Part I. **The Total Synthesis of (+)-Trehazolin: Optically Active Spiroheptadienes as Useful Precursors for the Synthesis of Aminocyclopentitols**

Part II. **An Inexpensive, Nonbasic Alternative to the Horner-Emmons Olefination Reaction**

A dissertation presented by

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The time has come to bid farewell to Southern California. It has been an interesting time and one I would not trade for anything. Before I go, there are a great many people I must thank (or blame, depending on your perspective).

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My parents and sister certainly deserve mention. They've been a steady source of love and support for as long as I can remember. They put up with the singlemindedness graduate school requires. They made the distance not so great. I would not be here without them.

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the hours of a grad student. She didn't complain about moving 3000 miles away from anyone else she knew. She thoroughly proofread everything I've ever written since we met. I literally would not have been able to do this without her.

Abstract

Polysubstituted cyclopentyl rings are a common structural feature in nature. Densely functionalized five-membered carbocycles feature prominently in many natural products. Because of this ubiquity, a versatile synthon for the construction of enantiomerically pure polyfunctional cyclopentanes would be a valuable addition to the armamentium of the organic chemist. We believed that spiro[2.4]hepta-4,6-diene-1-methanol could fill this role. As a demonstration of the power of this synthon, we describe a total synthesis of the trehalase inhibitor trehazolin. The synthesis of the trehalase inhibitor trehazolin is fairly concise; the fully functionalized aminocyclitol core is prepared in just 14 steps. Highlights include (1) preparation of optically active spiro[2.4]hepta-4,6-diene-1-methanol, (2) one-step aminohydroxylation of the cyclopentadiene moiety, (3) imidate opening with Li_2NiBr_4, and (4) the use of 1,6-anhydro-β-D-glucose in the preparation of the glycosylating agent. Optically active spiro[2.4]hepta-4,6-diene-1-methanol and its derivatives should prove valuable in the construction of other cyclopentanoid natural products.

A number of important enantioselective processes utilize allylic relationships to install chirality, and the Horner-Emmons olefination reaction has long been the gold standard for the stereoselective synthesis of these substrates from aldehydes and ketones. It was recently reported by Herrmann and coworkers that methyltrioxorhenium was capable of catalyzing the olefination of aldehydes with ethyl diazoacetate in the presence of a stoichiometric amount of triphenyl phosphine. We found that triethyl phosphite was capable of both reducing Re(VII) and promoting the reaction. With as little as 1% catalyst, a wide variety of aldehyes were converted into the corresponding (*E*)-enoates efficiently. An extremely mild, inexpensive alternative to the Horner-Emmons reaction has been described. The chemoselectivity of this process (aldehyde vs. ketone) should prove useful in organic synthesis.

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List of Abbreviations

$[\alpha]_D^{25}$	optical rotation at 589 nm and 25 °C
Å	angstrom
Ac	acetyl
aq	aqueous
Ar	aryl
Bn	benzyl
Bz	benzoyl
Bp	boiling point
Bu	butyl
℃	degrees Celcius
$CDCl_3$	deuteriochloroform
C_6D_6	hexadeuteriobenzene
cm^{-1}	reciprocal centimeters
Chx	cyclohexyl
δ	chemical shift
dba	dibenzilidineacetone
DCC	dicyclohexylcarbodiimide
DMAP	4-(dimethylamino)pyridine
DMF	N,N-dimethylforamide
DMSO	dimethylsulfoxide
E	entgegen
EDA	ethyl diazoacetate
equiv	equivalent
Et	ethyl

EtOAc	ethyl acetate
FAB	fast atom bombardment
4Å MS	4 angstrom molecular sieves
FT	Fourier transform
g	gram
h	hour
^1H	proton
HRMS	high resolution mass spectroscopy
hν	light
Hz	Hertz
i	iso
IR	infrared
J	coupling constant
L	liter
m	meta
M	molar
(M)+	molecular ion
m-CPBA	*meta*-chloroperoxybenzoic acid
MeOH	methyl alcohol
mg	milligram
MHz	megahertz
min	minute
mL	milliliter
mm Hg	millimeters of mercury
mmol	millimole
mol	mole
MOM	methoxymethyl

mp	melting point
Ms	methanesulfonyl
μL	microliter
MTO	methyltrioxorhenium
MTPA	methoxytrifluoromethylphenylacetyl
n	normal
N	normal (concentration)
NBS	N-bromosuccinamide
nm	nanometer
NMO	N-methylmorpholine N-oxide
NMR	nuclear magnetic resonance
o	ortho
p	para
pH	hydrogen ion concentration (log scale)
Ph	phenyl
ppm	parts per million
PPTS	pyridinium *para*-toluenesulfonate
Pr	propyl
Py	pyridine
R	rectus
R_f	retention factor
s	second
sec	secondary
t	tertiary
TBS	tert-butyldimethylsilyl
TES	triethylsilyl
Tf	trifluoromethanesulfonyl

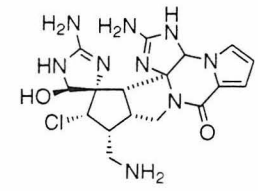
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	para-toluenesulfonyl
v/v	volume-to-volume ratio
xs	excess
Z	zusammen

Part I. The Total Synthesis of (+)-Trehazolin: Optically Active Spiroheptadienes as Useful Precursors for the Synthesis of Aminocyclopentitols

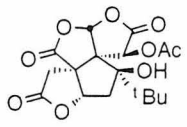
Introduction

Polysubstituted cyclopentyl rings are a common structural feature in nature (Figure 1). Densely functionalized five-membered carbocycles are prominent in natural products: for example, palau' amine (**1**),[1] bilobalide (**2**),[2] mannostatin A (**3**),[3] the sirodesmins (**4**),[4] allosamidin (**5**),[5] streptazolin (**6**),[6] and azadirachtin (**7**).[7] The syntheses of these molecules, when they exist, are as diverse as the target molecules themselves.

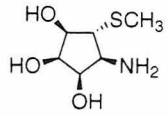
Figure 1. Cyclopentanoid natural products.



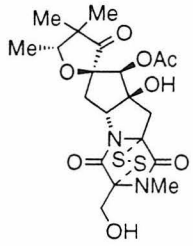
Palau' Amine
1



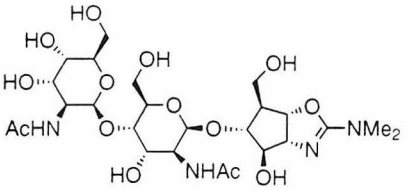
Bilobalide
2



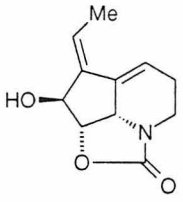
Mannostatin A
3



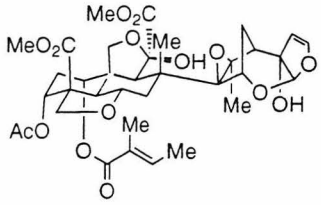
Sirodesmin A
4



Allosamidin
5



Streptazolin
6



Azadirachtin
7

---

1 Kinnel, R. B.; Gehrken, H.-P.; Scheuer, P. J. *J. Am. Chem. Soc.* **1993**, *115*, 3376.

2 (a) Corey, E. J.; Su, W. -g. *J. Am. Chem. Soc.* **1987**, *109*, 7534. (b) Crimmins, M. T., Jung, D. K.; Gray, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 3146.

3 Aoyagi, T.; Yamamoto, T.; Kojiri, K.; Morishima, H.; Nagai, M; Hamada, M.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1989**, *42*, 882.

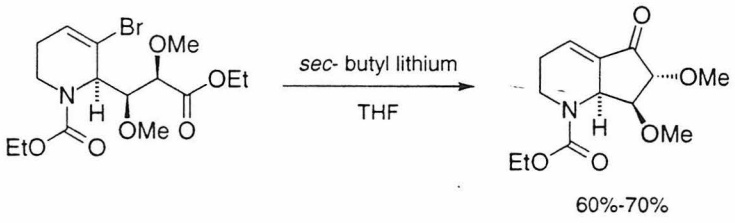
4 Curtis, P.J.; Greatbanks, D.; Hesp, B. *J. Chem. Soc., Perkins Trans. I* **1977**, 180.

5 Sakuda, S.; Isogai, A.; Matsumoto, S.; Suzuki, A. *Tetrahedron Lett.* **1986**, 2475.

6 Drautz, H.; Zahner, H; Kupfer, E.; Keller-Schlierlein, W. *Helv. Chim. Acta* **1981**, *64*, 1752.

7 Kraus, K.; Bokel, M.; Klenk, A.; Pohnl, H. *Tetrahedron Lett.* **1985**, *26*, 6435.

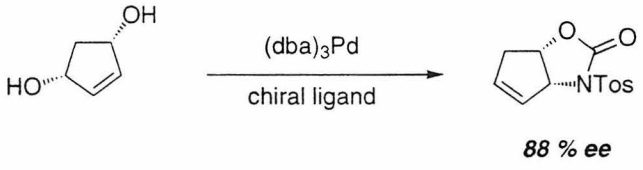
Figure 2. Cyclization of advanced acyclic precursor to streptazolin.



Because of the great strides made in acyclic stereocontrol (both enantioselection and diastereoselection), many successful syntheses have depended on the cyclization of a functionalized acyclic precursor. This strategy served Overman well in the synthesis of streptazolin (Figure 2).[8] Functionalization of a cyclopentadiene is also appealing. Trost's syntheses of mannostatin A and allosamidin[9] and Ganem's synthesis of mannostatin[10] employ this strategy (Figure 3). Neither strategy is without hazard, however. Closure of an acyclic structure is not invariably trivial, and conditions compatible with sensitive functionality can be difficult to find. When functionalizing a cyclopentadiene, difficulty arises in the enantioselective derivitization. In this regard, Trost and Ganem achieved only limited success, obtaining enantiomeric excesses of 44% and 80% respectively.[9,10]

Figure 3. Enantioselective steps of mannostatin syntheses.

Trost[9]

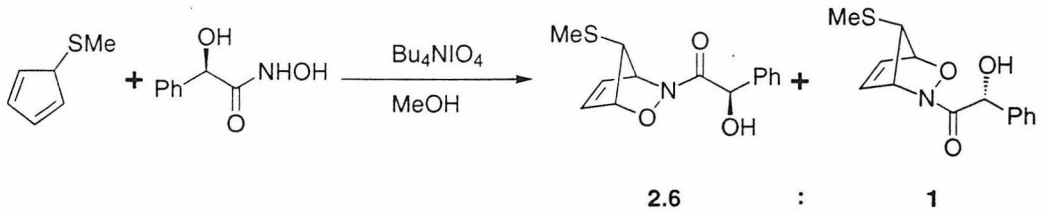


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8 Flann, C. J.; Overman, L. E. *J. Am. Chem. Soc.* **1987**, *109*, 6115.
9 Trost, B. M.; Van Vranken, D. L. *J. Am. Chem. Soc.* **1993**, *15*, 444.
10 King, S. B.; Ganem, B. *J. Am. Chem. Soc.* **1991**, *113*, 5089.

Figure 3 (cont.)

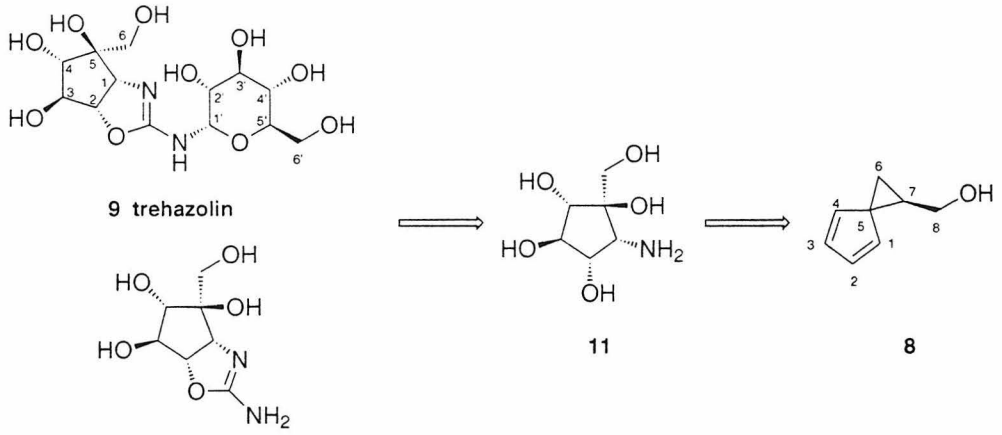
Ganem[10]



2.6 : **1**

Because of these difficulties and the wide variety of cyclopentanoid natural products, a versatile synthon for the construction of enantiomerically pure polyfunctional cyclopentanes would be a valuable addition to the armamentium of the organic chemist. We felt that spiro[2.4]hepta-4,6-diene-1-methanol (**8**) could fill this role. As a demonstration of the power of this synthon, the total synthesis of the trehalase inhibitor (+)-trehazolin (**9**) is described (Figure 4).[11]

Figure 4. Retrosynthesic analysis of (+) -trehazolin and trehalamine.



9 trehazolin

10 trehalamine

11

8

[11] Ando, O.; Satake, H.; Itoi, K; Sato, A.; Nakajima, M.; Takahashi, S.; Haruyama, H.; Ohkuma, Y.; Kinoshita, T.; Enokita, R. *J. Antibiot.* **1991**, *44*, 1168.

Background

Trehazolin was isolated in 1990 from the culture broth of *Micromonospora* by Japanese workers. It has proven a potent inhibitor of a number of trehalase enzymes. Both silkworm trehalase and porcine trehalase were inhibited at nanomolar concentrations.[11] The aglycon of trehazolin, trehalamine (**10**), is itself a natural product which was first isolated from the culture broths of *Micromonospora* and *Amycolatopsis* in 1992.[12] Trehalamine, however, is not as potent a trehalase inhibitor as trehazolin; it inhibits silkworm trehalase only at a concentration of 1.8×10^{-4} M.

The structures of trehalamine and trehazolin were determined using spectroscopic techniques and later confirmed by unambiguous synthesis. Interestingly, trehalostatin, a natural product initially identified as the C(4) epimer of trehazolin, was later shown to be identical to trehazolin, illustrating one of the inherent difficulties of substituted cyclopentanes-structural proof.[13] The conformational mobility of five-membered rings renders coupling constant analysis difficult and the close proximity of nearly all protons makes it difficult to obtain definitive nuclear Overhauser enhancements.

In addition to their biology, these molecules are intriguing to the synthetic chemist, for the challenge of five contiguous stereocenters on a cyclopentane is an alluring one. Presently, there are four other syntheses in the literature. In the Ogawa synthesis,[14] a derivative of *myo*-inostitol (**12**) is oxidatively degraded to the dialdehyde **13**. Dialdehyde **13** undergoes a Henry reaction to provide the desired 5-amino-1,2,3,4- cyclopentatetrol **14** as a minor product in approximately 5% yield. An additional 12 steps are required to obtain the racemic aminocyclitol portion of trehazolin **11.**

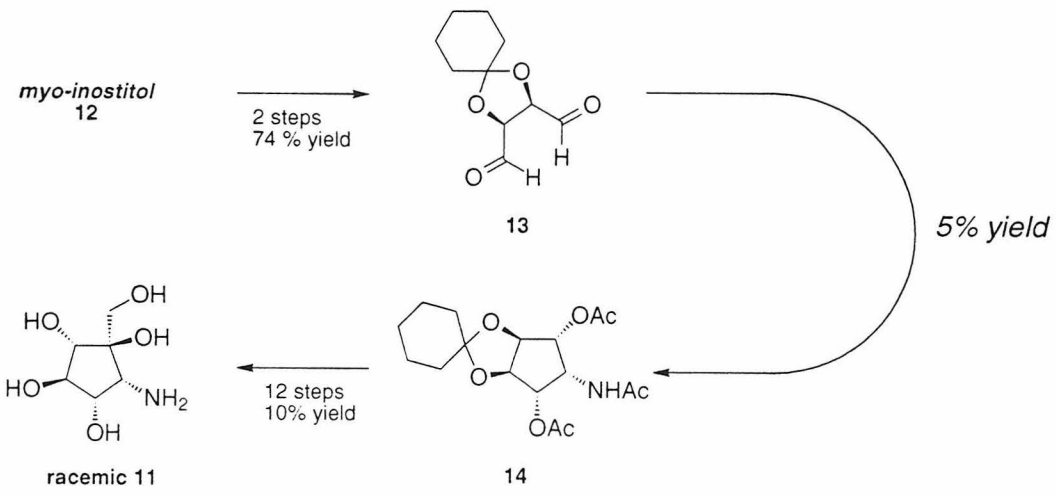
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12 Ando, O.; Nakajima, M.; Hamano, K.; Itoi, K.; Takahashi, S.; Takamatsu, Y.; Sato, A.; Enokita, R.; Okazaki, T.; Haruyama, H.; Kinoshita, T. *J. Antibiot.* **1993**, *46*, 1125.

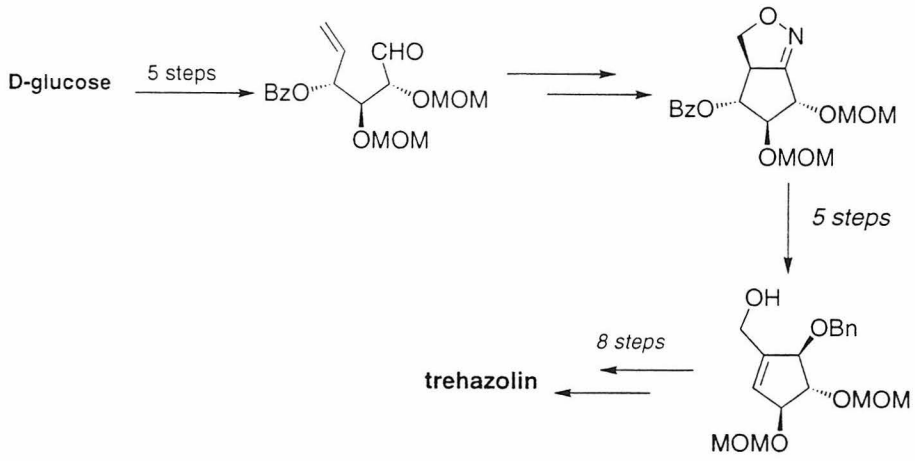
13 Nakayama, T.; Amachi, T.; Murao, S.; Sakai, T.; Shin, T.; Kenny, P. T. M.; Iwashita, T.; Zagorski, M.; Komura, H.; Nomoto, K. *J. Chem. Soc., Chem. Comm.* **1991**, 921.

Figure 5. Literature routes to the trehazolin core.

Ogawa[14]



Shiozaki[15]



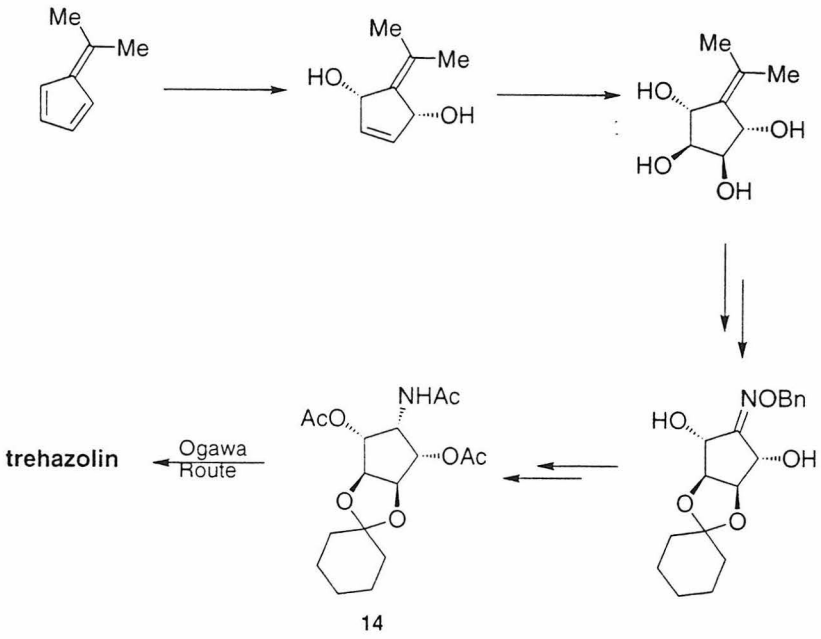
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14 Ogawa, S.; Uchida, C. *J. Chem. Soc., Perkins Trans. I* **1992**, 1939.

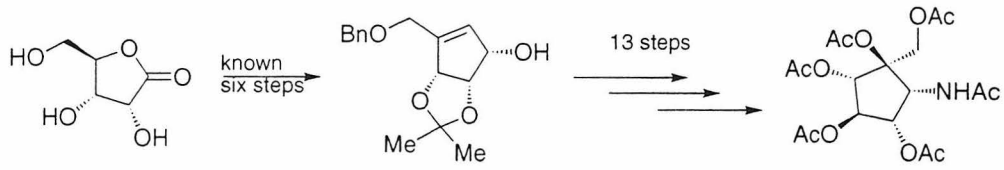
15 Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 10065.

Figure 5 (cont.)

Ganem[16]



Knapp[17]



In the first enantiospecific synthesis,[15] Shiozaki generates trehalamine from D-glucose in 18 steps. More recently, Ganem has completed a formal synthesis of trehazolin by synthesizing meso-aminocyclitol **14** from dimethylfulvene.[16] This aminocyclitol is an intermediate in the Ogawa route. Finally, Knapp has prepared the hexaacetate from ribonic acid in 18 steps.[17]

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16 Goering, B. K.; Li, J.; Ganem, B. *Tetrahedron Lett.* **1995**, *36*, 8905.

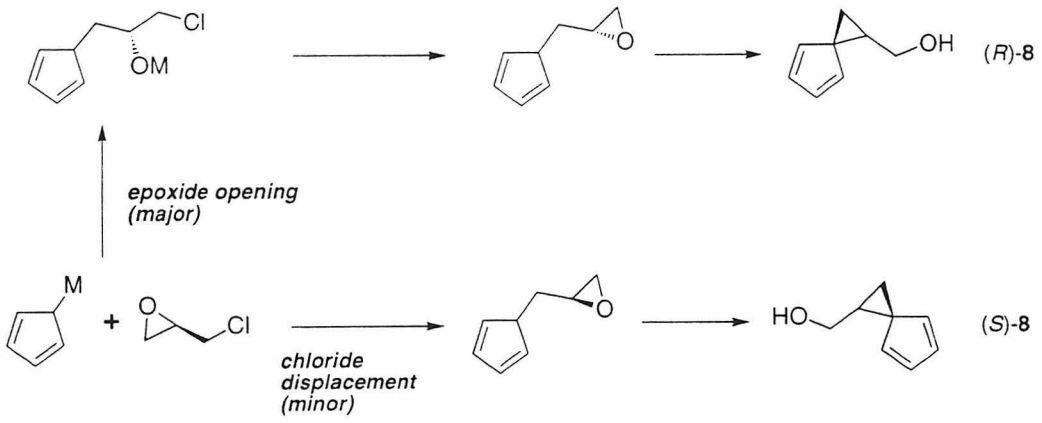
17 Knapp, S.; Purandare, A.; Rupitz, K.; Withers, S. G. *J. Am. Chem. Soc.* **1994**, *116*, 7461.

Basically, two approaches to the synthesis of trehazolin have been taken. Knapp and Shiozaki chose to convert stereochemically-dense carbohydrate starting materials, *via* multistep sequences, into appropriately sized carbocycles. The other tack, taken by Ganem and Ogawa, fairly efficiently assembles the aminocyclitol from achiral starting materials, but requires a late stage resolution to obtain optically pure materials. The route described here follows a third path–the starting material is chiral, but contains the bare minimum of extraneous functionality. This sparseness should hopefully give intermediate **8** a fair degree of versatility.

Preparation of (-)Spiro[2.4]hepta-4,6-diene-1-methanol (8).

Spiro[2.4]hepta-4,6-diene-1-methanol was first synthesized in 1962 by Schaltegger,[18] and has been used in a number of clever racemic syntheses.[19] However, a thorough literature search revealed no precedent for the synthesis or resolution of the racemate. Therefore, a means of obtaining optically pure **8** was the first goal.

Figure 6. Two pathways for spirocyclization.



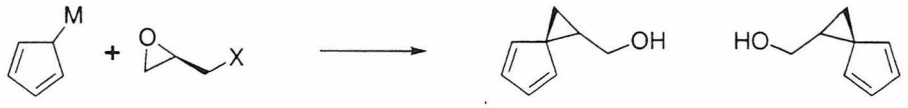
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18 (a) Bangert, K.; Boekelheide, V. *Tetrahedron Lett.* **1963**, 1119. (b) Schaltegger, H. *Helv. Chim. Acta* **1962**, *45*, 1368.

19 Lei, B.; Fallis, A. G. *J. Org. Chem.* **1993**, *58*, 2186. (b) Corey, E. J.; Shiner, C. S.; Volante, R. P.; Cyr, C. R. *Tetrahedron Lett.* **1975**, 1161.

At first glance, the solution would appear to be simple regiocontrol with regard to the epichlorohydrin–chloride displacement yields one enantiomer and epoxide opening the other (Figure 6). To test this hypothesis, a number of different conditions (Table 1) were tried, some of which proved more conducive to epoxide opening than others.

Table 1. Initial attempts at enantioselective spirocyclization.



(*R*)-**8** (*S*)-**8**

Metal	X	Additives	Solvent	Ratio ((*R*):(*S*))	ee(%)[a]	yield (%)
Na	OTosylate	None	THF	1:1	0	50
K	Cl	18-crown-6	THF	3:1	50	50
Na	Cl	none	THF	5:1	66	38
Li	Cl	none	THF	10:1	81	42
Li	Cl	$AlMe_3$	THF	6.5:1	73	36
Li	Cl	none	Et_2O	5.6:1	70	36
MgBr	Cl	none	THF	1:19	90	<5

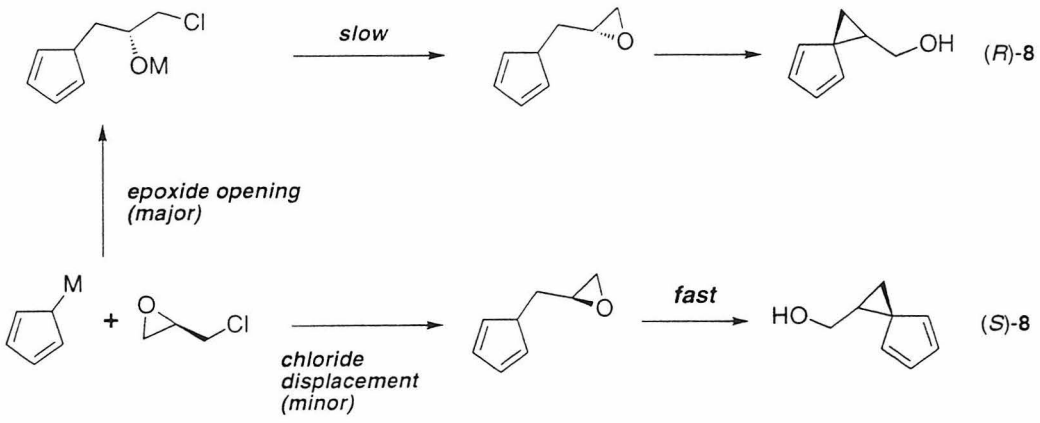
[a](*R*)- and (*S*)-**8** were converted to the corresponding (*S*)-MTPA esters.[20] The diastereomeric ratios were determined by integration of the ^1H NMR (300 MHz, C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H).

Our initial foray was somewhat disappointing: treatment of glycidol tosylate (91 % ee) with cyclopentadienyl sodium and excess NaH gave **8** in modest yield (50%) and with no enantioselection. Switching from glycidol tosylate to epichlorohydrin (91% ee) yielded a small improvement in enantioselection (66%), favoring epoxide opening. It was hoped that increasing the Lewis acidity of the counterion would favor epoxide opening even more; and, indeed, the use of cyclopentadienyl lithium afforded **8** in moderate yield (42%) and moderate selectivity (81% ee). This success suggested that even more acidic conditions might improve the enantioselection to useful levels. However, the addition of a stoichiometric amount of

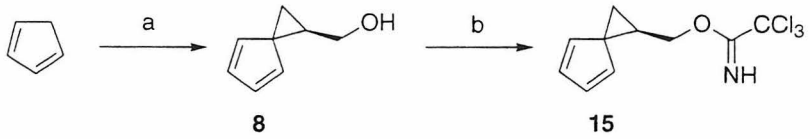
[20] Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

trimethylaluminum actually decreased both the yield (36%) and the ee (73 %). Switching to a less coordinating solvent had a similarly deleterious effect. The most surprising result came next–when cyclopentadienyl magnesium bromide was employed, **8** was obtained in extremely poor yield (5 %) but with good selectivity (90% ee) opposite that which was previously obtained. This result suggested that the observed optical purity was not solely the product of the initial reaction with the epichlorohydrin. The seemingly anomalous results could be neatly explained if the following were true: first, the addition to epichlorohydrin proceeds with excellent selectivity (>20:1) favoring epoxide opening; second, the closure to the epoxide is slow with Lewis acidic counter ions; and third, the intramolecular opening of the epoxide is fast. This allows for a kinetic resolution of sorts to occur-the minor product, which arises from initial chloride displacement, is quickly converted to (*S*)-**8**. The major product, however, is stalled at the secondary alcohol, indefinitely, it seems, in the case of the Grignard reagent. This discovery prompted an obvious and successful solution–longer reaction times. When allowed to stir for 8 or more hours, the reaction of the cyclopentadienyl lithium and epichlorohydrin produced **8** in 59% yield and greater than 90% ee.

Figure 7. Speed of spirocyclization affects observed ee.



Scheme 1.[a] Preparation of trichloroimidate **15**.

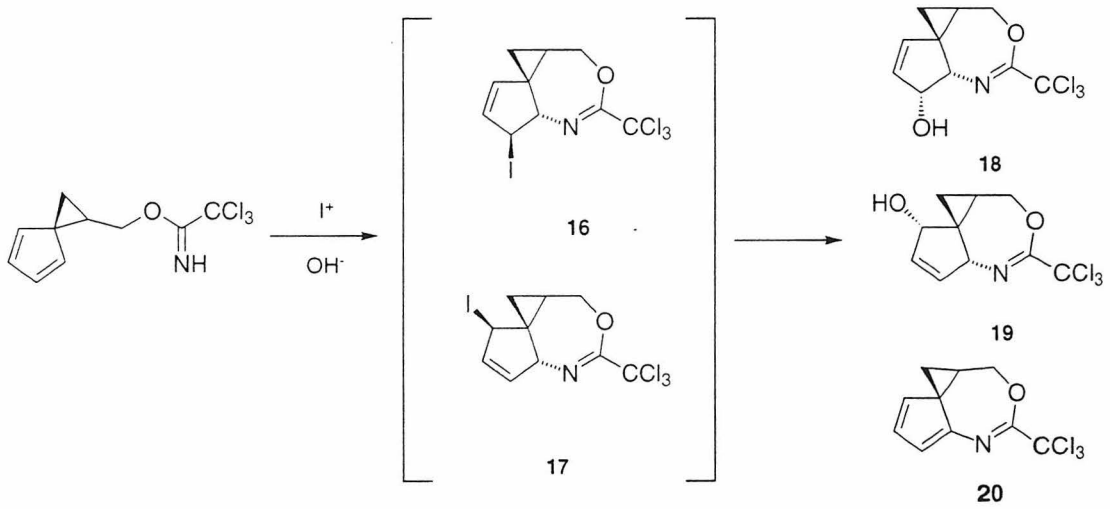


[a]Conditions: (a) *i.* *n*BuLi, THF, (*R*)-epichlorohydrin, NaH, 60%; (b) NaH, CCl_3CN, 95%.

Initial route to trehazolin core.

The first two stereocenters were to be set *via* an iodolactamization.[21] Toward that end, **8** was converted to the tricholorimidate **15**;[22] however, when treated with a number of halonium sources (I_2, NBS, di-*sym*-collidine-bromonium perchlorate[23]), **15** gave not the anticipated trans-aminoiodides (**16**, **17**), but instead the *cis*-aminoalcohols (**18**, **19**).

Figure 8. Products of the iodolactamization.



All attempts to conduct the reaction under nonaqueous conditions led to decomposition of the starting material; the major product isolated, albeit in poor yield,

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21 Pauls, H. W.; Fraser-Reid, B. *J. Org. Chem.* **1983**, *48*, 1392.
22 Overman, L. E. *J. Am. Chem. Soc.* **1974**, *96*, 597.
23 Lemieux, R.U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190.

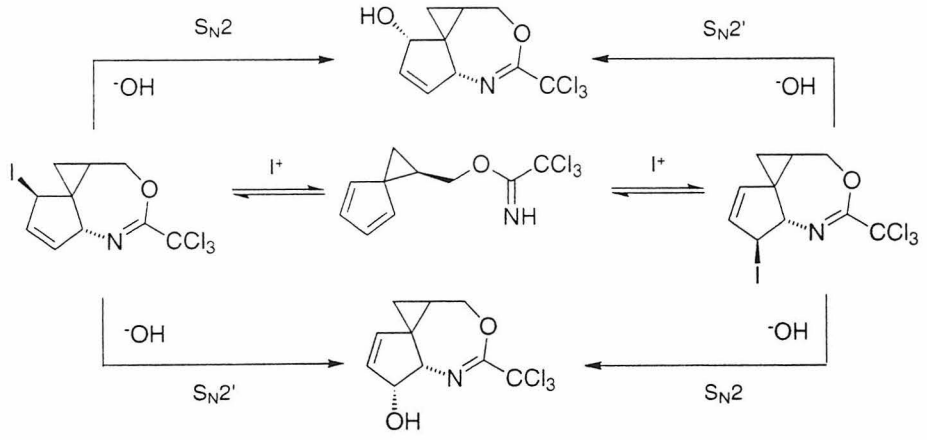
(<20%) was β,γ-unsaturated enamine **20**. The regiochemistry did not vary noticeably with either temperature or halonium source. However, solvent did influence the product ratio, as summarized in Table 2. The observed solvent effect is difficult to interpret, since the selectivity could occur at either of two junctures, and the formation of the intermediate iodide could be reversible. Because each iodide is able to undergo S_N2 or S_N2' displacement, both alcohol regioisomers can be generated from either iodide.[24]

Table 2. Solvent dependence of iodolactamization.

Solvent	Ratio (**19**:**18**)[a]
Diethyl ether	1.5:1
Tetrahydrofuran	2:1
Benzene	3:1
Acetone	3.75:1
Acetonitrile	4:1
Dichloromethane	5.2:1

[a]The ratio was determined by integration of the C(3)H at δ 5.85 ppm (major) relative to the C(3)H proton signal at δ 5.75 ppm (minor) in the ^{1}H NMR spectrum.

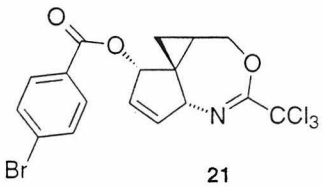
Figure 9. Possible pathways to the observed aminoalcohol products.



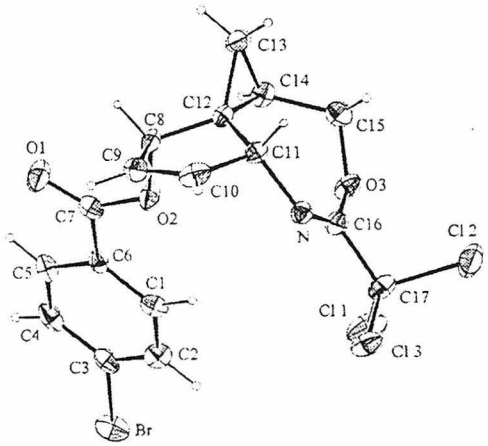
24 Bromination of acyclic 1,3 dienes to give 1,2 (kinetic) versus 1,4 (thermodynamic) addition products has been investigated as a function of reaction solvent and temperature, see: (a) Farmer, E.H.; Lawrence, C. D.; Thorpe, J. F. *J. Chem. Soc.* **1928**, 729. (b) Hatch, L. F.; Gardner, P. D.; Gilbert, R. E. *J. Am. Chem. Soc.* **1959**, *81*, 5943. (c) Heasley, V. L.; Frye, C. L.; Gore, R. T.; Wilday, P. S. *J. Org. Chem.* **1968**, *33*, 2342. (d) Heasley, V. L.; Heasley, G. E.; Taylor, S. K.; Frye, C. L. *J. Org. Chem.* **1970**, *35*, 2967.

In terms of overall yield acetonitrile was the solvent of choice; the major regioisomer was typically obtained in 60% yield. While the reaction in methylene chloride gave better regio- selectivity, the yields were degraded by the presence of **20**, and the 1,4 product (**19**) was obtained in only 40% yield. Both the relative and absolute stereochemistries were confirmed at this stage with a single crystal X-ray structure of *p*-bromobenzoate **21**.

Figure 10. Crystal structure of *p*-bromobenzoate **21**.



21

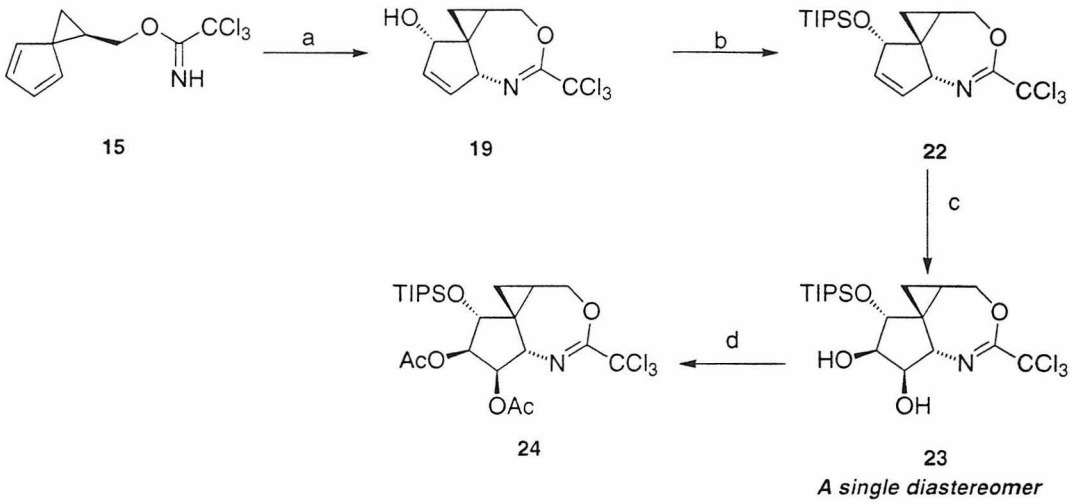


Alcohol **19** was converted to triisopropyl silyl ether **22** under standard conditions in 95% yield.[25] Dihydroxylation of **21** was facile, giving diol **23** in 93% yield as a single diastereomer.[26] Diol **23** was treated with excess acetic anhydride and DMAP, giving **24** in 85% yield.

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[25] Corey, E. J.; Cho, H.; RÅcker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.
[26] Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

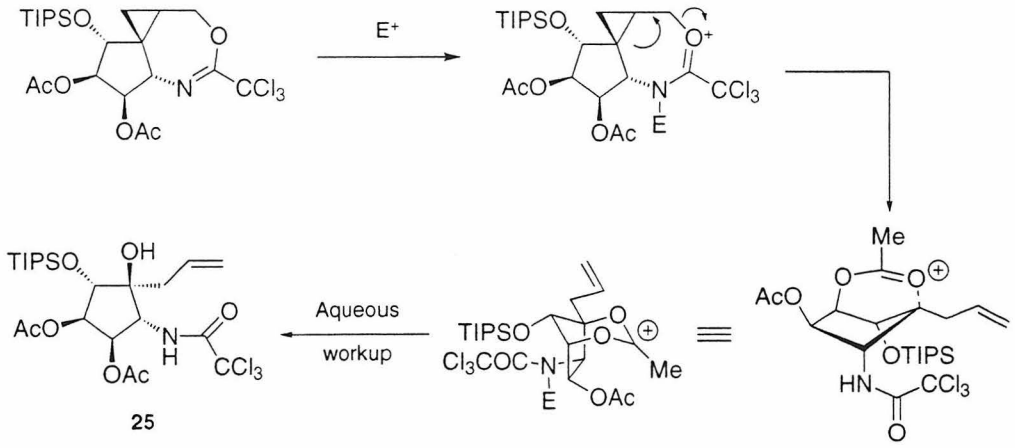
Scheme 2.[a] Installation of the *cis* diol.



[a]Conditions: (a) di-*sym*-collidine-iodonium perchlorate, $NaHCO_3$, CH_3CN, 60%; (b) TIPSOTf, lutidine, 95%; (c) OsO_4, NMO, 85%; (d) Ac_2O, DMAP, 85%.

It was hoped that treatment of **24** with the appropriate electrophile would induce solvolysis of the cyclopropane to give **25**, leaving inversion of C(3) and excision of a two-carbon fragment as the last remaining obstacles to the synthesis of trehalamine.[27]

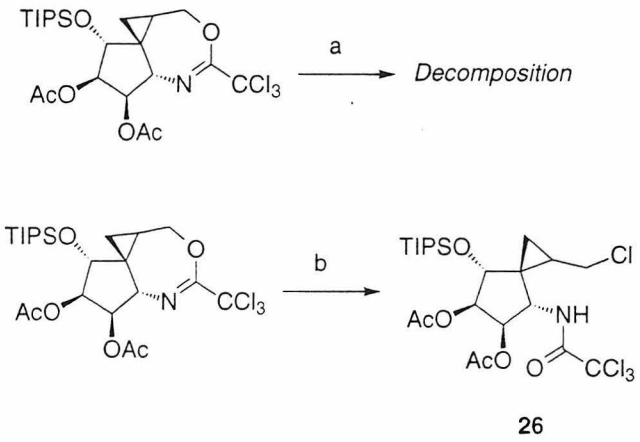
Figure 11. Initial strategy for installation of C(5) tertiary alcohol.



27 Salaün, J. "Rearrangements involving the cyclopropyl group" in *The Chemistry of the Cyclopropyl Group;* Rappoport. Z., Ed.; J. Wiley and Sons: New York, 1987; volume 2, chapter 13.

Treatment of **24** with R_3SiOTf led to decomposition of the starting material under all conditions attempted. All attempts to hydrolyze **24** were unsuccessful; only unidentifiable by-products were obtained. However, treatment of **24** with one equivalent of $SnCl_4$ gave chloride **26** in nearly quantitative yield.

Scheme 3.[a] Initial attempts to fragment the cyclopropane.

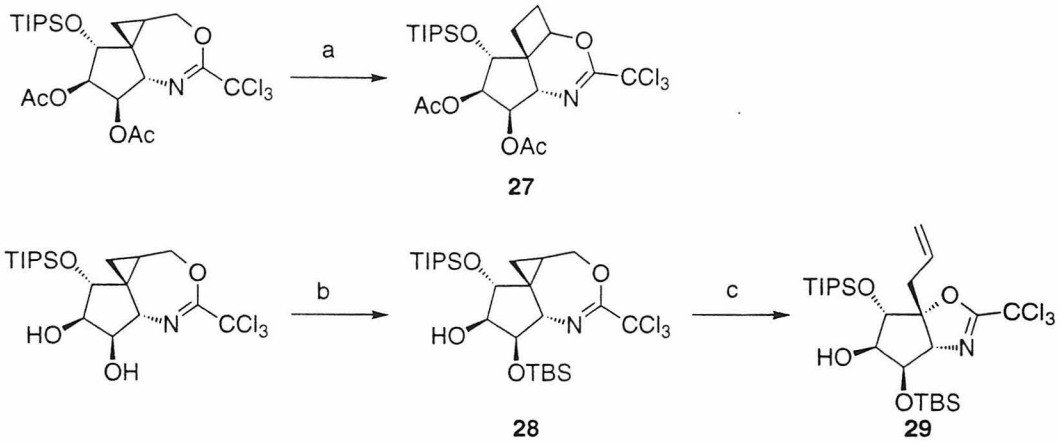


26

[a]Conditions: (a) TESOTf, CH_2Cl_2; (b) $SnCl_4$, toluene, 50 °C, 95%.

This was an encouraging result, as it was the first evidence that Lewis acids could activate the cyclopropyl carbinol towards displacement. Reasoning that displacement by the counterion was simply faster than the desired rearrangement, a Lewis acid lacking a counterion was employed–$BF_3 \cdot OEt_2$. *Bis*-acetate **24** reacted with one equivalent of $BF_3 \cdot OEt_2$ to give a mixture of products; surprisingly, the major product was spiro-fused cyclobutanol **27**. This unexpected result prompted further exploration of the acid-catalyzed chemistry of **23**. It was found that **23** could be monosilylated with TBSCl to give **28**. On treatment with $BF_3 \cdot OEt_2$, **28** rearranged to give an inseparable mixture of products, one of which was **29**.

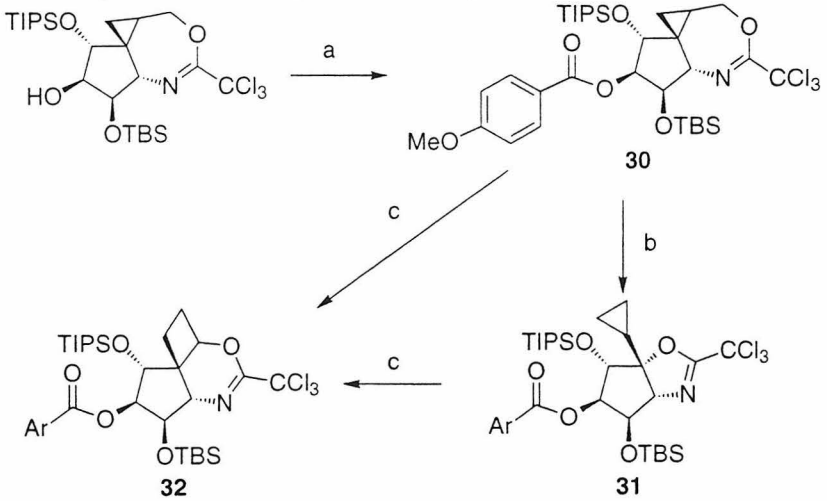
Scheme 4.[a] An unexpected rearrangement- example I.



[a]Conditions: (a) $BF_3 \cdot OEt_2$, toluene, 20%; (b) TBSCl, DMAP, TEA, 90%; (c) $BF_3 \cdot OEt_2$ 30%.

Next, mono silyl ether **28** was acylated with *p*-anisoyl chloride, generating **30** in good yield (80%).[28] On treatment with a single equivilent of $BF_3 \cdot OEt_2$ for 1 hour, exo-cyclopropane **31** was formed cleanly in good yield. Strangely, if **30** was allowed to stir for 24 hours or **31** was resubmitted to the reaction conditions, **32** was the only isolable compound, typically in greater than 80% yield.

Scheme 5.[a] An unexpected rearrangement- example II.



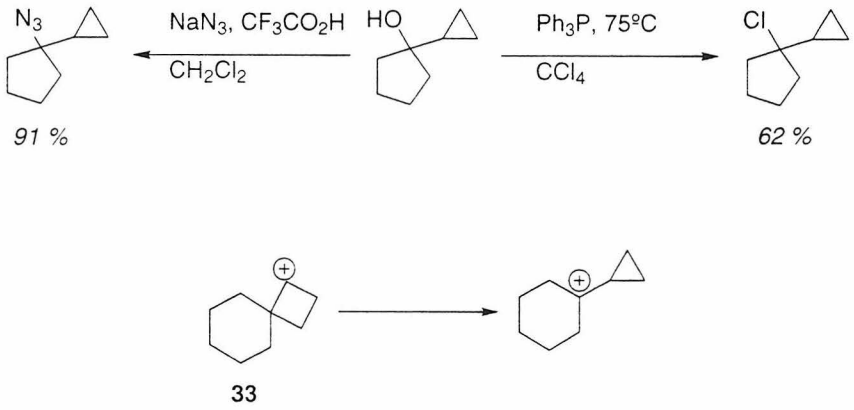
[a]Conditions: (a) *p*-anisoyl chloride, DMAP, TEA, 80%; (b) $BF_3 \cdot OEt_2$, 2 h, 68%; (c)$BF_3 \cdot OEt_2$, 24 h, 83%.

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28 For an example of a *p*-anisoyl ester being used in an intramolecular displacement, see: Corey, E. J.; Carpino, P. *J. Am. Chem. Soc.* **1989**, *111*, 5472.

This was rather unexpected. Upon first inspection, the tertiary cation of **31** would seem to be much more stable. Therefore, it was anticipated that only **31** would ever be observed. It is an especially surprising result given the literature precedents. For example, under acidic conditions 1-cyclopropylcyclopentanol shows no tendency to rearrange (Figure 12).[29]

Figure 12. A counterintuitive rearrangement.

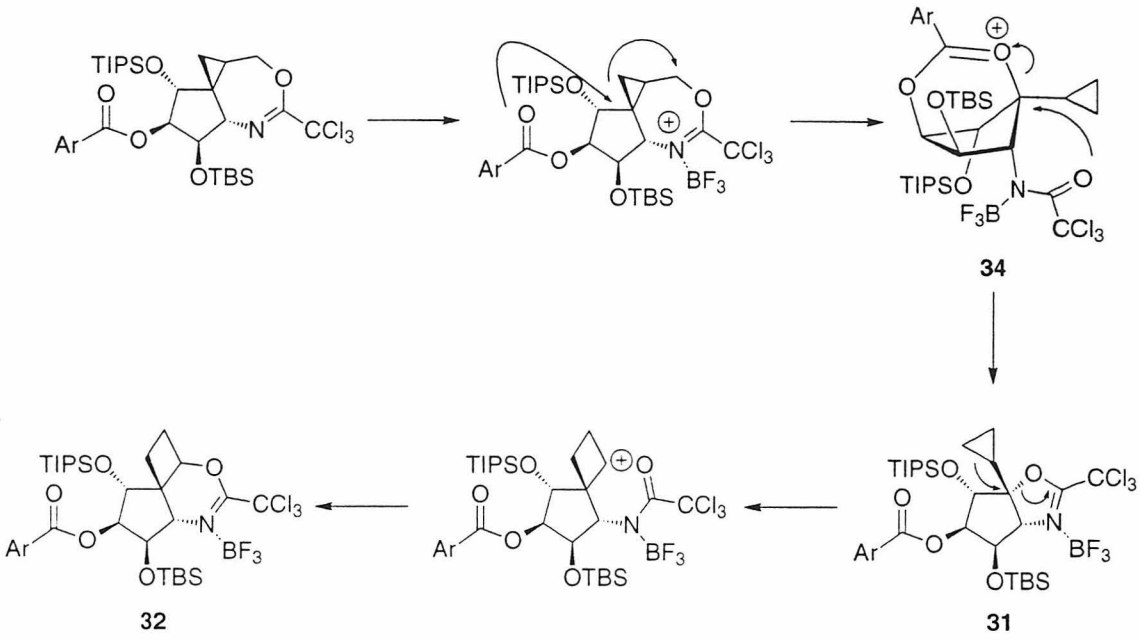


Furthermore, Olah has studied cations such as **33** and found that they rearrange to give the tertiary cation, not the spirofused structure.[30] It seems that the high degree of oxygenation of **31** destabilizes the tertiary cation at C(5) to the extent that the spirocyclobutane is the thermodynamic product. Formation of **32** could occur as illustrated in Figure 13.

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29 Engel, P. S.; Culotta, A. M. *J. Am. Chem. Soc.* **1991**, *113*, 2686.
30 Olah, G. A.; Prakash, G. K. S.; Rawda, T. N. *J. Org. Chem.* **1980**, *45*, 965.

Figure 13. Possible mechanism of rearrangement.

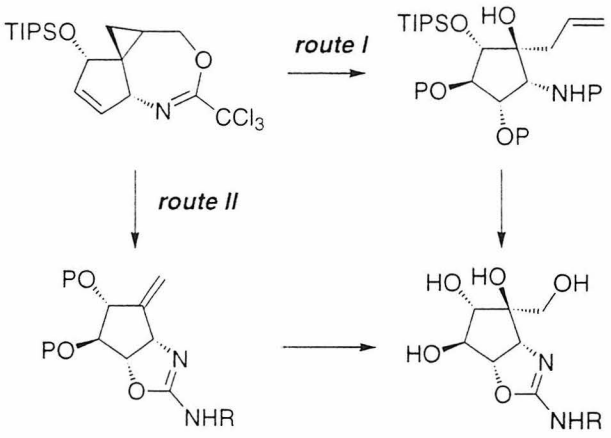


Apparently a carbonyl on the C(3) alcohol is able to assist in the solvolysis of the cyclopropyl imidate, generating the exocyclopropyl **34**. Once formed, this intermediate closes to form oxazoline **31**, which can rearrange further, generating spirocyclobutane **32**. The identity of the product is isolated seems to be a function of the nucleophilicity of the carbonyl. Poorer nucleophiles, such as the acetate, do not stabilize **34** well enough to stall conversion into the more stable **32**. The more nucleophilic *p*-anisoyl ester is able to stabilize **34** for at least a brief period. However, on continued stirring even the *p*-anisoyl ester is converted into the thermodynamically preferred spirocyclobutane. The electron-withdrawing effect of the additional ester could also be playing a role. The *bis*-acetate is more electron-poor than the monobenzoate, therefore it is more likely to rearrange to the spirocyclobutane.

Revised route to trehazolin core.

While interesting, the cationic chemistry of these compounds was not obviously applicable to the synthesis of trehazolin. In fact, the rearrangements observed suggested that it would be unwise to install the tertiary alcohol at this stage (Figure 14). Originally we had planned to install the hydroxyl at C(5) and degrade the side chain to generate a protected trehalamine (route I). This order of events was reversed; the two carbons were now to be excised prior to installation of the C(5) hydroxyl (route II).

Figure 14. New strategy for installation of tertiary carbinol.

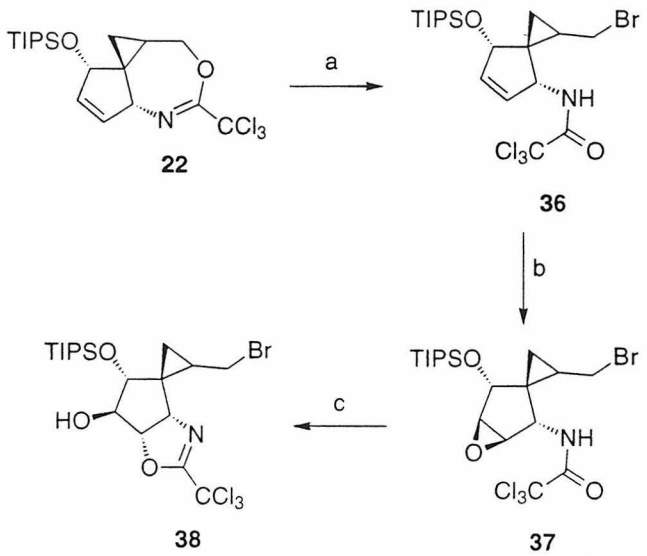


As before, alcohol **19** was converted to triisopropyl silyl ether **21** under standard conditions. While all attempts to hydrolyze **21** using aqueous acid or strong Lewis acids ($SnCl_4$, $TiCl_4$) were unsuccessful, treatment with Li_2NiBr_4 afforded the anticipated bromide (**36**) in good (80 %) yield.[31] The bromide was converted to epoxide **37** in 65 % yield using dimethyl dioxirane.[32] This olefin proved rather unreactive; it only slowly decomposed when treated with a number of other epoxidizing reagents (*m*-CPBA, trifluoroperacetic acid). The epoxide was cleanly converted with stoichimetric $BF_3 \cdot OEt_2$ into oxazoline **38**.

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[31] Dawe, R. D.; Molinski, T. F.; Turner, J. V. *Tetrahedron Lett.* **1984**, *25*, 2061.
[32] Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.

Scheme 6.[a] Preparation of the trehazolin oxazoline.



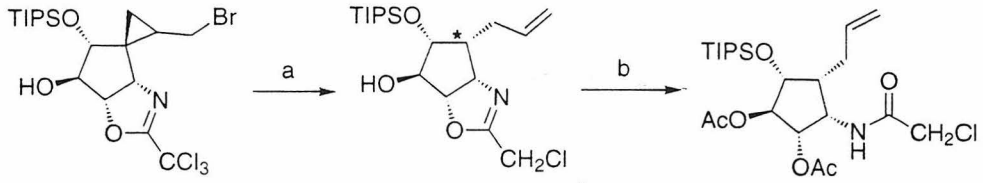
[a]Conditions: (a) Li_2NiBr_4, THF, 60 °C, 80%; (b) dimethyl dioxirane, acetone, 65%; (c) $BF_3 \cdot OEt_2$, toluene, 87%.

The oxazoline was converted into allyl oxazoline **39** using catalytic Bu_3SnH with stoichiometric $NaBH_4$.[33] These conditions were chosen because the trichloromethyl is reduced at a comparable rate to the cyclopropyl carbinyl bromide–at least three equivalents of Bu_3SnH would have been required had it been used stoichiometrically. The diastereoselection at C(5) was 5:1 (α:β). Because the oxazoline proved fairly sensitive to hydrolysis, it was converted in moderate yield (77% for two steps) to diacetate **40**. Alternatively, the crude reduction product could be hydrolyzed and acetylated directly (53 % yield for the two step sequence).

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[33] Giese, B.; Gonzalez-Gomez, J. A.; Witzel, T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 69.

Scheme 7.[a] Fragmentation of the cyclopropylcarbinyl bromide.



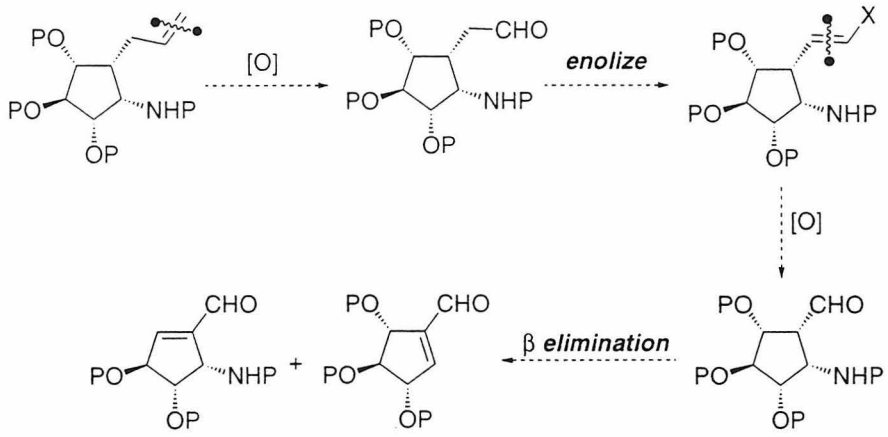
38 **39** **40**

diastereoselection 5:1

[a]Conditions: (a) Bu_3SnH, $NaBH_4$, Et_3B, EtOH, 75%; (b) *i.* PPTS, H_2O/CH_3CN, *ii.* Ac_2O, DMAP, 77%(2 steps).

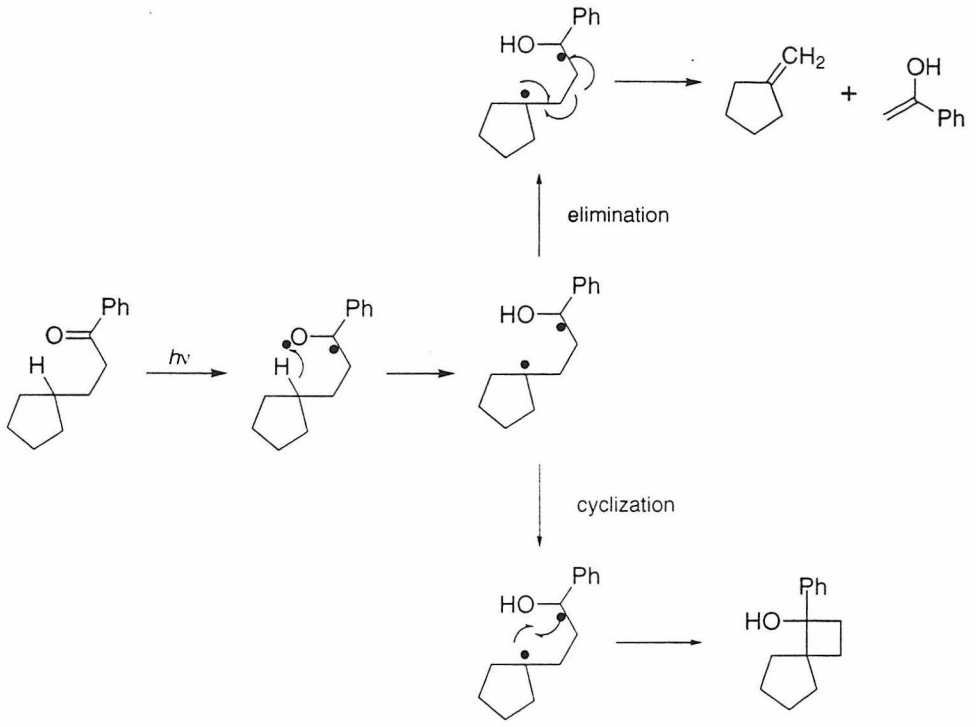
Excision of the two-carbon fragment could be accomplished *via* a number of iterative procedures. However, all these routes present the same difficulty: generation of a fairly acidic proton at C(5) in a molecule primed for β elimination (Figure 15).[34] To circumvent this potential hazard, we chose to remove both carbons simultaneously photochemically, via a Norrish type II fragmentation (Figure 16).[35]

Figure 15. β-elimination problem of the iterative route.



[34] Farr, R. A.; Peet, N. R.; Kang, M. S. *Tetrahedron Lett.* **1990**, *49*, 7109.
[35] Nuss, J. M.; Murphy, M. M. *Tetrahedron Lett.* **1994**, *35*, 37.

Figure 16. Norrish type II photofragmentation.

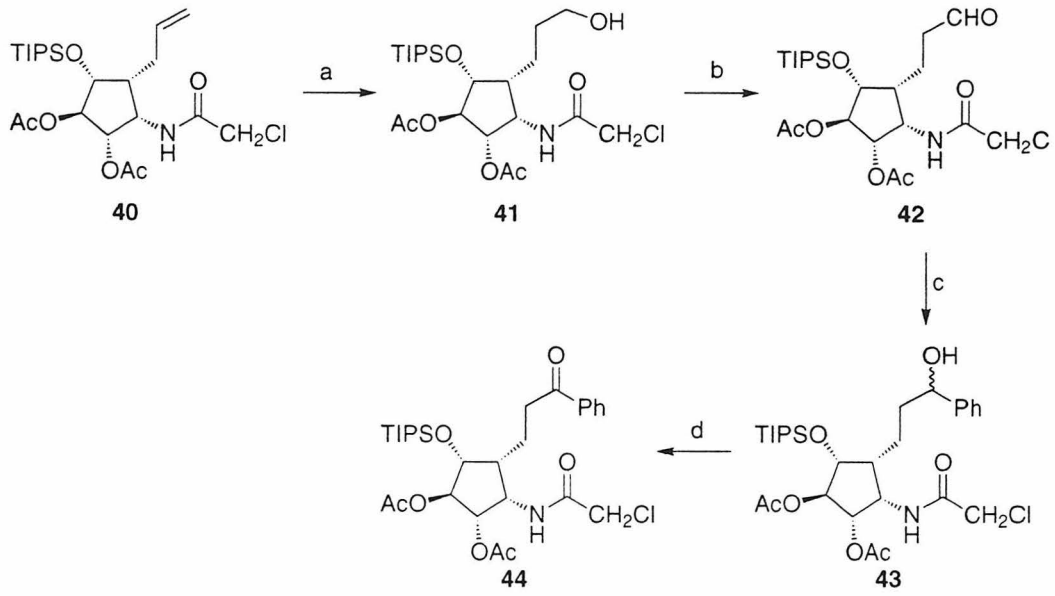


Execution of the photochemical excision required the conversion of the terminal olefin to an aryl ketone. Toward that end, **40** was hydroborated using dicyclohexyl borane. Following oxidative work-up, the primary alcohol **41** was obtained in 83% yield.[36] Oxidation to the aldehyde under Swern conditions proceeded smoothly–**42** was obtained in 83% yield.[37] Addition of phenyl magnesium bromide was only somewhat successful; a 2:1 mixture of the desired epimeric benzyl alcohols and starting aldehyde was obtained. When the reaction was run in 1 M LiBr, however, the ratio improved to 6:1 favoring the benzyl alcohols. The mixture was oxidized to the phenyl ketone **44** in good (89 %) yield.

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36 Zweifel, G.; Ayyanger, N. R.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2072.
37 Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

Scheme 8.[a] Preparation of the Norrish substrate.



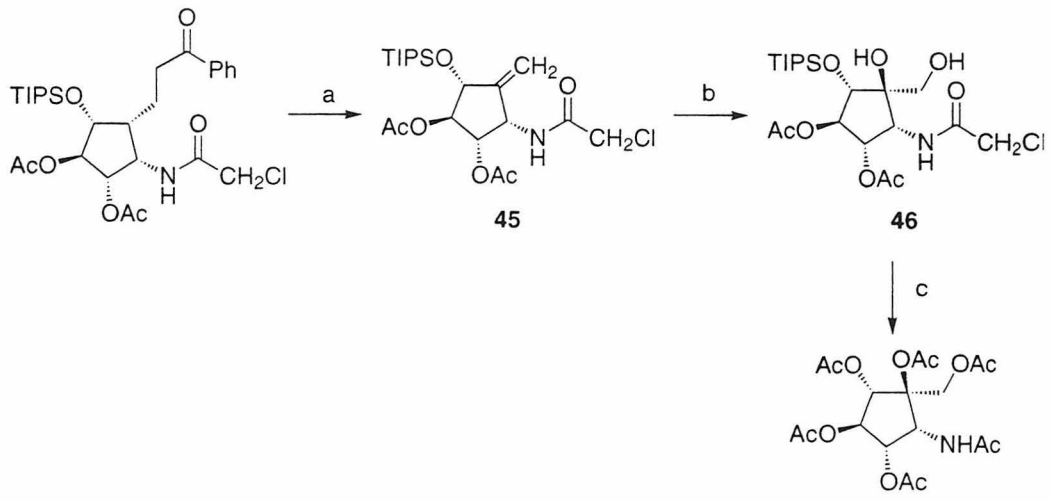
[a]Conditions: (a) Chx_2BH, H_2O_2, 83%; (b) DMSO, $(COCl)_2$, TEA, 83%; (c) PhMgBr, LiBr, THF, 60%; (d) DMSO, $(COCl)_2$, TEA, 89%.

Irradiation of a dilute solution of the phenyl ketone (1 mg/mL) in degassed benzene for 45 min yielded nearly quantitatively exomethylene **45**. The crude product was dissolved in acetone and dihydroxylated with OsO4 to give a single diol **46** in 80% yield from the phenyl ketone. Conversion to the previously synthesized hexaacetate confirmed both the absolute and relative stereochemistries.[38] This constituted completion of the aminocyclitol portion of trehazolin, leaving only the glucose-derived portion.

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[38] Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Org. Chem.* **1994**, *59*, 813.

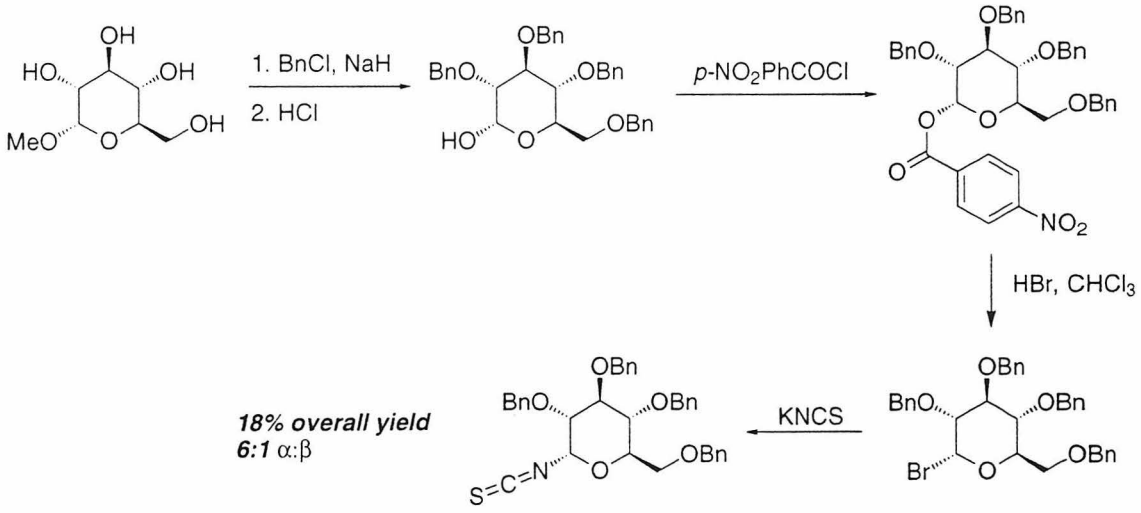
Scheme 9.[a] Synthesis of the trehalamine aminocyclitol.



[a]Conditions: (a) hν, benzene; (b) OsO_4, NMO 79% (2 steps); (c) Ac_2O, pyridine 90%.

Synthesis of the glycosidic coupling partner

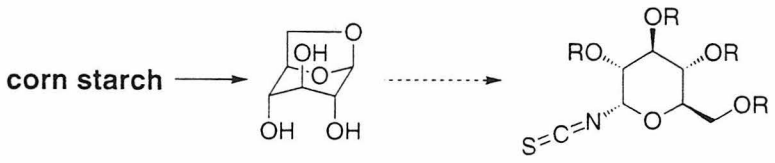
Figure 17. Literature route to α-glucose isothiocyanate.[39]



[39] Camarasa, M. J.; Fernández-Resa, P.; García-López, M. T.; De las Heras, F. G.; Méndez-Castrillón, P. P.; Felix, A. S. *Synthesis* **1984**, 509.

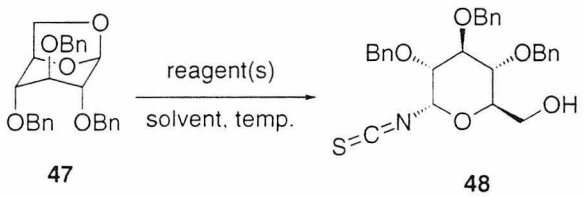
The literature synthesis of α-D-glucose isothiocyanate, tetrabenzyl ether, is somewhat laborious.[39] We hoped to circumvent this process through the use of a suitably protected anhydroglucose, which would be converted in but two steps into the desired isocyanate.

Figure 18. Anhydroglucose as a glycosylation agent.



Toward that end, anhydroglucose was prepared by pyrolysis of corn starch, and protected as the tribenzyl ether (**47**).[40] This compound proved surprisingly resistant to acidic opening with no reaction occurring with a variety of thiocyanate salts (Table 3). Finally, treatment of **47** with 3 equiv of tetrabutylammonium thiocyanate and 9 equiv of BF_3•OEt_2 in toluene for 48 h afforded the desired isothiocyanate **48** in 50% yield. The remaining material was unreacted starting material.

Table 3. Summary of unsuccessful attempts to solvolize 1,6-anhydroglucose.

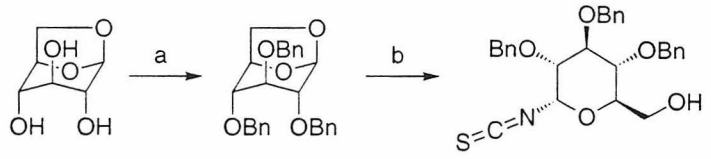


47 **48**

Reagent(s)	Solvent	Temp. (°C)	Result
TMSNCS/TMSOTf	toluene	-78-25	no reaction
TMSNCS/BF_3•OEt_2	toluene	25	no reaction
TMSNCS (neat)	n/a	138	no reaction
Ti(NCS)4	CH_2Cl_2	25	no reaction
Ti(NCS)4/BF_3•OEt_2	CH_2Cl_2	25	no reaction
Et_2AlNCS	toluene	110	no reaction

40 Cêrný, M.; Stanêk, *J. Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 23.

Scheme 10.[a] Synthesis of a protected α-glucose isothiocyanate.



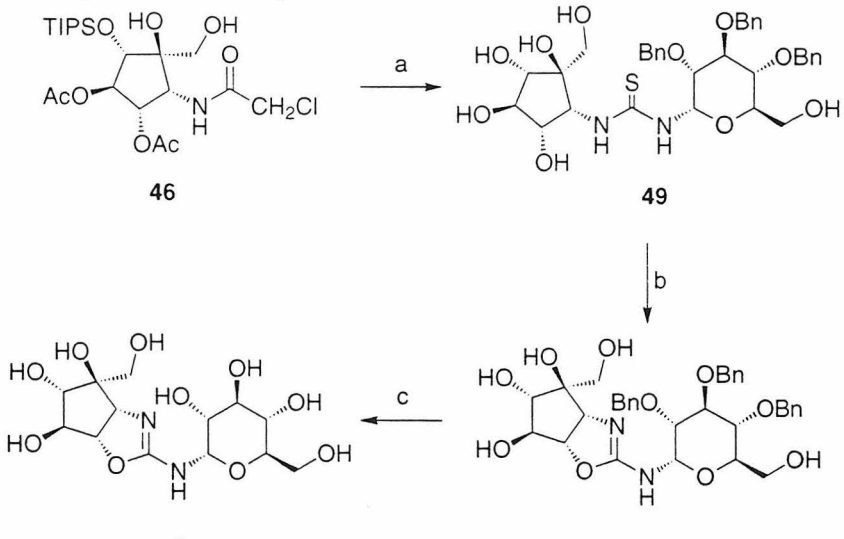
47 **48**

[a]Conditions: (a) BnCl, NaH, DMF, 65%; (b) *n*Bu4NNCS, BF_3•OEt_2 , 50%.

Final steps

With both coupling fragments in hand, the synthesis was concluded following the literature precedents.[14, 15] Diol **46** was treated with 4 N HCl at 60 °C for 8 h, yielding the aminocyclitol **14**. This was dissolved in pyridine/DMF and treated with isocyanate **48** and DMAP (5 equiv) to provide thiurea **49**. Closure to the amidine was effected by yellow mercury oxide. Finally, deprotection of the trehazolin tribenzyl ether afforded trehazolin, which was identical to the natural product in its optical rotation, by thin layer chromatography, and comparison of the ^1H NMR spectrum with an authentic sample.[41]

Scheme 11.[a] Completion of the synthesis of (+)-trehazolin.



46 **49** **50** **9**

[a]Conditions: (a) *i.* 4N HCl, MeOH, *ii.* **48**, DMAP, 60%; (b) yellow HgO; (c) PdOH/C, H_2, 40% (2 steps).

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41 We thank Dr. Nakajma (Sankyo Co., Ltd.) for generously providing a sample of (+)-trehazolin and Dr. Nakajima and Professor S. Ogawa (Keio University) for providing spectral data for comparison.

Conclusion

A concise synthesis of the trehalase inhibitor trehazolin from optically active spiro[2.4]hepta-4,6-diene-1-methanol has been described; the fully functionalized aminocyclitol core is prepared in just 14 steps. Highlights include (1) preparation of optically active **8**, (2) one-step aminohydroxylation of the cyclopentadiene moiety, (3) imidate opening with Li_2NiBr_4, and (4) the use of 1,6-anhydro-β-D-glucose in the preparation of the glycosylating agent. Optically active **8** and its derivatives should prove valuable in the construction of other cyclopentanoid natural products.

Appendix I-Experimental Section

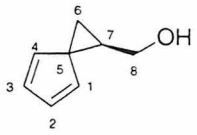
General procedures: All reagents were commercially obtained except where noted. Where appropriate, reagents were purified prior to use. All nonaqueous reactions were performed using oven dried glassware under an atmosphere of dry nitrogen. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl prior to use. N,N-di-*iso*-propyl-ethylamine, dichloromethane, 2,6-lutidine, pyridine, and triethylamine were distilled from calcium hydride prior to use. N,N-dimethylformamide was stood over 4 è molecular sieves prior to use. Hexanes were rendered olefin-free and distilled from sodium prior to use. Methanol was distilled from magnesium methoxide prior to use. Chromatographic purification of products was accomplished using forced flow chromatography on Baker 7024-R silica gel according to the method of Still.[42] Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60F plates (230-400 mesh). Visualization of the developed chromatogram was performed by either fluorescence quenching, aqueous ceric ammonium molybdate (CAM) stain, or an ethanolic *p*-anisaldehyde spray.

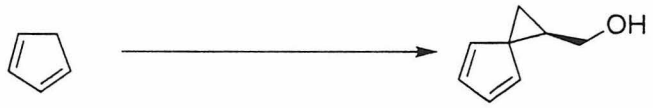
NMR spectra were recorded on a General Electric QE Plus operating at 300 and 75 MHz for ^{1}H and ^{13}C, respectively, and are referenced to residual protio solvent signals. Data for 1H are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and assignment. IR spectra were recorded on a Perkin-Elmer 1600 Series spectrometer. Optical rotations were determined on a Jasco DIP-18 polarimeter operating at the sodium D line are reported as follows: $[\alpha]_D^{25}$, concentration (g/100 mL), and solvent.

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42 Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Figure 19. Numbering scheme employed with spiro[2.4]hepta-2,4-diene-1-methanol derivatives.





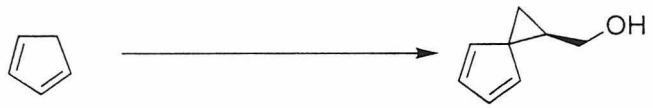
8

(±)Spiro[2,4]-2,4-heptadiene-1-methanol (**8**). To a 1000 mL three-necked flask equipped with a nitrogen line, jacketed addition funnel, and a stirbar was added 36.0 g (21.6 g, 900 mmol, 2.20 equiv) of NaH as a 60% dispersion in mineral oil. The NaH was washed with 2 x 20 mL of pentane an suspended in 300 mL of THF. The suspension was cooled to 0 °C. The addition funnel was cooled to -78 °C and charged with 27.0 g of freshly cracked cyclopentadiene (409 mmol, 1.00 equiv). Cyclopentadiene was added dropwise to the stirred suspension of NaH over a period of 2 h. A mild exotherm and gas evolution were noted. To the reddish-brown suspension was added dropwise 38.0 mL of epichlorohydrin (44.8 g, 484 mmol, 1.18 equiv). The addition was complete after 1 h. The reaction was stirred until gas evolution ceased and then quenched cautiously with 100 mL of ice water. The crude product was extracted into diethyl ether (2 x 300 mL) from water and dried over Na_2SO_4. The resulting solution was concentrated *via* rotary evaporation to a brown oil which was distilled (72-74 °C, 1 Torr) to give 27.0 g (221 mmol, 54.0% yield) of **8** as a clear oil.



8

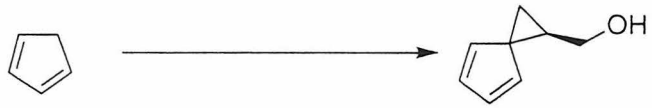
Cyclopentadienyl sodium and glycidol tosylate. A 100 mL round-bottomed flask was charged with 894 mg (536 mg, 22.4 mmol, 2.50 equiv) of a 60% dispersion of NaH in mineral oil. The dispersion was rinsed twice with 5 mL of pentane and suspended in 10 mL of THF. To the stirred suspension at 0 °C was added 646 mg (9.79 mmol, 1.09 equiv) of freshly cracked cyclopentadiene. After 30 min at 0 °C, a solution of 2.04 g (8.95 mmol, 1.00 equiv) of (*R*)- glycidol tosylate (91 % ee) in 5 mL of THF was added at 0 °C. The reaction was allowed to stir for 30 min and quenched by the addition of 10 mL of water. The layers were separated and the aqueous layer was extracted three times with 40 mL of Et_2O. The organic layers were combined, dried over anhydrous Na2SO4, and distilled under vacuum (72-74 °C, 1 Torr) to yield 547 mg (4.49 mmol, 50.2 % yield) of **8** as a clear oil. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 1:1 (0 % ee).



8

Cyclopentadienyl sodium and epichlorohydrin/THF. A 100 mL round-bottomed flask was charged with 2.13 g (1.28 g, 53.3 mmol, 2.32 equiv) of a 60% dispersion of NaH in mineral oil. The dispersion was rinsed twice with 5 mL of pentane and suspended in 10 mL of THF. To the stirred suspension at 0 °C was added 1.72 g (26.1 mmol, 1.13 equiv) of freshly cracked cyclopentadiene. After 30 min at 0 °C, a solution of 2.13 g (23.0

mmol, 1.00 equiv) of (*R*)-epichlorohydrin (91 % ee) in 5 mL of THF was added at 0 °C. The reaction was allowed to stir for 30 min and quenched by the addition of 10 mL of water. The layers were separated and the aqueous layer was extracted three times with 40 mL of Et_2O. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (2:1 hexanes:ethyl acetate w/1% TEA, R_f = 0.30) to afford 1.06 g (8.68 mmol , 38.8 % yield) of **8** as a clear oil. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 5:1 (66 % ee).

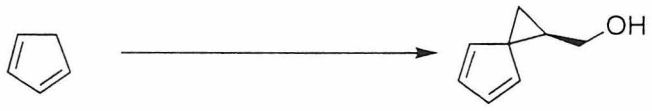


8

Cyclopentadienyl lithium with epichlorohydrin/THF. To a solution of 1.1 g (17 mmol, 1.0 equiv) of freshly cracked cyclopentadiene in 22 mL of THF at -78 °C was added via cannula 9.9 mL of *t*BuLi (1.7 M in hexanes, 17 mmol, 1 equiv). The reaction was stirred for 30 min, yielding a 0.51 M solution of cyclopentadienyl lithium, which was used without further purification.

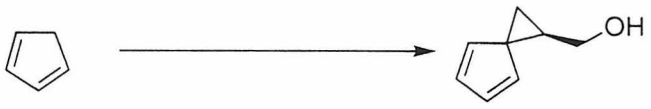
To a cooled solution of 380 mg (4.1 mmol, 1.0 equiv) of (*R*)-epichlorohydrin in 5 mL of THF at -78 °C was added 11 mL of cyclopentadienyl lithium (0.51 M, 5.6 mmol, 1.4 equiv). The reaction was warmed to 0 °C and stirred for 30 min. The reaction was then transferred via cannula to a suspension of 220 mg (60 % dispersion, 5.5 mmol, 1.1 equiv) of NaH in 2 mL of THF at 0 °C. After 30 min at 0 °C, the reaction was cautiously quenched by the addition of 10 mL of water. The layers were separated and the aqueous

layer was extracted three times with 30 mL of Et_2O. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel chromatography (200 x 10 mm, 2:1 hexanes:ethyl acetate w/1% TEA, R_f= 0.30) to afford 210 mg (1.8 mmol, 42 % yield) of **8** as a clear oil. A small portion (5 mg) of **8** was treated with (S)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 9.75:1 (81 % ee).



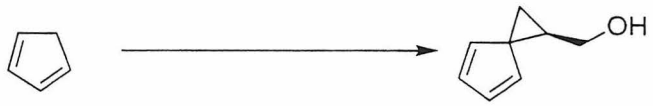
8

Cyclopentadienyl lithium and trimethyl aluminum/THF. To a cooled solution of 380 mg (4.1 mmol, 1.0 equiv) of (*R*)-epichlorohydrin in 5 mL of THF at -78 °C was added sequentially 2.5 mL (2.0 M, 5.0 mmol, 1.2 equiv) of trimethyl aluminum, and 11 mL of cyclopentadienyl lithium (0.51 M, 5.6 mmol, 1.4 equiv). The reaction was stirred for 30 min. The reaction was then transferred *via* cannula to a suspension of 300 mg (60% dispersion, 7.5 mmol, 1.8 equiv) of NaH in 2 mL of THF at 0 °C. After 30 min at 0 °C, the reaction was cautiously quenched by the addition of 10 mL of water. The layers were separated and the aqueous layer was extracted three times with 30 mL of Et_2O. The organic layers were combined, dried over anhydrous Na2SO4, and concentrated. The residue was purified by silica gel chromatography (200 x 10 mm, 2:1 hexanes:ethyl acetate w/1% TEA, R_f = 0.30) to afford 180 mg (1.5 mmol, 37 % yield) of **8** as a clear oil. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 6.5:1 (73 % ee).



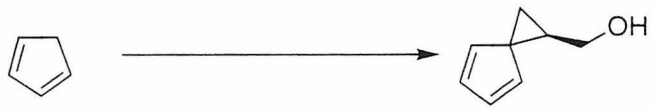
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Cyclopentadienyl lithium in Et_2O. To a solution of 570 mg (8.7 mmol, 2.1 equiv) of freshly cracked cyclopentadiene in 11 mL of Et_2O at -78 °C was added *via* cannula 5.1 mL of *t*BuLi (1.7 M in hexanes, 8.7 mmol, 2.1 equiv). The reaction was stirred for 30 min at -78 °C, and warmed to 25 ¯c for 30 min. The reaction was then cooled to 0 °C. To the yellowish suspension, was then added a solution of 380 mg (4.1 mmol, 1.0 equiv) of (*R*)- epichlorohydrin in 5 mL of Et2O. The reaction was stirred for 30 min at 0 °C and tranfered via cannula to a suspension of 300 mg (60 % dispersion, 7.5 mmol, 1.8 equiv) of NaH in 2 mL of Et_2O at 0 °C. After 30 min at 0 °C, the reaction was cautiously quenched by the addition of 10 mL of water. The layers were separated and the aqueous layer was extracted three times with 30 mL of Et_2O. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel chromatography (200 x 10 mm, 2:1 hexanes:ethyl acetate w/1% TEA, R_f= 0.30) to afford 180 mg (1.5 mmol, 36 % yield) of **8** as a clear oil. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 5.6:1 (70 % ee).



8

Cyclopentadienyl Potassium.[43] To a solution of 3.13 g (55.9 mmol, 4.05 equiv) of KOH, and 1.23 g (4.66 mmol, 0.338 equiv) of 18-crown-6 in 50 mL of THF was added 1.89 g (28.6 mmol, 2.07 equiv) of freshly cracked cyclopentadiene at 25 °C. After 45 min, a solution of 1.28 g (13.8 mmol, 1.00 equiv) of (*R*)-epichlorohydrin in 10 mL of THF was added *via* cannula. The reaction was stirred for 2 h at 25 °C. The reaction was poured into 100 mL of brine and extracted three times with 100 mL of Et_2O. The organic layers were combined, dried over anhydrous Na2SO4, and concentrated in vacuo. The residue was purified by silica gel chromatography (200 x 10 mm, 2:1 hexanes:ethyl acetate w/1% TEA, R_f= 0.30) to afford 850 mg (6.97 mmol, 50.5 % yield) of **8** as a clear oil. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 3:1 (50 % ee).



8

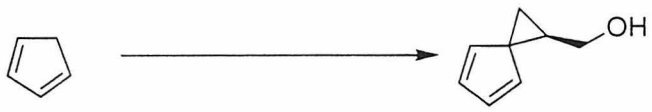
Cyclopentadienyl Magnesium bromide.[44] To a solution of 710 mg (11 mmol, 2.8 equiv) of cyclopentadiene in 5 mL of THF at -78 °C was added 4.0 mL (2.9 M, 11 mmol, 2.8 equiv) of ethyl magnesium bromide. The reaction was warmed to reflux and allowed to stir for 24 h. The solution was cooled to 0 °C and diluted with 5 mL of THF. To the reaction was added 380 mg (4.1 mmol, 1.00 equiv) of (*R*)-epichlorohydrin at 0 °C via

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[43] Ambler, H.; Laycock, D. E. *Synthesis* **1980**, 799.
[44] Ford, W. T. *J. Organomet. Chem.* **1971**, *32*, 27

cannula. After 2 h at 0 °C, the reaction was transfered via cannula to a suspension of 300 mg (60% dispersion, 7.5 mmol, 1.8 equiv) of NaH in 2 mL of THF. The reaction was stirred for 12 h, warming slowly to 25 °C. The reaction was then cautiously quenched with 10 mL of water. The layers were separated, and the aqueous layer was extracted three times with 50 mL of Et_2O. The organic layers were combined, dried over anhydrous Na2SO4, and concentrated in vacuo. The residue was purified by silica gel chromatography (200 x 10 mm, 2:1 hexanes:ethyl acetate w/1% TEA, R_f= 0.30) to afford 29 mg (0.24 mmol, 5.8% yield) of **8** as a clear oil. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 1:19 (90 % ee).

Cyclopentadienyl lithium. A 1000 mL three-necked flask was charged with 120 mL (190 mmol, 1.0 equiv) of 1.6 M BuLi in hexanes. The solution was cooled to 0 °C and diluted with 250 mL of THF. To the stirring reaction was added dropwise 13 g (190 mmol, 1.0 equiv) of freshly cracked cyclopentadiene. The reaction was stirred until gas evolution ceased. The white suspension was used without purification in the subsequent reaction.



8

Spiro[2.4]hepta-4,6-diene-1-methanol (8). A 1000 mL three-necked roundbottom flask was charged with 8.8 g (220 mmol, 3.0 equiv) of a 60% dispersion of NaH in mineral oil. The dispersion was rinsed twice with 15 mL pentane and suspended in 100 mL THF. To the stirred slurry at 0 °C was added 14 g (74 mmol, 1.0 equiv) of (*R*)-1-

chloro-2-hydroxy-3- (mesyloxy)- propane[45] in 20 mL THF via cannula; the reaction mixture was stirred until gas evolution ceased. To the reaction was then added, *via* cannula, 390 mL (190 mmol, 2.6 equiv) of 0.50 M cyclopentadienyl lithium. The reaction was stirred at 0 °C overnight and cautiously quenched by the addition of 20 mL of water. The organic layer was separated and the aqueous layer extracted three times with 200 mL Et_2O. The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (240 mm x 40 mm, 2:1 hexanes:ethyl acetate w/1% TEA, R_f= 0.30) to afford 5.30 g (43.4 mmol, 59% yield) of **8** as a clear oil: $[\alpha]_D^{25}$ = -40° (c = 0.8, $CHCl_3$); IR (thin film) ν 3883, 3073, 2928, 2361, 1627, 1479, 1383, 1256, 1140, 1083, 1007, 898, 856, 791, 617 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 6.54 (1 H, m, $C^{1\text{-}4}\mathbf{H}$), 6.45 (1 H, m, $C^{1\text{-}4}\mathbf{H}$), 6.09 (1 H, m, $C^{1\text{-}4}\mathbf{H}$), 5.88 (1 H, m, $C^{1\text{-}4}\mathbf{H}$), 3.59 (1 H, m, $C^8\mathbf{H}_2$), 3.30 (1 H, m, $C^8\mathbf{H}_2$), 2.05 (1 H, m, $C^7\mathbf{H}$), 1.40 (1 H, m, $C^7\mathbf{H}_2$), 1.26 (1 H, m, $C^7\mathbf{H}_2$) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 139.3, 134.3, 131.1, 128.4, 64.1, 41.9, 29.6, 16.9 ppm. HRMS: (FAB) Calcd for $C_8H_{10}O$ (M)+: 122.0731. Found: 122.0733. A small portion (5 mg) of **8** was treated with (*S*)-MTPACl (2 equiv) and DMAP (2 equiv) in CH_2Cl_2. Integration of the ^1H NMR (300 MHz C_6D_6) resonances at δ 3.95 (major, 2 H) and δ 3.69 (minor, 1 H) indicated a diastereomer ratio of 20.4:1.0 (90.5 % ee).



8 **15**

Imidate 15. A 1000 mL round-bottom flask was charged with 5.2 g (130 mmol, 1.6 equiv) of a 60% dispersion of NaH in mineral oil. The dispersion was washed twice with 10 mL of pentane and suspended in 100 mL THF. The stirred suspension was cooled to 0

[45] Baldwin, J. J.; Raab, A. W.; Mensler, K.; Arison, B. H.; McClure, D. E. *J. Org. Chem.* **1978**, *43*, 4876

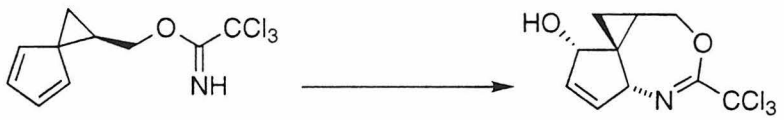
°C. To the reaction mixture was then added dropwise via syringe 17 mL (24 g, 160 mmol, 2.0 equiv) of trichloroacetonitrile. To the reaction was then added 10 g (82 mmol, 1.0 equiv) of **8** *via* cannula. The reaction was stirred for 30 min and cautiously quenched with 100 mL of water. The brown suspension was extracted 2 x 500 mL diethyl ether; the organic layers were the combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (250 mm x 40 cm, 8:1 hexanes:ethyl acetate with 1% TEA, R_f = 0.4) to give 20.0 g (76 mMol, 95% yield) of **15** as a light yellow oil: $[\alpha]_D^{25}$ = -4.2° (c = 5.6, $CHCl_3$); IR (thin film) ν 3339, 3073, 2952, 1763, 1662, 1482, 1411, 1353, 1167, 990, 877, 796, 708, 648, 612 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ 8.35 (1 H, s, N**H**), 6.50 (1 H, m, $C^{1\text{-}4}$**H**), 6.45 (1 H, m, $C^{1\text{-}4}$**H**), 6.09 (1 H, m, $C^{1\text{-}4}$**H**), 5.80 (1 H, m, $C^{1\text{-}4}$**H**), 4.18 (2 H, m, C^8H_2), 2.18 (1 H, m, C^7**H**), 1.30 (1 H, m, C^7H_2) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 162.3, 138.7, 134.2, 131.1, 128.9, 91.6, 70.5, 41.3, 24.4, 16.6 ppm. HRMS (FAB) Calcd for $C_{10}H_{10}Cl_3NO$ (M)+: 264.9827. Found: 264.9835.

General procedure for iodolactamization. To a solution of **15** (approx. 0.25 M) was added an equal volume of saturated aqueous $NaHCO_3$. The mixture was cooled to 0 °C and di-*sym*- collidine iodonium perchlorate[46] (2 equiv) were added. The reaction was stirred for 45 min and then quenched by the addition of Na_2SO_3 (4 equiv). The layers were separated and the aqueous phase was extracted twice with 50 mL of Et_2O. The organic layers were combined, dried over anhydrous Na2SO4, and concentrated in vacuo. Integration of the C(3)**H** ^1H NMR resonances (300 MHz C_6D_6) at δ 5.85 (**19**) and δ 5.75 (**18**) in the unpurified product revealed the product ratio:

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[46] Lemieux, R.U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190.

Solvent	Ratio (19:18)
Et_2O	1.5:1
THF	2:1
Benzene	3:1
Acetone	3.75:1
CH_3CN	4:1
CH_2Cl_2	5.2:1



15 19

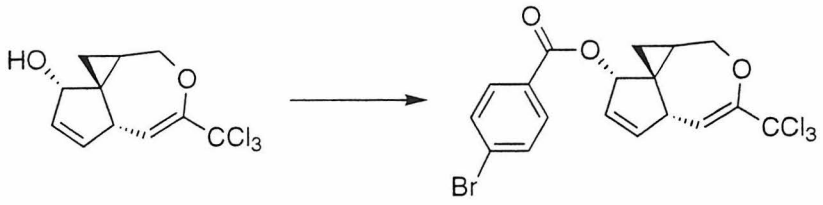
Alcohol 19. To a stirred solution of 12.2 g 15 (45.9 mmol, 1.00 equiv) in 200 mL acetonitrile was added 200 mL of saturated $NaHCO_3$. The mixture was cooled to 0 °C and 46.0 g of di-*sym* -collidine iodinium perchlorate (104 mmol, 2.27 equiv) was added as a single portion. The red suspension was stirred vigorously for 2 h at 0 °C and quenched with 25.0 g of Na_2SO_3 (195 mmol, 4.25 equiv) at 25 °C. The light yellow suspension was extracted twice with 600 mL of diethyl ether. The organic layers were combined, dried and concentrated to give a yellow oil. The crude product was purified by silica gel chromatography (600mm x 20 cm, 2:1 hexanes:ethyl acetate with 1% TEA) to give 2.00 g (7.12 mmol, 15.5 % yield) of **18** as a white solid, 8.00 g (28.5 mmol, 62.0% yield) of **19** as a white crystalline solid, and 250 mg of **20** (0.945 mmol, 2.06 % yield) as a yellow oil.

18: mp 100-105 °C (dec.); R_f = 0.25 (2:1 hexanes:ethyl acetate); $[\alpha]_D^{25}$ = -2.6° (c = 5.5, $CHCl_3$); IR (thin film) ν 3379, 2891, 1690, 1461, 1282, 1214, 1178, 1071, 994, 855, 827 cm^{-1}; ^1H NMR (300 MHz $CDCl_3$) δ 6.30 (1 H, m, $C^4\mathbf{H}$), 6.10 (1 H, m, $C^3\mathbf{H}$), 4.95(1 H, s, $C^{1\text{-}2}\mathbf{H}$), 4.92 (1H, s, $C^{1\text{-}2}\mathbf{H}$), 4.77 (1 H, dd,*J* = 6 Hz, 12 Hz, $C^8\mathbf{H}_2$), 3.96 (1 H, t, *J* = 12 Hz, $C^8\mathbf{H}_2$), 1.96 (1 H, m, $C^7\mathbf{H}$), 1.59 (1 H, br s, O**H**), 1.51 (1 H, dd, *J* = 5 Hz, 9 Hz, $C^6\mathbf{H}_2$), 0.76 (1 H, t, *J* = 5 Hz, $C^6\mathbf{H}_2$) ppm; ^{13}C NMR (75 MHz

$CDCl_3$) δ 149.6, 137.1, 136.5, 94.1, 78.5, 75.4, 69.5, 30.3, 21.4, 18.3 ppm. HRMS (FAB): Calcd for $C_{10}H_{10}Cl_3NO_2$ (M)+: 280.9777. Found: 280.9785.

19: R_f = 0.32 (2:1 hexanes:ethyl acetate); mp 110-115 °C (dec.); $[\alpha]_D^{25}$ = -18.3° (c = 2.17, CHCl3); IR (thin film) ν 3379, 2891, 1690, 1461, 1282, 1214, 1178, 1071, 994, 855, 827 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.33 (1 H, dd, *J* = 3 Hz, 6 Hz, $C^2\mathbf{H}$), 6.14 (1 H, m, $C^3\mathbf{H}$), 4.69 (1 H, dd, *J* = 6 Hz, 12 Hz, $C^4\mathbf{H}$), 4.61 (1H, br s, $C^8\mathbf{H}_2$), 3.97 (1 H, br s, $C^1\mathbf{H}$), 3.87 (1 H, t, *J* = 12 Hz, $C^8\mathbf{H}_2$), 2.11 (1 H, m, $C^7\mathbf{H}$), 1.59 (1 H, br s, O**H**), 1.15 (1 H, dd, *J* = 5 Hz, 9 Hz, $C^6\mathbf{H}_2$), 1.01 (1 H, t, *J* = 5 Hz, $C^6\mathbf{H}_2$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 138.5, 134.6, 94.1, 81.3, 74.8, 68.1, 37.1, 24.0, 19.0 ppm. HRMS (FAB): Calcd for $C_{10}H_{10}Cl_3NO_2$ (M)+: 280.9777. Found: 280.9785.

20: R_f = 0.58 (2:1 hexanes:ethyl acetate); IR ν 3070, 2942, 1694, 1651, 1463, 1383, 1289, 1219, 1116, 1034, 998, 882, 812 cm^{-1}; ^1H NMR (C_6D_6, 300 MHz) δ 6.71 (1H, dd, J = 1.5 Hz, 2 Hz, $C^{2\text{-}4}\mathbf{H}$), 6.38 (1H, dd, *J* = 2 Hz, 6 Hz, $C^{2\text{-}4}\mathbf{H}$), 5.63 (1H, dd, *J* = 1.5 Hz, 6 Hz, $C^{2\text{-}4}\mathbf{H}$), 3.82 (1 H, dd, *J* = 6 Hz, 18 Hz, $C^8\mathbf{H}_2$), 3.38 (1 H, d, *J* = 18 Hz, $C^8\mathbf{H}_2$), 1.74 (1H, dd, *J* = 6 Hz, 12 Hz, $C^6\mathbf{H}_2$), 1.50 (1 H, m, $C^7\mathbf{H}$), 1.05 (1 H, m, $C^6\mathbf{H}_2$) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 147.5, 139.9, 137.5, 130.0, 129.8, 94.1, 66.3, 40.0, 29.1, 13.8 ppm.



19 **21**

***p*-bromobenzoate 21**. To a stirred solution of 24 mg of DCC (0.12 mmol, 1.1 equiv) in 5 mL of dichloromethane was added 24 mg of *p*-bromobenzoic acid (0.12 mmol, 1.1

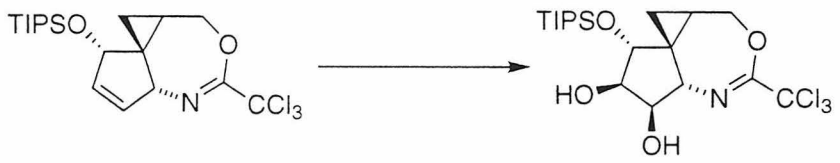
equiv). The mixture was stirred for 15 min. Next, a solution of 32 mg of 19 (0.11 mmol, 1.0 equiv) and 15 mg of DMAP (0.12 mmol, 1.1 equiv) was added. The reaction was stirred for 2 h at 25 °C. The solvent was then removed by rotary evaporation and the crude product was purified by silica gel chromatography(15 cm x 1 cm, 6:1 hexanes:diethyl ether, R_f = 0.40) yielding 40 mg (0.086 mmol, 78 % yield) of **21** as a crystalline solid: mp 151-152 °C; $[\alpha]_D^{25}$ = +15.0° (c=1.33, CHCl3); IR n 2933, 2856, 1713, 1644, 1590, 1531, 1267, 1181, 1012, 951, 756 cm-1; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (2H, d, *J* = 8 Hz, *p*-bromobenzoate), 7.58 (2H, d, *J* = 8 Hz, *p*-bromobenzoate), 6.57 (1 H, dd, *J* = 3 Hz, 6 Hz, $C^{2\text{-}3}\mathbf{H}$), 6.25 (1 H, d, *J* = 3 Hz, $C^{2\text{-}3}\mathbf{H}$), 5.41 (1 H, d, *J* = 3 Hz, $C^{1,4}\mathbf{H}$), 4.76 (1H, s, $C^{1,4}\mathbf{H}$), 4.69 (1H, dd, *J* = 7 Hz, 14 Hz, $C^8\mathbf{H}_2$), 3.98 (1H, t, *J* = 14 Hz, $C^8\mathbf{H}_2$), 2.10 (1 H, m, $C^7\mathbf{H}$), 1.41 (1 H, dd, *J* = 5 Hz, 9 Hz, $C^6\mathbf{H}_2$), 1.16 (1 H, t, *J* = 5 Hz, $C^6\mathbf{H}_2$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 150.0, 141.8, 132.3, 132.2, 131.8, 131.4, 128.9, 91.3, 83.8, 74.7, 68.5, 26.7, 24.2, 20.0 ppm. HRMS(CI) Calcd for $C_{17}H_{13}BrCl_3NO_3$(M)+: 462.9145. Found: 462.9144.



19 22

Silyl ether 22. To a solution of 5.50 g (19.6 mmol, 1.00 equiv) 19 in 100 mL CH_2Cl_2 at -40 °C was added sequentially 3.30 mL (3.05 g, 28.5 mmol, 1.45 equiv) of 2,6-lutidine and 5.9 mL (22.0 mmol, 1.10 equiv) of TIPSOTf. The reaction mixture was stirred at -40 °C for 2 h and poured into 100 mL saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted twice with 50 mL CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel chromatography (200x60 mm, 8:1 hexanes:ethyl acetate, R_f = 0.4) to

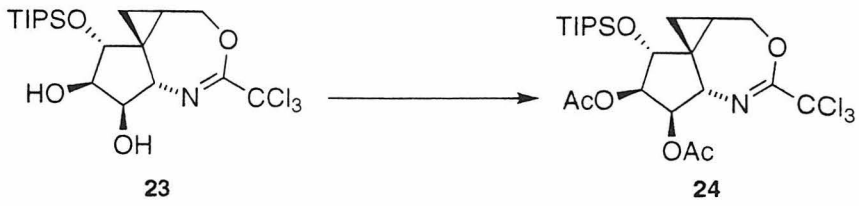
afford 8.40 g (19.2 mmol, 98.2% yield) of **22** as a white solid: mp 53-55 °C; = +7.45° (c = 1.65, $CHCl_3$); IR (thin film) ν 3850, 3667, 3625, 2942, 2358, 1651, 1415, 1368, 1245, 1181, 1058, 998, 918, 850, 812 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 6.26 (1 H, dd, *J* = 3 Hz, 6 Hz, $C^2\mathbf{H}$), 6.06 (1 H, dt, *J* = 1 Hz, 1 Hz, 6 Hz, $C^3\mathbf{H}$), 4.65 (1H, dd, *J* = 6 Hz, 12 Hz, $C^8\mathbf{H}_2$), 4.56 (1 H, t, *J* = 1 Hz, 1 Hz, $C^4\mathbf{H}$), 4.20 (1 H, d, *J* = 3 Hz, $C^1\mathbf{H}$), 3.85 (1 H, t, *J* = 12 Hz, $C^8\mathbf{H}_2$), 2.06 (1 H, m, $C^7\mathbf{H}$), 1.00 (23 H, m, $C^6\mathbf{H}_2$, TIPS) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 148.6, 137.4, 134.0, 102.6, 81.5, 73.8, 67.8, 37.2, 23.3, 18.9, 18.0, 12.5 ppm. HRMS (FAB) Calcd for $C_{19}H_{30}Cl_3NO_2Si$ (M)+: 437.1111. Found: 437.0180.



22 **23**

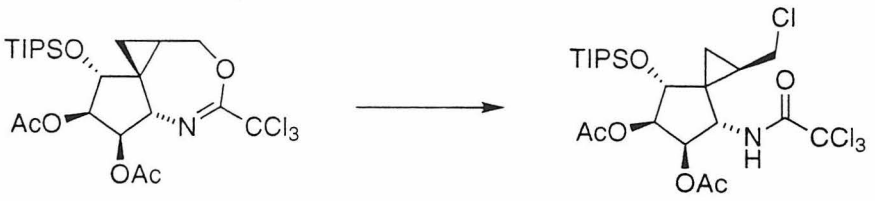
Diol 23. To a stirred solution of 1.1 g of **22** (2.4 mmol, 1.0 equiv) in 20 mL acetone and 5 mL distilled water was added 620 mg of NMO (5.3 mmol, 2.2 equiv) and 1.0 mL of a 4.0 % aqueous solution of OsO_4 (40 mg OsO_4, 0.15 mmol, 0.066 equiv). The yellow solution was stirred for 8 h and quenched with 200 mg of Na_2SO_3. The reaction was extracted into diethyl ether (2 x 15 mL) from saturated aqueous $NaHCO_3$; the organic layers were combined, dried over Na_2SO_4 and concentrated to a white solid. Purification by silica gel chromatography (19 mm x 20 cm, 2:1 hexanes: ethyl acetate, R_f=0.29) gave 1.1 g of **23** (2.2 mmol, 93 % yield): IR (thin film) ν 3402, 2943, 2724, 2251, 1463, 1384, 1333, 1180, 1012 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.617 (1 H, dd, *J* = 6 Hz, 12 Hz, $C^8\mathbf{H}_2$), 4.36 (1 H, dd, *J* = 3 Hz, 6 Hz, $C^2\mathbf{H}$), 4.09 (1 H, dd, *J* = 3 Hz, 6 Hz, $C^3\mathbf{H}$), 4.06 (1 H, d, *J* = 3 Hz, $C^4\mathbf{H}$), 3.90 (1 H, t, 12 Hz, $C^8\mathbf{H}_2$), 3.78 (1 H, d, *J* = 3 Hz, $C^1\mathbf{H}$), 3.56 (1 H, br, O**H**), 2.85 (1 H, br, O**H**), 1.86 (1 H, m, $C^7\mathbf{H}$), 1.1-0.92 (23

H, $C^6\mathbf{H}_2$, $Si(C\mathbf{H}(C\mathbf{H}_3)_2)_3$) ppm; ^{13}C (75 MHz, $CDCl_3$) δ 151.1, 107.3, 82.8, 80.8, 78.9, 74.8, 69.3, 36.1, 23.4, 18.3, 18.1, 17.5, 12.5 ppm.



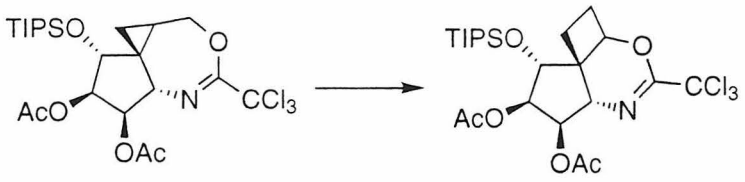
23 **24**

***Bis*-acetate 24.** To a stirred solution of 220 mg of **23** (0.464 mmol, 1.00 equiv) in 5 mL of CH_2Cl_2 was added 138 mg of DMAP (1.13 mmol, 2.40 equiv) and 116 mg of acetic anhydride (1.14 mmol, 2.44 equiv). The reaction was stirred for 15 min and concentrated to give a yellow solid. Purification by silica gel chromatography (19 mm x 20 cm, 4:1 hexanes:ethyl acetate, R_f = 0.35) afforded 220 mg of **24** as a white solid (0.394 mmol, 85.0% yield): mp 136-137 °C; IR (thin film) ν 3904, 3854, 3751, 3676, 2944, 2362, 1696, 1372, 1183, 1070, 922, 860, 791 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 5.89 (1 H, dd, J = 4 Hz, 3 Hz, $C^2\mathbf{H}$), 5.59 (1 H, t, *J* = 4 Hz, $C^3\mathbf{H}$), 4.05 (1 H, *J* = 4 Hz, $C^4\mathbf{H}$), 3.98 (1 H, dd, *J* = 12 Hz, 6 Hz, $C^8\mathbf{H}_2$), 3.88 (1 H, d, *J* = 3 Hz, $C^1\mathbf{H}$), 3.22 (1 H, t, *J* = 12 Hz, $C^8\mathbf{H}_2$), 1.76 (3 H, s, $C\mathbf{H}_3$), 1.722 (3 H, s, $C\mathbf{H}_3$), 1.07-0.85 (22 H, m, $C^7\mathbf{H}$, $Si(C\mathbf{H}(C\mathbf{H}_3)_2)_3$), 0.64 (1 H, dd, *J* = 5 Hz, 8 Hz, $C^6\mathbf{H}$), 0.41 (1 H, t, *J* = 5 Hz, $C^6\mathbf{H}$) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 168.9, 168.7, 150.9, 95.0, 79.7, 79.6, 79.2, 73.4, 65.6, 35.8, 22.1, 20.1, 20.0, 17.9, 17.8, 17.1, 12.4 ppm.



24 **26**

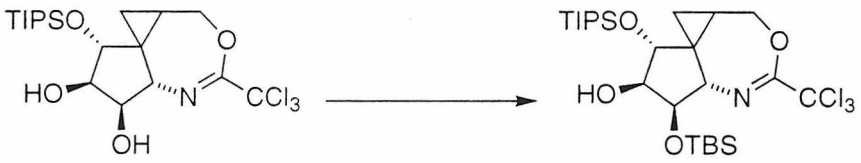
Chloride 26. To a stirred solution of 11 mg of **24** (0.020 mmol, 1.0 equiv) in 1 mL of toluene was added via syringe 25 μL of a 1:9 $SnCl_4$: toluene solution (1.1 mg $SnCl_4$, 0.021 mmol, 1.1 equiv). The nitrogen inlet was quickly replaced by a glass stopper and the reaction vessel was heated to 50 °C for 8 h. The reaction was quenched with 1 mL saturated aqueous $NaHCO_3$ and extracted with diethyl ether (2 x 5 mL). The organic layers were combined, dried over Na_2SO_4, and concentrated to a clear oil. Purification by silica gel chromatography (10 mm x 10 cm, 4:1 hexanes:ethyl acetate, R_f = 0.3) gave 11 mg of **26** as a clear oil (0.019 mmol, 95 % yield): ^{1}H NMR (300 MHz C_6D_6) δ 7.50 (1 H, d, *J* = 10 Hz, N**H**), 5.75 (1 H, dd, *J* = 4.5 Hz, 7 Hz, C^3**H**), 5.55 (1 H, dd, *J* = 1 Hz, 7 Hz, C^2**H**), 4.45 (1 H, dd, *J* = 4.5 Hz, 10 Hz, C^4**H**), 3.58 (1 H, d, *J* = 1 Hz, C^1**H**), 3.48 (1 H, dd, *J* = 8 Hz, 16 Hz, C^8**H**$_2$), 3.27 (1 H, dd, *J* = 9 Hz, 16 Hz), 1.65 (3 H, s, C**H**$_3$), 1.60 (3 H, s, C**H**$_3$), 1.45 (1 H, m, C^7**H**), 1.10-0.85 (22 H, m, C^6**H**$_2$, Si(C**H**(C**H**$_3$)$_2$)$_3$), 0.645 (1 H, t, *J* = 5 Hz, C^6**H**) ppm.



24 27

Spirocyclobutane 27. To a stirred solution of 10 mg of **24** (0.018 mmol, 1 equiv) in 1 mL of toluene was added 24 μL of a 1:9 BF_3•OEt_2:toluene solution (2.7 mg BF_3•OEt_2, 0.019 mmol, 1.0 equiv). After stirring for two hours at 25 °C, the reaction was quenched

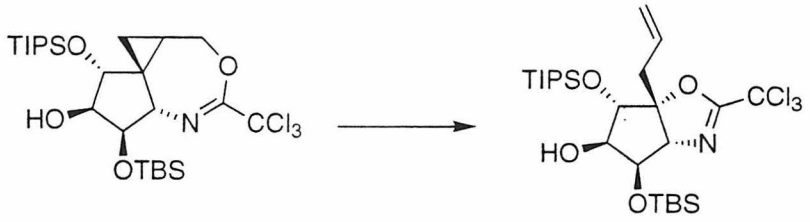
with 1 mL saturated $NaHCO_3$ and extracted with 2 x 5 mL Et_2O. The organic layers were combined, dried over Na_2SO_4 and concentrated to a yellow oil. Purification by silica gel chromatography (15 mm x 10 cm, 2:1 hexanes:ethyl acetate, R_f = 0.67) afforded 3 mg (0.006 mmol, 30% yield) of **27** as a clear oil: IR (thin film) ν 3904, 3854, 3751, 3676, 2944, 2362, 1696, 1372, 1183, 1070, 922, 860, 791 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 5.69 (1 H, t, *J* = 5.6 Hz, $C^2\mathbf{H}$), 5.42 (1H, t, *J* = 4 Hz, $C^3\mathbf{H}$), 4.83 (1 H, t, *J* = 4 Hz, $C^8\mathbf{H}$), 4.12 (1 H, d, *J* = 4 Hz, $C^4\mathbf{H}$), 3.95 (1 H, d, *J* = 4 Hz, $C^1\mathbf{H}$), 2.0 - 1.5 (4 H, m, $C^6\mathbf{H}_2$, $C^7\mathbf{H}_2$), 1.21-1.0 (21 H, s, $Si(C\mathbf{H}(C\mathbf{H}_3)_2)_3$) ppm.



23 **28**

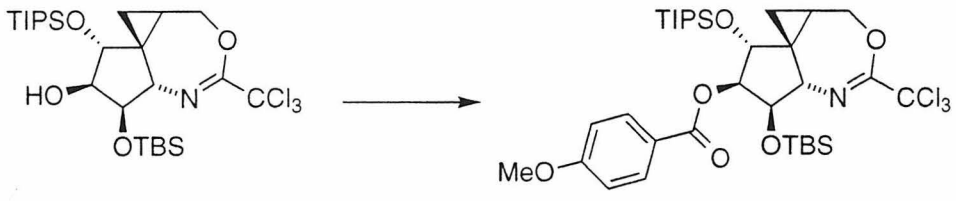
TBS ether 28. To a stirred solution of 1.53 g of **23** (3.23 mmol, 1.00 equiv) in 40 mL CH_2Cl_2 was added 2.25 mL of triethylamine (16.2 mmol, 5.02 equiv), 200 mg of DMAP(1.64 mmol, 0.509 equiv) and 1.46 g of TBSCl (9.70 mmol, 3.00 equiv) sequentially. The reaction was stirred for 24 h and quenched with 10 mL of saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous phase was extracted with 40 mL of CH_2Cl_2. The organic layers were combined, dried over Na_2SO_4, and concentrated. Purification by silica gel chromatography (19mm x 20 cm, 4:1 hexanes:ethyl acetate, R_f = 0.7) yielded 1.60 g of **28** (2.80 mmol, 87.1% yield) and 200 mg of **23** (13.1 % yield): IR (thin film) ν 3402, 2943, 2724, 2251, 1463, 1384, 1333, 1180 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 4.64 (1 H, t, *J* = 4 Hz, $C^3\mathbf{H}$), 4.13 (1 H, m, $C^2\mathbf{H}$), 4.00 (1 H, dd, *J* = 6 Hz, 12 Hz, $C^8\mathbf{H}_2$), 3.85 (1 H, d, *J* = 4 Hz, $C^4\mathbf{H}$), 3.72 (1 H, d, *J* = 4 Hz, $C^1\mathbf{H}$), 3.144 (1H, *J* = 12 Hz, $C^8\mathbf{H}_2$), 2.75 (1 H, s, O**H**), 1.62 (1 H, m, $C^7\mathbf{H}$), 1.06 (9 H, s, $SiC(C\mathbf{H}_3)_3$), 0.93 (21 H, s, $Si(C\mathbf{H}(C\mathbf{H}_3)_2)_3$), 0.17 (3 H, s, $SiC\mathbf{H}_3$), 0.15 (3 H, s, $SiC\mathbf{H}_3$) ppm; ^{13}C NMR (300 MHz, C_6D_6) δ 150.0, 95.0, 83.5, 83.2, 77.9, 74.1, 70.1,

36.2, 32.0, 31.6, 29.8, 29.7, 29.5, 23.4, 22.8, 22.7, 18.1, 17.9, 17.5, 14.0, 12.4, -4.5, -5.3 ppm.



28 **29**

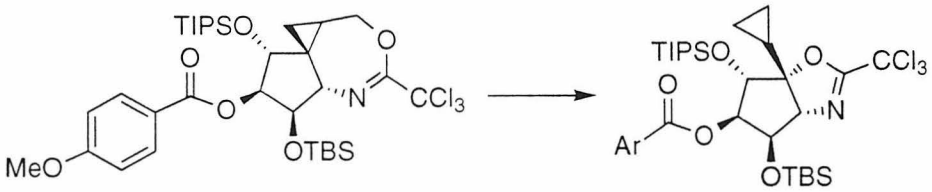
Oxazoline 29. To a stirred solution of 35 mg of **28** (0.059 mmol, 1.0 equiv) in 1 mL of toluene was added 60 µL of a 1:9 BF_3•OEt_2: toluene solution (0.048 mmol, 0.81 equiv). The reaction was stirred for 2 h and quenched with 200 mL of triethylamine. The reaction was concentrated and purified via silica gel chromatography (10 mm x 20 cm, 8:1 hexanes:ethyl acetate, R_f = 0.7). 10 mg of a clear oil were obtained (0.017 mmol, 28% yield): ^{1}H NMR (300 MHz C_6D_6) δ 5.78 (1 H, m, C^7**H**), 5.08 (2 H, dd, *J* = 11 Hz, 16 Hz, C^8**H**$_2$), 4.32 (1 H, d, *J* = 6.5 Hz, C^4**H**), 4.15 (1 H, m, C^2**H**), 3.95 (1 H, d, *J* = 2.5 Hz, C^1**H**), 3.92-3.88 (1 H, m, C^3**H**), 2.80 (1 H, dd, *J* = 6.6 Hz, 13 Hz, C^6**H**$_2$), 2.50 (1 H, dd, *J* = 6.6 Hz, 13 Hz, C^6**H**), 1.20 (21 H, s, Si(C**H**(C**H**$_3$)$_2$)$_3$), 0.87 (9 H, s, SiC(C**H**$_3$)$_3$, 0.06 (3 H, s, SiC**H**$_3$), 0.0 (3 H, s, SiC**H**$_3$) ppm.



28 **30**

***p*-methoxybenzoate 30**. To a stirred solution of 410 mg of **28** (0.0719 mmol, 1.00 equiv) in 10 mL CH_2Cl_2 was added sequentially 500 mL of triethylamine(3.59 mmol, 5.00 equiv), 100 mg of DMAP (0.820 mmol, 1.14 equiv), and 123 µL of *p*-

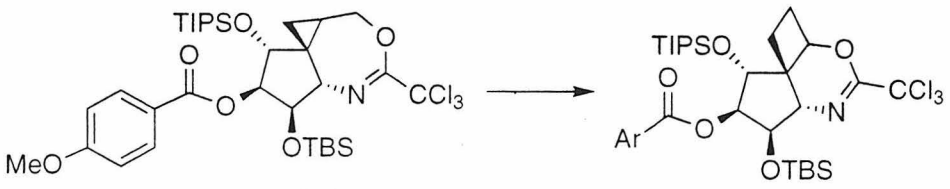
methoxybenzoyl chloride (1.05 mmol, 1.46 equiv). The reaction was stirred overnight and quenched with saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous phase was extracted with 10 mL CH_2Cl_2. The organic layers were combined, dried over Na_2SO_4 and concentrated to a yellow solid. Purification by silica gel chromatography (19mm x 25 cm., 8:1 hexanes: ethyl acetate, Rf = 0.47) afforded 420 mg of **30** (0.596 mmol, 82.9% yield) as a clear oil. ^1H NMR (300 MHz C_6D_6) δ 8.29 (2 H, d, *J* = 11 Hz, *p*-methoxybenzoate), 6.71 (2 H, d, *J* = 11 Hz, *p*-methoxybenzoate), 5.70 (1 H, t, *J* = 4 Hz, $C^2\mathbf{H}$), 5.05 (1 H, t, *J* = 4 Hz, $C^3\mathbf{H}$), 4.19 (1 H, d, *J* = 4 Hz, $C^4\mathbf{H}$), 4.05 (1 H, dd, *J* = 4 Hz, 12 Hz, $C^8\mathbf{H}_2$), 3.95 (1 H, d, *J* = 4 Hz, $C^1\mathbf{H}$), 3.28 (1 H, t, *J* = 12 Hz, $C^8\mathbf{H}_2$), 3.14 (3 H, s, $C\mathbf{H}_3$), 1.77-1.75 (1 H, m, $C^7\mathbf{H}$), 1.09 (21 H, s, $Si(C\mathbf{H}(C\mathbf{H}_3)_2)_3$), 0.95 (9 H, s, $SiC(C\mathbf{H}_3)_3$), 0.80 (1 H, dd, J = 5 Hz, 8Hz, $C^6\mathbf{H}_2$), 0.57 (1 H, t, J = 8Hz, $C^6\mathbf{H}_2$), 0.14 (3 H, s, $SiC\mathbf{H}_3$), 0.12 (3 H, s, $SiC\mathbf{H}_3$) ppm.



30 **31**

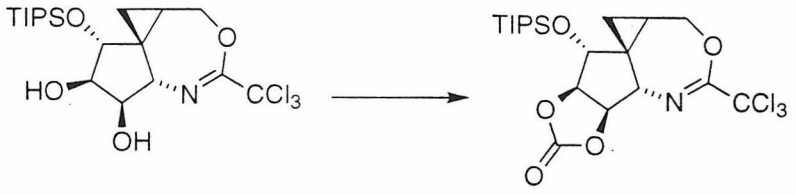
Exocyclopropane 31. To a stirred solution of 180 mg of **30** (0.25 mmol, 1 equiv) in 5 mL of toluene was added 31 μL of $BF_3{\bullet}OEt_2$. After stirring for one hr at 0 °C, the reaction was quenched with 2 mL saturated $NaHCO_3$ and extracted with 2 x 5 mL Et_2O. The organic layers were combined, dried over Na_2SO_4 and concentrated to a yellow oil. Purification by silica gel chromatography (20 mm x 10 cm, 8:1 hexanes:ethyl acetate, R_f = 0.49) afforded 120 mg of **31** (0.17 mmol, 69% yield) as a clear oil: IR (thin film) ν 2950, 2820, 1725, 1693, 1612, 1518, 1256 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 8.19 (2 H, d, *J* = 11 Hz, *p*-methoxybenzoate), 6.66 (2 H, d, *J* = 11 Hz, *p*-methoxybenzoate), 5.45 (1 H, t, *J* = 3 Hz, 5 Hz, $C^3\mathbf{H}$), 5.15 (1H, d, *J* = 5 Hz, $C^8\mathbf{H}$), 4.71 (1 H, t, J = 3 Hz, $C^4\mathbf{H}$),

4.01 (1 H, s, C^1**H**), 3.11 (3 H, s, C**H**$_3$), 1.48 (1 H, m, C^6**H**), 1.081 (21 H, s, Si(C**H**(C**H**$_3$)$_2$)$_3$), 0.96 (9 H, s, SiC(C**H**$_3$)$_3$), 0.76-0.75 (1 H, m, cyclopropane), 0.55-0.54 (1 H, m, cyclopropane), 0.40-0.39 (1 H, m, cyclopropane), 0.35-0.34 (1 H, m, cyclopropane), 0.24 (3 H, s, SiC**H**$_3$), 0.12 (3 H, s, SiC**H**$_3$) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 165.7, 164.1, 132.2, 122.9, 114.2, 95.8, 79.5, 79.4, 77.7, 72.9, 55.1, 26.0, 18.5, 18.3, 18.2, 16.5, 13.5, 13.3, 12.8, 1.8, 0.1, -4.9, -5.1 ppm.



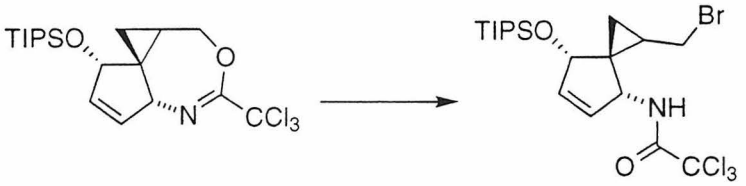
30 **32**

Spirocyclobutane 32. To a stirred solution of 230 mg of **30** (0.32 mmol , 1.0 equiv) in 6 mL of toluene was added 40 μL (0.32 mmol, 1.0 equiv) of BF_3•OEt_2. After stirring for 24 h at 25 °C, the reaction was quenched with 5 mL saturated $NaHCO_3$ and extracted with 2 x 20 mL Et_2O. The organic layers were combined, dried over Na_2SO_4 and concentrated to a yellow oil. Purification by silica gel chromatography (20 mm x 20 cm, 8:1 hexanes:ethyl acetate, R_f = 0.49) afforded 180 mg (0.25 mmol, 81 % yield) of **32** as a clear oil: IR (thin film) ν 2950, 2820, 1725, 1693, 1612, 1518, 1256 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 8.19 (2 H, d, *J* = 11 Hz, *p*-methoxybenzoate), 6.66 (2 H, d, *J* = 11 Hz, *p*-methoxybenzoate), 5.45 (1 H, t, *J* = 4 Hz, C^2**H**), 4.90 (1H, t, *J* = 4 Hz, C^8**H**), 4.71 (1 H, t, *J* = 4 Hz, C^3**H**), 4.33 (1 H, d, *J* = 4 Hz, C^1**H**), 4.00 (1 H, d, *J* = 4 Hz, C^1**H**), 3.11 (3 H, s, C**H**$_3$), 2.0 - 1.5 (4 H, m, C^7**H**$_2$, C^8**H**$_2$), 1.081 (21 H, s, Si(C**H**(C**H**$_3$)$_2$)$_3$), 0.96 (9 H, s, SiC(C**H**$_3$)$_3$), 0.24 (3 H, s, SiC**H**$_3$), 0.12 (3 H, s, SiC**H**$_3$) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 166.0, 164.5, 152.1, 132.3, 123.3, 115.0, 94.2, 81.0, 79.5,78.7, 71.0, 67.5, 55.6, 47.1, 27.5, 27.1, 26.1, 18.9, 23.2, -4.1, -4.2 ppm.



23 35

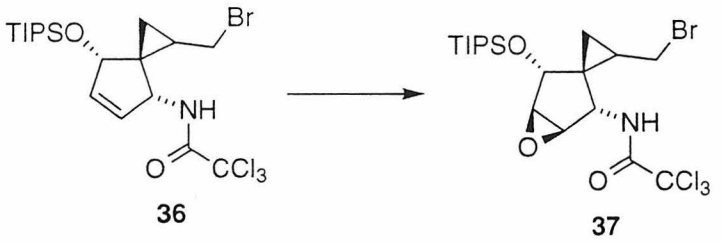
Carbonate 35. To a stirred solution of 20 mg **23** (0.04 mmol, 1 equiv) in 1.5 mL of CH_2Cl_2 at -78 °C was added 20 μL of pyridine (0.3 mmol, 8 equiv). A solution of 6 mg of triphosgene (0.02 mmol, 0.5 equiv) in 1 mL of CH_2Cl_2 was transfered to the reaction *via* cannula. The resulting orange slurry was allowed to slowly warm to 25 °C and quenched with 1 mL water. The organic layer was separated and the aqueous layer was extracted with 2 x 5 mL CH_2Cl_2. The organic layers were combined, dried over Na_2SO_4 and concentrated. Purification by silica gel chromatography (10 mm x 15 cm, 3:1 hexanes:ethyl acetate, R_f = 0.50) yielded 20 mg of **35** (0.04 mmol, 100% yield) as a white solid. ^{1}H NMR (300 MHz, C_6D_6) δ 4.85 (1 H, d, *J* = 6.5 Hz, C^2**H**), 4.36 (1 H, d, *J* = 6.5 Hz, C^3**H**), 3.72 (1 H, dd, *J* = 6 Hz, 12 Hz, C^8**H**$_2$), 3.68 (1 H, s, C^4**H**), 3.52 (1 H, s, C^1**H**), 3.08 (1 H, t, *J* = 12 Hz, C^8**H**$_2$), 1.45 (1 H, m, C^7**H**), 1.05-0.86 (21 H, s, Si(C**H**(C**H**$_3$)$_2$)$_3$), 0.32 (1 H, dd, *J* = 5 Hz, 8 Hz, C^6**H**$_2$), 0.14 (1 H, t, *J* = 5 Hz, C^6**H**$_2$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 151.5, 99.4, 88.5, 86.6, 83.4, 69.1, 37.7, 22.6, 18.6, 18.5, 16.3, 12.8 ppm.



22 36

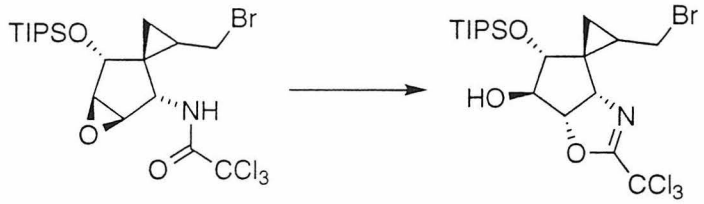
Bromide 36. A 500 mL three-necked flask was charged with 6.74 g (30.9 mmol, 5.00 equiv) of $NiBr_2 \cdot H_2O$. The flask was evacuated and heated at 140 °C for 3 hr to dry the

$NiBr_2$. A nitrogen atmosphere was reestablished and 5.32 g (61.8 mmol, 10.0 equiv) of LiBr were added. To the salts were added 100 mL THF, yielding a blue solution. To this solution were added *via* cannula 2.71 g (6.18 mmol, 1.00 equiv) of **22** in 30 mL of THF. The reaction was heated to 65 °C and stirred for 48 hr. The reaction was then carefully poured into 200 mL of water and filtered through Celite. The organic layer was separated and the aqueous layer was extracted twice with 200 mL of Et_2O. The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel chromatography (250 x 40 mm, 8:1 hexanes:Et_2O, R_f = 0.2) to afford 2.54 g (4.88 mmol, 79.7 % yield) of **36** as a clear oil: $[\alpha]_D^{25}$ = -72.6° (c = 4.0, $CHCl_3$); IR (thin film) ν 3408, 3066, 2944, 2892, 1713, 1504, 1384, 1310, 1219, 1048 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 6.97 (1 H, d, *J* = 9 Hz, N**H**), 5.84 (2 H, s, $C^{2\text{-}3}$**H**), 4.39 (1 H, d, *J* = 9 Hz, C^1**H**), 3.61 (1 H, s, C^4**H**), 3.55 (1 H, dd, *J* = 7 Hz, 10 Hz, C**H**$_2$Br), 3.21 (1 H, t, *J* = 10 Hz, C**H**$_2$Br), 1.71 (1 H, m, C^7**H**), 1.04-0.729 (21 H, m, TIPS), 0.60 (1 H, dd, *J* = 5 Hz, 10 Hz, C^6**H**$_2$), 0.314 (1 H, t, *J* = 5 Hz, C^6**H**$_2$) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 160.2, 137.4, 134.5, 93.0, 82.1, 59.6, 40.8, 34.2, 23.8, 21.85, 17.9, 17.8, 12.1 ppm. HRMS (FAB) Calcd for $C_{19}H_{32}BrCl_3NO_2$ (M+H)+: 518.0451. Found: 518.0410.



epoxide 37. To 1.5 g (2.9 mmol, 1.0 equiv) of **36** was added 90 mL (9.0 mmol, 3.0 equiv) 0.10 M dimethyl dioxirane in acetone. The light yellow solution was allowed to stir 6 h and concentrated. The residue was treated with an additional 90 mL of 0.10 M dimethyl

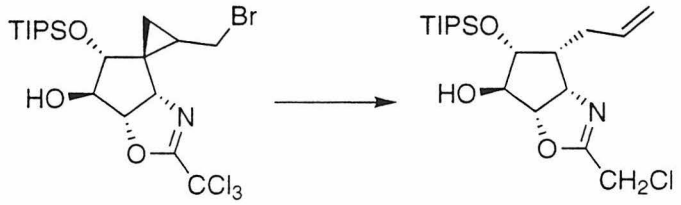
dioxirane. The procedure was repeated three times. The reaction was concentrated and the residue was purified by silica gel chromatography (200 x 20 mm, 8:1 hexanes:Et_2O, R_f = 0.15) to afford 1.0 g (1.8 mmol, 65% yield) of **37** as a clear oil: $[\alpha]_D^{25}$ = -32 (c = 1.0, $CHCl_3$); IR (thin film) ν 3402, 2867, 2361, 1714, 1503, 1330, 1223, 1086 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.20 (1 H, d, *J* = 9 Hz, N**H**), 4.17 (1 H, d, *J* = 9 Hz, C^1**H**), 3.69 (1 H, s, C^4**H**), 3.60 (1 H, d, *J* = 5 Hz, $C^{2\text{-}3}$**H**), 3.52 (1 H, d, *J* = 5 Hz, $C^{2\text{-}3}$**H**), 3.52 (1 H, t, *J* = 9 Hz, C**H**$_2$Br), 3.15 (1 H, t, *J* = 9 Hz, C**H**$_2$Br), 1.64 (1 H, m, C^7**H**), 1.05 - 0.68 (23 H, m, C^6**H**$_2$, TIPS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 92.4, 79.6, 56.8, 56.6, 56.1, 37.9, 34.2, 22.8, 19.8, 18.1, 18.0, 17.8, 12.4, 12.4 ppm. HRMS (FAB) Calcd for $C_{19}H_{31}BrCl_3NO_3Si$ (M)+: 533.0322. Found: 533.0342.



37 **38**

oxazoline 38. To a solution of 1.00 g (1.88 mmol, 1.00 equiv) **37** in 20 mL toluene at 0 °C was added via syringe 310 μL (2.48 mmol, 1.32 equiv) BF_3•OEt_2. The reaction was allowed to stir for 30 min and quenched by pouring into a separatory funnel containing 100 mL Et_2O and 20 mL saturated $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted twice with 50 mL Et_2O. The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated. The reaction was purified by silica gel chromatography (200 mm x 20 mm, 4:1 hexanes:ethyl acetate, R_f = 0.48) to afford 870 mg (1.63 mmol, 87.0 % yield) of **38** as a colorless solid: mp 96-98 °C; $[\alpha]_D^{25}$ = -107° (c = 1.00, $CHCl_3$); IR (thin film) ν 3417, 2866, 1771, 1660, 1384, 1219, 1066, 964, 882, 822 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.09 (1 H, d, *J* = 8 Hz, C^2**H**), 4.48 (1 H, d, *J*

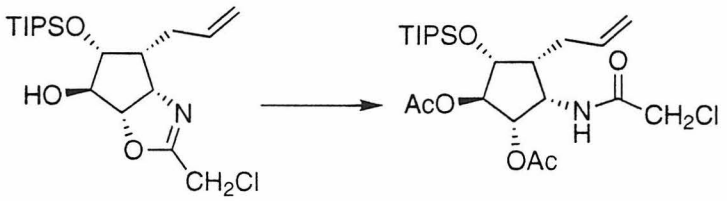
= 8 Hz, C^1**H**), 4.369 (1 H, s, C^3**H**), 4.04 (1 H, dd, *J* = 5 Hz, 11 Hz, C**H**$_2$Br), 3.55 (1 H, s, C^4**H**), 3.36 (1 H, t, *J* = 11 Hz, C**H**$_2$Br), 1.91 (1 H, s, O**H**), 1.80 (1 H, m, C^7**H**), 1.20 (1 H, t, *J* = 6 Hz, C^6**H**), 1.0 (21 H, s, TIPS), 0.846 (1 H, t, *J* = 6 Hz) ppm; ^{13}C (75 MHz, $CDCl_3$) δ 161.1, 92.4, 84.9, 81.8, 77.2, 40.2, 37.0, 23.3, 21.9, 18.3, 18.2, 12.5 ppm. HRMS (FAB) Calcd for $C_{19}H_{31}BrCl_3NO_3Si$ (M)+: 533.0322. Found: 533.0309.



38 **39**

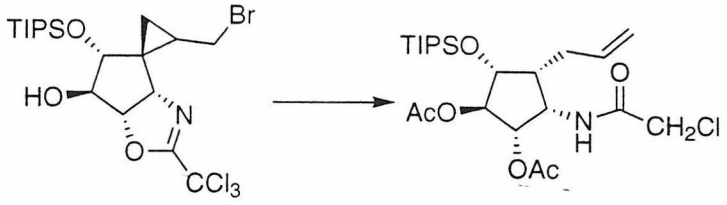
Allyl cyclopentane 39. To a solution of 800 mg (1.5 mmol, 1.0 equiv) of **38** in 20 mL of absolute ethanol was added sequentially 60 μL (0.23 mmol, 0.15 equiv) of Bu_3SnH, 500 mg (13 mmol, 8.8 equiv) of $NaBH_4$ and 230 μL of 1.0 M triethylborane (0.23 mmol, 0.15 equiv). The reaction was stirred for 8 h and an additional 40 μL (0.10 equiv) Bu_3SnH, 55 mg $NaBH_4$ (1.0 equiv), and 150 μL of 1.0 M triethylborane (0.10 equiv). The white slurry was allowed to stir for 12 h and quenched by the addition of 10 mL of water. The reaction mixture was extracted three times with Et_2O. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (150 x 20 mm, 4:1 hexanes:ethyl acetate, R_f = 0.25) to afford 430 mg (1.1 mmol, 75% yield) of **39** as a white solid: mp 68-70 °C; $[\alpha]_D^{25}$ = -49 (c = 1.3, $CHCl_3$); IR (thin film) ν 3260, 2943, 2866, 2362, 1660, 1464, 1361, 1243, 1100, 1067, 882 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.01 (1H, m, C^7**H**), 5.27 - 5.08 (2H, m, C^8**H**$_2$), 4.73 (1H, d, *J* = 8 Hz, C^2**H**), 4.63 (1 H, t, *J* = 8Hz, C^1**H**), 4.26 (1 H, s, C^3**H**), 4.07 (1 H, d, *J* = 12 Hz, C**H**$_2$Cl), 4.06 (1 H, d, *J* = 8 Hz, C^4**H**), 3.92 (1 H, d, *J* = 12 Hz, C**H**$_2$Cl), 2.53 - 2.13 (3 H, m, C$^{5\text{-}6}$**H**), 1.04 (21 H, s, TIPS) ppm; ^{13}C NMR

(75 MHz, $CDCl_3$) δ 161.3, 137.4, 115.6, 89.4, 81.0, 80.5, 72.9, 47.3, 36.6, 29.2, 18.2, 12.5 ppm. HRMS (FAB) Calcd for $C_{19}H_{35}ClNO_3$ $(M+H)^+$: 388.2075. Found: 388.2075.



39 **40**

***Bis* -acetate 40**. To a solution of 220 mg (0.59 mmol, 1.0 equiv) of **39** in 5 ml of CH_3CN:water (4:1 *v/v*) was added 30 mg (0.12 mmol, 0.20 equiv) of PPTS. After 12 h, the reaction was concentrated in vacuo and the residue was dissolved in 5 mL of CH_2Cl_2. To the stirring solution was added sequentially 280 μL (2.9 mmol, 5.0 equiv) of acetic anhydride and 350 mg (2.9 mmol, 5.0 equiv) of DMAP. The yellow solution was stirred 8 h and concentrated *in vacuo*. The residue was purified by silica gel chromatography (150 x 20 mm, 2:1 hexanes:ethyl acetate, R_f = 0.61) to afford 220 mg (0.450 mmol, 77 % yield) of **40** as a white solid: mp 76.5 - 78 °C; $[\alpha]_D^{25}$ = -7.3° (c = 2.04, $CHCl_3$); IR (thin film) ν 3411, 2867, 2867, 2364, 1749, 1682, 1521, 1369, 1111, 998, 882 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19 (1 H, d, *J* = 10 Hz, N**H**), 5.80 (1 H, m, C^7**H**), 5.14 - 5.08 (4 H, m, $C^{2\text{-}3}$**H**, C^8**H**$_2$), 4.82 (1 H, m, C^1**H**), 4.17 (1 H, d, *J* = 4 Hz, C^4**H**), 4.04 (2 H, s, **CH**$_2$Cl), 2.35 (2 H, t, *J* = 7 Hz, C^6**H**$_2$), 2.20 (1 H, m , C^5**H**), 2.08 (3 H, s, Ac), 2.06 (3 H, s, Ac), 1.2 - 0.9 (21 H, m, TIPS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 166.3, 136.3, 118.2, 83.9, 79.1, 78.7, 78.4, 77.9, 52.9, 45.5, 43.1, 29.3, 21.4, 21.1, 18.6, 12.8 ppm. HRMS (FAB) Calcd for $C_{23}H_{40}ClNO_6Si$ (M)+: 489.2313. Found: 489.2314.

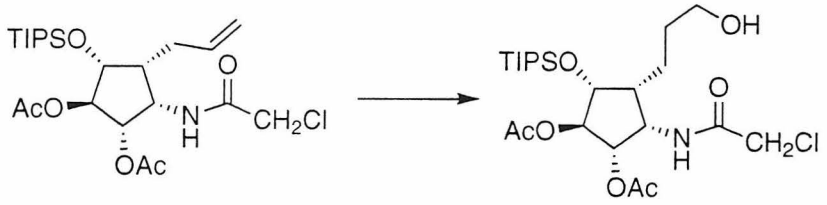


38 **40**

***Bis*-acetate 40.** To a solution of 3.0 g (5.6 mmol, 1.0 equiv) of **38** in 20 mL of absolute ethanol were added sequentially 250 μL (0.99 mmol, 0.17 equiv) of Bu_3SnH, 1.5 g (43 mmol, 7.6 equiv) of $NaBH_4$, and 1.0 μL (1.0 M, 1.0 mmol, 0.17 equiv) of triethylborane. After 4 hrs, additional $NaBH_4$ (1.0 g), and triethylborane (1.0 mL) were added. The reaction was stirred an additional 8 h and quenched by the addition of 20 mL of water. The aqueous layer was extracted three times with 100 mL of Et_2O; the organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was dissolved in 40 mL of 4:1 CH_3CN: water. To the stirring solution was added 200 mg (1.1 mmol, 0.18 equiv) of TsOH; the yellow solution was allowed to stir at 25 °C for 12 h. The reaction mixture was then concentrated to a yellow oil, which was dried azeotropically with CH_3CN (3 x 200 mL). The residue was dissolved in 150 mL of CH_2Cl_2 and treated with 5.0 mL (53 mmol, 9.5 equiv) of acetic anhydride, 1.0 g (8.2 mmol, 1.5 equiv) of DMAP, and 5.0 mL (36 mmol, 6.4 equiv) of triethylamine. The reaction was stirred overnight and quenched by the addition of 100 mL of water. The organic layer was separated and the aqueous layer was extracted twice with 100 mL of CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (200 mm x 30 mm, 2:1 hexanes:ethyl acetate, $R_f = 0.61$) to afford 1.43 g (2.97 mmol, 53.0 % yield) of **40** as a white solid: mp 76.5 - 78 °C; $[\alpha]_D^{25} = -7.3°$ (c = 2.04, $CHCl_3$); IR (thin film) ν 3411, 2867, 2867, 2364, 1749, 1682, 1521, 1369, 1111, 998, 882 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19 (1 H, d, *J* = 10 Hz, N**H**), 5.80 (1 H, m, C^7**H**), 5.14 - 5.08 (4

H, m, $C^{2-3}\mathbf{H}$, $C^{8}\mathbf{H}_2$), 4.82 (1 H, m, $C^{1}\mathbf{H}$), 4.17 (1 H, d, J = 4 Hz, $C^{4}\mathbf{H}$), 4.04 (2 H, s, $\mathbf{CH}_2Cl$), 2.35 (2 H, t, J = 7 Hz, $C^{6}\mathbf{H}_2$), 2.20 (1 H, m , $C^{5}\mathbf{H}$), 2.08 (3 H, s, Ac), 2.06 (3 H, s, Ac), 1.2 - 0.9 (21 H, m, TIPS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 166.3, 136.3, 118.2, 83.9, 79.1, 78.7, 78.4, 77.9, 52.9, 45.5, 43.1, 29.3, 21.4, 21.1, 18.6, 12.8 ppm. HRMS (FAB) Calcd for $C_{23}H_{40}ClNO_6Si$ (M)+: 489.2313. Found: 489.2314.

Preparation of dicyclohexylborane.[47] To a solution of 1.00 mL (9.81 mmol, 2.00 equiv) of cyclohexene in 5 mL of Et_2O at 0 °C was added 493 μL (10.0 M, 4.93 mmol, 1.00 equiv) of BH_3•SMe_2. The white slurry was stirred for 3 h at 0 °C, then diluted by the addition of 5 mL of Et_2O to give a 0.493 M solution of dicyclohexylborane, which was used without subsequent purification.



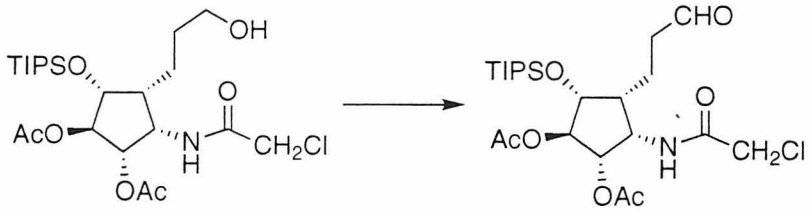
40 **41**

Alcohol 41. To a solution of 380 mg (0.788 mmol, 1.00 equiv) of **40** in 5 mL of Et_2O at 0 °C was added *via* syringe 3.19 mL (1.57 mmol, 1.99 equiv) of 0.493 M dicyclohexylborane. The reaction was stirred for 30 min; then the excess borane was quenched by the addition of 3 mL MeOH and the reaction was allowed to warm to 25 °C. To the clear solution was added sequentially 5 mL of phosphate buffer (pH 7) and 2 mL of 30% H_2O_2. The reaction was stirred for 8 h and extracted with 50 mL of 8:1 CH_2Cl_2:MeOH. The aqueous layer was reextracted twice with 50 mL of 8:1 CH_2Cl_2.

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[47] Zweifel, G.; Ayyanger, N. R.; Brown, H. C. *J. Am. Chem. Soc.* **1963**, *85*, 2072.

The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel chromatography (100 x 25 mm, 1:1 CH_2Cl_2:ethyl acetate, R_f = 0.3) to afford 320 mg (0.630 mmol , 81.0% yield) of **41** as a clear oil: $[\alpha]_D^{25}$ = +5.81° (c = 2.0, $CHCl_3$); IR (thin film) ν 3404, 2944, 2867, 1747, 1678, 1525, 1370, 1111, 998, 882 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.12 (1 H, d, 11 Hz, N**H**), 5.04 (2 H, m, $C^{2\text{-}3}$**H**), 4.81 (1 H, m, C^1**H**), 4.09 (1 H, d, *J* = 3 Hz, C^4**H**), 4.02 (1 H, d, *J* = 15 Hz, C**H**$_2$Cl), 3.97 (1 H, d, *J* = 15 Hz, C**H**$_2$Cl), 3.59 (2 H, m, C**H**$_2$OH), 2.06 (1 H, m, C^5**H**), 2.03 (3 H, s, Ac), 2.01 (3 H, s, Ac), 1.60 (4 H, m, $C^{6\text{-}7}$**H**$_2$), 1.01 (21 H, m, TIPS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 166.1, 83.3, 78.8, 78.3, 62.5, 52.5, 45.1, 42.5, 30.8, 21.0, 20.7, 20.6, 18.2, 18.1, 18.0, 17.9, 12.3 ppm. HRMS (FAB) Calcd for $C_{23}H_{43}ClNO_7Si$ (M+H): 508.2497. Found: 508.2540.

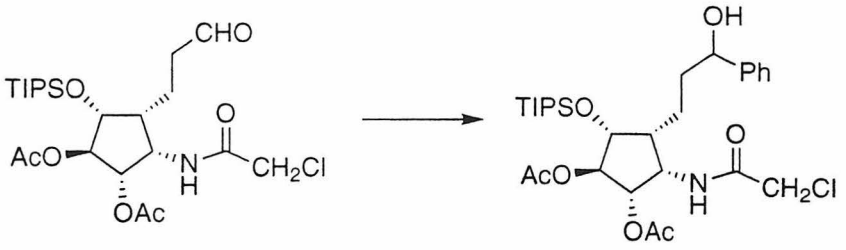


41 **42**

Aldehyde 42. To a solution of 200 μL (2.34 mmol, 3.96 equiv) of oxalyl chloride in 10 mL of CH_2Cl_2 at -78 °C was added dropwise 500 μL (7.04 mmol, 11.9 equiv) of DMSO. After 15 min, a solution of 300 mg (0.591 mmol, 1.00 equiv) of **41** in 5 mL of CH_2Cl_2 was added at -78 °C. After 1 hr at -78 °C, 2.00 mL (14.4 mmol, 24.3 equiv) of triethylamine were added. The reaction was allowed to warm slowly to 0 °C. After 30 min at 0 °C, the reaction was quenched with 10 mL of water. The organic layer was separated and the aqueous layer was reextracted twice with 50 mL of CH_2Cl_2. The organic layers were combined, dried over anhydrous Na2SO4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (100 mm x 20 mm, 1:1 hexanes:ethyl acetate,

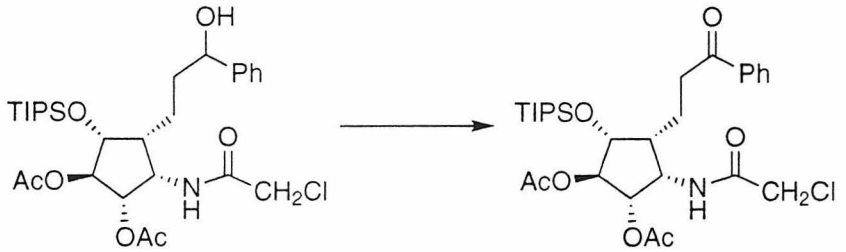
R_f = 0.30) to afford 250 mg (0.495 mmol, 83.8 % yield) of **42** as a colorless oil: $[\alpha]_D^{25}$ = +10.0° (c = 0.25, $CHCl_3$); IR (thin film) ν 3409, 2868, 2723, 1747, 1681, 1463, 1370, 1112, 883 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.768 (1 H, s, C**H**O), 7.09 (1 H, d, *J* = 11 Hz, N**H**), 5.07 (2 H, m, $C^{2\text{-}3}$**H**), 4.83 (1 H, m, C^1**H**), 4.12 (1 H, d, *J* = 3 Hz, C^4**H**), 4.05 (1 H, d, *J* = 15 Hz, C**H**$_2$Cl), 3.99 (1 H, d, *J* = 15 Hz, C**H**$_2$Cl), 2.54 (2 H, m, C^7**H**$_2$), 2.15 (1 H, m, C^5**H**$_2$), 2.05 (3 H, s, Ac), 2.04 (3 H, s, Ac), 1.85 (2 H, m, C^6**H**$_2$), 1.2 - 0.9 (21 H, m, TIPS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.4, 169.5, 169.4, 166.0, 83.2, 78.8, 78.2, 51.9, 44.4, 42.5, 41.7, 20.9, 20.6, 18.2, 18.1, 18.0, 17.9, 16.9, 12.3 ppm. HRMS (FAB) Calcd for $C_{23}H_{40}ClNO_7Si$ (M)+: 505.2262. Found: 505.2265.

Phenyl magnesium bromide. A 25 mL round-bottomed flask was charged with 48 mg (2 mmol, 1 equiv) of magnesium turnings. The flask was evacuated and flame dried. A nitrogen atmosphere was reestablished and the magnesium was suspended in 4 mL of THF. To the stirred suspension was added 240 μL (2.4 mmol, 1.2 equiv) of phenyl bromide. The reaction was stirred until the magnesium turnings were completely consumed, yielding a 0.5 M solution of phenyl magnesium bromide, which was used without further purification.



42 **43**

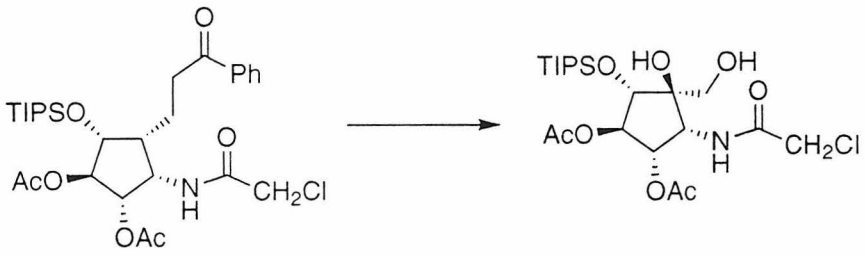
Benzyl alcohol 43. To a solution of 250 mg (0.500 mmol, 1 equiv) of **42** in 10 mL of 1.0 M LiBr in THF was added at -78 °C 2.0 mL of 0.5 M PhMgBr. After 3 h, the reaction was quenched by the addition of 2 mL of MeOH and warmed to 25 °C. The reaction was partitioned between Et_2O (50 mL) and water (50 mL) and the layers were separated. The aqueous layer was extracted twice with 50 mL of Et_2O; the organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (150 x 20 mm, 1:1 hexanes:ethyl acetate, $R_f = 0.30$) to afford 200 mg of an inseparable 6:1 (mol:mol) mixture of **43**:**42** (174 mg 43, 0.301 mmol, 60.0 % yield; 25 mg 42, 0.049 mmol, 10 %) as an oil.



43 **44**

Phenyl ketone 44. To a solution of 200 µL (2.34 mmol, 8.15 equiv) of oxalyl chloride in 10 mL of CH_2Cl_2 at -78 °C were added dropwise 500 µL (7.04 mmol, 24.5 equiv) of DMSO. After 15 min, a solution of 200 mg (174 mg, 0.287 mmol, 1.00 equiv) of a 6:1 mixture of **43**:**42** in 5 mL of CH_2Cl_2 was added at -78 °C. After 1 hr at -78 °C, 2 mL (14.4 mmol, 50.2 equiv) of triethylamine were added. The reaction was allowed to warm

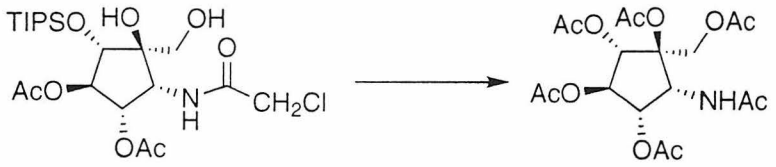
slowly to 0 °C. After 30 min at 0 °C, the reaction was quenched with 10 mL of water. The organic layer was separated and the aqueous layer was reextracted twice with 50 mL of CH_2Cl_2. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (150 x 20 mm, 2:1 hexanes:ethyl acetate, R_f = 0.24) to afford 150 mg (0.258 mmol, 90.0 % yield) of **44** as a colorless oil: $[\alpha]_D^{25}$ = -7.92° (c = 1.07, $CHCl_3$); IR ν 3411, 2944, 2867, 1747, 1681, 1520, 1370, 1239, 1044, 882 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.93 (2 H, d, *J* = 7 Hz, Ph), 7.54 (1 H, t, *J* = 7 Hz, Ph), 7.43 (2 H, t, *J* = 7 Hz, Ph), 7.15 (1 H, d, *J* = 10 Hz, N**H**), 5.05 (2 H, m, $C^{2\text{-}3}$**H**), 4.86 (1 H, m, C^1**H**), 4.16 (1 H, d, *J* = 3 Hz, C^4**H**), 4.03 (1 H, d, *J* = 15 Hz, C**H**$_2$Cl), 3.99 (1 H, d, *J* = 15 Hz, C**H**$_2$Cl), 3.02 (2 H, t, *J* = 7 Hz, C^7**H**$_2$), 2.22 (1 H, m, C^5**H**), 2.04 (3 H, s, Ac), 2.02 (3 H, s, Ac), 1.92 (2 H, m, C^6**H**$_2$), 1.1 - 0.88 (21 H, m, TIPS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.5, 169.5, 166.0, 136.8, 133.3, 128.7, 128.1, 83.3, 79.1, 78.4, 52.0, 44.5, 42.5, 36.0, 20.9, 20.6, 19.0, 18.2, 18.1, 12.4 ppm. HRMS (FAB) Calcd for $C_{29}H_{44}ClNO_7Si$ (M)+: 581.2576. Found: 581.2595.



44 **46**

Diol 46. A solution of 40 mg (0.06 mmol, 1 equiv) of **44** in 35 mL of benzene was subjected to 5 freeze-pump-thaw cycles and irradiated for 30 min. The crude product was concentrated and redissolved in 5 mL of 4:1 acetone:water. To the reaction was added sequentially 20 μL of a 4% OsO_4 solution (0.8 mg OsO_4, 0.003 mmol, 0.05 equiv) and 50 mg (0.4 mmol, 7 equiv) of NMO. The yellow solution was allowed to stir 12 h at 25 °C

and then was quenched by the addition of 50 mg of Na_2SO_3. The reaction was concentrated *in vacuo* and the residue was purified by silica gel chromatography (20 x 5 mm, 1:1 hexanes:ethyl acetate, R_f = 0.28) to afford 20 mg (0.05 mmol, 80 % yield) of **46** as a clear oil: $[\alpha]_D^{25}$ = -2.6° (c = 0.65, $CHCl_3$); IR (thin film) ν 3383, 2944, 2867, 1749, 1663, 1534, 1369, 1238, 1150, 882 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 (1 H, d, *J* = 7 Hz, N**H**), 5.44 (1 H, dd, *J* = 4 Hz, 7 Hz, C^2**H**), 5.12 (1 H, t, *J* = 4 Hz, C^3**H**), 4.44 (1 H, t, *J* = 7 Hz, C^1H), 4.18 (1 H, d, *J* = 4 Hz, C^4**H**), 4.06 (2 H, s, C**H**$_2$Cl), 3.83 (1 H, dd, *J* = 5 Hz, 12 Hz, C^6**H**), 3.63 (1 H, dd, *J* = 8 Hz, 12 Hz, C^6**H**), 3.41 (1 H, s, O**H**), 3.15 (1 H, dd, *J* = 5 Hz, 8 Hz, O**H**), 2.10 (3 H, s, Ac), 2.08 (3 H, s, Ac), 1.2 - 0.9 (21 H, m, TIPS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 169.8, 167.8, 84.5, 82.3, 81.6, 76.5, 63.0, 57.7, 43.0, 21.4, 21.1 18.5, 13.0, 12.8 ppm. HRMS (FAB) Calcd for $C_{21}H_{39}ClNO_8Si$ (M)+: 496.2133. Found: 496.2163.



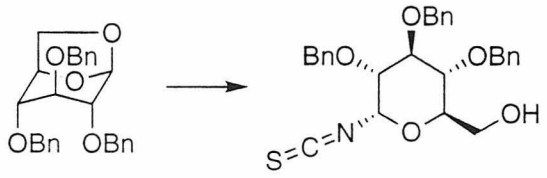
46

Hexaacetate.[48] To a solution of 9 mg (0.02 mmol, 1 equiv) of **46** in 15 mL of MeOH:H_2O (5:1) was added 2 mL of concentrated HCl. After stirring 8 hrs at 60 °C, the reaction was concentrated; the residue was dried azeotropically with CH_3CN (3 x 100 mL). The residue was dissolved in 10 mL pyridine and treated with 100 mL of acetic anhydride (1 mmol, 50 equiv) and 1 crystal of DMAP. After 48 hrs, the reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel chromatography (5 mm x 20 mm, 3:2 benzene:acetonitrile, R_f = 0.31) to afford 4 mg (0.009 mmol, 45% yield) of the trehazolin hexacetate as a white solid: $[\alpha]_D^{25}$ = +4.5° (c = 0.27, $CHCl_3$); IR (thin film)

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[48] Kobayashi, Y.; Miyazaki, H.; Shiozaki, M. *J. Org. Chem.* **1994**, *59*, 813.

ν 3382, 2058, 1652, 1455, 1323, 1154, 1069 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.82 (1 H, d, *J* = 9.4 Hz, N**H**), 5.78 (1 H, d, *J* = 5.5, C^4**H**), 5.35 (1H, dd, *J* = 4.8 Hz, 8.0 Hz, C_2**H**), 5.30 (1 H, dd, *J* = 8.0 Hz, 9.4 Hz, C^1**H**), 5.22 (1 H, t, *J* = 5.0 Hz, C^3**H**), 4.67 (1 H, d, *J* = 12.2 Hz, C^6H_2), 4.53 (1 H, d, *J* = 12.2 Hz, C^6H_2), 2.11 (3 H, s, Ac), 2.10 (3 H, s, Ac), 2.07 (3 H, s, Ac), 2.06 (3 H, s, Ac), 2.05 (3 H, s, Ac), 1.99 (3 H, s, Ac) ppm.

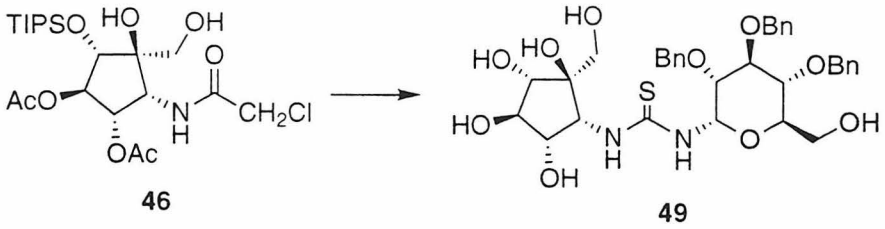


47 **48**

Isothiocyanate 48. To a solution of 650 mg (1.50 mmol, 1.00 equiv) of **47**[49] in 30 mL of toluene were added sequentially 1.30 g (4.51 mmol, 3.00 equiv) of Bu_4NNCS and 1.6 mL (13.5 mmol, 9.00 equiv) of BF_3•OEt_2. The orange solution was stirred for 48 h at 25 °C and concentrated to a brown oil. The residue was purified by silica gel chromatography (200 x 20mm, 2:1 hexanes:ethyl acetate, R_f = 0.38) to afford 368 mg (0.750 mmol, 50.0 % yield) of **48** as a purple oil: $[\alpha]_D^{25}$ = +20° (c = 0.5, $CHCl_3$); IR (thin film) ν 3445, 3063, 3030, 2918, 2026, 1718, 1604, 1454, 1359, 1209, 1028 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.5 - 7.0 (15 H, m, Ph), 5.06 (1 H, d, *J* = 4 Hz, C^1**H**), 4.81 (2 H, d, *J* = 11 Hz, C**H**$_2$Ph), 4.73 (1 H, d, *J* = 11 Hz, C**H**$_2$Ph), 4.67 (1 H, d, *J* = 11 Hz, C**H**$_2$Ph), 4.32(2 H, s, C**H**$_2$Ph), 3.88 (1 H, t, *J* = 9 Hz, C^3**H**), 3.65 - 3.48 (4 H, m, $C^{4\text{-}6}$**H**), 3.34 (1 H, dd, *J* = 4 Hz, 9 Hz, C^2**H**) ppm; ^{13}C NMR (75 MHz, C_6D_6) δ 142.5, 138.8, 138.4, 137.6, 128.5, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 83.6, 81.5, 79.8, 76.1, 75.5, 74.8, 74.5, 72.8, 60.9 ppm. HRMS(FAB) Calcd for $C_{28}H_{23}NO_5S$ (M)+: 491.1766. Found: 491.1736.

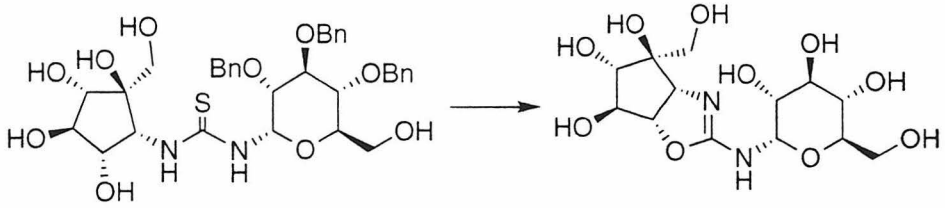
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[49] Zemplén, G.; Csürös, Z.; Angyal, S. *Chem. Ber.* **1937**, *70B*, 1848.



46 49

Thiourea 49. To a solution of 22 mg (0.045 mmol, 1.0 equiv) of **46** in 15 mL of MeOH:H_2O (5:1) was added 2 mL of concentrated HCl. After stirring 8 h at 60 °C, the reaction was concentrated; the residue was dried azeotropically with CH_3CN (3 x 100 mL). The residue was dissolved in 10 mL pyridine:DMF (10:1 *v/v*). To the reaction was added sequentially 1 crystal of DMAP and 24 mg (0.050 mmol, 1.1 equiv) of **48**. After 48 hrs, the reaction mixture was concentrated *in vacuo* and the residue was pushed though a plug of silica gel with 10 mL of MeOH to afford 18 mg (0.027 mmol, 60 %) of **49** as a yellow oil: $[\alpha]_D^{25}$ = -40° (c = 1.7, $CHCl_3$); IR (thin film) ν 3382, 2058, 162, 1455, 1323, 1154, 1069 cm^{-1}; ^1H NMR (300 MHz, CD_2Cl_2) δ 8.10 (1 H, d, *J* = 4 Hz, N**H**), 7.40 - 7.20 (15 H, m, Ph), 4.95 - 4.58 (7 H, m , C**H**$_2$Ph, C^1**H**), 4.2 - 3.1 (11 H) ppm; ^{13}C NMR (75 MHz, CD_3CN) δ 139.3, 138.5, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 117.9, 82.2, 81.8, 79.0, 78.1, 76.7, 75.3, 75.2, 75.0, 72.3, 72.2, 66.7, 61.7, 44.8, 41.6, 40.3 ppm.



49 9

Trehazolin (9). To a solution of 25 mg (0.037 mmol, 1.0 equiv) of **49** in 5 mL of 1:1 Et_2O: acetone was added 25 mg (0.12 mmol, 3.0 equiv) of yellow HgO. The yellow

slurry was stirred for 48 hrs and filtered through a plug of Celite. The Celite plug was washed with 20 mL of MeOH. The filtrate was concentrated by rotary evaporation and the residue was dissolved in 3 mL of MeOH. To the solution was added 300 mg of 10 % PdOH/C (Pearlman's catalyst). The black suspension was stirred at 25 °C for 2 h under a hydrogen atmosphere. The suspension was filtered through a Celite plug, which was washed thouroughly with MeOH (10 mL) and water (10 mL). The filtrate was combined and concentrated in vacuo. The residue was purified on a column of Dowex 50W x2 resin (H+ type), eluting with 0.5 M NH_4OH, to afford 5 mg (0.01 mmol, 40 % yield) of Trehazolin as a white solid: $[\alpha]_D^{25} = +90^\circ$ (c = 0.1, H_2O); IR (thin film) ν 3500, 1640 cm^{-1}; ^1H NMR (300 MHz, D_2O, HDO reference) δ 5.31 (1 H, d, *J* = 5 Hz, $C^{1'}\mathbf{H}$), 4.90 (1 H, d, *J* = 8.8 Hz, $C^2\mathbf{H}$), 4.33 (1 H, d, *J* = 8.8 Hz, $C^1\mathbf{H}$), 4.18 (1 H, m, $C^3\mathbf{H}$), 3.93 (1 H, d, *J* = 4.4 Hz), 3.82 - 3.70 (5 H, m, $C^6\mathbf{H}_2$, $C^{6'}\mathbf{H}$, $C^2\mathbf{H}$), 3.63 (1 H, t, *J* = 9 Hz, $C^3\mathbf{H}$), 3.55 (1 H, m, $C^{5'}\mathbf{H}$), 3.38 (1 H, t, *J* = 9 Hz, $C^{4'}\mathbf{H}$) ppm.

Appendix II - Crystal data and structural refinements for *p*-bromobenzoate **21**.

Crystals of *p*-bromobenzoate **21** were grown from a solution of ethyl acetate by slow evaporation. The solution structure confirms the absolute and relative stereochemistries of the parent compound.

Table 4. Crystal Data and Structure Refinement for *p*-bromobenzoate **21**.

Empirical Formula	$C_{17}H_{13}BrCl_3NO_3$
Formula weight	465.56
Crystal color	colorless
Solvent of crystallization	Ethyl acetate
Type of diffractometer	*Enraf-Nonius CAD-4*
Data collection method	Omega
Temperature	160 K
Wavelength	0.7107 Å
Crystal system	Monoclinic
Space group	$P2_12_12_1$ (#19)
Unit cell dimensions	a = 9.298(2) Å
	b = 12.334(3) Å
	c = 15.972(2) Å
Volume	1831.7(8) $Å^3$
Z	4
Density (calculated)	1.688 g cm^{-3}
Theta range for data collection	10.5 to 13°
Index ranges	$-12 \leq h \leq 12$, $0 \leq k \leq 16$, $0 \leq l \leq 20$
Reflections collected	6551

Independent reflections	4178 [R_{merge}= 0.051]
Data/restraints/parameters	4178/0/266
Goodness-of-fit on F2	1.29
Final R indices [I>2σ(I)]	R_1 = 0.039, wR_2 = 0.072
R indices (all data)	R_1 = 0.060
Largest diff. peak and hole	0.72 and -0.88 e•Å^{-3}
Lattice parameter determination	# of reflections = 25, range = 10.5°≤θ≤13°
Number of standard reflections	3
Interval (minutes)	60
(Δ/σ)max in final least squares cycle	< 0.005

Table 5. Atomic coordinates (x 10^4) and equivilent isotropic displacement parameters ($Å^2$ x 10^3) for **21**. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

Atom	*x*	*y*	*z*	U_{eq}
Br	6697(.5)	-4918(.3)	12148(.3)	320(1)
Cl1	1685(2)	-1594(1)	10360(1)	452(3)
Cl2	-835(1)	-428(1)	9761(1)	426(3)
Cl3	1433(1)	696(1)	10620(1)	341(3)
O1	1649(4)	-2546(2)	14697(2)	336(8)
O2	969(3)	-1933(2)	13433(2)	240(7)
O3	-932(3)	-1780(2)	11303(2)	259(7)
N	-472(3)	-51(3)	11942(2)	193(7)
C1	3332(5)	-2822(3)	12662(3)	220(9)
C2	4442(5)	-3366(3)	12265(3)	248(10)
C3	5189(4)	-4170(3)	12690(3)	236(10)
C4	4833(5)	-4432(4)	13504(3)	280(11)
C5	3750(5)	-3878(4)	13903(3)	255(10)
C6	2992(4)	-3070(3)	13488(3)	185(9)
C7	1814(5)	-2501(3)	13954(3)	219(9)
C8	-280(5)	1385(4)	13805(3)	203(10)
C9	111(5)	-222(4)	13989(3)	260(10)
C10	-437(5)	429(4)	13411(3)	268(10)
C11	-1257(4)	-161(3)	12746(2)	198(9)
C12	-1408(4)	-1277(3)	13147(2)	171(8)
C13	-2896(5)	-1739(4)	13308(3)	263(11)
C14	-1931(5)	-2240(3)	12663(3)	215(10)
C15	-2242(5)	-2016(4)	11756(3)	267(11)
C16	-374(5)	-768(3)	11389(3)	226(10)
C17	457(5)	-515(4)	10575(3)	261(10)

Table 6. Complete Distances for **21**.

Bond	Distance(Å)	Bond	Distance(Å)
Br-C3	1.889(4)	C11-C17	1.787(4)
C12-C17	1.773(4)	C13-C17	1.748(4)
O1-C7	1.198(5)	O2-C7	1.341(5)
O2-C8	1.469(5)	O3-C15	1.446(5)
O3-C16	1.359(5)	N-C11	1.483(5)
N-C16	1.253(5)	C1-C2	1.385(6)
C1-C6	1.391(6)	C1-H1	1.00(4)
C2-C3	1.387(6)	C2-H2	0.94(4)
C3-C4	1.380(6)	C4-C5	1.374(6)
C4-H4	0.92(4)	C5-C6	1.389(6)
C5-H5	0.93(4)	C6-C7	1.499(6)
C8-C9	1.508(6)	C8-C12	1.490(6)
C8-H8	1.03(4)	C9-C10	1.326(6)
C9-H9	0.96(4)	C10-C11	1.496(6)
C10-H10	0.81(6)	C11-C12	1.525(5)
C11-H11	0.95(4)	C12-C13	1.518(6)
C12-C14	1.499(6)	C13-C14	1.500(6)
C13-H13a	0.87(4)	C13-H13b	0.97(4)
C14-C15	1.502(6)	C14-C15	0.97(4)
C15-C15a	1.03(4)	C15-H15b	0.92(4)
C16-C17	1.544(6)		

Table 7. Complete bond angles for **21**.

	Angle(°)		Angle(°)
C8-O2-C7	116.9(3)	H11-C11-N	105.1(22)
C16-O3-C15	117.1(3)	C12-C11-C10	100.8(3)
C16-N-C11	125.6(3)	H11-C11-C10	109.9(22)
C6-C1-C2	119.8(4)	H11-C11-C12	112.7(22)
H1-C1-C2	120.2(22)	C11-C12-C8	108.2(3)
H1-C1-C6	120.0(22)	C13-C12-C8	119.3(3)
C3-C2-C1	119.7(4)	C14-C12-C8	121.4(3)
H2-C2-C1	121.6(25)	C13-C12-C11	119.6(3)
H2-C2-C3	118.7(25)	C14-C12-C11	121.9(3)
C2-C3-Br	119.8(3)	C14-C12-C13	59.6(3)
C4-C3-Br	119.7(3)	C14-C13-C12	59.6(3)
C4-C3-C2	120.5(4)	H13a-C13-C12	115.8(28)
C5-C4-C3	19.8(4)	H13b-C13-C12	119.6(25)
H4-C4-C3	124.8(25)	H13a-C13-C14	117.7(28)
H4-C4--C5	115.4(25)	H13b-C13-C14	125.2(25)
C6-C5-C4	120.4(4)	H13-C13-H13a	110.3(37)
H5-C5-C4	119.7(24)	C13-C14-C12	60.8(3)
H5-C5-C6	119.8(24)	C15-C14-C12	114.5(3)
C5-C6-C1	119.7(4)	H14-C14-C12	119.3(22)
C7-C6-C1	122.3(4)	C15-C14-C13	118.1(4)
C7-C6-C5	118.0(4)	H14-C14-C13	117.2(22)
O2-C7-O1	124.3(4)	H14-C14-C15	115.8(22)
C6-C7-O1	124.3(4)	C14-C15-O3	111.0(4)
C6-C7-O2	111.4(3)	H15a-C15-O3	106.7(23)
C9-C8-O2	109.1(3)	H15b-C15-O3	102.2(27)
C12-C8-O2	108.3(3)	H15a-C15-C14	117.2(23)
H8-C8-O2	107.1(21)	H15b-C15-C14	117.0(27)
C12-C8-C9	102.8(3)	H15b-C15-H15a	101.1(35)
H8-C8-C9	116.1(22)	N-C16-O3	133.8(4)
H8-C8-C12	113.2(21)	C17-C16-O3	106.9(3)
C10-C9-C8	110.3(4)	C17-C16-N	119.2(4)
H9-C9-C8	115.7(23)	Cl2-C17-Cl1	109.7(2)
H9-C9-C10	133.3(23)	Cl3-C17-Cl1	108.2(2)

C11-C10-C9	113.3(4)	C16-C17-Cl1	109.3(3)
H10-C10-C9	124.5(32)	Cl3-C17-Cl2	109.3(2)
H10-C10-C11	122.1(31)	C16-C17-Cl2	106.9(3)
C10-C11-N	108.6(3)	C16-C17-Cl3	113.4(3)
C12-C11-N	119.5(3)		

Table 8. Anisotropic Displacement Parameters for **21**.

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Br	255(2)	215(2)	491(3)	45(2)	25(2)	-57(2)
Cl1	536(8)	344(7)	475(8)	101(7)	249(7)	-12(6)
Cl2	550(8)	521(8)	208(6)	-68(6)	-29(6)	33(6)
Cl3	393(8)	300(6)	330(6)	-91(6)	115(6)	26(5)
O1	406(18)	422(18)	180(15)	112(19)	1(16)	1(14)
O2	271(16)	287(17)	161(15)	107(14)	-3(13)	22(13)
O3	366(18)	212(17)	198(16)	-61(15)	71(15)	-42(14)
N	200(16)	211(17)	169(17)	40(19)	0(13)	4(17)
C1	190(20)	143(18)	328(26)	-11(20)	-1(22)	-36(18)
C2	304(24)	167(21)	273(25)	-31(19)	12(21)	-8(21)
C3	195(22)	189(21)	325(28)	-15(18)	-54(20)	-79(20)
C4	239(25)	204(24)	398(30)	2(20)	-143(22)	51(22)
C5	246(25)	268(25)	251(24)	13(19)	-80(20)	2(20)
C6	191(23)	161(20)	202(22)	-37(17)	-60(18)	-1(18)
C7	195(21)	177(20)	285(25)	-10(20)	-13(20)	-43(18)
C8	241(24)	240(24)	129(21)	39(20)	9(18)	12(19)
C9	250(23)	291(29)	240(24)	-31(21)	21(19)	-89(22)
C10	335(27)	191(22)	278(25)	-17(21)	119(21)	-100(21)
C11	232(19)	158(21)	203(21)	6(17)	24(17)	34(19)
C12	208(24)	150(19)	156(19)	26(17)	19(16)	-1(16)
C13	250(26)	290(26)	248(26)	-9(20)	56(21)	44(22)
C14	293(25)	140(19)	212(24)	-20(19)	0(19)	14(17)
C15	288(26)	222(26)	292(27)	-84(21)	-18(21)	-36(21)
C16	250(24)	213(23)	215(24)	0(20)	0(19)	53(20)
C17	321(26)	257(24)	206(22)	40(21)	86(20)	3(20)

$U_{i,j}$ values have been multiplied by 10^4. The form of the displacement factor is:

$\exp -2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2Uhka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)$

Table 9. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **21**.

Atom	*x*	*y*	*z*	*B*
H1	2767(39)	-2260(32)	12355(23)	2.1
H2	4694(43)	-3217(33)	11706(26)	2.3
H4	5275(40)	-4966(38)	13818(23)	2.7
H5	3501(44)	-4063(31)	14448(23)	2.4
H8	-603(41)	-1843(31)	14308(24)	1.9
H9	785(39)	-114(35)	14439(22)	2.5
H10	-321(48)	1082(35)	13398(28)	2.5
H11	-2159(37)	184(32)	12655(22)	1.9
H13a	-3616(45)	-1347(33)	13131(26)	2.5
H13b	-3117(46)	-2052(33)	13851(26)	2.5
H14	-1539(41)	-2952(30)	12787(23)	2
H15a	-2949(46)	-1401(33)	11624(25)	2.5
H15b	-2629(45)	-2575(36)	11447(27)	2.5

The structure was solved using SHELXS-86. Twenty-five non-hydrogen atoms were located. All hydrogen atoms were placed in calculated positions. All non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined isotropically.

Table 10. Intermolecular Contacts less than 3.5 Å for **21**.

	Distance (Å)		Distance (Å)
Br-H14	3.10(4)	C5-H9	3.48(4)
Br-H15b	3.16(4)	C6-H11	2.93(4)
Br-H13a	3.39(4)	C8-H5	3.06(4)
Br-O2	3.427(3)	C9-H5	3.04(4)
Br-H1	3.04(4)	C10-H14	3.32(4)
Br-H9	3.46(4)	C14-H10	3.40(4)
Cl1-H9	3.48(4)	C15-H2	3.21(4)
Cl1-H15b	3.13(4)	C15-H10	3.35(4)
Cl2-H13a	3.44(4)	H1-H10	3.29(6)
Cl2-H5	3.25(4)	H1-H11	3.20(5)
Cl2-H2	2.92(4)	H2-H15a	3.14(6)
Cl3-O1	3.250(3)	H2-H15b	2.64(6)
Cl3-H9	3.28(4)	H2-H11	3.24(6)
Cl3-H8	3.13(4)	H4-H15a	2.88(6)
Cl3-H13b	3.30(4)	H4-H9	2.83(6)
Cl3-H14	3.04(4)	H5-H15a	3.39(6)
Cl3-H4	3.29(4)	H5-H8	2.43(5)
O1-C13	3.333(5)	H5-H9	2.95(5)
O1-H8	3.10(4)	H5-H13b	3.40(6)
O1-H13b	2.38(4)	H10-H14	2.83(6)
O3-H10	2.92(4)	H10-H15b	3.21(6)
N-C6	3.454(5)	N-H14	3.22(4)
C1-H13a	3.45(4)	C1-H11	2.74(4)
C2-H13a	3.37(4)	C2-H15b	3.17(4)
C2-H11	2.78(4)	C3-H14	3.40(4)
C3-H15b	3.45(4)	C3-H11	2.98(4)
C3-H13a	3.33(4)	C4-H11	3.14(4)
C4-H15a	3.00(4)	C4-C9	3.45(4)
C5-H11	3.12(4)	C5-H15a	3.31(4)
C5-H8	3.05(4)		

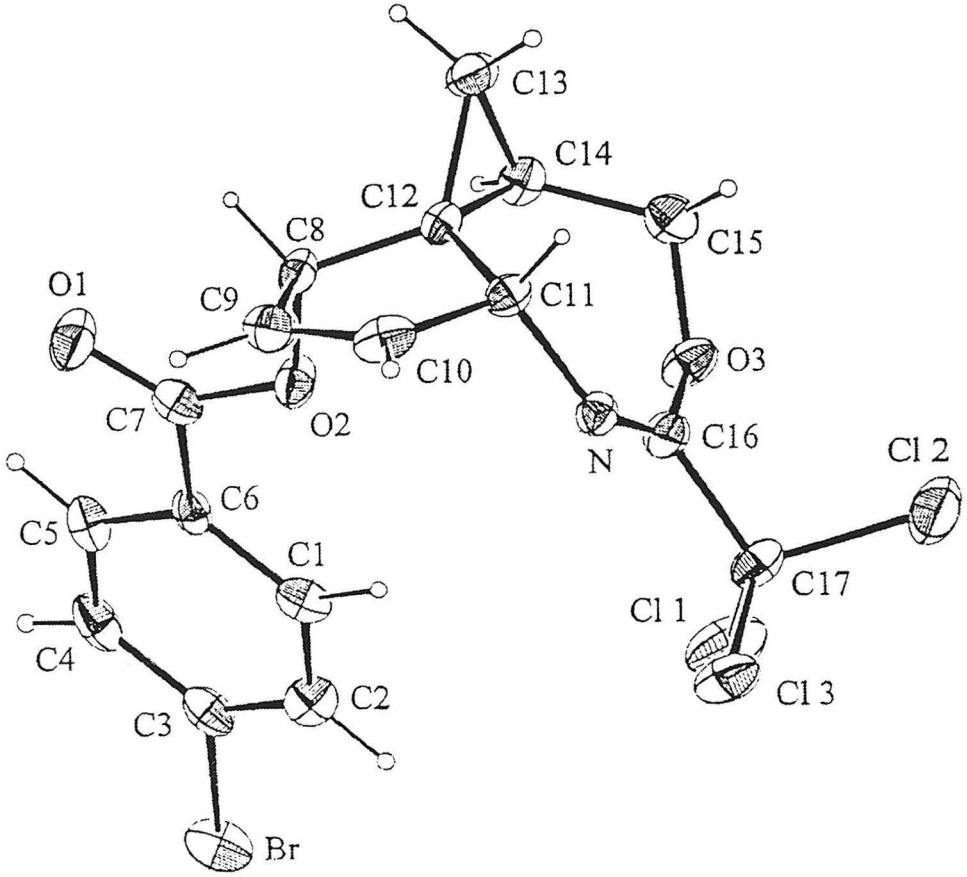


Figure 20. *p*-bromobenzoate **21** crystal structure.

Table 11. Observed and calculated structure factors for *p*-bromobenzoate **21**.

The columns contain, in order, l, $10F_{obs}$, $10F_{calc}$, $10\sigma F_{obs}$. A minus sign preceding F_{obs} indicates that F_{obs}^2 is negative.

h 1 -20

1	148	114	22
2	112	90	30
3	165	158	15

h 2 -20

1	76	95	39
2	167	175	22

h 3 -20

1	-60	67	46
2	89	76	35

h 4 -20

1	111	39	30

h 1 -19

1	199	208	17
2	7[illegible]	54	35
3	204	212	12
4	115	129	20

h 2 -19

1	97	89	31
2	[illegible]	[illegible]	[illegible]
3	[illegible]	[illegible]	[illegible]
4	[illegible]	107	29

h 3 -19

1	61	26	40
2	[illegible]	23	24
3	[illegible]	[illegible]	[illegible]
4	98	88	28

h 4 -19

1	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]
3	[illegible]	[illegible]	[illegible]
4	[illegible]	[illegible]	[illegible]
5	[illegible]	[illegible]	[illegible]
6	[illegible]	[illegible]	[illegible]

h 5 -19

1	[illegible]	76	35
2	[illegible]	[illegible]	[illegible]
3	[illegible]	[illegible]	[illegible]

h 6 -19

1	78	121	42

h 1 -18

1	198	201	17
2	81	66	32
3	179	201	14
4	59	91	32
5	83	116	36

h 2 -18

1	191	196	18
2	107	133	27
3	126	127	18
4	164	184	14
5	167	144	18

h 3 -18

1	249	263	15
2	181	117	23
3	130	134	17
4	143	111	16
5	111	39	30

h 4 -18

1	246	232	15
2	149	139	23
3	-40	32	41
4	102	70	21
5	149	152	24

h 5 -18

1	61	53	42
2	79	81	34
3	43	67	39
4	202	202	14

h 6 -18

1	164	120	21
2	145	93	23
3	98	44	24

h 7 -18

1	-68	26	42
2	50	125	52

h 1 -17

1	219	203	14
2	161	154	18
3	161	155	13
4	146	174	16
5	76	69	38
6	76	138	41

h 2 -17

1	-36	53	49
2	184	143	23
3	200	234	11
4	199	190	12
5	226	247	11
6	85	18	34

h 3 -17

1	96	69	37
2	428	430	10
3	67	84	28
4	237	242	11
5	-32	42	58
6	61	31	48

h 4 -17

1	119	78	23
2	61	68	41
3	46	115	37
4	145	104	16
5	200	218	18
6	-76	54	42

h 5 -17

1	157	116	19
2	113	81	26
3	227	209	11
4	212	195	12
5	116	31	28

h 6 -17

1	130	68	23
2	341	308	12
3	152	136	16
4	229	235	12
5	92	126	36

h 7 -17

1	168	157	21
2	37	57	55
3	152	175	17
4	169	151	16

h 8 -17

1	75	87	39
2	78	89	38
3	106	104	23

h 9 -17

1	154	144	24

h 1 -16

1	63	92	35
2	274	295	12
3	191	174	11
4	199	186	11
5	168	154	20
6	94	91	31
7	178	188	22

h 2 -16

1	111	130	24
2	47	48	42
3	200	198	11
4	-52	10	32
5	109	73	27
6	146	130	22
7	124	122	28

h 3 -16

1	140	110	19
2	-104	27	25
3	261	276	9
4	178	161	12
5	97	87	29
6	-28	54	61
7	248	198	15

h 4 -16

1	154	122	17
2	128	91	21
3	65	72	28
4	200	191	11
5	160	117	20
6	166	188	22
7	-40	85	59

h 5 -16

1	277	257	12
2	105	98	26
3	132	98	15
4	164	175	14
5	230	209	16
6	69	78	42

h 6 -16

1	294	261	12
2	168	178	17
3	108	119	20
4	222	226	11
5	161	107	21
6	213	207	19
7	358	348	11
8	141	123	21
9	148	152	15
10	110	61	20
11	226	225	18

h 8 -16

1	85	61	34
2	198	213	18
3	111	112	21
4	201	188	13

h 9 -16

1	172	189	22
2	66	36	42
3	86	104	28

h 10 -16

1	72	77	43

h 1 -15

1	256	268	11
2	167	179	15
3	186	147	12
4	385	368	7
5	78	68	24
6	-6	26	38
7	171	189	22
8	210	193	19

h 2 -15

1	380	388	9
2	169	157	14
3	269	245	8
4	130	147	14
5	249	256	10
6	-38	66	56
7	14	94	77
8	132	136	29

h 3 -15

1	134	137	16
2	366	368	11
3	169	168	12
4	290	307	9
5	217	216	11
6	66	63	38
7	148	112	23
8	198	218	21

h 4 -15

1	167	161	16
2	237	209	12
3	240	245	9
4	93	104	21
5	110	97	19
6	59	70	44
7	84	88	36

h 5 -15

1	41	28	44
2	152	102	17
3	36	62	38
4	261	272	10
5	-28	35	47
6	250	244	16
7	151	106	23

h 6 -15

1	125	141	22
2	227	235	14
3	243	243	10
4	76	88	26
5	225	226	11
6	79	105	38

h 7 -15

1	174	156	17
2	71	155	38
3	198	205	12
4	270	252	10
5	173	139	14
6	89	65	36

h 8 -15

1	52	77	44
2	149	130	21
3	200	178	12
4	87	68	28
5	46	109	41

h 9 -15

1	162	161	21
2	220	209	17
3	142	138	16
4	92	110	28

h 10 -15

1	186	110	22
2	73	108	42
3	186	170	18

h 1 -14

1	434	436	9
2	246	249	11
3	84	91	28
4	267	270	8
5	311	312	8
6	198	184	18
7	230	222	10
8	128	124	21

h 2 -14

1	166	155	14
2	436	436	9
3	309	298	10
4	217	219	9
5	96	104	19
6	516	519	10
7	187	164	18
8	116	131	29

h 3 -14

1	399	400	9
2	164	160	18
3	110	116	15
4	-16	47	47
5	264	268	9
6	121	90	22
7	352	347	13
8	117	81	27

h 4 -14

1	85	64	26
2	388	388	10
3	118	99	14
4	202	209	10
5	193	174	11
6	277	278	14
7	-78	62	36
8	111	57	29

h 5 -14

1	196	181	13
2	174	170	15
3	90	104	20
4	-68	24	25
5	77	47	24
6	120	111	26
7	221	212	17
8	140	111	25

h 6 -14

1	132	148	20
2	229	231	14
3	187	199	12
4	144	161	14
5	86	90	24
6	110	108	28
7	128	86	28

h 7 -14

1	206	181	18
2	86	42	29
3	[illegible]	[illegible]	[illegible]
4	[illegible]	[illegible]	[illegible]
5	[illegible]	[illegible]	[illegible]
6	[illegible]	[illegible]	[illegible]
7	[illegible]	64	21

h 8 -14

1	76	83	33
2	227	231	14
3	[illegible]	[illegible]	[illegible]
4	82	81	31
5	[illegible]	85	38
6	176	168	49

h 9 -14

1	288	283	14
2	[illegible]	[illegible]	[illegible]
3	36	64	42
4	80	69	28
5	203	201	13

h 10 -14

1	64	62	41
2	134	137	25
3	240	238	10
4	177	190	15

h 11 -14

1	122	98	27
2	319	314	14
3	76	89	31

h 1 -13

1	223	231	10
2	424	423	8
3	308	314	10
4	168	148	15
5	168	178	12
6	106	84	24
7	128	98	23
8	88	68	33
9	98	63	24

h 2 -13

1	194	207	12
2	349	339	9
3	262	247	10
4	186	228	15
5	332	324	7
6	207	201	15
7	162	156	17
8	64	131	35
9	223	206	13

h 3 -13

1	217	218	11
2	307	292	9
3	432	443	9
4	240	240	12
5	155	177	13
6	146	114	20
7	-86	43	32
8	110	93	29
9	99	82	25

h 4 -13

1	172	187	14
2	[illegible]	[illegible]	9
3	[illegible]	[illegible]	9
4	[illegible]	[illegible]	9
5	[illegible]	[illegible]	9
6	[illegible]	[illegible]	9
7	[illegible]	[illegible]	9
8	[illegible]	[illegible]	9

h 5 -13

1	428	419	9
2	[illegible]	[illegible]	9
3	[illegible]	[illegible]	9
4	[illegible]	[illegible]	9
5	[illegible]	[illegible]	9
6	[illegible]	[illegible]	9
7	[illegible]	[illegible]	9
8	[illegible]	[illegible]	9
9	[illegible]	[illegible]	9

h 6 -13

1	[illegible]	[illegible]	9
2	[illegible]	[illegible]	9
3	[illegible]	[illegible]	9
4	[illegible]	[illegible]	9
5	[illegible]	[illegible]	9
6	[illegible]	[illegible]	9
7	[illegible]	[illegible]	9
8	[illegible]	[illegible]	9
9	[illegible]	[illegible]	9

h 7 -13

1	186	210	15
2	389	413	10
3	238	241	9
4	417	400	8
5	80	122	26
6	-14	65	71
7	59	40	44

h 8 -13

1	375	360	10
2	129	115	21
3	401	398	8
4	49	47	34
5	107	102	16
6	260	241	15
7	184	195	21

h 9 -13

1	175	191	18
2	172	183	18
3	133	108	16
4	206	215	12
5	75	27	28
6	99	82	33

h 10 -13

1	211	200	15
2	-72	86	37
3	171	170	15
4	156	163	16
5	88	75	27

h 11 -13

1	34	25	56
2	179	168	20
3	84	93	27
4	150	155	18

h 12 -13

1	43	100	57
2	94	63	38

h 1 -12

1	401	437	8
2	[illegible]	[illegible]	8
3	[illegible]	[illegible]	11
4	[illegible]	[illegible]	9
5	[illegible]	[illegible]	9
6	[illegible]	[illegible]	9
7	[illegible]	[illegible]	9
8	[illegible]	[illegible]	9

h 2 -12

1	333	316	8
2	[illegible]	[illegible]	8
3	[illegible]	[illegible]	16
4	[illegible]	[illegible]	17
5	[illegible]	[illegible]	28
6	[illegible]	[illegible]	14
7	[illegible]	[illegible]	29
8	[illegible]	[illegible]	26
9	[illegible]	[illegible]	11

h 3 -12

1	274	264	9
2	242	246	10
3	534	532	8
4	97	78	22
5	177	183	15
6	246	221	13
7	205	192	16
8	110	103	26
9	86	89	27

h 4 -12

1	107	99	18
2	265	259	10
3	52	40	33
4	166	177	15
5	53	55	26
6	236	227	13
7	41	63	50
8	107	97	29
9	103	116	28

h 5 -12

1	548	541	8
2	-47	56	36
3	256	279	11
4	169	155	15
5	247	252	9
6	189	177	16
7	353	340	12
8	89	9	33
9	54	67	39

h 6 -12

1	441	442	9
2	282	285	11
3	-78	26	28
4	178	188	11
5	455	448	7
6	320	313	12
7	114	119	27
8	190	179	19

h 7 -12

1	330	323	10
2	59	46	33
3	179	199	11
4	296	289	8
5	314	301	8
6	248	230	14
7	252	214	15
8	169	154	23

h 8 -12

1	283	270	13
2	176	188	16
3	290	277	8
4	56	44	29
5	247	257	10
6	235	234	16
7	84	86	38

h 9 -12

1	216	206	14
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3	107	90	18
4	178	169	13
5	187	180	13
6	94	78	34
7	52	92	52

h 10 -12

1	144	142	21
2	109	122	27
3	128	91	17
4	64	66	30
5	163	151	15
6	174	162	22

h 11 -12

1	148	134	22
2	67	76	40
3	140	116	16
4	161	157	16
5	152	154	18

h 12 -12

1	40	67	54
2	159	137	22
3	177	196	16

h 13 -12

1	178	172	21

h 1 -11

1	438	411	7
2	339	336	8
3	443	443	8
4	493	489	8
5	199	227	12
6	-37	26	43
7	162	138	17
8	348	329	12
9	232	233	12
10	127	69	20

h 2 -11

1	529	535	8
2	358	360	7
3	804	796	9
4	15	21	51
5	123	124	18
6	349	332	10
7	196	193	15
8	238	197	14
9	329	343	10
10	98	100	27

h 3 -11

1	131	142	14
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3	[illegible]	[illegible]	9
4	504	498	8
5	[illegible]	[illegible]	9
6	82	81	28
7	181	208	18
8	42[illegible]	[illegible]	11
9	-39	52	43

h 4 -11

1	287	276	9
2	442	439	8
3	281	275	9
4	202	193	12
5	192	180	13
6	111	81	22
7	62	65	37
8	230	248	16
9	198	189	13

h 5 -11

1	163	165	13
2	336	326	9
3	201	197	12
4	311	316	10
5	114	109	15
6	140	121	20
7	188	148	17
8	-85	65	35
9	171	170	15

h 6 -11

1	217	218	11
2	318	296	9
3	180	190	14
4	354	339	10
5	138	143	14
6	209	196	15
7	88	98	33
8	249	245	16
9	111	113	24

h 7 -11

1	210	189	12
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3	380	394	9
4	78	64	20
5	342	350	8
6	238	220	14
7	181	142	18
8	203	150	18

h 8 -11

1	213	216	13
2	198	190	14
3	168	172	12
4	115	122	17
5	190	171	12
6	87	93	33
7	133	122	24
8	136	103	28

h 9 -11

1	60	111	36
2	232	255	13
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4	39	70	38
5	84	92	25
6	157	148	22
7	188	161	24

h 10 -11

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h 11 -11

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3	167	181	12
4	79	74	28
5	281	267	10

h 12 -11

1	106	124	31
2	191	194	18
3	105	106	22
4	267	276	11

h 13 -11

1	82	102	38
2	172	212	22

h 1 -10

1	102	108	14
2	128	150	13
3	261	234	8
4	329	327	8
5	223	229	11
6	165	179	15
7	364	361	10
8	198	197	16
9	101	78	22
10	121	77	20

h 2 -10

1	331	329	7
2	430	433	7
3	290	284	8
4	150	136	13
5	380	377	9
6	211	197	13
7	450	436	9
8	230	207	14
9	-12	64	60
10	-21	50	56

h 3 -10

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3	282	274	9
4	632	629	9
5	364	370	9
6	374	380	9
7	307	318	11
8	188	122	17
9	74	22	27
10	80	64	29

h 4 -10

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h 5 -10

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4	[illegible]	[illegible]	9
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6	[illegible]	[illegible]	9

h 6 -10

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4	[illegible]	[illegible]	9
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6	[illegible]	[illegible]	9
7	[illegible]	[illegible]	9
8	[illegible]	[illegible]	9
9	[illegible]	[illegible]	9

h 7 -10

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7	[illegible]	[illegible]	9
8	[illegible]	[illegible]	22
9	[illegible]	[illegible]	14

h 8 -10

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5	266	259	9
6	268	258	14
7	88	118	34

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 8   49   95   55
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 2  161  156   17
 3  116  122   17
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 6  193  196   19
 7  189  154   20
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 3  255  236   10
 4  245  230   10
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 6  300  270   16
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 3  230  234   13
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 6  183  212   16
 7  178  179   17
 8  119  110   22
 9  236  241   12
10   77   68   31
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 4  437  426    8
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 7  196  186   16
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 6   86   62   29
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 6  158  157   20
 7  176  146   20
 8  152  156   25
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 4   81   74   22
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 6   49  118   48
 7  231  240   18
 8  -64   44   47
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 1   56   37   37
 2  245  235   13
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 7   68  119   47
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 2   73   81   38
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 6  128   88   27
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 2  198  174   16
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 5  115  120   23
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 2  218  187   18
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h 10 -7

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8	219	208	19

h 11 -7

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3	513	503	7
4	207	212	11
5	128	136	18
6	248	227	16
7	161	113	24

h 12 -7

1	143	155	22
2	400	284	19
3	310	294	19
4	211	211	18
5	139	161	19

h 13 -7

1	220	198	18

h 1 -6

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3	371	361	6
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6	248	262	10
7	306	300	10
8	327	300	10
9	99	83	20
10	82	30	28
11	49	76	41

h 2 -6

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2	709	681	8
3	459	445	6
4	284	278	7
5	508	503	8
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7	537	544	9
8	128	140	21
9	208	222	11
10	97	39	22
11	177	186	16

h 3 -6

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3	702	672	8
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5	259	248	9
6	697	696	9
7	244	237	11
8	293	282	11
9	80	51	24
10	75	92	28
11	149	124	19

h 4 -6

1	931	978	10
2	598	588	7
3	179	173	9
4	566	572	8
5	681	677	9
6	388	391	8
7	586	588	9
8	116	89	23
9	100	97	16
10	266	281	18

h 5 -6

1	638	622	7
2	390	390	7
3	619	619	8
4	428	430	7
5	168	178	18
6	470	421	8
7	210	188	13
8	240	226	14
9	198	198	19
10	82	23	29

h 6 -6

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5	278	282	10
6	186	186	13
7	411	413	10
8	192	183	17
9	164	170	14
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h 7 -6

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6	408	410	10
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h 8 -6

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7	456	448	10
8	136	112	23
9	108	53	23

h 9 -6

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6	589	581	10
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9	48	79	43

h 10 -6

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3	193	185	14
4	164	153	11
5	282	281	9
6	275	286	14
7	407	397	12
8	180	142	22

h 11 -6

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3	388	397	10
4	191	189	12
5	197	209	12
6	300	301	13
7	130	181	28
8	164	150	26

h 12 -6

1	143	172	23
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3	11	24	19
4	241	224	10
5	149	140	16
6	222	196	16
7	199	167	21

h 13 -6

1	92	106	29
2	87	81	31
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4	103	91	22
5	147	141	17
6	22	132	76

h 14 -6

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2	179	118	19
3	134	116	18
4	158	143	17

h 15 -6

1	158	165	22
2	178	184	21

h 1 -5

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3	494	520	6
4	575	554	7
5	369	356	7
6	84	58	21
7	158	156	15
8	83	37	26
9	342	360	8
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11	271	247	11

h 2 -5

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5	666	656	8
6	235	215	10
7	149	141	16
8	291	304	11
9	241	257	10
10	148	130	17
11	194	178	14

h 3 -5

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6	73	92	28
7	66	109	31
8	332	346	11
9	371	373	8
10	156	144	16
11	272	246	12

h 4 -5

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4	692	698	8
5	166	191	12
6	347	343	9
7	181	210	18
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9	218	227	11
10	191	184	14
11	121	129	23

h 5 -5

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5	540	537	8
6	83	54	23
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8	158	141	20
9	342	354	9
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11	66	78	36

h 6 -5

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3	344	336	7
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5	316	312	9
6	241	256	12
7	275	262	12
8	339	349	12
9	156	125	15
10	178	189	16

h 7 -5

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4	182	187	12
5	451	448	9
6	259	248	11
7	243	245	13
8	226	228	15
9	385	377	9
10	91	112	28

h 8 -5

1	238	248	9
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3	419	405	8
4	556	543	9
5	436	440	9
6	245	216	12
7	332	305	11
8	256	228	15
9	141	170	19
10	250	249	14

h 9 -5

1	278	278	9
2	686	689	9
3	384	369	9
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5	208	208	19
6	164	180	19
7	166	166	21
8	296	287	14
9	211	187	14

h 10 -5

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3	385	376	9
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5	274	274	9
6	137	136	28
7	282	269	18
8	193	218	21

h 11 -5

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3	352	376	8
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5	269	259	10
6	155	162	31
7	226	188	17
8	141	119	29

h 12 -5

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3	93	127	22
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5	118	103	19
6	-69	39	43
7	136	130	28

h 13 -5

1	75	96	34
2	149	108	20
3	189	201	13
4	85	100	26
5	157	123	17
6	225	228	20

h 14 -5

1	281	268	13
2	224	193	15
3	-13	47	59
4	270	261	11
5	181	210	17

h 15 -5

1	56	73	47
2	122	128	29
3	58	73	38

h 1 -4

1	698	666	7
2	945	935	9
3	209	192	6
4	869	859	9
5	442	434	7
6	788	788	9
7	579	577	9
8	176	164	15
9	136	156	16
10	240	270	11
11	138	95	18

h 2 -4

1	966	941	10
2	388	388	6
3	429	429	6
4	691	691	7
5	880	880	8
6	611	611	9
7	1110	1110	12
8	1110	1110	12

h 3 -4

1	360	360	8
2	442	442	6
3	388	388	7
4	874	874	8
5	1110	1110	9
6	1110	1110	10
7	1110	1110	11
8	1110	1110	12

h 4 -4

1	580	576	7
2	568	542	7
3	192	172	8
4	760	747	9
5	334	326	8
6	356	359	8
7	367	374	9
8	154	136	17
9	-61	88	30
10	158	182	16
11	200	197	15

h 5 -4

1	719	716	8
2	588	585	7
3	490	480	7
4	191	184	10
5	372	366	8
6	399	406	9

7	302	293	10
8	269	259	12
9	160	166	15
10	-43	43	42
11	188	186	16

h 6 -4

1	670	664	8
2	590	570	7
3	256	233	8
4	320	316	8
5	348	346	9
6	429	439	9
7	479	476	9
8	198	193	16
9	217	211	12
10	207	215	13

h 7 -4

1	583	575	7
2	468	462	7
3	316	312	8
4	467	469	8
5	529	520	9
6	437	428	9
7	342	316	10
8	262	228	12
9	142	166	19

h 8 -4

1	148	167	24
2	198	99	28
3	218	231	14

h 1 -3

1	891	888	9
2	1629	1603	16
3	482	486	6
4	670	686	8
5	419	442	7
6	187	167	11
7	194	187	11
8	508	480	9
9	321	326	8
10	232	232	13
11	67	99	35

h 2 -3

1	199	199	4
2	1424	1415	10
3	431	438	6
4	502	479	7
5	579	583	8
6	92	94	19
7	301	316	10
8	249	255	12
9	213	243	11
10	261	250	10
11	128	85	20

h 3 -3

1	255	249	5
2	1036	1017	10
3	939	933	10
4	67	83	18
5	504	517	7
6	154	143	13
7	328	330	10
8	371	363	10
9	368	402	8
10	221	215	12
11	129	130	21

h 4 -3

8	71	90	46

h 12 -4

1	251	273	12
2	306	288	11
3	-26	51	56
4	241	238	10
5	348	340	9
6	262	265	15
7	204	190	20

h 13 -4

1	230	214	13
2	329	348	12
3	270	277	14
4	265	253	11
5	170	143	16
6	253	236	17

h 14 -4

1	350	371	12
2	288	283	14
3	250	244	16
4	342	341	10
5	241	242	13

h 15 -4

h 5 -3

1	327	315	6
2	655	635	7
3	446	439	7
4	568	557	8
5	524	505	8
6	554	539	9
7	205	215	14
8	205	187	14
9	227	243	11
10	300	311	11
11	84	91	31

h 6 -3

1	308	306	6
2	50	40	23
3	434	424	7
4	322	319	8
5	339	334	9
6	126	112	18
7	116	119	24
8	211	220	16
9	262	269	10
10	82	79	39
11	247	222	13

h 7 -3

1	429	431	7
2	361	364	7
3	288	280	8
4	518	522	8
5	110	88	19
6	104	96	22
7	166	137	12
8	238	210	14
9	199	197	13
10	330	316	10

h 8 -3

1	47	62	28
2	722	701	9
3	327	320	8
4	426	414	9
5	410	399	9
6	311	289	11
7	-61	39	39
8	268	232	14
9	212	211	13
10	-50	48	43

h 9 -3

1	659	665	8
2	282	279	9
3	321	312	9
4	168	172	15
5	417	388	10
6	117	143	25
7	180	198	19
8	136	132	25
9	235	261	13

h 10 -3

1	277	274	9
2	264	261	10
3	303	289	10
4	572	577	9
5	161	173	13
6	276	269	13
7	100	114	32
8	216	192	18
9	102	91	27

h 11 -3

1	513	516	9
2	299	311	11
3	178	214	17
4	338	315	8
5	198	187	12
6	226	205	16
7	-15	21	76
8	319	291	14

h 12 -3

1	403	409	9
2	232	226	13
3	483	478	10
4	248	268	13
5	206	210	19
6	191	181	21
7	222	208	19

h 13 -3

1	376	381	10
2	337	328	11
3	101	58	29
4	338	301	9
5	268	288	12
6	15	91	79

h 14 -3

1	209	197	16
2	103	105	32
3	264	273	14
4	191	178	15
5	74	58	33

h 15 -3

1	138	123	23
2	246	242	17
3	49	132	57

h 1 -2

1	211	210	4
2	679	668	7
3	-36	66	21
4	613	599	7
5	365	371	7
6	208	189	9
7	330	336	9
8	252	251	12
9	318	328	11
10	99	127	22
11	168	176	14

h 2 -2

1	341	332	4
2	792	785	8
3	270	269	5
4	239	221	7
5	119	110	13
6	893	902	10
7	397	404	9
8	215	229	13
9	23	89	45
10	226	209	16
11	116	69	21

h 3 -2

1	1388	1396	14
2	1089	1076	11
3	423	429	6
4	476	472	7
5	676	713	8
6	289	282	9
7	624	615	9
8	172	174	16
9	205	241	11
10	103	121	22
11	308	287	11

h 4 -2

1	801	782	8
2	768	768	8
3	491	499	7
4	397	395	7
5	459	448	7
6	716	716	9
7	642	600	9
8	611	606	8
9	191	196	12
10	288	248	14
11	91	91	42

h 5 -2

1	486	469	6
2	643	641	7
3	298	294	12
4	298	294	8
5	645	629	8
6	301	299	9
7	288	245	11
8	69	112	32
9	104	68	27
10	142	151	18
11	257	251	15

h 6 -2

1	270	268	6
2	607	598	7
3	664	665	8
4	514	511	8
5	483	483	8
6	367	372	9
7	176	168	16
8	251	243	13
9	67	108	31
10	230	205	12
11	86	125	32

h 7 -2

1	554	554	7
2	316	319	7
3	241	228	9
4	201	191	11
5	631	604	9
6	437	420	9
7	391	381	10
8	116	81	25
9	-15	19	58
10	255	217	12

h 8 -2

1	501	488	7
2	264	256	9
3	153	102	13
4	523	511	9
5	332	334	10
6	433	416	10
7	271	278	13
8	114	138	28
9	97	58	25
10	248	230	13

h 9 -2

1	633	622	8
2	156	157	14
3	97	84	21
4	162	178	16
5	556	548	10
6	386	378	10
7	422	408	11
8	153	160	22
9	90	85	28

h 10 -2

h 11 -2

h 12 -2

h 13 -2

1	-91	63	28
2	186	198	17
3	100	130	32
4	229	242	23
5	159	168	17
6	183	139	22

h 14 -2

1	152	177	21
2	73	76	39
3	76	91	40
4	84	97	30
5	141	131	20

h 15 -2

1	207	208	17
2	-26	68	67
3	150	37	24

4	153	162	20

h 1 -1

1	791	781	8
2	933	979	9
3	845	887	9
4	457	512	6
5	206	199	8
6	305	268	8
7	-55	67	31
8	497	498	9
9	256	292	9
10	256	263	11
11	64	71	34
12	93	82	30

h 2 -1

1	337	321	4
2	550	539	6
3	1102	1138	11
4	518	542	7
5	460	457	7
6	228	228	10
7	312	313	9
8	199	221	15
9	299	311	8
10	88	45	28
11	97	88	9

h 3 -1

1	1	1	1
2	1	1	1
3	1	1	1
4	1	1	1
5	1	1	1
6	1	1	1
7	1	1	1
8	1	1	1
9	1	1	1
10	1	1	1
11	1	1	1
12	1	1	1

h 4 -1

1	1	1	1
2	1	1	1
3	1	1	1
4	1	1	1
5	1	1	1
6	1	1	1
7	1	1	1
8	1	1	1
9	1	1	1
10	1	1	1
11	1	1	1
12	1	1	1

h 5 -1

1	223	213	6
2	1004	981	10
3	287	282	7
4	678	678	8
5	243	229	9
6	538	560	9
7	92	117	26
8	346	305	11
9	127	102	17
10	256	283	12
11	72	57	35

h 6 -1

1	469	472	6
2	188	177	8
3	1028	1012	11
4	488	491	8
5	491	489	8
6	463	461	9
7	111	121	23
8	233	224	13
9	431	448	8
10	229	240	13
11	135	129	23

h 7 -1

1	360	347	7
2	898	862	10
3	272	263	8
4	671	672	9
5	352	368	9
6	186	158	14
7	106	127	25
8	428	424	10
9	129	135	19
10	268	276	12

h 8 -1

1	288	303	8
2	123	147	16
3	693	678	9
4	218	207	12
5	259	258	11
6	38	41	49
7	247	241	14
8	308	301	10
9	284	308	11
10	82	28	41

h 9 -1

1	466	480	8
2	687	695	9
3	286	284	12
4	574	575	9
5	308	306	11
6	102	105	26
7	138	138	24
8	308	294	14
9	82	104	30

h 10 -1

1	256	244	11
2	237	238	13
3	642	641	10
4	111	126	24
5	408	403	7
6	76	97	36
7	281	286	15
8	259	228	11
9	390	380	14

h 11 -1

1	263	262	12
2	370	360	10
3	128	95	21
4	233	232	10
5	177	182	14
7	214	218	19
8	269	275	17

h 12 -1

1	172	202	18
2	309	286	11
3	238	234	15
4	84	115	26
5	262	273	11
6	229	253	19
7	94	65	38
8	488	491	8
9	491	489	8
10	463	461	9
11	111	121	23
12	233	224	13

h 13 -1

1	246	250	15
2	309	300	13
3	268	270	14
4	254	246	11
5	165	149	17
6	132	124	30
7	196	186	24

h 14 -1

1	182	188	20
2	263	263	16
3	252	223	16
4	160	149	18
5	202	174	15

h 15 -1

1	306	269	13
2	242	254	19
3	-65	45	49
4	164	130	19

h 0 0

2	112	109	4
4	1012	987	10
6	1121	1166	10
8	497	489	7
10	209	209	10
12	194	193	14

h 1 0

1	609	610	5
2	299	299	3
3	743	743	6
4	438	442	5
5	1261	1281	11
6	-68	43	16
7	664	662	7
8	114	77	14
9	21	29	46
10	178	168	11
11	339	323	8
12	122	82	20

h 2 0

0	1244	1225	16
1	1593	1593	16
2	1078	1082	9
3	76	48	9
4	259	267	5
5	109	99	10
6	527	543	6
7	88	79	16
8	77	71	21
9	35	74	39
10	269	287	8
11	123	117	18

h 3 0

1	1134	1149	9
2	877	875	7
3	432	431	5
4	197	202	6
5	583	545	8
6	488	474	6
7	602	593	7
8	89	73	19
9	-20	12	48
10	121	87	16
11	138	146	17

h 4 0

0	1383	1379	14
1	110	82	6
2	545	548	5
3	861	861	8
4	239	242	5
5	141	131	9
6	543	563	6
7	101	87	15
8	474	482	7
9	48	61	35
10	69	52	25
11	89	73	23

h 5 0

1	256	262	4
2	311	316	4
3	53	13	16
4	161	154	7
5	648	638	7
6	261	250	7
7	442	416	7
8	112	128	17
9	-27	10	46
10	-83	18	22
11	224	228	12

h 6 0

0	1065	1076	7
1	838	838	6
2	372	378	6
3	58	59	18
4	298	264	6
5	83	56	14
6	304	314	7
7	336	328	8
8	368	376	8
9	68	14	28
10	28	38	45
11	264	238	11

h 7 0

1	718	705	8
2	75	83	14
3	487	485	6
4	402	403	6
5	438	428	6
6	68	7	22
7	608	588	7
8	237	233	11
9	300	302	10
10	20	18	51

h 8 0

0	123	144	13
1	557	553	6
2	491	497	6
3	383	384	6
4	211	203	8
5	103	72	15
6	618	632	7
7	118	144	17
8	206	204	12
9	196	196	12
10	159	118	15

h 9 0

1	139	125	10
2	425	429	6
3	76	67	19
4	620	619	7
5	134	145	14
6	165	180	13
7	193	187	13
8	231	218	12
9	178	193	13

h 10 0

0	171	199	13
1	199	208	9
2	308	321	7
3	581	584	7
4	160	145	12
5	118	141	14
6	213	187	11
7	182	176	14
8	-45	24	42
9	-50	77	38

h 11 0

1	489	487	7
2	97	63	18
3	143	147	14
4	108	120	15
5	412	408	7
6	99	7	23
7	278	274	11
8	183	142	18

h 12 0

0	518	508	9
1	514	520	10
2	226	248	10
3	428	414	8
4	218	228	9
5	81	80	21
6	488	491	9
7	142	128	19

h 13 0

1	530	507	7
2	412	414	8
3	176	23	29
4	510	510	7
5	395	388	8
6	288	288	12
7	148	143	21

h 14 0

0	343	352	12
1	182	178	13
2	153	145	16
3	276	279	11
4	101	86	21
5	239	221	11

h 15 0

1	244	242	11
2	111	117	23
3	155	115	17
4	185	162	14

h 16 0

0	285	282	16

h 0 1

1	370	372	3
2	410	421	4
3	725	743	6
4	832	858	7
5	694	691	8
6	178	176	8
7	179	180	9
8	566	561	7
9	359	377	6
10	84	70	20
11	300	298	8
12	119	72	20

h 1 1

0	360	369	4
1	768	783	7
2	937	943	9
3	850	874	9
4	542	555	7
5	204	201	9
6	288	302	8
7	93	75	21
8	512	513	9
9	299	314	12
10	247	255	15
11	-61	88	51
12	127	71	31

h 2 1

0	330	345	5
1	220	223	7
2	897	906	10
3	268	262	7
4	719	730	9
5	220	243	10
6	570	574	8
7	178	178	8
8	178	180	9
9	565	561	7
10	359	377	6
11	84	70	20
12	300	298	8

h 3 1

0	330	345	5
1	220	223	7
2	897	906	10
3	268	262	7
4	719	730	9
5	220	243	10
6	570	574	8
7	178	178	8
8	178	180	9
9	565	561	7
10	359	377	6
11	84	70	20
12	300	298	8

h 4 1

0	1227	1228	7
1	692	706	7
2	669	677	7
3	943	957	10
4	171	161	9
5	457	477	7
6	111	89	55
7	343	352	9
8	89	59	30
9	448	438	10
10	117	84	27
11	219	223	20

h 5 1

0	350	345	5
1	220	223	7
2	897	906	10
3	268	262	7
4	719	730	9
5	220	243	10
6	570	574	8

7	93	102	25
8	327	320	11
9	111	102	27
10	308	265	14
11	-48	60	56

h 6 1

0	303	303	6
1	381	398	7
2	172	179	9
3	1057	1069	11
4	489	480	8
5	487	495	8
6	452	449	9
7	152	158	17
8	224	235	15
9	443	450	11
10	219	245	19
11	157	138	26

h 7 1

0	809	795	9
1	309	311	7
2	879	876	10
3	247	245	9
4	604	611	8
5	369	366	9
6	172	147	16
7	128	80	40
8	441	443	11
9	196	196	28
10	284	284	17

h 8 1

0	77	104	22
1	318	307	8
2	128	130	18
3	668	708	9
4	208	218	13
5	169	180	12
6	81	20	26
7	276	261	13
8	309	301	13
9	244	250	16
10	60	33	48

h 9 1

0	675	671	9
1	399	388	9
2	668	694	11
3	238	243	11
4	600	641	9
5	296	304	11
6	188	174	19
7	93	83	29
8	294	297	14
9	49	87	53

h 10 1

0	128	142	19
1	262	269	11
2	208	222	13
3	614	672	9
4	128	128	20
5	381	390	10
6	171	132	18
7	199	223	20
8	221	200	17
9	323	324	15

h 11 1

0	51	48	38

1	256	264	12
2	356	377	10
3	110	78	24
4	200	210	15
5	155	166	21
6	99	56	30
7	269	235	15
8	269	268	16

h 12 1

0	134	125	20
1	185	204	16
2	278	285	13
3	240	245	14
4	35	93	56
5	266	256	15
6	278	262	15
7	124	49	28

h 13 1

0	136	115	22
1	268	283	14
2	296	296	13
3	279	283	14
4	219	217	17
5	83	125	38
6	188	135	25
7	232	220	20

h 14 1

0	188	191	19
1	198	212	18
2	302	293	14
3	207	227	19
4	163	138	29
5	154	151	27

h 15 1

0	106	80	31
1	242	260	18
2	271	280	17
3	-50	61	52
4	75	125	49

h 0 2

0	906	969	9
1	503	522	4
2	478	454	5
3	33	35	17
4	338	339	4
5	44	56	19
6	512	528	6
7	108	96	13
8	294	270	8
9	173	192	10
10	-35	35	35
11	-36	23	40
12	-81	84	28

h 1 2

0	39	39	11
1	203	202	4
2	621	633	7
3	84	70	11
4	617	626	7
5	305	319	7
6	259	237	9
7	269	274	10
8	201	222	14
9	329	322	11
10	149	138	22
11	181	188	22

h 2 2

0	504	491	5
1	364	366	5
2	700	721	7
3	253	255	6
4	226	217	7
5	85	102	18
6	876	891	10
7	432	423	9
8	237	263	13
9	141	92	19
10	200	193	18
11	95	96	35

h 3 2

0	608	622	6
1	1424	1423	14
2	1063	1094	11
3	430	433	6
4	456	457	7
5	691	695	9
6	294	282	8
7	621	605	9
8	199	187	15
9	263	252	14
10	99	101	34
11	275	274	17

h 4 2

0	1049	1056	7
1	758	758	8
2	780	776	8
3	503	495	7
4	387	395	7
5	410	423	8
6	703	704	9
7	679	658	9
8	581	595	10
9	73	68	35
10	126	127	28
11	111	108	34

h 5 2

0	642	648	7
1	448	463	6
2	667	679	8
3	888	887	10
4	314	308	7
5	619	620	8
6	325	318	9
7	237	230	12
8	168	132	17
9	78	68	35
10	178	141	20
11	271	275	17

h 6 2

0	1051	1049	11
1	255	259	7
2	548	549	7
3	676	667	8
4	498	506	8
5	435	424	8
6	435	426	9
7	212	207	14
8	251	225	13
9	93	109	33
10	189	187	21
11	-49	123	59

h 7 2

0	786	772	9
1	577	582	8
2	342	342	7
3	250	253	9
4	182	172	12
5	562	558	9
6	431	430	9
7	362	352	11
8	87	78	33
9	39	36	54
10	226	218	19

h 8 2

0	796	822	9
1	431	439	8
2	309	308	8
3	16	92	54
4	472	493	9
5	382	372	9
6	434	422	10
7	276	274	13
8	174	146	19
9	149	76	23
10	210	220	22

h 9 2

0	448	444	8
1	584	582	8
2	88	102	23
3	138	91	17
4	199	211	14
5	571	564	10
6	369	371	10
7	429	426	11
8	80	73	36
9	91	66	38

h 10 2

0	1061	1059	7
1	439	437	9
2	366	376	10
3	501	510	10
4	328	342	11
5	222	244	15
6	428	438	11
7	138	166	26
8	248	251	17
9	191	179	23

h 11 2

0	62	42	33
1	343	357	10
2	258	272	13
3	196	183	15
4	211	194	15
5	352	351	12
6	167	205	22
7	345	365	13
8	74	105	45

h 12 2

0	289	277	11
1	121	131	24
2	220	212	15
3	215	217	16
4	65	91	38
5	-49	79	50
6	204	162	18
7	169	174	24

h 13 2

0	-101	57	29

1	29	38	59
2	145	157	23
3	147	159	24
4	187	226	21
5	189	209	21
6	132	115	28

h 14 2

0	350	360	13
1	187	207	21
2	123	100	28
3	44	57	54
4	118	74	31
5	69	88	45

h 15 2

0	61	32	47
1	203	185	20
2	-94	46	37
3	80	60	42
4	216	195	20

h 0 3

1	1428	1374	18
2	394	386	4
3	938	991	9
4	426	422	8
5	721	728	9
6	47	43	22
7	480	472	8
8	247	242	9
9	564	548	7
10	218	231	11
11	198	199	12

h 1 3

0	703	701	7
1	860	859	6
2	1564	1594	11
3	389	411	6
4	748	742	8
5	466	471	7
6	187	172	10
7	168	181	13
8	496	478	9
9	291	306	13
10	205	192	18
11	107	75	33

h 2 3

0	382	383	5
1	210	212	5
2	1104	1089	11
3	466	472	6
4	386	397	6
5	559	566	8
6	81	107	22
7	299	304	10
8	167	195	17
9	239	233	14
10	263	243	15
11	63	112	47

h 3 3

0	293	272	5
1	305	294	5
2	1007	1024	10
3	938	950	10
4	33	52	30
5	476	480	7
6	134	148	15
7	341	347	10

8	371	376	10
9	423	429	10
10	206	204	18
11	153	119	26

h 4 3

0	719	712	8
1	662	672	7
2	792	847	8
3	912	931	10
4	829	841	9
5	442	438	8
6	-54	38	32
7	317	310	10
8	249	229	13
9	348	331	12
10	329	321	13
11	172	224	25

h 5 3

0	477	471	6
1	328	321	6
2	681	701	8
3	471	498	7
4	532	501	8
5	488	490	8
6	538	540	9
7	211	211	13
8	201	196	16
9	224	211	14
10	151	144	24
11	91	62	38

h 6 3

0	61	20	18
1	32	38	6
2	-48	47	28
3	480	486	7
4	318	311	8
5	311	311	9
6	184	188	15
7	188	188	16
8	224	208	14
9	321	327	14
10	77	88	42
11	239	228	20

h 7 3

0	249	253	7
1	448	456	7
2	301	308	8
3	298	291	8
4	549	538	8
5	50	70	36
6	85	87	27
7	190	201	18
8	228	217	17
9	325	296	15

h 8 3

0	507	518	7
1	132	144	13
2	699	707	9
3	297	305	9
4	415	413	9
5	430	427	9
6	328	317	11
7	87	38	30
8	223	226	18
9	228	220	18
10	73	49	46

h 9 3

0	-26	39	44
1	648	658	9
2	396	391	9
3	338	350	10
4	193	199	14
5	400	403	10
6	138	152	21
7	218	198	17
8	192	178	20
9	249	267	18

h 10 3

0	104	85	20
1	314	317	9
2	253	237	11
3	225	216	13
4	559	569	10
5	150	141	20
6	274	262	15
7	84	111	37
8	219	211	19
9	80	83	44

h 11 3

0	78	103	28
1	503	521	9
2	283	283	11
3	257	264	12
4	191	186	15
5	179	164	21
6	191	84	38
7	212	254	18

h 12 3

0	228	240	12
1	388	385	11
2	167	174	22
3	478	491	11
4	281	284	14
5	211	211	16
6	181	198	23
7	199	210	28

h 13 3

0	220	226	14
1	388	391	11
2	287	288	13
3	188	197	20
4	199	201	19
5	284	311	16
6	-101	82	31

h 14 3

0	323	328	13
1	108	167	32
2	99	94	32
3	299	284	15
4	127	166	30
5	93	76	40

h 15 3

0	102	192	34
1	81	124	41
2	215	229	28
3	62	115	52

h 0 4

0	727	691	7
1	1337	1316	11
2	779	768	7
3	396	401	4
4	686	689	6
5	469	471	5
6	505	518	6
7	468	471	6
8	352	345	7
9	35	57	33
10	194	201	11
11	274	259	9

h 1 4

0	1311	1301	13
1	725	677	7
2	925	939	9
3	196	202	7
4	862	868	9
5	385	390	7
6	770	796	9
7	561	571	9
8	234	220	13
9	142	144	21
10	311	291	14
11	90	69	38

h 2 4

0	860	860	9
1	908	923	9
2	373	368	5
3	388	408	6
4	427	430	7
5	484	490	7
6	440	455	6
7	561	540	9
8	251	248	12
9	228	220	18
10	130	124	21
11	240	236	18

h 3 4

0	70	69	11
1	448	439	6
2	608	606	7
3	421	428	6
4	268	269	7
5	405	404	7
6	441	450	8
7	402	396	9
8	264	268	12
9	138	84	22
10	68	134	43
11	202	183	21

h 4 4

0	971	976	10
1	632	625	7
2	580	591	7
3	194	189	8
4	679	700	8
5	427	409	8
6	385	408	9
7	315	324	10
8	168	142	17
9	93	75	30
10	147	136	24
11	184	183	24

h 5 4

0	324	336	6
1	792	796	9
2	526	525	7
3	468	480	7
4	176	184	10
5	356	357	8
6	396	392	9
7	363	343	10
8	265	266	13
9	186	188	19
10	92	63	35
11	130	179	33

h 6 4

0	440	440	6
1	681	683	8
2	537	541	7
3	246	228	8
4	255	274	9
5	371	371	9
6	458	462	9
7	491	475	10
8	233	215	15
9	227	206	17
10	94	197	41

h 7 4

0	542	538	7
1	585	588	8
2	421	432	7
3	313	314	8
4	421	433	8
5	506	508	9
6	398	399	10
7	304	293	11
8	266	226	13
9	241	244	17
10	43	102	61

h 8 4

0	560	553	8
1	298	321	8
2	536	542	8
3	364	373	9
4	272	280	10
5	166	143	16
6	268	252	12
7	290	290	13
8	236	209	17
9	102	161	30
10	103	123	30

h 9 4

0	41	78	35
1	159	164	14
2	69	107	28
3	448	447	9
4	288	293	11
5	261	260	13
6	125	180	25
7	113	116	28
8	109	97	32
9	77	102	44

h 10 4

0	-19	103	52
1	334	334	9
2	239	233	11
3	252	251	12
4	104	135	25
5	139	141	22
6	325	336	13
7	212	195	18
8	161	137	24
9	118	75	32

h 11 4

0	262	278	12
1	432	454	10
2	177	173	16
3	304	333	12
4	308	279	12
5	185	197	18
6	183	173	20
7	242	244	18
8	52	57	54

h 12 4

0	306	300	11
1	241	255	13
2	257	265	13
3	96	85	30
4	241	256	16
5	336	355	14
6	263	254	17
7	226	209	20

h 13 4

0	413	406	11
1	199	199	17
2	311	335	13
3	248	261	16
4	265	261	16
5	138	140	28
6	239	254	20

h 14 4

0	278	292	14
1	347	362	12
2	237	252	17
3	212	245	20
4	329	341	15
5	229	232	21

h 15 4

0	166	118	19
1	159	174	24
2	69	83	45
3	265	231	17

h 0 5

1	474	466	4
2	497	501	5
3	681	667	6
4	1082	1102	9
5	347	351	5
6	108	105	13
7	281	278	7
8	428	422	7
9	125	121	13
10	358	355	7
11	140	142	16

h 1 5

0	269	286	5
1	1015	1005	10
2	501	511	6
3	506	527	6
4	577	567	7
5	345	352	7
6	64	48	26
7	182	197	14
8	66	66	32
9	352	358	11
10	26	74	65
11	225	219	19

h 2 5

0	692	685	7
1	344	351	5
2	392	417	6
3	433	452	6
4	759	774	9
5	618	642	8
6	198	201	12
7	128	162	19
8	354	338	10
9	265	253	13
10	156	155	24
11	183	169	23

h 3 5

0	654	656	7
1	632	637	7
2	340	332	6
3	487	496	7
4	604	617	8
5	454	468	8
6	91	72	21
7	89	96	25
8	333	341	11
9	420	425	11
10	214	166	18
11	269	251	17

h 4 5

0	265	270	6
1	111	114	15
2	648	643	7
3	564	554	7
4	699	726	8
5	155	164	12
6	346	351	9
7	147	126	16
8	352	331	11
9	208	205	13
10	224	204	18
11	94	134	40

h 5 5

0	380	380	6
1	738	735	8
2	510	508	7
3	483	485	7
4	420	434	7
5	548	556	8
6	101	88	21
7	264	273	12
8	178	159	18
9	392	384	12
10	-22	91	72
11	-94	59	42

h 6 5

0	349	367	7
1	325	330	7
2	732	748	9
3	343	353	7
4	733	756	9
5	275	269	10
6	250	268	12
7	264	260	12
8	394	347	11
9	97	102	33
10	247	187	17

h 7 5

0	490	491	7
1	630	643	8
2	338	336	8
3	464	480	8
4	196	199	12
5	450	459	9
6	248	220	12
7	249	243	14
8	249	224	15
9	408	396	12
10	76	86	45

h 8 5

0	203	205	10
1	257	261	9
2	566	568	8
3	419	421	8
4	530	531	9
5	447	449	9
6	208	210	15
7	247	273	18
8	212	214	19
9	168	184	24
10	189	223	28

h 9 5

0	476	471	8
1	300	318	9
2	681	681	9
3	316	322	11
4	188	188	14
5	229	197	18
6	196	215	18
7	189	189	23

h 10 5

0	148	148	14
1	284	284	14
2	380	380	14
3	196	196	17
4	282	282	17
5	269	269	18
6	141	140	30
7	282	282	17
8	190	196	21

h 11 5

0	164	168	14
1	220	220	13
2	410	410	11
3	377	387	11
4	162	162	20
5	264	271	14
6	182	197	23
7	181	172	28
8	64	98	50

h 12 5

0	-67	64	34
1	127	121	22
2	312	310	12
3	110	132	27
4	244	232	15
5	171	138	20
6	84	52	39
7	147	147	28

h 13 5

0	246	234	13
1	64	121	41
2	159	146	21
3	185	200	19
4	111	67	30
5	142	109	28

6	212	236	21

h 14 5

0	-100	31	31
1	275	265	14
2	248	233	16
3	-15	43	75
4	252	227	17
5	233	230	20

h 15 5

0	229	174	17
1	54	56	51
2	76	123	43
3	130	100	31

h 0 6

0	179	176	6
1	404	404	4
2	234	231	4
3	804	792	7
4	156	146	7
5	319	316	5
6	526	538	6
7	498	492	6
8	-64	33	28
9	49	42	28
10	126	106	15
11	211	203	11

h 1 6

0	797	802	8
1	[illegible]	695	8
2	[illegible]	528	6
3	[illegible]	[illegible]	[illegible]
4	502	500	6
5	286	286	8
6	166	186	13
7	288	306	11
8	299	286	12
9	114	87	20
10	116	85	21
11	48	62	25

h 2 6

0	411	410	6
1	648	642	7
2	[illegible]	703	6
3	430	407	6
4	278	281	7
5	448	486	8
6	211	238	11
7	502	528	9
8	169	127	16
9	204	223	17
10	-52	32	48
11	198	187	21

h 3 6

0	993	1006	10
1	453	448	6
2	672	671	8
3	659	648	8
4	513	519	7
5	207	219	10
6	653	673	9
7	215	230	13
8	291	277	11
9	-51	36	45
10	109	81	30
11	102	110	37

h 4 6

0	244	222	6
1	992	978	10
2	586	590	7
3	155	163	10
4	552	576	8
5	669	683	9
6	353	371	9
7	556	544	9
8	108	92	25
9	96	85	31
10	151	159	24
11	265	252	18

h 5 6

0	735	747	8
1	499	498	7
2	385	394	7
3	616	624	8
4	456	467	8
5	213	210	11
6	399	416	9
7	158	166	18
8	228	204	14
9	176	206	22
10	90	21	36

h 6 6

0	297	291	7
1	398	397	7
2	148	129	12
3	43	38	31
4	576	589	8
5	237	227	11
6	160	131	15
7	422	432	10
8	160	171	21
9	206	197	18
10	88	99	52

h 7 6

0	588	590	8
1	199	212	10
2	422	424	8
3	150	148	13
4	524	529	8
5	116	84	19
6	398	399	10
7	82	161	34
8	-107	42	29
9	169	186	23
10	137	188	31

h 8 6

0	362	365	8
1	755	739	9
2	200	211	12
3	340	355	9
4	159	195	16
5	228	229	13
6	160	135	17
7	397	435	12
8	108	120	30
9	74	50	43

h 9 6

0	539	557	8
1	117	94	18
2	538	548	9
3	229	239	12
4	356	376	10
5	-83	45	30
6	603	610	10
7	-14	13	73
8	97	67	35
9	103	69	36

h 10 6

0	133	129	18
1	585	594	9
2	138	148	19
3	168	189	17
4	114	126	23
5	277	275	13
6	317	298	13
7	431	422	12
8	138	119	29

h 11 6

0	362	373	10
1	166	163	16
2	233	248	13
3	429	423	10
4	132	164	22
5	195	210	18
6	290	301	15
7	122	156	31
8	137	150	31

h 12 6

0	289	285	11
1	190	191	16
2	80	68	33
3	-34	29	53
4	226	218	16
5	121	136	29
6	222	214	18
7	220	214	21

h 13 6

0	133	135	22
1	100	82	28
2	66	80	33
3	95	132	34
4	-88	59	36
5	129	112	28
6	157	119	26

h 14 6

0	226	229	17
1	270	272	14
2	180	139	20
3	127	120	28
4	92	106	39

h 15 6

0	49	111	52
1	217	193	18
2	126	166	31

h 0 7

1	267	263	4
2	1477	1473	15
3	533	534	5
4	741	745	7
5	93	72	12
6	289	287	6
7	300	292	7
8	252	244	9
9	223	222	9
10	354	361	7
11	161	184	15

h 1 7

0	149	158	8
1	585	588	7
2	468	531	6
3	832	855	9
4	190	197	9
5	498	513	8
6	79	72	24
7	307	307	10
8	142	117	19
9	490	466	10
10	92	110	34
11	-48	78	57

h 2 7

0	273	285	6
1	217	221	7
2	860	855	9
3	231	234	8
4	724	681	9
5	183	190	11
6	215	222	11
7	37	72	42
8	351	344	11
9	147	180	23
10	267	262	16
11	-86	82	42

h 3 7

0	420	420	6
1	388	386	6
2	172	177	8
3	664	698	8
4	277	289	8
5	526	541	8
6	195	196	13
7	291	288	11
8	177	177	17
9	421	429	11
10	57	79	48
11	142	94	28

h 4 7

0	817	796	9
1	213	206	7
2	745	745	8
3	264	269	8
4	592	595	8
5	259	257	10
6	-73	12	27
7	207	211	14
8	276	269	14
9	125	105	24
10	288	288	16

h 5 7

0	380	362	6
1	311	309	7
2	248	243	8
3	456	455	7
4	123	129	16
5	458	480	9
6	152	154	17
7	188	162	15
8	180	155	18
9	325	343	13
10	-110	67	34

h 6 7

0	512	493	7
1	255	275	8
2	367	342	7
3	289	286	8
4	486	489	8
5	77	125	27
6	18	43	56
7	110	145	26
8	121	52	25
9	238	216	16
10	205	224	22

h 7 7

0	235	226	9
1	338	316	8
2	185	205	11
3	476	486	8
4	305	309	9
5	401	417	9
6	216	231	14
7	136	108	22
8	155	157	22
9	317	330	15
10	71	77	47

h 8 7

0	30	78	41
1	270	262	9
2	262	262	10
3	113	94	19
4	534	538	9
5	190	184	15
6	181	168	17
7	98	100	30
8	224	211	15
9	-50	38	54

h 9 7

0	324	308	9
1	120	109	18
2	429	432	9
3	288	291	11
4	-67	62	33
5	118	77	24
6	260	277	15
7	100	48	31
8	128	108	29
9	142	150	32

h 10 7

0	160	160	15
1	430	438	9
2	328	308	10
3	151	120	17
4	288	290	12
5	308	315	12
6	91	67	33
7	232	224	17
8	236	220	19

h 11 7

0	298	308	11
1	149	204	19
2	186	173	16
3	480	506	10
4	215	219	16
5	116	119	27
6	179	202	22
7	137	136	29

h 12 7

0	-48	28	43
1	283	286	12
2	259	270	14
3	108	126	28
4	309	303	13
5	250	228	16
6	89	84	37

h 13 7

0	256	229	13
1	173	136	19
2	228	259	17
3	306	296	14
4	200	218	21
5	198	194	22

h 14 7

0	89	43	33
1	230	224	17
2	285	268	15
3	97	121	36
4	263	279	18

h 15 7

0	72	55	44
1	145	164	27

h 0 8

0	116	105	11
1	534	532	8
2	410	420	5
3	211	210	9
4	212	220	6
5	211	210	8
6	210	212	8
7	488	471	7
8	28	14	42
9	97	64	18
10	228	221	10
11	305	286	9

h 1 8

0	730	730	8
1	508	501	7
2	669	670	7
3	388	386	7
4	174	164	10
5	462	471	8
6	818	842	10
7	122	109	19
8	190	176	15
9	108	104	26
10	162	135	21
11	-108	39	35

h 2 8

0	509	500	6
1	1052	1042	11
2	210	215	8
3	310	316	7
4	382	391	7
5	214	237	11
6	290	291	10
7	334	341	10
8	135	160	21
9	200	194	18
10	207	229	19
11	192	167	22

h 3 8

0	329	320	6
1	191	189	8
2	369	351	7
3	112	83	14
4	294	315	8

5	300	289	9
6	555	559	9
7	166	193	17
8	119	126	24
9	175	161	20
10	-64	25	44

h 4 8

0	57	26	20
1	378	381	7
2	406	408	7
3	166	194	11
4	182	164	11
5	90	112	23
6	87	103	26
7	463	462	10
8	283	317	14
9	120	60	26
10	132	141	28

h 5 8

0	767	771	9
1	179	162	9
2	482	480	7
3	169	186	12
4	218	230	11
5	248	247	11
6	569	598	9
7	166	129	16
8	183	166	17
9	149	138	23
10	98	85	36

h 6 8

0	77	56	23
1	688	691	8
2	85	105	23
3	269	278	9
4	216	227	11
5	479	477	9
6	119	106	23
7	579	566	10
8	206	204	16
9	-42	33	66
10	79	162	46

h 7 8

0	771	777	9
1	309	309	8
2	340	334	8
3	333	326	9
4	337	334	9
5	387	390	10
6	426	435	10
7	181	179	18
8	216	216	17
9	127	142	28

h 8 8

0	65	82	28
1	437	429	8
2	372	368	9
3	167	179	15
4	214	208	13
5	307	292	11
6	170	138	17
7	326	321	12
8	103	70	31
9	39	118	64

h 9 8

0	339	340	9

1	228	220	11
2	263	267	10
3	197	211	15
4	180	144	15
5	193	185	16
6	70	137	40
7	153	156	24
8	164	150	24

h 10 8

0	60	29	34
1	152	172	18
2	257	254	12
3	193	188	15
4	-80	36	32
5	240	243	14
6	159	104	20
7	183	226	22
8	-42	35	60

h 11 8

0	380	407	10
1	-12	25	64
2	211	214	15
3	155	90	19
4	248	266	15
5	162	212	23
6	199	208	20
7	130	127	31

h 12 8

0	-59	60	40
1	289	300	13
2	23	46	60
3	234	250	16
4	302	312	31
5	309	315	14
6	-74	86	46

h 13 8

0	469	469	11
1	227	204	16
2	161	148	22
3	268	277	16
4	284	286	15
5	188	150	22

h 14 8

0	170	154	21
1	126	151	27
2	227	182	17
3	63	76	49

h 0 9

1	70	38	13
2	217	210	6
3	509	501	6
4	523	547	6
5	176	183	9
6	37	39	31
7	174	189	11
8	41	33	35
9	181	167	11
10	178	160	12

h 1 9

0	54	16	21
1	544	532	7
2	553	547	7
3	327	339	7
4	252	260	9

5	286	292	9
6	214	197	12
7	155	167	17
8	57	95	41
9	299	308	13
10	219	187	18

h 2 9

0	137	152	11
1	476	476	7
2	279	298	8
3	214	206	9
4	577	567	8
5	340	347	9
6	188	168	13
7	134	151	20
8	167	177	17
9	152	164	22
10	263	295	15

h 3 9

0	241	222	8
1	230	223	8
2	419	408	7
3	601	607	8
4	374	386	8
5	513	530	8
6	212	212	12
7	-64	34	32
8	100	30	27
9	300	296	13
10	120	106	30

h 4 9

0	386	381	7
1	342	346	7
2	758	701	9
3	310	323	8
4	600	586	8
5	336	343	9
6	188	197	14
7	191	191	14
8	187	218	18
9	94	69	33
10	268	239	16

h 5 9

0	36	64	34
1	457	460	7
2	426	428	8
3	493	497	8
4	249	238	10
5	136	130	17
6	190	197	15
7	175	160	17
8	140	196	24
9	226	234	18
10	89	74	40

h 6 9

0	219	208	10
1	391	385	8
2	591	589	8
3	411	416	8
4	413	396	9
5	255	255	12
6	136	128	20
7	207	201	16
8	260	259	14
9	137	109	26

h 7 9

0	346	349	9
1	411	404	8
2	331	358	9
3	595	598	9
4	247	280	12
5	211	199	13
6	79	59	31
7	245	249	14
8	320	296	13
9	291	292	15

h 8 9

0	101	62	20
1	193	180	12
2	643	654	9
3	244	237	12
4	236	253	13
5	189	164	15
6	245	243	14
7	117	85	27
8	363	339	13
9	101	106	36

h 9 9

0	182	155	13
1	229	208	12
2	121	103	20
3	488	464	9
4	83	82	30
5	227	231	15
6	70	52	37
7	178	169	21
8	115	114	33

h 10 9

0	185	208	15
1	218	244	13
2	560	561	9
3	113	82	23
4	324	308	12
5	139	152	22
6	74	70	39
7	224	220	18

h 11 9

0	73	30	32
1	87	147	31
2	111	91	25
3	299	306	12
4	181	147	18
5	182	191	20
6	123	91	28
7	-77	9	42

h 12 9

0	78	21	34
1	195	197	17
2	68	70	39
3	232	238	16
4	149	145	24
5	-85	40	39
6	-52	33	54

h 13 9

0	138	132	24
1	20	87	67
2	61	59	44
3	121	108	28
4	141	85	26

h 14 9

0	258	250	16
1	129	84	28
2	173	202	23

h 0 10

0	333	337	7
1	396	396	5
2	74	81	14
3	178	187	8
4	-10	48	44
5	573	591	6
6	173	159	10
7	323	318	7
8	40	20	35
9	65	50	26
10	88	67	22

h 1 10

0	788	792	9
1	31	65	32
2	188	166	10
3	237	238	9
4	336	339	8
5	164	178	14
6	204	204	12
7	307	323	11
8	200	199	14
9	42	76	52
10	91	82	38

h 2 10

0	518	514	7
1	356	349	7
2	405	406	7
3	290	289	8
4	148	148	12
5	320	348	9
6	235	230	12
7	406	406	10
8	238	198	10
9	132	65	24
10	-22	47	69

h 3 10

0	1094	1107	11
1	345	338	7
2	298	288	8
3	281	271	8
4	598	614	8
5	404	409	9
6	337	345	10
7	284	277	12
8	117	134	26
9	-131	30	28
10	-101	47	35

h 4 10

0	438	432	7
1	404	406	8
2	165	177	12
3	529	526	8
4	254	251	10
5	347	311	9
6	313	328	11
7	486	498	10
8	201	172	17
9	-77	46	38
10	124	38	29

h 5 10

0	465	461	8
1	543	519	8

2	382	383	8
3	327	348	9
4	380	373	9
5	425	394	9
6	236	235	13
7	177	178	17
8	178	182	20
9	46	80	54

h 6 10

0	378	395	8
1	86	95	22
2	248	258	11
3	204	214	12
4	164	135	15
5	109	104	22
6	260	261	12
7	120	93	24
8	196	176	18
9	204	212	20

h 7 10

0	239	234	11
1	288	278	9
2	91	85	23
3	79	81	27
4	159	140	16
5	260	268	12
6	188	189	20
7	130	130	22
8	124	123	27
9	82	84	40

h 8 10

0	828	828	10
1	289	307	10
2	116	104	18
3	64	60	23
4	245	253	13
5	241	241	15
6	265	265	14
7	136	132	30
8	104	42	31

h 9 10

0	298	290	11
1	498	502	9
2	279	277	11
3	98	92	25
4	88	97	41
5	304	302	13
6	248	255	16
7	197	169	19
8	101	111	36

h 10 10

0	305	307	11
1	298	303	12
2	191	180	15
3	-26	88	58
4	270	265	13
5	196	209	18
6	216	211	18
7	160	153	25

h 11 10

0	88	73	29
1	184	196	17
2	218	241	16
3	254	226	13
4	256	254	14
5	143	141	25

6	293	292	16

h 12 10

0	89	92	31
1	281	255	14
2	163	152	22
3	-69	36	41
4	122	116	29
5	200	203	21

h 13 10

0	170	181	21
1	32	44	60
2	107	110	32
3	225	236	19

h 14 10

0	-74	20	43

h 0 11

1	392	405	5
2	523	526	6
3	399	391	6
4	701	675	7
5	374	381	7
6	116	119	10
7	185	169	10
8	144	149	10
9	196	201	13
10	226	208	19

h 1 11

0	99	116	16
1	380	386	7
2	398	394	8
3	443	427	8
4	498	502	9
5	247	264	11
6	-82	20	28
7	181	183	28
8	301	316	12
9	255	239	15
10	101	88	38

h 2 11

0	96	116	17
1	538	535	8
2	374	386	6
3	781	769	9
4	88	47	22
5	148	133	15
6	338	339	10
7	167	173	17
8	218	208	16
9	348	331	12
10	126	137	30

h 3 11

0	184	177	11
1	139	108	12
2	248	226	9
3	363	359	8
4	497	494	9
5	308	323	10
6	74	87	31
7	229	226	14
8	366	395	12
9	-26	61	64

h 4 11

0	-74	72	23
1	315	308	8
2	436	426	8
3	314	316	9
4	186	175	13
5	116	148	21
6	138	95	19
7	94	92	29
8	251	261	15
9	169	177	22

h 5 11

0	344	349	9
1	136	126	15
2	364	354	9
3	269	259	10
4	265	266	11
5	119	131	21
6	100	111	27
7	153	146	19
8	106	63	29
9	159	156	23

h 6 11

0	291	283	9
1	182	184	13
2	283	274	10
3	188	177	14
4	335	333	10
5	144	151	16
6	214	218	15
7	23	78	66
8	259	245	15
9	169	134	21

h 7 11

0	223	233	12
1	186	199	14
2	107	83	21
3	392	385	9
4	108	22	28
5	360	361	11
6	241	205	14
7	148	152	23
8	129	121	27

h 8 11

0	112	122	22
1	168	185	22
2	198	199	14
3	187	199	16
4	-78	70	32
5	168	170	19
6	141	119	22
7	99	108	34
8	110	114	33

h 9 11

0	208	225	15
1	147	152	18
2	231	241	14
3	-97	93	28
4	96	43	27
5	120	101	25
6	119	146	29
7	129	154	28

h 10 11

0	310	300	11
1	191	183	16
2	198	216	17
3	317	335	12
4	293	274	13
5	85	127	36
6	167	140	22

h 11 11

0	80	80	33
1	347	356	12
2	309	316	13
3	149	175	23
4	14	83	75
5	228	251	19

h 12 11

0	272	264	15
1	-99	96	32
2	176	197	22
3	157	115	22
4	261	267	17

h 13 11

0	199	215	20
1	-25	100	68
2	240	212	17

h 0 12

0	711	710	9
1	90	95	14
2	120	89	11
3	93	110	15
4	336	336	7
5	69	30	21
6	372	366	7
7	75	26	23
8	190	172	13
9	208	216	10

h 1 12

0	268	277	9
1	429	421	8
2	329	322	8
3	222	222	12
4	387	388	9
5	418	403	9
6	123	114	21
7	310	295	11
8	148	164	22
9	21	59	67

h 2 12

0	472	485	8
1	293	281	9
2	475	472	8
3	149	153	15
4	103	134	22
5	146	131	17
6	242	241	12
7	154	113	18
8	159	168	21
9	236	250	17

h 3 12

0	62	42	27
1	201	205	12
2	278	267	9
3	533	540	9
4	31	93	45
5	162	159	16
6	198	206	15
7	262	245	13
8	136	116	23
9	63	96	46

h 4 12

0	280	267	9
1	-66	58	28
2	266	279	9
3	-74	24	26
4	191	191	14
5	66	43	30
6	179	219	18
7	113	86	26
8	112	100	29
9	144	121	24

h 5 12

0	488	492	8
1	486	493	9
2	45	35	37
3	280	276	10
4	160	147	16
5	243	259	13
6	178	178	17
7	358	354	12
8	-45	16	51
9	0	61	91

h 6 12

0	447	447	9
1	467	454	9
2	314	321	10
3	-38	25	42
4	169	207	15
5	415	427	10
6	319	324	13
7	138	130	24
8	168	169	23

h 7 12

0	592	598	9
1	322	307	10
2	27	24	48
3	284	277	12
4	297	288	13
5	308	299	12
6	235	229	15
7	224	242	17
8	152	144	25

h 8 12

0	396	391	10
1	233	234	13
2	185	189	16
3	279	285	12
4	-40	33	49
5	246	257	15
6	242	233	15
7	97	109	34

h 9 12

0	445	445	10
1	154	167	19
2	196	181	16
3	87	91	31
4	166	165	20
5	157	161	21
6	115	59	29
7	81	68	40

h 10 12

0	65	57	39
1	124	157	25
2	67	92	37
3	109	125	28
4	-81	86	37
5	149	132	23
6	137	138	28

h 11 12

0	250	255	15
1	64	127	42
2	58	42	44
3	-64	113	43
4	109	133	31
5	173	148	22

h 12 12

0	333	333	13
1	-45	35	51
2	115	113	30
3	216	217	18

h 13 12

0	97	142	37

h 0 13

1	144	165	10
2	209	198	8
3	324	336	6
4	152	164	12
5	407	423	6
6	127	118	18
7	255	278	11
8	98	80	22
9	199	192	11

h 1 13

0	232	244	10
1	241	243	10
2	452	448	8
3	269	293	10
4	130	111	18
5	154	160	17
6	-75	62	32
7	-92	90	31
8	108	104	28
9	-34	54	60

h 2 13

0	74	71	25
1	248	243	10
2	348	354	9
3	183	181	13
4	212	210	13
5	310	311	11
6	168	196	18
7	208	178	15
8	92	119	34
9	77	163	42

h 3 13

0	-46	32	35
1	243	236	11
2	287	288	10
3	416	436	9
4	241	243	12
5	197	165	14
6	99	107	28
7	80	33	34
8	90	92	33
9	86	69	38

h 4 13

0	97	74	22
1	193	190	13
2	504	509	9
3	418	437	9
4	209	212	14
5	330	332	11
6	299	285	12
7	138	132	24
8	232	239	16

h 5 13

0	85	66	24
1	441	436	9
2	498	512	9
3	204	224	13
4	199	221	15
5	145	160	20
6	148	128	20
7	81	75	35
8	164	170	23

h 6 13

0	-95	21	24
1	299	301	11
2	448	458	12
3	388	420	11
4	150	164	22
5	199	214	20
6	241	222	15
7	211	216	16
8	85	82	37

h 7 13

0	337	346	10
1	166	189	16
2	471	491	10
3	152	228	15
4	366	388	11
5	85	108	30
6	124	98	26
7	118	22	31

h 8 13

0	92	15	26
1	366	371	11
2	75	116	32
3	418	419	10
4	81	69	33
5	115	90	26
6	236	241	16
7	217	216	18

h 9 13

0	281	242	13
1	167	188	19
2	191	192	17
3	197	218	23
4	204	216	18
5	-58	23	47
6	59	88	50

h 10 13

0	-13	21	68
1	188	182	18
2	-64	64	42
3	161	179	22
4	225	182	17
5	69	90	46

h 11 13

0	37	17	53

1	-124	13	26
2	192	190	19
3	120	91	28
4	163	157	24

h 12 13

0	50	85	51
1	99	88	34
2	-86	56	37

h 0 14

0	110	111	19
1	15	29	44
2	-59	39	23
3	203	223	9
4	106	89	13
5	271	273	7
6	143	161	15
7	75	88	26
8	57	73	23

h 1 14

0	548	555	9
1	408	483	9
2	248	245	11
3	201	88	59
4	288	276	13
5	342	342	10
6	176	188	16
7	136	174	20
8	108	121	28

h 2 14

0	555	553	9
1	361	359	14
2	401	406	9
3	298	303	11
4	182	202	16
5	110	101	26
6	484	498	10
7	169	177	21
8	98	130	33

h 3 14

0	274	261	10
1	399	380	9
2	166	150	14
3	92	112	25
4	102	43	23
5	282	284	13
6	107	84	26
7	311	321	13
8	92	88	32

h 4 14

0	318	321	10
1	89	83	25
2	322	335	10
3	118	117	21
4	204	218	15
5	132	171	23
6	273	259	13
7	48	58	48
8	82	85	38

h 5 14

0	225	247	12
1	207	210	14
2	163	149	17
3	49	111	42
4	-82	41	31
5	38	58	51
6	83	118	35
7	184	194	20
8	103	112	34

h 6 14

0	182	163	16
1	133	138	20
2	183	214	17
3	185	214	17
4	143	158	20
5	135	106	23
6	145	93	22
7	120	85	28

h 7 14

0	72	74	32
1	253	238	13
2	57	55	39
3	85	98	31
4	108	140	28
5	239	232	15
6	55	59	47
7	128	153	28

h 8 14

0	76	57	33
1	37	48	50
2	189	190	17
3	161	120	20
4	60	66	41
5	67	82	42
6	135	104	26

h 9 14

0	231	200	15
1	287	287	14
2	196	188	17
3	-37	69	56
4	102	96	30
5	143	166	26

h 10 14

0	316	329	13
1	14	80	73
2	179	169	20
3	247	230	16
4	180	201	22

h 11 14

0	100	50	32
1	131	126	27
2	318	308	14
3	-62	94	47

h 0 15

1	442	437	6
2	170	165	11
3	283	299	6
4	56	20	23
5	227	225	10
6	77	7	25
7	90	10	23
8	-60	6	35

h 1 15

0	65	120	32
1	258	273	11
2	194	192	14
3	102	124	23
4	343	365	11
5	120	67	23
6	-19	24	63
7	189	191	19
8	222	203	18

h 2 15

0	241	254	12
1	349	367	10
2	154	165	17
3	220	229	14
4	137	130	20
5	270	291	13
6	121	100	25
7	82	86	36
8	164	130	22

h 3 15

0	334	319	10
1	148	144	17
2	341	339	10
3	132	152	21
4	342	352	11
5	219	213	15
6	98	67	30
7	149	119	23
8	167	189	24

h 4 15

0	100	51	23
1	198	181	14
2	238	224	13
3	211	236	15
4	66	101	38
5	152	121	21
6	-48	76	50
7	52	108	50

h 5 15

0	108	122	24
1	96	38	28
2	148	126	19
3	83	53	31
4	290	292	13
5	-68	48	38
6	198	236	20
7	138	97	26

h 6 15

0	210	199	15
1	114	133	24
2	236	225	14
3	197	215	17
4	19	93	66
5	231	251	16
6	122	92	28

h 7 15

0	137	119	22
1	108	139	26
2	176	139	18
3	204	198	17
4	266	260	14
5	93	149	34
6	72	78	43

h 8 15

0	288	297	13
1	-88	92	32
2	91	121	33
3	171	145	20
4	35	64	57
5	96	125	34

h 9 15

0	-90	39	34
1	183	170	18
2	207	230	18
3	142	134	23
4	-89	92	37

h 10 15

0	211	177	18
1	138	140	25
2	-29	92	65
3	203	159	19

h 11 15

0	214	200	19

h 0 16

0	452	461	9
1	124	155	15
2	144	127	13
3	46	4	27
4	93	86	16
5	86	59	23
6	187	177	13
7	227	230	12

h 1 16

0	94	122	26
1	82	104	29
2	307	304	11
3	149	172	20
4	162	183	20
5	143	161	22
6	133	110	23
7	192	184	19

h 2 16

0	134	142	20
1	57	147	39
2	0	36	75
3	211	200	14
4	95	23	28
5	-31	77	56
6	182	175	18
7	180	128	20

h 3 16

0	133	146	19
1	80	59	30
2	-18	39	60
3	296	280	12
4	164	154	18
5	-31	51	57
6	80	68	36
7	210	211	19

h 4 16

0	435	436	10
1	146	139	20
2	100	116	27
3	103	70	27
4	177	193	19
5	142	129	24
6	171	202	22
7	142	101	25

h 5 16

0	-79	14	32
1	247	243	14
2	124	84	23
3	118	92	24
4	158	166	20
5	177	178	20
6	-36	75	58

h 6 16

0	355	340	11
1	272	289	13
2	194	189	17
3	157	118	21
4	195	222	18
5	150	117	23
6	209	205	19

h 7 16

0	-65	14	39
1	359	353	12
2	127	109	24
3	57	142	47
4	86	61	35
5	216	233	19

h 8 16

0	95	133	33
1	8	75	55
2	229	211	16
3	136	159	25
4	150	165	25

h 9 16

0	-40	24	54
1	225	195	17
2	-70	23	41
3	144	88	24

h 10 16

0	-87	54	38
1	53	64	50

h 0 17

1	58	75	28
2	221	230	10
3	142	138	12
4	239	242	8
5	104	116	23
6	128	114	18

h 1 17

0	185	166	16
1	240	248	13
2	172	149	17
3	109	127	25
4	167	155	19
5	120	49	25
6	165	131	21

h 2 17

0	-18	16	60
1	50	71	41
2	137	141	22
3	189	252	18
4	211	190	16
5	253	236	14
6	65	15	42

h 3 17

0	392	383	10
1	95	63	27
2	408	424	11
3	-30	89	56
4	204	215	18
5	126	39	24
6	49	20	51

h 4 17

0	-81	15	32
1	116	89	28
2	-30	42	54
3	98	142	30
4	34	79	56
5	182	203	21
6	-68	57	43

h 5 17

0	133	136	24
1	124	103	24
2	88	77	32
3	228	226	16
4	223	179	16
5	132	42	24

h 6 17

0	110	103	27
1	8	65	55
2	229	211	16
3	136	159	25
4	150	165	25

h 7 17

0	69	74	41
1	199	183	21
2	79	79	52
3	144	126	28

h 8 17

0	48	47	50
1	21	83	70
2	84	99	45
3	103	12	34

h 9 17

0	84	131	39
1	191	182	20

h 0 18

0	118	151	25
1	291	294	9
2	150	133	16
3	140	145	13
4	27	6	40
5	131	122	18

h 1 18

0	137	123	22
1	194	206	17
2	-72	52	37
3	203	201	15
4	115	107	27
5	49	92	51

h 2 18

0	98	88	27

1	195	181	17
2	102	127	30
3	104	127	29
4	149	174	22
5	163	135	22

h 3 18

0	205	214	16
1	270	262	14
2	117	123	27
3	172	129	19
4	159	127	22
5	102	66	32

h 4 18

0	137	48	21
1	224	211	15
2	141	141	24
3	85	30	34
4	44	57	52
5	155	136	22

h 5 18

0	134	116	24
1	72	56	39
2	147	100	22
3	86	56	35
4	204	216	20

h 6 18

0	-77	74	38
1	108	94	30
2	-43	87	52
3	76	45	39

h 7 18

0	81	68	39
1	36	28	57
2	161	137	22

h 0 19

1	51	82	35
2	254	267	11
3	-76	27	23
4	148	111	14

h 1 19

0	129	116	24
1	191	192	19
2	108	69	28
3	189	199	20
4	145	138	24

h 2 19

0	128	112	25
1	67	32	39
2	312	304	14
3	105	69	30
4	84	138	39

h 3 19

0	114	97	27
1	-95	31	32
2	126	39	25
3	200	206	19
4	-95	103	37

h 4 19

0	200	159	18
1	-14	107	73
2	122	156	30
3	132	113	27

h 5 19

0	130	155	28
0	0	3	84
1	82	80	36
2	161	155	23
3	50	121	55

h 6 19

0	-33	15	61
1	82	117	40

h 0 20

0	207	228	19
1	116	85	20
2	45	27	40
3	85	105	23

h 1 20

0	130	155	28
1	133	106	25
2	-72	70	41
3	192	164	20

h 2 20

0	-88	24	35
1	104	126	32
2	149	173	24

h 3 20

0	77	44	39
1	-93	64	35
2	33	59	60

h 4 20

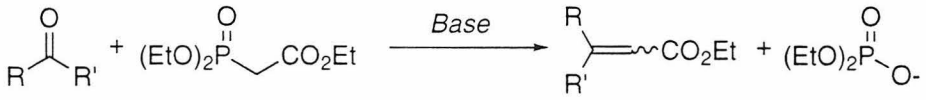
0	113	13	30
1	29	60	64

Part II. An Inexpensive, Nonbasic Alternative to the Horner-Emmons Olefination Reaction

Introduction

A number of important enantioselective processes utilize allylic relationships to install chirality, and the Horner-Emmons olefination reaction has long been the gold standard for the stereoselective synthesis of these substrates from aldehydes and ketones.[1,2,3] Water soluble byproducts and generally good (*E*):(*Z*) stereoselection have made it a valuable addition to the organic chemist's synthetic arsenal.

Figure 1. The Horner-Emmons condensation.



It was recently reported by Herrmann and coworkers that methyltrioxorhenium(VII) (MTO) was capable of catalyzing the olefination of aldehydes with ethyl diazoacetate in the presence of a stoichiometric amount of triphenyl phosphine.[4] This reaction was effective at catalyst load as low as 5% and with a wide variety of aldehydes. However, at lower catalyst loads dimerization of the diazoacetate outstripped the desired reaction.[5] Herrmann later reported that trichlorooxobis(triphenylphosphinio)rhenium(V) was also an effective

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1 For reviews of reactions of phosphonate anions with carbonyl compounds, see: (a) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87. (b) Wadsworth, W. S. *Org. React.* **1977**, *25*, 73.

2 For a leading reference on enantioselective allylic epoxidations, see: Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S.Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

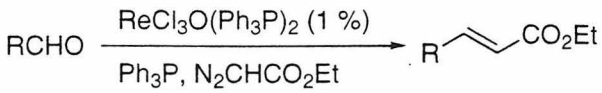
3 For leading references on enantioselective allylic cyclopropanations, see: (a) Denmark, S. E.; O'Connor, S. P. *J. Org. Chem.* **1997**, *62*, 3390. (b) Kobayashi, S.; Imai, N.; Sakamoto, K.; Takahashi, H. *Tetrahedron Lett.* **1994**, *35*, 7045. (c) Charlene, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367.

4 Herrmann, W. A.; Wang, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1641.

5 Herrmann, W. A.; Roesky, P. W.; Wang, M.; Scherer, W. *Organometallics* **1994**, *13*, 4531.

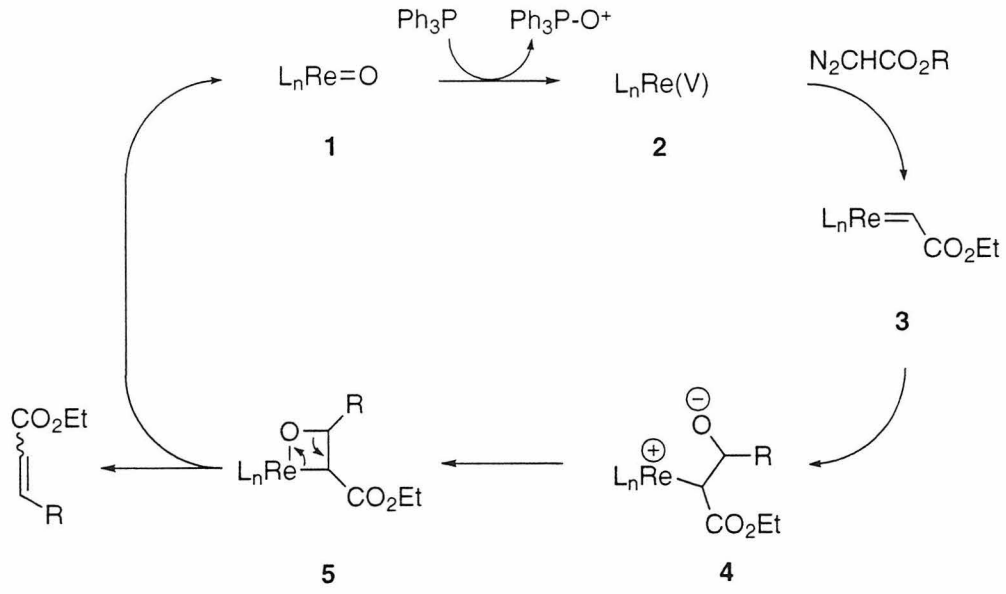
catalyst. In fact, it proved both more reactive (lower mol% catalyst) and more selective for a single aldehyde (*p*-nitro-benzaldehyde).[5]

Figure 2. Rhenium catalyzed olefination of aldehydes.



Two mechanisms have been proposed. Herrmann favors initial reduction of the rhenium (VII) oxo by the phosphine to a rhenium(V) complex. This complex then reacts directly with the diazoacetate to yield a rhenium alkylidene. On exposure to the aldehyde, the rhenium alkylide forms a metallooxetane, which extrudes the olefin and regenerates rhenium (VII) oxo species (Figure 3).

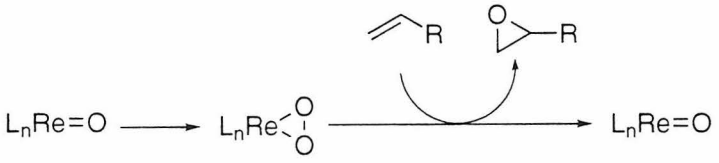
Figure 3. One possible mechanism - initial reduction of Re(VII).[4]



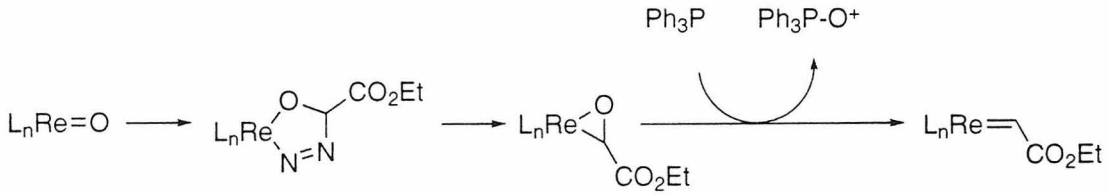
Another possible mechanism was proposed by Espenson and coworkers; in their scheme, the rhenium oxo complex undergoes a dipolar cycloaddition with the diazoacetate,

yielding **6**, which then extrudes nitrogen to give **7**. While neither **6** nor **7** has been observed spectroscopically, their formation parallels the MTO reaction with hydrogen peroxide to form **8** (Figure 4).[6] In the presence of an appropriate reductant, **7** is reduced to rhenium alkylidene **3**. Alkylidene **3** is sufficiently nucleophilic to add to an aldehyde, generating alcohol **4**.[7] Closure to oxometallocyclobutane **5** quickly follows. Finally, a retro [2+2] extrudes the olefin product and regenerates the Re carbonyl, completing the cycle.[8]

Figure 4. Formation of the putative metallooxirane intermediate.[8]



8



6 **7**

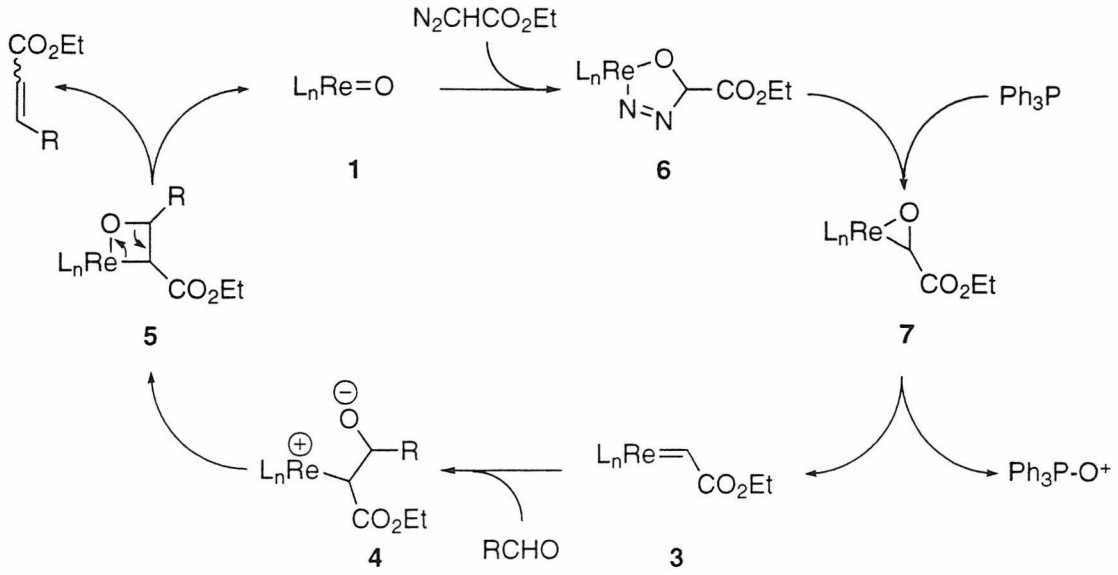
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6 Abuomar, M. M.; Hansen, P. J.; Espenson, J. H. *J. Am. Chem. Soc.* **1996,** *118*, 4966.

7 For reviews of the chemistry of metal carbenes (a) Schrock, R. R. *Pure. Appl. Chem.* **1986**, *19*, 342. (b) Schrock, R. R. *J. Organomet. Chem.* **1986**, *300*, 249. (c) Doyle, M. P. *Acc. Chem. Res.* **1986**, *19*, 348.

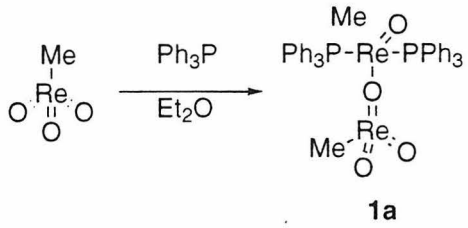
8 Zhu, Z.; Espenson, J. H. *J. Am. Chem. Soc.* **1996**, *118*, 9901.

Figure 5. Another mechanistic possiblity - reduction of Re occurs after reaction with EDA.[8]



The two proposed mechanisms differ only in the order of events–is the rhenium(VII) complex reduced before or after it reacts with the diazoester? While Herrmann has isolated a Re(V) complex generated on reaction of MTO and triphenylphosphine (Figure 4) that catalyzes the olefination, it behaves differently than the *in situ* prepared catalyst, both in activity and (*E*):(*Z*) selectivity (Table 1).[5]

Figure 6. Reaction of MTO and Ph3P in the absence of aldehyde or EDA.



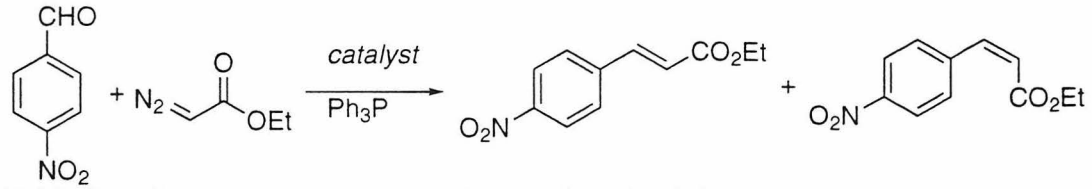
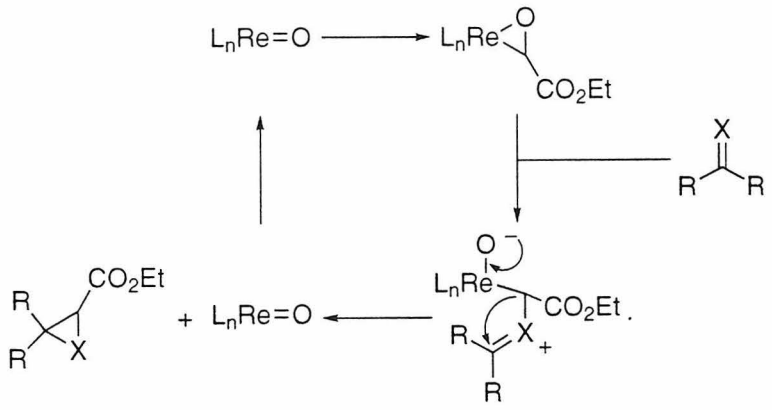


Table I. Effects of catalyst preparation on the selectivity of the olefination.

Catalyst	cat. load (mol %)	yield of olefin (%)	(*E*):(*Z*)
MTO	10	94	66:34
MTO	5	72	93:7
1a	10	95	59:41
1a	5	89	67:33

Regarding the Espenson mechanism, as stated above, neither of the key intermediates (**6** or **7**) has yet been isolated or observed spectroscopically. However, **6** and **7** have been implicated as likely intermediates in the reactions of EDA in the absence of reductant. For instance, it is interesting to note that while ketones and aldehydes are unreactive in the absence of a reductant at room temperature, they do react with diazoacetates in the presence of MTO at elevated temperatures. Espenson and coworkers have demonstrated that when stirred at 50-60 °C for several days, aldehydes and ketones are converted into the corresponding epoxides and imines are transformed into aziridines.[9]

Figure 7. Mechanism of formation of epoxides and aziridines.

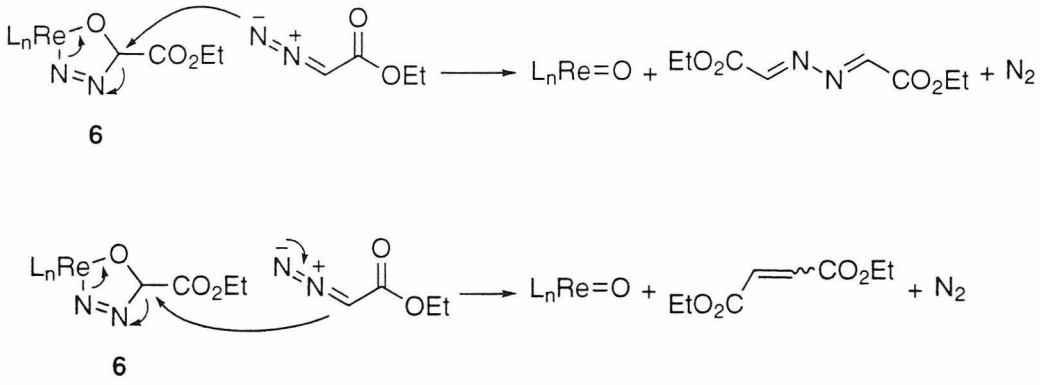


9 Zu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60*, 7090.

Espenson's metallooxirane also neatly accounts for the formation of the major byproducts of these reactions - the diazenes, fumarates and maleates. If a sufficiently reactive electrophile is not present, intermediate **6** is able to condense with diazoacetate at either of its nucleophilic centers. If the diazoester C-alkylates, extrusion of nitrogen generates a mixture of diethyl fumarate and maleate, whereas N-alkylation leads to diazene product. These byproducts are typically observed with ketones and stericly congested aldehydes (Figure 8).[10] Additionally, at very low catalyst loads, diazene begins to predominate regardless of the aldehyde present.

The stereochemistry of the dimerization byproduct is worthy of mention. When ethyl diazoacetate is allowed to dimerize, as catalyzed by methyltrioxorhenium, the major olefin product is diethyl fumarate. The *cis* isomer predominates in a 9:1 ratio over the *trans*. This is the exact opposite of the aldehyde olefination results, implying that a number of reactive intermediates are likely involved.

Figure 8. Formation of diazene, maleate, and fumarate byproducts.



In summary, it is almost certain that in the case of MTO, there are at least two catalytically active species present. It also seems likely that the actual sequence of events

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10 Herrmann, W. A.; Roesky, P. W.; Wang, M.; Scherer, W. *Organometallics* **1994**, *13*, 4531.

depends on a number of factors, including Re species, temperature, concentration and reductant.

Results and Discussion

While an excellent process for the synthesis of α,β-unsaturated esters, the Herrmann protocol is unsutiable as a practical replacement to the Horner-Wadsworth-Emmons olefination: (1) the requirement of stoichimetric triphenylphosphine gives triphenylphosphine oxide as a coproduct, which is oftentimes difficult to remove from a reaction mixture, complicating purification; (2) good (*E*):(*Z*) selectivity was observed for only a few aldehydes;[4] and (3) optimal yields of the enoate product required relatively large amounts of the expensive methyltrioxorhenium catalyst (5-10 mol%).[4]

From the outset, we had two goals: (1) we wished to substitute the expensive MTO with the cheaper $ReCl_3O(PPh_3)_2$ (500 mg/$53 and 1 g/$21.75, respectively, Aldrich); (2) we wished to substitute a more "user-friendly" reductant in place of triphenylphosphine. The replacement reductant had to be at least as inexpensive as triphenylphosphine ($0.12/g), and easily removed from the reaction mixture - the ideal reductant byproduct would be water soluble. Screening a variety of reductants (sulfides,[11] sulfites, hydrazine, disilanes,[12] silanes) garnered no success. A number of biphasic conditions were attempted (buffered sodium hypophosphites and benzene)[13] also with no success. Interestingly, the major product observed under mildly basic, biphasic conditions was the aldol product **9** (Figure 9).[14] Its formation requires only the presence of the hypophosphite and the

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11 MTO catalyzes the oxidation of sulfides to sulfones: Brown, K. N.; Espenson, J. H. *Inorg. Chem.* **1996**, *35*, 7211.

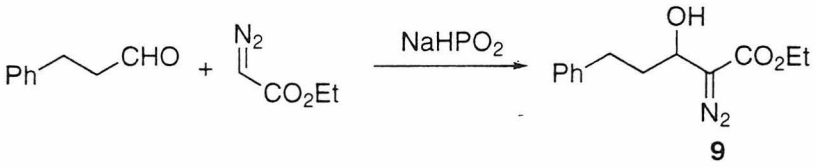
12 Triphenylsilane is the reagent of choice for reducing phosphine oxides to the corresponding phosphine. For a leading reference, see: Marsi, K. L. *J. Org. Chem.* **1977**, *39*, 265.

13 Abu-Omar, M. A.; Espenson, J. H. *Inorg. Chem.* **1995**, *34*, 6239.

14 For other examples of diazoacetate aldols, see: Wenkert, E.; McPherson, C. A. *J. Am. Chem. Soc.* **1972**, *94*, 8084.

diazoacetate-removing either the rhenium, the phosphine (added as a potential phase transfer catalyst), or both had no effect on the course of the reaction.

Figure 9. The diazo-aldol reaction observed at higher pH.



9

While some of the reductants were able to reduce Re(VII) to Re(V) (as demonstrated by a color change of the reaction mixture from pale yellow to brown), they were not able to promote olefination. Additionally, the pH of biphasic reactions is extremely important. Acidic solutions decompose the ethyl diazoacetate to ethyl glycolate, and basic conditions prompt the aldol. In fact, Espenson and coworkers observed significant decomposition of EDA under biphasic conditions.[6] However, triethyl phosphite was capable of both reducing Re(VII) and promoting the reaction. With as little as 1% catalyst, a wide variety of aldehyes were olefinated efficiently. Typically, only one equiv of stoichiometric reagents were required for complete conversion of the starting materials. The notable exception is entry **15**, methacrolein, where dimerization of the diazoacetate was competitive. In this case an additional equiv of ethyl diazoacetate was added after 1 h. The generality of the reaction is demonstrated in Table 2.

Figure 10. Re catalyzed olefination with triethylphosphite as stoichiometric reductant - general reaction.

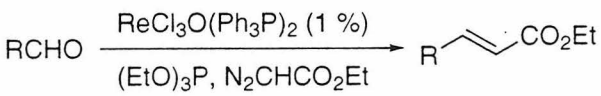
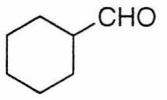
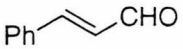
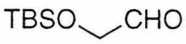
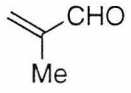
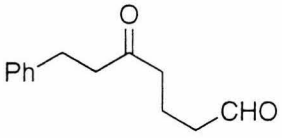
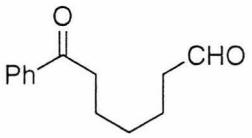
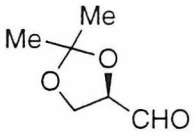
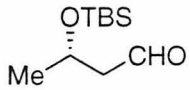


Table 2. Aldehyde olefination with N_2CHCO_2Et, $ReOCl_3(PPh_3)_2$, and $(EtO)_3P$.

Substrate	Structure	yield(%)	(*E*):(*Z*)[a,b]	^{1}H NMR data
10	PhCHO	90	>20:1	E: H_α δ 6.45; H_β δ 7.66
				Z: H_α δ 5.90; H_β δ 6.95
11		91	9.3:1	E: H_α δ 5.78; H_β δ 6.95
				Z: H_α δ 5.62; H_β δ 6.00
12		95	11:1	E: H_α δ 5.90; H_β δ 7.06
				Z: H_α δ 5.88; H_β δ 6.35
13		95	11:1	E: H_α δ 6.03; H_β δ 6.76
				Z: H_α δ 5.75; H_β δ 8.18
14		85	5.2:1	E: H_α δ 6.07; H_β δ 6.97
				Z: H_α δ 6.09; H_β δ 6.17
15		65	5:1	E: H_α δ 5.80; H_β δ 7.30
				Z: H_α δ 5.81; H_β δ 6.45
16		85	>20:1	E: H_γ δ 2.50
				Z: H_γ δ 2.80
17		85	>20:1	E: H_α δ 5.82; H_β δ 6.98
				Z: H_α δ 5.75; H_β δ 6.22
18		90	7:1	E: H_α δ 6.05; H_β δ 6.88
				Z: H_α δ 6.09; H_β δ 6.17
19		70	2.84:1	E: H_α δ 6.05; H_β δ 6.88
				Z: H_α δ 5.80; H_β δ 6.35
20		90	14:1	E: H_α δ 5.84; H_β δ 6.96
				Z: H_α δ 5.83; H_β δ 6.34

[a]The diastereomeric ratio of enoates was determined by analysis by ^{1}H NMR spectroscopy and comparison to published data for (*E*)- and (*Z*)- stereoisomers.[15] [b]In the cases where the (*Z*)-olefins were not known, authentic (*Z*)-olefins were prepared by the method of Still.[16]

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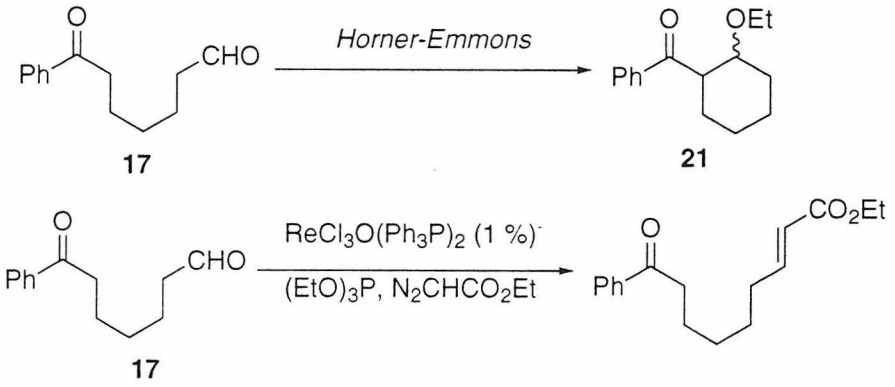
15 With the exception of enoates in entries 14, 16, 17, 18, 20, the enoate products are known: (a) Entry 10, see footnote 21. (b) entry 11 & 12, see footnote 22. (c) entry 13, see footnote 23. (d) entry 15, see footnote 24. (e) entry 19, see footnote 25.16 Still, W. C.; Gennari, C. *Tetrahedron Lett.***1983**, *24*, 4405.

16 Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

A wide array of functionality is tolerated by the reaction conditions. Even relatively fragile esters such as the enyne product of **19** survive the reaction conditions. The neutrality of these conditions is demonstated by the reaction with isopropylidene glyceradehyde-no racemization occurs during the reaction. Additionally no β-elimination is observed with **20**.

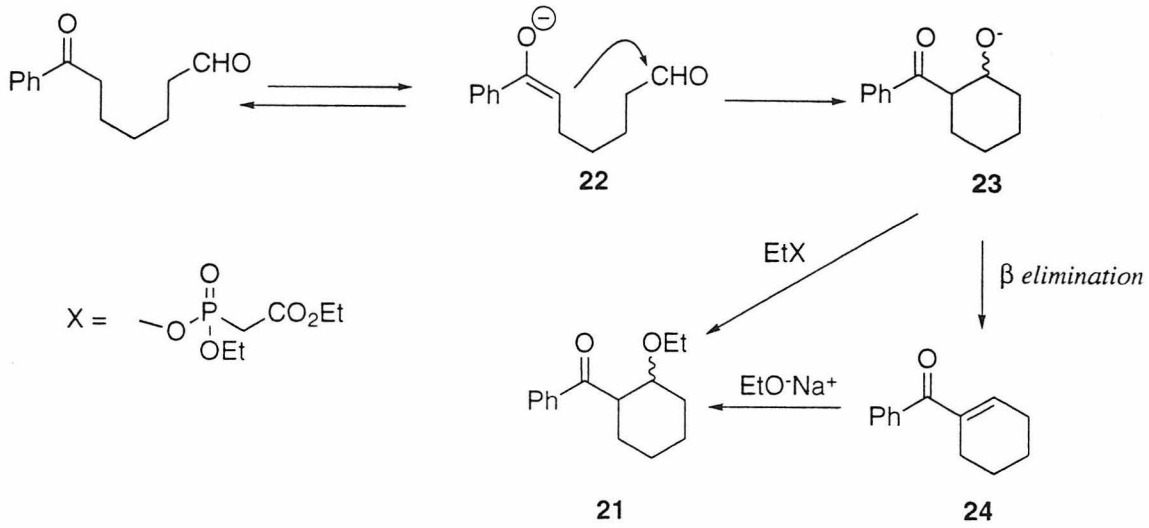
A couple of representative ketones were also tried. Neither acetophenone nor β-ionone was olefinated by these reagents. This emphasizes another valuable aspect of the rhenium-catalyzed olefination–its chemoselectivity. Even with a large excess of diazoacetate, only mono-olefination was observed with **16** and **17**. In fact, under typical Horner-Emmons conditions (NaH, triethylphosphonoacetate, THF) **17** was converted into aldol products **21** as an inseparable mixture of diastereomers.

Figure 11. Olefination of base-sensitive aldehydes - Horner-Emmons vs. Re(V) catalyzed.



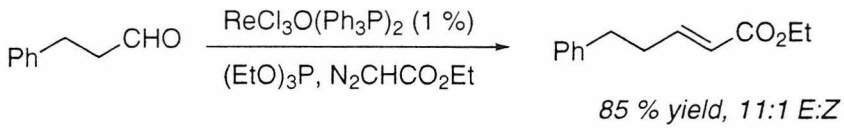
Ethyl ether **21** could be formed in the following manner. First, the ketone is deprotonated by the phosphonoacetate to give enolate **22** which condenses with the aldehyde to generate **23**. Aldol adduct **23** could dehydrate, generating α,β-unsaturated ketone **24**. Michael additon of ethanol (generated by the reaction of adventitious water with triethylphosphonoacetate) will then yield **21**. Alternatively, aldol adduct **23** could simply be ethylated by triethyl phosphonoacetate.

Figure 12. Potential mechanism for the formation of **21**.



Finally, the reaction works with reagent grade solvent and reagents; careful purification of solvent and the phosphite are not required. For example, hydrocinnamaldehyde is converted in good yield (85 %) to ethyl 5-phenyl-2-pentenoate ((*E*):(*Z*) 11:1) using THF and triethyl phosphite as purchased without further purification.

Figure 13. Large scale olefination with reagent-grade solvent.



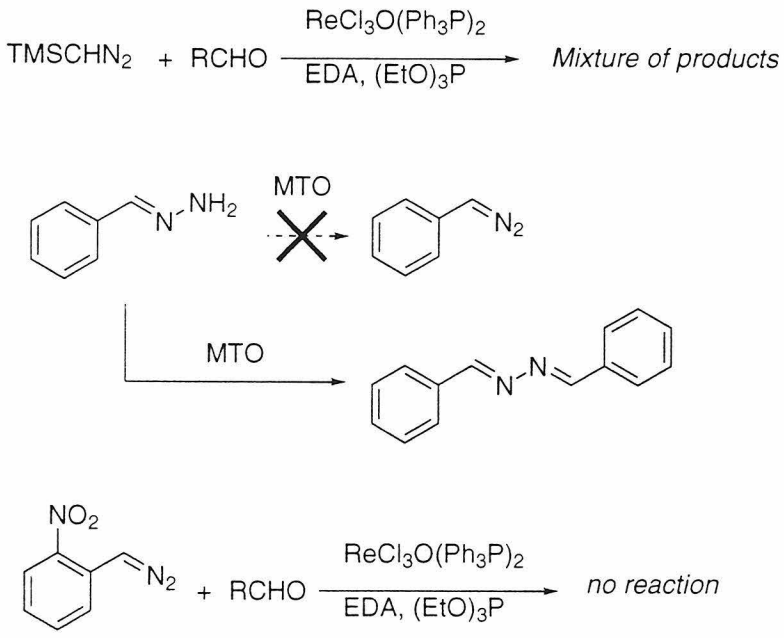
At present, the olefination only works with α-diazoesters. Several attempts to synthesize vinyl silanes (by reacting an aldehyde with trimethylsilyldiazomethane) failed, yielding only complex mixtures of products. Attempts to utilize benzaldehyde hydrazone[17]

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17 For an example of benzaldehyde hydrazone being oxidized with a metal oxide (HgO) to phenyldiazomethane, see: Gutsche, C. D.; Jason, E. F. *J. Am. Chem. Soc.* **1956**, *78*, 1184.

as both reductant and substrate were similarly unsuccessful–the only product isolated after prolonged stirring was the diazene (Figure 14). It also seems that the ester moiety is essential for reactivity; even nitrobenzyldiazomethane,[18] one of the more electron-withdrawn alkyldiazoacetates, was unreactive under the typical reaction conditions. However, it is hoped that through the use of a different Re complex or a different reductant, the range of diazosubstrates might be extended.

Figure 14. Unreactive diazoalkanes.



Conclusion

In conclusion, an extremely mild, inexpensive alternative to the Horner-Emmons reaction has been described. The commercial availability of all the reagents combined with a tolerance for reagent-grade solvents and reagents make this a practical process. The low catalyst load (1%), easy purification of enoates products, and generally good (*E*):(*Z*) ratios emphasize the utility of this protocol. The chemoselectivity (aldehyde vs. ketone) and

[18] Ohtsuka, E.; Wakabayashi, T.; Tanaka, S.;Tanaka, T.; Oshie, K.; Hasegawa, A.; Ikehara, M. *Chem. Pharm. Bull.* **1981**, *29*, 318.

mildness of this procedure should prove also useful in organic synthesis. Finally, the absence of a discrete phosphonate or phosphorane deprotonation step makes this an attractive alternative to the venerable Horner-Emmons olefination, especially for the olefination of sensitive aldehydes.

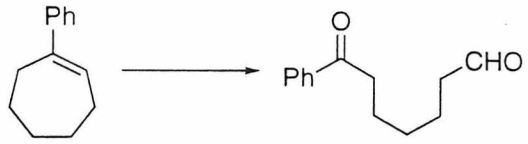
Appendix I - Experimental

General procedures: All reagents were commercially obtained except where noted. Where appropriate, reagents were purified prior to use. All nonaqueous reactions were performed using oven dried glassware under an atmosphere of dry nitrogen. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl prior to use. *N,N*-di-*iso*-propyl- ethylamine, dichloromethane, 2,6-lutidine, pyridine, and triethylamine were distilled from calcium hydride prior to use. *N,N*-dimethylformamide was stood over 4 Å molecular sieves prior to use. Hexanes were rendered olefin-free and distilled from sodium prior to use. Methanol was distilled from magnesium methoxide prior to use. Chromatographic purification of products was accomplished using forced flow chromatography on Baker 7024-R silica gel according to the method of Still.[19] Thin-layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60F plates (230-400 mesh). Visualization of the developed chromatogram was performed by fluorescence quenching, aqueous ceric ammonium molybdate (CAM) stain, or an ethanolic *p*-anisaldehyde spray.

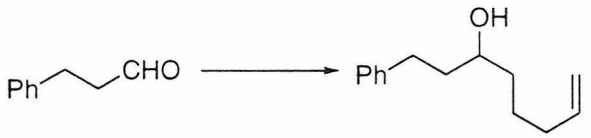
NMR spectra were recorded on a General Electric QE Plus operating at 300 and 75 MHz for ^{1}H and ^{13}C, respectively, and are referenced to residual protio or carbon solvent signals. Data for ^{1}H are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz), and assignment. IR spectra were recorded on a Perkin-Elmer 1600 Series spectrometer. Optical rotations were determined on a Jasco DIP-181 polarimeter operating at the sodium D line and are reported as follows: $[\alpha]_{D}^{25}$, concentration (g/100 mL), and solvent.

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19 Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.



Aldehyde 17. To a 100 mL three necked flask was added 6.0 g (35 mmol, 1.0 equiv) of 1-phenyl-1-cycloheptene[20] in 40 mL of 8:1 dichloromethane:methanol (*v:v*). The solution was cooled to -78 °C and a dilute stream of ozone was bubbled through the reaction. After 30 min, no starting material remained and the reaction was quenched with 11 g(40 mmol, 1.1 equiv) of triphenylphosphine at -78 °C. The reaction was allowed to warm to room temperature slowly and then concentrated by rotary evaporation. The crude product was purified *via* silica gel chromatography (10 cm x 2.5 cm, 6:1 hexanes:ethyl acetate, R_f = 0.2) to yield 5.0 g of **17** (25 mmol, 70% yield) as a clear oil: IR (thin film) ν 2937, 2863, 2721, 1723, 1685, 1597, 1448, 1216 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.62-9.60 (1 H, m, C**H**O), 7.83 (2 H, d, *J* = 8 Hz, Ph), 7.41-7.39 (2 H, m, Ph), 7.31 (1 H, d, *J* = 8 Hz, Ph), 2.84-2.80 (2 H, m, PhCOC**H**$_2$), 2.33-2.30 (2 H, m), 1.62-1.59 (2 H, m), 1.54-1.51 (2 H, m), 1.29-1.26 (2 H, m) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 200.4, 137.4, 133.4, 129.0, 128.4, 44.1, 38.6, 29.2, 24.3, 22.3 ppm. HRMS(CI) calculated for $C_{13}H_{16}O_3$ (M)+: 204.1150. Found: 204.1145.



8-phenyl-1-octen-6-ol. To a 250 mL round bottomed flask equipped with a stirbar and reflux condenser was added 1.0 g of magnesium turnings (42 mmol, 1.1 equiv). The turnings were flame-dried under high vacuum. A nitrogen atmosphere was reintroduced to the reaction vessel and the magnesium turnings were suspended in 100 mL of THF. To the

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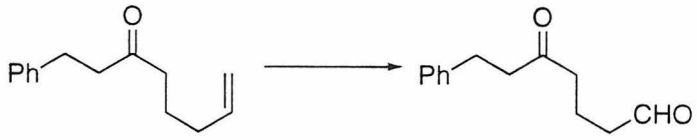
20 DeCosta, B.R.; George, C.; Li, G.; He, X. *J. Org. Chem.* **1994**, *59*, 482.

reaction was added cautiously 5.4 mL of 5-bromo-1-pentene (6.8 g, 46 mmol, 1.2 equiv). The addition was moderated to control the subsequent exotherm. The reaction was stirred until the exotherm subsided and 5.0 mL of hydrocinnamaldehyde (38 mmol, 1.0 equiv) was added dropwise. The reaction was stirred for 5 hrs at room temperature and quenched by the addition of 50 mL of 1 N HCl. The reaction was partitioned between diethyl ether and water (100 mL:100 mL). The aqueous layer was extracted three times with 100 mL of diethyl ether. The organic layers were combined, dried over Na_2SO_4, and concentrated via rotary evaporation to give a yellow oil. Purification by silica gel chromatography (15 cm x 2.5 cm, 6:1 hexanes:ethyl acetate, R_f = 0.2) yielded 5.0 g of 8-phenyl-1-octen-6-ol (25 mmol, 65 % yield) as clear oil: IR (thin film) ν 3374, 2932, 2859, 1640, 1495, 1454, 911, 747, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35-7.22 (5 H, m, Ph), 5.85-5.82 (1 H, m, CH_2=C**H**-), 5.04-5.01 (2 H, m, C**H**$_2$=CH-), 3.71-3.69 (1H, m, C**H**OH), 2.87-2.66 (2 H, m), 2.05-2.03 (2 H, m), 1.82-1.79 (2H, m), 1.52-1.44 (4 H, m) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 128.9, 126.4, 121.1, 115.2, 71.7, 39.6, 37.5, 34.2, 32.6, 25.4 ppm.

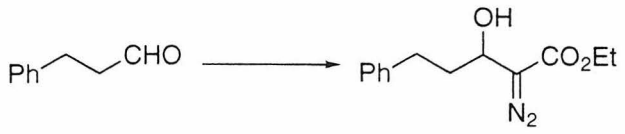


8-phenyl-1-octen-6-one. To a 100 mL round-bottomed flask equipped with a stirbar was added 2.0 g of 8-phenyl-1-octen-6-ol (9.1 mmol, 1.0 equiv) in 40 mL of dichloromethane. To the solution was then added sequentially 10 g of celite and 3.8 g of pyridinium dichromate (10 mmol, 1.1 equiv). The brown slurry was stirred for 8 hrs and quenched by filtering through 5 g of celite on a sintered glass funnel. The brown solution was concentrated to a yellow oil. Purification of the oil by silica gel chromatography (15 cm x 2.5 cm, 4:1 hexanes:ethyl acetate, R_f = 0.2) yielded 1.3 g of phenyl-1-octen-6-one (7.9 mmol, 65 % yield) as a clear oil: IR (thin film) ν 3063, 3027, 2931, 2861, 1714,

1640, 1603, 1496, 1453, 1410, 1370 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.99-6.86 (5 H, m, Ph), 5.47-5.44 (1 H, m, CH_2=C**H**-), 4.70-4.68 (2 H, m, C**H**$_2$=CH-), 2.61-2.58 (2 H, m, COC**H**$_2$), 2.41-2.39 (2 H, m, C**H**$_2$CH=CH), 2.08-2.06 (2 H, m), 1.73-1.70 (2 H, m), 1.38-1.35 (2 H, m) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 141.4, 138.1, 128.8, 126.3, 115.4, 44.5, 42.3, 33.3, 30.0, 22.9 ppm.



Aldehyde 16. A 100 mL three-necked flask equipped with a stirbar, and gas inlet was charged with 1.3 g of 8-phenyl-1-octen-6-one (6.4 mmol, 1.0 equiv) in 50 mL of 4:1 dichloromethane: methanol (*v:v*). The reaction was cooled to -78 °C and a dilute stream of ozone was bubbled into the flask. After 30 min, the reaction had taken on a bluish tinge and nitrogen was bubbled through the reaction to displace the excess ozone. The reaction was then quenched by the addition of 1.8 g of triphenylphosphine (6.8 mmol, 1.06 equiv). The reaction was allowed to warm slowly to 25 °C and was then concentrated to a yellow oil. Purification by silica gel chromatography (10 cm x 2.5 cm, 6:1 hexanes:ethyl acetate, R_f = 0.2) yielded 1.1 g of **16** (5.5 mmol, 85 %, yield) as a clear oil : IR (thin film) ν 2937, 2863, 2721, 1723, 1685, 1597, 1448, 1216 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.64-9.63 (1H, m, C**H**O), 7.83 (2 H, d, *J* = 8 Hz, Ph), 7.42-7.40 (2H, m, Ph), 7.31 (1 H, d, *J* = 8 Hz, Ph), 2.84-2.80 (2 H, m, PhCOC**H**$_2$), 2.35-2.30 (2 H, m), 1.62-1.58 (2 H, m), 1.54-1.52 (2 H, m), 1.29-1.27 (2 H, m) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.9, 200.4, 137.4, 133.4, 129.0, 128.4, 44.1, 38.6, 29.2, 24.3, 22.3 ppm. HRMS(CI) calculated for $C_{13}H_{16}O_2$ (M)+: 204.1150. Found: 204.1153.



Aldol reaction. To a 25 mL round-bottomed flask equipped with a stirbar was added 3 mL of a 1 M solution of $NaHPO_2$. To the reaction mixture was then added 320 mL (2.4 mmol, 1.0 equiv) of hydrocinnamaldehyde and 300 mL (2.6 mmol, 1.1 equiv) of ethyl diazoacetate. The yellow reaction mixture was stirred at room temperature for 2 hrs and then quenched by pouring into a 100 mL separatory funnel containing 50 mL of dichloromethane and 50 mL of distilled water. The aqueous layer was extracted twice with 50 mL of dichloromethane and the organic layers were combined and dried over anhydrous Na_2SO_4. The pale yellow solution was concentrated *via* rotary evaporation and purified by silica gel chromatography (15 cm x 2.5 cm, 4:1 hexanes:ethyl acetate, R_f=0.4) to give 550 mg (2.2 mmol, 92 % yield) of ethyl 3-hydroxy-2-diazo-5-phenylpentanoate as a clear yellow oil: IR (thin film) ν 3300, 2980, 2870, 2100, 1690, 1100 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.34 (2 H, m, Ph), 7.27-7.24 (3 H, m, Ph), 4.45 (1 H, t, *J* = 2 Hz, C**H**OH), 4.23 (2 H, q, *J* = 7.0 Hz, C**H**$_2$CH$_3$), 2.95-2.82 (2 H, m, PhC**H**$_2$), 2.10-1.90 (2 H, m, PhCH$_2$C**H**$_2$), 1.10 (3 H, t, *J* = 7.0 Hz, CH$_2$C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.1, 165.5, 129.0, 128.9, 126.7, 122.4, 60.8, 34.9, 34.5, 14.8 ppm.

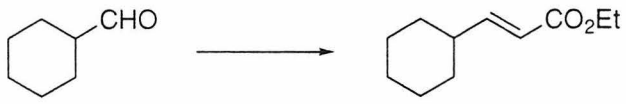
General procedure for olefination. To a 25 mL round-bottomed flask equipped with a stirbar was added 20 mg of $ReCl_3O(Ph_3P)_2$ (0.024 mmol, 0.010 equiv). The yellow powder was suspended in 5 mL of THF and 400 μL (2.4 mmol, 1.0 equiv) of triethylphosphite was added . To the stirring mixture was added 2.4 mmol of aldehyde followed by 270 μL (2.4 mmol, 1.0 equiv) of ethyl diazoacetate. Gas evolution was observed and the reaction color turned dark brown. The reaction was stirred for 2 hrs and quenched by pouring into a separatory funnel containing 50 mL of diethyl ether and 50 mL

of water. The layers were separated and the aqueous layer was extracted twice with 50 mL of diethyl ether. The organic layers were combined and dried over anhydrous Na_2SO_4. The solution was concentrated *via* rotary evaporation to a yellow oil which was purified by silica gel chromatography. The stereoselectivity was typically estimated by integrating the olefinic region (consult Table 2 for relevant ^1H NMR signals).



Isolated as a clear colorless oil in 90% yield.[21]

R_f = 0.55, (6:1 hexanes ethyl acetate); IR (thin film) ν 2983, 2920, 1705, 1645, 1449, 1275 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (1 H, d, *J* = 16 Hz, C**H**=CH-CO_2Et), 7.58-7.56 (2 H, m, Ph), 7.42-7.39 (3 H, m, Ph), 6.47 (1 H, d, *J* = 16 Hz, CH=C**H**-CO_2Et), 4.30 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 1.37 (3 H, t, *J* = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 145.1, 135.0, 130.8, 129.4, 128.6, 118.8, 61.0, 14.9 ppm.



Isolated as a clear colorless oil in 91 % yield.[22]

R_f = 0.55, (6:1 hexanes ethyl acetate); IR (thin film) ν 2980, 2927, 2853, 1721, 1651, 1449, 1275, 1173 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.98-6.95 (1H, m, C**H**=CHCO_2Et), 5.78 (1 H, d, *J* = 15 Hz, CH=C**H**CO_2Et), 4.21 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 2.20-2.13 (1H, m, CH=CH-C**H**), 1.77-1.65 (6 H, m, Chx), 1.31 (3H, t, *J* = 7 Hz, CH_3), 1.38-1.15 (10 H, m, Chx) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 154.8, 119.4, 60.7, 40.9, 32.2, 26.5, 26.3, 14.8 ppm.

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21 Nonnemacher, A.; Mayer, R.; Plienger, H.; *Liebings Ann. Chem.* **1983**, 2135.
22 Vedejs, E.; Fleck, T.S.; *J. Am. Chem. Soc.* **1989**, *111*, 5861.



Isolated as a clear colorless oil in 95% yield.

R_f = 0.50, (6:1 hexanes ethyl acetate); IR (thin film) ν 2983, 2925, 2850, 1718, 1651, 1449, 1275, 1173 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.32 (2 H, m, Ph), 7.27-7.22 (3H, m, Ph), 7.06 (1H, dt, *J* = 7, 15 Hz, C**H**=CH-CO_2Et), 5.90 (1 H, d, *J* =15 Hz, CH=C**H**-CO_2Et), 4.23 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 2.82 (2 H, t, *J* = 8 Hz, PhC**H**$_2$), 2.56 (2 H, dd, J = 7 Hz, 8 Hz, CH-C**H**$_2$), 1.33 (3 H, t, *J* = 7 Hz, CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 148.6, 141.4, 129.0, 128.9, 126.7, 122.4, 60.8, 34.9, 34.5, 14.8 ppm.



Isolated as a clear colorless oil in 95% yield.[23]

R_f = 0.60, (6:1 hexanes ethyl acetate); IR (thin film) ν 3027, 2982, 2935, 1720, 1654, 1603, 1314, 1267, 1197, 1039 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74-7.51 (6 H, m, Ph, olefin), 6.93 (1 H, m, C**H**-CH=CHCO_2Et), 6.76 (1 H, dd, *J* = 7 Hz, 15 Hz, CH=C**H**CO_2Et), 6.03 (1 H, d, *J* = 15 Hz, CH=C**H**CO_2Et), 4.29 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 1.36 (3 H, t, *J* = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 140.9, 129.6, 129.3, 129.2, 129.0, 127.4, 126.8, 121.8, 60.9, 14.9 ppm.

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23 Takahashi, H.; Fujiwara, K.; Ohta, M. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1498.



Isolated as clear colorless oil in 85% yield.[24]

R_f = 0.45, (6:1 hexanes ethyl acetate); IR (thin film) ν 2982, 2935, 2850, 1720, 1654, 1603, 1314, 1267 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.97 (1 H, dd, *J* = 16 Hz, 3 Hz, C**H**=CH-CO_2Et), 6.07 (1 H, dt, *J* = 16 Hz, 2.4 Hz, CH=C**H**CO_2Et), 4.31 (2 H, dd, *J* = 2.4 Hz, 3 Hz, C**H**$_2$OTBS), 4.17 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 1.90, (9 H, s, TBS), 1.27 (3 H, t, *J* = 7 Hz, CH_2CH_3), 1.06 (3 H, s, TBS), 1.04 (3 H, s, TBS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 147.8, 120.1, 77.2, 60.7, 16.8, 14.6, -4.9 ppm.

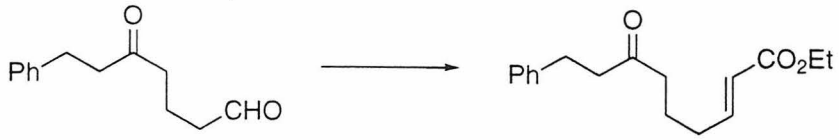


Isolated as clear, colorless oil in 65% yield.[25]

R_f = 0.45, (6:1 hexanes ethyl acetate); IR (thin film) ν 3027, 2982, 2935, 1720, 1645, 1599, 1300, 1267, 1197, 1039 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30 (1 H, d, *J* = 16 Hz, C**H**=CH-CO_2Et), 5.80 (1 H, d, *J* = 16 Hz, CH=C**H**CO_2Et), 5.4 (2 H, s, C**H**$_2$=C), 4.20 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 1.90, (3 H, s, CH_3), 1.30 (3 H, t, *J* = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 151.2, 147.4, 124.6, 119.2, 68.4, 35.7, 18.5 ppm.

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24 Hudlicky, T; Fleming, A.; Radesca, L. *J. Am. Chem. Soc.* **1989**, *111*, 6691.
25 Sundberg, R. J.; Bukowick, P.A.; Holcombe, F. U. *J. Org. Chem.* **1967**, *32, 2938.*



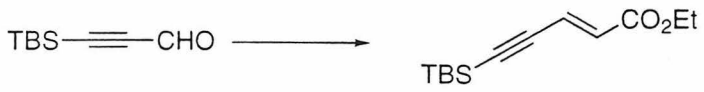
Isolated as a clear colorless oil in 85% yield.

R_f = 0.50, (6:1 hexanes ethyl acetate); IR (thin film) ν 3010, 2950, 1720, 1686, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 (2 H, d, J = 7 Hz, Ph) , 7.25-7.05 (3 H, m, Ph), 6.99-6.97 (1H, m, C**H**=CH-CO_2Et), 5.85 (1 H, d, *J* = 15 Hz, CH=C**H**-CO_2Et), 4.15 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 2.52-2.49 (2 H, m), 1.76-1.74 (2 H, m), 1.51-1.49 (2 H, m), 1.44-1.42 (2 H, m), 1.23-1.22 (4 H, m), 1.20 (3 H, t, J = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4, 167.2, 149.6, 133.4, 130.3, 129.1, 128.5, 121.9, 61.7, 38.9, 32.5, 29.3, 28.4, 24.5, 14.8 ppm.



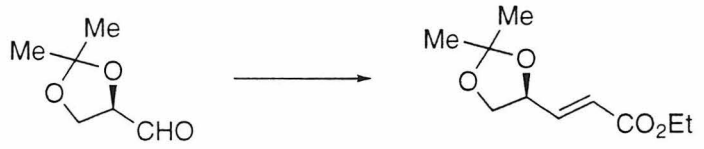
Isolated as a clear colorless oil in 85% yield.

R_f = 0.50, (6:1 hexanes ethyl acetate); IR (thin film) ν 3015, 2950, 1718, 1682, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 (2 H, d, J = 7 Hz, Ph) , 7.54 (2 H, m, Ph), 7.47 (1 H, m, Ph), 6.98 (1H, m, C**H**=CH-CO_2Et), 5.82 (1 H, d, *J* = 15 Hz, CH=C**H**-CO_2Et), 4.25 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 2.95 (2 H, m, PhCOC**H**$_2$), 2.23-2.21 (2 H, m), 1.77-1.75 (2 H, m), 1.54-1.52 (2 H, m), 1.44-1.40 (2 H, m), 1.31 (3 H, t, J = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4, 167.2, 149.6, 133.4, 130.3, 129.1, 128.5, 121.9, 61.7, 38.9, 32.5, 29.3, 28.4, 24.5, 14.8 ppm.



Isolated as a clear colorless oil in 90% yield.

R*f* = 0.60, (6:1 hexanes ethyl acetate); IR (thin film) ν 3020, 2935, 2010, 1720, 1654, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.78 (1 H, d, *J* = 16 Hz, C**H**=CH-CO_2Et), 6.28 (1 H, d, *J* = 16Hz, CH=C**H**-CO_2Et), 4.23 (2 H, q, *J* = 7 Hz, C**H**$_2$$CH_3$), 1.31 (3 H, t, *J* = 7 Hz, CH_2C**H**$_3$), 0.982 (9 H, s, TBS), 0.18 (6 H, s, TBS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 131.7, 125.5, 103.9, 102.6, 61.3, 26.6, 17.2, 14.9, -4.3 ppm.



Isolated as clear, colorless oil in 70% yield.[26]

R*f* = 0.15, (6:1 hexanes ethyl acetate); $[\alpha]_D^{25}$ = +43° (*c* = 0.50, $CHCl_3$); IR (thin film) ν 1720, 1657 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.88 (1 H, dd, *J* = 16 Hz, 5 Hz, C**H**=CH-CO_2Et), 6.05 (1 H, dd, *J* = 16 Hz, 2 Hz, CH=C**H**-CO_2Et), 4.67 (1 H, m, C**H**OR), 4.23 (2H, m, ROC**H**$_2$CH), 3.67 (2H, q, *J* = 7 Hz, C**H**$_2$$CH_3$), 1.44 (3 H, s, C(C**H**$_3$)$_2$), 1.40 (3 H, s, C(C**H**$_3$)$_2$), 1.28 (3 H, t, *J* = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 146.5, 120.7, 68.2, 60.6, 55.5, 26.6, 24.3, 17.2, 16.5 ppm.

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26 Takano, S.; Kurotaki, A.; Takahashi, M.; Ogasawara, K. *Synthesis* **1986**, 403.



Isolated as a clear, colorless oil in 90% yield.

R_f = 0.55, (6:1 hexanes ethyl acetate); $[\alpha]_D^{25}$ = +25° (c=0.50, $CHCl_3$); IR (thin film) ν 3027, 2982, 2935, 1720, 1654, 1603, 1314, 1267, 1197, 1039 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.96 (1 H, dt, *J* = 7, 16 Hz, **CH**=CH-CO_2Et), 5.84 (1 H, d, *J* = 16 Hz, CH=C**H**-CO_2Et), 4.17 (2 H, q, *J* = 7 Hz, CH_2CH_3), 3.94 (1 H, m, **CH**OTBS), 2.3-2.335 (2 H, m, CH=CH-CH_2), 1.29 (3 H, t, *J* = 7 Hz, CH_2CH_3), 1.17 (3 H, d, *J* = 6 Hz, CH_3CHOTBS), 0.89 (9 H, s, TBS), 0.05 (6 H, s, TBS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 146.5, 123.7, 68.2, 60.6, 43.0 39.1, 26.3, 24.3, 14.8, -4.0, -4.3 ppm.



Large scale olefination - reagent grade solvent. To a 100 mL round-bottomed flask equipped with a stirbar was added 62 mg (0.075 mmol, 0.010 equiv) of $ReCl_3O(Ph_3P)_2$. The yellow powder was suspended in 20 mL of THF and 1.2 mL (7.5 mmol, 1.0 equiv) of triethylphosphite was added. To the stirring mixture was added 1.0 g mmol of hydrocinnamaldehyde (7.5 mmol, 1 equiv) followed by 850 mL (7.5 mmol, 1.0 equiv) of ethyl diazoacetate. Gas evolution was observed and the reaction color turned dark brown. The reaction was stirred for 2 hrs and quenched by pouring into a separatory funnel containing 50 mL of diethyl ether and 50 mL of water. The layers were separated and the aqueous layer was extracted twice with 50 mL of diethyl ether. The organic layers were combined and dried over anhydrous Na_2SO_4. The solution was concentrated *via* rotary evaporation to a yellow oil which was purified by silica gel chromatography (15 cm x 2.5 cm, R_f = 0.5, 6:1 hexanes ethyl acetate) to give 1.3 g of (Z)-ethyl- 5-phenyl-2-pentenoate (6.3 mmol, 85 % yield) as a clear oil: IR (thin film) ν 3027, 2982, 2935,

1720, 1654, 1603, 1314, 1267, 1197, 1039 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37-7.32 (2 H, m, Ph), 7.27-7.22 (3 H, m, Ph), 7.06 (1H, dt, *J* = 7, 15 Hz, **CH**=CH-CO_2Et), 5.90 (1 H, d, *J* =15 Hz, CH=C**H**-CO_2Et), 4.23 (2 H, q, *J* = 7 Hz, CH_2CH_3), 2.82 (2 H, t, *J* = 8 Hz, $PhCH_2$), 2.56 (2 H, dd, J = 7 Hz, 8 Hz, CH-CH_2), 1.33 (3 H, t, *J* = 7 Hz, CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1, 148.6, 141.4, 129.0, 128.9, 126.7, 122.4, 60.8, 34.9, 34.5, 14.8 ppm.

Preparation of authentic (*Z*)-olefins - Still modified Horner-Emmons.[27] To a 25 mL flask equipped with a stirbar was added 410 mg (1.5 mmol, 5.0 equiv) of 18-crown-6 in 5 mL of THF. To the stirred solution was then added 66 μL (0.31 mmol, 1.0 equiv) of *bis* (2,2,2-trifluoroethyl) (methoxycarbonylmethyl)phosphonate. The solution was cooled to -78°C and 630 μL (0.50 M, 0.31 mmol, 1.0 equiv) of KHMDS in toluene was added *via* syringe. To the reaction was added immediately 0.31 mmol of aldehyde *via* cannula in 2 x 1 mL of THF. After stirring for 30 min, the reaction was quenched by pouring into a separatory funnel containing 15 mL of Et_2O and 15 mL of saturated ammonium chloride. The aqueus layer was extracted once with 15 mL of Et_2O. The organic layers were combined, dried over Na_2SO_4, and concentrated *via* rotary evaparation. The crude methyl ester was then dissolved in 10 mL of ethanol. To the stirred solution was then added one sodium sphere. The resulting mixture was allowed to stir for 30 min at 25 °C and then quenched by pouring into a separatory funnel containing 15 mL of Et_2O and 15 mL of saturated ammonium chloride. The aqueus layer was extracted once with 15 mL of Et_2O. The organic layers were combined, dried over Na_2SO_4, and concentrated *via* rotary evaporation. The crude ethyl esters were purified by silica gel chromatography (15 cm x 2 cm, 6:1 hexanes:Et_2O).

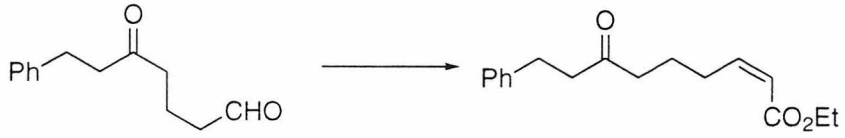
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27 Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.



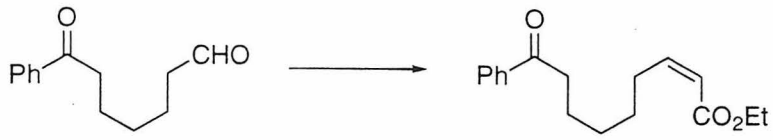
Isolated as clear colorless oil in 70% yield.

R_f = 0.45, (6:1 hexanes ethyl acetate); IR (thin film) ν 2982, 2935, 2850, 1720, 1654, 1603, 1200 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.35 (1 H, dt, *J* = 11.5 Hz, 5 Hz, **CH**=CH-CO_2Et), 5.72 (1 H, dt, *J* = 11.5 Hz, 2.5 Hz, CH=C**H**CO_2Et), 4.75 (2 H, dd, *J* = 5 Hz, 2.5 Hz, **CH**$_2$OTBS), 4.15 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 1.27 (3 H, t, *J* = 7 Hz, CH_2CH_3), 0.89 (9 H, TBS), 0.065 (6 H, s, TBS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 152.7, 118.5, 62.2, 60.6, 26.4, 18.8, 14.7, -4.7 ppm. HRMS(CI) calculated for $C_{12}H_{24}O_3Si$ (M)+: 244.1495. Found: 244.1490.



Isolated as a clear colorless oil in 80% yield.

R_f = 0.50, (6:1 hexanes ethyl acetate); IR (thin film) ν 3010, 2950, 1720, 1686, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.96-7.94 (2 H, d, J = 7 Hz, Ph), 7.20-7.05 (6 H, m, Ph, C**H**=CH-CO_2Et), 5.82 (1 H, d, *J* = 11 Hz, CH=C**H**-CO_2Et), 4.25 (2 H, q, *J* = 7 Hz, C**H**$_2CH_3$), 2.82-2.78 (2 H, m, PhCOC**H**$_2$), 2.55-2.50 (2 H, m), 1.78-1.74 (2 H, m), 1.53-1.44 (4 H, m), 1.31 (3 H, t, J = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4, 167.2, 149.6, 133.4, 130.3, 129.1, 128.5, 121.9, 61.7, 38.9, 32.5, 29.3, 28.4, 24.5, 14.8 ppm. HRMS(CI) calculated for $C_{17}H_{23}O_3$ (M+H)+: 275.1647. Found: 275.1649.



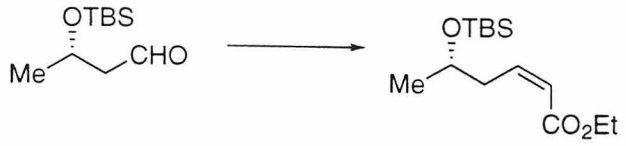
Isolated as a clear colorless oil in 80% yield.

R_f = 0.60, (6:1 hexanes ethyl acetate); IR (thin film) ν 3010, 2950, 1720, 1686, 1597 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 (2 H, d, J = 7 Hz, Ph) , 7.55- 7.46 (3 H, m, Ph), 6.22 (1H, dt, *J* = 11.5 Hz, 7 Hz, C**H**=CH-CO_2Et), 5.75 (1 H, d, *J* = 11.5 Hz, CH=C**H**-CO_2Et), 4.15 (2 H, q, *J* = 7 Hz, C**H**$_2$$CH_3$), 2.98-2.95 (2 H, m, PhCOC**H**$_2$), 2.68-2.66 (2 H, m), 1.80-1.65 (2 H, m), 1.53-1.44 (4 H, m), 1.27 (3 H, t, J = 7 Hz, CH_2C**H**$_3$) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.9, 167.7, 150.8, 133.5, 133.4, 129.2, 128.6, 120.4, 60.4, 39.0, 29.6, 29.4, 24.7, 14.8 ppm. HRMS(CI) calculated for $C_{17}H_{23}O_3$ (M+H)+: 275.1647. Found: 275.1638.



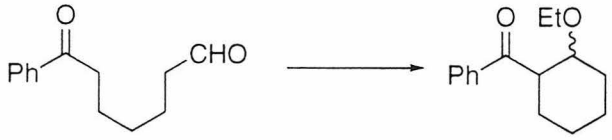
Isolated as a clear colorless oil in 85% yield.

R_f = 0.55, (6:1 hexanes ethyl acetate); IR (thin film) ν 3015, 2835, 2005, 1705, 1310, 1009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.17 (1 H, d, *J* = 11 Hz, C**H**=CH-CO_2Et), 6.09 (1 H, d, *J* = 11Hz, CH=C**H**-CO_2Et), 4.25 (2 H, q, *J* = 7 Hz, C**H**$_2$$CH_3$), 1.31 (3 H, t, *J* = 7 Hz, CH_2C**H**$_3$), 0.982 (9 H, s, TBS), 0.18 (6 H, s, TBS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 130.0, 122.7, 107.0, 101.8, 60.9, 26.6, 14.8, -4.3 ppm. HRMS(CI) calculated for $C_{13}H_{22}O_2Si$ (M)+: 238.1389. Found: 238.1388.



Isolated as a clear, colorless oil in 85% yield.

R_f = 0.55, (6:1 hexanes ethyl acetate), $[\alpha]_D^{25}$ = +20° (c=0.50, $CHCl_3$); IR (thin film) ν 3027, 2982, 2935, 1720, 1654, 1603, 1314, 1267, 1197, 1039 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.34 (1 H, dt, *J* = 11.5, 4 Hz, C**H**=CH-CO_2Et), 5.83 (1 H, d, *J* = 11.5 Hz, CH=C**H**-CO_2Et), 4.16 (2 H, q, *J* = 7 Hz, C**H**$_2$$CH_3$), 3.95 (1 H, m, **CH**OTBS), 2.80 (2 H, m, CH=CH-C**H**$_2$), 1.32 (3 H, t, *J* = 7 Hz, CH_2C**H**$_3$), 1.22 (3 H, d, *J* = 6 Hz, C**H**$_3$CHOTBS), 0.87 (9 H, s, TBS), 0.05 (6 H, s, TBS) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 147.5, 121.3, 68.4, 60.6, 39.2, 26.4, 24.3, 14.8, 11.1, -4.0, -4.3 ppm. HRMS(CI) calculated for $C_{14}H_{29}O_3Si$ (M+H)+: 273.1808. Found: 273.1896.



Horner-Emmons reaction with 17. A 25 mL Schlenk flask equipped with a stirbar was charged with 20 mg (0.50 mmol, 1.0 equiv) of NaH as a 60 % dispersion in oil. The dispersion was washed with pentanes (2 x 5 mL) and suspended in 5 mL of THF. To the stirred mixture was added *via* syringe 130 μL of triethyl phosphonoacetate (0.58 mmol, 1.2 equiv). The reaction was stirred until gas evolution ceased and then cooled to 0 °C. To the reaction was then added 100 mg of **17** (0.49 mmol, 1.0 equiv) in 2 x 2 mL of THF. The mixture was stirred for 30 min and quenched by the cautious addition of 2 mL of distilled water. The reaction was partioned between 50 mL of diethyl ether and 50 mL of water. The aqueous layer was extracted twice with 50 mL of diethyl ether. The organic layers were combined and dried over anhydrous Na_2SO_4. The solution was concentrated

by rotary evaporation to a yellow oil. Purification by silica gel chromatography (15 cm x 2.5 cm, R_f = 0.5, 6:1 hexanes:ethyl acetate) yielded 85 mg of **21** (0.37 mmol, 75% yield) as an inseparable mixture of isomers: IR (thin film) ν 2932, 1731, 1678, 1448 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.05-7.95 (2 H, m, Ph), 7.65-7.45 (3 H, m, Ph), 4.37-4.34 (2 H, m, minor isomer, C**H**$_2$CH$_3$), 4.23 (2 H, q, *J* = 7.0 Hz, C**H**$_2$CH$_3$), 3.75-3.65 (1 H, m, C**H**OEt), 3.42 (1 H, t, *J* = 2.0 Hz, minor isomer), 3.0 (1 H, t, *J* = 2.0 Hz, minor isomer), 2.45-2.5 (3 H, m, Chx), 2.0-1.15 (6 H, m, Chx), 1.15 (3 H, t, *J* = 7.0 Hz, CH$_2$C**H**$_3$).