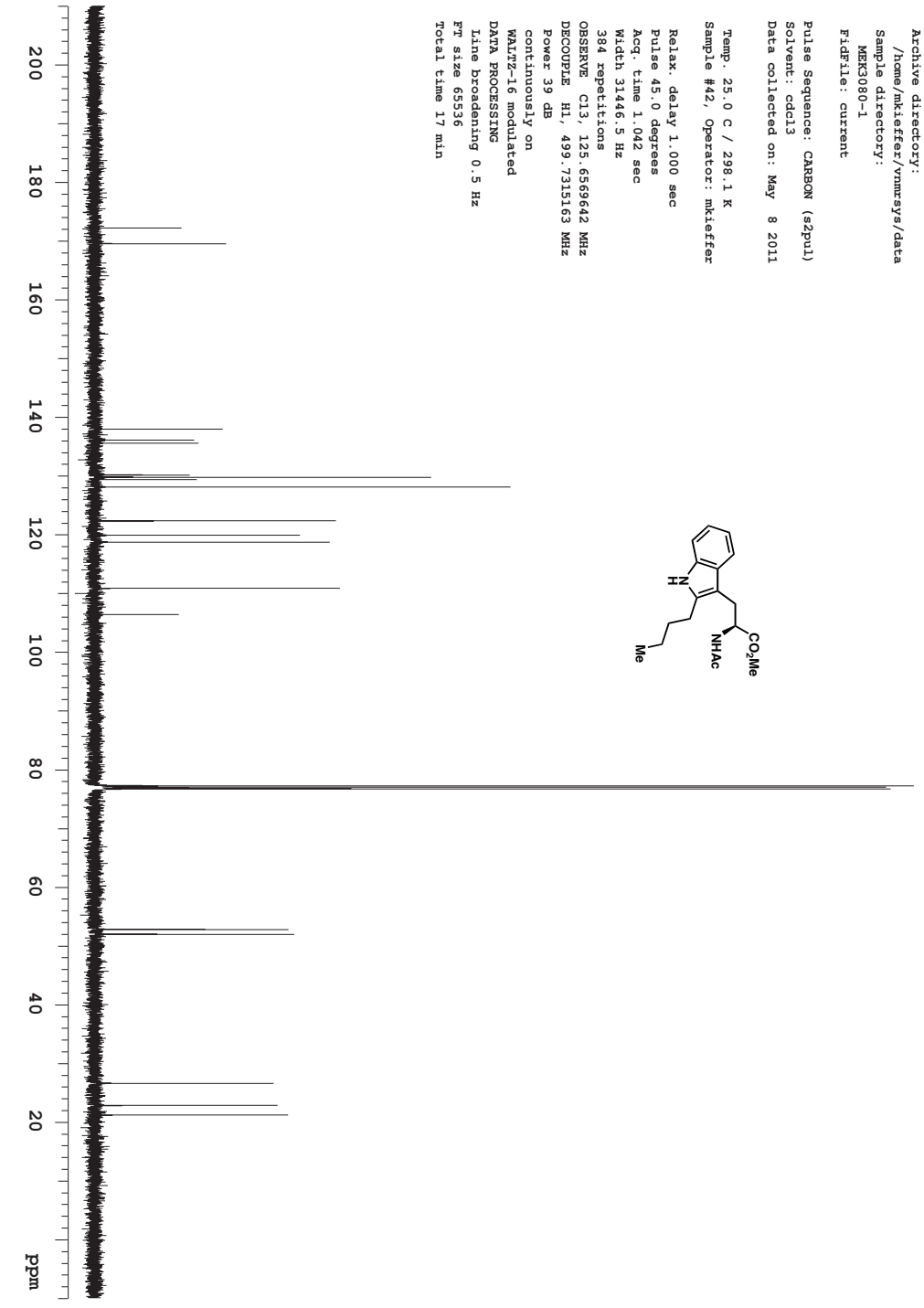

MEK-ortho-fluoro-1
Sample Name:
MEK-ortho-fluoro-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-ortho-fluoro-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 26 2011
Sample #33, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
0.91
1.01
1.02
0.84
1.15
0.82
0.56
1.47
1.01
0.94
0.97
2.18
3.00
3.32
10
9
8
7
6
5
4
3
2
1
ppm
F
NH
NHAc
CO2Me

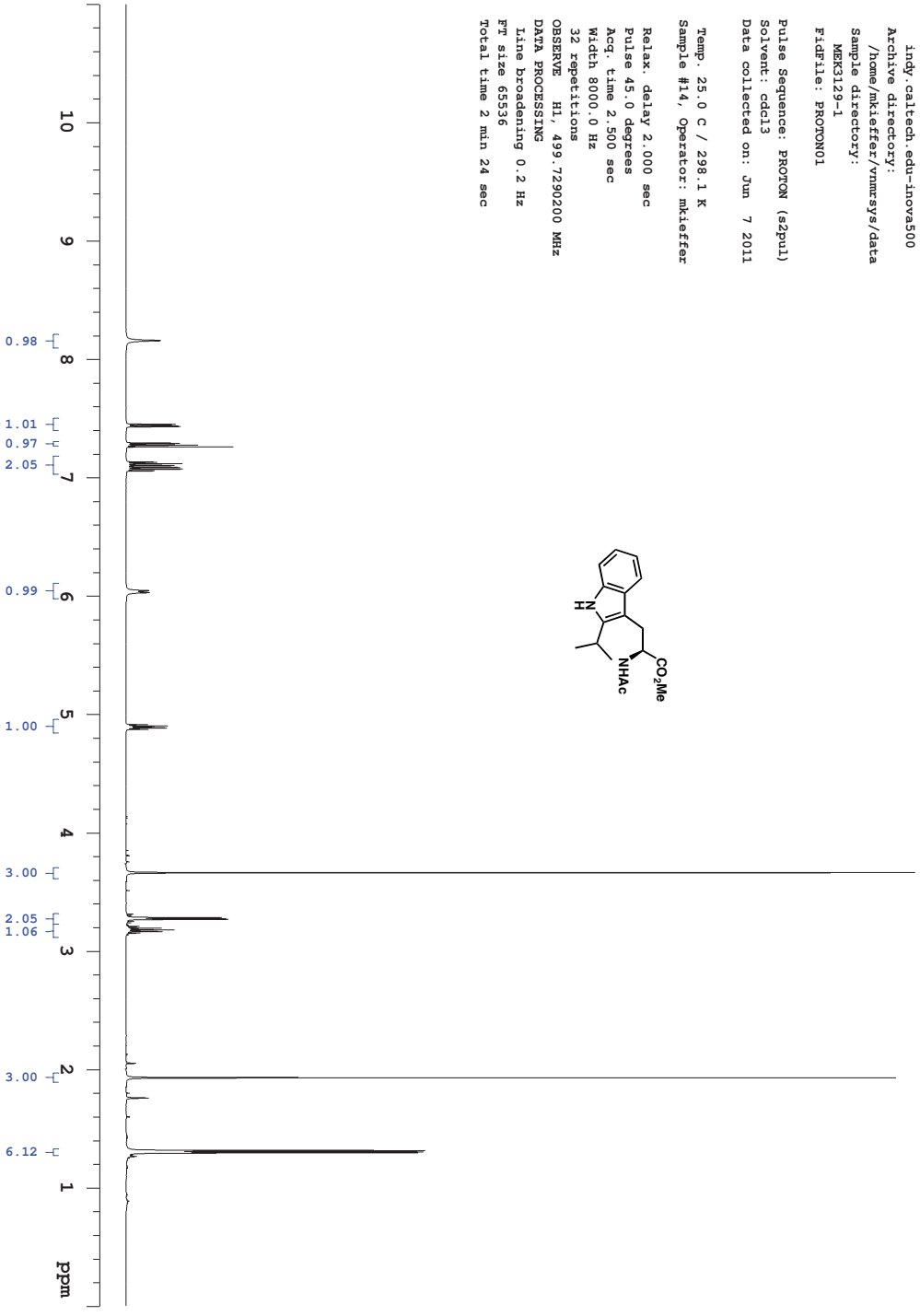

MEK3219-2
Sample Name:
MEK3219-2
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3219-2
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 17 2011
Sample #7, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 50 min
HN
F
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

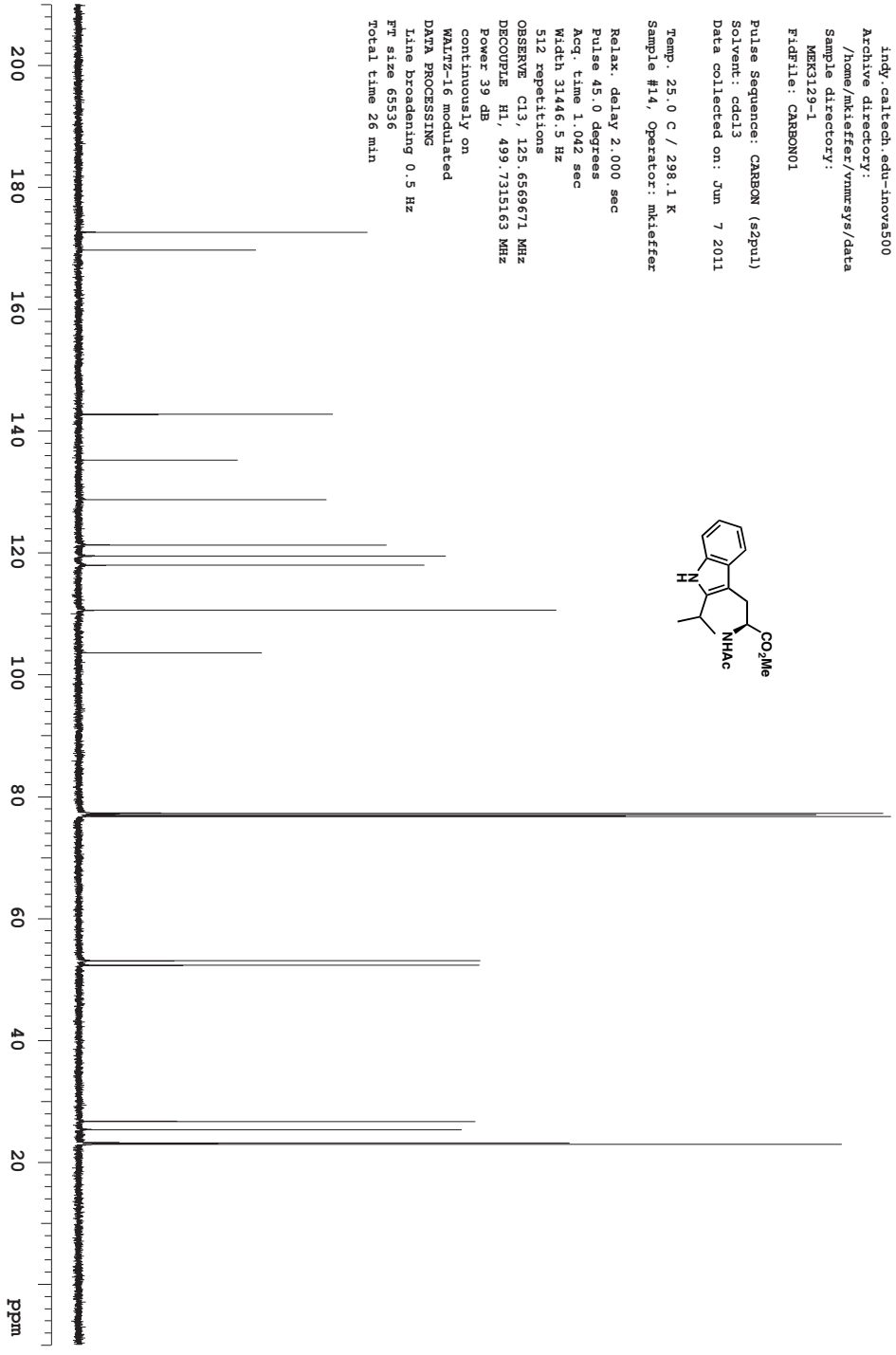

MEK-m-OMe
Sample Name:
MEK-m-OMe
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-m-OMe
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2011
Sample #16, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
0.98
1.05
2.11
1.06
2.02
0.99
0.98
0.99
1.00
3.19
2.19
3.00
2.89
10
9
8
7
6
5
4
3
2
1
ppm
H
N
NHAc
CO2Me
OMe

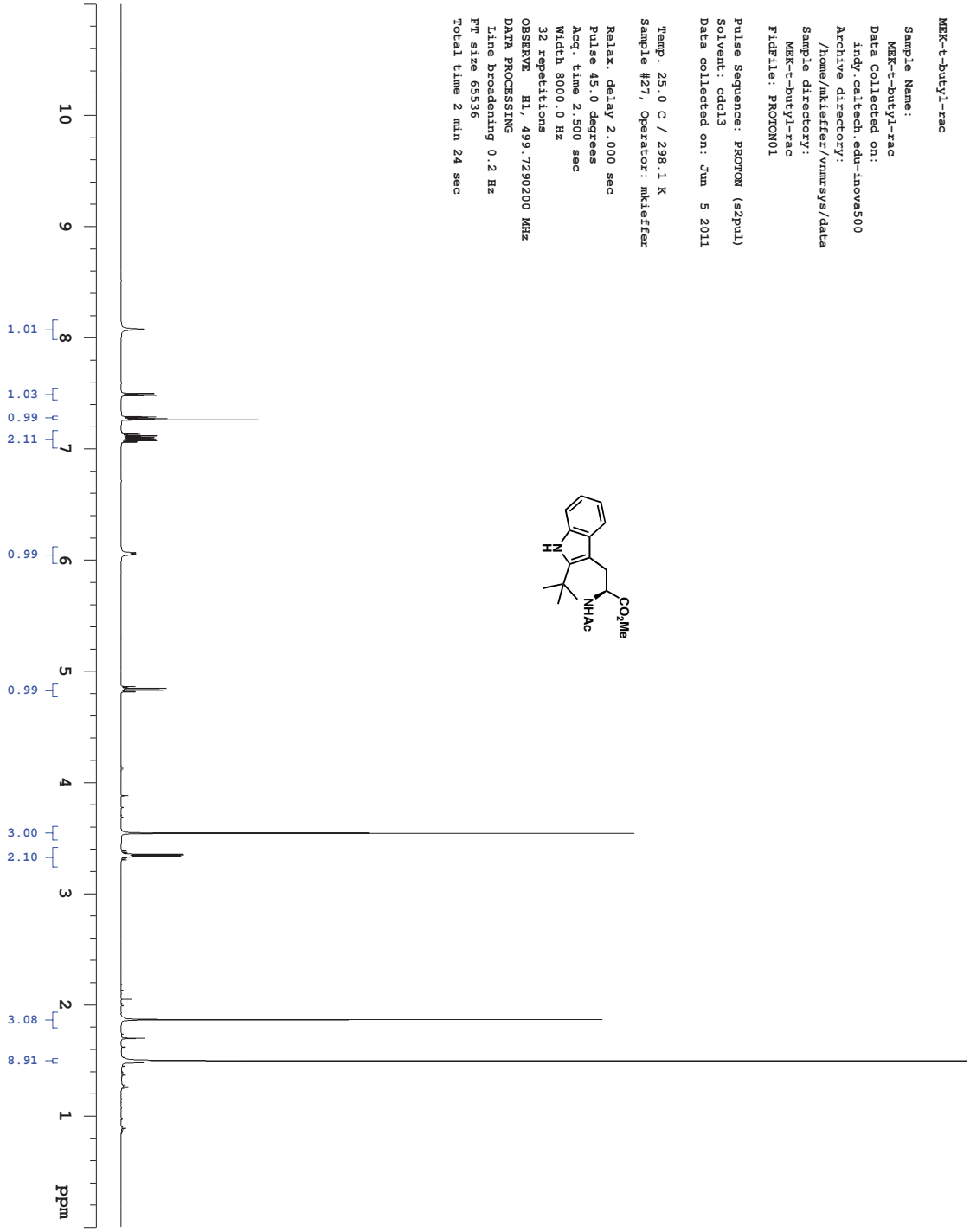

MEK-m-OMe
Sample Name:
MEK-m-OMe
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-m-OMe
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 25 2011
Sample #16, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6569681 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
NH
NHAc
CO2Me
OMe
200
180
160
140
120
100
80
60
40
20
ppm

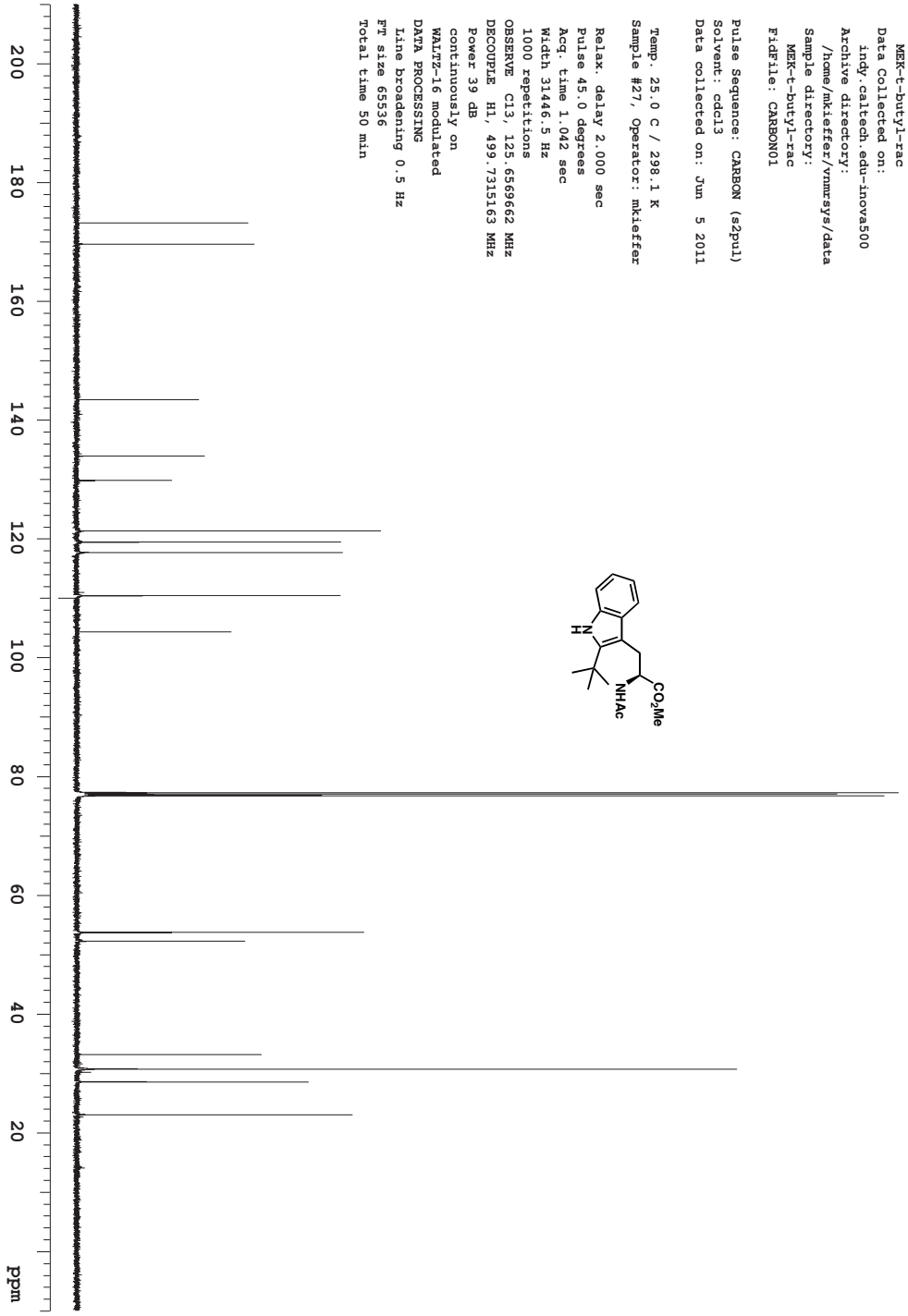

MEK3083-1
Sample Name:
MEK3083-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3083-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 9 2011
Temp. 25.0 C / 298.1 K
Sample #38, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
FT size 65536
Total time 4 min 0 sec
2.59
2.75
3.83
5.61
2.63
2.73
8.17
5.44
5.49
8.20
5.66
5.57
8.27
10
9
8
7
6
5
4
3
2
1
ppm
H
N
Me
NHAc
CO2Me

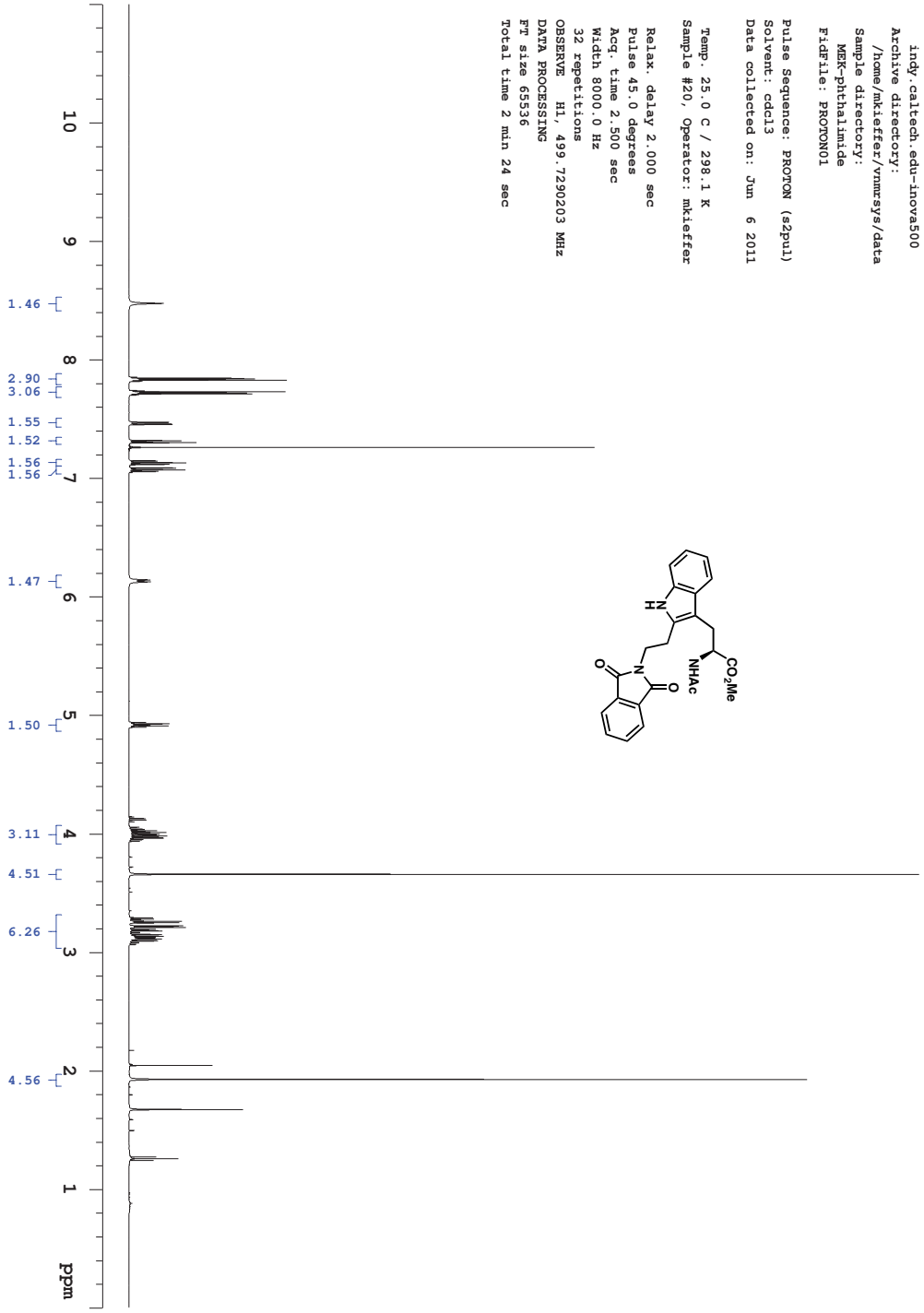

MEK3080-1
Sample Name:
MEK3080-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3080-1
FidFile: current
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 8 2011
Temp. 25.0 C / 298.1 K
Sample #42, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
384 repetitions
OBSERVE C13, 125.6569642 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
H
N
Me
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

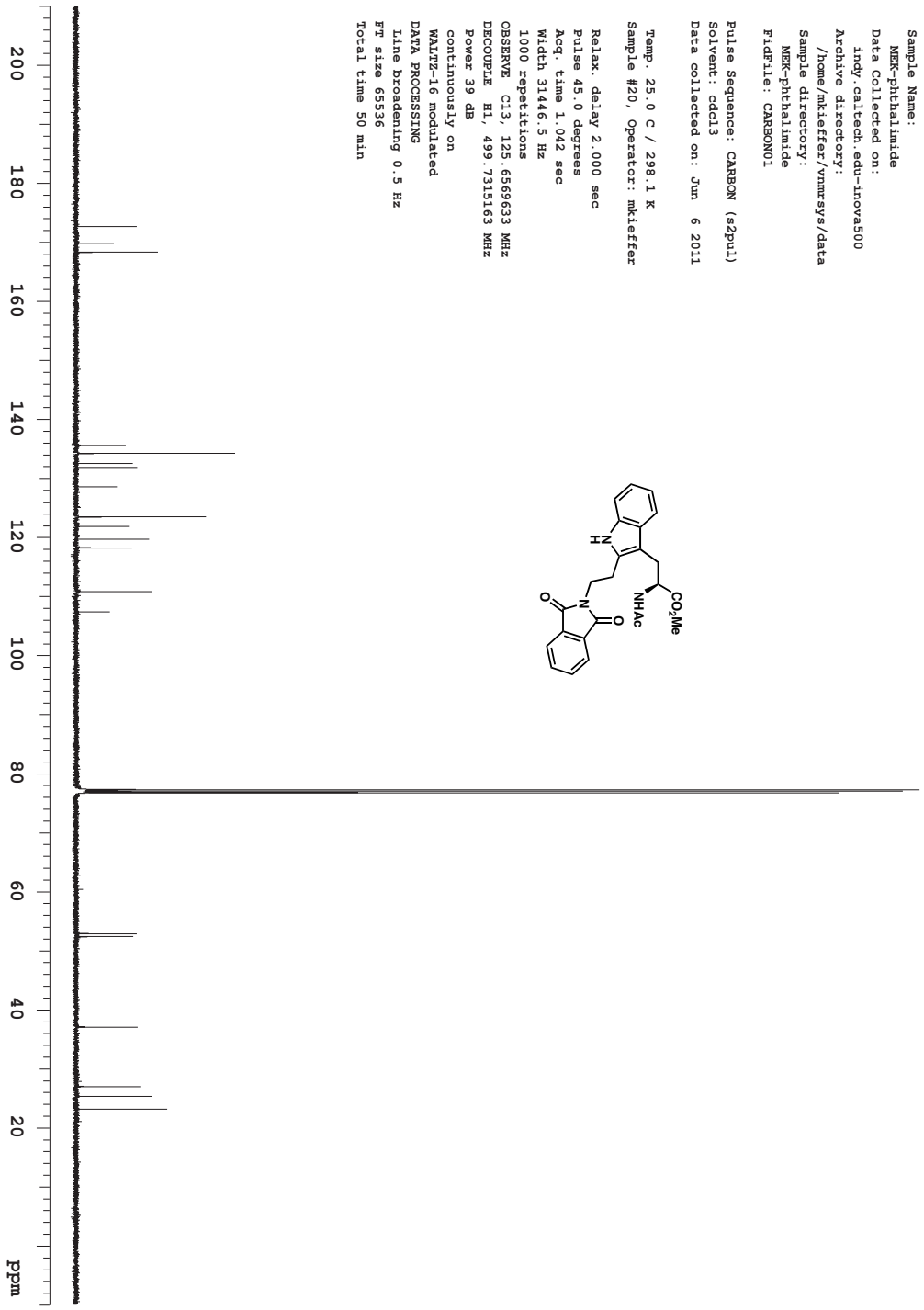

MEK3129-1
Sample Name:
MEK3129-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3129-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 7 2011
Temp. 25.0 C / 298.1 K
Sample #14, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
0.98
1.01
0.97
2.05
0.99
1.00
3.00
2.05
1.06
3.00
6.12
10
9
8
7
6
5
4
3
2
1
ppm
NHAc
CO2Me

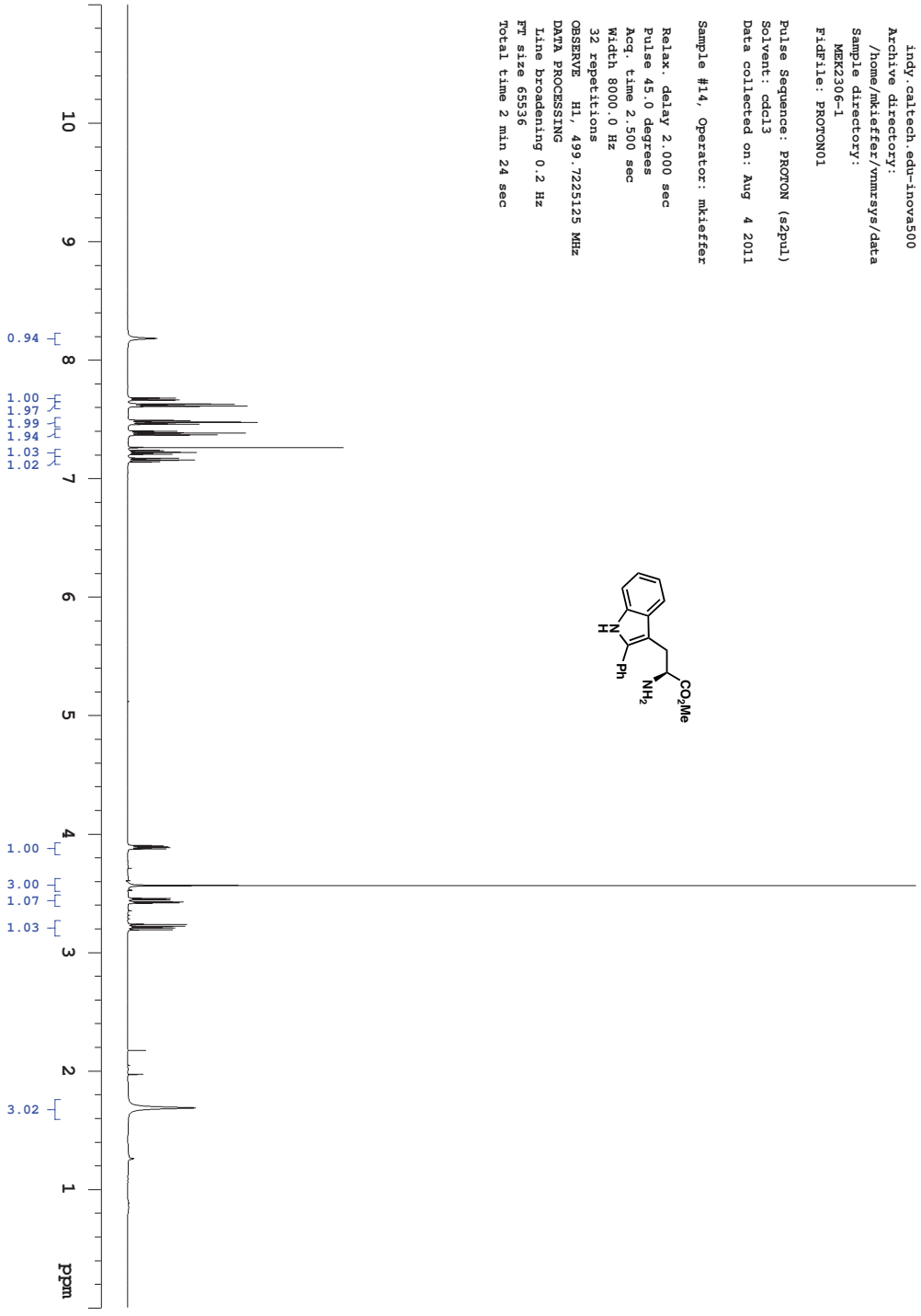

MEK3129-1
Sample Name:
MEK3129-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3129-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 7 2011
Temp. 25.0 C / 298.1 K
Sample #14, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6569671 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 26 min
NH
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

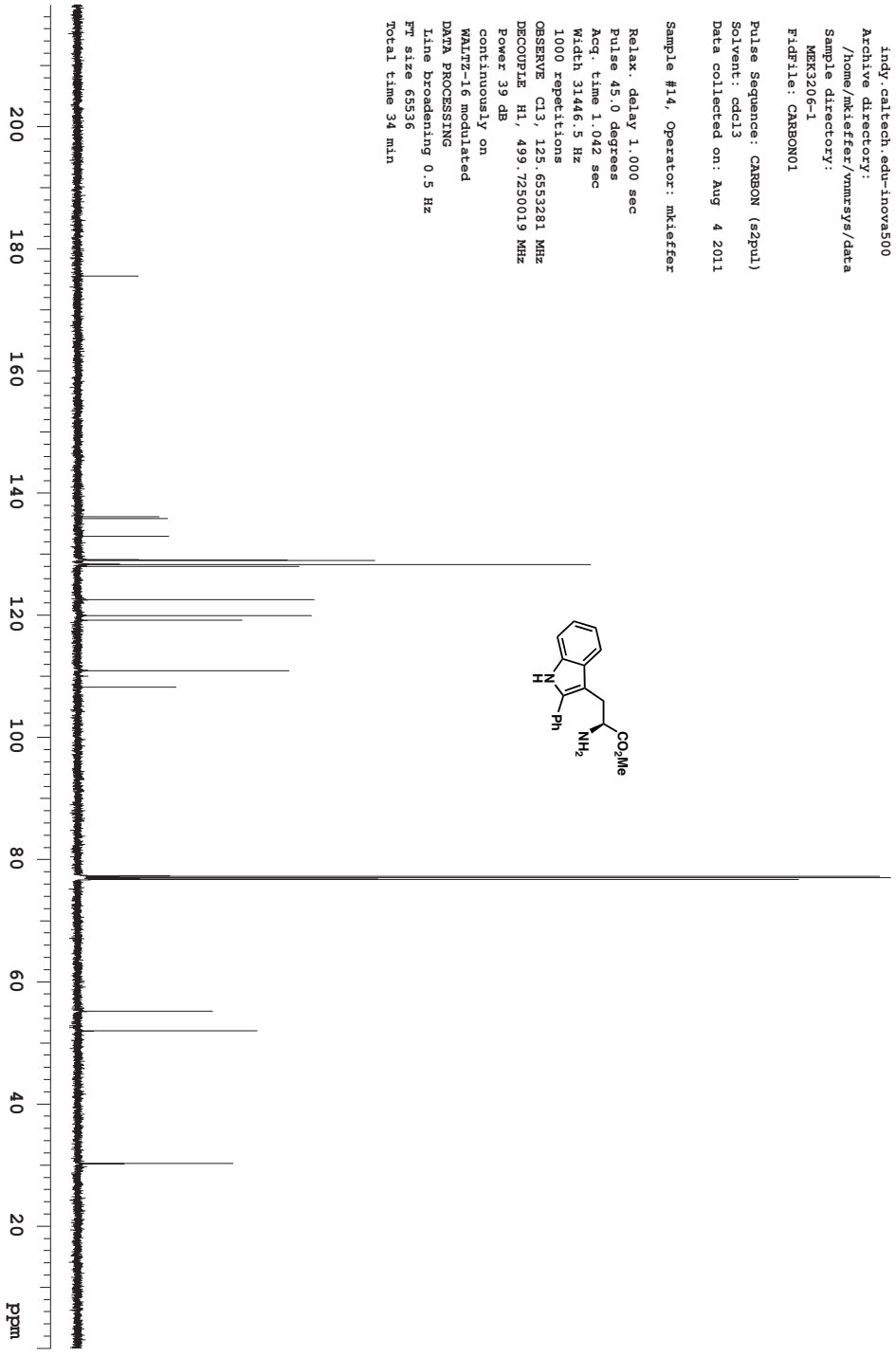

MEK-t-butyl-rac
Sample Name:
MEK-t-butyl-rac
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-t-butyl-rac
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 5 2011
Temp. 25.0 C / 298.1 K
Sample #27, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290200 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
1.01
1.03
0.99
2.11
0.99
0.99
3.00
2.10
3.08
8.91
NHAc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm

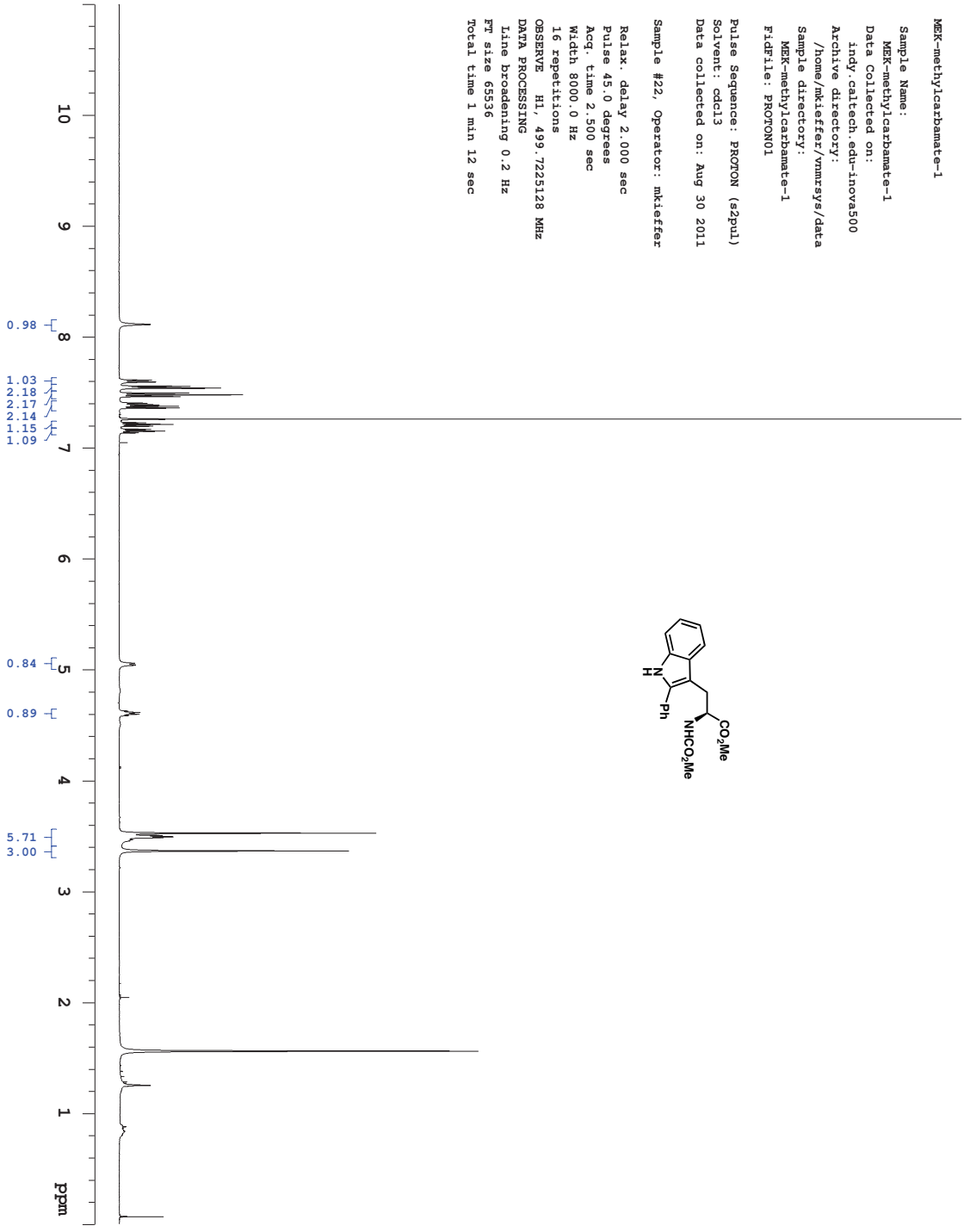

MEK-t-butyl-rac
Sample Name:
MEK-t-butyl-rac
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-t-butyl-rac
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 5 2011
Temp. 25.0 C / 298.1 K
Sample #27, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6569662 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 50 min
NH
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm


MEK-phthalimide
Sample Name:
MEK-phthalimide
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-phthalimide
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2011
Temp. 25.0 C / 298.1 K
Sample #20, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7290203 MHz
DATA PROCESSING
FT size 65536
Total time 2 min 24 sec
1.46
2.90
3.06
1.55
1.52
1.56
1.56
1.47
1.50
3.11
4.51
6.26
4.56
10
9
8
7
6
5
4
3
2
1
ppm
NHAc
CO2Me


MEK-phthalimide
Sample Name:
MEK-phthalimide
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-phthalimide
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 6 2011
Temp. 25.0 C / 298.1 K
Sample #20, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6569633 MHz
DECOUPLE H1, 499.7315163 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 50 min
NHAc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm


MEK2306-1
Sample Name:
MEK2306-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK2306-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 4 2011
Sample #14, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7225125 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 24 sec
0.94
1.00
1.97
1.99
1.94
1.03
1.02
1.00
3.00
1.07
1.03
3.02
10
9
8
7
6
5
4
3
2
1
ppm
N
H
Ph
NH2
CO2Me


MEK3206-1
Sample Name:
MEK3206-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3206-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 4 2011
Sample #14, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553281 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
N
H
Ph
NH2
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm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Data Collected on:
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Archive directory:
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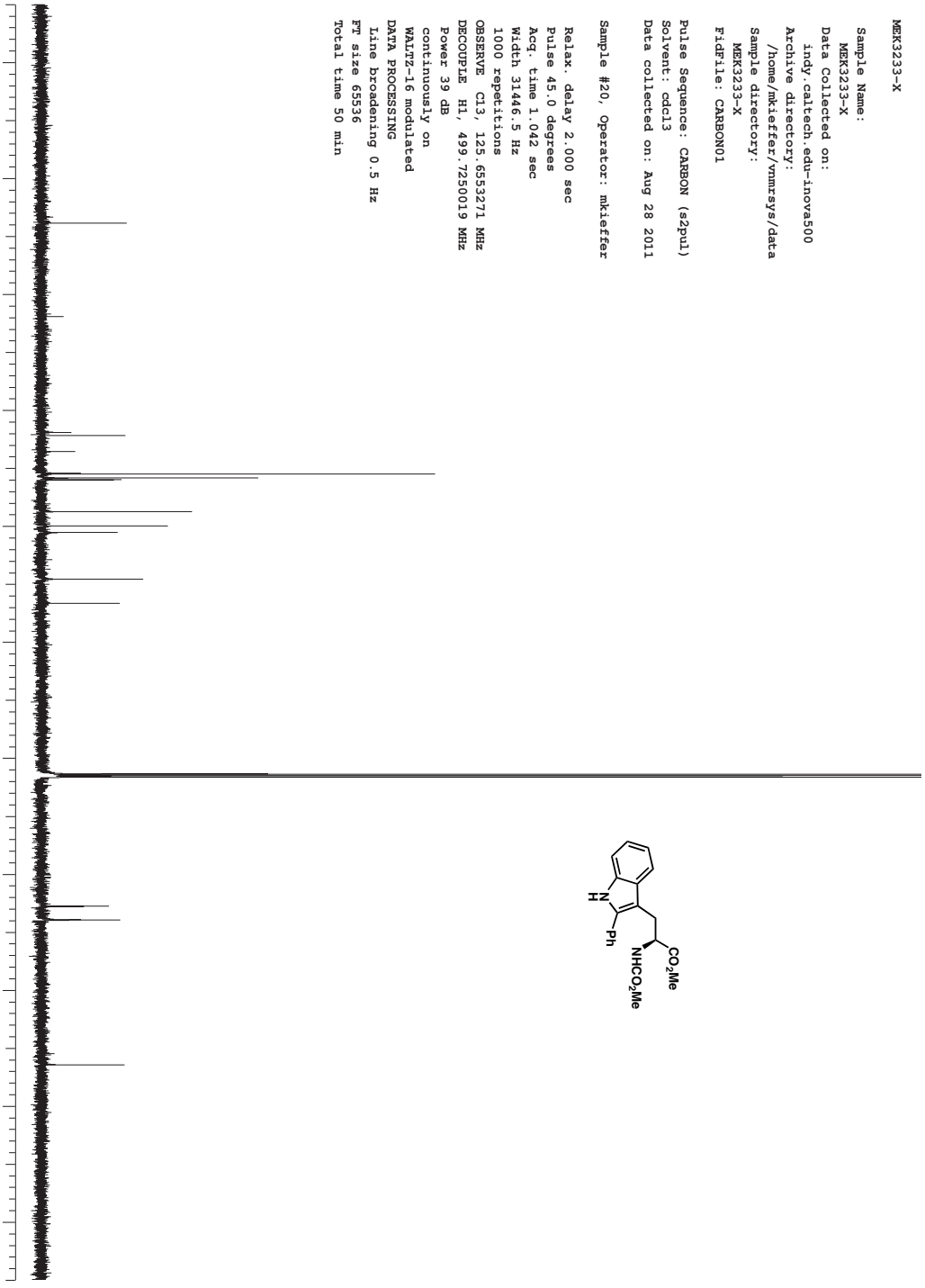
Sample directory:
MEK-methylcarbamate-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 30 2011
Sample #22, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225128 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min 12 sec
0.98
1.03
2.18
2.17
2.14
1.15
1.09
0.84
0.89
5.71
3.00
10
9
8
7
6
5
4
3
2
1
ppm
N
H
Ph
NHCO2Me
CO2Me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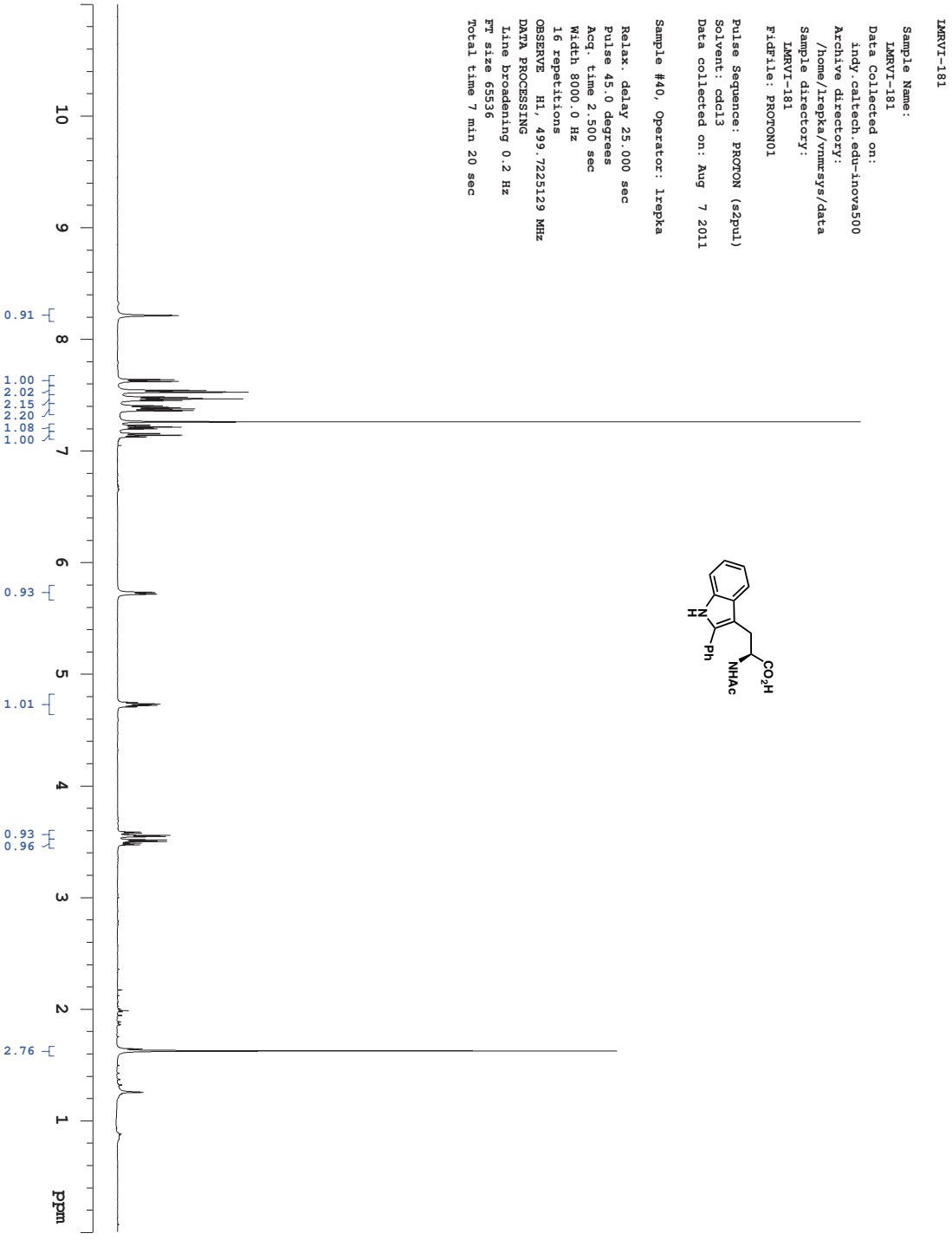
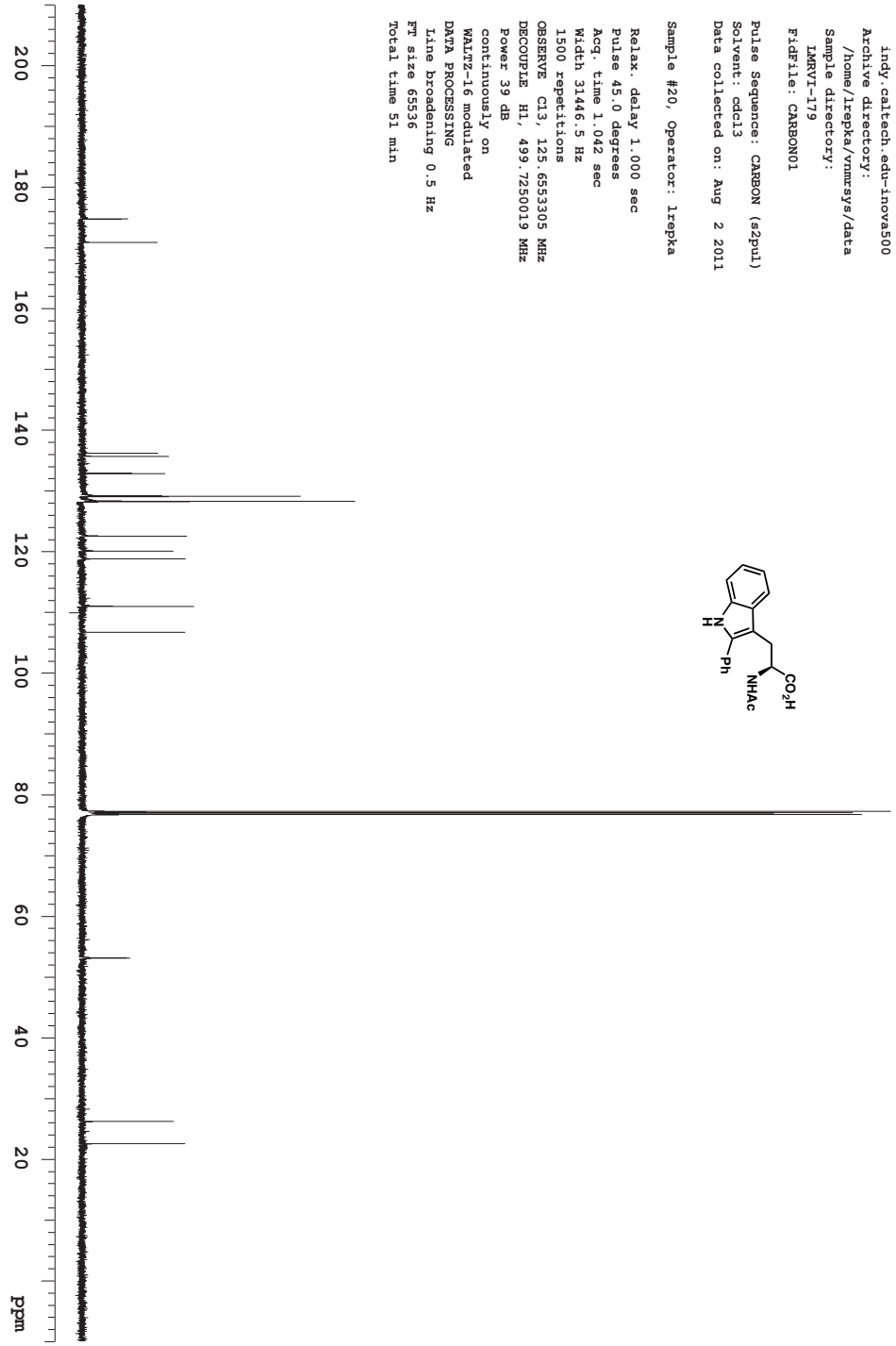
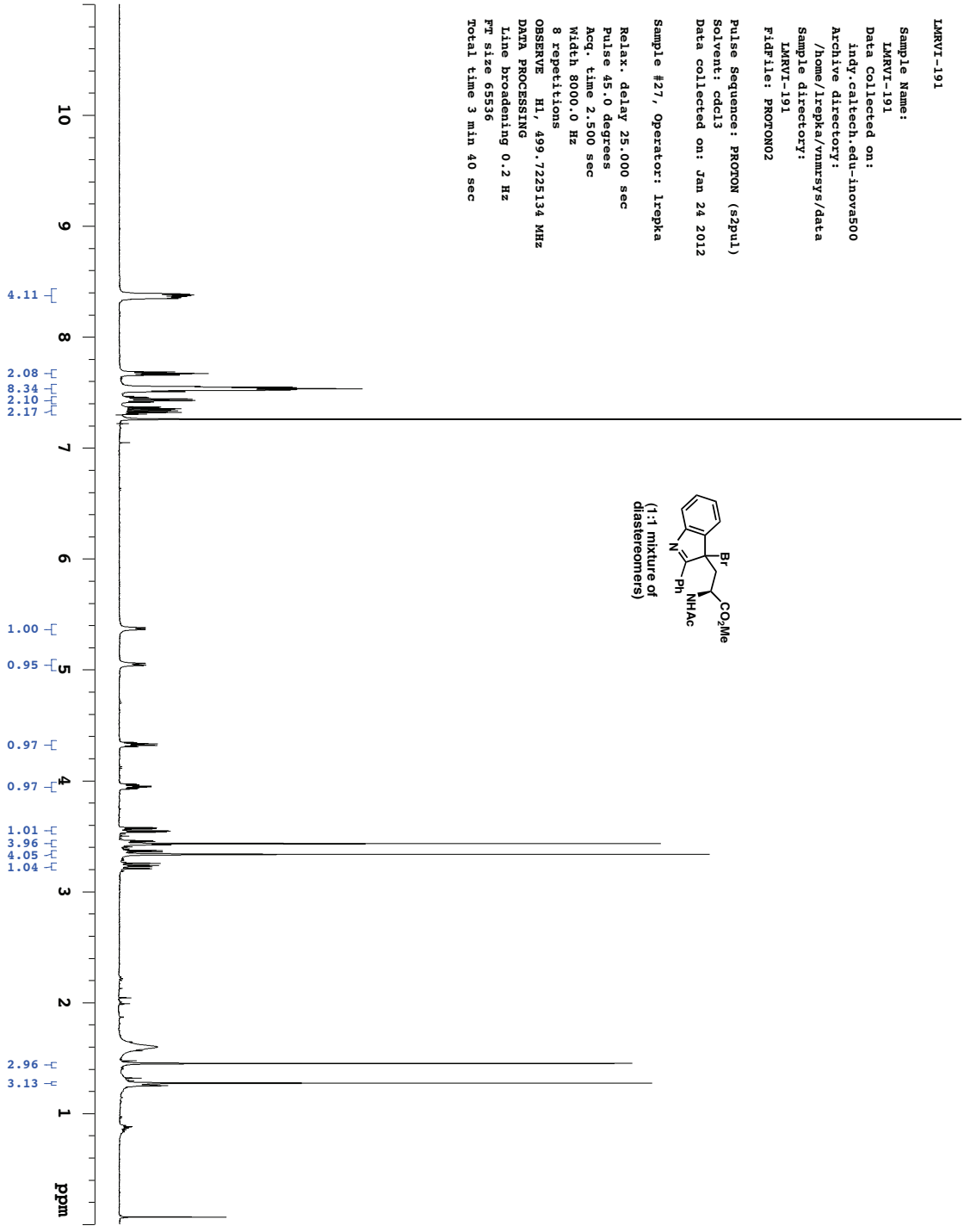
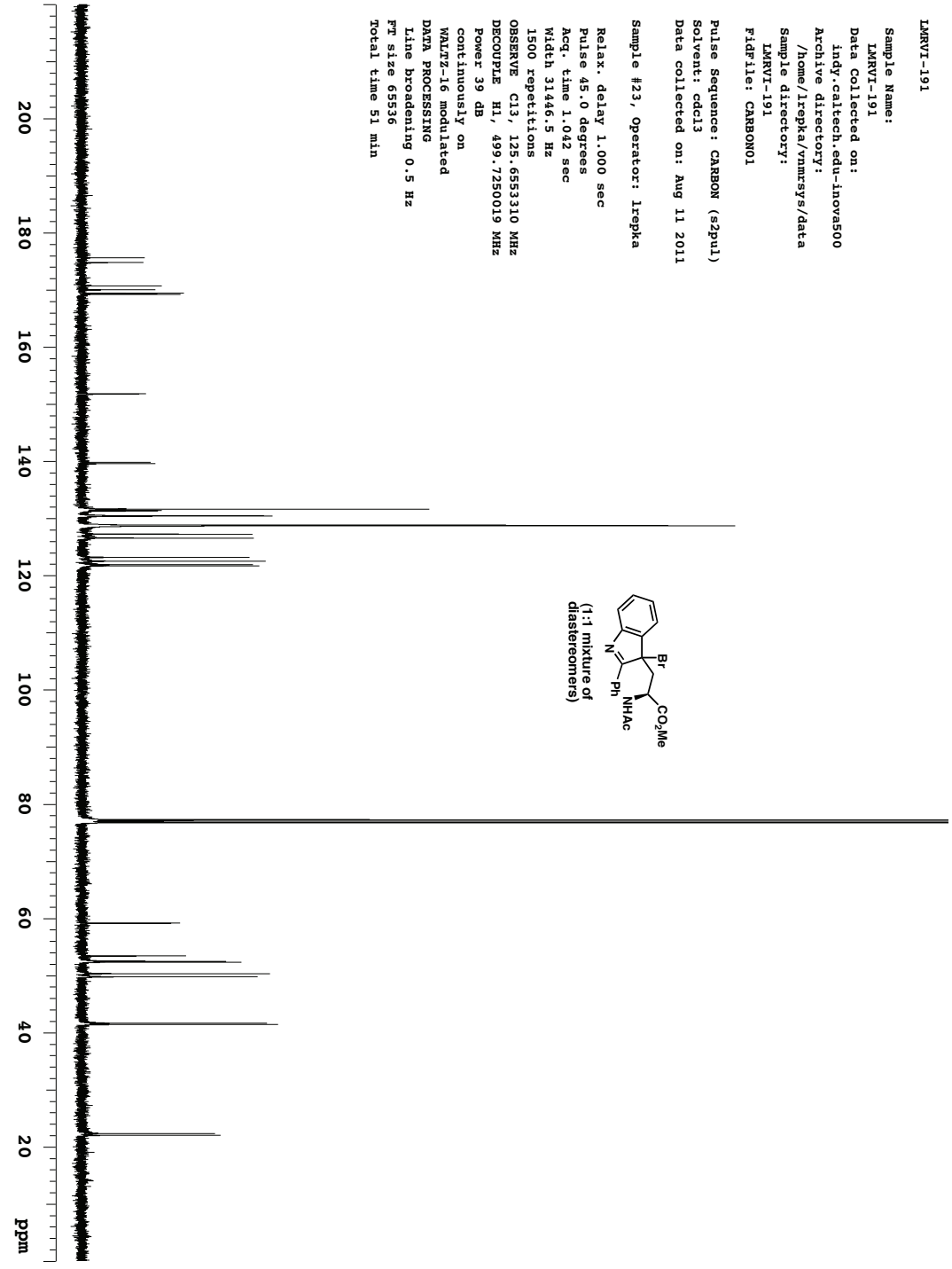
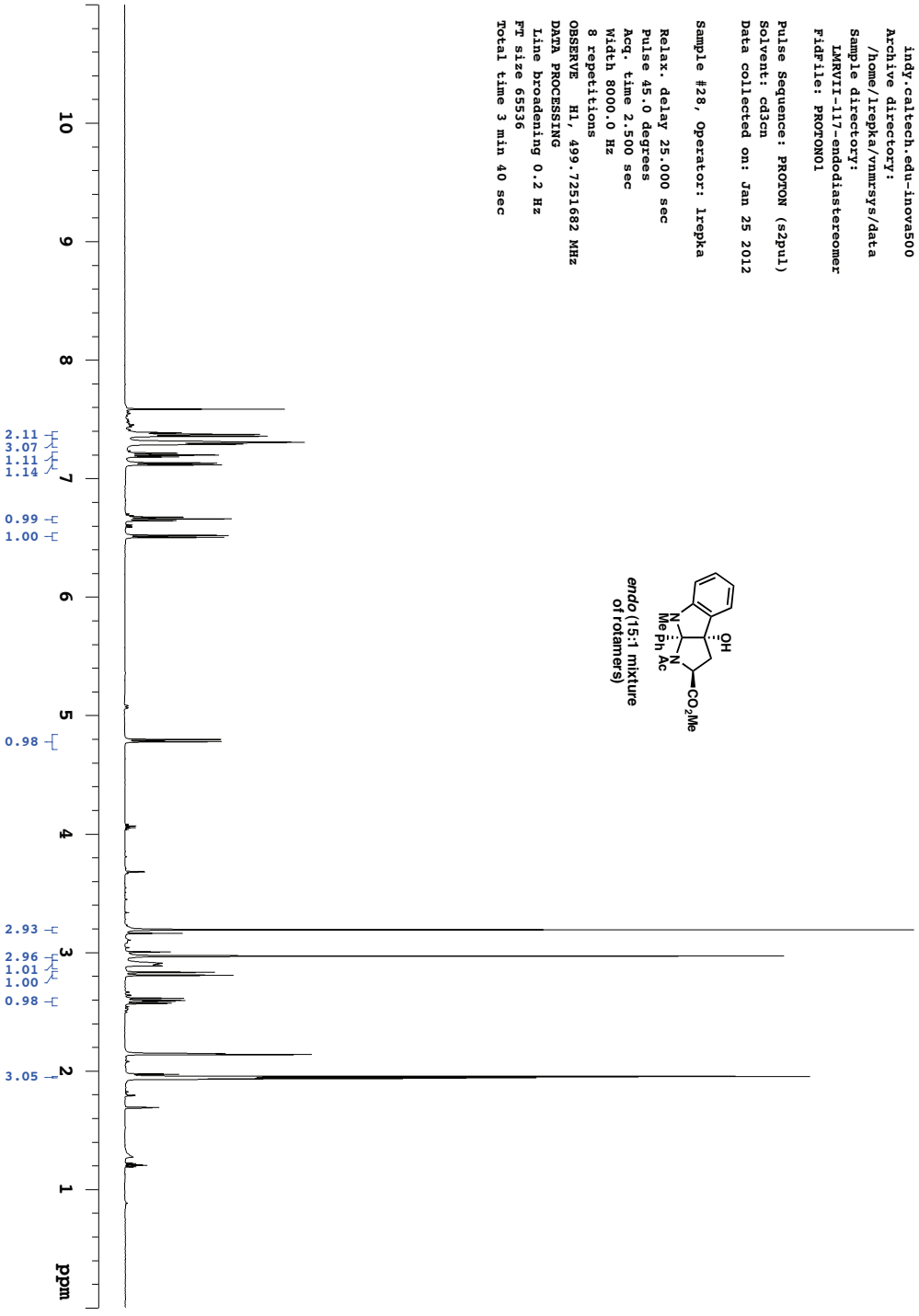
Sample Name:
MEK3233-X
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK3233-X
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 28 2011
Sample #20, Operator: mkieffer
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6553271 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 50 min
N
H
Ph
NHCO2Me
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

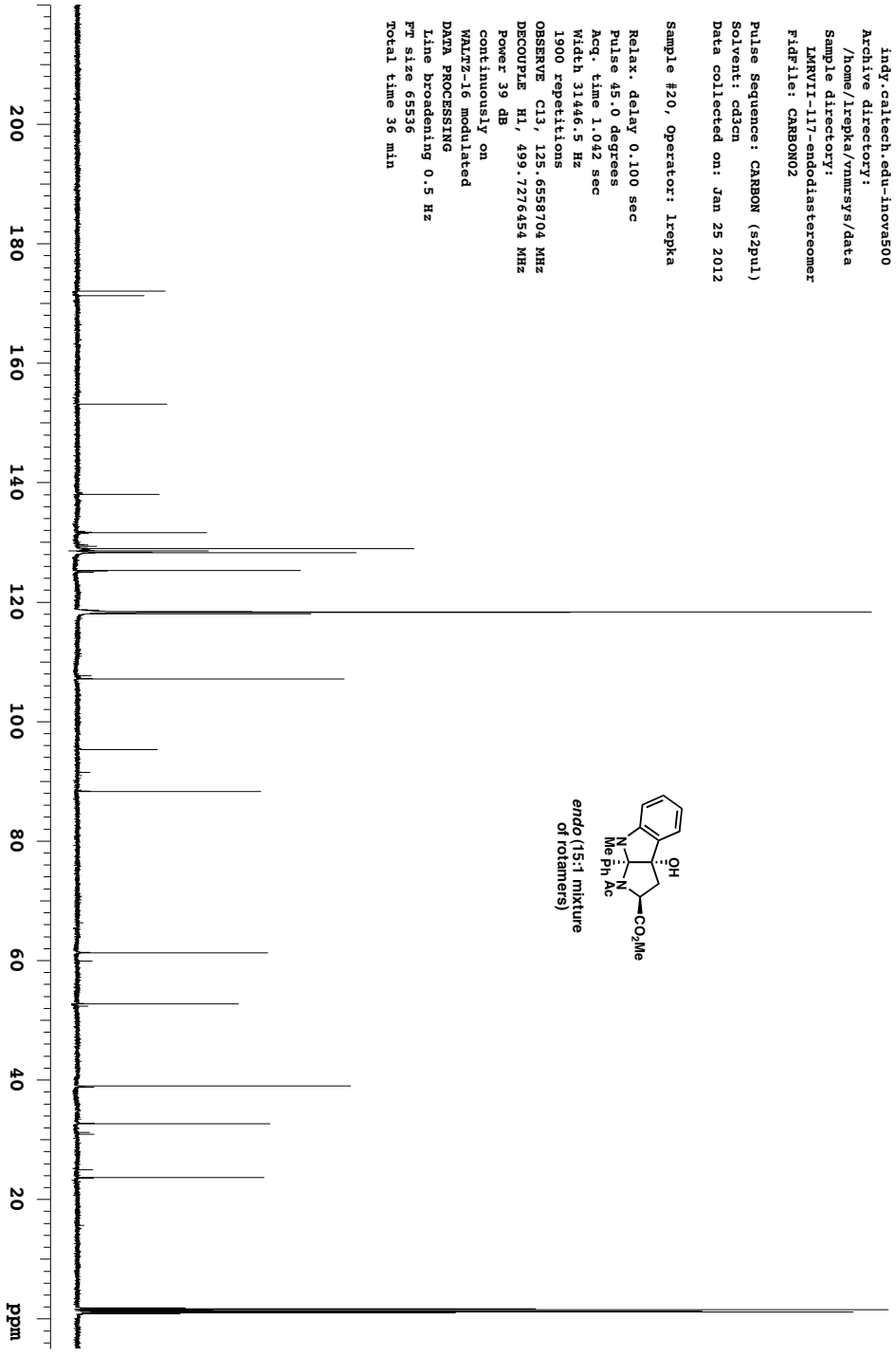

IMRVI-181
Sample Name:
IMRVI-181
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
IMRVI-181
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Aug 7 2011
Sample #40, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.7225129 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 7 min 20 sec
0.91
1.00
2.02
2.15
2.20
1.08
1.00
0.93
1.01
0.93
0.96
2.76
10
9
8
7
6
5
4
3
2
1
ppm
N
H
Ph
NHAc
CO2H

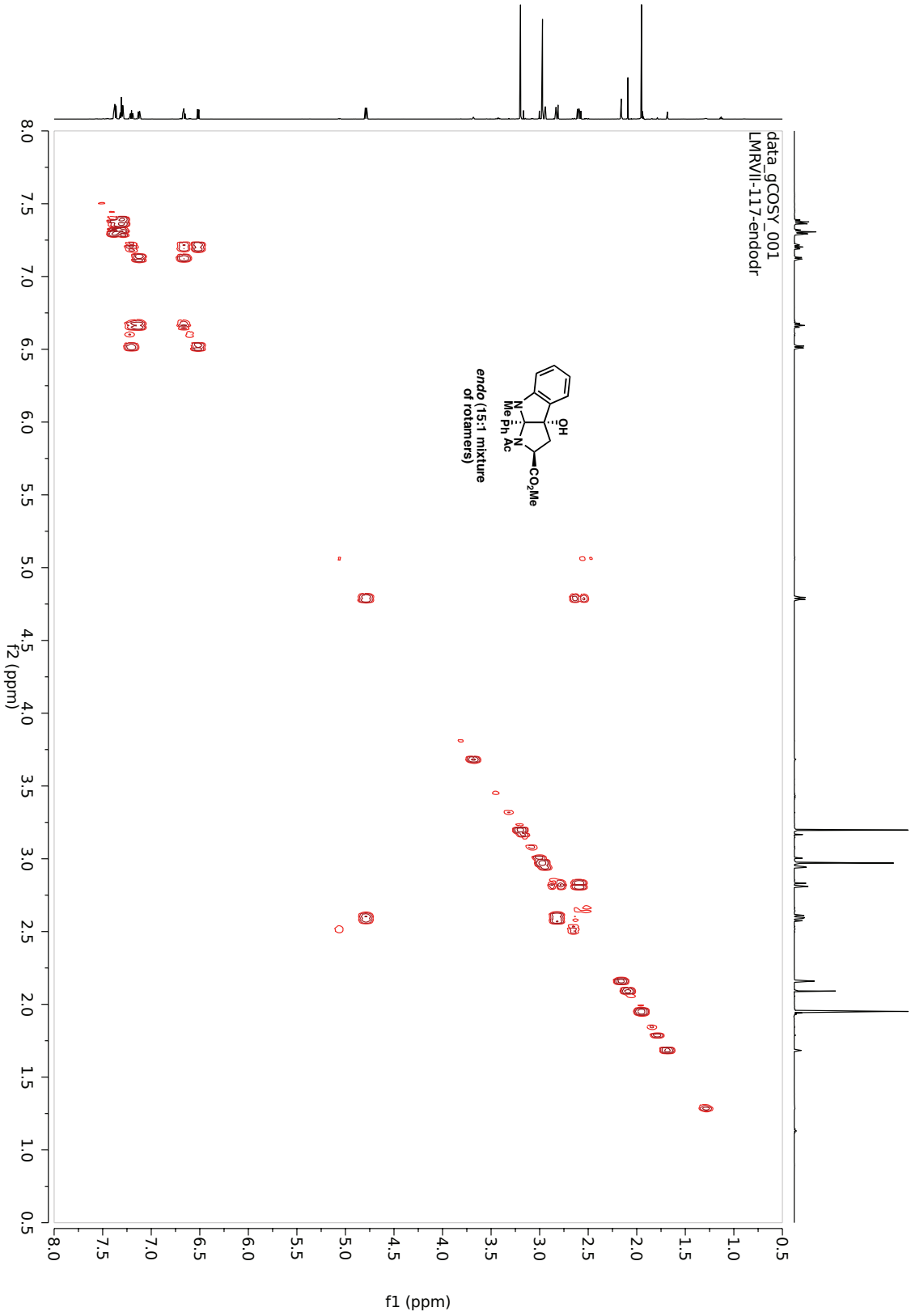

IMRVI-179
Sample Name:
IMRVI-179
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
IMRVI-179
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 2 2011
Sample #20, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6553305 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
H
N
Ph
NHAc
CO2H
200
180
160
140
120
100
80
60
40
20
ppm

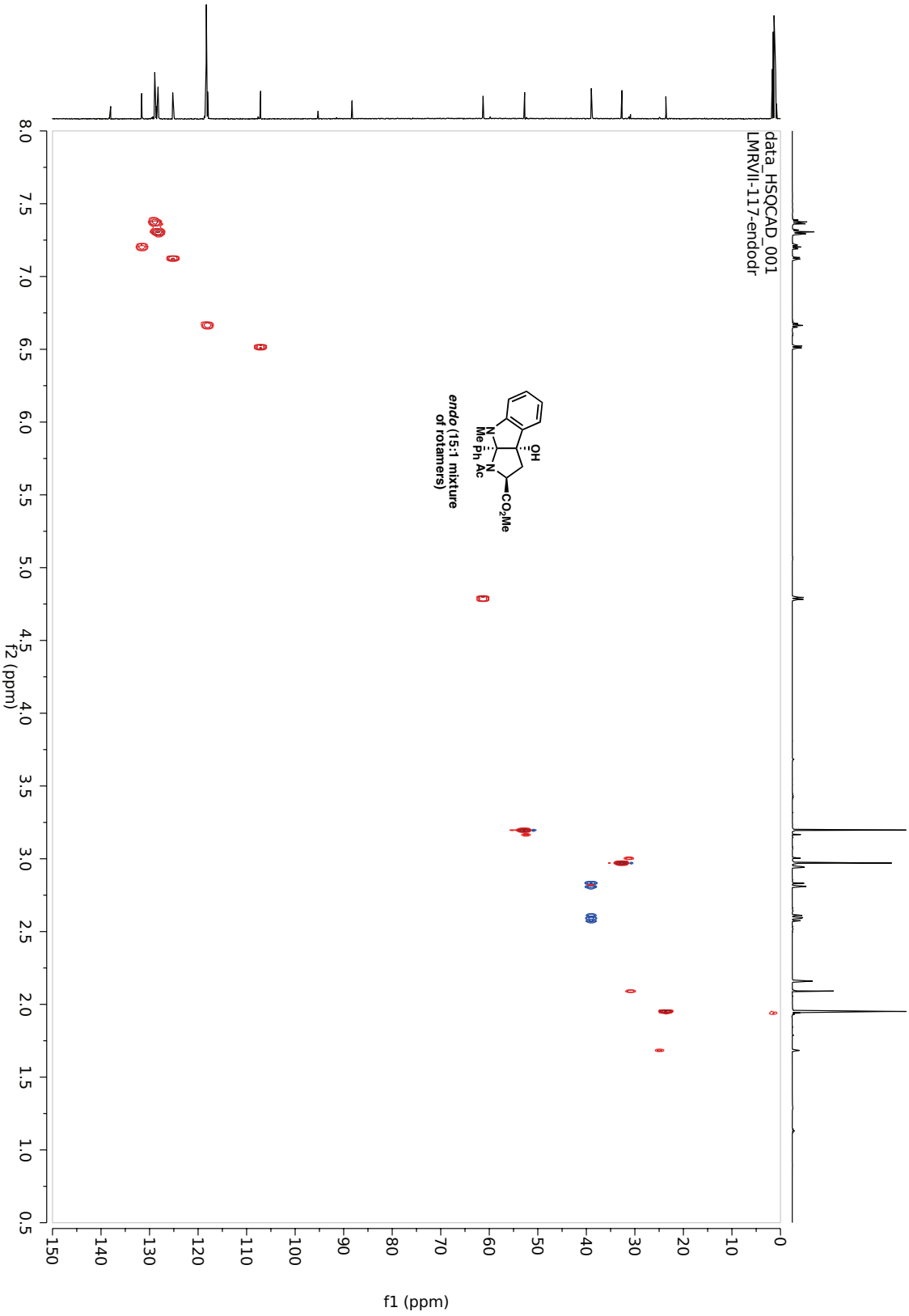

LMRVI-191
Sample Name:
LMRVI-191
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-191
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 24 2012
Sample #27, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7225134 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
(1:1 mixture of diastereomers)
Br
CO2Me
NHAc
Ph
N
4.11
2.08
8.34
2.10
2.17
1.00
0.95
0.97
0.97
1.01
3.96
4.05
1.04
2.96
3.13
10
9
8
7
6
5
4
3
2
1
ppm

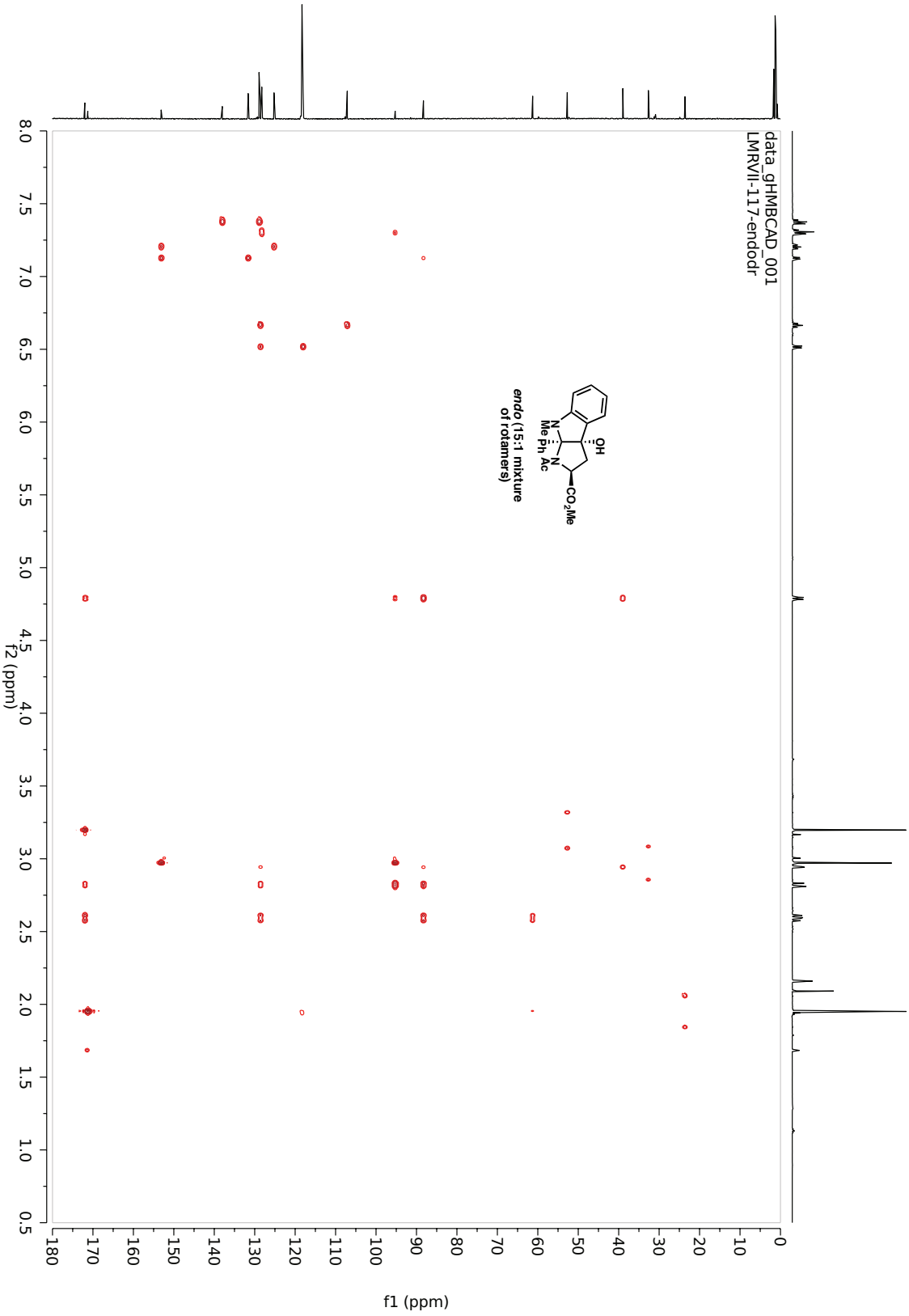

LMRVI-191
Sample Name:
LMRVI-191
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVI-191
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Aug 11 2011
Sample #23, Operator: lrepka
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.655310 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
Br
N
Ph
NHAc
CO2Me
(1:1 mixture of diastereomers)
200
180
160
140
120
100
80
60
40
20
ppm

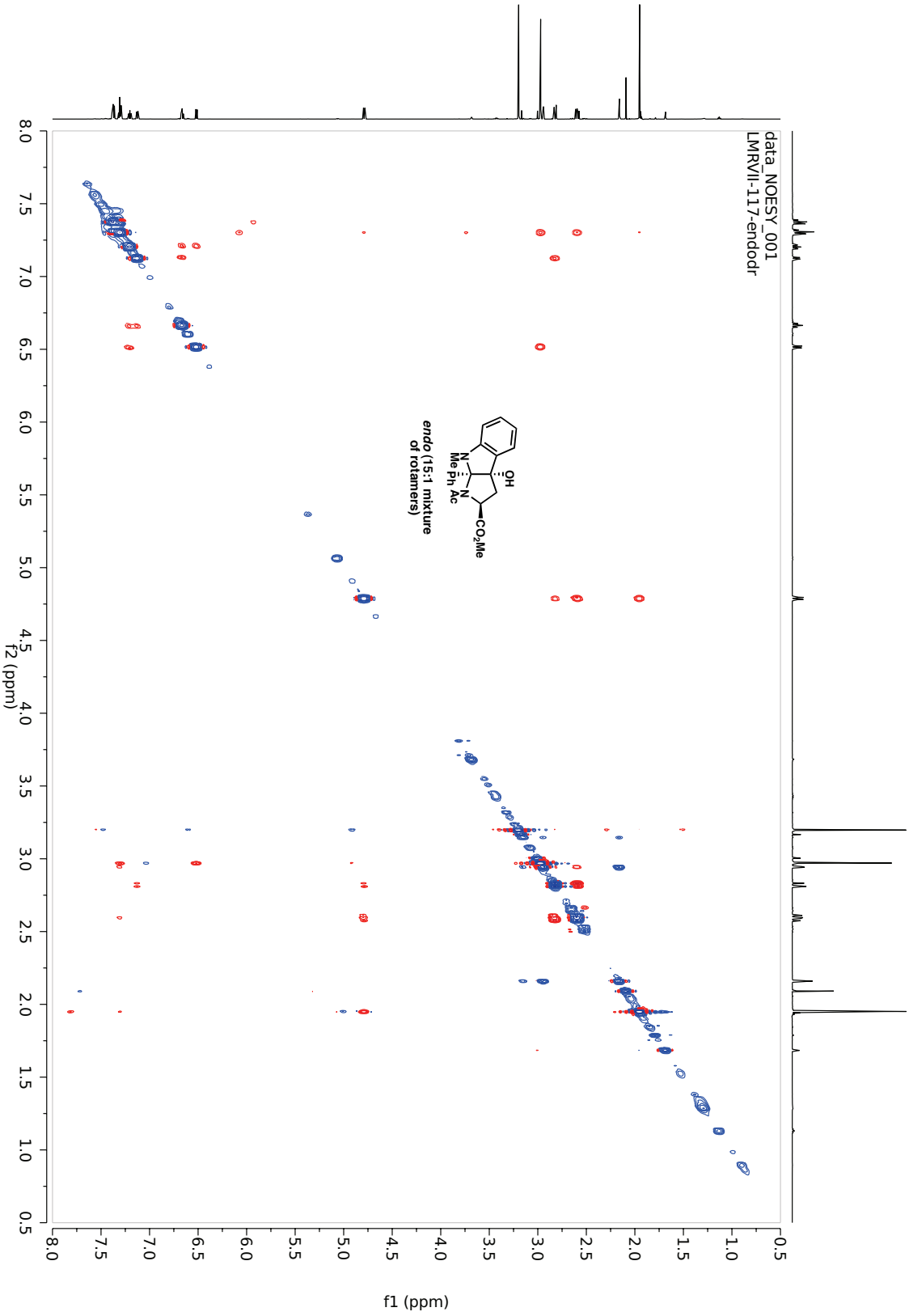

LMRVII-117-endodiastereomer
Sample Name:
LMRVII-117-endodiastereomer
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVII-117-endodiastereomer
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jan 25 2012
Sample #28, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7251682 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
endo (15:1 mixture of rotamers)
Me
Ph
Ac
OH
CO2Me
2.11
3.07
1.11
1.14
0.99
1.00
0.98
2.93
2.96
1.01
1.00
0.98
3.05
10
9
8
7
6
5
4
3
2
1
ppm

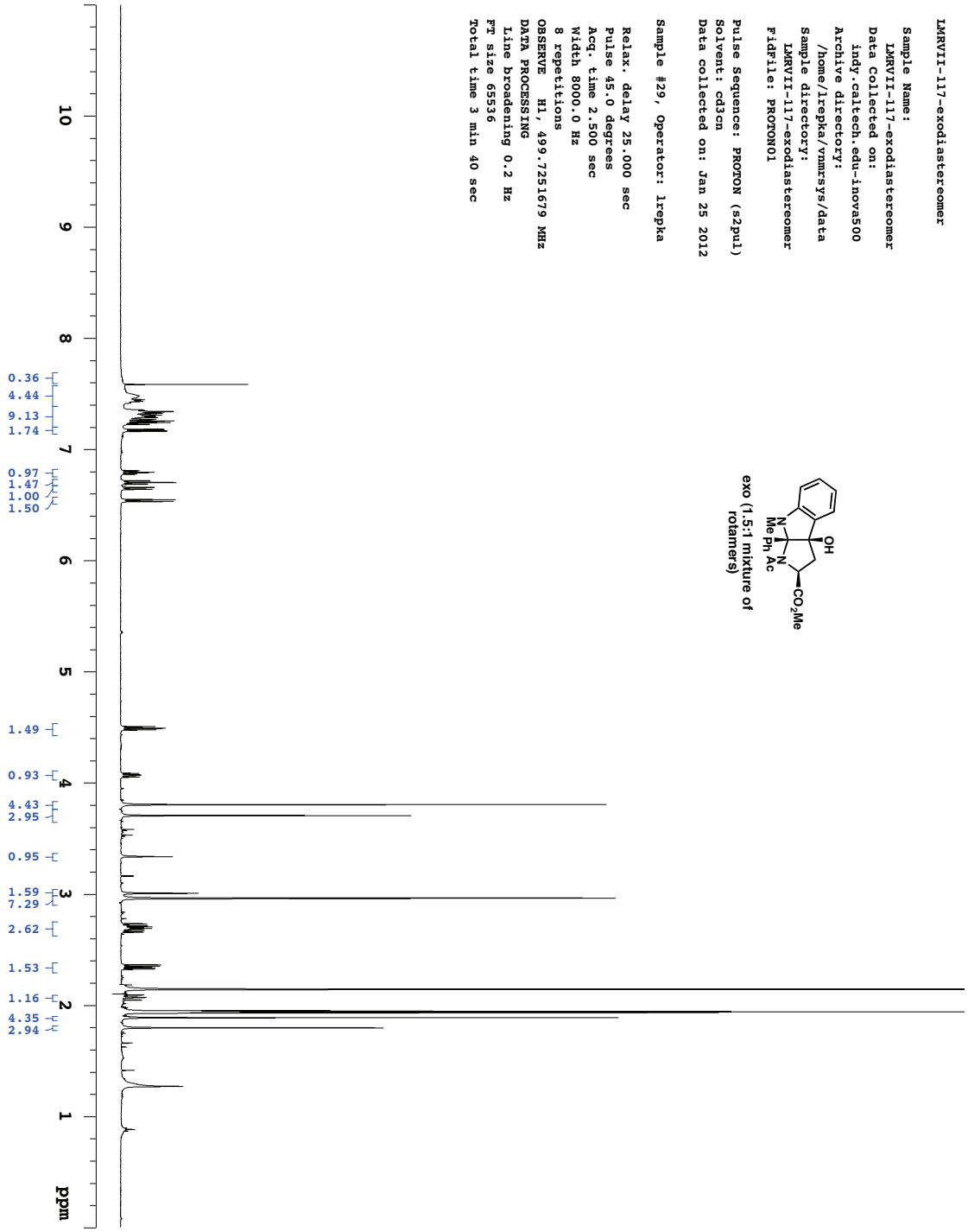

LMRVII-117-endodiastereomer
Sample Name:
LMRVII-117-endodiastereomer
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVII-117-endodiastereomer
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jan 25 2012
Sample #20, Operator: lrepka
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1900 repetitions
OBSERVE C13, 125.6558704 MHz
DECOUPLE H1, 499.7276454 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 36 min
OH
N
Me
Ph
N
Ac
CO2Me
endo (15:1 mixture of rotamers)
200
180
160
140
120
100
80
60
40
20
ppm

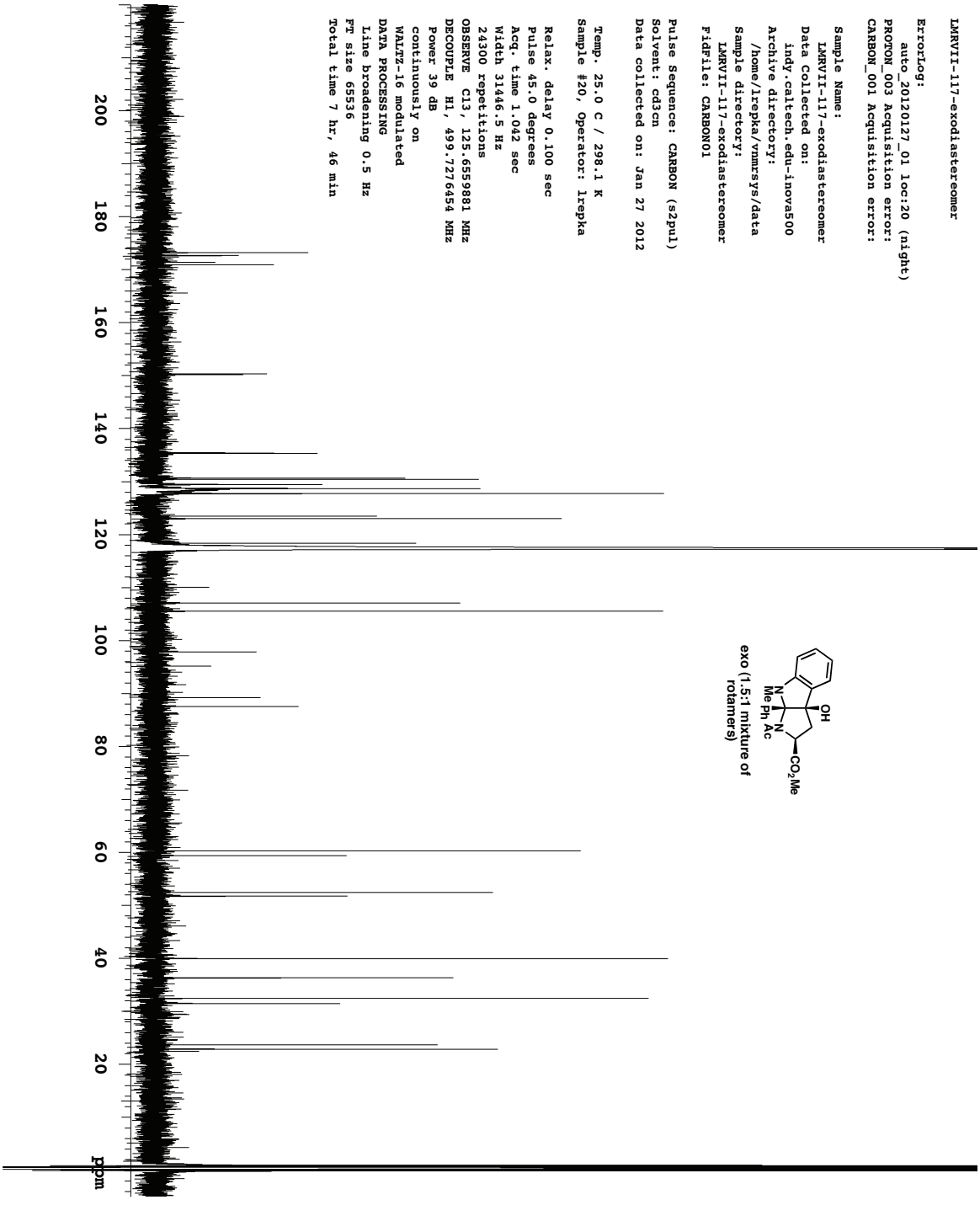

data_gCOSY_001
LMRVII-117-endodr
endo (15:1 mixture of rotamers)
OH
CO2Me
Me
Ph
Ac
f2 (ppm)
f1 (ppm)

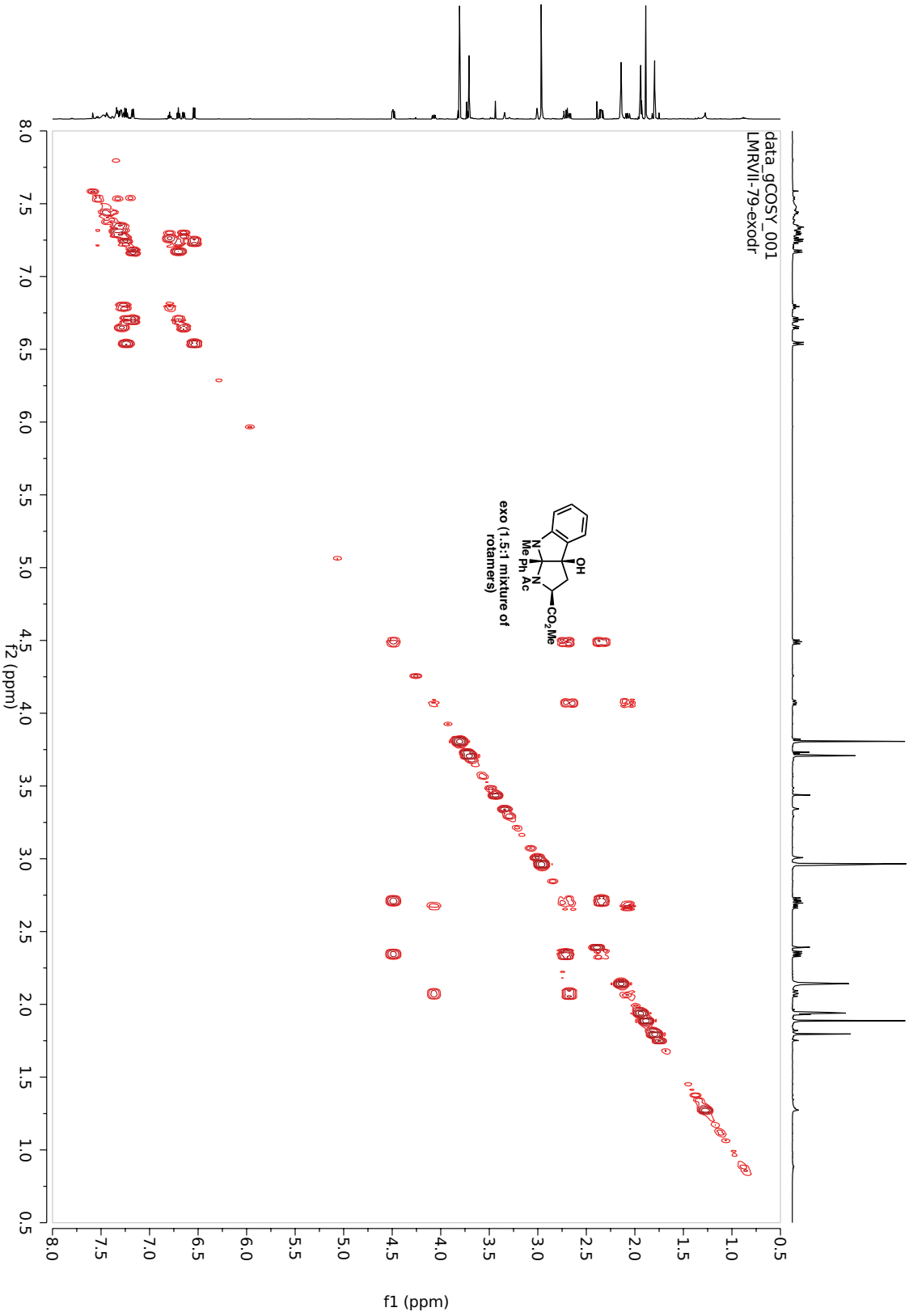

data_HSQCAD_001
LMRVII-117-endodr
endo (15:1 mixture of rotamers)
f1 (ppm)
f2 (ppm)

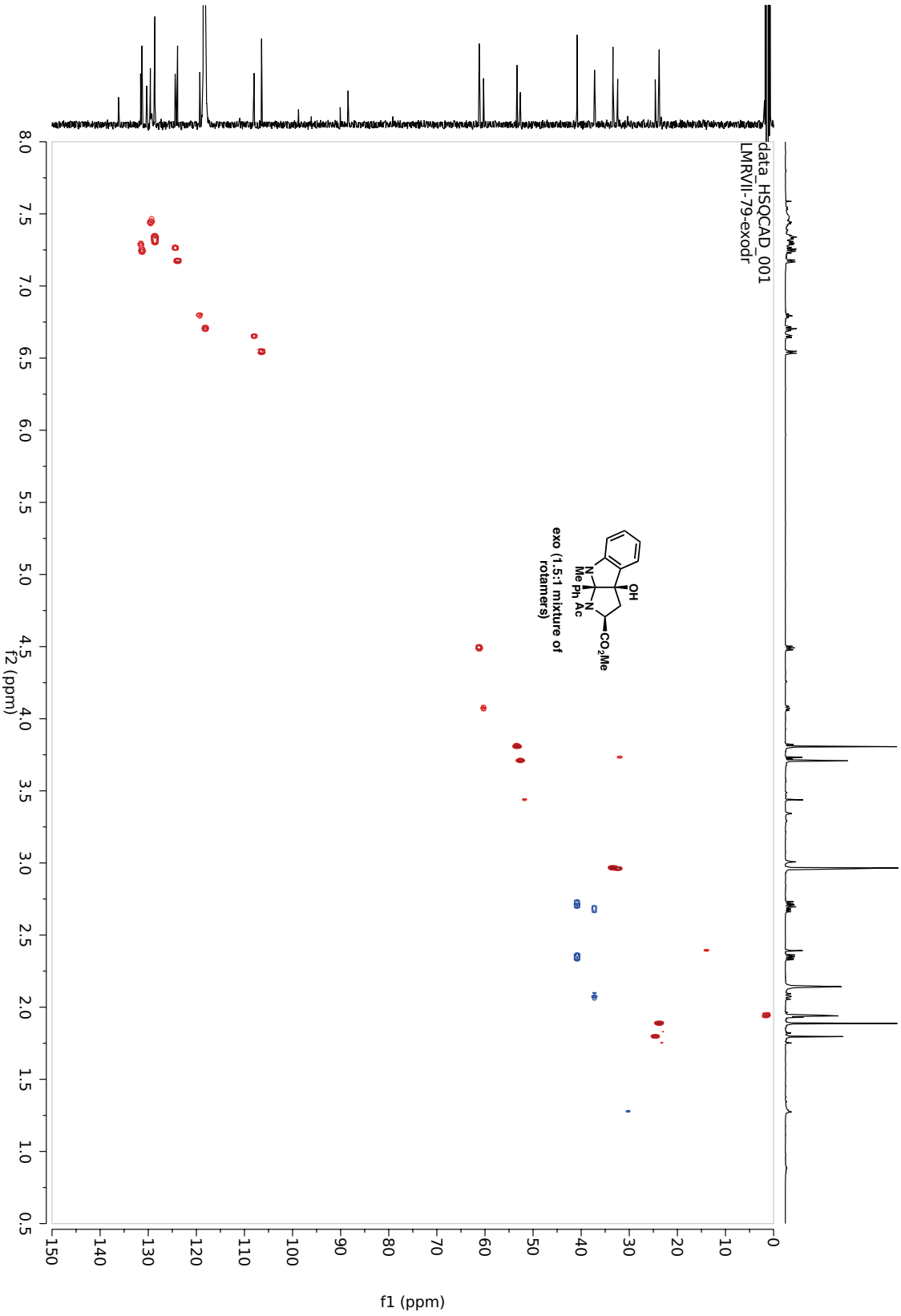

data_gHMBCAD_001
LMRVII-117-endodr
endo (15:1 mixture of rotamers)
f2 (ppm)
f1 (ppm)

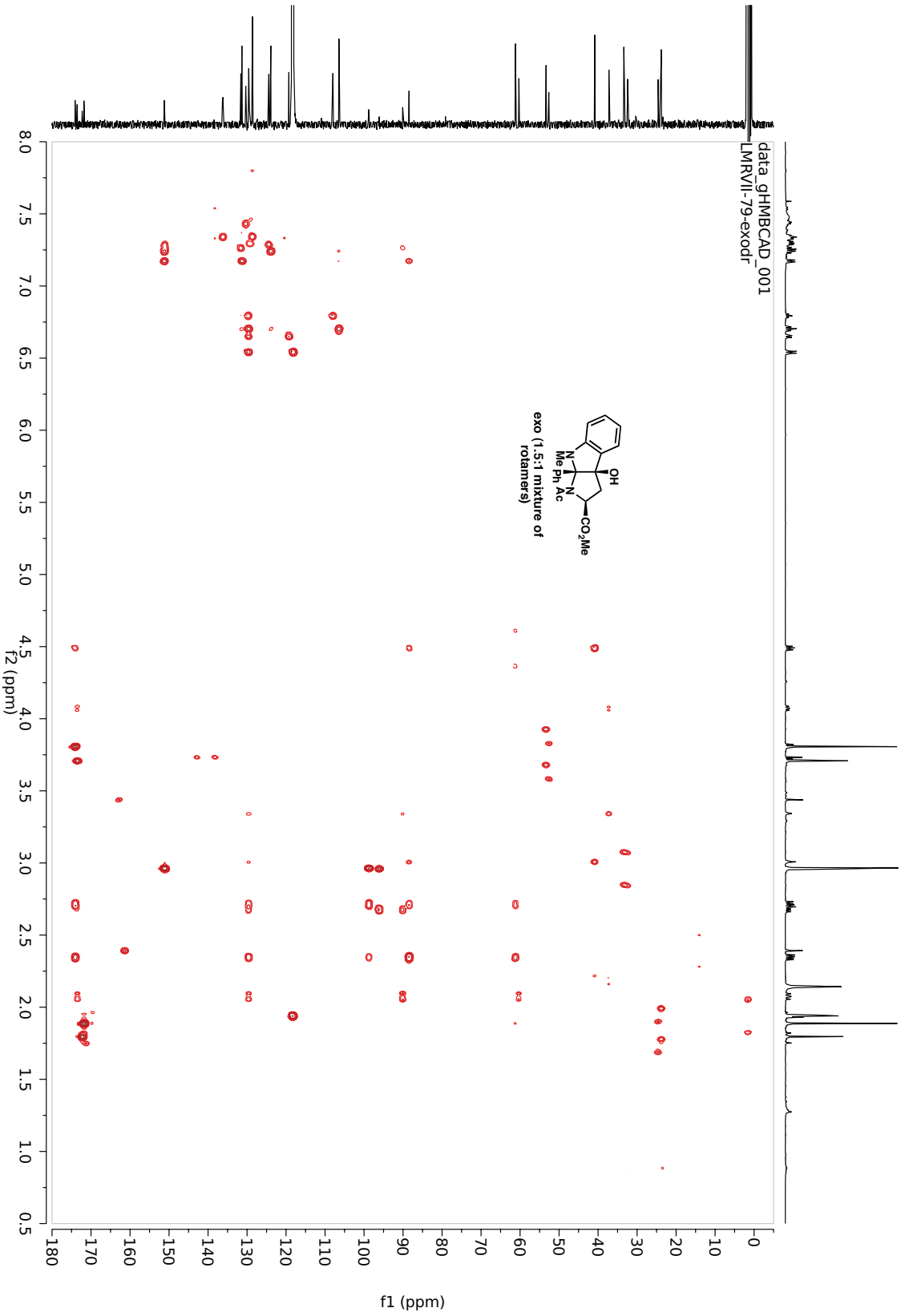

data_NOESY_001
LMRVII-117-endodr
endo (15:1 mixture of rotamers)
f1 (ppm)
f2 (ppm)

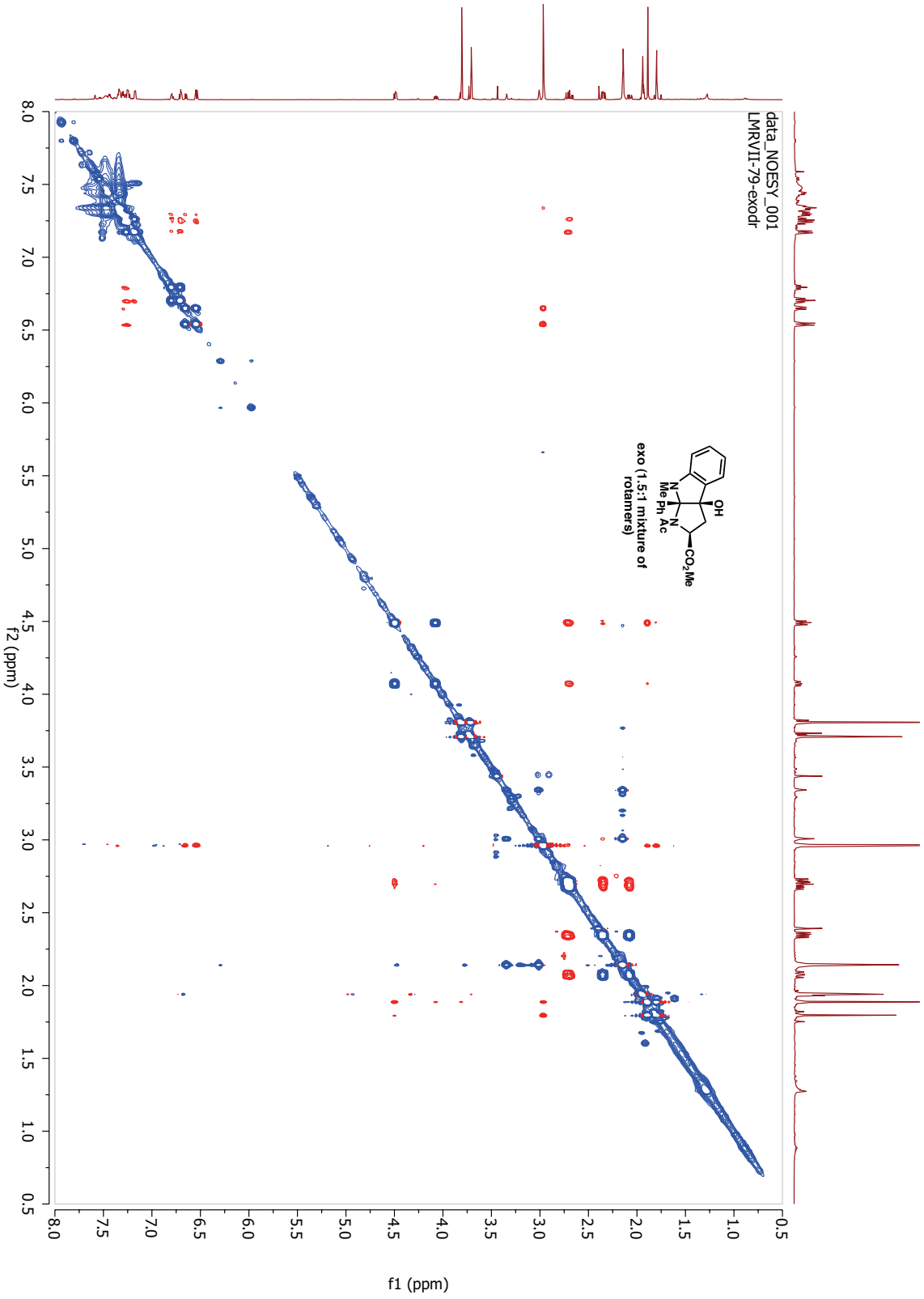

LMRVII-117-exodiastereomer
Sample Name:
LMRVII-117-exodiastereomer
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVII-117-exodiastereomer
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jan 25 2012
Sample #29, Operator: lrepka
Relax. delay 25.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7251679 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 3 min 40 sec
exo (1.5:1 mixture of rotamers)
OH
N
N
Me
Ph
Ac
CO2Me
0.36
4.44
9.13
1.74
0.97
1.47
1.00
1.50
1.49
0.93
4.43
2.95
0.95
1.59
7.29
2.62
1.53
1.16
4.35
2.94
10
9
8
7
6
5
4
3
2
1
ppm


LMRVII-117-exodiastereomer
ErrorLog:
auto_20120127_01 loc:20 (night)
PROTON_003 Acquisition error:
CARBON_001 Acquisition error:
Sample Name:
LMRVII-117-exodiastereomer
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/lrepka/vnmrsys/data
Sample directory:
LMRVII-117-exodiastereomer
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jan 27 2012
Temp. 25.0 C / 298.1 K
Sample #20, Operator: lrepka
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
24300 repetitions
OBSERVE C13, 125.6559881 MHz
DECOUPLE H1, 499.7276454 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 7 hr, 46 min
OH
N
Me
Ph
N
Ac
CO2Me
exo (1.5:1 mixture of rotamers)
200
180
160
140
120
100
80
60
40
20
ppm


data_gCOSY_001
LMRVII-79-exodr
exo (1.5:1 mixture of rotamers)
f1 (ppm)
f2 (ppm)


data_HSQCAD_001
LMRVII-79-exodr
exo (1.5:1 mixture of rotamers)
f1 (ppm)
f2 (ppm)


data_gHMBCAD_001
LMRVII-79-exodr
exo (1.5:1 mixture of rotamers)
f1 (ppm)
f2 (ppm)


data_NOESY_001
LMRVII-79-exodr
exo (1.5:1 mixture of rotamers)
f1 (ppm)
f2 (ppm)

Chapter 3

Direct and Selective Copper-Catalyzed Arylation of Tryptamines and Tryptophans: Total Synthesis of (+)-Naseseazines A and B[†]

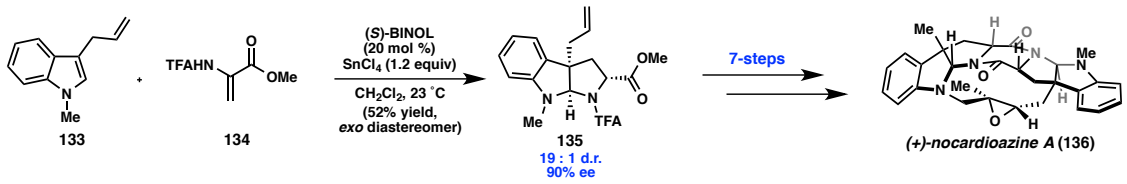
3.1 INTRODUCTION

3.1.1 Limitation of the Formal (3+2) Methodology

The pyrroloindoline is a common structural motif that unites several biosynthetically distinct families of alkaloids.[1] As discussed in **Chapters 1** and **2**, our lab has developed an enantioselective method to access this scaffold through the formal (3+2) cycloaddition of 3-substituted indoles and 2-amido acrylates. This strategy has been subsequently applied in the synthesis of several distinct natural products.[2] For example, 3-allyl pyrroloindoline **135,** prepared in 52% yield and 90% ee from 3-allylindole, can be advanced in only seven-steps to the macrocyclic natural product, (+)-nocardioazine A (**136**), a p-glycoprotein inhibitor.[3]

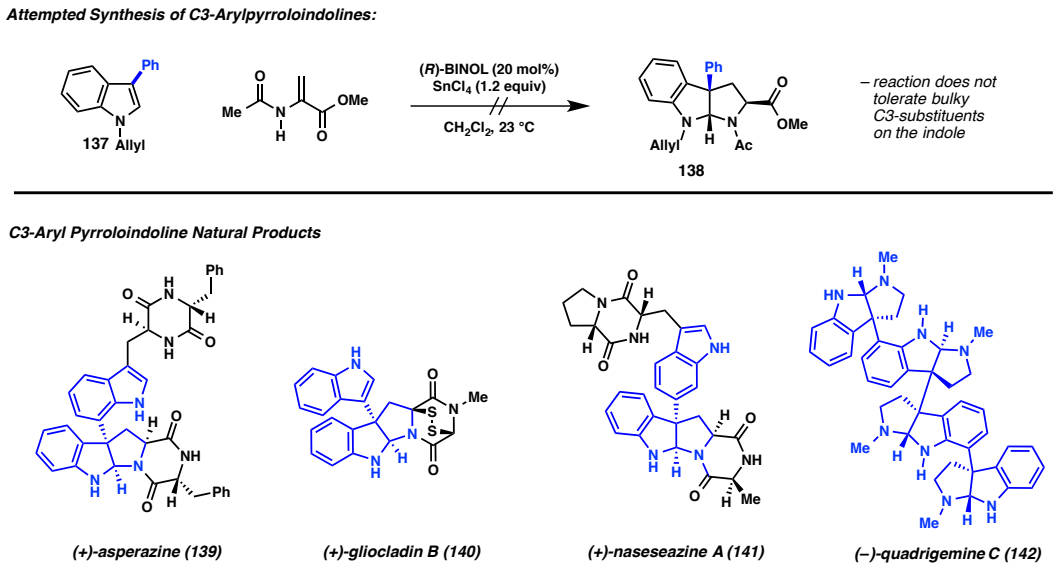
[†] Portions of this chapter have been reproduced from published studies (Kieffer, M. E.; Chuang, K. V.; Reisman, S. E. *Chem. Sci.* **2012**, *3*, 3170 – and – Kieffer, M. E.[★]; Chuang, K. V.[★]; Reisman, S. E. *J. Am. Chem. Soc.* **2013**, *135*, 5557) and the supporting information found therein. Work was conducted in collaboration with Kangway V. Chuang.

Scheme 3.1. *Total synthesis of (+)-nocardioazine A*



One major limitation of this convergent methodology is the inability to utilize indoles bearing bulky C3 substituents. For instance, *N*-allyl-3-phenylindole (**137**) fails to react under the optimized conditions, even after prolonged reaction times and more forcing conditions. This finding proved to be particularly unfortunate due to the prevalence of an important subclass of pyrroloindoline natural products characterized by a C3-quaternary center bearing an *aryl* substituent (**Figure 3.1**). These compounds, including quadrigemine C (**142**) and gliocladine B (**140**), exhibit potent biological activity, yet methods for their efficient preparation have remained a challenge in modern synthetic chemistry.[4,5] This chapter describes our efforts towards the development of a complementary and direct arylation reaction in order to gain convergent access to this subclass of natural products.

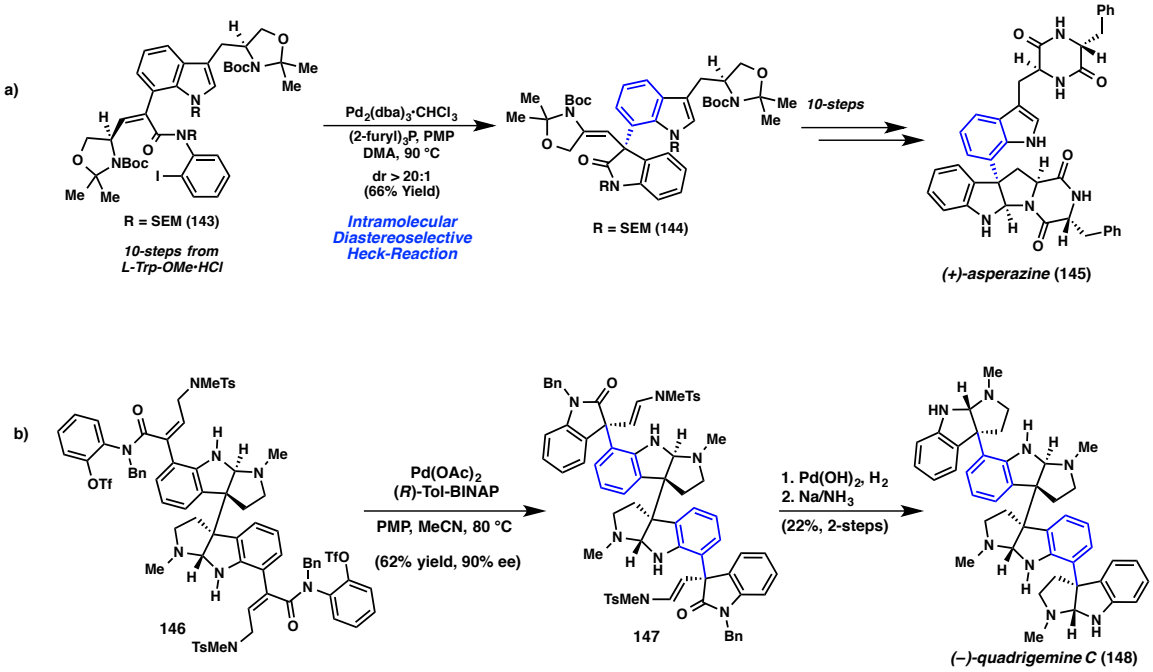
Figure 3.1. *C3-Aryl pyrroloindoline natural products*



3.1.2 Previous Syntheses of C3-arylated Pyrroloindolines

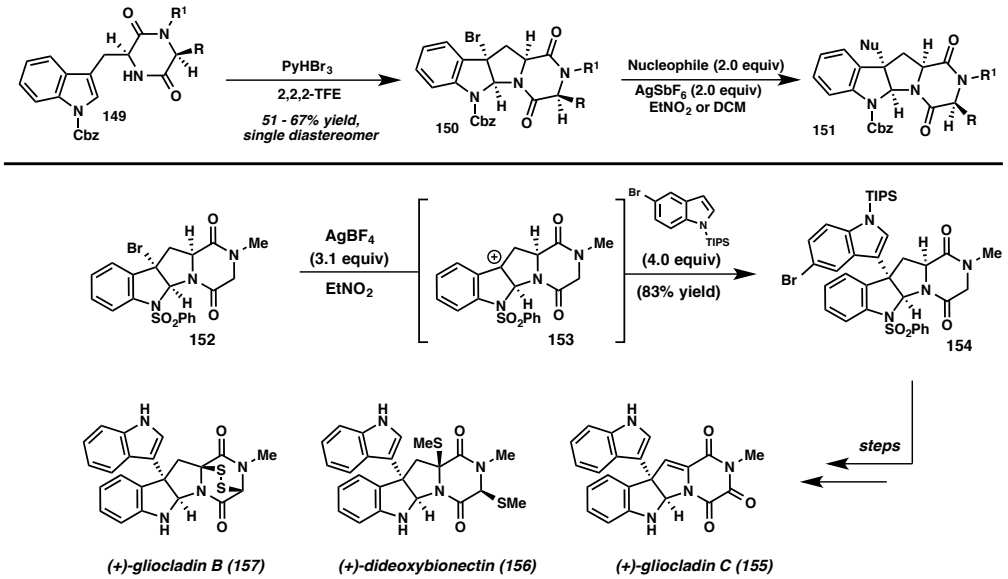
In a seminal 2001 report, Overman and Govek reported the successful implementation of an intramolecular Heck strategy in the synthesis of (+)-asperazine, a bisindole alkaloid containing a unique C3-C7 aryl linkage.[6] In 10-steps (*L*)-tryptophan methylester hyrdrochloride was advanced to iodoanilide **143** that, in a key step, was subjected to $Pd_2(dba)_3$, $(2\text{-furyl})_3P$, and PMP to effect a highly diastereoselective, intramolecular Heck reaction to form the C3-arylated quaternary center found in the natural product. Oxindole **144** was further advanced to (+)-asperazine in another 10-steps. The following year, Overman reported the total synthesis of the polypyrroloindoline alkaloid (–)-quadrigemine C, now utilizing a key, *enantioselective* Heck desymmetrization of a meso compound (**Scheme 3.2**, **b**).[7] Treatment of meso-**146** with $Pd(OAc)_2$ and *(R)*-tol-BINAP with pentamethylpiperidine affords bisoxindole **147**, which is efficiently cyclized under reductive conditions to the natural product.

Scheme 3.2. *Overman's approach to C3-aryl pyrroloindolines*



A decade later, Movassaghi and co-workers reported a general strategy towards this class of compounds using a bromocyclization/Friedel–Crafts approach (**Scheme 1.16, Chapter 1**).[5c] A subsequent publication details the extension of this strategy towards the completion of indole-bearing natural products **155**–**157** (**Scheme 3.3**). Again, starting with tryptophan-derived bromo tetracycle **152**, subjection to superstoichiometric $AgBF_4$ to generate the benzylic tertiary carbocation followed by the addition of four equivalents of an indole nucleophile, provides C3-aryl pyrroloindoline **154**. This common intermediate can be further functionalized to access (+)-gliocladins B and C and (+)-dideoxybionectin, demonstrating the power and versatility of this approach.[5d]

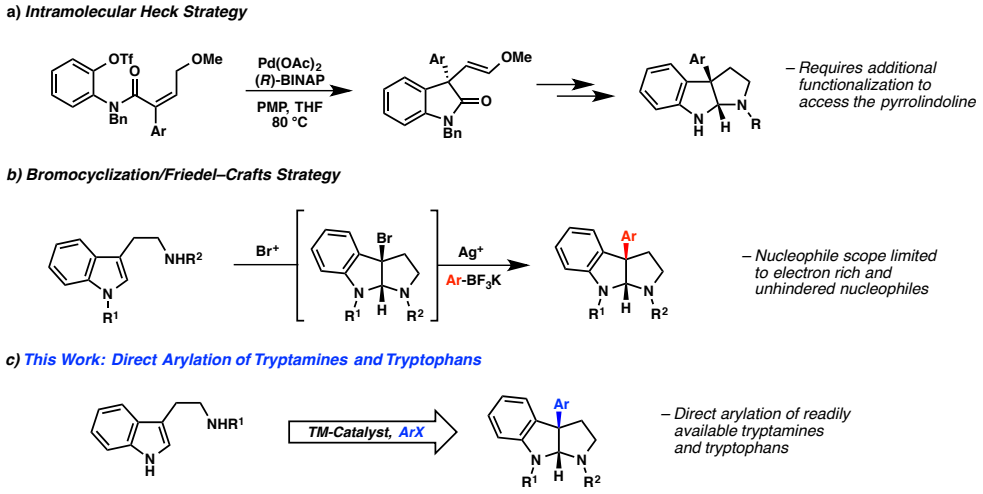
Scheme 3.3. *Movassaghi's approach to C3-aryl pyrroloindolines*



At the outset of our studies, the strategies presented by Overman and Movassaghi represented the state-of-the-art in the preparation of C3-aryl pyrroloindolines. Despite the ability of these elegant approaches to provide access to the desired scaffold, we believed there might be room for improvement (**Scheme 3.4**). For example, while the Heck reaction is a powerful tool for the generation of quaternary centers, the preparation of the cyclization precursor is lengthy, and additional steps are required for advancement to pyrroloindolines. In contrast, Movassaghi's approach is potentially more general and allows for late-stage aryl group installation, yet the reported conditions only provide moderate yields and require superstoichiometric amounts of silver salts and precious nucleophiles. Furthermore, only electron-rich and sterically unencumbered nucleophiles are tolerated with this approach. In considering various strategies, we recognized that there existed *no direct method* for the preparation of C3-arylpyrroloindolines, and therefore anticipated that the development of a direct arylation/cyclization cascade of tryptamines and tryptophans would significantly streamline the assembly and preparation

of a diverse array of C3-arylpyrroloindolines and enable the concise preparation of related natural products.

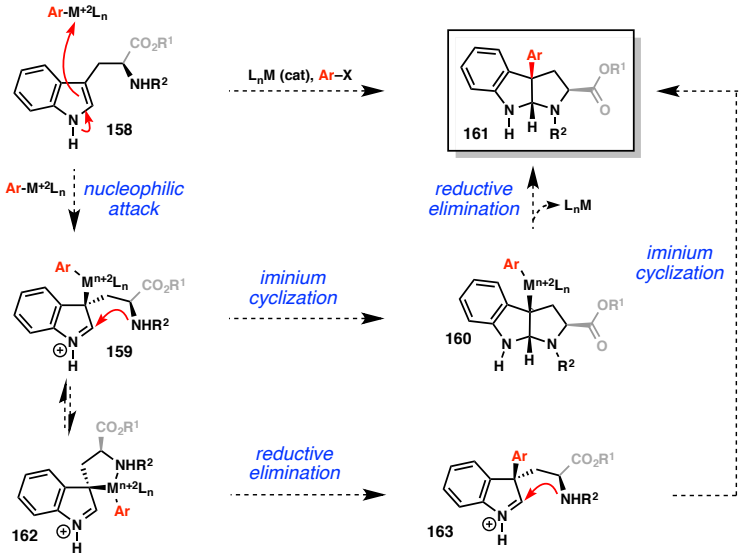
Scheme 3.4. *Strategies to access C3-aryl pyrroloindolines*



3.2 REACTION DESIGN

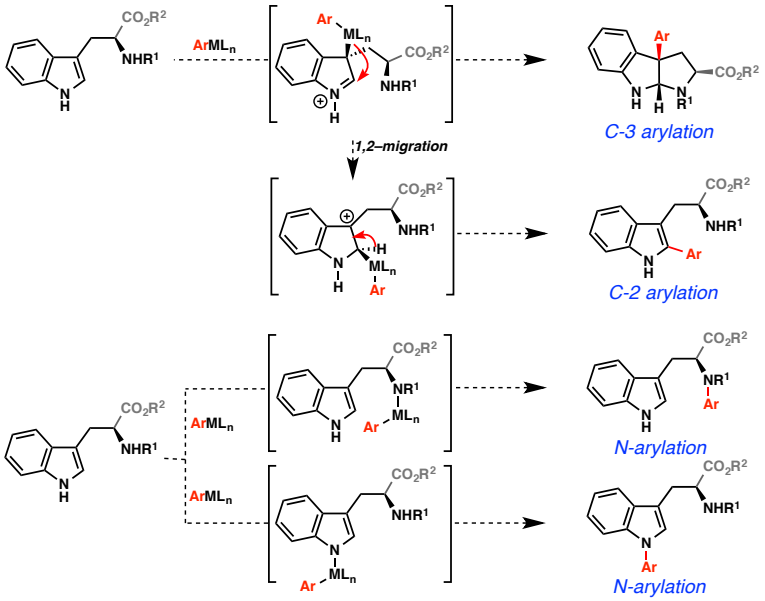
One possible strategy to effect this transformation is through transition metal catalysis. Although C3-functionalization/cyclization has been a widely employed approach for pyrroloindoline synthesis, and furthermore has been utilized successfully in the context of Pd-mediated C3-allylation and benzylation reactions, at the outset of our studies no equivalent *arylation* reaction had been reported.[8,9,10] Mechanistically, we hypothesized such a transformation could proceed through initial nucleophilic attack of a tryptamine or tryptophan onto an electrophilic metal center to form C3-metallated intermediate **159** (**Scheme 3.5**). Iminium cyclization to form the pyrrolidine ring, followed by reductive elimination to furnish the all carbon quaternary center, would provide the desired product (**161**). Alternatively, we imagined that the pendant amine might stabilize C3-metallated **159**. Reductive elimination from a spirocyclic intermediate (**162**) and subsequent iminium cyclization could also provide the pyrroloindoline product.

Scheme 3.5. *Proposed transition metal mechanism*



Although a transformation proceeding *via* indole C3-metallation seemed attractive, we recognized from the outset that this design was not without inherent challenges in chemoselectivity. Specifically, key to the success of this transformation is the generation of C3-metallated species **159**, which must undergo reductive elimination and cyclization to provide the desired product (**Scheme 3.6**). One major concern was the relative stability of such an intermediate, which is known to undergo facile migration to the C2 position of the indole.[11] Reductive elimination and rearomatization could then furnish 2-aryl indoles. Additionally, one could imagine coordination of the transition metal catalyst to either the indole nitrogen or the pendant amine to yield Buchwald-Hartwig type products.

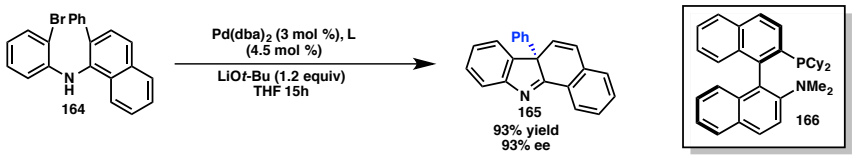
Scheme 3.6. *Possible indole reactivity*



3.2.1 Initial Investigation into Palladium Catalysis

Our initial strategy was inspired by 2009 work from Buchwald and co-workers in which they utilized a Pd(0-II) cycle in the asymmetric dearomatization of naphthalenes (**Scheme 3.7**).[12] Using chiral Davephos **166**, a variety of substituted arenes served as competent substrates in the generation of sterically demanding, arylated quaternary centers.

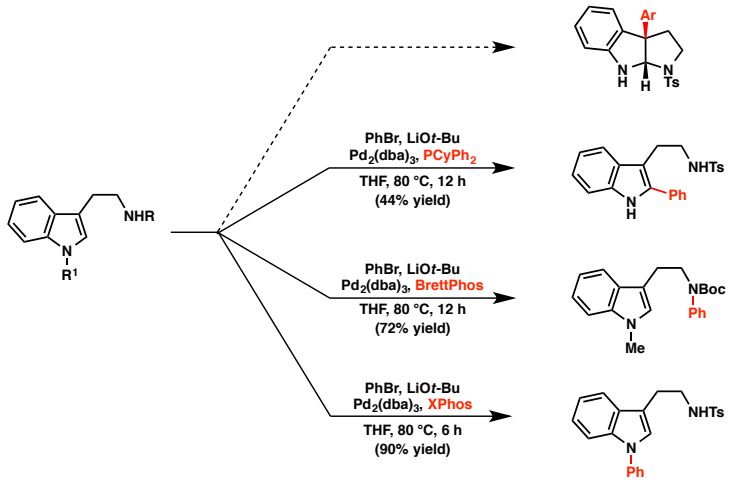
Scheme 3.7. *Buchwald's Pd-catalyzed intramolecular arylation*



Drawing an analogous mechanism, we wondered if Pd(0)/(II) catalysis could be applied to the direct arylation of tryptamine derivatives. A systematic screen of substrates, palladium sources, and ligands revealed the ability to selectivity access each of the predicted product isomers, except for the desired pyrroloindoline (**Scheme 3.8**).

Employing slightly smaller ligands, C2-arylation was observed while the use of bulky ligands, perhaps unsurprisingly, resulted in the formation of C–N bonds. With these negative results, a change in strategy was deemed necessary.

Scheme 3.8. *Pd-catalyzed arylation*



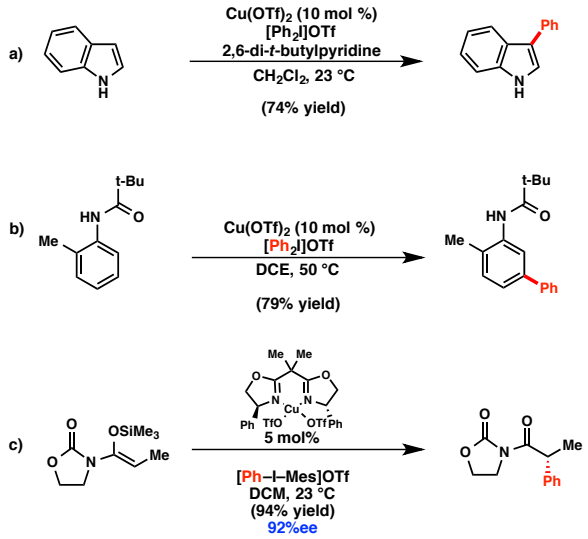
3.2.2 Investigation into Copper Catalysis

In our previous palladium approach, a variety of strong bases were used deprotonate the indole in order to increase its reactivity and nucleophilicity. Given the undesired reactivity observed, we decided to employ an alternative tactic to modify the reactivity. We reasoned that, rather than increasing substrate nucleophilicity, increasing metal electrophilicity might facilitate the rate of reductive elimination over 1,2-migration, thereby enabling the preparation of C3-arylated products.

To this end, we were encouraged by several reports from the Gaunt group, in which mild arylation of nucleophiles with diaryliodonium salts could be effected through Cu-catalysis (**Scheme 3.9**).[13] Specifically, Gaunt invokes a highly electrophilic Cu(III)-aryl intermediate, which is generated under mild conditions due to the ease of oxidative addition to diaryliodonium salts. We hypothesized that it may be possible to harness the

reactivity of this Cu/iodonium system to effect the direct arylation of tryptamines to form pyrroloindolines, but recognized from the outset that the generation of a sterically-demanding, aryl quaternary center may test the limits of this technology. Specifically, at the outset of our exploratory efforts, *no examples* of quaternary-center formation using Cu/ArI_2X had been reported in the literature.

Scheme 3.9. *Gaunt's Cu-catalyzed arylation*



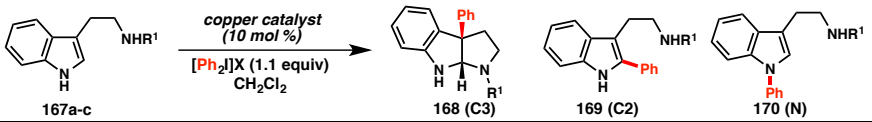
3.3 SCREENING AND OPTIMIZATION

Excited about the application of this new catalyst system, tosyl tryptamine **167a** was easily prepared and treated with Ph_2IBF_4, di-*tert*-butylpyridine, and 10 mol % $Cu(OTf)_2$, identical conditions to those reported by Gaunt and co-workers. Disappointingly, these efforts were met with extremely low conversion of starting material; however, trace masses corresponding to arylated products were detected by UHPLCMS. In considering the reaction conditions, we wondered whether di-*tert*-butylpyridine was potentially acting as a ligand and coordinating the copper catalyst, thereby mitigating its reactivity. Closer inspection of Gaunt's reported conditions

revealed that stoichiometric base was employed to suppress acid-catalyzed dimerization of the 2,3-unsubstituted indoles. As 3-substituted indoles have a significantly lower propensity to dimerize, the reaction was repeated in the absence of base. To our delight, 3-aryl pyrroloindoline **168a** was isolated in 60% yield along with 27% yield of migratory side product **169a** (**Table 3.1**).

Our optimization efforts began with a screen of Cu(I) and Cu(II) sources (**Table 3.1**). Whereas copper catalysts with highly coordinating ligands such as halides and acetonitrile (entries **6**–**7**) showed no reactivity, $Cu(OAc)_2$ exhibited an incredibly clean reaction profile (entry **8**) and moderate yields. Surprisingly, a low yield of side product **169a** did not necessarily correspond to a higher yield of product. In fact, it appears that 2-aryl indole **169a** converts to an unknown oxidative dimer as the reaction proceeds. In terms of the iodonium salts, the best results were obtained using the non-coordinating tetrafluoroborate counterion. Interestingly, use of a TFA counterion results in chemoselective *N*-arylation of the indole nitrogen (**170a**). The non-symmetric iodonium salt [Ph-I-Mes]BF_4, for which the mesityl group serves as a non-transferable ligand, is also a competent coupling partner, although longer reaction times are required.

Table 3.1. *Optimization of Cu-source and protecting group*



167a-c 168 (C3) 169 (C2) 170 (N)

entry	R^1	Cu source	X	additive	C3 : C2 : N	pdt	yield[a] (%)
1	Ts	$Cu(OTf)_2$	BF_4	–	2.3 : 1 : 0	168a	62[b]
2	Ts	–	BF_4	–	–	168a	0
3	Boc	$Cu(OTf)_2$	BF_4	–	–	168b	<5
4	Ac	$Cu(OTf)_2$	BF_4	–	–	168c	<5
5	Ts	$(CuOTf)_2$•PhMe	BF_4	–	3.4 : 1 : 0	168a	64
6	Ts	CuI	BF_4	–	–	168a	0
7	Ts	$Cu(MeCN)_4PF_6$	BF_4	–	–	168a	0
8	Ts	$Cu(OAc)_2$	BF_4	–	2.9 : 1	168a	64
9	Ts	$Cu(OTf)_2$	PF_6	–	2.5 : 1	168a	28
10	Ts	$Cu(OTf)_2$	OTf	–	2.9 : 1	168a	32
11	Ts	$Cu(OTf)_2$	Cl	–	–	168a	0
12	Ts	$Cu(OTf)_2$	TFA	–	0 : 0 : 1	170a	nd
13	Ts	$Cu(OTf)_2$	BF_4	dtbpy	–	168a	<5
14	Ts	$Cu(OTf)_2$	BF_4	–	2.6 : 1	168a	65[b]

[a] Determined by HPLC *versus* an internal standard. [b] Isolated yield. [c] $[Ph\text{-}I\text{-}Mes]BF_4$ was employed as the electrophile.

Although both $Cu(OTf)_2$ and $Cu(OAc)_2$ furnished comparable yields of pyrroloindoline **168a** when using $[Ph_2I]BF_4$ as the electrophile, the $Cu(OAc)_2$-catalyzed reaction profile was cleaner overall, thereby simplifying purification. As a result, $Cu(OAc)_2$ was the catalyst of choice for arylation reactions employing $[Ph_2I]BF_4$ or other symmetric iodonium salts. On the other hand, $Cu(OTf)_2$ proved superior for arylation reactions that employed less reactive, mesityl-substituted iodonium salts.

3.4 SUBSTRATE SCOPE OF RACEMIC ARYLATION

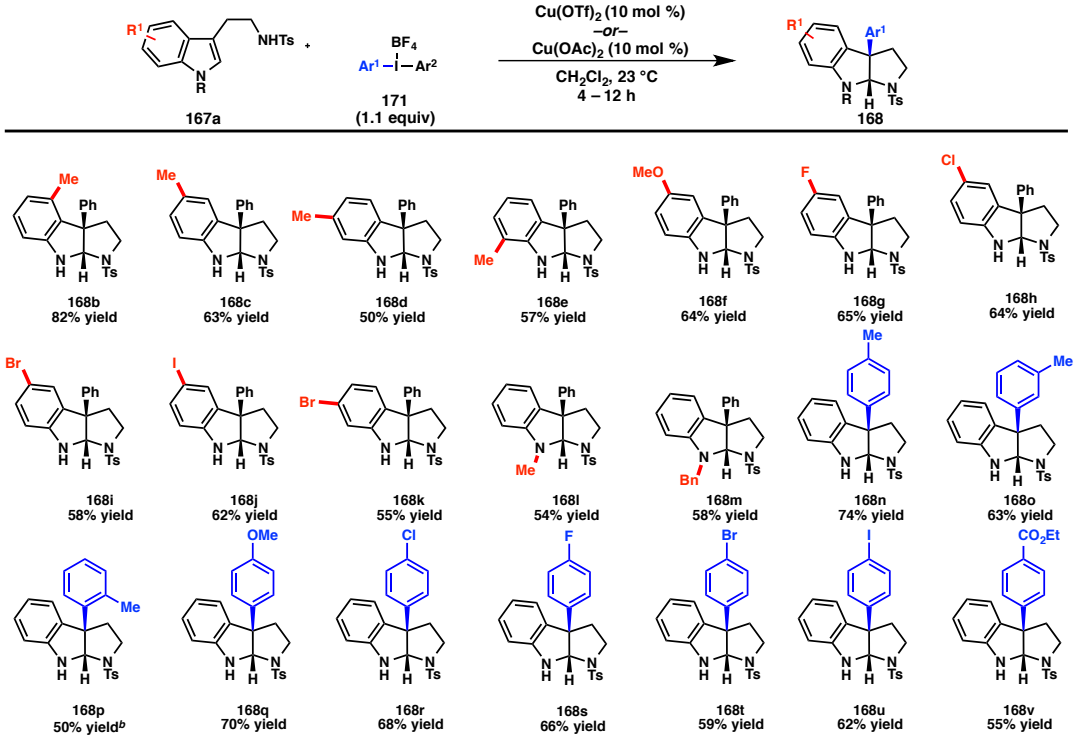
3.4.1 Tryptamine and Iodonium Scope

Using this method, a variety of arylated pyrroloindolines can be prepared in a single step from the corresponding *N*-tosyl tryptamines at ambient temperatures (**Table 3.2**). We were pleased to find that tryptamine substrates bearing alkyl substitution at C4, C5, C6, and C7 are accommodated, providing the corresponding pyrroloindolines in good

yields (**168b–168e**). Additionally, a variety of electron-donating and electron-withdrawing substituents are tolerated at C5. Although comparable yields are obtained, slower rates are observed in the reactions of indoles substituted with electron-withdrawing groups. *N*-tosyltryptamines bearing alkyl substitution on the indole nitrogen are also competent reaction partners (**168l–168m**).

We next investigated the scope of the aryl coupling partner. We were pleased to find that a range of electron-donating and withdrawing substituents were well tolerated at the *para*- and *meta*- positions, utilizing both symmetric and non-symmetric iodoniums. Unfortunately, *ortho*-substitution was poorly tolerated, providing the product in low yield (**168p**, 15% yield). Fortunately, reactivity could be restored by switching to the symmetric iodonium salt (**168p**, 50% yield).

Table 3.2. *Substrate Scope*

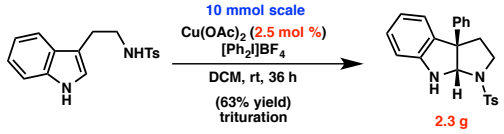


[a] Reactions were conducted on 0.30 mmol scale. Isolated yields are reported. [b] The symmetric iodonium was utilized.

3.4.2 Scale-up Procedure

Our screening protocol was conducted using 10–20 mol% catalyst loading to ensure uniformly good yields over a range of substrates. However, to demonstrate the scalability and efficiency of this transformation, the reaction has been carried out on a 3 g scale using N-tosyltryptamine and $[Ph_2I]BF_4$ with only 2.5 mol % catalyst loading. Purification by filtration followed by trituration provides analytically pure pyrroloindoline in 63% yield, without the need for column chromatography. Notably, the reaction proceeds at ambient temperature with nearly equimolar ratios of indole and $[Ph_2I]BF_4$.

Scheme 3.10. *Scale-up reaction*

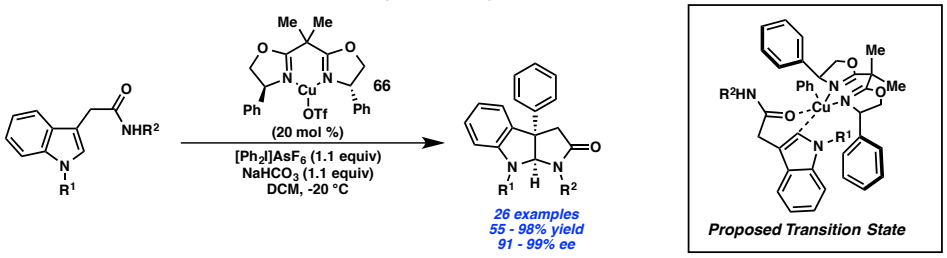


3.5 DIASTEREOSELECTIVE ARYLATION REACTION DESIGN

3.5.1 Macmillan's Enantioselective Method

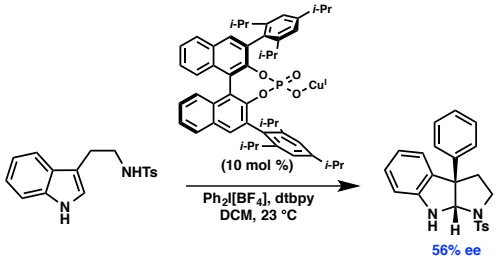
As the manuscript for this methodology was being prepared, a similar enantioselective transformation was reported by MacMillan and co-workers.[14] Utilizing chiral copper box complexes, they were able to effect both a chemoselective and enantioselective arylation of indole carboxamides. Their method proved general for a variety of substituted indoles and diaryliodonium salts (**Scheme 3.11**).

Scheme 3.11. *MacMillan's Cu-catalyzed arylation*



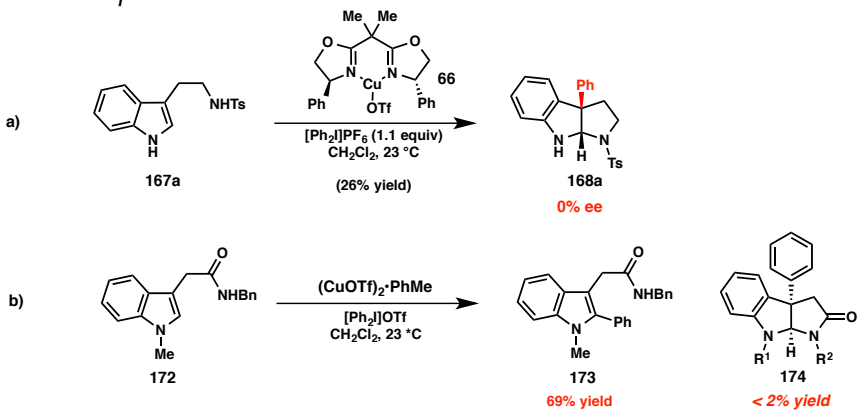
This report was particularly disappointing as we had already gathered preliminary data on an enantioselective variant of our arylation reaction. Employing catalytic copper and chiral copper phosphates, C3-aryl pyrroloindoline **168a** was recovered in moderate but promising enantioselectivities (**Scheme 3.12**).

Scheme 3.12. *Enantioselective result.*



Regardless, we resolved to investigate the differences and similarities between our conditions and MacMillan's conditions to gain a better understanding of the reactivity of these types of systems. Based on MacMillan's work, it has been established that indole carboxamides in conjunction with copper catalysis and diaryliodonium salts provide pyrroloindoline products in a chemoselective and enantioselective fashion. Interestingly, subjection of our substrate (**167a**) to MacMillan's conditions, provides low yields of arylated product and in racemic form. Similarly, subjection of MacMillan's substrate (**172**) to our ligandless copper conditions, provided almost exclusive C2-arylation (**173**).

Scheme 3.13. *Comparison Studies*



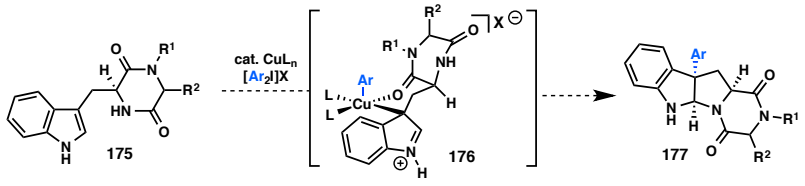
3.5.2 New Reaction Design

We rationalized that a careful matching of the directing group (Lewis-basicity) and catalyst stereoelectronics likely determined product ratios. Specifically, it appeared that MacMillan's more Lewis-basic directing group may compensate for the diminished electrophilicity of the ligated copper complex, allowing for the complex to still coordinate strongly to the substrate. Similarly, the diminished electrophilicity of the ligated copperbox complex may prevent meaningful coordination of *N*-tosyltryptamine, resulting in poor reactivity, yield, and no enantioinduction.

Acknowledging that our ultimate goal was to develop methodology useful in the application of natural product total synthesis, we recognized that neither our arylation method, nor that of MacMillan and co-workers, provides products with the functionality necessary for advancement to natural products. Instead, perhaps the most straightforward and useful approach was the direct and *diastereoselective* arylation of tryptophan derivatives. Starting with tryptophan-derived diketopiperazines **175**, we hoped to use the inherent Lewis basicity of the amide to selectively direct a copper catalyst to a single face of the indole to provide pyrroloindoline products in a diastereoselective fashion (**177**).

Successful execution would represent the most convergent route to this class of compounds reported to date.

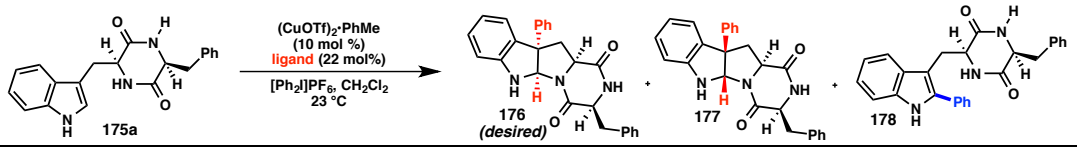
Scheme 3.14. *Proposed diastereoselective arylation*



3.6 OPTIMIZATION OF DIASTEREOSELECTIVE ARYLATION

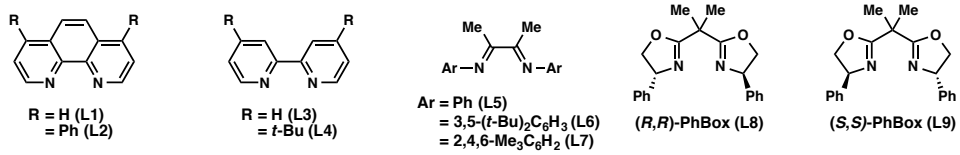
Our efforts to effect this diastereoselective transformation began with subjection of tryptophan-derived diketopiperazine **175a**, to our previously optimized conditions of ligandless copper (**Table 3.3**, **entry 1**). We were encouraged to recover the desired isomer in 22% yield. However, pyrroloindoline **176** was also formed in a 1:1 C3:C2 mixture (**178**), as well as a 3:1 diastereomeric ratio (**177**). In an effort to test our hypothesis on the necessary matching of directing group ability and the catalyst electronics, we conducted a screen of bidentate ligands. While more conventional bipy and phenanthroline based ligands provided minimal increases in yield, we were pleased to find that they were able to modulate the selectivities. We were delighted to find that use of the sterically congested bis(mesityl)-α-diimine ligand (**L7**) furnished the product in 70% yield. Further investigation into the sterics of the diimine ligand revealed that the precise substitution around the adjacent arene exerts a significant effect on the reactivity and selectivity of the reaction. The yield of pyrroloindoline was further improved through the use of a triflate counterion, providing the product in 85% isolated yield as a single diastereomer (**entry 14**).

Table 3.3. *Diastereoselective optimization*



entry	ligand	[Ph$_2$I]X	C3:C2[a]	dr[a]	yield (%)[a]
1	–[b]	[Ph$_2$I]PF$_6$	–	–	0
2	–	[Ph$_2$I]PF$_6$	1:1	3:1	22
3	L1	[Ph$_2$I]PF$_6$	1:1	3:1	15
4	L2	[Ph$_2$I]PF$_6$	1:2	2:1	<5
5	L3	[Ph$_2$I]PF$_6$	6:1	10:1	20
6	L4	[Ph$_2$I]PF$_6$	12:1	12:1	38
7	L5	[Ph$_2$I]PF$_6$	2:1	5:1	26
8	L6	[Ph$_2$I]PF$_6$	1:1	4:1	24
9	L7	[Ph$_2$I]PF$_6$	>20:1	>20:1	70
10	L8	[Ph$_2$I]PF$_6$	1:1	4:1	15
11	L9	[Ph$_2$I]PF$_6$	2:1	20:1	35
12	L7	[Ph$_2$I]BF$_4$	>20:1	>20:1	76
13	L7	[Ph$_2$I]AsF$_6$	>20:1	>20:1	81
14	L7	[Ph$_2$I]OTf	>20:1	>20:1	83 (85)[c]

[a]Yield of major diastereomer as determined by ^{1}H NMR analysis of the crude reaction mixture. [b] No (CuOTf)$_2$•PhMe was used. [c] Isolated yield.

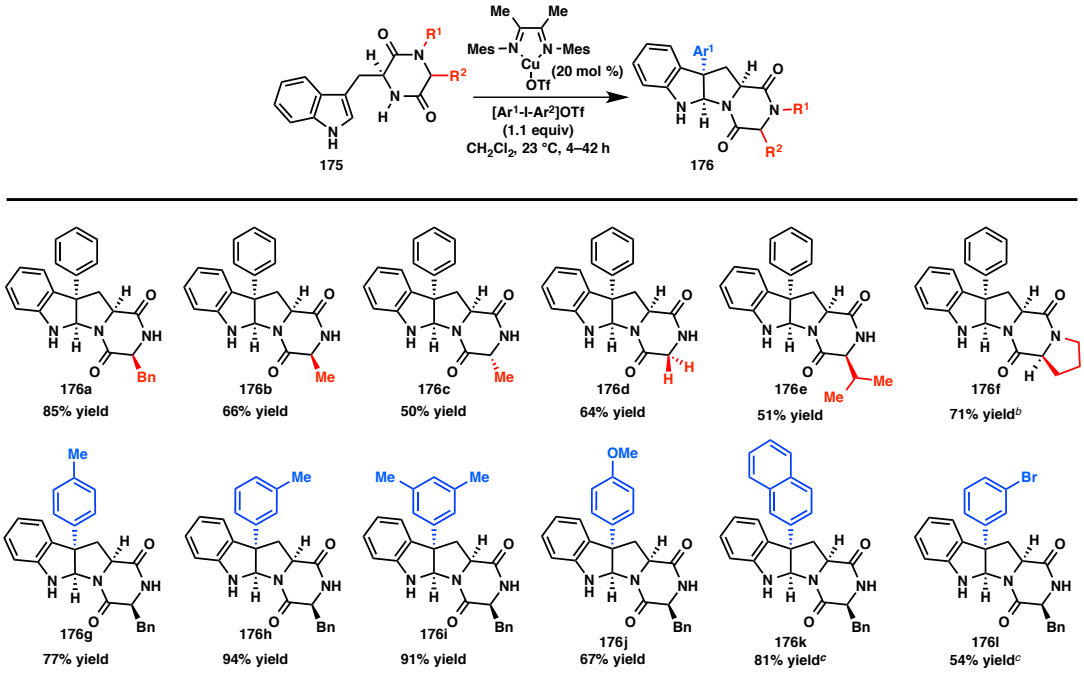


3.7 SCOPE OF DIASTEREOSELECTIVE ARYLATION

With optimized conditions in hand, the substrate scope of this diastereoselective reaction was examined (**Table 3.4**). A variety of arylated pyrroloindolines (**176**) can be prepared in one step from the corresponding diketopiperazines (**175**). Interestingly, the diketopiperazines derived from either L- or D-alanine react to deliver diastereomeric pyrroloindolines **176b** and **176c**, respectively, which possess the same configuration at the newly formed quaternary center. This observation indicates that the configuration at the tryptophan-derived stereogenic center is the dominant stereocontrolling factor. The scope of the aryl coupling partner was also investigated and was found to be tolerant of both electron-rich and electron-poor arenes (**176j–176l**).

In contrast, diketopiperazine **175f**, derived from *L*-Pro, proved to be a challenging substrate and provided **176f** in low yield as a result of poor C3:C2 selectivity under our standard conditions. We hypothesized that the increased substitution at nitrogen may result in a destabilizing interaction with the bulky Cu^{I}(**L7**) catalyst. A screen of more sterically-accessible ligands revealed that the use 40 mol % **L6** in conjunction with [Ph-$_2$I]PF_6 restores the C3:C2 selectivity and delivers pyrroloindoline **176f** in 71% yield. At this time, we believe that the need for increased ligand loading with **L6** is likely due to the formation of bridging Cu-catalyst dimers. This hypothesis is further supported by the fact that reaction rates utilizing **L6** are considerably accelerated at higher dilutions.

Table 3.4. *Substrate scope of diastereoselective arylation*

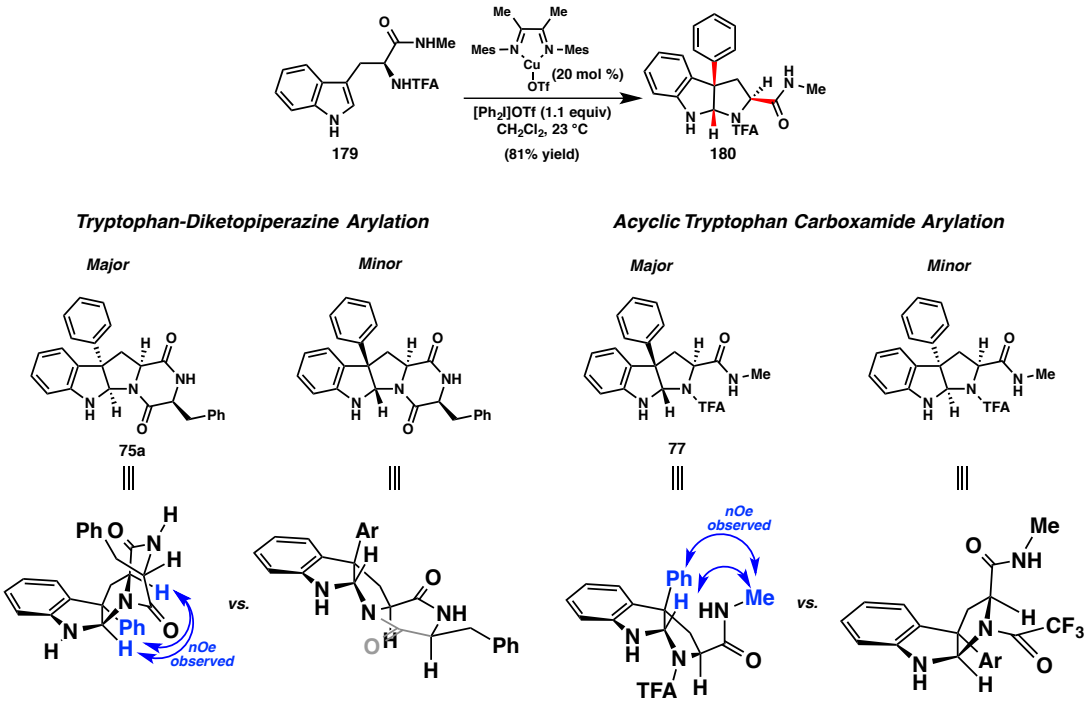


[a] Reactions conducted on 0.3 mmol scale using symmetric diaryliodonium triflate unless otherwise noted. Isoltaed yields are reported. [b] 40 mol % ligand **L6** was used with diphenyliodonium hexfluorophosphate. [c] Non-symmetric aryl[*p*-xylyl]iodonium triflate was used.

Given the success of a range of diketopiperazine-containing substrates, we next turned our attention to a more flexible system. Specifically, we wondered if an acyclic

tryptophan-derived carboxamide would behave similarly under our reaction conditions. Remarkably, subjection of *acyclic* **179** to our optimized conditions provided pyrroloindoline products in which arylation occurred with opposite facial selectivity at the quaternary center to that seen with diketopiperazine substrates (**180**). From a synthetic standpoint, this presents the exciting opportunity to access either enantiomeric series of pyrroloindoline products from naturally occurring (*L*)-tryptophan.

Figure 3.2. *Reversal in diastereoselectivity*

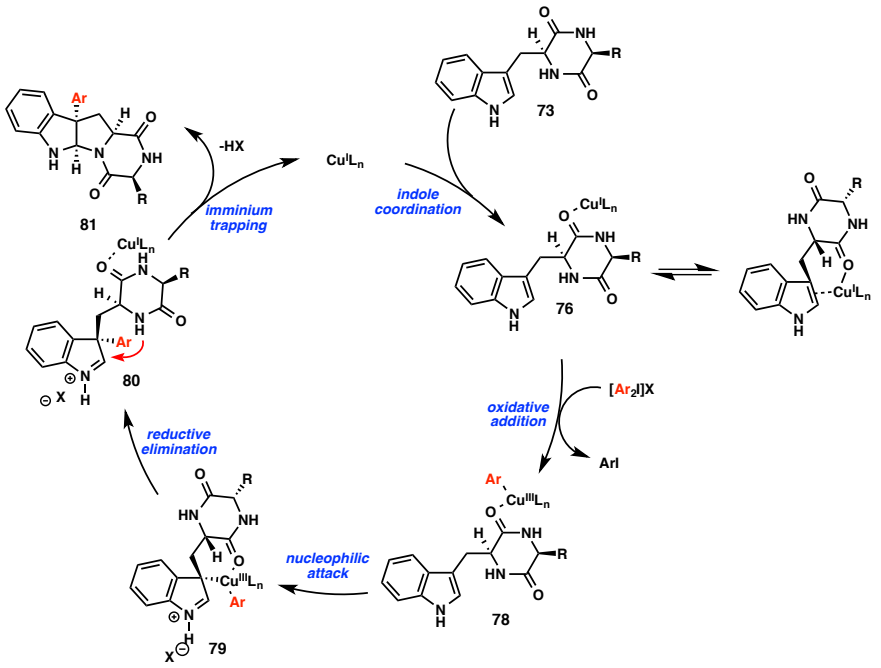


3.8 MECHANISTIC HYPOTHESIS

The mechanism of this reaction is still under investigation and our attempted studies have been complicated by the presence of paramagnetic species in ^{1}H NMR experiments as well as the heterogeneous nature of this reaction. Currently, we can only speculate on the possible mechanisms based on circumstantial evidence. However, in analogy to that proposed by Gaunt for the Cu-catalyzed C3-arylation of unsubstituted

indoles, we currently favor a Cu(I–III) catalytic cycle (**Scheme 3.15**). Although Gaunt proposes oxidative addition prior to indole coordination, our studies suggest indole coordination is likely necessary for oxidation to a Cu(III) species.

Scheme 3.15. *Possible arylation mechanism*



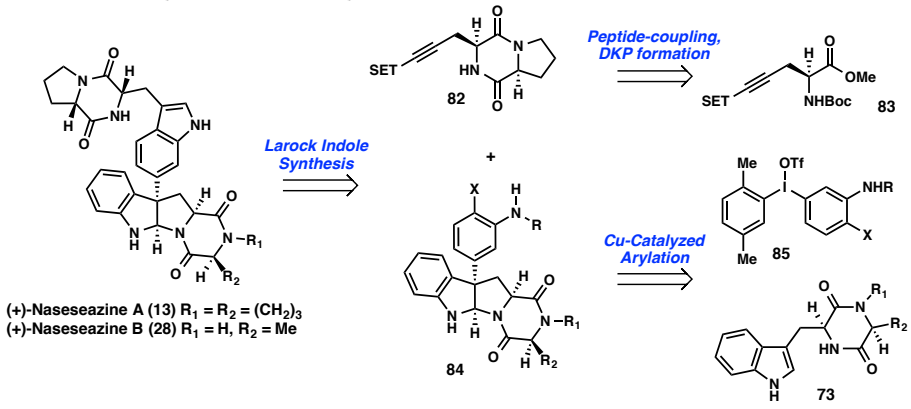
3.9 TOTAL SYNTHESIS OF (+)-NASESEAZINES A AND B

3.9.1 Retrosynthetic Analysis

Having successfully optimized this diastereoselective transformation, we set out to demonstrate the versatility and efficiency of this transformation through the total synthesis of C3-arylpyrroloindoline-containing natural products (+)-naseseazines A and B. Retrosynthetically, we imagined a disconnection through the tryptophan indole *via* a late stage Larock indole synthesis between an appropriate haloaniline and alkynyl diketopiperazine. We hoped to synthesize the necessary haloaniline from our newly developed diastereoselective arylation of a tryptophan-derived diketopiperazine and a

functionalized iodoniun. Alkynyl diketopiperazine **82** was expected to be available *via* a peptide coupling followed by cyclocondensation of the corresponding propargylglycine derivative.

Scheme 3.16. *Retrosynthetic Analysis*

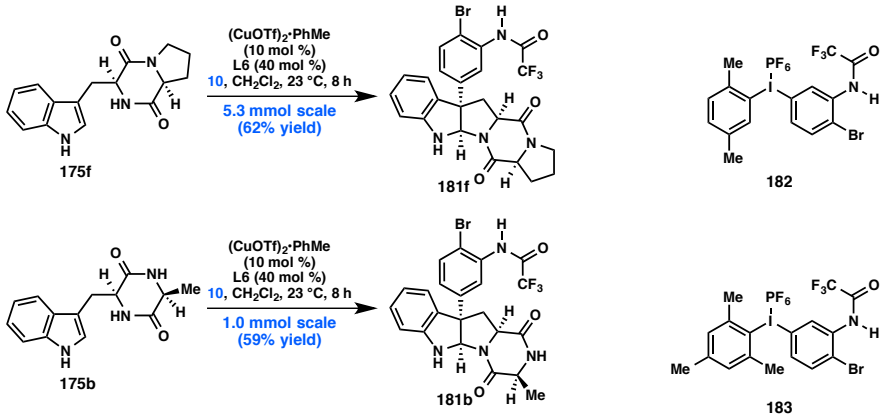


3.9.2 Forward Synthesis

In the forward sense, we began by investigating the arylation reaction of cyclo-L-Trp-L-Pro (**175f**) with diaryliodonium salt **182**, readily prepared in 80% yield over two-steps from commercially available 2-bromo-5-iodoaniline. We were pleased to find that subjecting these two coupling partners to a prestirred solution of 10 mol% (CuOTf)$_2$•PhMe and 40 mol% $^{t\text{-Bu}}$DAB$_{Me}$ (**L6**), conditions previously optimized for (L)-proline-derived diketopiperazine **175f**, provided **181f** in modest yield. Unfortunately competitive *p*-xylyl transfer was also observed, resulting in an inseparable mixture of arylation products. Although our previous studies had indicated that Cu(**L7**)OTf was incapable of transferring ortho-substituted arenes, this new observation led us to believe that the active Cu(**L6**) species was significantly more sterically accessible, and may tolerate a bulkier, nontransferable ligand. As a result, mesityl iodonium **183** was readily prepared and subjected to the reaction conditions. Gratifyingly, pyrroloindoline **181f** was cleanly isolated in 62% yield with good selectivity. This direct and efficient procedure is easily

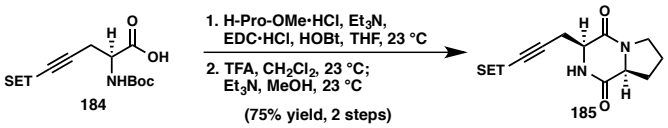
performed on large scale and provides the desired pyrroloindoline with excellent levels of diastereocontrol. Moreover, the same conditions could be applied to alanine-derived **175b** to give pyrroloindoline **181b** in 59% yield.

Scheme 3.17. *Arylation using a functionalized iodonium*



To prepare the other coupling fragment for a Larock indolization, alkynyl diketopiperazine **185** was synthesized on gram scale via initial peptide coupling of amino acid **184** with (*L*)-proline methyl ester hydrochloride. One-pot Boc deprotection and base-mediated cyclocondensation provide the desired coupling partner.

Scheme 3.18. *Preparation of a propargyl diketopiperazine*

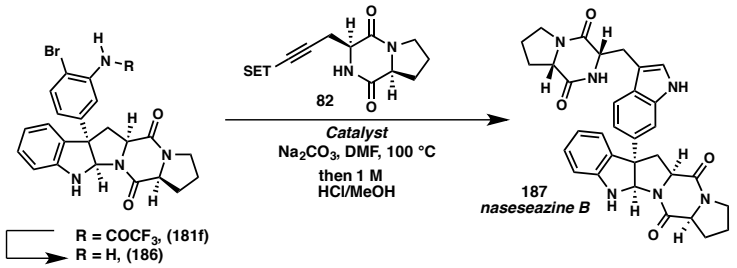


With these coupling partners in hand, all that remained in the synthesis was a late-stage Larock indolization to access the natural product. Although Larock indole syntheses between iodoanilines and alkynes are commonplace in the literature, the corresponding reaction of bromoanilines has been considerably less developed.[15,16] We were encouraged that this reaction could be viable based on reports by Boger and co-workers on an intramolecular Larock macrocyclization of a bromoaniline en route to the total synthesis

of the complestatin natural products.[16] Despite the use of superstoichiometric $Pd(OAc)_2$ and ditertbutylferrocenylphosphine as a ligand, this precedent demonstrated the viability of such a reaction in the context of advanced stage total synthesis and in the presence of numerous peptide bonds.

We were therefore encouraged to find that the use of stoichiometric palladium with 1,1'-bis(di-*tert*-butylphosphino)ferrocene (dtbpf) gave traces of the natural product (**Table 3.5**, **entry 2**). Unfortunately, a closer analysis of the reaction mixture showed that the major products of this reaction consisted of hydrodebrominated starting material, *epi*-naseseazine B, and *iso*-naseseazine B. Furthermore, subsequent attempts to optimize this reaction based on the conditions identified by Boger and co-workers proved completely unfruitful, and we therefore embarked on an extensive screen of less conventional ligands. Interestingly, treatment of stoichiometric amounts of the *N*-heterocyclic carbene-based catalyst PEPPSI-IPr greatly reduced debromination, although **187** was recovered in low yield. Subjecting the free aniline to identical conditions improved the recovery, providing a 39% isolated yield (entry 7). Additional screening revealed that the bulky preformed catalyst $Pd[P(o\text{-tol})_3]_2$ was highly active, reaching full conversion in only 15 minutes and providing 27% yield of the product. Intrigued by the reactivity, we wondered whether catalysis might be achieved under these conditions. Gratifyingly, treatment with only 25 mol % $Pd[P(o\text{-tol})_3]_2$ afforded **187** in 51% yield, constituting the first catalytic Larock indolization on a bromoaniline in total synthesis.

Table 3.5. *Optimization of the Larock indole synthesis*



entry	R	catalyst	time	product:debromo	yield (%)
1	TFA	$Pd(OAc)_2$ (1.1 equiv), LiCl	8 h	–	–
2	TFA	$Pd(OAc)_2$ (1.1 equiv), dtbpf (1.2 equiv)	2 h	1 : 1	<10
3	TFA	$Pd_2(dba)_3$ (0.5 equiv), dtbpf (1.2 equiv)	2 h	1 : 1	<10
4	TFA	$Pd(OAc)_2$ (1.1 equiv), DavePhos (1.2 equiv)	2 h	1 : 1	<10
5	TFA	$Pd(OAc)_2$ (1.1 equiv), PCy_3 (1.2 equiv)	8 h	0 : 1	–
6	TFA	PEPPSI-IPr (1.1 equiv)	8 h	>20 :1	<20
7	H	PEPPSI-IPr (1.1 equiv)	8 h	>20 :1	39
8	H	$Pd[P(o\text{-tol})_3]_2$ (1.1 equiv)	15 min	10 :1	27
9	H	$Pd[P(o\text{-tol})_3]_2$ (25 mol %)	90 min	>20 : 1	51

An analogous sequence was applied to furnish the related natural product (+)-naseseazine A by utilizing alanine-derived diketopiperazine **181b**. Through this Cu-catalyzed arylation chemistry, these complex polycyclic alkaloids are available in only five steps (longest linear sequence) from commercially available starting materials in 19% and 25% overall yield respectively, highlighting the ability to generate structurally diverse pyrroloindolines in an extremely convergent manner.

3.10 CONCLUSION

In conclusion, this report describes the discovery and development of new, Cu-catalyzed arylation reactions of tryptamine and tryptophan-derivatives to form 3-arylpyrroloindolines. Direct and selective C3-arylation is achieved through the use of copper catalysts in conjunction with hypervalent iodine(III) salts as the aryl source. *N*-sulfonyltryptamines were found to react uniquely using copper(I) or (II) salts and

diaryliodonium tetrafluoroborates to afford racemic C3-aryl pyrroloindolines in good yields. Furthermore, the addition of α-diimine ligands to the system has enabled the development of an efficient and highly diastereoselective tryptophan arylation reaction. Using this transformation to assemble the pyrroloindoline core enables the concise, stereoselective syntheses of the bisindole alkaloids (+)-naseseazines A and B in overall yields of 25 and 19%, respectively.

3.11 EXPERIMENTAL SECTION

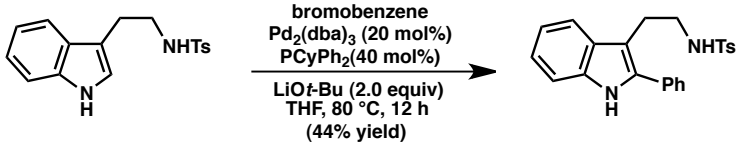
3.11.1 Materials and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), dimethylformamide (DMF), and toluene (PhMe) were dried by passing through activated alumina columns. Triethylamine (Et_3N) was distilled over calcium hydride prior to use. Unless otherwise stated, chemicals and reagents were used as received. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, *p*-anisaldehyde, or $KMnO_4$ staining. Reaction samples were analyzed on an Agilent 1290 Series LC/MS using an Eclipse Plus C18 column (RRHD 1.8 μm, 2.1 x 50 mm, 11,072 plates). Flash column chromatography was performed either as described by Still et al. using silica gel (particle size 0.032-0.063) purchased from Silicycle or using pre-packaged RediSep®Rf columns on a CombiFlash Rf system (Teledyne ISCO Inc.). Alumina was purchased from Sigma-Aldrich (Aluminum oxide, ~150 mesh, 58Å pore size, activated, basic, Brockmann I) and deactivated with 3% v/w H2O (30.0 mL / 970 g). ^{1}H and ^{13}C NMR

spectra were recorded on a Varian 400 MR (at 400 MHz and 101 MHz, respectively), a Varian Inova 500 (at 500 MHz and 126 MHz, respectively), or a Varian Inova 600 (at 600 MHz and 150 MHz, respectively), and are reported relative to internal $CHCl_3$ (^1H, δ = 7.26) or DMSO (^1H, δ = 2.50), and $CDCl_3$ (^{13}C, δ = 77.0), or DMSO (^{13}C, δ = 40.0). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode.

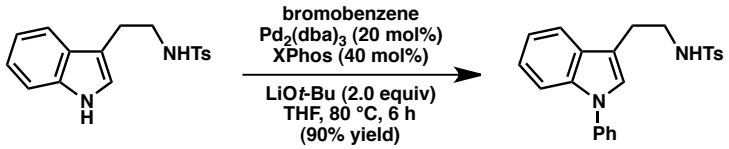
3.11.2 Optimization of Racemic Arylation

A. Palladium-Catalyzed Reaction Screens

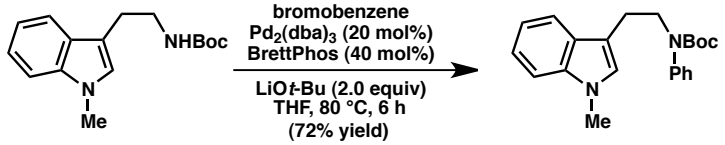


To a flame-dried vial in the glove box was charged $PCyPh_2$ (11 mg, 0.04 mmol), $Pd_2(dba)_3$ (11 mg, 0.02 mmol), N-tosyltryptamine (31 mg, 0.1 mmol), bromobenzene (51 μL, 0.5 mmol), LiOtBu (16 mg, 0.2 mmol) and THF (1 mL). The vial was sealed and heated to 80 ^oC for 12 hours. The reaction mixture was filtered through a plug of silica and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (20% EtoAc in hexanes) to afford 2-phenyl tryptamine **17** (16.9 mg, 0.04 mmol, 44%). ^1H NMR ($CDCl_3$, 500 MHz) δ 8.11 (s, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.52 – 7.42 (m, 5H), 7.40 (ddd, *J* = 4.1, 1.5, 1.5 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.20

(dd, J = 16.1, 7.8 Hz, 3H), 7.09 (dd, J = 7.8, 7.2 Hz, 1H), 4.35 (t, J = 5.8 Hz, 1H), 3.28 (dd, J = 13.3, 6.8 Hz, 2H), 3.08 (dd, J = 7.1, 7.1 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.2, 136.7, 135.8, 132.5, 129.6, 129.0, 128.5, 128.10, 128.09, 127.0, 122.6, 120.0, 118.8, 110.9, 108.3, 43.2, 25.0, 21.5;HRMS (MM) calc'd for $[M+H]^+$ 391.1475, found 391.1491.



To a flame-dried vial in the glove box was charged XPhos (19 mg, 0.04 mmol), $Pd_2(dba)_3$ (11 mg, 0.02 mmol), N-tosyltryptamine (31 mg, 0.1 mmol), bromobenzene (51 μL, 0.5 mmol), LiOtBu (16 mg, 0.2 mmol) and THF (1 mL). The vial was sealed and heated to 80 ^{o}C for 6 hours. The reaction mixture was filtered through a plug of silica and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (20% EtoAc in hexanes) to afford N-phenyl tryptamine (35.2 mg, 0.09 mmol, 90%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.70 – 7.65 (m, 2H), 7.57 – 7.43 (m, 6H), 7.39 – 7.32 (m, 1H), 7.23 (dd, J = 11.6, 4.5 Hz, 3H), 7.16 – 7.10 (m, 1H), 7.09 (s, 1H), 4.54 (t, J = 6.1 Hz, 1H), 3.34 (q, J = 6.6 Hz, 2H), 2.99 (t, J = 6.7 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.3, 139.4, 136.8, 136.1, 129.6, 128.3, 127.0, 126.4, 126.2, 124.1, 122.7, 120.1, 118.8, 112.7, 110.7, 43.1, 25.4, 21.5. HRMS (MM) calc'd for $[M+H]^+$ 391.1475, found 391.1470.



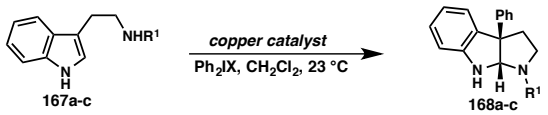
To a flame-dried vial in the glove box was charged BrettPhos (6.4 mg, 0.012 mmol), $Pd_2(dba)_3$ (3.5 mg, 0.006 mmol), *N*-Boc-*N'*-methyltryptamine (8 mg, 0.1 mmol), bromobenzene (16 μL, 0.15 mmol), LiOtBu (4.8 mg, 0.06 mmol) and THF (1 mL). The vial was sealed and heated to 80 ^oC for 6 hours. The reaction mixture was filtered through a plug of silica and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (20% EtoAc in hexanes) to afford N-phenyl tryptamine (28.0 mg, 0.02 mmol, 72%). ^1H NMR ($CDCl_3$, 500 MHz) δ 7.54 (d, J = 7.9 Hz, 1H), 7.34 (dd, J = 10.7, 4.9 Hz, 2H), 7.28 (d, J = 8.2 Hz, 1H), 7.24 – 7.18 (m, 4H), 7.07 (ddd, J = 7.9, 7.0, 1.0 Hz, 1H), 6.85 (s, 1H), 3.97 – 3.87 (m, 2H), 3.72 (s, 3H), 3.06 – 2.95 (m, 2H), 1.42 (s, 10H). ^{13}C NMR ($CDCl_3$, 126 MHz) 148.4, 143.5, 139.4, 136.4, 135.6, 132.6, 131.9, 129.6, 128.5, 127.2, 127.1, 127.0, 125.7, 124.3, 119.2, 109.4, 84.4, 62.1, 47.4, 37.9, 21.4, 20.8. FTIR (NaCl, thin film): 3056, 3027, 2949, 2891, 2827, 1762, 1605, 1491, 1347, 1160, 1092, 1022. HRMS (MM) calc'd for $[M+H]^+$ 409.1381, found 409.1363.

B. Copper-Catalyzed Reaction Screen

General Procedure – To a flame-dried, 1-dram vial was charged the appropriate tryptamine (0.10 mmol), 4,4'-di-*tert*-butylbiphenyl, diaryl iodonium salt (0.11 mmol), copper catalyst (0.010 mmol), and additive (0.10 mmol, if applicable). Anhydrous CH_2Cl_2 (1.0 mL) was then added and the reaction stirred under inert atmosphere and monitored by UHPLC-MS for optimal yield.

The following response factors relative to an internal standard of 4,4'-di-*tert*-butylbiphenyl were measured and calculated based on three runs of varied concentration at λ = 254 nm:

N-Tosyltryptamine **167a** (Starting Material): Response Factor = 0.117
N-Tosylpyrroloindoline **168a** (Product): Response Factor = 0.253
UHPLC samples were analyzed at λ = 254 nm and yields calculated based on the above factors.



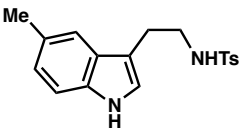
entry	R	Cu source	X	additive	pdt	yield (%)[a]
1	Ts	$Cu(OTf)_2$	BF_4	–	**19a**	62[b]
2	Ts	–	BF_4	–	**19a**	0
3	Boc	$Cu(OTf)_2$	BF_4	–	**19b**	<5
4	Ac	$Cu(OTf)_2$	BF_4	–	**19c**	<5
5	Ts	$(CuOTf)_2$•PhMe	BF_4	–	**19a**	64
6	Ts	CuI	BF_4	–	**19a**	0
7	Ts	$Cu(MeCN)PF_6$	BF_4	–	**19a**	0
8	Ts	$Cu(OAc)_2$	BF_4	–	**19a**	64
9	Ts	$Cu(OTf)_2$	PF_6	–	**19a**	28
10	Ts	$Cu(OTf)_2$	OTf	–	**19a**	32
11	Ts	$Cu(OTf)_2$	Cl	–	**19a**	0
12	Ts	$Cu(OTf)_2$	BF_4	dtbpy	**19a**	<5
13	Ts	$Cu(OTf)_2$	BF_4	$NaHCO_3$	**19a**	55
14	Ts	$Cu(OTf)_2$	BF_4	AcOH	**19a**	62
15	Ts	$Cu(OTf)_2$	BF_4	–[c]	**19a**	65

[a] Determined by HPLC versus an internal standard. [b] Isolated yield. [c] [Ph-I-Mes]BF_4 was employed as the electrophile

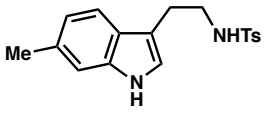
3.11.3 Preparation of N-tosyl tryptamine derivatives

General Procedure A – To a solution of tryptamine (1.00 equiv) in CH_2Cl_2 (0.1 M) was added Et_3N (1.50 equiv). The solution was cooled to 0 °C in an ice bath and *p*-toluenesulfonyl chloride (1.01 equiv) added in one portion as solid against a positive steam of nitrogen. The solution was stirred for 15 minutes, then the ice bath removed and allowed to warm up to ambient temperature (20 to 25 °C) and stirred for an additional 4

hours. The reaction was then quenched with 1 N aq. HCl (equal volume to CH_2Cl_2 used) and the organic layer separated and washed with another portion of 1N aq. HCl. The combined aqueous layers were then combined and back extracted with CH_2Cl_2 (20 mL), then the organic layers combined, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by flash chromatography (SiO_2) to afford *N*-tosyltryptamine as a white or off-white solid.



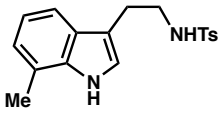
***N*-Tosyltryptamine 167b**: Prepared according to General Procedure A. Reaction run on 6.40 mmol (1.30 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167b** as a white, amorphous solid (1.58 g, 4.81 mmol, 75 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.98 (s, 1H), 7.67 – 7.60 (m, 2H), 7.25 – 7.19 (m, 3H), 7.17 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.01 (dd, *J* = 8.3, 1.6 Hz, 1H), 6.92 (d, *J* = 2.3 Hz, 1H), 4.46 (t, *J* = 6.0 Hz, 1H), 3.26 (q, *J* = 6.5 Hz, 2H), 2.89 (dd, *J* = 6.9, 6.3 Hz, 2H), 2.41 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) 143.2, 136.7, 134.7, 129.6, 128.7, 127.0, 127.0, 123.8, 122.7, 118.1, 110.9, 110.9, 42.9, 25.4, 21.5, 21.4; FTIR (NaCl, thin film): 3401, 3290, 3042, 2919, 2864, 1597, 1423, 1320, 1303, 1157, 1093. HRMS (MM) calc'd for $[M+H]^+$ 329.1318, found 329.1316.



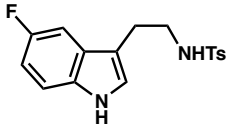
***N*-Tosyltryptamine 167c**: Prepared according to General Procedure A. Reaction run on 3.68 mmol (641 mg) scale. The

crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167c** as a white, amorphous solid (940 mg, 2.87 mmol, 78 % yield).

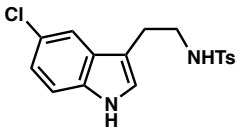
^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.94 (s, 1H), 7.67 – 7.59 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 6.92 – 6.86 (m, 2H), 4.46 (t, *J* = 6.1 Hz, 1H), 3.25 (q, *J* = 6.5 Hz, 2H), 2.90 (t, *J* = 6.6 Hz, 2H), 2.45 (s, 3H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.2, 136.8, 136.7, 132.1, 129.6, 127.0, 124.7, 121.9, 121.3, 118.1, 111.3, 111.2, 43.0, 25.5, 21.6, 21.5. FTIR (NaCl, thin film): 3401, 3280, 2913, 2859, 1456, 1404, 1320, 1301, 1157, 1093. HRMS (MM) calc'd for $[M+H]^+$ 329.1318, found 329.1307.



***N*-Tosyltryptamine 167d**: Prepared according to General Procedure A. Reaction run on 3.84 mmol (669 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167d** as a white, amorphous solid (1.02g, 3.11 mmol, 81 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.27 (s, 1H), 7.90 (d, *J* = 8.2 Hz, 2H), 7.57 – 7.50 (m, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.24 (dd, *J* = 9.7, 2.0 Hz, 3H), 4.75 (t, *J* = 6.1 Hz, 1H), 3.53 (q, *J* = 6.5 Hz, 2H), 3.18 (t, *J* = 6.6 Hz, 2H), 2.73 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (126 MHz, $cdcl_3$) δ 143.3, 136.7, 136.0, 129.6, 127.0, 126.3, 122.7, 122.3, 120.5, 119.7, 116.2, 112.0, 43.0, 25.6, 21.5, 16.6l FTIR (NaCl, thin film): 3400, 3275, 3047, 2908, 2849, 1436, 1320, 1303, 1157, 1093, 1063. HRMS (MM) calc'd for $[M+H]^+$ 329.1318, found 329.1307.

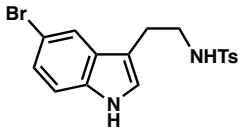


***N*-Tosyltryptamine 167e:** Prepared according to General Procedure A. Reaction run on 3.43 mmol (610 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167e** as an off-white, amorphous solid (940 mg, 2.83 mmol, 82 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.12 (s, 1H), 7.64 – 7.60 (m, 2H), 7.28 – 7.24 (m, 1H), 7.22 (dd, J = 8.5, 0.6 Hz, 2H), 7.02 (d, J = 2.4 Hz, 1H), 6.99 – 6.89 (m, 2H), 4.45 (t, J = 6.0 Hz, 1H), 3.24 (q, J = 6.6 Hz, 2H), 2.87 (dd, J = 6.8, 6.4 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6 (d, $J_{C\text{-}F}$ = 233.8 Hz), 143.5, 136.4, 132.8, 129.6, 127.1 (d, $J_{C\text{-}F}$ = 10.0 Hz), 127.0, 124.4, 111.9 (d, $J_{C\text{-}F}$ = 8.8 Hz), 111.6 (d, $J_{C\text{-}F}$ = 5.0 Hz), 110.6 (d, $J_{C\text{-}F}$ = 26.3 Hz), 103.4 (d, $J_{C\text{-}F}$ = 22.5 Hz), 42.71, 25.32, 21.47; FTIR (NaCl, thin film): 3392, 3275, 2933, 2864, 1486, 1457, 1319, 1301, 1157, 1093 cm^{-1}. HRMS (MM) calc'd for $[M+H]^+$ 333.1068, found 333.1058.

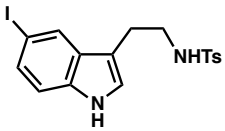


***N*-Tosyltryptamine 167f**: Prepared according to General Procedure A. Reaction run on 3.34 mmol (650 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167f** as an off-white, amorphous solid (1.08 g, 3.10 mmol, 92 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.18 (s, 1H), 7.65 – 7.57 (m, 2H), 7.28 (d, J = 2.0 Hz, 1H), 7.24 (d, J = 0.5 Hz, 1H), 7.21 (dd, J = 8.5, 0.6 Hz, 2H), 7.11 (dd, J = 8.7, 1.9 Hz, 1H), 7.00 (d, J = 2.3 Hz, 1H), 4.49 (t, J = 6.0 Hz, 1H), 3.23 (q, J = 6.6 Hz, 2H), 2.86 (td, J = 6.7, 0.6 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.5, 136.4, 134.7, 129.7, 127.9, 126.9, 125.2, 124.1, 122.5, 117.9, 112.3, 111.2, 42.7, 25.2, 21.5; FTIR

(NaCl, thin film): 3385, 3275, 2913, 2859, 1464, 1422, 1319, 1156, 1093 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 349.0772, found 349.0766.

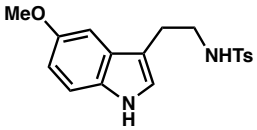


5-Bromo-*N*-Tosyltryptamine 167g: Reaction run on 7.99 mmol (1.91 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167g** as a white amorphous solid (2.63g, 6.69 mmol, 84% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.17 (s, 1H), 7.68 – 7.65 (m, 1H), 7.63 – 7.59 (m, 2H), 7.41 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.23 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.12 (dd, *J* = 8.5, 0.4 Hz, 1H), 6.95 (d, *J* = 2.3 Hz, 1H), 4.48 (t, *J* = 6.0 Hz, 1H), 3.23 (q, *J* = 6.5 Hz, 2H), 2.85 (t, *J* = 6.6 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.5, 136.4, 135.4, 130.5, 129.7, 129.4, 127.3, 126.9, 123.5, 113.3, 110.9, 82.9, 42.8, 25.2, 21.6; FTIR (NaCl, thin film): 3376, 3290, 2922, 2864, 1598, 1460, 1420, 1320, 1157, 1093 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 393.0267, found 393.0260.

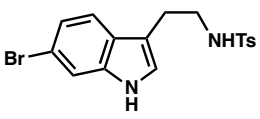


5-Iodo-*N*-tosyltryptamine 167h: To a 50-mL Schlenk tube was charged 5-bromo-*N*-tosyltryptamine **167g** (858 mg, 2.18 mmol, 1.00 equiv), CuI (42.0 mg, 0.220 mmol, 0.10 equiv), and NaI (654 mg, 4.36 mmol, 2.00 equiv). The vessel was then evacuated and backfilled with N_2 three times, and *N,N'*-dimethylethylene diamine (47 μL, 0.44 mmol, 0.20 equiv) and 1,4-dioxane (2.2 mL) added. The vessel was then sealed and heated to 100 °C for 23 hours, then cooled to room temperature, and quenched with concentrated aqueous NH_4OH (10 mL), then diluted with H_2O (30 mL). The mixture was then extracted with CH_2Cl_2 (3 x 30 mL), the organic layers combined, dried over anhydrous Na_2SO_4, filtered, and concentrated *in*

vacuo. Flash chromatography (gradient elution, 10-60% EtOAc in Hexanes) afforded 5-iodo-N-tosyltryptamine as a white solid (900 mg, 2.04 mmol, 94% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.27 (s, 1H), 7.63 – 7.57 (m, 2H), 7.44 (d, *J* = 1.8 Hz, 1H), 7.24 – 7.17 (m, 4H), 6.96 (d, *J* = 2.4 Hz, 1H), 4.62 (t, *J* = 6.0 Hz, 1H), 3.22 (q, *J* = 6.6 Hz, 2H), 2.83 (t, *J* = 6.6 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.5, 136.3, 134.9, 129.7, 128.5, 126.9, 124.9, 124.0, 120.9, 112.8, 112.6, 111.0, 42.7, 25.1, 21.5; FTIR (NaCl, thin film): 3391, 3290, 2928, 2854, 1598, 1456, 1417, 1319, 1288, 1157, 1093 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 441.0128, found 441.0130.



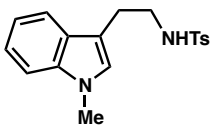
5-Methoxy-*N*-Tosyltryptamine 167i: Prepared according to General Procedure A. Reaction run on 5.94 mmol (1.13 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167i** as a white amorphous solid (1.68g, 4.88 mmol, 82 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.98 (s, 1H), 7.64 – 7.58 (m, 2H), 7.24 (dd, *J* = 8.7, 0.5 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 2H), 6.95 (d, *J* = 2.3 Hz, 1H), 6.87 – 6.81 (m, 2H), 4.45 (t, *J* = 6.0 Hz, 1H), 3.80 (s, 3H), 3.25 (q, *J* = 6.5 Hz, 2H), 2.91 (t, *J* = 6.6 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 154.0, 143.3, 136.6, 131.6, 129.6, 127.2, 127.0, 123.3, 112.5, 112.0, 111.2, 100.2, 55.8, 42.8, 25.4, 21.5; FTIR (NaCl, thin film): 3390, 3285, 2928, 2824, 1486, 1459, 1437, 1319, 1215, 1156, 1092 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 345.1267, found 345.1266.



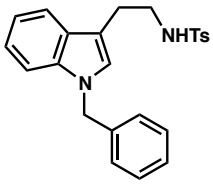
***N*-Tosyltryptamine 167j**: Prepared according to General

Procedure A. Reaction run on 10.90 mmol (2.61 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **167j** as a white, amorphous solid (3.42g, 8.70 mmol, 80 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.11 (s, 1H), 7.63 – 7.56 (m, 2H), 7.49 (dd, *J* = 1.7, 0.5 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.21 – 7.18 (m, 2H), 7.13 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.95 (d, *J* = 2.4 Hz, 1H), 4.44 (t, *J* = 6.1 Hz, 1H), 3.24 (q, *J* = 6.5 Hz, 2H), 2.89 (t, *J* = 6.4 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.4, 137.1, 36.5, 129.6, 126.9, 125.8, 123.2, 122.8, 119.7, 115.8, 114.2, 111.8, 42.9, 25.3, 21.5; FTIR (NaCl, thin film): 3368, 3270, 2933, 2864, 1457, 1399, 1319, 1156, 1092. HRMS (MM) calc'd for $[M+H]^+$ 393.0267, found 393.0252.

General procedure B – To a solution of *N*-tosyltryptamine (1.57 g, 5.00 mmol, 1.00 equiv) in DMF (17 mL) at 20 °C was added NaH (60% dispersion in mineral oil, 0.700 g, 17.5 mmol, 3.5 equiv) slowly, with vigorous stirring, and stirring continued at 20 °C. After 30 minutes, the solution was cooled to 0 °C in an ice bath, and the appropriate alkyl halide (5.00 mmol, 1.00 equiv) was added dropwise by syringe over three minutes. Stirring was continued at 0 °C for two hours, and the reaction allowed to warm to 20 °C and stirring continued for 13 hours. The reaction was then carefully quenched by the dropwise addition of saturated, aqueous ammonium chloride (10 mL), and the mixture diluted with EtOAc (100 mL), and washed with brine (2 x 50 mL). The organic layer was then dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. Flash chromatography (SiO_2) afforded *N'*-alkylated tryptamines as a white solid.



***N*-tosyl-*N'*-methyltryptamines 167k**: Prepared according to General Procedure B. Reaction run on 5.00 mmol (1.57 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 20-40% EtOAc in Hexane) to afford **20k** as a white, amorphous solid (1.18 g, 3.59 mmol, 72 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.05 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.82 (s, 1H), 4.41 (t, *J* = 6.0 Hz, 1H), 3.73 (s, 3H), 3.26 (q, *J* = 6.5 Hz, 2H), 2.92 (t, *J* = 6.6 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.1, 143.1, 137.0, 136.8, 129.6, 129.5, 129.5, 129.5, 129.5, 129.5, 127.3, 127.2, 126.9, 121.7, 118.9, 118.9, 118.5, 109.9, 109.9, 109.3, 109.3, 43.2, 43.2, 32.6, 32.5, 25.3, 25.3, 21.5, 21.4, 14.1; FTIR (NaCl, thin film):3292, 3051, 2929, 1616, 1473, 1325, 1158, 1093 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 329.1318, found 329.1314.



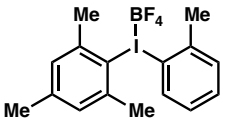
***N*-tosyl-*N'*-benzyltryptamines**: Prepared according to General Procedure B. Reaction run on 5.00 mmol (1.57 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 20-30% EtOAc in Hexane) to afford **167l** as a white, amorphous solid (1.52 g, 3.76 mmol, 75 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.33 – 7.22 (m, 4H), 7.21 – 7.13 (m, 3H), 7.12 – 7.07 (m, 2H), 7.06 – 7.01 (m, 1H), 6.85 (s, 1H), 5.23 (s, 2H), 4.44 (t, *J* = 6.1 Hz, 1H), 3.27 (q, *J* = 6.6 Hz, 2H), 2.91 (t, *J* = 6.7 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 143.2, 137.3, 136.8, 136.8, 129.6, 128.8, 127.7, 127.5, 127.0, 126.8, 126.5, 122.0, 119.3, 118.7, 110.7, 109.8,

49.9, 43.1, 25.5, 21.5; FTIR (NaCl, thin film): 3284, 3057, 3029, 2922, 1597, 1466, 1326, 1159, 1094, 1076 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 405.1557, found 405.1630.

3.11.4 Preparation of Diaryliodonium Tetrafluoroborates

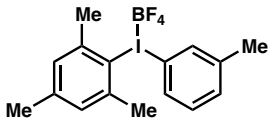
General Procedure C – To a solution of aryl iodide (1.00 equiv) in Ac_2O (0.5 M) was added *m*CPBA (1.50 equiv). After stirring 1 hour at 23 °C, the mixture was cooled to 0 °C and mesitylene (1.10 equiv) was added followed by dropwise addition of HBF_4 (50% *aq* solution, 2.00 equiv). The reaction continued stirring at 0 °C for 30 minutes, followed by 6 hours at 23 °C. The mixture was diluted with water, extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Crude reaction mixtures were dissolved in minimal CH_2Cl_2 and precipated with Et_2O to yield fine, white powders. The precipitate was filtered and dried overnight under high vacuum at 100 °C.

(2-Methylphenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared



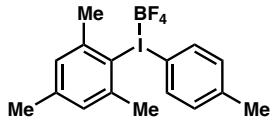
according to General Procedure C. Reaction run on 10.0 mmol (2.18 g) scale. Trituration afforded the product as a white powder (3.0 g, 7.1 mmol, 71 % yield). ^1H NMR (500 MHz, DMSO) δ 7.96 (d, J = 7.8 Hz, 1H), 7.56 – 7.54 (m, 2H), 7.29 – 7.23 (m, 1H), 7.21 (s, 2H), 2.56 (s, 6H), 2.56 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (DMSO, 125 MHz) δ 143.5, 142.1, 141.2, 137.2, 132.9, 132.4, 130.4, 129.8, 122.3, 119.1, 26.6, 24.9, 21.0. FTIR (NaCl, thin film): 1587, 1558, 1457, 1382, 1301, 1064, 1024. HRMS (MM) calc'd for $[M]^+$ 337.0448, found 337.0443.

(3-Methylphenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.18 g) scale. Trituration afforded the product as a white powder (3.9 g, 9.2 mmol, 92 % yield).



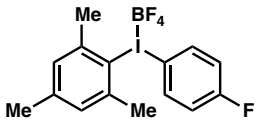
^{1}H NMR (500 MHz, DMSO) δ 7.85 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.22 (s, 2H), 2.60 (s, 6H), 2.32 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (DMSO, 126 MHz) δ 143.5, 142.45, 142.1, 135.1, 133.0, 132.2, 132.0, 130.3, 122.9, 114.8, 26.8, 21.2, 21.0. FTIR (NaCl, thin film): 2913, 1595, 1558, 1452, 1301, 1063, 1024 cm^{-1}; HRMS (MM) calc'd for $[M]^+$ 337.0448, found 337.0443.

(4-Methylphenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.18 g) scale. Trituration afforded the product as a white powder (3.4 g, 8.2 mmol, 80 % yield).



^{1}H NMR (500 MHz, DMSO) δ 7.90 – 7.84 (m, 2H), 7.31 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.20 (s, 2H), 2.60 (s, 6H), 2.33 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (DMSO, 125 MHz) δ 143.5, 142.7, 141.9, 135.0, 133.0, 130.2, 123.2, 111.4, 26.8, 21.7, 21.0. FTIR (NaCl, thin film): 1586, 1451, 1381, 1064, 1024. HRMS (MM) calc'd for $[M]^+$ 337.0448, found 447.0446.

(4-Fluorophenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.22 g) scale. Trituration afforded the product as a white powder (1.7 g, 4.1 mmol, 40 % yield). ^{1}H NMR (500 MHz, DMSO) δ 8.08 – 8.01 (m, 2H), 7.40 –

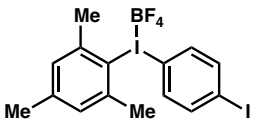


7.34 (m, 2H), 7.22 (s, 2H), 2.60 (s, 6H), 2.30 (s, 3H). ^{13}C NMR (DMSO, 125 MHz) δ 164.2 (d, $J_{C\text{-}F}$ = 250.0 Hz), 143.7, 142.00, 137.8 (d, $J_{C\text{-}F}$ = 8.75 Hz), 130.3, 123.4, 119.7 (d, $J_{C\text{-}F}$ = 22.5 Hz), 109.1, 26.8, 21.0; FTIR (NaCl, thin film): 1576, 1482, 1301, 1237, 1165, 1064, 1024 cm^{-1}; HRMS (MM) calc'd for $[M–BF_4]^+$ 341.0197, found 341.0188.

(4-Chlorophenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.39 g) scale. Trituration afforded the product as a white powder (1.92 g, 4.3 mmol, 44 % yield). ^{1}H NMR (500 MHz, DMSO) δ 7.99 – 7.93 (m, 2H), 7.60 – 7.55 (m, 2H), 7.23 (d, J = 0.5 Hz, 2H), 2.59 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (DMSO, 125 MHz) δ 143.7, 142.1, 137.5, 136.7, 132.3, 130.3, 123.3, 112.8, 26.77, 21.02; FTIR (NaCl, thin film): 1469, 1380, 1301, 1064, 1027 cm^{-1}; HRMS (MM) calc'd for $[M–BF_4]^+$ 356.9901, found 356.9895.

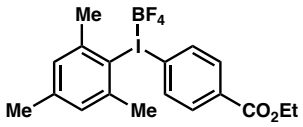
(4-Bromophenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.83 g) scale. Trituration afforded the producct as a white powder (2.67 g, 5.5 mmol, 55 % yield). ^{1}H NMR (500 MHz, DMSO) δ 7.91 – 7.86 (m, 2H), 7.73 – 7.68 (m, 2H), 7.23 (d, J = 0.5 Hz, 2H), 2.59 (s, 6H), 2.30 (s, 3H). ^{13}C NMR (DMSO, 126 MHz) δ 143.8, 142.1, 136.8, 135.2, 130.3, 126.3, 123.2, 113.5, 26.8, 21.0; FTIR (NaCl, thin film): 1085, 1469, 1388, 1303, 1064 1024 cm^{-1}; HRMS (MM) calc'd for $[M–BF_4]^+$ 400.9396, found 400.9392.

(4-iodophenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared



according to General Procedure C. Reaction run on 5.0 mmol (1.24 g) scale. Trituration afforded the product as a white powder (1.59 g, 3.0 mmol, 30 % yield). ^{1}H NMR (500 MHz, DMSO) δ 7.88 – 7.82 (m, 2H), 7.73 – 7.69 (m, 2H), 7.22 (s, 2H), 2.58 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (DMSO, 125 MHz) δ 143.71, 142.06, 140.93, 136.50, 130.31, 123.13, 114.38, 100.25, 26.77, 21.02; FTIR (NaCl, thin film): 1464, 1380, 1303, 1064, 1024, 984 cm^{-1}; HRMS (MM) calc'd for $[M–BF_4]^+$ 448.9258, found 448.9248.

(4-ethoxycarbonyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate: Prepared



according to General Procedure C. Reaction run on 10.0 mmol (2.76 g) scale. Trituration afforded the product as a white powder (2.20 g, 4.6 mmol, 46 % yield).

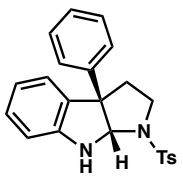
^{1}H NMR (500 MHz, DMSO) δ 8.11 – 8.05 (m, 2H), 8.02 – 7.96 (m, 2H), 7.24 (d, J = 0.5 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 2.59 (s, 6H), 2.30 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (DMSO, 125 MHz) δ 165.03, 143.8, 142.2, 135.2, 133.1, 132.4, 130.4, 123.2, 119.8, 62.0, 26.8, 21.0, 14.5; FTIR (NaCl, thin film): 2984, 1719, 1583, 1449, 1395, 1365, 1277, 1064, 1024 cm^{-1}; HRMS (MM) calc'd for $[M–BF_4]^+$ 395.0502, found 395.0493.

3.11.5 Preparation of N-Tosylpyrroloindolines

General Procedure D – To a flame-dried flask was charged the appropriate *N*-tosyltryptamine derivative (0.300 mmol, 1.0 equiv), the appropriate iodonium (0.330 mmol, 1.1 equiv), $Cu(OAc)_2$ or $Cu(OTf)_2$ (0.030 mmol or 0.060 mmol, 0.10 equiv or 0.20

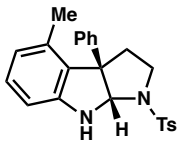
mmol) and CH_2Cl_2 (3.0 mL). The reaction was stirred for the time indicated, at which point the reaction was diluted with CH_2Cl_2 (10 mL), and quenched with saturated aq. $NaHCO_3$ (15 mL). The organic layer was separated and washed with additional $NaHCO_3$ (2 x 15 mL) and the resulting aqueous layers were then combined and back extracted with CH_2Cl_2 (15 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (SiO_2 or basic alumina) to afford the *N*-tosylpyrroloindoline as a white or off-white solid.

Pyrroloindoline 168a: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 4 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in hexanes) to afford **168a** as a white, amorphous solid (72.6 mg, 0.19 mmol, 62 % yield).



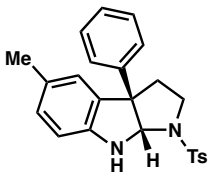
^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 – 7.71 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.25 – 7.15 (m, 3H), 7.14 – 7.09 (m, 3H), 7.00 (ddd, *J* = 7.4, 1.1, 0.5 Hz, 1H), 6.80 – 6.74 (m, 1H), 6.70 (dd, *J* = 7.8, 0.6 Hz, 1H), 5.43 (s, 1H), 4.91 (s, 1H), 3.65 (ddd, *J* = 10.6, 7.8, 1.4 Hz, 1H), 3.25 (td, *J* = 11.0, 5.6 Hz, 1H), 2.48 (ddd, *J* = 12.4, 5.6, 1.0 Hz, 1H), 2.44 (s, 3H), 2.34 (ddd, *J* = 12.4, 11.3, 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.8, 143.6, 143.0, 136.3, 131.4, 129.8, 128.8, 128.6, 127.0, 127.0, 125.7, 123.9, 119.6, 110.1, 85.6, 61.8, 48.1, 37.3, 21.5. FTIR (NaCl, thin film): 3366, 2978, 2878, 1610, 1595, 1491, 1466, 1332, 1318, 1303, 1159, 1094. HRMS (MM) calc'd for $[M+H]^+$ 391.1475, found 391.1473.

Pyrroloindoline 168a: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168a** as a white foam (99.4 mg, 0.25 mmol, 82 % yield).



^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.78 – 7.70 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.24 – 7.15 (m, 3H), 7.12 – 7.08 (m, 2H), 6.95 (dd, *J* = 6.5, 0.8 Hz, 1H), 6.89 – 6.82 (m, 1H), 6.72 (dd, *J* = 7.4, 7.4 Hz, 1H), 5.47 (s, 1H), 4.70 (s, 1H), 3.67 (ddd, *J* = 10.5, 7.8, 1.5 Hz, 1H), 3.24 (ddd, *J* = 10.9, 10.9, 5.6 Hz, 1H), 2.47 (ddd, *J* = 12.4, 5.6, 1.1 Hz, 1H), 2.44 (s, 3H), 2.35 (ddd, *J* = 12.4, 11.2, 7.8 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ147.4, 143.6, 143.1, 136.5, 130.8, 129.8, 129.7, 128.6, 126.98, 126.94, 125.7, 121.4, 119.7, 119.5, 85.5, 62.2, 48.2, 37.6, 21.5, 16.7. FTIR (NaCl, thin film): 3351, 3059, 2892, 1595, 1447, 1332, 1153, 1089. HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1629.

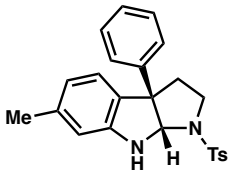
Pyrroloindoline 168b: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168b** as a white, amorphous solid (76.6 mg, 0.19 mmol, 63 % yield).



^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.25 – 7.16 (m, 3H), 7.15 – 7.10 (m, 2H), 6.91 (dd, *J* = 7.9, 1.0 Hz, 1H), 6.79 (d, *J* = 0.4 Hz,

1H), 6.61 (d, *J* = 7.9 Hz, 1H), 5.41 (s, 1H), 3.64 (ddd, *J* = 10.5, 7.8, 1.3 Hz, 1H), 3.25 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, *J* = 12.3, 11.3, 7.9 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 146.4, 143.5, 143.1, 136.3, 131.7, 129.8, 129.2, 129.0, 128.6, 126.97, 126.95, 125.7, 124.4, 110.1, 85.9, 61.8, 48.1, 37.1, 21.5, 20.9. FTIR (NaCl, thin film): 3385, 2922, 1617, 1597, 1496, 1448, 1340, 1159, 1093. HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1644.

Pyrroloindoline 168c: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168c** as a white foam (61.0 mg, 0.15 mmol, 50 % yield).

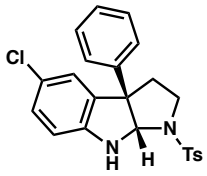


^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.77 – 7.70 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.25 – 7.14 (m, 3H), 7.13 – 7.07 (m, 2H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.59 (ddd, *J* = 7.6, 1.4, 0.7 Hz, 1H), 6.55 – 6.51 (m, 1H), 5.41 (s, 1H), 4.83 (s, 1H), 3.64 (ddd, *J* = 10.6, 7.8, 1.4 Hz, 1H), 3.27 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.41 (m, 1H), 2.44 (s, 3H), 2.31 (ddd, *J* = 7.9, 6.9, 5.7 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 149.0, 143.6, 143.2, 138.8, 136.4, 129.8, 128.6, 128.6, 127.0, 126.9, 125.7, 123.6, 120.4, 111.0, 85.9, 61.6, 48.2, 37.3, 21.5, 21.5. FTIR (NaCl, thin film): 3353, 2889, 1595, 1490, 1448, 1331, 1307, 1159, 1119, 1092. HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1609.

Pyrroloindoline 168d: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168d** as a white, crystalline solid (69.2 mg, 0.17 mmol, 57% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.81 – 7.70 (m, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.25 – 7.15 (m, 3H), 7.13 – 7.07 (m, 2H), 6.95 (d, *J* = 7.4 Hz, 1H), 6.86 (d, *J* = 7.1 Hz, 1H), 6.72 (dd, *J* = 7.4, 7.4 Hz, 1H), 5.47 (s, 1H), 4.70 (s, 1H), 3.67 (ddd, *J* = 10.5, 7.8, 1.4 Hz, 1H), 3.24 (ddd, *J* = 10.9, 10.9, 5.6 Hz, 1H), 2.47 (ddd, *J* = 12.4, 5.6, 1.1 Hz, 1H), 2.44 (s, 3H), 2.35 (ddd, *J* = 12.4, 11.2, 7.8 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 147.4, 143.6, 143.1, 136.5, 130.8, 129.8, 129.7, 128.6, 127.0, 126.9, 125.7, 121.4, 119.7, 119.5, 85.5, 62.2, 48.2, 37.6, 21.5, 16.7; FTIR (NaCl, thin film): 3350, 2892, 1594, 1490, 1465, 1448, 1331, 1319, 1305, 1243, 1151, 1109, 1089 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1590.

Pyrroloindoline 168e: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (99.7 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168e** as a white, crystalline solid (80.1 mg, 0.20 mmol, 65 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.26 – 7.17 (m, 3H), 7.15 – 7.08 (m, 2H), 6.82 (ddd, *J* = 8.9, 8.9, 2.6 Hz, 1H), 6.71 (dd, *J* = 8.2, 2.6 Hz, 1H), 6.63 (dd, *J* = 8.5, 4.2 Hz, 1H), 5.43 (s, 1H), 3.65 (ddd, *J* = 10.5, 7.8, 1.4 Hz, 1H), 3.27 (ddd, *J* = 10.9, 10.9, 5.7 Hz, 1H), 2.48 – 2.39 (m, 1H), 2.44 (s, 3H), 2.33 (ddd, *J* = 12.5, 11.2, 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ

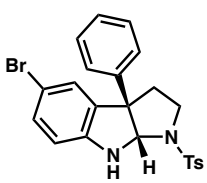
157.4 (d, $J_{C\text{-}F}$ = 235.0 Hz), 144.7, 143.7, 142.3, 136.1, 133.3 (d, $J_{C\text{-}F}$ = 7.5 Hz), 129.9, 128.7, 127.3, 127.0, 125.6, 115.2 (d, $J_{C\text{-}F}$ = 22.5 Hz), 111.2 (d, $J_{C\text{-}F}$ = 23.8 Hz), 110.8 (d, $J_{C\text{-}F}$ = 7.5 Hz), 86.2, 62.0, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3365, 2891, 1996, 1593, 1488, 1448, 1329, 1306, 1154, 1091. HRMS (MM) calc'd for $[M+H]^+$ 409.1381, found 409.1375.



Pyrroloindoline 168f: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (105 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168f** as a white, crystalline solid (81.7 mg, 0.19 mmol, 64 % yield).

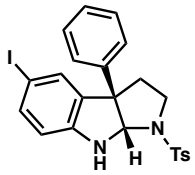
^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.74 – 7.69 (m, 2H), 7.29 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.27 – 7.19 (m, 3H), 7.13 – 7.09 (m, 2H), 7.06 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.62 (d, *J* = 8.3 Hz, 1H), 5.44 (s, 1H), 4.95 (s, 1H), 3.64 (ddd, *J* = 10.6, 7.8, 1.5 Hz, 1H), 3.27 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.40 (m, 1H), 2.43 (s, 3H), 2.33 (ddd, *J* = 12.5, 11.2, 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 126 MHz) δ 147.3, 143.8, 142.3, 136.1, 133.6, 129.9, 128.8, 128.7, 127.3, 126.9, 125.5, 124.1, 111.0, 85.8, 61.8, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3386, 3059, 2971, 1598, 1481, 1447, 1336, 1258, 1158, 1090 1037. HRMS (MM) calc'd for $[M+H]^+$ 425.1085, found 425.1083.

Pyrroloindoline 168g: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (118.0 g) scale. The crude material was purified on basic alumina (gradient elution,



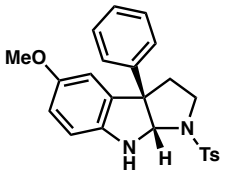
40% THF in Hexane) to afford **168g** as a white, crystalline solid (82.1 mg, 0.18 mmol, 58 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.75 – 7.69 (m, 2H), 7.29 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.27 – 7.18 (m, 4H), 7.10 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.06 (d, *J* = 2.0 Hz, 1H), 6.58 (d, *J* = 8.3 Hz, 1H), 5.43 (s, 1H), 4.96 (s, 1H), 3.64 (ddd, *J* = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.48 – 2.44 (m, 1H), 2.43 (s, 3H), 2.33 (ddd, *J* = 8.2, 6.4, 4.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 126 MHz) 147.8, 143.8, 142.3, 136.1, 134.1, 131.5, 129.9, 128.7, 127.3, 126.9, 126.9, 125.5, 111.5, 111.1, 85.7, 61.8, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3386, 3059, 2971, 1598, 1477, 1336, 1258, 1093, 1037. HRMS (MM) calc'd for $[M+H]^+$ 469.0580, found 469.0578.

Pyrroloindoline 168h: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (132.1 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168h** as a white, amorphous solid (92.6 mg, 0.19 mmol, 62 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.33 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 2H), 7.23 – 7.15 (m, 4H), 7.08 – 7.03 (m, 2H), 6.45 (d, *J* = 8.3 Hz, 1H), 5.38 (d, *J* = 6.8 Hz, 1H), 4.93 (s, 1H), 3.59 (ddd, *J* = 10.6, 7.8, 1.5 Hz, 1H), 3.23 (ddd, *J* = 10.9, 10.9, 5.6 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.39 (s, 3H), 2.28 (ddd, *J* = 12.5, 11.2, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.4, 143.6, 142.4, 137.4, 136.1, 134.6, 132.6, 129.9, 128.7, 127.3, 126.9, 125.5, 112.2, 85.5, 80.3, 61.6, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3385, 3057, 2968, 1597, 1476, 1446,

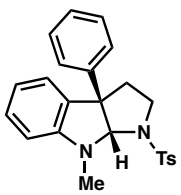


1420, 1334, 1260, 1159, 1093 cm $^{-1}$; HRMS (MM) calc'd for $[M+H]^+$ 517.0441, found 517.0436.

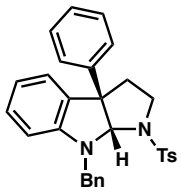
Pyrroloindoline 168i: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 6 hours. Reaction run on 0.30 mmol (103.3 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168i** as a white, amorphous solid (72.6 mg, 0.19 mmol, 62 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 – 7.70 (m, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.25 – 7.15 (m, 3H), 7.15 – 7.08 (m, 2H), 6.69 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.60 (d, *J* = 2.5 Hz, 1H), 5.40 (s, 1H), 4.71 (s, 1H), 3.71 (s, 3H), 3.65 (ddd, *J* = 10.5, 7.8, 1.3 Hz, 1H), 3.25 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.44 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, *J* = 12.4, 11.3, 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) 153.9, 143.6, 142.7, 142.6, 136.3, 133.0, 129.8, 128.6, 127.1, 127.0, 125.7, 113.6, 110.8, 110.6, 86.3, 62.1, 55.8, 48.1, 37.0, 21.5; FTIR (NaCl, thin film): 3380, 3057, 3025, 2947, 2832, 1598, 1492, 1336, 1159, 1093, 1035; HRMS (MM) calc'd for $[M+H]^+$ 421.1580, found 421.1577.



Pyrroloindoline 168k: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 20 – 25% THF in Hexane) to afford **168k** as a white, solid (65.1 mg, 0.16 mmol, 54% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.71 – 7.65 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.20 – 7.17 (m, 3H), 7.17 – 7.13 (m, 1H), 6.96 – 6.89 (m, 2H), 6.85 (dd, *J* = 7.3, 1.1 Hz,

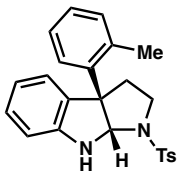


1H), 6.67 (ddd, *J* = 7.4, 7.4, 0.8 Hz, 1H), 6.50 (d, *J* = 7.9 Hz, 1H), 5.53 (s, 1H), 3.76 (ddd, *J* = 12.1, 7.0, 1.0 Hz, 1H), 3.13 (ddd, *J* = 11.9, 11.9, 5.2 Hz, 1H), 3.06 (s, 3H), 2.44 (s, 3H), 2.21 (ddd, *J* = 12.2, 5.0, 1.2 Hz, 1H), 2.05 (ddd, *J* = 12.0, 12.0, 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) 150.5, 143.6, 143.0, 136.5, 132.2, 129.7, 128.8, 128.4, 127.2, 126.7, 125.9, 123.62, 117.8, 106.2, 91.9, 61.1, 48.8, 38.0, 31.2, 21.5; FTIR (NaCl, thin film): 3056, 3027, 2949, 2891, 2827, 1762, 1605, 1491, 1347, 1160, 1092, 1022 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1600.

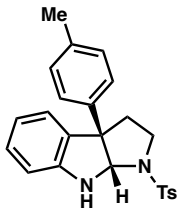


Pyrroloindoline 168l: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (121 mg) scale. The crude material was purified on basic alumina (gradient elution, 20 – 25% THF in Hexane) to afford **168l** as a white foam (83.4 mg, 0.17 mmol, 58% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.64 – 7.52 (m, 2H), 7.41 – 7.36 (m, 2H), 7.36 – 7.30 (m, 2H), 7.29 – 7.24 (m, 1H), 7.19 – 7.12 (m, 5H), 7.09 – 7.02 (m, 1H), 6.89 – 6.81 (m, 3H), 6.64 (ddd, *J* = 7.4, 7.4, 0.9 Hz, 1H), 6.42 (d, *J* = 7.8 Hz, 1H), 5.69 (s, 1H), 4.89 (d, *J* = 16.4 Hz, 1H), 4.63 (d, *J* = 16.4 Hz, 1H), 3.82 (dd, *J* = 12.5, 6.8 Hz, 1H), 3.25 (ddd, *J* = 12.2, 12.2, 5.1 Hz, 1H), 2.41 (s, 3H), 2.24 (dd, *J* = 11.9, 4.7 Hz, 1H), 2.06 (ddd, *J* = 12.1, 12.1, 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 149.7, 143.6, 143.5, 138.5, 136.4, 132.2, 129.7, 128.7, 128.4, 128.4, 127.3, 127.2, 126.9, 126.7, 125.8, 123.9, 117.9, 106.5, 90.7, 61.3, 48.5, 48.1, 38.2, 21.5; FTIR (NaCl, thin film): 3062, 3027, 2898, 1604, 1493, 1346, 1158, 1089 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 481.1944, found 481.1947.

Pyrroloindoline 168a: Prepared according to General Procedure D using 20 mol% $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale with the symmetric di-*o*-tolyliodonium tetrafluoroborate. The crude material was purified by silica gel chromatography (gradient elution, 20% EtOAc in Hexane) to afford **168a** as a white, amorphous solid (60.6 mg, 0.15 mmol, 50 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.69 – 7.63 (m, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.14 – 7.04 (m, 4H), 7.03 – 6.98 (m, 1H), 6.92 (dd, *J* = 7.4, 0.8 Hz, 1H), 6.76 (ddd, *J* = 7.4, 7.4, 1.0 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 5.67 (s, 1H), 4.94 (s, 1H), 3.59 (ddd, *J* = 10.1, 7.7, 4.0 Hz, 1H), 3.36 (ddd, *J* = 10.1, 8.6, 6.6 Hz, 1H), 2.69 (ddd, *J* = 12.9, 7.9, 7.9 Hz, 1H), 2.40 (s, 3H), 2.39 – 2.34 (m, 1H), 2.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.4, 143.5, 139.4, 136.4, 135.6, 132.6, 131.9, 129.6, 128.5, 127.2, 127.1, 127.0, 125.7, 124.3, 119.2, 109.4, 84.4, 62.1, 47.4, 37.9, 21.4, 20.8; FTIR (NaCl, thin film): 3390, 3057, 2975, 2883, 1606, 1485, 1338, 1158 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1633.

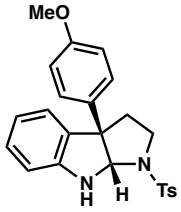


Pyrroloindoline 168b: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 20% EtOAc in Hexane) to afford **168b** as a white, amorphous solid (90.0 mg, 0.22 mmol, 74 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 – 7.71 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.11 (ddd, *J* = 7.7, 7.7, 1.3 Hz, 1H), 7.04 (dd, *J* = 4.7, 4.0 Hz, 2H), 6.99 (ddd, *J* = 3.8, 3.8, 1.6 Hz, 3H), 6.77 (ddd, *J* = 7.4, 1.0 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.39 (s, 1H), 3.64 (ddd, *J* = 10.6, 7.8, 1.4 Hz, 1H), 3.25

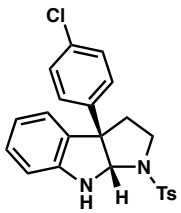


(ddd, *J* = 10.9, 10.9, 5.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.44 (s, 3H), 2.37 – 2.29 (m, 1H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.7, 143.6, 140.0, 136.7, 136.31, 131.6, 129.8, 129.2, 128.7, 127.0, 125.6, 123.8, 120.0, 110.1, 85.7, 61.5, 48.1, 37.3, 21.5, 20.9; FTIR (NaCl, thin film): 3395, 3052, 3022, 2913, 1607, 1465, 1336, 1159, 1094, 1035 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1624.

Pyrroloindoline 168c: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 4 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 6:3:1 Hexanes:CH_2Cl_2:Acetone) to afford **168c** as a white foam (88.1 mg, 0.21 mmol, 70 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.75 – 7.70 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.11 (ddd, *J* = 7.9, 7.4, 1.3 Hz, 1H), 7.04 – 6.96 (m, 3H), 6.80 – 6.72 (m, 3H), 6.71 – 6.67 (m, 1H), 5.36 (s, 1H), 4.89 (br s, 1H), 3.74 (s, 3H), 3.63 (ddd, *J* = 10.6, 7.8, 1.5 Hz, 1H), 3.23 (td, *J* = 10.9, 5.6 Hz, 1H), 2.47 – 2.40 (m, 1H), 3.2.44 (s, 3H) 2.32 (ddd, *J* = 12.4, 11.2, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 158.5, 148.77, 143.6, 136.3, 135.0, 131.7, 129.8, 128.7, 127.0, 126.8, 123.8, 119.6, 113.9, 110.1, 85.8, 61.2, 55.2, 48.2, 37.3, 21.5; FTIR (NaCl, thin film): 3390, 3047, 2953, 2834, 1608, 1512, 1483, 1466, 1336, 1251, 1183, 1159, 1094 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 421.1580, found 421.1580.

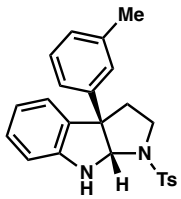


Pyrroloindoline 168d: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF



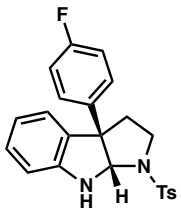
in Hexane) to afford **168d** as a white, amorphous solid (86.5 mg, 0.20 mmol, 68 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 – 7.69 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.21 – 7.15 (m, 2H), 7.15 – 7.09 (m, 1H), 7.06 – 7.00 (m, 2H), 6.95 (ddd, *J* = 7.4, 1.2, 0.5 Hz, 1H), 6.77 (ddd, *J* = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (dd, *J* = 4.5, 4.0 Hz, 1H), 5.37 (s, 1H), 4.91 (br s, 1H), 3.65 (ddd, *J* = 10.7, 7.8, 1.5 Hz, 1H), 3.24 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.44 (s, 3H), 2.28 (ddd, *J* = 12.4, 11.2, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.7, 143.7, 141.5, 136.2, 132.9, 131.0, 129.9, 129.0, 128.7, 127.1, 126.9, 123.7, 119.7, 110.2, 85.6, 61.3, 48.1, 37.1, 21.5; FTIR (NaCl, thin film): 3386, 3051, 2970, 2893, 1607, 1493, 1466, 1483, 1399, 1336, 1159, 1093 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 425.1085, found 425.1077.

Pyrroloindoline 168e: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 20% EtOAc in Hexane) to afford **168e** as a white, amorphous solid (75.2 mg, 0.19 mmol, 63% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.77 – 7.72 (m, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.14 – 7.08 (m, 2H), 7.02 – 6.97 (m, 2H), 6.92 – 6.86 (m, 2H), 6.77 (ddd, *J* = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.42 (s, 1H), 3.66 (ddd, *J* = 10.6, 7.8, 1.4 Hz, 1H), 3.25 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.45 (m, 1H), 2.44 (s, 3H), 2.32 (ddd, *J* = 12.5, 11.4, 7.9 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.8, 143.6, 143.0, 138.2, 136.4, 131.4, 129.9, 128.7, 128.4, 127.8, 127.0, 126.3, 124.0, 122.8, 119.6, 110.1, 85.7, 61.8, 48.2, 37.6, 21.5, 21.5; FTIR (NaCl, thin

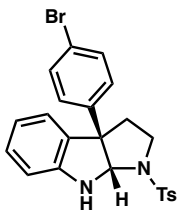


film): 3390, 2047, 2970, 1607, 1483, 1466, 1340, 1159, 1094 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 405.1631, found 405.1626.

Pyrroloindoline 168f: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168f** as a white, amorphous solid (80.3 mg, 0.20 mmol, 66 % yield). ^1H NMR ($CDCl_3$, 500 MHz) δ 7.77 – 7.70 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.16 – 7.09 (m, 1H), 7.09 – 7.04 (m, 2H), 6.97 (ddd, *J* = 7.4, 1.2, 0.5 Hz, 1H), 6.93 – 6.86 (m, 2H), 6.78 (ddd, *J* = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.38 (s, 1H), 3.66 (ddd, *J* = 10.6, 7.8, 1.4 Hz, 1H), 3.24 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.42 (m, 1H), 2.44 (s, 3H), 2.30 (ddd, *J* = 12.4, 11.2, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 161.6 (d, J_{C-F} = 245.0 Hz), 148.7, 143.7, 138.7, 138.7, 136.2, 131.3, 129.8, 128.9, 127.3 (d, J_{C-F} = 7.5 Hz), 126.9, 123.7, 119.7, 115.3 (d, J_{C-F} = 20.0 Hz), 110.2, 109.9, 85.7, 61.2, 48.1, 37.3, 21.5; FTIR (NaCl, thin film): 3391, 3051, 2970, 2892, 1607, 1510, 1483, 1466, 1400, 1336, 1233, 1160, 1095 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 409.1381, found 409.1363.



Pyrroloindoline 168g: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **168g** as a white, amorphous solid (83.4 mg, 0.19 mmol, 59 %

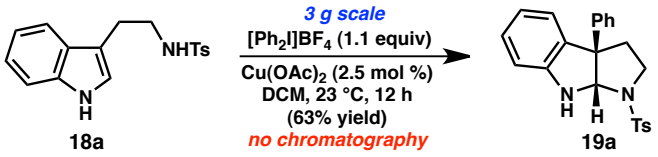


yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.76 – 7.69 (m, 2H), 7.36 – 7.28 (m, 4H), 7.12 (ddd, *J* = 7.7, 7.7, 1.2 Hz, 1H), 7.00 – 6.92 (m, 3H), 6.77 (ddd, *J* = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.37 (s, 1H), 4.91 (s, 1H), 3.65 (ddd, *J* = 10.7, 7.8, 1.4 Hz, 1H), 3.24 (ddd, *J* = 10.9, 10.9, 5.6 Hz, 1H), 2.49 – 2.40 (m, 1H), 2.44 (s, 3H), 2.27 (ddd, *J* = 12.4, 11.2, 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.6, 143.7, 142.0, 136.1, 131.6, 130.9, 129.9, 129.0, 127.5, 126.9, 123.71, 121.0, 119.7, 110.2, 85.5, 61.4, 48.1, 37.0, 21.5; FTIR (NaCl, thin film): 3391, 3051, 2970, 2892, 1608, 1597, 1484, 1466, 1396, 1336, 1159, 1095 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 469.0580, found 469.0553.

Pyrroloindoline 168h: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexanes) to afford **168h** as a white, amorphous solid (95.8 mg, 0.19 mmol, 62 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.75 – 7.69 (m, 2H), 7.55 – 7.51 (m, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.12 (ddd, *J* = 7.7, 7.7, 1.2 Hz, 1H), 6.96 – 6.92 (m, 1H), 6.88 – 6.83 (m, 2H), 6.76 (ddd, *J* = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 5.35 (s, 1H), 3.64 (ddd, *J* = 10.7, 7.8, 1.4 Hz, 1H), 3.24 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.39 (m, 1H), 2.44 (s, 3H), 2.26 (ddd, *J* = 12.4, 11.2, 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 148.7, 143.8, 142.8, 137.6, 136.2, 130.9, 129.9, 129.0, 127.7, 126.9, 123.7, 119.8, 110.3, 92.5, 85.5, 61.5, 48.1, 36.9, 21.6; FTIR (NaCl, thin film): 3390, 3047, 2948, 2878, 1612, 1486, 1336, 1158, 1005 cm^{-1}; HRMS (MM) calc'd for $[M+H]^+$ 517.0441, found 517.0424.

Pyrroloindoline 168i: Prepared according to General Procedure D using 20 mol % $Cu(OTf)_2$ for 12 hours. Reaction run on 0.30 mmol (94.0 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 6:3:1 Hexanes:DCM:Acetone) to afford **168i** as a colorless oil (78.2 mg, 0.17 mmol, 56 % yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.91 – 7.85 (m, 2H), 7.75 – 7.69 (m, 2H), 7.29 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.21 – 7.15 (m, 2H), 7.14 – 7.08 (m, 1H), 6.96 (ddd, *J* = 7.4, 1.2, 0.5 Hz, 1H), 6.76 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.71 (dd, *J* = 7.2, 0.7 Hz, 1H), 5.43 (s, 1H), 4.92 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.66 (ddd, *J* = 10.7, 7.8, 1.4 Hz, 1H), 3.26 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.49 (ddd, *J* = 12.3, 5.5, 1.0 Hz, 1H), 2.43 (s, 3H), 2.31 (ddd, *J* = 12.4, 11.3, 7.9 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 166.1, 148.7, 148.0, 143.8, 136.2, 130.9, 129.9, 129.9, 129.7, 129.0, 126.9, 125.63, 123.8, 119.7, 110.2, 85.4, 61.8, 60.9, 48.1, 37.1, 21.5, 14.3; FTIR (NaCl, thin film): 3387, 3052, 2979, 2895, 1713, 1610, 1483, 1467, 1343, 1278, 1160, 1110 cm^{-1}. HRMS (MM) calc'd for $[M+H]^+$ 463.1686, found 463.1666.

3.11.6 Catalyst Efficiency and Scalability



To a flame-dried, 100 mL flask was charged *N*-tosyltryptamine (3.15 g, 10.0 mmol, 1.0 equiv), Ph_2IBF_4 (4.04 g, 11.0 mmol, 1.1 equiv) and $Cu(OAc)_2$ (45.4 mg, 0.25 mmol, 0.025 equiv). The dissolved in 50 mL CH_2Cl_2 and allowed to stir at room temperature

for 12 hours at which point the reaction was diluted with CH_2Cl_2 (100 mL), washed with saturated aqueous $NaHCO_3$ (2 x 50 mL) and the resulting aqueous layers were then combined and back extracted with CH_2Cl_2 (50 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The resultant yellow solid was dissolved in 50 mL CH_2Cl_2, 100 mL Et_2O and 200 mL hexanes to afford a light yellow powder. The powder was filtered and dried under vacuum to give **168a** (2.55g, 6.5 mmol, 65% yield).

3.11.7 Preparation of Diimine Ligands

α-Diimine ligands were prepared following literature precedent by Bercaw et al. $^{Mes}DAB_{Me}$ (**L7**) and $^{t\text{Bu}}DAB_{Me}$ (**L6**) were readily prepared on greater than 40 gram scale in comparable yields to those reported in the literature. Ligands were thoroughly dried under high-vacuum (< 1.0 mTorr) at 50 °C for 4 hours prior to use and stored in a glovebox under inert atmosphere.

3.11.8 Preparation of Diketopiperazine Substrates

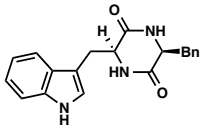
The preparation of diketopiperazines **175a-f** have been previously prepared in the literature. Diketopiperazine substrates **175d** and **175e** were prepared according to known literature procedures. Improved yields were obtained for substrates **175a-175c** using an analogous procedure as reported by Movassaghi et al.

General Procedure (I) *for the Synthesis of Diketopiperazine Substrates:*

To a solution of L-tryptophan methyl ester hydrochloride (1.0 equiv) in CH_2Cl_2 (0.1 M) at 0 °C was added Et_3N (4.5 equiv) dropwise. HOBt•H_2O (1.5 equiv) and Boc-

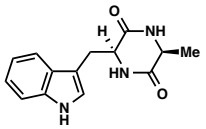
amino acid (2.0 equiv) were sequentially added and stirred vigorously. Once homogenous, EDC•HCl (1.5 equiv) was added in a single portion and the solution allowed to warm to 23 °C. The reaction was stirred for 15 hours, at which time it was quenched by the addition of 1N HCl, and the aqueous layer extracted with CH_2Cl_2 (2 x). The combined organics were then washed with saturated aqueous $NaHCO_3$, and the aqueous layer back extracted with CH_2Cl_2 (2 x). The organics were pooled, then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The resulting oil/foam was subsequently dissolved in CH_2Cl_2 (0.2 M), and cooled to 0 °C. TFA (1.5 mL/5 mL CH_2Cl_2) was added dropwise, then the solution was warmed to 23 °C and stirred for 2 h. The mixture was concentrated *in vacuo* and the resulting viscous residue dissolved in methanol (0.25 M), and cooled to 0°C. Ammonium hydroxide (28–30% in H_2O, 1 mL/ 6 mL MeOH) was then added dropwise and the reaction mixture allowed to warm to 23 °C and stirred for 24 h. The resulting suspension was cooled to 0 °C, and the fine white precipitate was filtered and rinsed with cold methanol. The white solid is then crushed and dried under high vacuum (< 1 mTorr) at 50 °C for a minimum of 2 h.

Cyclo-(L)-Trp-(L)-Phe (175a)



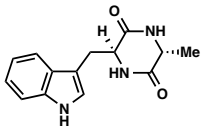
Prepared from L-tryptophan methyl ester hydrochloride following *General Procedure I* on 19.6 mmol scale. The crude reaction mixture was filtered to yield 5.8 g (89% yield) of **175a** as a white solid. Spectral data matches that reported in the literature.

Cyclo-(L)-Trp-(L)-Ala (175b)



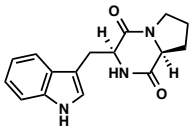
Prepared from L-tryptophan methyl ester hydrochloride following *General Procedure I* on 9.8 mmol scale. The crude reaction mixture was filtered to yield 2.3 g (92% yield) of **175b** as a white solid. Spectral data matches that reported in the literature.

Cyclo-(L)-Trp-(D)-Ala (175c)



Prepared from L-tryptophan methyl ester hydrochloride following *General Procedure I* on 7.9 mmol scale. The crude reaction mixture was filtered to yield 1.8 g (89% yield) of **175c** as a white solid. Spectral data matches that reported in the literature.

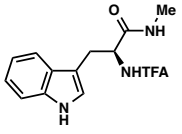
Large Scale Preparation of Cyclo-(L)-Trp-(L)-Pro (175f):



To a solution of L-proline methyl ester hydrochloride (11.0 g, 66.6 mmol, 1.00 equiv) in CH_2Cl_2 (700 mL) at 0 °C was added triethylamine (32.5 mL, 233 mmol, 3.50 equiv) dropwise by addition funnel. *N*-hydroxybenzotriazole monohydrate (15.3, 100 mmol, 1.50 equiv) and Boc-(L)-tryptophan (31.8 g, 100 mmol, 1.50 equiv) were then added successively. After 10 minutes, EDC•HCl (19.2 g, 100 mmol, 1.50 equiv) was added in a single portion and the mixture allowed to warm to 23 °C over 2.0 hours. After 20 hours, the solution was quenched by the addition of 1N HCl (1.0 L), and the aqueous layer extracted with CH_2Cl_2 (2 x 150 mL). The combined organics were then washed with saturated aqueous $NaHCO_3$ (1.0 L), and the aqueous layer back extracted with CH_2Cl_2 (200 mL). The combined organics were then dried over anhydrous sodium sulfate, filtered, and concentrated in

vacuo. The resulting white foam was then dissolved in CH_2Cl_2 (200 mL), and trifluoroacetic acid (60 mL) added dropwise by addition funnel. After 2 h, the solution was concentrated in vacuo and the viscous residue dissolved in methanol (900 mL) and cooled to 0 °C. Ammonium hydroxide (28 to 30% in H_2O, 35.0 mL) was added dropwise by addition funnel. The solution was then stirred for 14 hours, concentrated in vacuo, and redissolved in CH_2Cl_2 (1.0 L). The solution was next washed with H_2O (3 x 500 mL), and the aqueous layer back extracted with CH_2Cl_2 (250 mL). The organic layers were then dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was dissolved in MeOH (200 mL) and the solution cooled to 0 °C. After 20 minutes, the resulting white precipitate was collected. The filtrate was then concentrated to 100 mL and recooled to 0 °C, and a second crop of precipitate collected. The process was repeated a third time to collect a third crop of product. The resulting precipitates were combined, powdered, and dried under high vacuum at 50 °C for 12 hours to afford analytically pure cyclo-L-Pro-L-Trp as a white solid (12.4 g, 43.8 mmol, 66% yield). Spectral data matches that reported in the literature.

Preparation of Trifluoroacetyltryptophan methyl carboxamide (7):



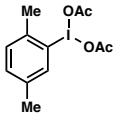
To (L)-Tryptophan methyl ester hydrochloride (5.84 g, 22.9 mmol) was added methylamine (33% solution in EtOH, 50 mL). The mixture was stirred for 48 h at 20 °C, then concentrated *in vacuo*, and the mixture co-evaporated with CH_2Cl_2 (50 mL), then Et_2O (3 x 100 mL), sequentially to afford a white solid. The solid was then suspended in anhydrous CH_2Cl_2 (250 mL), and Et_3N (9.6 mL, 68.7 mmol, 3.0 equiv) added dropwise by syringe at 20 °C. The resulting mixture was then cooled to 0

°C, and TFAA (3.23 mL, 22.9 mmol, 1.00 equiv) added dropwise by syringe. After 24 hours, the reaction was quenched with 1N HCl (200 mL), extracted with CH_2Cl_2 (200 mL), dried over Na_2SO_4, filtered and concentrated. The residue was then dissolved in EtOAc (250 mL), and filtered through a short plug of silica gel, and the filter cake washed with additional EtOAc (250 mL). The filtrate was then concentrated, and the resulting yellow solid was treated with Et_2O/pentane to afford **7** as a white, amorphous powder (2.97 g, 42% yield). ^{1}H NMR (500 MHz, DMSO-d_6) 10.82 (d, J = 0.9 Hz, 1H), 9.61 (d, J = 8.2 Hz, 1H), 8.21 (q, J = 4.3 Hz, 1H), 7.65 (d, J = 7.9 Hz, 1H), 7.33 (d, J = 8.1 Hz, 1H), 7.13 (d, J = 2.3 Hz, 1H), 7.10 – 7.04 (m, 1H), 6.99 (ddd, J = 7.9, 7.1, 1.0 Hz, 1H), 4.52 (ddd, J = 9.9, 8.5, 4.8 Hz, 1H), 3.20 (dd, J = 14.6, 4.6 Hz, 1H), 3.08 (dd, J = 14.6, 10.0 Hz, 1H), 2.62 (d, J = 4.6 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) 170.3, 156.2 (q, $J_{C\text{-}F}$ = 36.4 Hz), 136.1, 127.1, 123.7, 121.0, 118.4, 118.3, 115.8 (q, $J_{C\text{-}F}$ = 288.2 Hz), 111.4, 109.7, 54.3, 27.2, 25.7; FTIR (NaCl, thin film): 3277, 1700, 1696, 1653, 1636, 1560, 1347, 1185; $[\alpha]_D^{25}$ = +8.53 (c = 0.44, $CHCl_3$); LRMS (EI+) calc'd $[M+H]^+$ 314.1, found 314.1.

3.11.9 Preparation of Diaryliodonium Triflate Salts

The following diaryliodonium salts were prepared following known procedures: diphenyliodonium tetrafluoroborate, diphenyliodonium hexafluoroarsentate, diphenyliodonium triflate, bis-*p*-tolyliodonium triflate, and bis-*p*-methoxyiodonium triflate. Diphenyliodonium hexafluorophosphate was purchased from Alfa-Aesar. *m*-CPBA (Sigma-Aldrich, <77%) was dried under high vacuum (< 1 mTorr) at 23 °C for 4 hours as reported by Oloffson and coworkers.

Preparation of 2-iodo-*p*-xylene diacetate (SI-1):



To a solution of 2-iodo-1,4-dimethylbenzene (11.6 g, 50.0 mmol, 1.00 equiv) in AcOH (1.0 L) at 50 °C was added $NaBO_3$•$4H_2O$ (84.7 mmol, 0.55 mmol, 11.0 equiv) portion wise over 30 minutes. The solution was vigorously stirred at 50 °C for 5 hours, then cooled to ambient temperature and diluted with H_2O (500 mL) and extracted with CH_2Cl_2 (3 x 500 mL). The combined organics were then washed with water (3 x 500 mL), dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude residue was suspended in a minimum of Et_2O, then triturated with hexanes and the precipitate collected by vacuum filtration. 2-Iodo-*p*-xylene diacetate was obtained as a white, crystalline solid (14.0 g, 40.0 mmol, 80% yield). Spectral data obtained match that previously reported, ^{1}H and ^{13}C NMR data is reported for convenience. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 1.2 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.30 (dd, *J* = 7.8, 1.2 Hz, 1H), 2.65 (s, 3H), 2.36 (s, 3H), 1.97 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 176.3, 138.5, 137.3, 137.3, 133.5, 130.4, 126.8, 24.9, 20.6, 20.2.

General Procedure II

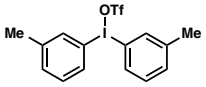
To a solution of iodoarene in CH_2Cl_2 (0.25 M) was added *m*CPBA (1.1 equiv), and BF_3•OEt_2 (2.5 equiv). The solution was stirred for 45 minutes, then the solution cooled to 0 °C in a dry ice corresponding aryl boronic acid (1.00 equiv) added a solid in a single portion. The solution was stirred for 15 minutes, then warmed to room temperature and stirring continued for 45 minutes. The solution was then recooled to 0 °C and TfOH (2.00

equiv) added dropwise via syringe. The solution was stirred for 5 minutes at 0 °C, then warmed to room temperature and concentrated under reduced pressure. The resulting solution was then filtered through a plug of silica gel, eluting with 5% MeOH/CH_2Cl_2, the filtrate concentrated, and the residue triturated from Et_2O to afford pure diaryliodonium triflate, typically as a white, crystalline solid.

General Procedure III

To a solution of aryl boronic acid (1.00 equiv) in CH_2Cl_2 (0.25 M) at 0 °C was added BF_3•OEt_2 (1.1 equiv) dropwise by syringe. The solution was stirred for 15 minutes, then a solution of iodoxylene diacetate (1.00 equiv) in CH_2Cl_2 (0.5 M) added dropwise by cannula transfer over 15 minutes. The solution was slowly warmed to 23 °C over 1 h, then recooled to 0 °C and TfOH (2.00 equiv) added dropwise via syringe. The solution was stirred for 5 minutes at 0 °C, then warmed to room temperature and concentrated under reduced pressure. The resulting solution was then filtered through a plug of silica gel, eluting with 5 % MeOH/CH_2Cl_2, the filtrate concentrated, and the residue triturated from Et_2O to afford pure diaryliodonium triflate salt, typically as a white, crystalline solid.

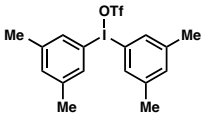
Di-(3-tolyl)iodonium triflate (SI-2)



Prepared by *General Procedure II* from 3-methylphenyl boronic acid and 3-methyliodobenzene on 5.00 mmol scale. Trituration from Et_2O afforded the product as a white, crystalline solid (1.54 g, 3.36 mmol, 67% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.10 (td, J = 1.8, 0.9 Hz, 2H), 8.04 (ddt, J = 7.9, 1.8, 0.9

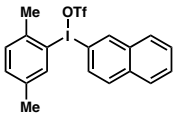
Hz, 2H), 7.48 (ddt, *J* = 7.7, 1.8, 1.0 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 2.34 (d, *J* = 0.8 Hz, 6H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 142.3, 135.78, 133.2, 132.7, 131.9, 116.6, 21.2; FTIR (NaCl, thin film): 3744, 3675, 1596, 1259, 1172, 1036, 1026 cm^{-1}; LRMS (EI+) calc'd $[M–OTf]^+$ 309.1, found 309.0.

Di-(3,5-dimethylphenyl)iodonium triflate (SI-3)



Prepared by *General Procedure II* from 3,5-dimethyliodobenzene and 3,5-dimethylphenylboronic acid on 10.0 mmol scale. Trituration from Et_2O afforded the product as a white, crystalline solid (3.72 g, 7.65 mmol, 77% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 (dt, *J* = 1.5, 0.8 Hz, 4H), 7.30 (tt, *J* = 1.5, 0.8 Hz, 2H), 2.30 (d, *J* = 0.9 Hz, 12H); ^{13}C NMR (500 MHz, DMSO-d_6): δ 141.9, 133.9, 132.9, 116.2, 21.1; FTIR (NaCl, thin film): 1599, 1558, 1451, 1381, 1243, 1221, 1171, 1154, 1026 cm^{-1}; LRMS (EI+) calc'd $[M–OTf]^+$ 337.2, found 337.2.

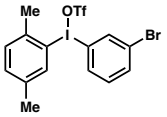
(2-naphthyl)(*p*-xylyl)iodonium triflate (SI-4)



Prepared by *General Procedure III* from 2-naphthyl boronic acid on 5.00 mmol scale. Trituration from Et_2O afforded the product as a white, crystalline solid (2.15 g, 4.23 mmol, 85% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.93 (d, *J* = 1.9 Hz, 1H), 8.29 (dd, *J* = 1.7, 0.9 Hz, 1H), 8.18 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.10 – 7.99 (m, 4H), 7.73 – 7.66 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.38 (ddd, *J* = 7.7, 1.7, 0.8 Hz, 1H), 2.61 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (500 MHz, DMSO-d_6): δ 139.6, 137.9, 137.6, 136.5, 134.4, 133.9, 133.8, 132.00, 131.5, 130.6, 129.4, 128.6, 128.6, 128.4, 121.6,

113.0, 25.0, 20.5; FTIR (NaCl, thin film): 3670, 3588, 1653, 1635, 1490, 1347, 1259, 1172, 1036, 1024 cm^{-1}; LRMS (EI+) calc'd $[M–OTf]^+$ 359.0, found 359.0.

(3-bromophenyl)(*p*-xylyl)iodonium triflate (SI-5)



Prepared by *General Procedure III* from 3-bromophenyl boronic acid on 5.00 mmol scale. Trituration from Et_2O afforded the product as a white, crystalline solid (1.33 g, 2.48 mmol, 50% yield). ^1H NMR (500 MHz, DMSO-d_6) δ 8.53 (dd, J = 1.8, 1.8 Hz, 1H), 8.28 (dd, J = 1.8, 0.9 Hz, 1H), 8.18 (ddd, J = 8.0, 1.8, 0.9 Hz, 1H), 7.85 (ddd, J = 8.1, 1.9, 0.9 Hz, 1H), 7.51 - 7.42 (m, 2H), 7.44 - 7.38 (m, 1H), 2.57 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (500 MHz, DMSO-d_6): δ 139.2, 137.5, 137.1, 136.7, 134.9, 133.9, 133.6, 133.5, 131.1, 123.3, 121.2, 116.1, 24.5, 20.0; FTIR (NaCl, thin film): 3074, 1569, 1554, 1490, 1456, 1275, 1242, 1170, 1025 cm^{-1}; LRMS (EI+) calc'd $[M–OTf]^+$ 388.1, found 388.9.

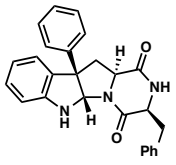
3.11.10 Optimization of Reaction Parameters for Diastereoselective Arylation

Optimization Procedure – In a glovebox, $(CuOTf)_2$•PhMe (20.7 mg, 0.040 mmol), and ligand (0.088 mmol) were dissolved in anhydrous CH_2Cl_2 (4.0 mL). The solution was stirred vigorously for 1.0 hr, filtered through a plug of cotton and removed from the glovebox. A portion of the solution (1.00 mL, 0.020 mmol, 20 mol % in Cu) was added to an oven-dried, 1-dram vial containing diketopiperazine (0.100 mmol) and diaryliodonium salt (0.110 mmol). The solution was stirred at 23 °C (care was taken not to exceed 25 °C) for 24 hrs, then quenched by the addition of concentrated ammonia (28–30% in H_2O, 1.0 mL). After 5 minutes, the mixture was diluted with EtOAc (30 mL) and

washed with a mixture water (20 mL) and brine (20 mL). The aqueous layer was then back extracted with EtOAc (2 x 10 mL) and the combined organics dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to afford a solid residue.

The residue was then dissolved in a standard solution of maleic acid in DMSO-d_6, and the solution analyzed for yield, C3:C2 ratio, and dr. NMR yields were obtained via careful integration against the standard.

Preparation of minor diastereomer 177



To an oven dried vial was added diketopiperazine **175a** (33 mgs, 0.1 mmol), diaryliodonium hexafluorophosphate (47 mgs, 0.11 mmol) and $(CuOTf)_2$•PhMe (5.2 mgs, 0.01 mmol). The solids were dissolved in 1 mL CH_2Cl_2 and the reaction was allowed to stir for 24 hours, then quenched by the addition of 1 mL NH_4OH. The mixture was diluted with EtOAc and extracted with EtOAc (2 X 10 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated. The minor diastereomer was purified from the crude residue by silica gel chromatography (50% hexanes, 47.5% ethyl acetate, 2.5% methanol) to afford **177** as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) 7.30 – 7.27 (m, 2H), 7.26 – 7.22 (m, 3H), 7.22 – 7.16 (m, 3H), 7.15 – 7.09 (m, 2H), 7.04 (ddd, *J* = 7.7, 7.7, 1.3 Hz, 1H), 6.88 – 6.83 (m, 1H), 6.67 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.61 (d, *J* = 7.8 Hz, 1H), 5.77 (s, 1H), 5.69 (d, *J* = 9.3 Hz, 1H), 4.40 – 4.32 (m, 1H), 4.16 (ddd, *J* = 10.5, 3.8, 1.3 Hz, 1H), 3.51 (dd, *J* = 14.5, 3.8 Hz, 1H), 3.15 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.69 (ddd, *J* = 16.6, 14.1, 10.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) 168.8, 166.8, 147.2, 142.3, 135.6, 133.3, 129.2, 128.9, 128.8, 128.6, 127.5, 127.3, 126.5, 124.1, 119.6, 109.6, 85.5, 59.2, 58.6, 56.1, 38.6, 36.2;

FTIR (NaCl, thin film): 3306, 3058, 2929, 1674, 1607, 1482, 1447, 1318, 1223, 1071 cm^{-1}; $[\alpha]_D^{25} = -329$ ($c = 0.31$, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 410.2, found 410.2.

3.11.11 Substrate Scope for Diastereoselective Arylation – Characterization Data

General Procedure IV: Tryptophan Arylation

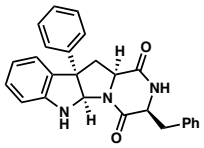
Catalyst Preparation – In a glovebox, copper(I)trifluoromethanesulfonate toluene complex (0.10 equiv) and alpha-diimine-ligand (0.22 equiv) were dissolved in anhydrous CH_2Cl_2 (0.1 M in Cu). The solution was vigorously stirred for 1.0 hour, and then filtered through a plug of cotton.[1] The solution was then removed from the glovebox for immediate use.

Arylation Reaction – A flame-dried flask containing a magnetic stirbar was charged with tryptophan substrate (0.300 mmol, 1.00 equiv) and diaryliodonium salt (0.330 mmol, 1.1 equiv), then equipped with a rubber septum. To the solids was added the freshly-prepared Cu-catalyst solution prepared above (3.00 mL, 0.030 mmol, 20 mol %) and the solution vigorously stirred at 20 °C. After the time indicated below, the solution was quenched with aqueous ammonia (3.00 mL of a 27-33% solution in H_2O) and stirred for 5 minutes. The reaction was then diluted with EtOAc (30 mL) and washed with a mixture of H_2O (30 mL) and brine (30 mL). The aqueous portion was back extracted with EtOAc (2 x 10 mL) and the combined organics dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography on silica gel to

[1] Filtering the catalyst solution was found to improve the overall selectivity, reactivity, and reproducibility of the reaction.

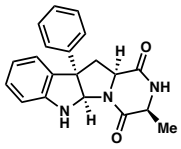
afford pure arylpyrroloindoline product, typically as either a white, amorphous powder or a white foam.

Pyrroloindoline 176a



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and diphenyliodonium triflate. The crude residue was purified by silica gel chromatography (50% hexanes, 47.5% ethyl acetate, 2.5% methanol) to afford **176a** as a white solid (104.0 mg, 0.254 mmol, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 6H), 7.28 (ddd, *J* = 5.1, 2.3, 2.3 Hz, 2H), 7.20 (d, *J* = 7.0 Hz, 2H), 7.12 (ddd, *J* = 7.7, 7.7, 1.2 Hz, 1H), 6.97 – 6.89 (m, 1H), 6.75 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.69 (d, *J* = 7.9 Hz, 1H), 5.85 (s, 1H), 5.60 (s, 1H), 4.44 (dd, *J* = 8.4, 8.4 Hz, 1H), 4.24 (ddd, *J* = 10.7, 3.7, 1.1 Hz, 1H), 3.61 (dd, *J* = 14.5, 3.7 Hz, 1H), 3.23 (dd, *J* = 13.7, 7.4 Hz, 1H), 2.77 (ddd, *J* = 13.6, 10.2, 2.2 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 166.8, 147.1, 142.3, 135.6, 133.3, 129.3, 128.9, 128.9, 128.7, 127.6, 127.6, 126.5, 124.2, 119.7, 109.7, 85.5, 59.3, 58.7, 56.2, 38.6, 36.3; FTIR (NaCl, thin film): 3315, 3087, 3052, 3027, 2928, 2849, 1676, 1605, 1498, 1407, 1348, 1306, 1261, 1221 cm^{-1}; $[\alpha]_D^{25}$ = +113 (*c* = 1.8, $CHCl_3$); LRMS (EI+) calc'd $[M+H]^+$ 410.2, found 410.2.

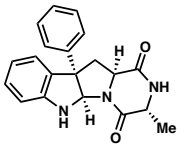
Pyrroloindoline 176b



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and diphenyliodonium triflate for 24 h. Reaction was run with additional CH_2Cl_2 (3.00 mL) for solubility. The crude residue was purified by silica gel chromatography (20% hexanes : 77.5% ethyl acetate: 2.5% methanol) to afford **176b**

as a white solid (66.2 mg, 0.199 mmol, 66% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 4H), 7.32 – 7.26 (m, 1H), 7.09 (dd, *J* = 7.7, 7.7 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 7.5, 7.5 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 5.82 (d, *J* = 8.3 Hz, 1H), 5.79 (s, 1H), 4.48 (dd, *J* = 8.3, 8.3 Hz, 1H), 4.15 – 4.05 (m, 1H), 3.21 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.84 (dd, *J* = 13.8, 9.3 Hz, 1H), 1.46 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 167.9, 147.2, 142.3, 133.2, 128.9, 128.7, 127.4, 126.5, 124.2, 119.7, 109.8, 85.5, 59.4, 59.0, 51.3, 38.3, 15.7; FTIR (NaCl, thin film): 3255, 2928, 2849, 1669, 1653, 1486, 1419, 1219 cm^{-1}; $[\alpha]_D^{25}$ = +158 (*c* = 0.85, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 334.2, found 334.1.

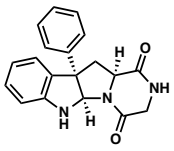
Pyrroloindoline 176c



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and diphenyliodonium triflate for 24 h. Reaction was run with additional CH_2Cl_2 (3.00 mL) for solubility. The crude residue was purified by silica gel chromatography (77.5% ethyl acetate, 20% hexanes, 2.5% methanol) to afford **5c** as a white solid (49.5 mg, 0.149 mmol, 50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 4H), 7.31 – 7.26 (m, 1H), 7.09 (ddd, *J* = 7.6, 7.6, 1.0 Hz, 1H), 7.01 (d, *J* = 3.8 Hz, 1H), 6.88 (dd, *J* = 7.4, 0.5 Hz, 1H), 6.72 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 1H), 5.84 (d, *J* = 3.0 Hz, 1H), 5.54 (d, *J* = 3.0 Hz, 1H), 4.43 (dd, *J* = 10.6, 7.0 Hz, 1H), 4.01 (qd, *J* = 7.2, 4.2 Hz, 1H), 3.29 (dd, *J* = 13.7, 7.0 Hz, 1H), 2.65 (dd, *J* = 13.7, 10.7 Hz, 1H), 1.46 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 167.9, 147.1, 142.2, 133.6, 128.9, 128.7, 127.3, 126.7, 124.0, 119.5, 109.6, 86.0, 58.8, 57.2, 53.6, 39.4,

19.8; FTIR (NaCl, thin film): 3275, 3042, 2913, 1684, 1652, 1437, 1308, 1266, 1221 cm^{-1}; $[\alpha]_D^{25}$ = +119 (*c* = 1.1, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 334.2, found 334.1

Pyrroloindoline 176d



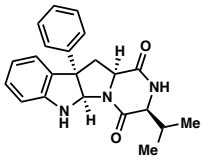
Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and diphenyliodonium triflate for 24 h. Reaction was run with additional CH_2Cl_2 (3.00 mL) for solubility. The crude residue was purified by silica gel chromatography (77.5% ethyl acetate, 20% hexane, 2.5% methanol) to afford **176d** as a white solid (61.5 mg, 0.193 mmol, 64% yield).

^1H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 4H), 7.29 – 7.26 (m, 1H), 7.09 (ddd, *J* = 7.7, 7.7, 1.3 Hz, 1H), 6.96 – 6.90 (m, 1H), 6.86 (d, *J* = 4.2 Hz, 1H), 6.73 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 5.81 (s, 1H), 4.43 (dd, *J* = 8.5, 8.5 Hz, 1H), 4.02 (dd, *J* = 17.0, 1.6 Hz, 1H), 3.85 (dd, *J* = 17.0, 4.6 Hz, 1H), 3.23 (dd, *J* = 13.7, 7.4 Hz, 1H), 2.77 (dd, *J* = 13.8, 9.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4, 165.2, 147.1, 142.3, 133.3, 128.9, 128.7, 127.3, 126.5, 124.2, 119.7, 109.8, 85.4, 59.2, 58.0, 46.7, 38.7; FTIR (NaCl, thin film): 3280, 3047, 2928, 2854, 1674, 1602, 1483, 1441, 1310, 1263, 1219, 1155 cm^{-1}; $[\alpha]_D^{25}$ = +80.2 (*c* = 0.59, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 320.1, found 320.1.

Pyrroloindoline 176e

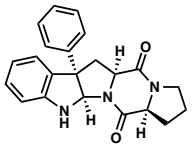
Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and diphenyliodonium triflate for 24 h. The crude residue was purified by silica gel chromatography (20% hexanes,

77.5% ethyl acetate, 2.5% methanol) to afford **176e** as a white solid (55.5 mg, 0b.154 mmol, 51% yield).



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.31 (m, 4H), 7.30 – 7.26 (m, 1H), 7.11 – 7.06 (m, 1H), 6.96 – 6.92 (m, 1H), 6.73 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.66 – 6.62 (m, 1H), 5.87 (s, 1H), 5.80 (d, *J* = 2.6 Hz, 1H), 5.44 (d, *J* = 2.4 Hz, 1H), 4.47 – 4.39 (m, 1H), 3.91 – 3.87 (m, 1H), 3.23 (dd, *J* = 13.7, 7.4 Hz, 1H), 2.79 (dd, *J* = 13.7, 9.7 Hz, 1H), 2.60 (heptd, *J* = 7.1, 2.6 Hz, 1H), 1.05 (d, *J* = 7.2 Hz, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4, 166.7, 147.3, 142.4, 133.3, 128.9, 128.6, 127.3, 126.5, 124.3, 119.6, 109.5, 85.5, 60.4, 59.1, 58.2, 38.8, 28.4, 19.3, 16.0; FTIR (NaCl, thin film): 3292, 2964, 1669, 1609, 1483, 1465, 1419, 1347, 1291, 1222 cm^{-1}; $[\alpha]_D^{25}$ = +107 (*c* = 0.52, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 362.2, found 362.2.

Pyrroloindoline 176f

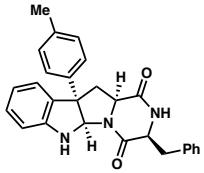


Prepared following *General Procedure IV* using 40 mol % $^{t\text{-}Bu}DAB_{Me}$ and diphenyliodonium hexafluorophosphate for 4 h. The crude residue was purified by silica gel chromatography (77.5% ethyl acetate, 20% hexanes, 2.5% methanol) to afford **176f** as a white solid (76.6 mg, 0.213 mmol, 71% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 - 7.34 (m, 4H), 7.31 - 7.27 (m, 1H), 7.08 (ddd, *J* = 7.9, 7.5, 1.3 Hz, 1H), 6.91 (ddd, *J* = 7.5, 1.3, 0.6 Hz, 1H), 6.73 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.67 - 6.61 (m, 1H), 5.83 (s, 1H), 5.36 (s, 1H), 4.55 - 4.48 (m, 1H), 4.14 (ddd, *J* = 9.1, 7.3, 1.6 Hz, 1H), 3.54 - 3.46 (m, 2H), 3.21 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.81 (dd, *J* =

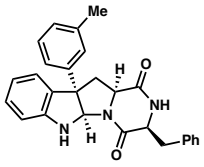
13.9, 9.8 Hz, 1H), 2.31 (dddd, *J* = 12.8, 7.0, 7.0, 3.4 Hz, 1H), 2.17 (dddd, *J* = 12.9, 10.7, 9.2, 7.2 Hz, 1H), 2.07 - 1.96 (m, 1H), 1.90 (dddd, *J* = 14.9, 6.8, 4.0, 1.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.9, 165.7, 147.0, 142.3, 133.6, 128.8, 128.8, 128.6, 127.3, 126.7, 124.1, 119.7, 109.7, 85.3, 60.5, 60.3, 59.9, 45.2, 38.1, 27.6, 23.2; FTIR (NaCl, thin film): 3330, 2952, 2878, 1665, 1607, 1484, 1467, 1423, 1340, 1313, 1219, 1154, 1068 cm^{-1}; $[\alpha]_D^{25}$ = +108 (*c* = 0.63, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 360.2, found 360.2.

Pyrroloindoline 176g



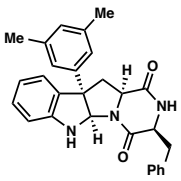
Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and di(*p*-tolyl)iodonium triflate for 32 h. The crude residue was purified by silica gel chromatography (50% hexanes, 47.5% ethyl acetate, 2.5% methanol) to afford **176g** as a white solid (98.2 mg, 0.232 mmol, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.28 (ddd, *J* = 4.7, 1.9, 1.9 Hz, 1H), 7.24 – 7.18 (m, 4H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.11 (ddd, *J* = 7.7, 7.7, 1.3 Hz, 1H), 6.93 – 6.89 (m, 1H), 6.74 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 1H), 5.84 (d, *J* = 2.9 Hz, 1H), 5.56 (s, 1H), 5.43 (d, *J* = 2.8 Hz, 1H), 4.48 – 4.38 (m, 1H), 4.23 (ddd, *J* = 10.8, 3.7, 1.3 Hz, 1H), 3.61 (dd, *J* = 14.5, 3.7 Hz, 1H), 3.21 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.74 (ddd, *J* = 18.4, 14.1, 10.4 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 166.8, 147.1, 139.3, 137.1, 135.6, 133.5, 129.5, 129.3, 128.9, 128.6, 127.6, 126.4, 124.1, 119.7, 109.6, 85.6, 59.0, 58.7, 56.2, 38.7, 36.3, 20.9; FTIR (NaCl, thin film): 3315, 3027, 2923, 2859, 1686, 1602, 1412, 1343, 1308, 1219 cm^{-1}; $[\alpha]_D^{25}$ = +208 (*c* = 0.61, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 424.2, found 424.2.

Pyrroloindoline 176h



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and di(*m*-tolyl)iodonium triflate for 4 h. The crude residue was purified by silica gel chromatography (50% hexanes, 47.5% ethyl acetate, 2.5% methanol) to afford **176h** as a white solid (119.0 mg, 0.280 mmol, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.1 Hz, 2H), 7.16 – 7.07 (m, 4H), 6.93 (d, *J* = 7.4 Hz, 1H), 6.74 (dd, *J* = 13.8, 6.3 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 5.87 (d, *J* = 2.9 Hz, 1H), 5.60 (s, 1H), 5.46 (d, *J* = 2.7 Hz, 1H), 4.49 – 4.39 (m, 1H), 4.24 (dd, *J* = 10.8, 2.7 Hz, 1H), 3.61 (dd, *J* = 14.5, 3.7 Hz, 1H), 3.23 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.81 – 2.68 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 166.8, 147.1, 142.2, 138.6, 135.6, 133.4, 129.3, 128.9, 128.7, 128.6, 128.1, 127.6, 127.2, 124.1, 123.6, 119.6, 109.6, 85.5, 59.2, 58.7, 56.2, 38.7, 36.3, 21.6; FTIR (NaCl, thin film): 3385, 3270, 3032, 2918, 2839, 1676, 1602, 1409, 1350, 1313, 1234, 1197 cm^{-1}; $[\alpha]_D^{25}$ = +169 (*c* = 0.81, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 424.2, found 424.2.

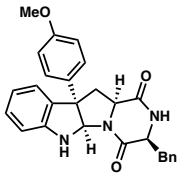
Pyrroloindoline 176i



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and bis(3,5-dimethylphenyl)iodonium triflate for 4 h. The crude residue was purified by silica gel chromatography (50% hexanes, 47.5% ethyl acetate, 2.5% methanol) to afford **176i** as a white solid (119.4 mg, 0.273 mmol, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 7.37 – 7.31 (m, 2H), 7.30 – 7.26 (m, 1H), 7.23 – 7.18 (m, 2H), 7.14 –

7.09 (m, 1H), 6.97 – 6.94 (m, 2H), 6.94 – 6.90 (m, 2H), 6.74 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.71 – 6.65 (m, 1H), 5.88 (d, *J* = 2.9 Hz, 1H), 5.61 (s, 1H), 5.44 (d, *J* = 2.8 Hz, 1H), 4.43 (ddd, *J* = 9.8, 7.1, 1.0 Hz, 1H), 4.24 (ddd, *J* = 10.8, 3.7, 1.4 Hz, 1H), 3.62 (dd, *J* = 14.5, 3.7 Hz, 1H), 3.23 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.77 (dd, *J* = 14.5, 10.8 Hz, 1H), 2.68 (dd, *J* = 13.7, 10.1 Hz, 1H), 2.30 (d, *J* = 0.4 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) 168.9, 166.7, 147.1, 142.1, 138.4, 135.7, 133.5, 129.3, 129.0, 128.9, 128.5, 127.6, 124.4, 124.1, 119.6, 109.6, 85.5, 59.1, 58.7, 56.2, 38.8, 36.3, 21.4; FTIR (NaCl, thin film): 3288, 3051, 2919, 2854, 1684, 1604, 1484, 1455, 1418, 1346, 1312, 1255, 1204, 1156, 1109 cm^{-1}; $[\alpha]_D^{25}$ = +101 (*c* = 2.0, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 438.2, found 438.2.

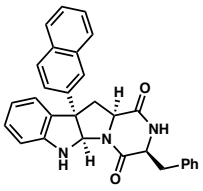
Pyrroloindoline 176j



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ using di(*p*-methoxyphenyl)iodonium triflate for 42 h. The crude residue was purified by silica gel chromatography (50% hexanes, 47.5% ethyl acetate, 2.5% methanol) to afford **176j** as a white solid (88.1 mg, 0.200 mmol, 67% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 7.36 – 7.30 (m, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.27 – 7.23 (m, 2H), 7.20 (d, *J* = 7.0 Hz, 2H), 7.11 (ddd, *J* = 7.7, 7.7, 1.2 Hz, 1H), 6.91 (dd, *J* = 7.4, 0.7 Hz, 1H), 6.89 – 6.86 (m, 2H), 6.74 (ddd, *J* = 7.5, 7.5, 0.9 Hz, 1H), 6.67 (d, *J* = 7.8 Hz, 1H), 5.81 (s, 1H), 5.57 (s, 1H), 4.48 – 4.40 (m, 1H), 4.24 (ddd, *J* = 10.8, 3.7, 1.2 Hz, 1H), 3.79 (s, 3H), 3.61 (dd, *J* = 14.5, 3.5 Hz, 1H), 3.18 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.74 (ddd, *J* = 20.3, 14.1, 10.4 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) 168.9, 166.8, 158.7, 147.1, 135.6, 134.2, 133.5, 129.3, 128.9, 128.6, 127.7, 127.6, 124.1, 119.7, 114.2, 109.7, 85.7, 58.8, 58.7, 56.2, 55.3, 38.7, 36.3; FTIR (NaCl, thin film): 3309, 3052, 2938, 2839, 1684,

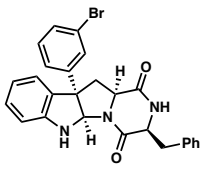
1653, 1609, 1513, 1457, 1419, 1312, 1251, 1183, 1032 cm^{-1}; $[\alpha]_D^{25}$ = +70 (*c* = 0.80, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 440.2, found 440.2.

Pyrroloindoline 176k



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and (2-naphthyl)(*p*-xylyl)iodonium triflate for 42 h. The crude residue was purified by silica gel chromatography (50% hexanes, 47.5% ethyl acetate, 2.5% methanol) to afford **176k** as a white solid (113.0 mg, 0.246 mmol, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 7.85 – 7.78 (m, 4H), 7.54 – 7.45 (m, 2H), 7.38 (ddd, *J* = 11.4, 3.9, 3.9 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.31 – 7.26 (m, 1H), 7.23 – 7.18 (m, 2H), 7.14 (ddd, *J* = 7.7, 7.7, 1.2 Hz, 1H), 6.93 (dd, *J* = 7.4, 0.9 Hz, 1H), 6.78 – 6.68 (m, 2H), 5.98 (s, 1H), 5.59 (s, 1H), 5.50 (s, 1H), 4.57 – 4.49 (m, 1H), 4.25 (ddd, *J* = 10.8, 3.7, 1.3 Hz, 1H), 3.62 (dd, *J* = 14.5, 3.7 Hz, 1H), 3.39 (ddd, *J* = 16.0, 8.0, 8.0 Hz, 1H), 2.80 (ddd, *J* = 14.4, 12.1, 10.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 166.7, 147.2, 139.2, 135.6, 133.3, 133.0, 132.4, 129.3, 129.0, 128.9, 128.8, 128.0, 127.6, 127.5, 126.6, 126.4, 125.5, 124.3, 124.2, 119.7, 109.7, 85.4, 59.5, 58.8, 56.2, 38.5, 36.3; FTIR (NaCl, thin film): 3330, 3052, 2918, 1676, 1605, 1483, 1409, 1343, 1303 cm^{-1}; $[\alpha]_D^{25}$ = +237 (*c* = 0.57, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 460.2, found 460.2.

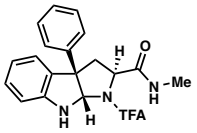
Pyrroloindoline 176l



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and (3-bromophenyl)(*p*-xylyl)iodonium triflate for 42 h. The crude residue was purified by silica gel chromatography (50% hexanes, 47.5% ethyl

acetate, 2.5% methanol) to afford **176l** as a white solid (79.3 mg, 0.163 mmol, 54% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 7.48 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.33 (dd, *J* = 7.3, 7.3 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.24 – 7.18 (m, 3H), 7.13 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.76 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 5.79 (d, *J* = 1.3 Hz, 1H), 5.59 (s, 1H), 5.50 (s, 1H), 4.42 (dd, *J* = 8.4, 8.4 Hz, 1H), 4.25 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.60 (dd, *J* = 14.5, 3.7 Hz, 1H), 3.15 (dd, *J* = 13.8, 7.5 Hz, 1H), 2.78 (ddd, *J* = 18.5, 14.2, 10.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) 168.6, 166.9, 147.1, 144.8, 135.5, 132.5, 130.6, 130.4, 129.6, 129.3, 129.0, 128.9, 127.6, 125.3, 124.2, 123.1, 119.9, 109.9, 85.4, 59.1, 58.5, 56.2, 38.5, 36.2; FTIR (NaCl, thin film): 3315, 3057, 2933, 2864, 1679, 1612, 1560, 1482, 1412, 1343, 1313, 1221 cm^{-1}; $[\alpha]_D^{25}$ = -+91.4 (*c* = 2.8, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 488.1, found 488.1.

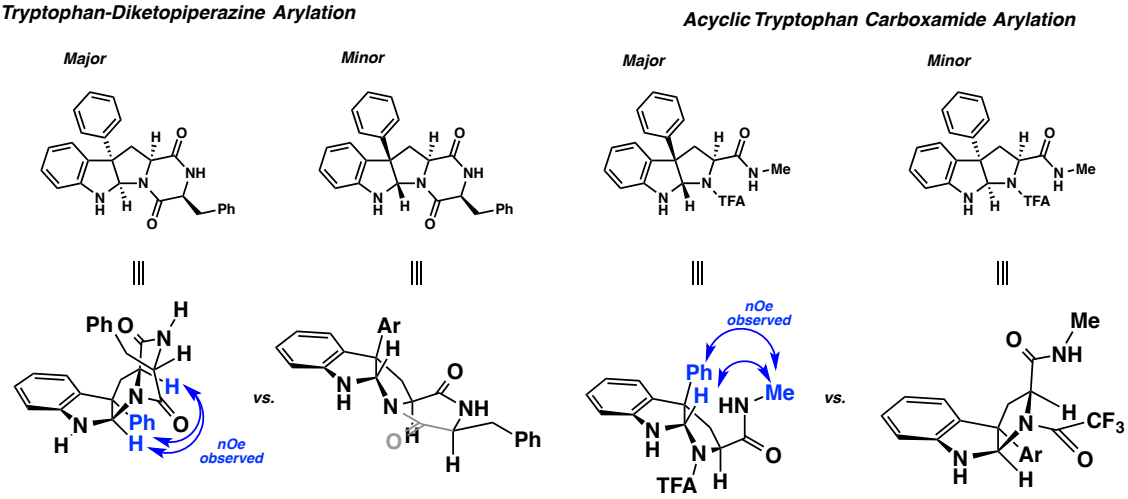
Pyrroloindoline 180



Prepared following *General Procedure IV* using $^{Mes}DAB_{Me}$ and diphenyliodonium triflate for 3 h. The crude residue was purified by silica gel chromatography (60% hexanes, 37.5% ethyl acetate, 2.5% methanol) to afford 1**80** as a white solid (94.6 mg, 0.243 mmol, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) 7.55 (d, *J* = 2.9 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.30 – 7.27 (m, 1H), 7.27 – 7.23 (m, 1H), 7.23 – 7.18 (m, 3H), 6.96 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.17 (d, *J* = 2.8 Hz, 1H), 4.63 (d, *J* = 2.3 Hz, 1H), 4.25 (ddd, *J* = 12.6, 4.2, 4.2 Hz, 1H), 3.24 (dd, *J* = 12.6, 4.1 Hz, 1H), 3.07 (s, 3H), 2.48 (dd, *J* = 12.6, 12.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) 169.0, 156.9 (q, J_{C-F} = 37.6 Hz), 148.0, 144.9, 130.1, 129.4, 128.9, 127.5, 125.9, 125.3, 120.9, 115.5 (q, J_{C-F} = 287.7 Hz), 110.3, 83.8, 53.4, 49.1, 35.9, 33.3; FTIR

(NaCl, thin film): 3361, 3057, 2937, 1718, 1653, 1608, 1559, 1487, 1469, 1320, 1268, 1216, 1187, 1163, 1058, 1034 cm^{-1}; $[\alpha]_D^{25}$ = +215 (*c* = 1.3, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 390.1, found 390.1.

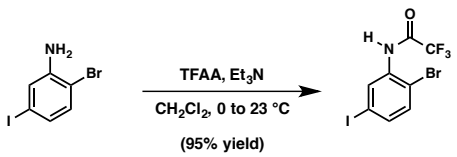
3.11.12 Stereochemical Assignment of Tryptophan Arylation



The stereochemical assignment of the pyrroloindole products was assigned by ^1H, ^{13}C, COSY, HSQC, HMBC, and NOESY 2D experiments on L-Trp-L-Phe derived pyrroloindoline and assigned by spectroscopic analogy for pyrroloindoles 1**76b-f**. Acyclic tryptophan-derived carboxamide **180** was independently analyzed by ^1H, ^{13}C, COSY, HSQC, HMBC, and NOESY 2D experiments and found to arylate from the opposite face of the prochiral indole moiety. Selected NOESY 2D data is included in the spectral data

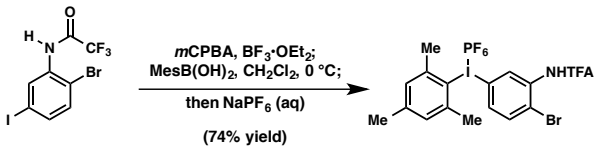
3.11.13 Total Synthesis of (+)-Naseseazines A and B

Preparation of *N*-**(2-bromo-5-iodophenyl)-2,2,2-trifluoroacetamide**



To a solution of 2-bromo-5-iodoaniline (14.9 g, 50.0 mmol, 1.0 equiv) in CH_2Cl_2 (250 mL) was added Et_3N (10.4 mL, 75.0 mmol, 1.50 equiv). The solution was cooled to 0 °C and trifluoroacetic anhydride (7.8 mL, 55.0 mmol, 1.10 equiv) added dropwise by syringe. The solution was stirred for 30 minutes and slowly warmed to 23 °C and stirring continued for 4 hours. The reaction was then quenched by the addition of 0.5 N HCl (150 mL), and the reaction washed with 0.5 N HCl (2 x 100 mL). The combined organics were then back extracted with Et_2O (100 mL), and the organics dried over Na_2SO_4, filtered, and concentrated in vacuo to afford pure 2-bromo-5-iodotrifluoroacetanilide as a white fluffy solid (18.8 g, 47.7 mmol, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.63 (d, J = 2.0 Hz, 1H), 8.37 (s, 1H), 7.42 (dd, J = 8.4, 2.1 Hz, 1H), 7.29 (d, J = 8.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 154.58 (q, J = 38.0 Hz), 136.2, 134.0, 133.7, 130.5, 115.3 (q, J = 288.7 Hz), 113.8, 93.0; IR (NaCl, thin film): 3267, 3081, 1709, 1574, 1529, 1459, 1395, 1260, 1186, 1165, 1034 cm^{-1}; LRMS (EI+) calc'd for $[M+H]^+$ 393.9, found 393.9.

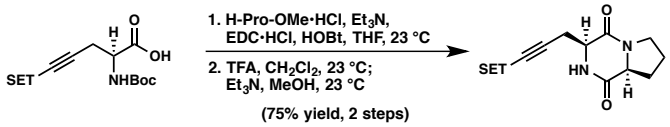
Preparation of (3-trifluoroacetamido-4-bromophenyl)(mesityl)iodonium hexafluorophosphate



To a solution of 2-bromo-5-iodotrifluoroacetanilide (11.8 g, 30.0 mmol, 1.00 equiv) in CH_2Cl_2 (120 mL) was added *m*CPBA (80%, 7.15 g, 33.0 mmol, 1.10 equiv). The solution was stirred for 5 minutes, then BF_3•OEt_2 (9.26 mL, 75.0 mmol, 2.50 equiv) was added dropwise by syringe to afford a bright orange solution. After 45 minutes, the solution was cooled to 0 °C and 2,4,6-trimethylphenylboronic acid (5.41 g, 33.0 mmol, 1.10 equiv)

added in a single portion. The mixture was stirred for an additional 15 minutes, warmed to 23 °C over 15 minutes, then stirred for an additional 20 minutes at room temperature. Saturated aqueous $NaPF_6$ (150 mL) was added to the solution, and the heterogeneous mixture stirred vigorously for 1 hr. The solution was diluted with CH_2Cl_2 (100 mL) and H_2O (150 mL), the layers separated, and the aqueous layer extracted with CH_2Cl_2 (2 x 100 mL). The combined organics were then dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo* to afford a thick oil. The oil was co-evaporated once from Et_2O (100 mL), and diluted with Et_2O (500 mL). The clear supernatant was decanted and the residual oil co-evaporated from Et_2O (200 mL), resulting in precipitation. The resulting solid was suspended in Et_2O (500 mL) and cooled in an ice-bath for 20 minutes, then collected by vacuum filtration and dried under high vacuum (<1 mTorr) for 15 h to afford diaryliodonium hexafluorophosphate **183** as an off-white, powdery solid (14.6 g, 22.2 mmol, 74 % yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.53 (s, 1H), 8.24 (d, J = 1.8 Hz, 1H), 7.91 (dd, J = 8.6, 1.9 Hz, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.27 – 7.21 (m, 2H), 2.62 (s, 6H), 2.30 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 155.9 (q, J = 37.6 Hz), 143.8, 142.1, 136.5 (d, J = 13.8 Hz), 135.7 (d, J = 35.8 Hz), 130.4, 126.0, 123.4, 116.3 (q, J = 288.2 Hz), 113.2 , 26.8, 21.0; FTIR (NaCl, thin film): 3365, 3092, 2926, 1735, 1582, 1523, 1457, 1405, 1267, 1204, 1157, 1031 cm^{-1}; LRMS (EI+) calc'd $[M–PF_6]^+$ 511.9, found 511.9.

Preparation of Diketopiperazine 185

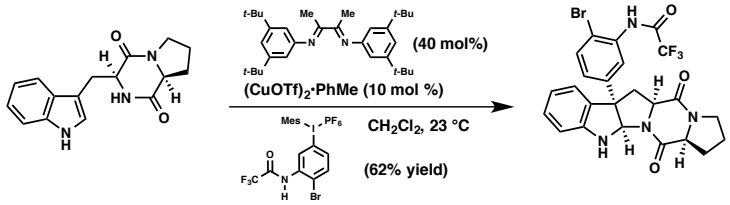


To a solution of freshly prepared amino acid (4.75 g, 14.5 mmol, 1.00 equiv) in THF (0.4 M, 240 mL) at 0 °C was added EDC•HCl (3.34 g, 17.4 mmol, 1.20 equiv), anhydrous HOBt (2.74 g, 20.3 mmol, 1.40 equiv) and Et_3N (4.5 mL, 32 mmol, 2.2 equiv). The mixture was then stirred for 5 minutes, and *L*- proline methyl ester hydrochloride (2.89 g, 17.4 mmol, 1.20 equiv) was added. The reaction was slowly warmed to 23 °C over 2 hours and stirring continued for 20 hours. The reaction was then quenched with 1 N HCl (500 mL) and extracted with EtOAc (3 x 250 mL), then the combined organics washed with saturated aqueous $NaHCO_3$ (500 mL), and aqueous layer back extracted with EtOAc (200 mL). The combined organic layers were then dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to afford crude dipeptide as a viscous oil.

The residue was then dissolved in CH_2Cl_2 (100 mL), and trifluoroacetic acid (30 mL) was added dropwise by addition funnel at room temperature over 10 minutes. Stirring was continued for 20 minutes, then the solution diluted with toluene (100 mL) and the mixture concentrated in vacuo to afford a thick oil. The residue was then redissolved in MeOH (75 mL) and the mixture cooled to 0 °C. Et_3N (55 mL) was then added dropwise the stirring solution over 10 minutes by addition funnel. Upon completion of the addition, the cooling bath was removed and the reaction was warmed to 23 °C over 1 hr. After an additional 3 hrs at room temperature, the solution was concentrated, the crude residue dissolved in Et_2O (500 mL), and the solution washed with water (2 x 500 mL). The organic layers were back extracted with Et_2O (250 mL), and the combined organic layers washed with brine (200 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to afford a yellow oil. The residue was purified by silica gel flash chromatography (5% MeOH in EtOAc) to afford diketopiperazine **185** as a white solid (3.32 g, 10.8

mmol, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.15 (s, 1H), 4.17 – 4.10 (m, 2H), 3.65 – 3.57 (m, 1H), 3.53 (ddd, *J* = 12.0, 8.9, 3.2 Hz, 1H), 3.10 (dd, *J* = 17.5, 3.6 Hz, 1H), 2.58 (dd, *J* = 17.5, 10.5 Hz, 1H), 2.43 – 2.32 (m, 1H), 2.14 – 1.97 (m, 2H), 1.97 – 1.83 (m, 1H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.59 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 163.9, 101.9, 86.6, 59.3, 53.9, 45.4, 28.4, 22.6, 22.5, 7.4, 4.3; FTIR (NaCl, thin film): 3233, 2954, 2908, 2873, 2176, 1675, 1457, 1417, 1338, 1306, 1018 cm^{-1}; $[\alpha]_D^{25}$ = -–108 (*c* = 0.93, $CHCl_3$); HRMS (MM) calc'd for $[M+H]^+$ 307.1836, found 307.1839.

Preparation of Pyrroloindoline 181f



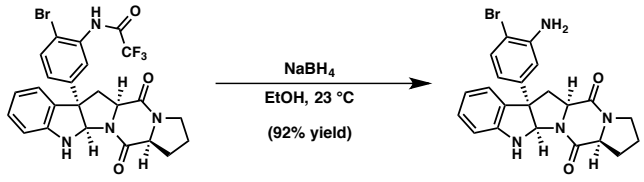
In a glovebox, $Cu(OTf)_2$•PhMe (310 mg, 0.600 mmol) and $^{t\text{Bu}}DAB_{Me}$ (1.10 g, 2.40 mmol) were added to an oven-dried, 200 mL round-bottomed flask. Anhydrous CH_2Cl_2 (60.0 mL) was then added by syringe, and the resulting deep-purple solution was stirred for 1 hr at 25 °C in the glovebox. The solution was then filtered through a tight plug of cotton, and the resulting solution removed from the glovebox.

To a flame-dried, 1-liter round-bottomed flask was charged cyclo-L-Pro-L-Trp **175f** (1.50 g, 5.30 mmol, 1.00 equiv), (4-bromo-3-trifluoroacetamidophenyl)mesityliodonium hexafluorophosphate (4.19 g, 6.36 mmol, 1.20 equiv) in anhydrous CH_2Cl_2 (480 mL). The solution was stirred at 23 °C for 10 minutes, then cooled to 15 °C in a cold water bath. To the flask was then added the freshly prepared catalyst solution of $Cu^I(^{t\text{Bu}}DAB_{Me})$ (53.0 mL, 1.06 mmol, 0.20 equiv) dropwise over 20 minutes. The deep-purple solution

was allowed to warm to 23 °C over 2 hours, then stirred for 20 hours at 23 °C by which time the solution had turned to a deep red. The solution was then quenched by the addition of aqueous ammonium hydroxide (1.8 M, 500 mL). The mixture was transferred to a separatory funnel, vigorously shaken, and the layers partitioned. The aqueous layer was then back extracted with EtOAc (2 x 100 mL), and the combined organic layers dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Repeated silica gel chromatography (5% MeOH, 25% Hexanes, 70% EtOAc) afforded aryl pyrrolodine **181f** as an amorphous white solid (1.79 g, 3.26 mmol, 62% yield).

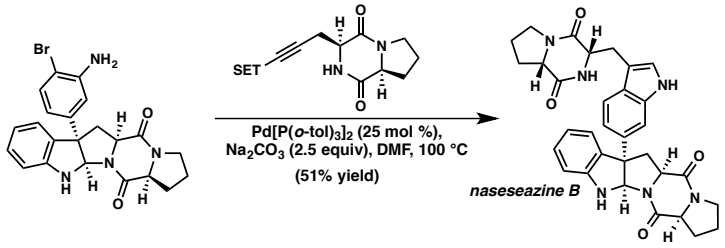
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.42 (d, *J* = 2.3 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 7.10 (ddd, *J* = 7.7, 7.7, 1.3 Hz, 1H), 7.04 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.97 (ddd, *J* = 7.6, 1.2, 0.5 Hz, 1H), 6.76 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.64 (ddd, *J* = 7.8, 0.8, 0.8 Hz, 1H), 5.73 (s, 1H), 4.59 - 4.51 (m, 1H), 4.20 - 4.11 (m, 1H), 3.51 - 3.40 (m, 2H), 3.09 (dd, *J* = 14.0, 7.9 Hz, 1H), 2.96 (dd, *J* = 14.0, 8.9 Hz, 1H), 2.30 (dddd, *J* = 12.9, 7.0, 7.0, 3.5 Hz, 1H), 2.15 (dddd, *J* = 13.0, 10.5, 9.0, 7.2 Hz, 1H), 2.02 - 1.93 (m, 1H), 1.88 (ddddd, *J* = 17.2, 10.5, 8.6, 4.3, 4.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 165.4, 154.8 (q, $J_{C\text{-}F}$ = 38.0 Hz), 147.2, 144.1, 133.5, 132.8, 132.0, 129.0, 125.9, 124.2, 120.0, 119.9, 115.46 (q, $J_{C\text{-}F}$ = 288.7 Hz), 112.8, 110.0, 85.0, 60.5, 60.1, 59.8, 45.2, 38.1, 27.5, 23.3; FTIR (NaCl, thin film): 3270, 1733, 1683, 1586, 1539, 1485, 1467, 1418, 1312, 1245, 1198, 1162 cm^{-1}; $[\alpha]_D^{25}$ = +67.8 (*c* = 1.8, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 549.1, found 549.1.

Preparation of Aniline 186:



To a solution of pyrroloindoline **181f** (150 mg, 0.273 mmol, 1.00 equiv) in EtOH at 23 °C was added $NaBH_4$ (77.0 mg, 2.02 mmol, 7.4 equiv). The solution was stirred vigorously for 1 h, then cooled to 0 °C and slowly quenched with saturated aqueous ammonium chloride (5 mL). The mixture was then diluted with H_2O (50 mL) and extracted with EtOAc (3 x 25 mL). The combined organics were then dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude residue by flash silica gel chromatography (75% EtOAc, 20% Hexanes, 5% MeOH) afforded bromoaniline **186** as a white, amorphous solid (114 mg, 0.252 mmol, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.3 Hz, 1H), 7.08 (ddd, *J* = 7.7, 7.7, 1.3 Hz, 1H), 6.93 - 6.89 (m, 1H), 6.72 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 6.70 (d, *J* = 2.3 Hz, 1H), 6.65 - 6.58 (m, 2H), 5.76 (d, *J* = 2.8 Hz, 1H), 5.35 (d, *J* = 3.0 Hz, 1H), 4.52 - 4.44 (m, 1H), 4.18 - 4.07 (m, 3H), 3.48 (ddd, *J* = 8.6, 5.2, 5.2 Hz, 2H), 3.11 (dd, *J* = 13.9, 7.4 Hz, 1H), 2.76 (dd, *J* = 13.9, 9.7 Hz, 1H), 2.31 (dddd, *J* = 12.8, 7.0, 7.0, 3.3 Hz, 1H), 2.15 (dddd, *J* = 12.9, 10.6, 9.2, 7.2 Hz, 1H), 2.05 - 1.96 (m, 1H), 1.95 - 1.86 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ167.9, 165.6, 147.1, 144.3, 143.0, 133.1, 132.8, 128.7, 124.1, 119.7, 117.4, 114.0, 109.6, 108.0, 85.1, 60.5, 60.2, 59.5, 45.2, 38.0, 27.6, 23.3; FTIR (NaCl, thin film): 3457, 3341, 3003, 2953, 2881, 1661, 1612, 1572, 1484, 1466, 1422, 1341, 1293, 1252, 1214, 1152 cm^{-1}; $[\alpha]_D^{25}$ = +118 (*c* = 0.80, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 453.1, found 453.1.

Preparation of (+)-Naseseazine B (187)



In a glovebox, a 1-dram vial was charged with bromoaniline **186** (74.6 mg, 0.165 mmol, 1.00 equiv), alkyne **10** (127 mg, 0.412 mmol, 2.50 equiv), Na_2CO_3 (43.7 mg, 0.412 mmol, 2.50 equiv), and $Pd[P(o\text{-tol})_3]_2$ (29.5 mg, 0.0412 mmol, 25 mol %). DMF (1.70 mL) was then added and the solution stirred vigorously for 3 minutes at 25 °C. The solution was then heated to 100 °C for 1.5 h, cooled, and concentrated under reduced pressure and dried under high vacuum to ensure complete removal of residual DMF. The residue was then dissolved in CH_2Cl_2 (3 mL) and filtered through a plug of silica gel (50 g) to remove residual catalyst and base, then the filter cake rinsed (5% MeOH in CH_2Cl_2, 200 mL). The filtrate was then concentrated, and the crude residue dissolved in 1M methanolic HCl (10 mL), and stirred for 2 h at 23 °C. The solution was then concentrated and the residue was quenched by the addition of methanolic NH_3 (1 N, 5 mL) and reconcentrated. The residue was purified by flash chromatography on silica gel (2 to 7% MeOH in CH_2Cl_2) afforded Naseseazine B (**187)** as a white, powdery solid (47.3 mg, 0.837 mmol, 51% yield). Excess TES-alkyne **185** could be recovered during chromatography.

Spectroscopic and physical data, including ^1H, ^{13}C NMR in CD_3OD, DMSO-*d6,* IR, MS, and $[\alpha]_D^{25}$, obtained for Naseseazine B matched that as reported during isolation by Raju

et. al and data obtained by Movassaghi and Kim. See below for ^{1}H and ^{13}C comparison table. The use of natural amino acids in this report to synthesize (+)-naseseazine B is in agreement with Movassaghi and Kim's structural reassignment of the natural product.[2] During the course of this study, we determined that the exact chemical shifts (δ) of Naseseazine B observed in CD_3OD had a slight concentration dependence.

^{1}H NMR (600 MHz, CD_3OD) δ 7.56 (d, *J* = 8.5 Hz, 1H), 7.40 (d, *J* = 0.6 Hz, 1H), 7.12 (s, 1H), 7.04 (td, *J* = 7.6, 1.1 Hz, 1H), 7.00 (dd, *J* = 8.5, 1.1 Hz, 1H), 6.82 (dd, *J* = 7.2, 1.0 Hz, 1H), 6.69 – 6.64 (m, 2H), 5.82 (s, 1H), 4.71 – 4.61 (m, 1H), 4.38 (app t, *J* = 4.4 Hz, 1H), 4.24 (app t, *J* = 8.1, 1H), 3.96 (dd, *J* = 9.6, 6.6 Hz, 1H), 3.51 – 3.36 (m, 3H), 3.30 – 3.27 (m, 2H), 3.26 – 3.21 (m, 2H), 2.57 (dd, *J* = 13.7, 10.1 Hz, 1H), 2.24 (dddd, *J* = 10.0, 6.9, 6.9, 3.1 Hz, 1H), 2.13 – 2.03 (m, 1H), 2.00 – 1.93 (m, 2H), 1.93 – 1.84 (m, 1H), 1.72 – 1.60 (m, 1H), 1.49 – 1.40 (m, 1H), 1.01 – 0.92 (m, 1H); ^{13}C NMR (126 MHz, CD_3OD) δ 170.8, 170.1, 168.4, 167.3, 149.1, 137.9, 137.0, 136.0, 129.4, 127.7, 126.4, 124.9, 120.5, 119.6, 111.1, 110.4, 109.7, 86.9, 61.8, 61.7, 61.5, 60.0, 57.1, 46.2, 45.9, 39.5, 29.2, 29.0, 28.5, 24.2, 22.6.

^{1}H NMR (600 MHz, DMSO-d_6) δ 10.80 (d, *J* = 2.4 Hz, 1H), 7.68 (s, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.31 (d, *J* = 1.6 Hz, 1H), 7.19 (d, *J* = 2.4 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.80 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.75 (s, 1H), 6.61 (d, *J* = 6.6, 1 H), 6.58 (dd, *J* = 6.6, 1H), 5.68 (s, 1H), 4.72 (ddd, *J* = 9.3, 7.7, 1.3 Hz, 1H), 4.34 (ddd, *J* = 8.9, 7.4, 1.4 Hz, 1H), 4.29 (app t *J* = 5.3 Hz, 1H), 4.06 (ddd, *J* = 9.9, 6.8, 1.4 Hz, 1H), 3.37 – 3.33 (m, 2H), 3.25 (ddd, *J* = 12.1, 9.0, 3.9 Hz, 1H), 3.22 (dd, *J* = 14.9, 4.8 Hz, 1H), 3.13 (dd, *J* = 13.7, 7.4

Hz, 1H), 3.05 (dd, *J* = 14.9, 5.8 Hz, 1H), 2.37 (dd, *J* = 13.7, 10.4 Hz, 1H), 2.16 (dddd, *J* = 12.4, 7.0, 7.0, 3.6 Hz, 1H), 2.03 - 1.91 (m, 2H), 1.90 - 1.78 (m, 2H), 1.69 (dddd, *J* = 10.7, 8.7, 5.8, 2.5 Hz, 1H), 1.67 - 1.57 (m, 1H), 1.46 - 1.38 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 169.1, 167.9, 165.9, 165.5, 148.1, 135.9, 135.6, 134.6, 127.9, 126.1, 125.1, 123.4, 119.2, 118.0, 117.9, 109.3, 109.2, 84.9, 60.0, 59.8, 59.5, 58.4, 55.2, 44.6, 38.7, 27.7, 27.1, 25.7, 23.0, 21.9. IR: 3270, 2943, 2859, 1653, 1559, 1419, 1340 cm^{-1}; $[\alpha]_D^{25}$ = +97 (*c* = 0.45, MeOH) LRMS (EI+) calc'd for $[M+H]^+$ 565.3, found 565.3.

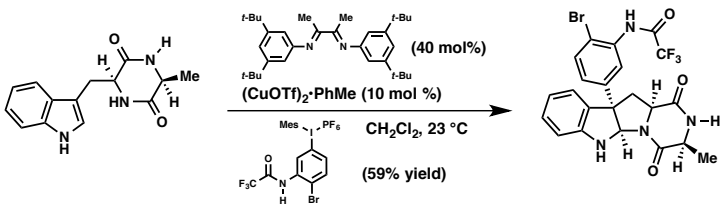
Comparison of ^{1}H NMR data for Natural vs. Synthetic (+)-Naseseazine B

Raju et al. Report, Natural (+)–Naseseazine B ^{1}H NMR, 600 MHz, CD_3OD	This Work, Synthetic (+)–Naseseazine B ^{1}H NMR, 600 MHz, CD_3OD
δ 7.58 (d, *J* = 8.4 Hz, 1H)	δ 7.56 (d, *J* = 8.5 Hz, 1H)
7.41 (d, *J* = 1.4 Hz, 1H)	7.40 (d, *J* = 0.6 Hz, 1H)
7.12 (s, 1H)	7.12 (s, 1H)
7.06 (td, *J* =7.6, 1.3 Hz)	7.04 (td, *J* = 7.6, 1.1 Hz, 1H)
7.03 (dd, *J* = 8.4, 1.8 Hz, 1H)	7.00 (dd, *J* = 8.5, 1.1 Hz, 1H)
6.84 (dt, *J* =7.2, 0.9 Hz, 1H)	6.82 (dt, *J* = 7.2 Hz, 1.0 Hz, 1H),
6.69 (t, *J* = 7.6 Hz, 1H)	6.69 – 6.64 (m, 2H)
6.68 (t, *J* = 7.6 Hz, 1H)	–
5.85 (s, 1H)	5.82 (s, 1H)
4.75 (dd, *J* = 10.2, 8.7 Hz, 1H)	4.71 – 4.61 (m, 1H)
4.40 (br t, *J* =4.7 Hz, 1H)	4.38 (app t, *J* = 4.4, 1H)
4.33 (dd, *J* = 9.5, 7.1 Hz, 1H)	4.24 (app t, *J* = 8.1, 1H)
3.99 (ddd, *J* = 11.4, 6.6 , 1.6 Hz, 1H)	3.96 (dd, *J* = 9.6, 6.6 Hz, 1H)
3.49 (m, 1H)	3.51 – 3.36 (m, 3H)
3.44 (m, 1H)	–
3.44 (m, 1H)	–
3.32 (m, 1H)	3.30 – 3.27 (m, 2H)
3.28 (m, 1H)	–
3.27 (m, 1H)	3.26 – 3.21 (m, 2H)
3.24 (m, 1H)	–
2.59 (dd, *J* = 13.8, 10.2 Hz, 1H)	2.57 (dd, *J* = 13.7, 10.1 Hz, 1H)
2.28 (m, 1H)	2.24 (dddd, *J* = 10.0, 6.9, 6.9, 3.1 Hz, 1H)
2.11 (m, 1H)	2.13 – 2.03 (m, 1H)
2.00 (m, 1H)	2.00 – 1.93 (m, 2H)
1.97 (m, 1H)	–
1.95 (m, 1H)	1.93 – 1.84 (m, 1H)
1.67 (m, 1H)	1.72 – 1.60 (m, 1H)
1.44 (m, 1H)	1.49 – 1.40 (m, 1H)
0.92 (m, 1H)	1.01 – 0.92 (m, 1H)

Comparison of ^{13}C NMR data for Natural vs. Synthetic (+)-Naseseazine B

Raju et al. Report, Natural (+)–Naseseazine B ^{13}C NMR, 151 MHz, CD_3OD	This Work, Synthetic (+)–Naseseazine B ^{13}C NMR, 126 MHz, CD_3OD	Chemical Shift Difference, Δδ
δ 170.7	δ 170.8	0.1
170.2	170.1	0.1
168.4	168.4	0.0
167.3	167.3	0.0
149.0	149.1	0.1
137.9	137.9	0.0
136.9	137.0	0.1
136.0	136.0	0.0
129.1	129.4	0.3
127.6	127.7	0.1
126.1	126.4	0.3
124.8	124.9	0.1
120.3	120.5	0.2
120.3	–	–
119.4	119.6	0.2
111.0	111.1	0.1
110.3	110.4	0.1
109.5	109.4	0.1
86.8	86.9	0.1
61.8	61.8	0.0
61.7	61.7	0.0
61.3	61.5	0.2
59.9	60.0	0.1
57	57.1	0.1
45.9	46.2	0.3
45.8	45.9	0.1
39.5	39.5	0.0
29.2	29.2	0.0
29.1	29.0	0.1
28.3	28.5	0.2
24.1	24.2	0.1
22.4	22.6	0.2

Preparation of Pyrroloindoline 181b

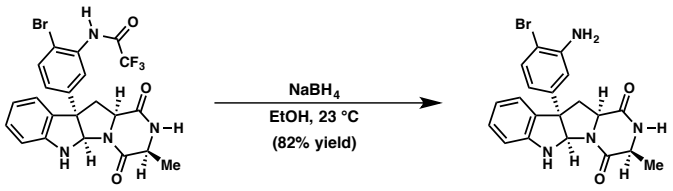


In a glovebox, $Cu(OTf)_2$•PhMe (77.6 mg 0.150 mmol) and $^{t\text{Bu}}DAB_{Me}$ (277 mg, 0.600 mmol, 2.40 mmol) were added to an oven-dried, 50 mL round-bottomed flask. Anhydrous CH_2Cl_2 (27.0 mL) was then added by syringe, and the resulting deep-purple solution was stirred for 1 hr at 25 °C in the glovebox. The solution was then filtered through a tight plug of cotton, and the resulting solution removed from the glovebox.

To a flame-dried, 100-mL round-bottomed flask was charged cyclo-L-Ala-L-Trp **175b** (334 mg, 1.30 mmol, 1.00 equiv) and (4-bromo-3-trifluoroacetamidophenyl)mesityliodonium hexafluorophosphate (940 mg, 1.43 mmol, 1.10 equiv)). To the flask was then added the freshly prepared catalyst solution of $Cu^{I}(^{tBu}DAB_{Me})$ (26.0 mL, 0.260 mmol, 0.20 equiv) dropwise over 20 minutes. The deep-purple solution was allowed to warm to 23 °C over 2 hours, then stirred for 8 hours at 23 °C. The solution was then quenched by the addition of aqueous ammonium hydroxide (1.8 M, 20 mL). The mixture was then diluted with EtOAc (100 mL), transferred to a separatory funnel, vigorously shaken, and the layers partitioned. The aqueous layer was then back-extracted with EtOAc (2 x 100 mL), and the combined organic layers dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. Repeated silica gel chromatography (78% EtOAc, 20% hexanes, 2 % MeOH) afford aryl pyrrolodine **181b** as a white solid (402.0 mg, 0.767 mmol, 59% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.39 (d, *J* = 2.3 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.20 (s, 1H), 7.09 (ddd, *J* = 7.7, 7.7, 1.0 Hz, 1H), 7.03 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.95 (d, *J* = 7.4 Hz, 1H), 6.73 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 1H), 5.73 (s, 1H), 5.68 (br s, 1H), 4.47 (dd, *J* = 8.3, 8.3 Hz, 1H), 4.10 – 4.03 (m, 1H), 3.09 (dd, *J* = 13.9, 7.9 Hz, 1H), 2.89 (dd, *J* = 13.9, 8.9 Hz, 1H), 1.41 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 168.4, 154.8

(q, $J_{C\text{-}F}$ = 38.0 Hz) 147.3, 144.0, 133.4, 132.8, 131.9, 129.0, 125.9, 124.0, 120.0, 119.7, 115.4 (q, $J_{C\text{-}F}$ = 288.6 Hz) 113.0, 110.1, 85.1, 59.3, 58.7, 51.2, 38.2, 15.2; FTIR (NaCl, thin film): 3270, 1733, 1683, 1586, 1539, 1485, 1467, 1418, 1312, 1245, 1198, 1162 cm^{-1}; $[\alpha]_D^{25}$ = +84 (*c* = 0.42, $CHCl_3$); LRMS (EI+) calc'd for $[M+H]^+$ 523.1, found 523.1.

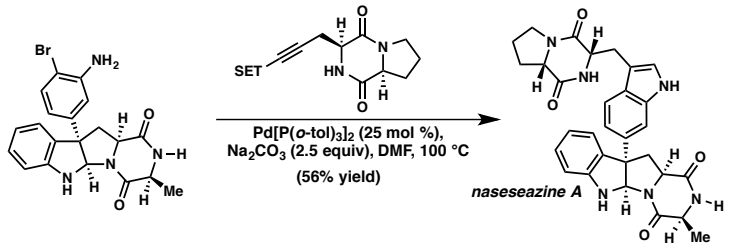
Preparation of Aniline 186b



To a solution of pyrroloindoline **181b** (140 mg, 0.268 mmol, 1.00 equiv) in EtOH (5.4 mL) at 23 °C was added $NaBH_4$ (76.3 mg, 2.00 mmol, 7.5 equiv). The solution was stirred vigorously for 1 h, then cooled to 0 °C and slowly quenched with saturated aqueous ammonium chloride (5 mL). The mixture was then diluted with H_2O (50 mL) and extracted with EtOAc (3 x 45 mL). The combined organics were then dried over sodium sulfate, filtered, and concentrated in vacuo. Purification of the crude residue by flash silica gel chromatography (75% EtOAc, 20% Hexanes, 5% MeOH) afforded bromoaniline **186b** as a white, amorphous solid (94.0 mg, 0.220 mmol, 82% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.4 Hz, 1H), 7.04 (ddd, *J* = 7.6, 7.6, 1.3 Hz, 1H), 6.91 - 6.85 (m, 1H), 6.85 (d, *J* = 2.3 Hz, 1H), 6.67 (ddd, *J* = 19.2, 7.7, 1.0 Hz, 2H), 6.56 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.72 (s, 1H), 4.56 (ddd, *J* = 10.0, 7.4, 1.6 Hz, 1H), 4.14 (qd, *J* = 6.8, 1.5 Hz, 1H), 3.10 (ddd, *J* = 14.0, 7.5, 1.7 Hz, 1H), 2.52 (dd, *J* = 13.6, 9.9 Hz, 1H), 1.37 (d, *J* = 6.9 Hz, 2H); FTIR (NaCl, thin film): 3345, 2919, 1668, 1605, 1483, 1418,

1300, 1209 cm^{-1}; $[\alpha]_D^{25}$ = +156 (*c* = 0.38, MeOH); LRMS (EI+) calc'd for $[M+H]^+$ 427.1, found 427.1.

Preparation of (+)-Naseseazine A



In a glovebox, a 1-dram vial was charged with bromoaniline **186b** (79.8 mg, 0.187 mmol, 1.00 equiv), alkyne **185** (143 mg, 0.467 mmol, 2.50 equiv), Na_2CO_3 (49.5 mg, 0.467 mmol, 2.50 equiv), and $Pd[P(o\text{-tol})_3]_2$ (33.4 mg, 0.0467 mmol, 25 mol %). DMF (1.90 mL) was then added and the solution stirred vigorously for 3 minutes at 25 °C. The solution was then heated to 100 °C for 1 h, cooled, and concentrated under reduced pressure and dried under high vacuum to ensure complete removal of residual DMF. The residue was then dissolved in CH_2Cl_2 (3 mL) and filtered through a plug of silica gel (50 g) to remove residual catalyst and base, then the filter cake rinsed (6% MeOH in CH_2Cl_2, 260 mL). The filtrate was then concentrated, and the crude residue dissolved in 1M methanolic HCl (12 mL), and stirred for 2 h at 23 °C. The solution was then concentrated and the residue was quenched by the addition of methanolic NH_3 (1 N, 12 mL) and reconcentrated. The residue was purified by flash chromatography on silica gel (2 to 10% MeOH in CH_2Cl_2) afforded Naseseazine A as a white, powdery solid (56.5 mg, 0.105 mmol, 56% yield). Excess TES-alkyne **185** could be recovered during chromatography.

Spectroscopic and physical data, including ^{1}H, ^{13}C NMR in CD_3OD, DMSO-*d6,* IR, MS, and $[\alpha]_D^{25}$, obtained for Naseseazine A matched that as reported during isolation by Raju et. al[15] and data obtained by Movassaghi and Kim.[2] See below for ^{1}H and ^{13}C comparison table. The use of natural amino acids in this report to synthesize (+)-naseseazine A is in agreement with Movassaghi and Kim's structural reassignment of the natural product.[2] During the course of this study, we determined that the exact chemical shifts (δ) of Naseseazine A observed in CD_3OD had a slight concentration dependence.

^{1}H NMR (600 MHz, CD_3OD) δ 7.55 (d, *J* = 8.4 Hz, 1H), 7.38 (s, 1H), 7.11 (s, 1H), 7.04 (app t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 6.83 (d, *J* = 7.4 Hz, 1H), 6.70 – 6.62 (m, 2H), 5.80 (s, 1H), 4.58 (app t, *J* = 8.6 Hz, 1H), 4.37 (dd, *J* = 4.7, 4.7 Hz, 1H), 4.10 (q, *J* = 6.8 Hz, 1H), 3.95 (dd, *J* = 10.7, 6.5 Hz, 1H), 3.41 (dt, *J* = 11.8, 8.3 Hz, 1H), 3.29 – 3.25 (m, 3H), 3.23 (dd, *J* = 13.2, 7.8 Hz, 2H), 2.58 (dd, *J* = 13.5, 10.0 Hz, 1H), 2.00 – 1.91 (m, 1H), 1.71 – 1.60 (m, 1H), 1.48 – 1.40 (m, 1H), 1.36 (d, *J* = 6.8 Hz, 3H), 1.01 – 0.91 (m, 1H); ^{13}C NMR (126 MHz, CD_3OD) δ 172.5, 170.8, 170.7, 167.3, 149.1, 137.9, 137.2, 135.9, 129.4, 127.6, 126.4, 125.0, 120.5, 120.4, 119.6, 111.1, 110.3, 109.7, 87.1, 61.2, 60.3, 60.0, 57.1, 52.2, 45.9, 39.7, 29.2, 29.0, 22.6, 15.3.

^{1}H NMR (600 MHz, DMSO-*d6*) δ 10.80 (s, 1H), 8.18 (s, 1H), 7.68 (s, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.29 (s, 1H), 7.19 (s, 1H), 7.01 – 6.96 (m, 2H), 6.83 (d, *J* = 7.3 Hz, 1H), 6.73 (s, 1H), 6.65 – 6.54 (m, 2H), 5.66 (s, 1H), 4.61 (dd, *J* = 8.6, 8.6 Hz, 1H), 4.28 (dd, *J* = 4.6, 4.6 Hz, 1H), 4.14 (q, *J* = 6.7 Hz, 1H), 4.10 – 4.03 (m, 1H), 3.40 – 3.35 (m, 1H), 3.28 – 3.18 (m, 2H), 3.07 (ddd, *J* = 26.8, 14.2, 6.7 Hz, 2H), 2.42 (dd, *J* = 13.1, 10.3 Hz,

1H), 2.02 – 1.93 (m, 1H), 1.70 (ddd, *J* = 27.0, 9.2, 9.2 Hz, 1H), 1.65 – 1.56 (m, 1H), 1.48 – 1.37 (m, 1H), 1.23 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-*d6*) δ 170.0, 169.1, 168.6, 165.5, 148.1, 135.9, 135.7, 134.4, 127.9, 126.1, 125.0, 123.6, 119.1, 117.9, 117.8, 109.3, 109.2, 109.1, 85.0, 59.3, 58.4, 58.4, 55.2, 50.3, 44.6, 38.8, 27.7, 25.7, 21.9, 14.8. FTIR: 3306, 2913, 2859, 1668, 1449, 1418, 1343, 1308 cm^{-1}; $[\alpha]_D^{25}$ = +121 (*c* = 0.30, MeOH); LRMS (EI+) calc'd for $[M+H]^+$ 539.2, found 539.2.

Comparison of ^{1}H NMR data for Natural vs. Synthetic (+)-Naseseazine A

Raju et al. Report, (+)–Naseseazine A ^{1}H NMR, 600 MHz, CD_3OD	**This Work (+)–Naseseazine A ^{1}H NMR, 600 MHz, CD_3OD**
δ 7.57 (d, *J* = 8.4 Hz, 1H)	δ 7.55 (d, *J* = 8.4 Hz, 1H)
7.40 (s, 1H)	7.38 (s, 1H)
7.11 (s, 1H)	7.11 (s, 1H)
7.05 (t, 7.2 Hz, 1H)	7.04 (app t, *J* = 7.6 Hz, 1H)
7.02 (d, *J* = 8.4 Hz, 1H)	7.00 (d, *J* = 8.4 Hz, 1H)
6.85 (d, *J* = 7.4 Hz, 1H)	6.83 (d, *J* = 7.4 Hz, 1H)
6.69 (d, *J* = 7.6 Hz, 1H)	6.70 – 6.62 (m, 2H)
6.67 (t, *J* = 8.5 Hz, 1H)	–
5.83 (s, 1H)	5.80 (s, 1H)
4.64 (dd, *J* = 8.4, 7.4 Hz, 1H)	4.58 (app t, *J* = 8.6 Hz, 1H)
4.39 (br t, *J* = 4.5 Hz, 1H)	4.37 (dd, *J* = 4.7, 4.7 Hz, 1H)
4.15 (q, *J* = 6.9 Hz, 1H)	4.10 (q, *J* = 6.8 Hz, 1H)
3.97 (dd, *J* = 10.8, 6.6 Hz, 1H)	3.95 (dd, *J* = 10.7, 6.5 Hz, 1H
3.42 (dt, *J* = 11.8, 8.1 Hz, 1H)	3.41 (dt, *J* = 11.8, 8.3 Hz, 1H)
3.30 (m, 1H)	3.29 – 3.25 (m, 3H)
3.29 (m, 1H)	–
3.26 (m, 1H)	–
3.24 (m, 1H)	3.23 (dd, *J* = 13.2, 7.8 Hz, 2H)
2.59 (dd, *J* = 13.7, 10.2 Hz, 1H)	2.58 (dd, *J* = 13.5, 10.0 Hz, 1H)
1.97 (m, 1H)	2.00 – 1.91 (m, 1H)
1.66 (m, 1H)	1.71 – 1.60 (m, 1H)
1.43 (m, 1H)	1.48 – 1.40 (m, 1H)
1.38 (d, *J* = 6.9 Hz, 1H)	1.36 (d, *J* = 6.8 Hz, 3H)
0.93 (m, 1H)	1.01 – 0.91 (m, 1H)

Comparison of ^{13}C NMR data for Natural vs. Synthetic (+)-Naseseazine A

Raju et al. Report, (+)–Naseseazine A ^{13}C NMR, 151 MHz, CD_3OD	This Work (+)–Naseseazine A ^{13}C NMR, 126 MHz, CD_3OD	Chemical Shift Difference, Δδ
172.6	172.5	0.1
170.6	170.8	0.2
170.6	170.7	0.1
167.3	167.3	0.0
149.1	149.1	0.0
137.9	137.9	0.0
137.2	137.2	0.0
135.8	135.9	0.1
129.2	129.4	0.2
127.6	127.6	0.0
126.2	126.4	0.2
124.9	125.0	0.1
120.3	120.5	0.2
120.2	120.4	0.2
119.5	119.6	0.1
110.9	111.1	0.2
110.1	110.3	0.2
109.5	109.7	0.2
87.1	87.1	0.0
61.2	61.2	0.0
60.2	60.3	0.1
60.0	60.0	0.0
57.2	57.1	0.1
52.1	52.2	0.1
45.8	45.9	0.1
39.7	39.7	0.0
29.0	29.2	0.2
29.0	29.0	0.0
22.5	22.6	0.1
15.2	15.3	0.1

3.12 NOTES AND REFERENCES

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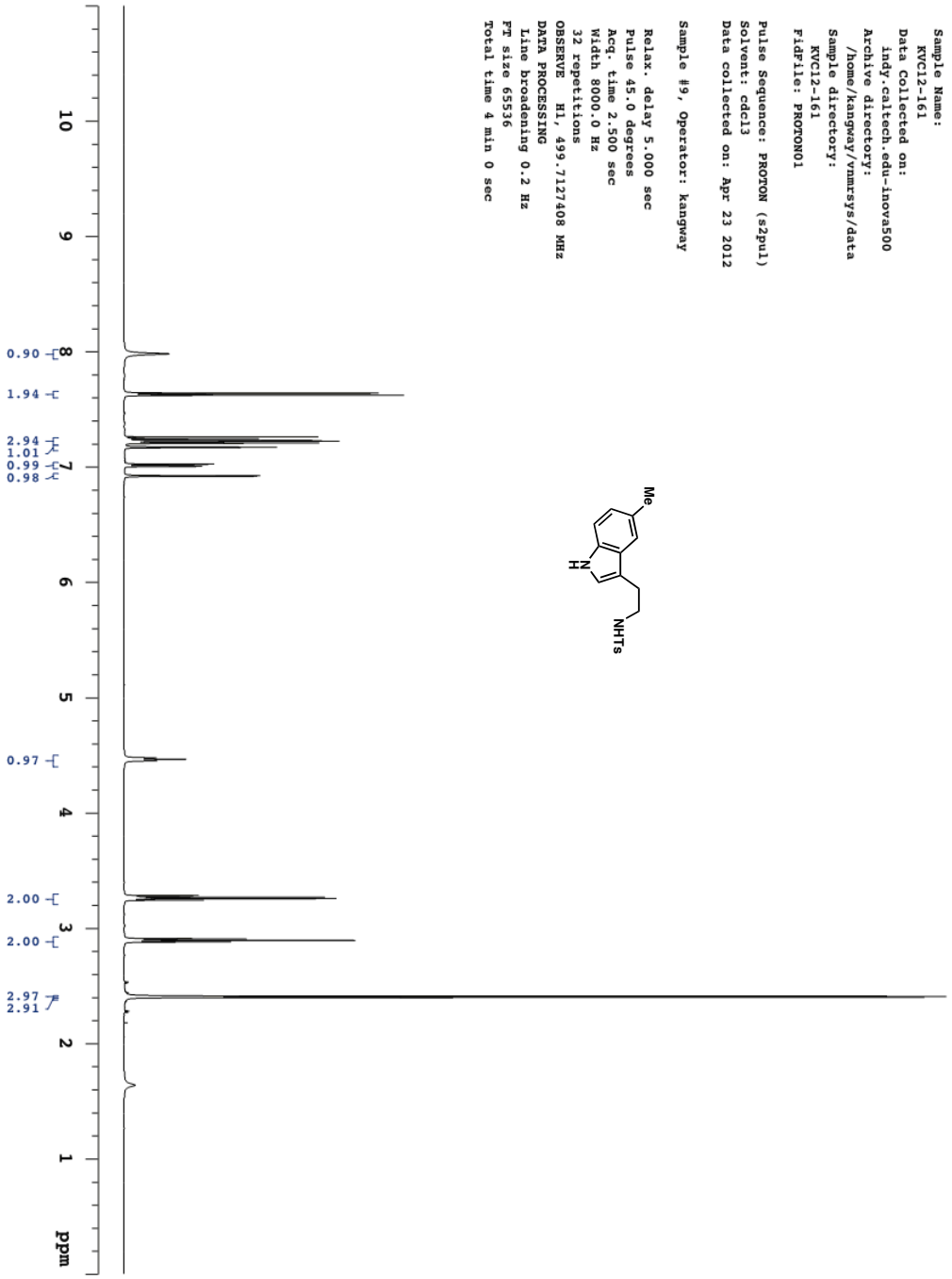
Appendix 2

Spectra Relevant to Chapter 3: Direct and Selective Copper-Catalyzed Arylation of Tryptamines and Tryptophans: Total Synthesis of (+)-Naseseazines A and B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Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #9, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
N
H
NHTs
0.90
1.94
2.94
1.01
0.99
0.98
0.97
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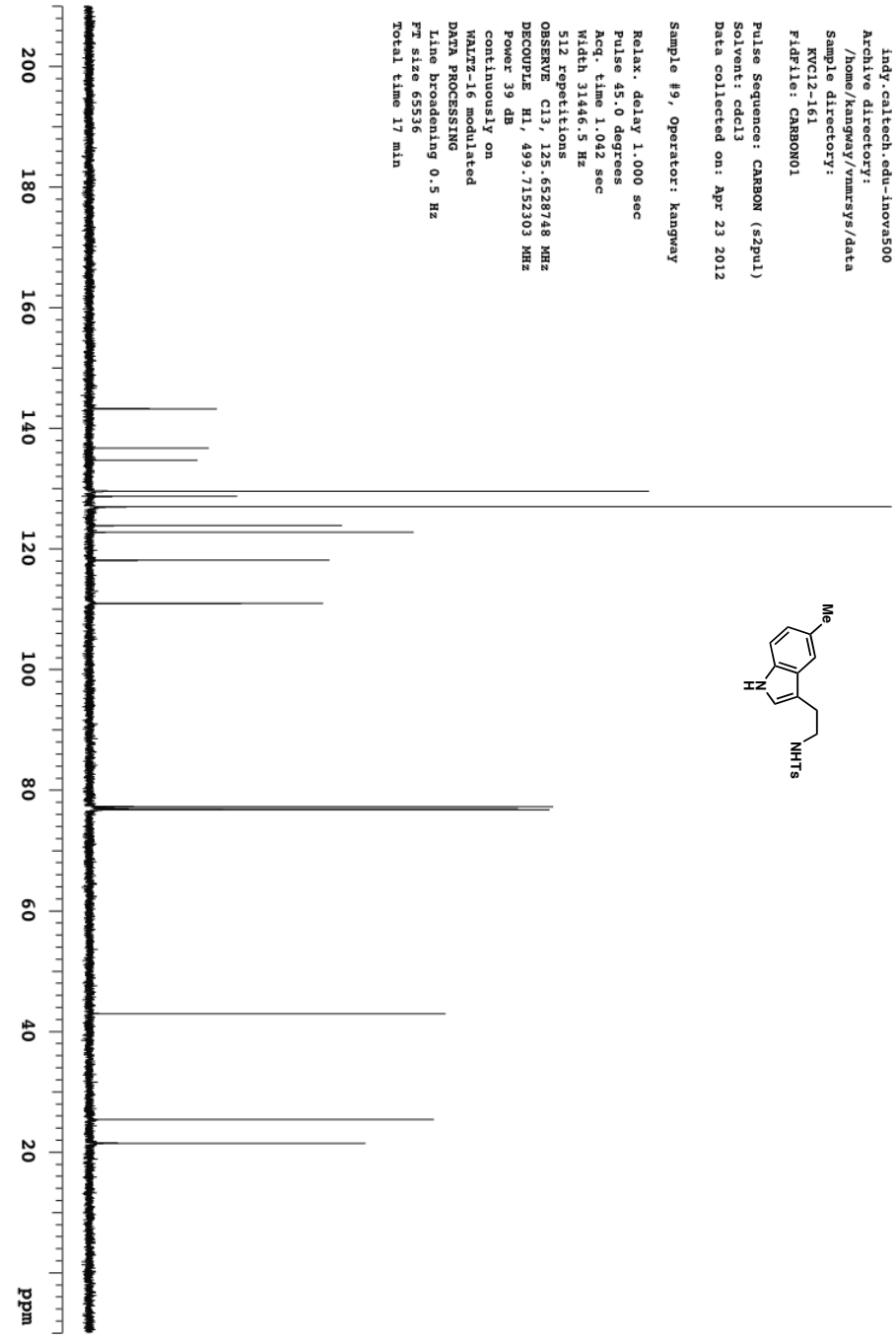
2.00
2.97
2.91
10
9
8
7
6
5
4
3
2
1
ppm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Sample directory:
KVC12-161
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Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #9, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528748 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
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Me
H
N
NHTs
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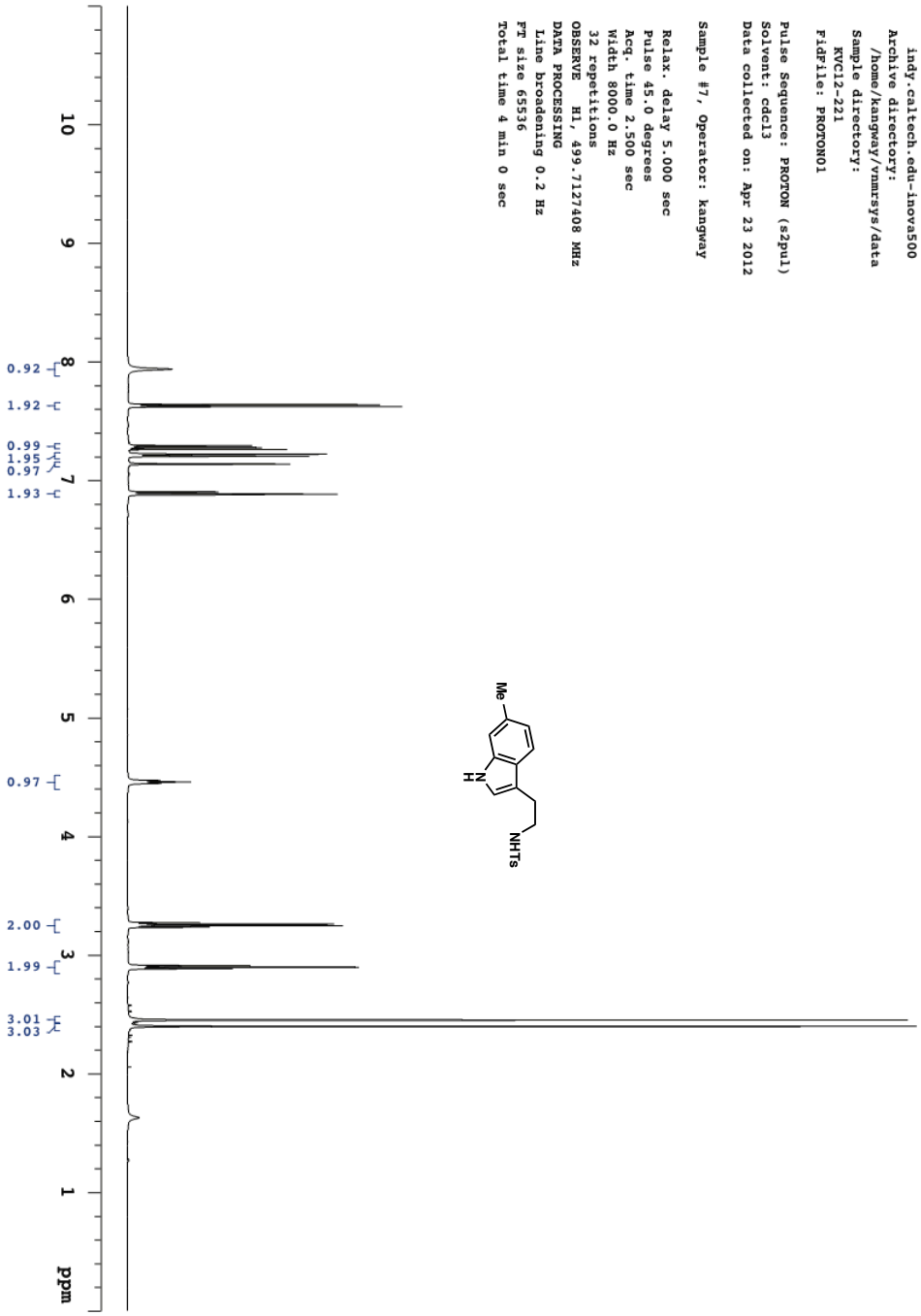
160
140
120
100
80
60
40
20
ppm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Sample directory:
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Solvent: cdcl3
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Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
NHTs
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1.92
0.99
1.95
0.97
1.93
0.97
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1.99
3.01
3.03
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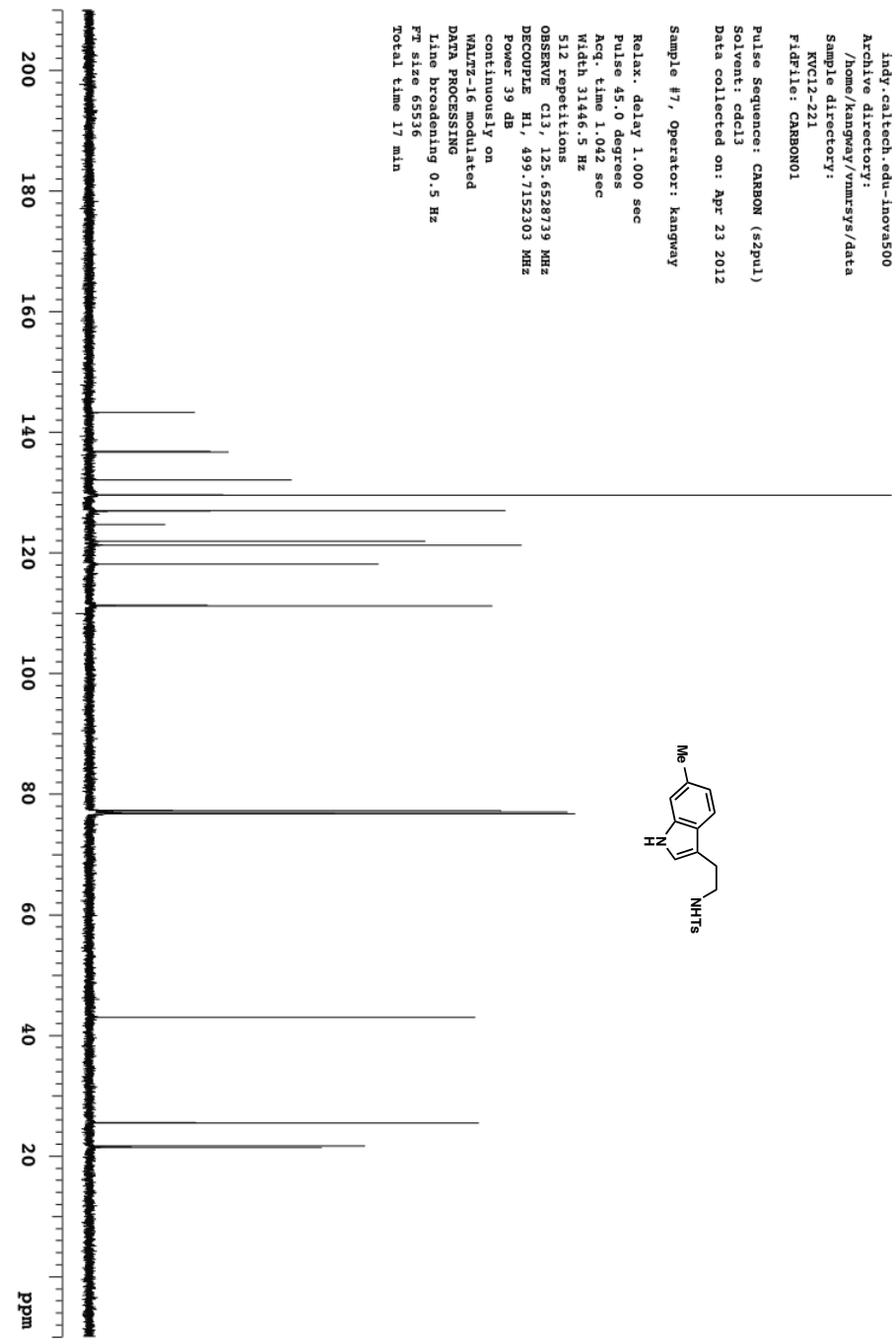
8
7
6
5
4
3
2
1
ppm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Archive directory:
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Sample directory:
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Solvent: cdcl3
Data collected on: Apr 23 2012
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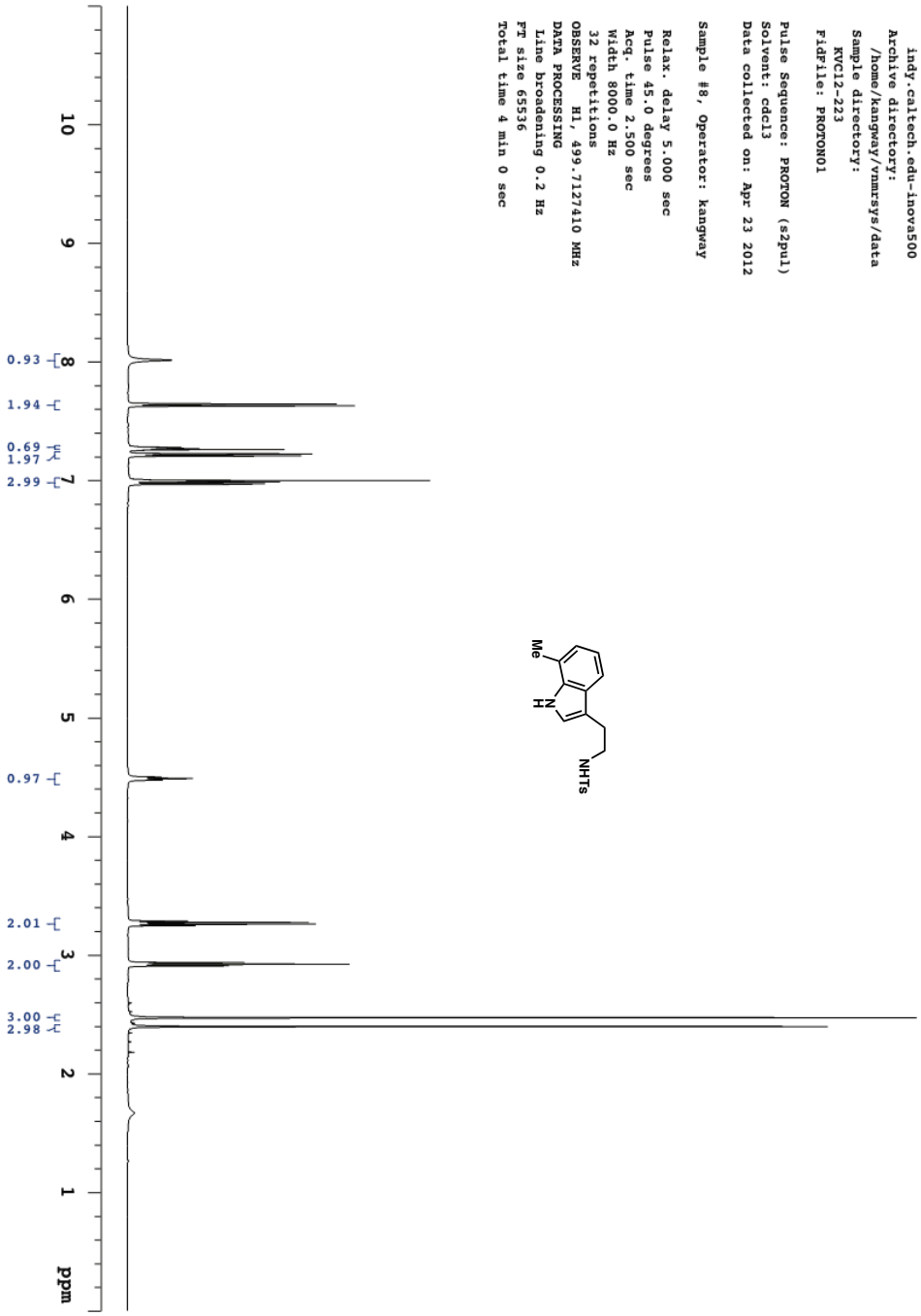
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528739 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
NHTs
200
180
160
140
120
100
80
60
40
20
ppm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Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
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Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
N
H
NHTs
0.93
1.94
0.69
1.97
2.99
0.97
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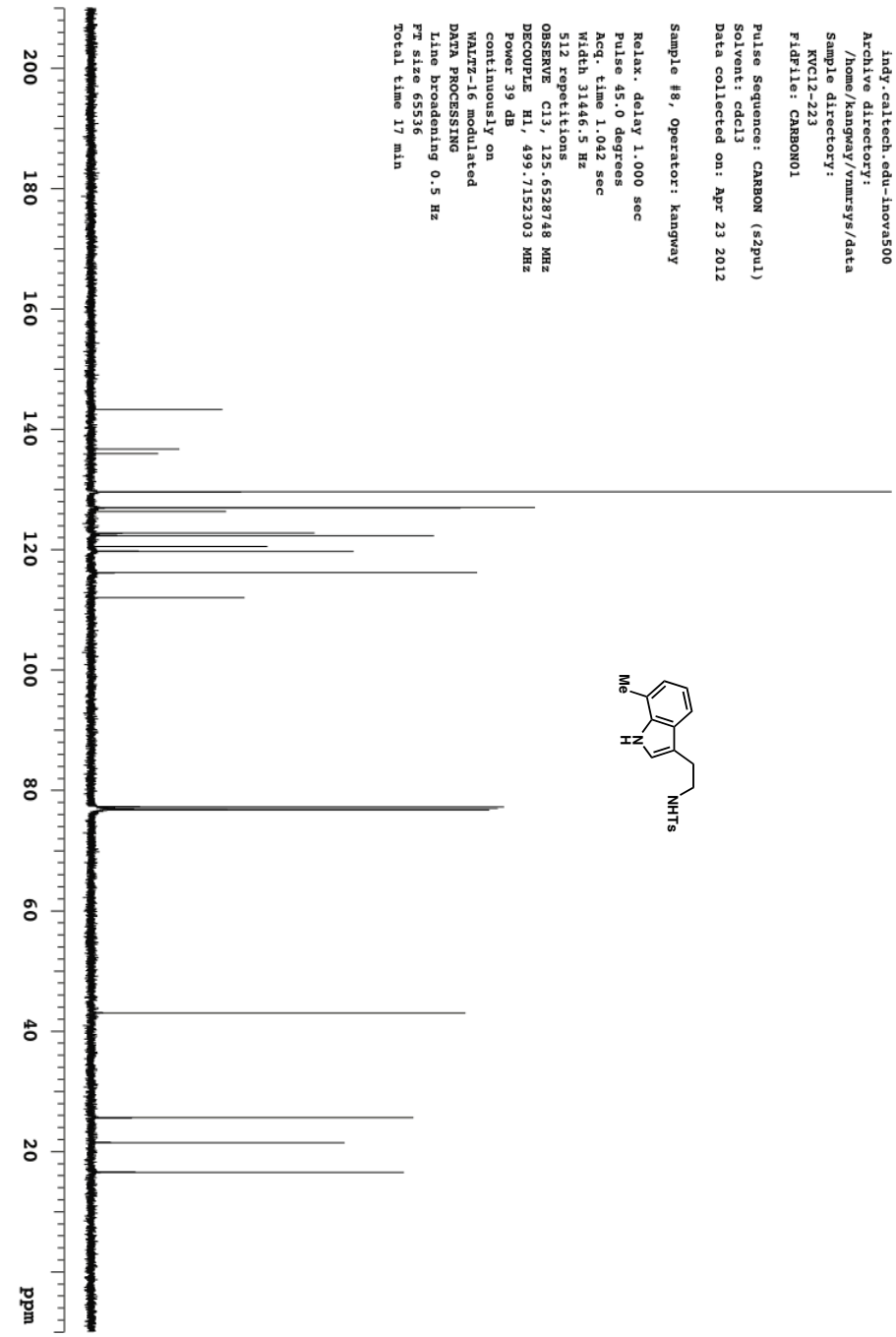
2.00
3.00
2.98
10
9
8
7
6
5
4
3
2
1
ppm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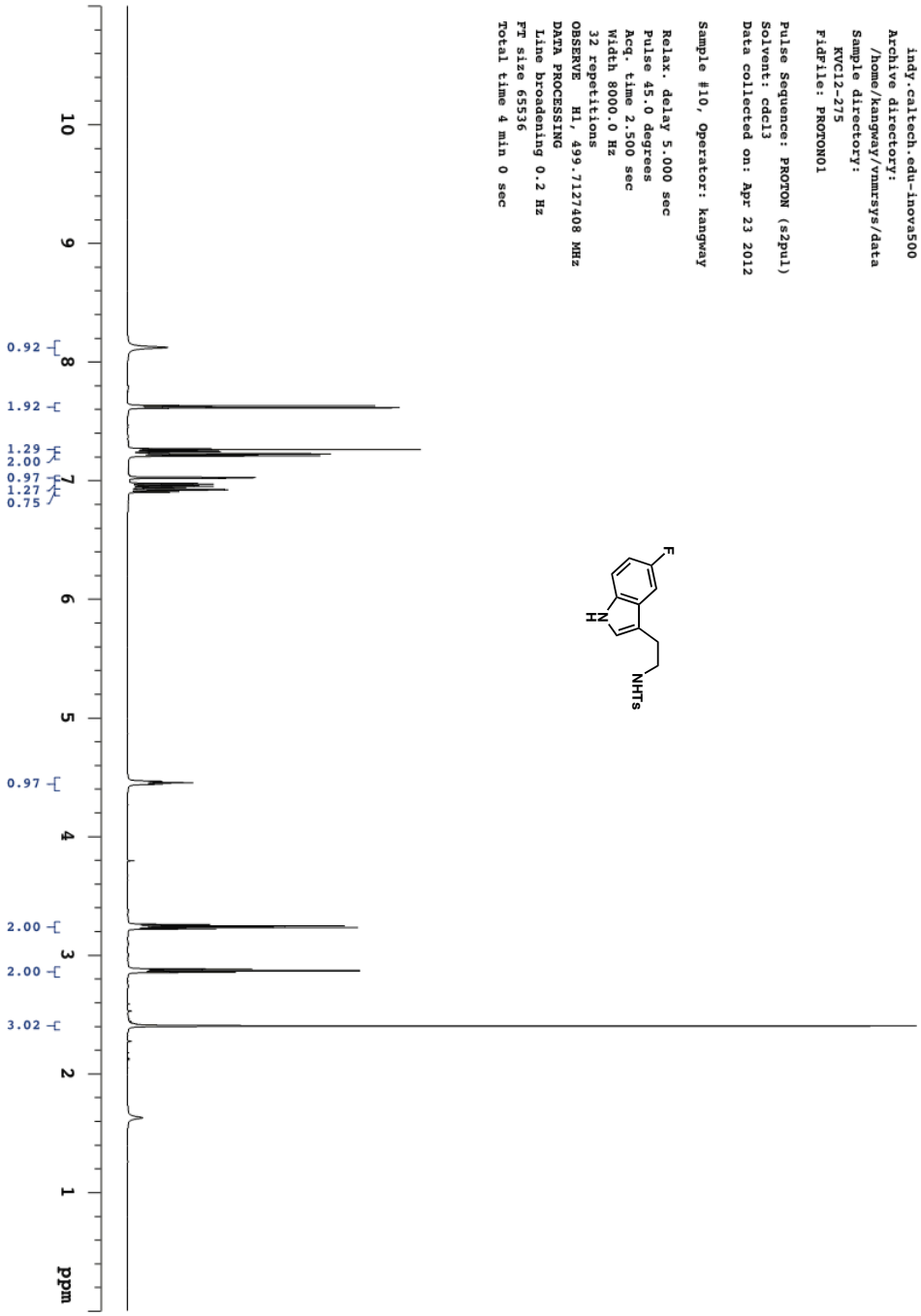
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #8, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528748 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
H
N
NHTs
200
180
160
140
120
100
80
60
40
20
ppm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Sample directory:
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FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #10, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
F
N
H
NHTs
0.92
1.92
1.29
2.00
0.97
1.27
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2.00
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9
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7
6
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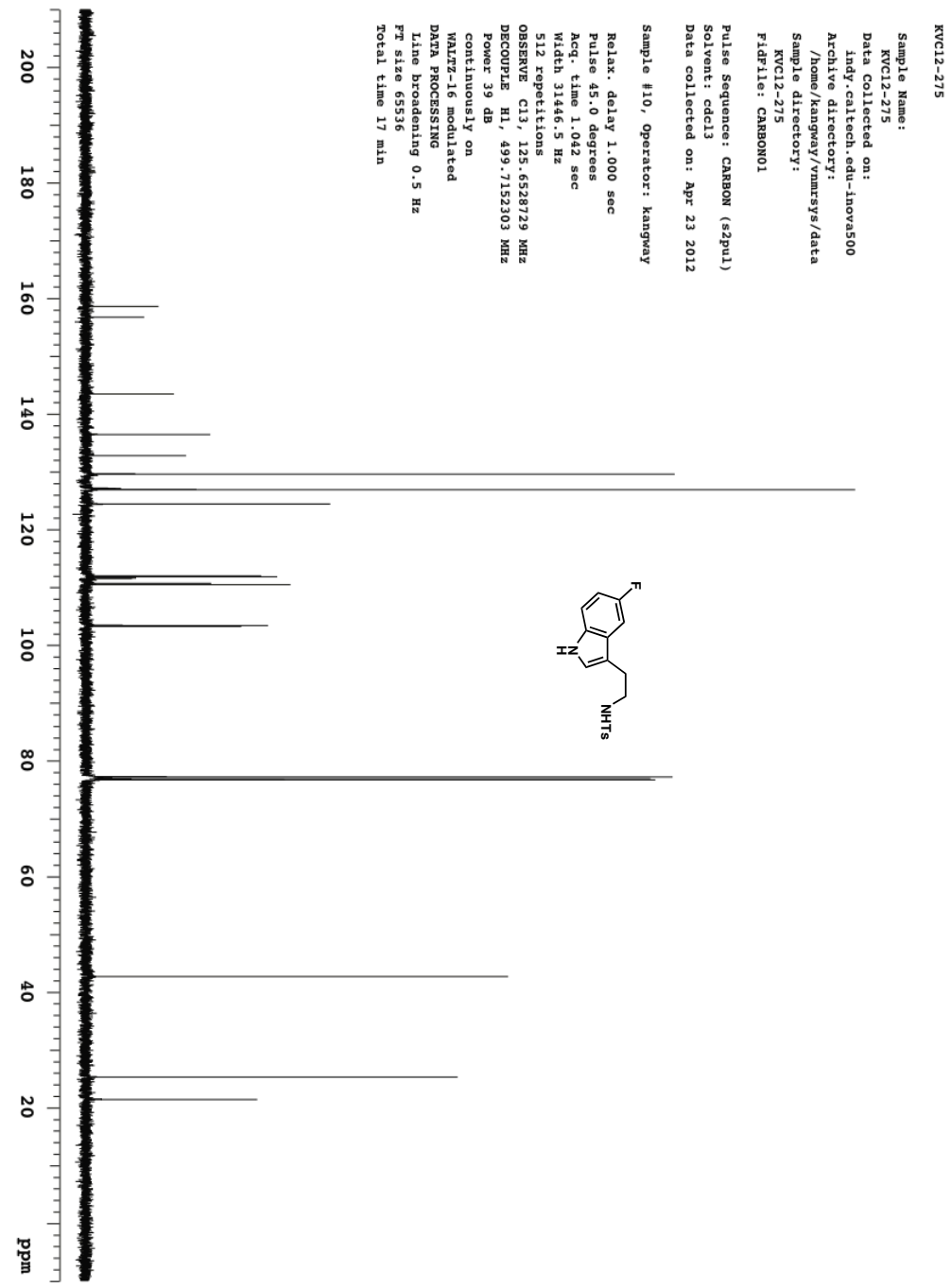
4
3
2
1
ppm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Sample directory:
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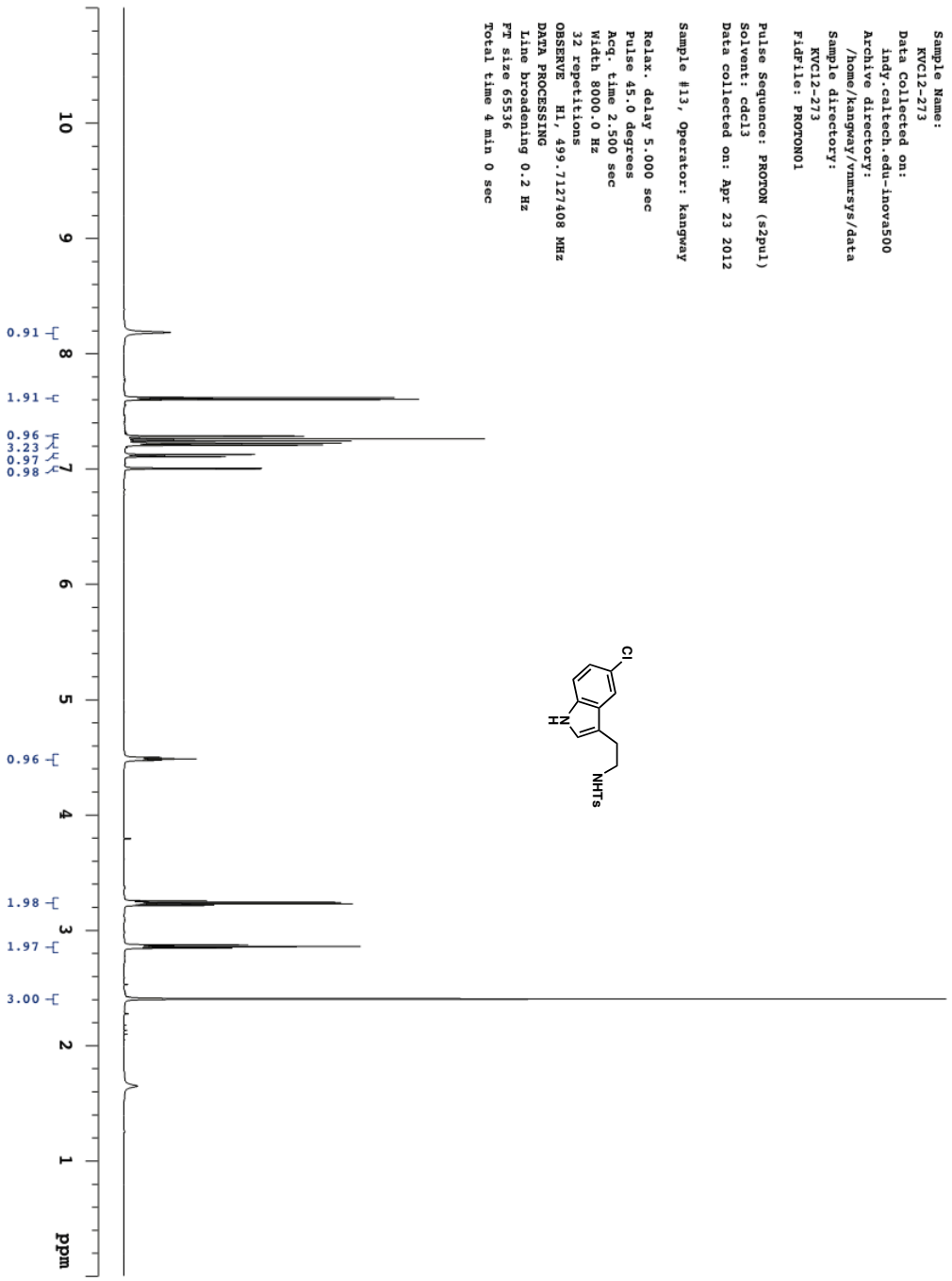
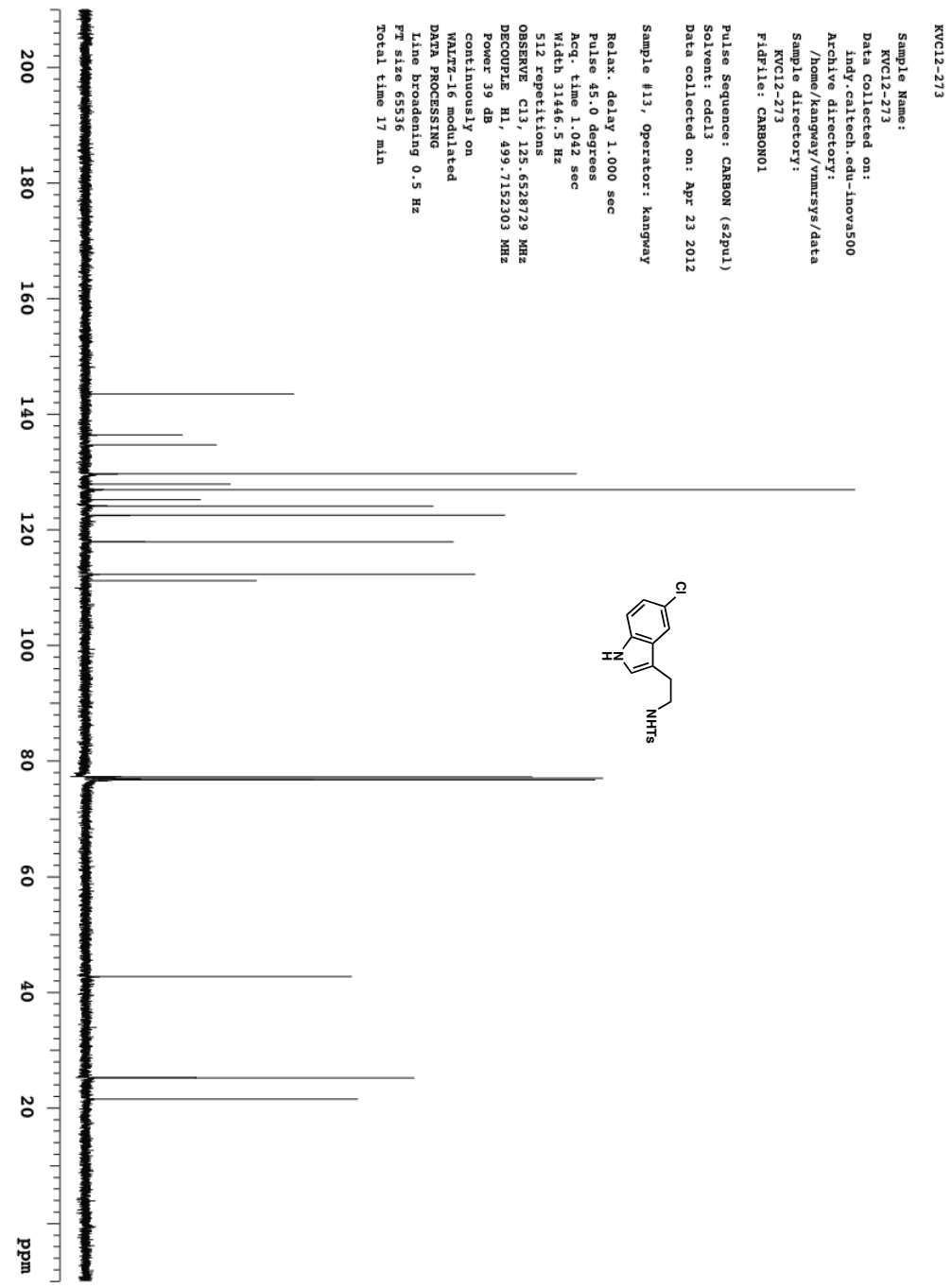
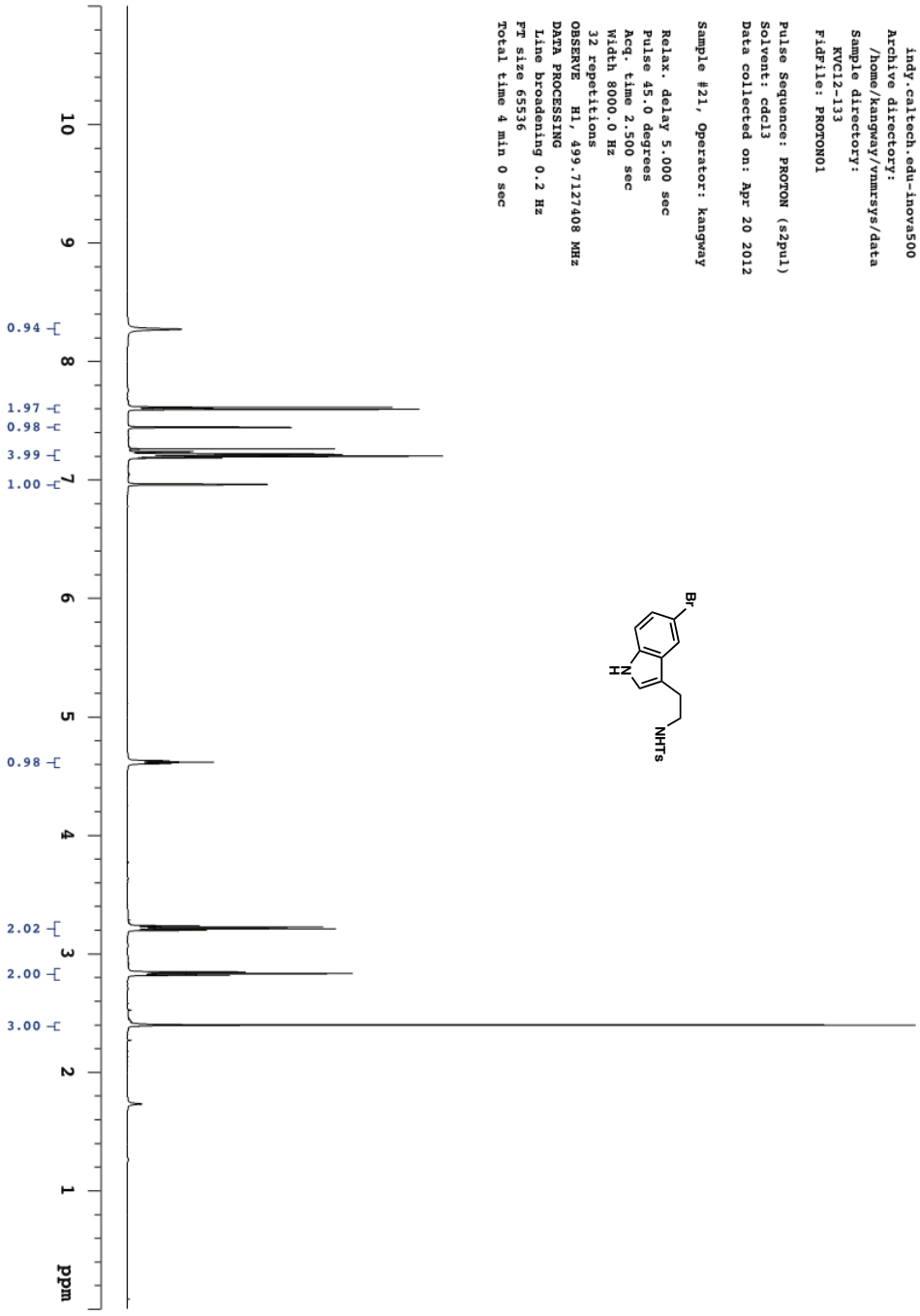
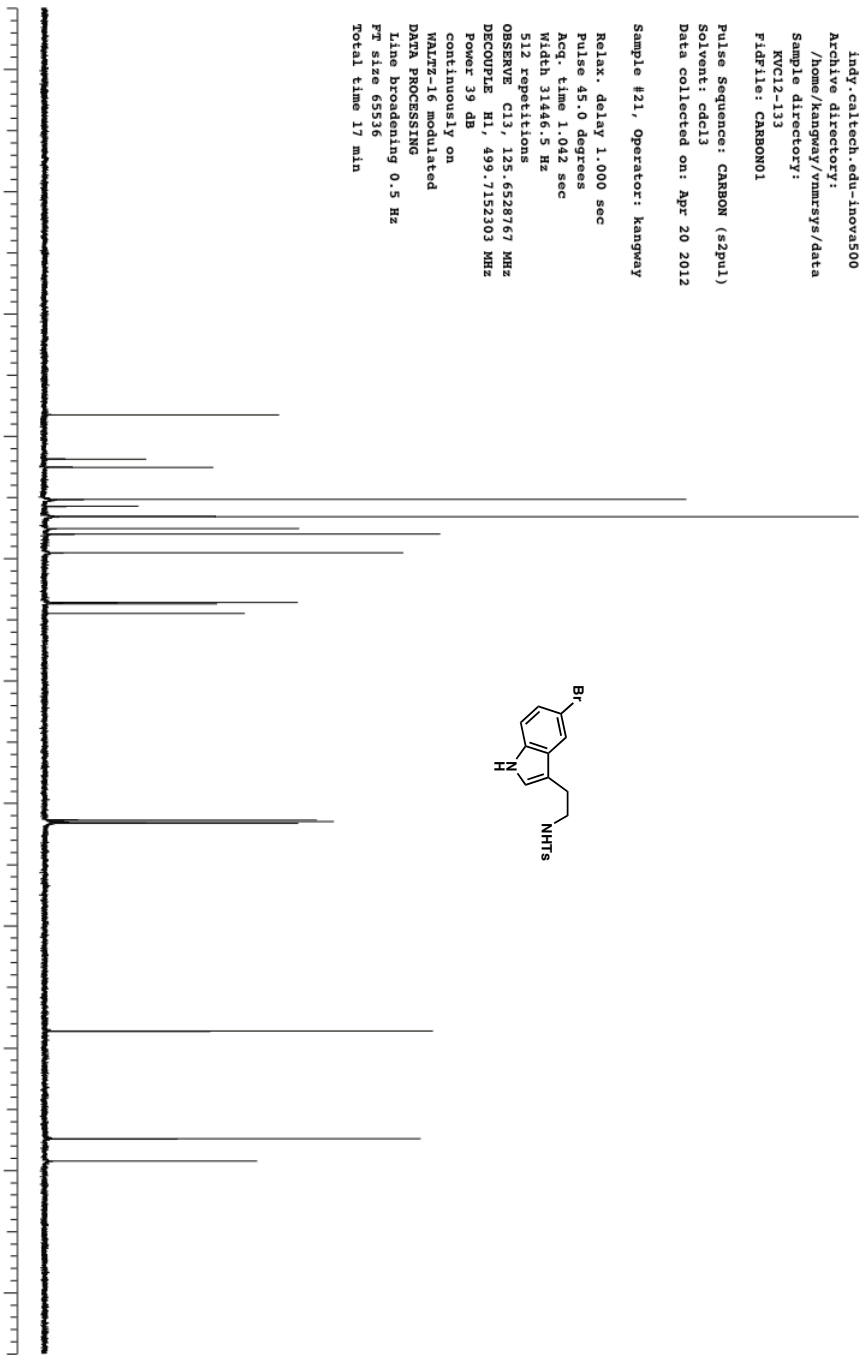
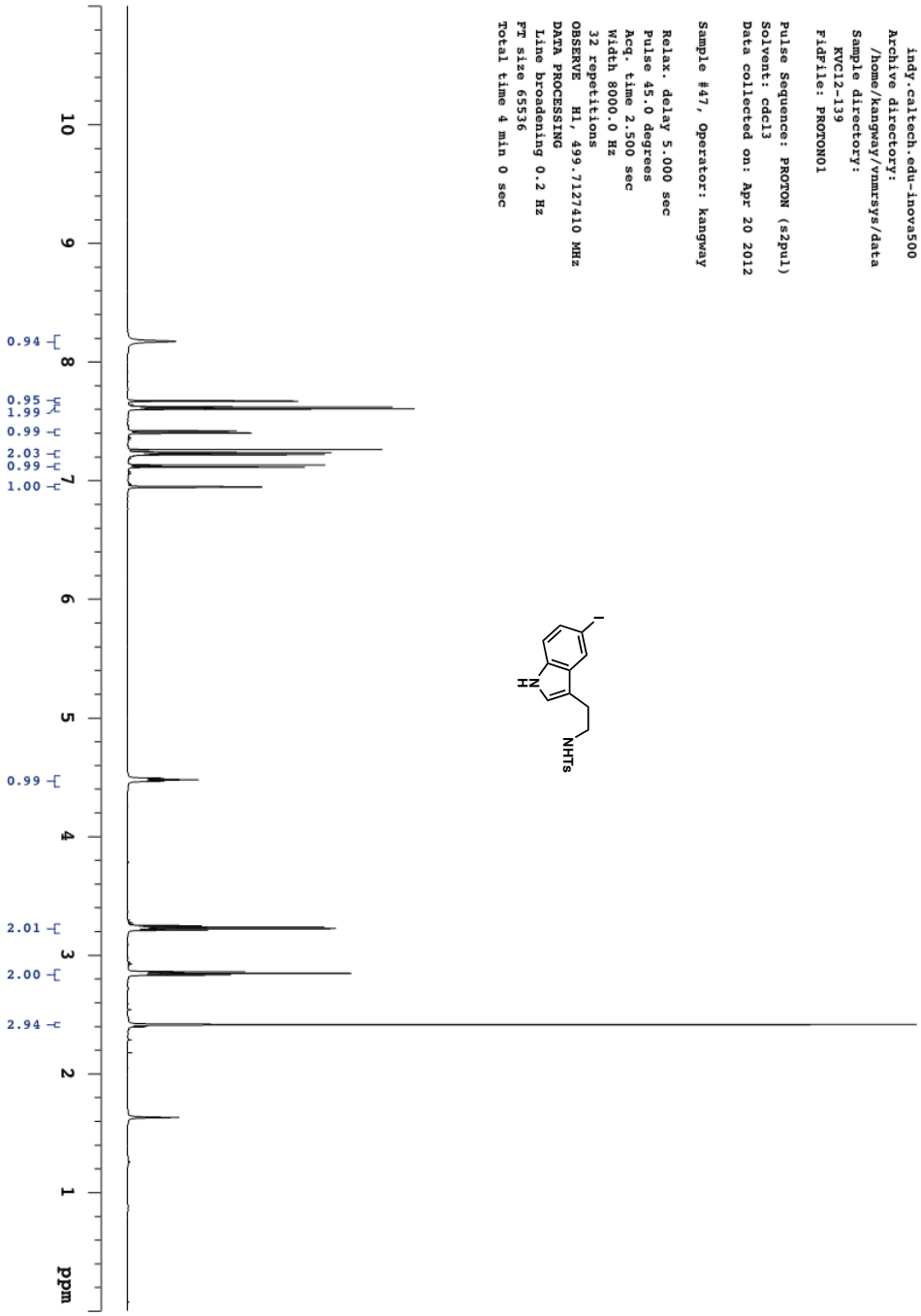
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #10, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
F
H
N
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

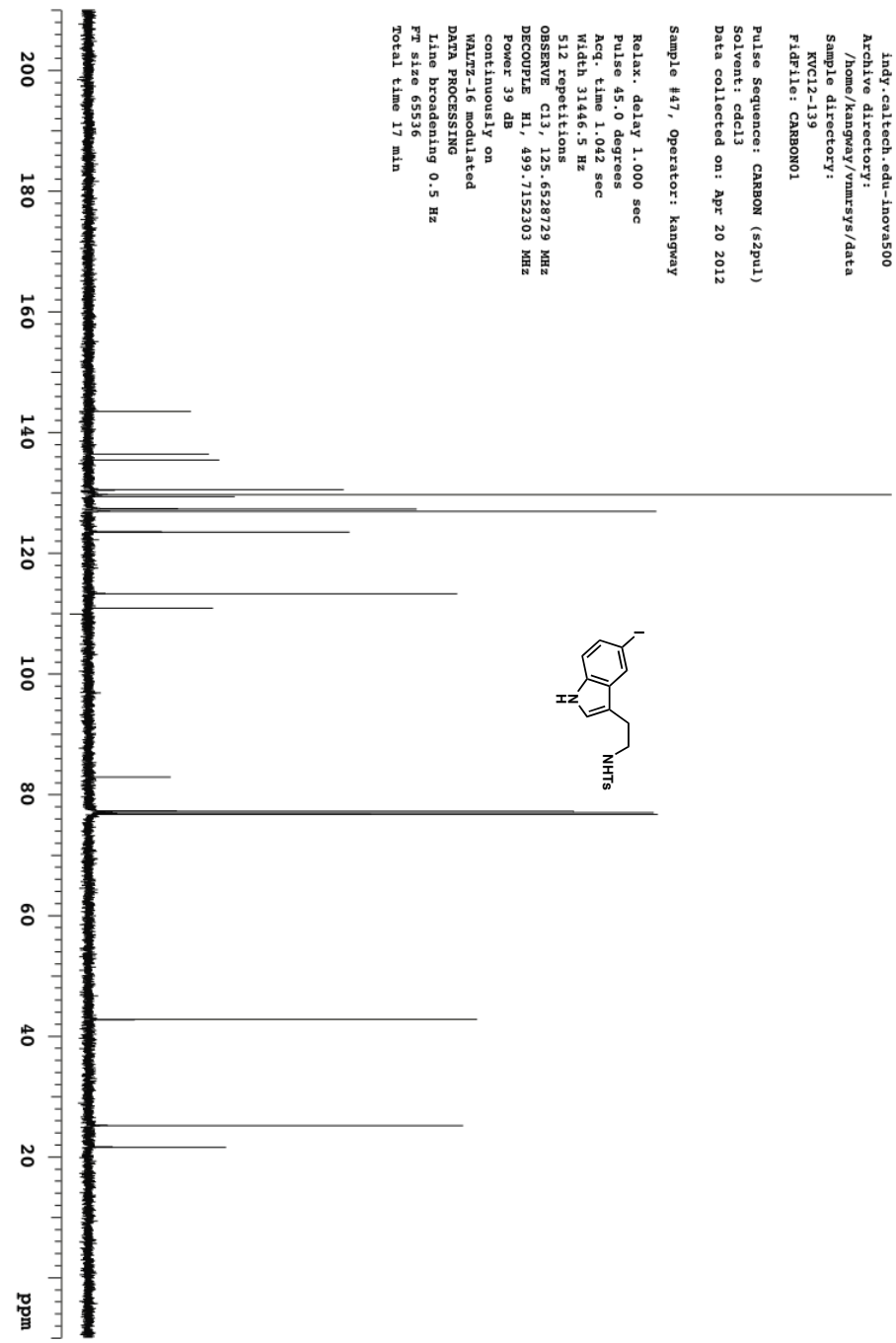

KVC12-273
Sample Name:
KVC12-273
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-273
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #13, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
0.91
1.91
0.96
3.23
0.97
0.98
0.96
1.98
1.97
3.00
Cl
NH
NHTs
10
9
8
7
6
5
4
3
2
1
ppm

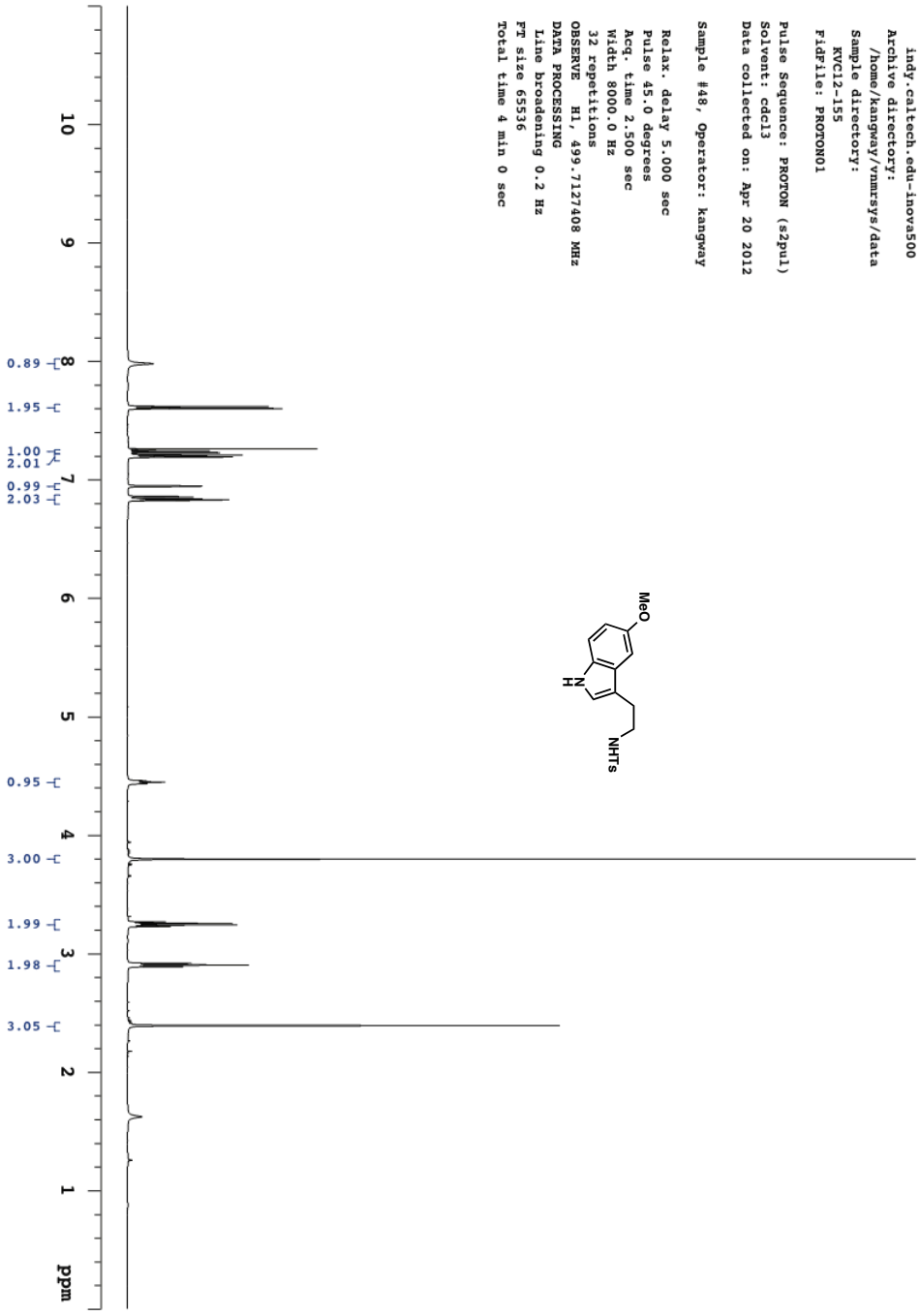

KVC12-273
Sample Name:
KVC12-273
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-273
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #13, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Cl
N
H
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

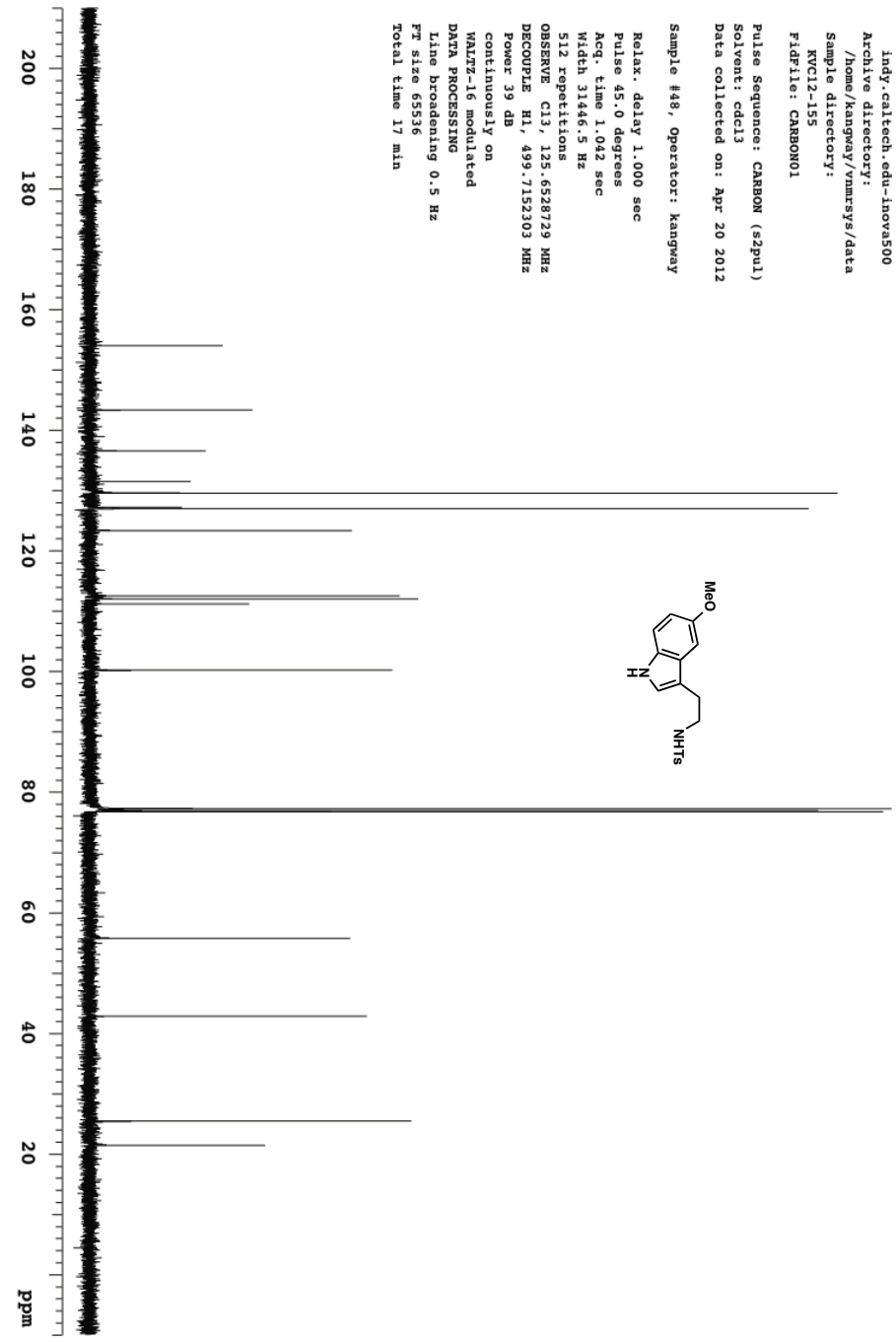

KVC12-133
Sample Name:
KVC12-133
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-133
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 20 2012
Sample #21, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Br
NH
NHTs
0.94
1.97
0.98
3.99
1.00
0.98
2.02
2.00
3.00
10
9
8
7
6
5
4
3
2
1
ppm

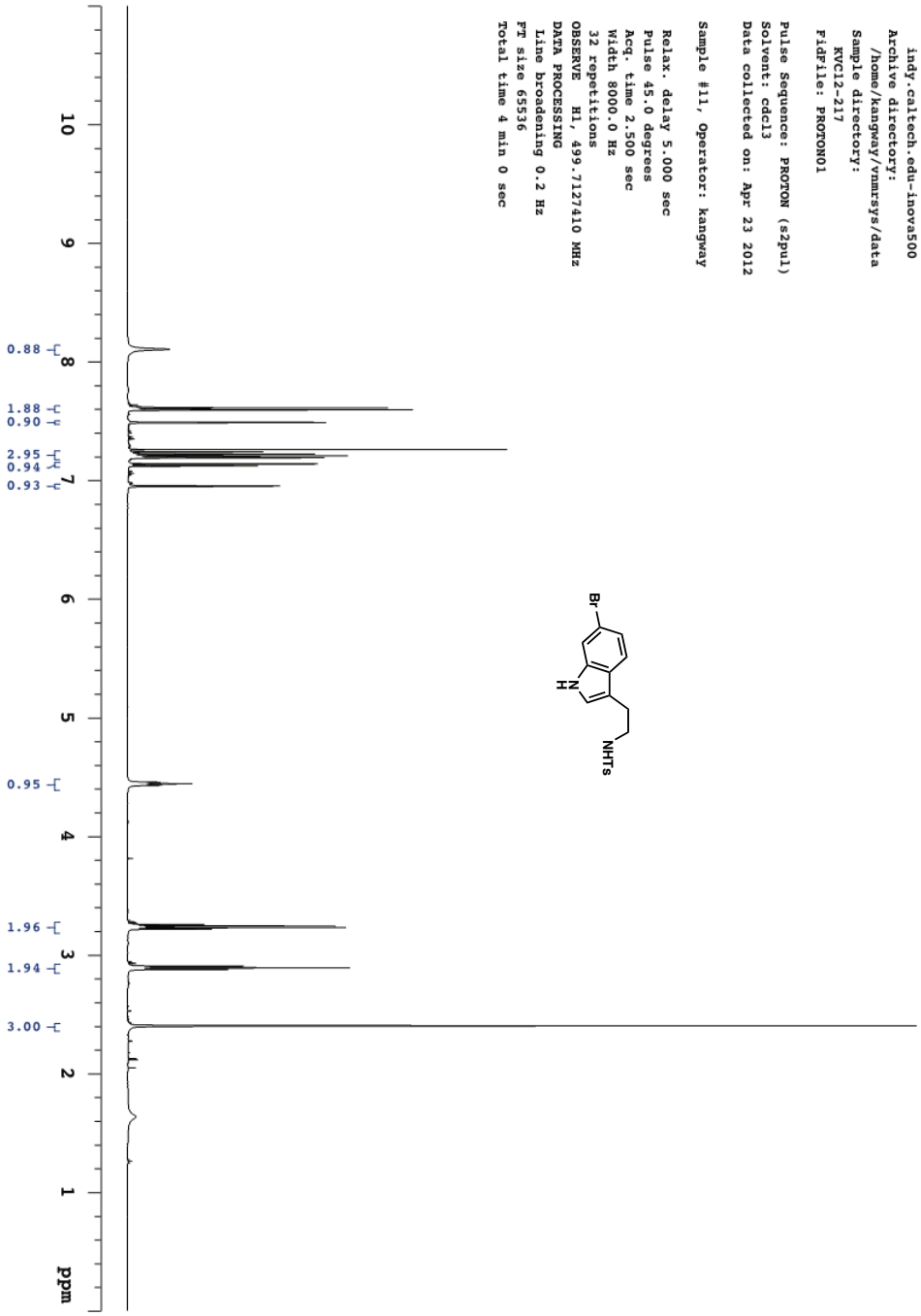

KVC12-133
Sample Name:
KVC12-133
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-133
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 20 2012
Sample #21, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528767 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Br
NH
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

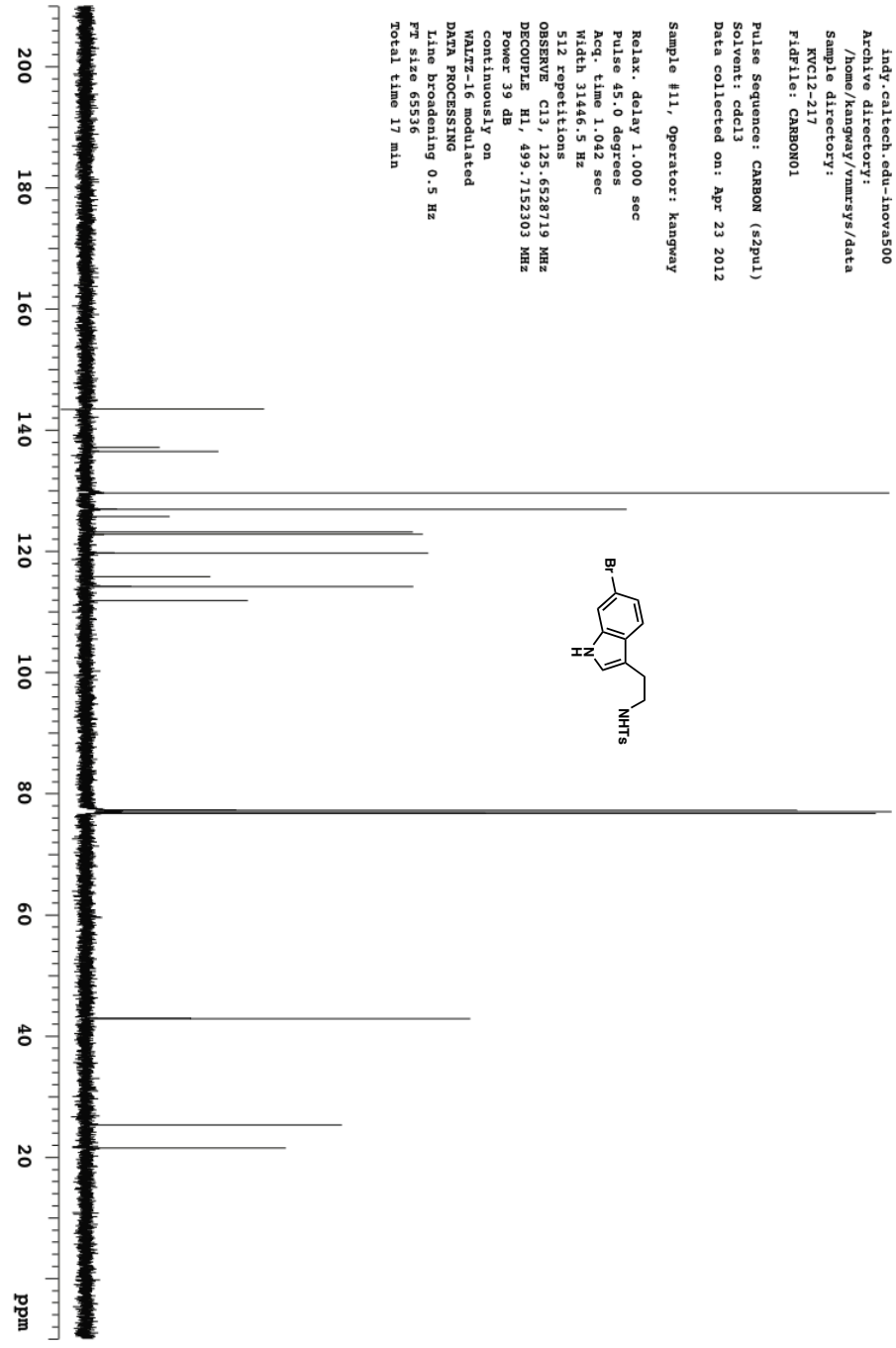

KVC12-139
Sample Name:
KVC12-139
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-139
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 20 2012
Sample #47, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
0.94
0.95
1.99
0.99
2.03
0.99
1.00
0.99
2.01
2.00
2.94
10
9
8
7
6
5
4
3
2
1
ppm
I
H
N
NHTs

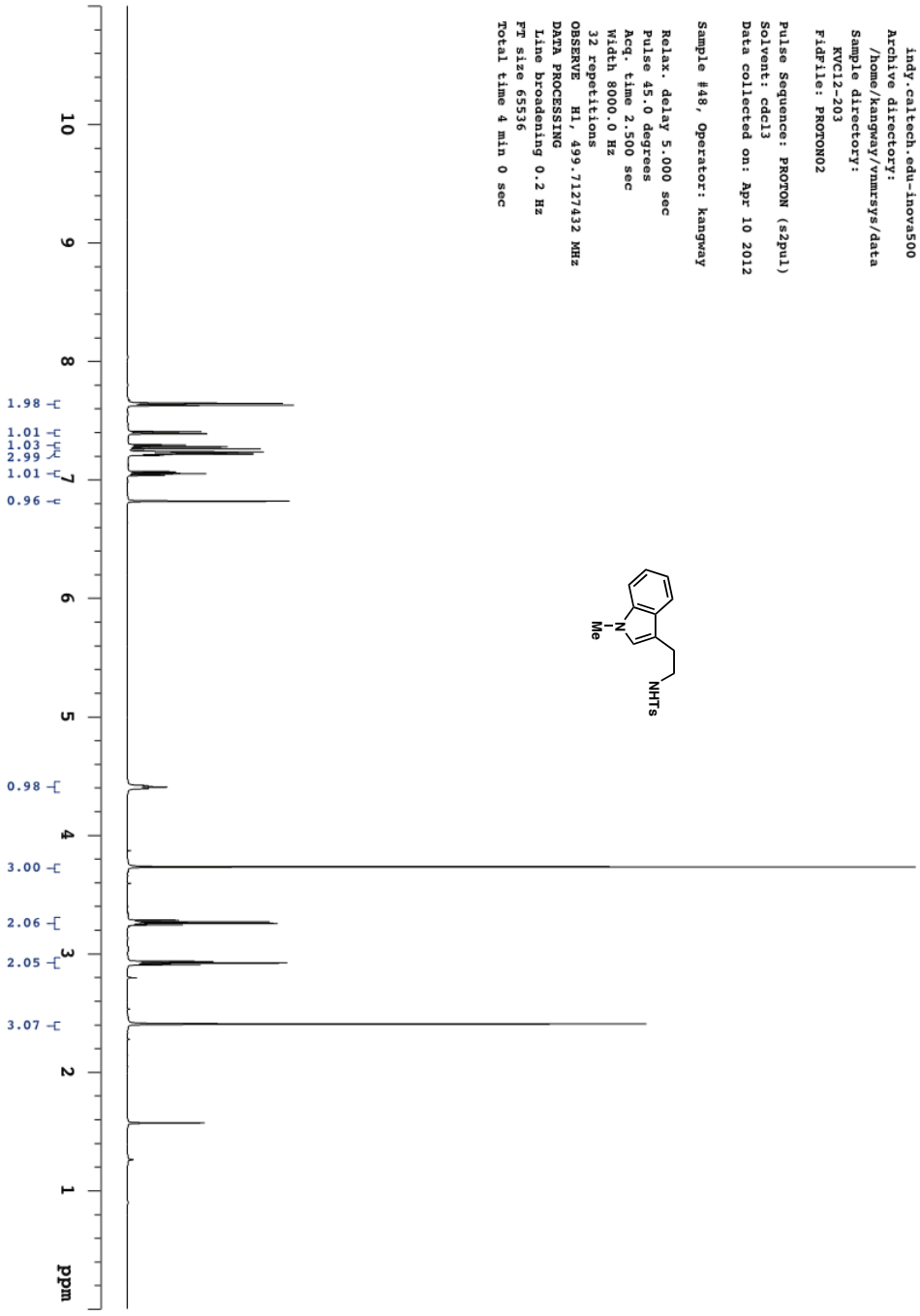

KVC12-139
Sample Name:
KVC12-139
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-139
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 20 2012
Sample #47, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

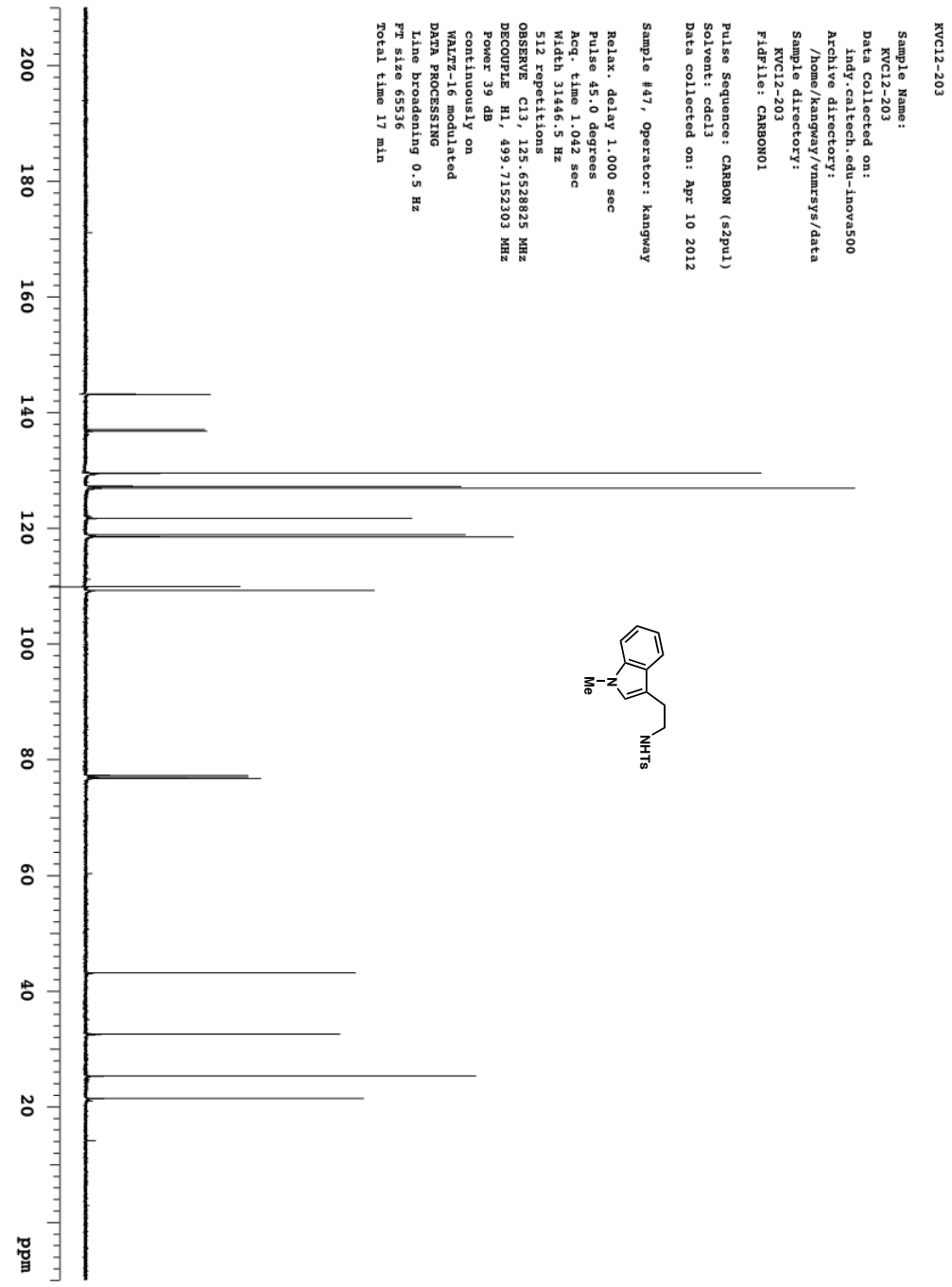

KVC12-155
Sample Name:
KVC12-155
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-155
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 20 2012
Sample #48, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
MeO
NHTs
0.89
1.95
1.00
2.01
0.99
2.03
0.95
3.00
1.99
1.98
3.05
10
9
8
7
6
5
4
3
2
1
ppm

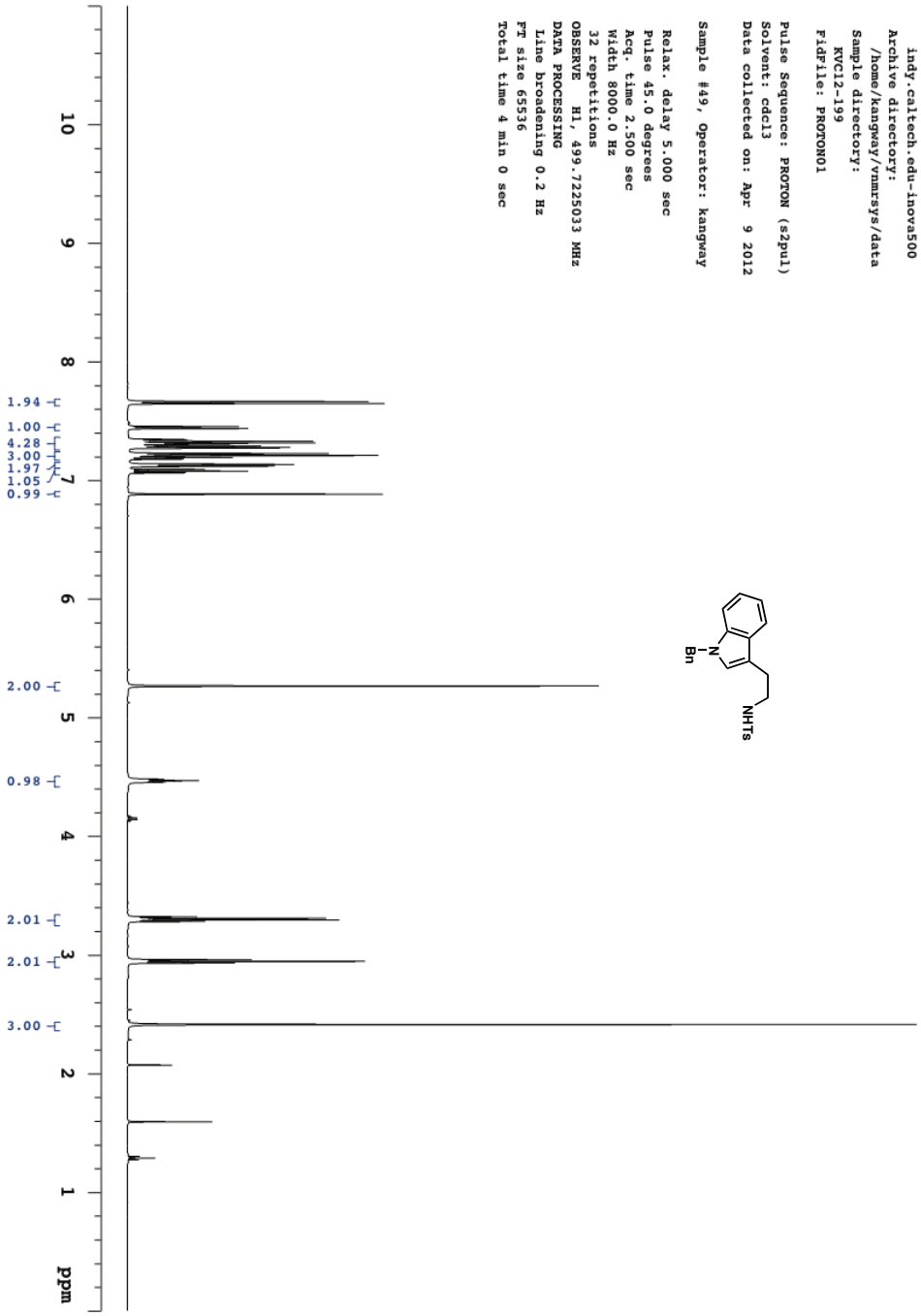

KVC12-155
Sample Name:
KVC12-155
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-155
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 20 2012
Sample #48, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
MeO
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

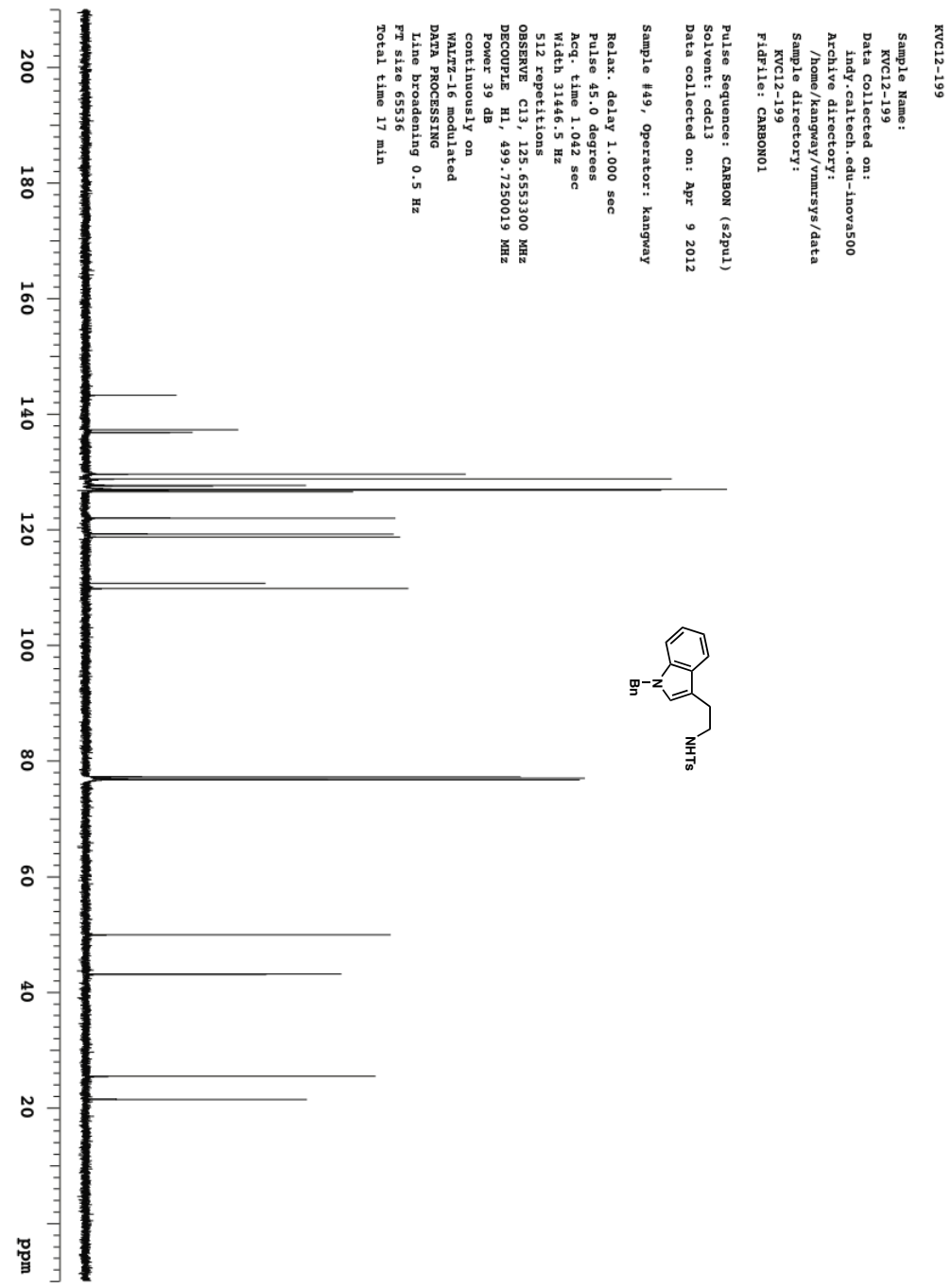

KVC12-217
Sample Name:
KVC12-217
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-217
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #11, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
0.88
1.88
0.90
2.95
0.94
0.93
0.95
1.96
1.94
3.00
Br
NH
NHTs
10
9
8
7
6
5
4
3
2
1
ppm

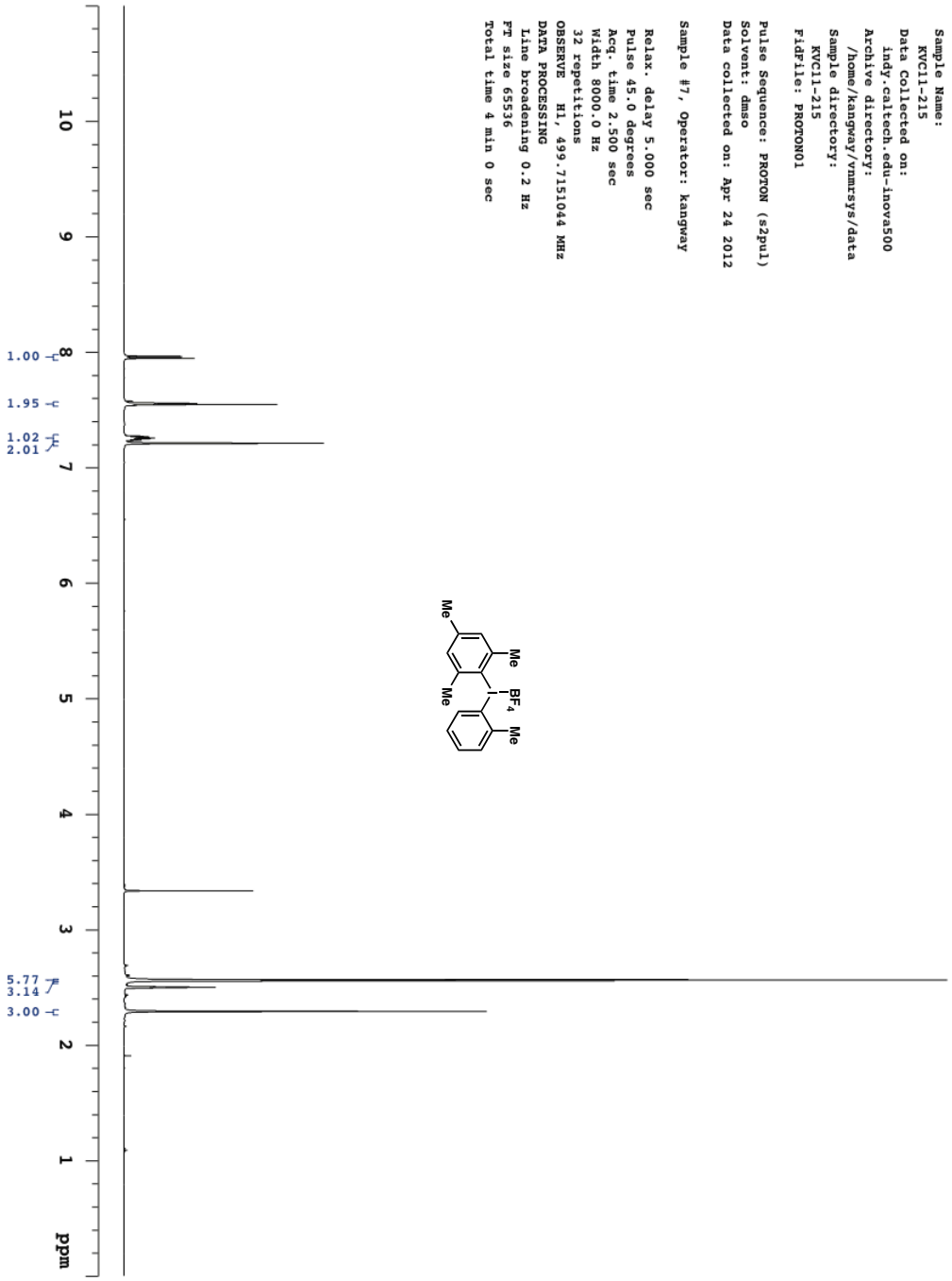

KVC12-217
Sample Name:
KVC12-217
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-217
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 23 2012
Sample #11, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528719 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Br
N
H
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

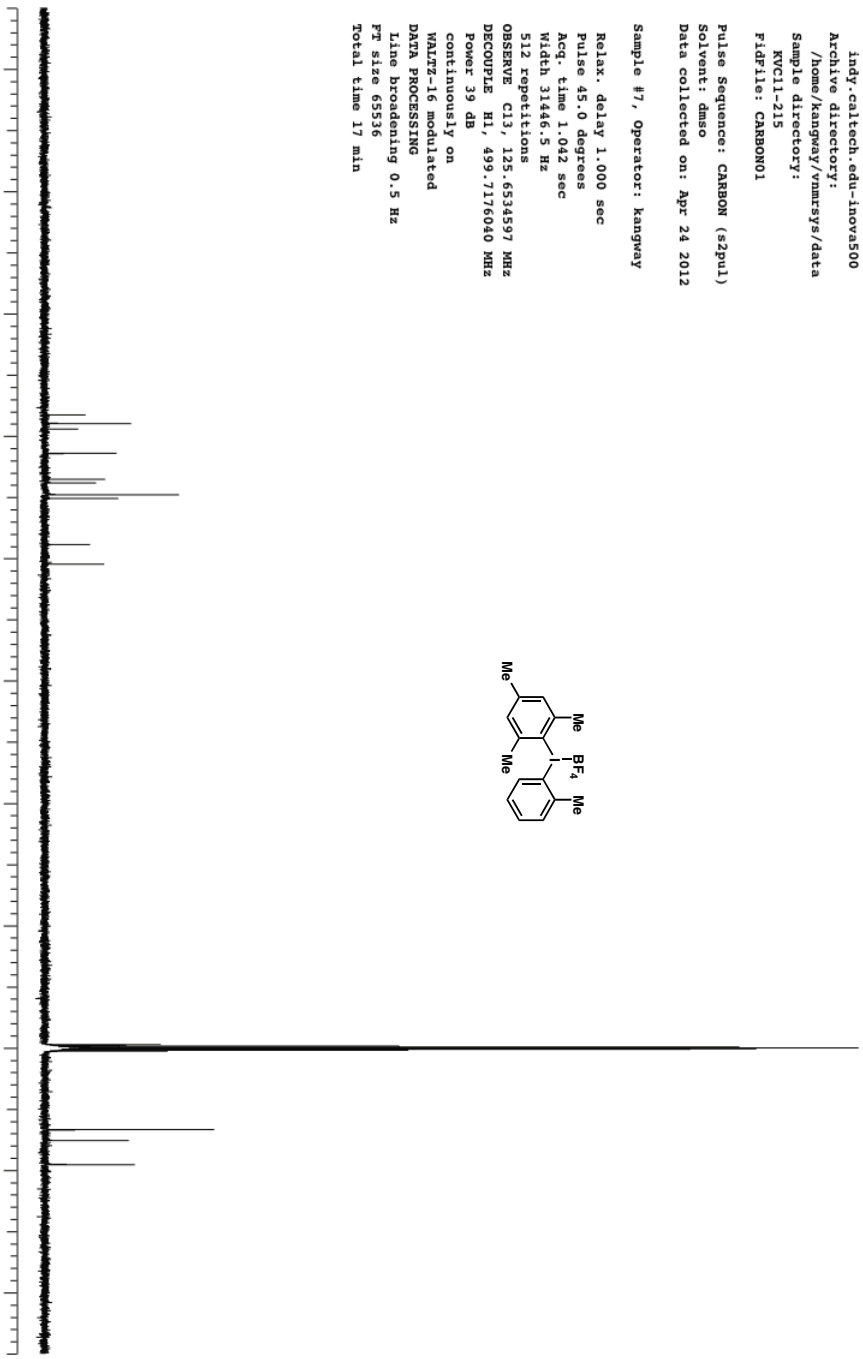

KVC12-203
Sample Name:
KVC12-203
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-203
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 10 2012
Sample #48, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127432 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
N
Me
NHTs
1.98
1.01
1.03
2.99
1.01
0.96
0.98
3.00
2.06
2.05
3.07
10
9
8
7
6
5
4
3
2
1
ppm

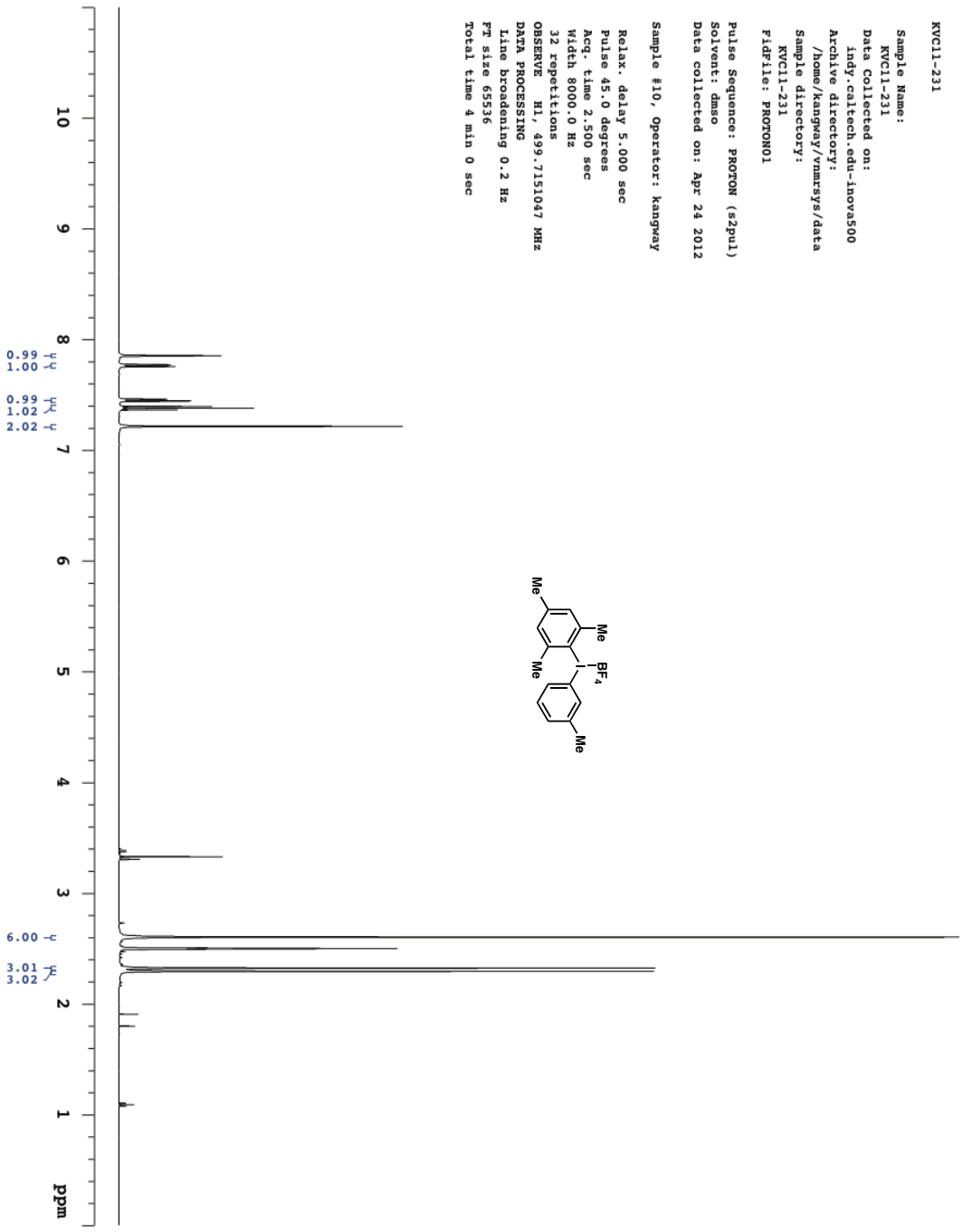

KVC12-203
Sample Name:
KVC12-203
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-203
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 10 2012
Sample #47, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528825 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
Me
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

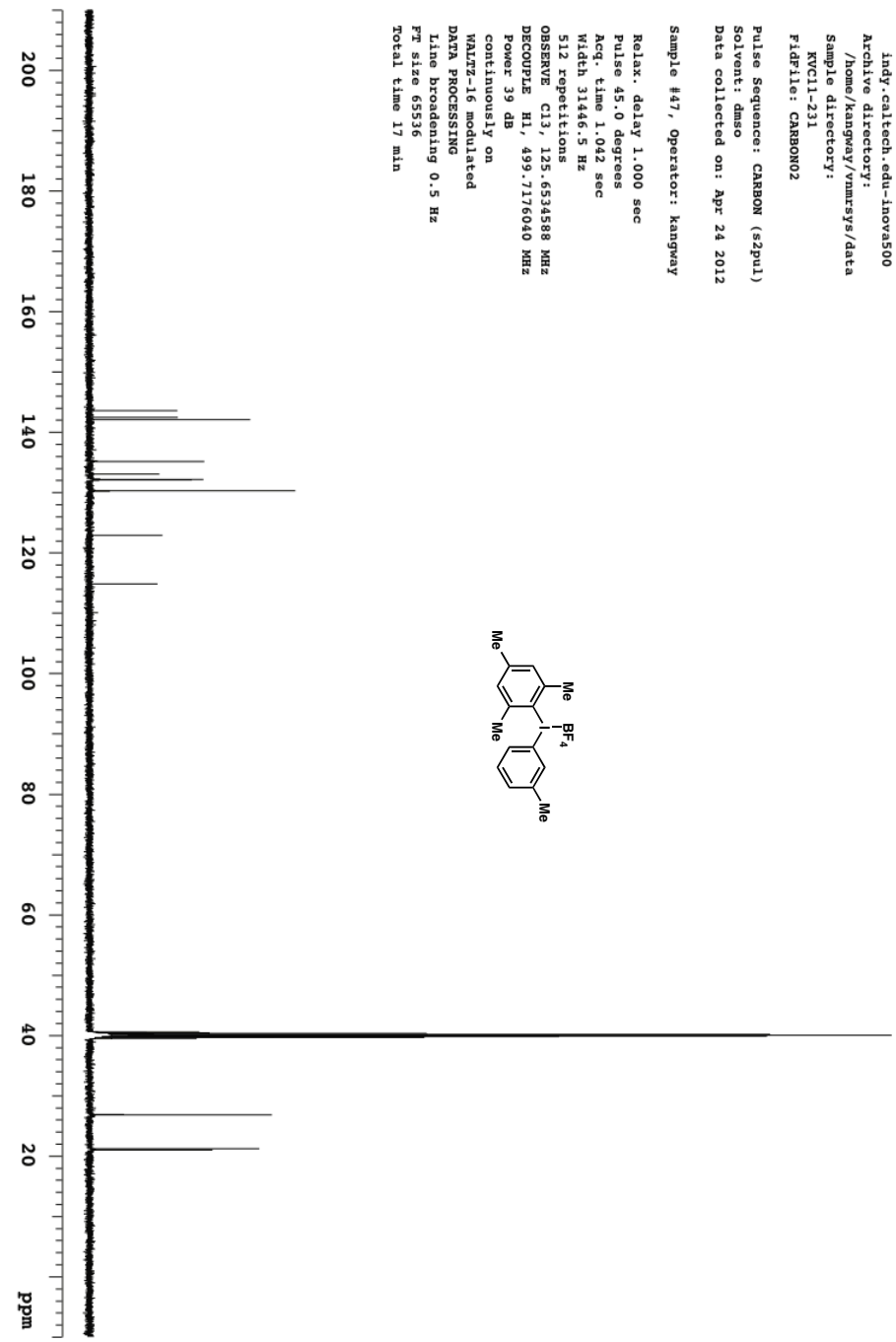

KVC12-199
Sample Name:
KVC12-199
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-199
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 9 2012
Sample #49, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7225033 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
1.94
1.00
4.28
3.00
1.97
1.05
0.99
2.00
0.98
2.01
2.01
3.00
N
Bn
NHTs
10
9
8
7
6
5
4
3
2
1
ppm

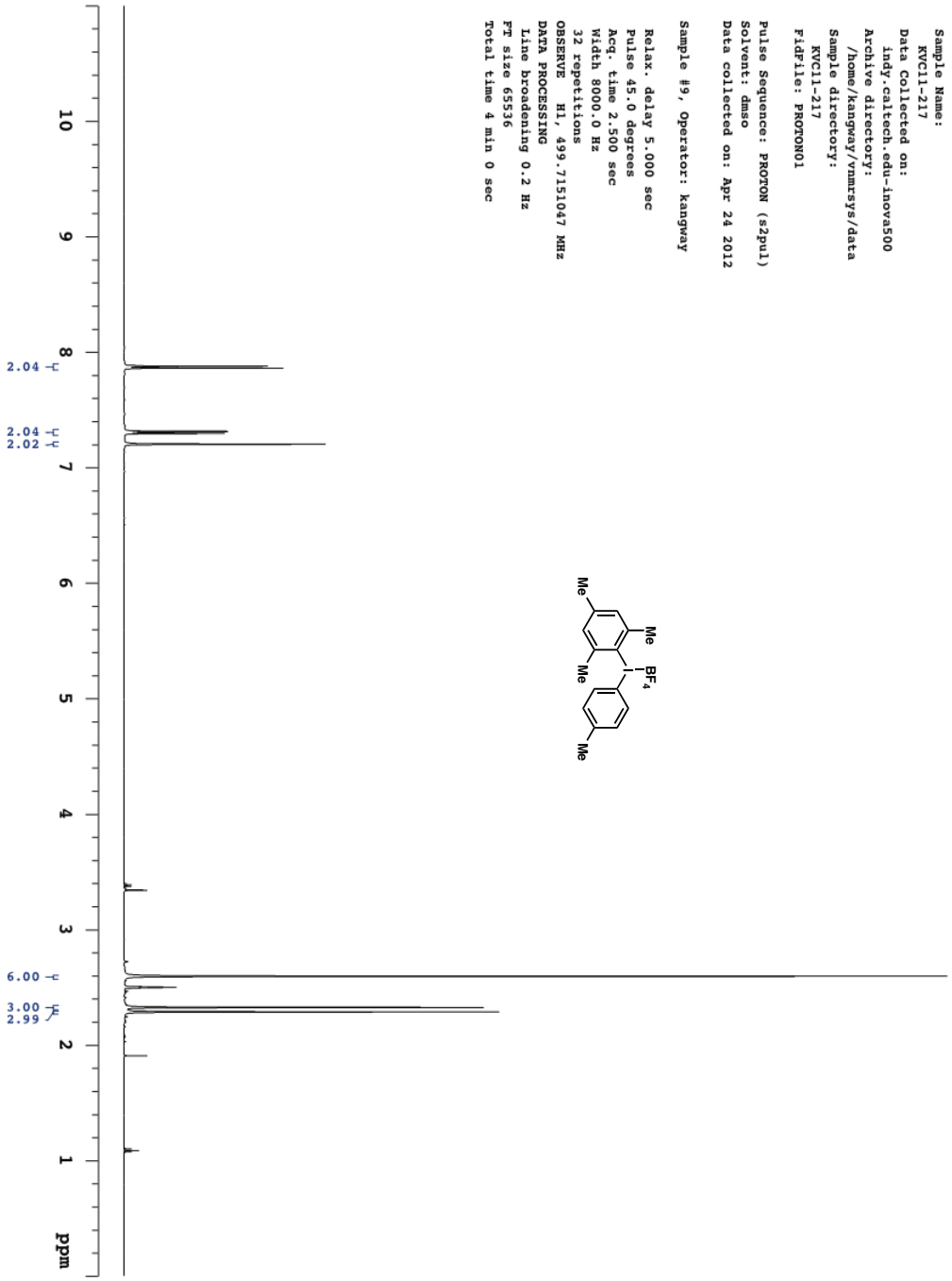

KVC12-199
Sample Name:
KVC12-199
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-199
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 9 2012
Sample #49, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6553300 MHz
DECOUPLE H1, 499.7250019 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
Bn
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

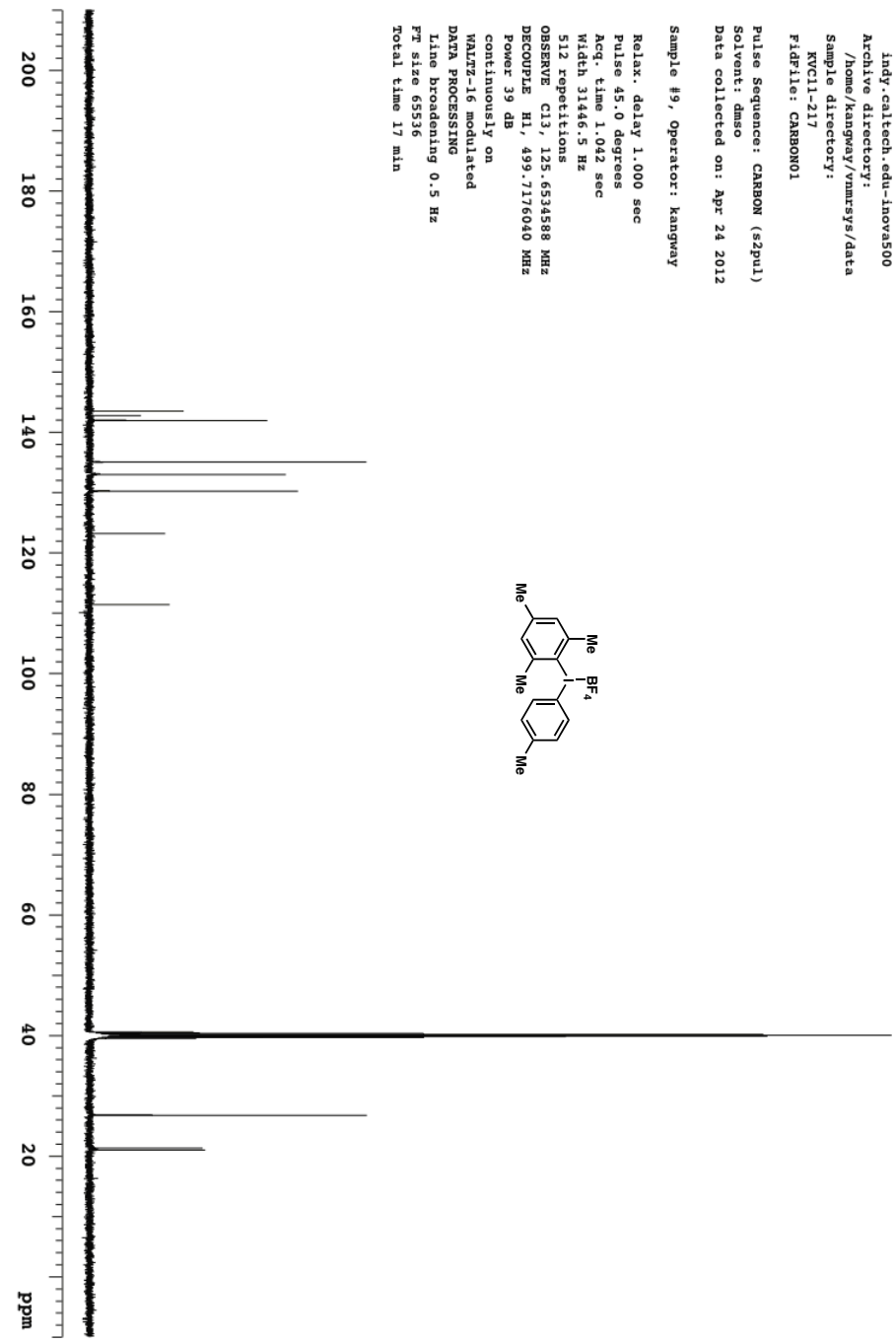

KVC11-215
Sample Name:
KVC11-215
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-215
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #7, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7151044 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Me
Me
BF4
Me
1.00
1.95
1.02
2.01
5.77
3.14
3.00
10
9
8
7
6
5
4
3
2
1
ppm

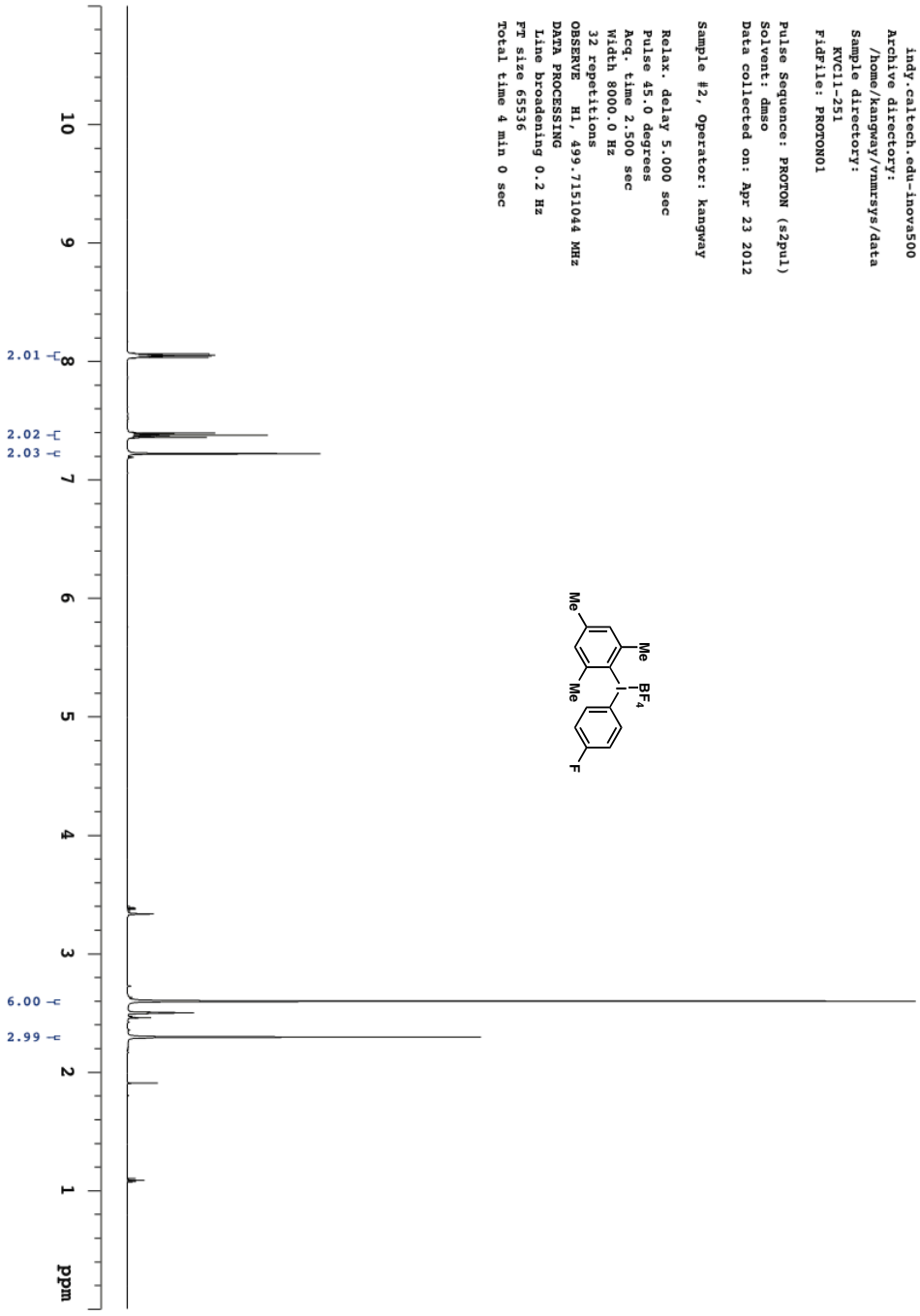

KVC11-215
Sample Name:
KVC11-215
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-215
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #7, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534597 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
Me
BF4
200
180
160
140
120
100
80
60
40
20
ppm

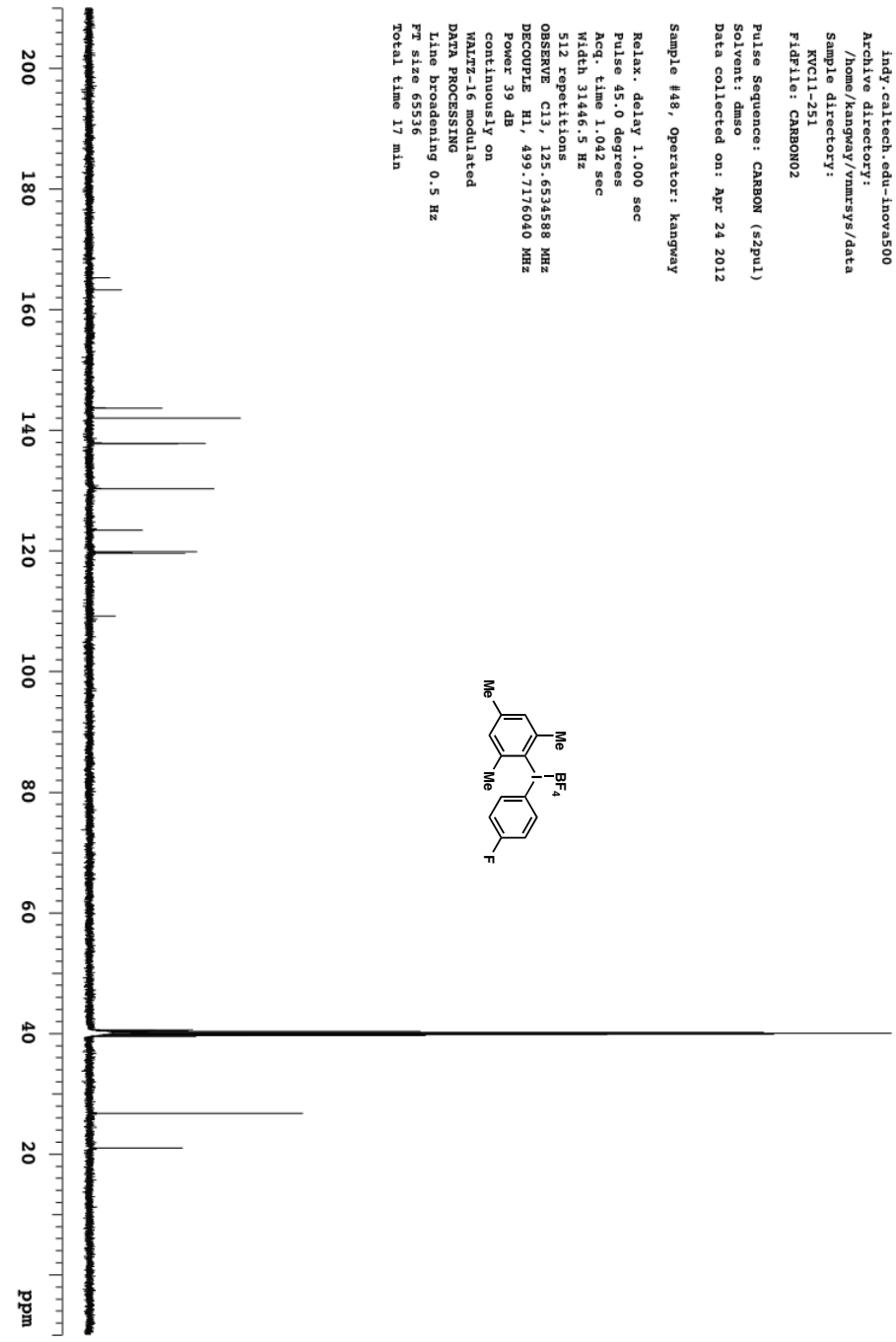

KVC11-231
Sample Name:
KVC11-231
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-231
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #10, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7151047 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Me
Me
Me
BF4
0.99
1.00
0.99
1.02
2.02
6.00
3.01
3.02
10
9
8
7
6
5
4
3
2
1
ppm

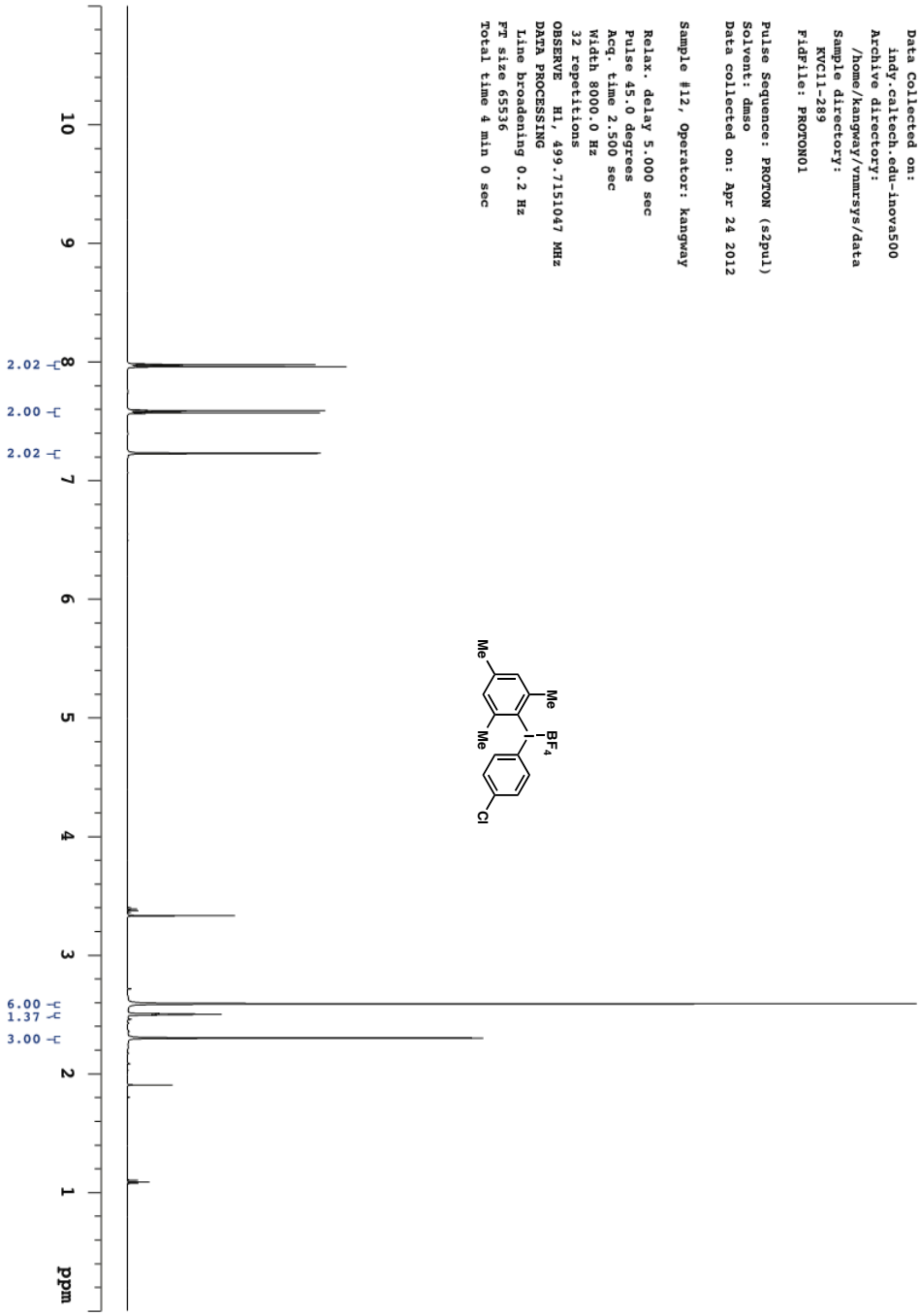

KVC11-231
Sample Name:
KVC11-231
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-231
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #47, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534588 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
Me
BF4
200
180
160
140
120
100
80
60
40
20
ppm

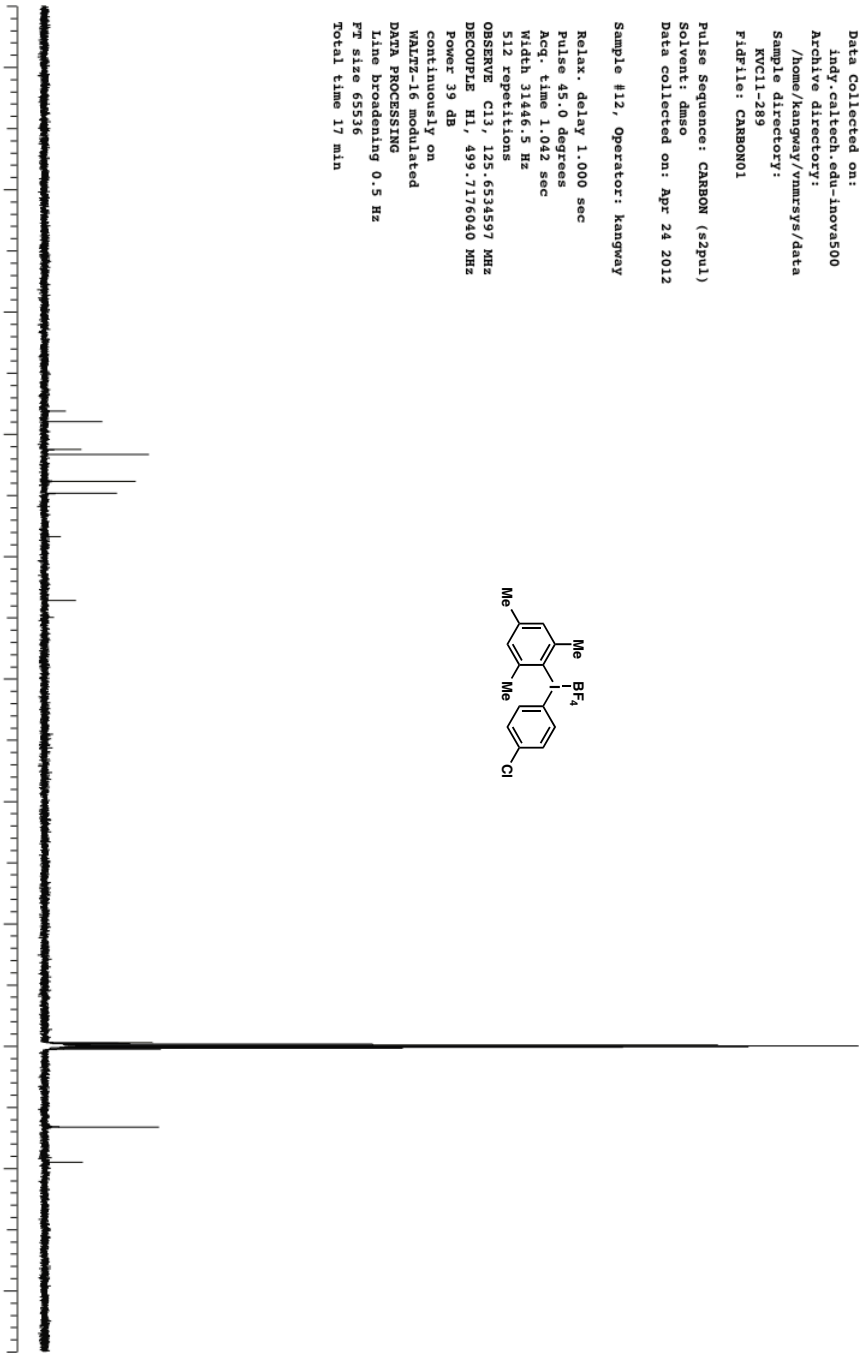

KVC11-217
Sample Name:
KVC11-217
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-217
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #9, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7151047 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Me
Me
Me
BF4
2.04
2.04
2.02
6.00
3.00
2.99
10
9
8
7
6
5
4
3
2
1
ppm

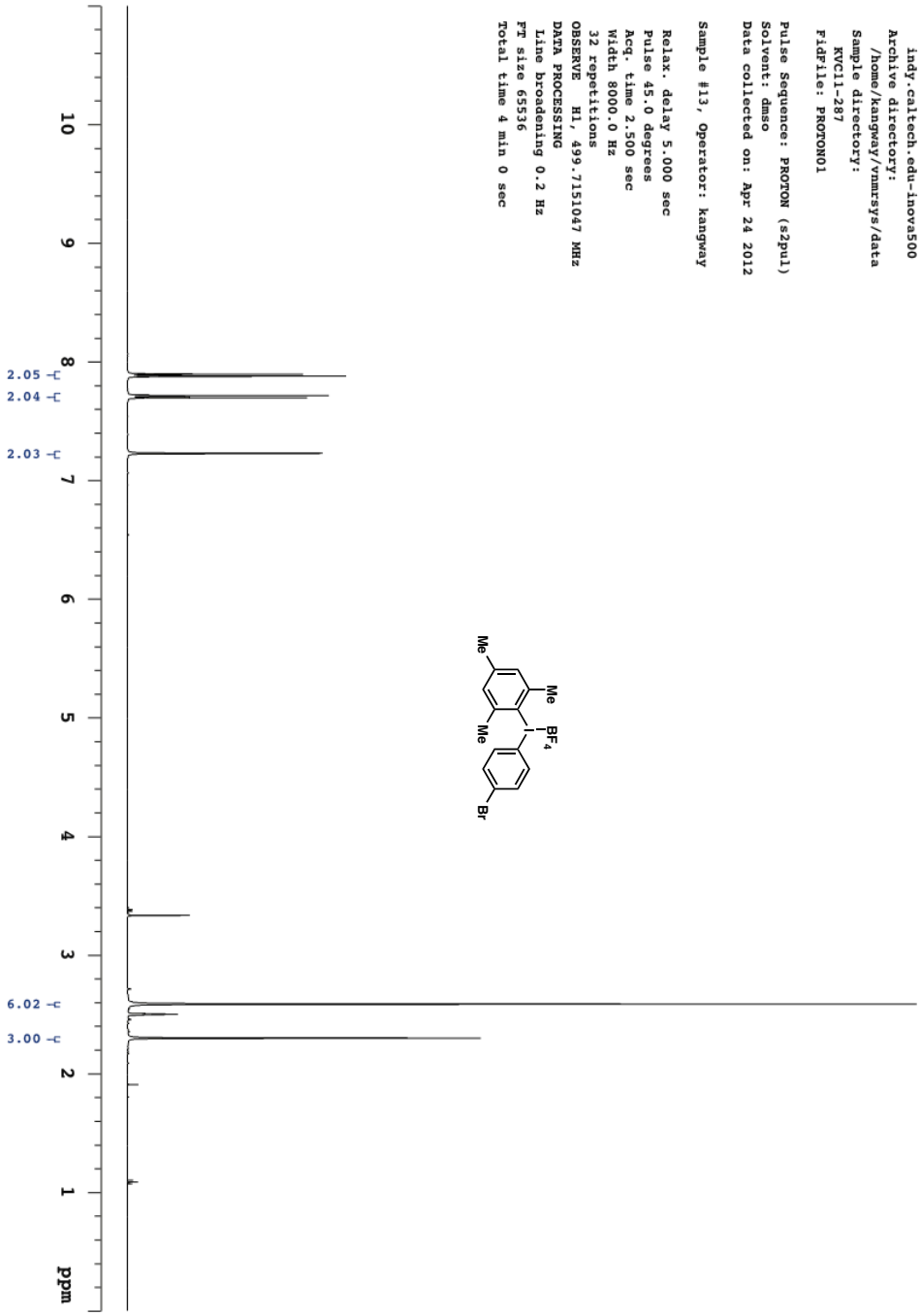

KVC11-217
Sample Name:
KVC11-217
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-217
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #9, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534588 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
Me
I
BF4
200
180
160
140
120
100
80
60
40
20
ppm

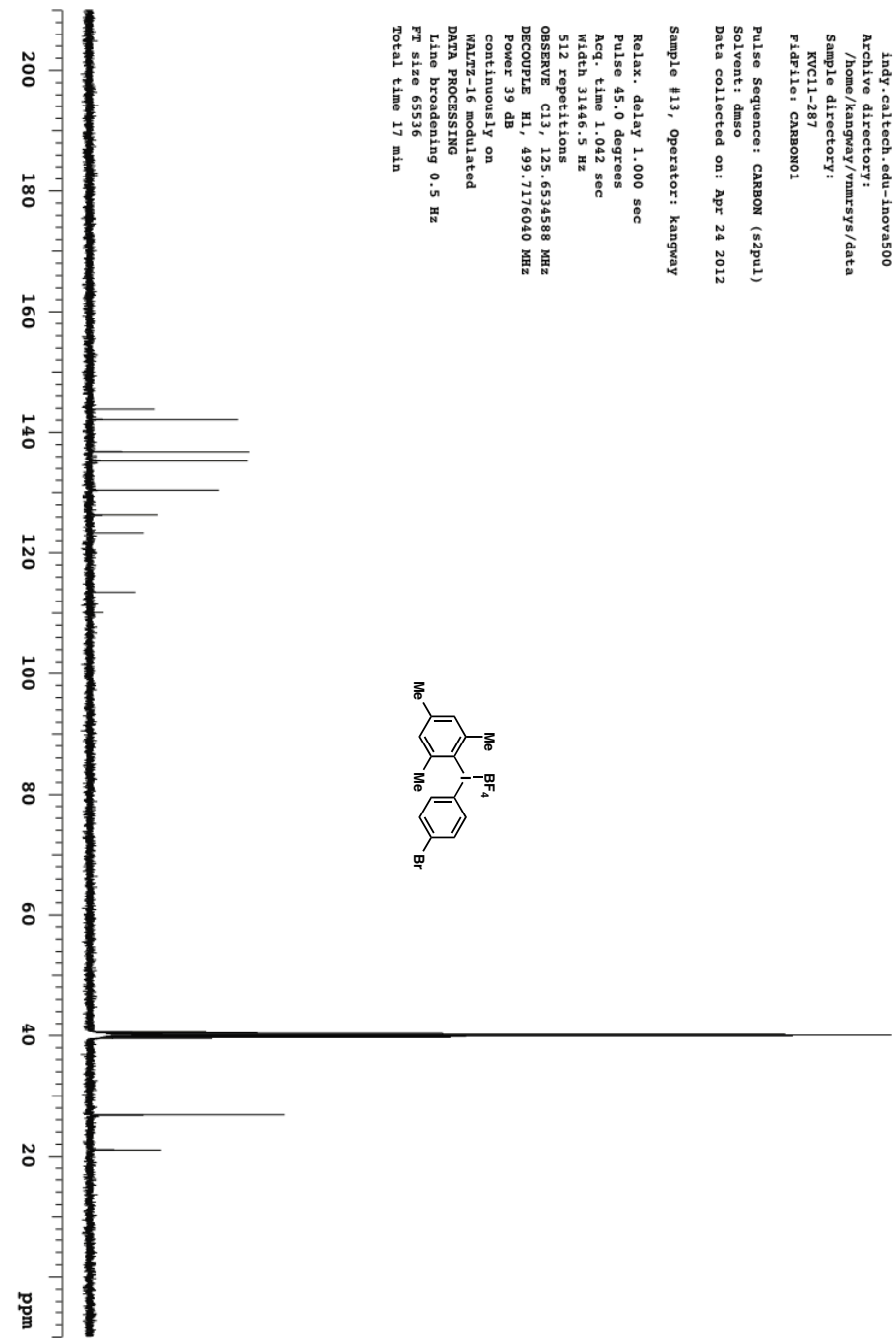

KVC11-251
Sample Name:
KVC11-251
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-251
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 23 2012
Sample #2, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7151044 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Me
Me
I
BF4
F
2.01
2.02
2.03
6.00
2.99
10
9
8
7
6
5
4
3
2
1
ppm

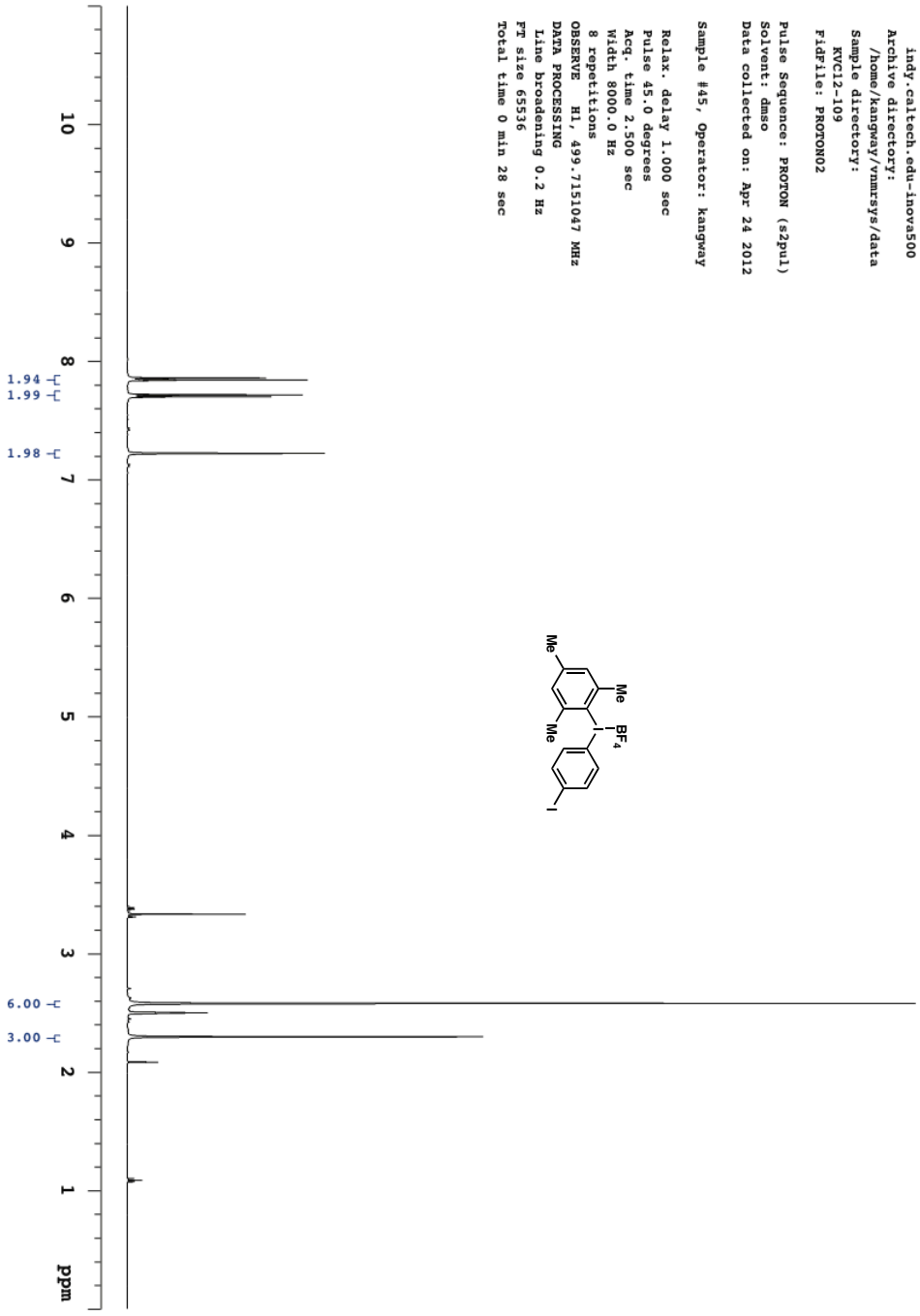

KVC11-251
Sample Name:
KVC11-251
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-251
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #48, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534588 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
I
BF4
F
200
180
160
140
120
100
80
60
40
20
ppm

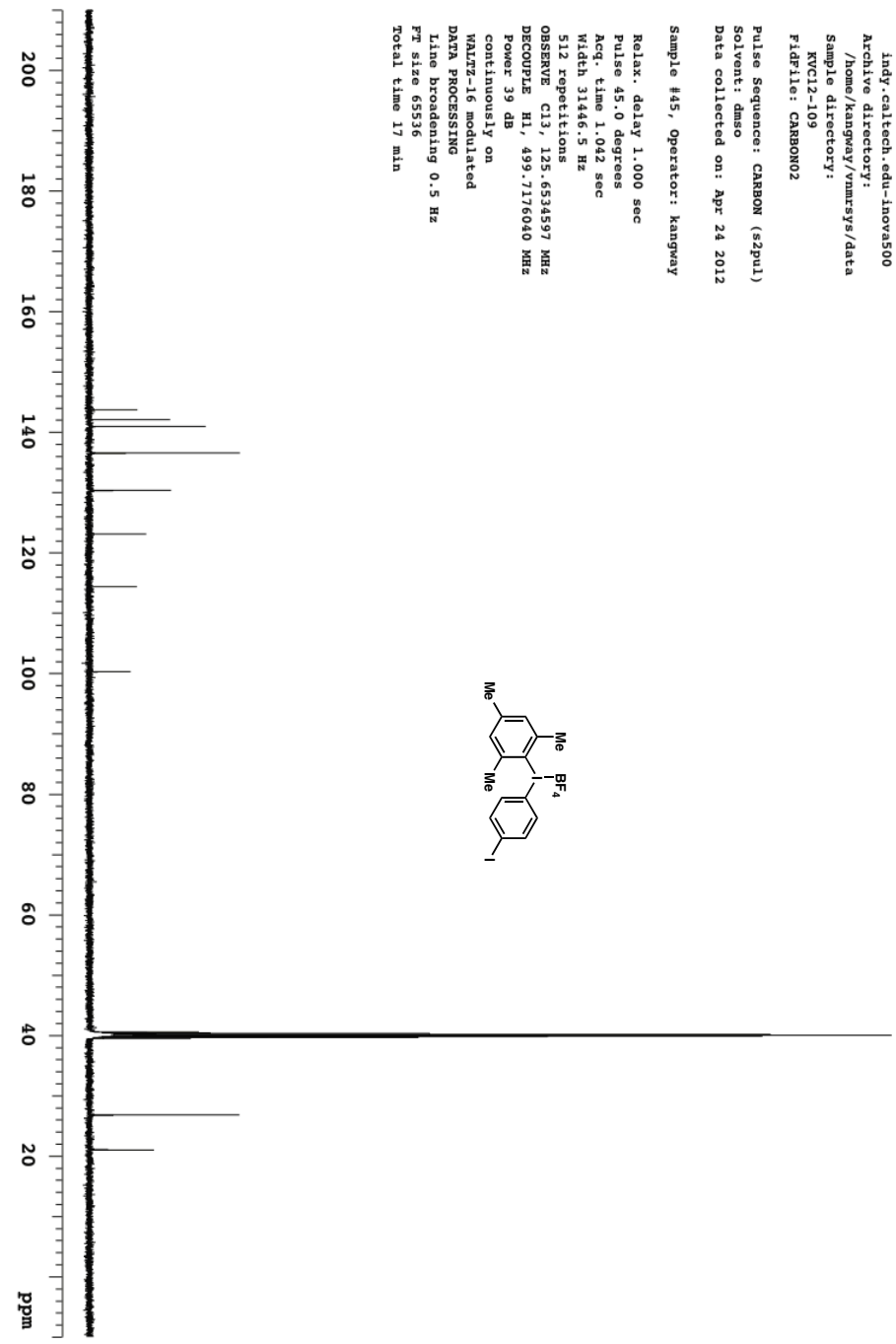

KVC11-289
Sample Name:
KVC11-289
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-289
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #12, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7151047 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Me
Me
BF4
Cl
2.02
2.00
2.02
6.00
1.37
3.00
10
9
8
7
6
5
4
3
2
1
ppm

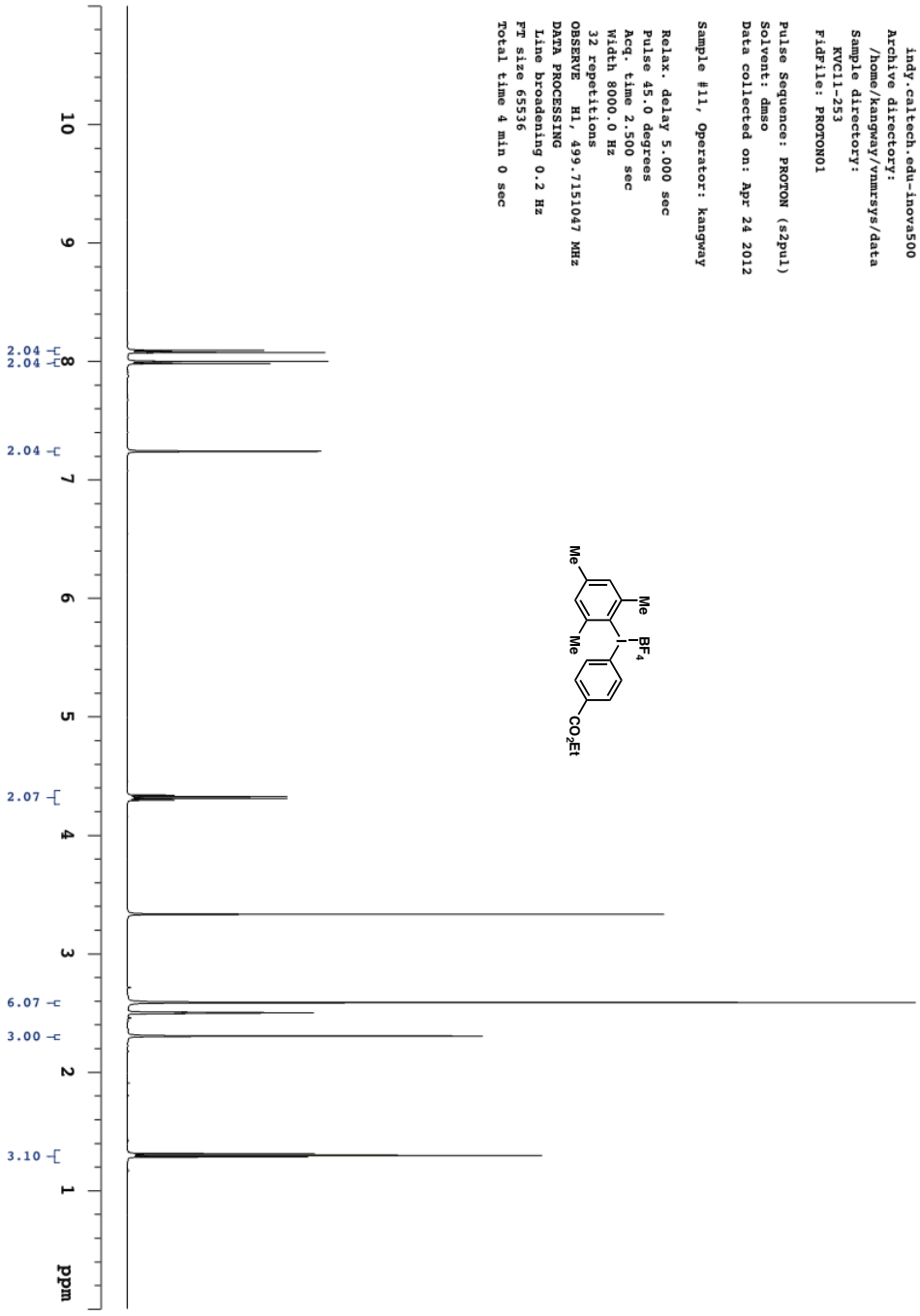

KVC11-289
Sample Name:
KVC11-289
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-289
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #12, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534597 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
I
BF4
Cl
200
180
160
140
120
100
80
60
40
20
ppm

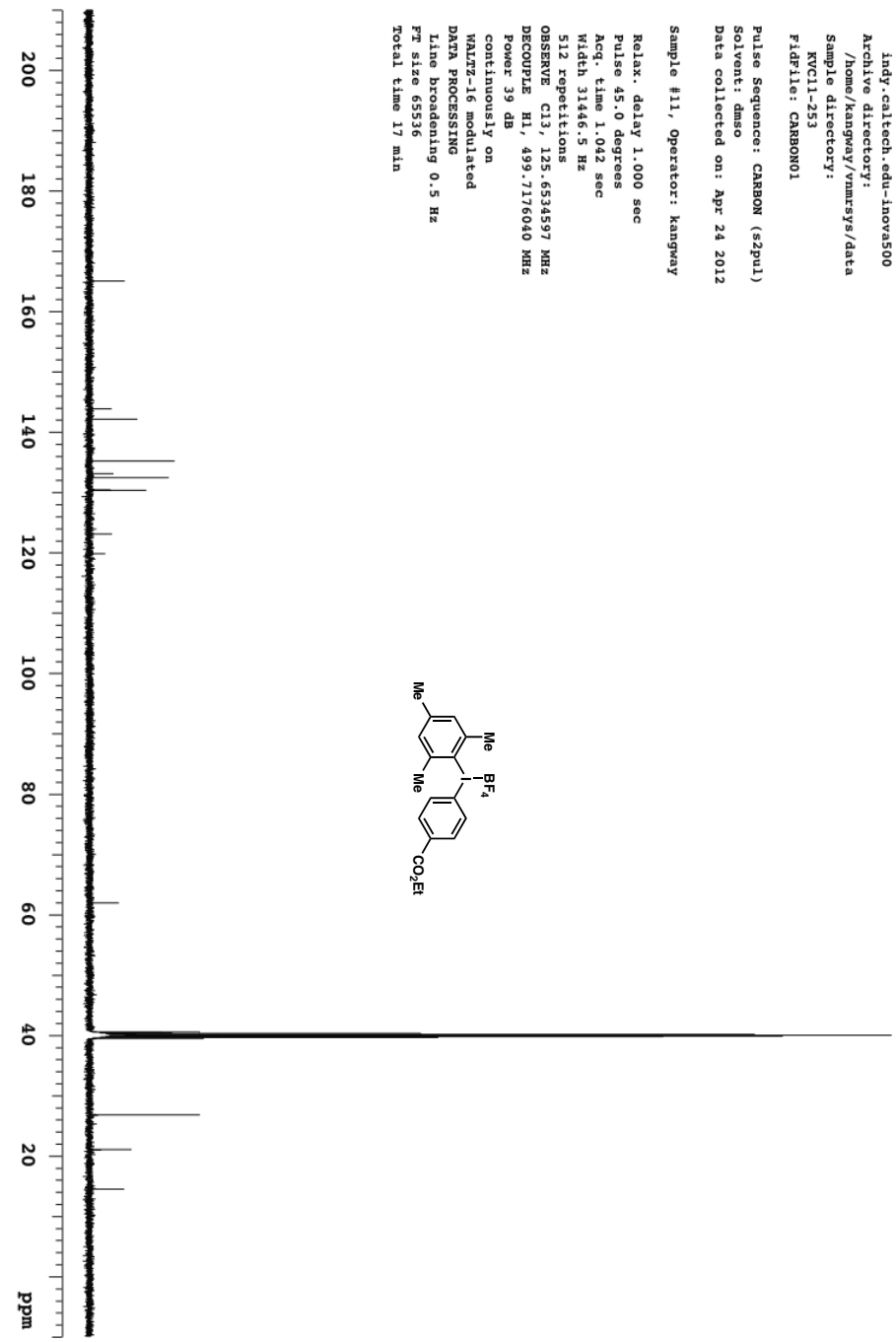

KVC11-287
Sample Name:
KVC11-287
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-287
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #13, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7151047 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.05
2.04
2.03
6.02
3.00
Me
Me
Me
Br
BF4
10
9
8
7
6
5
4
3
2
1
ppm

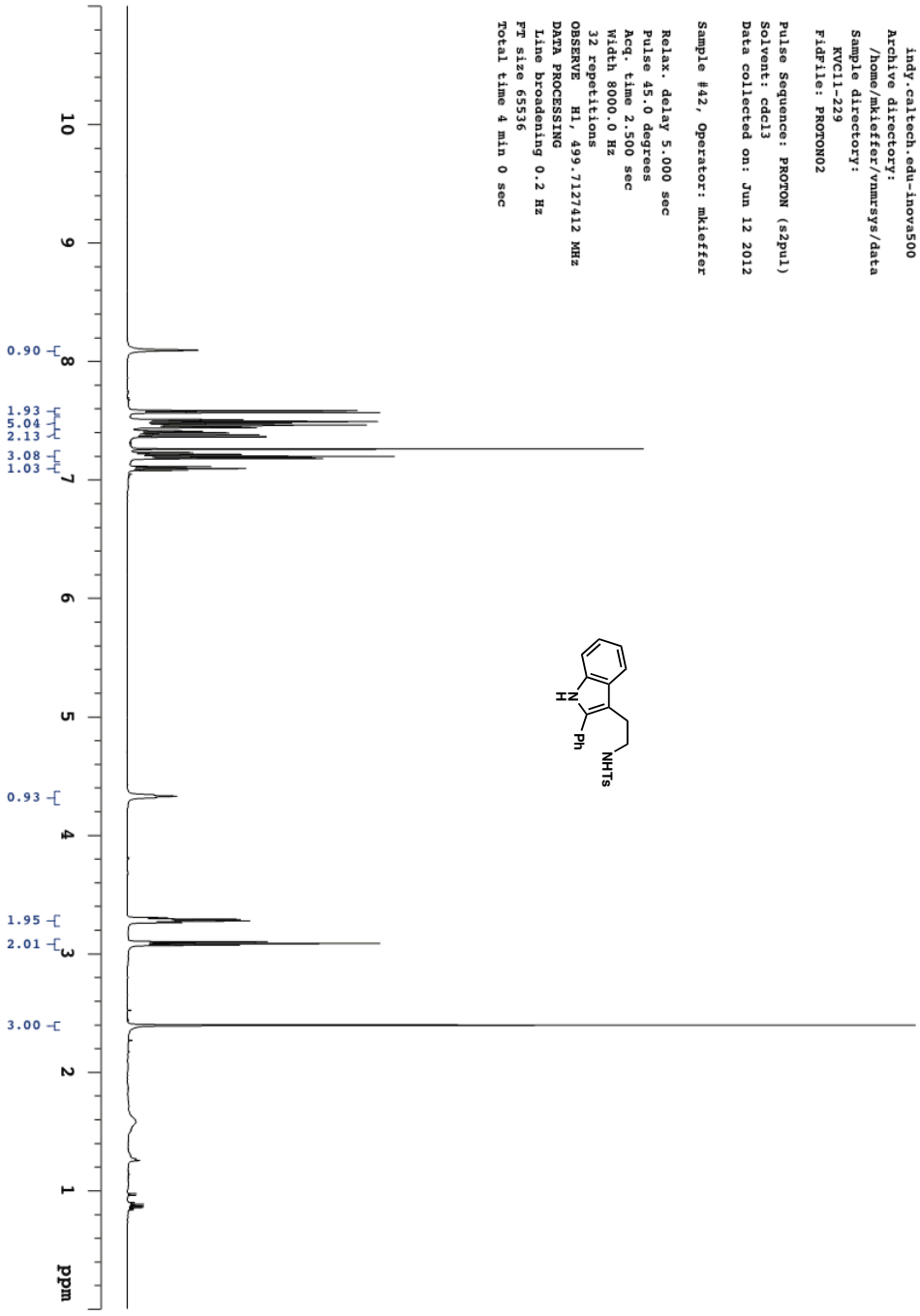

KVC11-287
Sample Name:
KVC11-287
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-287
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #13, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534588 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
Br
BF4
200
180
160
140
120
100
80
60
40
20
ppm

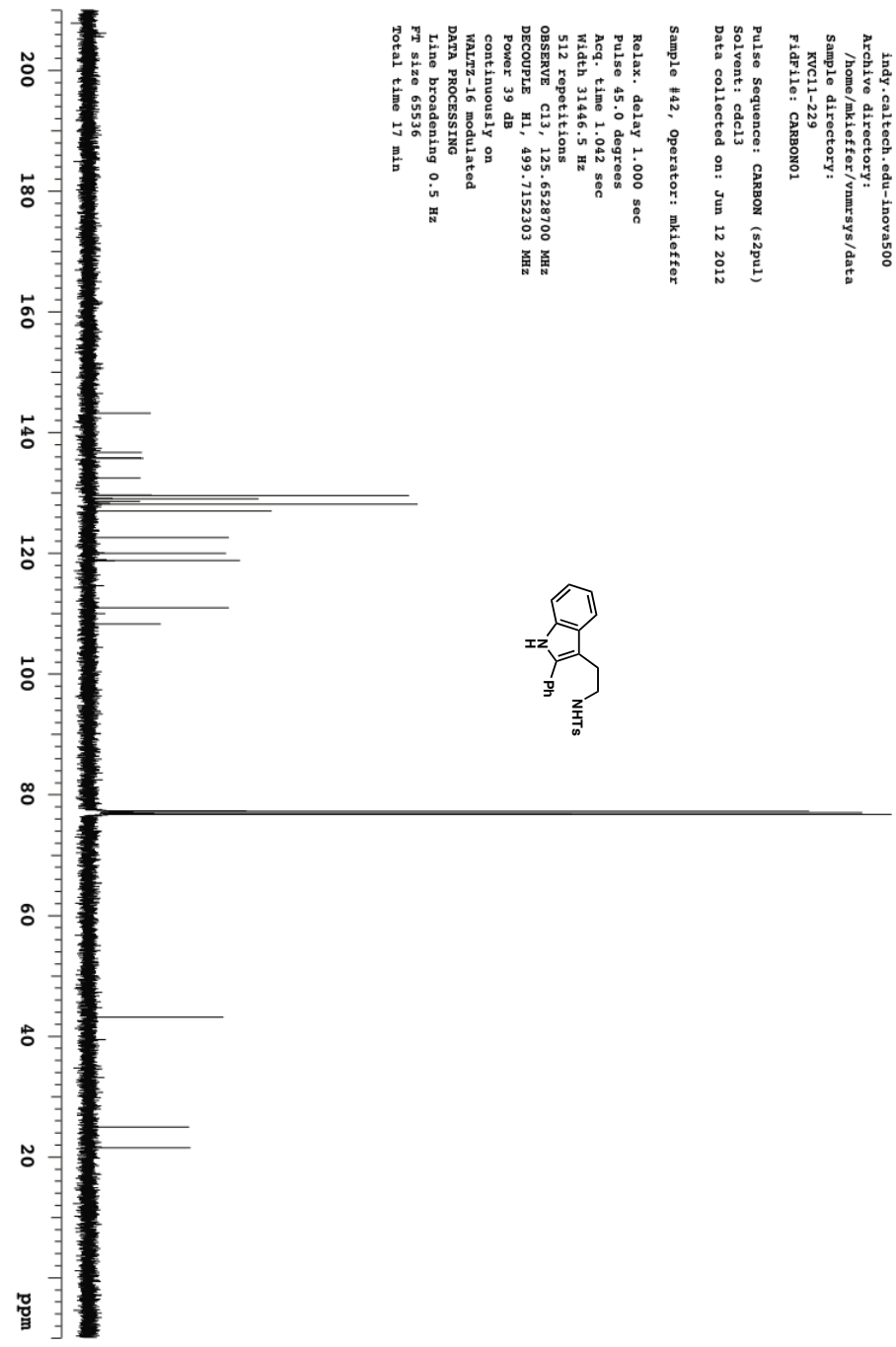

KVC12-109
Sample Name:
KVC12-109
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-109
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #45, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7151047 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
Me
Me
Me
I
I
BF4
1.94
1.99
1.98
6.00
3.00
10
9
8
7
6
5
4
3
2
1
ppm

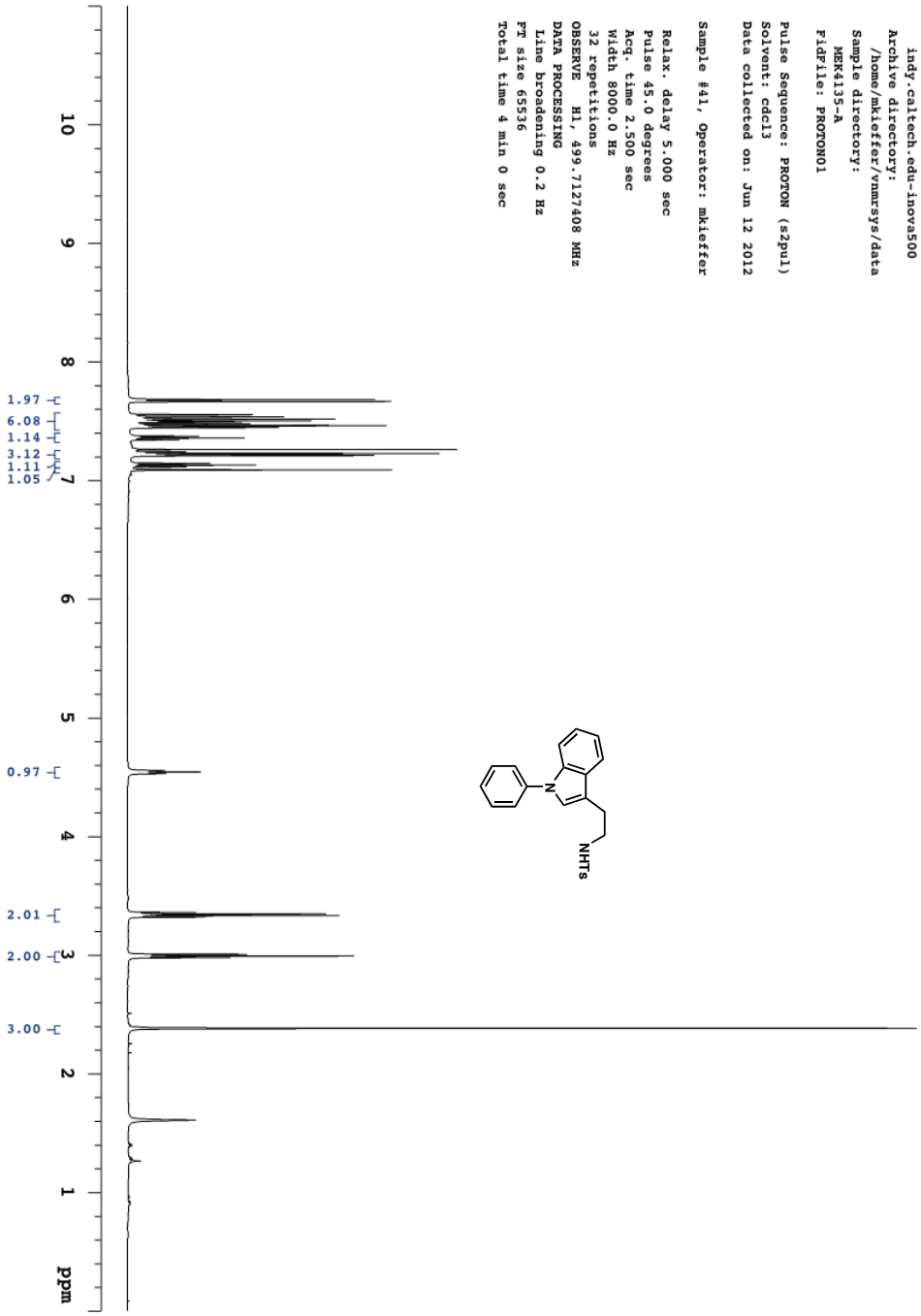

KVC12-109
Sample Name:
KVC12-109
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC12-109
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #45, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534597 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
I
BF4
200
180
160
140
120
100
80
60
40
20
ppm

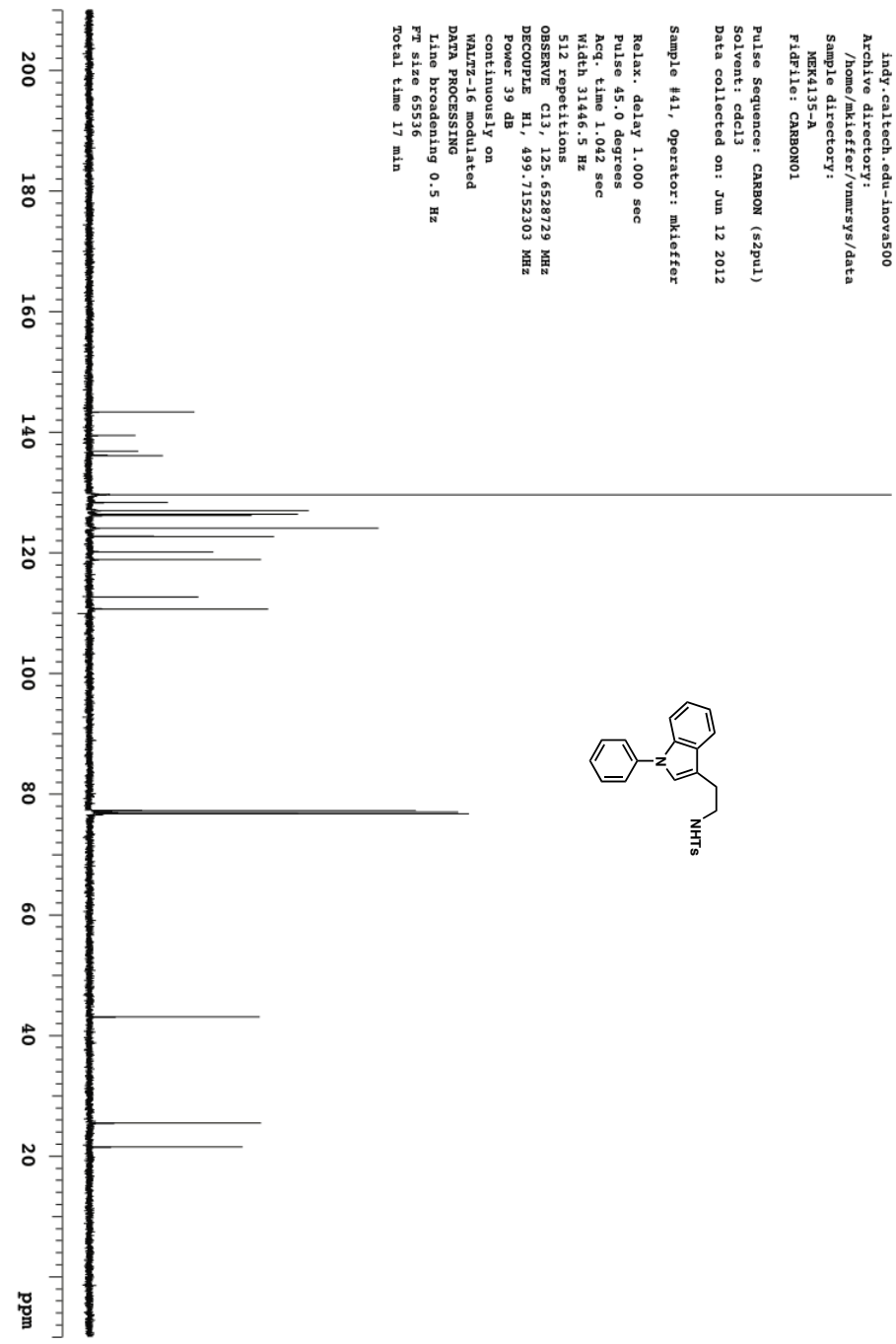

KVC11-253
Sample Name:
KVC11-253
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-253
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #11, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7151047 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Me
Me
I
BF4
CO2Et
2.04
2.04
2.04
2.07
6.07
3.00
3.10
10
9
8
7
6
5
4
3
2
1
ppm

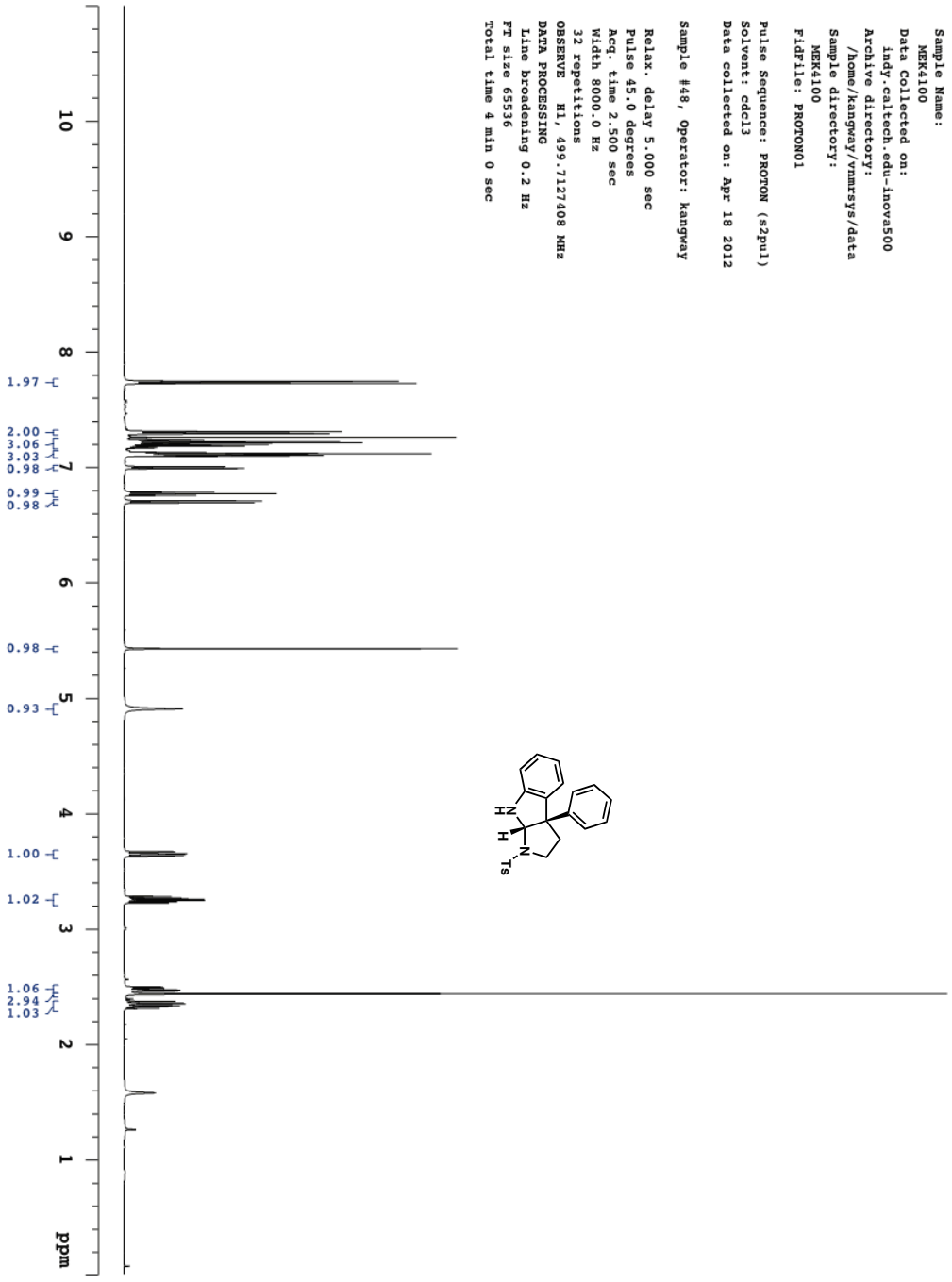

KVC11-253
Sample Name:
KVC11-253
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC11-253
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Apr 24 2012
Sample #11, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6534597 MHz
DECOUPLE H1, 499.7176040 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
I
BF4
CO2Et
200
180
160
140
120
100
80
60
40
20
ppm

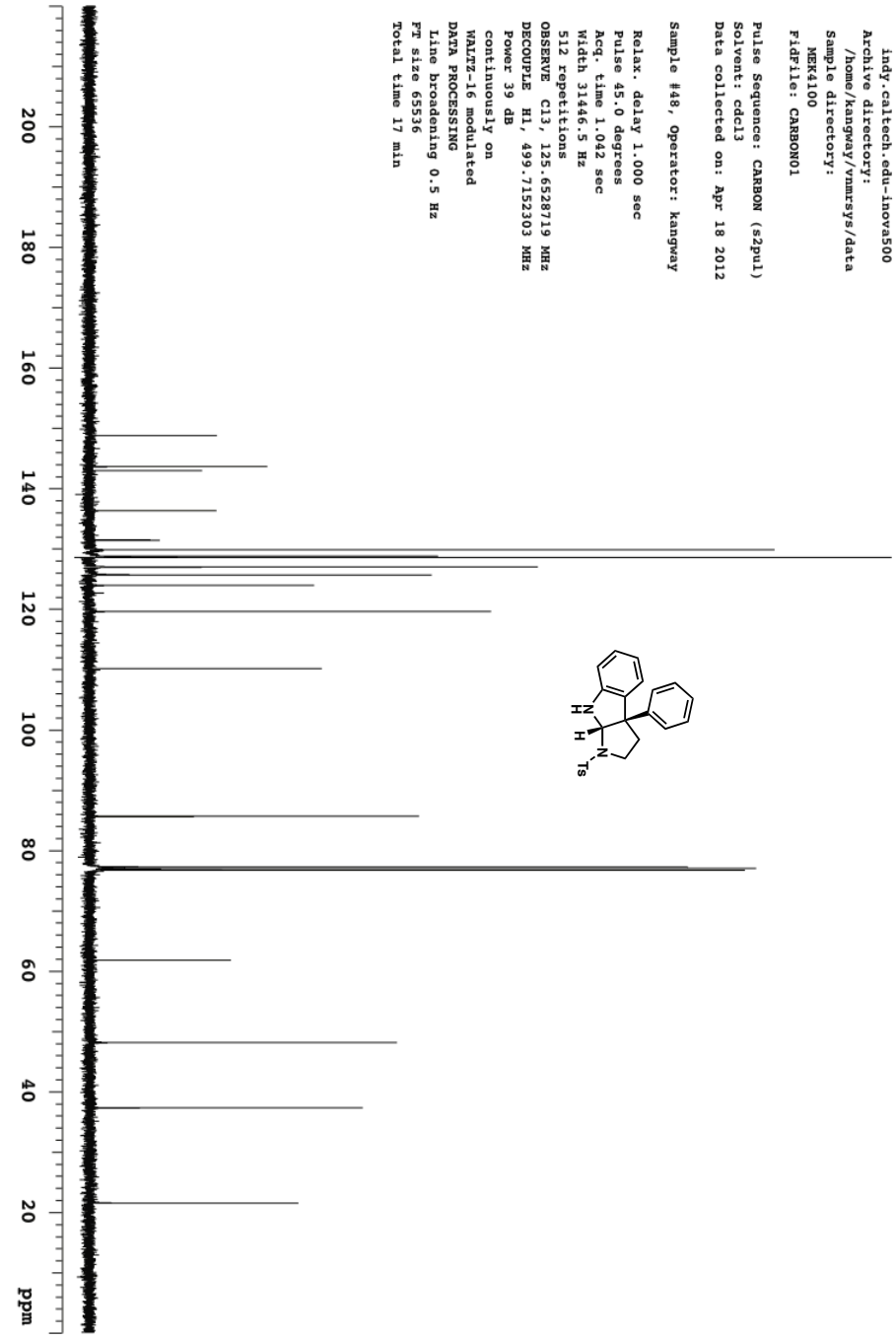

Sample Name:
KVC11-229
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC11-229
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012
Sample #42, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127412 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
0.90
1.93
5.04
2.13
3.08
1.03
0.93
1.95
2.01
3.00
10
9
8
7
6
5
4
3
2
1
ppm
NHTs
Ph
H
N

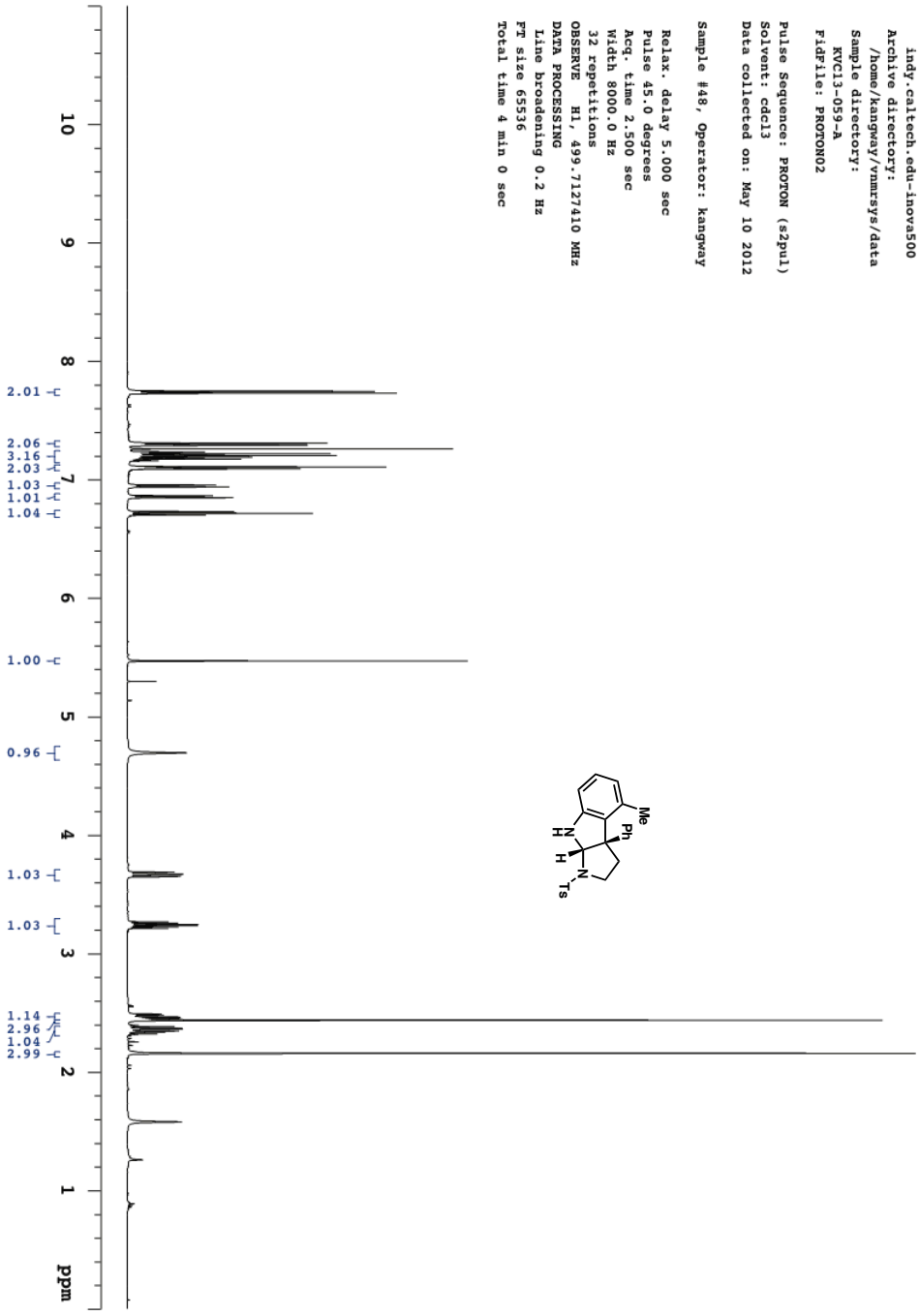

Sample Name:
KVC11-229
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC11-229
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012
Sample #42, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528700 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
NHTs
Ph
200
180
160
140
120
100
80
60
40
20
ppm

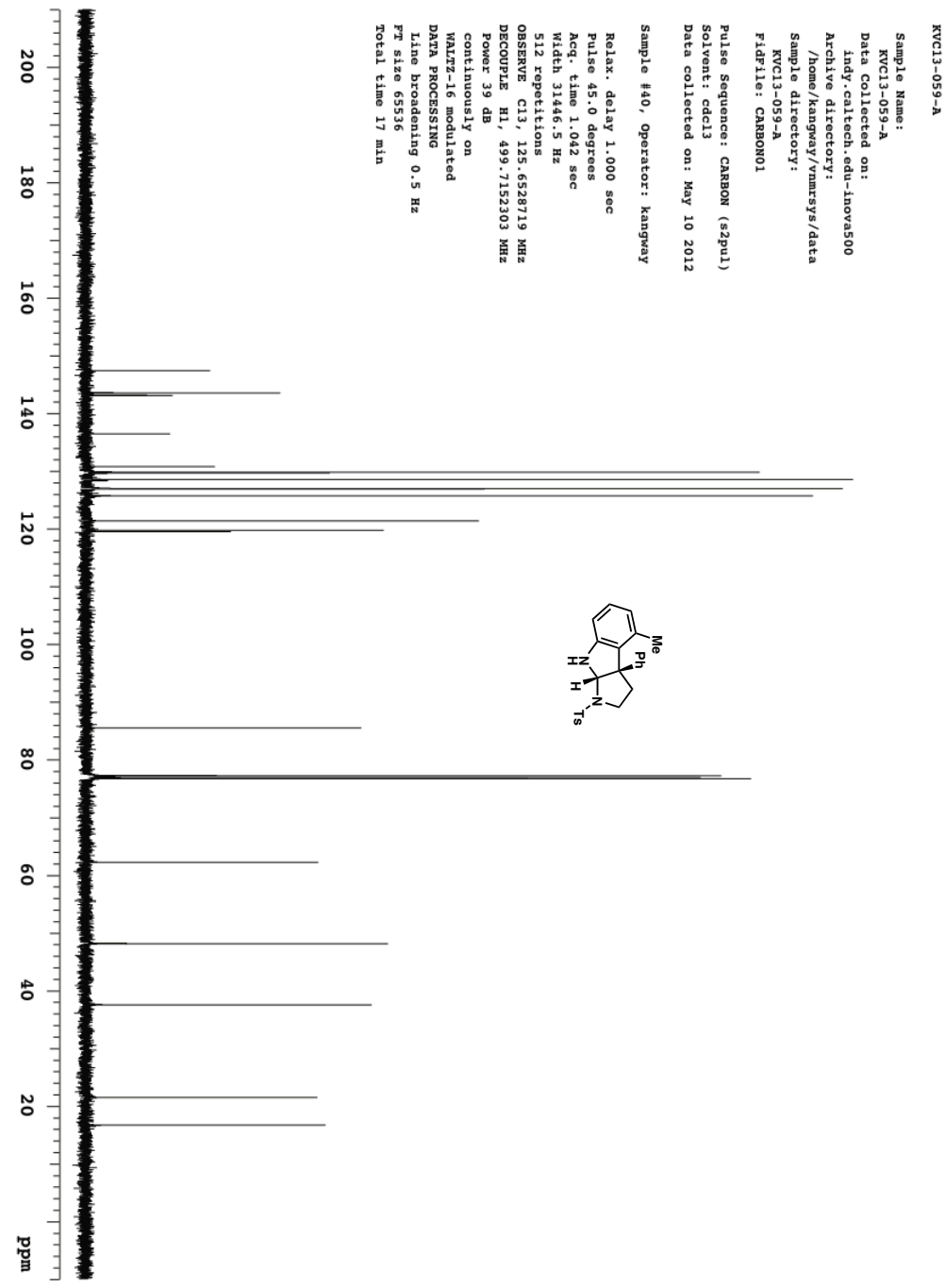

Sample Name:
MEK4135-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4135-A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012
Sample #41, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
1.97
6.08
1.14
3.12
1.11
1.05
0.97
2.01
2.00
3.00
N
NHTs
10
9
8
7
6
5
4
3
2
1
ppm

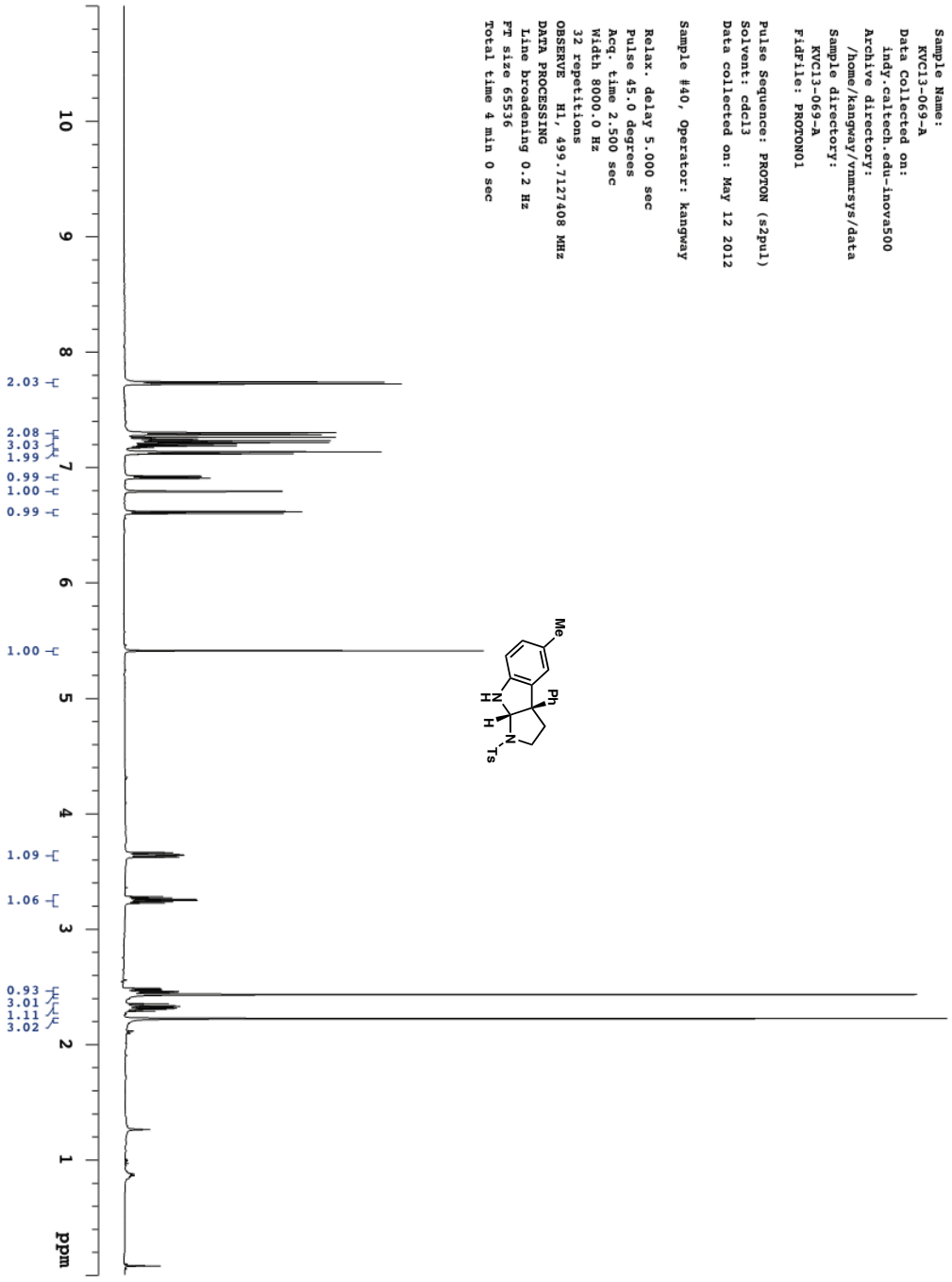

Sample Name:
MEK4135-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4135-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012
Sample #41, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
NHTs
200
180
160
140
120
100
80
60
40
20
ppm

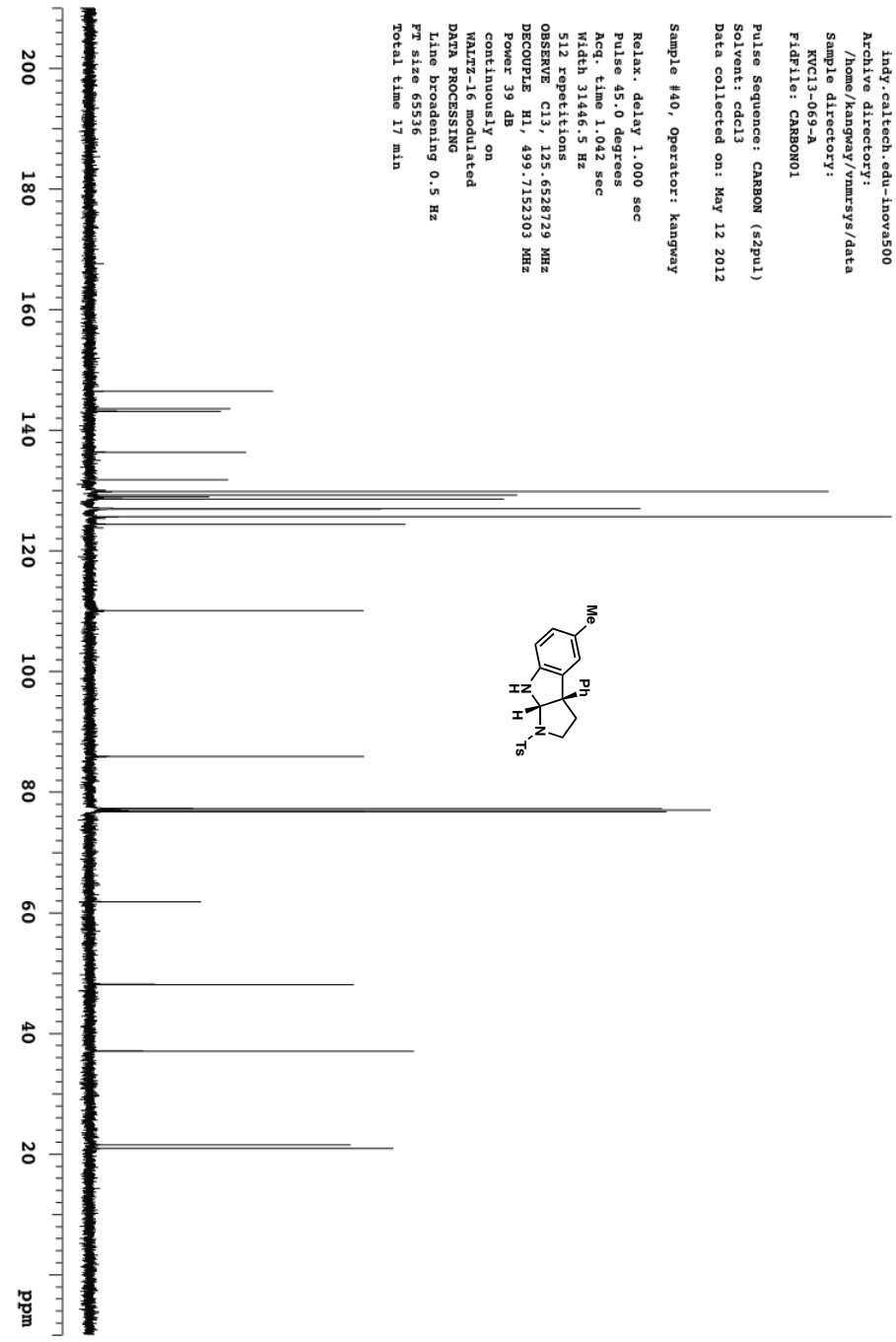

MEK4100
Sample Name:
MEK4100
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK4100
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 18 2012
Sample #48, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
1.97
2.00
3.06
3.03
0.98
0.99
0.98
0.98
0.93
1.00
1.02
1.06
2.94
1.03
10
9
8
7
6
5
4
3
2
1
ppm
N
H
N
H
Ts

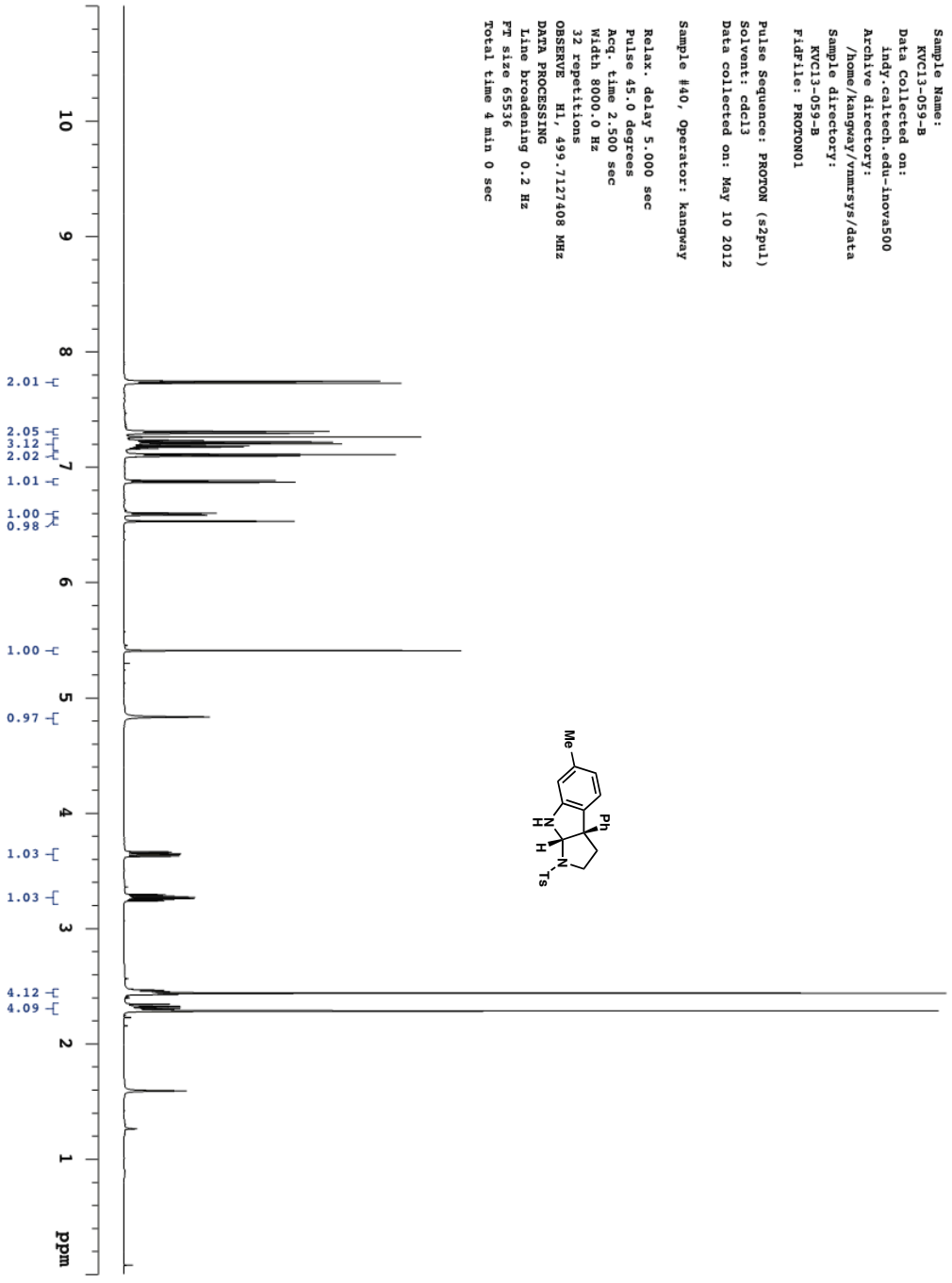

MEK4100
Sample Name:
MEK4100
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK4100
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 18 2012
Sample #48, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528719 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
200
180
160
140
120
100
80
60
40
20
ppm
H
N
H
N
Ts

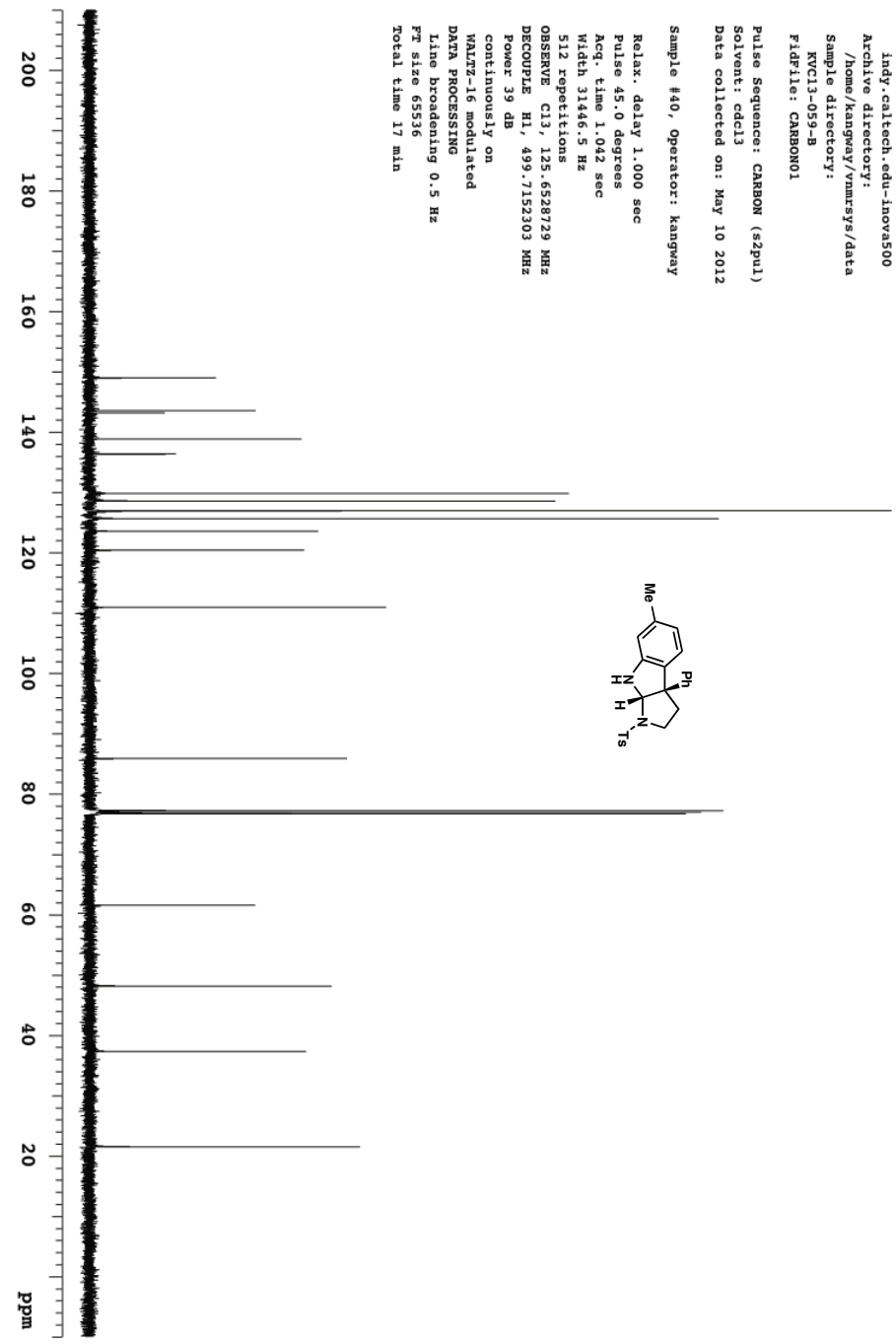

KVC13-059-A
Sample Name:
KVC13-059-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-A
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #48, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.01
2.06
3.16
2.03
1.03
1.01
1.04
1.00
0.96
1.03
1.03
1.14
2.96
1.04
2.99
Me
Ph
H
N
H
N
Ts
10
9
8
7
6
5
4
3
2
1
ppm

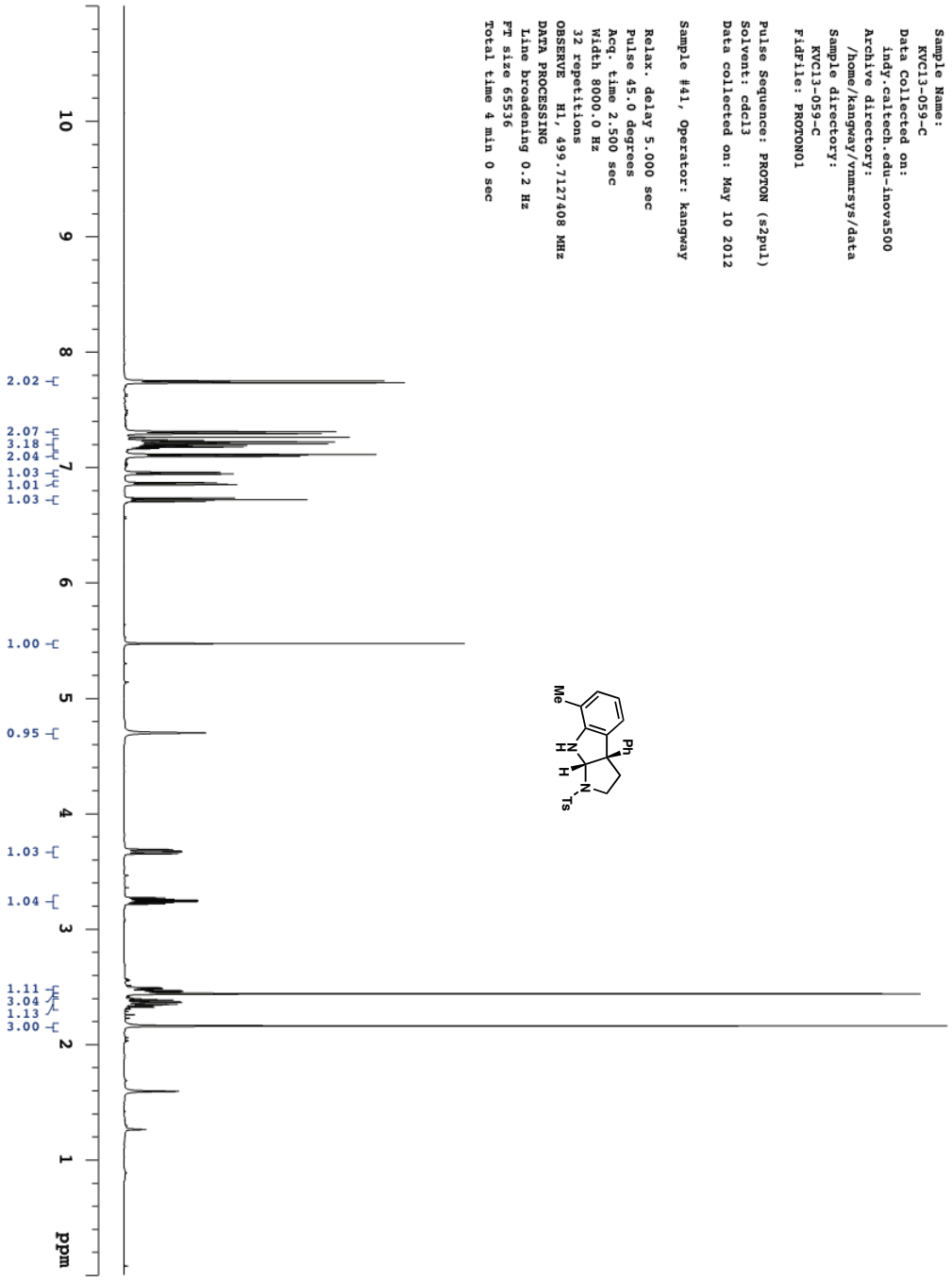

KVC13-059-A
Sample Name:
KVC13-059-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #40, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528719 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Ph
H
N
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

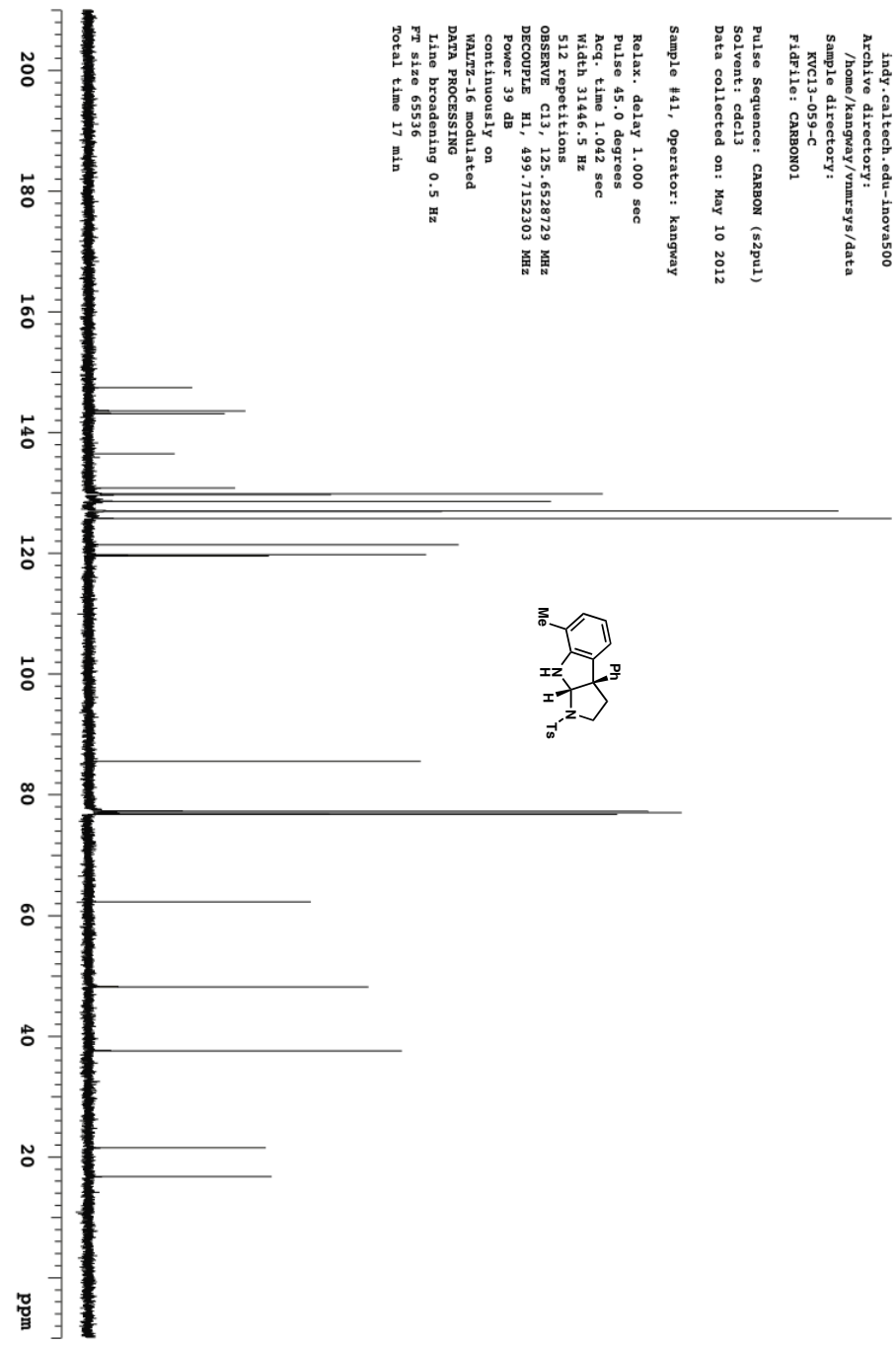

KVC13-069-A
Sample Name:
KVC13-069-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 12 2012
Sample #40, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Ph
N
H
H
N
Ts
2.03
2.08
3.03
1.99
0.99
1.00
0.99
1.00
1.09
1.06
0.93
3.01
1.11
3.02
10
9
8
7
6
5
4
3
2
1
ppm

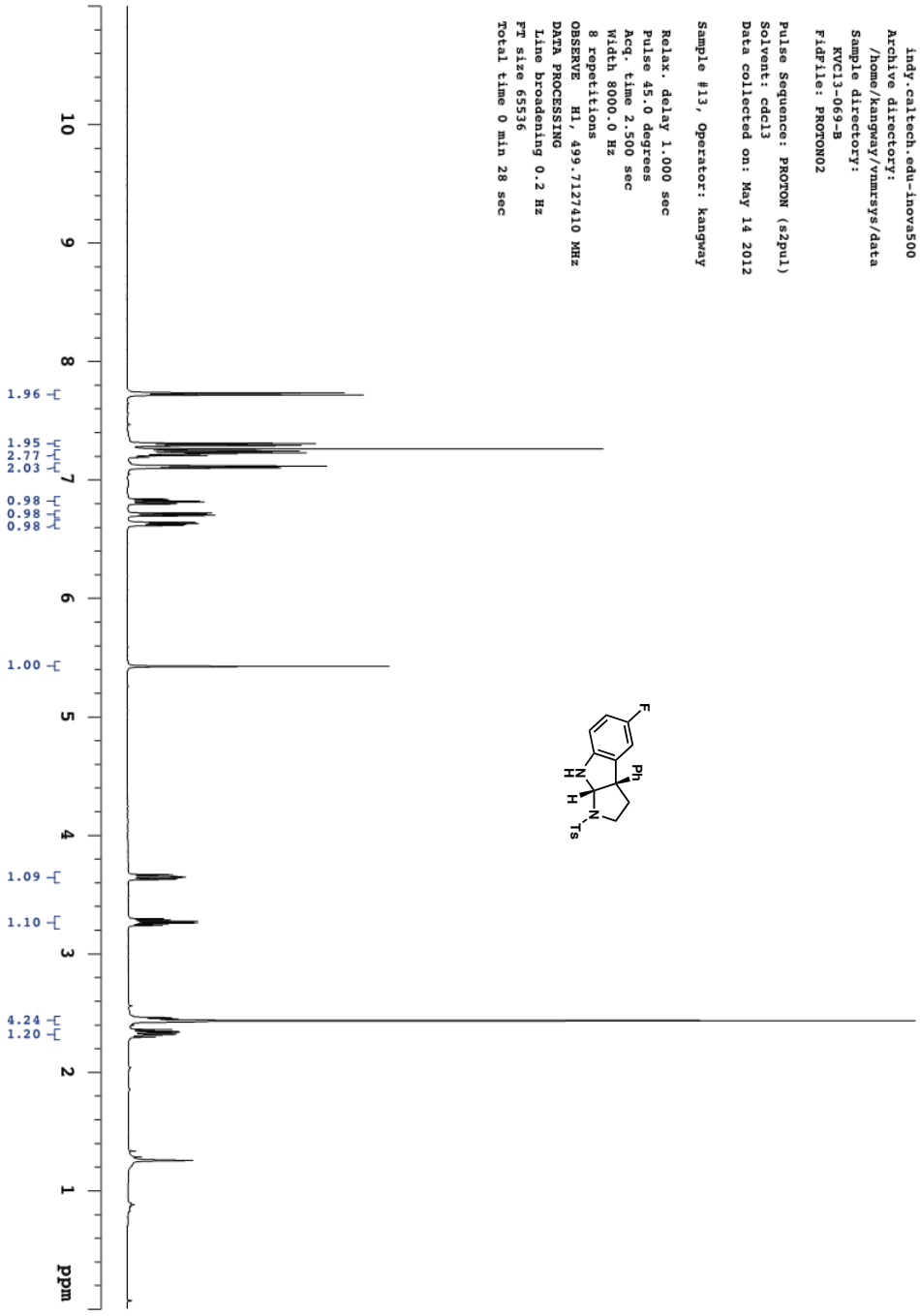

KVC13-069-A
Sample Name:
KVC13-069-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 12 2012
Sample #40, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Ph
H
N
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

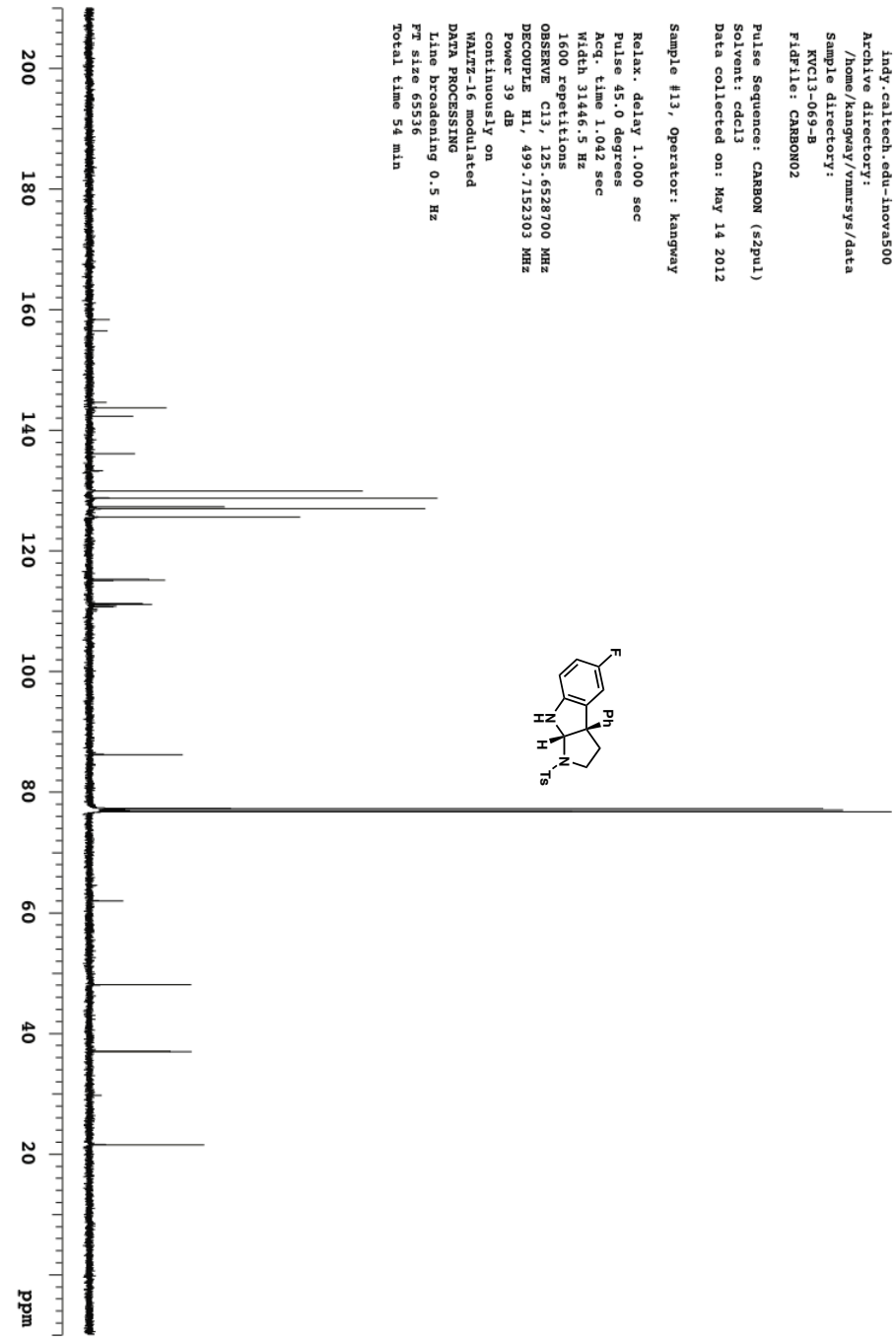

KVC13-059-B
Sample Name:
KVC13-059-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-B
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #40, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Ph
N
H
N
H
Ts
2.01
2.05
3.12
2.02
1.01
1.00
0.98
1.00
0.97
1.03
1.03
4.12
4.09
10
9
8
7
6
5
4
3
2
1
ppm

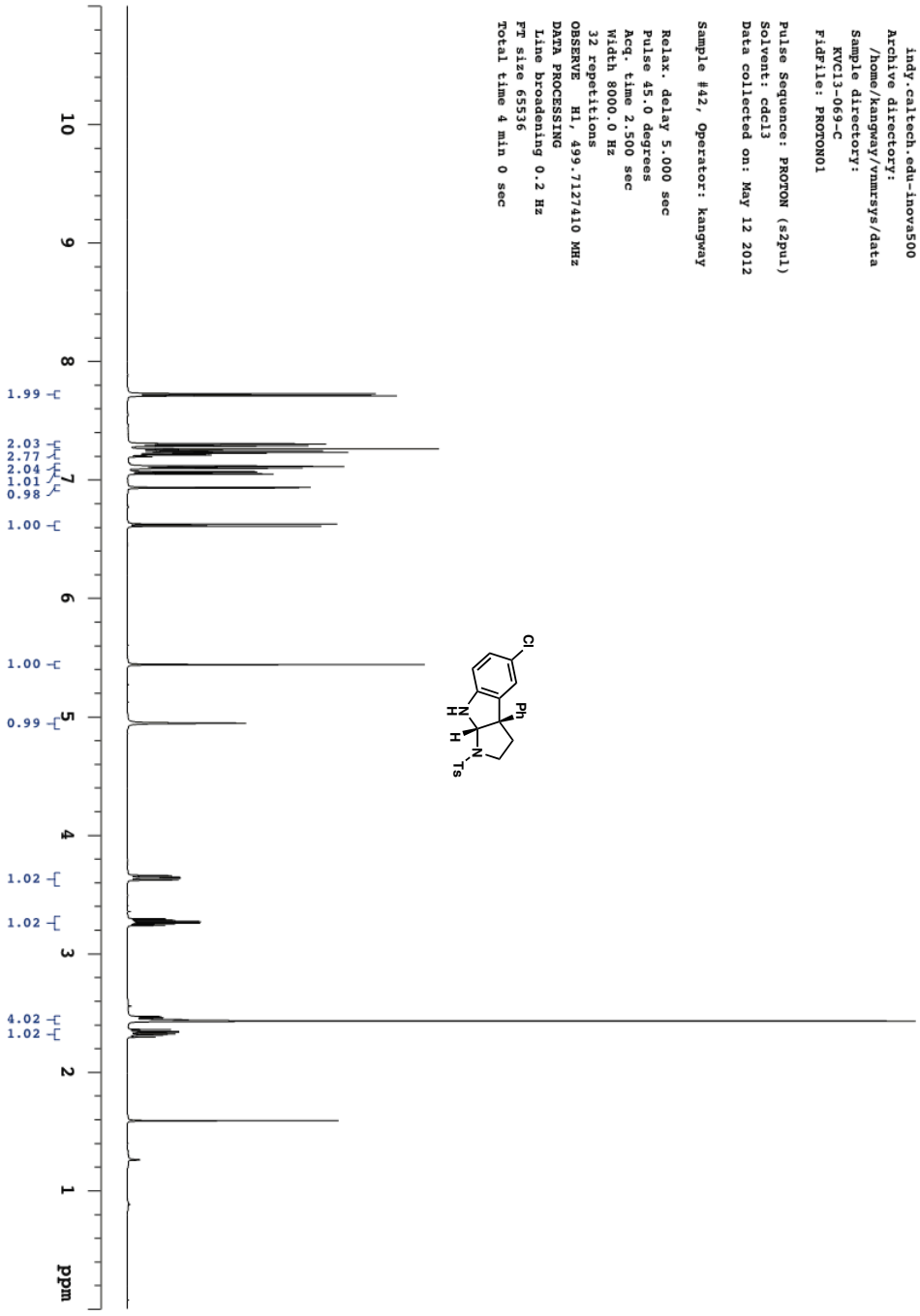

KVC13-059-B
Sample Name:
KVC13-059-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #40, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Ph
N
H
N
H
Ts
200
180
160
140
120
100
80
60
40
20
ppm

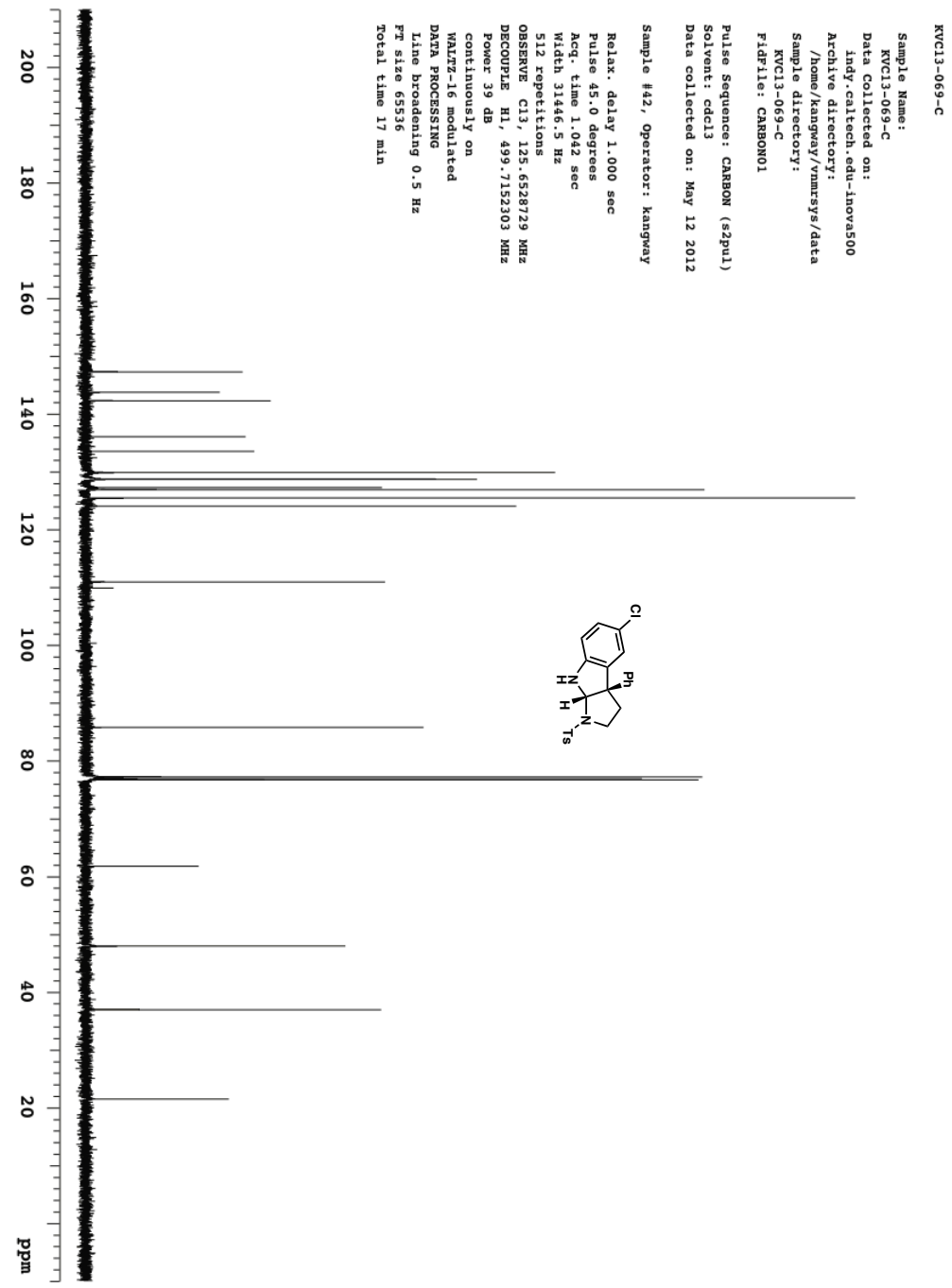

KVC13-059-C
Sample Name:
KVC13-059-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-C
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #41, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Me
Ph
Ts
2.02
2.07
3.18
2.04
1.03
1.01
1.03
1.00
0.95
1.03
1.04
1.11
3.04
1.13
3.00
ppm

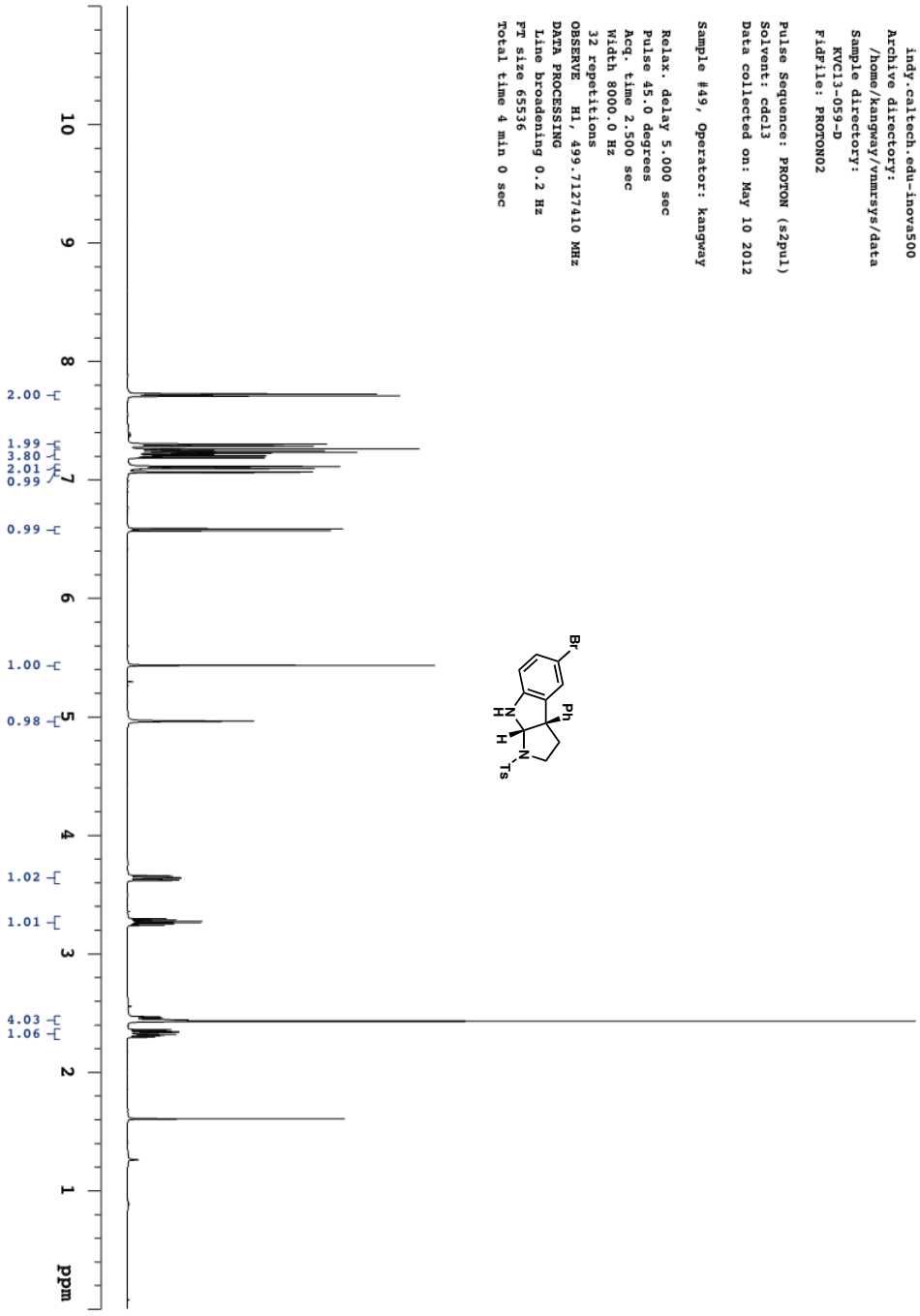

KVC13-059-C
Sample Name:
KVC13-059-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-C
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #41, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Ph
Ts
200
180
160
140
120
100
80
60
40
20
ppm

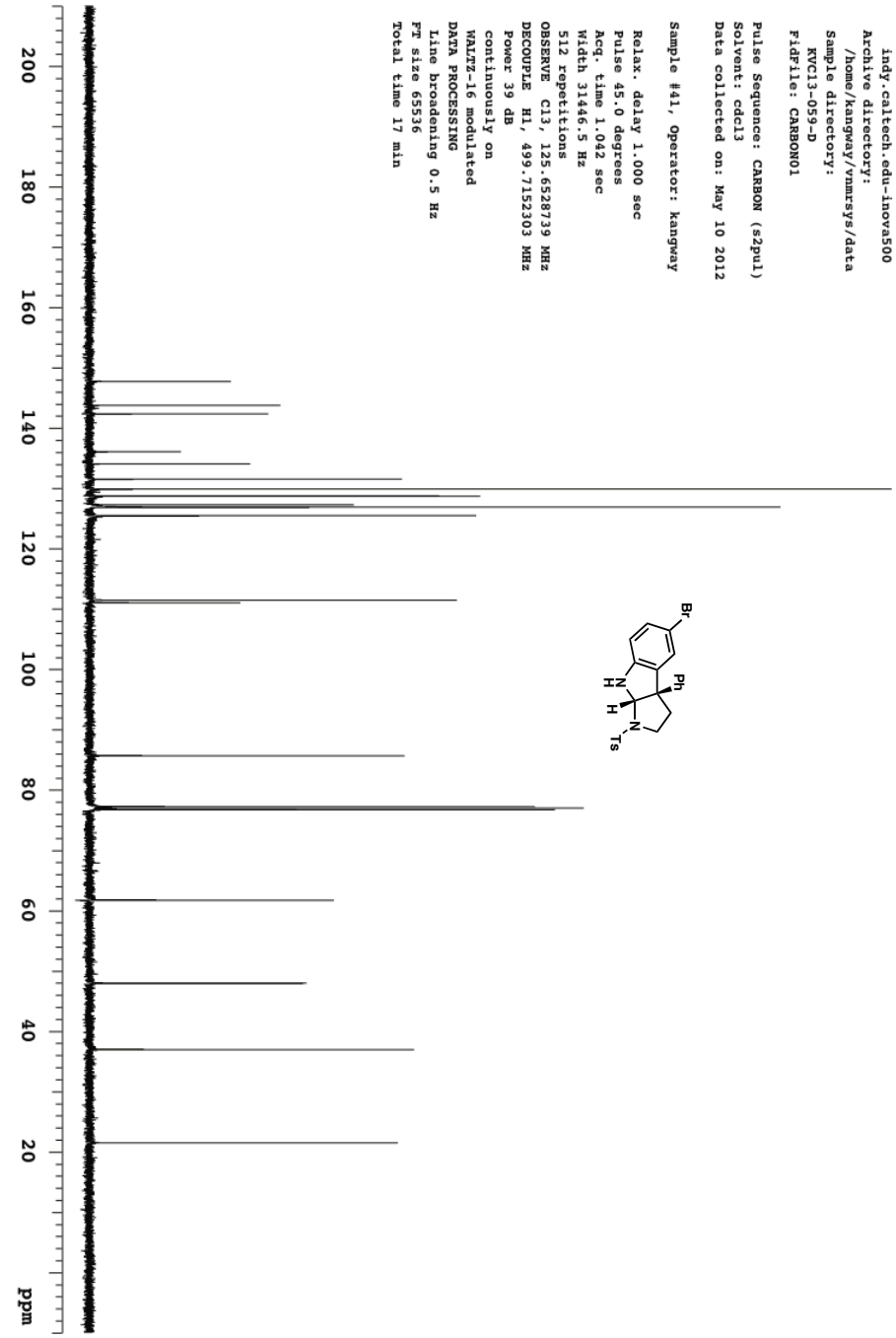

KVC13-069-B
Sample Name:
KVC13-069-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-B
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 14 2012
Sample #13, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 28 sec
1.96
1.95
2.77
2.03
0.98
0.98
0.98
1.00
1.09
1.10
4.24
1.20
10
9
8
7
6
5
4
3
2
1
ppm
F
Ph
N
H
H
N
Ts

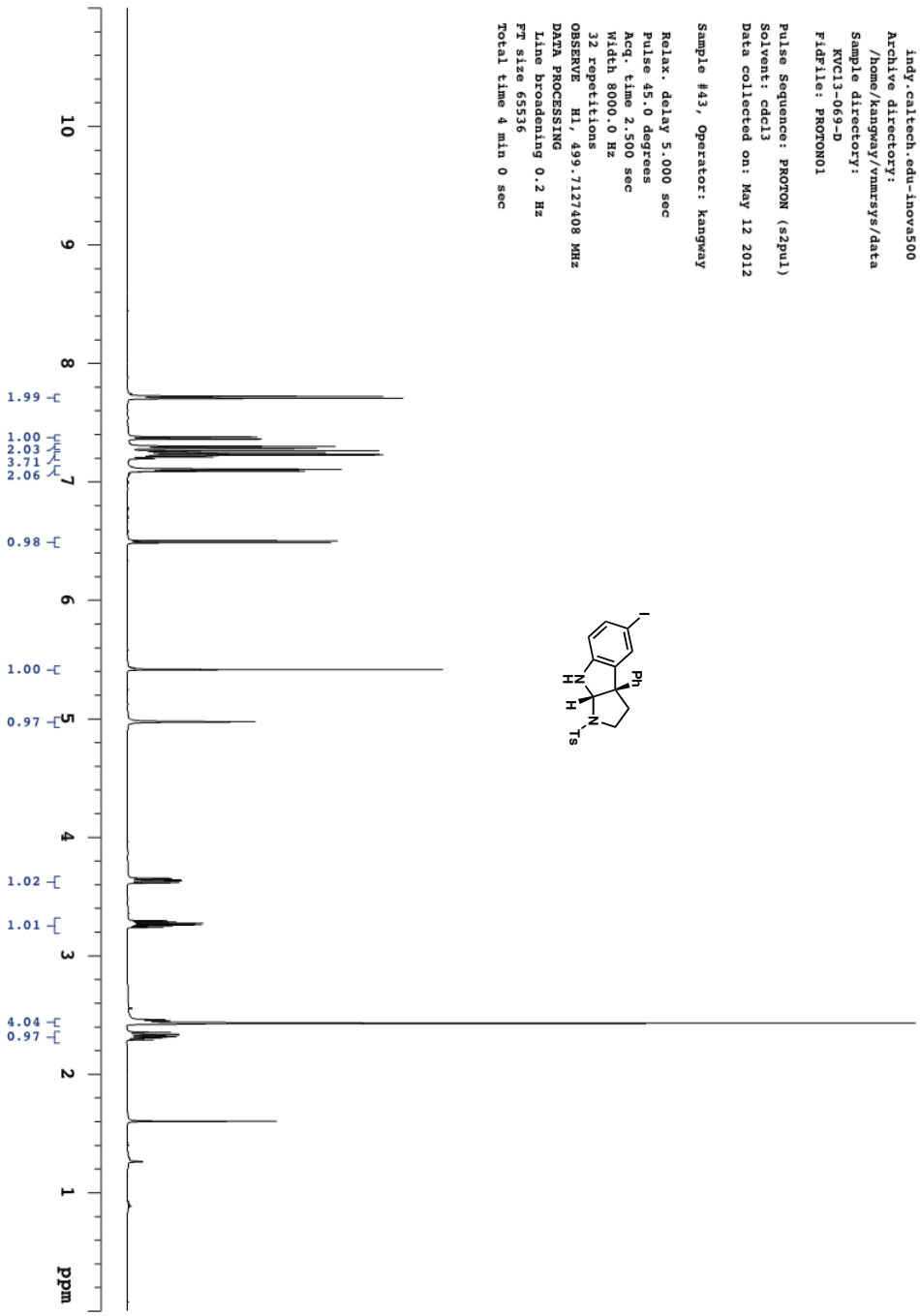

KVC13-069-B
Sample Name:
KVC13-069-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-B
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 14 2012
Sample #13, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1600 repetitions
OBSERVE C13, 125.6528700 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 54 min
F
Ph
N
H
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

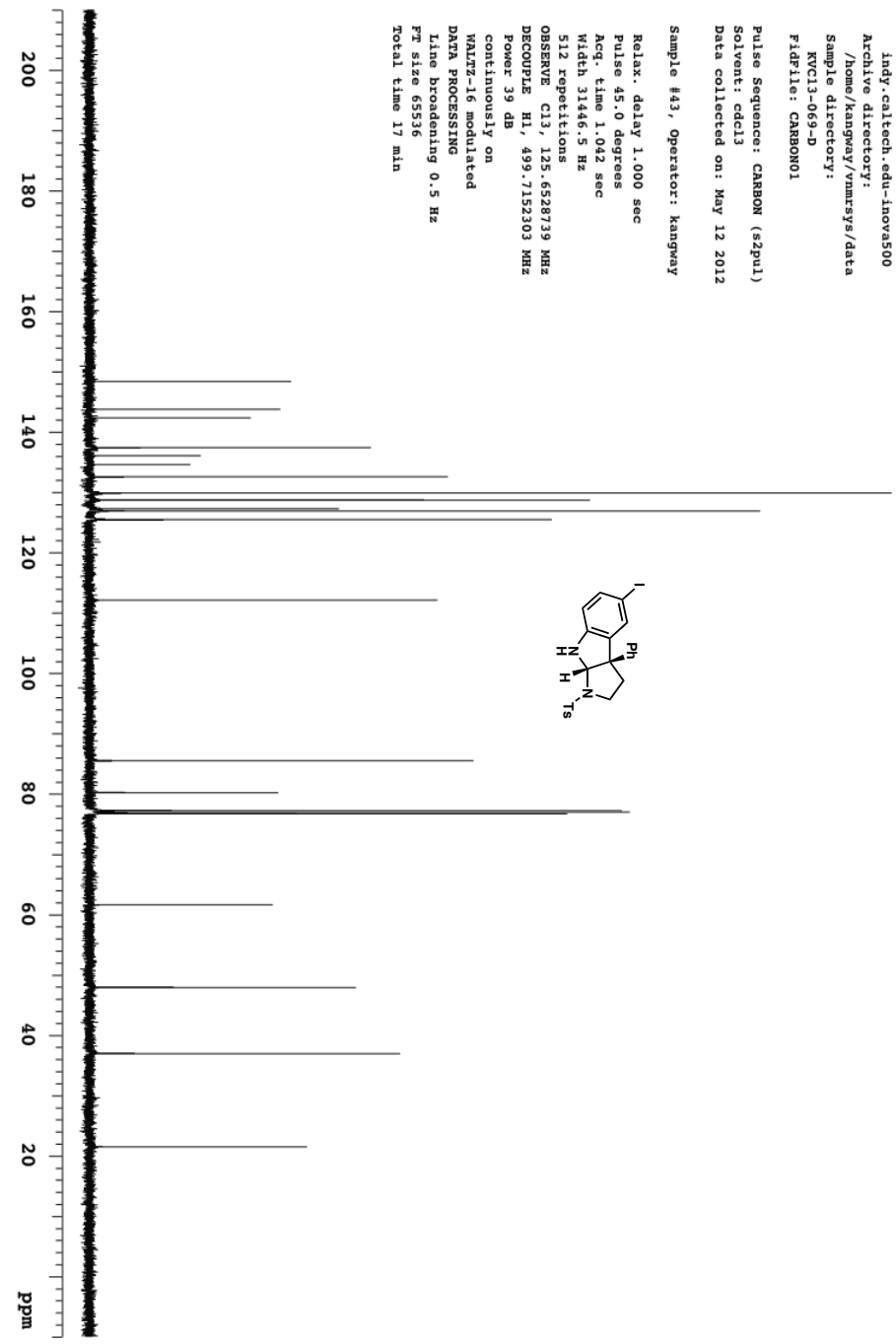

KVC13-069-C
Sample Name:
KVC13-069-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-C
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 12 2012
Sample #42, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
1.99
2.03
2.77
2.04
1.01
0.98
1.00
1.00
0.99
1.02
1.02
4.02
1.02
10
9
8
7
6
5
4
3
2
1
ppm
Cl
Ph
H
N
N
Ts

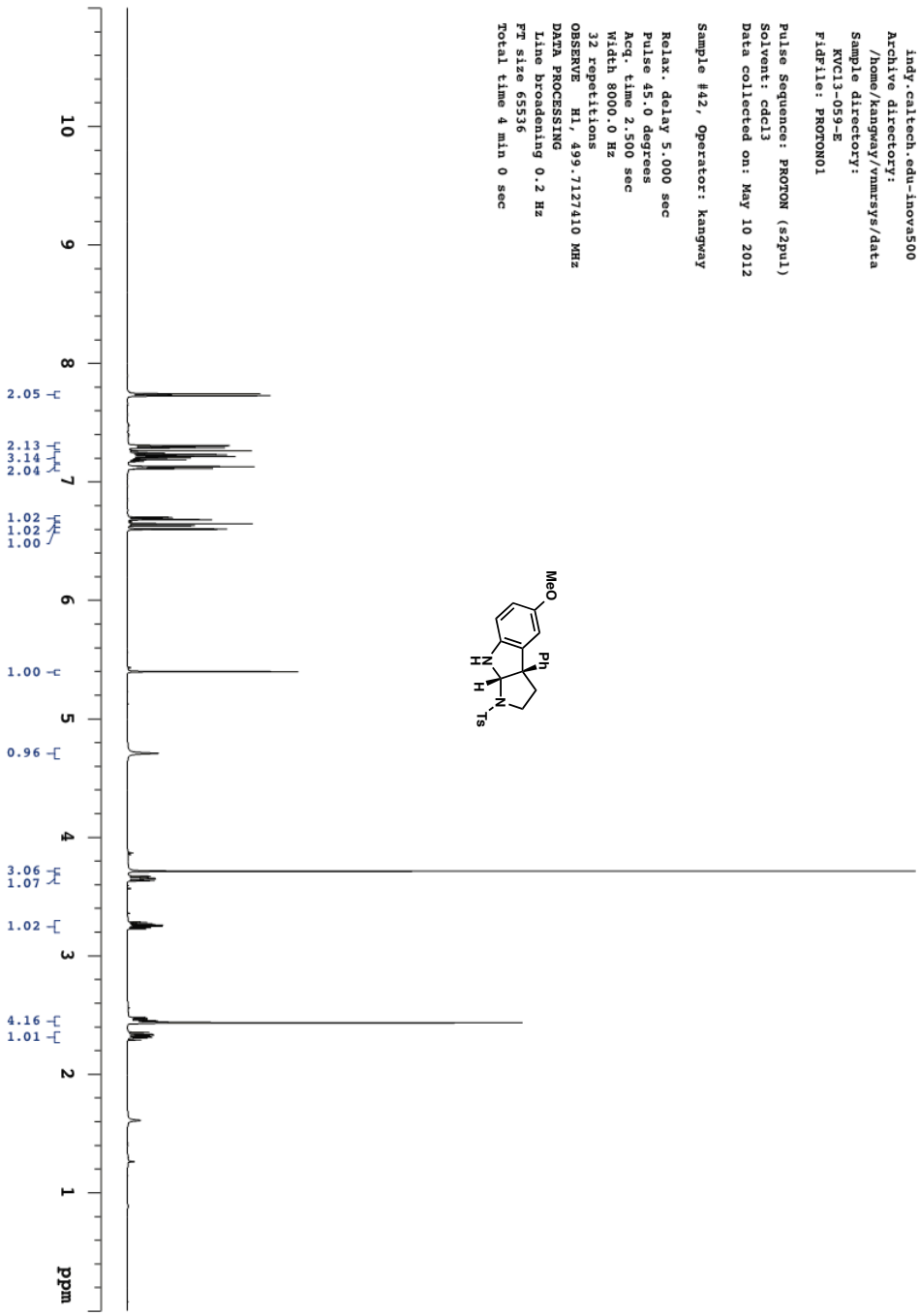

KVC13-069-C
Sample Name:
KVC13-069-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-C
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 12 2012
Sample #42, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Cl
Ph
H
N
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

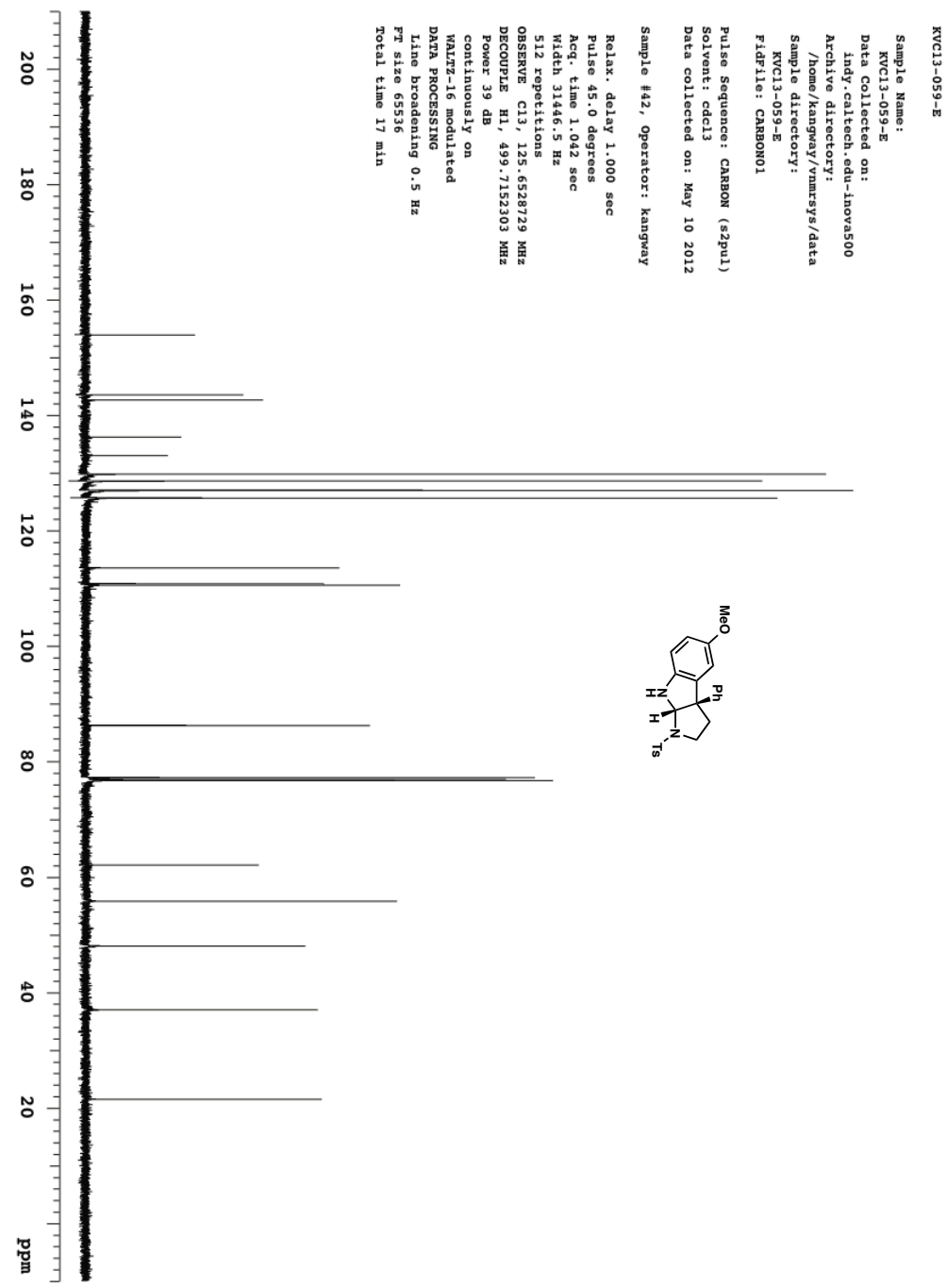

KVC13-059-D
Sample Name:
KVC13-059-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-D
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #49, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
Br
Ph
N
H
H
N
Ts
2.00
1.99
3.80
2.01
0.99
0.99
1.00
0.98
1.02
1.01
4.03
1.06
10
9
8
7
6
5
4
3
2
1
ppm

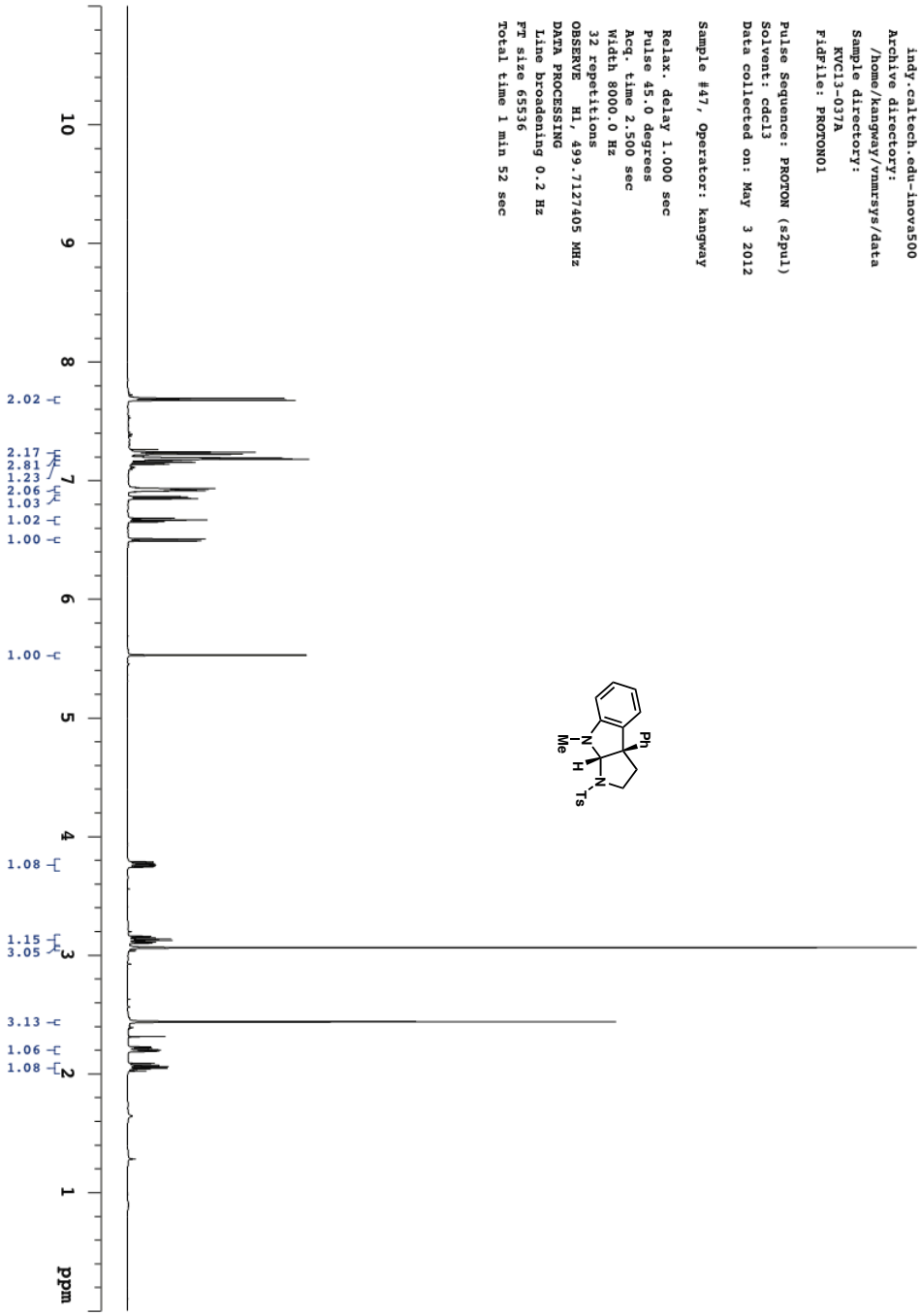

KVC13-059-D
Sample Name:
KVC13-059-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-D
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #41, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528739 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Br
Ph
H
N
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

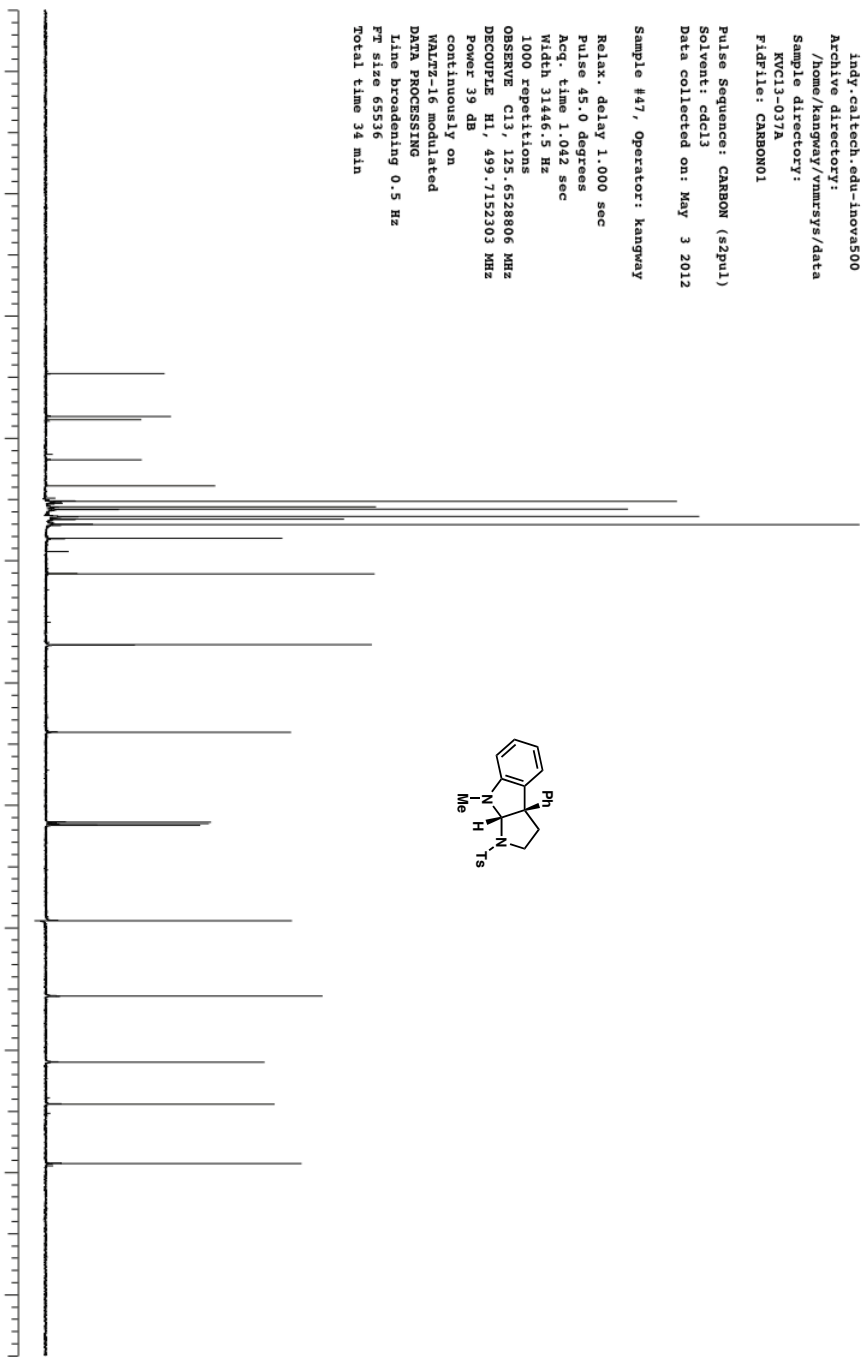

KVC13-069-D
Sample Name:
KVC13-069-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-D
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 12 2012
Sample #43, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
1.99
1.00
2.03
3.71
2.06
0.98
1.00
0.97
1.02
1.01
4.04
0.97
10
9
8
7
6
5
4
3
2
1
ppm
I
Ph
N
H
H
N
Ts

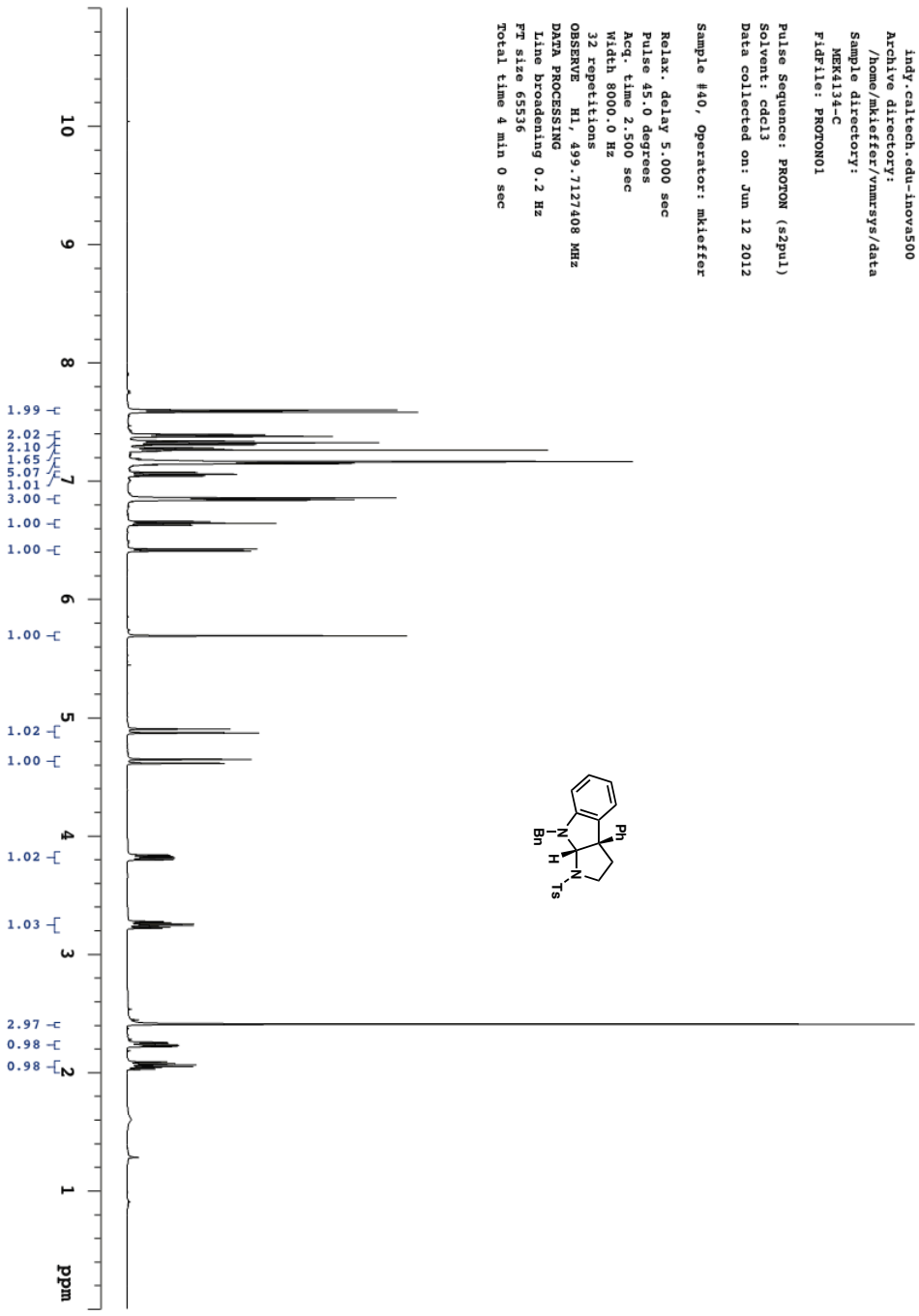

KVC13-069-D
Sample Name:
KVC13-069-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-069-D
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 12 2012
Sample #43, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528739 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
I
Ph
N
H
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

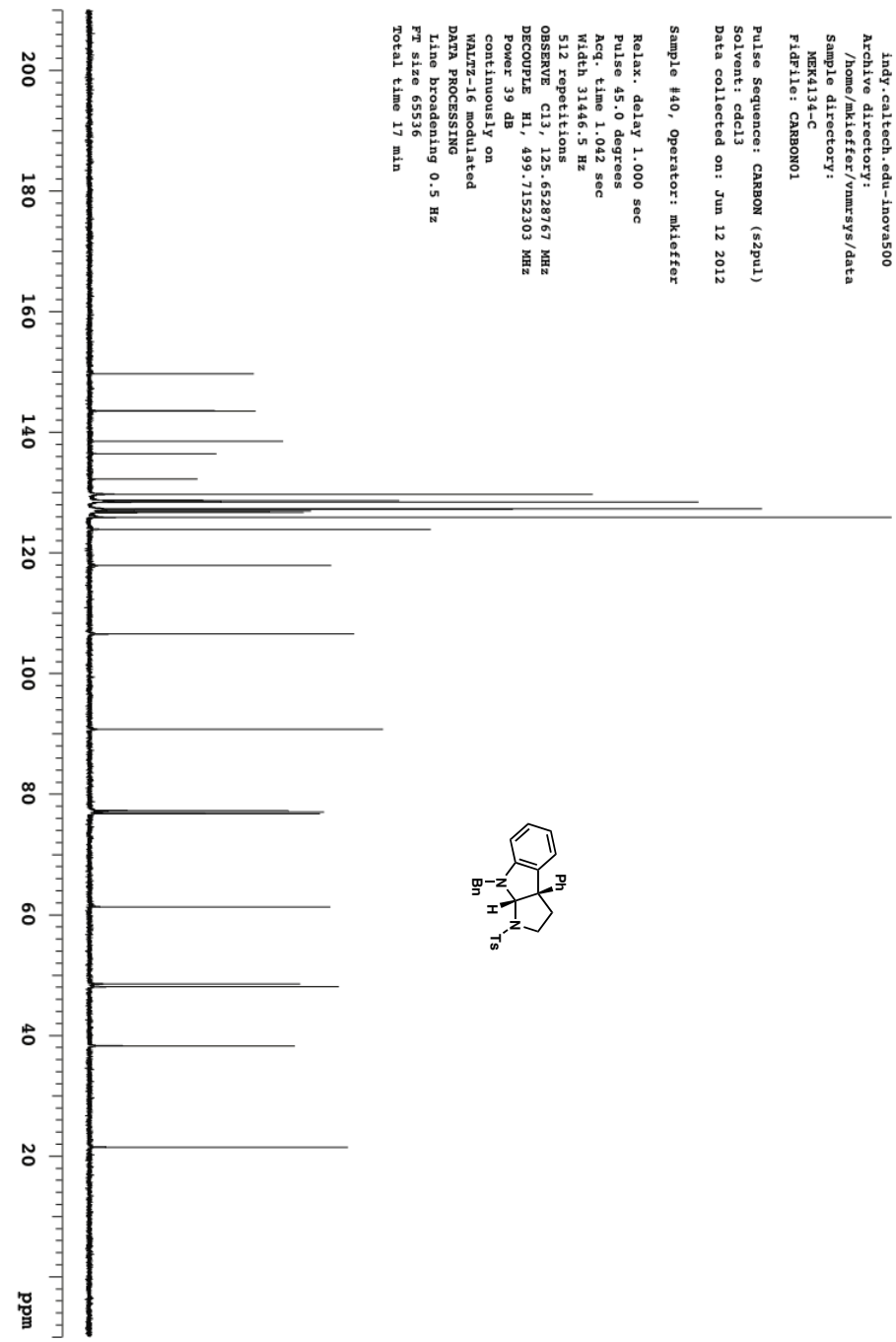

KVC13-059-E
Sample Name:
KVC13-059-E
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-E
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #42, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
MeO
Ph
Ts
2.05
2.13
3.14
2.04
1.02
1.02
1.00
1.00
0.96
3.06
1.07
1.02
4.16
1.01
ppm

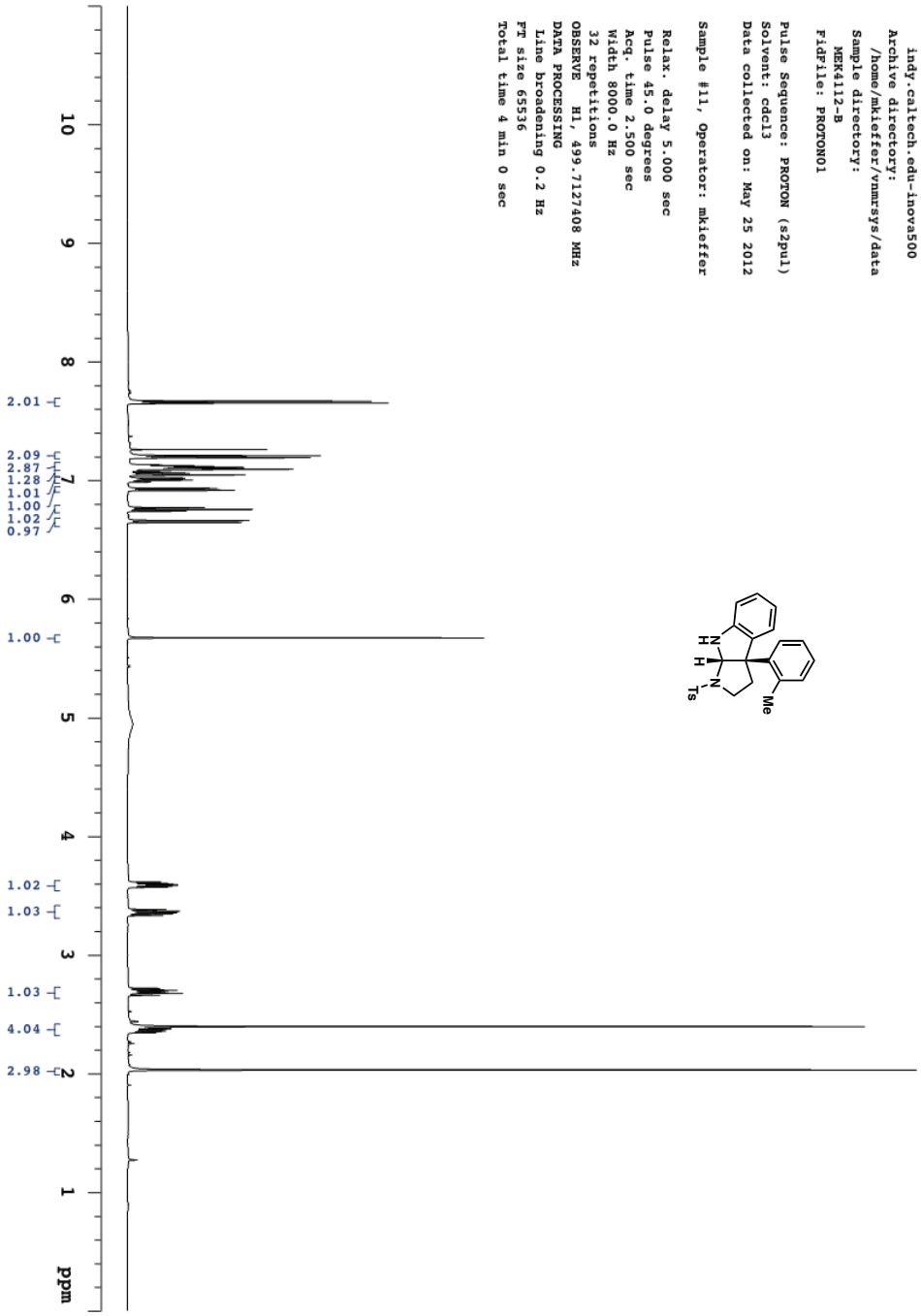

KVC13-059-E
Sample Name:
KVC13-059-E
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-059-E
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 10 2012
Sample #42, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
MeO
Ph
H
N
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

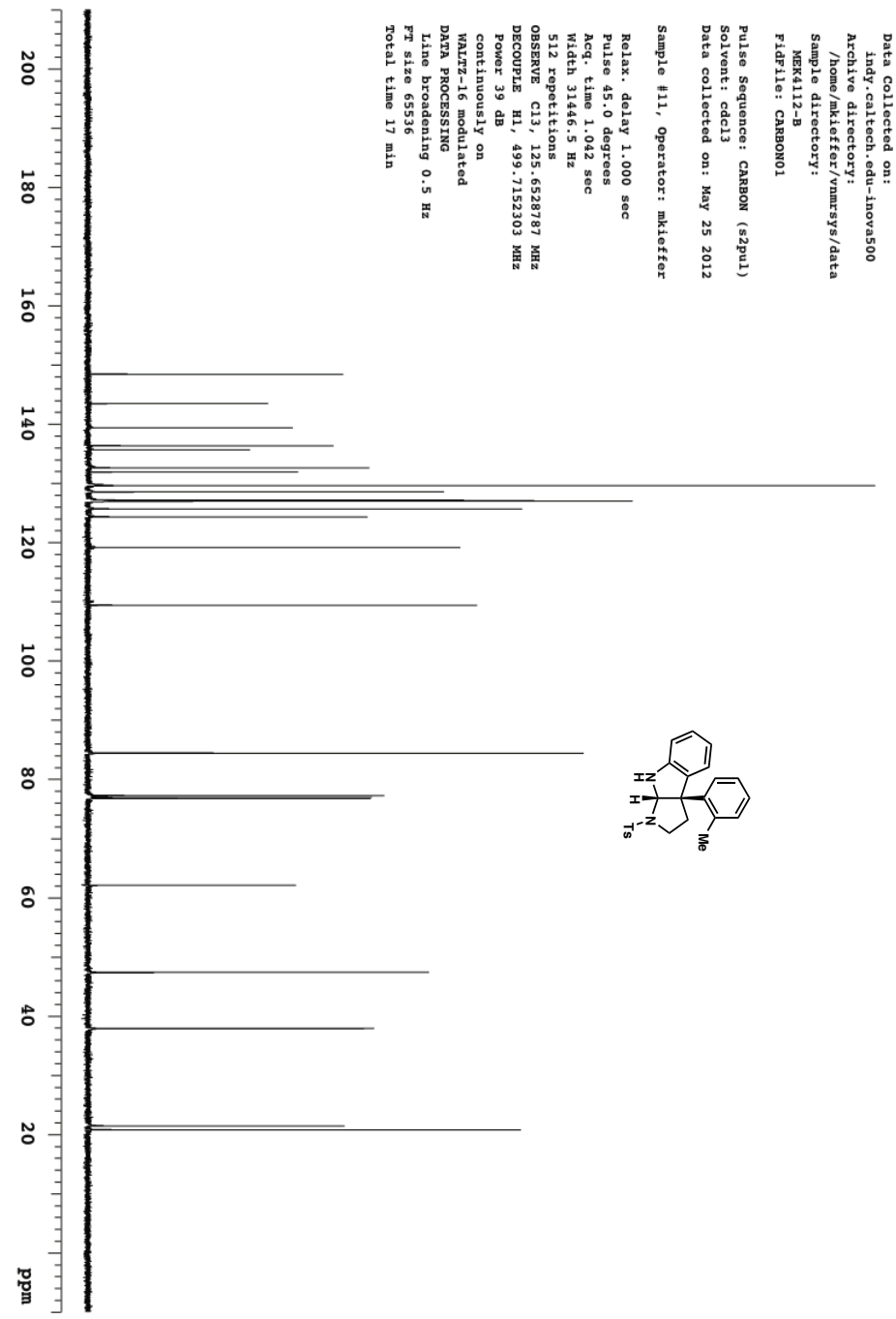

KVC13-037A
Sample Name:
KVC13-037A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-037A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 3 2012
Sample #47, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127405 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min 52 sec
Ph
Me
H
Ts
2.02
2.17
2.81
1.23
2.06
1.03
1.02
1.00
1.00
1.08
1.15
3.05
3.13
1.06
1.08
10
9
8
7
6
5
4
3
2
1
ppm

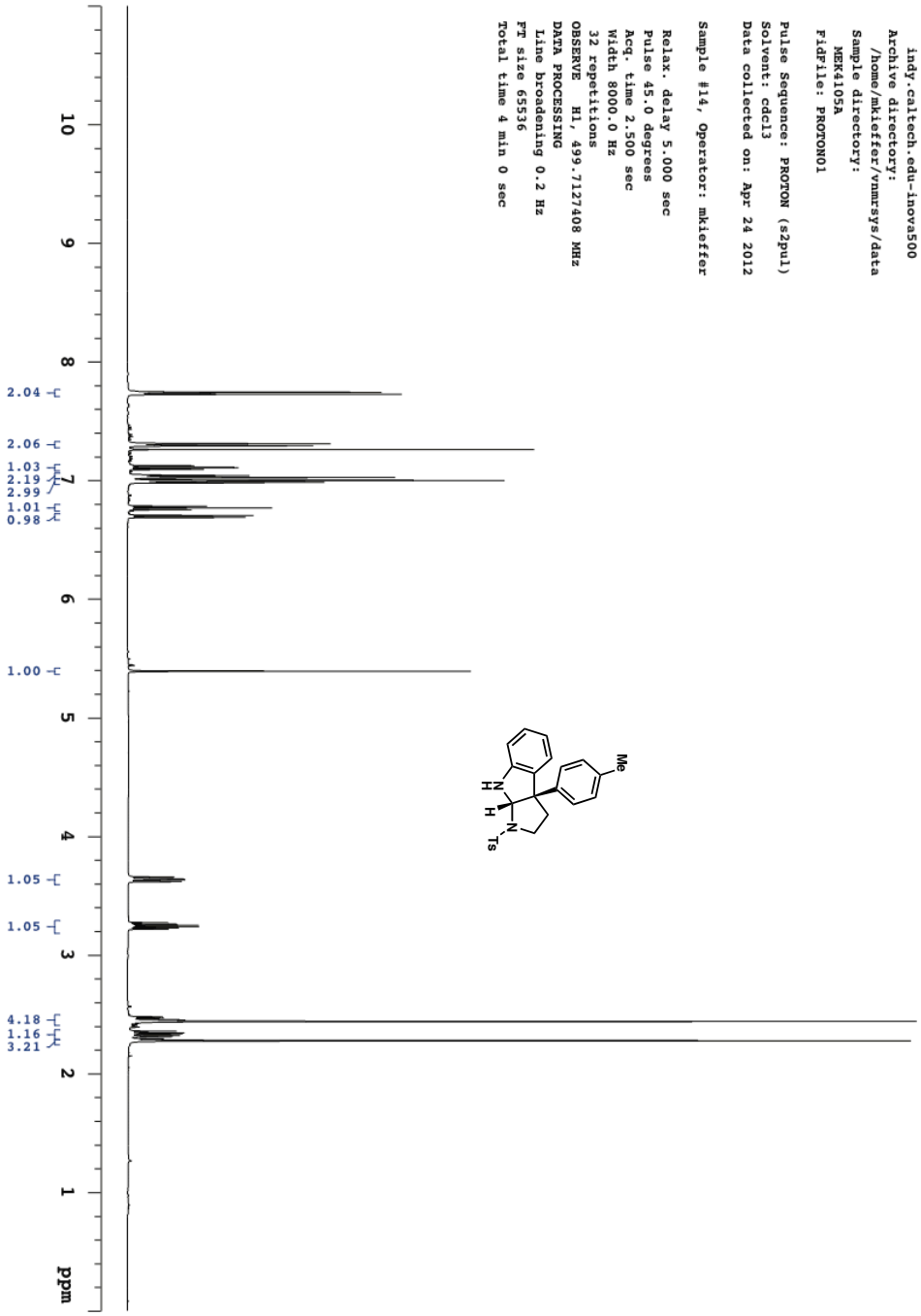

KVC13-037A
Sample Name:
KVC13-037A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC13-037A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 3 2012
Sample #47, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6528806 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Ph
N
Me
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

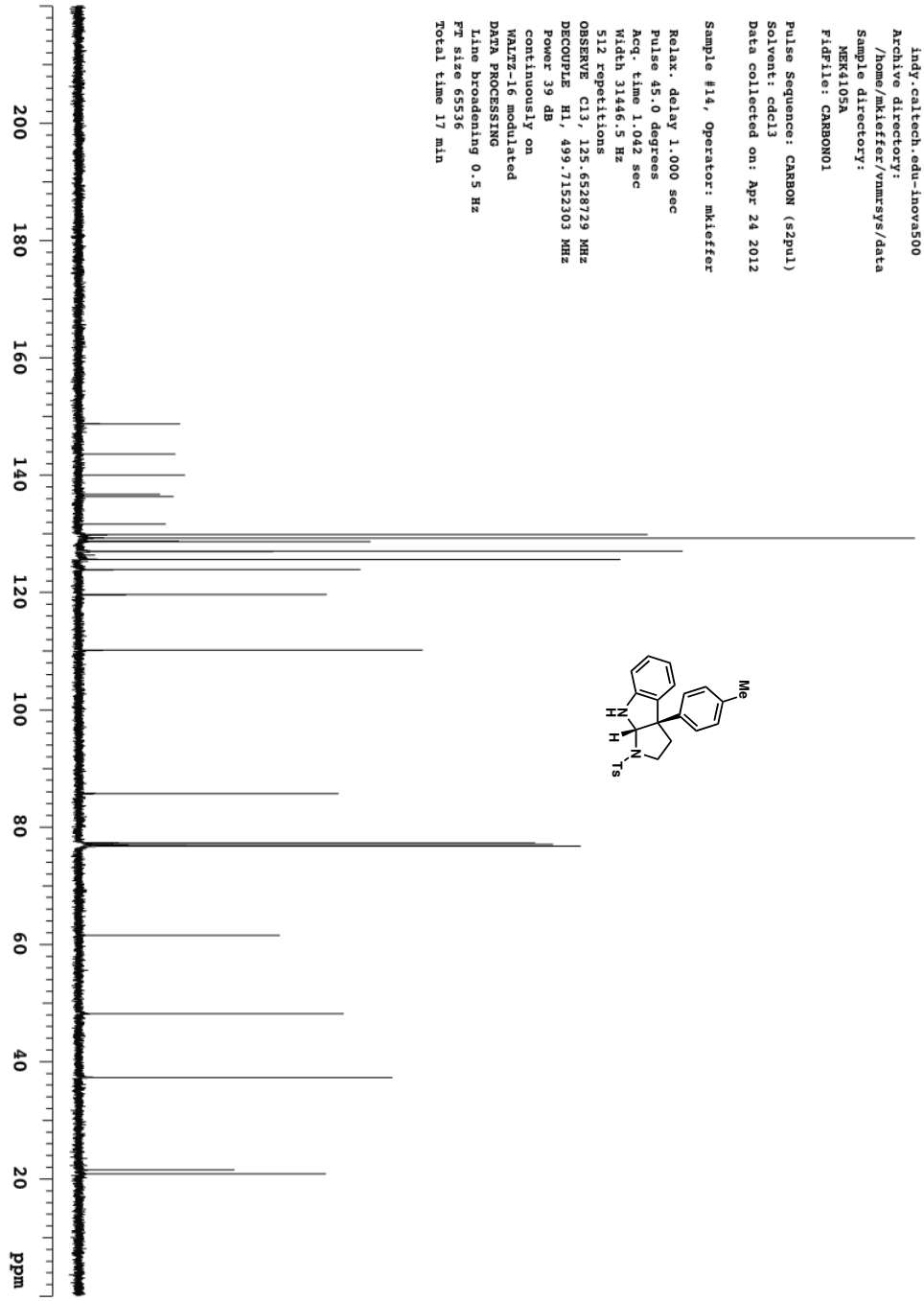

Sample Name:
MEK4134-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4134-C
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012
Sample #40, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
1.99
2.02
2.10
1.65
5.07
1.01
3.00
1.00
1.00
1.00
1.02
1.00
1.02
1.03
2.97
0.98
0.98
Ph
Bn
H
Ts
10
9
8
7
6
5
4
3
2
1
ppm

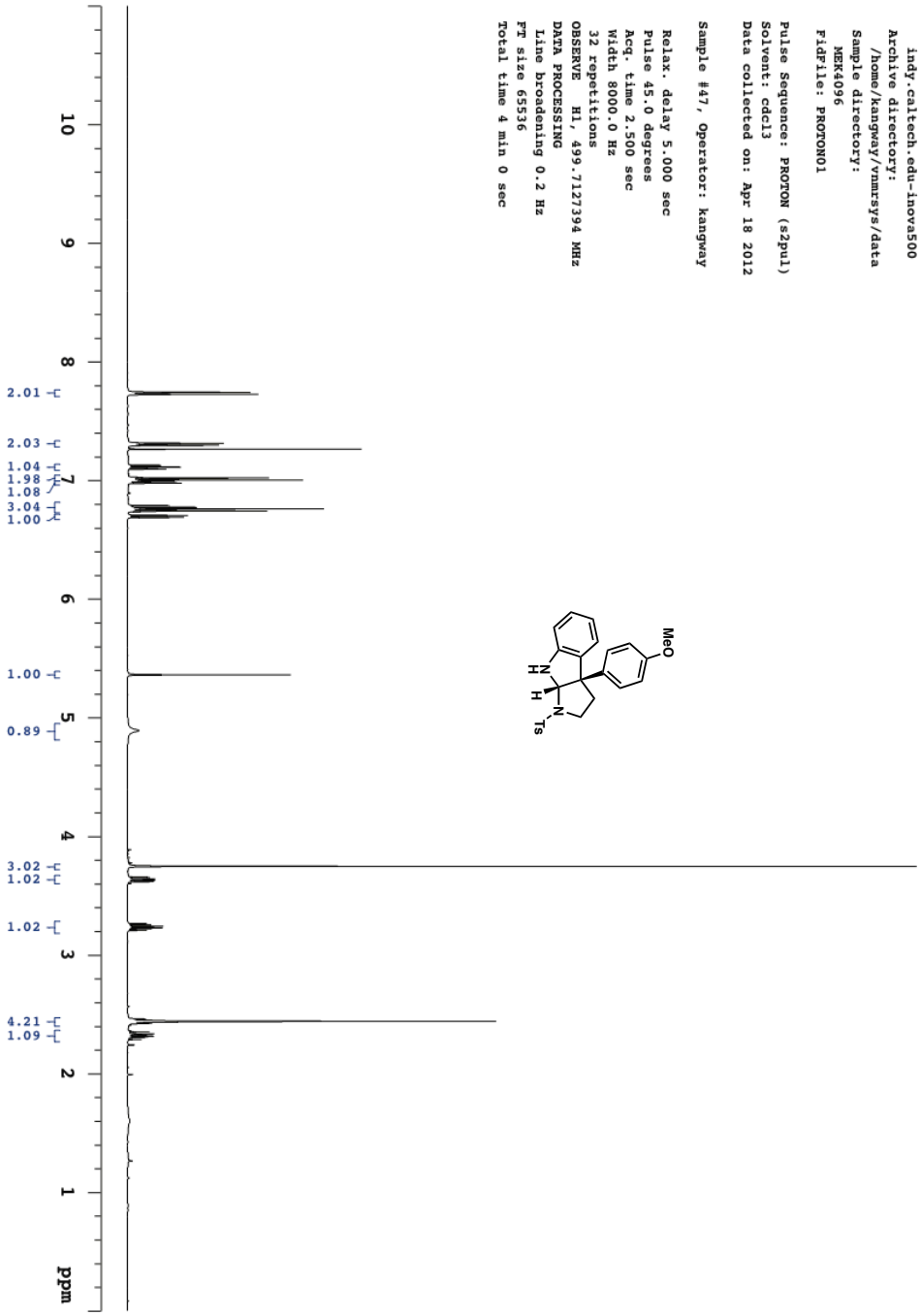

Sample Name:
MEK4134-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4134-C
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jun 12 2012
Sample #40, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528767 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Ph
Bn
H
Ts
200
180
160
140
120
100
80
60
40
20
ppm

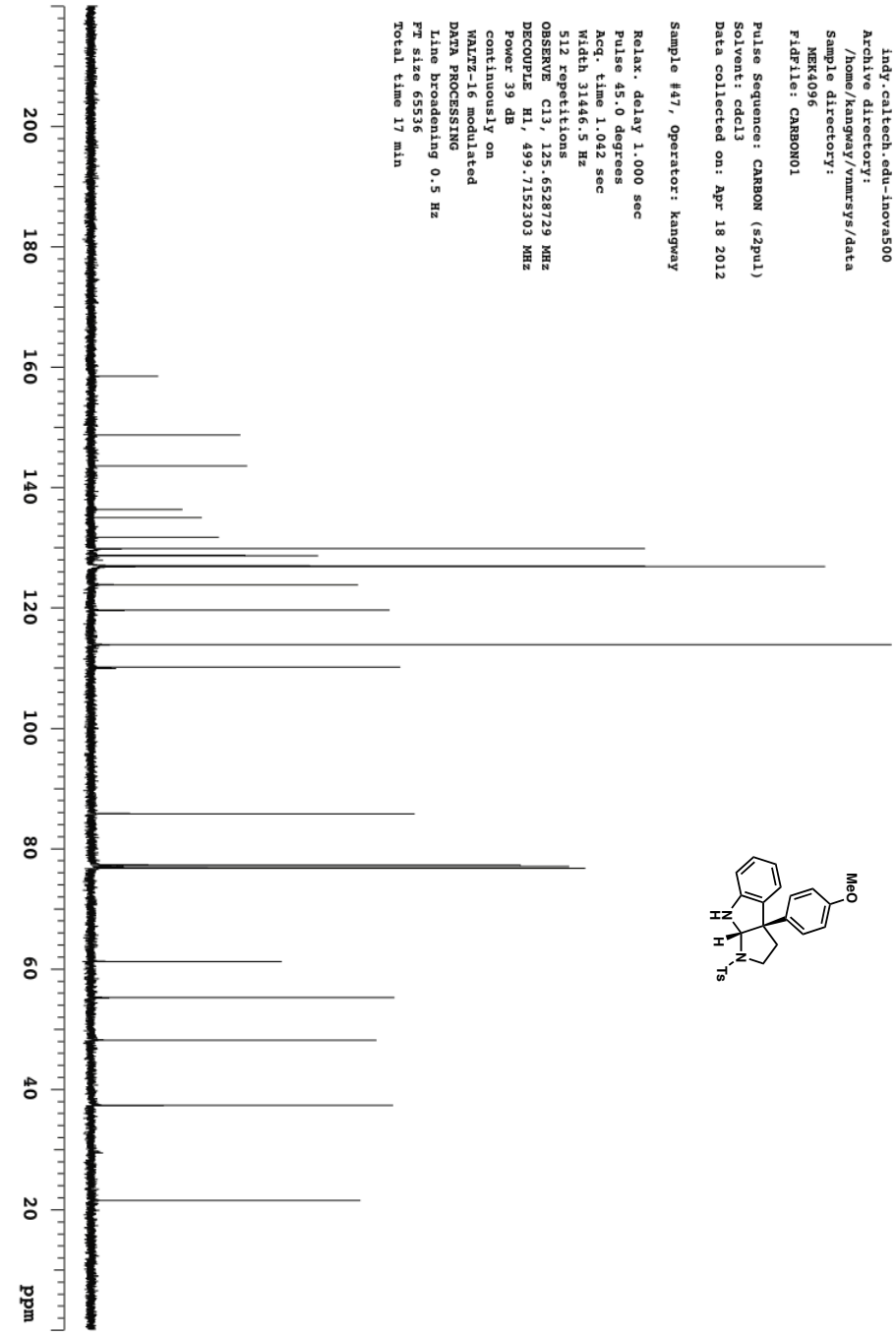

Sample Name:
MEK4112-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4112-B
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 25 2012
Sample #11, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.01
2.09
2.87
1.28
1.01
1.00
1.02
0.97
1.00
1.02
1.03
1.03
4.04
2.98
10
9
8
7
6
5
4
3
2
1
ppm
H
N
H
N
Ts
Me

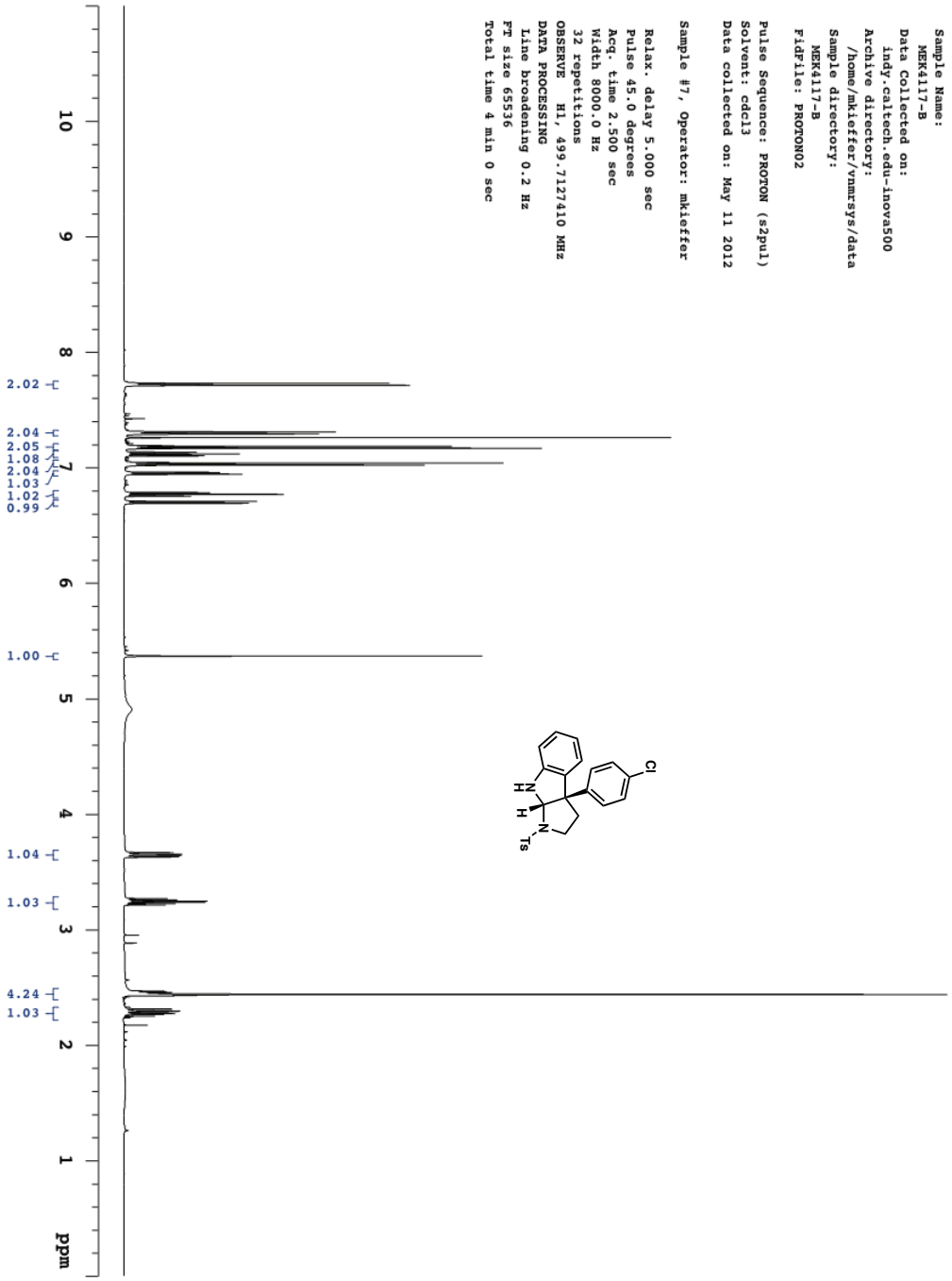

Sample Name:
MEK4112-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4112-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 25 2012
Sample #11, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528787 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
H
H
N
Ts
Me
200
180
160
140
120
100
80
60
40
20
ppm

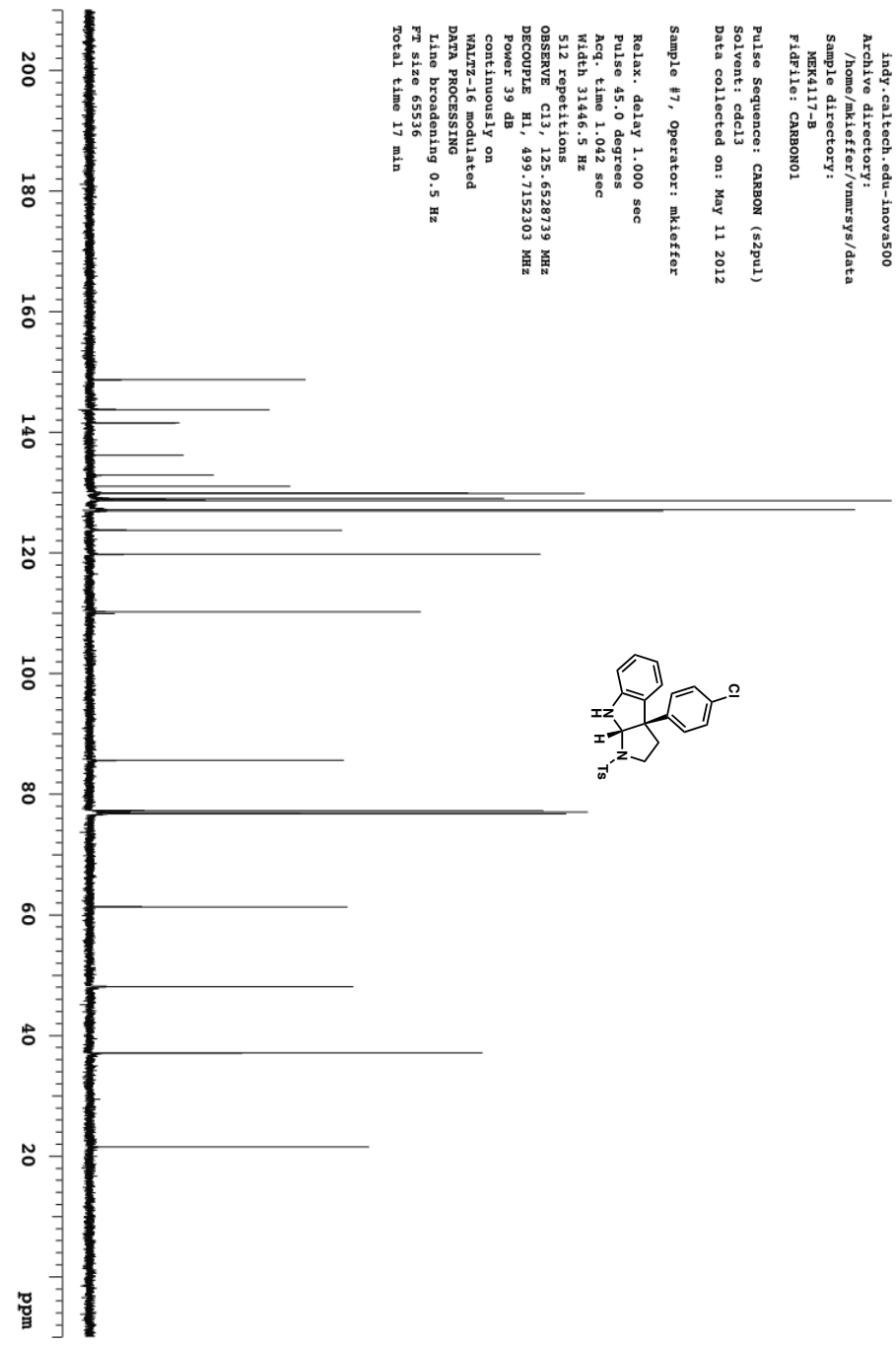

MEK4105A
Sample Name:
MEK4105A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4105A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 24 2012
Sample #14, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.04
2.06
1.03
2.19
2.99
1.01
0.98
1.00
1.05
1.05
4.18
1.16
3.21
Me
Ts
10
9
8
7
6
5
4
3
2
1
ppm

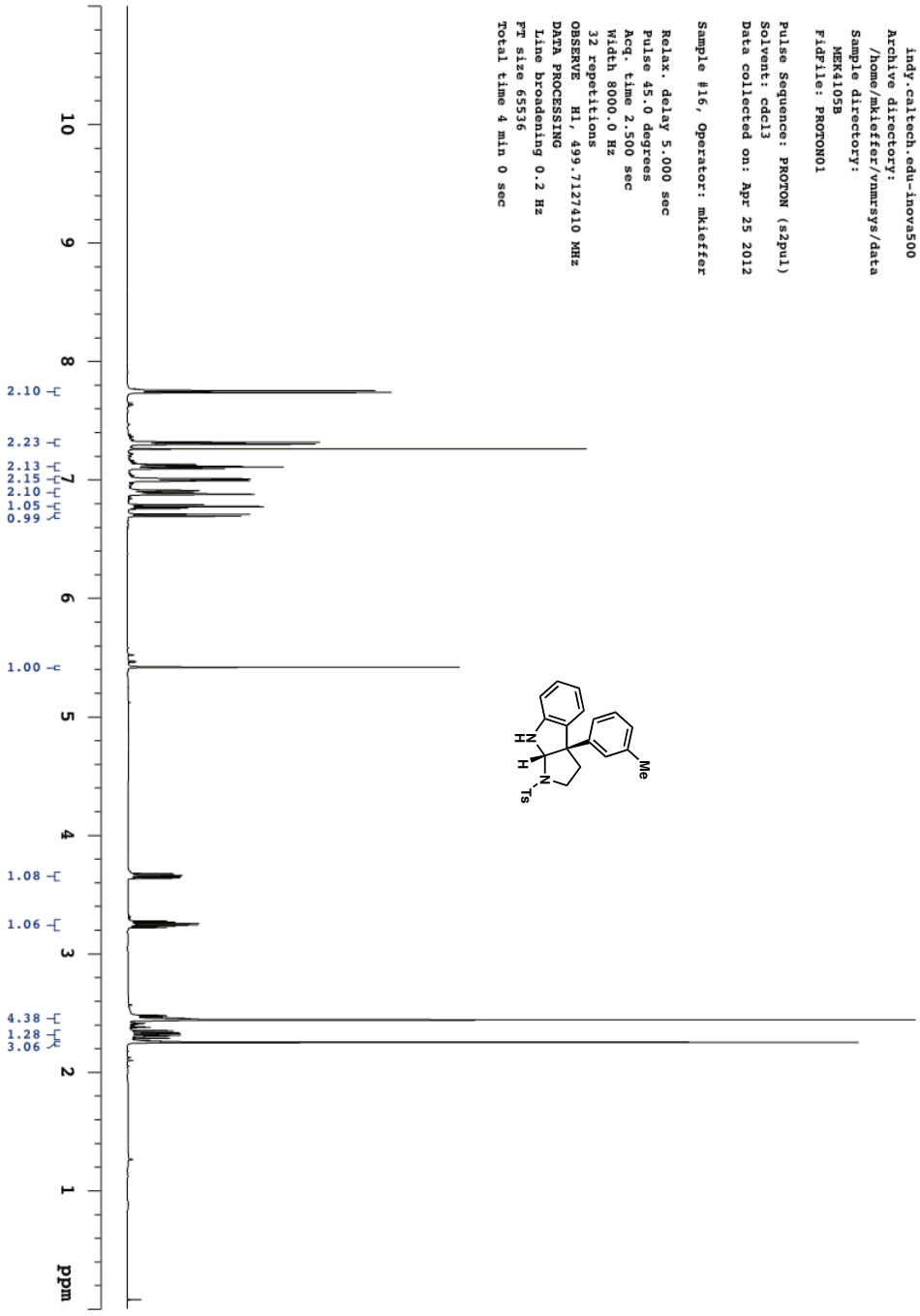

MEK4105A
Sample Name:
MEK4105A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4105A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 24 2012
Sample #14, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
N
H
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

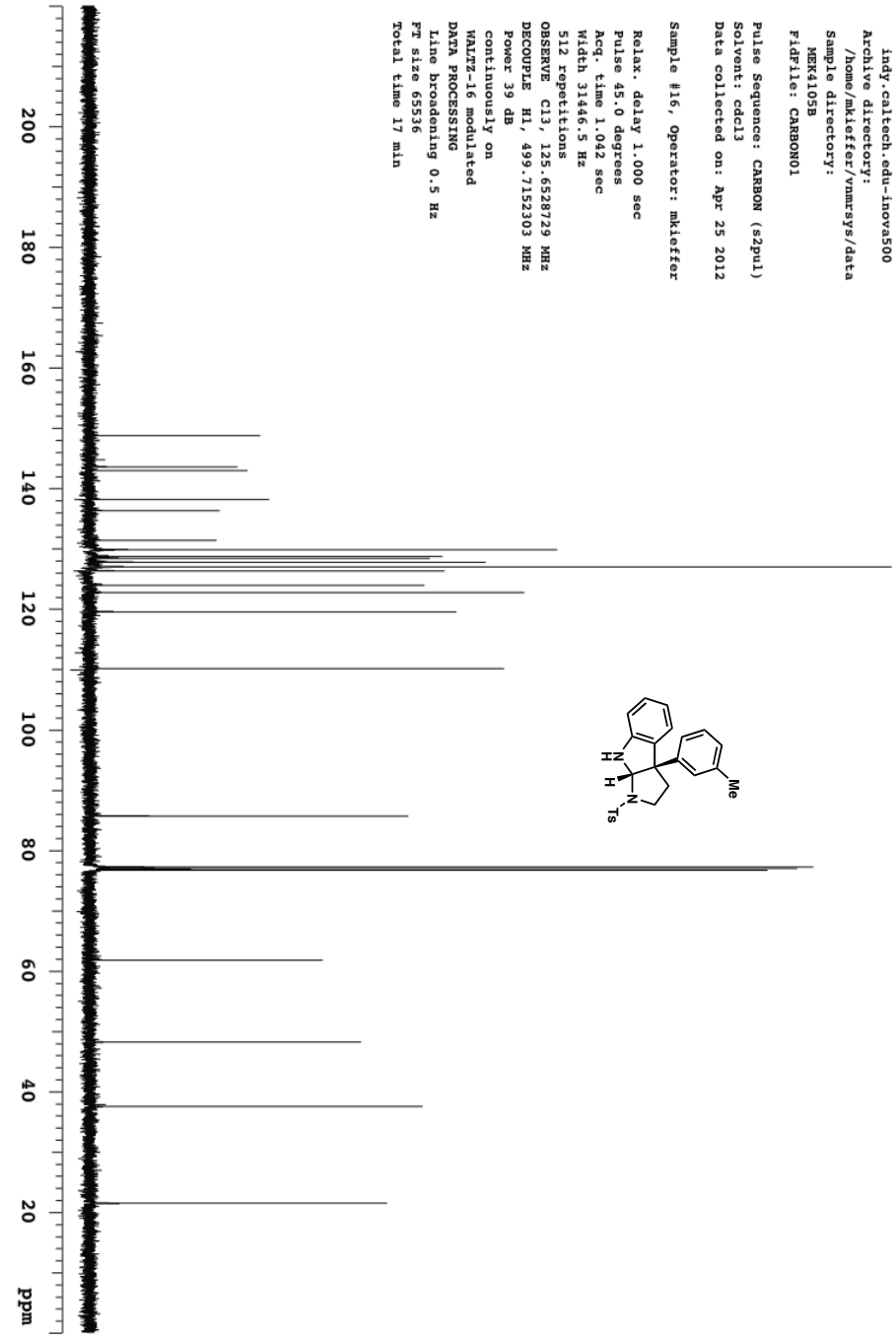

MEK4096
Sample Name:
MEK4096
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK4096
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 18 2012
Sample #47, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127394 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
MeO
Ts
2.01
2.03
1.04
1.98
1.08
3.04
1.00
1.00
0.89
3.02
1.02
1.02
4.21
1.09
10
9
8
7
6
5
4
3
2
1
ppm

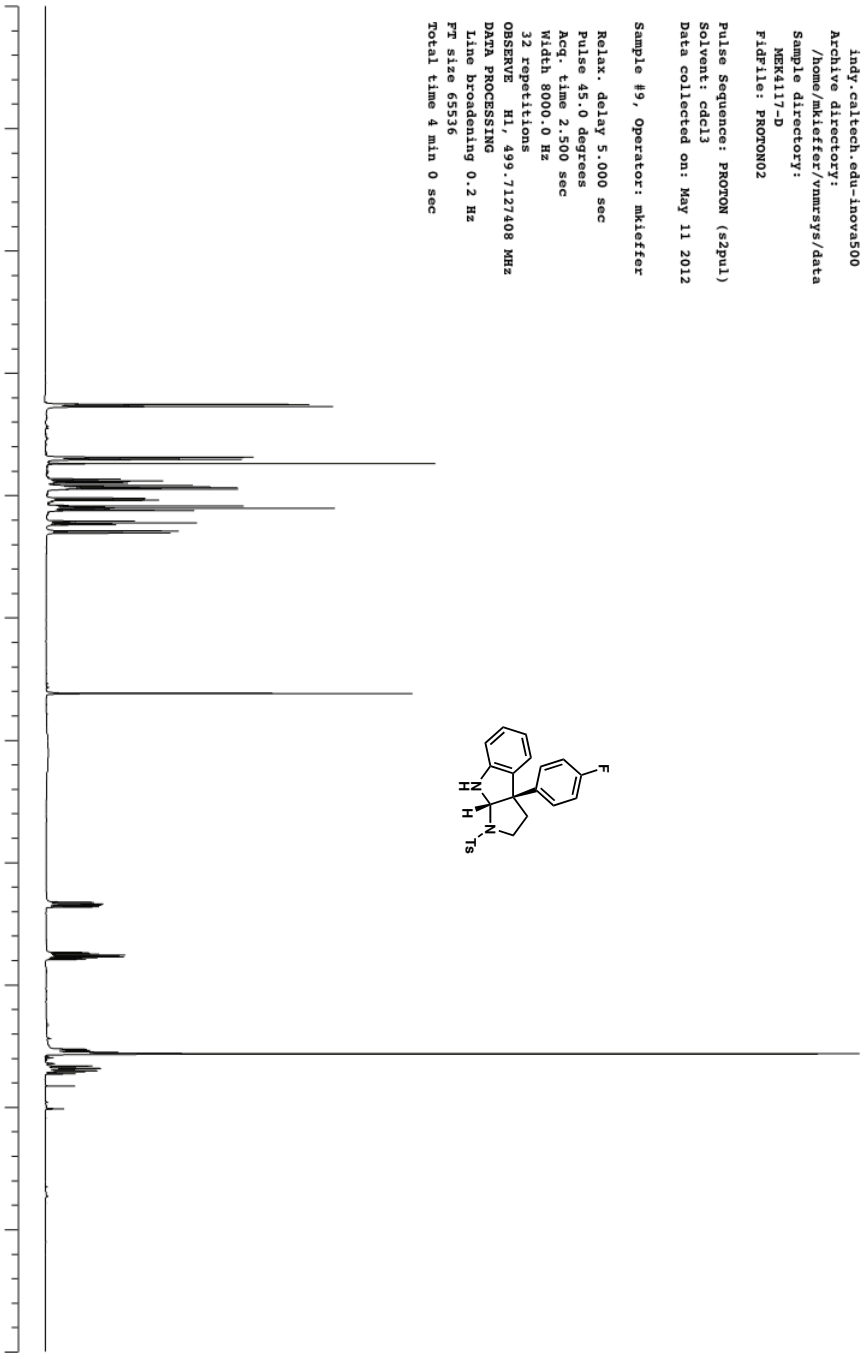

MEK4096
Sample Name:
MEK4096
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK4096
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 18 2012
Sample #47, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
MeO
Ts
200
180
160
140
120
100
80
60
40
20
ppm

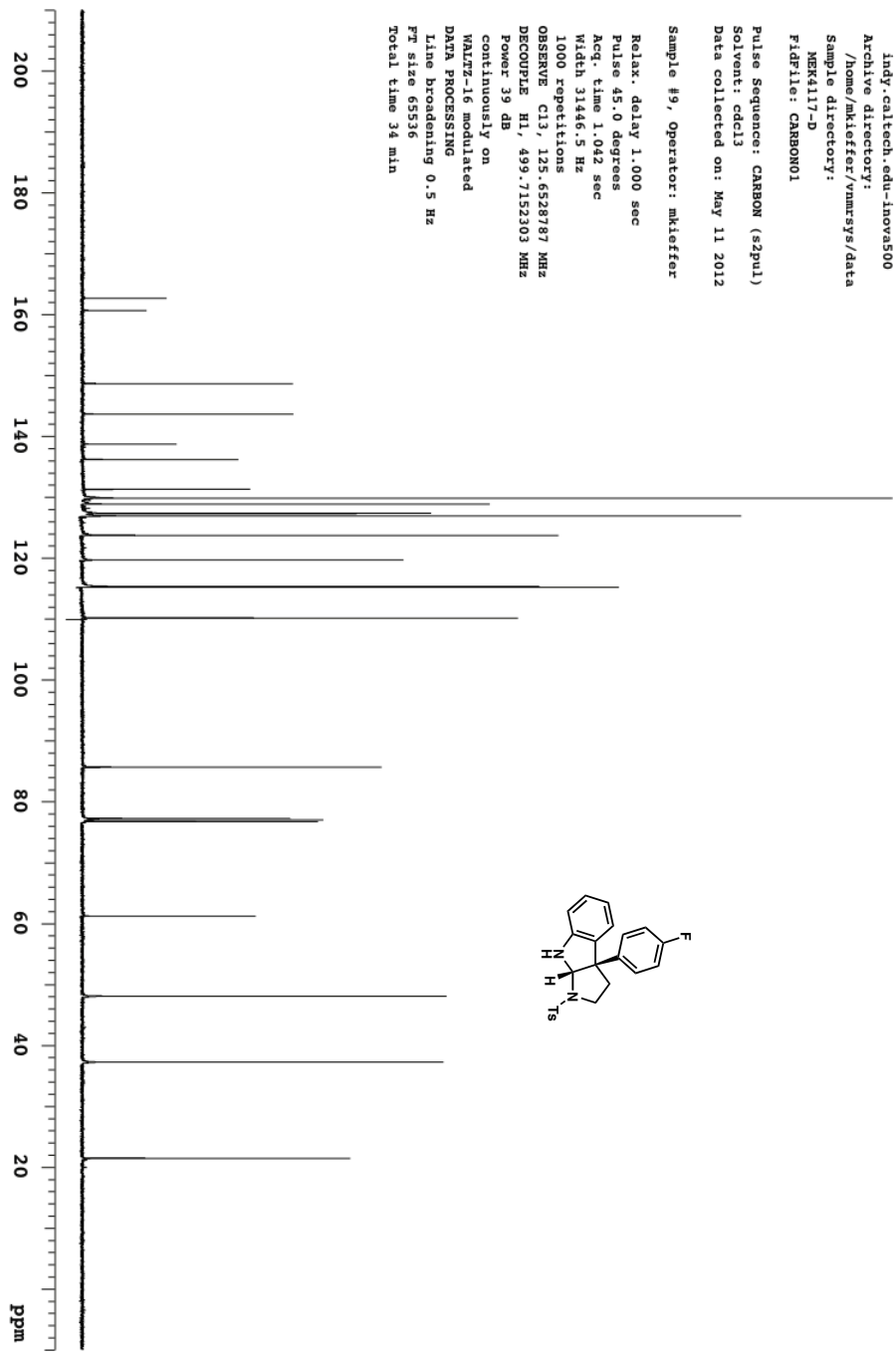

Sample Name:
MEK4117-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4117-B
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012
Sample #7, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.02
2.04
2.05
1.08
2.04
1.03
1.02
0.99
1.00
1.04
1.03
4.24
1.03
Cl
H
N
H
N
Ts
10
9
8
7
6
5
4
3
2
1
ppm

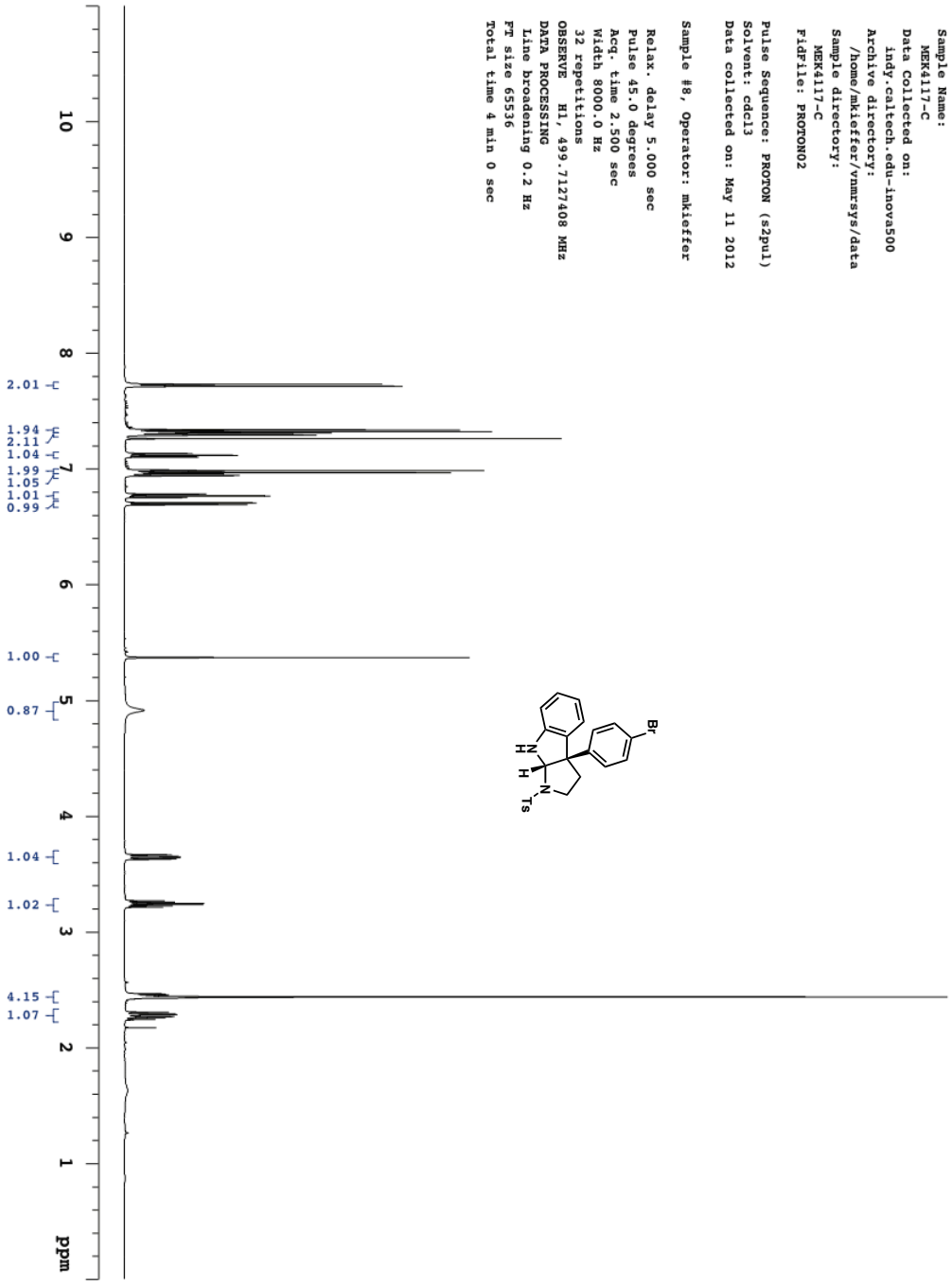

Sample Name:
MEK4117-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4117-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012
Sample #7, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528739 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Cl
H
N
H
N
Ts
200
180
160
140
120
100
80
60
40
20
ppm

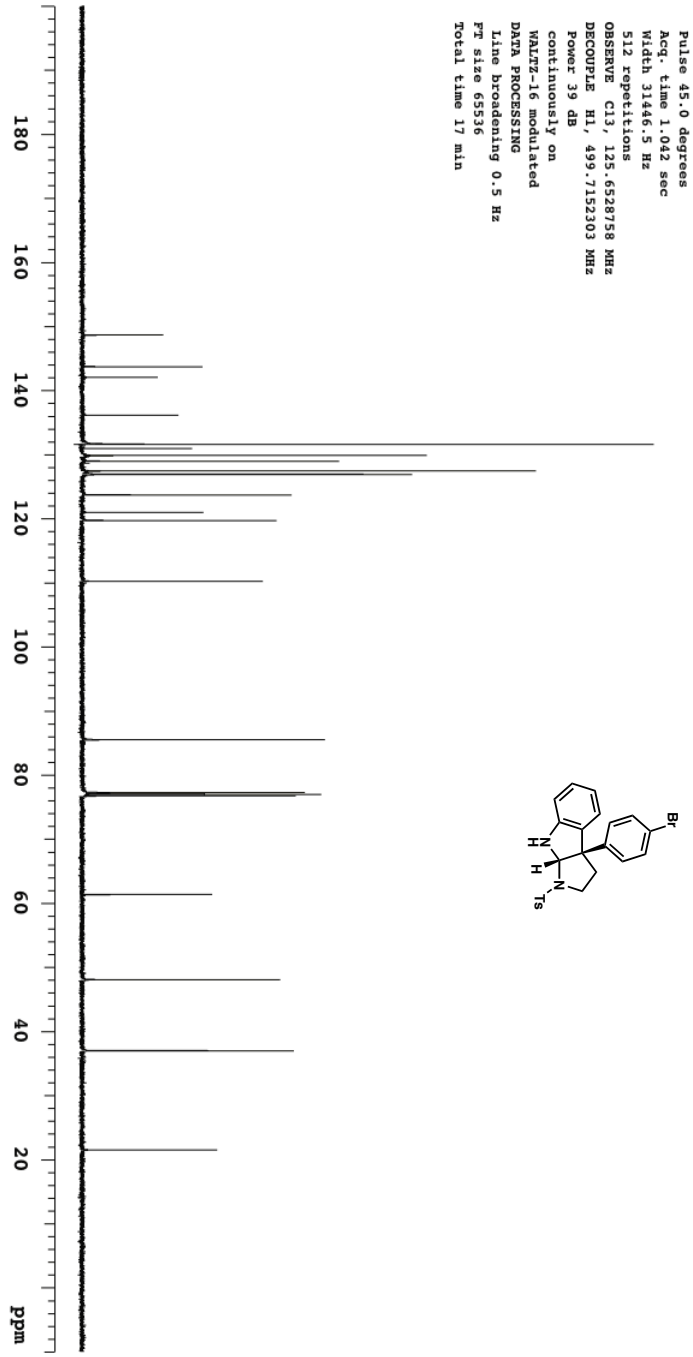

MEK4105B
Sample Name:
MEK4105B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4105B
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 25 2012
Sample #16, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.10
2.23
2.13
2.15
2.10
1.05
0.99
1.00
1.08
1.06
4.38
1.28
3.06
10
9
8
7
6
5
4
3
2
1
ppm
H
N
H
N
Ts
Me

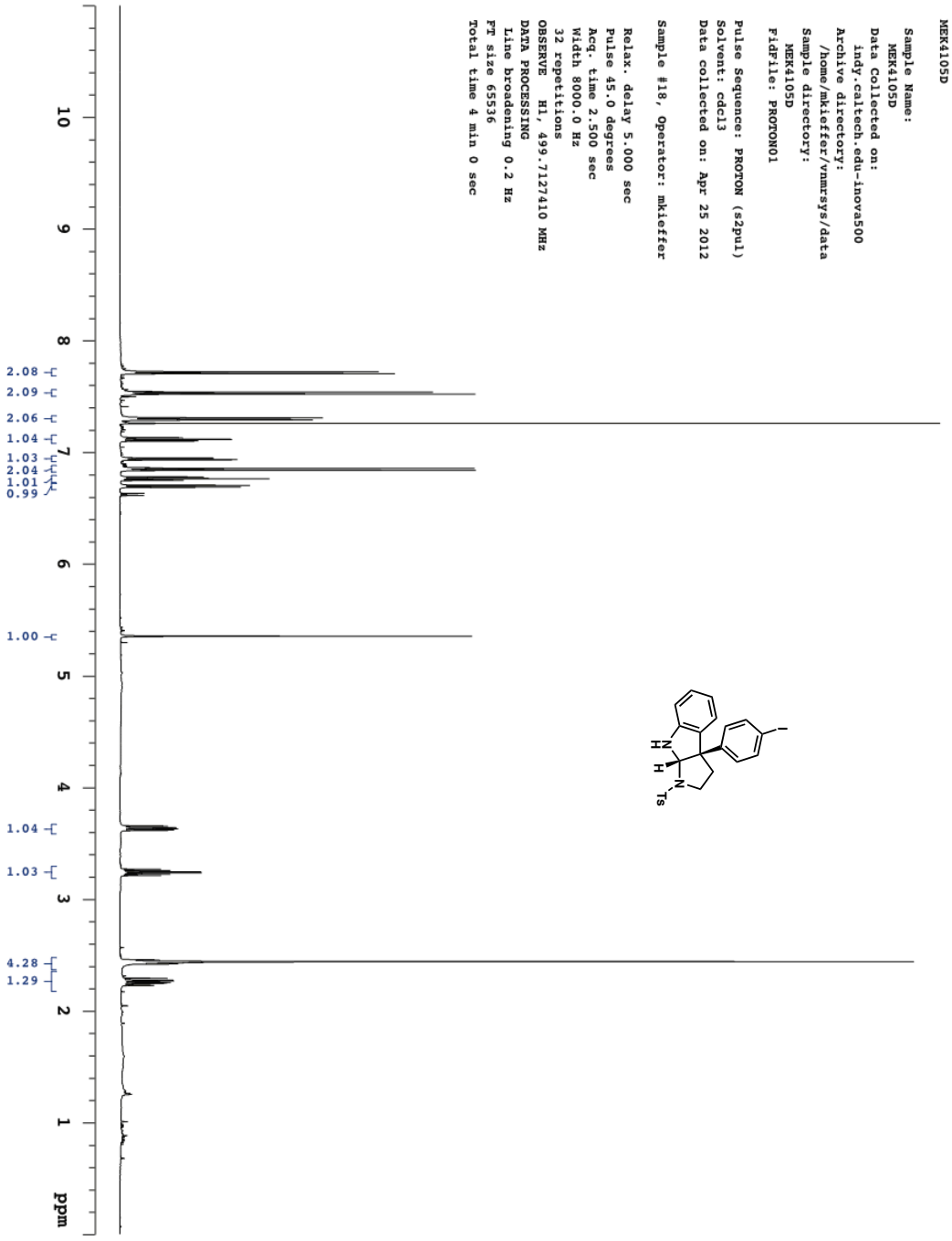

MEK4105B
Sample Name:
MEK4105B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4105B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 25 2012
Sample #16, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528729 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Ts
200
180
160
140
120
100
80
60
40
20
ppm

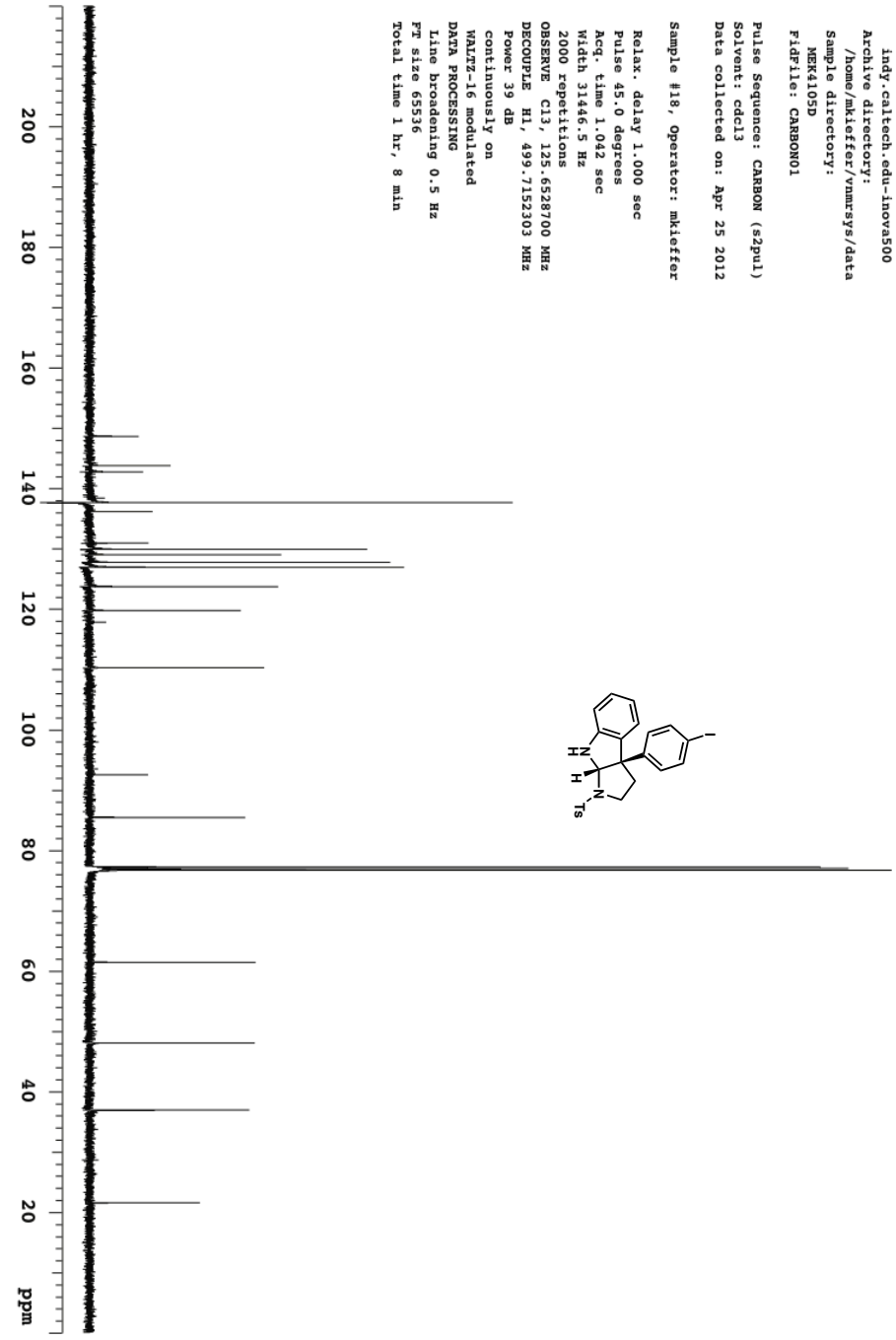

Sample Name:
MEK4117-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4117-D
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012
Sample #9, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
10
9
8
7
6
5
4
3
2
1
ppm
F
H
N
H
N
Ts

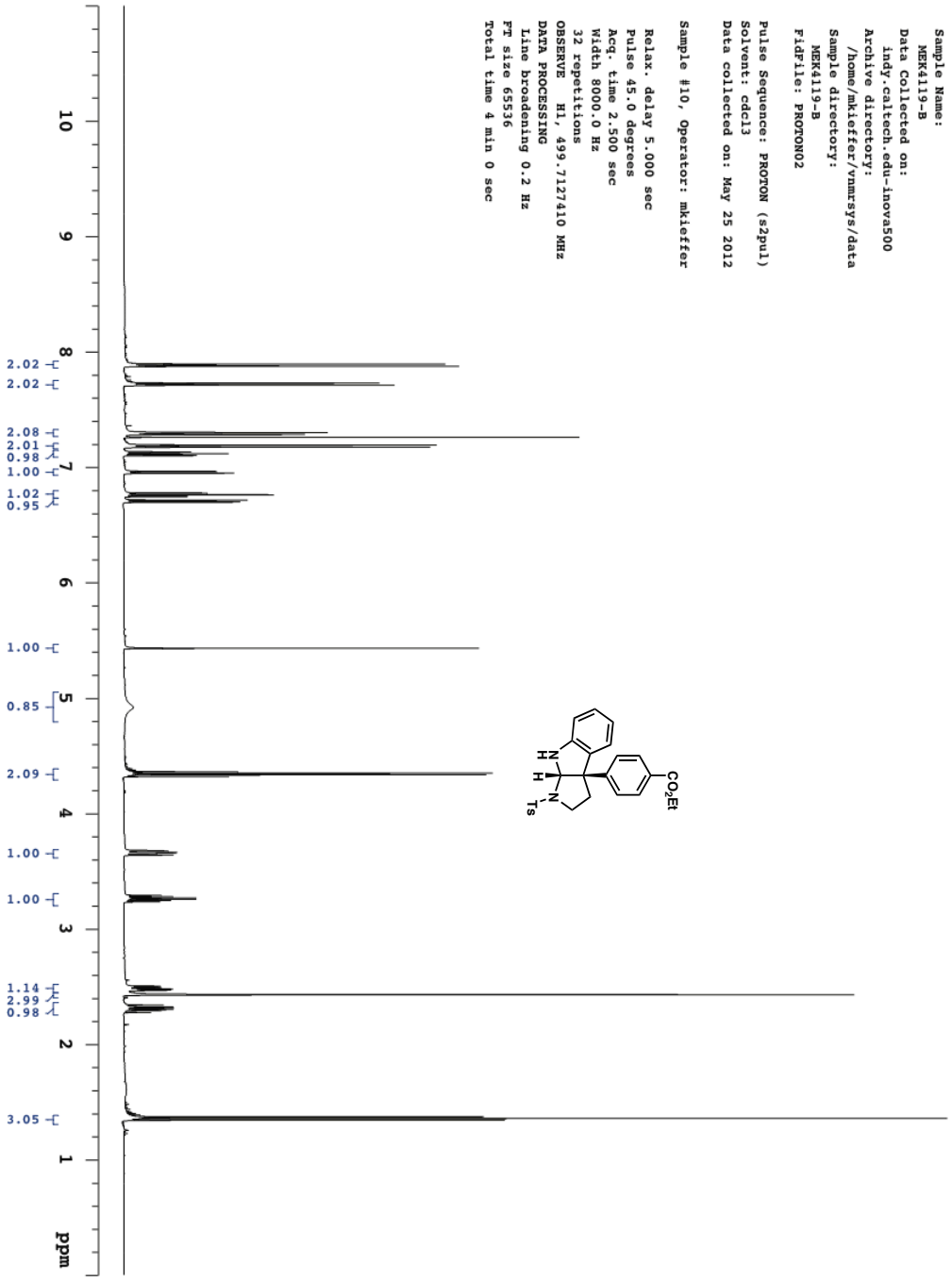

Sample Name:
MEK4117-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4117-D
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012
Sample #9, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6528787 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
200
180
160
140
120
100
80
60
40
20
ppm
F
H
N
H
N
Ts

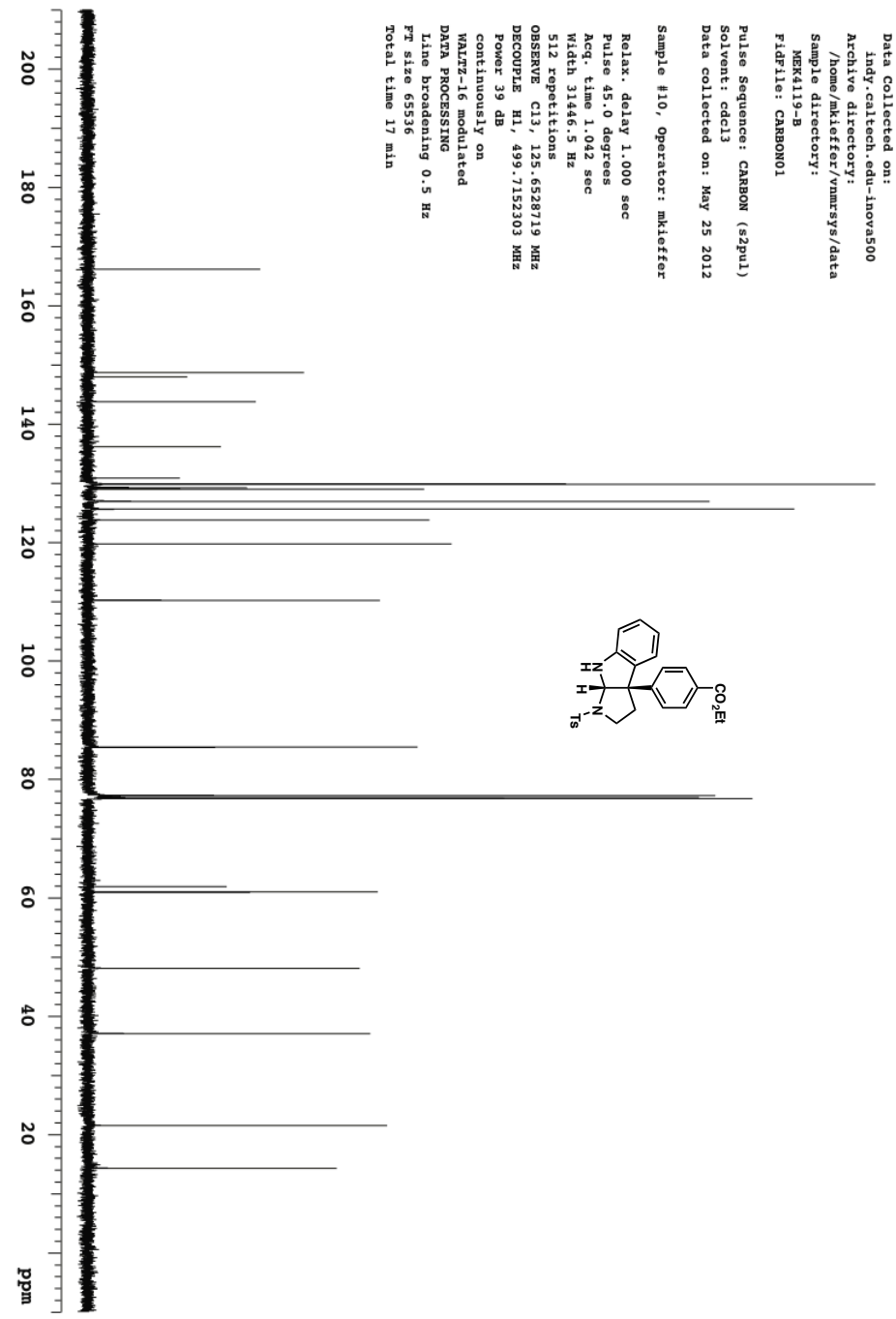

Sample Name:
MEK4117-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4117-C
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012
Sample #8, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127408 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.01
1.94
2.11
1.04
1.99
1.05
1.01
0.99
1.00
0.87
1.04
1.02
4.15
1.07
Br
N
H
H
N
Ts
10
9
8
7
6
5
4
3
2
1
ppm

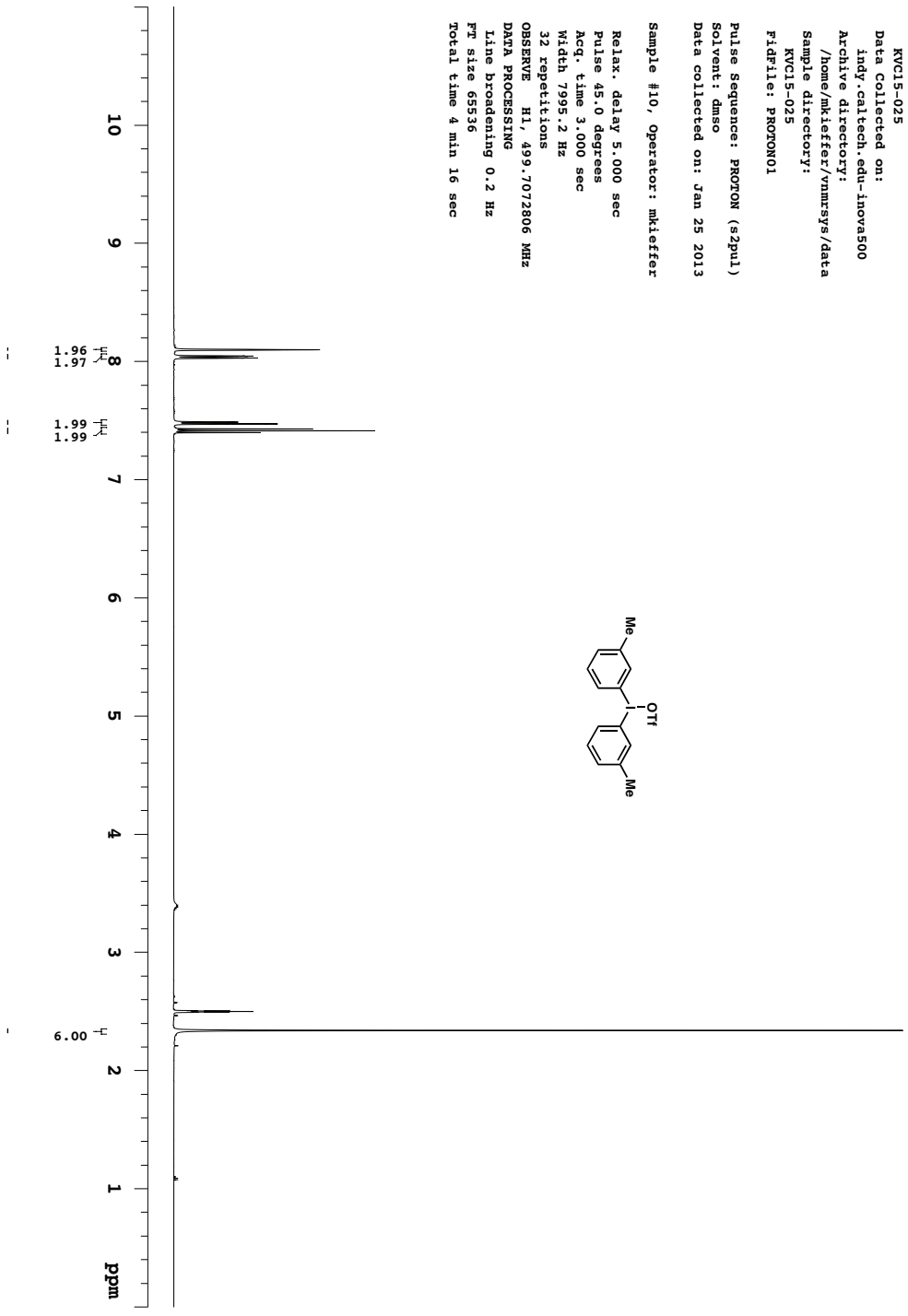

Sample Name:
MEK4117-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4117-C
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2012
Sample #8, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528758 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Br
H
N
H
N
Ts
180
160
140
120
100
80
60
40
20
ppm

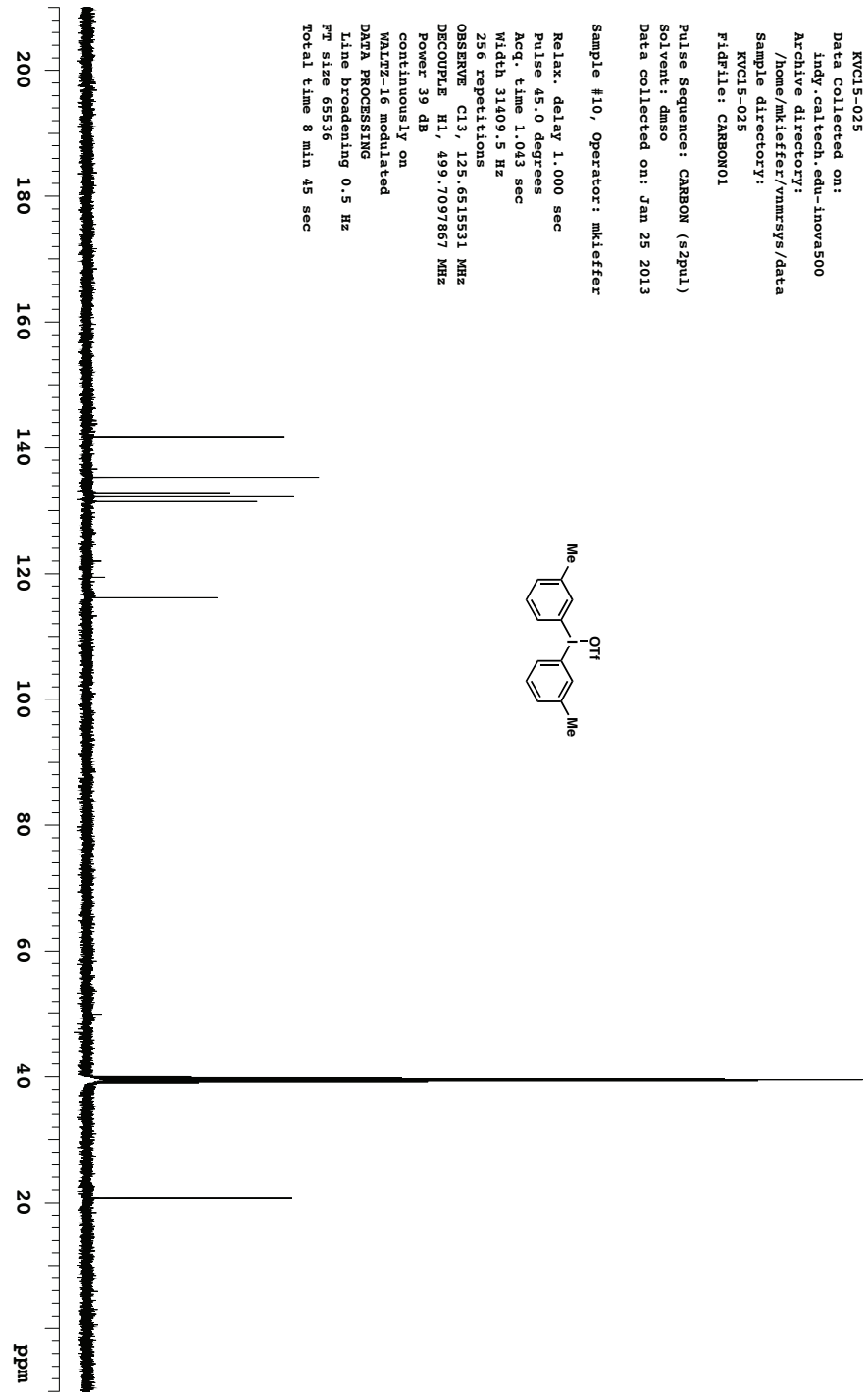

MEK4105D
Sample Name:
MEK4105D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4105D
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Apr 25 2012
Sample #18, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.08
2.09
2.06
1.04
1.03
2.04
1.01
0.99
1.00
1.04
1.03
4.28
1.29
10
9
8
7
6
5
4
3
2
1
ppm
H
N
H
N
Ts

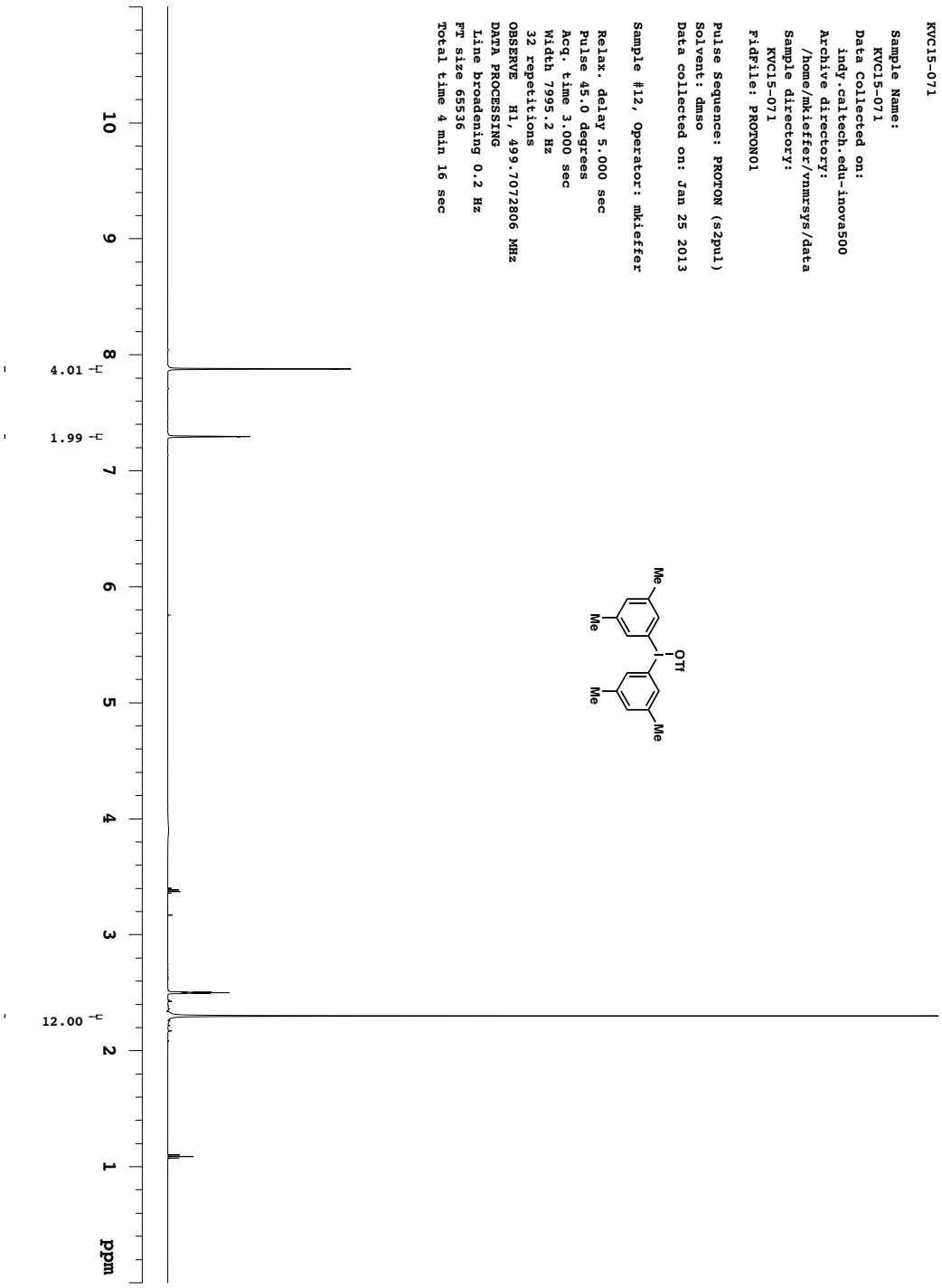

MEK4105D
Sample Name:
MEK4105D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4105D
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Apr 25 2012
Sample #18, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6528700 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
200
180
160
140
120
100
80
60
40
20
ppm
H
N
H
N
Ts
I

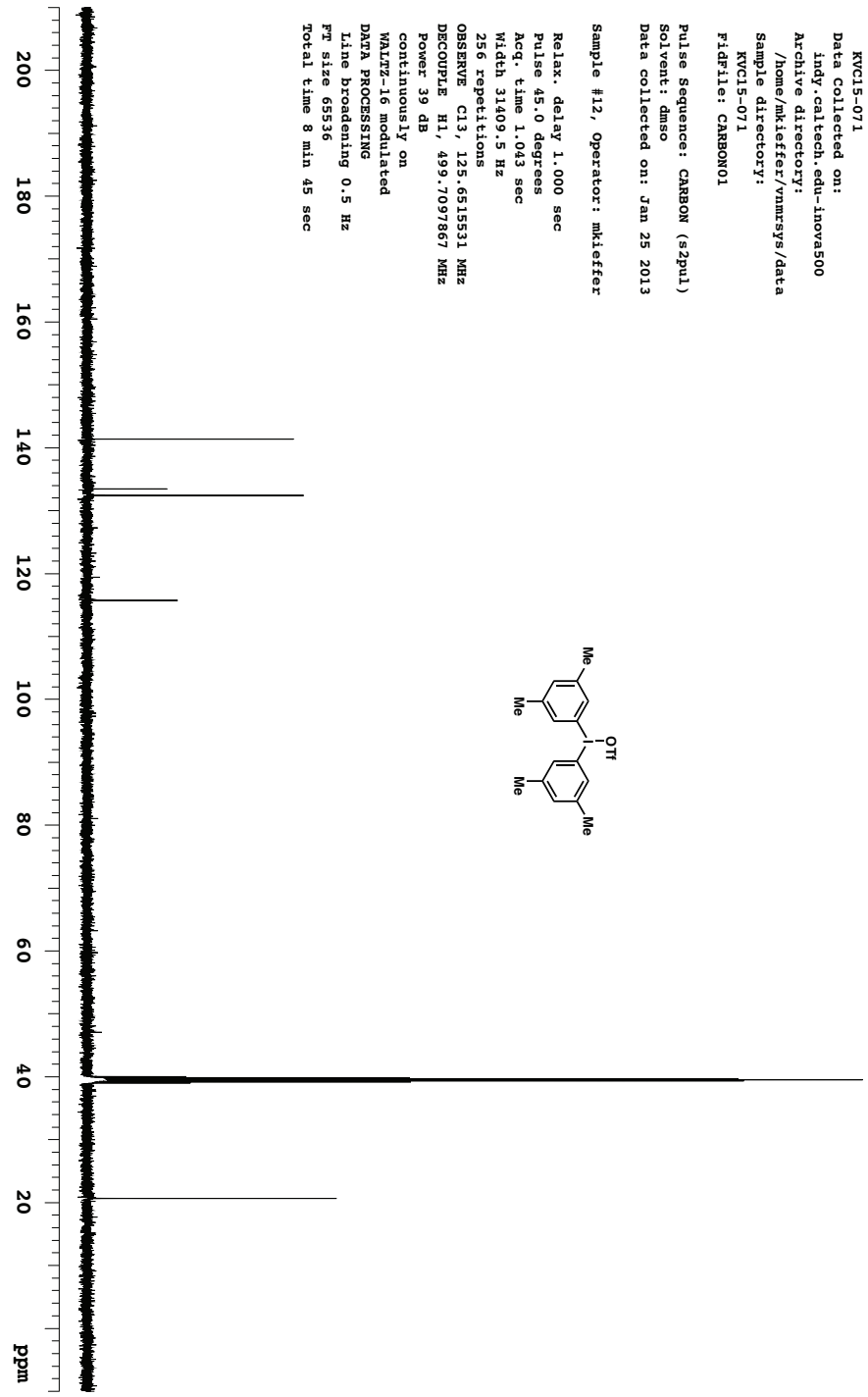

Sample Name:
MEK4119-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4119-B
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 25 2012
Sample #10, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7127410 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
2.02
2.02
2.08
2.01
0.98
1.00
1.02
0.95
1.00
0.85
2.09
1.00
1.00
1.14
2.99
0.98
3.05
Ts
CO2Et
ppm

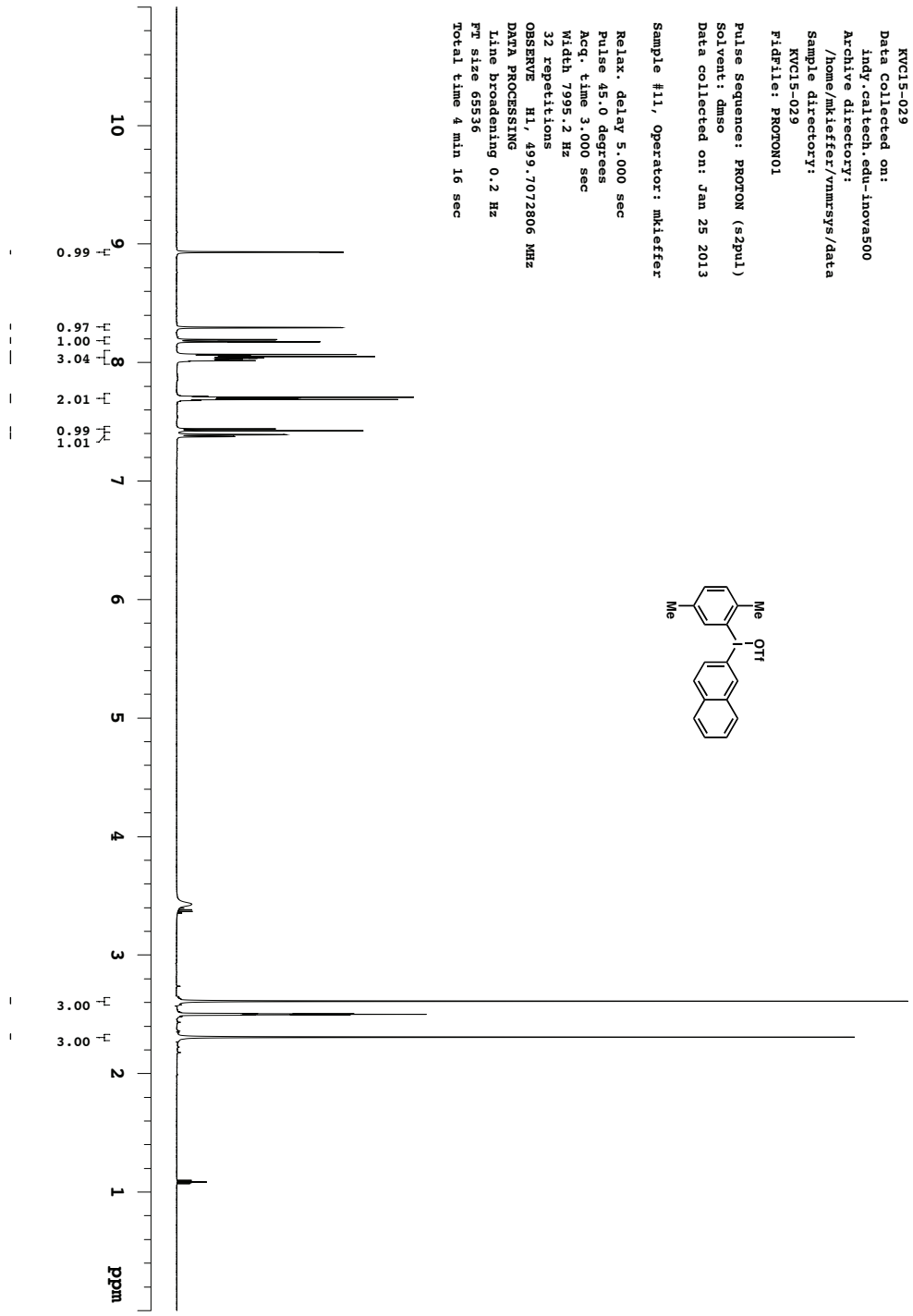

Sample Name:
MEK4119-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK4119-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 25 2012
Sample #10, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6528719 MHz
DECOUPLE H1, 499.7152303 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
200
180
160
140
120
100
80
60
40
20
ppm
N
H
H
N
Ts
CO2Et

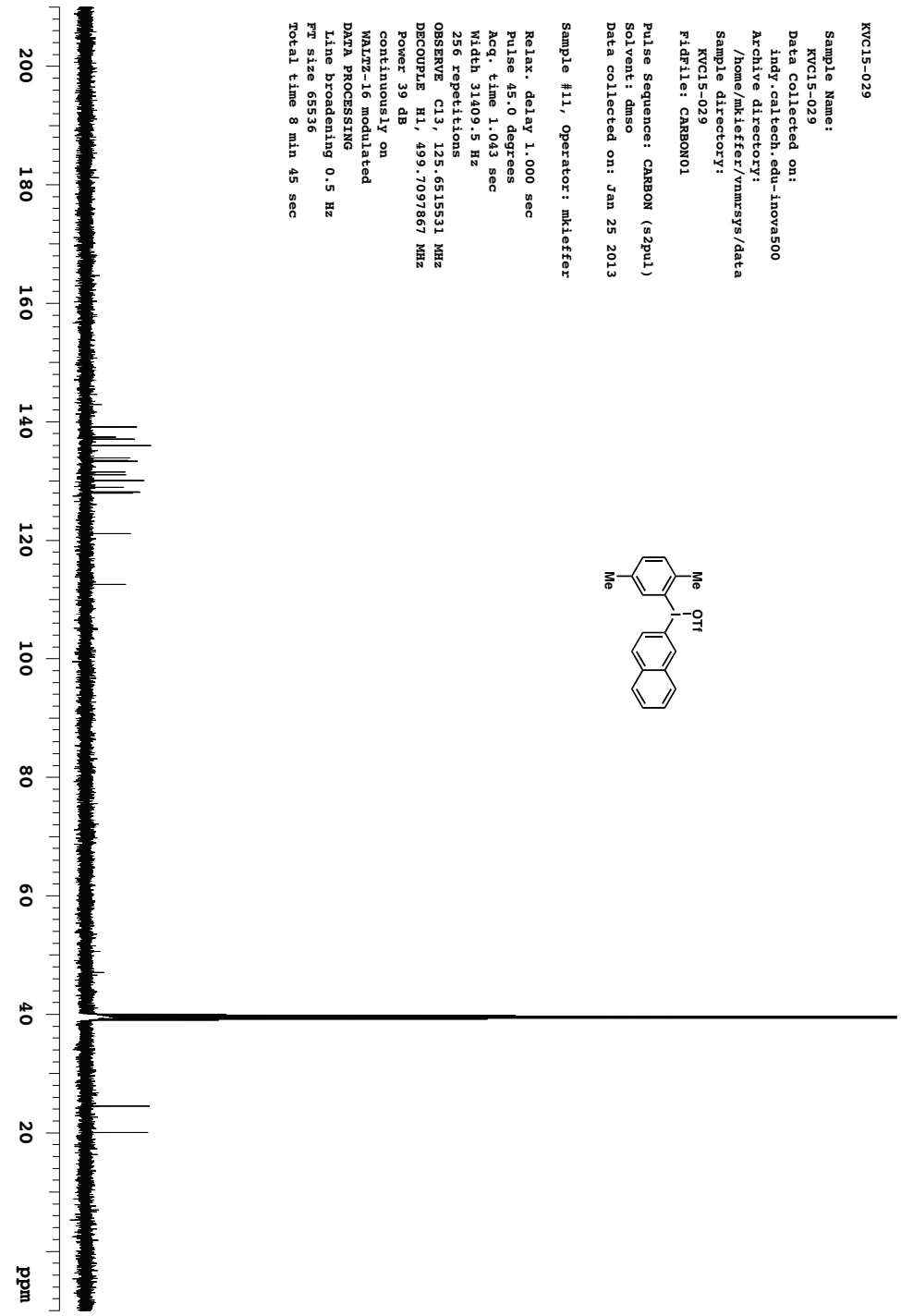

KVC15-025
Sample Name:
KVC15-025
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-025
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Jan 25 2013
Sample #10, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7072806 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Me
OTf
Me
1.96
1.97
1.99
1.99
6.00
10
9
8
7
6
5
4
3
2
1
ppm

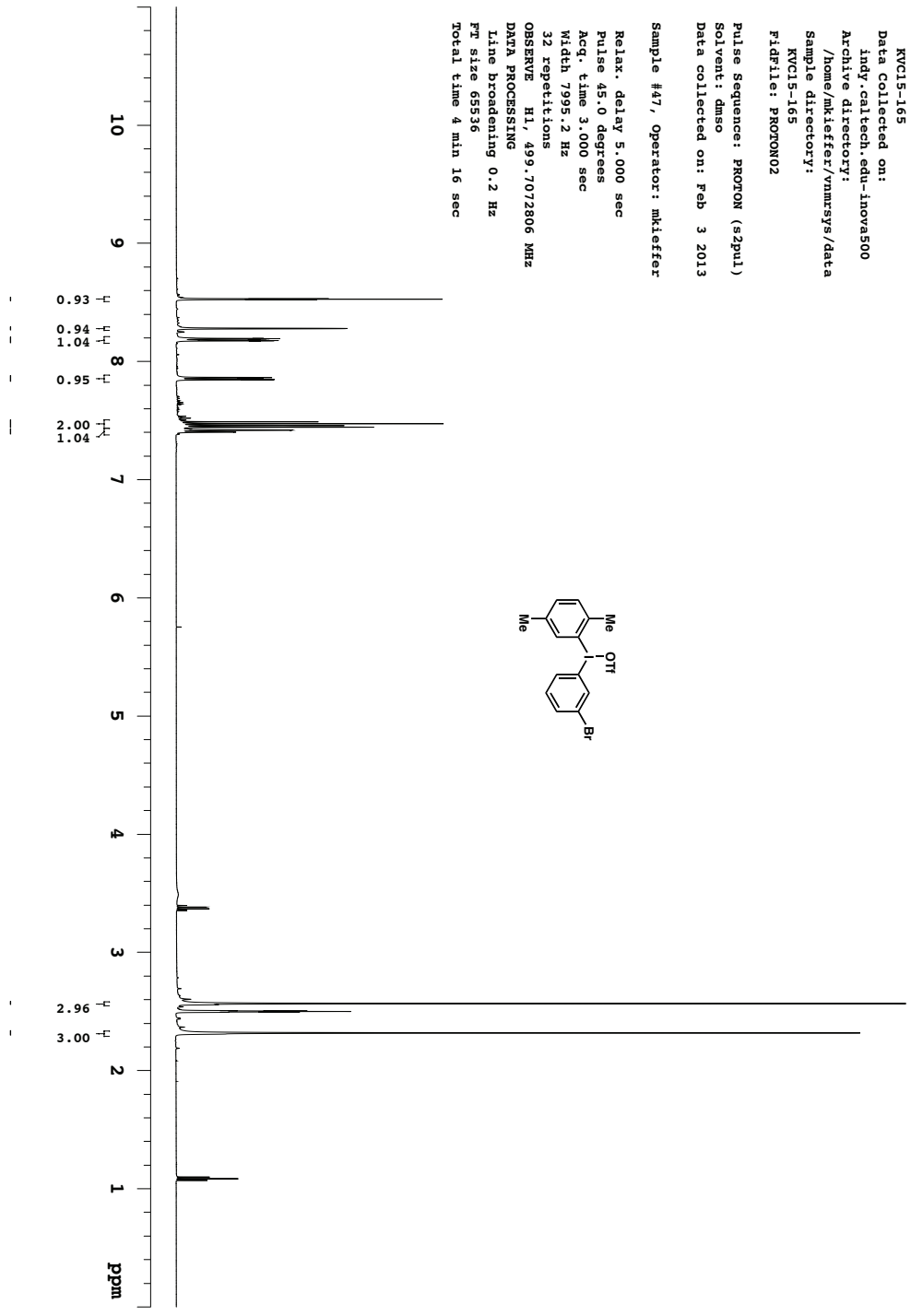

KVC15-025
Sample Name:
KVC15-025
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-025
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Jan 25 2013
Sample #10, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
256 repetitions
OBSERVE C13, 125.6515531 MHz
DECOUPLE H1, 499.7097867 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
Me
OTf
Me
200
180
160
140
120
100
80
60
40
20
ppm

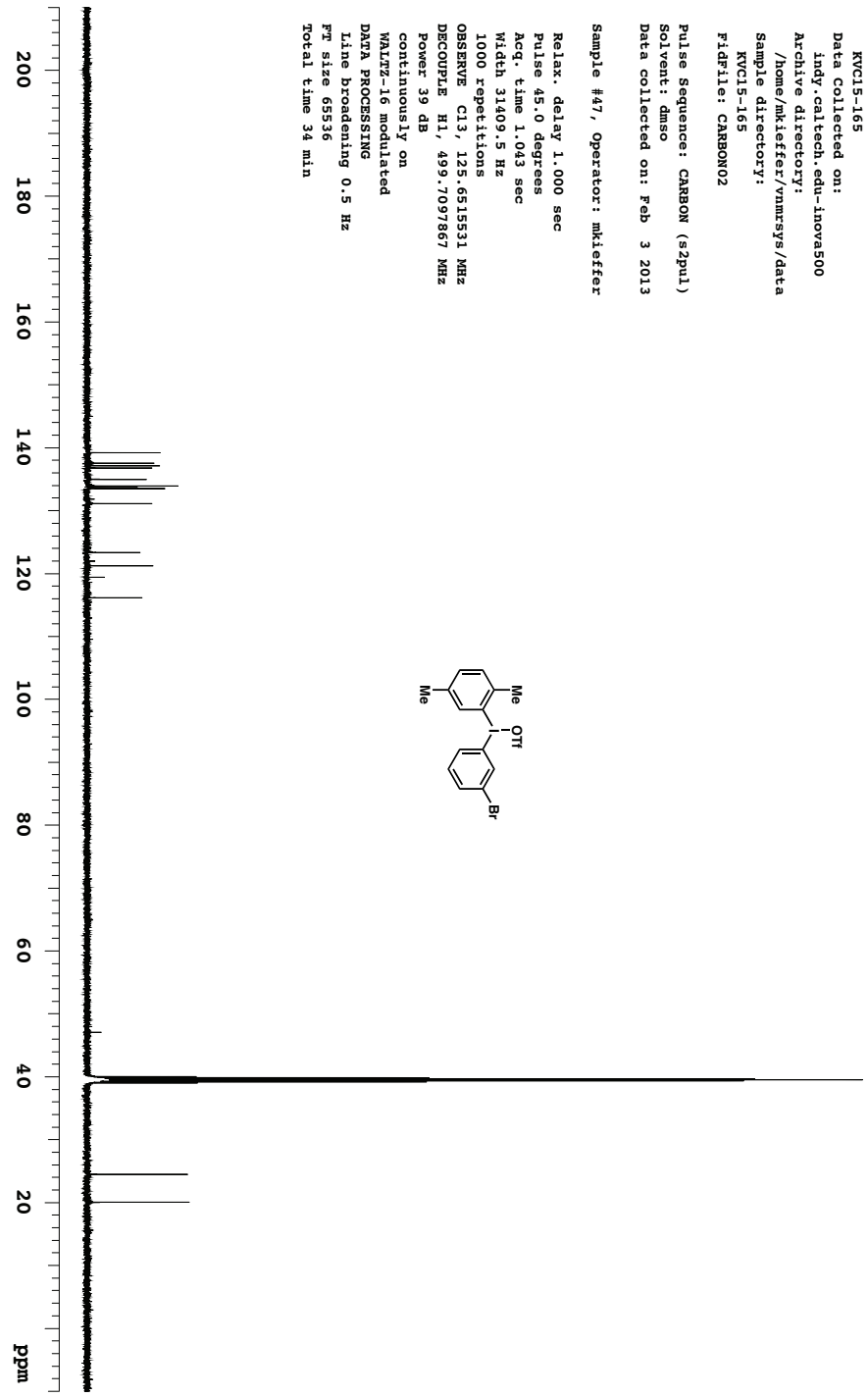

KVC15-071
Sample Name:
KVC15-071
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-071
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Jan 25 2013
Sample #12, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7072806 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Me
Me
Me
Me
OTf
4.01
1.99
12.00
10
9
8
7
6
5
4
3
2
1
ppm

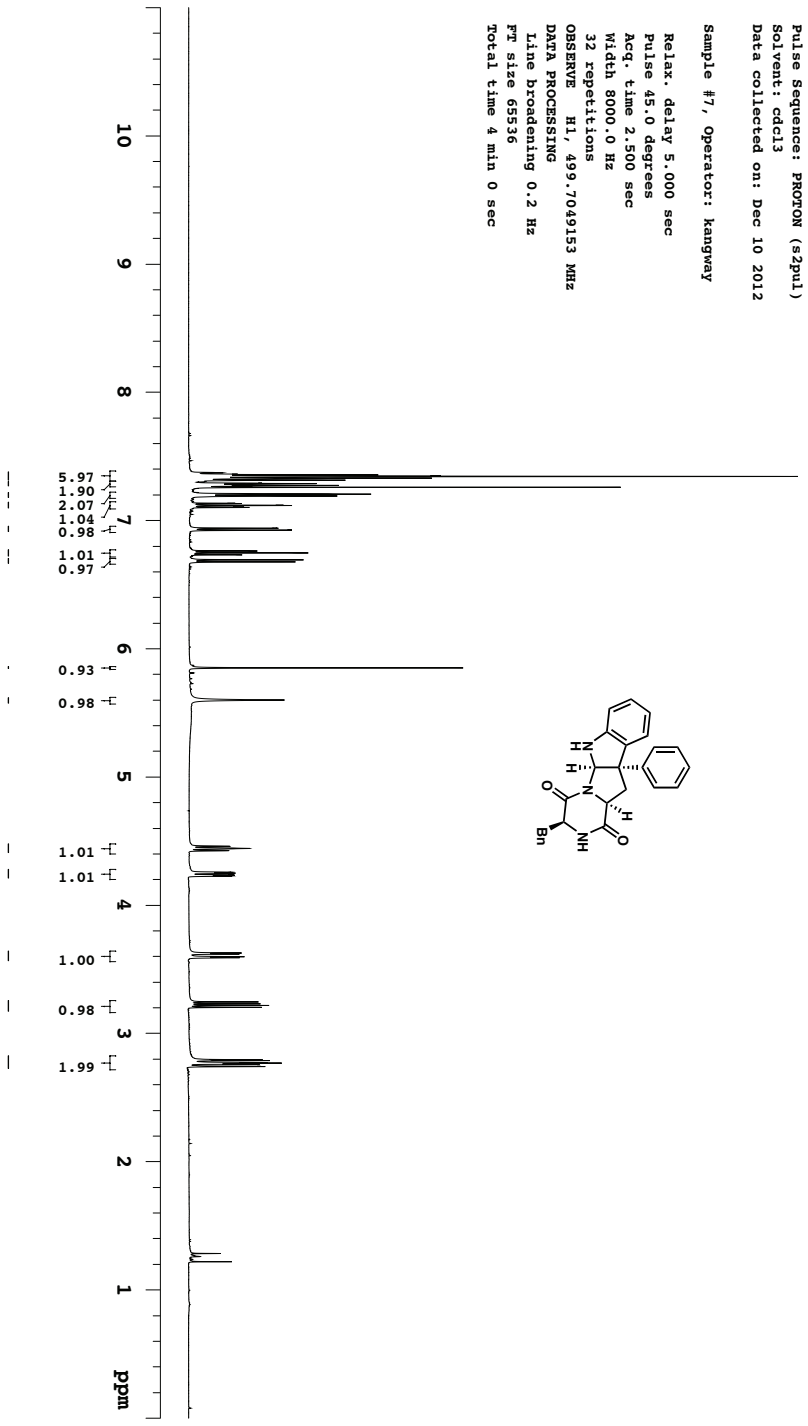

KVC15-071
Sample Name:
KVC15-071
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-071
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Jan 25 2013
Sample #12, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
256 repetitions
OBSERVE C13, 125.6515531 MHz
DECOUPLE H1, 499.7097867 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
Me
Me
I
OTf
Me
Me
200
180
160
140
120
100
80
60
40
20
ppm

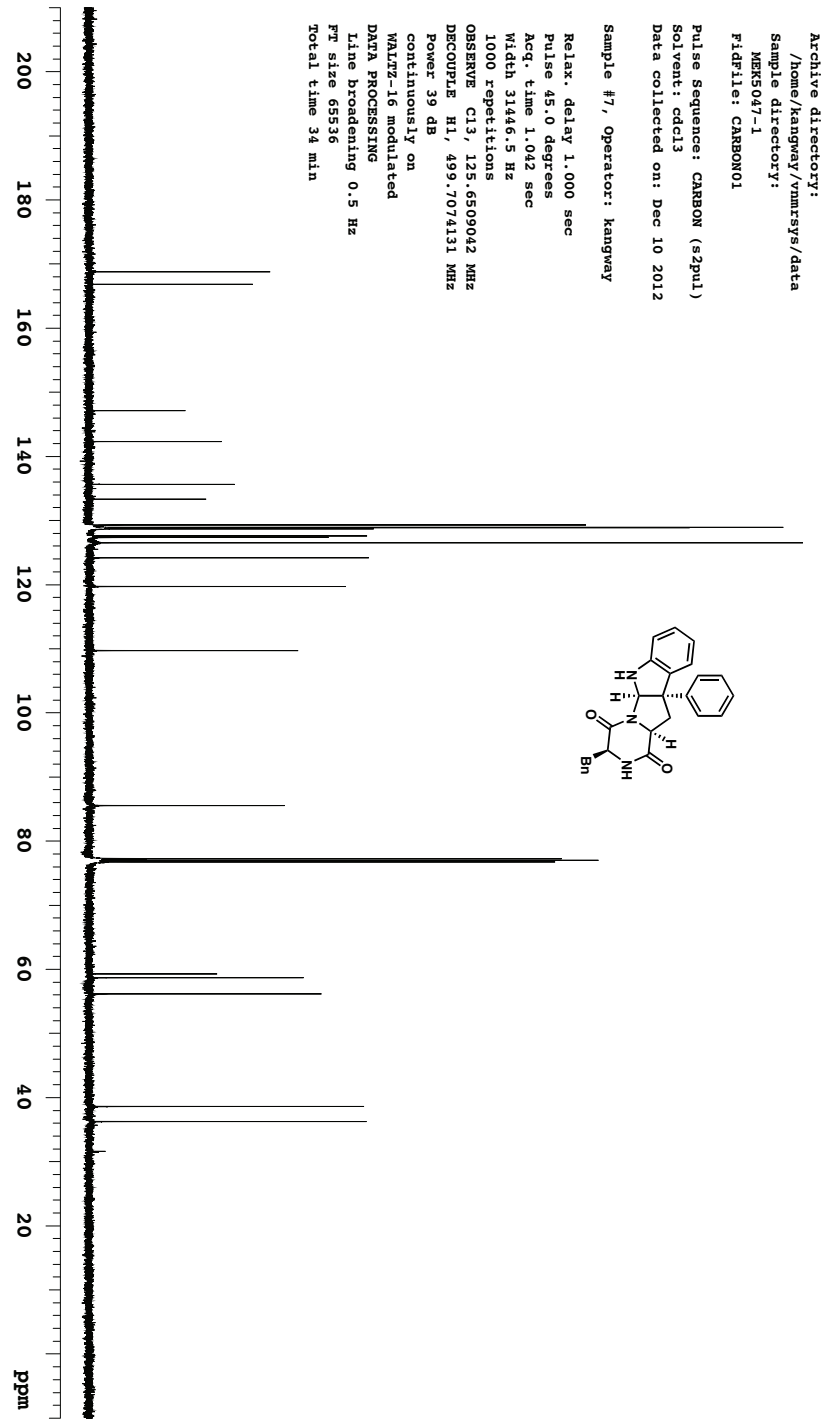

KVC15-029
Sample Name:
KVC15-029
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-029
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Jan 25 2013
Sample #11, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7072806 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Me
Me
OTf
0.99
0.97
1.00
3.04
2.01
0.99
1.01
3.00
3.00
10
9
8
7
6
5
4
3
2
1
ppm

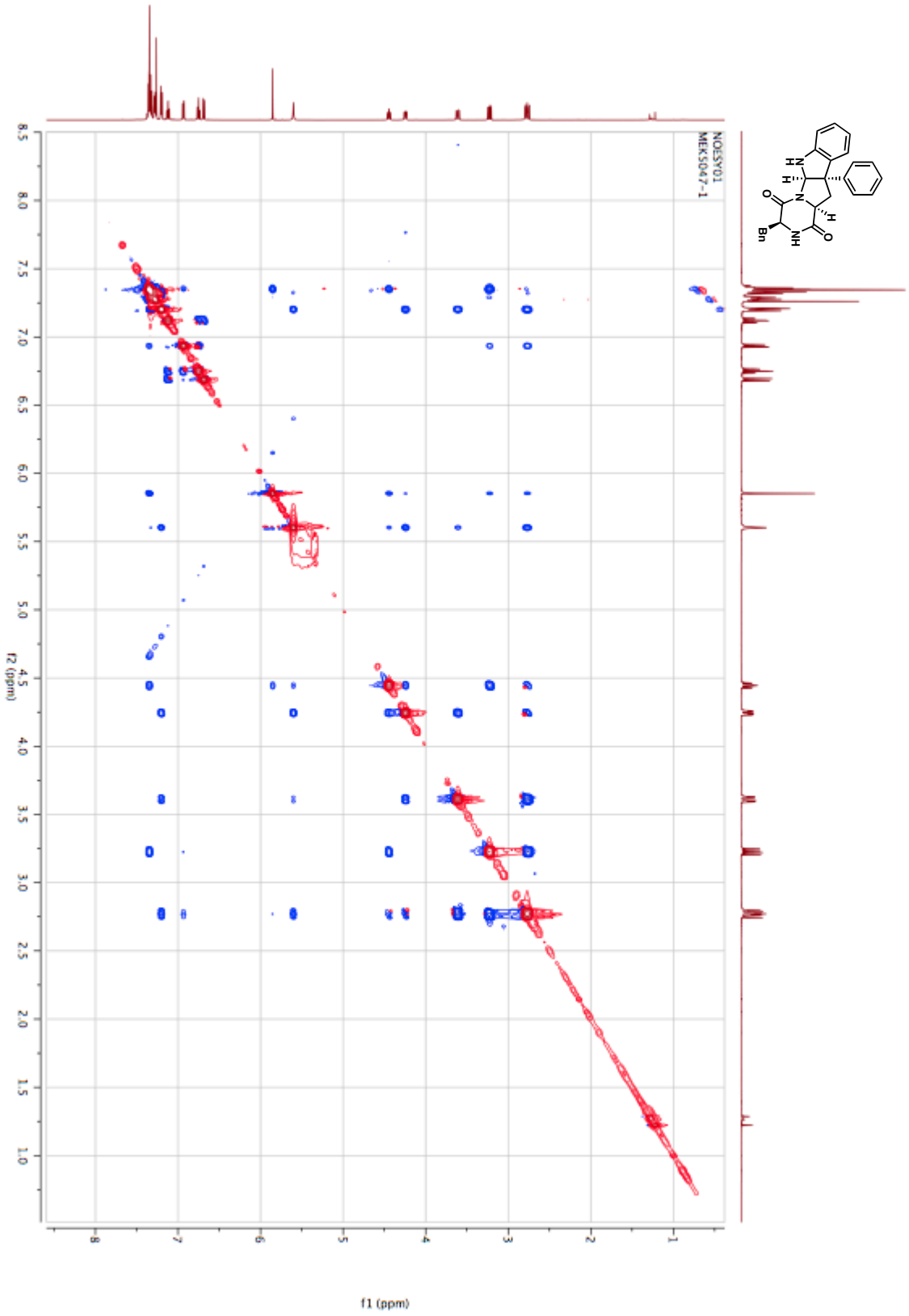

KVC15-029
Sample Name:
KVC15-029
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-029
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Jan 25 2013
Sample #11, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
256 repetitions
OBSERVE C13, 125.6515531 MHz
DECOUPLE H1, 499.7097867 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
Me
Me
OTf
200
180
160
140
120
100
80
60
40
20
ppm

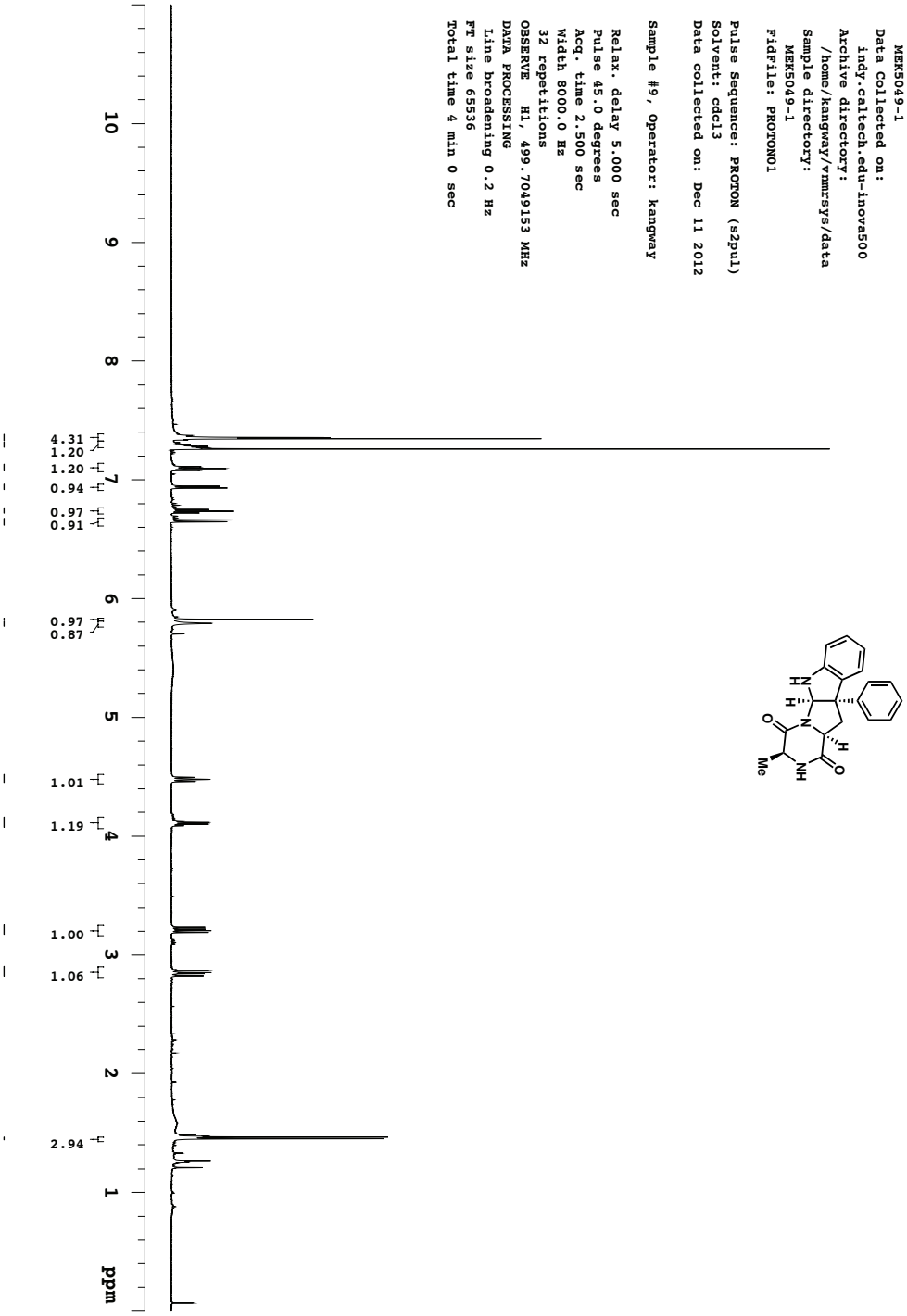

KVC15-165
Sample Name:
KVC15-165
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-165
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Feb 3 2013
Sample #47, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7072806 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Me
Me
OTf
Br
0.93
0.94
1.04
0.95
2.00
1.04
2.96
3.00
10
9
8
7
6
5
4
3
2
1
ppm

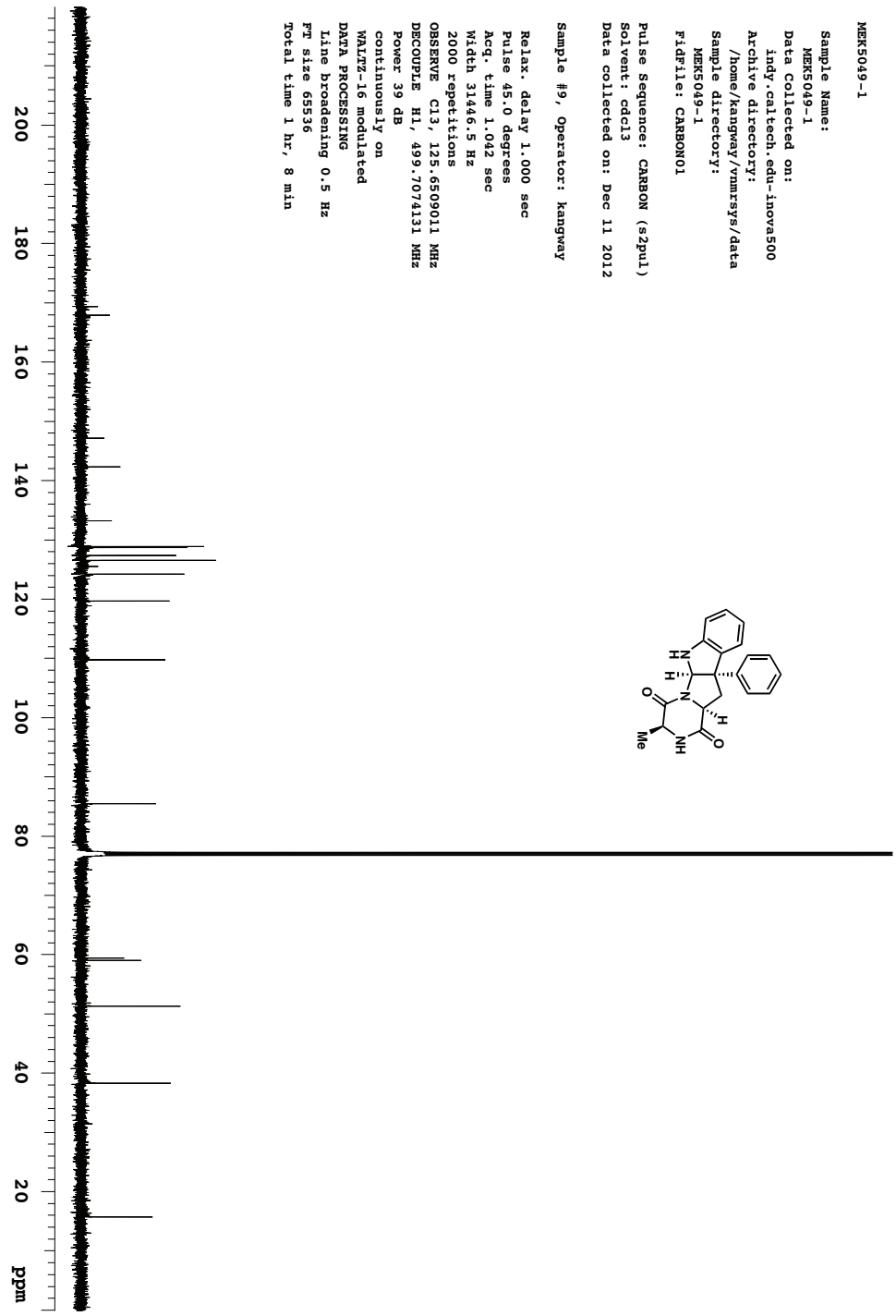

KVC15-165
Sample Name:
KVC15-165
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-165
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Feb 3 2013
Sample #47, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6515531 MHz
DECOUPLE H1, 499.7097867 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
Me
OTf
Br
200
180
160
140
120
100
80
60
40
20
ppm

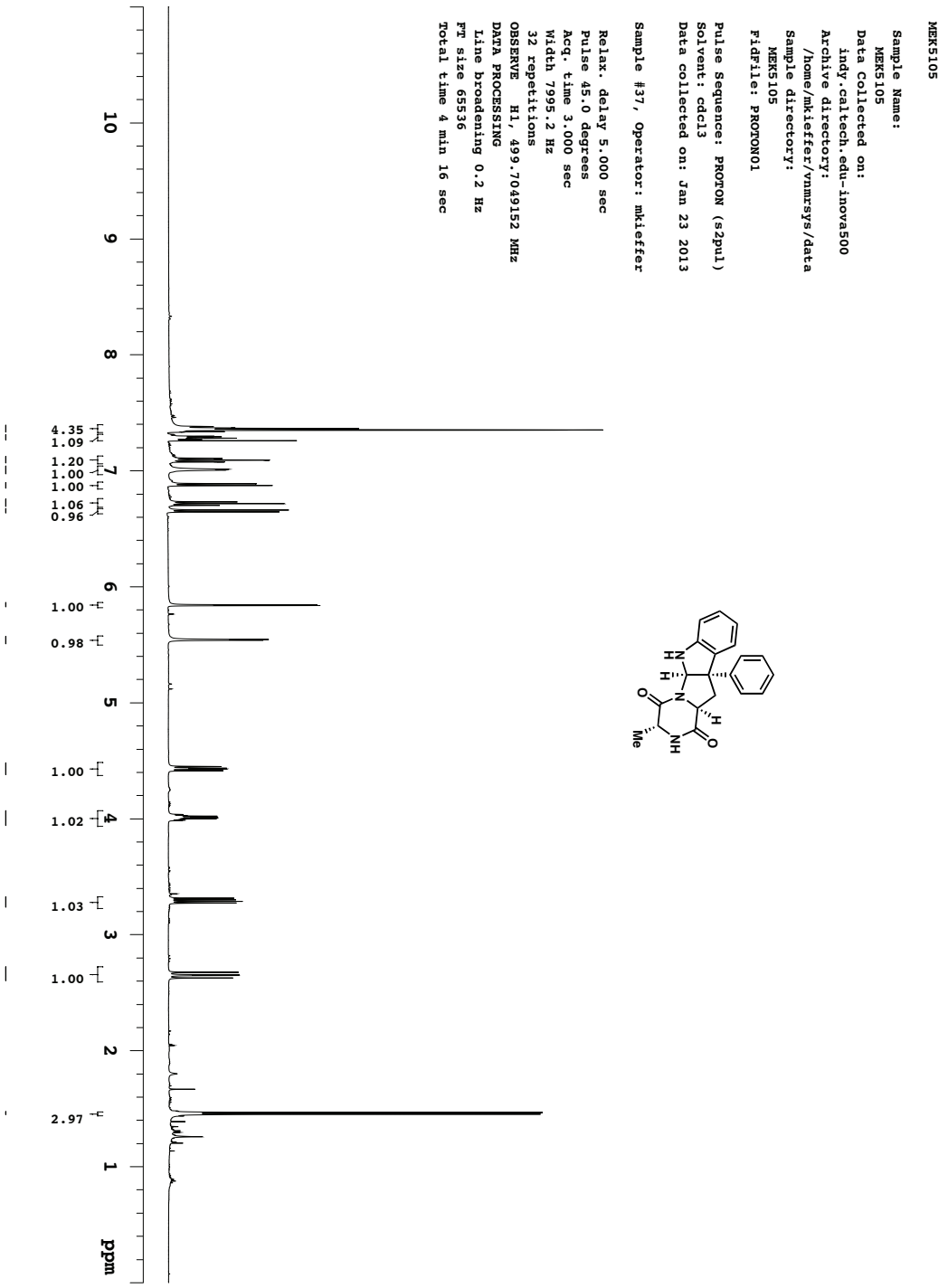

MEK5047-1
Sample Name:
MEK5047-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK5047-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 10 2012
Sample #7, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7049153 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
5.97
1.90
2.07
1.04
0.98
1.01
0.97
0.93
0.98
1.01
1.01
1.00
0.98
1.99
10
9
8
7
6
5
4
3
2
1
ppm
Bn


MEK5047-1
Sample Name:
MEK5047-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK5047-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 10 2012
Sample #7, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6509042 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Bn
200
180
160
140
120
100
80
60
40
20
ppm

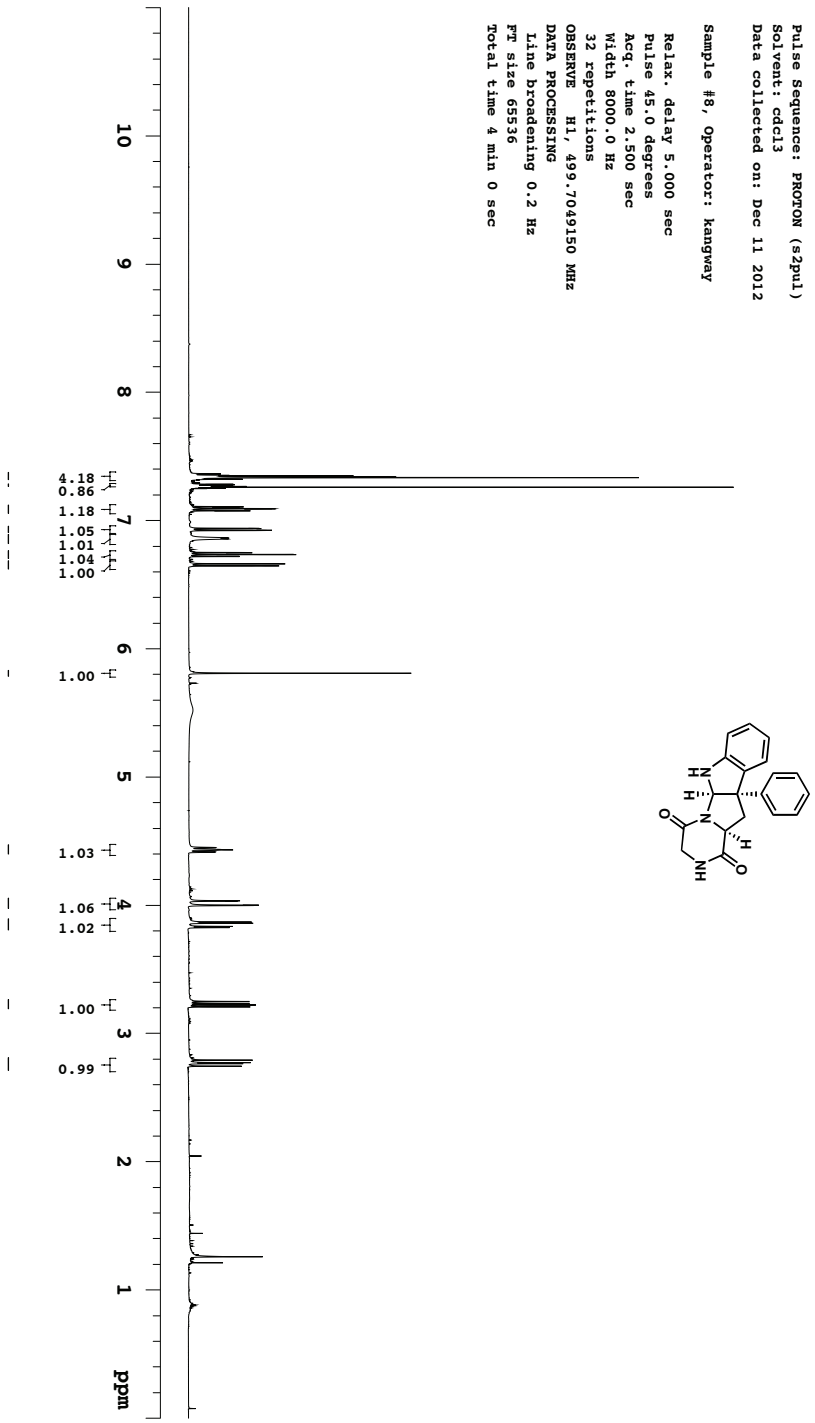

NOESY01
MEK5047-1
f2 (ppm)
f1 (ppm)
Bn

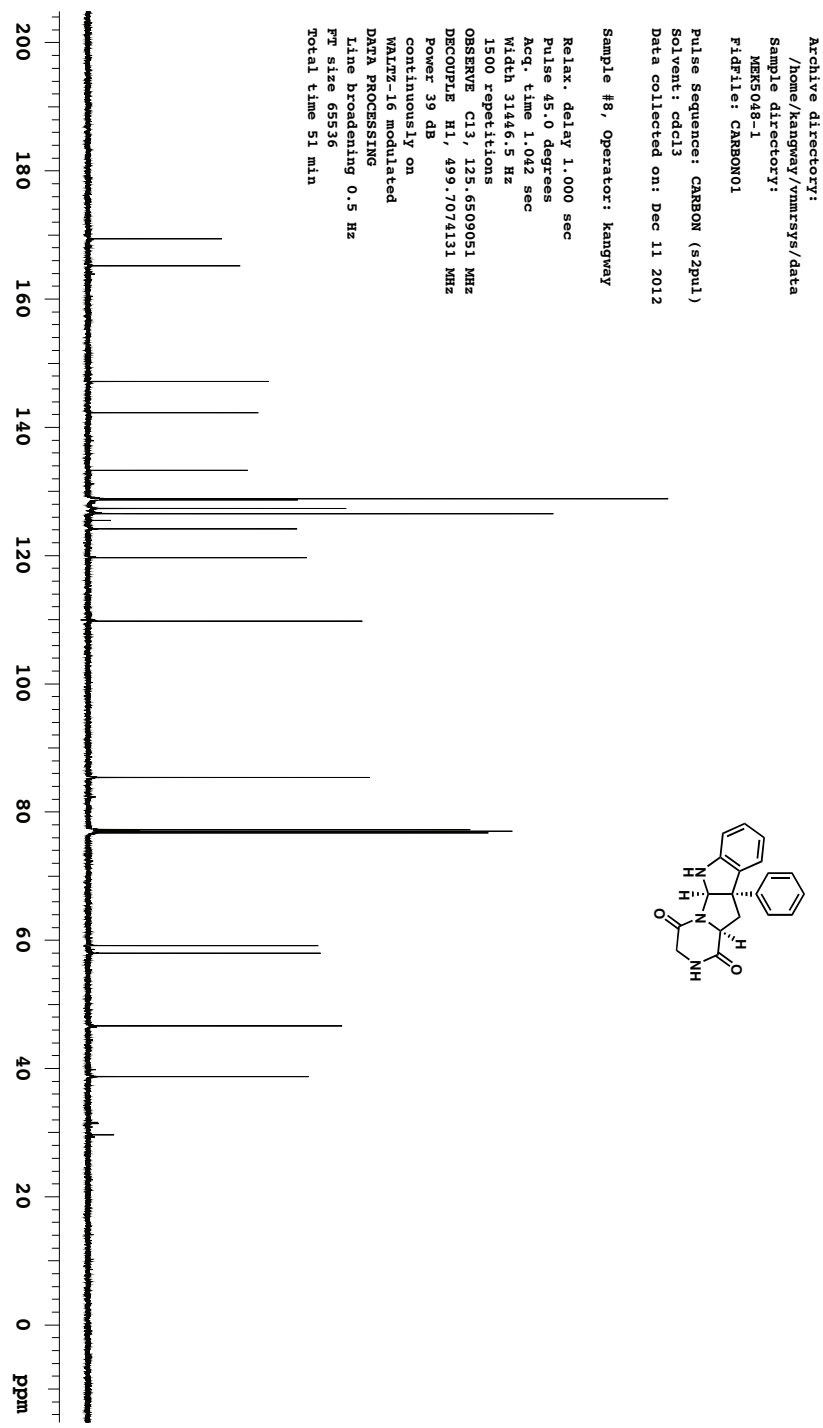

MEK5049-1
Sample Name:
MEK5049-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK5049-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 11 2012
Sample #9, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7049153 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
4.31
1.20
1.20
0.94
0.97
0.91
0.97
0.87
1.01
1.19
1.00
1.06
2.94
10
9
8
7
6
5
4
3
2
1
ppm
H
N
H
N
O
O
H
NH
O
Me

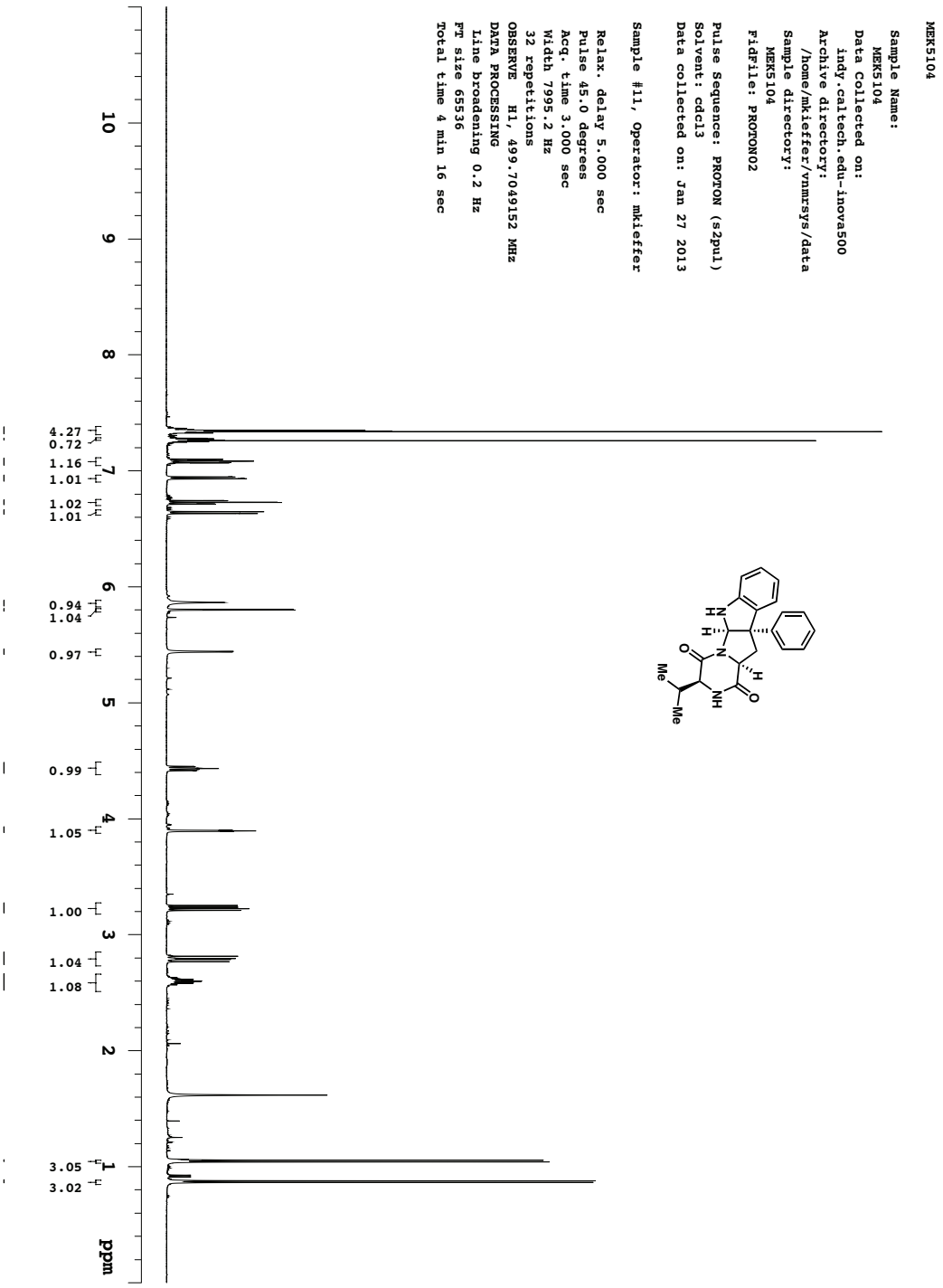

MEK5049-1
Sample Name:
MEK5049-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK5049-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 11 2012
Sample #9, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6509011 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
H
N
H
N
O
O
NH
Me
H
O
200
180
160
140
120
100
80
60
40
20
ppm

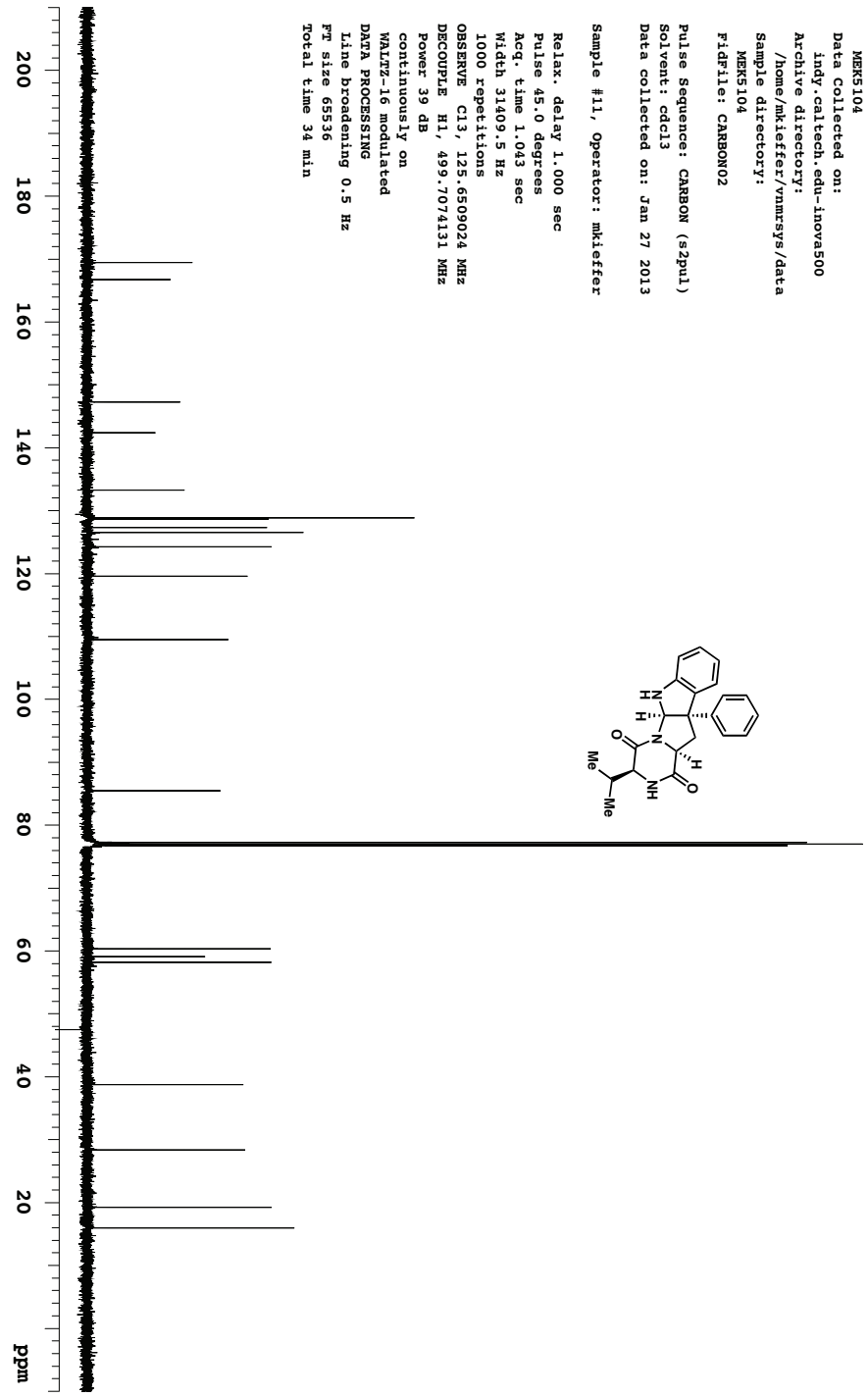

MEK5105
Sample Name:
MEK5105
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5105
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2013
Sample #37, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049152 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
4.35
1.09
1.20
1.00
1.00
1.06
0.96
1.00
0.98
1.00
1.02
1.03
1.00
2.97
Me
10
9
8
7
6
5
4
3
2
1
ppm

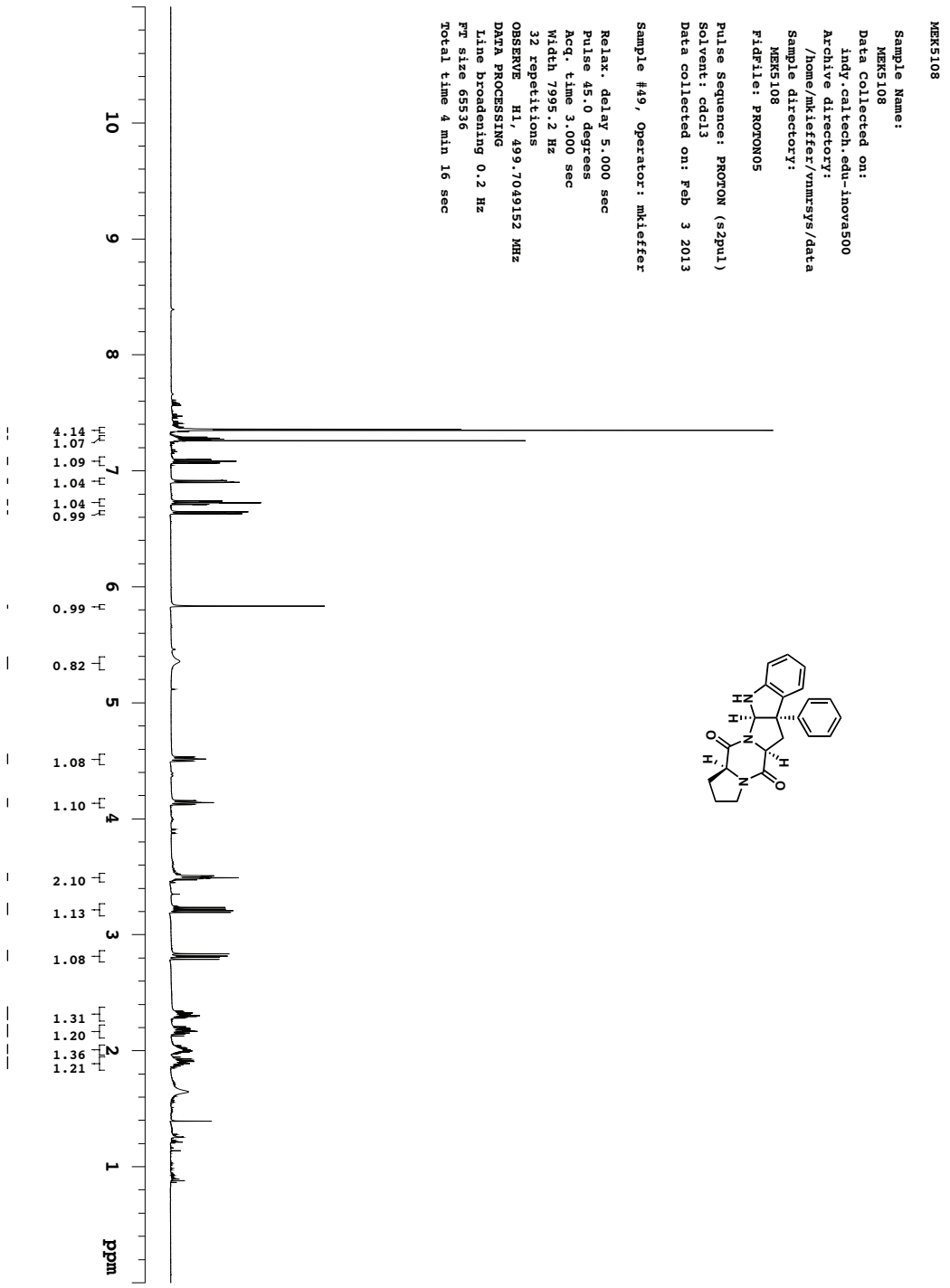
MEK5105
Sample Name:
MEK5105
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5105
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 23 2013
Sample #37, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509063 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
200
180
160
140
120
100
80
60
40
20
ppm

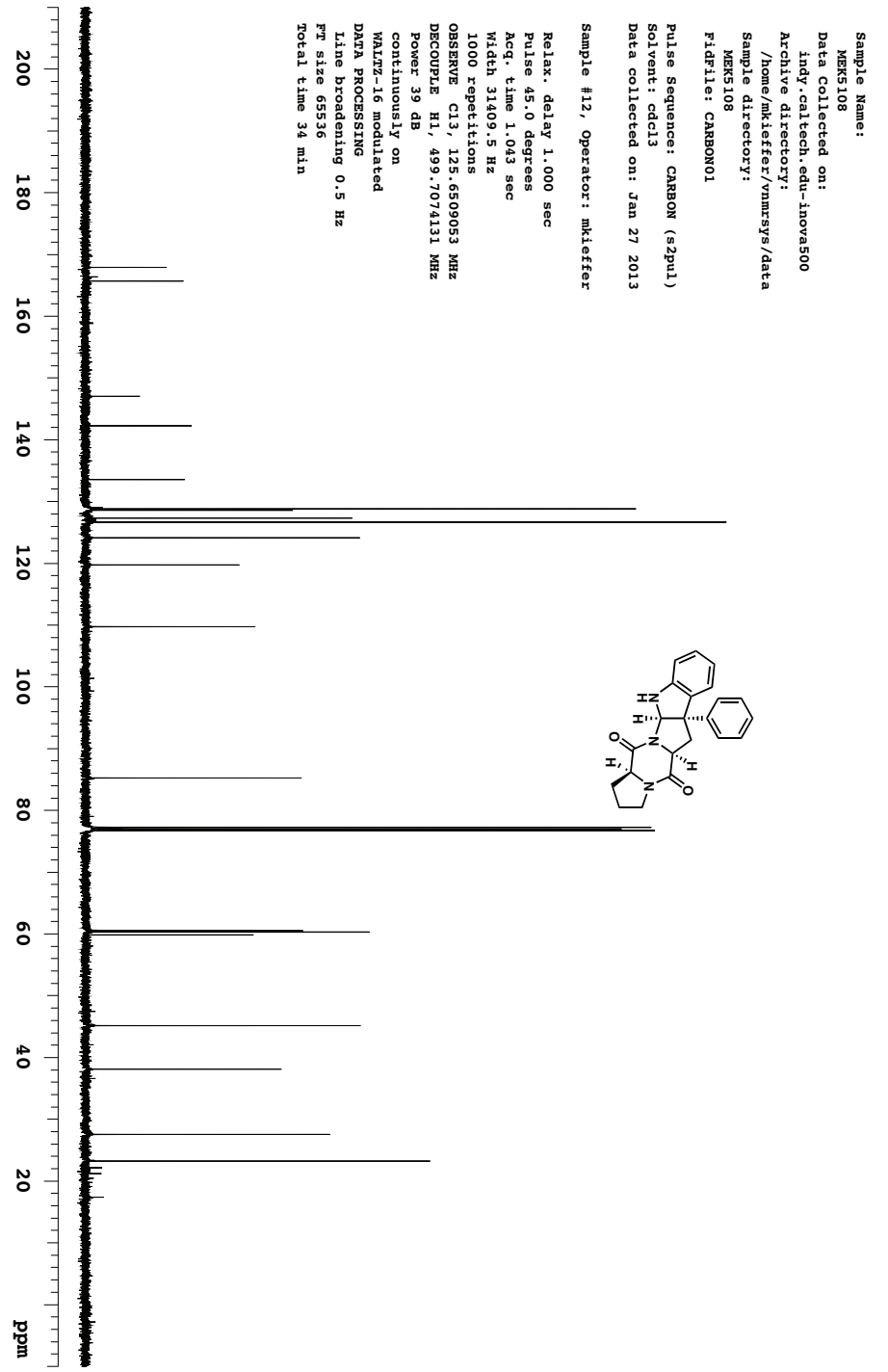

MEK5048-1
Sample Name:
MEK5048-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK5048-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 11 2012
Sample #8, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7049150 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 0 sec
4.18
0.86
1.18
1.05
1.01
1.04
1.00
1.00
1.03
1.06
1.02
1.00
0.99
10
9
8
7
6
5
4
3
2
1
ppm

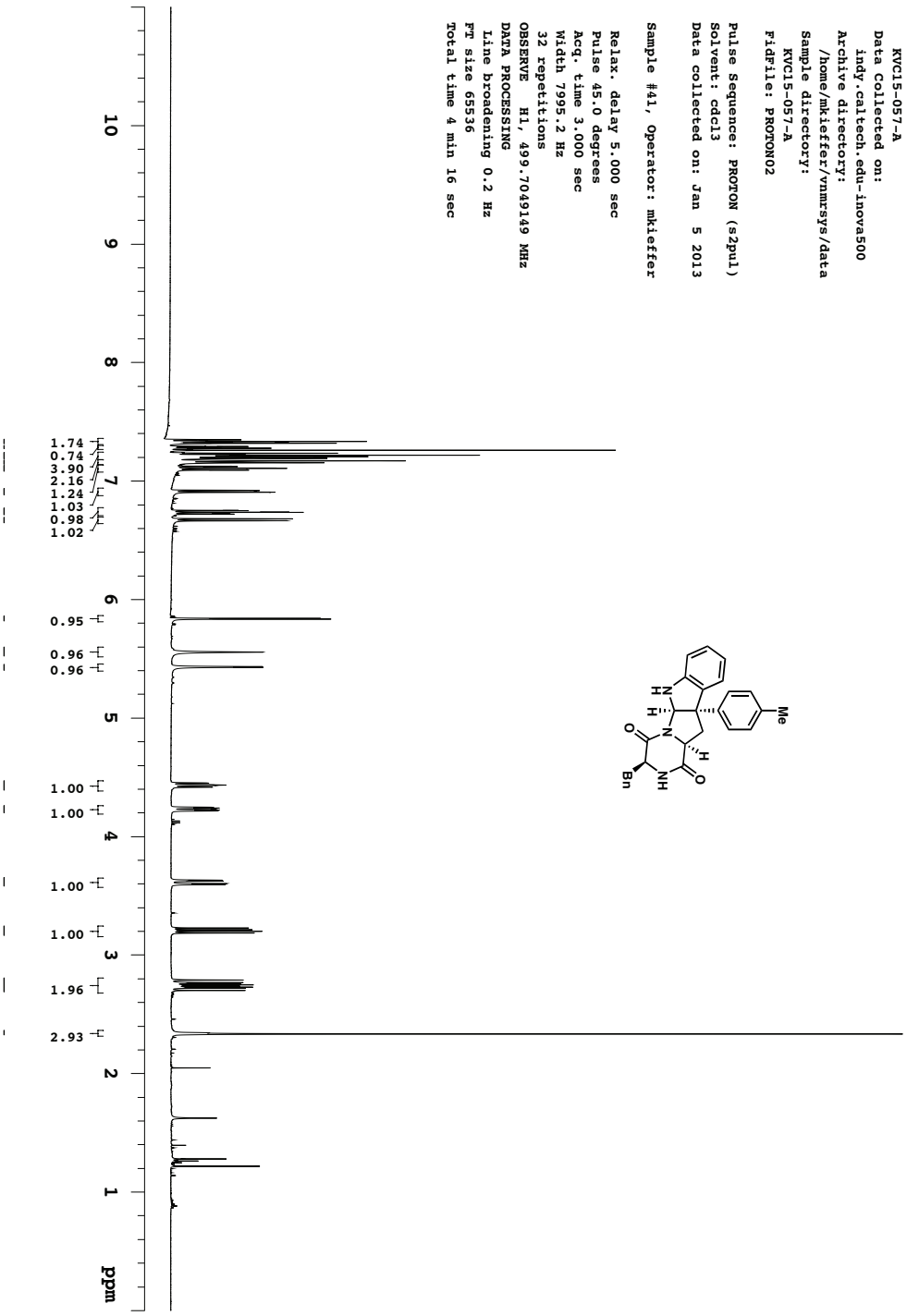

MEK5048-1
Sample Name:
MEK5048-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK5048-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 11 2012
Sample #8, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6509051 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
200
180
160
140
120
100
80
60
40
20
0
ppm

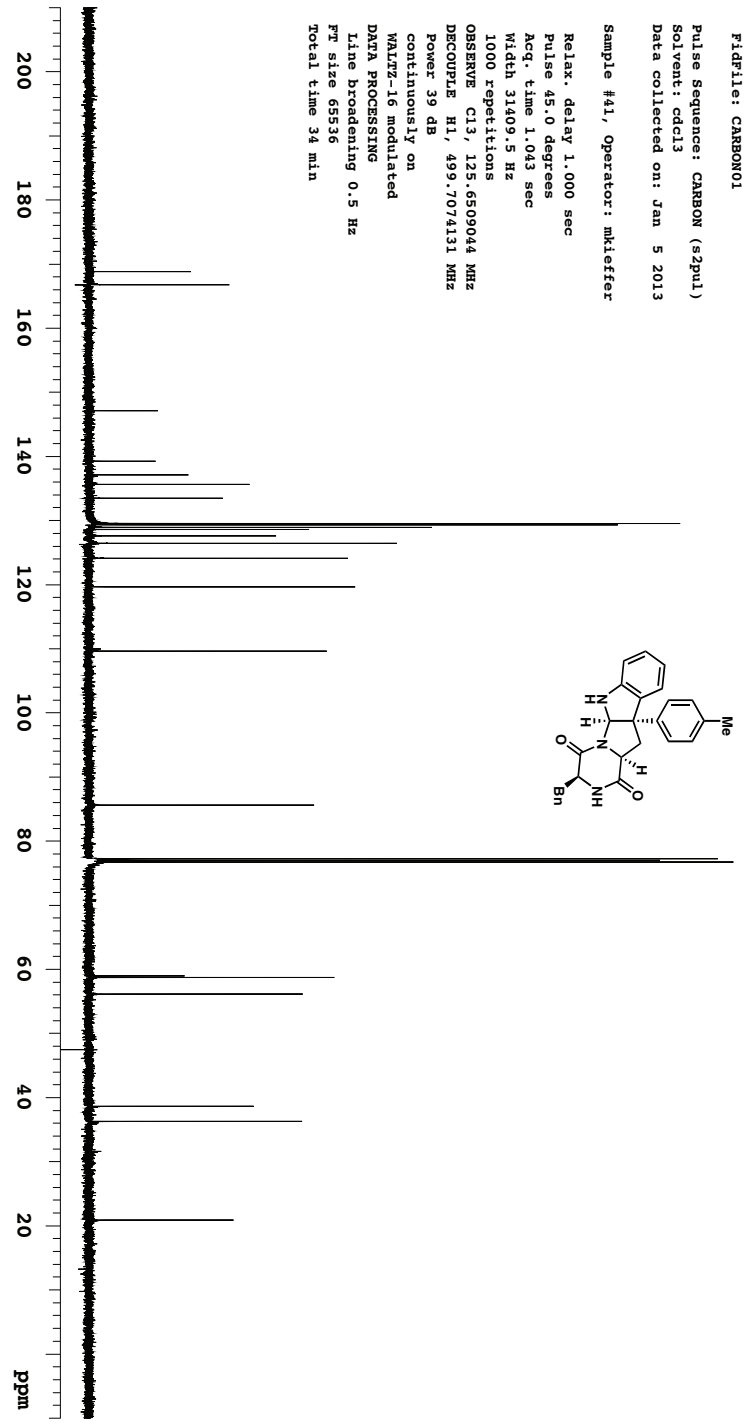

MEK5104
Sample Name:
MEK5104
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5104
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #11, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049152 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
4.27
0.72
1.16
1.01
1.02
1.01
0.94
1.04
0.97
0.99
1.05
1.00
1.04
1.08
3.05
3.02
ppm

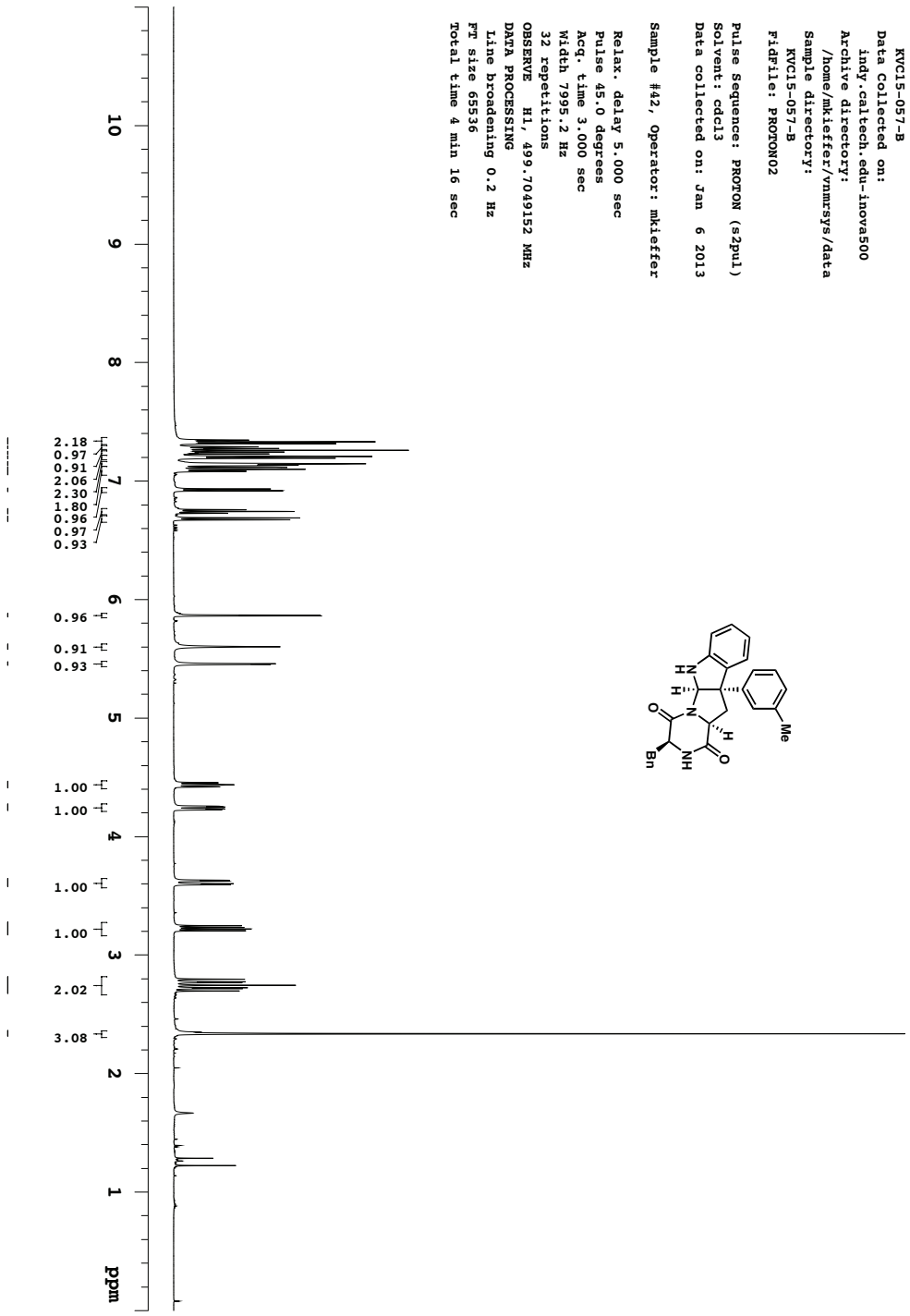

MEK5104
Sample Name:
MEK5104
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5104
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #11, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509024 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
200
180
160
140
120
100
80
60
40
20
ppm

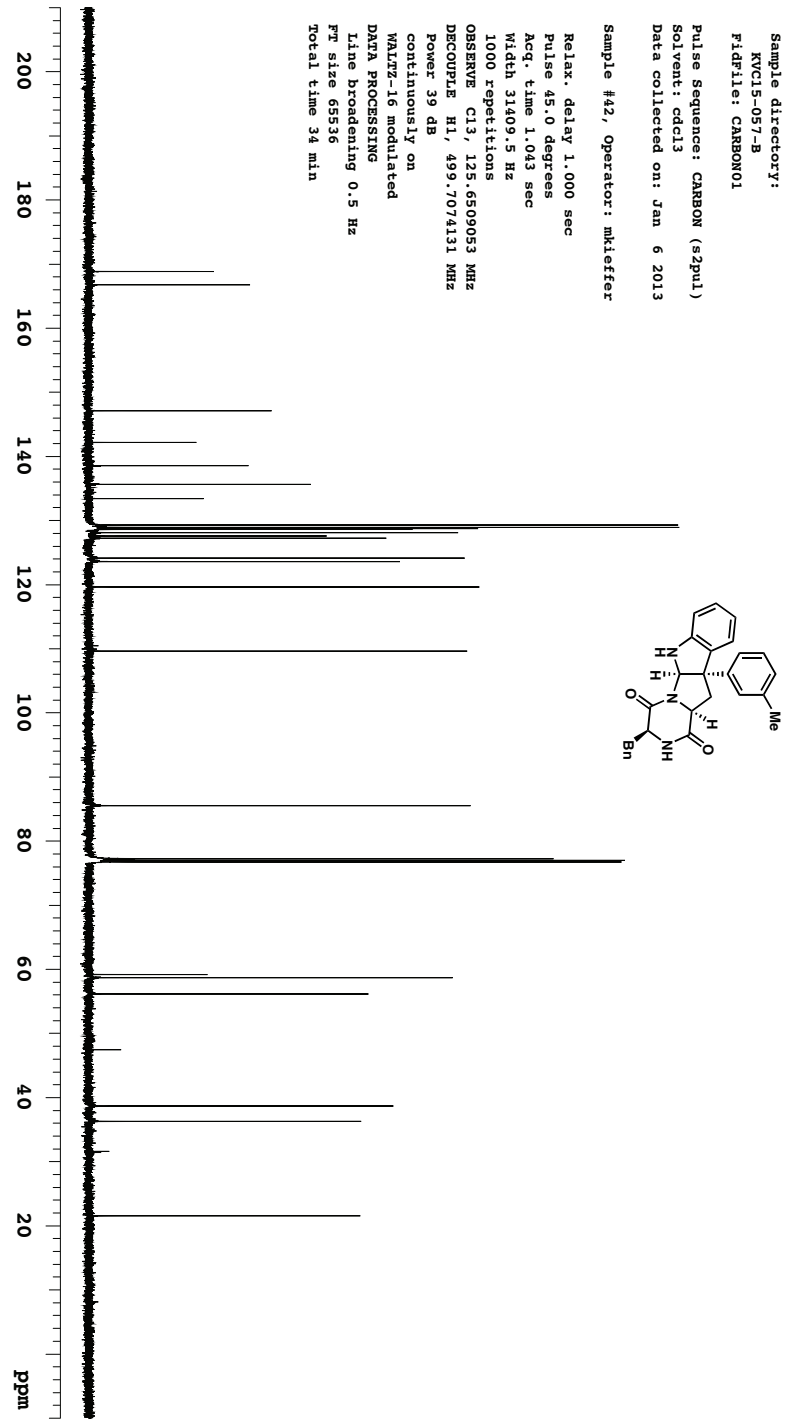

MEK5108
Sample Name:
MEK5108
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5108
FidFile: PROTON05
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 3 2013
Sample #49, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049152 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
4.14
1.07
1.09
1.04
1.04
0.99
0.99
0.82
1.08
1.10
2.10
1.13
1.08
1.31
1.20
1.36
1.21
10
9
8
7
6
5
4
3
2
1
ppm

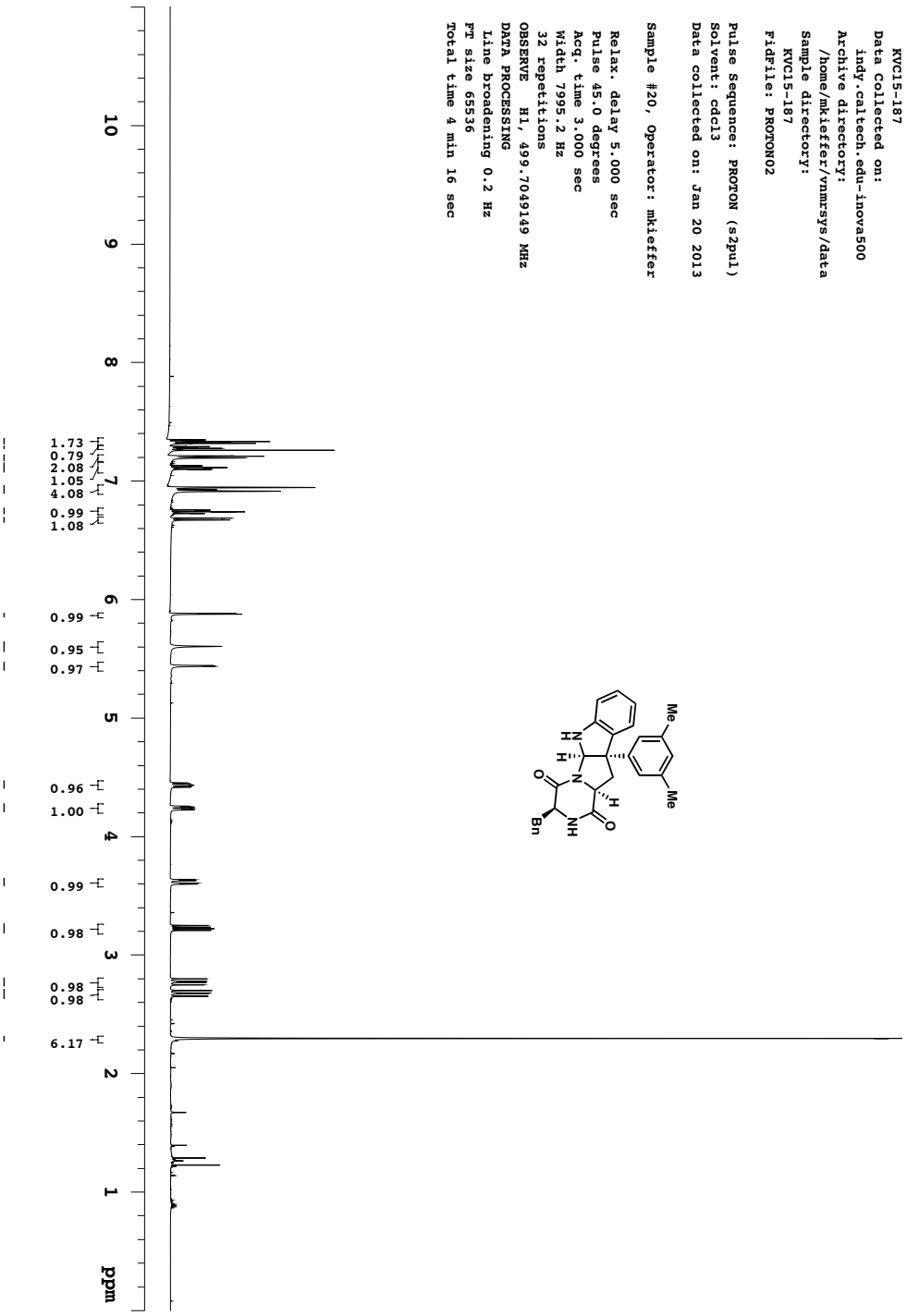

MEK5108
Sample Name:
MEK5108
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5108
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #12, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509053 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
200
180
160
140
120
100
80
60
40
20
ppm

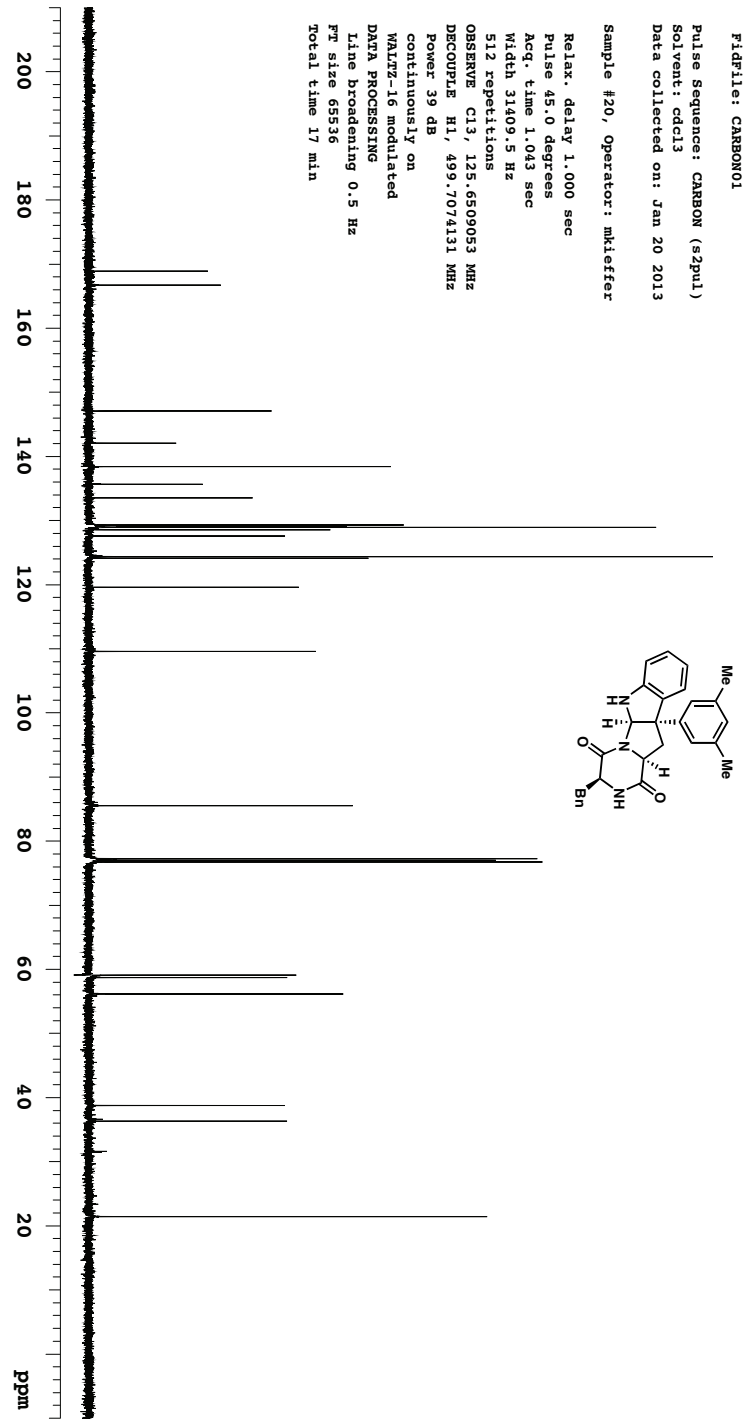

KVC15-057-A
Sample Name:
KVC15-057-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-057-A
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 5 2013
Sample #41, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
1.74
0.74
3.90
2.16
1.24
1.03
0.98
1.02
0.95
0.96
0.96
1.00
1.00
1.00
1.00
1.96
2.93
Me
Bn
ppm

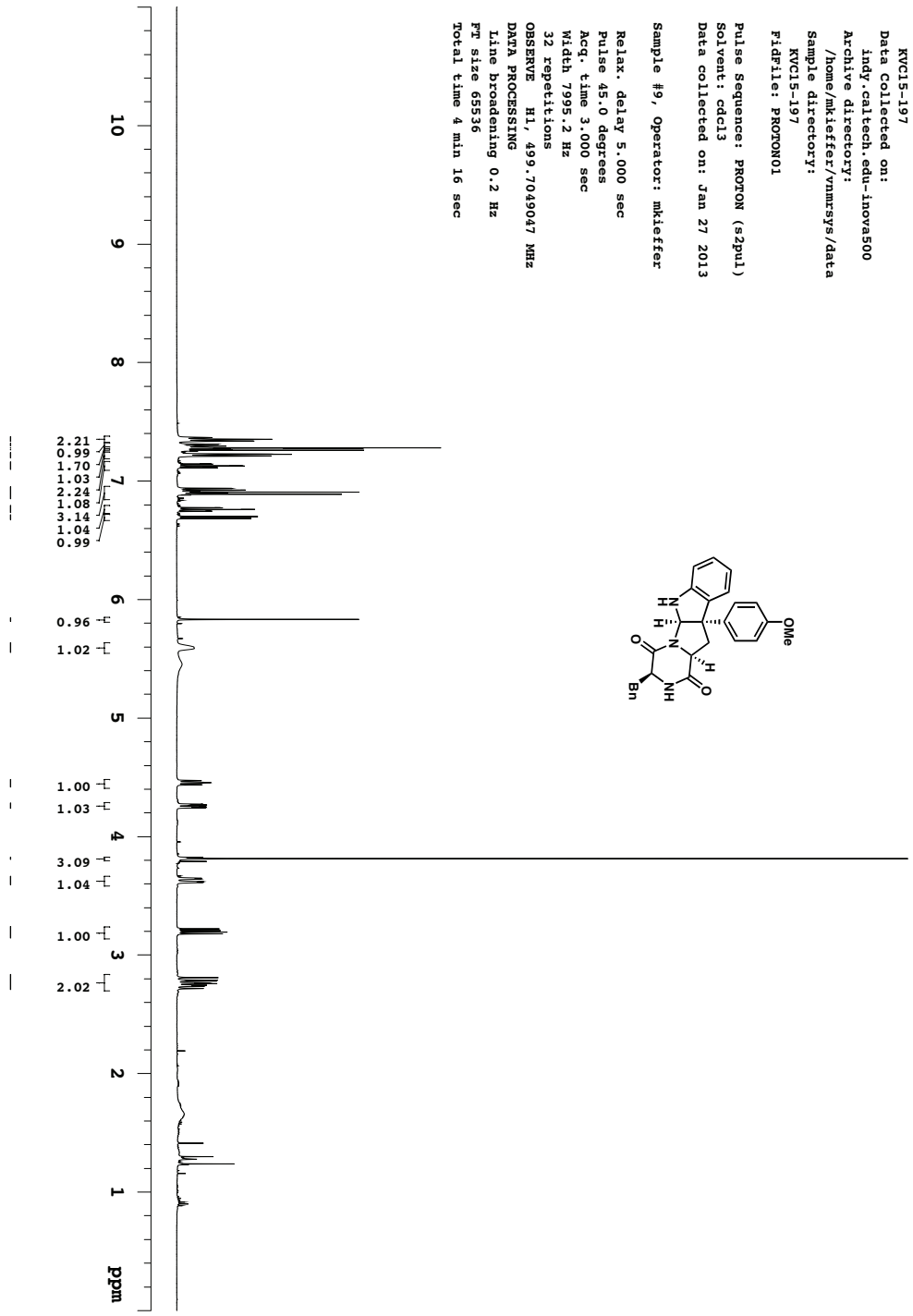

KVC15-057-A
Sample Name:
KVC15-057-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-057-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 5 2013
Sample #41, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509044 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
Bn
200
180
160
140
120
100
80
60
40
20
ppm

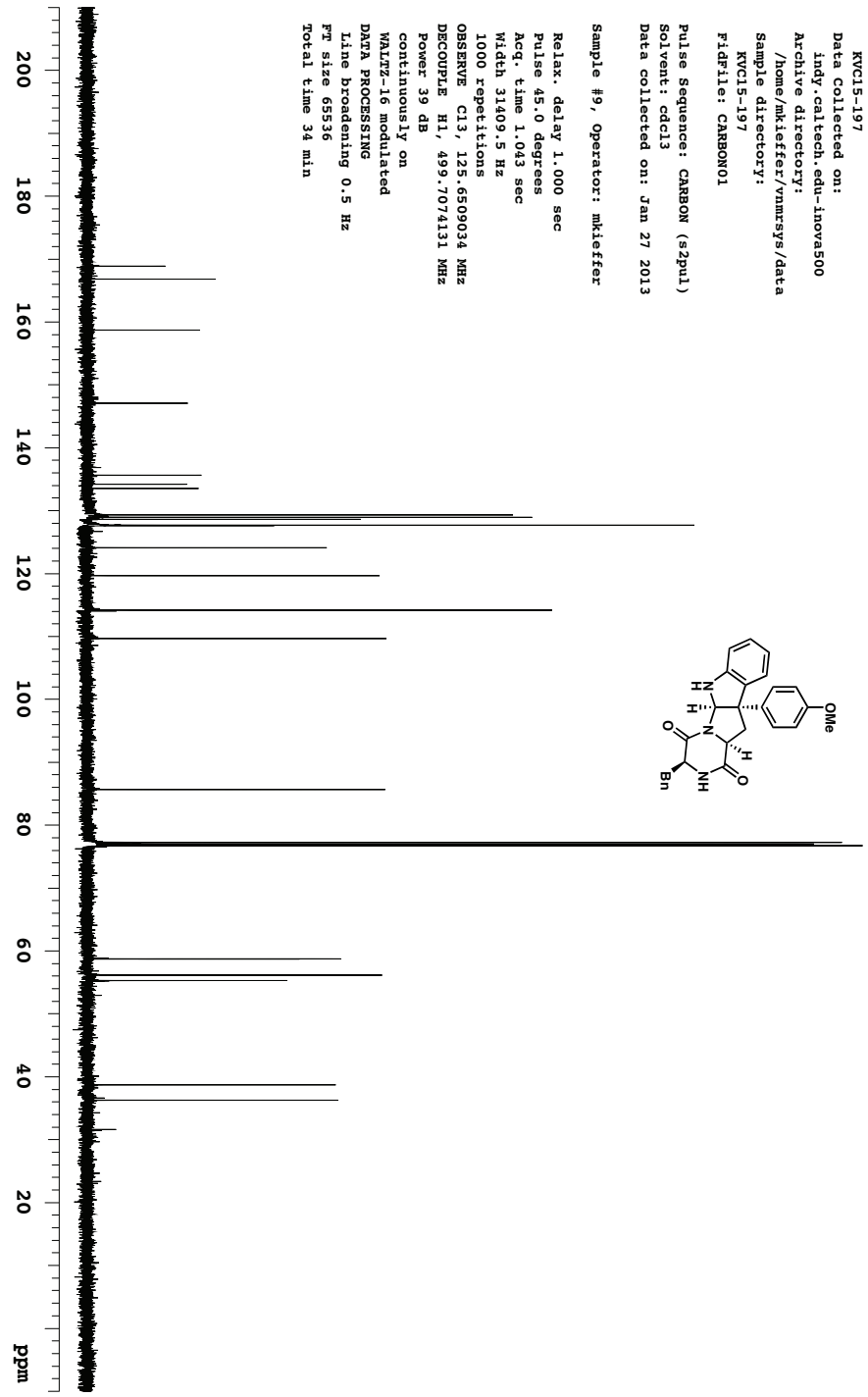

KVC15-057-B
Sample Name:
KVC15-057-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-057-B
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2013
Sample #42, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049152 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
2.18
0.97
0.91
2.06
2.30
1.80
0.96
0.97
0.93
0.96
0.91
0.93
1.00
1.00
1.00
1.00
2.02
3.08
Me
Bn
ppm

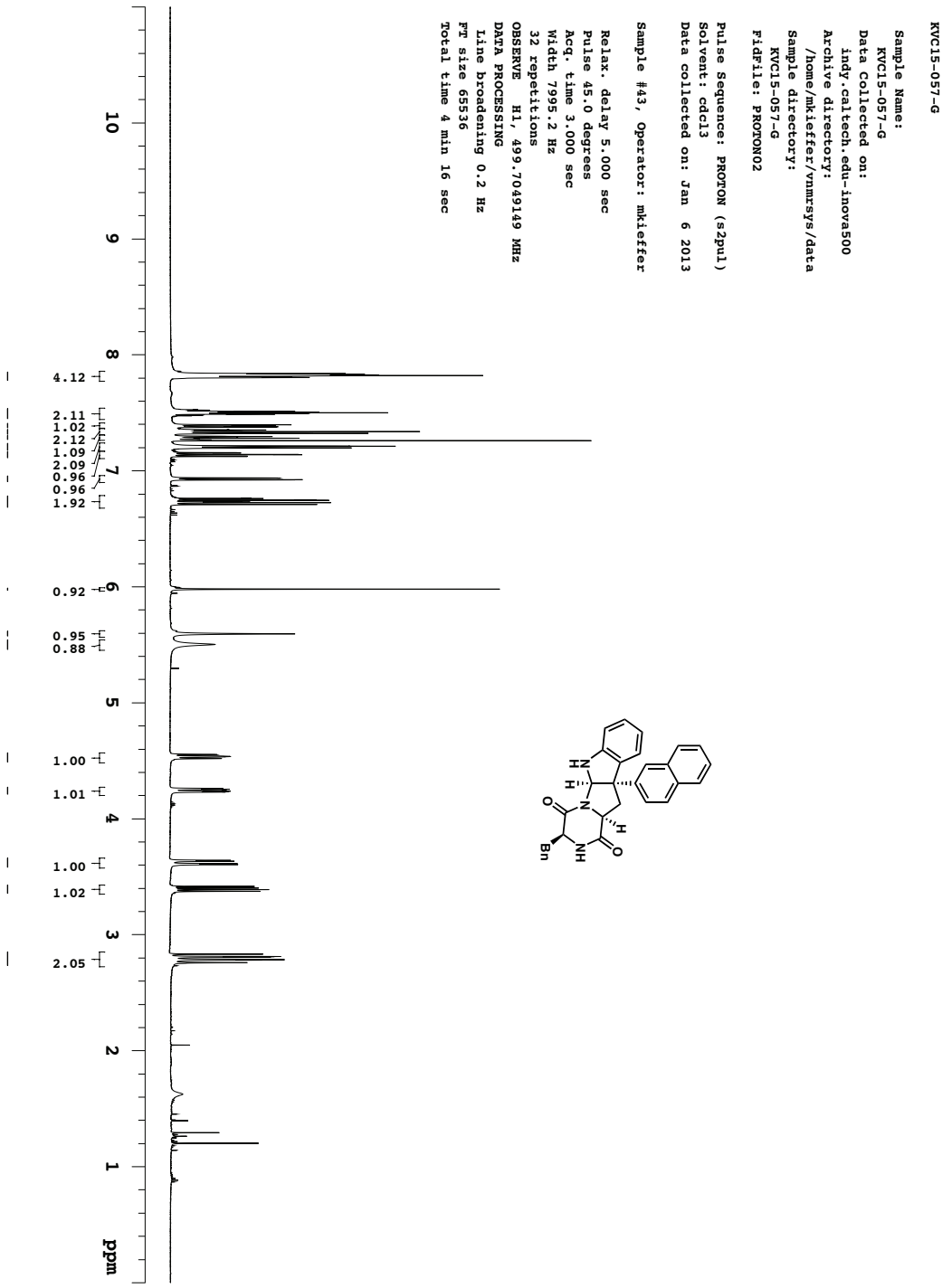

KVC15-057-B
Sample Name:
KVC15-057-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-057-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2013
Sample #42, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509053 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Me
Bn
200
180
160
140
120
100
80
60
40
20
ppm

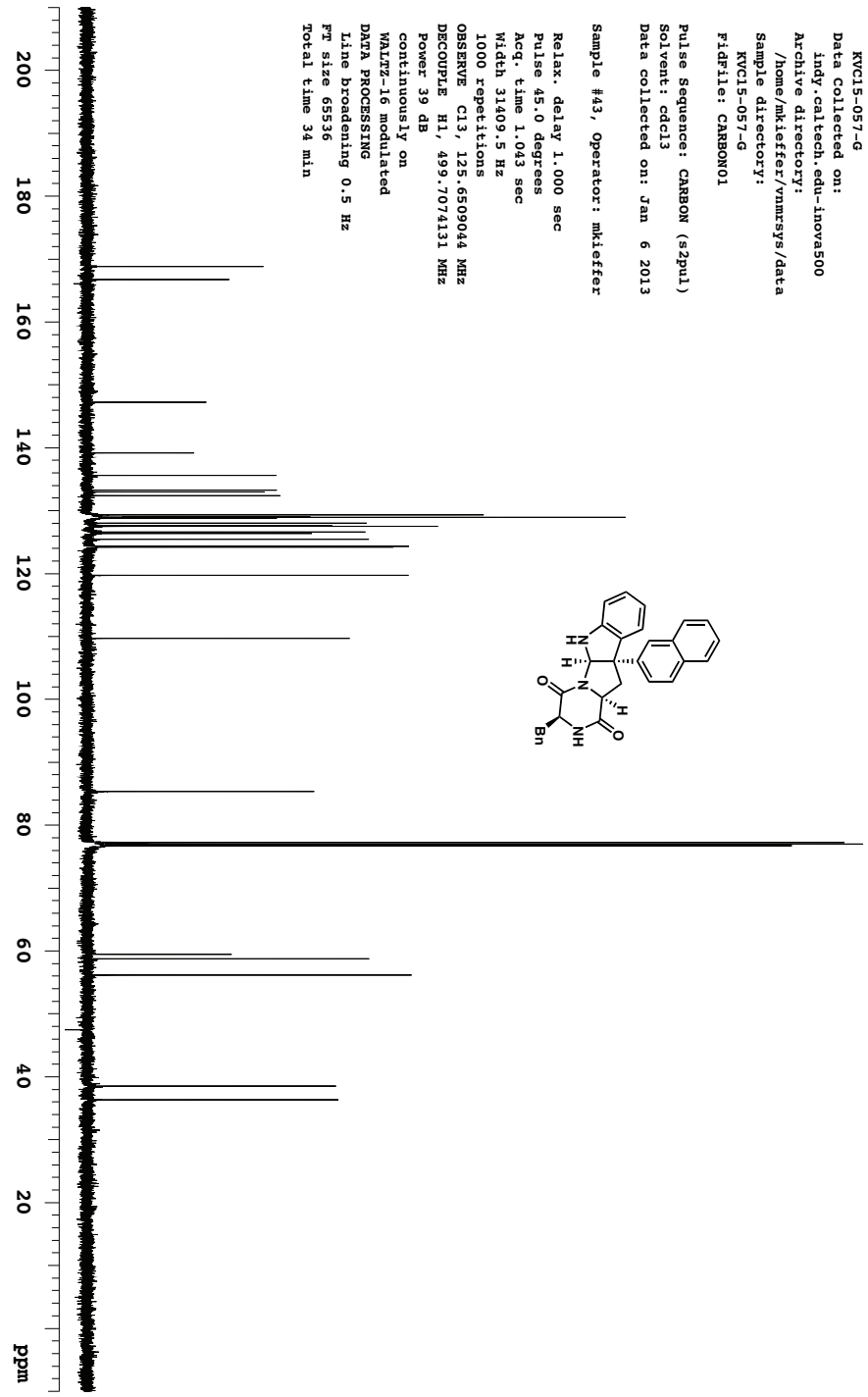

KVC15-187
Sample Name:
KVC15-187
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-187
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 20 2013
Sample #20, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
1.73
0.79
2.08
1.05
4.08
0.99
1.08
0.99
0.95
0.97
0.96
1.00
0.99
0.98
0.98
0.98
6.17
10
9
8
7
6
5
4
3
2
1
ppm
Me
Me
Bn
NH
H
O
O

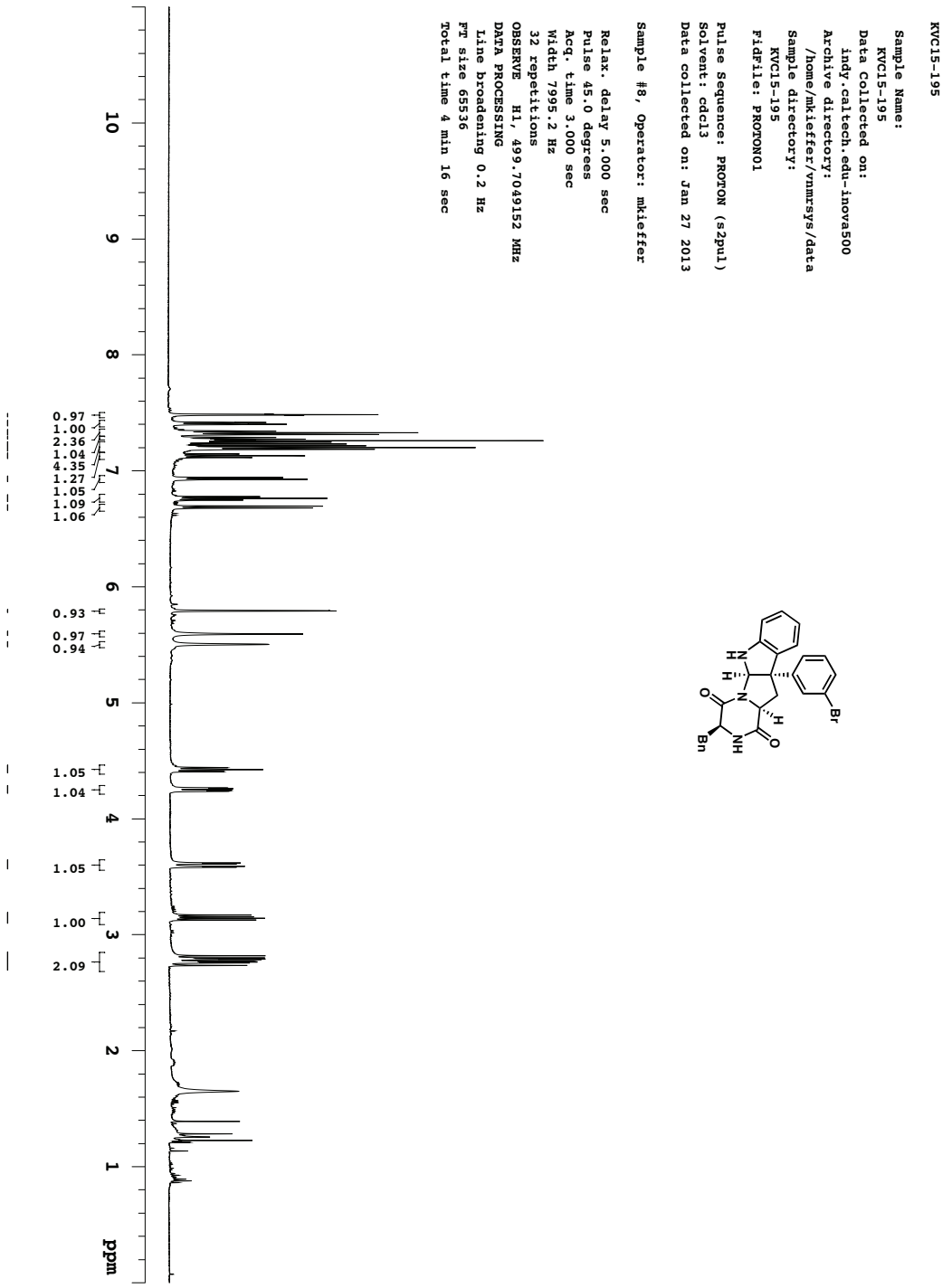

KVC15-187
Sample Name:
KVC15-187
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-187
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 20 2013
Sample #20, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
512 repetitions
OBSERVE C13, 125.6509053 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Bn
200
180
160
140
120
100
80
60
40
20
ppm

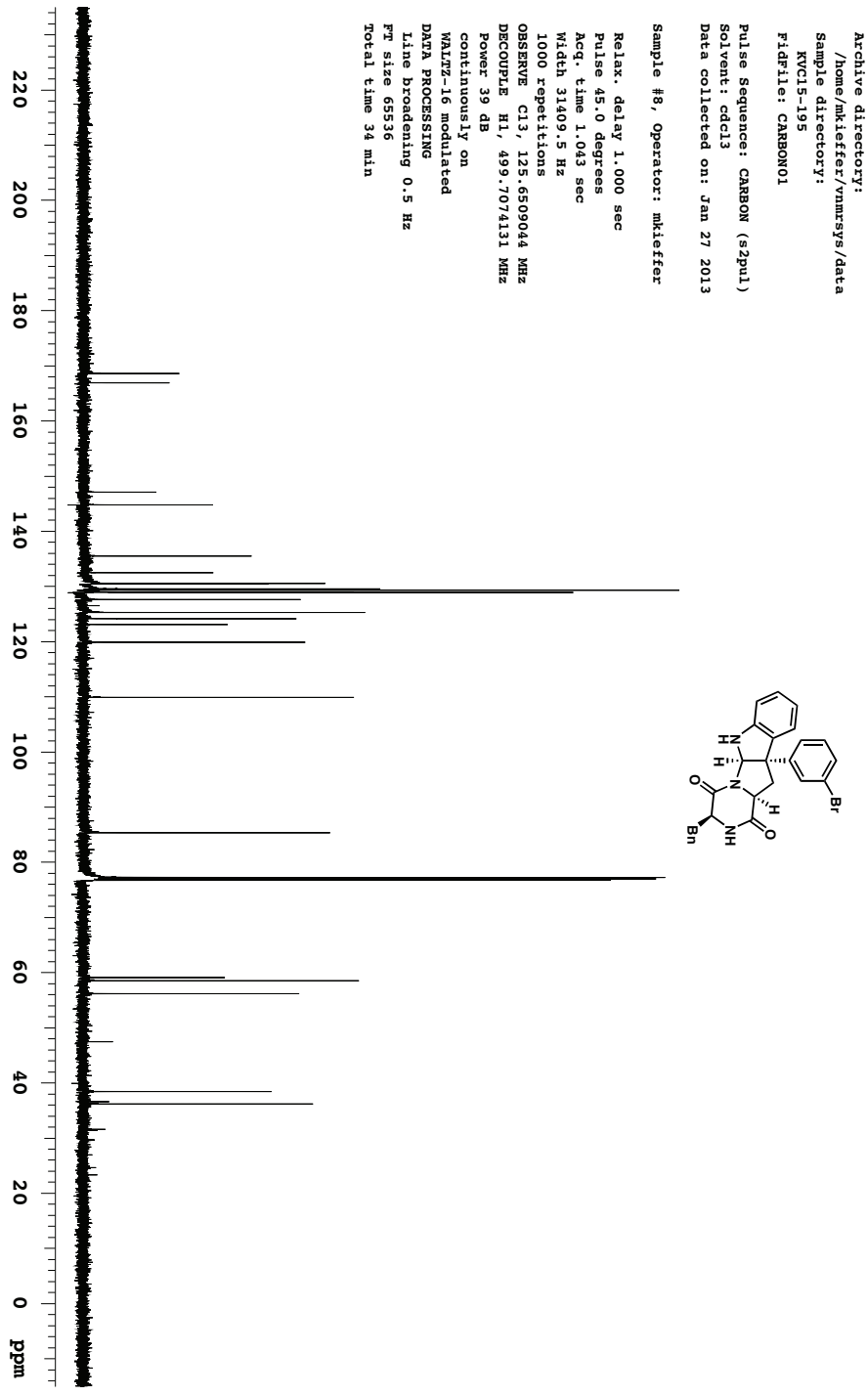

KVC15-197
Sample Name:
KVC15-197
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-197
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #9, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049047 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
2.21
0.99
1.70
1.03
2.24
1.08
3.14
1.04
0.99
0.96
1.02
1.00
1.03
3.09
1.04
1.00
2.02
OMe
Bn
10
9
8
7
6
5
4
3
2
1
ppm

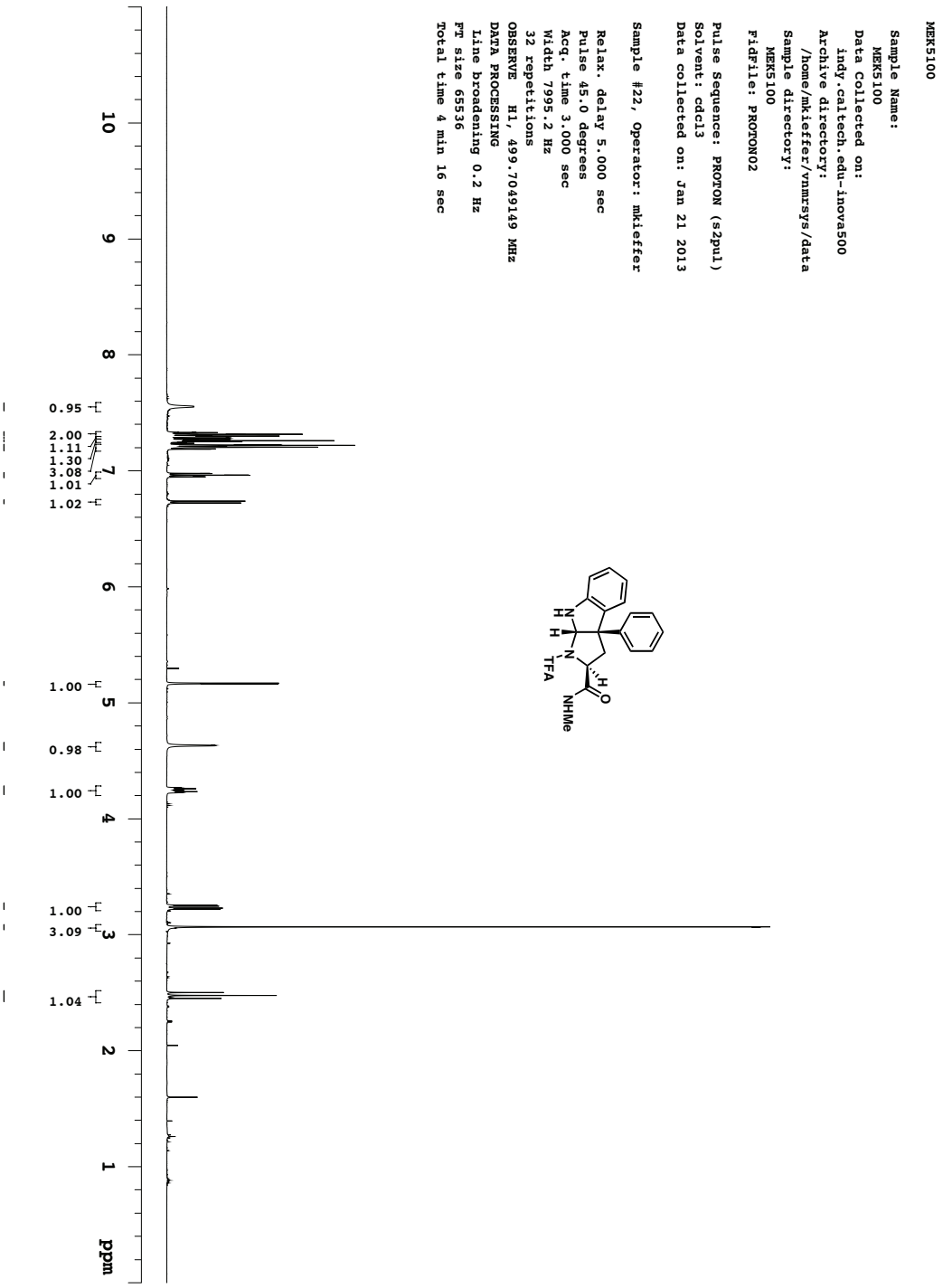

KVC15-197
Sample Name:
KVC15-197
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-197
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #9, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509034 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
OMe
Bn
200
180
160
140
120
100
80
60
40
20
ppm

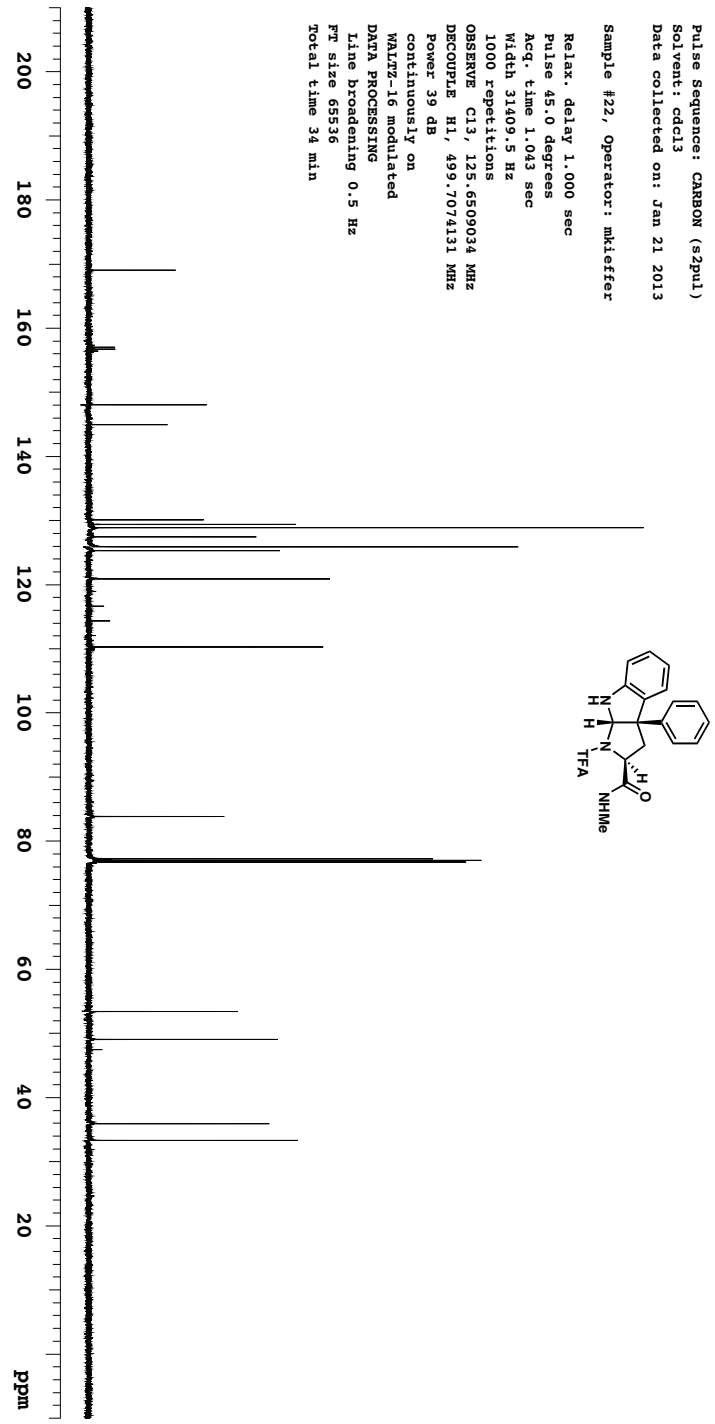

KVC15-057-G
Sample Name:
KVC15-057-G
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-057-G
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2013
Sample #43, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
4.12
2.11
1.02
2.12
1.09
2.09
0.96
0.96
1.92
0.92
0.95
0.88
1.00
1.01
1.00
1.02
2.05
10
9
8
7
6
5
4
3
2
1
ppm
Bn

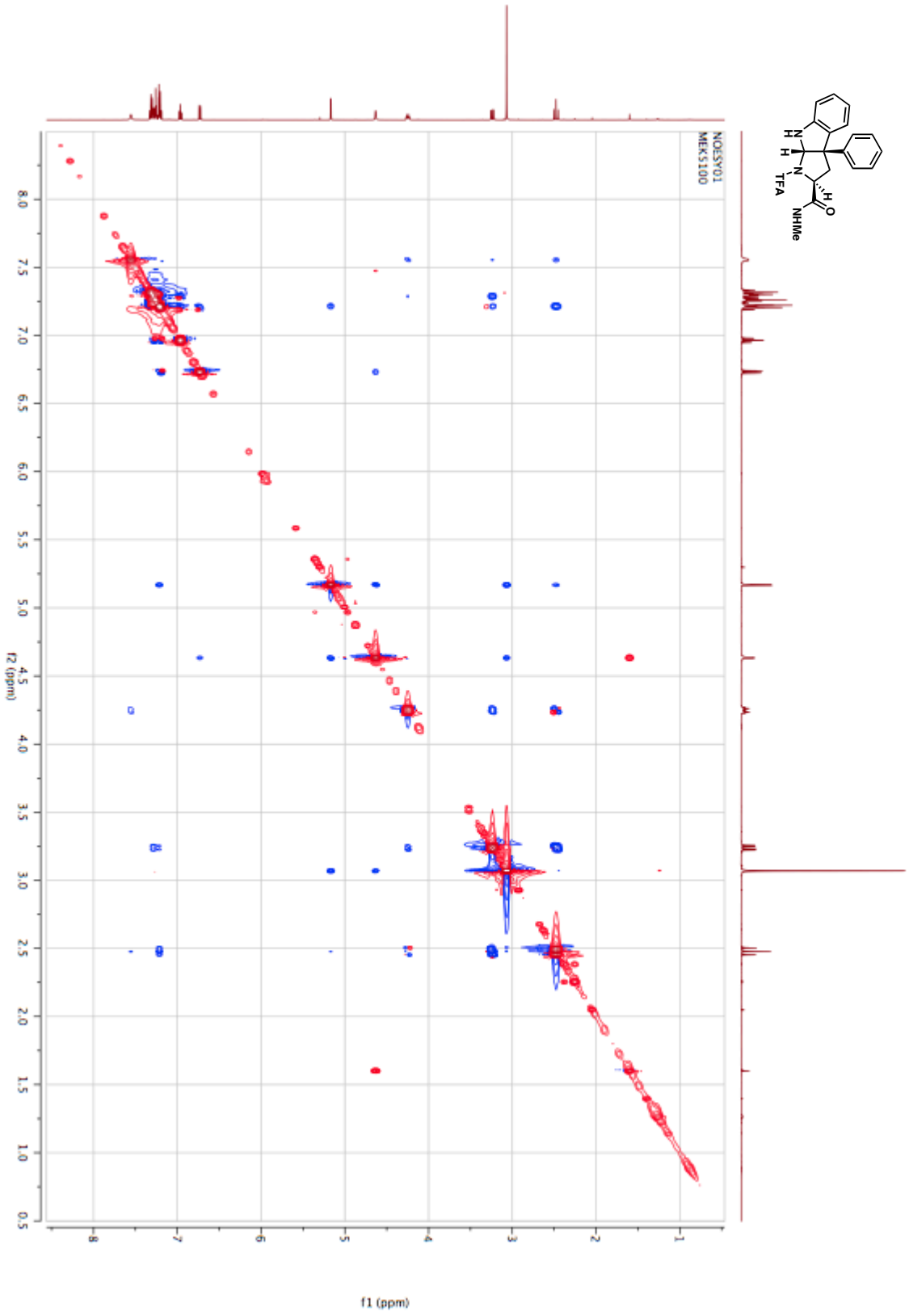

KVC15-057-G
Sample Name:
KVC15-057-G
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-057-G
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2013
Sample #43, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509044 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
200
180
160
140
120
100
80
60
40
20
ppm
N
H
H
N
O
O
NH
H
O
Bn

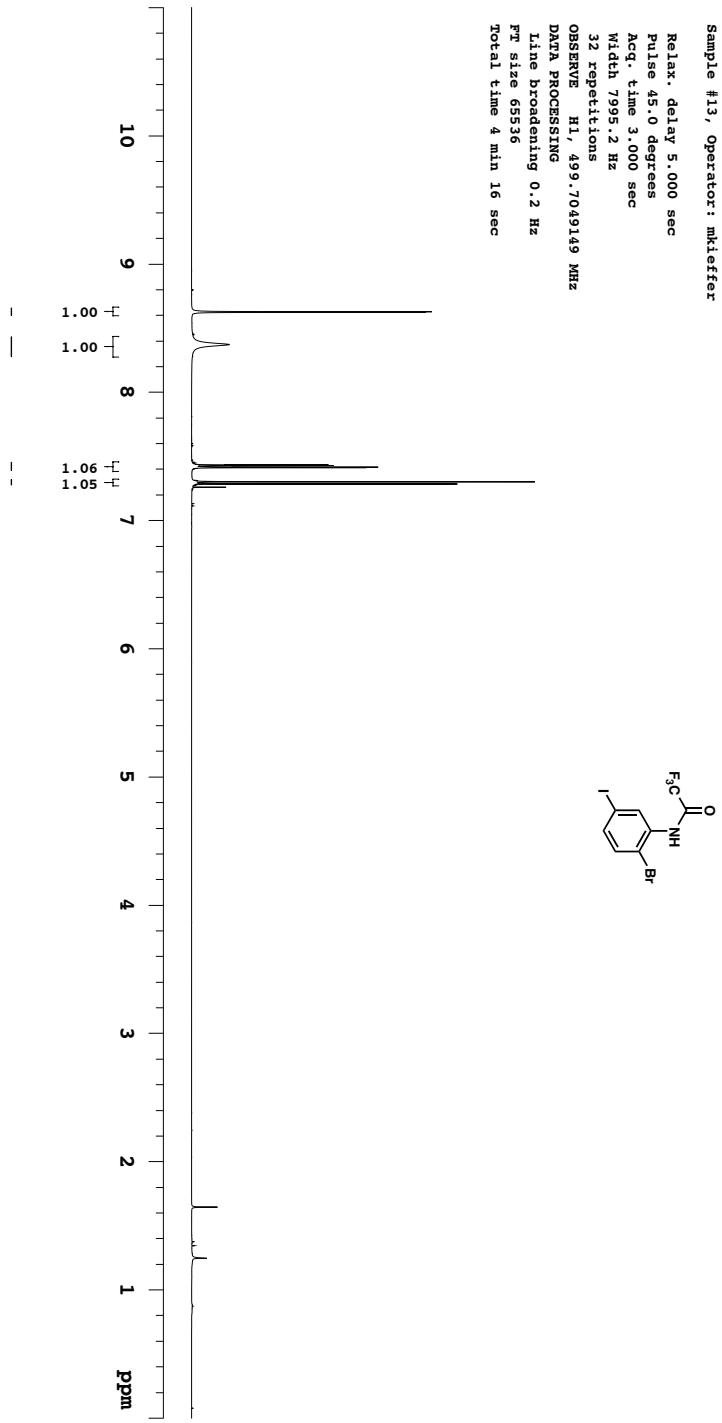

KVC15-195
Sample Name:
KVC15-195
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-195
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #8, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049152 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.97
1.00
2.36
1.04
4.35
1.27
1.05
1.09
1.06
0.93
0.97
0.94
1.05
1.04
1.05
1.00
2.09
10
9
8
7
6
5
4
3
2
1
ppm
Br
Bn

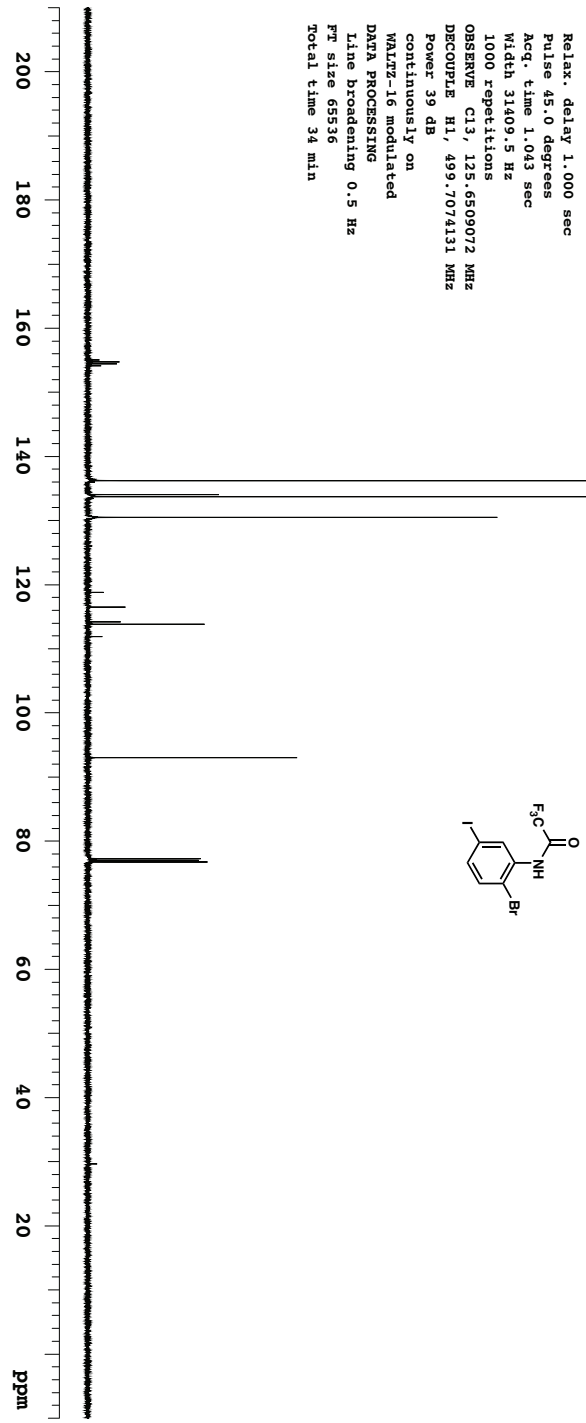

KVC15-195
Sample Name:
KVC15-195
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-195
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #8, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509044 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
220
200
180
160
140
120
100
80
60
40
20
0
ppm
H
N
H
N
O
O
NH
H
Br
Bn

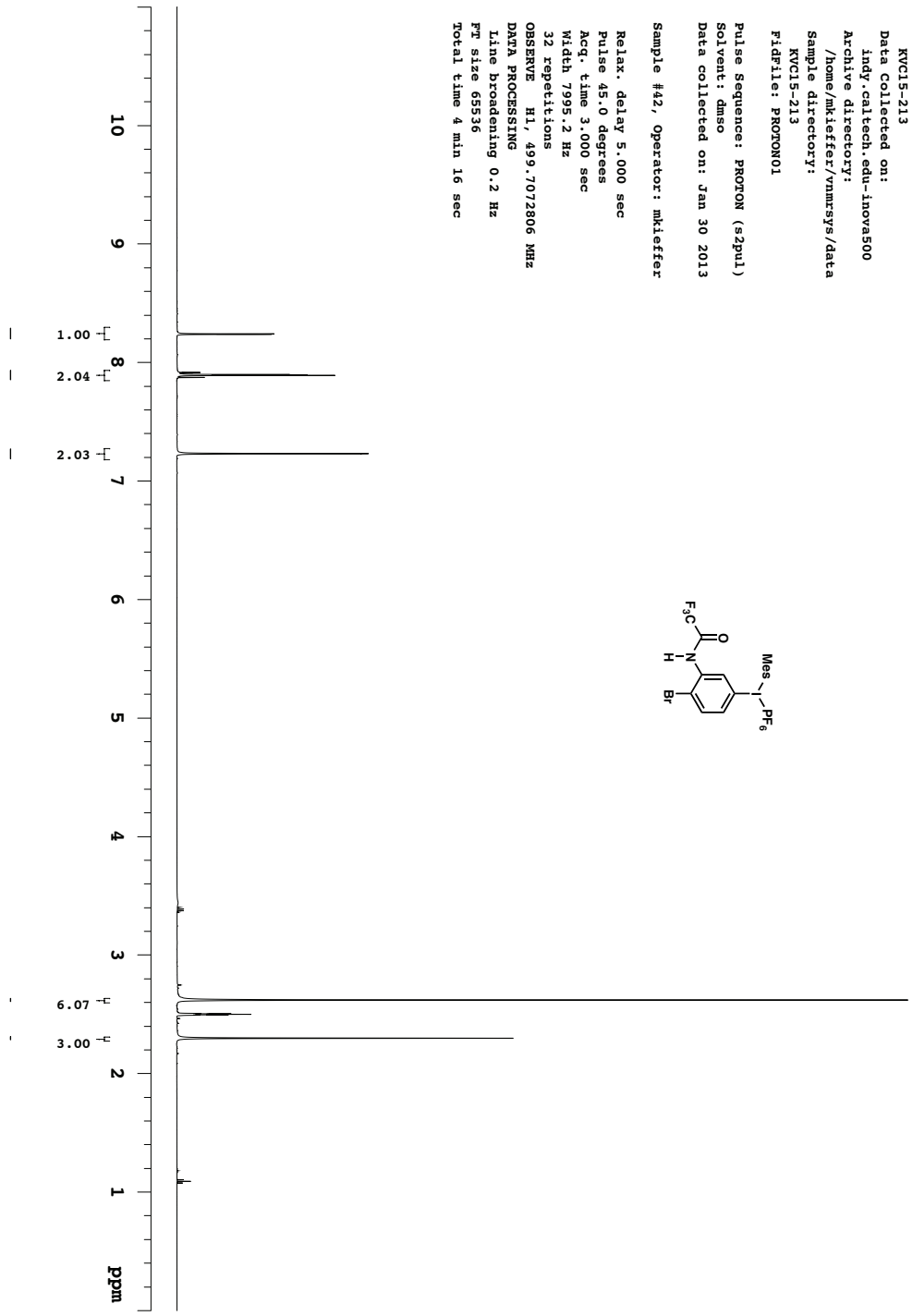

MEK5100
Sample Name:
MEK5100
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5100
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2013
Sample #22, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.95
2.00
1.11
1.30
3.08
1.01
1.02
1.00
0.98
1.00
1.00
3.09
1.04
TFA
NHMe
10
9
8
7
6
5
4
3
2
1
ppm

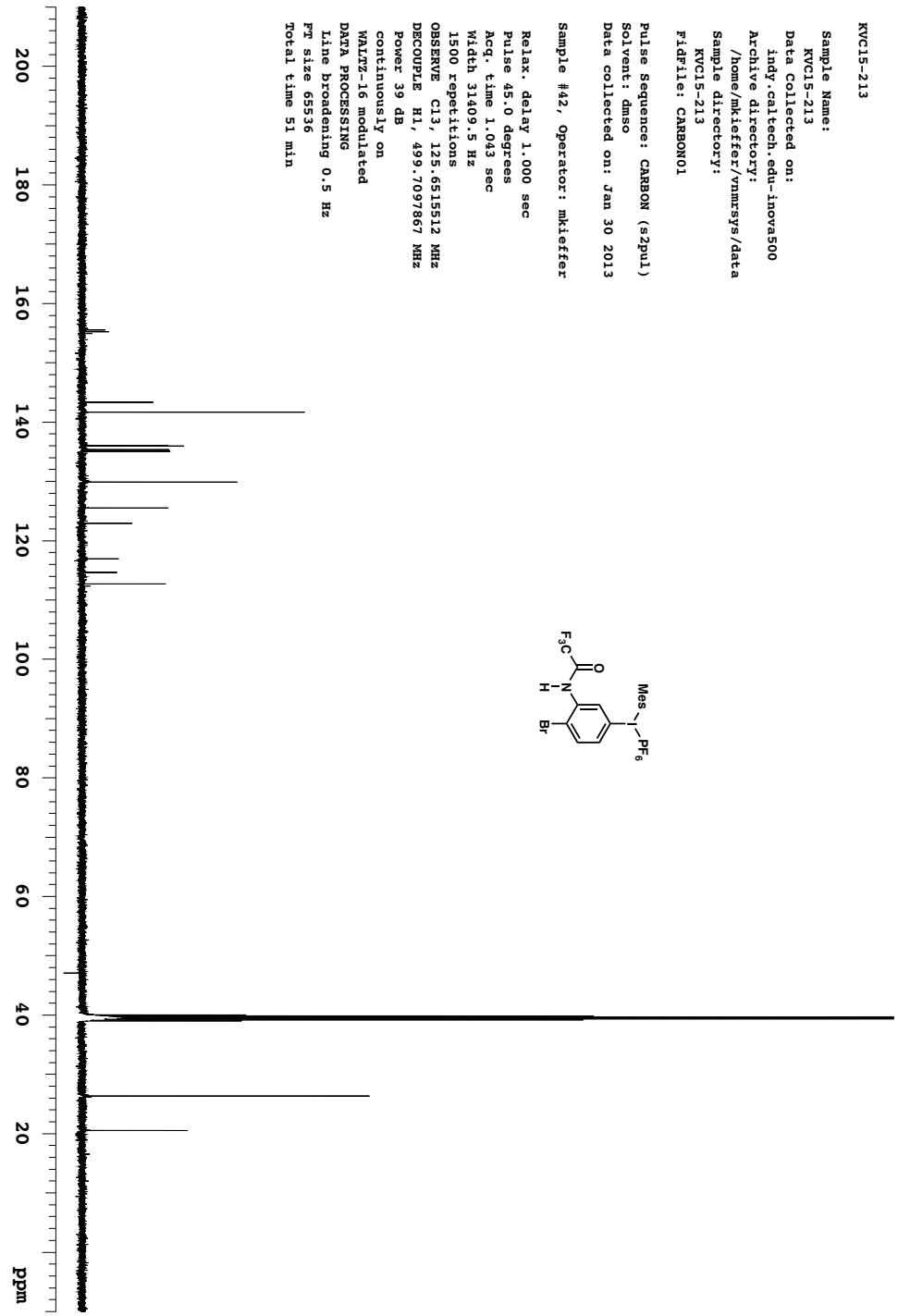

MEK5100
Sample Name:
MEK5100
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5100
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 21 2013
Sample #22, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509034 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
NHMe
TFA
200
180
160
140
120
100
80
60
40
20
ppm

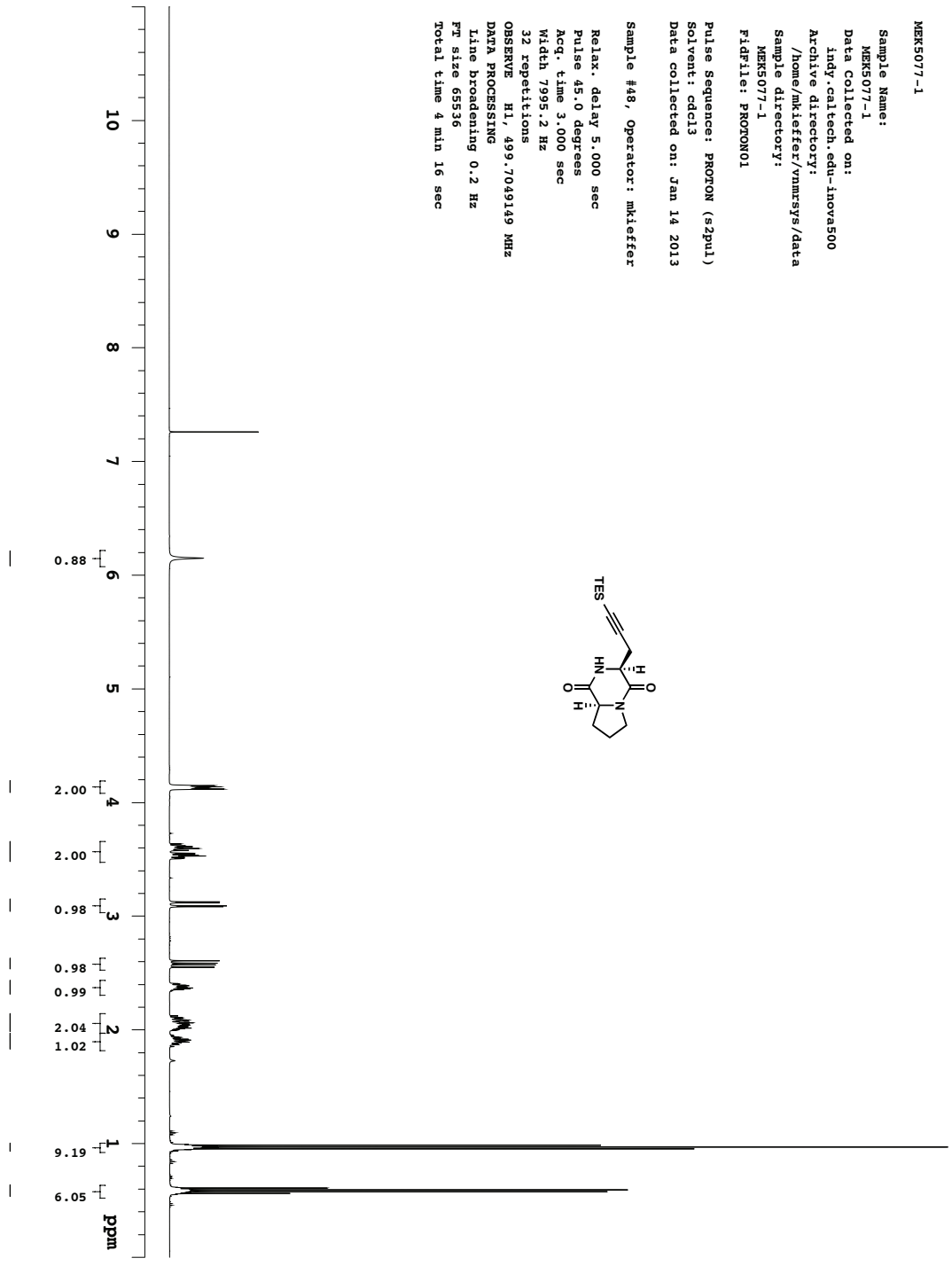

NOESY01
MEK5100
f2 (ppm)
f1 (ppm)
TFA
NHMe

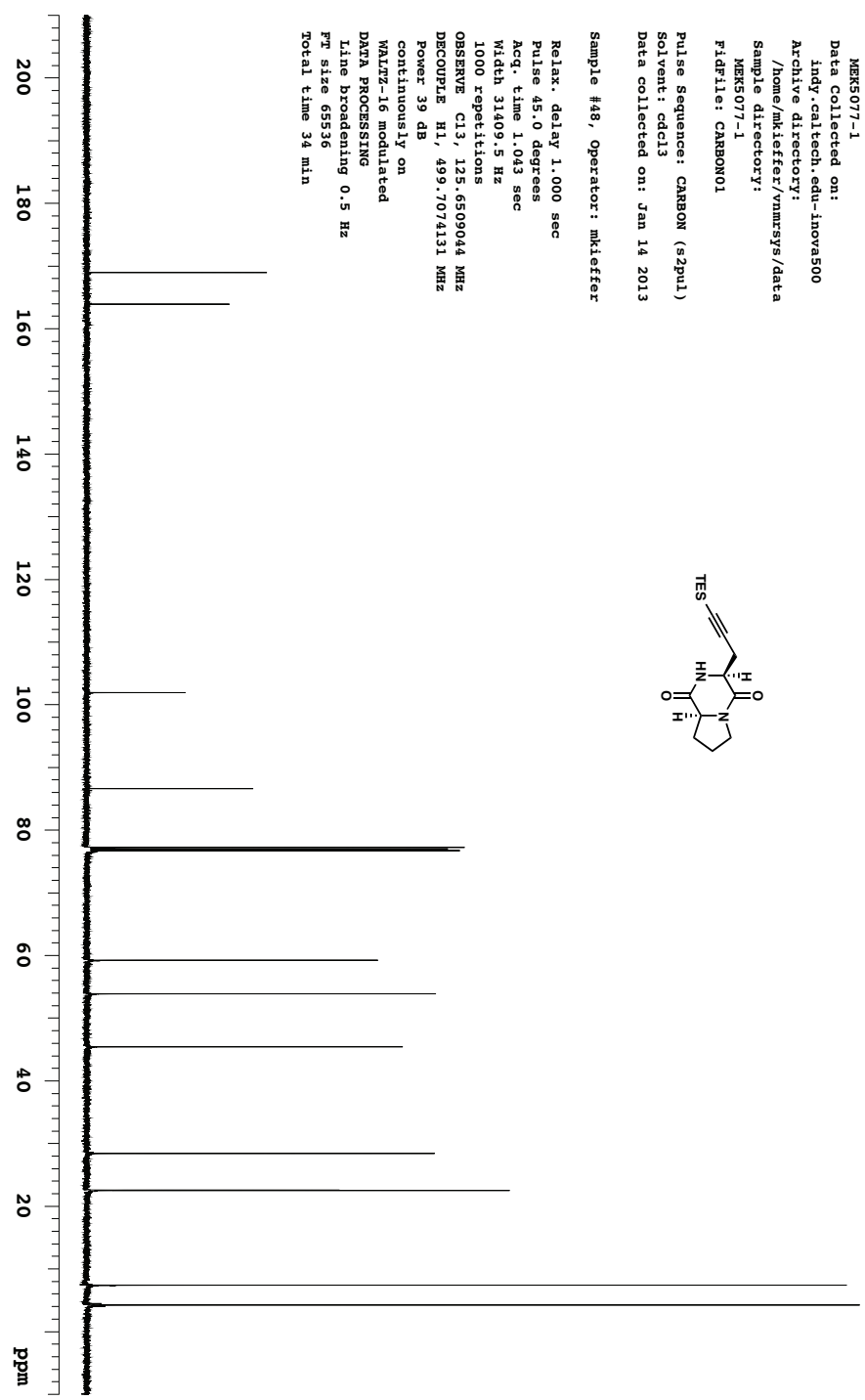

KVC15-023
Sample Name:
KVC15-023
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-023
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #13, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
1.00
1.00
1.06
1.05
10
9
8
7
6
5
4
3
2
1
ppm

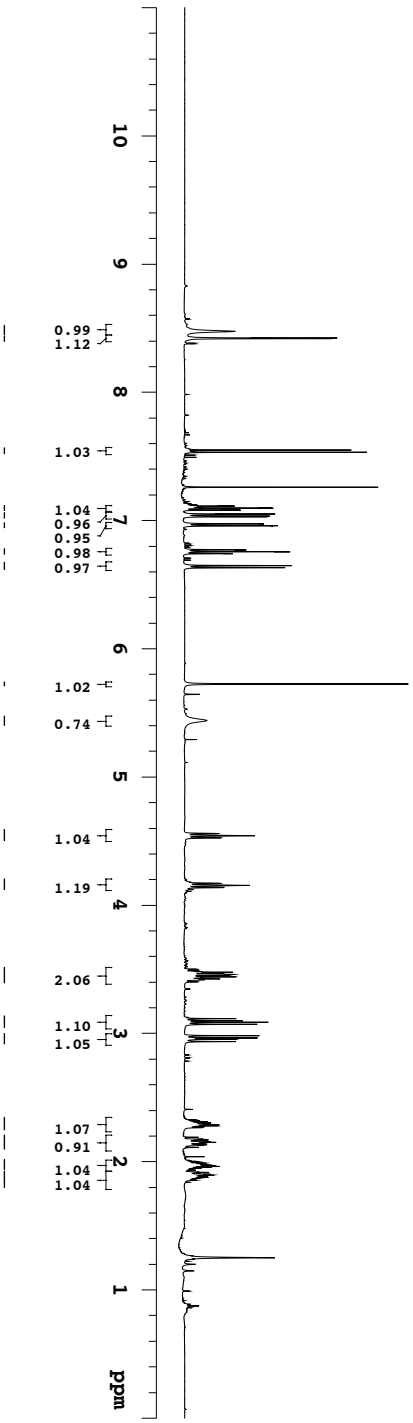

KVC15-023
Sample Name:
KVC15-023
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-023
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 27 2013
Sample #13, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509072 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
O
NH
Br
I
200
180
160
140
120
100
80
60
40
20
ppm

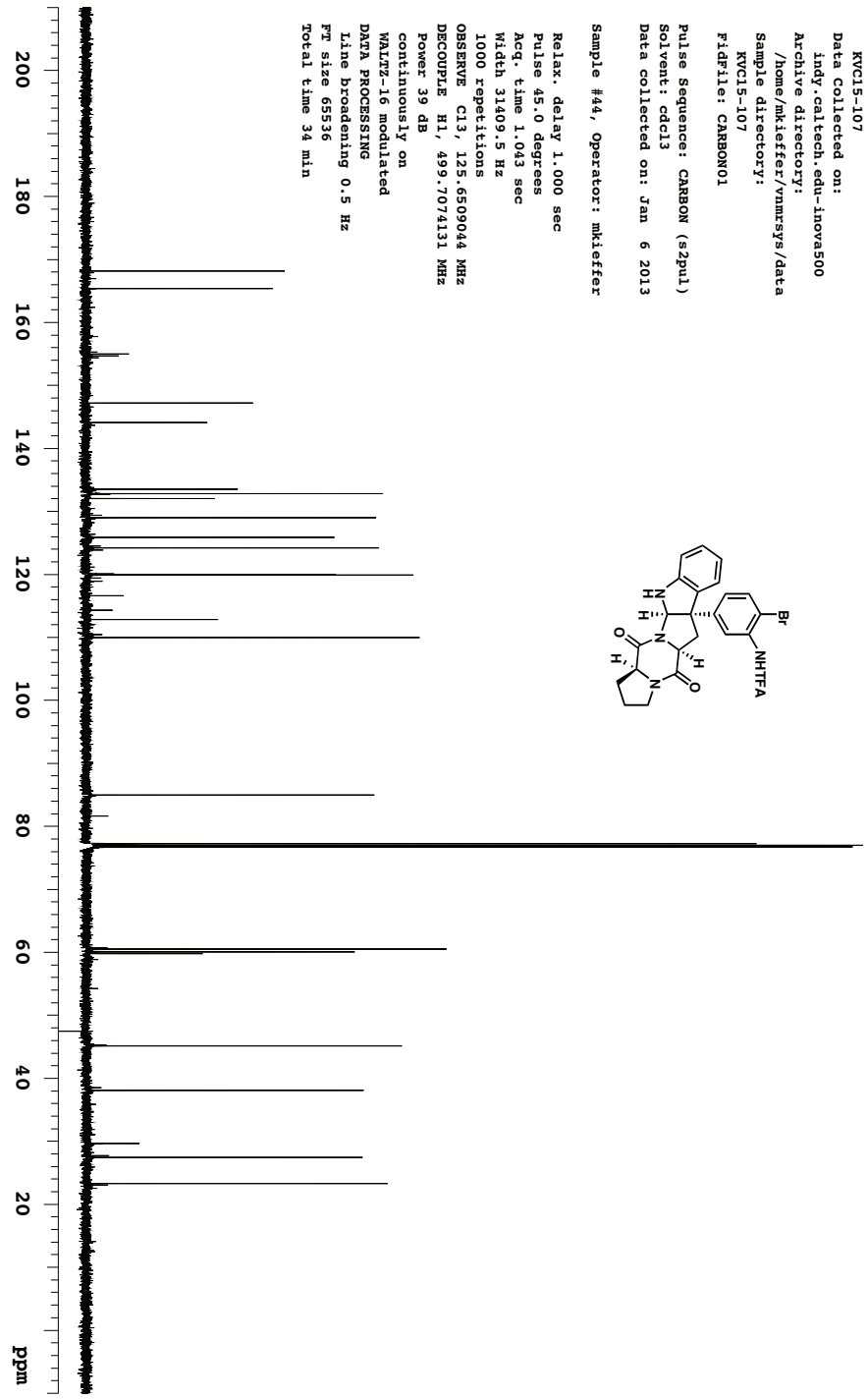

KVC15-213
Sample Name:
KVC15-213
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-213
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Jan 30 2013
Sample #42, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7072806 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
1.00
2.04
2.03
6.07
3.00
10
9
8
7
6
5
4
3
2
1
ppm
F3C
O
N
H
Br
Mes
PF6

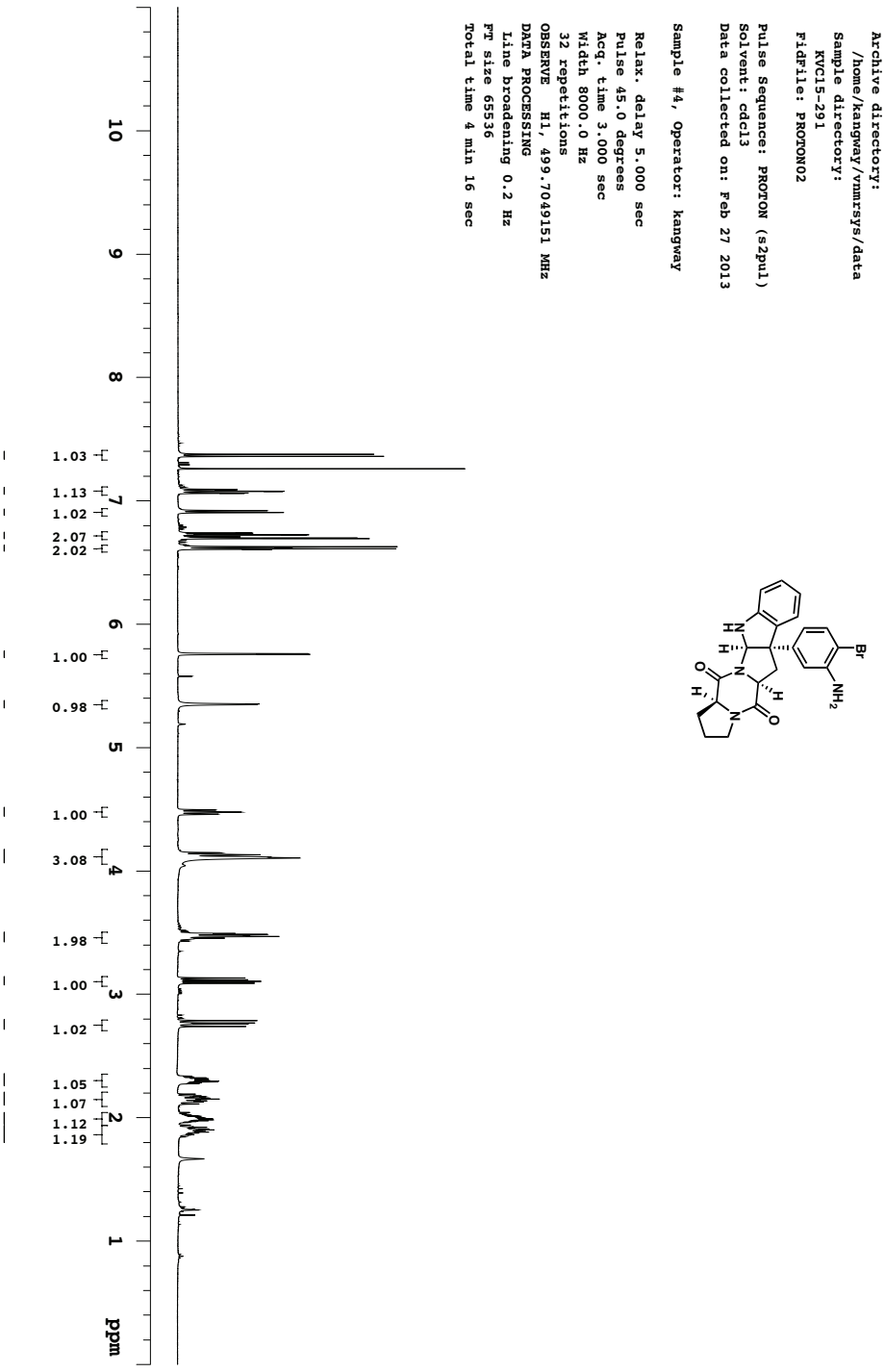

KVC15-213
Sample Name:
KVC15-213
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-213
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Jan 30 2013
Sample #42, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1500 repetitions
OBSERVE C13, 125.6515512 MHz
DECOUPLE H1, 499.7097867 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
F3C
O
N
H
Br
Mes
I
PF6
200
180
160
140
120
100
80
60
40
20
ppm

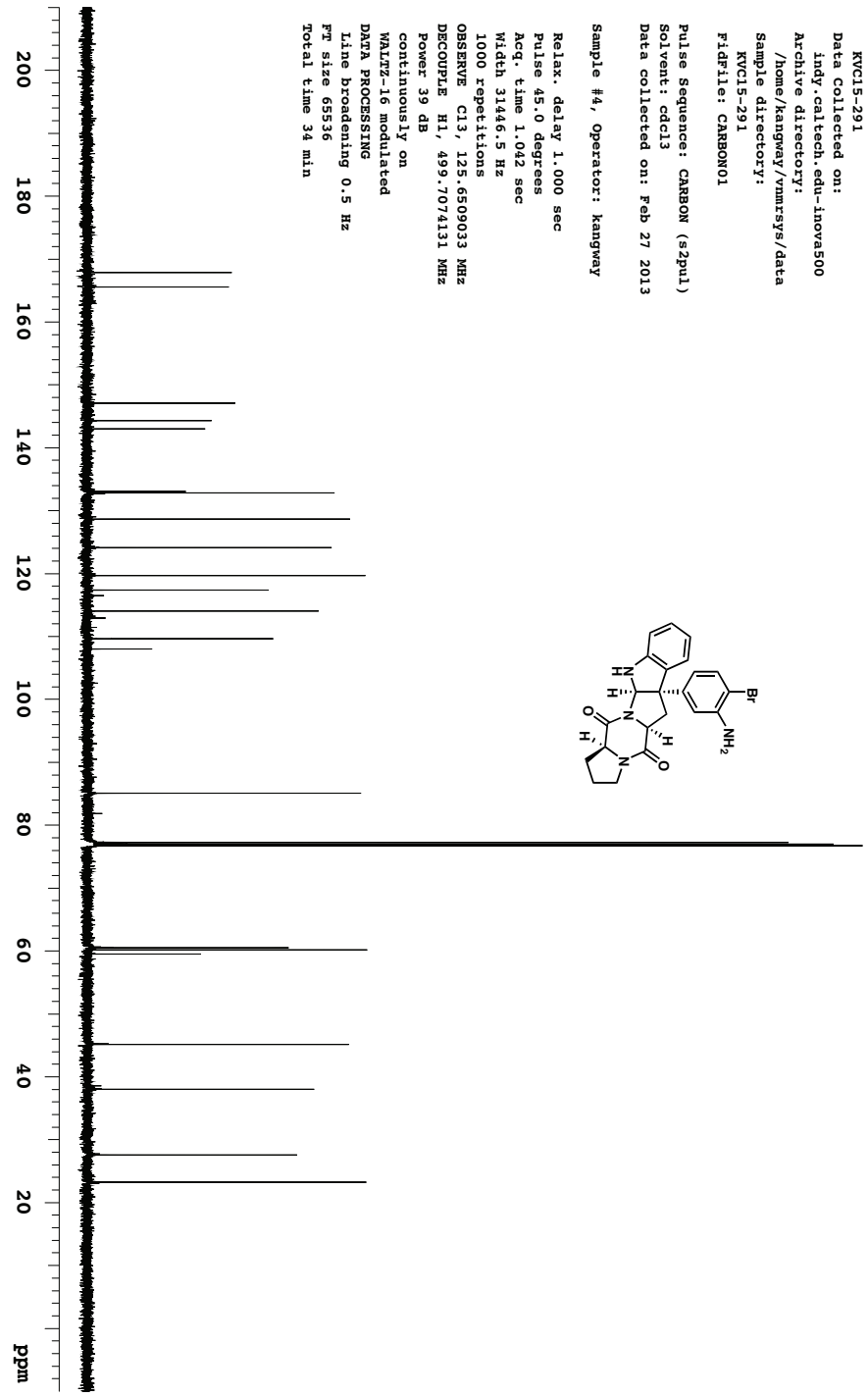

MEK5077-1
Sample Name:
MEK5077-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5077-1
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 14 2013
Sample #48, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
TES
HN
O
N
H
H
O
10
9
8
7
6
5
4
3
2
1
ppm
0.88
2.00
2.00
0.98
0.98
0.99
2.04
1.02
9.19
6.05

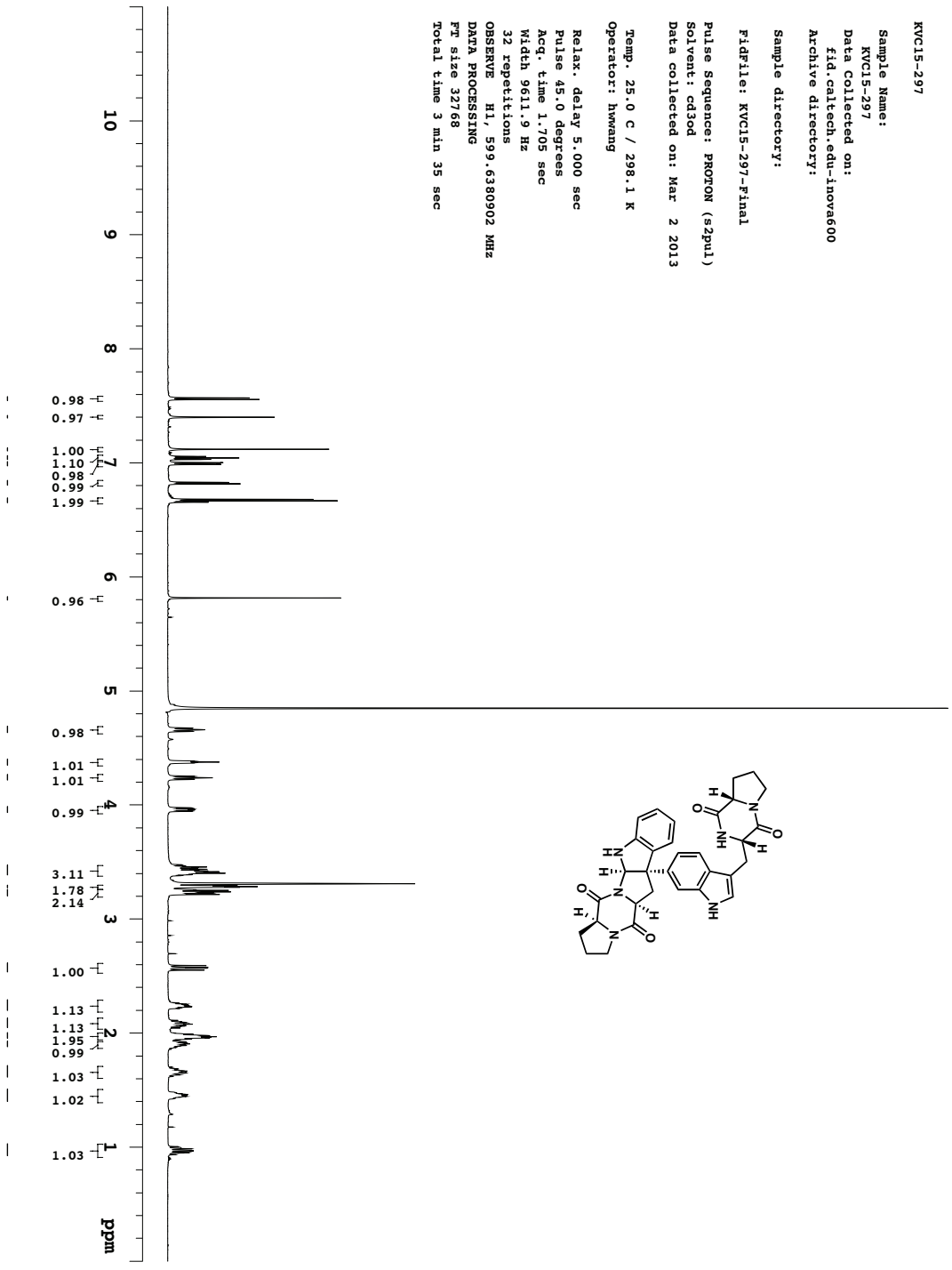

MEK5077-1
Sample Name:
MEK5077-1
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK5077-1
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 14 2013
Sample #48, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509044 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
TES
HN
O
O
H
H
N
200
180
160
140
120
100
80
60
40
20
ppm

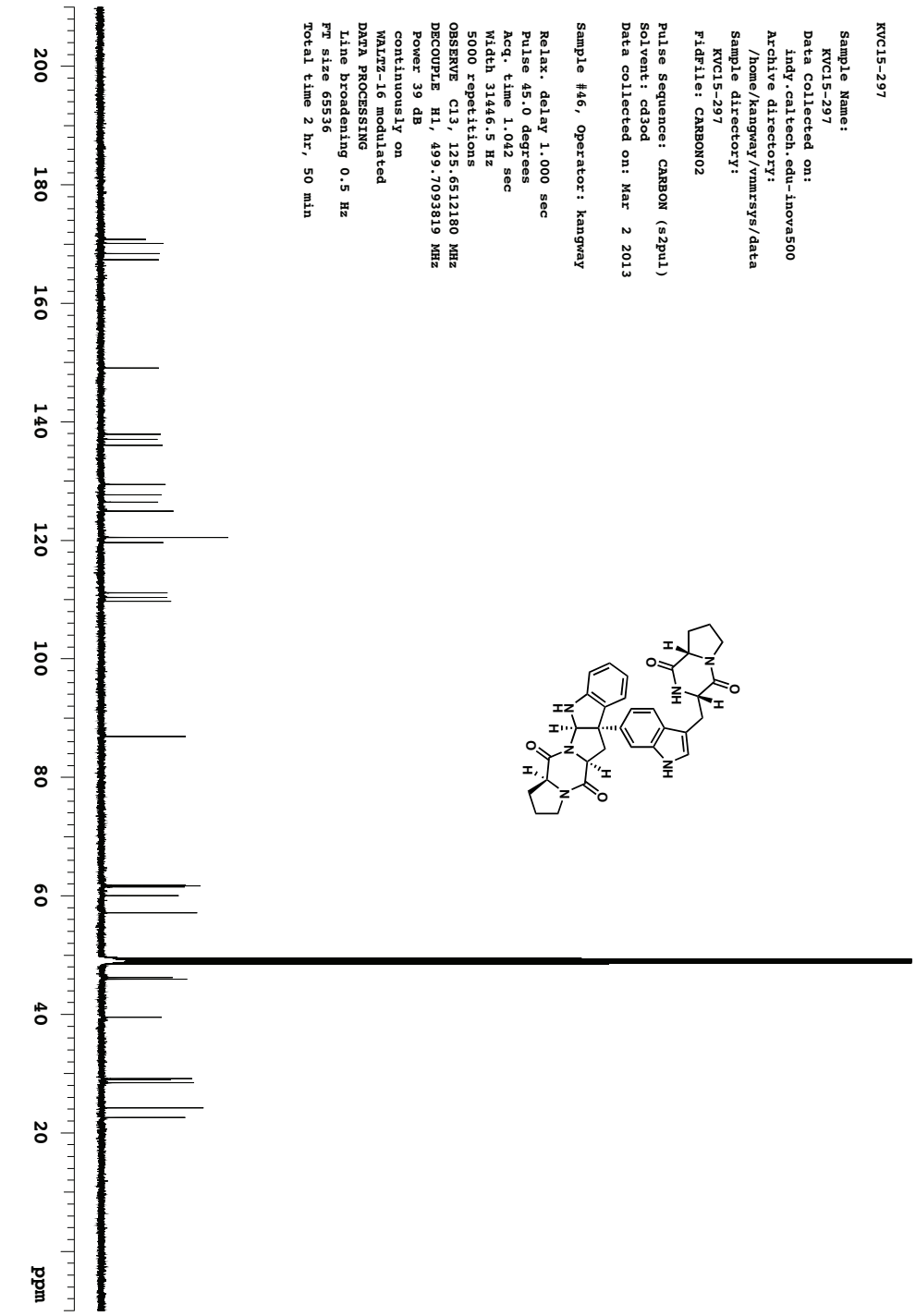

KVC15-107
Sample Name:
KVC15-107
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-107
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2013
Sample #44, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Br
NHTFA
0.99
1.12
1.03
1.04
0.96
0.95
0.98
0.97
1.02
0.74
1.04
1.19
2.06
1.10
1.05
1.07
0.91
1.04
1.04
10
9
8
7
6
5
4
3
2
1
ppm

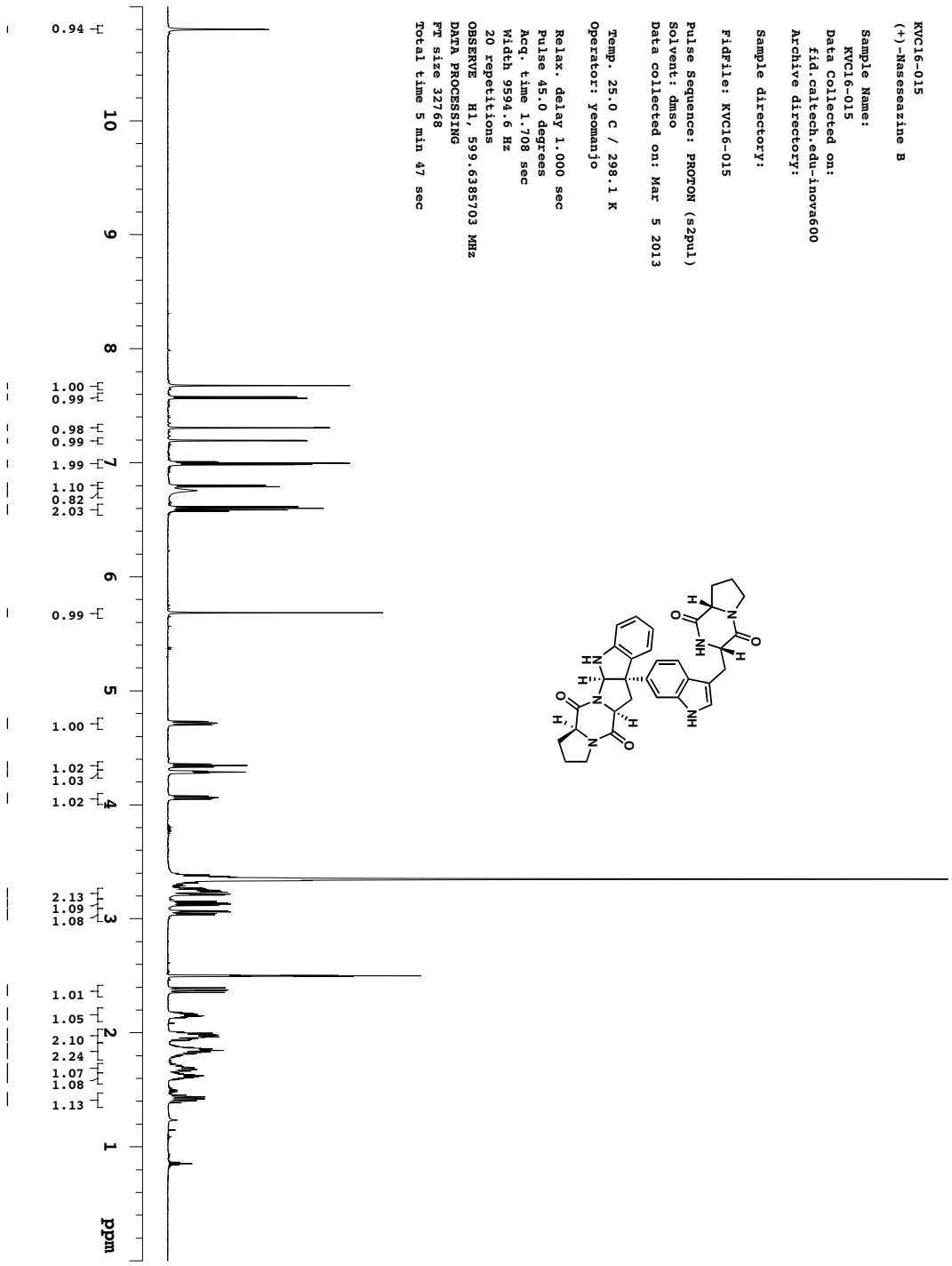

KVC15-107
Sample Name:
KVC15-107
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-107
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 6 2013
Sample #44, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
1000 repetitions
OBSERVE C13, 125.6509044 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Br
NHTFA
200
180
160
140
120
100
80
60
40
20
ppm

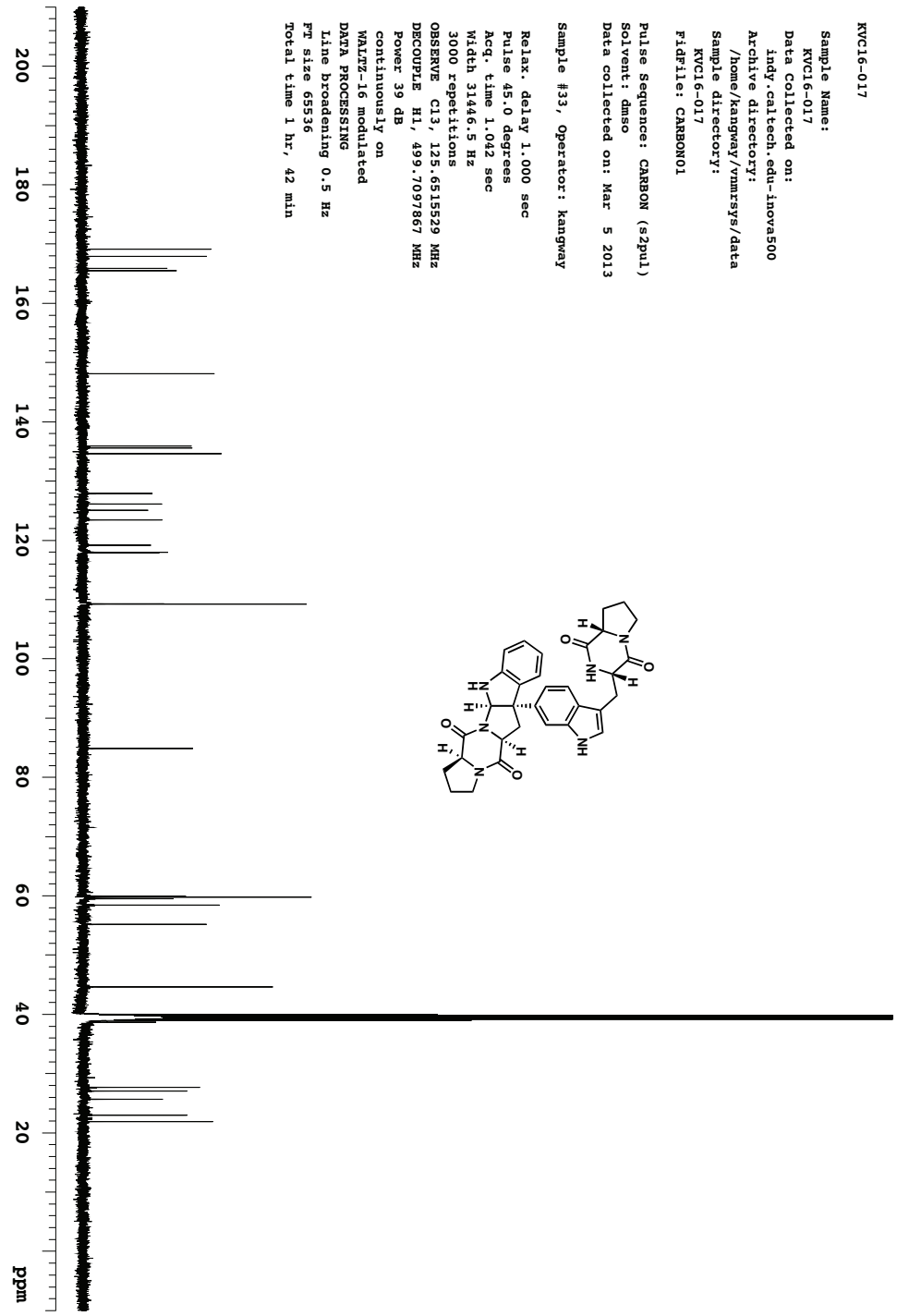

KVC15-291
Sample Name:
KVC15-291
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC15-291
FidFile: PROTONO2
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 27 2013
Sample #4, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7049151 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Br
NH2
1.03
1.13
1.02
2.07
2.02
1.00
0.98
1.00
3.08
1.98
1.00
1.02
1.05
1.07
1.12
1.19
10
9
8
7
6
5
4
3
2
1
ppm

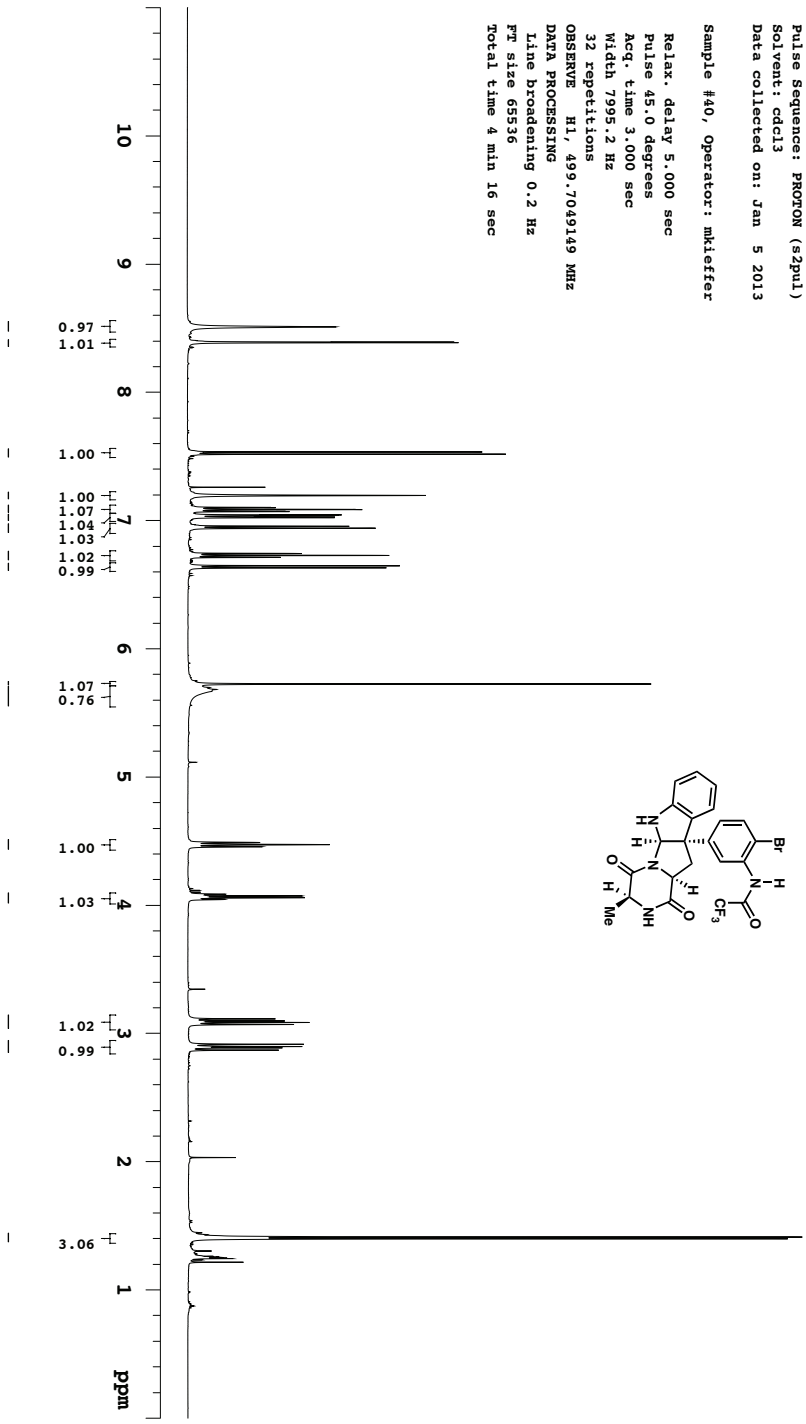

KVC15-291
Sample Name:
KVC15-291
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC15-291
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 27 2013
Sample #4, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6509033 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Br
NH2
200
180
160
140
120
100
80
60
40
20
ppm

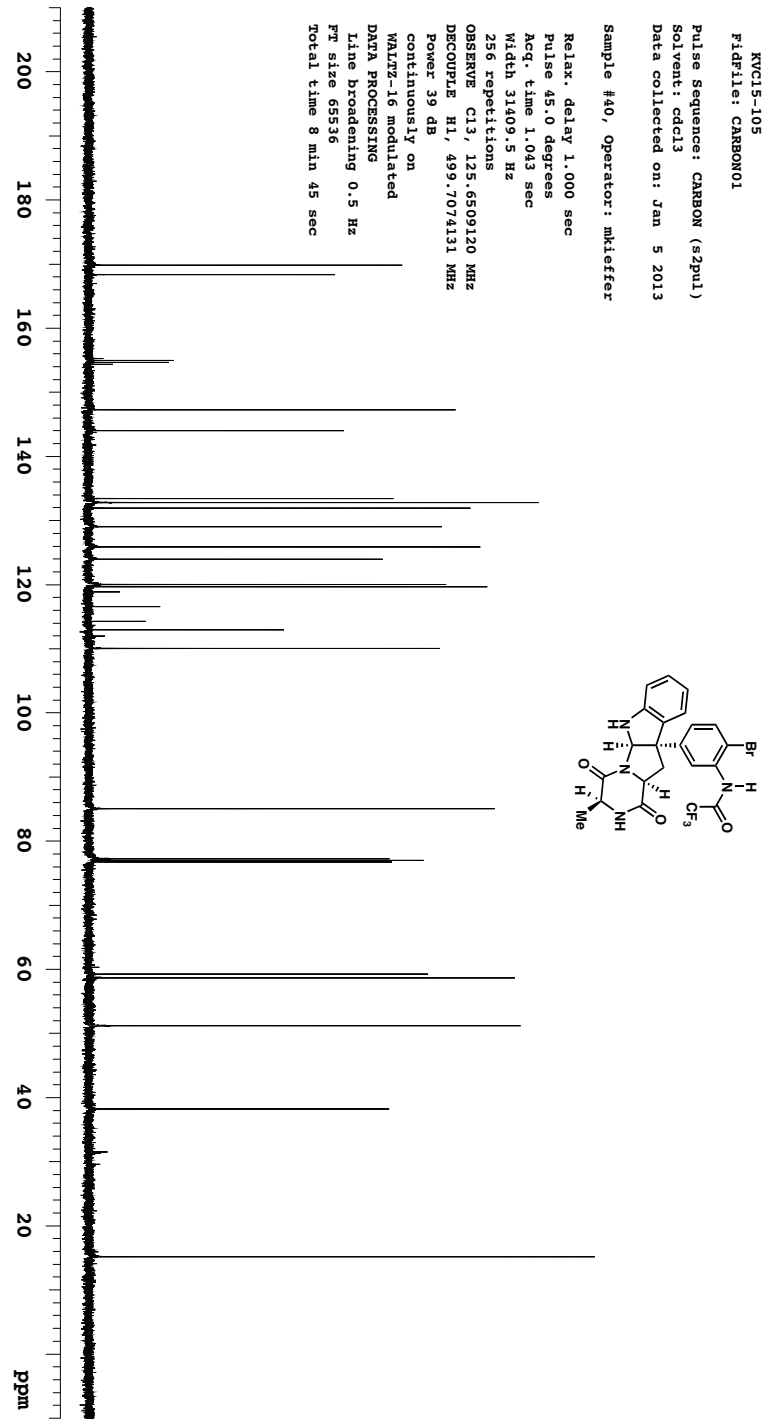

KVC15-297
Sample Name:
KVC15-297
Data Collected on:
fid.caltech.edu-inova600
Archive directory:
Sample directory:
FidFile: KVC15-297-Final
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Mar 2 2013
Temp. 25.0 C / 298.1 K
Operator: hwang
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 1.705 sec
Width 9611.9 Hz
32 repetitions
OBSERVE H1, 599.6380902 MHz
DATA PROCESSING
FT size 32768
Total time 3 min 35 sec
0.98
0.97
1.00
1.10
0.98
0.99
1.99
0.96
0.98
1.01
1.01
0.99
3.11
1.78
2.14
1.00
1.13
1.13
1.95
0.99
1.03
1.02
1.03
10
9
8
7
6
5
4
3
2
1
ppm


KVC15-297
Sample Name:
KVC15-297
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC15-297
FidFile: CARBON02
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Mar 2 2013
Sample #46, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
5000 repetitions
OBSERVE C13, 125.6512180 MHz
DECOUPLE H1, 499.7093819 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 2 hr, 50 min
200
180
160
140
120
100
80
60
40
20
ppm


KVC16-015
(+)-Naseseazine B
Sample Name:
KVC16-015
Data Collected on:
fid.caltech.edu-inova600
Archive directory:
Sample directory:
FidFile: KVC16-015
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Mar 5 2013
Temp. 25.0 C / 298.1 K
Operator: yeomanjo
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.708 sec
Width 9594.6 Hz
20 repetitions
OBSERVE H1, 599.6385703 MHz
DATA PROCESSING
FT size 32768
Total time 5 min 47 sec
0.94
1.00
0.99
0.98
0.99
1.99
1.10
0.82
2.03
0.99
1.00
1.02
1.03
1.02
2.13
1.09
1.08
1.01
1.05
2.10
2.24
1.07
1.08
1.13
10
9
8
7
6
5
4
3
2
1
ppm


KVC16-017
Sample Name:
KVC16-017
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC16-017
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Mar 5 2013
Sample #33, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3000 repetitions
OBSERVE C13, 125.6515529 MHz
DECOUPLE H1, 499.7097867 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 42 min
200
180
160
140
120
100
80
60
40
20
ppm


KVC15-105
Sample Name:
KVC15-105
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC15-105
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 5 2013
Sample #40, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 7995.2 Hz
32 repetitions
OBSERVE H1, 499.7049149 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.97
1.01
1.00
1.00
1.07
1.04
1.03
1.02
0.99
1.07
0.76
1.00
1.03
1.02
0.99
3.06
10
9
8
7
6
5
4
3
2
1
ppm


KVC15-105
Sample Name:
KVC15-105
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
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FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 5 2013
Sample #40, Operator: mkieffer
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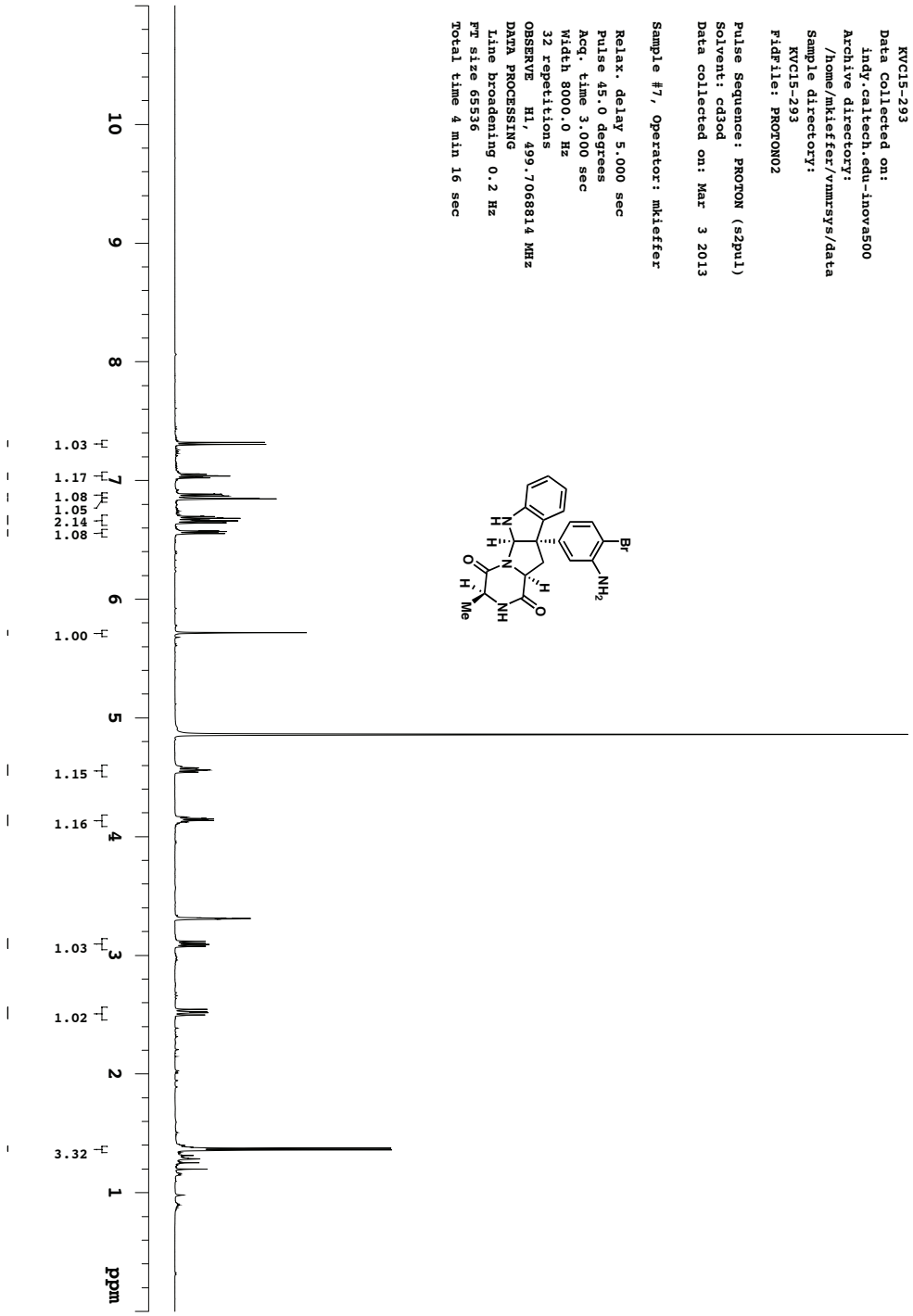
Pulse 45.0 degrees
Acq. time 1.043 sec
Width 31409.5 Hz
256 repetitions
OBSERVE C13, 125.6509120 MHz
DECOUPLE H1, 499.7074131 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
Br
H
N
O
CF3
H
N
H
O
H
N
Me
NH
O
200
180
160
140
120
100
80
60
40
20
ppm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KVC15-293
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
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Sample directory:
KVC15-293
FidFile: PROTONO2
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Mar 3 2013
Sample #7, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.7068814 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
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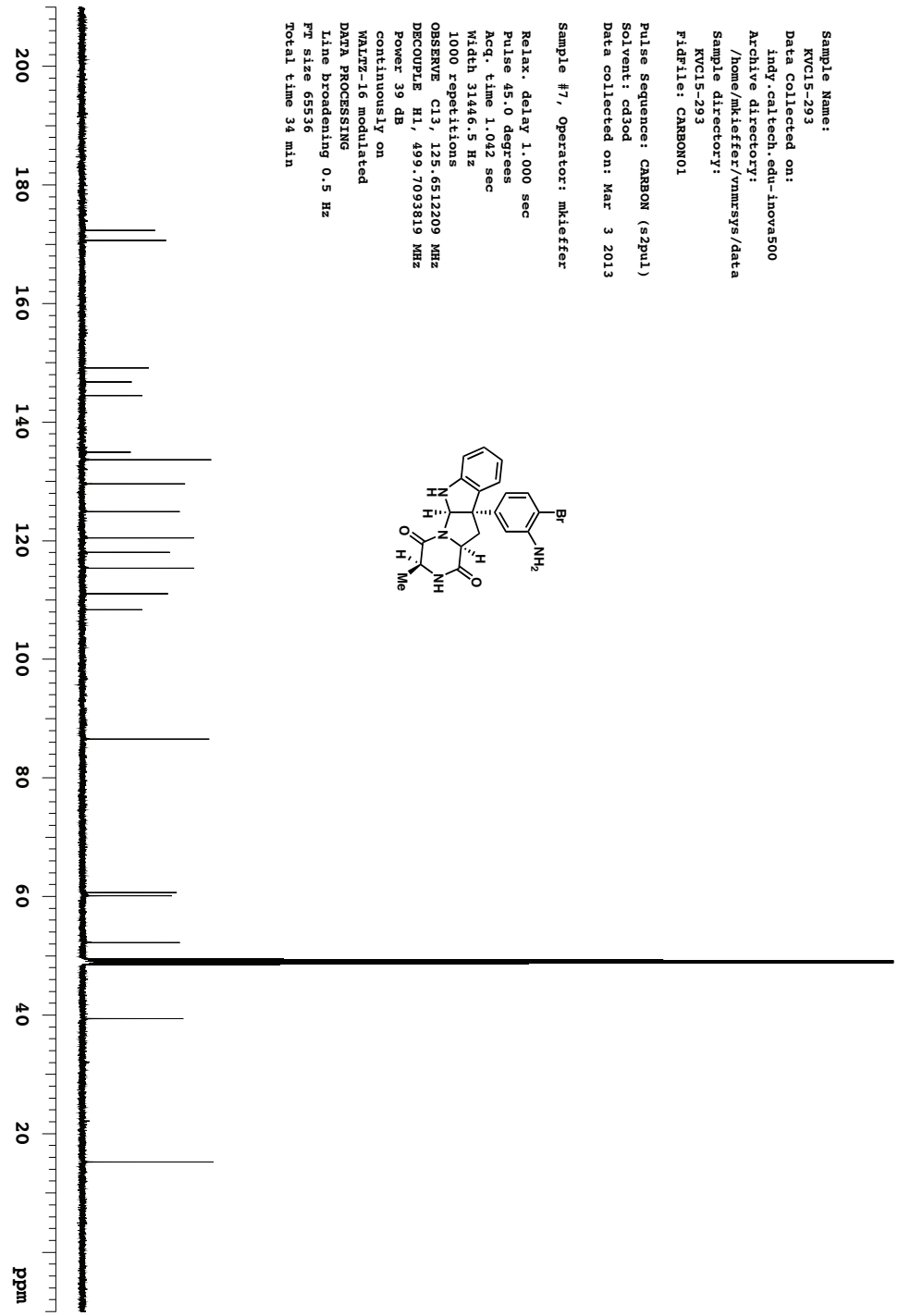
1.17
1.08
1.05
2.14
1.08
1.00
1.15
1.16
1.03
1.02
3.32
ppm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KVC15-293
Data Collected on:
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Archive directory:
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Sample directory:
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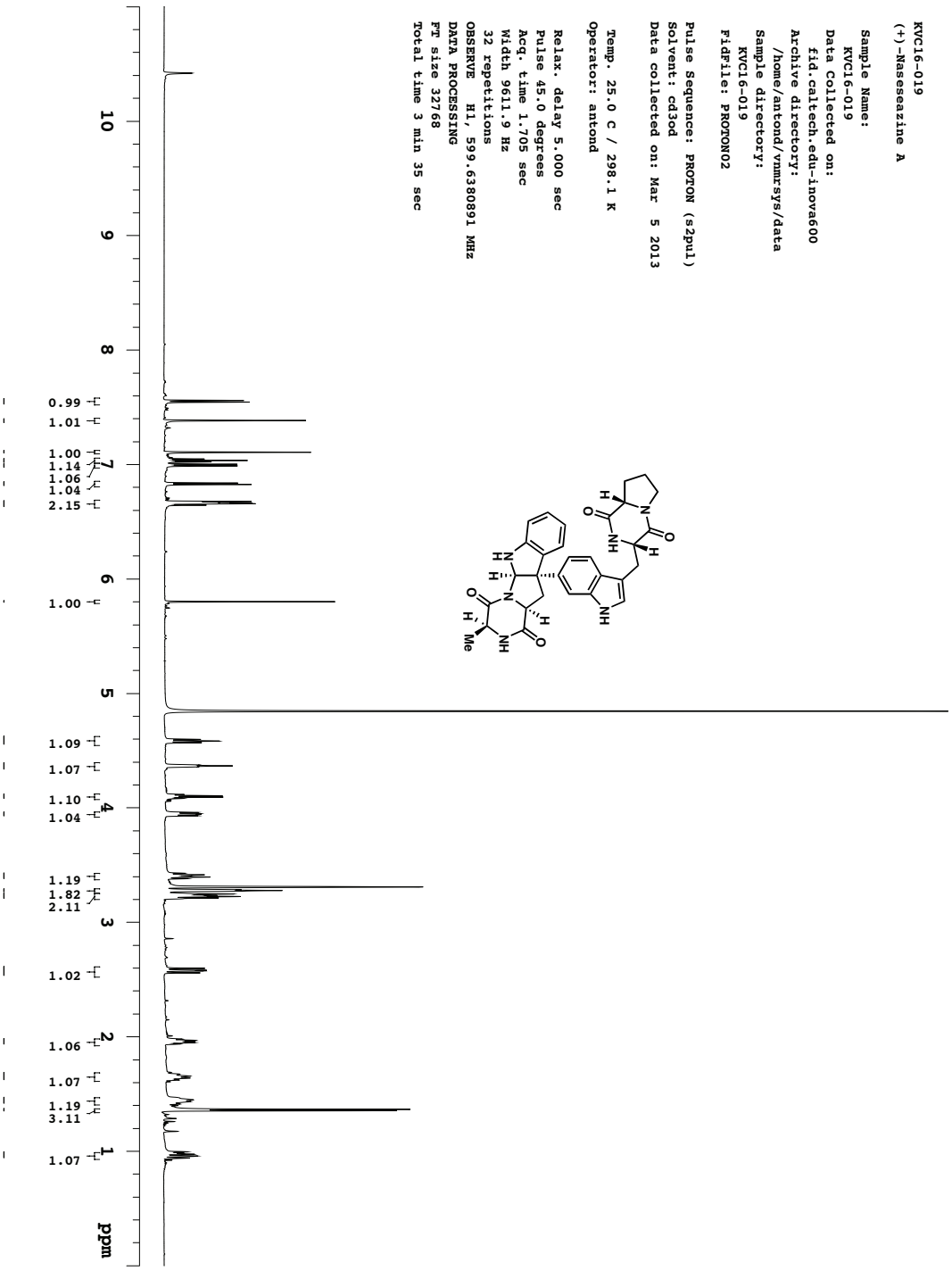
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Mar 3 2013
Sample #7, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6512209 MHz
DECOUPLE H1, 499.7093819 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Br
NH2
H
N
H
N
O
H
Me
NH
O
200
180
160
140
120
100
80
60
40
20
ppm


KVC16-019
(+)-Naseseazine A
Sample Name:
KVC16-019
Data Collected on:
fid.caltech.edu-inova600
Archive directory:
/home/antond/vnmrsys/data
Sample directory:
KVC16-019
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Mar 5 2013
Temp. 25.0 C / 298.1 K
Operator: antond
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 1.705 sec
Width 9611.9 Hz
32 repetitions
OBSERVE H1, 599.6380891 MHz
DATA PROCESSING
FT size 32768
Total time 3 min 35 sec
0.99
1.01
1.00
1.14
1.06
1.04
2.15
1.00
1.09
1.07
1.10
1.04
1.19
1.82
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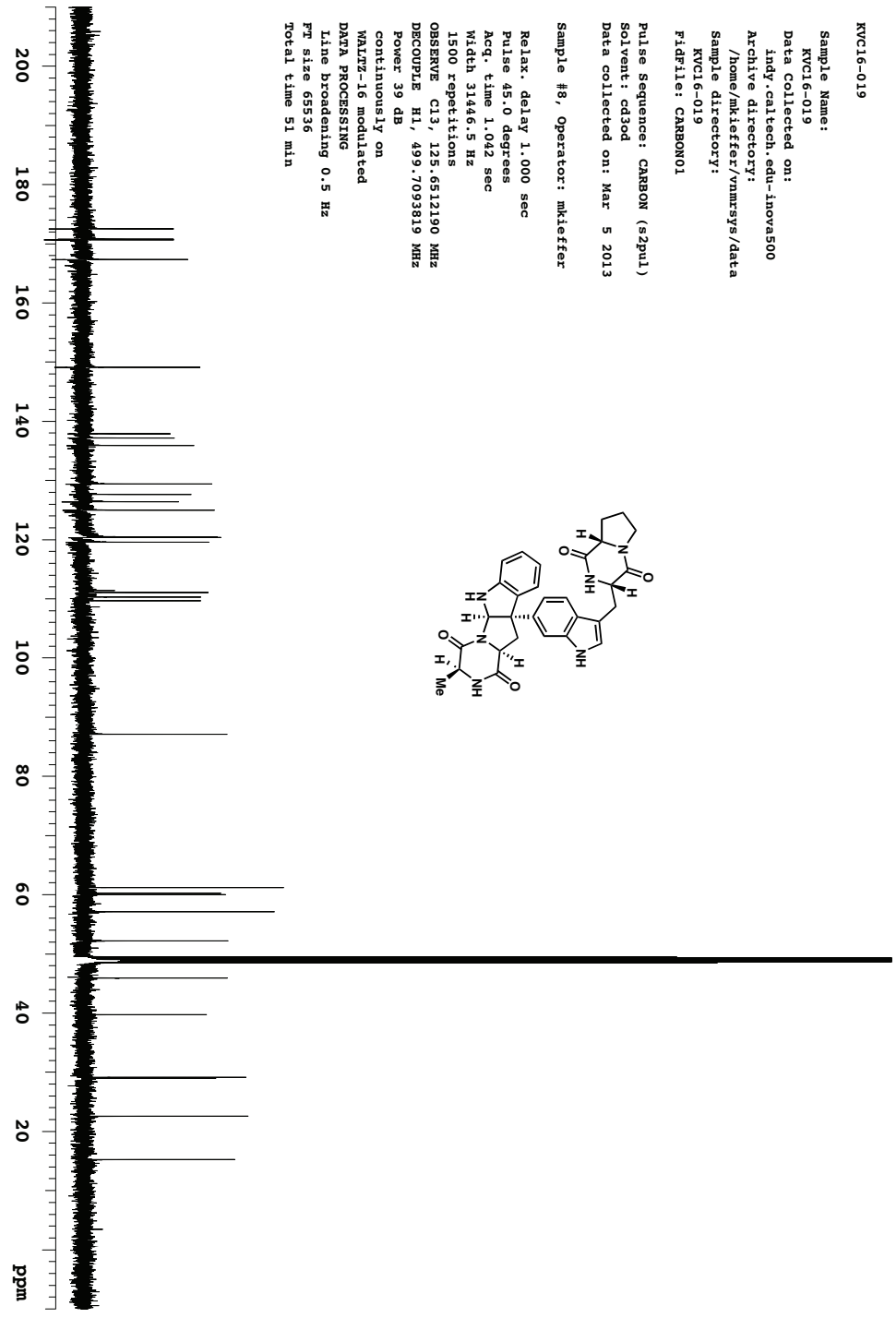
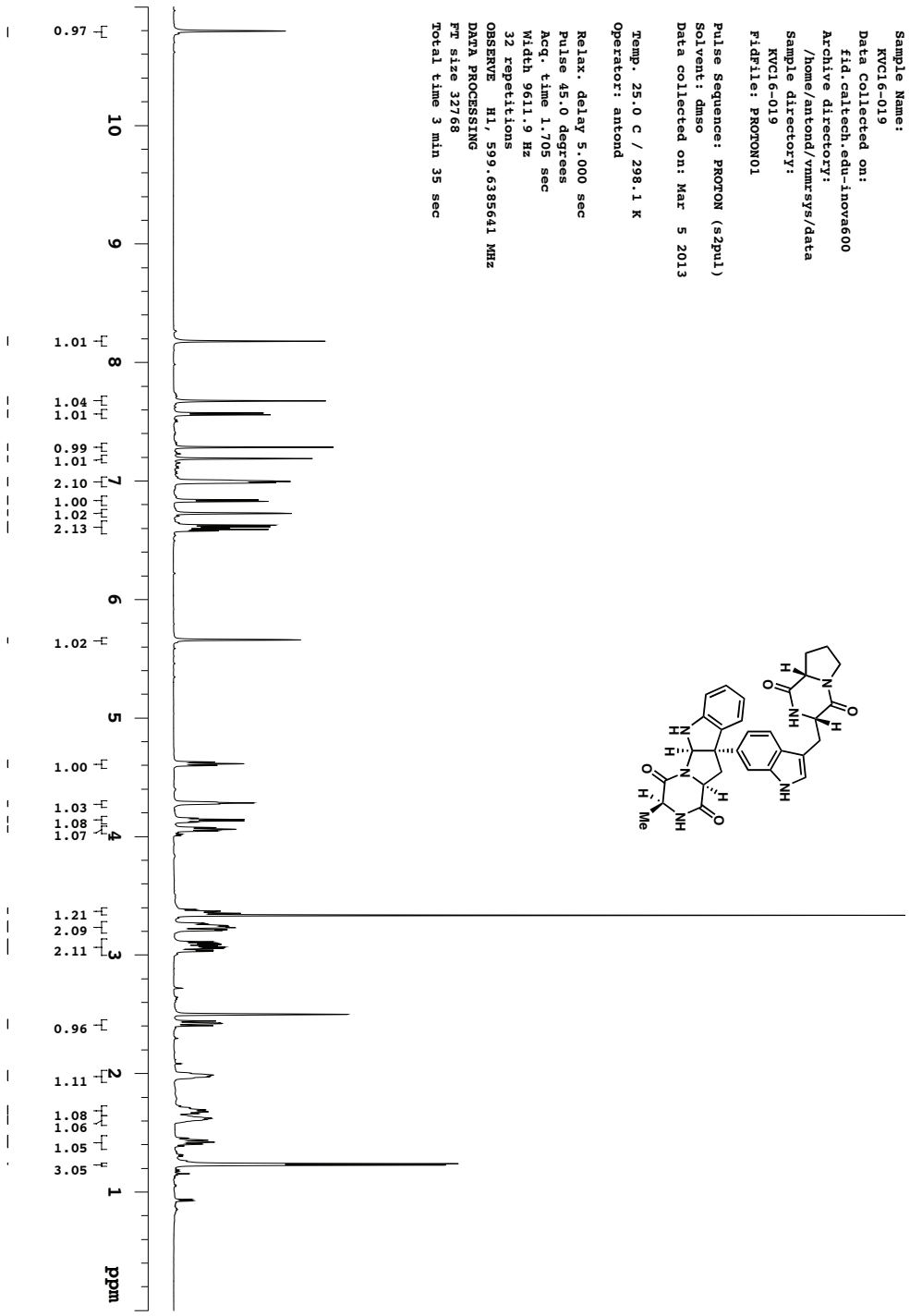
1.06
1.07
1.19
3.11
1.07
ppm


KVC16-019
Sample Name:
KVC16-019
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
KVC16-019
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3od
Data collected on: Mar 5 2013
Sample #8, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6512190 MHz
DECOUPLE H1, 499.7093819 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
200
180
160
140
120
100
80
60
40
20
ppm


KVC16-019
(+)-Naseseazine A
Sample Name:
KVC16-019
Data Collected on:
fid.caltech.edu-inova600
Archive directory:
/home/antond/vnmrsys/data
Sample directory:
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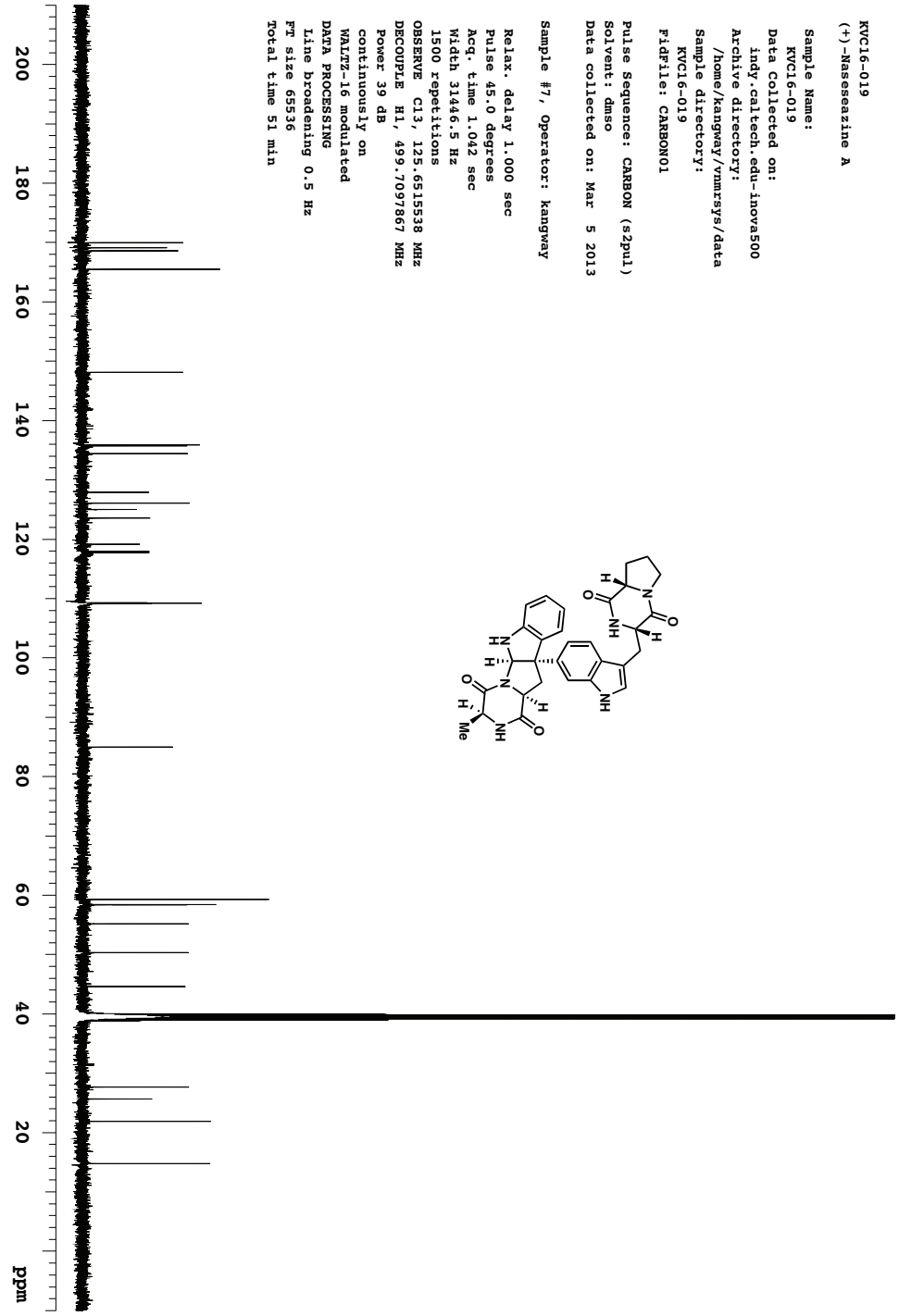
Solvent: dmso
Data collected on: Mar 5 2013
Temp. 25.0 C / 298.1 K
Operator: antond
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 1.705 sec
Width 9611.9 Hz
32 repetitions
OBSERVE H1, 599.6385641 MHz
DATA PROCESSING
FT size 32768
Total time 3 min 35 sec
0.97
1.01
1.04
1.01
0.99
1.01
2.10
1.00
1.02
2.13
1.02
1.00
1.03
1.08
1.07
1.21
2.09
2.11
0.96
1.11
1.08
1.06
1.05
3.05
10
9
8
7
6
5
4
3
2
1
ppm


KVC16-019
(+)-Naseseazine A
Sample Name:
KVC16-019
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
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Sample directory:
KVC16-019
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Mar 5 2013
Sample #7, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.651538 MHz
DECOUPLE H1, 499.709787 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
200
180
160
140
120
100
80
60
40
20
ppm

Chapter 4

A Mild and General Larock Indolization Protocol for the Synthesis of Unnatural Tryptophan Derivatives: Total Synthesis of (–)-Aspergilazine A.[†]

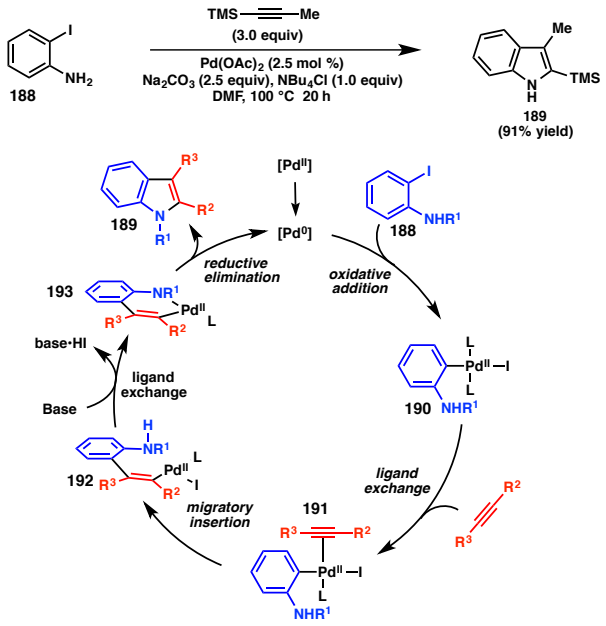
4.1 INTRODUCTION

The Pd(0)-catalyzed heteroannulation of disubstituted alkynes and 2-haloanilines, widely known as the Larock indole synthesis, is a powerful method for the preparation of structurally complex 2,3-disubstituted indoles that has found tremendous utility in accessing indole building blocks, unnatural tryptophan derivatives, and indole-containing natural products.[1,2,3,4] Mechanistically, it is expected to proceed through an active Pd(0) catalyst which can then undergo oxidative addition into 2-iodoaniline **188**. Coordination of an internal alkyne to adduct **190**, followed by migratory insertion and reductive elimination furnishes the indole product **189** and regenerates the Pd(0) catalyst. To date, Larock's original conditions – which couple an *o*-iodoaniline to an internal alkyne in the

[†] Portions of this chapter have been reproduced from submitted studies (Chuang, K. V.; Kieffer, M. E.; Reisman, S. E. *submitted*) and the supporting information found therein. Work was conducted in collaboration with Kangway V. Chuang.

presence of a "ligandless" Pd-catalyst, an inorganic base, and a chloride additive – still remain the most widely employed.[5]

Scheme 4.1. *The Larock indole synthesis catalytic cycle*



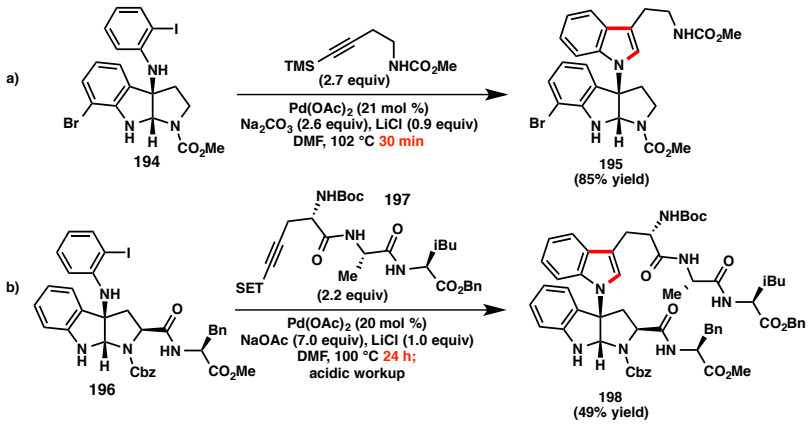
Despite the broad utility of the Larock indole synthesis, a surprisingly small portion of the literature has been dedicated to improving reaction conditions and expanding the substrate scope. From the standpoint of transition-metal catalysis, significant challenges remain, as the application of this reaction in the presence of more complex functionality requires increased catalyst loadings and reaction times due to diminished catalytic activity and poor catalyst turnover. These challenges were highlighted in our synthesis of (+)-naseseazines A and B (**Chapter 3**).[6] Specifically, low reactivity was observed with substoichiometric amounts of Pd catalyst, whereas use of higher Pd-loadings or more forcing conditions resulted in competitive hydrodehalogenation, problematic epimerization of the diketopiperazine, poor regioselectivity, and low mass recovery. This chapter describes our efforts to better

understand the intricacies of this transformation to aid in the development of a modified Larock indolization protocol. The mild procedure described herein enables the coupling of 2-bromoanilines with high functional group compatibility to provide structurally complex and synthetically useful indoles.

4.1.1 The Larock Indole Synthesis in Natural Products

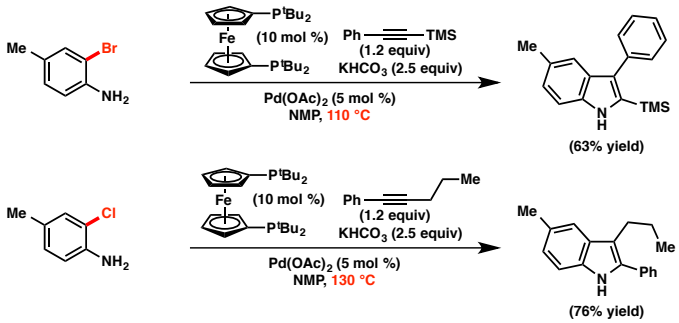
Following its initial disclosure in 1991, the Larock indole synthesis has been beautifully employed in a variety of total syntheses. Elegant examples from the Baran lab demonstrate the ability to quickly advance iodoaniline substrates **194** and **196** to highly functionalized intermediates *en route* to natural products such as psychotrimine and (+)-kapakahine B.[3] Despite the impressive and rapid generation of substrate complexity, these examples highlight the limitations of this catalyst system in tolerating functionalized substrates. For example, in their synthesis of kapakahine B, 20 mol % $Pd(OAc)_2$ is necessary to effect two productive turnovers on a complex iodoaniline substrate (**Scheme 4.2**, **b**). Generally, increased substrate complexity, especially with respect to *polar functionality* and *epimerizable centers*, necessitates increased catalyst loadings and reaction times, and typically results in lower product yields.

Scheme 4.2. *Iodoanilines in natural product synthesis*



It was not until 2004 that modifications to Larock's original conditions allowed for the successful implementation of bromo- and chloro-electrophiles. Employing 10 mol % of bidentate phosphine ligand 1,1'bis(di-*tert*-butylphosphino)ferrocene at elevated temperatures (110 – 130 °C), Senanayake and co-workers found that haloaniline substrates underwent smooth reaction to provide simple indoles in moderate to good yields (**Scheme 4.3**).[7]

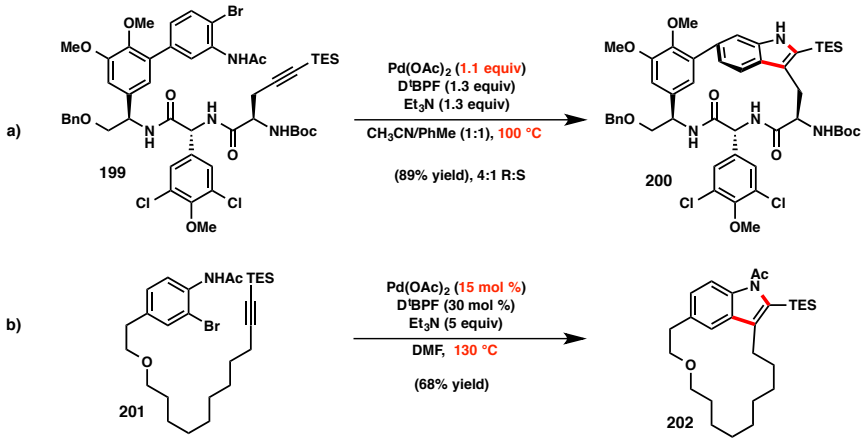
Scheme 4.3. *Larock modfications to include bromo- and chloroelectrophiles.*



Boger and co-workers have further explored the application of this phosphine ligand and bromoanilines in the context of total synthesis.[4] Utilizing a strategic intramolecular Larock reaction to assemble the key macrocyclic framework (**200**), early efforts resulted in poor mass recovery, competitive hydrodechlorination, and undesired epimerization of several critical α-stereocenters. Only after extensive optimization and

use of superstoichiometric Pd-catalyst and ligand were high yields obtained (**Scheme 4.4**, **a**). In a follow-up report, a catalytic Larock macrocyclization reaction was reported using 15 mol % $Pd(OAc)_2$ and 30 mol % ligand at 130 °C, but *only substrates without polar functionality and epimerizable centers* are competent in this transformation.[4]

Scheme 4.4. *Bromoanilines as electrophiles for the Larock indole synthesis*



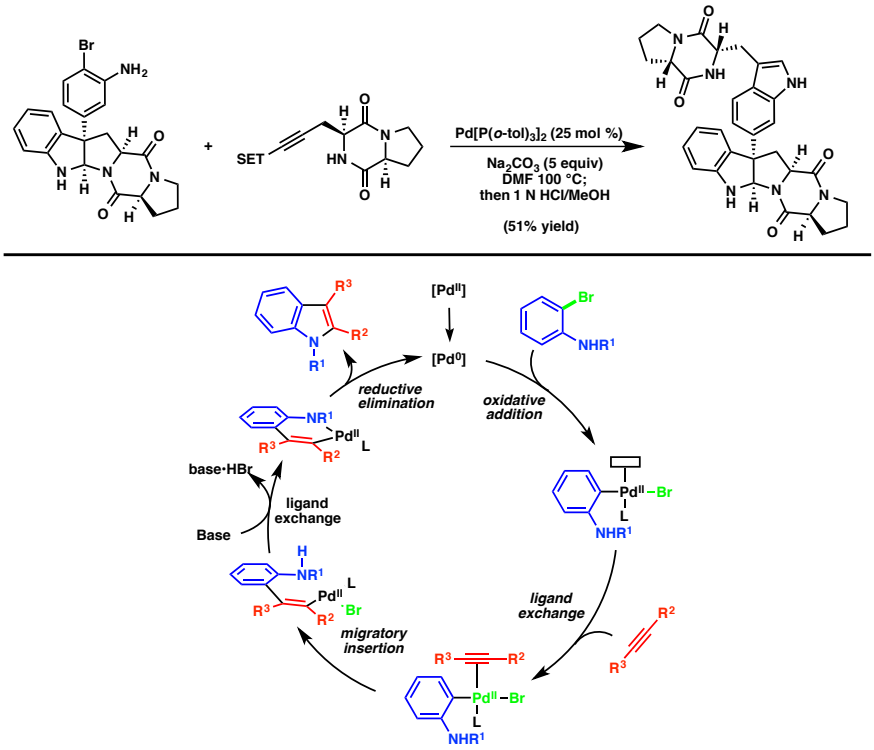
4.2 REACTION DESIGN

Our synthesis of (+)-naseseazines A and B constitutes the first *catalytic* Larock indolization on a bromoaniline in the context of total synthesis. We wondered whether these conditions could be further improved to create a low temperature, mild, and general protocol for the indolization of *2*-bromoaniline starting materials, which serve as more desirable substrates due to their increased ease of synthesis as well as commercial availability compared to *2*-iodoanilines. Specifically, we aimed to develop conditions compatible with highly functionalized substrates in order to directly access tryptophan derivatives. We hoped to identify conditions that would 1) increase substrate scope by enabling less reactive *2*-bromoaniline substrates; 2) proceed with synthetically useful

catalyst loadings; and 3) deliver products at lower temperatures in order to mitigate deleterious side reactivity. To accomplish this, we sought to understand why Pd[P(*o*-tol)$_3$]$_2$, our optimal catalyst in the preparation of the (+)-naseseazines, appeared to be uniquely effective in catalyzing our desired transformation.

In assessing the existing limitations of the Larock indolization, we rationalized that the poor reactivity of 2-bromoanilines under Larock's ligandless conditions was likely due to slow rates of oxidative addition. Although this elementary step could be easily remedied by the addition of an electron-donating phosphine ligand, we recognized that the limited success of this approach might be due to diminished rates of alkyne insertion due to coordinative saturation of Pd.[8] We hypothesized that the use of sterically demanding phosphines, such as P(*o*-tol)$_3$ and P(^{t}Bu)$_3$, which have been demonstrated to proceed *via* Pd-monophosphine rather than Pd-bisphosphine intermediates as the active catalyst, may serve to balance these opposing factors by providing a vacant coordination site to facilitate alkyne insertion (**Scheme 4.5**).[9]

Scheme 4.5. *Improving the Larock indole synthesis*

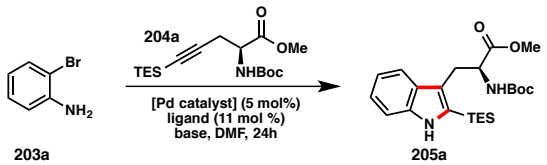


4.3 REACTION OPTIMIZATION

With the goal of identifying conditions tolerant of more complex functionality, we elected to study the coupling of 2-bromoaniline (**203a**) and alkyne **204a**[10] to afford 2-triethylsilyl-Boc-Trp-OMe (**205a**). Treatment with 5 mol % $Pd(OAc)_2$ with Na_2CO_3 at 100 °C, Larock's original conditions, surprisingly provided 27% yield of the desired coupling product. Turning our attention to the addition of phosphine ligands, the addition of 11 mol % PPh_3, PCy_3, DavePhos, or the dtbpf, the optimal ligand in Senanayake's report, suppressed the desired reactivity (**entries 2–5**). Returning to the preformed complex $Pd[P(o\text{-tol})_3]_2$, our most successful catalyst in the synthesis of the (+)-naseseazines, we were gratified to obtain 70% yield of the desired product. Moreover, by increasing the steric demand through the use of $Pd[P(^tBu)_3]_2$, a yield increase to 78% was

observed. We next investigated whether this reaction was competent at decreased temperatures. Lowering the temperature to 60 °C enabled a clean reaction and provided the product in an improved 85% yield (**entry 8**). To the best of our knowledge, this reaction represents the lowest temperature Larock indolization of *any 2-haloaniline* previously reported in the literature. Additionally, a soluble organic base (Cy_2NMe), and non-polar solvent could also be employed without loss in reaction efficiency (**entries 9 and 10**). Finally, in support of a highly active, Pd-monophosphine complex, use of a 1:1 [Pd]/L ratio generated by the addition of $Pd_2(dba)_3$ and $P(^tBu)_3$ offered improved initial rates of the reaction (**entry 11**). However, application of this catalyst system did not significantly reduce the overall reaction time, and furnished in the product in nearly identical yield. Although these final variations did not significantly affect yield, these data illustrate the robust nature of the active catalyst, as well as flexibility in the reaction conditions that may prove useful in individual substrate optimization. For simplicity of reaction setup, we elected to conduct our scope studies using the air-stable and crystalline $Pd[P(^tBu)_3]_2$.

Table 4.1. *Optimization Studies*



entry	[Pd cat.]	ligand	base	temp (°C)	yield (%)[b]
1	$Pd(OAc)_2$	–	Na_2CO_3	100	27
2	$Pd(OAc)_2$	PPh_3	Na_2CO_3	100	17
3	$Pd(OAc)_2$	DavePhos	Na_2CO_3	100	8
4	$Pd(OAc)_2$	PCy_3	Na_2CO_3	100	<5
5	$Pd(OAc)_2$	dtbpf	Na_2CO_3	100	<5
6	$Pd[P(o\text{-tol})_3]_2$	–	Na_2CO_3	100	70
7	$Pd[P(^t Bu)_3]_2$	–	Na_2CO_3	100	78
8	$Pd[P(^t Bu)_3]_2$	–	Na_2CO_3	60	85
9	$Pd[P(^t Bu)_3]_2$	–	Cy_2NMe	60	85
10[e]	$Pd[P(^t Bu)_3]_2$	–	Cy_2NMe	60	84 (87)[d]
11[e]	$Pd_2(dba)_3$	$P(^t Bu)_3$	Cy_2NMe	60	83

[a] Reactions conducted on 0.1 mmol scale with 2.0 equiv alkyne **204a** and 2.5 equiv base in DMF (0.5 mL). [b] Yield determined by ^1H NMR analysis of the crude reaction mixture relative to an internal standard. [c] 1:1 [Pd]/ligand used. [d] Isolated yield on 0.3 mmol scale. [e] Reaction performed in 1,4-dioxane.

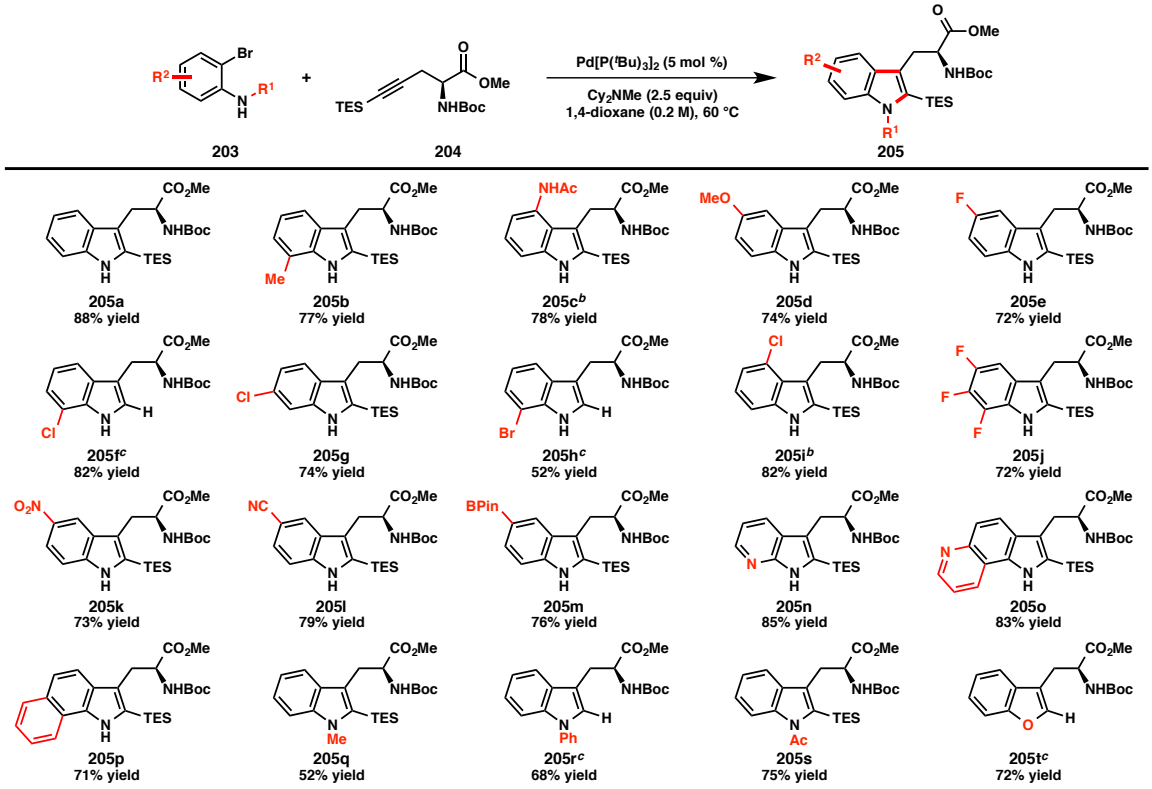
4.4 REACTION SCOPE

4.4.1 Bromoaniline scope

As shown in **Table 4.2**, the reaction exhibits excellent scope; both electron-rich (**205a**–**205d**) and electron-deficient (**205e**–**205l**) substrates react efficiently to provide a structurally diverse array of unnatural tryptophan derivatives. Substitution is readily tolerated at all positions of the indole, including the indole nitrogen, although the preparation of sterically demanding 4-substituted indoles requires slightly elevated temperatures to improve reaction rates (**205c** and **205l**). Halogenated substrates perform with excellent chemoselectivity for the aryl bromide over potentially reactive aryl chloride functionality, and a variety of useful chlorinated (**205f**, **205g**, **205l**) and fluorinated (**205e**, **205j**) tryptophans are readily accessed. Remarkably, even additional bromide functionality can be tolerated to provide bromotrytophan **205h**. Furthermore, we were pleased to find that Lewis-basic heterocycles also perform well under these

conditions (**205n** and **205o**). It is noteworthy that tryptophan **205o**, readily prepared here in two steps from commercially available materials, has recently been reported as a new fluorescent probe with interesting photophysical properties.[11] Finally, these conditions are also readily extended to 2-bromophenol to provide direct access to a substituted benzofuran derivative (**205t**). Importantly, chiral SFC analysis verified that this reaction proceeds without deleterious racemization, providing all products in enantiopure form. The 2-triethylsilyl group is easily removed using aqueous acid or fluoride sources, or alternatively can serve as a useful functional handle for a variety of transformations.[12]

Table 4.2. *Bromoaniline scope*

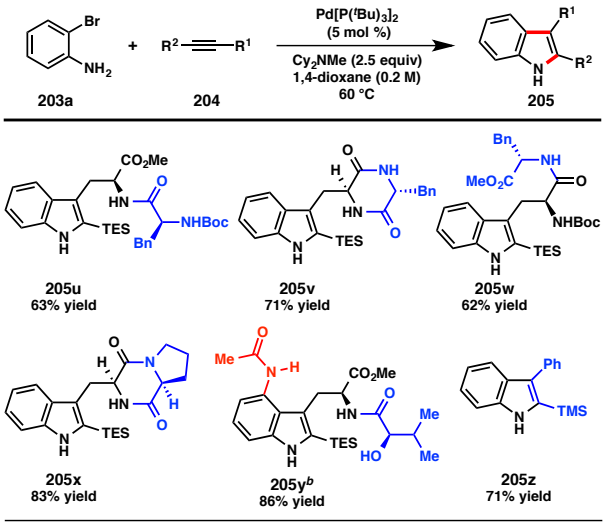


[a] Reactions conditions: Substituted 2-bromoaniline, alkyne (2.0 equiv), Cy2NMe (2.5 equiv) in 1,4-dioxane (0.2 M) at 60 °C. Isolated yields are reported. [b] Reaction performed at 80 °C. [c] To facilitate purification, desilylation with 1 M TBAF or 1 N HCl in MeOH was performed prior to chromatography.

4.4.2 Alkyne scope

To investigate the scope of the alkyne, several dipeptide-and diketopiperazine-based substrates were prepared and subjected to the reaction conditions (**Table 4.3**). In all cases, the products are obtained in good yields and with no observed epimerization of the α-stereocenters. Excellent functional group tolerance is demonstrated by the preparation of **205y** in 86% yield. Although the focus of this study was the coupling of peptide-based alkynes, simple alkynes such as TMS-phenyl acetylene can also be used (**3z**), reacting under considerably milder conditions than those previously reported.[13]

Table 4.3. *Alkyne scope*



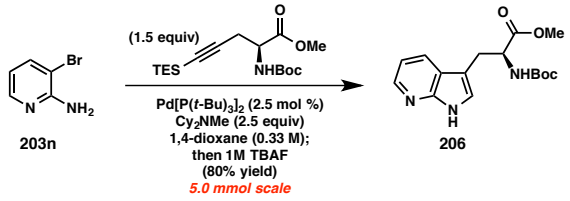
[a] Reactions conditions: **203a** (1.0 equiv), **204** (2.0 equiv), CyNMe (2.5 equiv), in 1,4-dioxane (0.2 M) at 60 °C. Isolated yields are reported. [b] Reaction performed at 80 °C.

4.4.3 Scale-up Reaction

The synthetic studies described above utilized 5 mol % catalyst for operational simplicity; however, individual couplings can be reoptimized for preparatively useful scales with lower catalyst loadings. For example, the coupling between 3-bromo-2-aminopyridine (**203n**) and alkyne **204a** was carried out on 5 mmol scale using 2.5 mol % $Pd[P(^tBu)_3]_2$ and 1.5 equiv alkyne, which upon quenching with 1M TBAF in THF to

effect protodesilylation, provided 1.28 g (80% yield) of *N*-Boc-7-aza-tryptophan methyl ester **206** (**Scheme 4.6**).

Scheme 4.6. *Reaction scale-up*

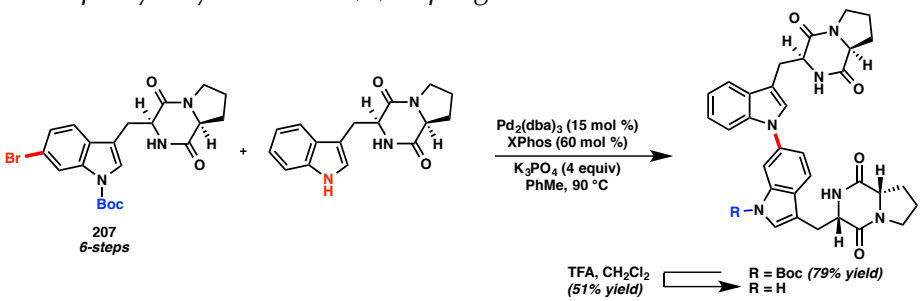


4.5 TOTAL SYNTHESIS OF (–)-ASPERGILAZINE A

4.5.1 Previous Synthesis of (–)-Aspergilazine A

With optimized conditions in hand, we set out to demonstrate the versatility and efficiency of this transformation through the total synthesis of (–)-aspergilazine A. (–)-aspergilazine A is (bis)diketopiperazine-containing indole natural product with a distinctive C6–N1 linkage.[14] First synthesized in 2014, Sperry and co-workers adopted a traditional approach utilizing a protecting group strategy.[15] In six-steps, they are able to synthesize Boc-protected 6-bromo tryptophan **207** via enzymatic resolution, which upon subjection to 30 mol % [Pd] and 60 mol % Xphos, undergoes C–N bond formation. Trifluoroacetic acid mediated removal of the Boc-protecting group then affords the natural product.

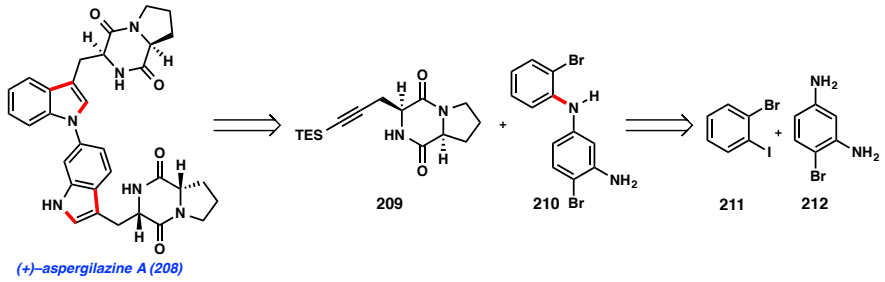
Scheme 4.6. *Sperry's synthesis of (–)-aspergilazine A*



4.5.2 Our Synthesis of (–)-Aspergilazine A

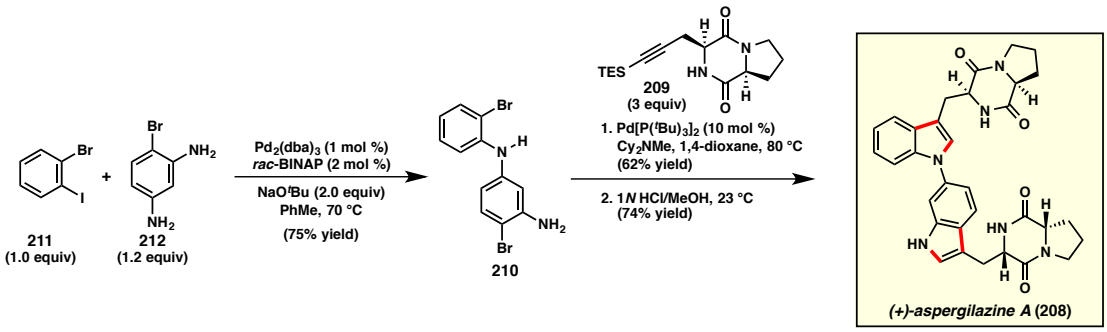
Retrosynthetically, we imagined a slightly more direct disconnection that could highlight our newly developed methodology. We proposed a disconnection through both tryptophan indoles *via* a sequential Larock indolization between known diketopiperazine **209** and diarylamine **210**. We hoped to synthesize diarylamine **210** using a selective Buchwald-Hartwig reaction of 1-bromo-2-iodobenzene (**211**) and commercially-available 4-bromo-1,2-diaminobenzene (**212**). Importantly, the success of this strategy hinges largely on the ability of this new protocol to enable the coupling of 2-bromoanilines; the preparation of the diiodinated analog of diarylamine **210** via C–N bond formation is a considerably more challenging synthetic undertaking.

Scheme 4.7. *Retrosynthetic analysis of (–)-aspergilazine A*



To this end, the requisite bis-bromoaniline (**210**) was readily prepared via coupling of 1-bromo-2-iodobenzene with 4-bromo-*m*-phenylenediamine (**212**).[16] Subjection of a mixture of dibromide **210** and alkyne **209** to 10 mol % Pd[P(^{t}Bu)$_3$] and 2.5 equiv of Cy_2NMe in 1,4-dioxane at 80 °C furnished bis-triethylsilyl-(–)-aspergilazine A in 62% isolated yield, representing an average reaction efficiency of 79% per indolization. Subsequent HCl-mediated desilylation cleanly provided the natural product. This highly convergent synthesis underscores the utility of this methodology in the direct preparation of complex molecular scaffolds.

Scheme 4.8. *Total synthesis of (–)-aspergilazine A*



4.6 CONCLUSION

In summary, this chapter describes the development of a mild and general protocol for the Pd-catalyzed synthesis of functionalized tryptophan derivatives. The reaction proceeds with low catalyst loadings, displays excellent substrate scope, and is readily scalable to provide gram quantities of synthetically useful indoles and unnatural tryptophans. Furthermore, the synthetic utility of this transformation has been demonstrated in the concise synthesis of the natural product (–)-aspergilazine A. We anticipate that this versatile protocol will find broad applicability in the preparation of complex indole and tryptophan scaffolds, and provide efficient entry to a broad array of natural products.

4.7 EXPERIMENTAL SECTION

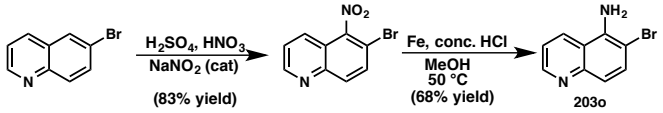
4.7.1 Materials and Methods

Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), dimethylformamide (DMF), and toluene (PhMe) were dried by passing through activated alumina columns. 1,4-Dioxane was dried by passing through activated alumina columns or purchased from Sigma-Aldrich (>99.8%, anhydrous).

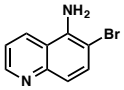
Triethylamine (Et_3N), diisopropylamine (i-Pr_2NH), diisopropylethylamine (i-Pr_2NEt), and dicyclohexylmethylamine (Cy_2NMe) were distilled over calcium hydride prior to use. Unless otherwise stated, chemicals and reagents were used as received. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, p-anisaldehyde, or $KMnO_4$ staining. Flash column chromatography was performed either as described by Still et al. using silica gel (particle size 0.032-0.063) purchased from Silicyle. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^1H and ^{13}C NMR spectra were recorded on a Varian 400 MR (at 400 MHz and 101 MHz, respectively), a Varian Inova 500 (at 500 MHz and 126 MHz, respectively), or a Varian Inova 600 (at 600 MHz and 150 MHz, respectively), and are reported relative to internal $CHCl_3$ (^1H, $\delta = 7.26$), MeCN (^1H, $\delta = 1.94$), or DMSO (^1H, $\delta = 2.50$), and $CDCl_3$ (^{13}C, $\delta = 77.0$), MeCN (^{13}C, $\delta = 118.26$), or DMSO (^{13}C, $\delta = 40.0$). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Preparatory HPLC was performed with either an Agilent 1200 Series HPLC utilizing an Agilent XDB-C18 5μm column (30 x 250 mm). Analytical SFC was performed with a Mettler SFC supercritical CO2 analytical chromatography system with Chiralcel AD-H column (4.6 mm x 25 cm). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode.

4.7.2 Preparation of haloaniline substrates

Bromoaniline 203o

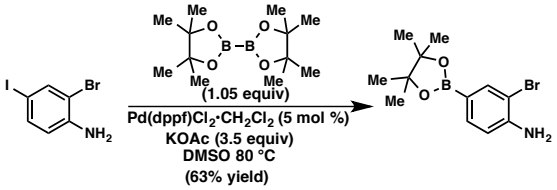


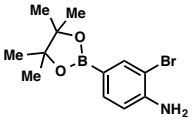
6-bromoquinoline was purchased from Combi-Blocks and nitrated using a known procedure. 5-nitro,6-bromo-quinloline (500 mg, 2.0 mmol, 1.0 equiv) was dissolved in MeOH (6 mL). Fe powder (331 mg, 5.9 mmol, 3.0 equiv) and concentrated HCl (2 mL) were added and the reaction was heated to 50 °C for 1 h. Upon cooling, the reaction was basified with NH_4OH to pH 9, filtered through celite, and extracted with EtOAc (2X, 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by chromatography on silica gel (40% acetone, 60% hexanes) to provide a light yellow, amorphous solid (300 mg, 1.3 mmol, 68% yield).



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.16 (ddd, *J* = 8.6, 1.5, 0.9 Hz, 1H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.45 (dd, *J* = 9.0, 0.7 Hz, 1H), 7.39 (dd, *J* = 8.6, 4.2 Hz, 1H) , 4.68 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.31, 148.1, 139.6, 133.3, 129.4, 120.7, 120.2, 118.7, 104.3; FTIR (NaCl, thin film): cm^{-1}; 3423, 3297, 3162, 1635, 1581, 1569, 1457, 1398, 1357, 1323; HRMS (MM) calc'd $[M+H]^+$ 222.9865, found 222.9862.

Bromoaniline 203m

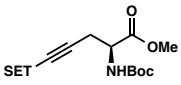




In a glovebox, a 2 dram vial was charged with 4-iodo,2-bromoaniline (500 mg, 1.7 mmol, 1.0 equiv), Pd(dppf)Cl_2•CH_2Cl_2 (69 mg, 0.08 mmol, 0.05 equiv), bis(pinacolato)diboron (448 mg, 1.8 mmol, 1.05 equiv), KOAc (557 mg, 5.9 mmol (3.5 equiv), and DMSO (5 mL). The vial was sealed, removed from the glove box and heated to 80 °C. After 24 h, the reaction was cooled, filtered through celite and flushed with ethyl acetate. This mixture was then washed with water (3 X), dried Na_2SO_4, filtered and concentrated. The crude reaction mixture was purified by chromatography on silica gel (10% ethyl acetate, 90% hexanes) to give white, amorphous solid **203m** (315 mg, 1.1 mmol, 63% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 1.3 Hz, 1H), 7.52 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 1.32 (s, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ146.6, 139.2, 135.0, 114.8, 108.8, 83.58, 24.8 (carbon adjacent to Boron was not observed); FTIR (NaCl, thin film): cm^{-1}; 3477, 3368, 2977, 2930, 1616, 1594, 1385, 1372, 1319, 1143, 1098; HRMS (MM) calc'd $[M+H]^+$ 297.0645, found 297.0637.

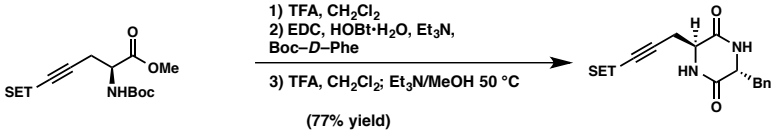
4.7.3 Preparation of alkyne substrates



Alkyne 204a

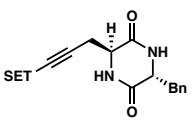
Alkyne **204a** was prepared on decagram scale according to the procedure reported by Baran and co-workers.

Alkyne 204v



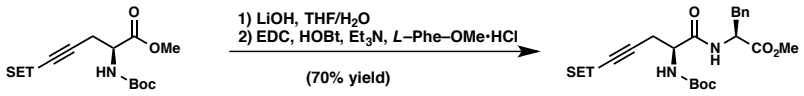
Methyl ester **204a** (1.02 g, 3.0 mmol, 1.00 equiv) was dissolved in a 5:1 mixture of CH_2Cl_2:TFA (20 mL) . After one hour, the reaction was concentrated and dissolved in 34 mL CH_2Cl_2. The solution was cooled to 0 °C under a positive pressure of N_2 and EDC•HCl (0.862 g, 4.5 mmol, 1.50 equiv), HOBt•H_2O (0.680 g, 4.5 mmol, 1.50 equiv) and Et_3N (1.88 mL, 13.5 mmol, 4.5 equiv) were added sequentially. The mixture was then stirred for 5 minutes, and Boc–*D*–phenylalanine (1.59 g, 6.0 mmol, 2.0 equiv) was added. The reaction was slowly warmed to 23 °C over 2 hours and stirring continued for 20 hours. The reaction was then quenched with 1 N HCl (500 mL) and extracted with EtOAc (3 x 250 mL), then the combined organics washed with saturated aqueous NaHCO3 (500 mL), and aqueous layer back extracted with EtOAc (200 mL). The combined organic layers were then dried over anhydrous Na2SO4, filtered, and concentrated in *vacuo* to afford crude dipeptide as a viscous oil.

The residue was then dissolved in CH_2Cl_2 (50 mL), and trifluoroacetic acid (15 mL) was added dropwise by addition funnel at room temperature over 10 minutes. Stirring was continued for 20 minutes, then the solution diluted with toluene (100 mL) and the mixture concentrated in *vacuo* to afford a thick oil. The residue was then redissolved in MeOH (35 mL) and the mixture cooled to 0 °C. Et_3N (27 mL) was then added dropwise the stirring solution over 10 minutes by addition funnel. Upon completion of the addition, the cooling bath was removed and the reaction was heated to 50 °C over 16 h. The mixture was cooled to 0 °C to yield a milky solution, which was filtered and washed with cold methanol to provide alkyne **204v** as a colorless solid (771 mg, 72% yield)

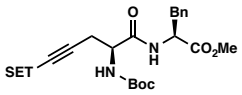


^{1}H NMR (500 MHz, DMSO) δ 8.35 (d, *J* = 1.6 Hz, 1H), 8.02 (d, *J* = 1.0 Hz, 1H), 7.29 – 7.19 (m, 3H), 7.18 – 7.12 (m, 2H), 4.15 (s, 1H), 3.19 – 3.11 (m, 2H), 2.88 (dd, *J* = 13.5, 4.9 Hz, 1H), 2.63 (dd, *J* = 16.9, 3.2 Hz, 1H), 2.40 (dd, *J* = 17.0, 4.7 Hz, 1H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.50 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (126 MHz, DMSO) δ 166.6, 166.0, 135.8, 130.1, 128.0, 126.7, 104.0, 83.9, 55.4, 52.6, 38.4, 24.8, 7.3, 3.9; FTIR (NaCl, thin film): cm^{-1}; 2916, 2350, 1732, 1651, 1557, 1455; $[\alpha]_D^{25}$ = –19.4 (*c* = 0.28, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 357.1993, found 357.1992.

Alkyne 204w

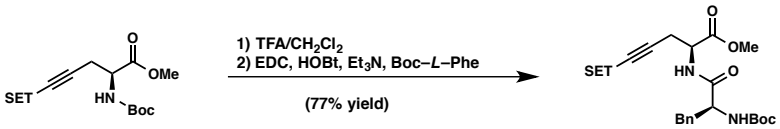


To a solution of methyl ester **204a** (550 mg, 1.5 mmol, 1.00 equiv) in THF/H_2O (4 mL/2 mL) at 0 °C under a positive pressure of N_2 was added aqueous LiOH (1 M, 1.9 mL, 1.2 equiv). After 1 hour, the reaction was quenched by slow addition of 1 M HCl (3 mL) and Et_2O (6 mL). The layers were separated and the aqueous was extracted with Et_2O (3X, 10 mL). The organics were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford a colorless oil. The oil was dissolved in 24 mL THF and cooled to 0 °C under a positive pressure of N_2. EDC (337 mg, 1.8 mmol, 1.2 equiv), anhydrous HOBt (277 mg, 2.0 mmol, 1.4 equiv) and Et_3N (610 μL, 4.4 mmol, 3.0 equiv) were added sequentially. After 5 minutes of stirring, a solution of (*l*)-Phe-OMe•HCl (347 mg, 1.6 mmol, 1.1 equiv) in THF (10 mL) was added via cannula. The reaction was warmed to room temperature and stirred for 12 h. The heterogeneous solution was concentrated and purified by chromatography on silica gel (20% ethyl acetate, 80% hexanes) to give white, amorphous solid **204w** (500 mg, 1.02 mmol, 70% yield)



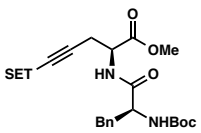
^{1}H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 7.30 – 7.19 (m, 3H), 7.13 – 7.04 (m, 2H), 6.84 (d, *J* = 4.9 Hz, 1H), 5.25 (s, 1H), 4.81 (ddd, *J* = 7.5, 6.0, 6.0 Hz, 1H), 4.22 (d, *J* = 4.9 Hz, 1H), 3.67 (s, 3H), 3.18 – 3.01 (m, 2H), 2.74 (dd, *J* = 17.1, 6.1 Hz, 1H), 2.65 (dd, *J* = 17.1, 6.5 Hz, 1H), 1.42 (s, 9H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.55 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 169.9, 155.3, 135.7, 129.1, 128.4, 127.0, 102.5, 85.5, 80.2, 53.4, 53.0, 52.2, 38.0, 28.1, 23.3, 7.7, 4.2; FTIR (NaCl, thin film): cm^{-1}; 3319, 2954, 2935, 2874, 2177, 1746, 1689, 1660, 1527, 1498, 1456, 1367, 1274, 1251, 1172, 1048, 1017; $[\alpha]_D^{25}$ = +39.2 (*c* = 4.29, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 433.2153, found 433.2138.

Alkyne 204u



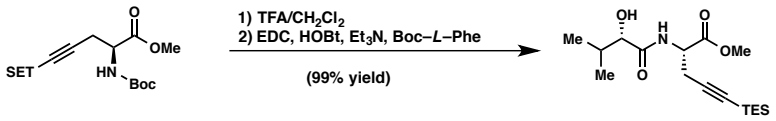
To a solution of Boc-alkyne **204a** (500 mg, 1.5 mmol, 1.00 equiv) in CH_2Cl_2 (15 mL) at 0 °C was added TFA (2.0 mL). The mixture was warmed to room temperature and stirred for 3 hours, after which PhMe (30 mL) was added and the reaction concentrated. The resultant oil was dissolved in THF (10 mL) and cooled to 0 °C under a positive pressure of N_2. In a separate flask, (*l*)-Boc-Phe-OH (466 mgs, 1.8 mmol, 1.2 equiv) was dissolved in THF (24 mL) and cooled to 0 °C. EDC (337 mg, 1.8 mmol, 1.2 equiv), anhydrous HOBt (277 mg, 2.0 mmol, 1.4 equiv) and Et_3N (610 μL, 4.4 mmol, 3.0 equiv) were added sequentially. After stirring for 5 minutes, the alkyne was transferred via cannula. The reaction was warmed to room temperature and stirred for 12 h. The heterogeneous reaction was concentrated and purified by chromatography on silica gel

(20% ethyl acetate, 80% hexanes) to provide the product as a colorless oil (552 mg, 1.13 mmol, 77% yield).



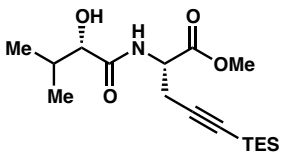
^{1}H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 7.28 – 7.22 (m, 2H), 7.19 (dd, *J* = 7.1, 7.1 Hz, 3H), 6.77 (d, *J* = 6.3 Hz, 1H), 5.16 (d, *J* = 5.9 Hz, 1H), 4.67 (d, *J* = 6.5 Hz, 1H), 4.44 (d, *J* = 6.1 Hz, 1H), 3.70 (s, 3H), 3.11 (dd, *J* = 13.9, 6.3 Hz, 1H), 2.98 (dd, *J* = 12.8, 6.6 Hz, 1H), 2.73 (dd, *J* = 17.0, 4.0 Hz, 1H), 2.57 (dd, *J* = 17.1, 5.3 Hz, 1H), 1.35 (s, 9H), 0.98 – 0.87 (m, 9H), 0.57 – 0.46 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ170.8, 170.4, 155.2, 136.4, 129.2, 128.4, 126.7, 101.3, 85.5, 79.8, 55.3, 52.4, 50.8, 38.4, 28.1, 23.5, 7.3, 4.1; FTIR (NaCl, thin film): cm^{-1}; 3419, 3335, 2963, 2868, 2179, 1743, 1661, 1518, 1451, 1365; $[\alpha]_D^{25}$ = +52.7 (*c* = 5.4, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 489.2779, found 489.2793.

Alkyne 204y



To a solution of Boc-alkyne **204a** (1.00 g, 2.9 mmol, 1.00 equiv) in CH_2Cl_2 (30 mL) at 0 °C was added TFA (4 mL). The mixture was warmed to room temperature and stirred for 3 hours, after which PhMe (100 mL) was added and the reaction concentrated. The resultant oil was dissolved in THF (10 mL) and cooled to 0 °C under a positive pressure of N_2. In a separate flask, (*R*)-2-hydroxy-3-methylbutanoic acid (346 mgs, 2.9 mmol, 1.0 equiv) was dissolved in THF (100 mL) and cooled to 0 °C. EDC (674 mg, 3.5 mmol, 1.2 equiv), anhydrous HOBt (554 mg, 4.1 mmol, 1.4 equiv) and hünigs base (1.5 mL, 8.6 mmol, 3.0 equiv) were added sequentially. After stirring for 5 minutes, the alkyne was transferred via cannula. The reaction was warmed to room temperature and stirred for 12 h. The heterogeneous reaction was concentrated and purified by

chromatography on silica gel (100% ethyl acetate) to provide the product as a colorless oil (995 mg, 2.9 mmol, 99% yield).



^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 7.43 (d, *J* = 7.6 Hz, 1H), 4.59 (dt, *J* = 8.2, 5.3 Hz, 1H), 3.89 (dd, *J* = 5.5, 3.1 Hz, 1H), 3.71 (d, *J* = 5.6 Hz, 1H), 3.69 (s, 3H), 2.80 (dd, *J* = 17.2, 5.5 Hz, 1H), 2.73 (dd, *J* = 17.2, 5.2 Hz, 1H), 2.07 (heptd, *J* = 6.9, 3.1 Hz, 1H), 1.01 – 0.93 (m, 12H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.61 – 0.52 (m, 6H); ^{13}C NMR (126 MHz, CD_3CN) δ 174.2, 171.7, 118.3, 103.6, 85.8, 76.4, 53.0, 51.4, 32.7, 23.9, 19.5, 15.9, 7.8, 5.0; FTIR (NaCl, thin film): cm^{-1}; 3385, 2952, 2863, 2176, 1744, 1653, 1507; $[\alpha]_D^{25}$ = -+89.4 (*c* = 3.40, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 342.2095, found 342.2087.

4.7.4 Optimization of reaction parameters

Optimization Procedure – In a glovebox, an oven-dried 1 dram vial was charged with 2-bromoaniline (17.2 mg, 0.1 mmol, 1.0 equiv), alkyne **204a** (68.3 mg, 0.2 mmol, 2.0 equiv), base (2.5 equiv), Pd-catalyst (0.05 equiv), and appropriate solvent (0.5 mL). The vial was sealed and heated to the required temperature for 2 – 36 h. Upon cooling, the crude reaction mixture was filtered through a silica plug, thoroughly washed with ethyl acetate and concentrated *in vacuo* to provide a crude oil.

The crude residue was dissolved in a standard solution of 2,3,5,6-tetrachloronitrobenzene in DMSO-d_6, and the yield of **205** was determined by ^{1}H NMR by integration relative to the internal standard.

** In entry 9 of Table 1, $Pd_2(dba)_3$ and P^tBu_3 were prestired for 1 h before being added to a vial containing the other reagents.

4.7.5 Substrate scope – characterization data

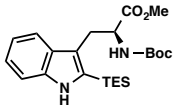
General Procedure I: In a glovebox, a 2 dram vial was charged with bromoaniline (0.3 mmol, 1.0 equiv), alkyne **204a** (0.6 mmol, 2.0 equiv), Cy_2NMe (0.75 mmol, 2.5 equiv), $Pd[P(P^tBu)_3]_2$ (0.015 mmol, 0.05 mmol) and anhydrous 1,4-dioxane (1.5 mL, 0.2 M). The vial was sealed and heated to 60 °C until there was complete consumption of starting material (12 – 72 h). In most cases the solution became cloudy as the reaction progressed. Upon cooling, the crude mixture was filtered through a plug of silica, which was subsequently flushed with ethyl acetate. The organics were concentrated and the crude residue was purified by chromatography on silica gel to provide tryptophan derivatives.

General Procedure II: In a glovebox, a 2 dram vial was charged with bromoaniline (0.3 mmol, 1.0 equiv), alkyne **204a** (0.6 mmol, 2.0 equiv), Cy_2NMe (0.75 mmol, 2.5 equiv), $Pd[P(P^tBu)_3]_2$ (0.015 mmol, 0.05 mmol) and anhydrous 1,4-dioxane (1.5 mL, 0.2 M). The vial was sealed and heated to 80 °C until there was complete consumption of starting material (12 – 72 h). In most cases the solution became cloudy as the reaction progressed. Upon cooling, the crude mixture was filtered through a plug of silica, which was subsequently flushed with ethyl acetate. The organics were concentrated and the crude residue was purified by chromatography on silica gel to provide tryptophan derivatives.

General Procedure III: In a glovebox, a 2 dram vial was charged with bromoaniline (0.3 mmol, 1.0 equiv), alkyne **204a** (0.6 mmol, 2.0 equiv), Cy_2NMe (0.75 mmol, 2.5

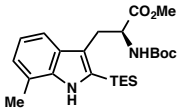
equiv), $Pd[P(P^tBu)_3]_2$ (0.015 mmol, 0.05 mmol) and anhydrous 1,4-dioxane (1.5 mL, 0.2 M). The vial was sealed and heated to 80 °C until there was complete consumption of starting material (12 – 72 h). In most cases the solution became cloudy as the reaction progressed. Upon cooling, the crude mixture was filtered through a plug of silica, which was subsequently flushed with ethyl acetate. The organics were concentrated and the crude residue was dissolved in 1M TBAF in THF. After 20 minutes, aqueous NH_4Cl was added and the reaction mixture was partitioned in a separatory funnel. The aqueous layer was back extracted with ethyl acetate (3 X 15 mL). The organics were then recombined, washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude residue was purified using silica gel chromatography.

Tryptophan **205a**



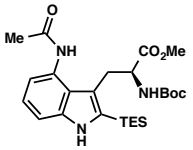
Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl acetate) to afford **3a** as a colorless oil (113.6 mg, 0.26 mmol, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 8.04 (s, 1H), 7.57 (d, J = 7.9 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.21 – 7.15 (m, 1H), 7.09 (dd, J = 7.4, 7.4 Hz, 1H), 4.93 (d, J = 7.7 Hz, 1H), 4.57 (dd, J = 14.4, 7.1 Hz, 1H), 3.63 (s, 3H), 3.36 – 3.18 (m, 2H), 1.36 (s, 9H), 1.05 – 0.98 (m, 9H), 0.97 – 0.89 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.7, 155.1, 138.5, 132.8, 128.6, 122.4, 119.5, 119.3, 118.9, 110.8, 79.6, 54.2, 52.2, 29.3, 28.2, 7.4, 3.7; FTIR (NaCl, thin film): cm^{-1}; 3383, 2954, 2911, 2875, 1739, 1700, 1501, 1456, 1367, 1284, 1164; $[\alpha]_D^{25}$ = +1.4 (c = 1.4, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 433.2517, found 433.2519.

Tryptophan **205b**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl acetate) to afford **205b** as a colorless oil (102.9 mg, 0.230 mmol, 77% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 8.68 (s, 1H), 7.37 (dd, *J* = 7.0, 1.3 Hz, 1H), 6.99 – 6.91 (m, 2H), 5.41 (d, *J* = 7.8 Hz, 1H), 4.37 (dd, *J* = 14.9, 7.6 Hz, 1H), 3.57 (s, 3H), 3.29 (dd, *J* = 14.5, 6.7 Hz, 1H), 3.13 (dd, *J* = 14.5, 7.8 Hz, 1H), 2.51 (s, 3H), 1.32 (s, 9H), 1.01 – 0.95 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.9, 156.1, 139.4, 133.2, 129.3, 123.6, 121.7, 121.5, 120.2, 117.2, 79.9, 56.1, 52.6, 29.6, 28.4, 17.4, 7.8, 4.3; FTIR (NaCl, thin film): cm^{-1}; 3396, 2954, 2912, 2874, 1704, 1498, 1366, 1279, 1217, 1163, 1018; $[\alpha]_D^{25}$ = –5.8 (*c* = 0.40, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 391.2048, found 391.2038.

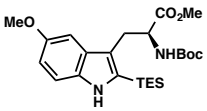
Tryptophan **205c**



Prepared following *General Procedure II* (12 h). The crude residue was purified by silica gel chromatography (80% hexanes, 20% acetone) to afford **205c** as a white, amorphous solid (114.3 mg, 0.234 mmol, 78% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.22 (s, 1H), 8.33 (s, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.08 (t, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 7.4 Hz, 1H), 5.54 (s, 1H), 4.34 (dd, *J* = 15.7, 7.6 Hz, 1H), 3.60 (s, 3H), 3.37 (dd, *J* = 14.7, 6.1 Hz, 1H), 3.14 – 2.95 (m, 1H), 2.13 (s, 3H), 1.34 – 1.18 (m, 9H), 1.03 – 0.89 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 174.3, 171.1, 156.2, 141.6, 134.4, 130.5, 124.7, 122.8, 119.8, 118.5, 110.7, 79.9, 57.0, 52.6, 29.3, 28.4, 23.8, 7.7, 4.3; FTIR (NaCl, thin film): cm^{-1}; 3313, 2953,

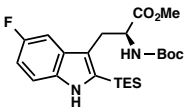
1700, 1672, 1506, 1367, 1168; $[\alpha]_D^{25}$ = –18.3 (*c* = 1.10, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 490.2732, found 490.2719.

Tryptophan **205d**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (85% hexanes, 15% ethyl acetate) to afford **205d** as a colorless oil (102.2 mg, 0.220 mmol, 74% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 8.95 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.03 (d, *J* = 1.5 Hz, 1H), 6.77 (dd, *J* = 8.8, 2.4 Hz, 1H), 5.53 (d, *J* = 8.2 Hz, 1H), 4.36 (dd, *J* = 14.6, 8.2 Hz, 1H), 3.82 (s, 3H), 3.60 (s, 3H), 3.26 (dd, *J* = 14.5, 6.1 Hz, 1H), 3.08 (dd, *J* = 14.5, 8.2 Hz, 1H), 1.28 (s, 9H), 1.01 – 0.95 (m, 9H), 0.95 – 0.91 (m, 6H); ^{13}C NMR (126 MHz, CD_3CN) δ 174.0, 156.1, 154.7, 135.2, 134.1, 130.0, 120.5, 113.3, 112.6, 101.1, 79.8, 56.3, 56.2, 52.6, 29.8, 28.4, 7.7, 4.2; FTIR (NaCl, thin film): cm^{-1}; 3379, 2953, 2874, 1700, 1620, 1506, 1437, 1391, 1366, 1218, 1164; $[\alpha]_D^{25}$ = +6.3 (*c* = 3.75, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 407.1997, found 407.1994.

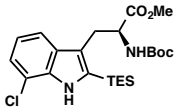
Tryptophan **205e**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl acetate) to afford **205e** as a colorless oil (97.2 mg, 0.216 mmol, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 8.01 (s, 1H), 7.26 – 7.22 (m, 1H), 7.21 – 7.14 (m, 1H), 6.91 (ddd, *J* = 8.9, 8.9, 2.2 Hz, 1H), 4.93 (d, *J* = 8.2 Hz, 1H), 4.53 (dd, *J* = 14.7, 7.0 Hz, 1H), 3.65 (s, 3H), 3.30 – 3.14 (m, 2H), 1.35 (s, 9H), 1.05 – 0.97 (m, 9H), 0.96 – 0.88 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.17, 157.69 (d, $J_{C\text{-}F}$ = 234.9 Hz), 155.00, 135.12 (d,

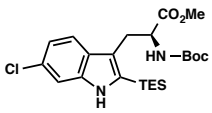
$J_{C\text{-}F}$ = 13.4 Hz), 129.00 (d, $J_{C\text{-}F}$ = 9.2 Hz), 119.56 (d, $J_{C\text{-}F}$ = 4.7 Hz), 111.30 (d, $J_{C\text{-}F}$ = 9.8 Hz), 110.83 (d, $J_{C\text{-}F}$ = 26.5 Hz), 103.61 (d, $J_{C\text{-}F}$ = 23.6 Hz), 79.75, 54.15, 52.26, 29.48, 28.17, 7.38, 3.62; FTIR (NaCl, thin film): cm^{-1}; 3372, 2956, 2875, 1734, 1718, 1700, 1502, 1437, 1367, 1166, 1073, 1010; $[\alpha]_D^{25}$ = +3.6 (*c* = 2.0, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 395.1797, found 395.1804.

Trytophan **205f**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (80% hexanes, 20% acetone) to afford **205f** as a colorless oil (114.3 mg, 0.245 mmol, 82% yield). ^1H NMR (500 MHz, CD_3CN, Major Rotamer) δ 8.87 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.08 – 6.97 (m, 1H), 5.50 (d, *J* = 8.1 Hz, 1H), 4.37 (dd, *J* = 15.1, 7.9 Hz, 1H), 3.56 (s, 3H), 3.29 (dd, *J* = 14.5, 6.5 Hz, 1H), 3.12 (dd, *J* = 14.5, 8.0 Hz, 1H), 1.29 (s, 9H), 1.02 – 0.96 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.7, 156.1, 136.6, 135.3, 131.5, 122.6, 122.4, 120.8, 118.6, 116.9, 79.9, 56.2, 52.6, 29.7, 28.4, 7.7, 4.2; FTIR (NaCl, thin film): cm^{-1}; 3380, 2954, 2875, 1734, 1718, 1507, 1499, 1366, 1164; $[\alpha]_D^{25}$ = +6.9 (*c* = 0.87, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 411.1501, found 411.1504.

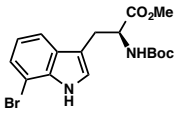
Tryptophan **205g**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl acetate) to afford **205g** as a colorless oil (103.9 mg, 0.222 mmol, 74% yield). ^1H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 7.98 (s, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.33 (s, 1H),

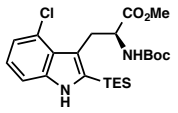
7.04 (d, J = 8.5 Hz, 1H), 4.92 (d, J = 8.1 Hz, 1H), 4.55 (dd, J = 14.7, 7.1 Hz, 1H), 3.61 (s, 3H), 3.22 (d, J = 6.6 Hz, 2H), 1.35 (s, 9H), 1.04 – 0.97 (m, 9H), 0.94 – 0.88 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 155.0, 138.8, 133.9, 128.4, 127.3, 120.1, 119.7, 110.7, 79.8, 54.2, 52.3, 29.5, 28.2, 7.4, 3.6; FTIR (NaCl, thin film): cm^{-1}; 3369, 2954, 2875, 1738, 1699, 1505, 1439, 1392, 1367, 1338, 1163, 1062; $[\alpha]_D^{25}$ = +7.1 (c = 1.63, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 467.2127, found 467.2129.

Tryptophan **205h**



Prepared following *General Procedure III* (36 h). The crude residue was purified by silica gel chromatography (80% hexanes, 20% acetone) to afford **205h** as a colorless oil (61.2 mg, 0.245 mmol, 52% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.33 (s, 1H), 7.54 (d, J = 7.9 Hz, 1H), 7.34 (d, J = 7.2 Hz, 1H), 7.17 (d, J = 1.7 Hz, 1H), 7.00 (dd, J = 7.8, 7.8 Hz, 1H), 5.51 (d, J = 7.4 Hz, 1H), 4.43 (dd, J = 13.5, 7.6 Hz, 1H), 3.64 (s, 3H), 3.23 (dd, J = 14.7, 5.4 Hz, 1H), 3.10 (dd, J = 14.7, 7.7 Hz, 1H), 1.35 (s, 89H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.5, 156.2, 135.6, 130.0, 125.5, 125.0, 121.3, 119.0, 112.5, 105.2, 79.9, 55.3, 52.7, 28.4, 28.3; FTIR (NaCl, thin film): cm^{-1}; 3365, 2968, 1738, 1696, 1501, 1434, 1365, 1335; $[\alpha]_D^{25}$ = +44.0 (c = 0.385, $CHCl_3$); HRMS (MM) calc'd $[M–C_5H_{10}O_2]^+$ 297.0233, found 297.0229.

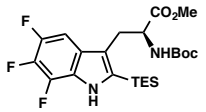
Tryptophan **205i**



Prepared following *General Procedure II* (12 h, 80 °C). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl acetate) to afford **205i** as a white, amorphous solid (113.7 mg, 0.243 mmol, 82%

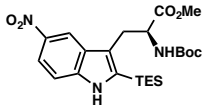
yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.29 (s, 1H), 7.38 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.06 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.02 (dd, *J* = 7.5, 1.2 Hz, 1H), 5.41 (d, *J* = 7.7 Hz, 1H), 4.53 (dd, *J* = 15.2, 8.8 Hz, 1H), 3.61 (s, 3H), 3.55 (dd, *J* = 14.3, 5.7 Hz, 1H), 3.28 – 3.17 (m, 1H), 1.23 (s, 9H), 1.02 – 0.89 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.8, 156.1, 141.7, 136.0, 125.8, 125.7, 123.5, 121.1, 120.5, 111.4, 79.8, 57.2, 52.5, 29.8, 28.3, 7.7, 4.2; FTIR (NaCl, thin film): cm^{-1}; 3369, 2954, 2934, 2875, 1721, 1700, 1499, 1456, 1436, 1366, 1167; $[\alpha]_D^{25}$ = –9.0 (*c* = 4.1, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 411.1501, found 411.1505.

Tryptophan **205j**



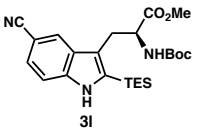
Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl acetate) to afford **205j** as a colorless oil (109.1 mg, 0.188 mmol, 72% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.36 (s, 1H), 7.25 (dd, *J* = 10.0, 7.1 Hz, 1H), 5.58 (d, *J* = 8.4 Hz, 1H), 4.32 (dd, *J* = 14.7, 8.5 Hz, 1H), 3.59 (s, 3H), 3.24 (dd, *J* = 14.7, 6.0 Hz, 1H), 3.04 (dd, *J* = 14.6, 8.7 Hz, 1H), 1.27 (s, 9H), 1.03 – 0.90 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.5, 156.0, 147.0 (dd, $J_{C\text{-}F}$ = 236.4, 11.9 Hz), 139.5 – 137.1 (m), 137.4 (d, $J_{C\text{-}F}$ = 3.6 Hz), 137.2 (ddd, $J_{C\text{-}F}$ = 239.4, 18.9, 12.5 Hz), 125.8 (dd, $J_{C\text{-}F}$ = 9.1, 5.4 Hz), 124.3 (dd, $J_{C\text{-}F}$ = 10.4, 2.1 Hz), 122.5 – 122.1 (m), 101.08 (d, $J_{C\text{-}F}$ = 19.1 Hz), 79.87, 56.24, 52.70, 29.44, 28.32, 7.62, 4.04; FTIR (NaCl, thin film): cm^{-1}; 3351, 2956, 2876, 1700, 1514, 1467, 1436, 1367, 1350, 1165; $[\alpha]_D^{25}$ = +4.2 (*c* = 0.65, $CHCl_3$); LRMS (ESI) calc'd $[M–C_4H_9]^+$ 431.5, found 431.2.

Tryptophan **205k**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (85% hexanes, 15% ethyl acetate) to afford **205k** as a yellow oil (105.0 mg, 0.219 mmol, 73% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.66 (s, 1H), 8.30 (d, *J* = 2.0 Hz, 1H), 7.91 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.66 (d, *J* = 8.9 Hz, 1H), 5.59 (d, *J* = 8.4 Hz, 1H), 4.37 (dd, *J* = 15.0, 8.3 Hz, 1H), 3.57 (s, 3H), 3.32 (dd, *J* = 14.6, 6.3 Hz, 1H), 3.15 (dd, *J* = 14.6, 8.4 Hz, 1H), 1.26 (s, 9H), 1.05 – 0.92 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.5, 156.1, 144.0, 142.1, 138.1, 134.1, 121.9, 119.8, 114.9, 108.6, 79.9, 56.3, 52.7, 29.6, 28.3, 7.6, 4.0; FTIR (NaCl, thin film): cm^{-1}; 3380, 2968, 2873, 1736, 1716, 1696, 1508, 1330, 1162, 1065, 1004; $[\alpha]_D^{25}$ = +7.9 (*c* = 0.75, $CHCl_3$); LRMS (ESI) calc'd $[M+H]^+$ 478.3, found 478.3.

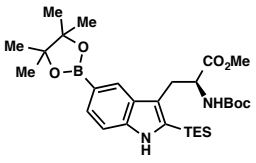
Tryptophan **205l**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (80% hexanes, 20% ethyl acetate) to afford **205l** as a white, amorphous solid (109.0 mg, 0.238 mmol, 79% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.48 (s, 1H), 8.03 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.38 (dd, *J* = 8.5, 1.5 Hz, 1H), 5.66 (d, *J* = 8.8 Hz, 1H), 4.35 (ddd, *J* = 9.0, 9.0, 5.5 Hz, 1H), 3.62 (s, 3H), 3.31 (dd, *J* = 14.6, 5.4 Hz, 1H), 3.10 (dd, *J* = 14.6, 9.2 Hz, 1H), 1.23 (s, 9H), 1.00 – 0.93 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.5, 155.9, 141.4, 136.9, 129.6, 126.0, 125.3, 122.3, 121.8, 113.0, 102.4, 79.8, 56.5, 52.7, 29.6, 28.3, 7.6, 4.0; FTIR (NaCl, thin film): cm^{-1}; 3350, 2953, 2878, 2218, 1728, 1696, 1508, 1370,

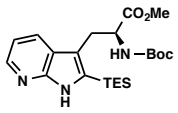
1167; $[\alpha]_D^{25}$ = –2.3 (*c* = 2.2, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 458.2470, found 458.2454.

Tryptophan **205**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (85% hexanes, 15% ethyl acetate – 80% hexanes, 20% ethyl acetate) to afford **205m** as a white, amorphous solid (127.0 mg, 0.227 mmol, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 8.10 – 7.98 (m, 2H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 4.90 (d, *J* = 8.1 Hz, 1H), 4.56 (dd, *J* = 14.4, 6.7 Hz, 1H), 3.75 (s, 3H), 3.39 – 3.24 (m, 2H), 1.36 (d, *J* = 2.8 Hz, 12H), 1.32 (s, 9H), 1.03 – 0.97 (m, 9H), 0.96 – 0.90 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ173.1, 155.2, 140.5, 133.1, 128.6, 128.4, 126.7, 120.1, 110.2, 83.4, 79.5, 54.0, 52.3, 28.8, 28.2, 24.9, 7.4, 3.7 (carbon adjacent to Boron was not observed); FTIR (NaCl, thin film): cm^{-1}; 3379, 2976, 2874, 1741, 1700, 1499, 1351, 1146; $[\alpha]_D^{25}$ = +15.0 (*c* = 1.0, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 558.3406, found 558.3388.

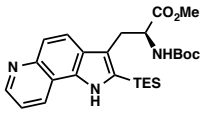
Tryptophan **205n**



Prepared following *General Procedure I* (12 h). The crude residue was purified by silica gel chromatography (98% dichloromethane, 2% methanol) to afford **205n** as a light yellow oil (111.2 mg, 0.256 mmol, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 9.78 (d, *J* = 14.4 Hz, 1H), 8.28 (d, *J* = 3.8 Hz, 1H), 7.90 (d, *J* = 7.7 Hz, 1H), 7.03 (dd, *J* = 7.7, 4.8 Hz, 1H), 5.14 (d, *J* = 8.4 Hz, 1H),

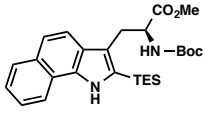
4.59 (dd, *J* = 15.0, 7.1 Hz, 1H), 3.59 (s, 3H), 3.25 (d, *J* = 6.8 Hz, 2H), 1.33 (s, 9H), 1.02 – 0.88 (m, 15H); ^{13}C NMR (126 MHz, $CDCl_3$) δ173.3, 155.0, 150.8, 143.3, 134.0, 127.3, 120.9, 118.1, 115.2, 79.7, 54.2, 52.2, 29.8, 28.1, 7.3, 3.6; FTIR (NaCl, thin film): cm^{-1}; 3380, 3226, 2953, 1743, 1691, 1582, 1496, 1439, 1367, 1283, 1172; $[\alpha]_D^{25}$ = +8.7 (*c* = 2.5, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 434.2470, found 434.2490.

Tryptopahn **205o**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (98% dichloromethane, 2% methanol) to afford **205o** as a light yellow oil (119.5 mg, 0.249 mmol, 83% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.79 (s, 1H), 8.78 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.76 (ddd, *J* = 8.3, 1.5, 0.7 Hz, 1H), 7.86 (d, *J* = 8.9 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.47 (dd, *J* = 8.3, 4.3 Hz, 1H), 5.60 (d, *J* = 8.3 Hz, 1H), 4.40 (dd, *J* = 15.0, 7.8 Hz, 1H), 3.57 (s, 3H), 3.37 (dd, *J* = 14.5, 6.6 Hz, 1H), 3.22 (dd, *J* = 14.5, 8.0 Hz, 1H), 1.26 (s, 9H), 1.01 (s, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.8, 156.1, 148.6, 147.4, 133.9, 133.3, 130.0, 125.6, 123.3, 123.1, 122.0, 121.2, 117.8, 80.0, 56.6, 52.7, 29.5, 28.4, 7.8, 4.4; FTIR (NaCl, thin film): cm^{-1}; 3350, 2953, 2873, 1734, 1717, 1700, 1696, 1570, 1496, 1377, 1164; $[\alpha]_D^{25}$ = +8.7 (*c* = 1.2, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$484.2626, found 484.2621.

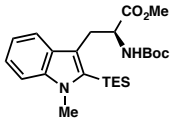
Tryptophan **205p**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl

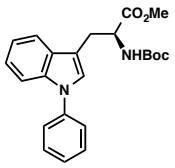
acetate) to afford **205p** as a colorless foam (103.2 mg, 0.213 mmol, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$, Major Rotamer) δ 8.67 (s, 1H), 8.05 (d, *J* = 8.1 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 7.44 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 4.97 (d, *J* = 7.9 Hz, 1H), 4.61 (*app* q, *J* = 7.1 Hz, 1H), 3.62 (s, 3H), 3.34 (d, *J* = 6.8 Hz, 2H), 1.35 (s, 9H), 1.08 – 1.02 (m, 9H), 1.02 – 0.97 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ173.3, 155.1, 133.6, 130.7, 130.6, 128.8, 125.4, 124.6, 124.2, 121.4, 121.3, 120.4, 119.4, 118.9, 79.7, 54.4, 52.3, 28.2, 24.7, 7.5, 3.8; FTIR (NaCl, thin film): cm^{-1}; 3409, 3350, 2953, 2868, 1743, 1694, 1501, 1392, 1362, 1165; $[\alpha]_D^{25}$ = +54.8 (*c* = 0.97, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 427.2048, found 427.2066.

Tryptophan **205q**



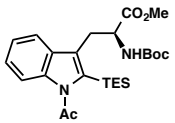
Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (88% hexanes, 12% ethyl acetate) to afford **205q** as a colorless oil (70.1 mg, 0.156 mmol, 52% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 7.51 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.20 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 1H), 7.04 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 5.41 (d, *J* = 7.3 Hz, 1H), 4.33 (dd, *J* = 15.1, 7.5 Hz, 1H), 3.83 (s, 3H), 3.52 (s, 3H), 3.33 (dd, *J* = 14.6, 7.1 Hz, 1H), 3.18 (dd, *J* = 14.5, 7.4 Hz, 1H), 1.37 – 1.23 (m, 9H), 1.03 – 0.95 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.9, 156.1, 141.0, 135.5, 129.6, 123.2, 121.8, 119.6, 119.5, 110.2, 80.0, 56.4, 52.5, 33.8, 28.9, 28.4, 7.9, 5.2; FTIR (NaCl, thin film): cm^{-1}; 3350, 2956, 2876, 1700, 1516, 1465, 1367, 1165; $[\alpha]_D^{25}$ = +4.9 (*c* = 0.34, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 391.20480, found 391.2034.

Tryptophan **205r**



Prepared following *General Procedure III* (12 h). The crude residue was purified by silica gel chromatography (20% acetone, 80% hexanes) to afford **205r** as a colorless oil (80.2 mg, 0.203 mmol, 68% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ7.63 (d, *J* = 7.8 Hz, 1H), 7.58 – 7.50 (m, 5H), 7.41 – 7.35 (m, 1H), 7.31 (s, 1H), 7.25 – 7.19 (m, 1H), 7.19 – 7.14 (m, 1H), 5.58 (d, *J* = 7.8 Hz, 1H), 4.51 (dd, *J* = 13.5, 7.7 Hz, 1H), 3.67 (s, 3H), 3.31 (dd, *J* = 14.7, 5.4 Hz, 1H), 3.18 (dd, *J* = 14.7, 7.6 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.6, 156.3, 140.4, 136.7, 130.7, 130.0, 127.9, 127.3, 124.8, 123.5, 121.1, 120.0, 118.3, 113.0, 111.4, 79.9, 55.2, 52.7, 28.5; FTIR (NaCl, thin film): cm^{-1}; 3380, 2966, 2930, 1741, 1714, 1501, 1455, 1367; $[\alpha]_D^{25}$ = +32.1 (*c* = 1.86, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 339.1339, found 339.1326.

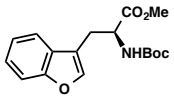
Tryptophan **205s**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (86% hexanes, 14% ethyl acetate) to afford **205s** as a colorless oil (107.0 mg, 0.226 mmol, 75% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 7.75 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.35 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 7.27 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 5.57 (d, *J* = 8.3 Hz, 1H), 4.40 (dd, *J* = 15.2, 8.0 Hz, 1H), 3.54 (s, 3H), 3.37 (dd, *J* = 14.4, 6.7 Hz, 1H), 3.20 (dd, *J* = 14.3, 8.2 Hz, 1H), 2.78 (s, 3H), 1.30 (s, 9H), 1.00 – 0.89 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.4, 171.0, 156.1, 138.0, 137.1, 133.7, 131.2, 125.9, 123.4,

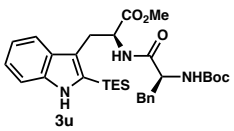
120.4, 115.2, 80.0, 55.9, 52.7, 28.8, 28.4, 27.0, 8.6, 6.9; FTIR (NaCl, thin film): cm^{-1}; 3373, 2953, 2874, 1746, 1700, 1499, 1435, 1369, 1321, 1223, 1167, 1109; $[\alpha]_D^{25}$ = +5.0 (*c* = 0.69, $CHCl_3$); HRMS (MM) calc'd $[M–C_4H_9]^+$ 419.1997, found 419.1986.

Tryptophan **205t**



Prepared following *General Procedure III* (24 h). The crude residue was purified by silica gel chromatography (25% acetone, 75% hexanes) to afford **205t** as a colorless oil (68.9 mg, 0.216 mmol, 72% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 7.60 (d, *J* = 7.2 Hz, 1H), 7.58 (s, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.36 – 7.30 (m, 1H), 7.27 (ddd, *J* = 7.5, 7.5, 1.0 Hz, 1H), 5.63 (d, *J* = 6.5 Hz, 1H), 4.48 (dd, *J* = 13.5, 7.9 Hz, 1H), 3.67 (s, 3H), 3.20 (dd, *J* = 14.8, 5.3 Hz, 1H), 3.07 (dd, *J* = 14.8, 8.0 Hz, 1H), 1.35 (s, 9H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.2, 156.0, 144.1, 128.8, 125.4, 123.6, 120.7, 118.3, 116.8, 112.2, 80.0, 54.5, 52.8, 28.4, 26.6; FTIR (NaCl, thin film): cm^{-1}; 3375, 2977, 2925, 1744, 1716, 1690, 1505, 1455, 1367, 1165; $[\alpha]_D^{25}$ = +16.8 (*c* = 0.64, $CHCl_3$); LRMS (MM) calc'd $[M–C_4H_9]^+$ 263.2, found 263.2.

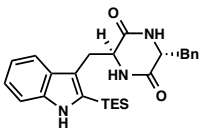
Tryptophan **205u**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (80% hexanes, 20% acetone) to afford **205u** as a colorless oil (109.1 mg, 0.188 mmol, 63% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.10 (s, 1H), 7.59 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.19 (m, 3H), 7.16 – 7.05 (m, 3H), 7.05 – 7.01 (m, 1H), 6.69 (d, *J* = 6.1 Hz, 1H), 5.24 (d, *J* = 6.4 Hz, 1H), 4.62 (dd, *J* = 13.1, 6.8 Hz, 1H), 4.23 (ddd, *J*

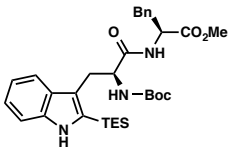
= 8.4, 8.4, 5.7 Hz, 1H), 3.60 (s, 3H), 3.24 (ddd, *J* = 14.4, 6.5, 4.7 Hz, 1H), 3.08 – 2.91 (m, 3H), 1.25 (s, 9H), 1.03 – 0.88 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ173.2, 172.1, 156.2, 139.8, 138.3, 133.3, 130.2, 129.7, 129.1, 127.4, 122.8, 120.4, 119.8, 119.4, 112.1, 79.9, 56.2, 55.4, 52.6, 38.4, 29.7, 28.4, 7.7, 4.2; FTIR (NaCl, thin film): cm^{-1}; 3380, 2948, 2878, 1736, 1666, 1506, 1367, 1244, 1165; $[\alpha]_D^{25}$ = –4.2 (*c* = 1.6, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 580.3201, found 580.3206.

Tryptophan **205v**



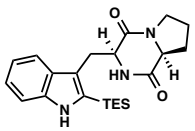
Prepared following *General Procedure I* (72 h). The crude residue was purified by silica gel chromatography (55% hexanes, 40% ethyl acetate, 5% methanol) to afford **205v** as a colorless oil (95.2 mg, 0.213 mmol, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.36 – 7.32 (m, 2H), 7.29 (ddd, *J* = 6.3, 5.1, 2.1 Hz, 2H), 7.22 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 7.18 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.10 (ddd, *J* = 7.9, 7.0, 0.9 Hz, 1H), 6.94 (d, *J* = 2.2 Hz, 1H), 5.64 (s, 1H), 4.24 (ddd, *J* = 5.2, 5.2, 2.5 Hz, 1H), 3.59 (dd, *J* = 14.5, 3.8 Hz, 1H), 3.45 (dd, *J* = 11.5, 3.8 Hz, 1H), 3.14 (d, *J* = 5.1 Hz, 2H), 2.87 (dd, *J* = 14.5, 11.5 Hz, 1H), 1.02 – 0.94 (m, 9H), 0.90 – 0.82 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 167.0, 138.7, 134.8, 133.9, 129.9, 128.9, 127.6, 127.6, 122.8, 119.7, 118.7, 118.0, 111.1, 56.6, 53.3, 40.2, 30.0, 7.4, 7.4, 3.7; FTIR (NaCl, thin film): cm^{-1}; 3356, 3226, 2958, 2864, 1676, 1451, 1437, 1316; $[\alpha]_D^{25}$ = +5.6 (*c* = 0.47, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 448.2415, found 448.2426.

Tryptophan **205w**



Prepared following *General Procedure I* (36 h). The crude residue was purified by silica gel chromatography (80% hexanes, 20% acetone) to afford **205w** as a colorless oil (108.0 mg, 0.186 mmol, 62% yield).[1]H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.10 (s, 1H), 7.59 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.29 – 7.19 (m, 3H), 7.16 – 7.05 (m, 3H), 7.05 – 7.01 (m, 1H), 6.69 (d, *J* = 6.1 Hz, 1H), 5.24 (d, *J* = 6.4 Hz, 1H), 4.62 (dd, *J* = 13.1, 6.8 Hz, 1H), 4.23 (ddd, *J* = 8.4, 8.4, 5.7 Hz, 1H), 3.60 (s, 3H), 3.24 (ddd, *J* = 14.4, 6.5, 4.7 Hz, 1H), 3.08 – 2.91 (m, 3H), 1.25 (s, 9H), 1.03 – 0.88 (m, 15H); ^{13}C NMR (126 MHz, CD_3CN) δ 172.6, 172.3, 156.0, 140.1, 137.6, 133.4, 130.3, 129.6, 129.3, 127.7, 122.9, 121.0, 119.8, 119.7, 112.0, 80.0, 57.1, 54.3, 52.7, 38.2, 29.6, 28.3, 7.8, 4.3, 4.2; FTIR (NaCl, thin film): cm^{-1}; 3370, 2953, 2878, 1745, 1666, 1508, 1449, 1370, 1241, 1170; $[\alpha]_D^{25}$ = +10.0 (*c* = 1.06, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 580.3201, found 580.3206.

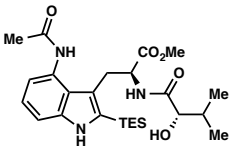
Tryptophan **205x**



Prepared following *General Procedure I* (72 h). The crude residue was purified by silica gel chromatography (55% hexanes, 40% ethyl acetate, 5% methanol) to afford **3x** as an amorphous, white solid (98.6 mg, 0.249 mmol, 83% yield). [1]H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.56 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.40 (ddd, *J* = 8.2, 0.8, 0.8 Hz, 1H), 7.22 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.11 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H), 5.59 (s, 1H), 4.42 (dd, *J* = 11.8, 2.4 Hz, 1H), 4.07 (dd, *J* = 11.6, 4.5 Hz, 1H), 3.84 (dd, *J* = 15.0, 3.9 Hz, 1H), 3.75 – 3.66 (m, 1H), 3.65 – 3.54 (m, 1H), 3.00 (dd, *J* = 15.0, 11.8 Hz, 1H), 2.39 – 2.29 (m, 1H), 2.13 – 2.00 (m, 2H), 1.99 – 1.87 (m, 1H), 1.04

– 0.98 (m, 9H), 0.94 – 0.85 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 165.7, 138.9, 133.6, 127.9, 123.0, 119.9, 118.8, 118.3, 111.3, 59.2, 54.8, 45.4, 28.4, 27.5, 22.6, 7.4, 3.8; FTIR (NaCl, thin film): cm^{-1}; 3365, 2953, 2873, 1671, 1456, 1412, 1303, 1239; $[\alpha]_D^{25}$ = –34.4 (*c* = 0.82, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 398.2258, found 398.2272.

Tryptophan **205y**

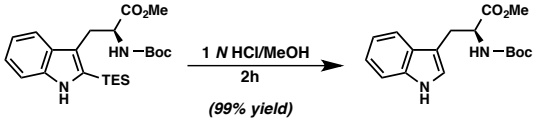


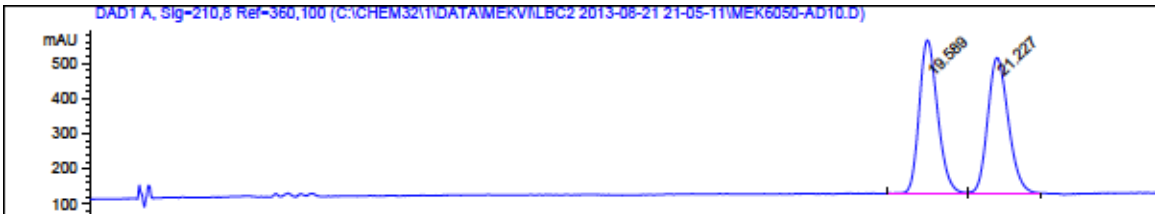
Prepared following *General Procedure II* (0.87 mmol scale, 12 h). The crude residue was purified by silica gel chromatography (100% ethyl acetate) to afford **205y** as a light yellow oil (370.2 mg, 0.756 mmol, 86% yield). ^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 9.28 (s, 1H), 8.44 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.17 (d, *J* = 5.6 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 7.4 Hz, 1H), 4.53 (dt, *J* = 10.3, 6.3 Hz, 1H), 3.65 (s, 3H), 3.64 – 3.62 (m, 1H), 3.59 (d, *J* = 5.9 Hz, 1H), 3.45 (dd, *J* = 14.7, 6.2 Hz, 1H), 3.17 (dd, *J* = 14.7, 10.3 Hz, 1H), 2.19 (s, 3H), 1.91 – 1.79 (m, 1H), 1.07 – 0.94 (m, 15H), 0.87 (dd, *J* = 15.7, 4.0 Hz, 3H), 0.70 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, CD_3CN) δ 174.4, 173.6, 171.5, 141.7, 134.9, 130.2, 124.9, 122.9, 119.4, 118.9, 110.9, 76.3, 52.6, 32.6, 29.5, 29.3, 23.8, 19.4, 15.6, 7.7, 4.3; FTIR (NaCl, thin film): cm^{-1}; 3324, 2956, 2875, 1742, 1657, 1516, 1435, 1369; $[\alpha]_D^{25}$ = –1.8 (*c* = 1.3, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 490.2732, found 490.2772.

4.7.6 Stability of tryptophan center

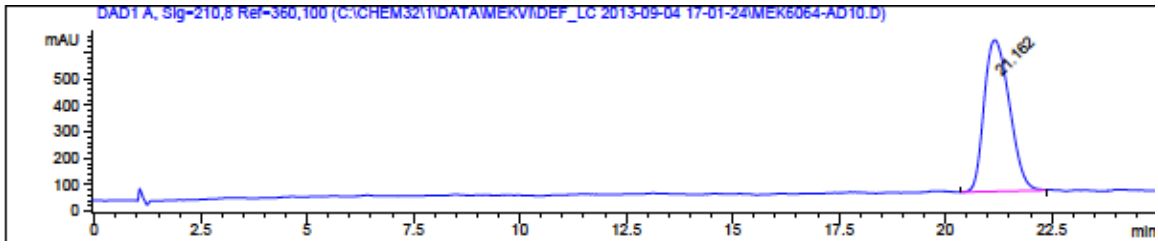
In order to confirm that the tryptophan products were not undergoing deleterious racemization under the reaction conditions, tryptophan **205a** was desilylated with 1 *N* HCl/MeOH and compared to *racemic N*-Boc-tryptophan methyl ester through chiral SFC

analysis (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R(minor) = 19.6 min, t_R(major) = 21.2 min. We observed no racemization of the tryptophan stereocenter under the reaction conditions. Additionally, Larock indole syntheses using dipeptide-derived alkynes to provide tryptohans **205u** – **205y** show the formation of a single diastereomer of product by crude ^{1}H NMR and LCMS, further supporting the stability of the tryptophan stereocenter under Larock conditions. The low optical rotations exhibited by tryptophans **205a** – **205z** are consistent with literature values of related compounds.





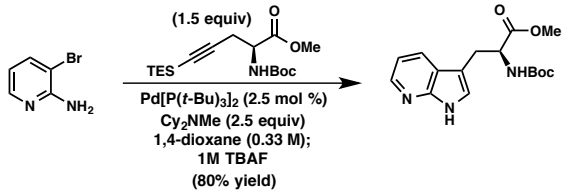
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.589	BV	0.4601	1.31030e4	436.62933	50.0927
2	21.227	VB	0.5243	1.30545e4	386.23413	49.9073



Signal 1: DAD1 A, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.162	VB	0.6657	2.36458e4	570.35565	100.0000

4.7.7 Scale-up and desilylation of tryptophan 205o

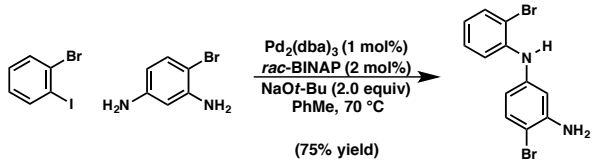


In a glovebox, pyridyl aniline **203o** (865 mg, 5.0 mmol, 1.0 equiv), alkyne **204a** (2.56 g, 7.5 mmol, 1.5 equiv), $Pd[P(^tBu)_3]_2$ (64 mg, 0.125 mmol, 0.025 equiv), and Cy_2NMe (2.7 mL, 12.5 mmol, 2.5 equiv) were combined in a 50 mL flask. The solids were dissolved in 15 mL 1,4-dioxane and the solution was heated to 60 °C for 30 h. Upon cooling, the milky yellow solution was filtered through a silica plug, which was washed thoroughly with ethyl acetate. The solution was concentrated and then redissolved in 50 mL ethyl acetate and 1 M TBAF in THF (5 mL). After 20 minutes, aqueous NH_4Cl was added and the reaction mixture was partitioned in a separatory funnel. The aqueous layer was back extracted with ethyl acetate (3 X 150 mL). The organics were then recombined, washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude residue was purified using silica gel chromatography (60% hexanes, 35% ethyl acetate, 5% methanol) to afford tryptophan as a light yellow solid (1.28 g, 80% yield).

^{1}H NMR (500 MHz, CD_3CN, Major Rotamer) δ 10.06 (s, 1H), 8.30 – 8.18 (m, 1H), 7.94 – 7.85 (m, 1H), 7.20 (s, 1H), 7.06 (dd, *J* = 7.9, 4.7 Hz, 1H), 5.64 (d, *J* = 7.7 Hz, 1H), 4.45 (dd, *J* = 13.4, 7.6 Hz, 1H), 3.64 (s, 3H), 3.23 (dd, *J* = 14.7, 5.4 Hz, 1H), 3.11 (dd, *J* = 14.7, 7.5 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (126 MHz, CD_3CN) δ 173.6, 156.2, 149.6, 143.8, 127.8, 125.0, 120.7, 116.3, 110.0, 79.9, 55.3, 52.7, 28.4, 28.4; FTIR (NaCl, thin

film): cm^{-1}; 3365, 2978, 1743, 1698, 1511, 1434, 1362; $[\alpha]_D^{25}$ = 49.1 (*c* = 1.25, $CHCl_3$); HRMS (MM) calc'd $[M+H]^+$ 320.1605, found 320.1594.

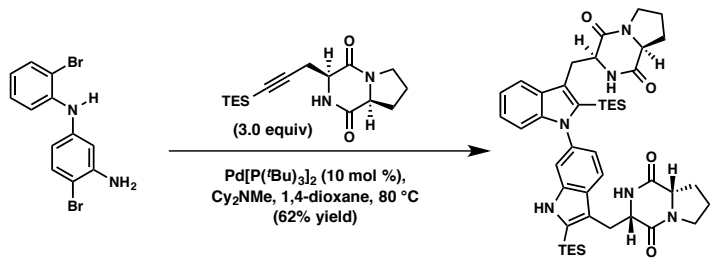
4.7.8 Total synthesis of (–)-aspergilazine A



In a glove box, a flame-dried 250 mL flask was charged with iodobromobenzene (771 μL, 6.0 mmol, 1.0 equiv), dianiline **212** (1.34 g, 7.2 mmol, 1.2 equiv), $Pd_2(dba)_3$ (54 mg, 0.06 mmol, 0.01 equiv), *rac*-BINAP (75 mg, 0.12 mmol, 0.02 equiv), and NaO^{t}Bu (865 mg, 9.0 mmol, 1.5 equiv). 60 mL of PhMe was added and the reaction flask was sealed and heated to 70 °C for 3.5 hours. Upon cooling, the reaction mixture was filtered through a plug of silica gel, which was flushed with ethyl acetate. The organics were concentrated and purified by silica gel chromatography (20% acetone, 80% hexanes) to provide the diarylamine **7** as a light yellow oil (1.54 g, 75% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.31 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.27 – 7.20 (m, 1H), 6.83 (ddd, *J* = 8.0, 7.2, 1.6 Hz, 1H), 6.56 (d, *J* = 2.5 Hz, 1H), 6.49 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.03 (s, 1H), 4.11 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ144.6, 141.9, 140.7, 132.9, 132.8, 128.0, 121.2, 116.6, 112.5, 111.2, 106.3, 101.9; FTIR (NaCl, thin film): cm^{-1}; 3464, 3380, 1612, 1582, 1511, 1459, 1407, 1330, 1303, 1276; HRMS (MM) calc'd $[M+H]^+$ 340.9284, found 340.9264.

Synthesis of bis-triethylsilyl-(–)-aspergilazine A



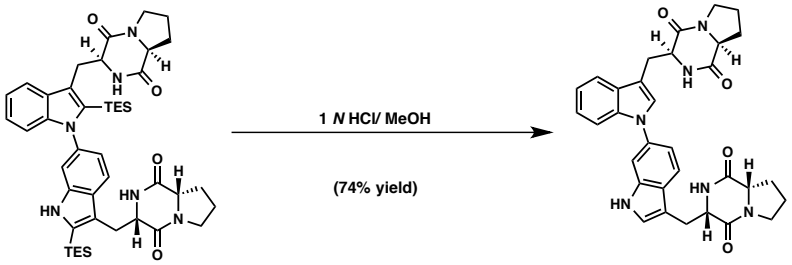
In a glovebox, a one dram vial was charged with diarylamine (35 mg, 0.1 mmol, 1.0 equiv), alkyne **209** (94 mg, 0.3 mmol, 3.0 equiv), Cy_2NMe (55 μL, 0.25 mmol, 2.5 equiv), $Pd[P(^tBu)_3]_2$ (5.2 mg, 0.01 mmol, 0.1 equiv) and 1,4-dioxane (500 μL). The vial was sealed and heated to 80 °C for 4 hours. Upon cooling, the reaction mixture was filtered through celite, which was washed with ethyl acetate (15 mL). The organics were concentrated and the crude reaction mixture was purified by preparative reverse phase HPLC (65–85% acetonitrile in H_2O, 30 mL/min, 20 min) to give the product as a colorless solid (49.5 mg, 62% yield).

^{1}H NMR (500 MHz, CD_2Cl_2, Major Rotamer) δ 8.47 (d, J = 11.0 Hz, 1H), 7.72 (dd, J = 8.3, 2.5 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.47 (dd, J = 7.6, 1.6 Hz, 1H), 7.21 – 7.11 (m, 3H), 7.03 – 6.94 (m, 1H), 5.71 (s, 1H), 5.56 (s, 1H), 4.60 – 4.52 (m, 1H), 4.52 – 4.47 (m, 1H), 4.25 – 4.08 (m, 2H), 3.98 – 3.84 (m, 2H), 3.78 – 3.68 (m, 2H), 3.67 – 3.57 (m, 2H), 3.22 (ddd, J = 14.7, 11.7, 2.9 Hz, 1H), 3.11 (ddd, J = 14.9, 11.7, 1.4 Hz, 1H), 2.46 – 2.30 (m, 2H), 2.18 – 2.03 (m, 4H), 2.05 – 1.89 (m, 2H), 1.19 – 1.08 (m, 9H), 1.08 – 0.98 (m, 6H), 0.98 – 0.84 (m, 9H), 0.75 – 0.52 (m, 6H); FTIR (NaCl, thin film): cm^{-1}; 3375, 2963, 2859, 1671, 1446, 1414; $[\alpha]_D^{25}$ = –79.5 (c = 0.055, 1:1 DCM:MeOH); HRMS (MM) calc'd $[M–SiC_6H_{15}]^+$ 679.3423, found 679.3426.

The ^{1}H NMR was found to coalesce in deuterated acetonitrile at 60 °C. The ^{13}C NMR was still rotameric, even at elevated temperature.

^{1}H NMR (400 MHz, CD_3CN) δ 9.42 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.72 – 7.65 (m, 1H), 7.51 (s, 1H), 7.22 – 7.04 (m, 3H), 6.94 (s, 1H), 5.60 (s, 1H), 5.49 (s, 1H), 4.47 (dd, *J* = 11.4, 11.4 Hz, 2H), 4.15 (t, *J* = 7.7 Hz, 2H), 3.85 (d, *J* = 14.7 Hz, 1H), 3.79 (dd, *J* = 15.0, 4.2 Hz, 1H), 3.72 – 3.58 (m, 2H), 3.50 (ddd, *J* = 11.6, 8.1, 3.8 Hz, 2H), 3.28 – 3.16 (m, 1H), 3.12 (dd, *J* = 14.9, 10.8 Hz, 1H), 2.33 – 2.15 (m, 2H), 2.06 – 1.70 (m, 6H), 1.23 – 0.94 (m, 11H), 0.88 (t, *J* = 7.7 Hz, 6H), 0.74 – 0.51 (m, 5H).

Synthesis of (–)-aspergilazine A



The silylated compound (49.5 mg, 0.06 mmol, 1.0 equiv) was dissolved in 1 *N* HCl in MeOH (10 mL) and allowed to stir for 15 minutes. The reaction was quenched by addition of aqueous $NaHCO_3$ and diluted with ethyl acetate. The organics were removed *in vacuo* and the aqueous extracted with ethyl acetate (3 X 20 mL). The organics were combined, dried over Na_2SO_4, filtered, and concentrated. The crude residue was purified by silica gel chromatography (5% MeOH, 95% CH_2Cl_2) to provide (–)-aspergilazine A as a colorless solid (26.0 mg, 74% yield).

Spectroscopic and physical data, including ^{1}H, ^{13}C NMR in DMSO-*d6,* IR, and MS obtained for (–)-aspergilazine A matched that as reported during isolation by Gu et. Al and data obtained by Sperry and co-workers. See below for ^{1}H and ^{13}C comparison table.

^{1}H NMR (500 MHz, DMSO) δ 11.05 (s, 1H), 7.98 (s, 1H), 7.87 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 7.9 Hz, 1H), 7.47 (d, J = 8.3 Hz, 1H), 7.45 (s, 1H), 7.43 (d, J = 1.7 Hz, 1H), 7.28 (d, J = 2.0 Hz, 1H), 7.18 – 7.14 (m, 1H), 7.14 – 7.11 (m, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 4.39 (t, *J* = 4.8 Hz, 1H), 4.35 (t, *J* = 4.7 Hz, 1H), 4.12 – 4.05 (m, 2H), 3.45 – 3.35 (m, 3H), 3.33 – 3.20 (m, 3H), 3.19 – 3.10 (m, 2H), 2.05 – 1.89 (m, 2H), 1.79 – 1.49 (m, 4H), 1.47 – 1.31 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 169.6, 169.5, 165.9, 165.9, 136.5, 136.0, 133.5, 129.0, 128.8, 126.5, 126.2, 122.5, 120.2, 119.9, 115.7, 111.4, 110.5, 110.2, 107.1, 58.9, 55.7, 55.6, 45.1, 28.2, 26.3, 26.2, 22.3, 22.3; FTIR (NaCl, thin film): cm^{-1}; 3365, 3246, 2933, 1666, 1459, 1414; $[\alpha]_D^{25}$ = –90.6 (*c* = 0.625, 1:1 CH_2Cl_2:MeOH); HRMS (MM) calc'd $[M+H]^+$ 565.2558, found 565.2555.

Comparison of ^{1}H NMR data for Natural vs. Synthetic (-)-Aspergilazine A

Isolation (–)-Aspergilazine A ^{1}H NMR, 600 MHz, DMSO	**This Work (–)-Aspergilazine A ^{1}H NMR, 500 MHz, DMSO**
δ 11.09 (s, 1H)	11.05 (s, 1H)
8.00 (s, 1H)	7.98 (s, 1H)
7.89 (s, 1H)	7.87 (s, 1H)
7.75 (br d, *J* = 8.4 Hz, 1H)	7.73 (d, *J* = 8.4 Hz, 1H)
7.68 (br d, *J* = 7.8 Hz, 1H)	7.67 (d, *J* = 7.9 Hz, 1H)
7.48 (d, *J* = 8.2 Hz, 1H)	7.47 (d, *J* = 8.3 Hz, 1H)
7.47 (s, 1H)	7.45 (s, 1H)
7.45 (d, *J* = 1.9 Hz, 1H)	7.43 (d, *J* = 1.7 Hz, 1H)
7.29 (d, *J* = 1.7 Hz, 1H)	7.28 (d, *J* = 2.0 Hz, 1H)
7.16 (ddd, *J* = 7.7, 7.4, 1.0 1H)	7.18 – 7.14 (m, 1H)
7.14 (dd, *J* = 8.3, 1.9, 1H)	7.14 – 7.11 (m, 1H)
7.09 (ddd, *J* = 7.4, 7.4, 0.8 1H)	7.09 (t, *J* = 7.4 Hz, 1H)
4.41 (dd, *J* = 4.9, 5.0 Hz, 1H)	4.39 (dd, *J* = 4.8, 4.8 Hz, 1H)
4.37 (dd, *J* = 5.0, 5.0 Hz, 1H)	4.35 (t, *J* = 4.7 Hz, 1H)
4.07 (dd, *J* = 8.3, 8.3 Hz, 2H)	4.12 – 4.05 (m, 2H)
3.38 (m, 3H)	3.45 – 3.35 (m, 3H)
3.26 (m, 3H)	3.33 – 3.20 (m, 3H)
3.16 (m, 2H)	3.19 – 3.10 (m, 2H)
1.98 (m, 2H)	2.05 – 1.89 (m, 2H)
1.65 (m, 4H)	1.79 – 1.49 (m, 4H)
1.37 (m, 2H)	1.47 – 1.31 (m, 2H)

Comparison of ^{13}C NMR data for Natural vs. Synthetic (–)-Aspergilazine A

Isolation (–)-Aspergilazine A ^{13}C NMR, 150 MHz, DMSO	**This Work (–)-Aspergilazine A ^{13}C NMR, 126 MHz, DMSO**	**Chemical Shift Difference, Δδ**
169.7	169.6	0.1
169.6	169.5	0.1
166.0	165.9	0.1
165.9	165.9	0.0
136.7	136.5	0.2
136.2	136.0	0.2
133.6	133.5	0.1
129.1	129.0	0.1
128.9	128.8	0.1
126.6	126.5	0.1
126.3	126.2	0.1
122.6	122.5	0.1
120.3	120.2	0.1
119.9	119.9	0.0
115.8	115.7	0.1
111.5	111.4	0.1
110.6	110.5	0.1
110.3	110.2	0.1
107.2	107.1	0.1

59.0	58.9	0.1
59.0	58.9	0.1
55.8	55.7	0.1
55.7	55.6	0.1
45.2	45.1	0.1
45.2	45.1	0.1
28.3	28.2	0.1
28.3	28.2	0.1
26.4	26.3	0.1
26.3	26.2	0.1
22.4	22.3	0.1
22.4	22.3	0.1

4.8 NOTES AND REFERENCES

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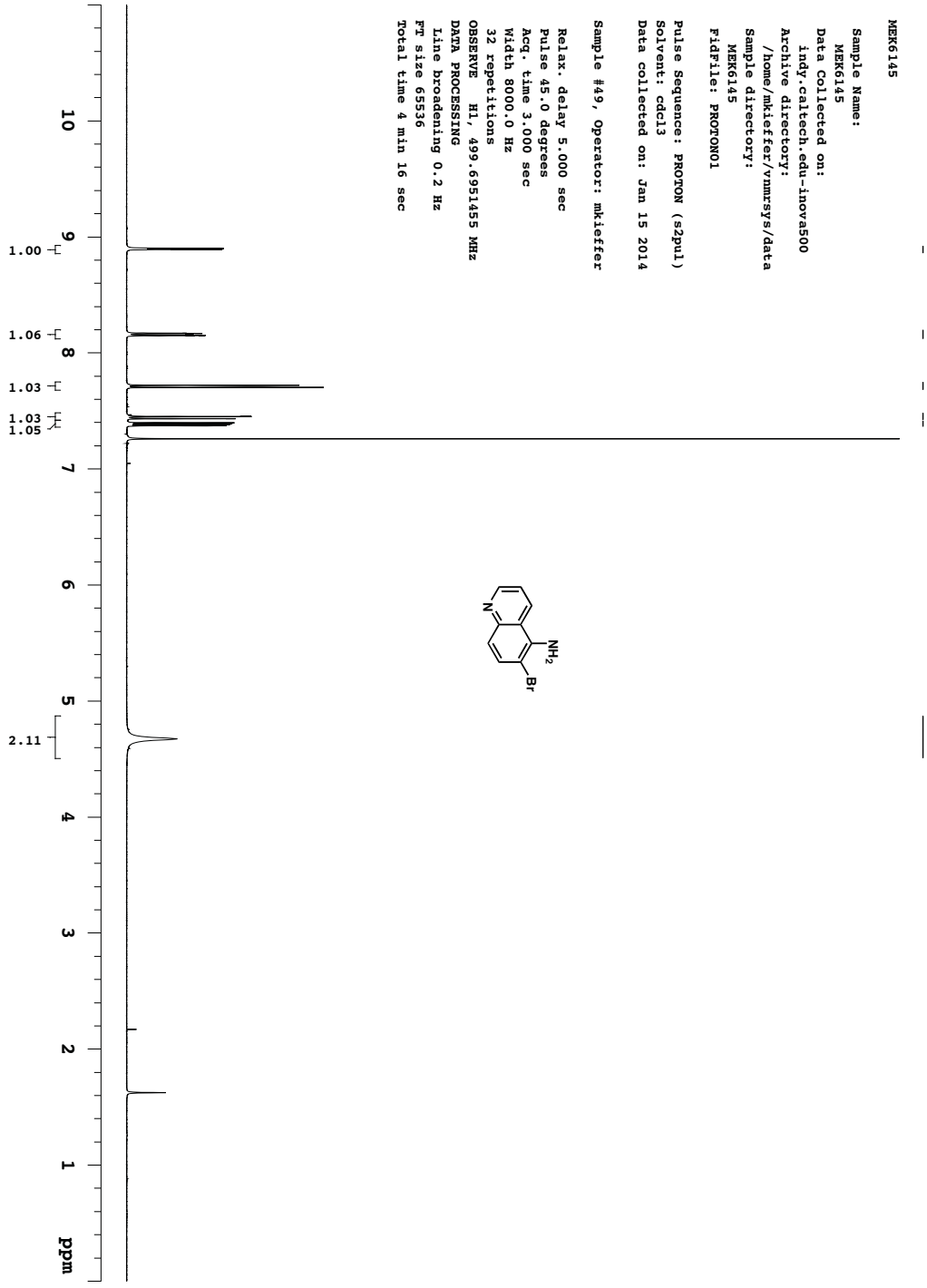
Appendix 3

Spectra Relevant to Chapter 4: A Mild and General Larock Indolization Protocol for the Synthesis of Unnatural Tryptophan Derivatives: Total Synthesis of (–)-Aspergilazine A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Data Collected on:
indy.caltech.edu-inova500
Archive directory:
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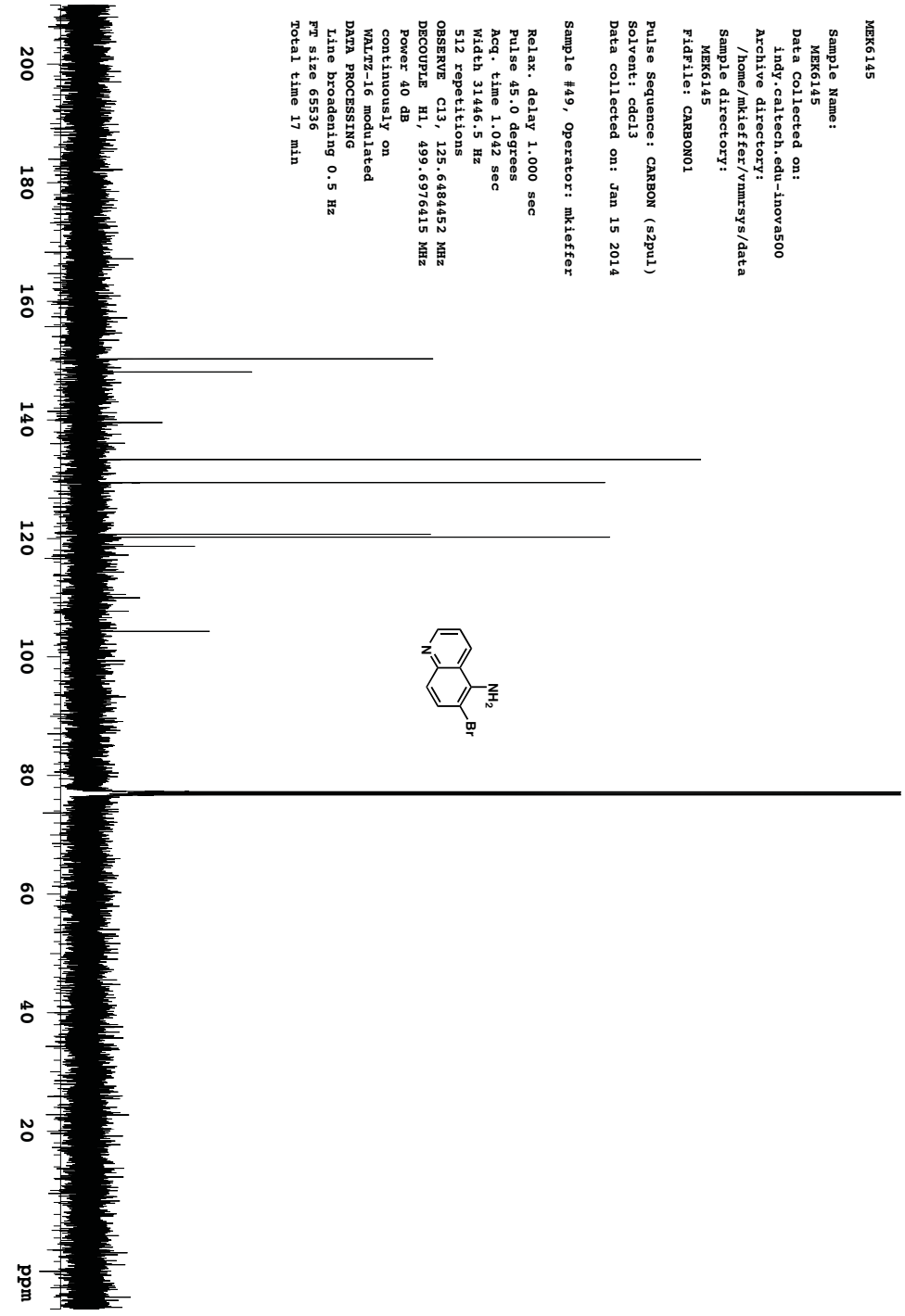
Sample directory:
MEK6145
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 15 2014
Sample #49, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
1.00
1.06
1.03
1.03
1.05
2.11
N
NH2
Br
10
9
8
7
6
5
4
3
2
1
ppm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Sample Name:
MEK6145
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
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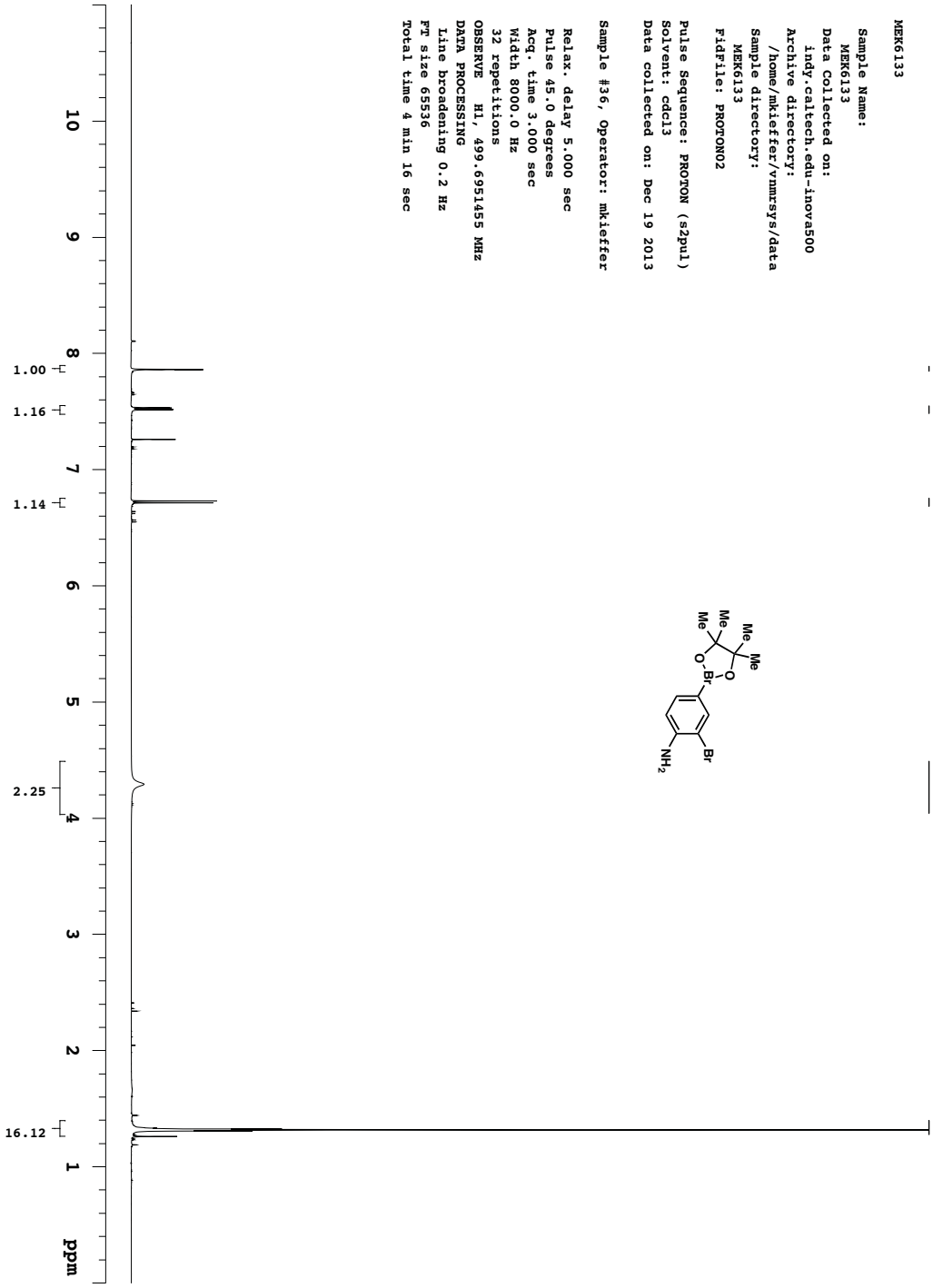
Sample directory:
MEK6145
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 15 2014
Sample #49, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484452 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
NH2
Br
200
180
160
140
120
100
80
60
40
20
ppm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Data Collected on:
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Archive directory:
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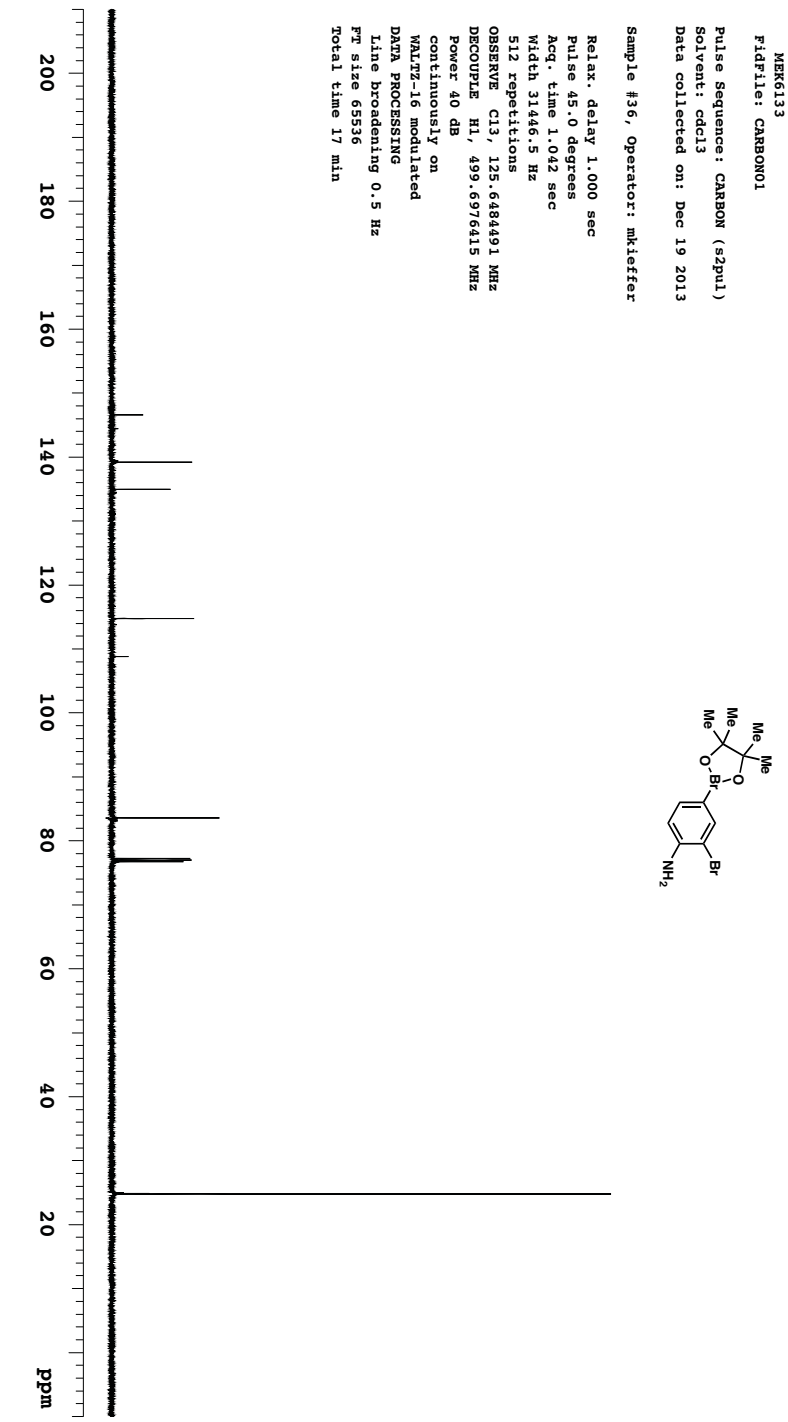
Sample directory:
MEK6133
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 19 2013
Sample #36, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Me
Me
Me
Me
O
Br
O
Br
NH2
1.00
1.16
1.14
2.25
16.12
10
9
8
7
6
5
4
3
2
1
ppm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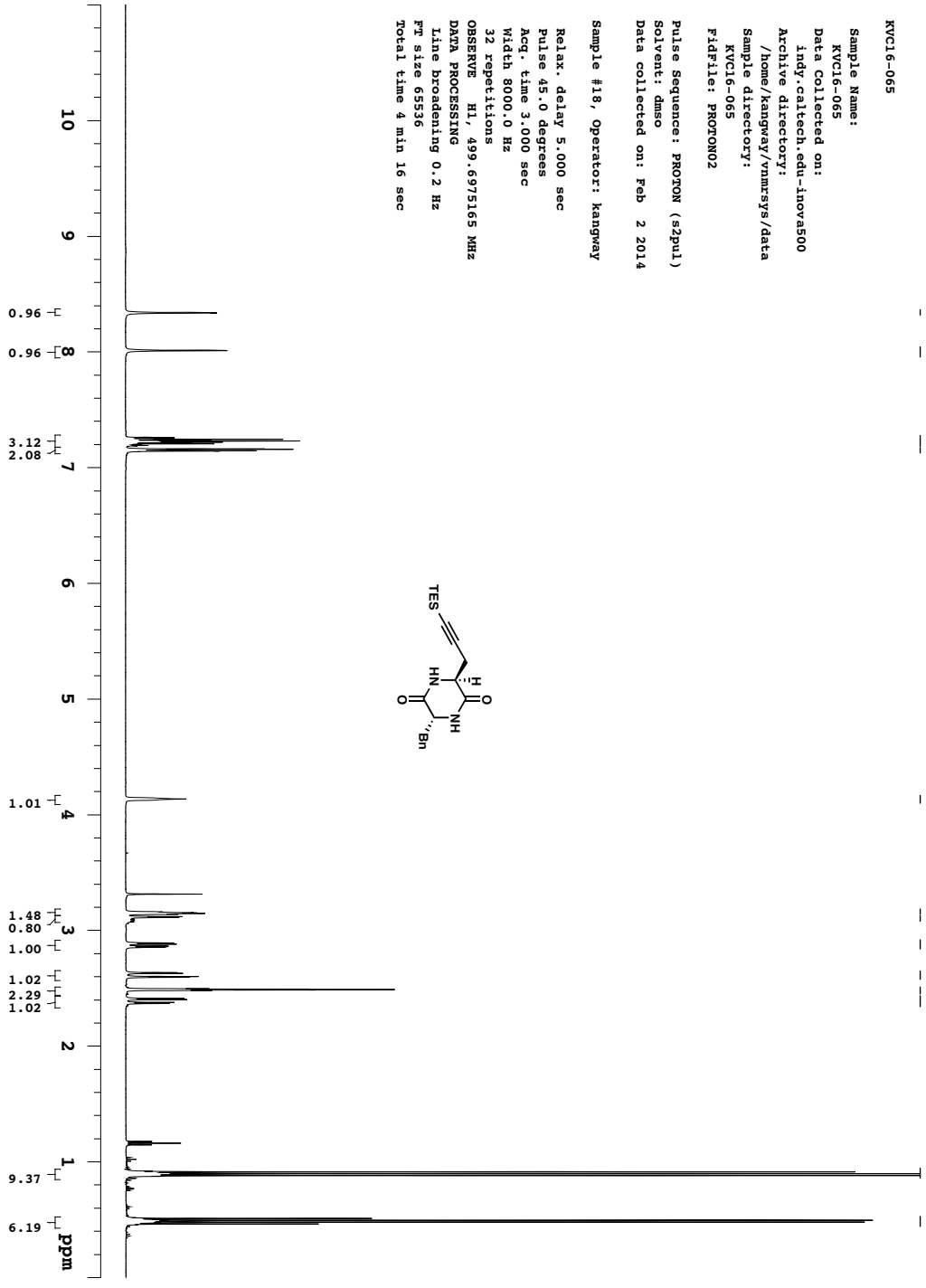
MEK6133
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6133
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 19 2013
Sample #36, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484491 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
O
Br
O
Br
NH2
200
180
160
140
120
100
80
60
40
20
ppm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KVC16-065
Data Collected on:
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Archive directory:
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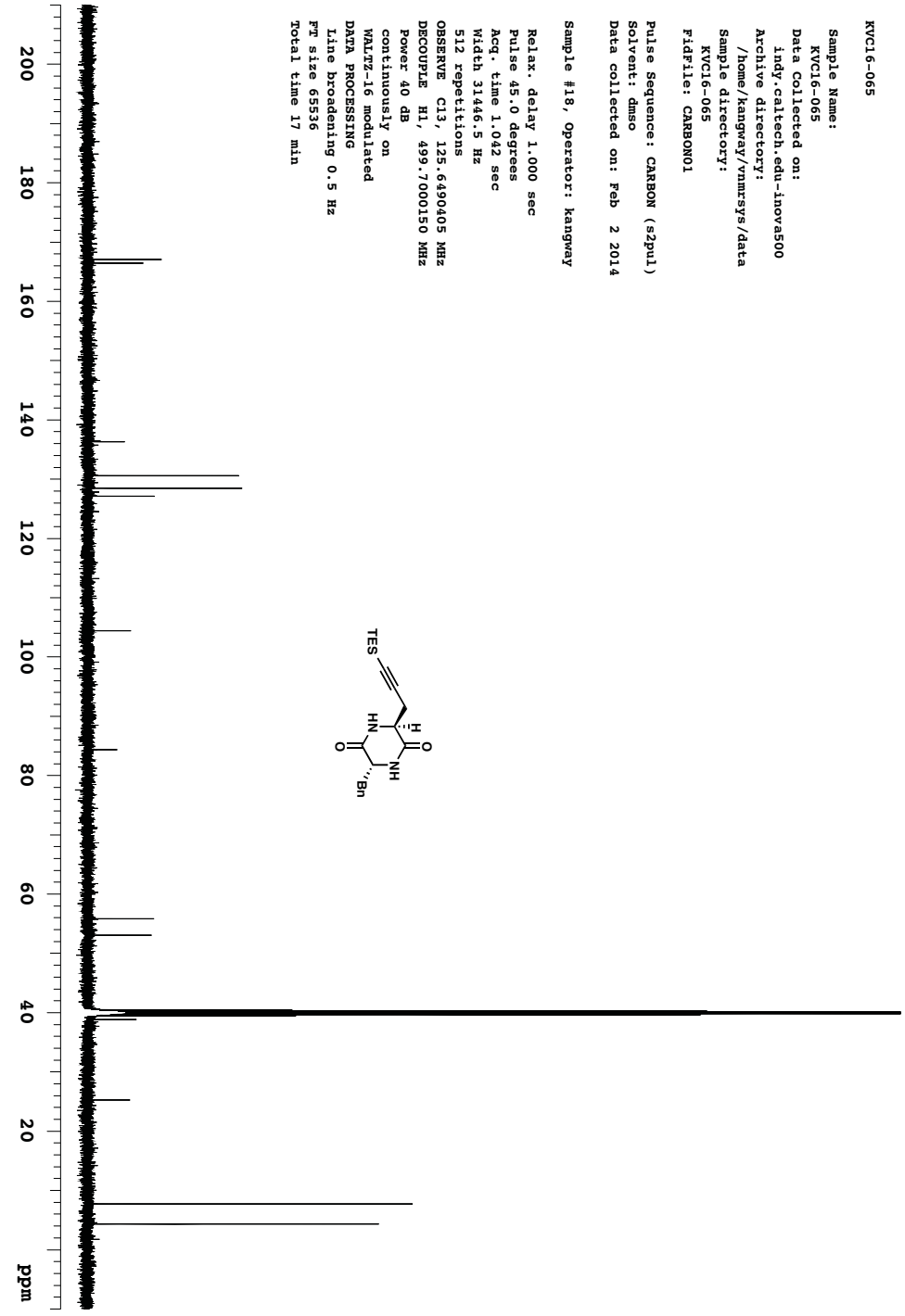
Sample directory:
KVC16-065
FidFile: PROTONO2
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Feb 2 2014
Sample #18, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6975165 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
TES
HN
NH
Bn
0.96
0.96
3.12
2.08
1.01
1.48
0.80
1.00
1.02
2.29
1.02
9.37
6.19
ppm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KVC16-065
Data Collected on:
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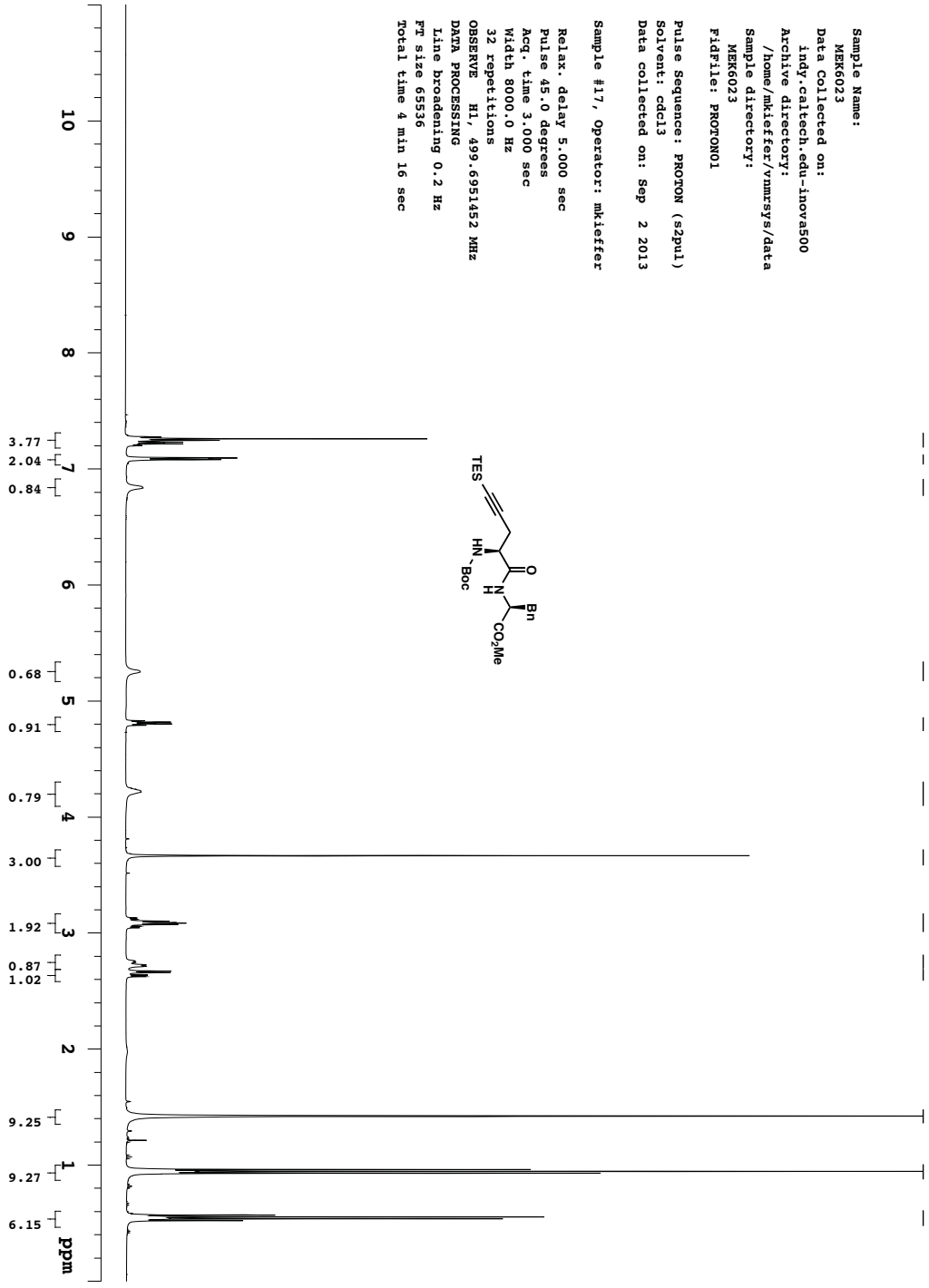
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
KVC16-065
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Feb 2 2014
Sample #18, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6490405 MHz
DECOUPLE H1, 499.7000150 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
TES
HN
NH
O
O
H
Bn
200
180
160
140
120
100
80
60
40
20
ppm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Data Collected on:
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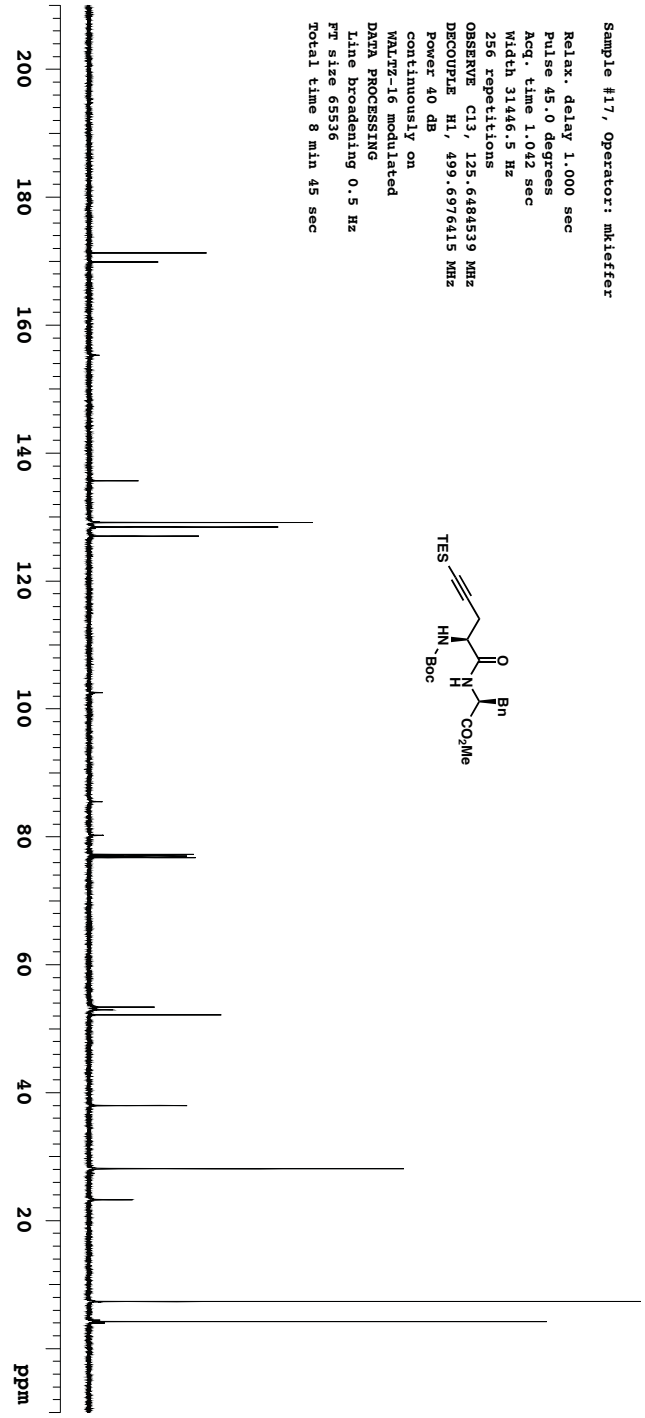
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6023
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2013
Sample #17, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951452 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
TES
HN
Boc
O
N
H
Bn
CO2Me
3.77
2.04
0.84
0.68
0.91
0.79
3.00
1.92
0.87
1.02
9.25
9.27
6.15
10
9
8
7
6
5
4
3
2
1
ppm


Sample Name:
MEK6023
Data Collected on:
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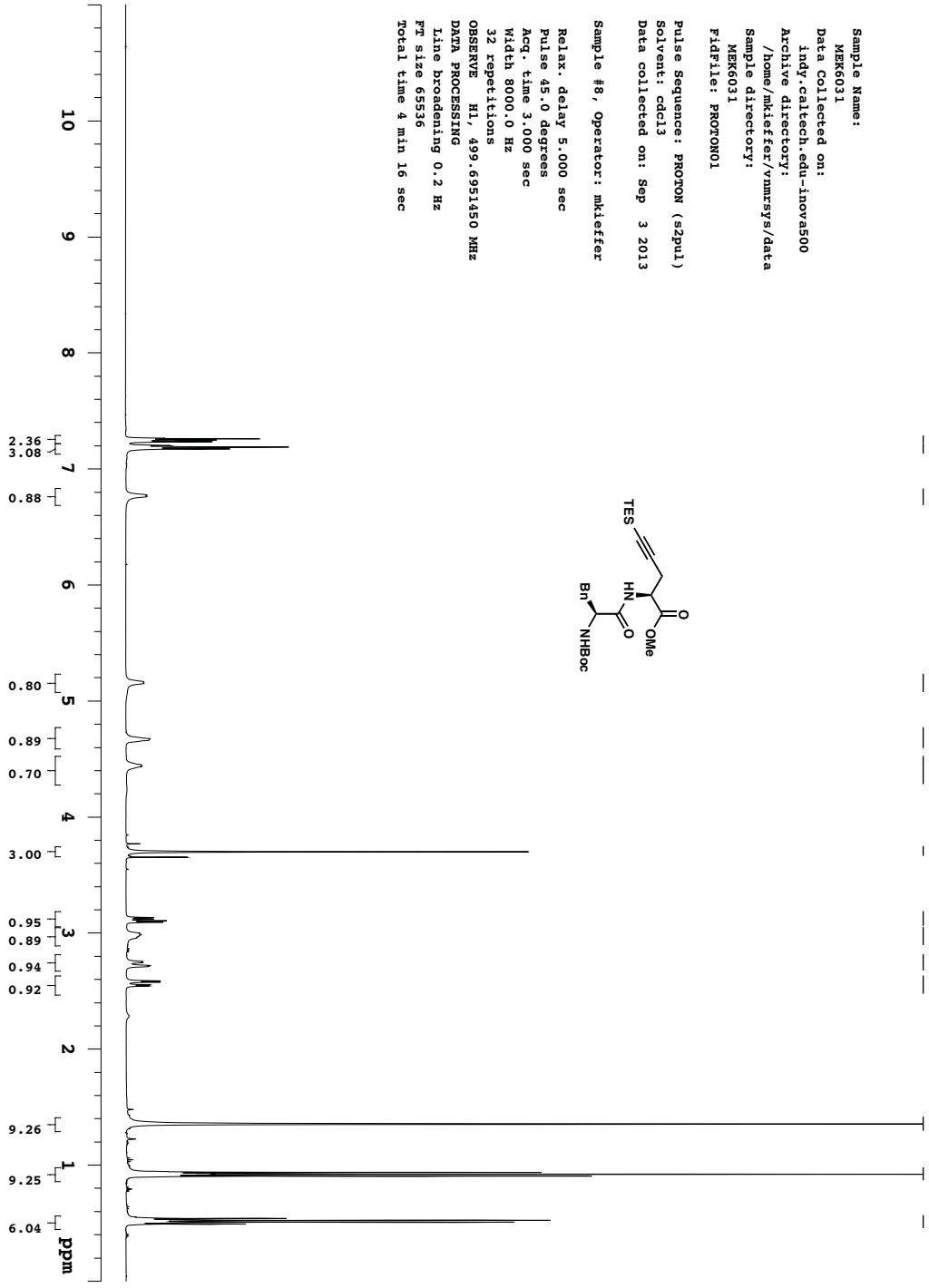
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6023
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2013
Sample #17, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6484539 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
TES
HN
Boc
O
N
H
Bn
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm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Data Collected on:
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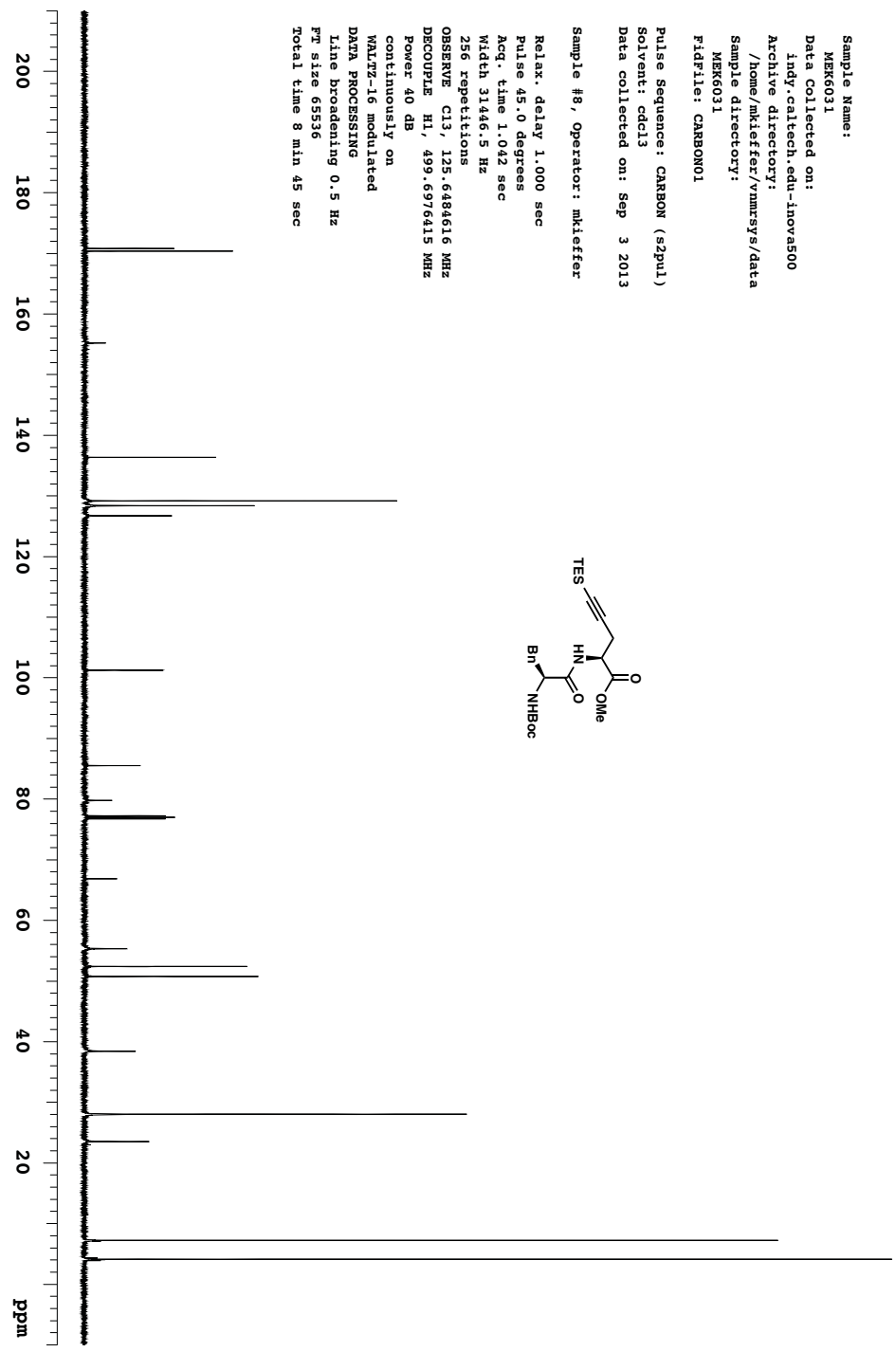
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6031
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 3 2013
Sample #8, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.695450 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
TES
HN
O
OMe
O
Bn
NHBoc
2.36
3.08
0.88
0.80
0.89
0.70
3.00
0.95
0.89
0.94
0.92
9.26
9.25
6.04
10
9
8
7
6
5
4
3
2
1
ppm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Data Collected on:
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Archive directory:
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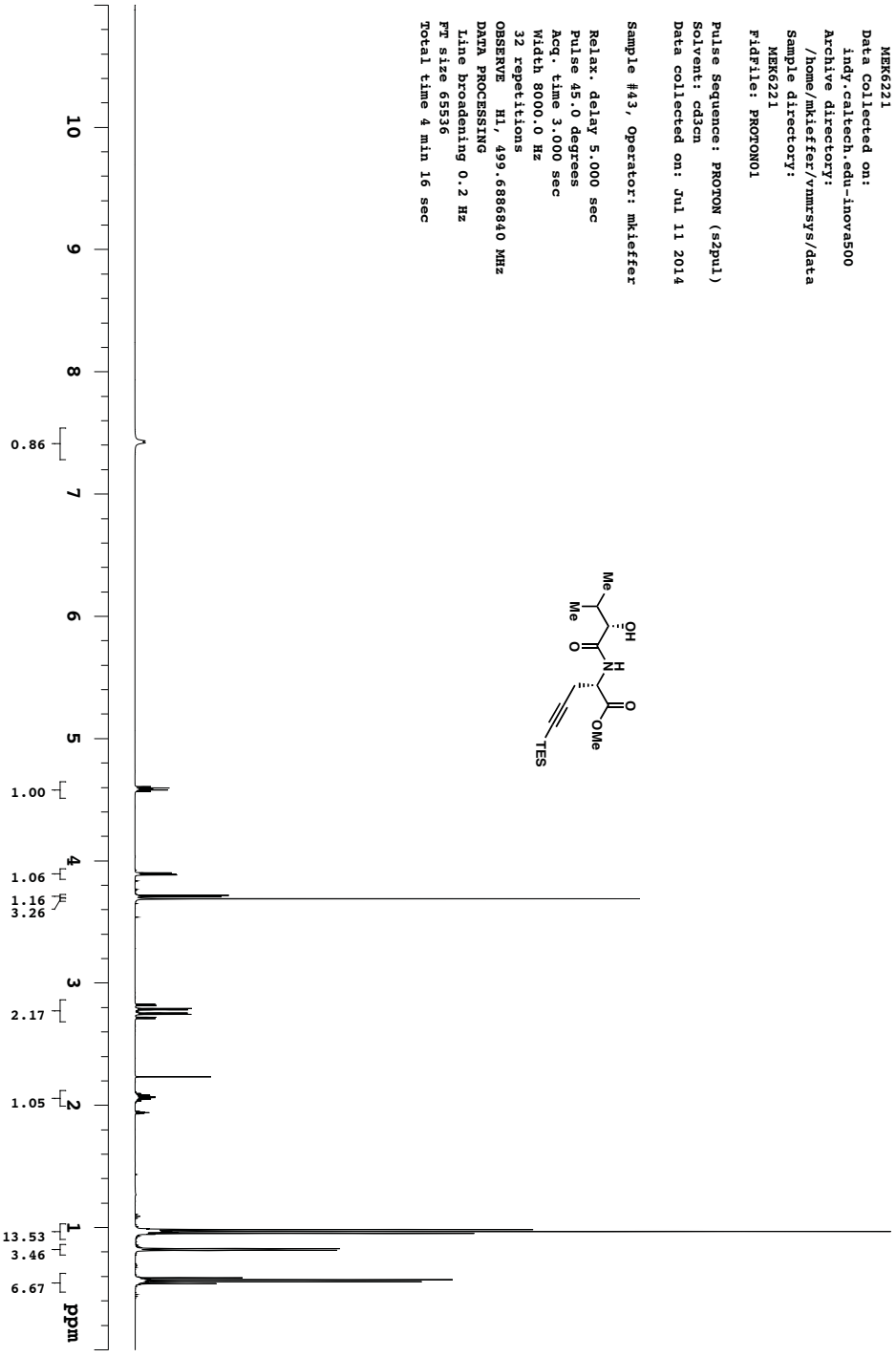
Sample directory:
MEK6031
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 3 2013
Sample #8, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6484616 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
TES
HN
O
OMe
Bn
NHBoc
O
200
180
160
140
120
100
80
60
40
20
ppm


MEK6221
Sample Name:
MEK6221
Data Collected on:
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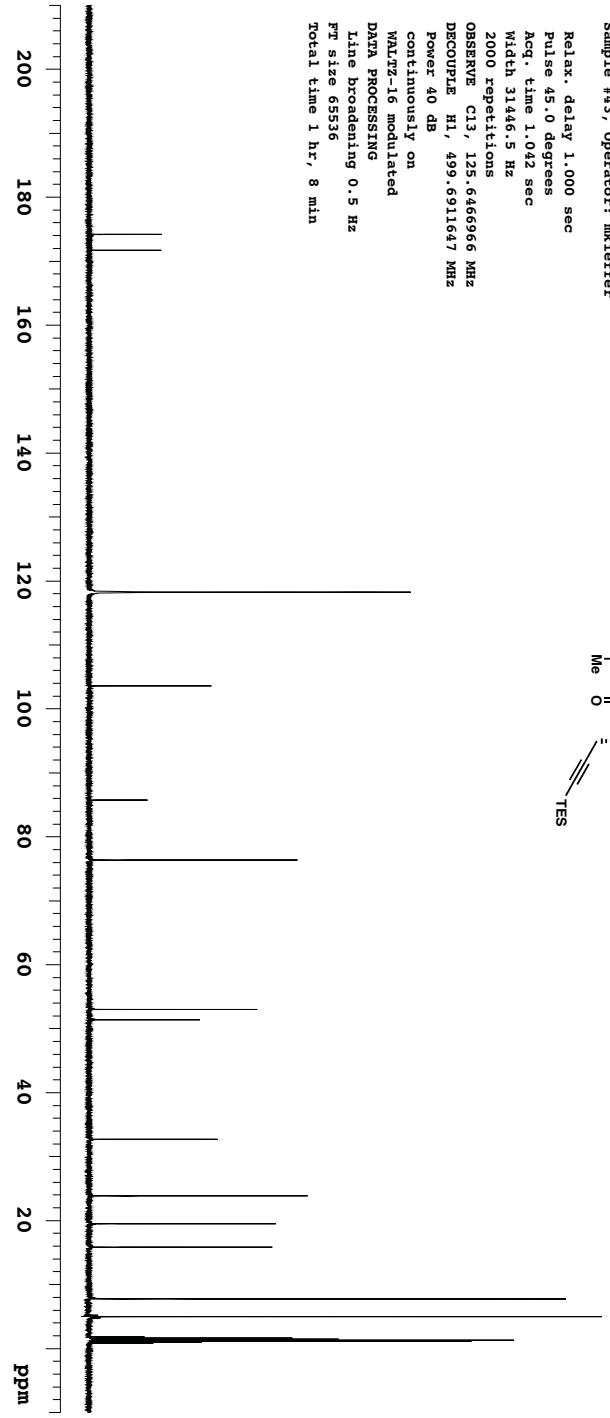
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6221
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jul 11 2014
Sample #43, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6886840 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Me
OH
Me
O
H
N
O
OMe
TES
0.86
1.00
1.06
1.16
3.26
2.17
1.05
13.53
3.46
6.67
10
9
8
7
6
5
4
3
2
1
ppm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MEK6221
Data Collected on:
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Archive directory:
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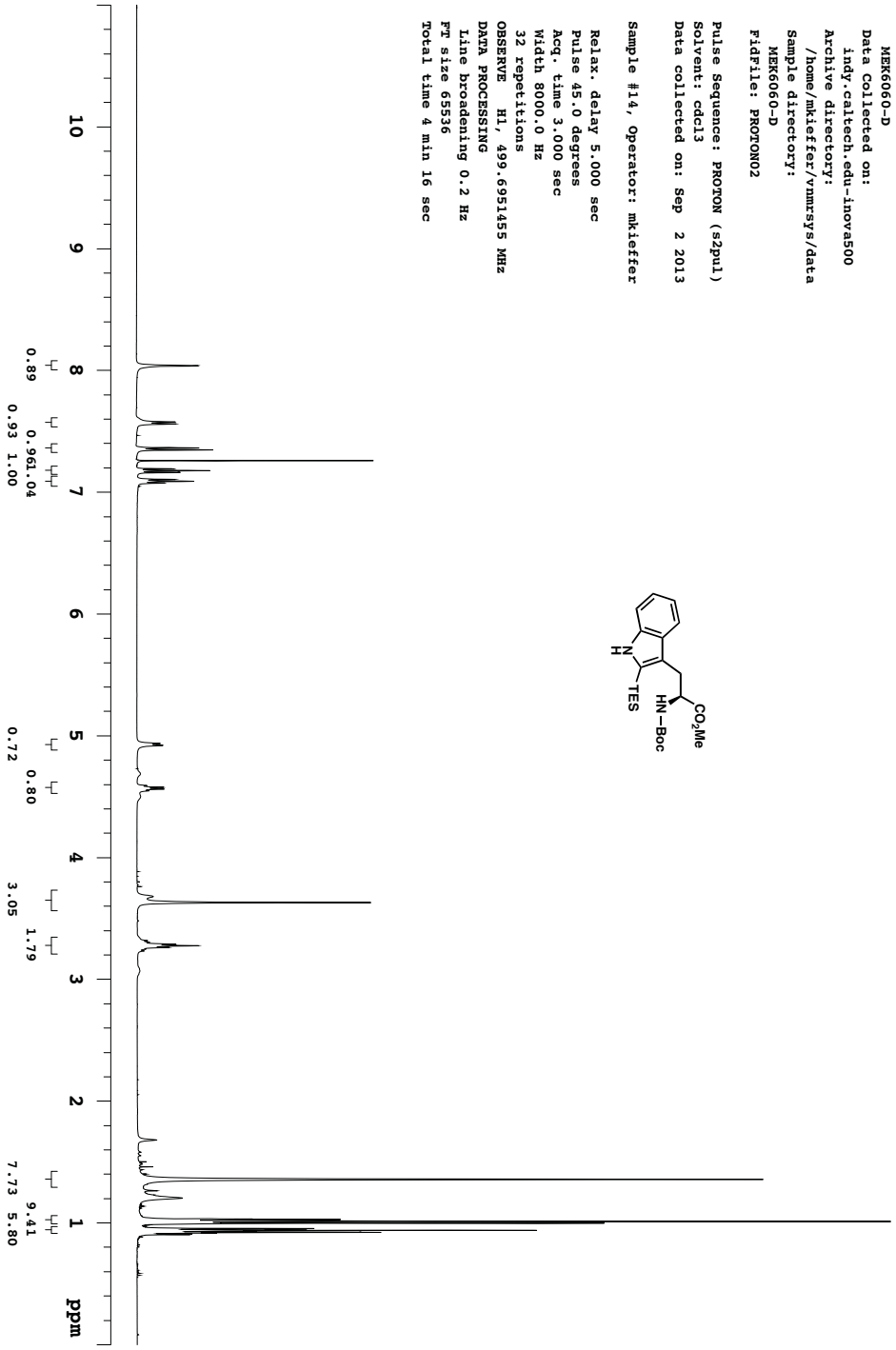
Sample directory:
MEK6221
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jul 11 2014
Sample #43, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6466966 MHz
DECOUPLE H1, 499.6911647 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
Me
Me
OH
O
N
H
O
OMe
TES
200
180
160
140
120
100
80
60
40
20
ppm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Archive directory:
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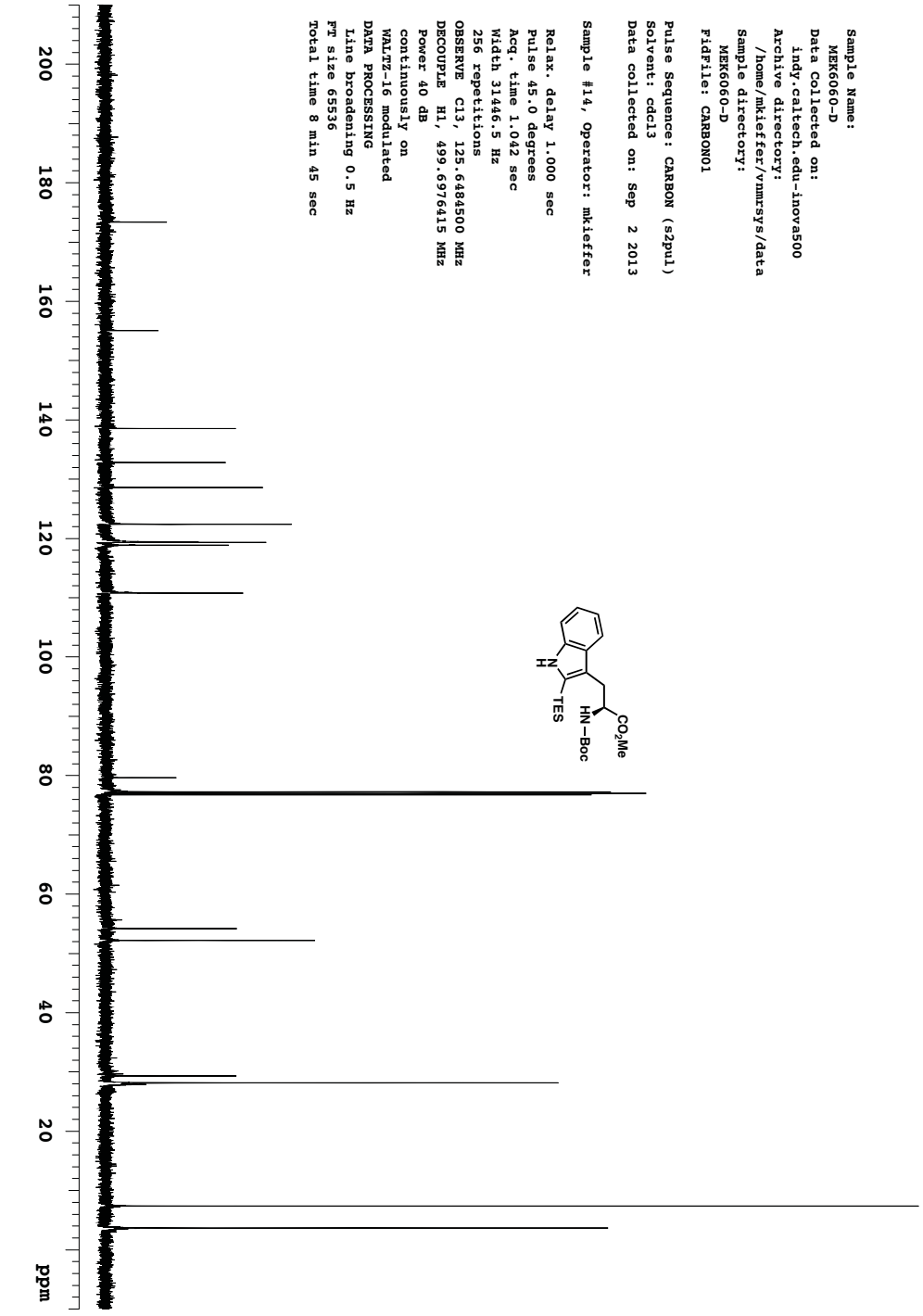
Sample directory:
MEK6060-D
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2013
Sample #14, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
HN
TES
HN—Boc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.89
0.93
0.96
1.00
1.04
0.72
0.80
3.05
1.79
9.41
7.73
5.80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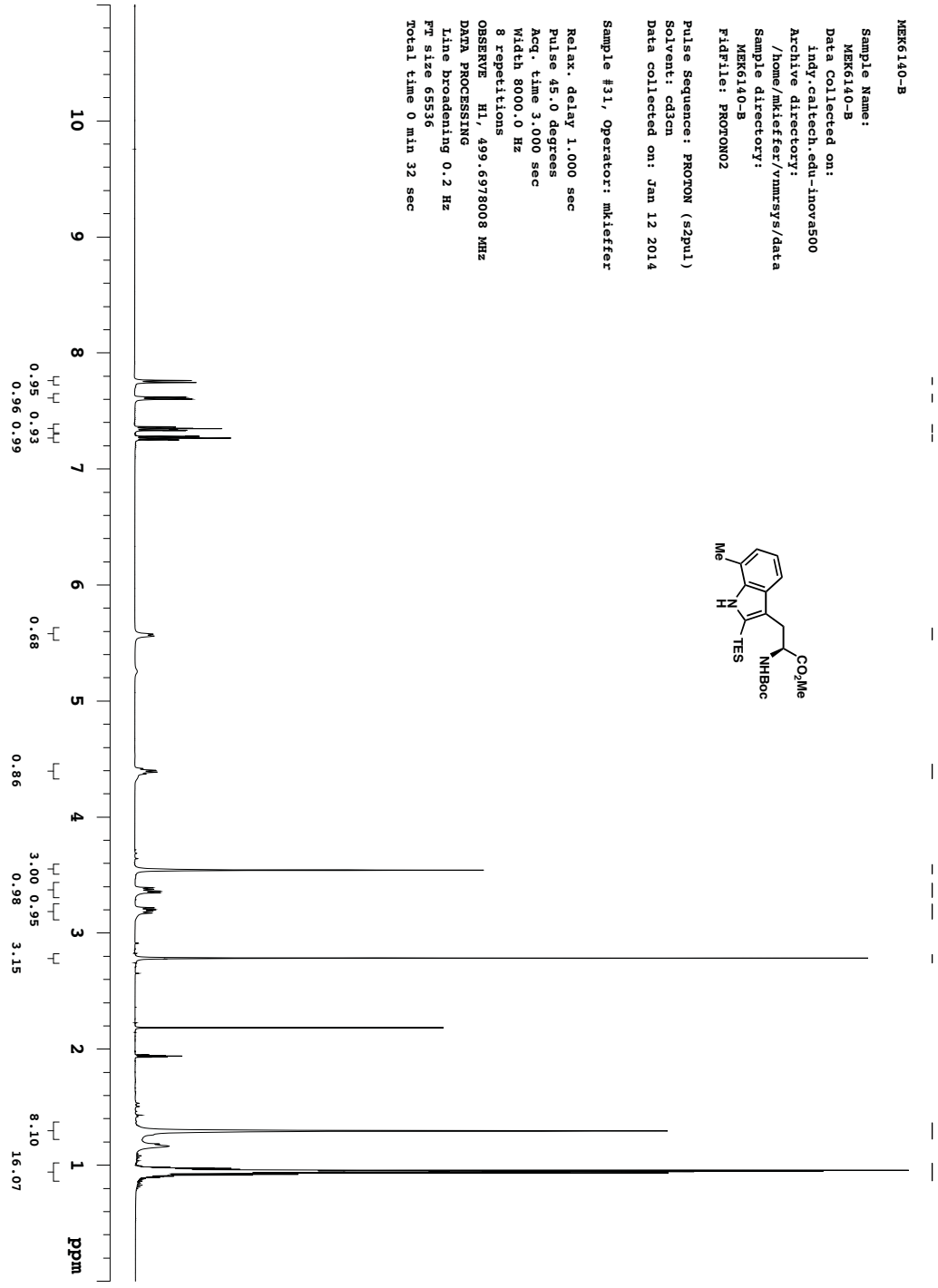
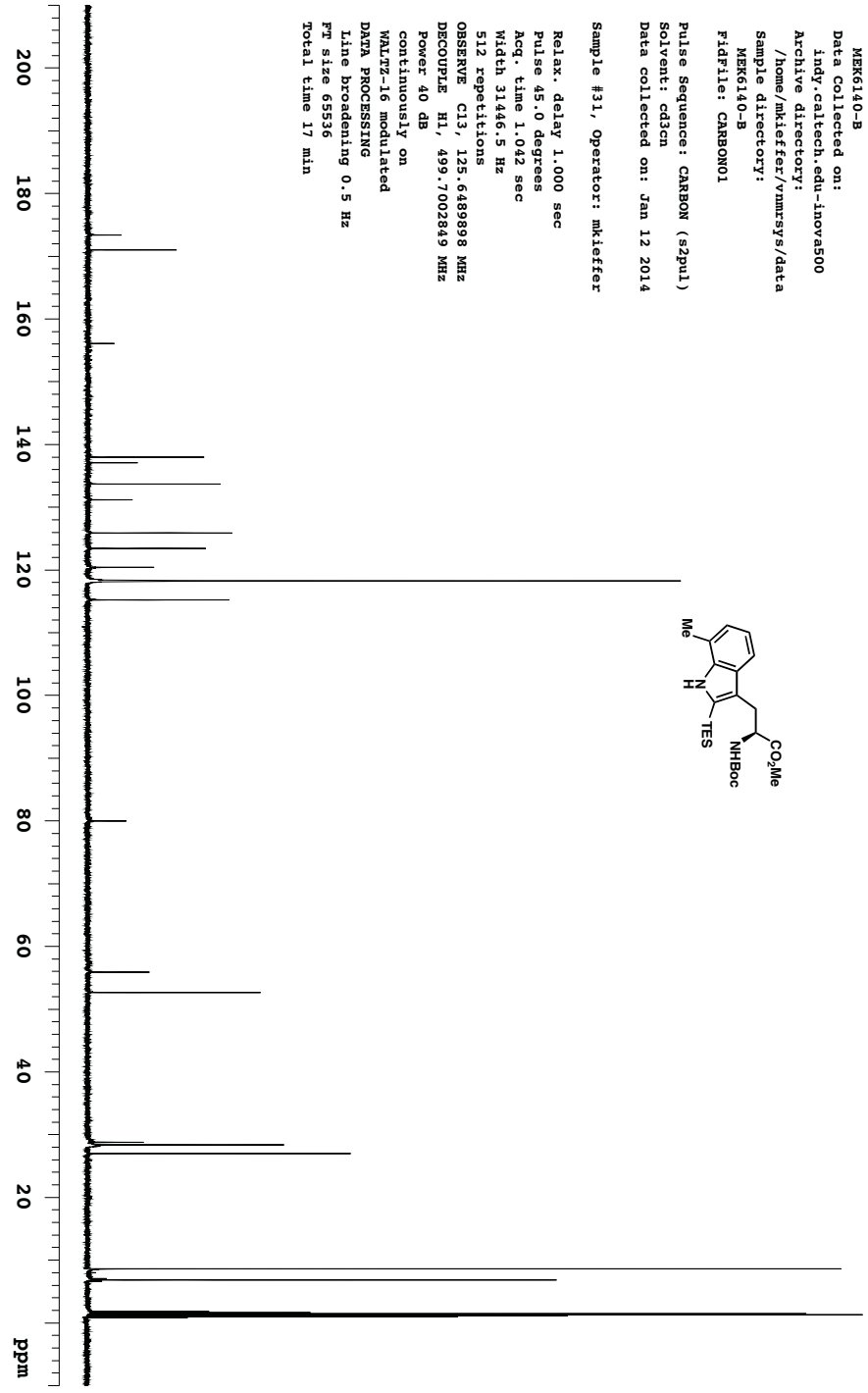
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6060-D
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2013
Sample #14, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6484500 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
N
H
TES
HN—Boc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm


MEK6140-B
Sample Name:
MEK6140-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6140-B
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jan 12 2014
Sample #31, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
Me
N
H
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.95 0.93
0.96 0.99
0.68
0.86
3.00 0.95
0.98 3.15
8.10
16.07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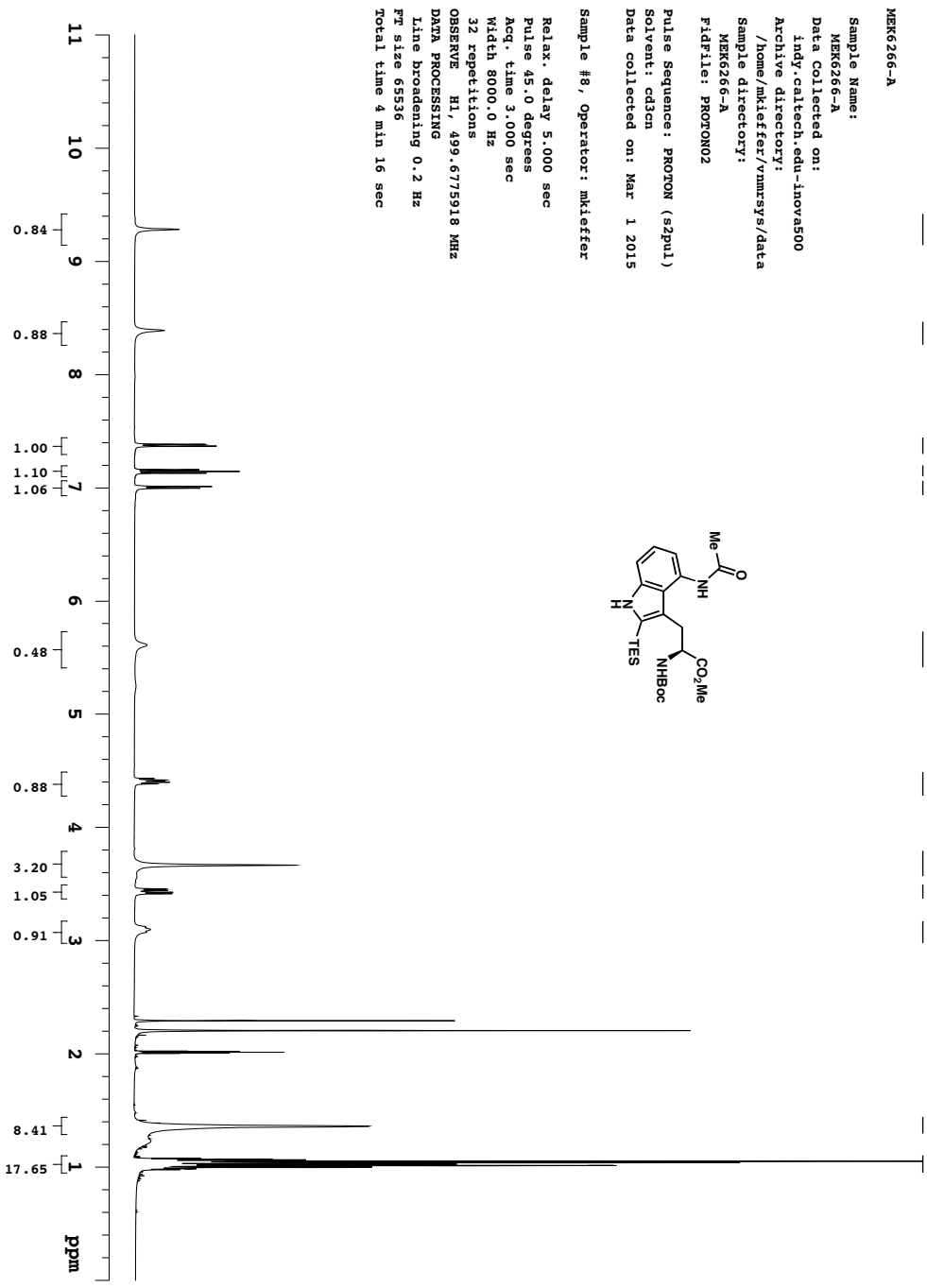
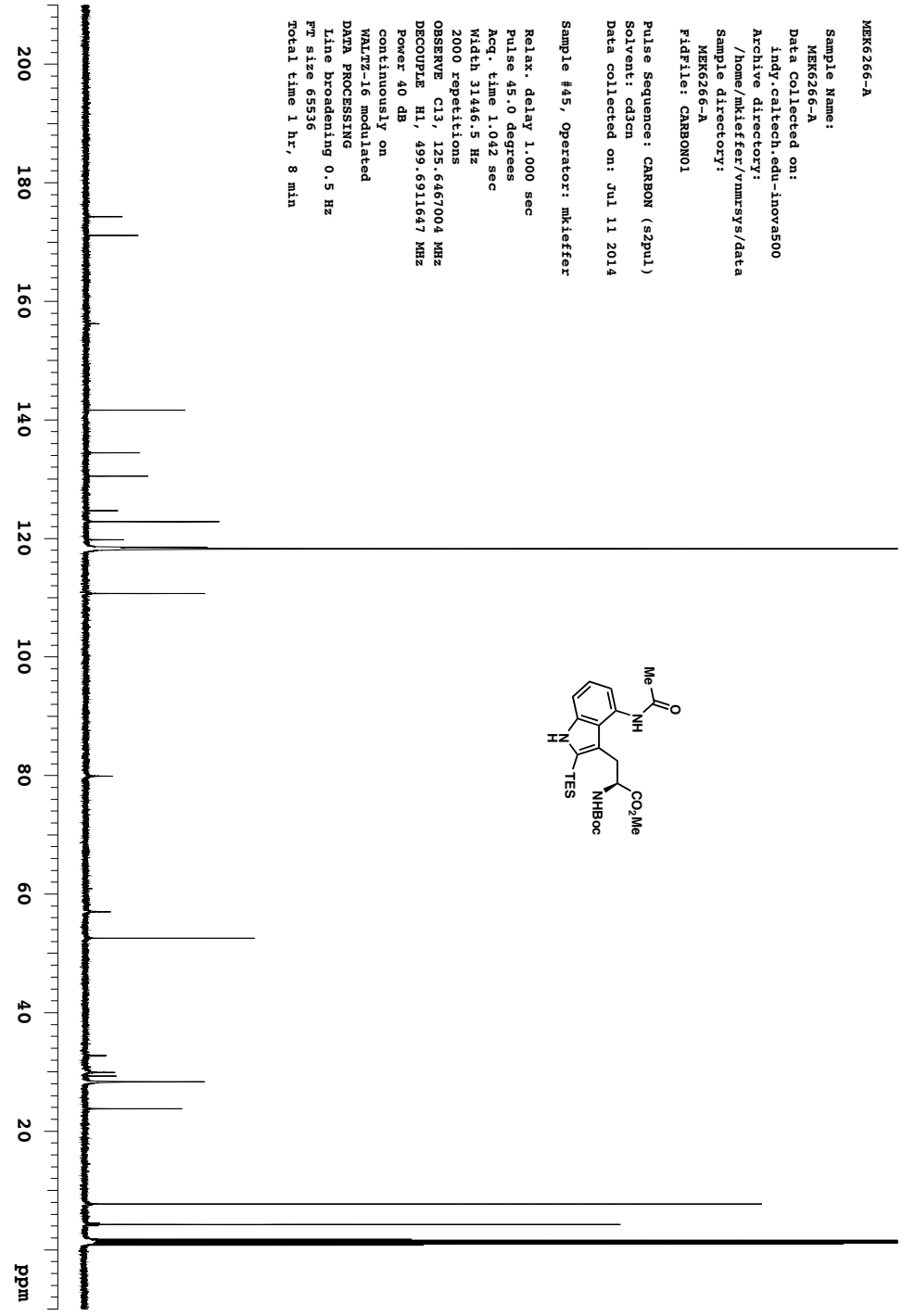
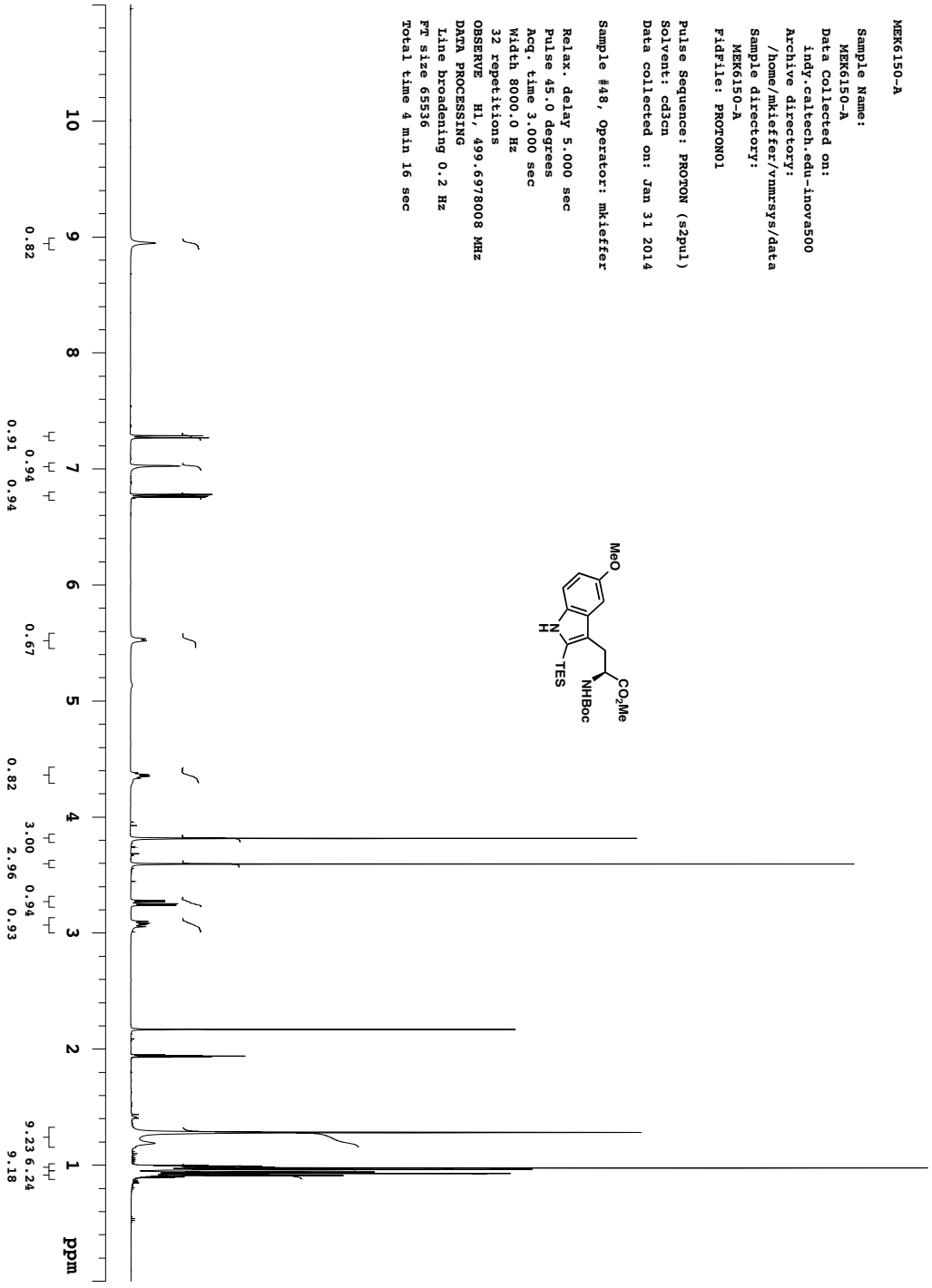
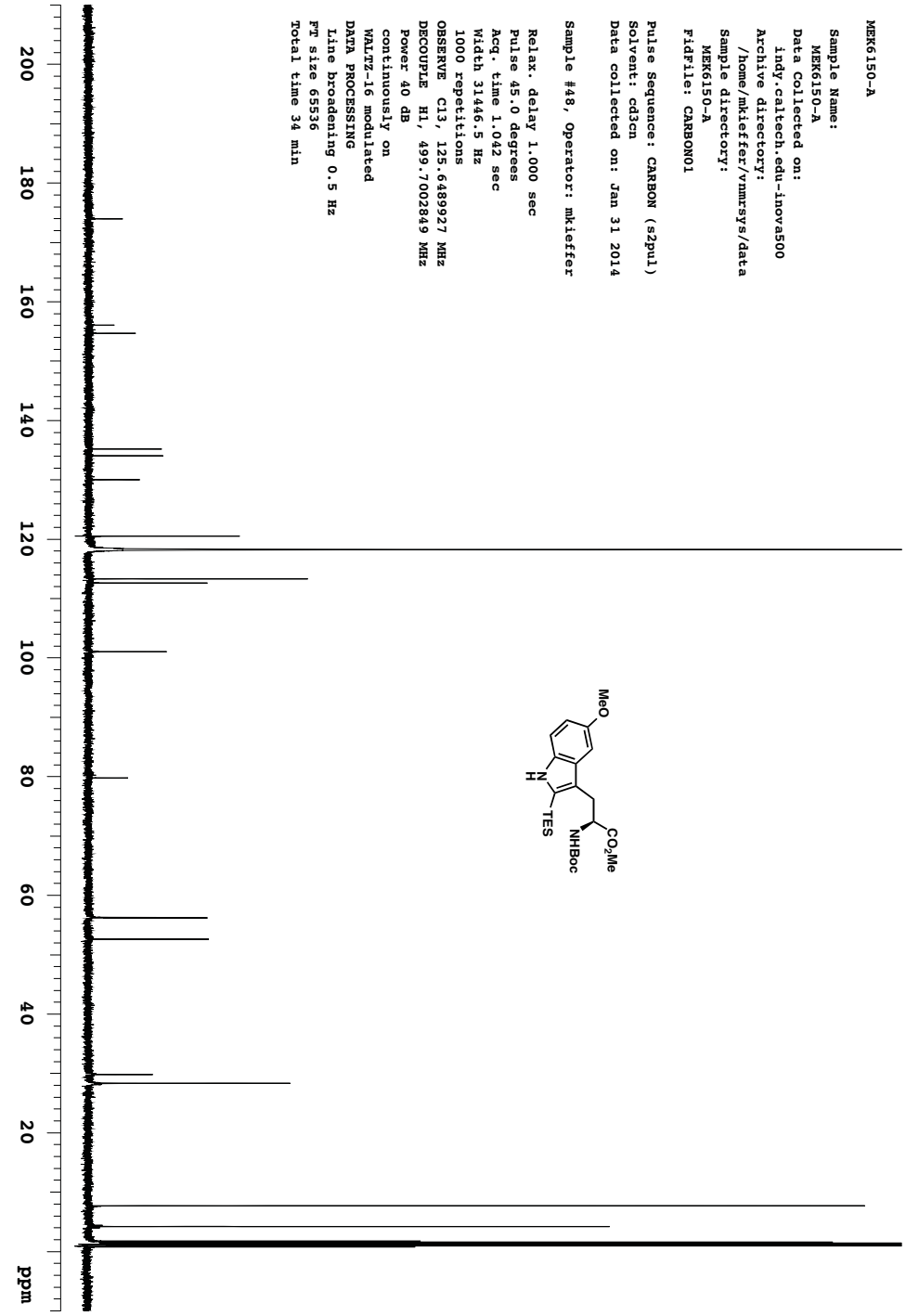
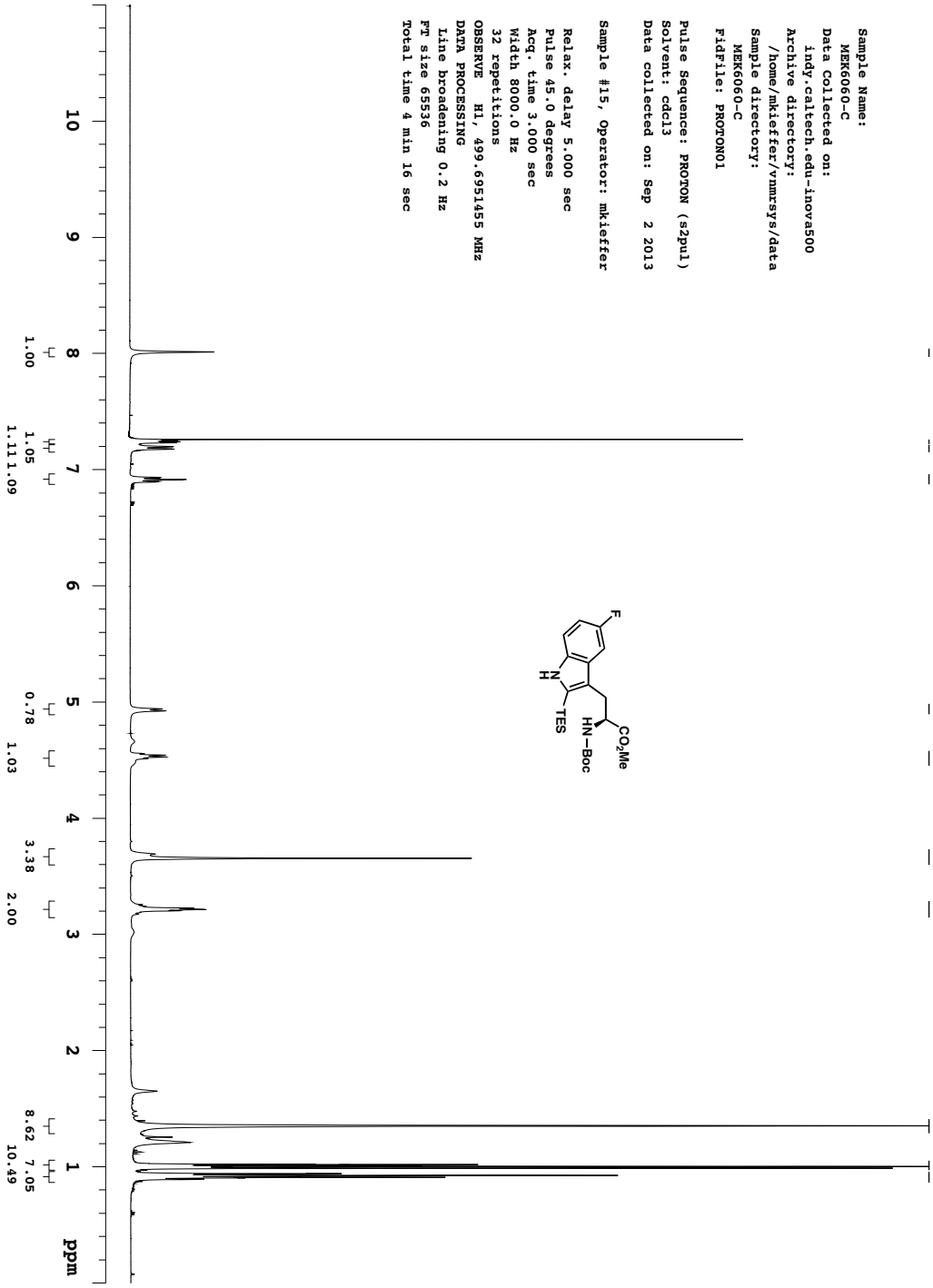
MEK6140-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6140-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jan 12 2014
Sample #31, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6489898 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

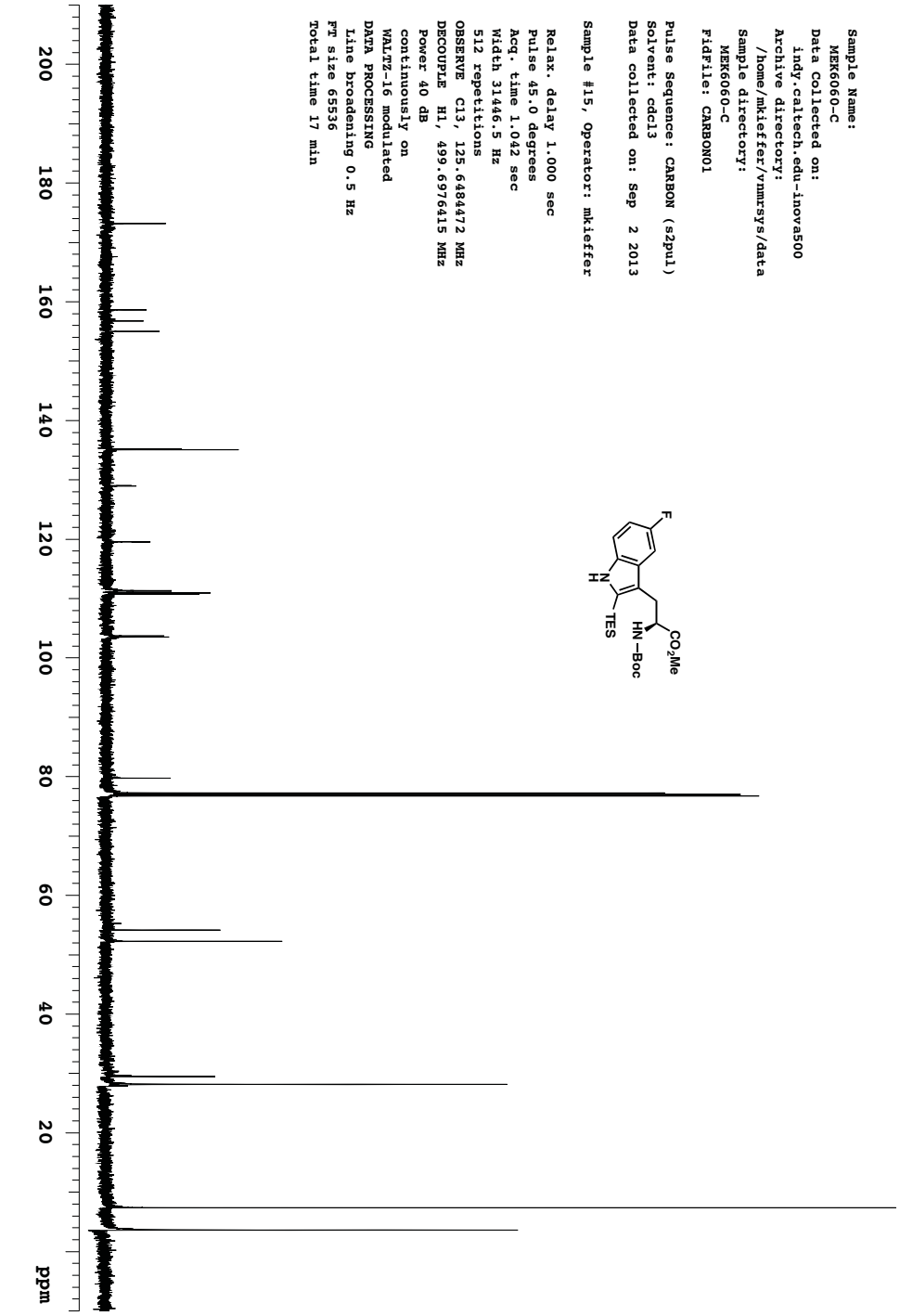

MEK6266-A
Sample Name:
MEK6266-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6266-A
FidFile: PROTONO2
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Mar 1 2015
Sample #8, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6775918 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Me
O
NH
N
H
TES
NHBoc
CO2Me
0.84
0.88
1.00
1.10
1.06
0.48
0.88
3.20
1.05
0.91
8.41
17.65
11
10
9
8
7
6
5
4
3
2
1
ppm

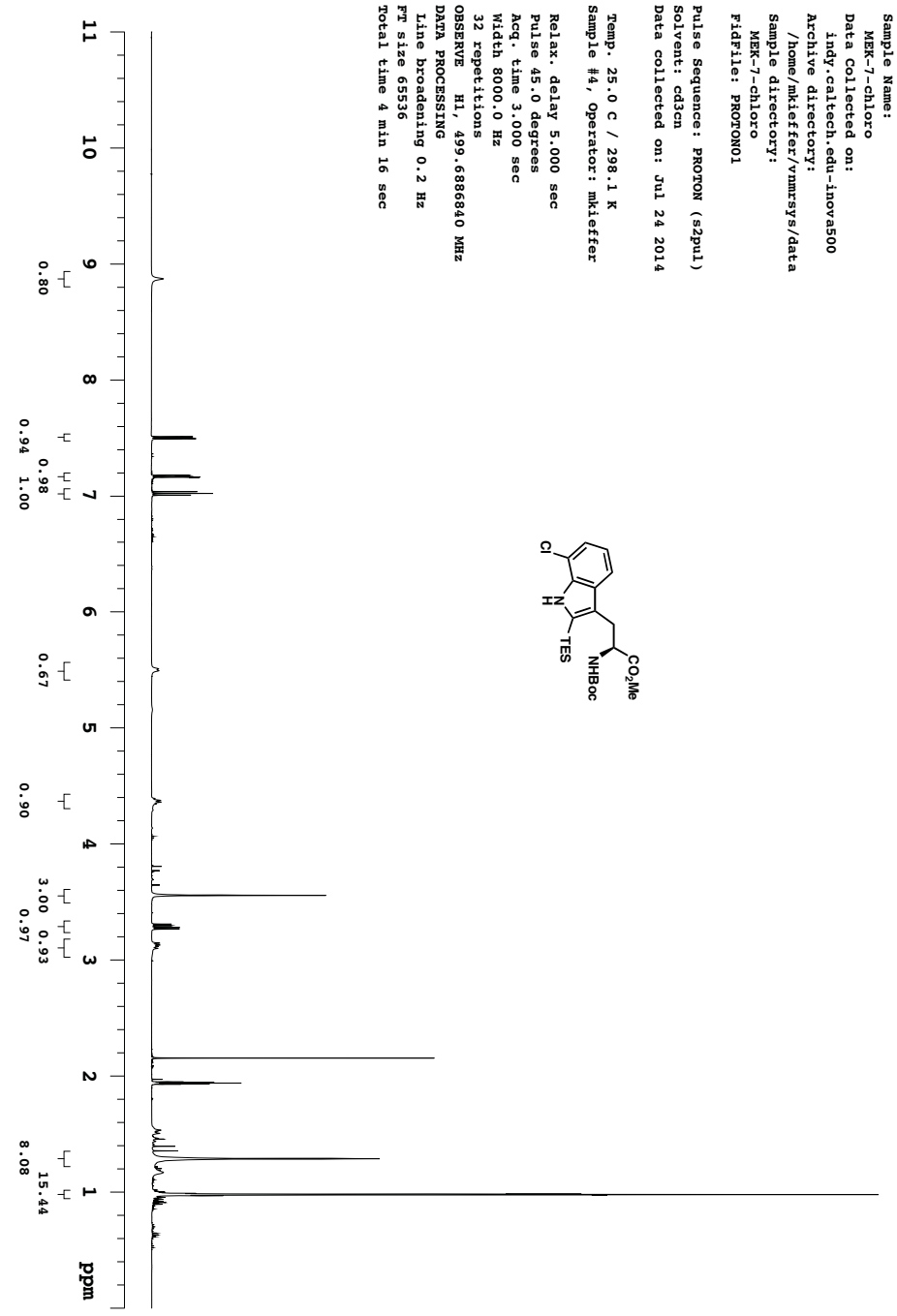

MEK6266-A
Sample Name:
MEK6266-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6266-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jul 11 2014
Sample #45, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.6467004 MHz
DECOUPLE H1, 499.6911647 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
Me
O
NH
H
N
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

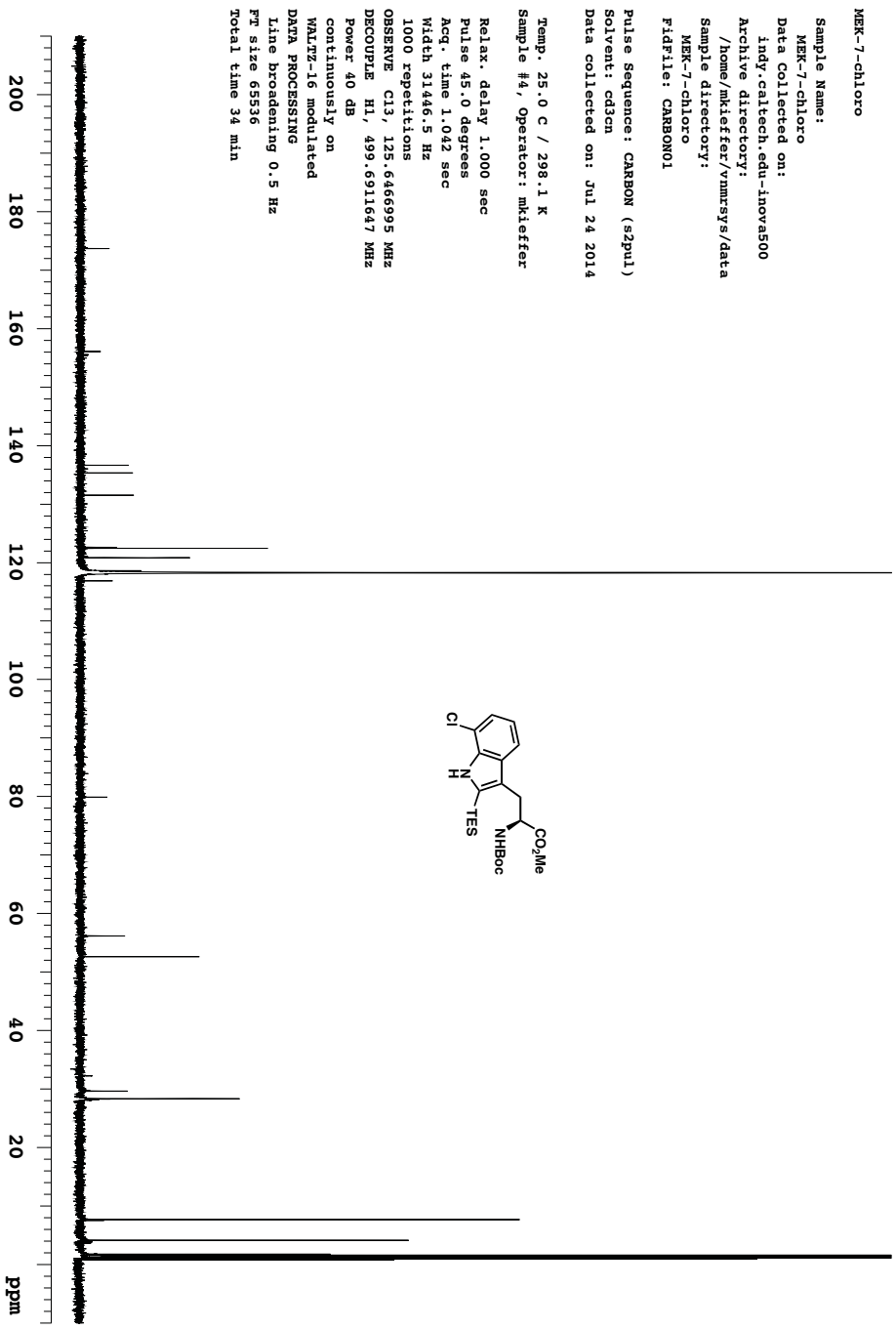

MEK6150-A
Sample Name:
MEK6150-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6150-A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jan 31 2014
Sample #48, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
MeO
NH
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.82
0.91
0.94
0.94
0.67
0.82
3.00
2.96
0.94
0.93
9.23
6.24
9.18

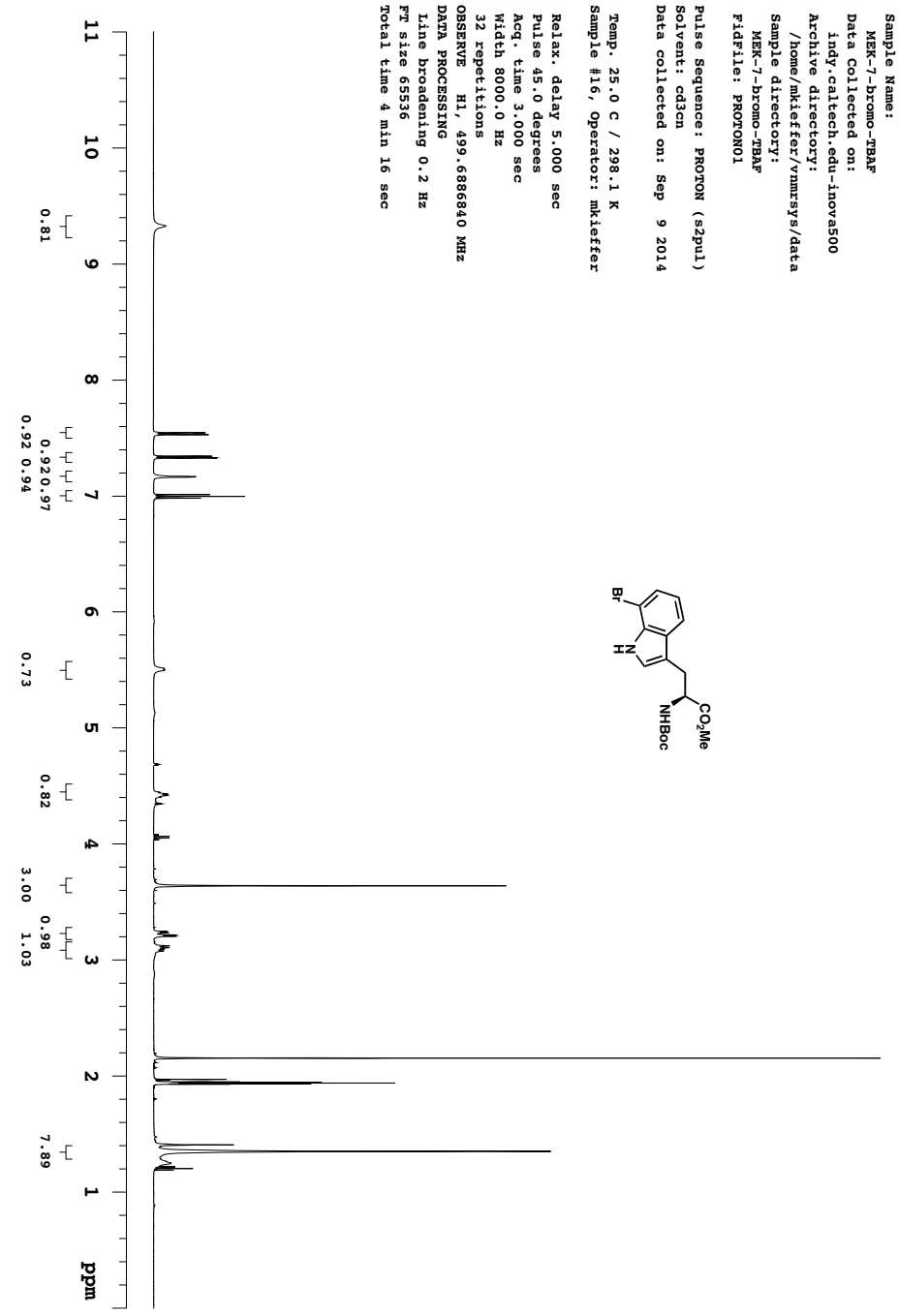

MEK6150-A
Sample Name:
MEK6150-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6150-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jan 31 2014
Sample #48, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6489927 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
MeO
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

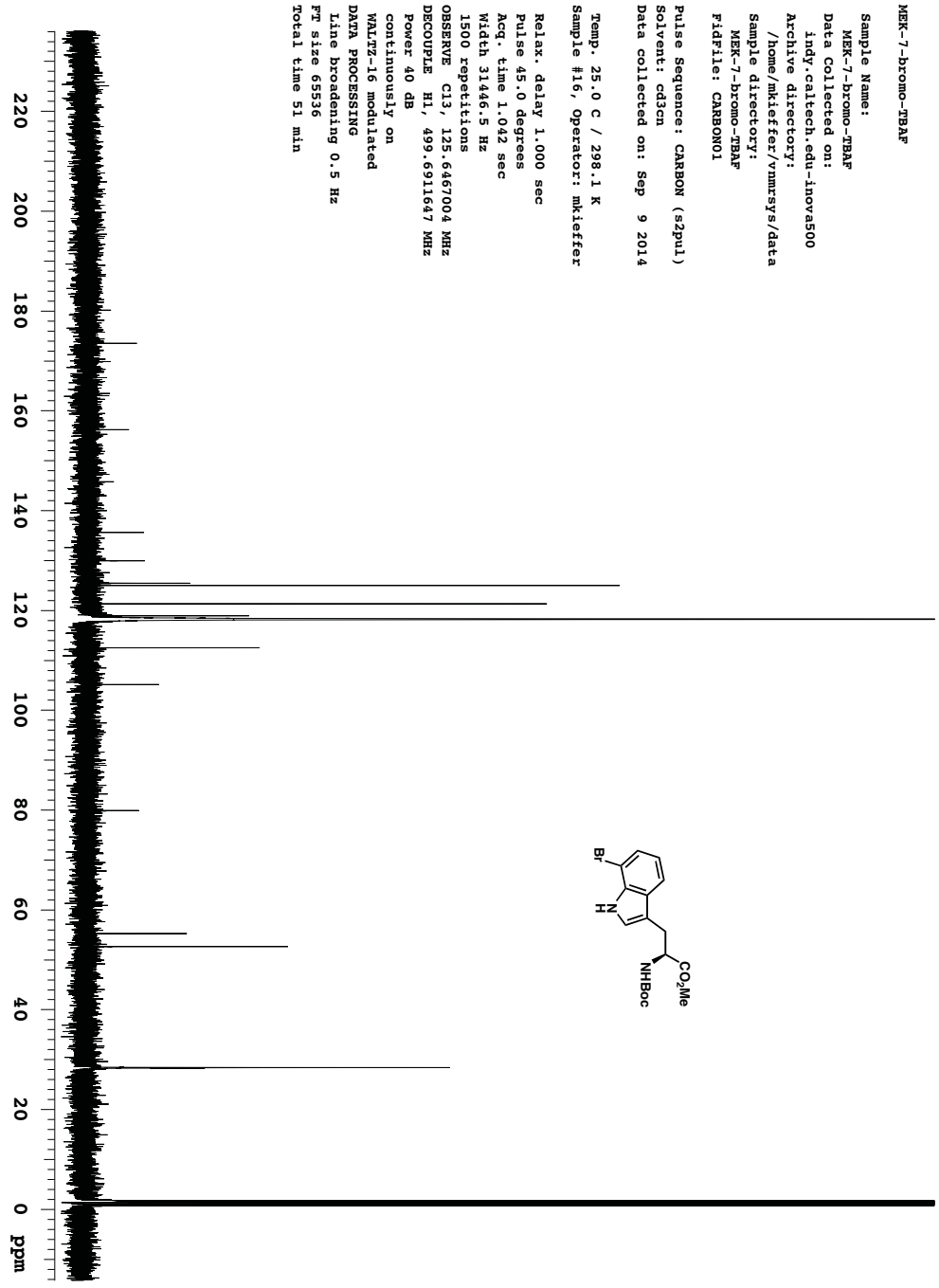

Sample Name:
MEK6060-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6060-C
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2013
Sample #15, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
F
N
H
TES
HN–Boc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.05
1.11
1.09
0.78
1.03
3.38
2.00
8.62
7.05
10.49

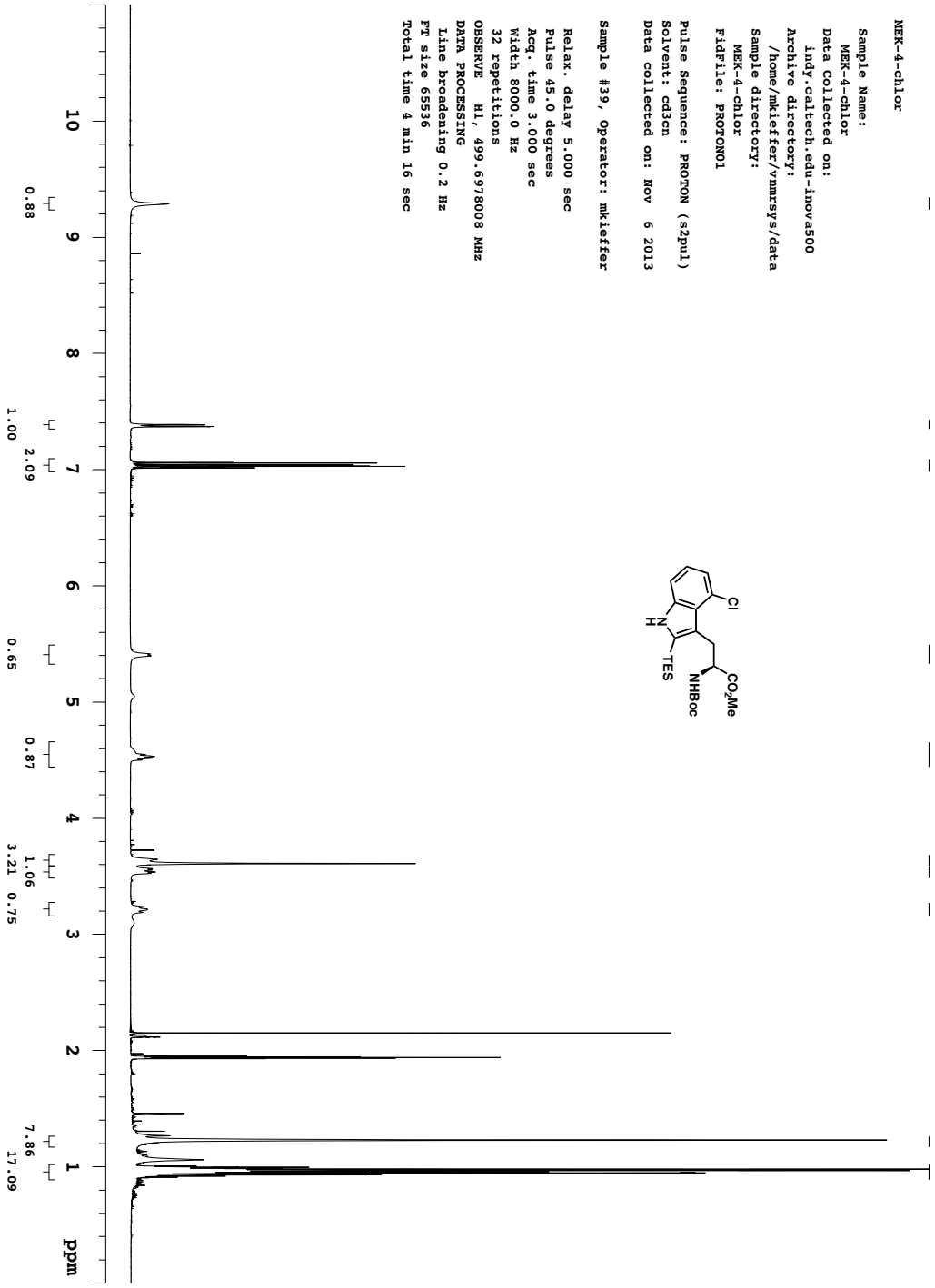

Sample Name:
MEK6060-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6060-C
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 2 2013
Sample #15, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484472 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
F
N
H
TES
HN–Boc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

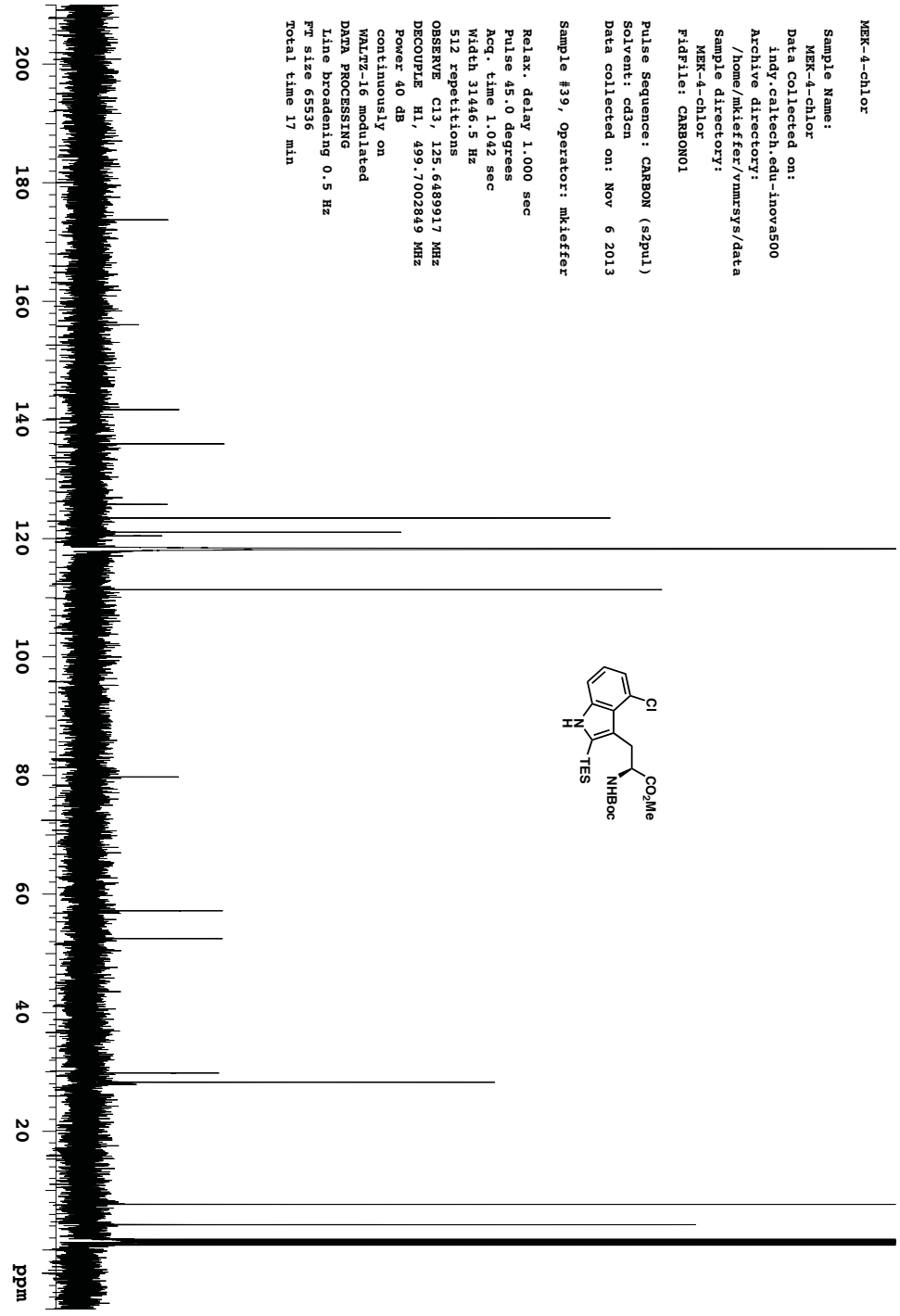

MEK-7-chloro
Sample Name:
MEK-7-chloro
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-7-chloro
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jul 24 2014
Temp. 25.0 C / 298.1 K
Sample #4, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6886840 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Cl
N
H
TES
NHBoc
CO2Me
0.80
0.98
0.94
1.00
0.67
0.90
3.00
0.93
0.97
15.44
8.08
11
10
9
8
7
6
5
4
3
2
1
ppm

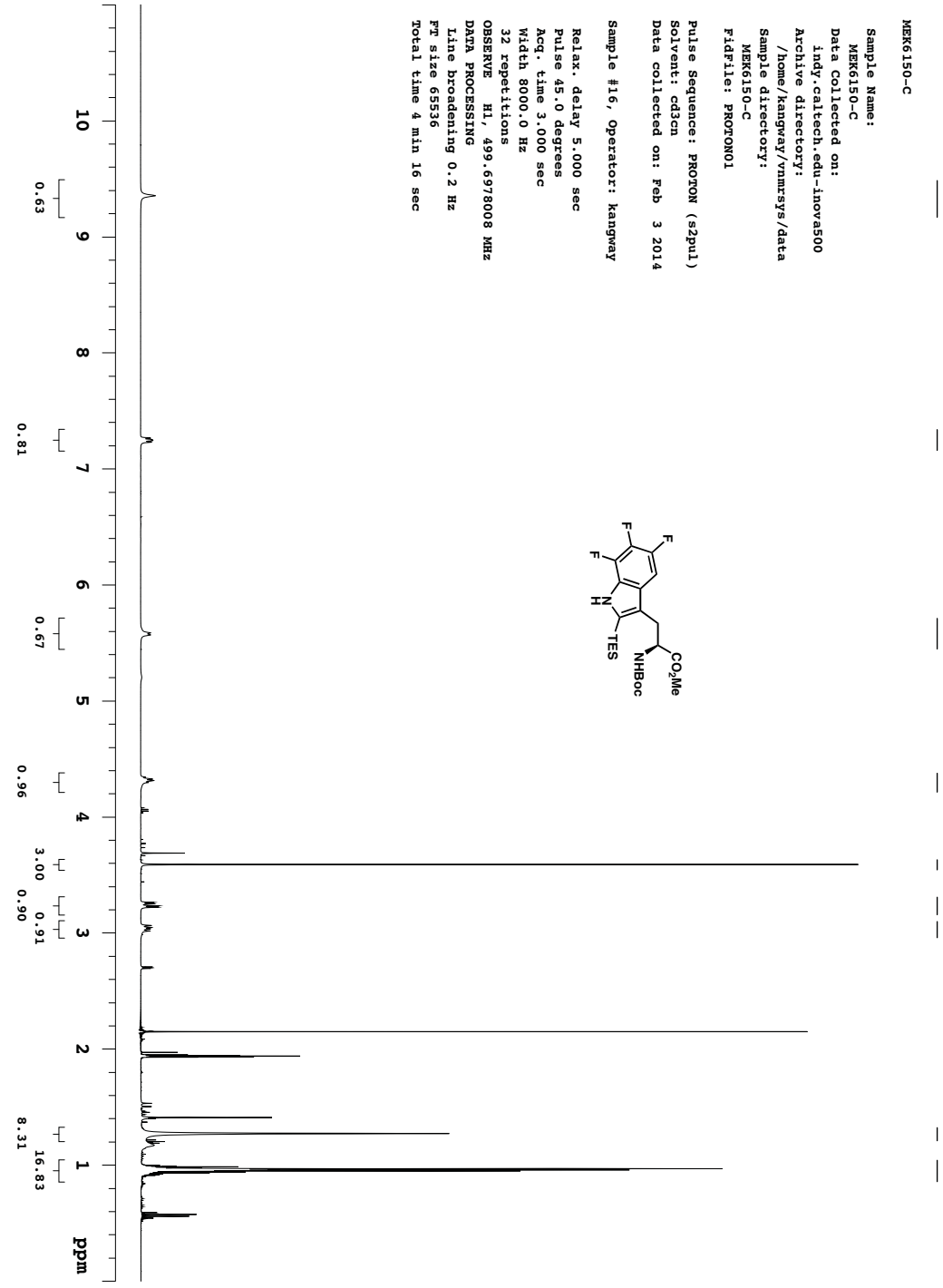

MEK-7-chloro
Sample Name:
MEK-7-chloro
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-7-chloro
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jul 24 2014
Temp. 25.0 C / 298.1 K
Sample #4, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6466995 MHz
DECOUPLE H1, 499.691647 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
Cl
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

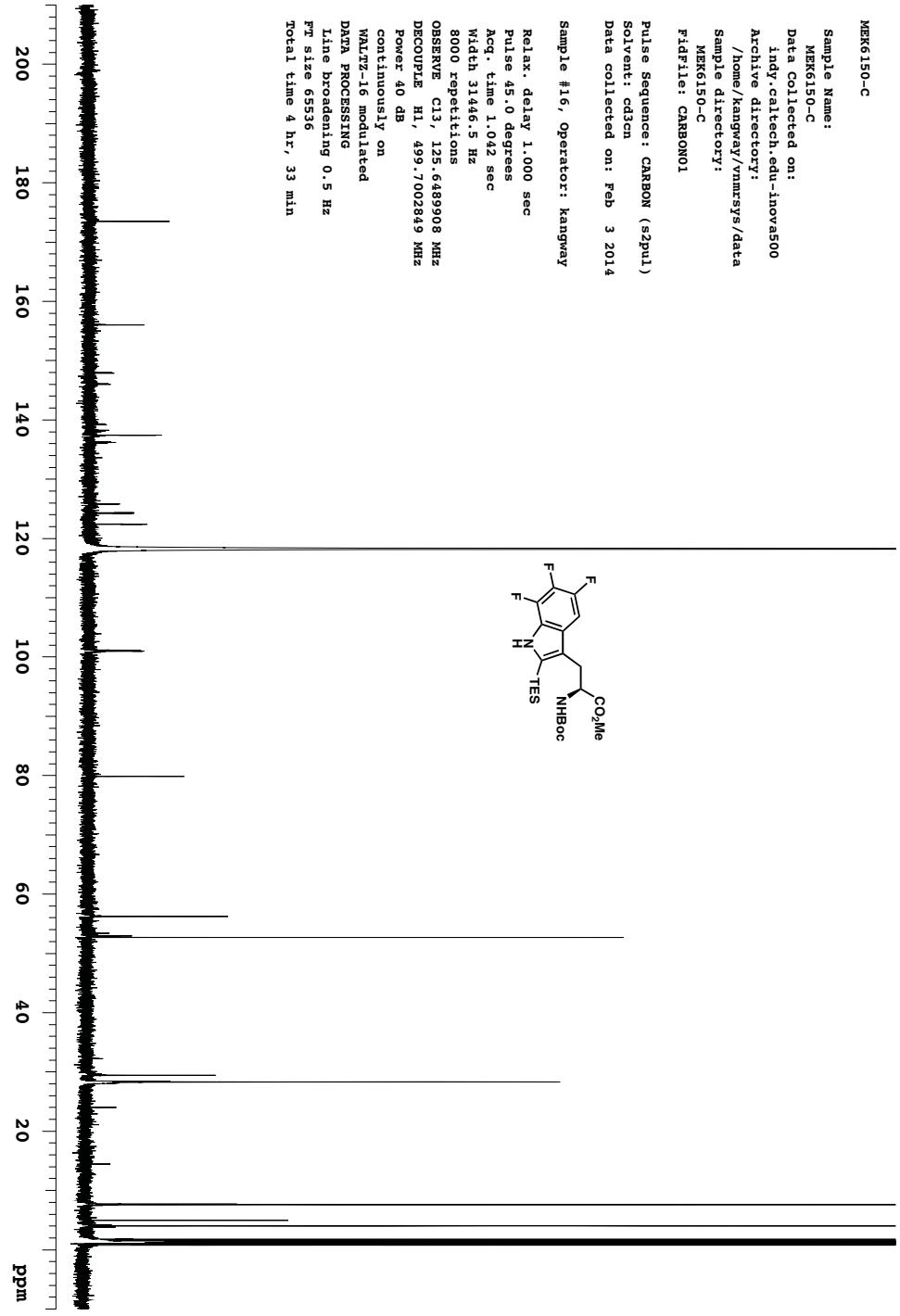

MEK-7-bromo-TBAF
Sample Name:
MEK-7-bromo-TBAF
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-7-bromo-TBAF
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Sep 9 2014
Temp. 25.0 C / 298.1 K
Sample #16, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6886840 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Br
N
H
CO2Me
NHBoc
11
10
9
8
7
6
5
4
3
2
1
ppm
0.81
0.92
0.97
0.92
0.94
0.73
0.82
3.00
0.98
1.03
7.89

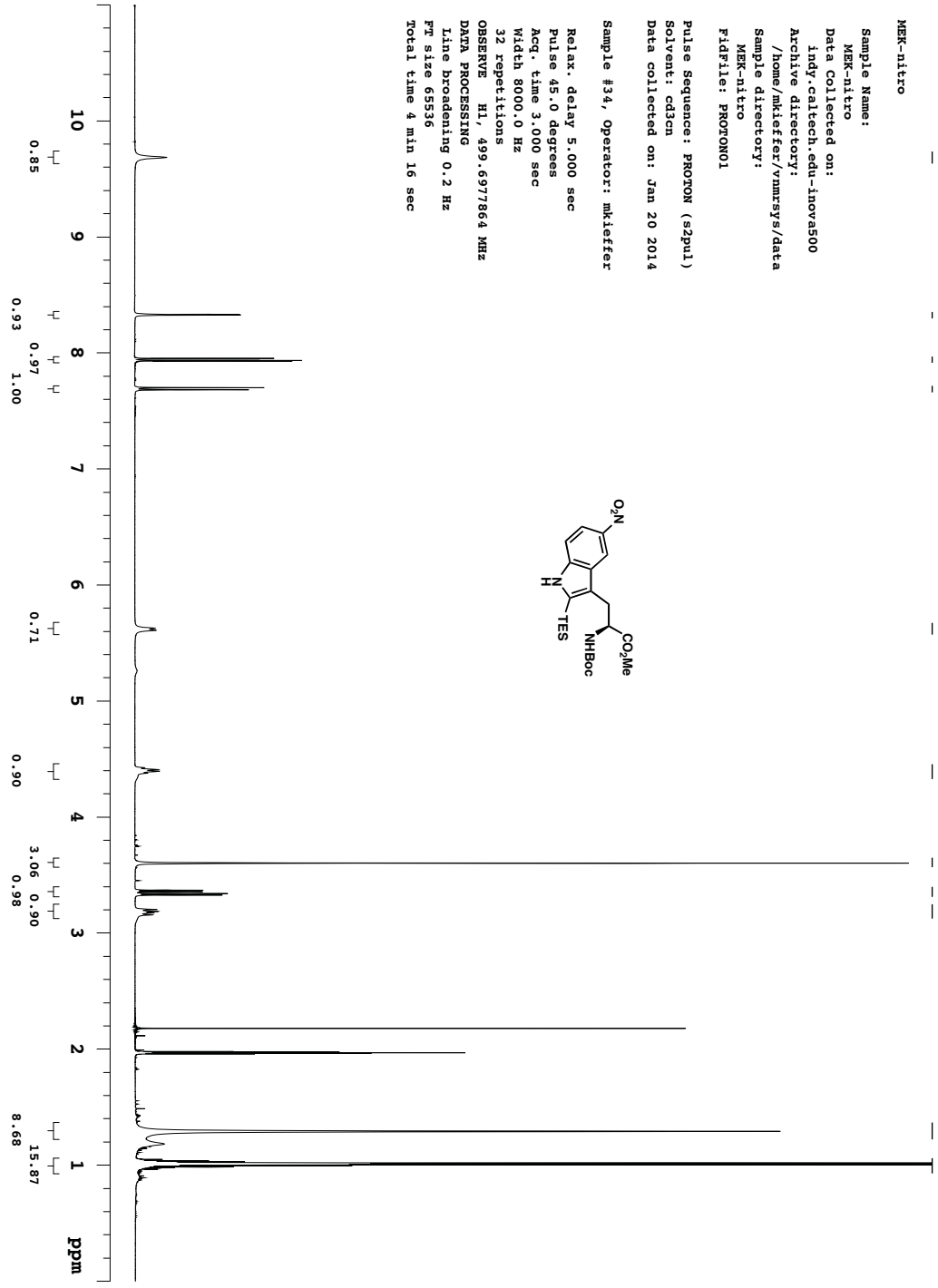

MEK-7-bromo-TBAF
Sample Name:
MEK-7-bromo-TBAF
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-7-bromo-TBAF
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Sep 9 2014
Temp. 25.0 C / 298.1 K
Sample #16, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6467004 MHz
DECOUPLE H1, 499.691647 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
Br
N
H
NHBoc
CO2Me
220
200
180
160
140
120
100
80
60
40
20
0
ppm

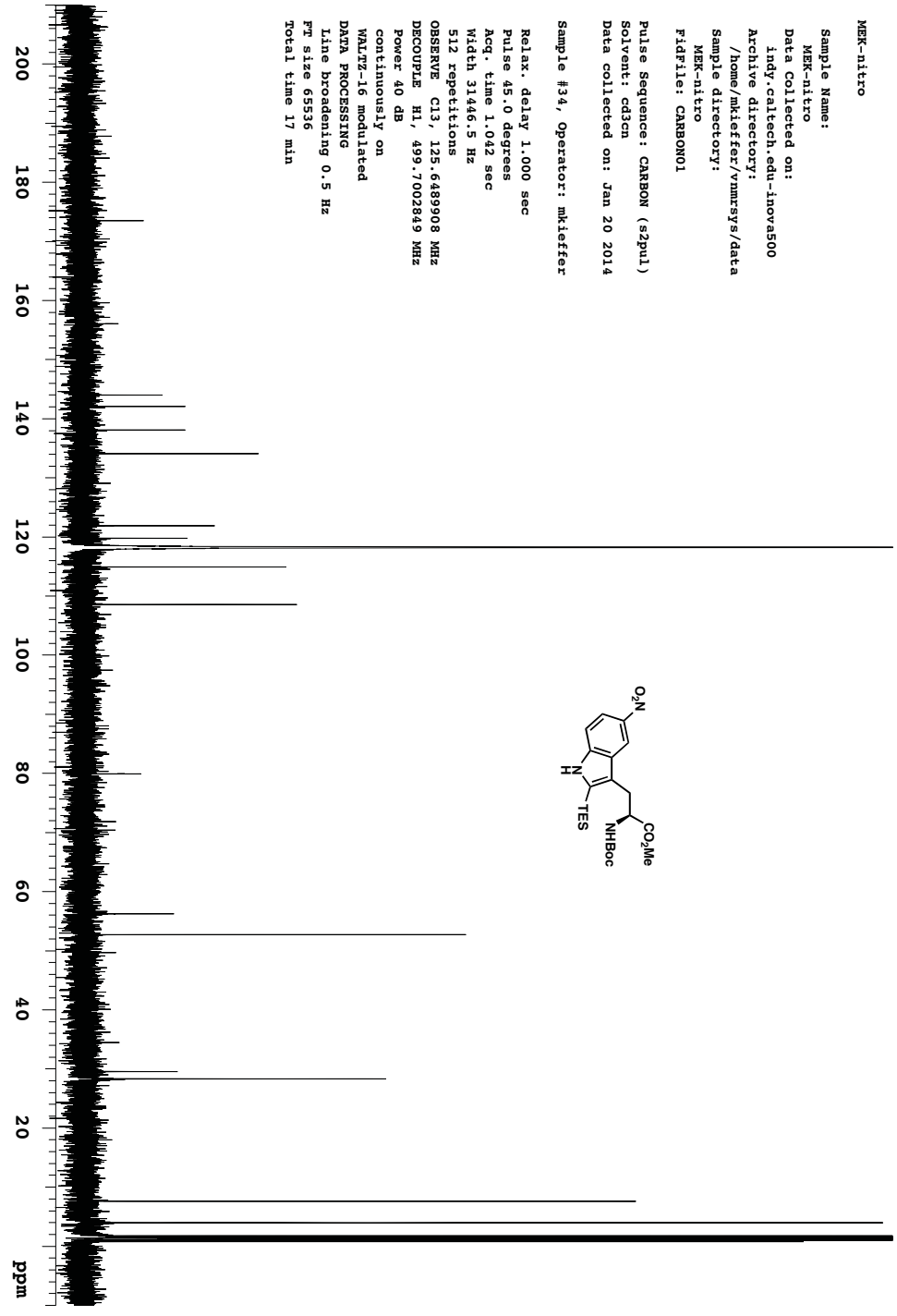

MEK-4-chlor
Sample Name:
MEK-4-chlor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-4-chlor
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Nov 6 2013
Sample #39, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
Cl
N
H
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.88
1.00
2.09
0.65
0.87
1.06
3.21
0.75
7.86
17.09

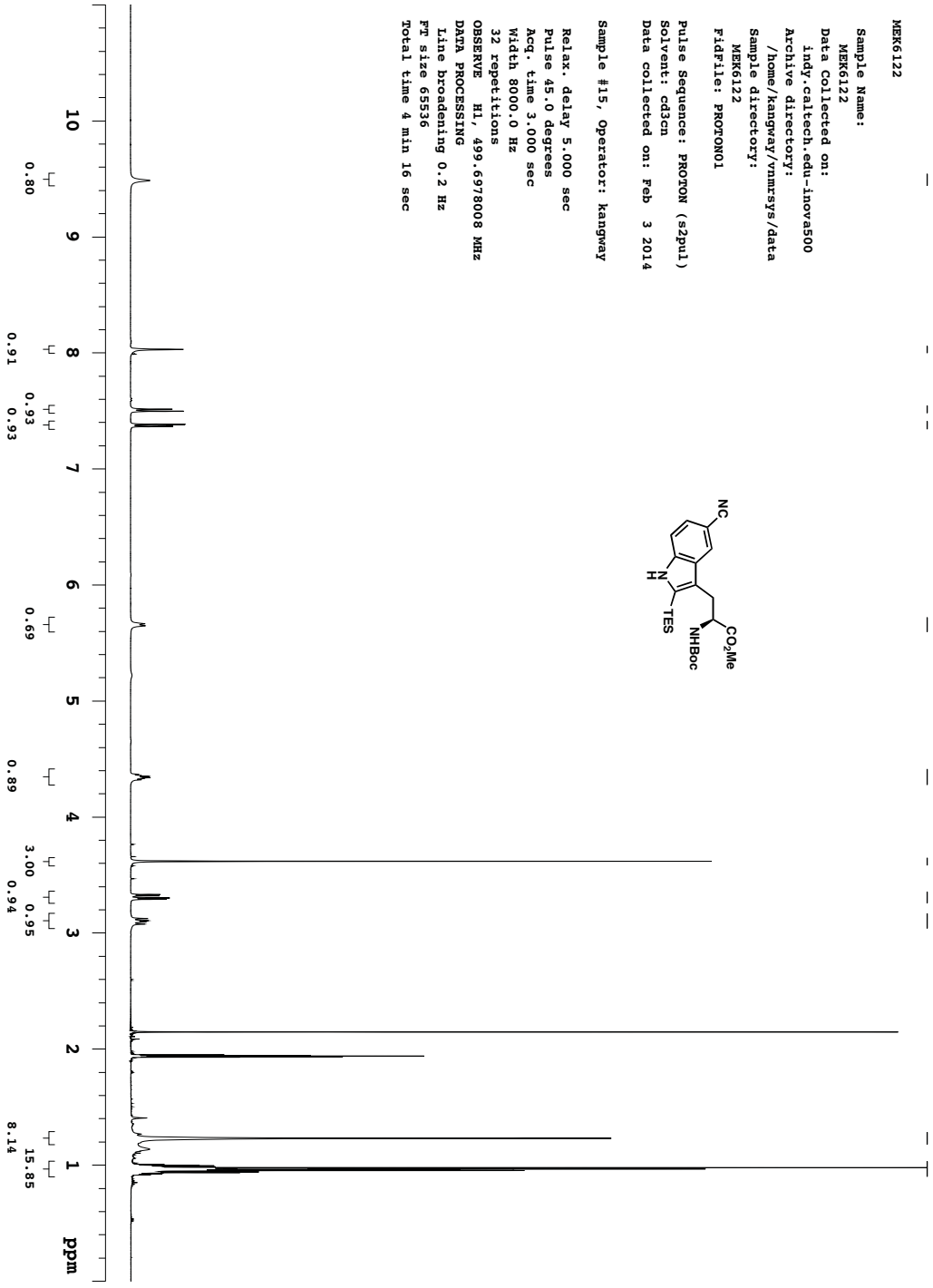

MEK-4-chlor
Sample Name:
MEK-4-chlor
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-4-chlor
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Nov 6 2013
Sample #39, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6489917 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Cl
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

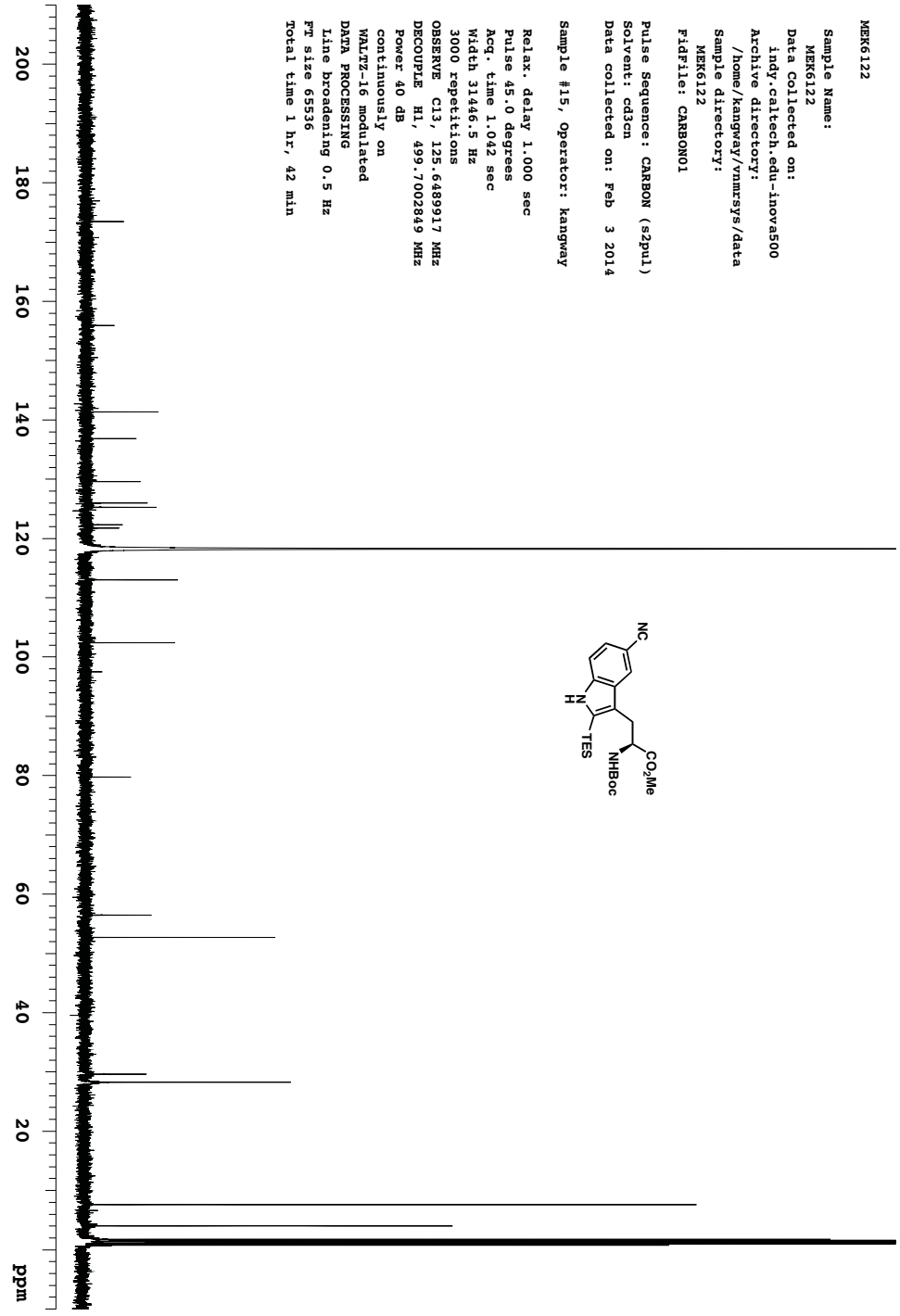

MEK6150-C
Sample Name:
MEK6150-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK6150-C
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Feb 3 2014
Sample #16, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
F
F
F
N
H
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.63
0.81
0.67
0.96
3.00
0.91
0.90
16.83
8.31

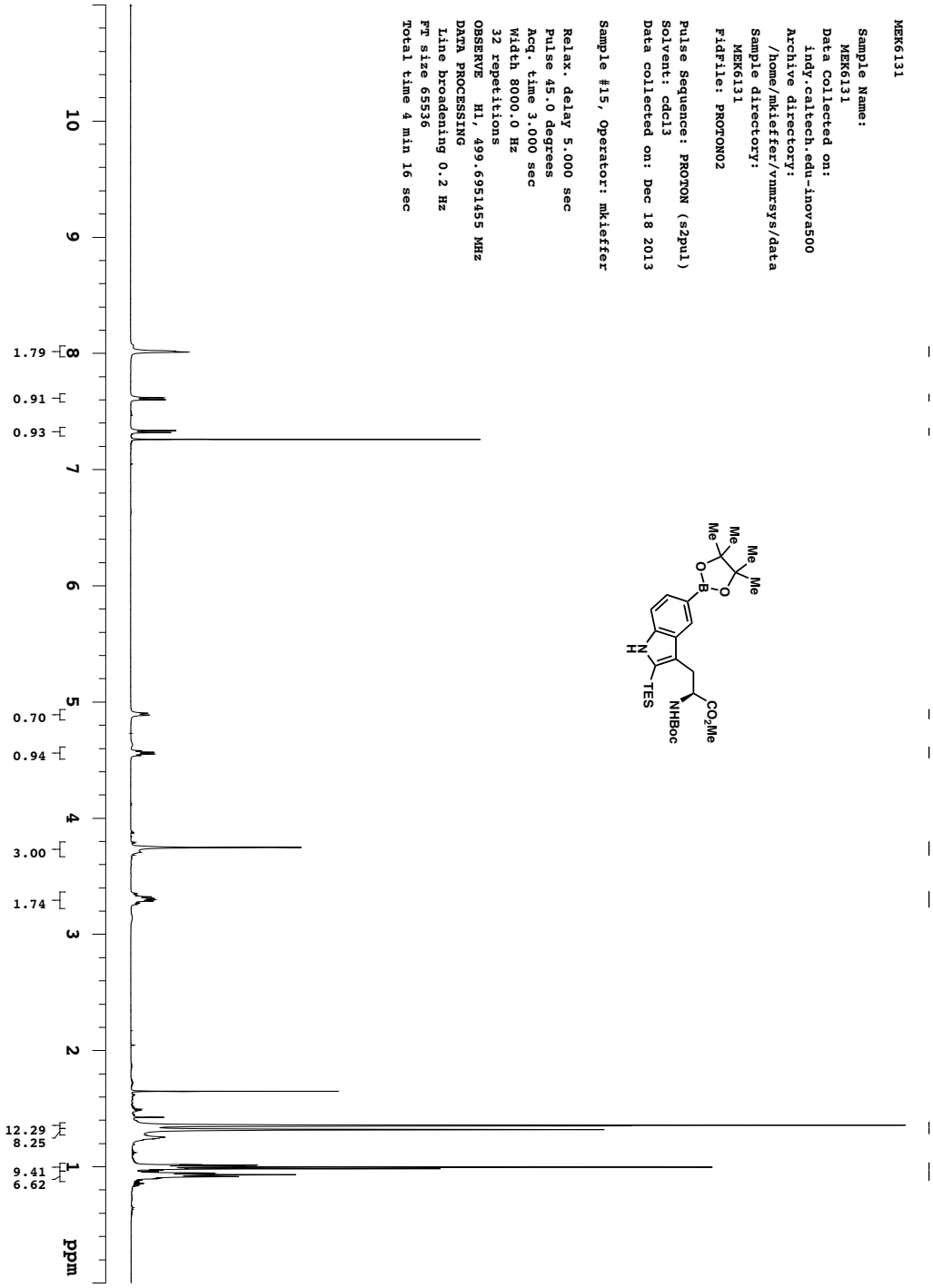

MEK6150-C
Sample Name:
MEK6150-C
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK6150-C
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Feb 3 2014
Sample #16, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
8000 repetitions
OBSERVE C13, 125.6489908 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 4 hr, 33 min
F
F
F
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

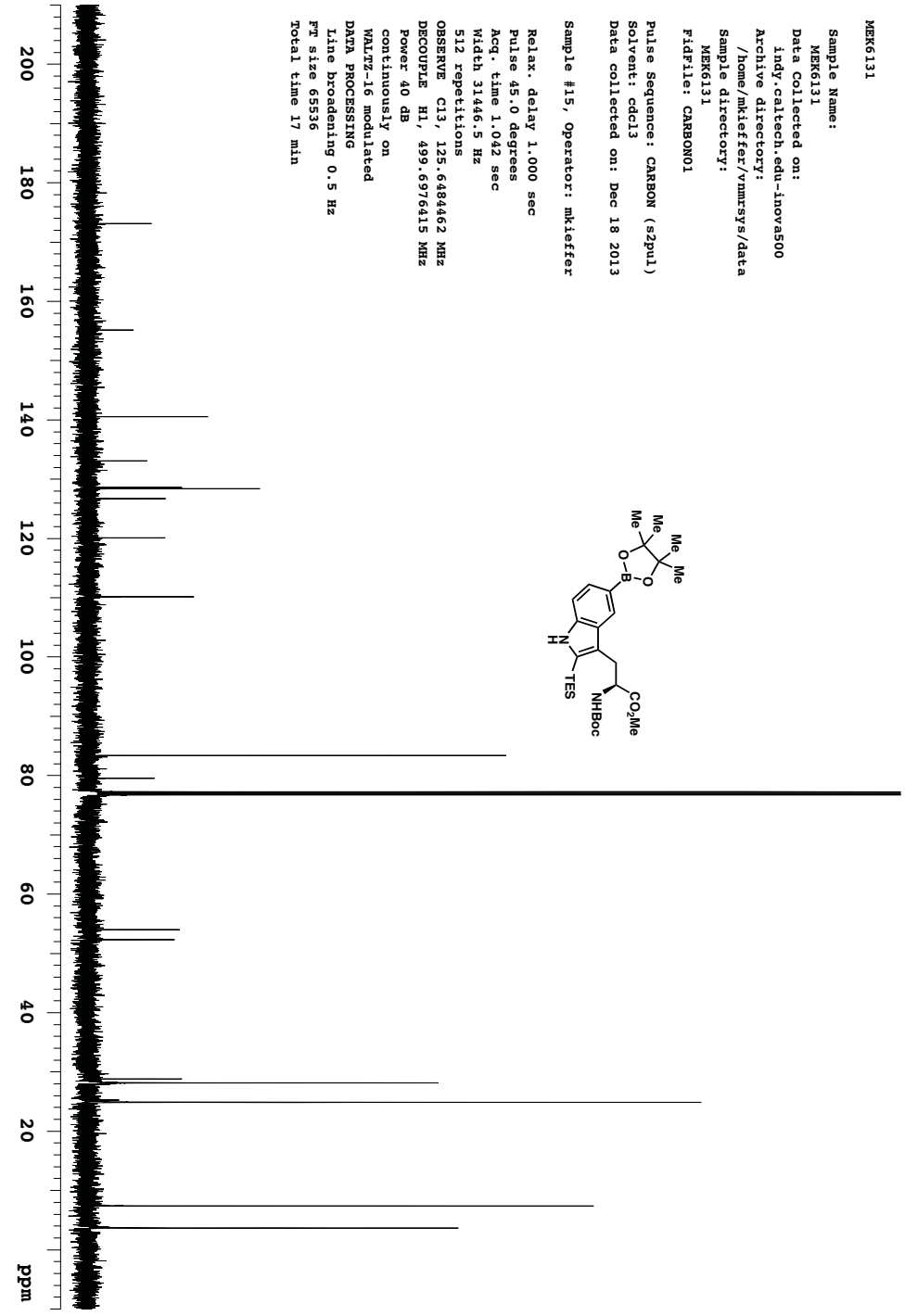

MEK-nitro
Sample Name:
MEK-nitro
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-nitro
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jan 20 2014
Sample #34, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.697864 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
O2N
H
N
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.85
0.93
0.97
1.00
0.71
0.90
3.06
0.90
0.98
15.87
8.68

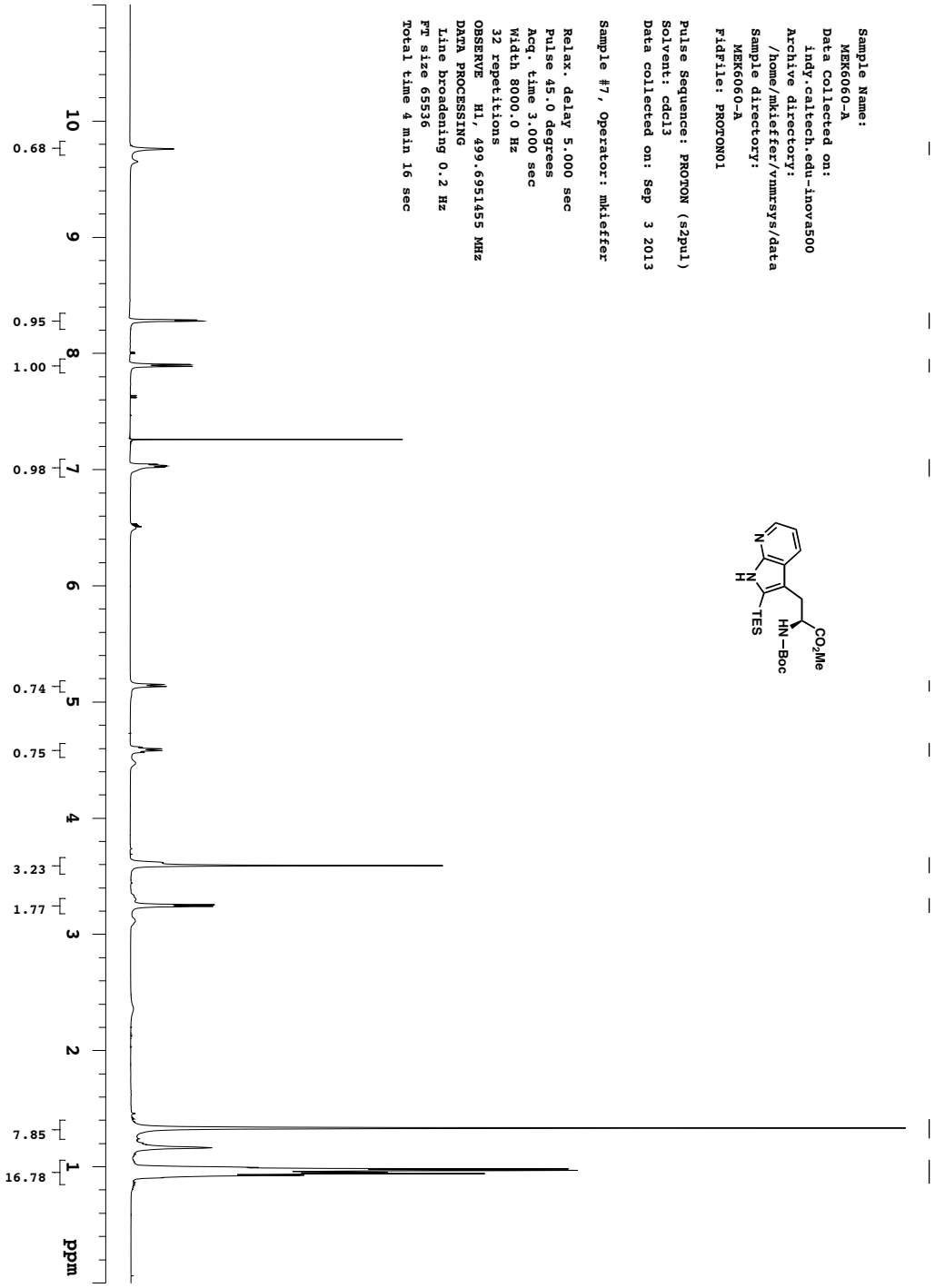

MEK-nitro
Sample Name:
MEK-nitro
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-nitro
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jan 20 2014
Sample #34, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6489908 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
O2N
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

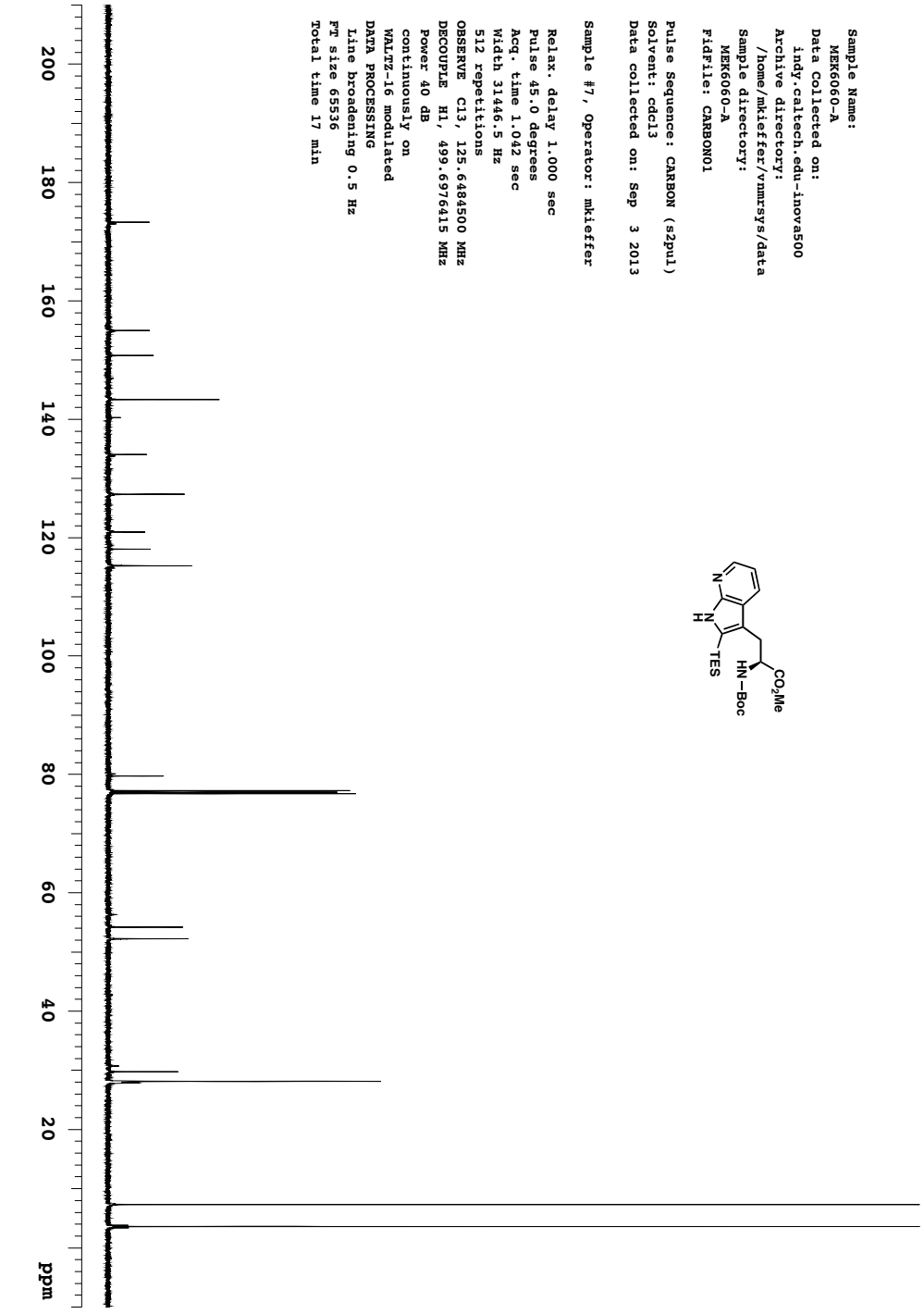

MEK6122
Sample Name:
MEK6122
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK6122
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Feb 3 2014
Sample #15, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
NC
N
H
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.80
0.91
0.93
0.93
0.69
0.89
3.00
0.94
0.95
15.85
8.14

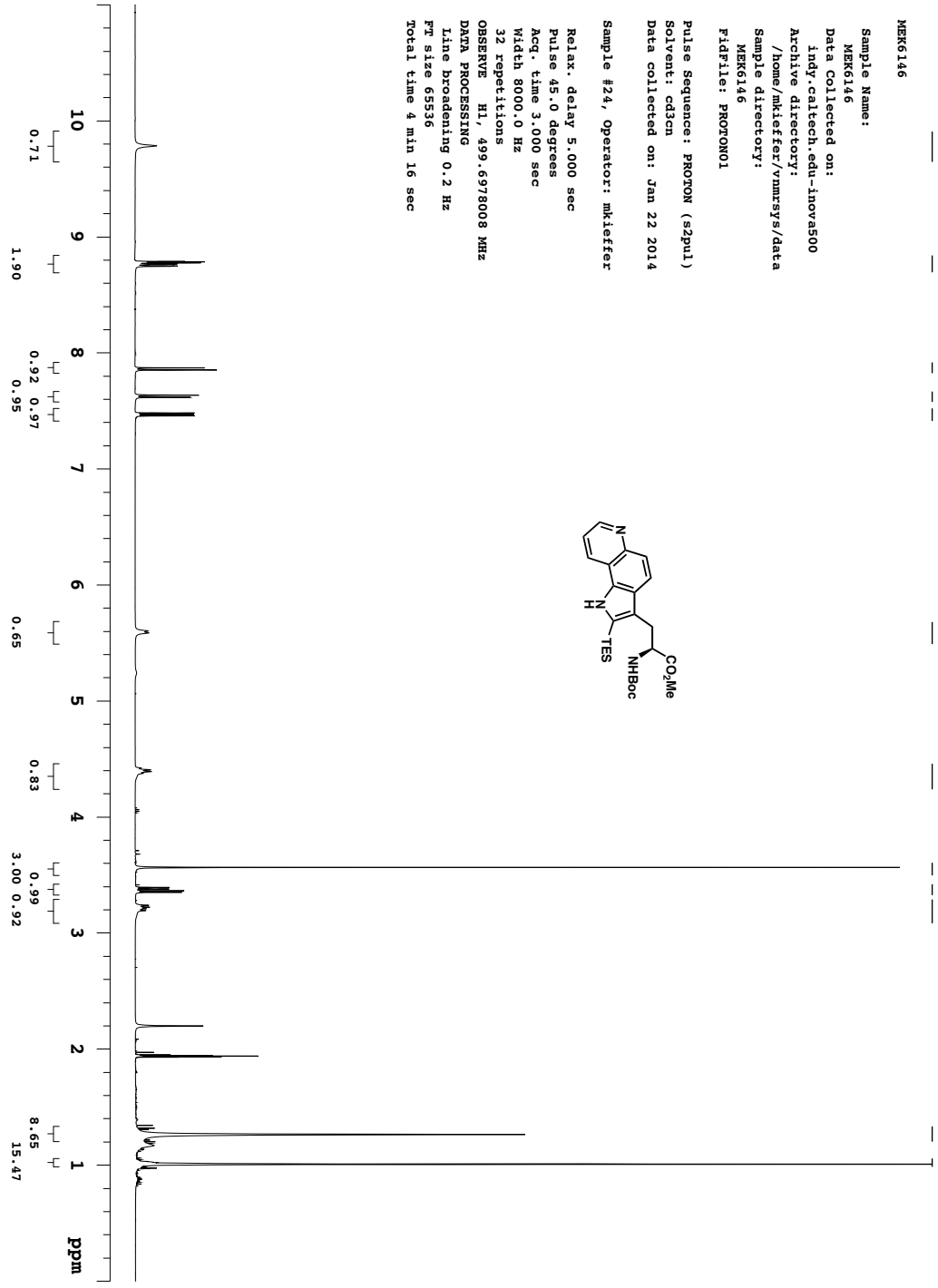

MEK6122
Sample Name:
MEK6122
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK6122
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Feb 3 2014
Sample #15, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3000 repetitions
OBSERVE C13, 125.6489917 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 42 min
NC
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

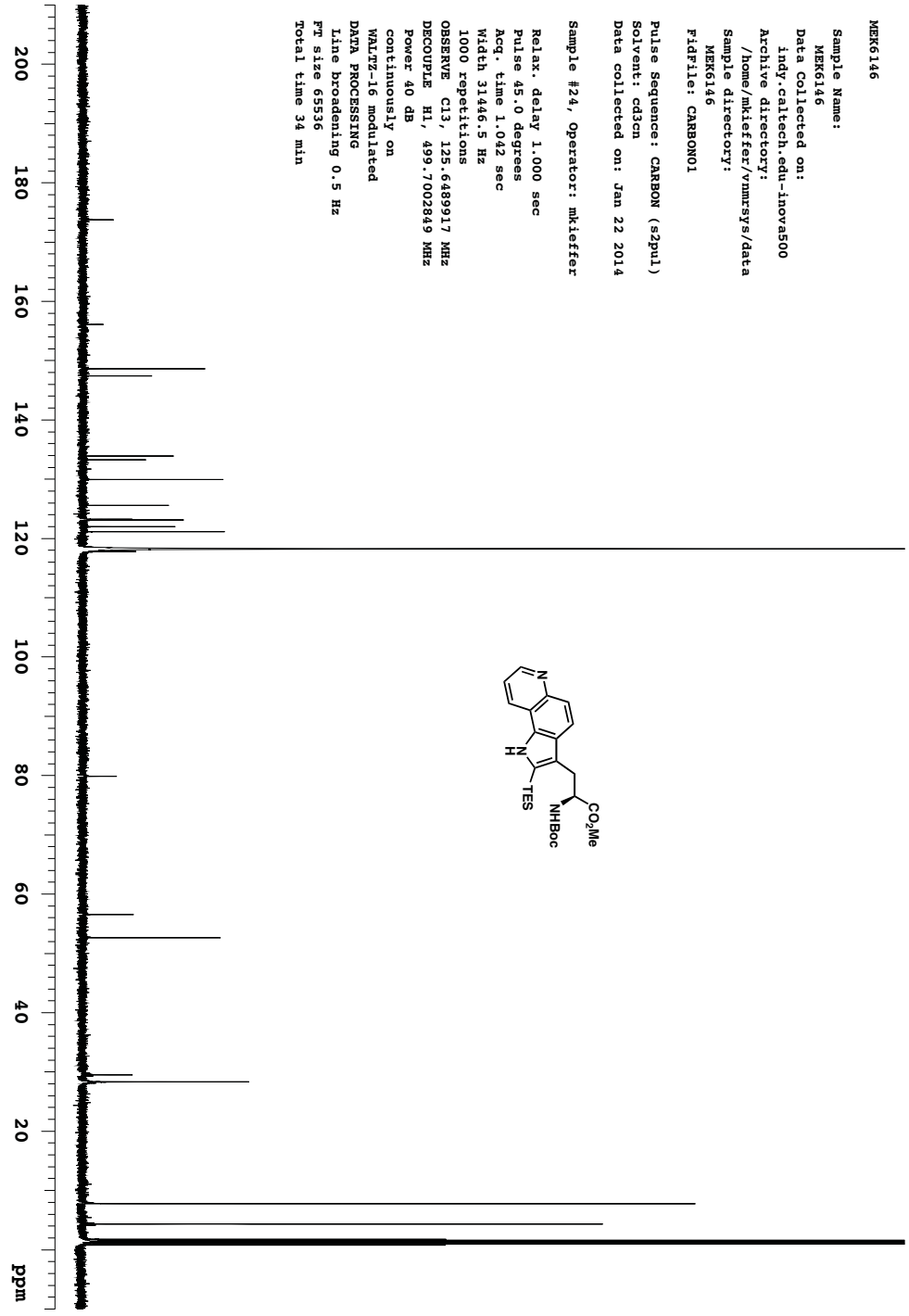

MEK6131
Sample Name:
MEK6131
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6131
FidFile: PROTONO2
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 18 2013
Sample #15, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
1.79
0.91
0.93
0.70
0.94
3.00
1.74
12.29
8.25
9.41
6.62
Me
Me
Me
Me
O
O
B
O
O
N
H
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm

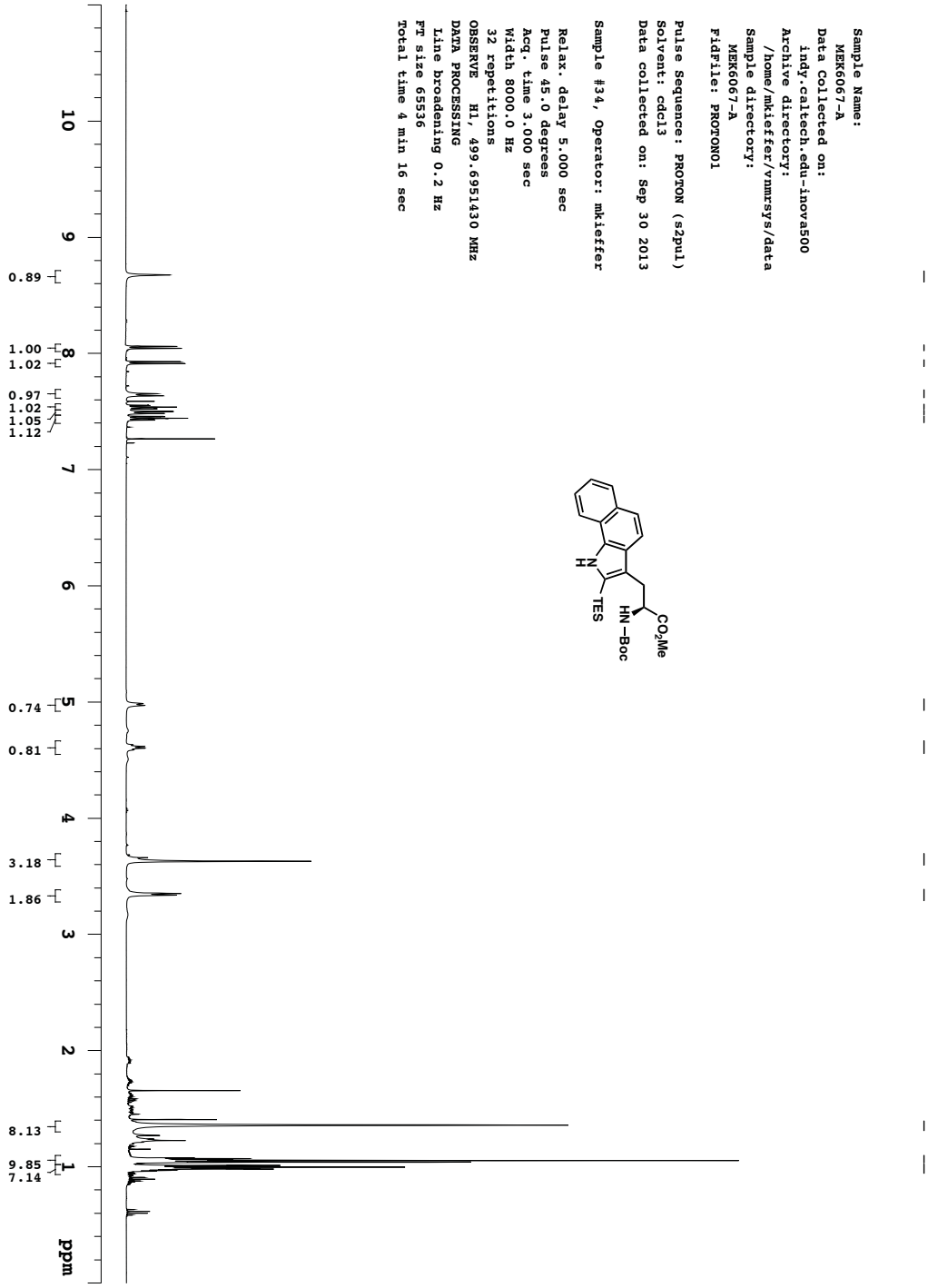

MEK6131
Sample Name:
MEK6131
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6131
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Dec 18 2013
Sample #15, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484462 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
Me
Me
Me
Me
O
B
O
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

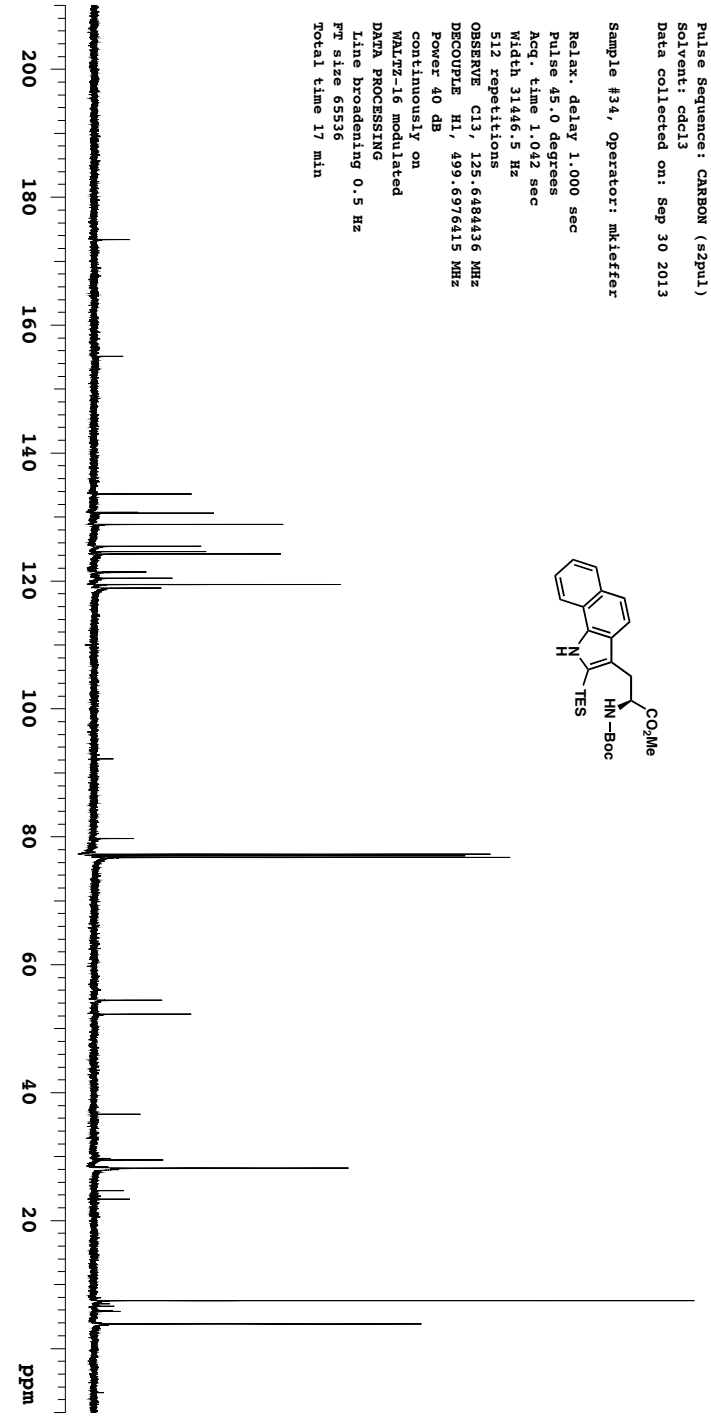

Sample Name:
MEK6060-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6060-A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 3 2013
Sample #7, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.68
0.95
1.00
0.98
0.74
0.75
3.23
1.77
7.85
16.78
10
9
8
7
6
5
4
3
2
1
ppm
N
H
N
TES
HN—Boc
CO2Me

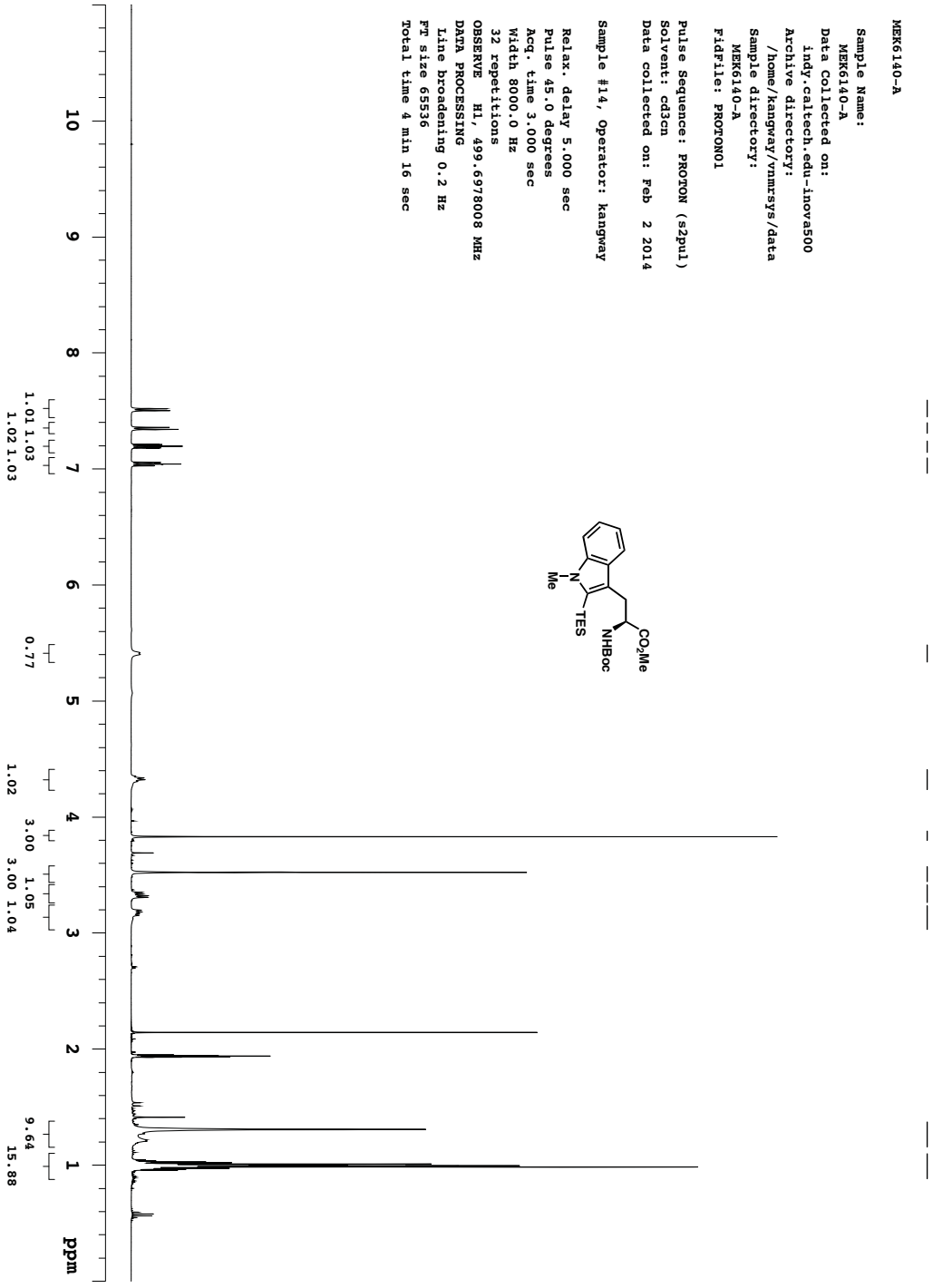

Sample Name:
MEK6060-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6060-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 3 2013
Sample #7, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484500 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
H
N
TES
HN–Boc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

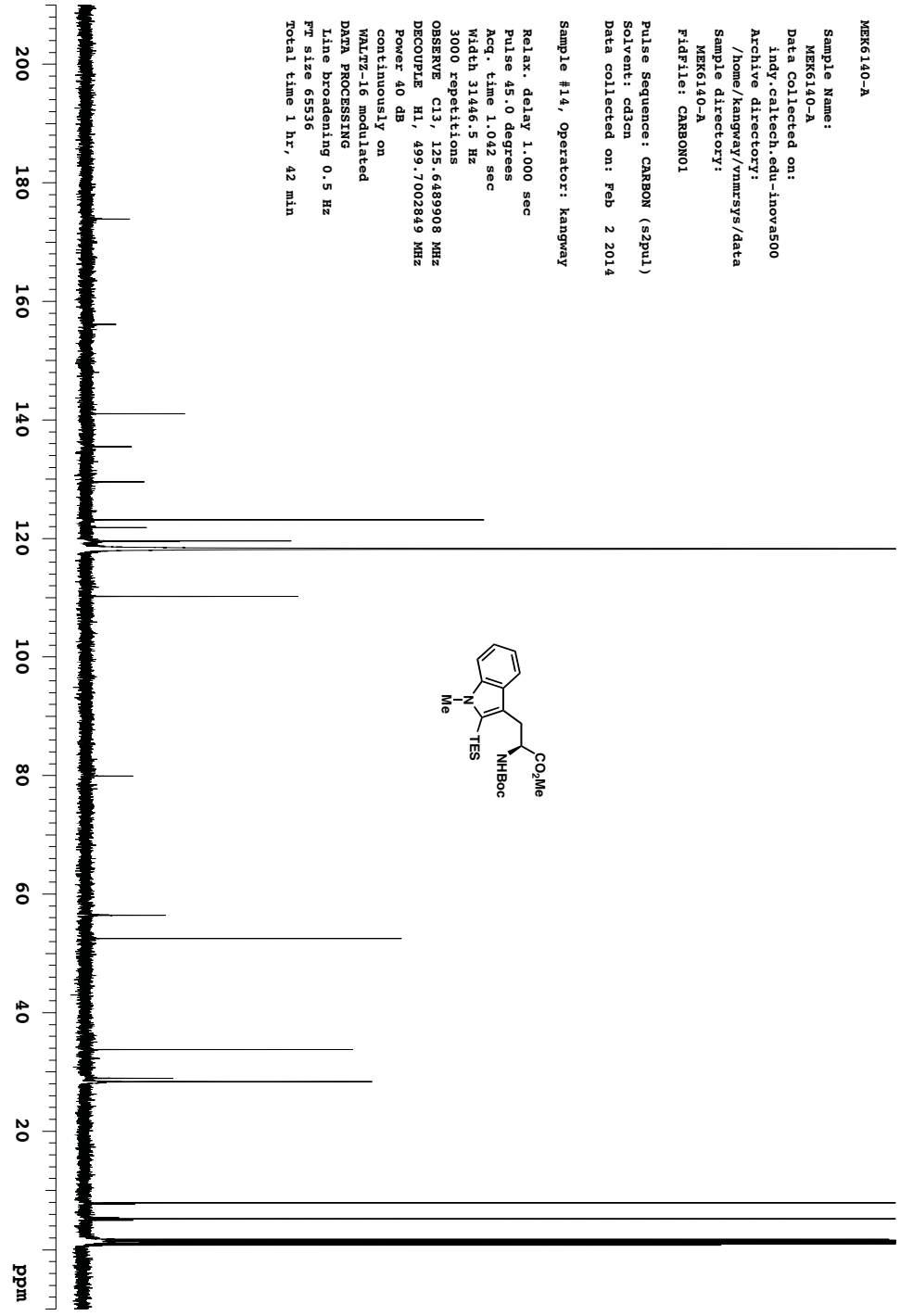

MEK6146
Sample Name:
MEK6146
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6146
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jan 22 2014
Sample #24, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
N
H
N
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.71
1.90
0.92
0.97
0.95
0.65
0.83
0.99
3.00
0.92
8.65
15.47

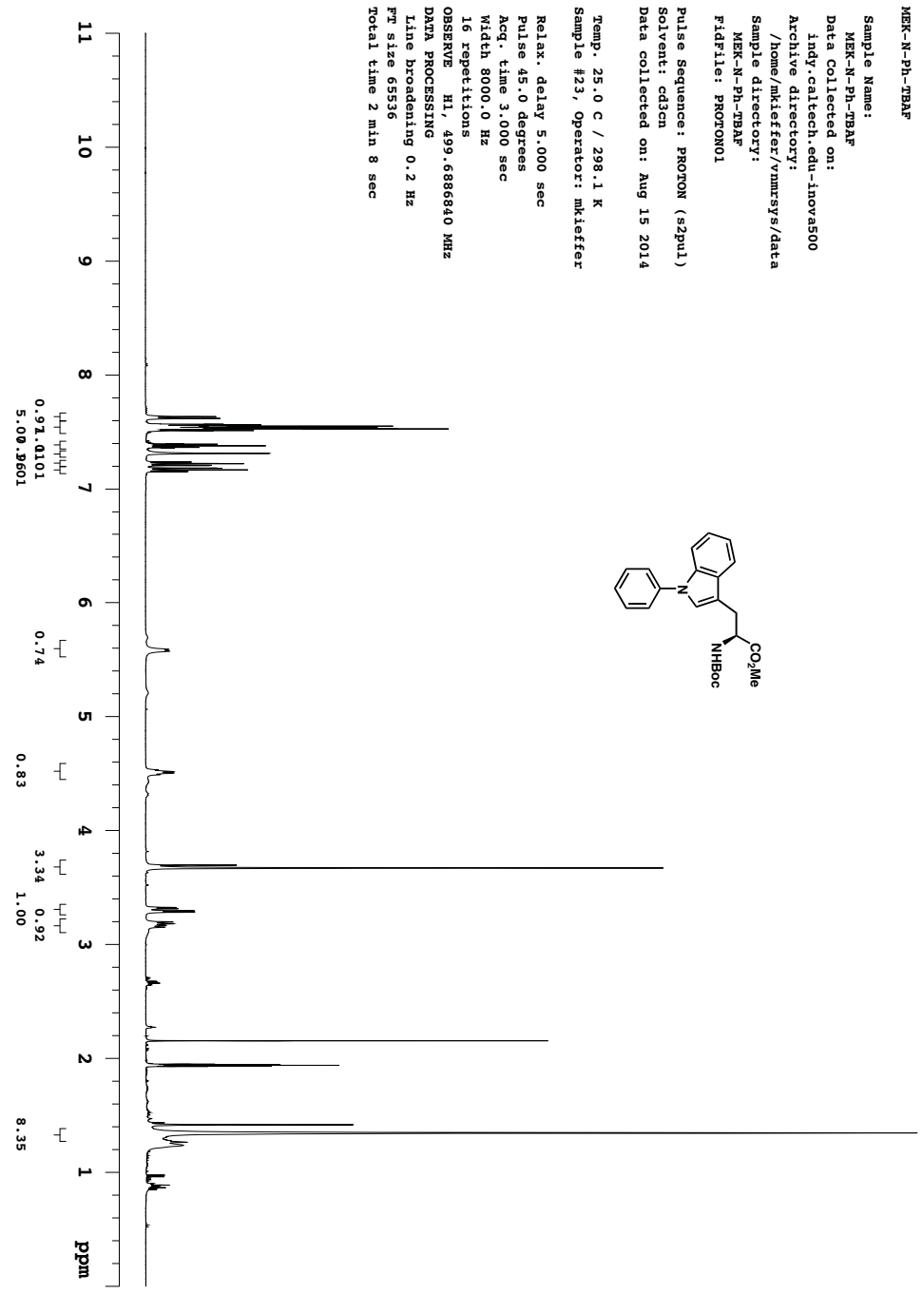

MEK6146
Sample Name:
MEK6146
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6146
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jan 22 2014
Sample #24, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6489917 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
N
H
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

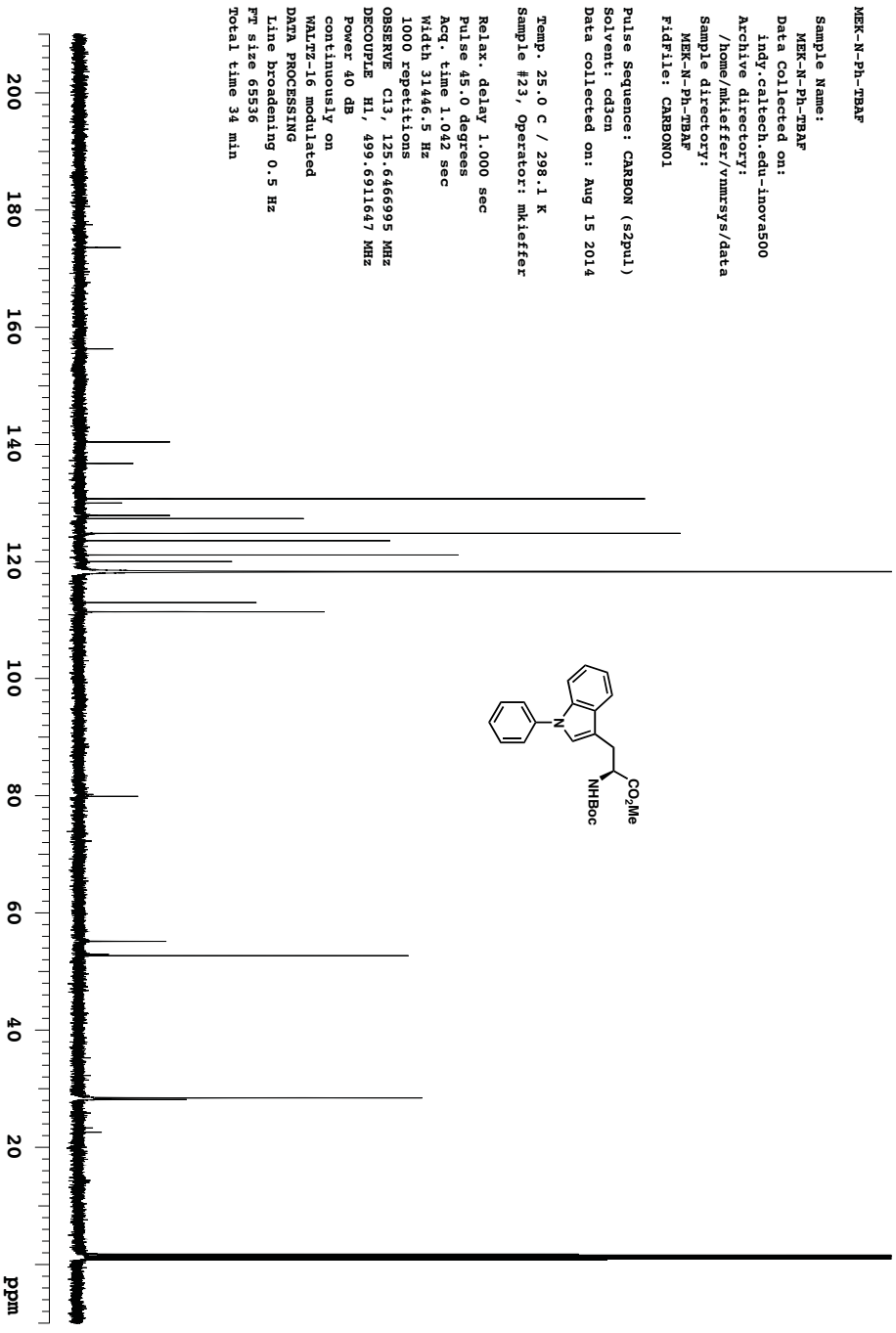

Sample Name:
MEK6067-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6067-A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 30 2013
Sample #34, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951430 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.89
1.00
1.02
0.97
1.02
1.05
1.12
0.74
0.81
3.18
1.86
8.13
9.85
7.14
TES
HN—Boc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm

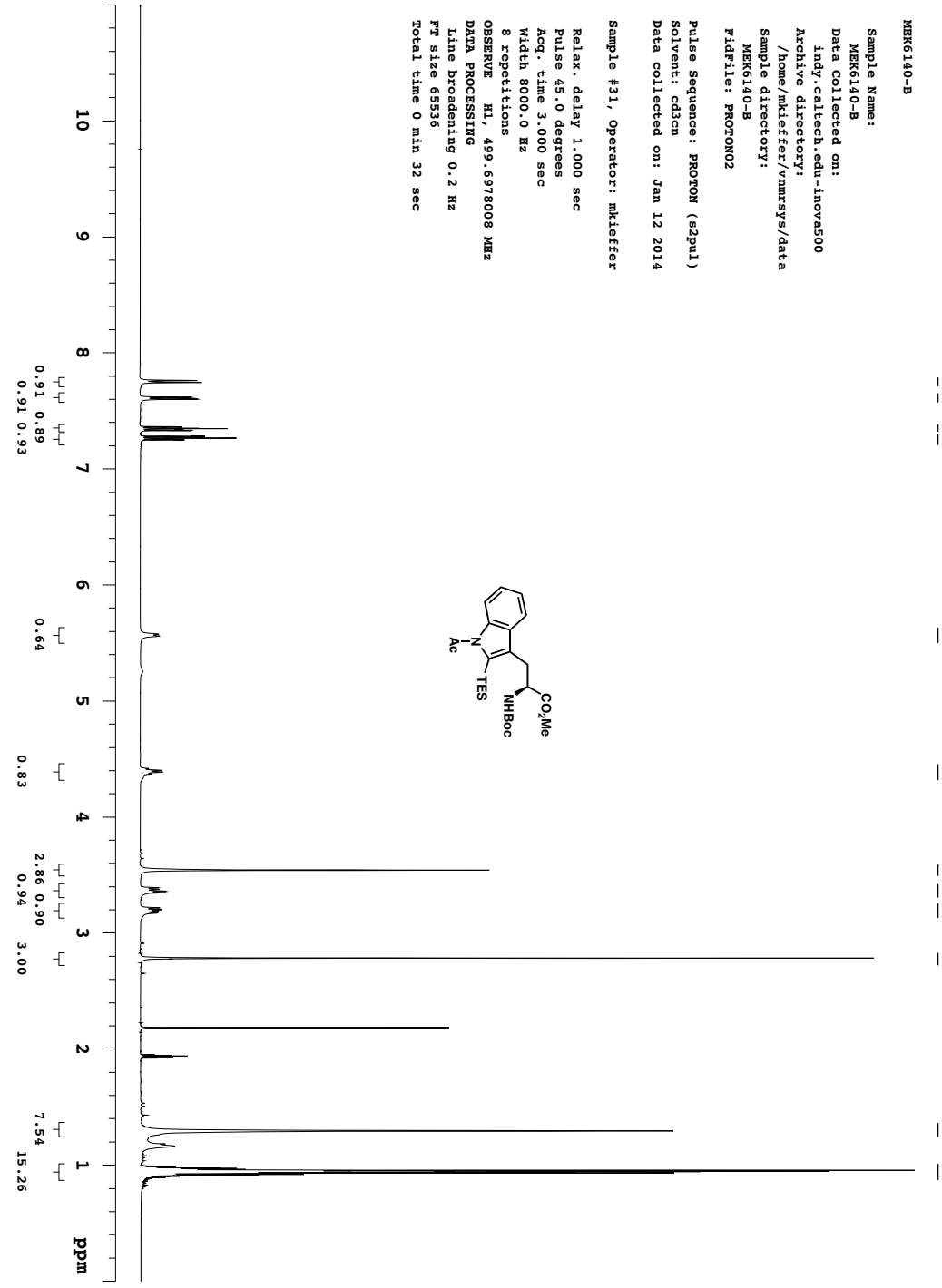

Sample Name:
MEK6067-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6067-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 30 2013
Sample #34, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484436 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
TES
HN–Boc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

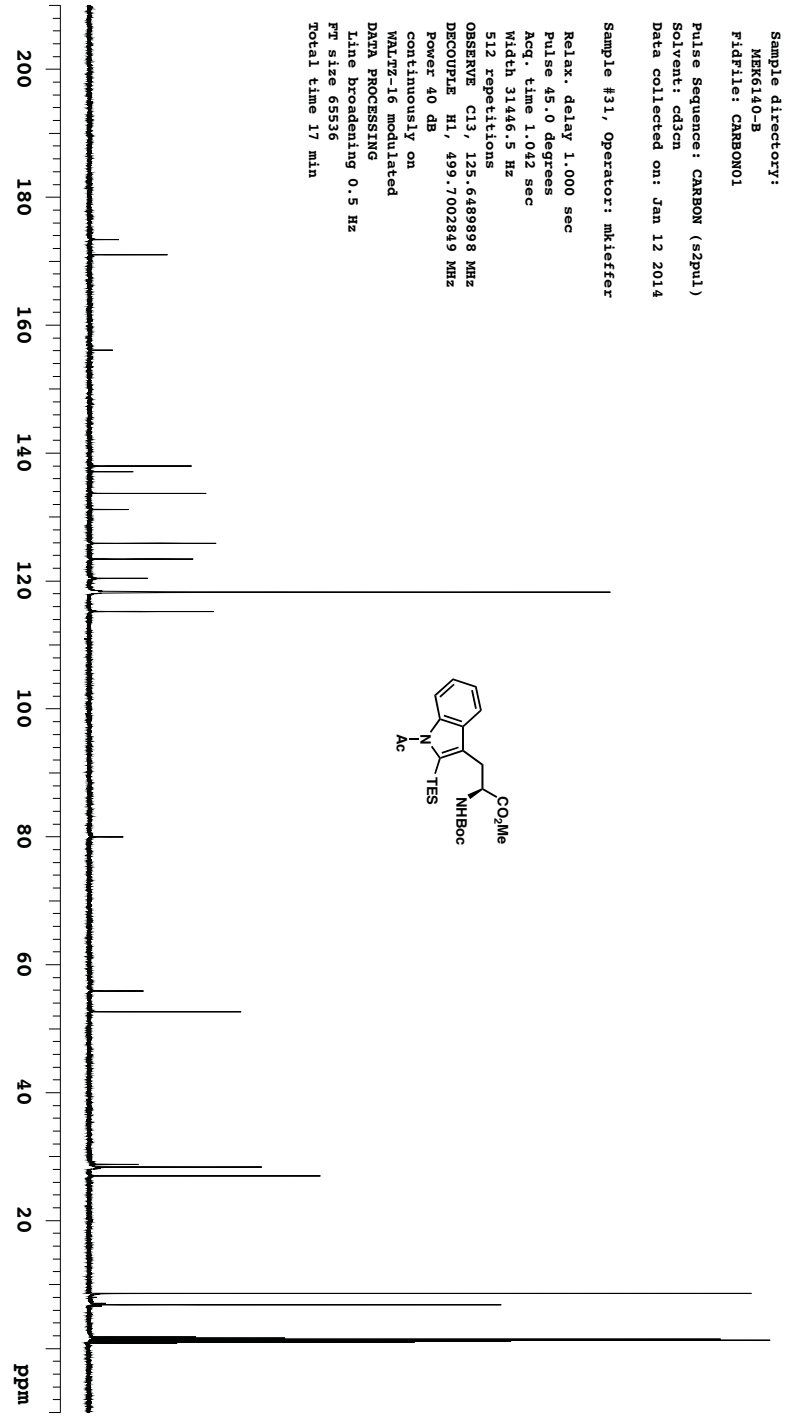

MEK6140-A
Sample Name:
MEK6140-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK6140-A
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Feb 2 2014
Sample #14, Operator: kangway
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
N
Me
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
1.01 1.03
1.02 1.03
0.77
1.02
3.00
1.05
3.00 1.04
9.64
15.88

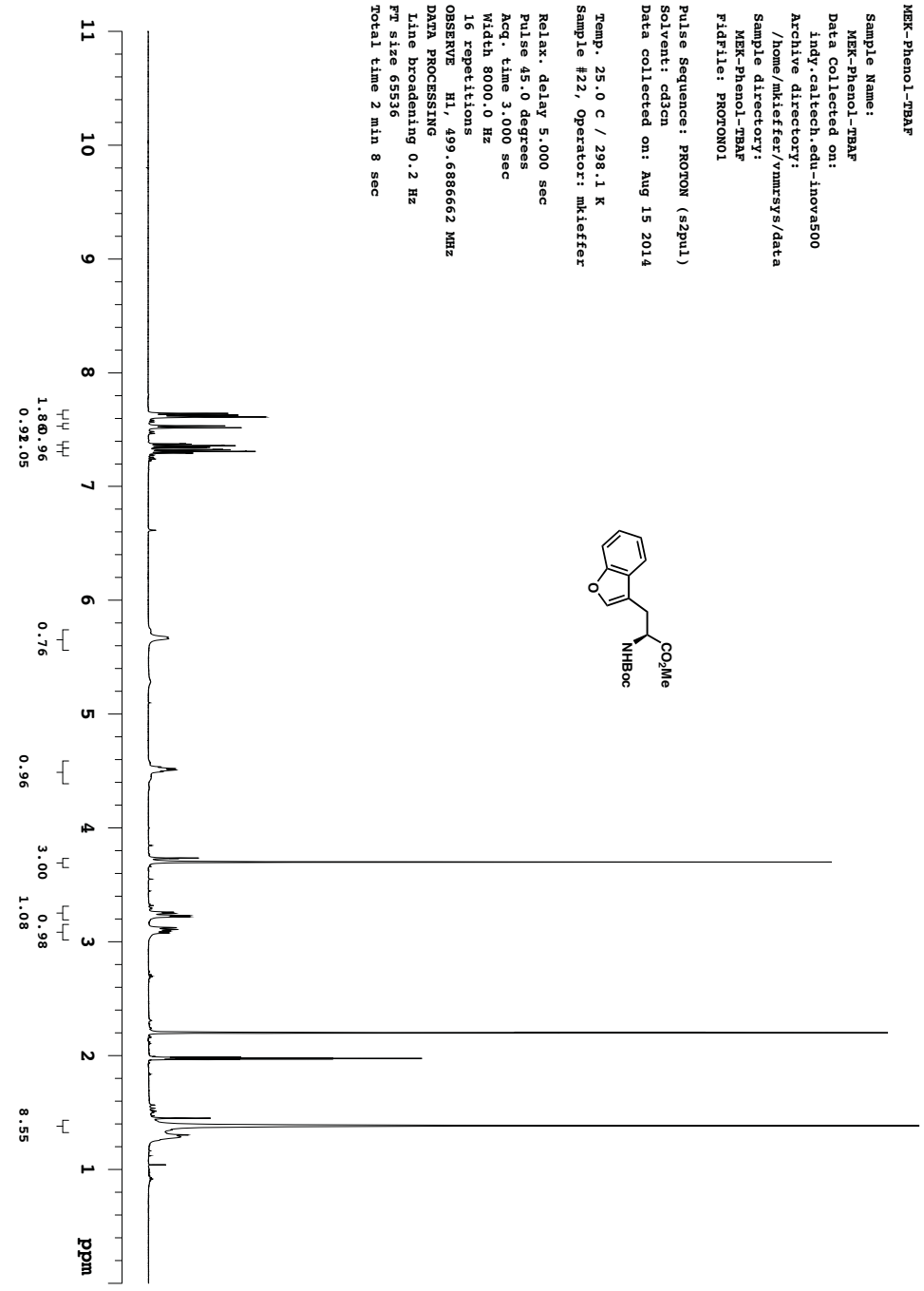

MEK6140-A
Sample Name:
MEK6140-A
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/kangway/vnmrsys/data
Sample directory:
MEK6140-A
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Feb 2 2014
Sample #14, Operator: kangway
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
3000 repetitions
OBSERVE C13, 125.6489908 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 42 min
N
Me
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

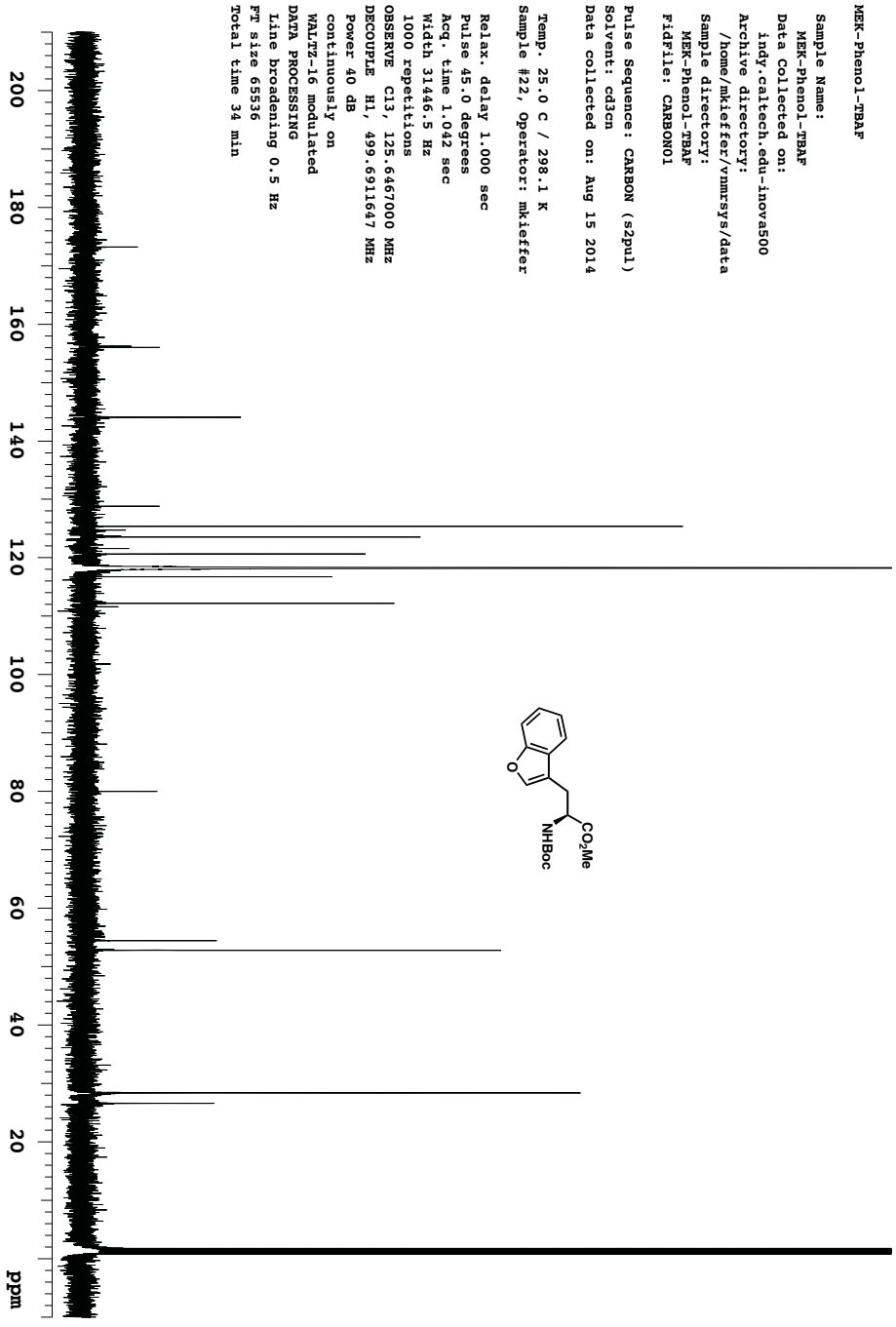

MEK-N-Ph-TBAF
Sample Name:
MEK-N-Ph-TBAF
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-N-Ph-TBAF
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Aug 15 2014
Temp. 25.0 C / 298.1 K
Sample #23, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.6886840 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 8 sec
N
NHBoc
CO2Me
0.91
1.01
5.00
1.96
01
0.74
0.83
3.34
0.92
1.00
8.35
11
10
9
8
7
6
5
4
3
2
1
ppm

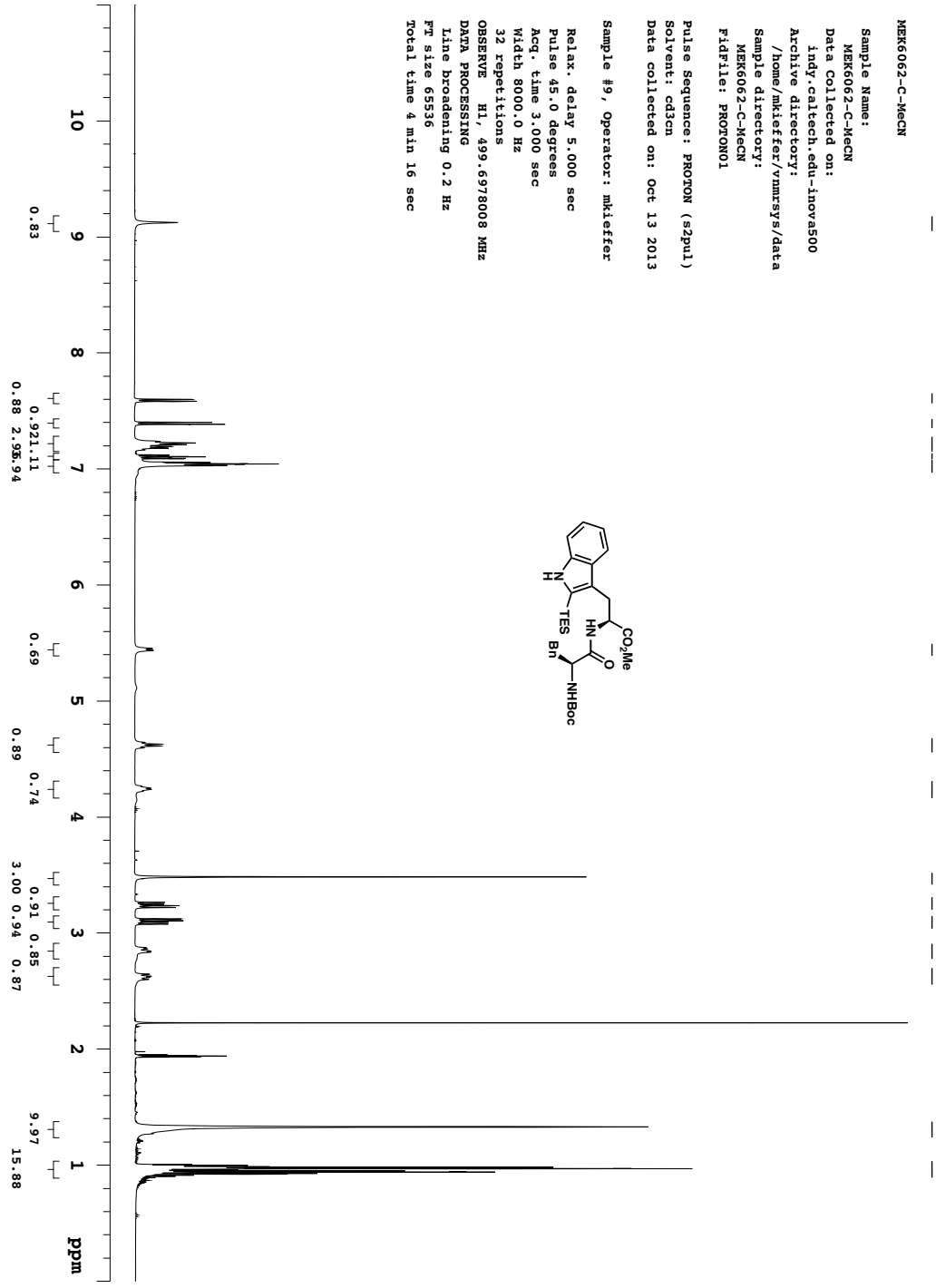

MEK-N-Ph-TBAF
Sample Name:
MEK-N-Ph-TBAF
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-N-Ph-TBAF
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Aug 15 2014
Temp. 25.0 C / 298.1 K
Sample #23, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6466995 MHz
DECOUPLE H1, 499.691647 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
N
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

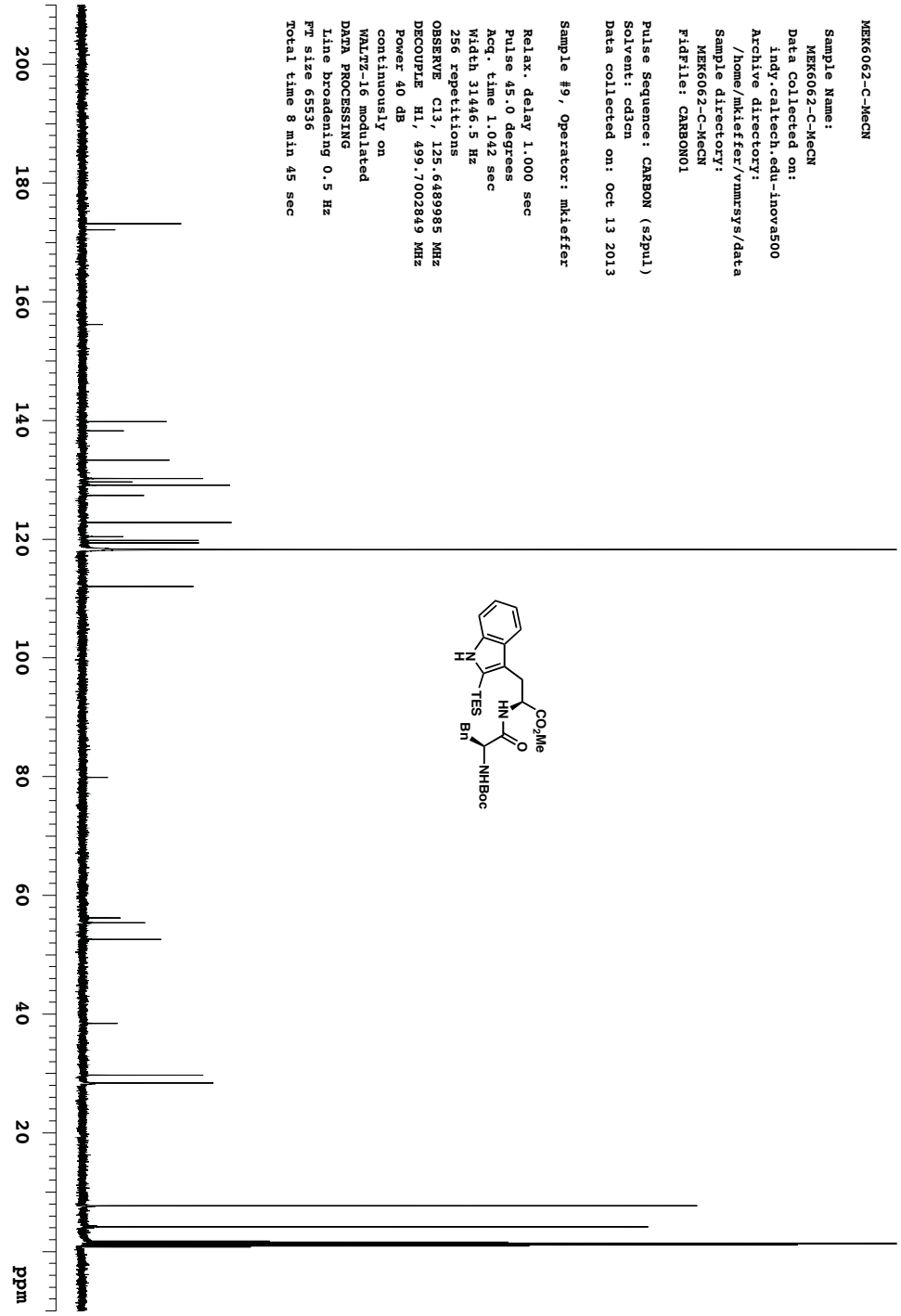

MEK6140-B
Sample Name:
MEK6140-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6140-B
FidFile: PROTON02
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jan 12 2014
Sample #31, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
8 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min 32 sec
N
Ac
TES
NHBoc
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.91 0.89
0.91 0.93
0.64
0.83
2.86 0.90
0.94
3.00
7.54
15.26

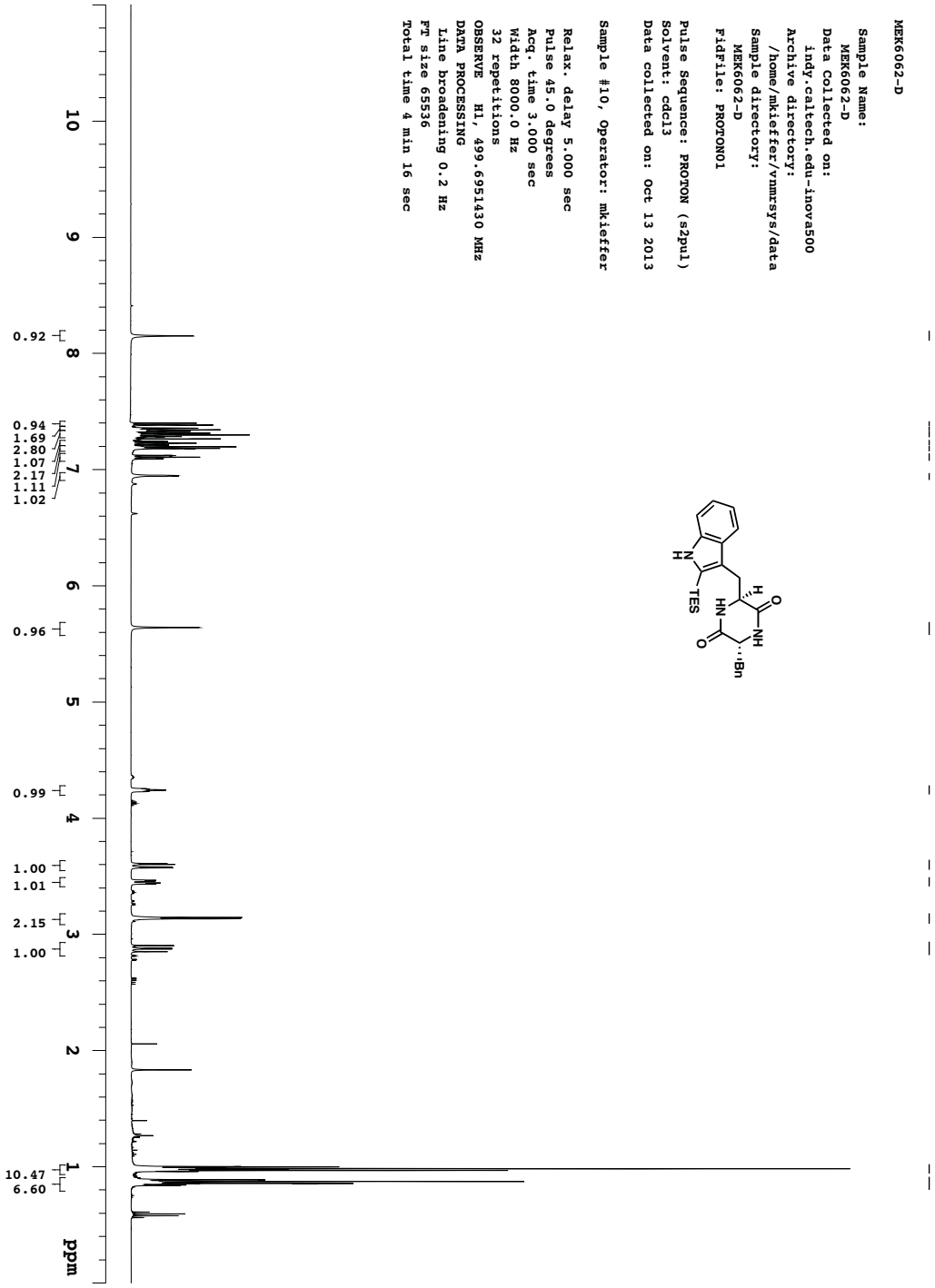

MEK6140-B
Sample Name:
MEK6140-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6140-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jan 12 2014
Sample #31, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6489898 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
Ac
TES
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

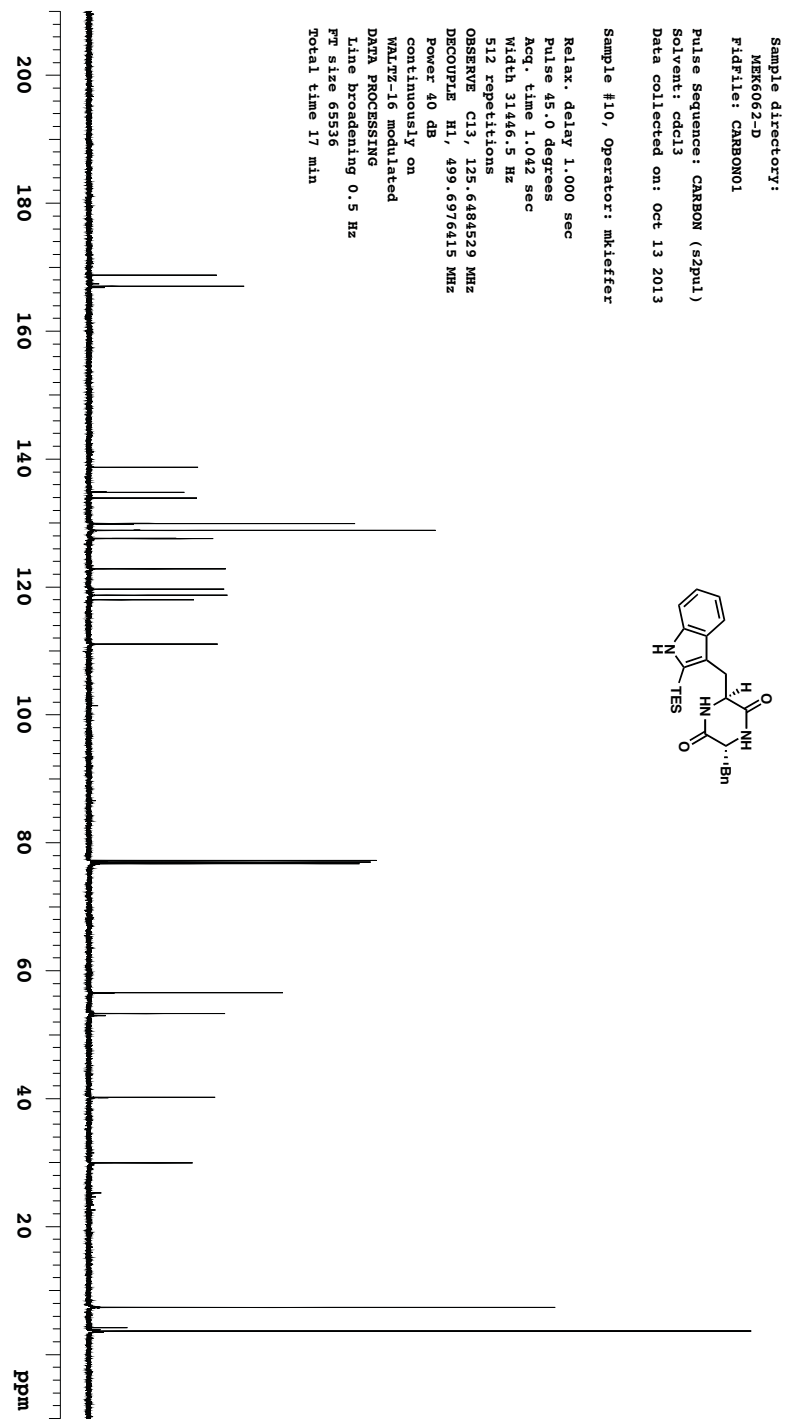

MEK-Phenol-TBAF
Sample Name:
MEK-Phenol-TBAF
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-Phenol-TBAF
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Aug 15 2014
Temp. 25.0 C / 298.1 K
Sample #22, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.6886662 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 8 sec
CO2Me
NHBoc
O
11
10
9
8
7
6
5
4
3
2
1
ppm
1.80
0.96
0.92
2.05
0.76
0.96
3.00
0.98
1.08
8.55

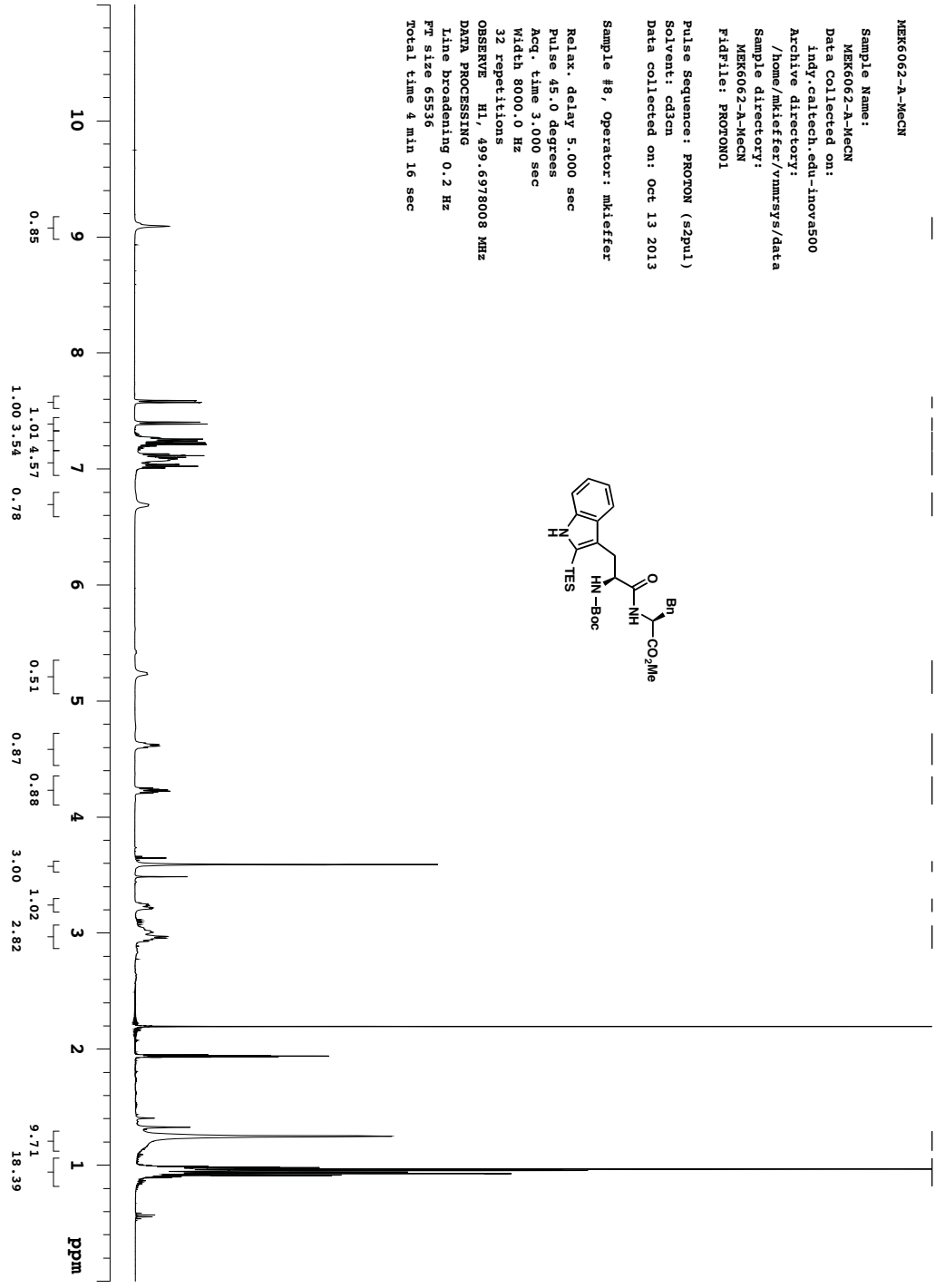

MEK-Phenol-TBAF
Sample Name:
MEK-Phenol-TBAF
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK-Phenol-TBAF
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Aug 15 2014
Temp. 25.0 C / 298.1 K
Sample #22, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1000 repetitions
OBSERVE C13, 125.6467000 MHz
DECOUPLE H1, 499.691647 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 34 min
NHBoc
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

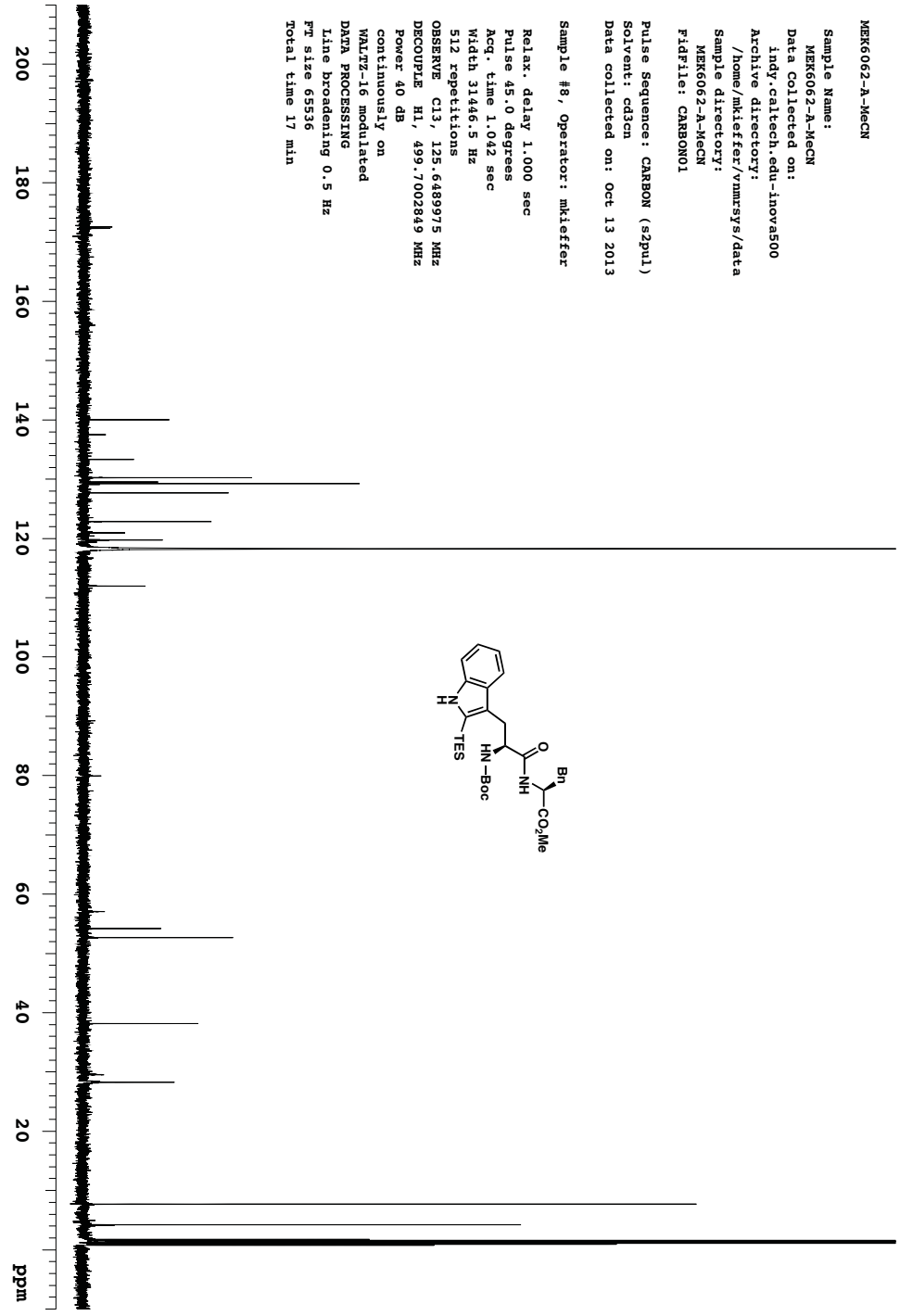

MEK6062-C-MeCN
Sample Name:
MEK6062-C-MeCN
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-C-MeCN
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Oct 13 2013
Sample #9, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
CO2Me
HN
O
TES
Bn
NHBoc
N
H
10
9
8
7
6
5
4
3
2
1
ppm
0.83
0.92
1.11
0.88
2.92
5.94
0.69
0.89
0.74
3.00
0.91
0.94
0.85
0.87
9.97
15.88

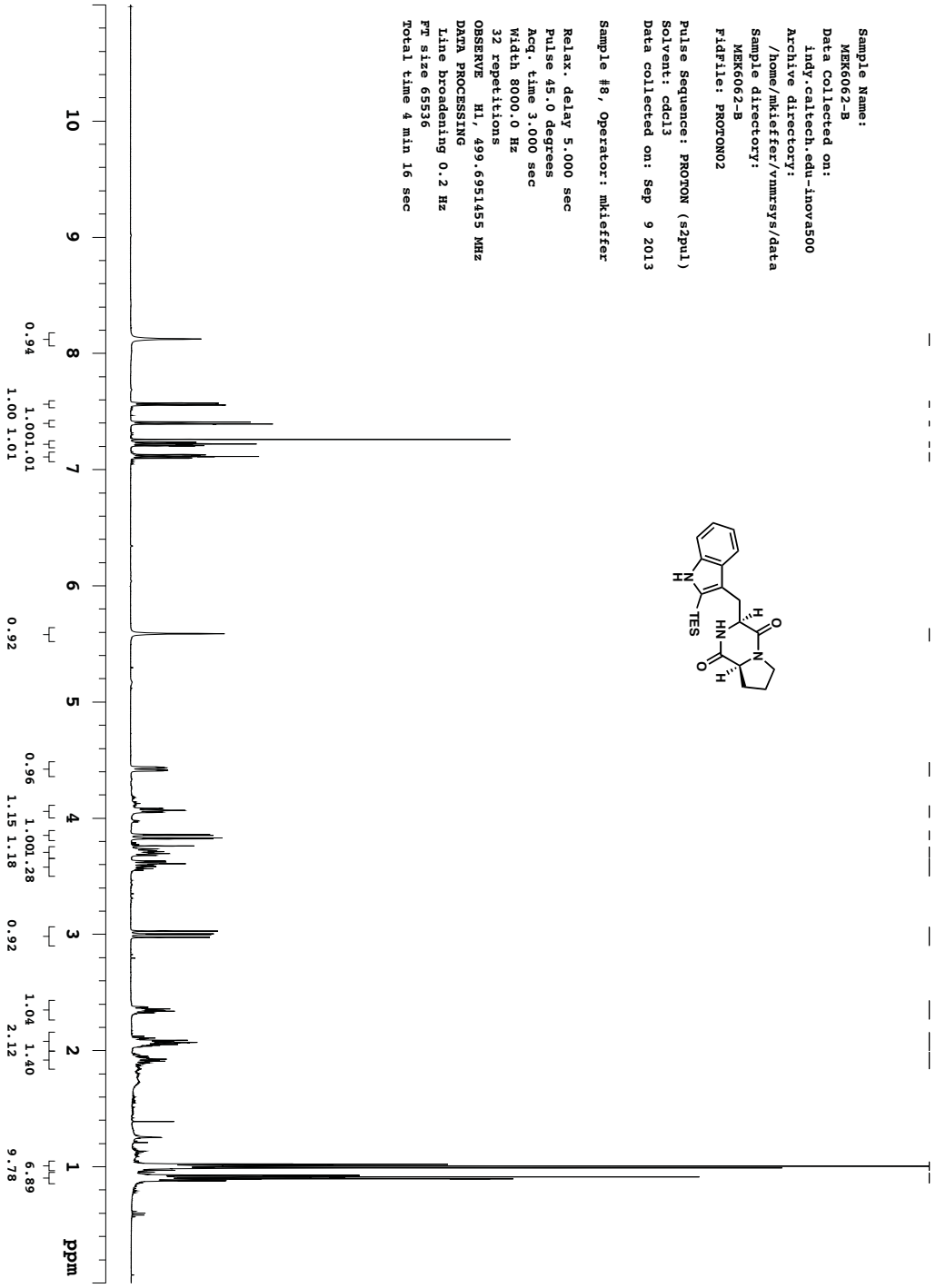

MEK6062-C-MeCN
Sample Name:
MEK6062-C-MeCN
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-C-MeCN
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Oct 13 2013
Sample #9, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6489985 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
200
180
160
140
120
100
80
60
40
20
ppm
N
H
TES
Bn
HN
O
CO2Me
NHBoc

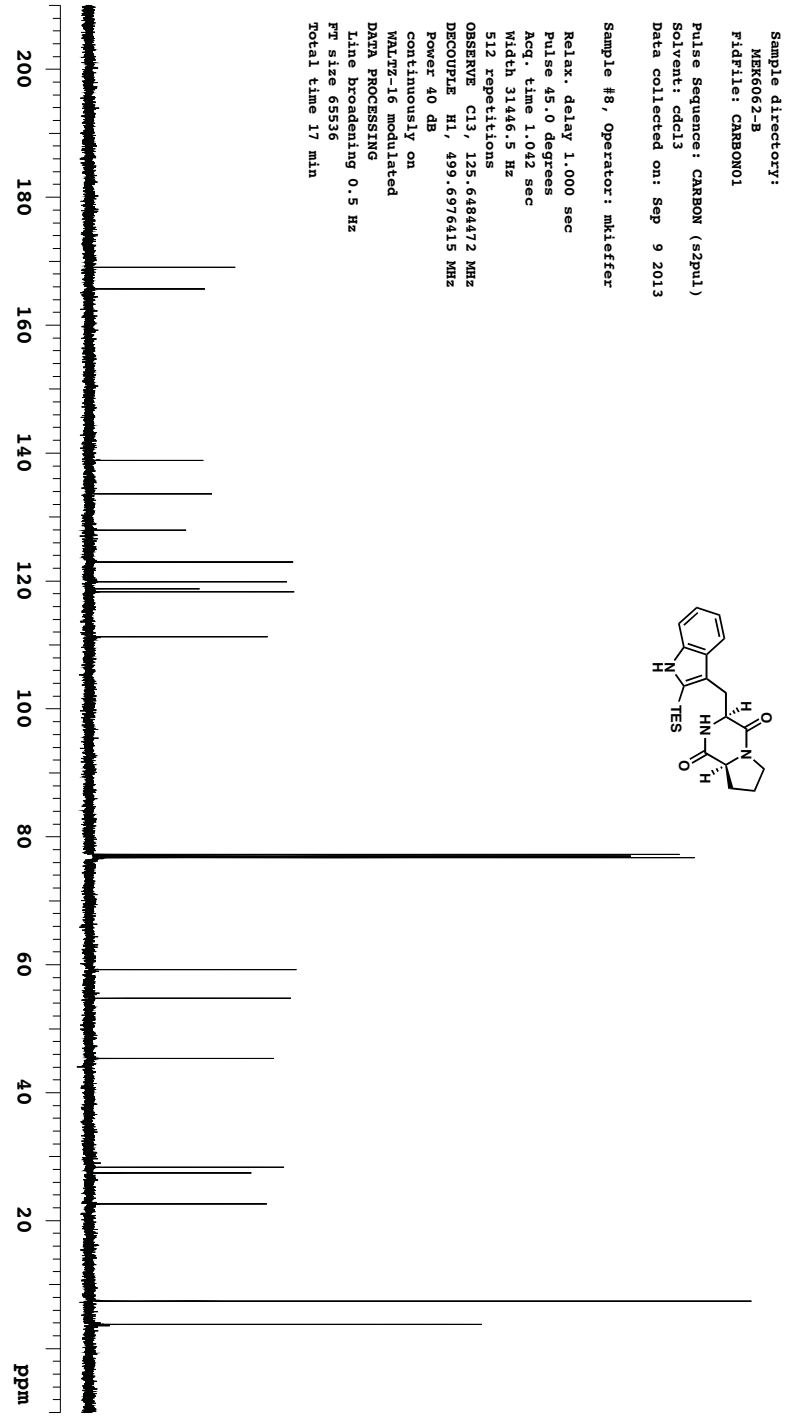

MEK6062-D
Sample Name:
MEK6062-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-D
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Oct 13 2013
Sample #10, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951430 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.92
0.94
1.69
2.80
1.07
2.17
1.11
1.02
0.96
0.99
1.00
1.01
2.15
1.00
10.47
6.60
TES
HN
NH
Bn
ppm

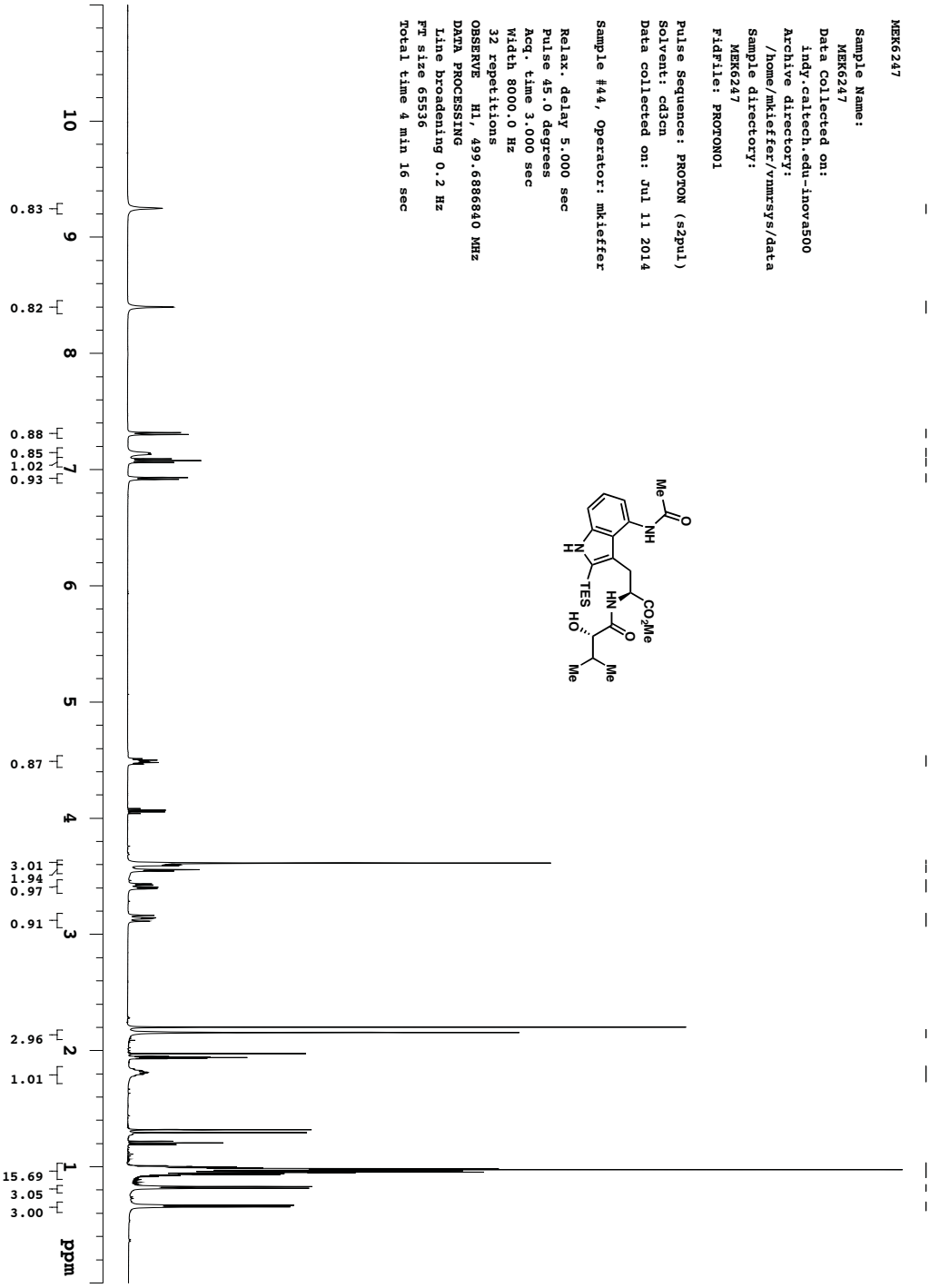

MEK6062-D
Sample Name:
MEK6062-D
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-D
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Oct 13 2013
Sample #10, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484529 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
TES
Bn
200
180
160
140
120
100
80
60
40
20
ppm

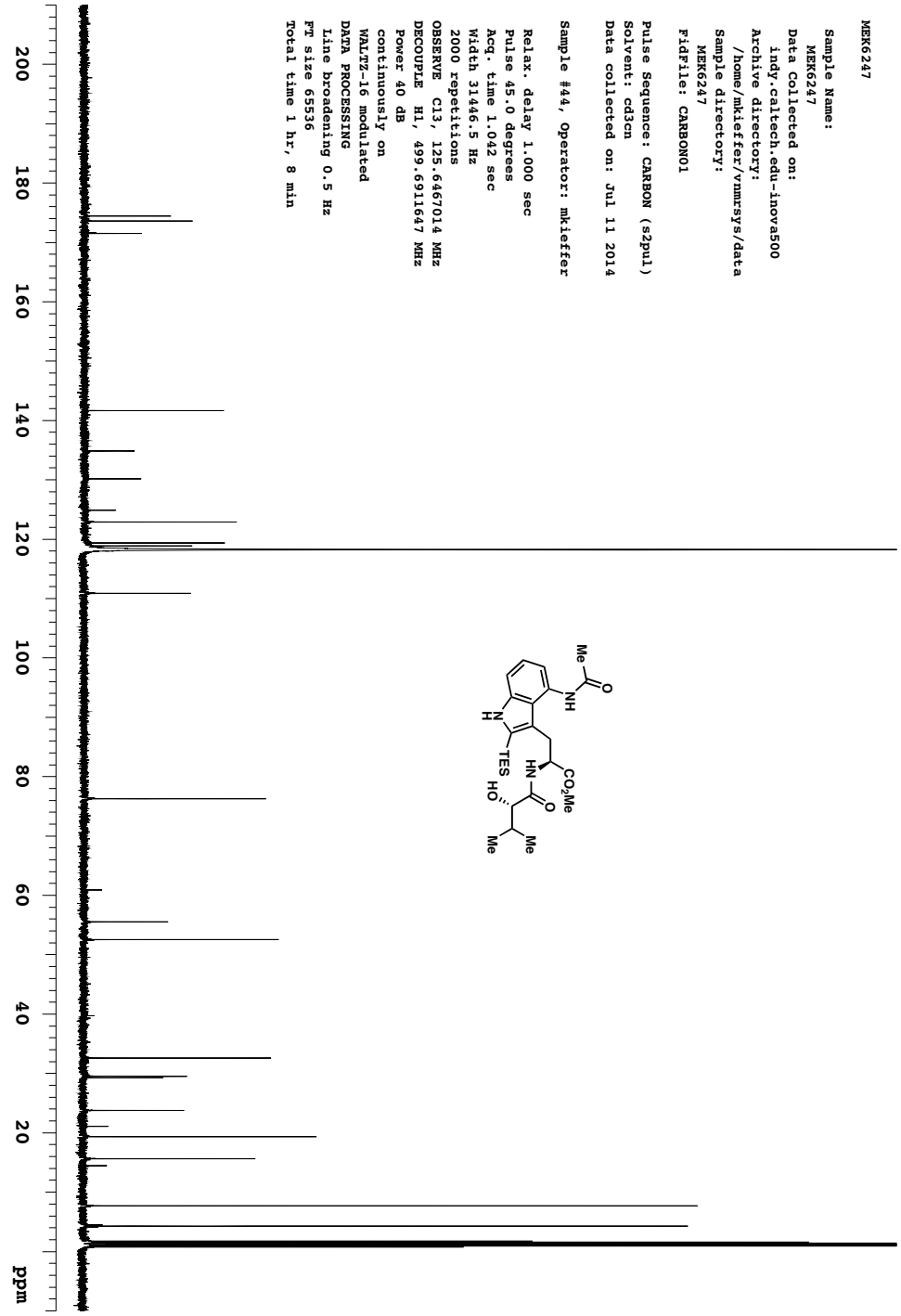

MEK6062-A-MeCN
Sample Name:
MEK6062-A-MeCN
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-A-MeCN
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Oct 13 2013
Sample #8, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6978008 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
HN
TES
HN–Boc
O
NH
Bn
CO2Me
10
9
8
7
6
5
4
3
2
1
ppm
0.85
1.00
3.54
1.01
4.57
0.78
0.51
0.87
0.88
3.00
1.02
2.82
9.71
18.39

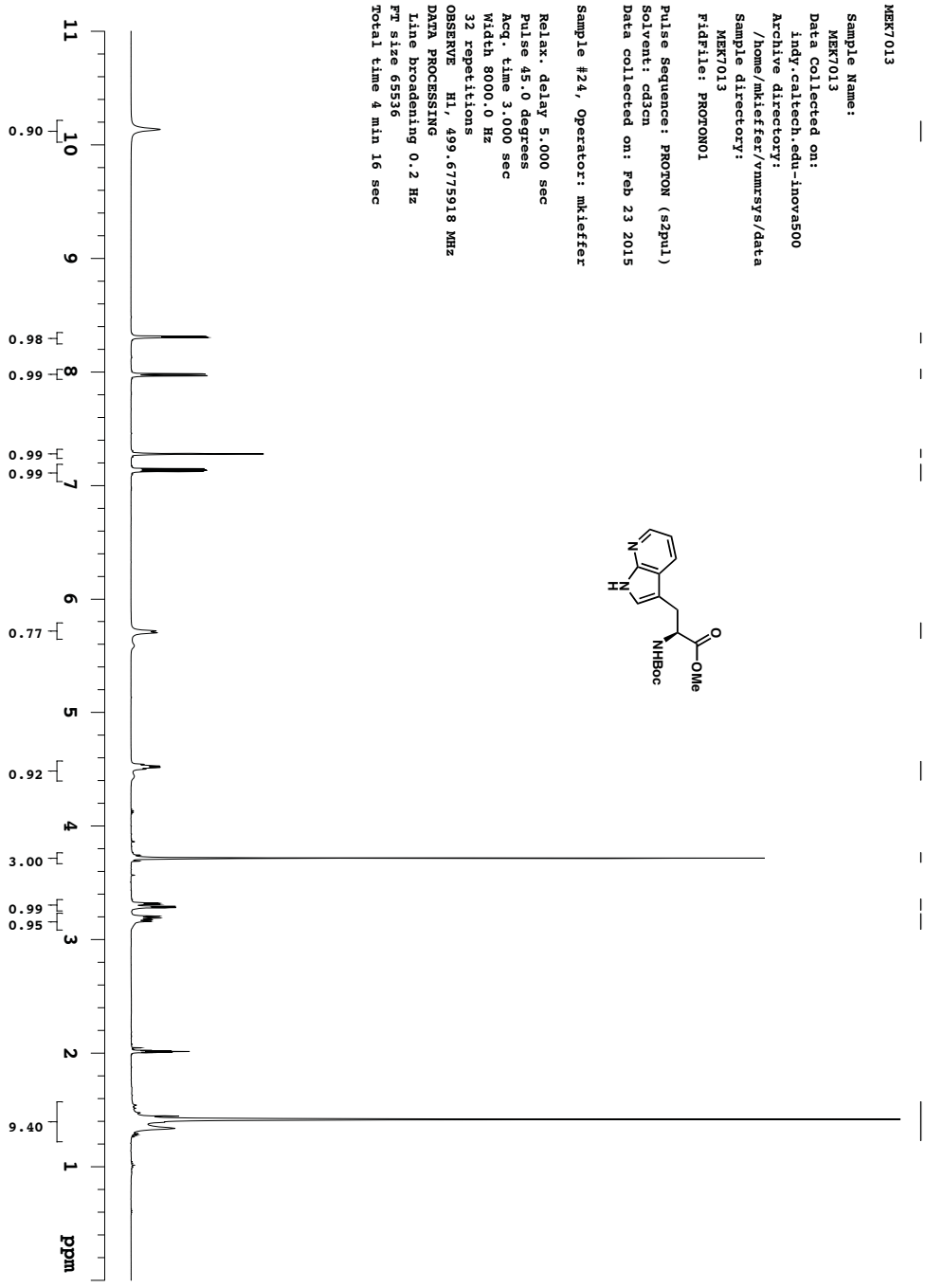

MEK6062-A-MeCN
Sample Name:
MEK6062-A-MeCN
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-A-MeCN
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Oct 13 2013
Sample #8, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6489975 MHz
DECOUPLE H1, 499.7002849 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
TES
HN—Boc
NH
Bn
CO2Me
200
180
160
140
120
100
80
60
40
20
ppm

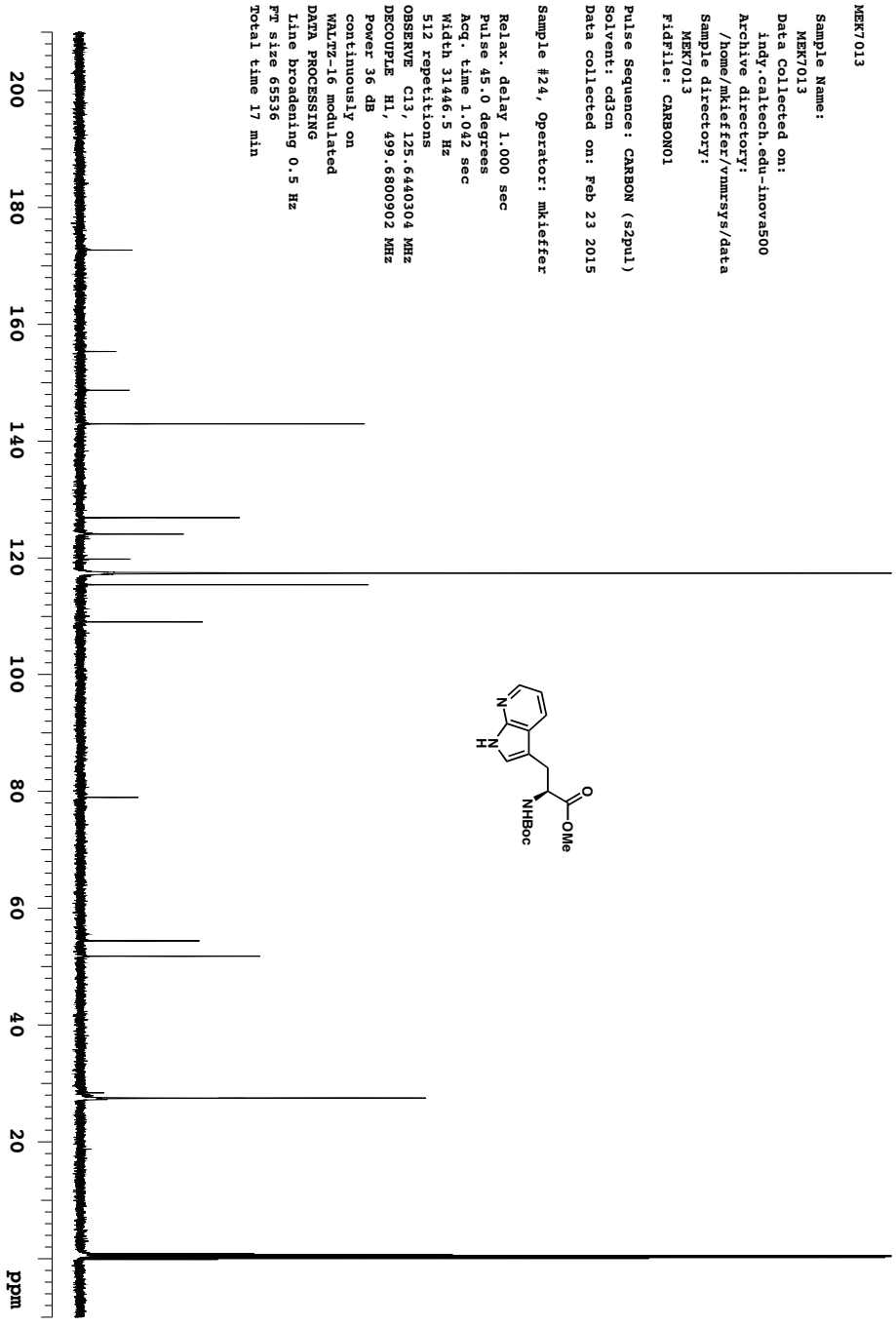

Sample Name:
MEK6062-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-B
FidFile: PROTONO2
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 9 2013
Sample #8, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6951455 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
TES
HN
O
N
H
ppm
10
9
8
7
6
5
4
3
2
1
0.94
1.00
1.00
1.01
0.92
0.96
1.15
1.00
1.18
1.28
0.92
1.04
2.12
1.40
6.89
9.78

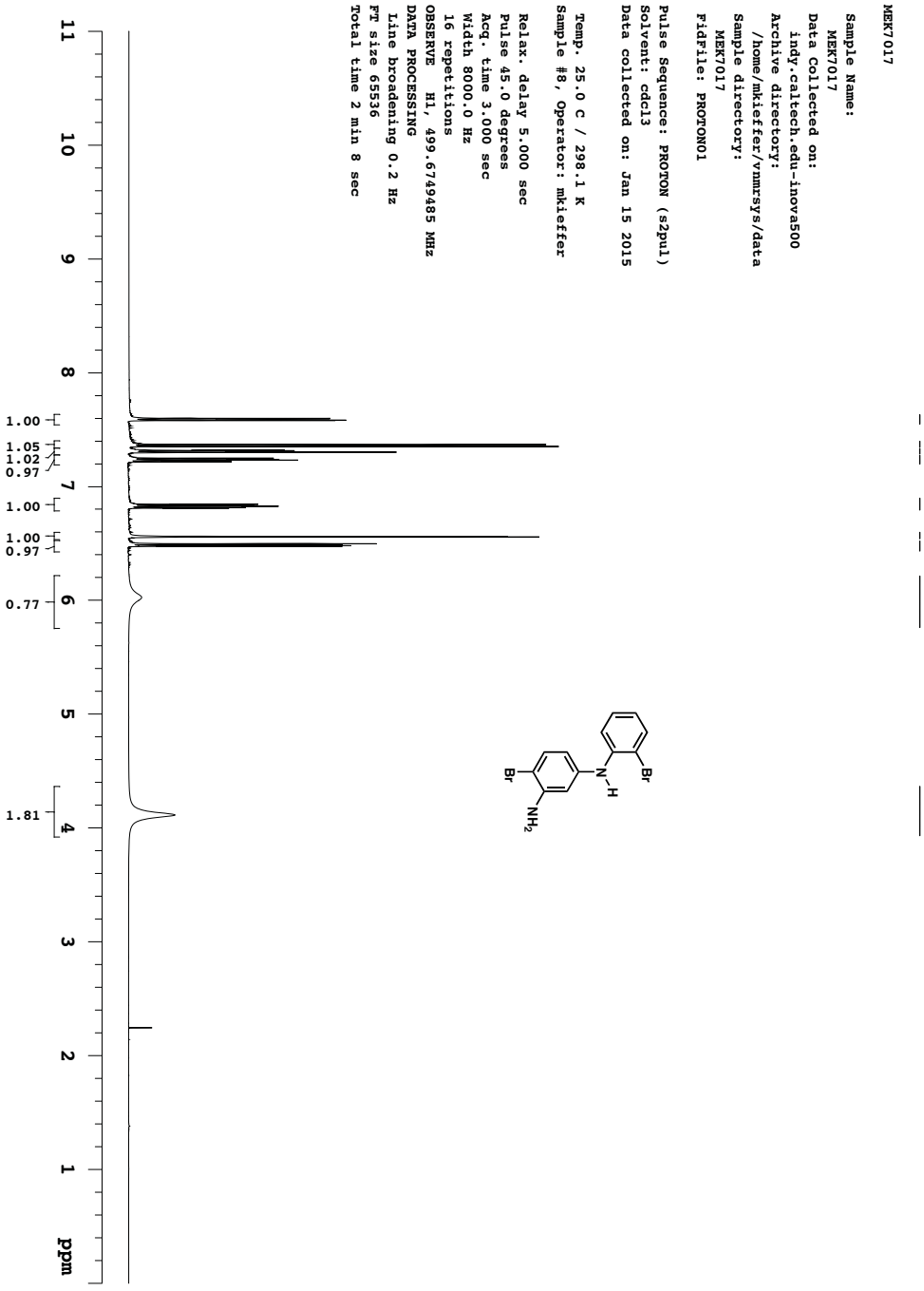

Sample Name:
MEK6062-B
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6062-B
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Sep 9 2013
Sample #8, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.6484472 MHz
DECOUPLE H1, 499.6976415 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
TES
200
180
160
140
120
100
80
60
40
20
ppm

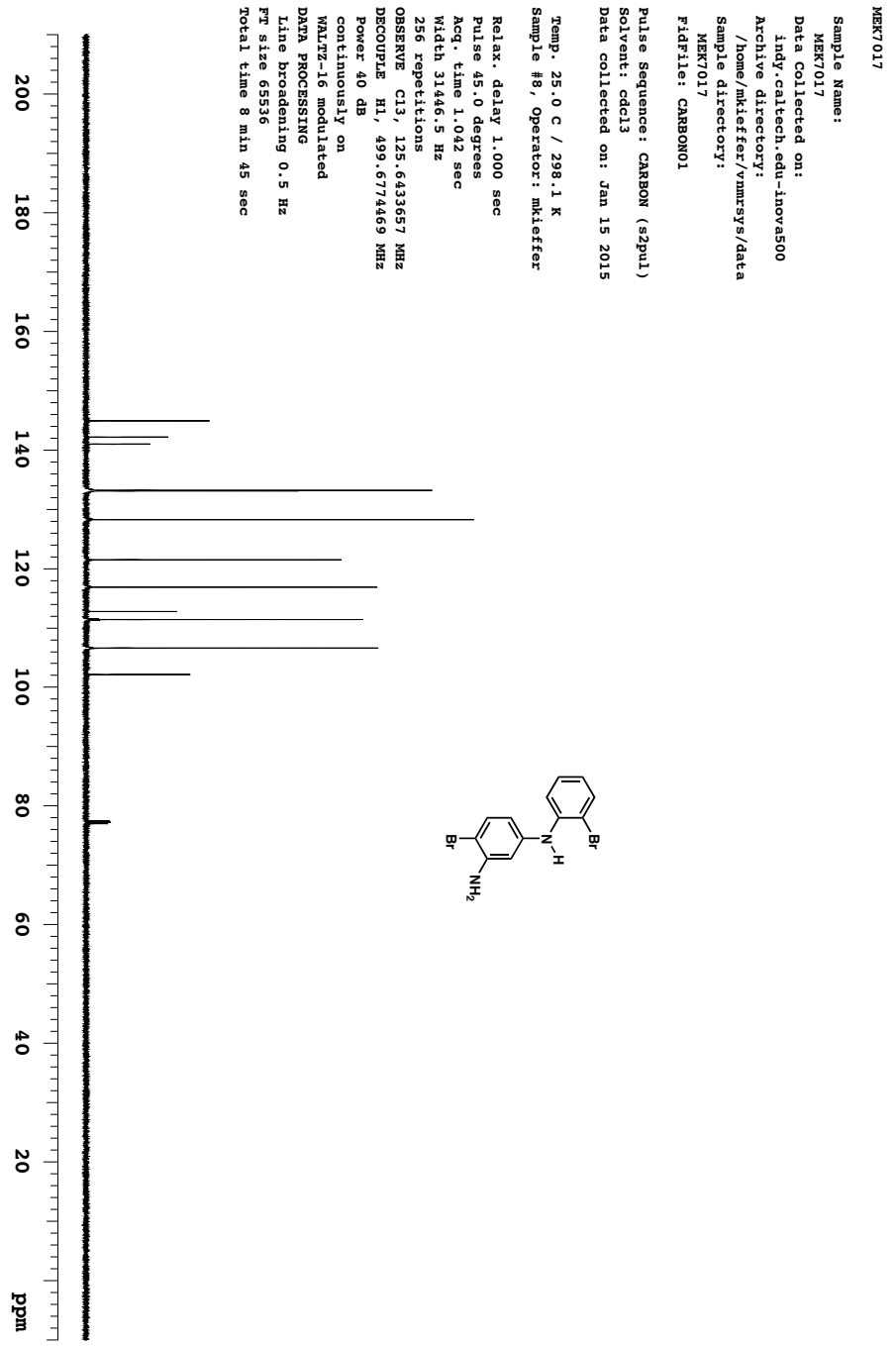

MEK6247
Sample Name:
MEK6247
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6247
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Jul 11 2014
Sample #44, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6886840 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.83
0.82
0.88
0.85
1.02
0.93
0.87
3.01
1.94
0.97
0.91
2.96
1.01
15.69
3.05
3.00
10
9
8
7
6
5
4
3
2
1
ppm
Me
O
NH
N
H
TES
HO
HN
CO2Me
O
Me
Me

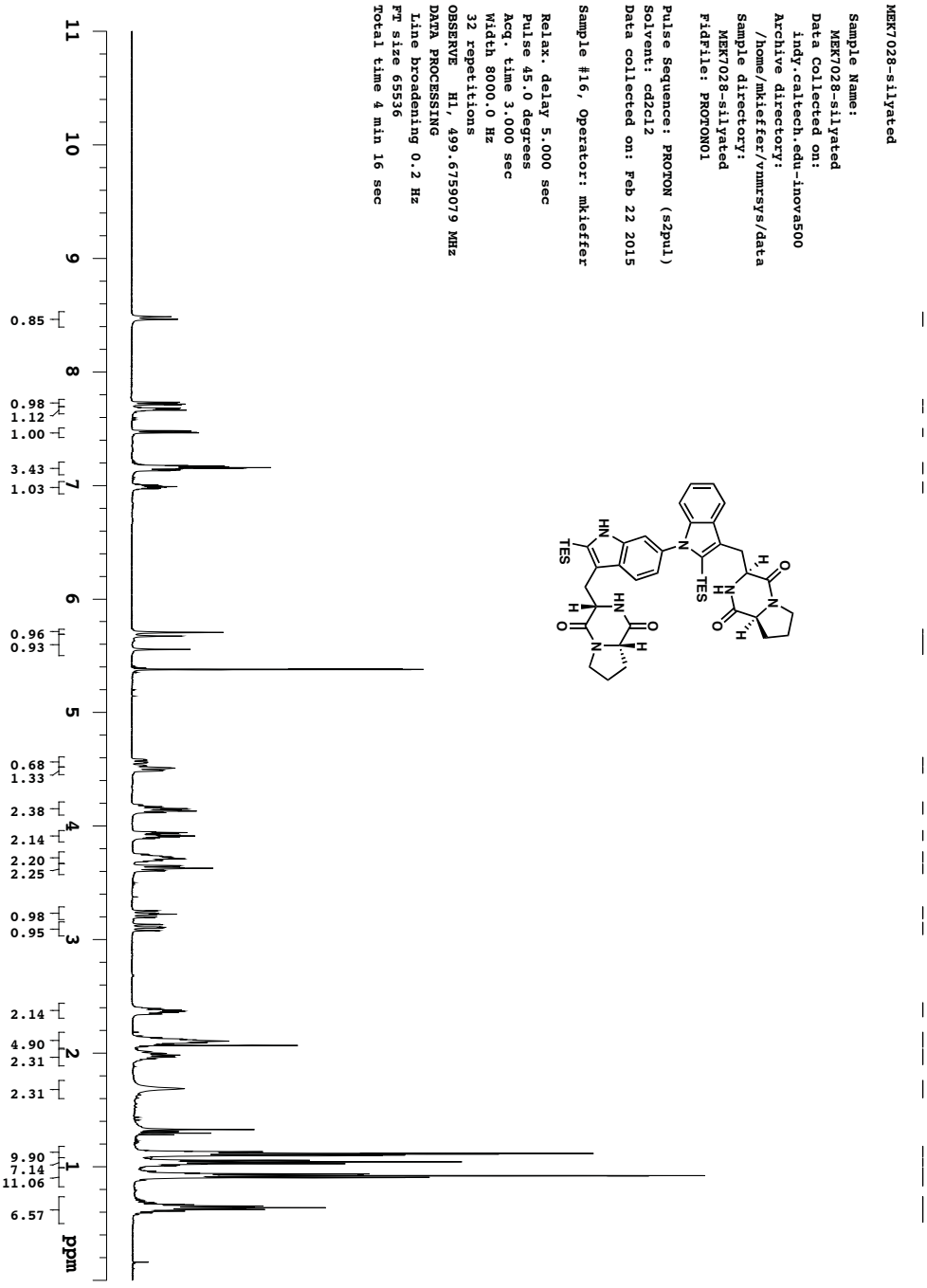

MEK6247
Sample Name:
MEK6247
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK6247
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Jul 11 2014
Sample #44, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
2000 repetitions
OBSERVE C13, 125.646704 MHz
DECOUPLE H1, 499.6911647 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 8 min
Me
O
NH
H
N
TES
HO
HN
CO2Me
O
Me
Me
200
180
160
140
120
100
80
60
40
20
ppm

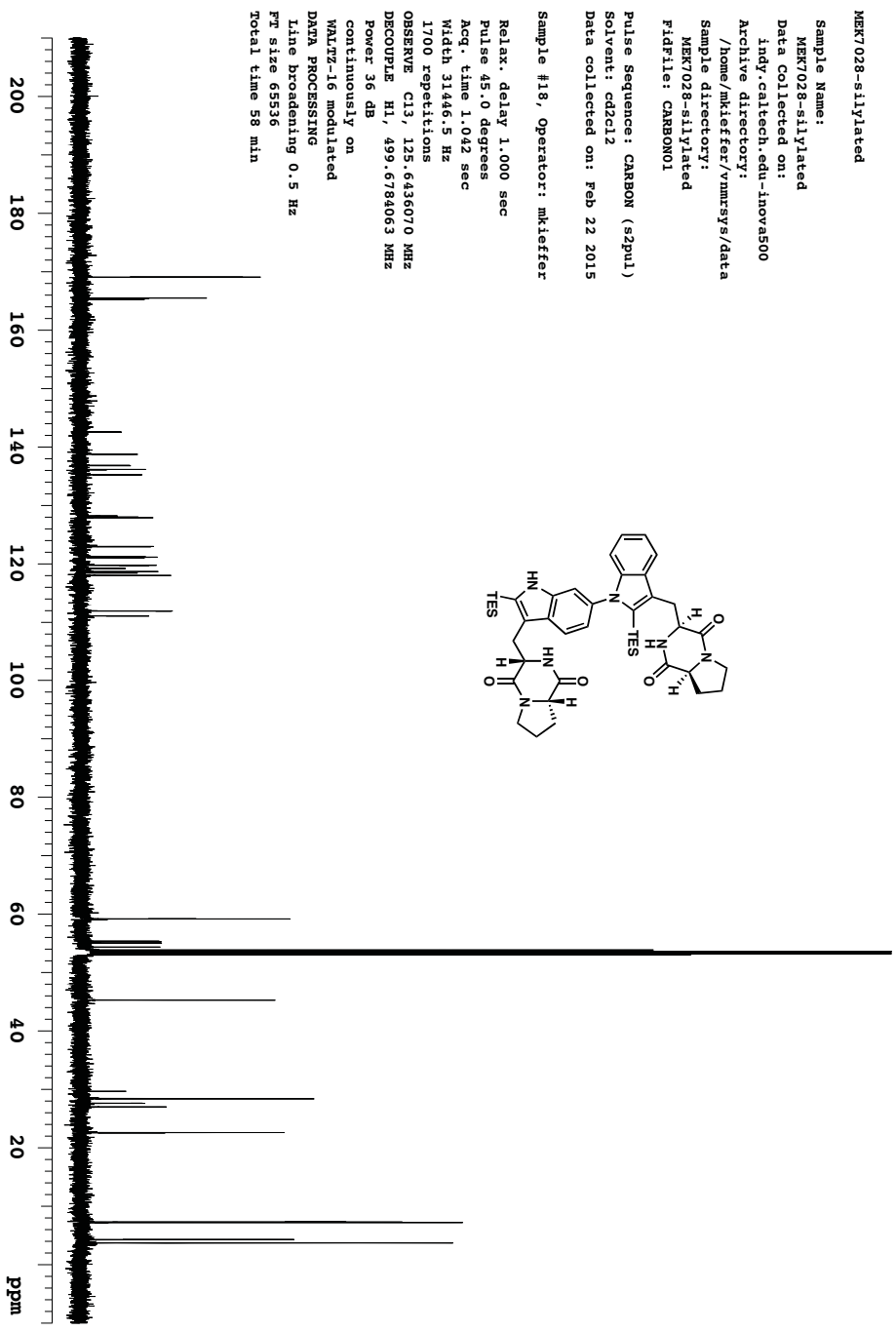

MEK7013
Sample Name:
MEK7013
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK7013
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Feb 23 2015
Sample #24, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6775918 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
N
N
H
NHBoc
O
OMe
0.90
0.98
0.99
0.99
0.99
0.77
0.92
3.00
0.99
0.95
9.40
11
10
9
8
7
6
5
4
3
2
1
ppm

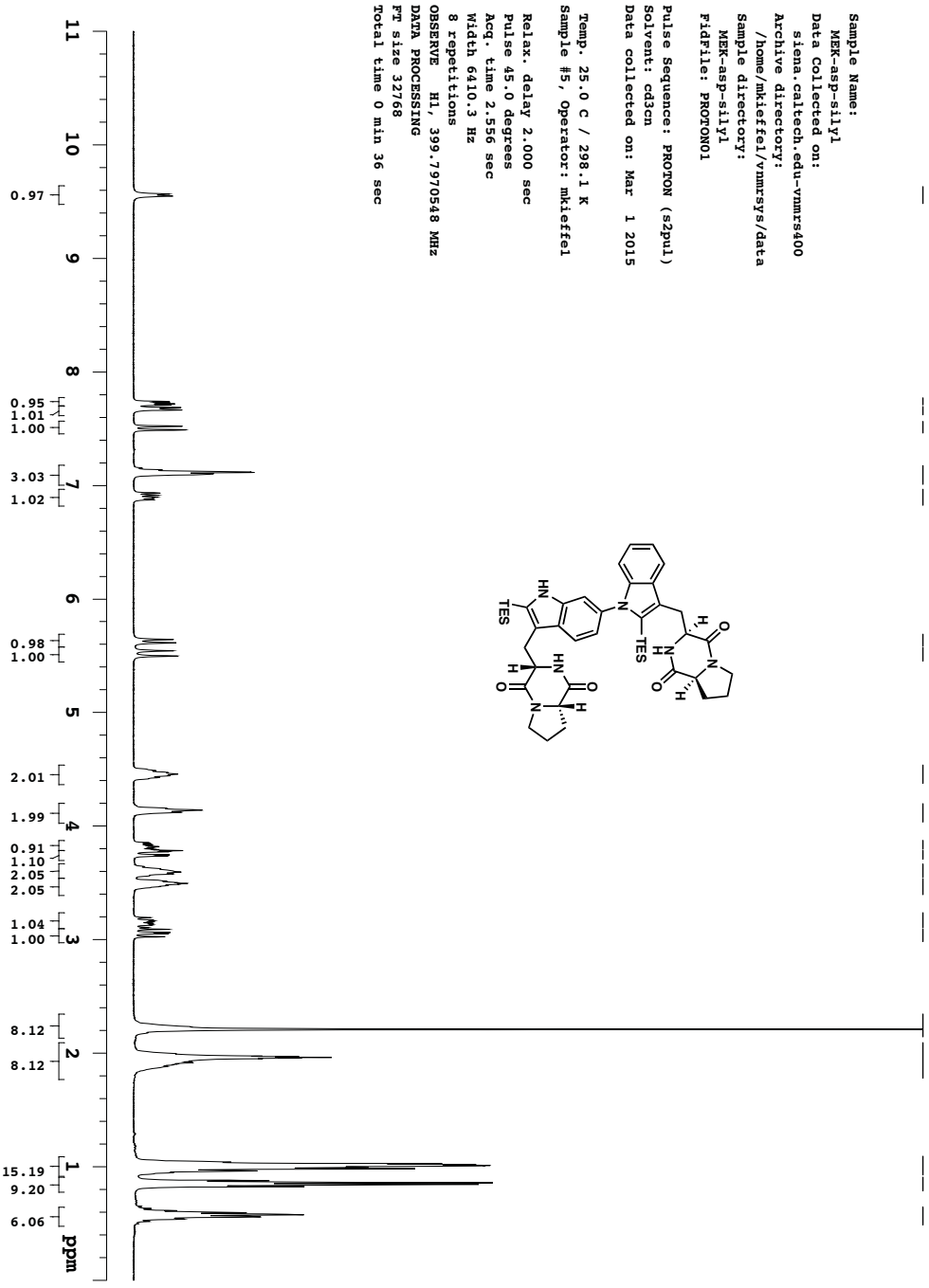

MEK7013
Sample Name:
MEK7013
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK7013
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd3cn
Data collected on: Feb 23 2015
Sample #24, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
512 repetitions
OBSERVE C13, 125.640304 MHz
DECOUPLE H1, 499.6800902 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 17 min
N
H
NHBoc
O
OMe
200
180
160
140
120
100
80
60
40
20
ppm

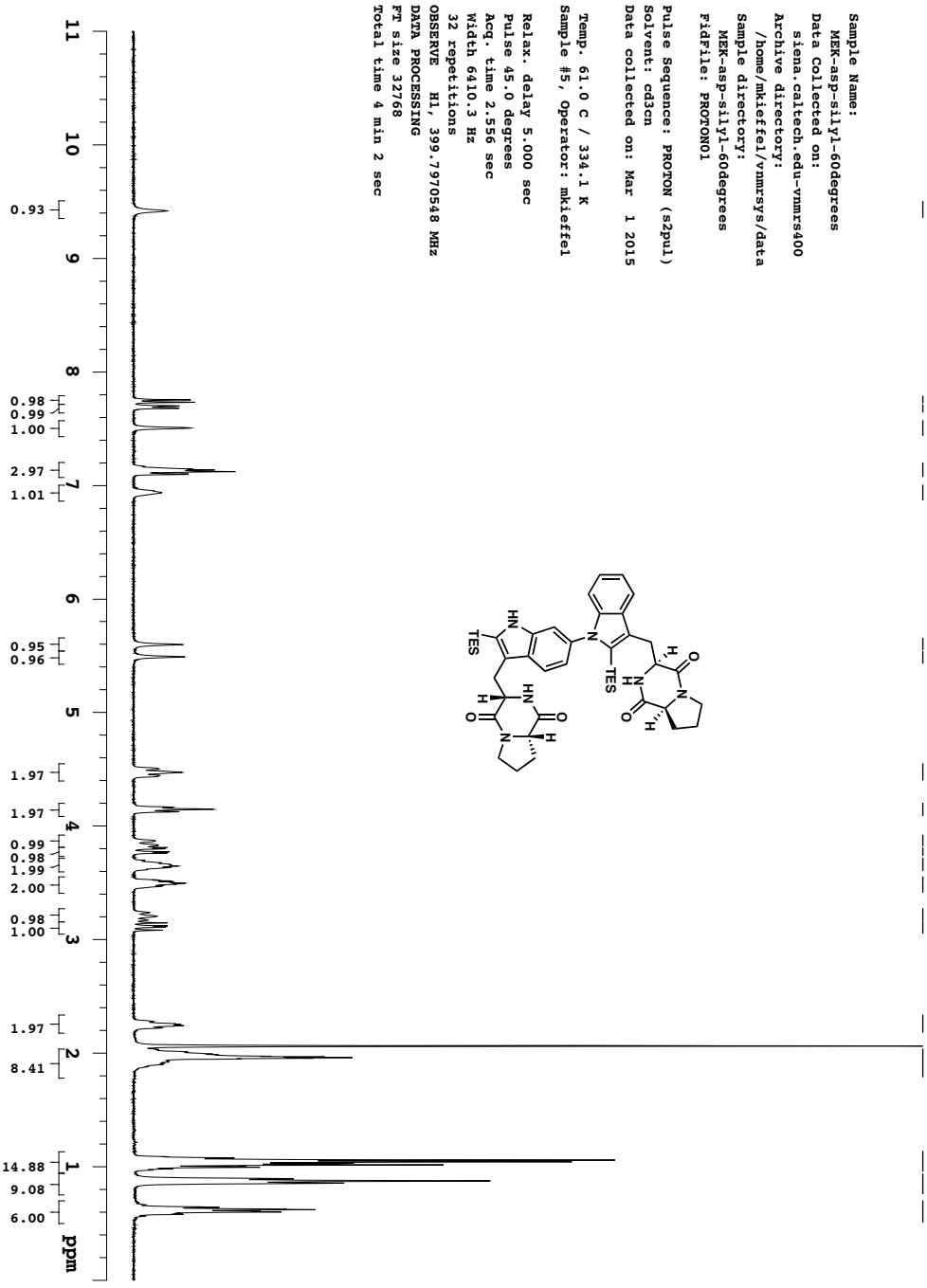

MEK7017
Sample Name:
MEK7017
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK7017
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 15 2015
Temp. 25.0 C / 298.1 K
Sample #8, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
16 repetitions
OBSERVE H1, 499.6749485 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 2 min 8 sec
Br
N
H
Br
NH2
1.00
1.05
1.02
0.97
1.00
1.00
0.97
0.77
1.81
11
10
9
8
7
6
5
4
3
2
1
ppm

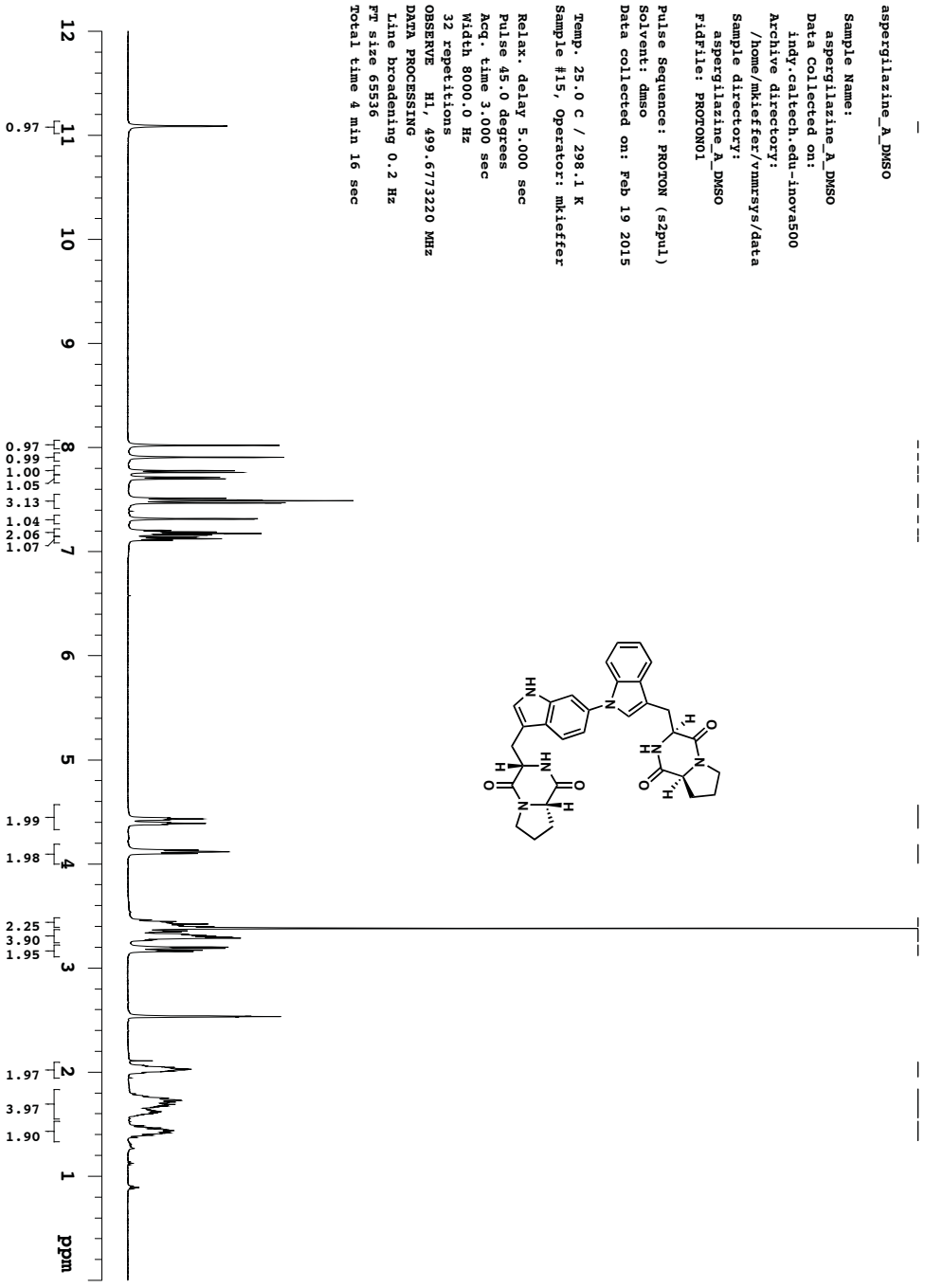

MEK7017
Sample Name:
MEK7017
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK7017
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Jan 15 2015
Temp. 25.0 C / 298.1 K
Sample #8, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
256 repetitions
OBSERVE C13, 125.6433657 MHz
DECOUPLE H1, 499.6774469 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 8 min 45 sec
Br
N
H
Br
NH2
200
180
160
140
120
100
80
60
40
20
ppm

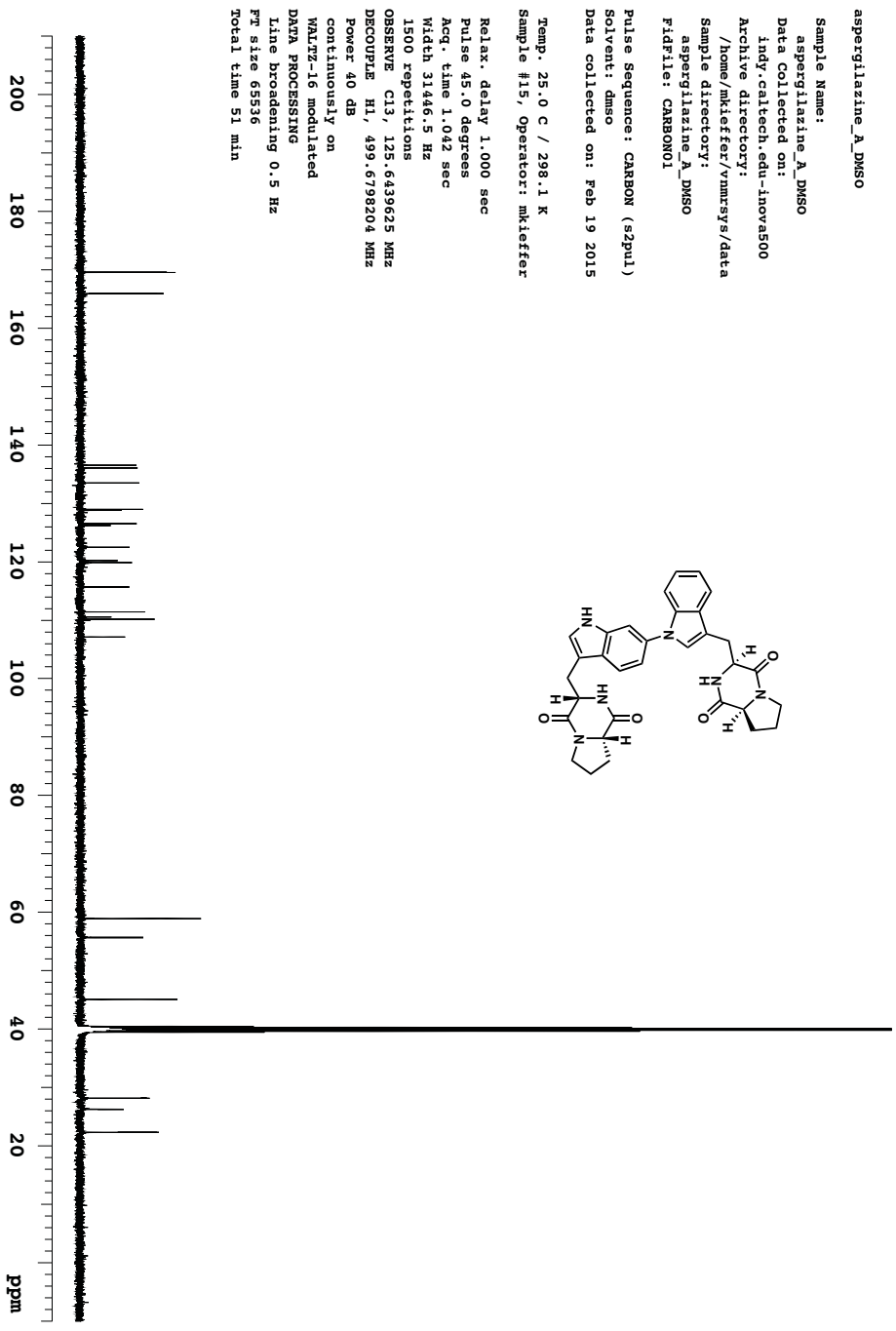

MEK7028-silyated
Sample Name:
MEK7028-silyated
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK7028-silyated
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd2cl2
Data collected on: Feb 22 2015
Sample #16, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6759079 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
TES
TES
0.85
0.98
1.12
1.00
3.43
1.03
0.96
0.93
0.68
1.33
2.38
2.14
2.20
2.25
0.98
0.95
2.14
4.90
2.31
2.31
9.90
7.14
11.06
6.57
11
10
9
8
7
6
5
4
3
2
1
ppm

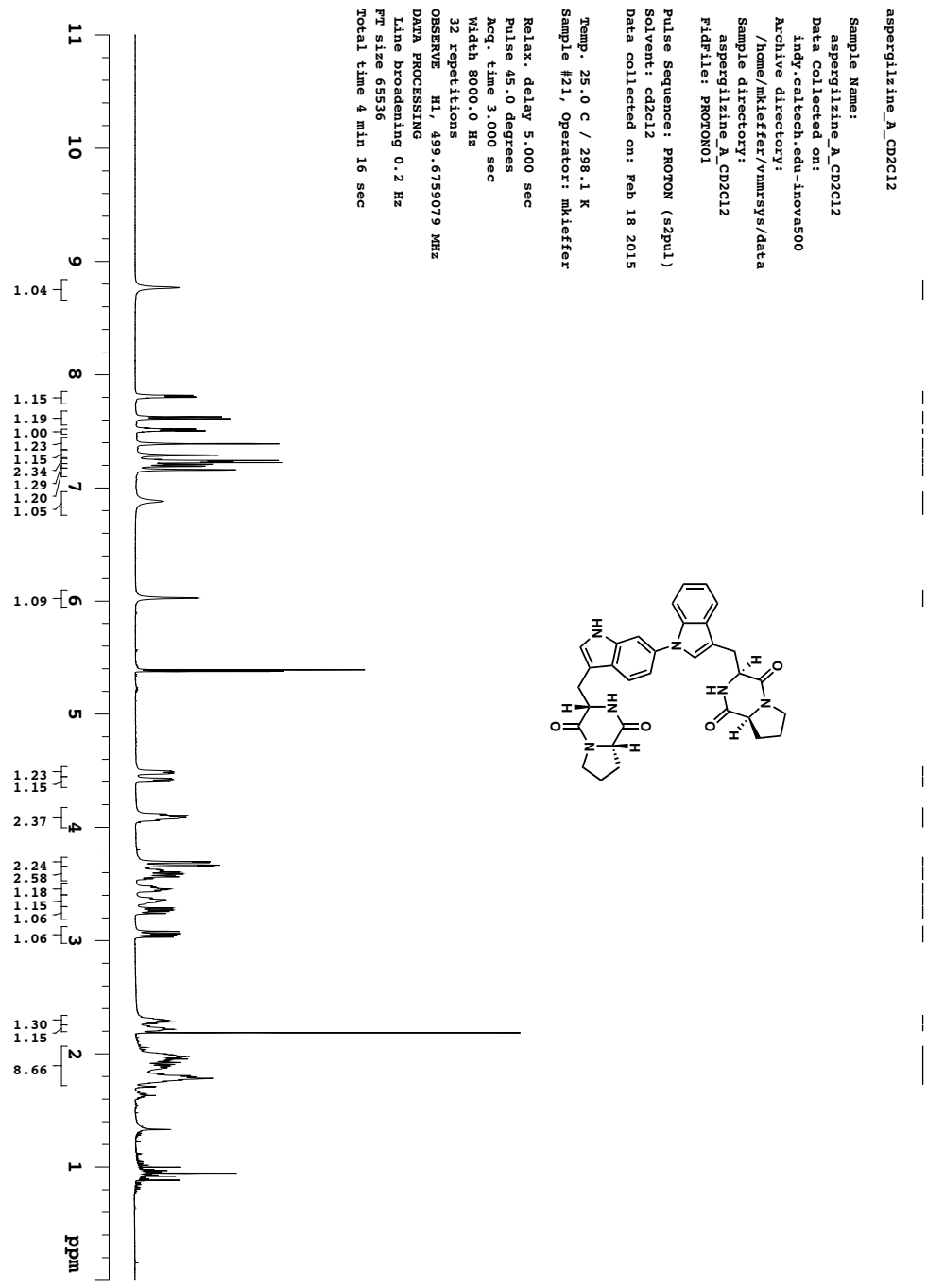

MEK7028-silylated
Sample Name:
MEK7028-silylated
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
MEK7028-silylated
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd2cl2
Data collected on: Feb 22 2015
Sample #18, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1700 repetitions
OBSERVE C13, 125.6436070 MHz
DECOUPLE H1, 499.6784063 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 58 min
TES
TES
200
180
160
140
120
100
80
60
40
20
ppm

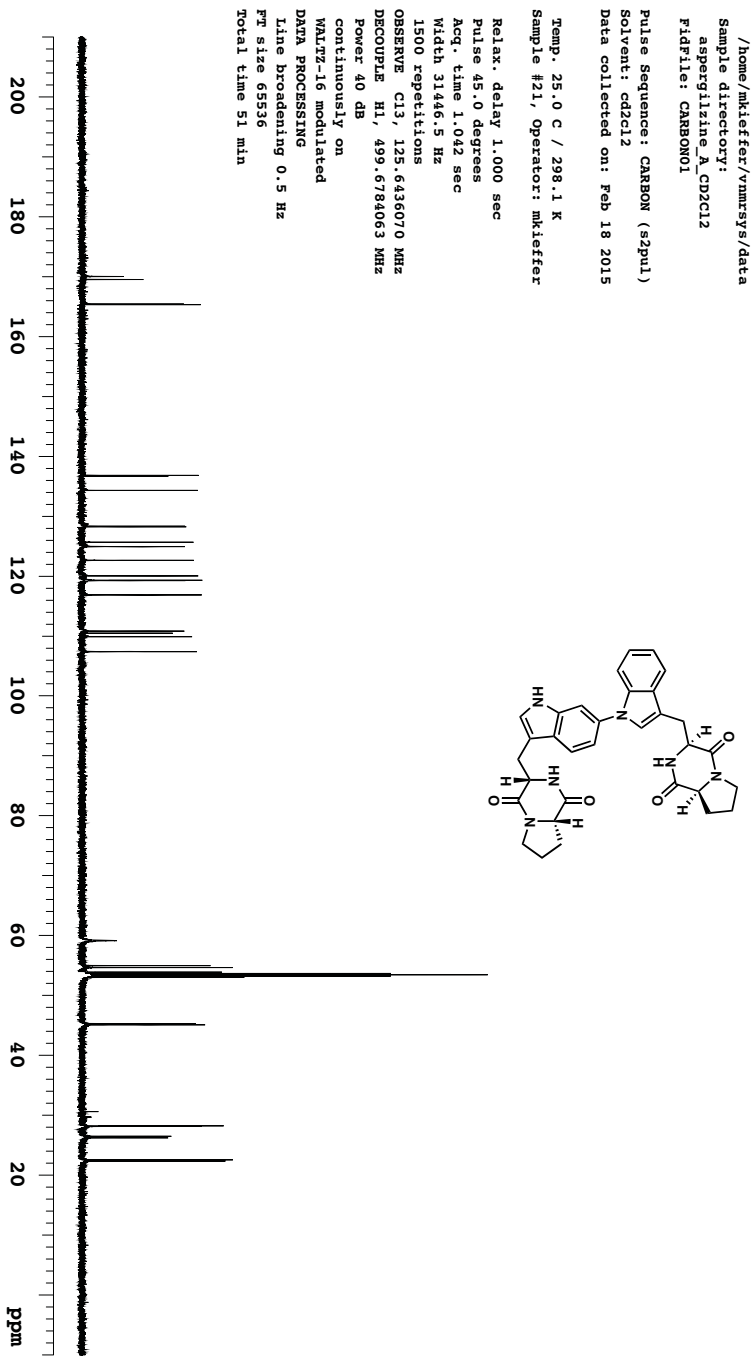

Sample Name:
MEK-asp-silyl
Data Collected on:
siena.caltech.edu-vnmrs400
Archive directory:
/home/mkieffel/vnmrsys/data
Sample directory:
MEK-asp-silyl
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Mar 1 2015
Temp. 25.0 C / 298.1 K
Sample #5, Operator: mkieffel
Relax. delay 2.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.7970548 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 36 sec
TES
TES
0.97
0.95
1.01
1.00
3.03
1.02
0.98
1.00
2.01
1.99
0.91
1.10
2.05
2.05
1.04
1.00
8.12
8.12
15.19
9.20
6.06
ppm


Sample Name:
MEK-asp-silyl-60degrees
Data Collected on:
siena.caltech.edu-vnmrs400
Archive directory:
/home/mkieffel/vnmrsys/data
Sample directory:
MEK-asp-silyl-60degrees
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3cn
Data collected on: Mar 1 2015
Temp. 61.0 C / 334.1 K
Sample #5, Operator: mkieffel
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
32 repetitions
OBSERVE H1, 399.7970548 MHz
DATA PROCESSING
FT size 32768
Total time 4 min 2 sec
0.93
0.98
0.99
1.00
2.97
1.01
0.95
0.96
1.97
1.97
0.99
0.98
1.99
2.00
0.98
1.00
1.97
8.41
14.88
9.08
6.00
11
10
9
8
7
6
5
4
3
2
1
ppm
HN
TES
N
H
O
TES
HN
H
O
N
H
O
N
H
O


asper gilazine_A_DMSO
Sample Name:
asper gilazine_A_DMSO
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
asper gilazine_A_DMSO
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: dmso
Data collected on: Feb 19 2015
Temp. 25.0 C / 298.1 K
Sample #15, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6773220 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
0.97
0.97
0.99
1.00
1.05
3.13
1.04
2.06
1.07
1.99
1.98
2.25
3.90
1.95
1.97
3.97
1.90
12
11
10
9
8
7
6
5
4
3
2
1
ppm


aspergilazine_A_DMSO
Sample Name:
aspergilazine_A_DMSO
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
aspergilazine_A_DMSO
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: dmso
Data collected on: Feb 19 2015
Temp. 25.0 C / 298.1 K
Sample #15, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6439625 MHz
DECOUPLE H1, 499.6798204 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
200
180
160
140
120
100
80
60
40
20
ppm


asperglizine_A_CD2Cl2
Sample Name:
asperglizine_A_CD2Cl2
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
asperglizine_A_CD2Cl2
FidFile: PROTON01
Pulse Sequence: PROTON (s2pul)
Solvent: cd2cl2
Data collected on: Feb 18 2015
Temp. 25.0 C / 298.1 K
Sample #21, Operator: mkieffer
Relax. delay 5.000 sec
Pulse 45.0 degrees
Acq. time 3.000 sec
Width 8000.0 Hz
32 repetitions
OBSERVE H1, 499.6759079 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 4 min 16 sec
1.04
1.15
1.19
1.00
1.23
1.15
2.34
1.29
1.20
1.05
1.09
1.23
1.15
2.37
2.24
2.58
1.18
1.15
1.06
1.06
1.30
1.15
8.66
11
10
9
8
7
6
5
4
3
2
1
ppm


asperglizine_A_CD2Cl2
Sample Name:
asperglizine_A_CD2Cl2
Data Collected on:
indy.caltech.edu-inova500
Archive directory:
/home/mkieffer/vnmrsys/data
Sample directory:
asperglizine_A_CD2Cl2
FidFile: CARBON01
Pulse Sequence: CARBON (s2pul)
Solvent: cd2cl2
Data collected on: Feb 18 2015
Temp. 25.0 C / 298.1 K
Sample #21, Operator: mkieffer
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.042 sec
Width 31446.5 Hz
1500 repetitions
OBSERVE C13, 125.6436070 MHz
DECOUPLE H1, 499.6784063 MHz
Power 40 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 51 min
200
180
160
140
120
100
80
60
40
20
ppm

ABOUT THE AUTHOR

Madeleine Eileen Kieffer was born on July 26th, 1988 in Greenville, South Carolina, but spent the majority of her early life in Milwaukee, Wisconsin. In 2006, she moved to Massachusetts to attend Wellesley College, where he developed an interest in organic chemistry working in the labs of Profs. David Haines, Larry Overman (UCI), and Andrew Smith (University of St. Andrews). Upon graduating in 2010, she relocated to Pasadena, CA to attend the California Institute of Technology, conducting her doctoral studies in the laboratory of Prof. Sarah Reisman. There, her research focused on the development of new methods for the preparation of functionalized tryptophans and their application in the synthesis of complex indole containing natural products.