CHAPTER 2

Mo-Catalyzed Asymmetric Allylic Alkylation Enabling the Construction of Highly Enantioenriched 1,4-Dicarbonyl Scaffolds[†]

2.1 INTRODUCTION

The construction of all-carbon quaternary stereocenters in enantioenriched form has been an ongoing challenge for organic chemists,[1] motivated in part by increasing evidence correlating molecular complexity with therapeutic value.[2] Transition-metal catalyzed allylic alkylation has emerged as an effective means for accessing these motifs.[3] In general, our group's approaches have centered on Pd-catalyzed decarboxylative allylic alkylation,[4] as well as Ir-catalyzed reactions favoring the branched isomer of product.[5] Within the latter class of reactions, our group has pioneered the use of tri-substituted allylic electrophiles to construct scaffolds containing quaternary stereocenters that originate from the electrophile. We found that masked acyl cyanides,[6] substituted malononitriles,[7] and dialkyl malonates[8] could be employed in conjunction with these electrophiles to access enantioenriched structures of high synthetic value (Scheme 2.1A).

Aiming to explore more abundant metals in branched-selective allylic alkylation, we were encouraged that molybdenum, a non-precious second-row transition metal, has

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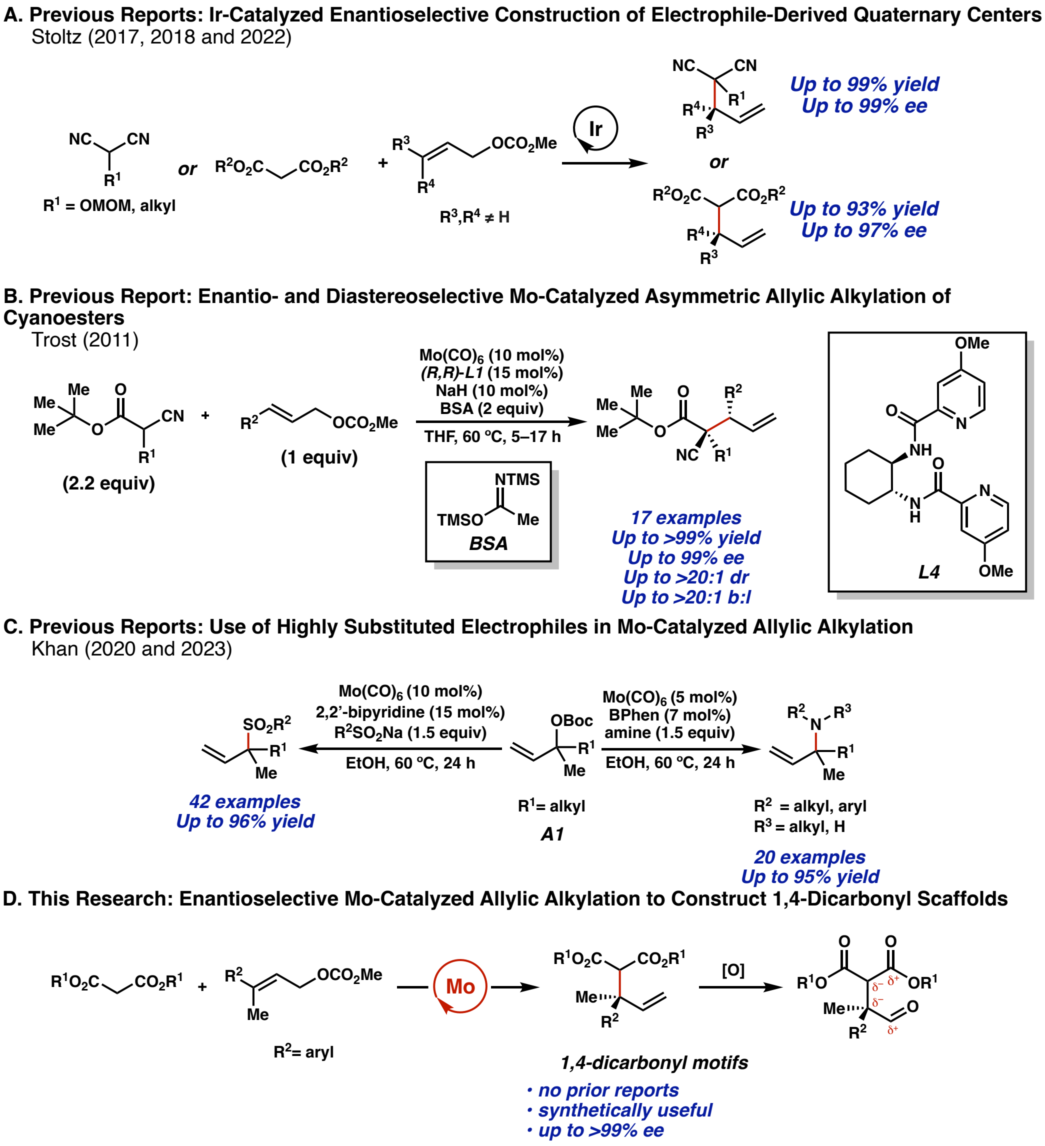
demonstrated exquisite preference for the branched product in prior reports.[9] Of particular significance, Trost and coworkers demonstrated a doubly stereoselective molybdenum-catalyzed allylic alkylation of substituted cyanoesters with disubstituted allylic electrophiles, constructing products bearing vicinal quaternary and tertiary stereocenters with excellent yields and stereocontrol (Scheme 2.1B).[10] This transformation features an electron-rich *para*-methoxy bispyridylamide ligand (**L4**), which helps to promote oxidative addition of the allylic electrophile and improves regioselectivity.

Despite molybdenum ($29.137/ lb)[11 a] being significantly cheaper than palladium ($992.00/lb)[11b] and iridium ($4150.00/oz)[11c], Mo-catalyzed allylic alkylation remains relatively less-developed for transformations involving challenging, tri-substituted linear allylic electrophiles. To our knowledge, there have only been two publications utilizing highly substituted electrophiles in Mo-catalyzed allylic substitution reactions to construct tetrasubstituted centers, limited to ofully alkyl allylic electrophiles (Scheme 2.1C).[12] However, there have been no studies detailing the construction of electrophile-derived all-carbon quaternary stereocenters via compound **A1** or its linear congener. Herein, we report a highly enantioselective Mo-catalyzed allylic alkylation, representing the first example of the formation of electrophile-derived all-carbon quaternary centers by Mo catalysis. We found that rapid ozonolysis following the allylic alkylation affords 1,4-dicarbonyl compounds, which are synthetically challenging to access due to the intrinsic mismatch of the carbonyl polarity (Scheme 2.1D).[13]

Scheme 2.1. *Asymmetric Allylic Alkylation: State of the Art*



A. Previous Reports: Ir-Catalyzed Enantioselective Construction of Electrophile-Derived Quaternary Centers
Stoltz (2017, 2018 and 2022)

B. Previous Report: Enantio- and Diastereoselective Mo-Catalyzed Asymmetric Allylic Alkylation of Cyanoesters
Trost (2011)

C. Previous Reports: Use of Highly Substituted Electrophiles in Mo-Catalyzed Allylic Alkylation
Khan (2020 and 2023)

D. This Research: Enantioselective Mo-Catalyzed Allylic Alkylation to Construct 1,4-Dicarbonyl Scaffolds

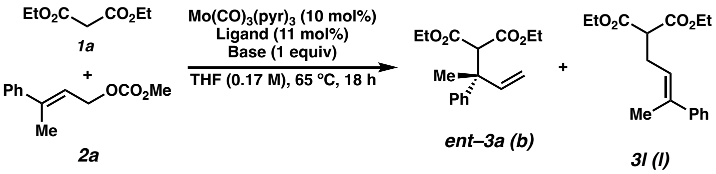
2.2 OPTIMIZATION EFFORTS

Given the stability of Mo(CO)$_6$, which necessitates high reaction times and temperatures to perform ligand exchange,[14] we first selected a more reactive Mo(0) source. While Mo(CO)$_3$(EtCN)$_3$[15] and Mo(CO)$_3$(C$_7$H$_8$)[16] have been leveraged in allylic alkylation processes, these precatalysts suffer from poor bench stability and require synthesis in the absence of air and water. We instead employed bench stable $Mo(CO)_3(pyr)_3$ [17] as a precatalyst in combination with the DACH-pyridyl ligand **L5** and NaH as a base. This reaction provided a 20% yield of the desired branched product (b) in a 2:1 ratio with the linear isomer (l) [Table 2.1, entry 1], constituting the first application of $Mo(CO)_3(pyr)_3$ in allylic substitution. Surprisingly, a non-symmmetrical picolinamide/benzamide ligand **L6**, which has been previously demonstrated to improve regioselectivity,[18] resulted in no conversion of starting material (entry 2). Other changes to the scaffold, such as replacement of the amides with esters, replacement of the carbonyls with thiocarbonyls, modification of the diamide backbone, and employment of a traditional Trost DACH ligand all led to a complete loss of reactivity (Experimental Section, Table 2.8). Moreover, a chiral Schiff base ligand **L7** resulted in trace conversion (entry 3).[19] In terms of the base additive, LiH performed similarly to NaH but exhibited poor mass balance (entry 4). Intriguingly, the counterion effect with the HMDS bases was quite pronounced, with LiHMDS delivering an improved 30% yield, while KHMDS resulted in trace product (entries 5-7). It is possible that either the lithiated diethyl malonate is more reactive, or that the lithium additive serves as both a base and Lewis acid to ionize the allylic electrophile.

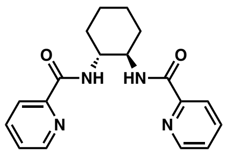
To improve reaction conversion, pyridyl substitution patterns on the C_2-symmetric ligand were explored. Electron-rich *para*-morpholine substitution on the pyridine ring led to enhanced reactivity and selectivity, delivering the product in an improved 32% yield and

3.4:1 b:l ratio with NaH as the base (entry 8). This could be improved further to 38% yield with LiHMDS as the base (entry 9). Intriguingly, an electron-deficient *para*-CF_3

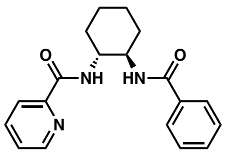
Table 2.1. *Optimization Studies*[a,b,c]



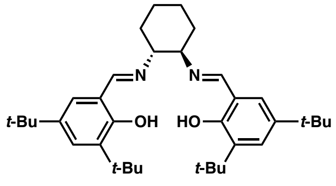
Entry	Ligand	Base	Yield (%)[a]	b/l[b]
1	*rac*-L5	NaH	20	2:1
2	*rac*-L6	NaH	0	-
3	*rac*-L7	NaH	0	-
4	*rac*-L5	LiH	23	1:1
5	*rac*-L5	LiHMDS	30	1.6:1
6	*rac*-L5	NaHMDS	19	1.8:1
7	*rac*-L5	KHMDS	<5	-
8	*rac*-L8	NaH	32	3.4:1
9	*rac*-L8	LiHMDS	38	2.4:1
10	*rac*-L9	NaH	31	1.6:1
11	*rac*-L10	LiHMDS	52	2.6:1
12[c]	*rac*-L10	LiHMDS	61	2.6:1



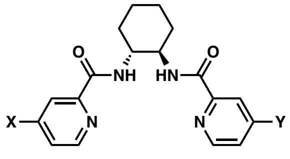
rac-L5



rac-L6



rac-L7



rac-L8: X = Y = N-morpholine

rac-L9: X = Y = CF_3

rac-L10: X = N-morpholine, Y = CF_3

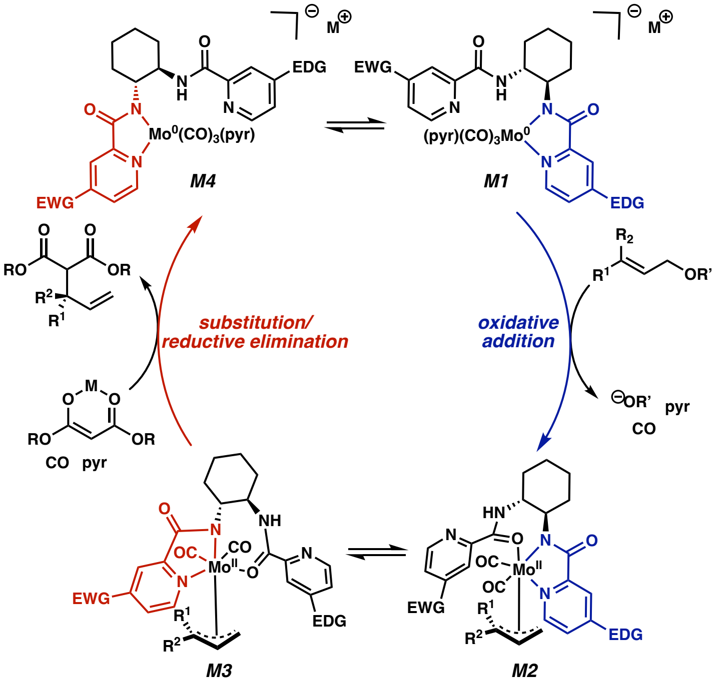
[a] Yields determined by ^1H NMR relative to a CH_2Br_2 internal standard. Reactions conducted on a 0.1 mmol scale. [b] b/l = branched to linear isomeric ratio. [c] Reaction performed with 15 mol% $Mo(CO)_3pyr_3$, 17 mol% ligand and a 48 h reaction time.

substituted ligand led to a similar yield with NaH, albeit with poor regioselectivity (entry 10). Given these results, we envisioned that employment of a C_1-symmetric ligand containing both electron-rich and electron-deficient pyridyl moieties could be beneficial. Inspired by the elementary steps proposed by Moberg with disubstituted allylic electrophiles,[20] we imagined that at first, an electron-rich pyridine could be bound to the Mo catalyst (**M1**) (Figure 2.1), facilitating oxidative addition to **M2**. At this point, a dynamic equilibration process could result in the electron-poor pyridine becoming bound to the metal (**M3**), accelerating the reductive elimination step to form product and **M4**.

Given our mechanistic hypothesis, various non-symmetrical ligands were explored in the transformation (Experimental Section, Table 2.6). We were delighted to find that C_1-symmetric *ShabyDACH* (**L10**), which contains both electron-rich *para*-morpholine and electron-deficient *para*-CF_3 fragments, promoted the desired transformation in 52% yield (Table 2.1, entry 11). This could be further improved to 61% yield when both an increased 48 h reaction time and 15 mol% Mo catalyst were employed (entry 12). Unfortunately, an extensive evaluation of additives demonstrated to be beneficial in other branched-selective allylic alkylation systems proved ineffective at improving the regioselectivity.[21]

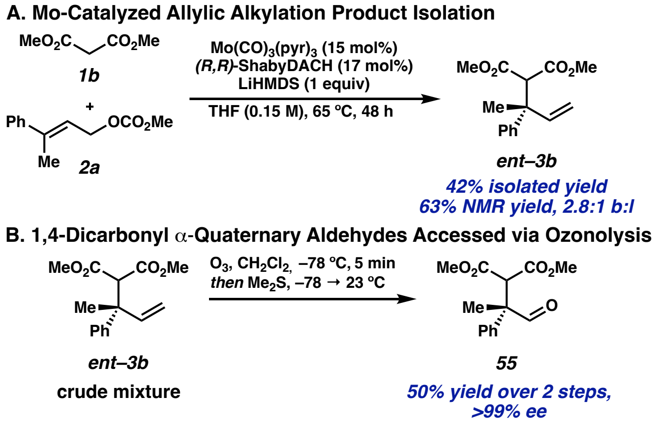
Separation of the branched and linear isomers by silica gel chromatography proved challenging. Sequential elutions by preparatory TLC allowed for isolation of branched product ***ent*-3b** in a diminished 42% yield (Scheme 2.2A). Given the inconsistencies in yield upon direct isolation of ***ent*-3b**, we considered an alternative approach to separate the

Figure 2.1. *Proposed Catalytic Cycle*



product isomers while also enhancing the synthetic value of the product. Ozonoloysis of the crude reaction mixture containing ***ent*-3b** could be performed to access the corresponding α-quaternary aldehyde **55** as a single constitutional isomer in 50% yield over two steps and excellent enantiopurity (>99% ee) (Scheme 2.2B). It is spectulated that the high enantioselectivity originates from rapid π-σ-π equilibration prior to nucleophilic attack. In support of this hypothesis, a racemic branched tri-substituted allylic electrophile **17a** preformed similarly to the achiral linear allylic electrophile, providing 96% ee (Experimental Section, Scheme 2.10).

Scheme 2.2. *Isolation of β-Quaternary Carbonyl Products*

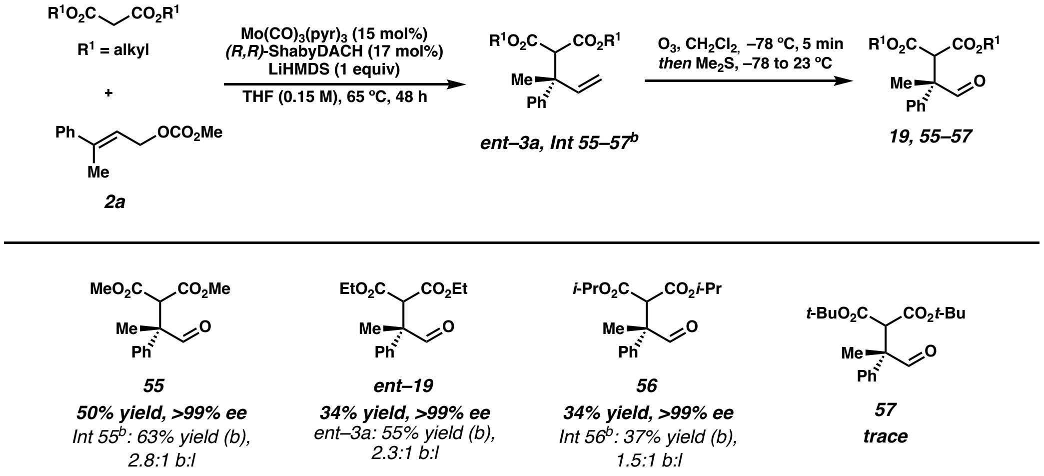


2.3 SUBSTRATE SCOPE

We next evaluated other dialkyl malonates under the optimized reaction conditions (Scheme 2.3). A substantial and predictable trend was observed favoring the linear product as the size of the malonate alkyl chain increased (***ent*–19, 55–57**).[22] Di-*tert*-butyl malonate proved too sterically hindered to participate in the reaction. Nevertheless, ee's of >99% were operative for each substrate. Unfortunately, other stabilized nucleophiles performed poorly in comparison to malonate nucleophiles (Experimental Section, Scheme 2.11).

We were pleased to find that our methodology could be applied to allylic electrophiles with a range of substitution patterns on the arene fragment (Scheme 2.4). The *para*-methyl substituted electrophile underwent the alkylation-ozonolysis sequence in 53% overall yield and >99% ee (**58**). Similarly, electron-rich *para*-methoxy substitution performed well in the alkylation-ozonolysis sequence (**59**), but an electron-deficient *para*-CF_3 substrate underwent the allylic alkylation with lower regioselectivity and yield (**60**). The *para*-nitro

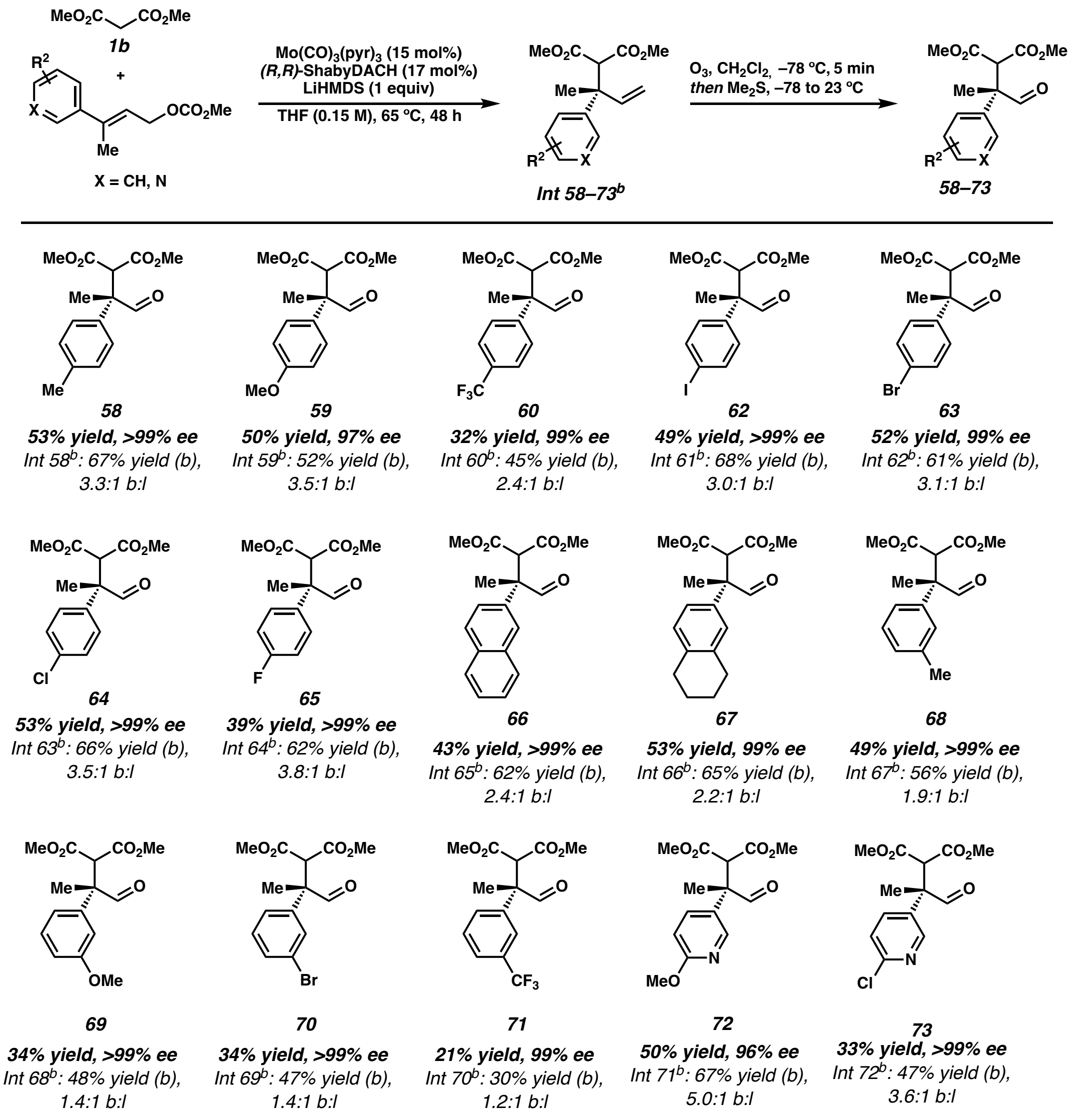
Scheme 2.3. *Performance of Malonate Nucleophiles*[a,b]



[a] Reactions conducted at 0.1 mmol scale, with 1 equiv of both nucleophile and electrophile. [b] Yield of branched product and b:l for intermediates determined by ^{1}H NMR relative to a CH_2Br_2 internal standard and as an average of two experiments. Crude mixture with linear isomer was advanced to ozonolysis.

product was not accessible under the reaction conditions *(***61**). To our delight, *para*-substitution with halides gave uniformly good yields in the allylic alkylation, as well as high enantioselectivities (**62**–**65**), offering a useful synthetic handle for future elaboration of the stereoenriched compounds and providing a stark contrast with Pd catalysts prone to oxidative addition into these bonds. More sterically demanding naphthyl and tetrahydronaphthyl substrates were also tolerated, though they led to diminished b:l regioselectivity (**66** and **67**). *Meta*-substitution was also accommodated with our protocol, though diminished regioselectivity was observed in all cases (**68** – **71**). Substrates bearing 2,5-disubstituted pyridine fragments resulted in moderate to high yields, enhanced

Scheme 2.4. *Electrophile Investigation*[a,b]

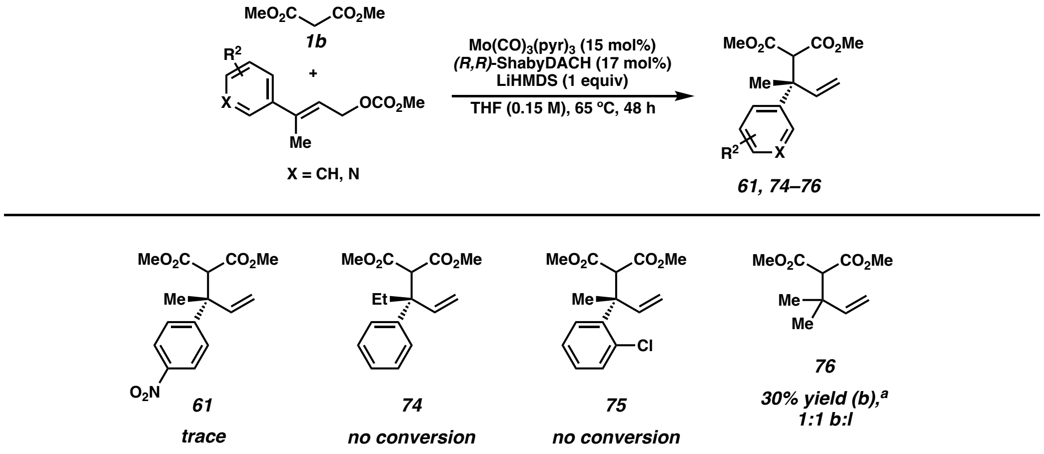


[a] Reactions conducted at 0.1 mmol scale, with 1 equiv of both nucleophile and electrophile. [b] Yield of branched product and b:l for intermediates determined by ^{1}H NMR relative to a CH_2Br_2 internal standard and as an average of two experiments. Crude mixture with linear isomer was advanced to ozonolysis.

regioselectivity and excellent enantioselectivity, offering further potential for product elaboration through pyridinone reactivity or cross-coupling (**72** and **73**).

Generally, this methodology is limited to a methyl substituent *ipso* to the arene on the electrophile (**74**) and fails with *ortho*-substituted arenes (**75**), similar to the Ir-catalyzed approach (Scheme 2.5). Furthermore, the employment of a fully-alkyl allylic electrophile resulted in the reverse-prenylated product (**76**) in a decreased 30% NMR yield and an observed 1:1 b:l mixture, possibly due to a slower rate of oxidative addition into the molybdenum center. Related substrates were ineffective in the transformation (Scheme 2.9)

Scheme 2.5. *Limitations*[a]

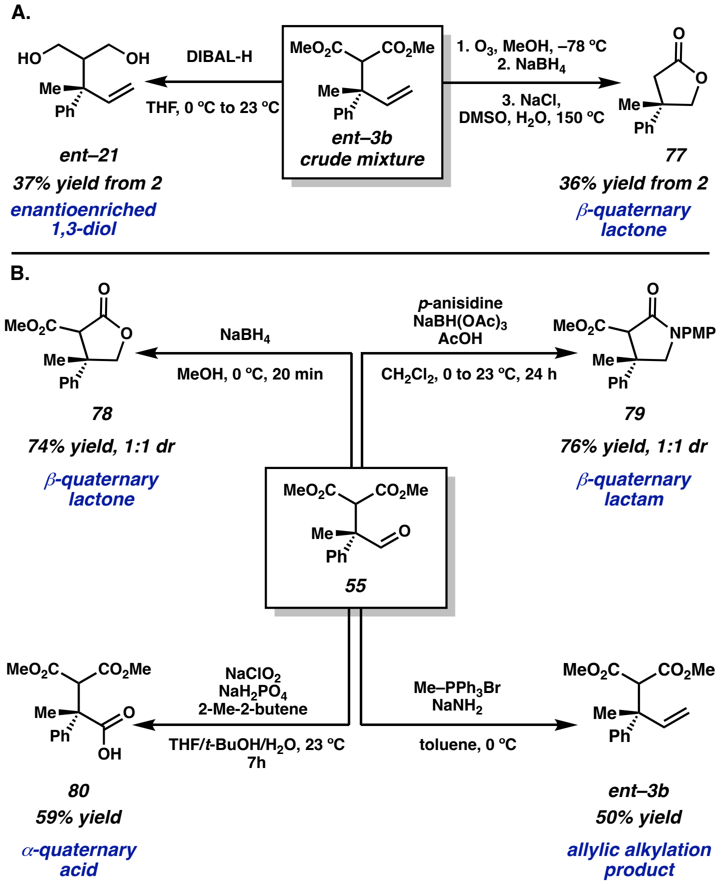


[a]Yield of branched product and b:l for intermediates determined by ^{1}H NMR relative to a CH_2Br_2 internal standard and as an average of two experiments.

2.4 DERIVATIZATIONS AND CONCLUSION

We were next interested in derivatizations of the allylic alkylation and ozonolysis products to demonstrate their synthetic utility (Scheme 2.6). Subjecting the crude product mixture containing ***ent*–3b** to DIBAL-H following allylic alkylation effected an exhaustive reduction of the malonate to the corresponding 1,3-diol ***ent*–21** (Scheme 2.6A). The constitutional isomers arising in this case were readily separable by preparatory TLC, and ***ent*–21** was isolated in a 37% yield over two steps. Moreover, we found that quenching the ozonolysis reaction with $NaBH_4$ (rather than Me_2S) then performing a Krapcho decarboxylation provided the enantioenriched β-quaternary lactone **77** in 36% overall yield from **2a**. Starting instead from α-quaternary aldehyde **55**, which could be prepared on a 2 mmol scale in 47% overall yield and >99% ee, reduction with $NaBH_4$ afforded lactone **78** as a mixture of diastereomers in 74% yield (Scheme 2.6B). Reductive

Scheme 2.6. *Product Diversification*

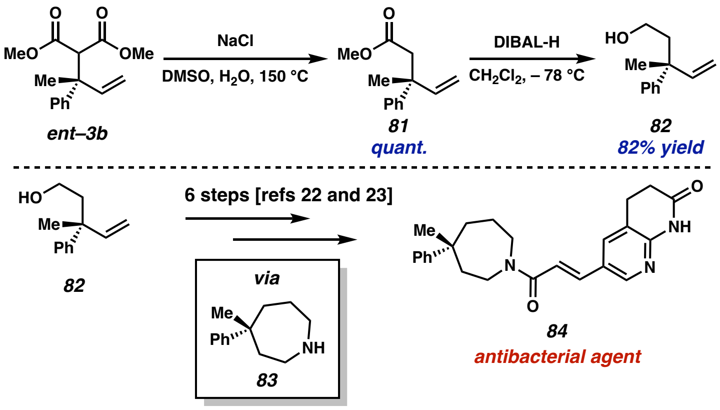


amination/lactamization of aldehyde **55** with *p*-anisidine delivered the protected lactam **79** in 76% yield. Pinnick oxidation was also successful, delivering a 59% yield of the crystalline α-quaternary acid product **80** and enabling determination of absolute stereochemistry by X-ray crystallography (see Experimental Section). Lastly, a salt-free Wittig olefination of **55** gave rise to the Mo-catalyzed allylic alkylation product ***ent*–3b** in 50% yield.

Lastly, we hoped to apply our methodology toward an asymmetric formal synthesis of an antibacterial agent (Scheme 2.7). To that end, ***ent*–3b** was demonstrated to undergo a Krapcho decarboxylation to afford ester **81**. This intermediate was then reduced exhaustively with DIBAL-H to deliver alcohol **82**. Alcohol **82** is a known intermediate in the synthesis of enantioenriched azepane **83**.[23] This intermediate could be further elaborated to access antibacterial agent **84** in nearly perfect levels of enantiopurity for the first time.[24]

In summary, we have developed the first example of a Mo-catalyzed asymmetric allylic alkylation that forges a quaternary stereocenter derived from the electrophile. This reaction proceeds with nearly perfect enantioselectivity, broadly improving upon the enantiomeric excesses observed in our Ir-catalyzed protocol. The transformation exhibits modest regioselectivity and electronic limitations not observed with Ir. Overall, the two-step alkylation-ozonolysis procedure provides access to electronically dissonant 1,4-dicarbonyl scaffolds, which are often synthetically difficult to access.[13] As the importance of sustainable, inexpensive, and non-toxic base metal catalysts grows, we envision that this

Scheme 2.7. *Formal Synthesis of Enantioenriched Antibacterial Azepane*



Mo-mediated technique will motivate further development of alternatives to precious metal catalysis in asymmetric allylic alkylation in our laboratory and other research groups around the globe.

2.5 EXPERIMENTAL SECTION

2.5.1 MATERIALS AND METHODS

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon.[25] Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-MS. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or $KMnO_4$ staining. Silicycle Silia*Flash*® P60 Academic Silica gel (particle size 40–63 µm) and Teledyne Isco CombiFlash Rf+ UV with Luknova standard silica (avg particle size 50µm) flash columns were used for flash chromatography. ^{1}H NMR spectra were recorded on Varian Inova 500 MHz, Varian 600 MHz, and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm) or CH_2Cl_2 (δ 5.30 ppm). ^{13}C NMR spectra were recorded on a Varian Inova 500

MHz spectrometer (125 MHz) and Bruker 400 MHz spectrometers (100 MHz) and are reported relative to $CDCl_3$ (δ 77.16 ppm). ^{19}F NMR spectra were recorded on a Bruker 400 MHz spectrometer (376 MHz) and referenced to an external standard: hexafluorobenzene; ^{19}F NMR (376 MHz, $CDCl_3$) δ -161.64. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell. Analytical SFC was performed with an Agilent 1260 Infinity II supercritical CO_2 analytical chromatography system utilizing Chiralpak (IC-3, AD-3, ID-3, IF-3, IG-3, IH-3) or Chiralcel (OD-3, OJ-3) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer in field ionization (FI+) or field desorption (FD+) mode, or an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI), or mixed ionization mode (MM: ESI-APCI+). Reagents were purchased from commercial sources and used as received unless otherwise stated.

Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON II CPAD detector with Mo K_α radiation (λ = 0.71073 Å) or Cu K_α radiation (λ = 1.54178 Å) from an IμS micro-source for the structure of compound V24319. The structure was solved by direct methods using SHELXS[26] and refined against F^2 on all data by full-matrix least squares with SHELXL-2019[27] using established refinement techniques.[28] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups).

Compound V24319 crystallizes in the triclinic space group *P*1 with four molecules in the asymmetric unit. The coordinates for the hydrogen atoms bound to O2, O22, O42 and O62 were located in the difference Fourier synthesis and refined semi-freely with the help of a restraint on the O-H distance (0.84(4) Å).

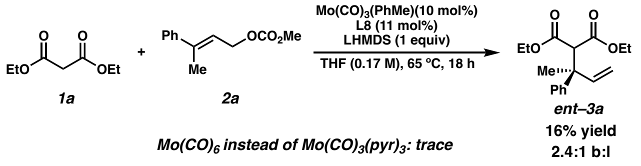
The crystal was non-merohedrally twinned. Two independent orientation matrices for the unit cell were determined using the program CELL_NOW[29], and data reduction taking into account the twinning was performed with SAINT[30]. The program TWINABS[31] was used to perform absorption correction and scaling, as well as detwin the data using a single domain. This procedure resulted in the merging of equivalent reflections.

List of Abbreviations:

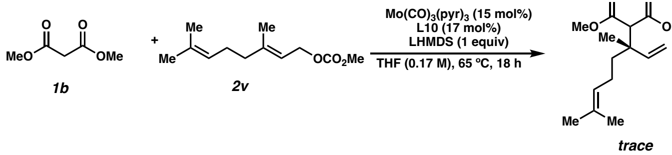
ee – enantiomeric excess, SFC – supercritical fluid chromatography, HPLC – high-performance liquid chromatography, TLC – thin-layer chromatography, Dr – dram, DACH – diaminocyclohexane

2.5.2 EXPERIMENTAL PROCEDURES AND SPECTROSCOPIC DATA

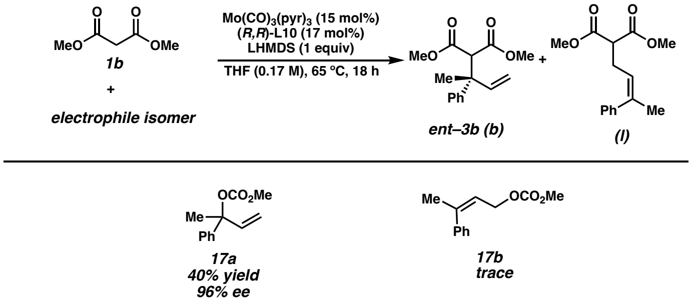
Scheme 2.8. *Alternative Mo Precatalyst*



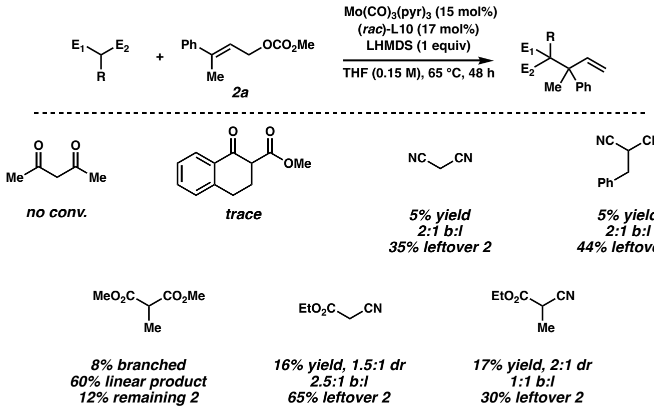
Scheme 2.9. *All-Alkyl Electrophile*



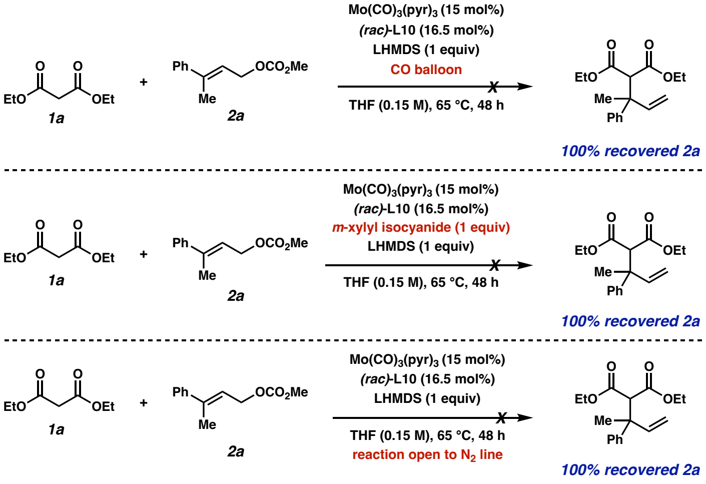
Scheme 2.10. *Reactivity of Electrophile Isomers*



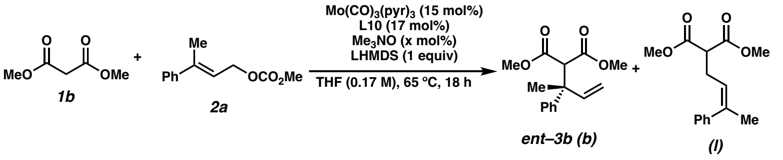
Scheme 2.11. *Compatibility of Other Stabilized Carbon Nucleophiles*



Scheme 2.12. *Probing the Role of CO*

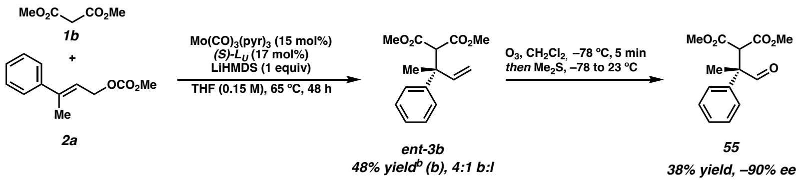


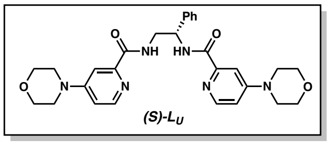
Scheme 2.13. *Trimethylamine Oxide as CO Scavenger*



Me$_3$NO	Result
15 mol%	55% yield, 3:0:1 b:l
30 mol%	12% yield, 1.9:1 b:l
45 mol%	trace

Scheme 2.14. *Performance of Ligand with Unsymmetrical Backbone*

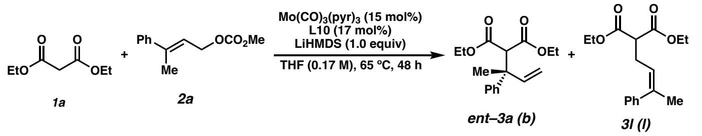




(S)-L$_U$

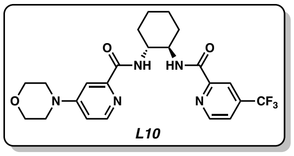
^{a}Reaction conducted at 0.1 mmol scale, with 1 equiv of both nucleophile and electrophile. ^{b}Yield of branched product and b:l for intermediates determined by ^{1}H NMR relative to a CH$_2$Br$_2$ internal standard and as an average of two experiments. Crude mixture with linear isomer was advanced to ozonolysis.

Table 2.2. *Control Reactions*



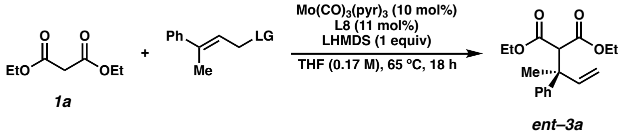
Entry	Deviation from Standard	Leftover SM (%)	Yield 3 (%)^a	b/l^b
1	None	<5	61	2.6:1
2	No Precatalyst	100	0	-
3	No Ligand	64	<5	-
4	No LHMDS	100	0	-
5	34 mol% L10	6	35	2.3:1
6	2.0 equiv LiHMDS	50	4	1:3
7	0.5 equiv LiHMDS	31	32	2.3:1
8	2.0 equiv 2a	9	49	2.5:1
9	2.0 equiv 1a and LiHMDS	<5	48	1.6:1

^{a}Yields determined by ^{1}H NMR relative to a CH$_2$Br$_2$ internal standard. Reactions conducted on a 0.1 mmol scale. ^{b}b/l = branched to linear isomeric ratio.



L10

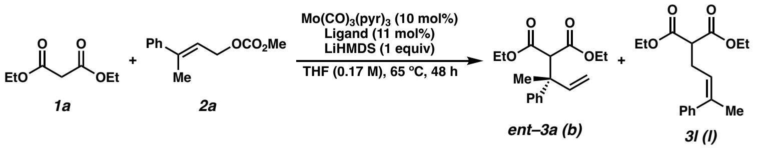
Table 2.3. *Leaving Group Survey*



Entry	LG =	Yield (%)[a]	b/l[b]
1	OCO_2Me	38	2.4:1
2	Cl	5	1:7
3	$OPO(OEt)_2$	42	2.2:1
4	$OC(O)CF_3$	22	1:1.25
5	OBz	5	3.3:1
6	$(4\text{-}CF_3)OBz$	15	2.3:1
7	(2,4,6-Me)OBz	<5	-

[a]Yields determined by ^1H NMR relative to a CH_2Br_2 internal standard. Reactions conducted on a 0.1 mmol scale. [b]b/l = branched to linear isomeric ratio.

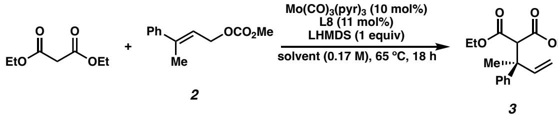
Table 2.4. *Enantiomeric Excess with Other Ligands*



Entry	Ligand	Yield 3 (%)[a]	b:l[a]	ee[b]
1	(*R,R*)-L5	37	1.7:1	>99%
2	(*R,R*)-L8	40	2.4:1	>99%
3	(*R,R*)-L10	52	2.6:1	>99%

[a]Yields determined by ^1H NMR relative to a CH_2Br_2 internal standard. Reactions conducted on a 0.1 mmol scale. [b]Ee determined by chiral SFC following DIBAL-H reduction.

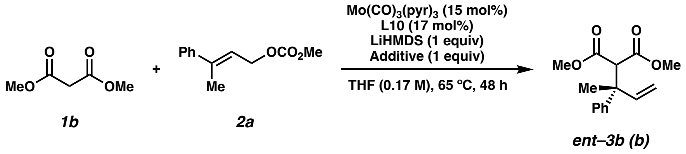
Table 2.5. *Solvent Investigation*



Entry	solvent	Yield (%)[a]	b/l[b]
1	2-MeTHF	46	2.2:1
2	DME	39	2.2:1
3	MTBE	16	1.2:1
4	Dioxane	31	2.3:1
5	Toluene	16	1:1
6	DMF	0	-
7	DCE	29	2:1

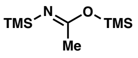
[a]Yields determined by ^1H NMR relative to a CH_2Br_2 internal standard. Reactions conducted on a 0.1 mmol scale. [b]b/l = branched to linear isomeric ratio.

Table 2.6. *Additive Study*

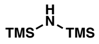


Entry	Additive	Leftover SM (%)	Yield 5 (%)[a]	b/l[b]
1	none	<5	61	2.6:1
2	BEt_3	<5	33	1:1.2
3	BPh_3	<5	46	1.8:1
4	LiBr	10	30	2:1
5	LiCl	19	34	2:1
6	ZnI_2	<5	<5	1:10
7	$MgBr_2$	22	0	28% linear
8	$ZrCl_4$	100	0	-
9	pyridine	<5	48	2.4:1
10	BSA	<5	52	2.4:1
11	HMDS (2 equiv)	<5	62	2.7:1
12	HMDS (4 equiv)	<5	58	2.6:1

[a]Yields determined by ^{1}H NMR relative to a CH_2Br_2 internal standard. Reactions conducted on a 0.1 mmol scale. [b]b/l = branched to linear isomeric ratio.



BSA



HMDS

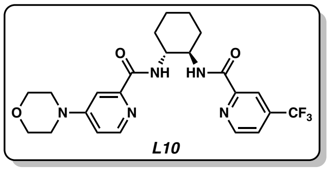
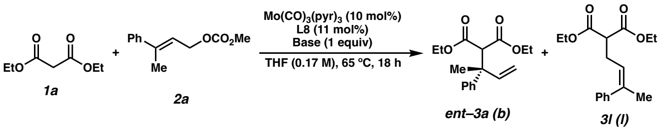


Table 2.7. *Base Investigation with* ***L8***



Entry	Base	Yield 3 (%)[a]	b/l[b]
1	LiO*t*-Bu	41	2.5:1
2	NaO*t*-Bu	<5	-
3	LiOMe	31	2.5:1
4	NaOMe	<5	-

[a]Yields determined by ^{1}H NMR relative to a CH_2Br_2 internal standard. Reactions conducted on a 0.1 mmol scale. [b]b/l = branched to linear isomeric ratio.

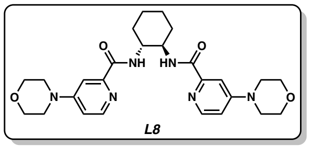
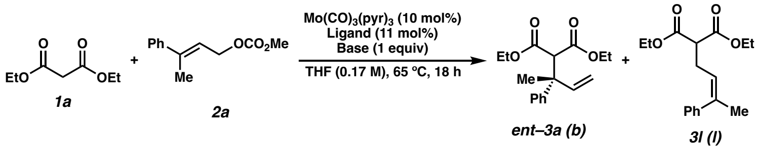
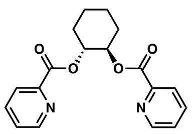


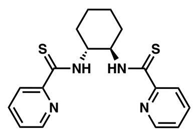
Table 2.8. *Ligand Evaluation*



Entry	Ligand	Base	Yield 3 (%)[a]	b/l[b]
1	*L11*	NaH	0	-
2	*L12*	NaH	0	-
3	*L13*	NaH	<5	-
4	*L14*	NaH	<5	-
5	*L15*	NaH	<5	-
6	*L16*	NaH	<5	-
7	*L17*	NaH	23	2.4:1
8	*L4*	NaH	15	1.6:1
9	*L18*	LiHMDS	33	2.2:1
10	*L19*	LiHMDS	22	1.7:1
11	*L20*	LiHMDS	31	1.9:1
12	*L21*	LiHMDS	0	-
13	*L22*	LiHMDS	<5	-
14	*L23*	LiHMDS	36	2:1

[a] Yields determined by ^1H NMR relative to a CH_2Br_2 internal standard. Reactions conducted on a 0.1 mmol scale. [b] b/l = branched to linear isomeric ratio.


L11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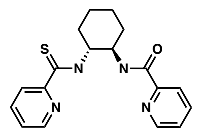
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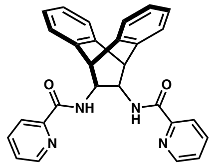
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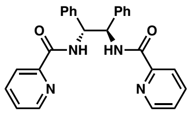
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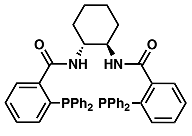
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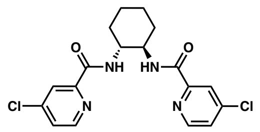
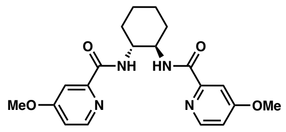

L17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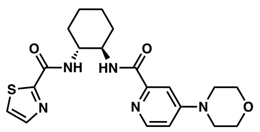
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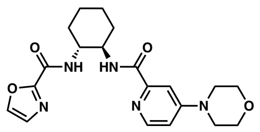
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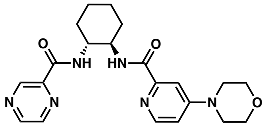
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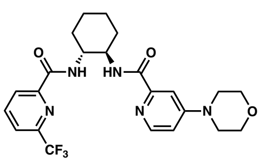
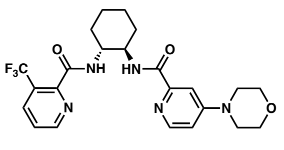
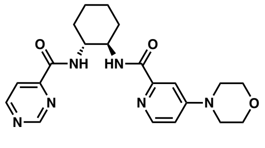
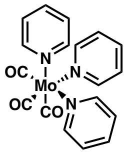

L21


L22

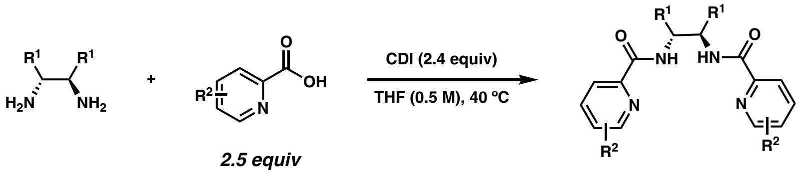

L23

Synthesis of $Mo(CO)_3(pyr)_3$

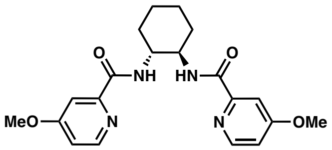


Following a modified literature procedure,[17] $Mo(CO)_6$ (1.06 g, 4.0 mmol) was dissolved in pyridine (2.689 g, 34 mmol, 2.7 mL) and the mixture was heated to 80 ºC for 2 h. At this point, the temperature was increased to 130 ºC and the reaction proceeded for 17 h at this temperature. Upon completion of the reaction, the solution was slowly cooled to ambient temperature without stirring. The resultant slurry was further cooled to 0 ºC then diluted with cold pyridine. The product was obtained as a crystalline yellow solid following filtration and repeated rinsing with cold pyridine (1.536 g, 3.7 mmol, 92% yield). ^{1}H NMR (500 MHz, DMSO) δ 8.61 – 8.54 (m, 6H), 7.78 (tt, *J* = 7.6, 1.8 Hz, 3H), 7.38 (ddd, *J* = 7.6, 4.2, 1.5 Hz, 6H).

Synthesis of C_2-Symmetric Ligands: General Procedure A

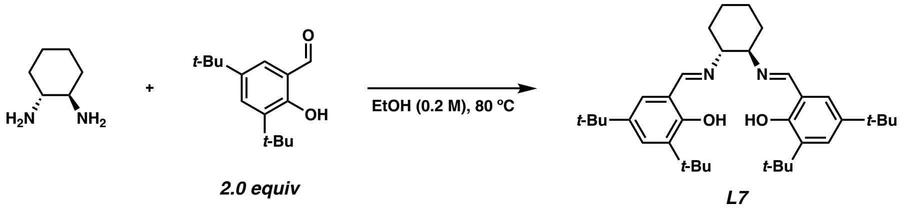


A flame-dried flask equipped with a stir bar was charged with carbonyldiimidazole (2.4 equiv) and then subjected to three purge-backfill cycles with N_2. THF (0.5 M) was added, followed by the picolinic acid derivative (2.5 equiv). The mixture was stirred at 40 ºC for 1 h. The diamine (1 equiv) was then added slowly via syringe. The reaction was monitored by TLC and LCMS. Upon completion (typically 16–24 h), the vessel was cooled to 23 °C and quenched by the addition of H_2O. Three extractions were performed with ethyl acetate, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel chromatography to afford the desired product.



N,*N*'-(cyclohexane-1,2-diyl)bis(4-methoxypicolinamide) (L4)

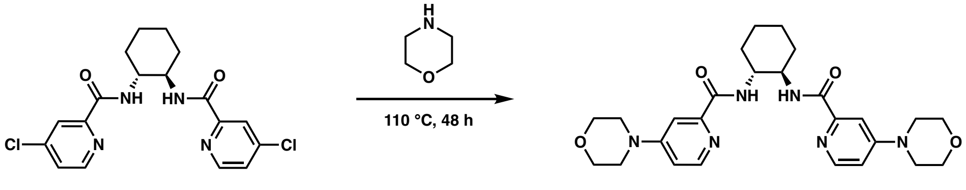
Prepared according to General Procedure A and purified by silica gel chromatography to afford **L4** as a white solid (350 mg, 0.91 mmol, 57% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dd, *J* = 5.7, 0.6 Hz, 2H), 8.23 (d, *J* = 6.8 Hz, 2H), 7.61 (dd, *J* = 2.7, 0.5 Hz, 2H), 6.84 (dd, *J* = 5.6, 2.6 Hz, 2H), 4.09 – 3.98 (m, 2H), 3.85 (s, 6H), 2.25 – 2.14 (m, 2H), 1.87 – 1.78 (m, 2H), 1.51 – 1.39 (m, 4H). Characterization data was in agreement with the literature.[32]



6,6'-((1E,1'E)-(((1*R*,2*R*)-cyclohexane-1,2-diyl)bis(azaneylylidene))bis(methaneylylidene))bis(2,4-di-tert-butylphenol) (L7)

Preparation: In accordance with a literature protocol,[3] 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (0.469 g, 2 mmol, 2 equiv) was added to a solution of *trans*-1,2-diaminocyclohexane (0.12 mL, 1 mmol, 1 equiv) in absolute ethanol (5 mL, 0.2 M). The mixture was heated to reflux for 1 h and then cooled to 23 °C. The resulting solid was collected by filtration and washed with a small portion of ethanol (2 mL) to afford **L7** as a fluffy yellow solid (0.546 g, quant.). ^{1}H NMR (600 MHz, $CDCl_3$) δ 13.69 (s, 2H), 8.29 (s, 2H), 7.29 (d, *J* = 2.4 Hz, 2H), 6.97 (d, *J* = 2.4 Hz, 2H), 3.33 – 3.28 (m, 2H), 1.90 (dd, *J* =

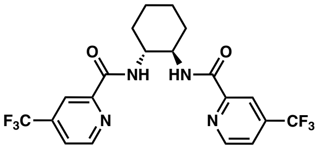
41.5, 11.3 Hz, 4H), 1.73 (m, 2H), 1.49 – 1.42 (m, 2H), 1.40 (s, 18H), 1.22 (s, 18H). Characterization data was in agreement with the literature.[33]



L17 *L5*

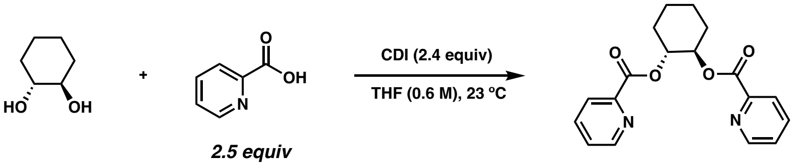
N,N'-((1R,2R)-cyclohexane-1,2-diyl)bis(4-morpholinopicolinamide) (L8)

Preparation: (R,R)-**L17** (500mg, 1.28 mmol, 1 equiv) was added to a flame-dried flask equipped with a reflux condenser and stir bar then subjected to three purge-backfill cycles with N_2. Morpholine (15 mL, 174 mmol, 136 equiv) was then added and the mixture was heated to 110 ºC. The reaction was monitored by LCMS and after 48 h all starting material was consumed. The reaction was then cooled to 23 °C and then concentrated by rotary evaporation. The residue was purified by silica gel chromatography (100% EtOAc then 0–10% MeOH/CH_2Cl_2) to afford **L8** as a yellow-orange solid (470 mg, 0.95 mmol, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 7.1 Hz, 2H), 8.19 (d, J = 5.8 Hz, 2H), 7.51 (d, J = 2.7 Hz, 2H), 6.65 (dd, J = 5.9, 2.7 Hz, 2H), 4.02 (t, J = 5.0 Hz, 2H), 3.79 (dd, J = 6.0, 3.9 Hz, 8H), 3.31 (dd, J = 6.0, 3.9 Hz, 8H), 2.23 – 2.12 (m, 2H), 1.81 (s, 4H), 1.52 – 1.34 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 156.1, 150.8, 149.0, 109.6, 106.8, 66.5, 53.2, 46.3, 32.8, 24.9. IR (thin film, NaCl) 3355, 2930, 2856, 1659, 1598, 1518, 1447, 1373, 1256, 1120, 993, 918, 731 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{26}H_{34}N_6O_4$ $[M]^{+\bullet}$: 494.2636, found 494.2617. $[\alpha]_D^{23}$ +57.35 (c 1.0, $CHCl_3$).



N,N'-(cyclohexane-1,2-diyl)bis(4-(trifluoromethyl)picolinamide) (L9)

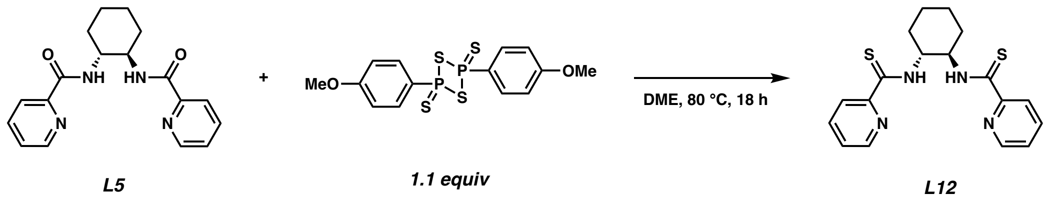
Prepared according to General Procedure A and purified by silica gel chromatography (20% EtOAc/Hexanes) to afford **L9** as a white solid (446 mg, 0.97 mmol, 97% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (d, *J* = 5.0 Hz, 2H), 8.35 – 8.24 (m, 2H), 8.24 – 8.11 (m, 2H), 7.58 (dd, *J* = 5.2, 1.7 Hz, 2H), 4.20 – 3.93 (m, 2H), 2.28 – 2.14 (m, 2H), 1.93 – 1.79 (m, 2H), 1.58 – 1.39 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 151.3, 149.4, 139.8 (q, *J* = 34.5 Hz), 121.8 (q, *J* = 3.6 Hz), 121.3, 118.3 (q, *J* = 3.6 Hz), 53.7, 32.7, 24.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.7. IR (thin film, NaCl) 3308, 2936, 2857, 1666, 1609, 1531, 1409, 1335, 1320, 1268, 1230, 1136, 1079, 914, 781, 732, 666 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{20}H_{18}N_4O_2F_6$ $[M]^{+\bullet}$: 460.1329, found 460.1318.



L11

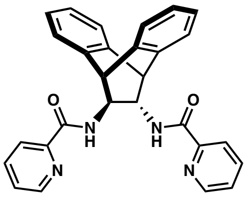
Cyclohexane-1,2-diyl dipicolinate (L11)

Preparation: Adopted from a literature protocol,[4] a flame-dried flask equipped with a stir bar was charged with carbonyldiimidazole (2.175 g, 13.4 mmol, 2.4 equiv) and then subjected to three purge-backfill cycles with N_2. THF (10 mL, 0.6 M) was added, followed by picolinic acid (1.725 g, 14 mmol, 2.5 equiv). The mixture was stirred at 23 ºC for 1 h. *Trans*-1,2-cyclohexanediol (650 mg, 5.6 mmol, 1 equiv) was then added slowly via syringe. The reaction was stirred at 23 °C for 18 h and monitored by LCMS. Upon completion, the reaction was quenched by the addition of water. Three extractions were performed with CH_2Cl_2 and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (5% MeOH/EtOAc). To remove remaining impurities, trituration was performed with hot hexanes, delivering **L11** as a white solid (1.10 g, 3.37 mmol, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (ddd, J = 4.7, 1.8, 0.9 Hz, 2H), 8.01 (dt, J = 7.9, 1.1 Hz, 2H), 7.75 (td, J = 7.7, 1.7 Hz, 2H), 7.39 (ddd, J = 7.7, 4.7, 1.2 Hz, 2H), 5.46 – 5.30 (m, 2H), 2.41 – 2.22 (m, 2H), 1.91 – 1.80 (m, 2H), 1.77 – 1.61 (m, 2H), 1.54 – 1.44 (m, 2H). Characterization data was in agreement with the literature.[34]



N,N'-(cyclohexane-1,2-diyl)bis(pyridine-2-carbothioamide) (L12)

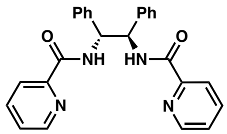
Preparation: In accordance with a literature protocol,[35] Lawesson's reagent (134 mg, 0.33 mmol, 1.1 equiv) was added to a stirring solution of *rac*-**L5** (100 mg, 0.3 mmol, 1 equiv) in DME (1 mL, 0.3 M), and the reaction was heated to 80 ºC for 18 h. The crude reaction was passed through a plug of Al_2O_3 and rinsed several times with CH_2Cl_2. The residue was purified by silica gel chromatography (0 – 50% EtOAc/Hexanes) to afford **L12** as a yellow solid (83.2 mg, 0.23 mmol, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.44 (s, 2H), 8.54 (dt, J = 8.0, 1.1 Hz, 2H), 8.46 (ddd, J = 4.7, 1.8, 0.9 Hz, 2H), 7.72 (td, J = 7.7, 1.7 Hz, 2H), 7.34 (ddd, J = 7.6, 4.7, 1.2 Hz, 2H), 5.06 – 4.88 (m, 2H), 2.47 – 2.38 (m, 2H), 1.97 – 1.85 (m, 2H), 1.55 (m, 4H). ^{13}C NMR (100 MHz, CDC13) δ 191.1, 150.9, 147.0, 137.0, 125.9, 124.9, 58.5, 31.0, 24.6. IR (thin film, NaCl) 3247, 2931, 1509, 1433, 1344, 989, 734 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{18}H_{20}N_4S_2[M]^{+\bullet}$: 356.1124, found 356.1119.



N,N'-(9,10-dihydro-9,10-ethanoanthracene-11,12-diyl)dipicolinamide (L14)

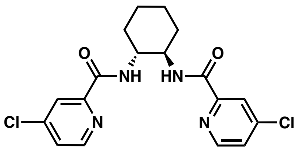
Prepared according to General Procedure A and purified by silica gel chromatography (0–100% EtOAc/Hexanes) to afford **L14** as a white solid (1.24 g, 2.78 mmol, 92% yield). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.43 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 2H), 8.14 (dt, *J* = 7.8, 1.1 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 2H), 7.79 (td, *J* = 7.7, 1.7 Hz, 2H), 7.46 (dd, *J* = 7.1, 1.4 Hz, 2H), 7.40 – 7.31 (m, 4H), 7.25 – 7.16 (m, 4H), 4.54 (d, *J* = 2.5 Hz, 2H), 4.41 – 4.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 149.5, 148.2, 141.3, 139.0, 137.3, 127.0, 126.9, 126.3, 126.0, 124.9, 122.23, 57.1, 49.6. IR (thin film, NaCl) 3374, 3353, 2950, 1672, 1590, 1514, 1462, 1434, 1226, 996, 912, 746, 631 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{28}H_{23}N_4O_2[M+H]^+$: 447.1816, found 447.1786.



N,N′-(1,2-diphenylethane-1,2-diyl)dipicolinamide (L15)

Prepared according to General Procedure A and purified by silica gel chromatography (0–100% EtOAc then 5% MeOH/EtOAc) to afford **L15** as a white solid (422 mg, 1.00 mmol, 20% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 9.02 – 8.90 (m, 2H), 8.58 (ddd, *J* = 4.8, 1.7, 0.9 Hz, 2H), 8.15 (dt, *J* = 7.8, 1.1 Hz, 2H), 7.80 (td, *J* = 7.7, 1.7 Hz, 2H), 7.41 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 2H), 7.32 – 7.22 (m, 10H), 5.67 (dd, *J* = 6.1, 2.6 Hz, 2H). Characterization data was in agreement with the literature.[36]

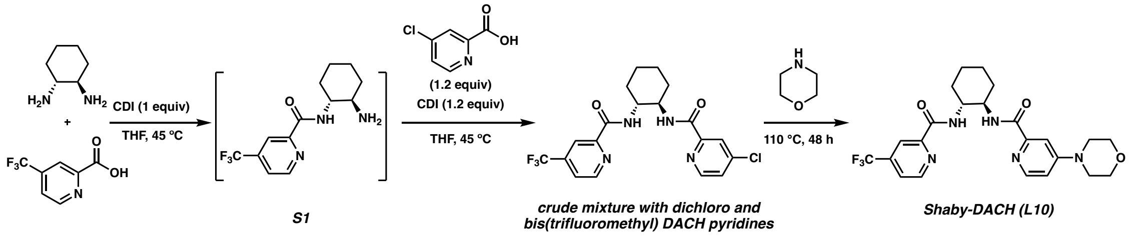


N,N'-(cyclohexane-1,2-diyl)bis(4-chloropicolinamide) (L17)

Prepared according to General Procedure A and purified by silica gel chromatography (0–100% EtOAc/Hexanes) to afford **L17** as a yellow solid (1.74 g, 4.42 mmol, 88% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 8.43 (d, *J* = 5.2 Hz, 2H), 8.19 – 8.11 (m, 2H), 8.06 (d, *J* = 2.1 Hz, 2H), 7.36 (dd, *J* = 5.2, 2.1 Hz, 2H), 4.10 – 3.95 (m, 2H), 2.27 – 2.10 (m, 2H), 1.94 –

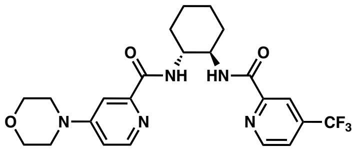
1.78 (m, 2H), 1.52 – 1.40 (m, 4H). Characterization data was in agreement with the literature.[32]

Synthesis of Shaby-DACH (L10) (Two-step, one-pot)



A flame-dried flask equipped with a stir bar was subjected to three purge-backfill cycles with N_2. (*R,R*)-1,2-diaminocyclohexane (114 mg, 1 mmol, 1 equiv) was added via syringe, followed by THF (2 mL, 0.5 M). In another flame-dried flask equipped with a stir bar, carbonyldiimidazole (162 mg, 1 mmol, 1 equiv) was added and the vessel was placed under N_2 atmosphere then charged with THF (1 mL). 4-CF_3 picolinic acid (191 mg, 1 mmol, 1 equiv) was added to the carbonyldiimidazole slurry, and the mixture was stirred at 45 ºC for 1 h. This solution was then transferred dropwise to the diamine solution via cannula at 45 ºC. The resulting mixture was stirred for 4 h. In a separate flame-dried flask equipped with a stir bar, carbonyldiimidazole (195 mg, 1.2 mmol, 1.2 equiv) was added and the vessel was placed under N_2 atmosphere then charged with THF (1 mL). 4-Cl picolinic acid (189 mg, 1.2 mmol, 1.2 equiv) was added to the carbonyldiimidazole slurry, and the mixture was stirred at 45 ºC for 1 h. This solution was added to the picolinamide mixture containing **S1** via cannula at 45 °C, which was then stirred for another 8 h and monitored by TLC and LCMS. Upon completion, the reaction was cooled to 23 °C and quenched by the addition of H_2O. Three extractions were performed with ethyl acetate, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (20–50 % EtOAc/Hexanes) to isolate an inseparable statistical mixture of DACH pyridines from other impurities.

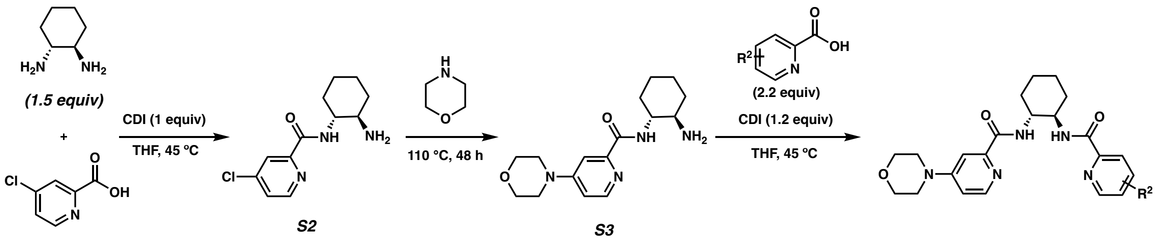
The mixture of DACH pyridines was then added to a flame-dried flask equipped with a reflux condenser and stir bar and then subjected to three purge-backfill cycles with N_2. Morpholine (10 mL, 116 mmol) was then added and the mixture was heated to 110 ºC. The reaction was monitored by LCMS and after 48 h all starting material was consumed. The reaction was then cooled to 23 °C and then concentrated by rotary evaporation. The residue was purified by silica gel chromatography (20–100% EtOAc/Hexanes then 10% $MeOH/CH_2Cl_2$) to isolate **L10** as an off-white solid (146 mg, 0.31 mmol, 31% yield over three steps).



4-morpholino-N-((1*R*,2*R*)-2-(4-(trifluoromethyl)picolinamido)cyclohexyl)picolinamide (L10)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 5.0 Hz, 1H), 8.29 (dt, *J* = 1.6, 0.8 Hz, 1H), 8.23 (dd, *J* = 16.3, 8.1 Hz, 2H), 8.17 (d, *J* = 5.8 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.46 (d, *J* = 2.7 Hz, 1H), 6.64 (dd, *J* = 5.9, 2.8 Hz, 1H), 4.13 – 3.94 (m, 2H), 3.82 – 3.71 (m, 4H), 3.32 – 3.23 (m, 4H), 2.26 – 2.08 (m, 2H), 1.89 –1.74 (m, 2H), 1.56 – 1.35 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 163.2, 156.1, 151.6, 150.5, 149.3, 149.0, 139.7 (q, *J* = 34.6 Hz), 124.0, 121.5 (q, *J* = 3.2 Hz), 118.3 (q, *J* = 3.5 Hz), 109.7, 106.6, 66.4, 54.2, 52.8, 46.2, 32.7, 32.6, 25.0, 24.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.7. IR (thin film, NaCl) 3329, 2931, 2858, 1661, 1600, 1519, 1335, 1168, 1145, 993, 735 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{23}H_{26}F_3N_6O_3$ $[M]^{+\bullet}$: 477.1982, found 477.1980. $[\alpha]_D^{23}$ –60.86 (*c* 1.0, $CHCl_3$).

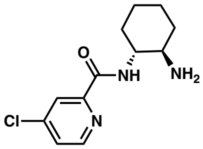
Synthesis of C_1-Symmetric Ligands (Stepwise): General Procedure B



A flame-dried flask equipped with a stir bar was subjected to three purge-backfill cycles with N_2. *Trans*-1,2-diaminocyclohexane (3.60 mL, 30 mmol, 1.5 equiv) was added via syringe, followed by THF (15 mL, 1.3 M). In another flame-dried flask equipped with a stir bar, carbonyldiimidazole (3.243 g, 20 mmol, 1 equiv) was added and the vessel was placed under N_2 atmosphere then charged with THF (40 mL, 0.5 M). 4-Cl picolinic acid (3.151 g, 20 mmol, 1 equiv) was added to the carbonyldiimidazole slurry, and the mixture was stirred at 45 ºC for 1 h. The diamine solution was then added dropwise to the carbonyldiimidazole/carboxylic acid solution via cannula at 45 ºC. The reaction was stirred at 45 °C and monitoried via TLC and LCMS. Upon completion (typically 8 h), the reaction was cooled to 23 °C and quenched by the addition of H_2O. Three extractions were performed with ethyl acetate, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The residue was purified via silica gel chromatography (2/10/88 Et_3N/MeOH/CH_2Cl_2) to isolate the product as a mixture with imidazole. A trituration was performed with hot H_2O to remove most of the imidazole, affording mono-picolinamide **S2** as a white solid (3.031 g, 11.95 mmol, 50% yield).

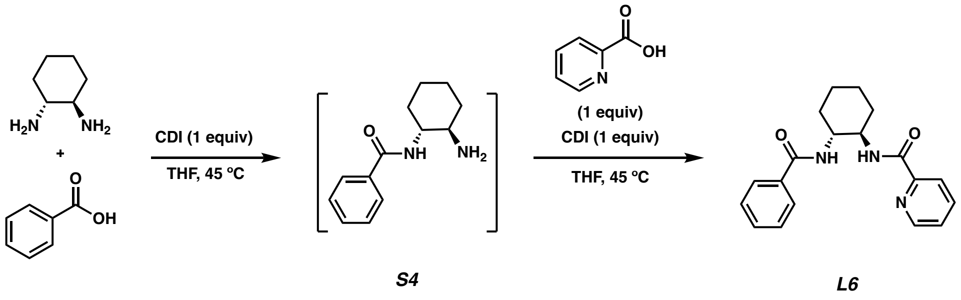
S2 (300 mg, 1.18 mmol, 1 equiv) was then added to a flame-dried flask equipped with a reflux condenser and stir bar, then subjected to three purge-backfill cycles with N_2. Morpholine (4.5 mL, 52 mmol, 44 equiv) was then added and the mixture was heated to 110 ºC. The reaction was monitored by LCMS and after 48 h all starting material was consumed. The reaction was then cooled to 23 °C and then concentrated by rotary evaporation. The crude product **S3** was advanced to the next step without additional purification.

S3 was then added to a flame-dried flask equipped with a stir bar under N_2 atmosphere and was then charged with THF (0.2 M). In another flame-dried flask equipped with a stir bar, the corresponding carboxylic acid (2.2 equiv) and THF (0.25 M) were added under N_2 atmosphere. Carbonyldiimidazole (2.2 equiv) was then added to the carboxylic acid solution and the mixture was stirred at 45 ºC for 1 h. This solution was then added to the picolinamide mixture containing **S3** via syringe or cannula. The mixture was stirred at 45 ºC and monitored by LCMS. Upon completion (typically 8 h), the reaction was cooled to 23 °C and quenched by the addition of H_2O. Three extractions were performed with ethyl acetate, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography to afford the desired product.



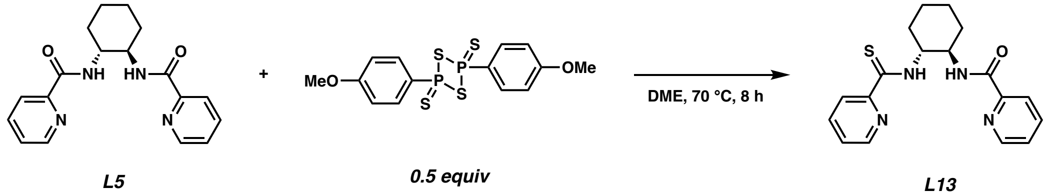
N-(2-aminocyclohexyl)-4-chloropicolinamide (S2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (dd, *J* = 5.2, 0.6 Hz, 1H), 8.22 (dd, *J* = 2.1, 0.6 Hz, 1H), 7.90 (d, *J* = 9.2 Hz, 1H), 7.43 (dd, *J* = 5.2, 2.1 Hz, 1H), 3.77 – 3.64 (m, 1H), 2.55 (td, *J* = 10.2, 4.0 Hz, 1H), 2.10 – 1.97 (m, 2H), 1.81 – 1.74 (m, 2H), 1.47 – 1.18 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 157.3, 122.4, 53.3, 45.7, 32.4, 24.6, 8.5. IR (thin film, NaCl) 3378, 3044, 2937, 2858, 2597, 2472, 2359, 2232, 1693, 1680, 1555, 1536, 1451, 1414, 1281, 1185, 1104, 996, 909, 837, 806, 730, 682, 645 cm^{-1}. HRMS (MM:ESI+) m/z calc'd for $C_{12}H_{17}N_3OCl$ $[M+H]^+$: 254.1055, found 254.1052.



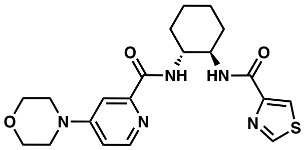
N-(2-benzamidocyclohexyl)picolinamide) (L6)

Preparation: In accordance with a literature protocol,[18] a flame-dried flask equipped with a stir bar was subjected to three purge-backfill cycles with N_2. *Trans*-1,2-diaminocyclohexane (1.884 g, 16.5 mmol, 1 equiv) was added via syringe, followed by THF (7.5 mL, 2.2 M). In another flame-dried flask equipped with a stir bar, benzoic acid (2.015 g, 16.5 mmol, 1 equiv) and THF (12 mL, 1.4 M) were added under N_2 atmosphere. Carbonyldiimidazole (2.675 g, 16.5 mmol, 1 equiv) was then added to the carboxylic acid solution and the mixture was stirred at 23 ºC for 1 h. This solution was then transferred dropwise to the diamine solution via syringe pump over 30 minutes. The resulting mixture was stirred at 23 °C for 18 h. In a separate flame-dried flask equipped with a stir bar, 2-picolinic acid (2.031 g, 16.5 mmol, 1 equiv) and THF (12 mL, 1.4 M) were added under N_2 atmosphere. Carbonyldiimidazole (2.675 g, 16.5 mmol, 1 equiv) was then added to the carboxylic acid solution and the mixture was stirred at 23 ºC for 1 h. This solution was then added to the benzamide solution containing **S4** via syringe pump over 1 hour. An additional 8 mL of THF was added to decrease the viscosity of the slurry. The mixture was stirred at 23 °C for 4 hours. Upon completion, dichloromethane (25 mL) and water (38 mL) were added and the two layers were partitioned. The organic layer was concentrated to a solid and then redissolved in CH_2Cl_2 (20 mL). This solution was extracted five times with 3 M aq. HCl (20 mL). The aqueous layer was made alkaline by adding 50% aq. NaOH (20 mL), then was extracted two times with CH_2Cl_2 (38 mL) and concentrated. The resulting solid was purified by silica gel chromatography (20% EtOAc/Hexanes) to afford **L6** as a white solid (746 mg, 2.31 mmol, 14% yield). ^1H NMR (600 MHz, $CDCl_3$) δ 8.52 (ddd, $J = 4.8$, 1.8, 1.0 Hz, 1H), 8.16 (d, *J* = 8.6 Hz, 1H), 8.13 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.82 – 7.74 (m, 3H), 7.43 – 7.34 (m, 4H), 7.24 (d, *J* = 7.0 Hz, 1H), 4.06 (tdd, *J* = 12.1, 8.8, 4.0 Hz, 1H), 3.91 (tdd, *J* = 11.1, 7.2, 4.0 Hz, 1H), 2.45 – 2.33 (m, 1H), 2.17 – 2.08 (m, 1H), 1.92 – 1.72 (m, 2H), 1.58 (qd, *J* = 12.5, 3.8 Hz, 1H), 1.48 – 1.41 (m, 2H),1.32 (tdd, *J* = 12.8, 11.3, 3.6 Hz, 1H). Characterization data was in agreement with the literature.[7]



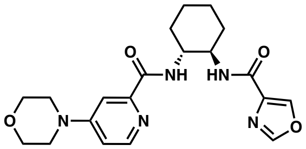
N-(2-(pyridine-2-carbothioamido)cyclohexyl)picolinamide (L13)

Preparation: In a modified procedure,[5] Lawesson's reagent (61 mg, 0.15 mmol, 0.5 equiv) was added to a stirring solution of *rac*-**L5** (100 mg, 0.3 mmol) in DME (2 mL, 0.15 M), and the temperature was elevated to 70 ºC. After 8 h, the reaction was allowed to cool slowly to 23 °C, at which point the crude mixture was plugged through Al_2O_3 with CH_2Cl_2 and EtOAc. The residue was purified by silica gel chromatography (0-100% EtOAc/Hexanes) to deliver the **L13** as a yellow solid (40.2 mg, 0.12 mmol, 39% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (d, *J* = 8.7 Hz, 1H), 8.56 (dt, *J* = 8.0, 1.1 Hz, 1H), 8.48 (dddd, *J* = 6.6, 4.7, 1. 8, 0.9 Hz, 2H), 8.29 – 8.22 (m, 1H), 8.05 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.72 (tdd, *J* = 7.8, 4.4, 1.7 Hz, 2H), 7.33 (ddt, *J* = 7.7, 4.8, 0.9 Hz, 2H), 4.79 – 4.66 (m, 1H), 4.36 – 4.23 (m, 1H), 2.49 – 2.38 (m, 1H), 2.27 – 2.15 (m, 1H), 1.92 – 1.81 (m, 2H), 1.63 – 1.39 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 164.6, 151.1, 149.6, 148.2, 147.0, 137.1, 136.9, 126.1, 125.8, 124.9, 122.1, 59.1, 52.7, 32.6, 30.8, 24.9, 24.5. IR (thin film, NaCl) 3254, 3054, 2929, 2858, 1668, 1516, 1447, 1433, 1348, 1151, 1045, 996, 981, 913, 734, 684 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{18}H_{20}N_4OS[M]^{+\bullet}$: 340.1352, found 340.1346.



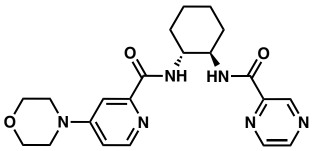
N-(2-(4-morpholinopicolinamido)cyclohexyl)thiazole-4-carboxamide (L18)

Prepared according to General Procedure B and purified by silica gel chromatography (100% CH_2Cl_2 to 1/10/89 Et_3N/MeOH/CH_2Cl_2) to afford **L18** as a yellow solid (103 mg, 0.25 mmol, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 2.2 Hz, 1H), 8.31 – 8.12 (m, 2H), 8.05 (d, J = 2.1 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 2.7 Hz, 1H), 6.66 (dd, J = 5.9, 2.8 Hz, 1H), 4.01 (tdd, J = 11.5, 8.4, 3.5 Hz, 2H), 3.84 – 3.77 (m, 4H), 3.35 – 3.28 (m, 4H), 2.38 – 2.02 (m, 2H), 1.81 (d, J = 7.5 Hz, 2H), 1.55 – 1.32 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 161.1, 156.2, 152.6, 151.4, 150.6, 149.0, 123.0, 109.7, 106.8, 66.5, 54.1, 52.8, 46.3, 32.7, 32.7, 25.0, 24.8. IR (thin film, NaCl) 3353, 2929, 2856, 1654, 1598, 1533, 1485, 1446, 1261, 1121, 992, 912, 885, 731 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{20}H_{25}N_5O_3S$ $[M]^{+\bullet}$: 415.1673, found 415.1657.



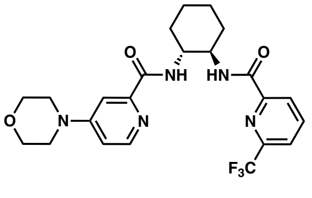
N-(2-(4-morpholinopicolinamido)cyclohexyl)oxazole-4-carboxamide (L19)

Prepared according to General Procedure B and purified by silica gel chromatography (100% CH_2Cl_2 to 1/10/89 Et_3N/MeOH/CH_2Cl_2) to afford **L19** as a yellow solid (89 mg, 0.23 mmol, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 5.9 Hz, 2H), 8.11 (d, J = 1.0 Hz, 1H), 7.80 (d, J = 1.0 Hz, 1H), 7.55 (d, J = 2.7 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 6.67 (dd, J = 5.9, 2.8 Hz, 1H), 4.08 – 3.87 (m, 2H), 3.86 – 3.74 (m, 4H), 3.33 (dd, J = 5.9, 4.1 Hz, 4H), 2.29 – 2.04 (m, 2H), 1.99 – 1.66 (m, 2H), 1.59 – 1.27 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 160.5, 156.2, 150.6, 150.5, 149.0, 141.2, 136.2, 109.7, 106.8, 66.5, 54.3, 52.6, 46.3, 32.60, 32.57, 25.0, 24.7. IR (thin film, NaCl) 3340, 3131, 2930, 2856, 2239, 1658, 1598, 1517, 1448, 1383, 1319, 1257, 1121, 1100, 1061, 993, 971, 953, 913, 891, 822, 730, 644 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{20}H_{25}N_5O_4$ $[M]^{+\bullet}$: 399.1901, found 399.1886.



N-(2-(4-morpholinopicolinamido)cyclohexyl)pyrazine-2-carboxamide (L20)

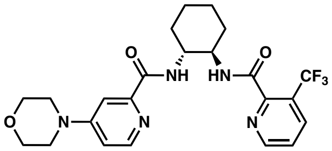
Prepared according to General Procedure B and purified by silica gel chromatography (100% CH_2Cl_2 to 1/10/89 Et_3N/MeOH/CH_2Cl_2) to afford **L20** as a yellow solid (52 mg, 0.13 mmol, 41% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (d, J = 1.5 Hz, 1H), 8.63 (d, J = 2.5 Hz, 1H), 8.48 (dd, J = 2.5, 1.5 Hz, 1H), 8.27 – 8.00 (m, 3H), 7.45 (d, J = 2.7 Hz, 1H), 6.63 (dd, J = 5.9, 2.8 Hz, 1H), 4.14 – 3.88 (m, 2H), 3.86 – 3.73 (m, 4H), 3.32 – 3.20 (m, 4H), 2.37 – 2.09 (m, 2H), 1.80 (s, 2H), 1.59 – 1.33 (m, 4H).^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 163.1, 156.0, 150.3, 148.9, 146.9, 144.6, 144.3, 142.7, 109.6, 106.5, 66.3, 54.1, 52.6, 46.1, 32.54, 28.7, 24.9, 24.7. IR (thin film, NaCl) 3333, 3053, 2931, 2855, 2352, 1666, 1599, 1519, 1448, 1400, 1383, 1321, 1265, 1256, 1155, 1122, 1068, 1048, 1019, 993, 971, 928, 891, 869, 783, 753, 732 cm^{-1}. HRMS (MM:ESI+) m/z calc'd for $C_{21}H_{27}N_6O_3$ $[M+H]^+$: 411.2139, found 411.2138.



4-morpholino-N-(2-(6-(trifluoromethyl)picolinamido)cyclohexyl)picolinamide (L21)

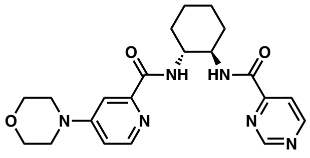
Prepared according to General Procedure B and purified by silica gel chromatography (100% EtOAc) to afford **L21** as a yellow solid (61 mg, 0.13 mmol, 64% yield). ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.40 (d, *J* = 7.8 Hz, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 8.16 (dd, *J* = 10.1, 7.2 Hz, 2H), 7.95 (t, *J* = 7.8 Hz, 1H), 7.73 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.57 (d, *J* = 2.7 Hz, 1H), 6.64 (dd, *J* = 5.9, 2.8 Hz, 1H), 4.19 – 4.04 (m, 1H), 4.05 – 3.84 (m, 1H), 3.87 – 3.73 (m, 4H), 3.40 – 3.23 (m, 4H), 2.37 – 2.09 (m, 2H) , 1.92 – 1.73 (m, 2H), 1.59 – 1.36 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.3, 156.1, 150.6, 150.5, 148.9, 146.9 (q, *J* = 35.4 Hz), 138.9, 125.0, 122.6, 122.5, 109.6, 106.9, 66.5, 55.0, 52.6, 46.2, 32.6, 32.4, 25.1, 24.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.5. IR (thin film, NaCl) 3332, 2933, 2856, 1673, 1599, 1523, 1449, 1343, 1257, 1191, 1141, 1112, 1079, 993, 909, 730 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{23}H_{26}F_3N_5O_3$ $[M]^{+\bullet}$: 477.1982, found 477.1957.



4-morpholino-*N*-(2-(3-(trifluoromethyl)picolinamido)cyclohexyl)picolinamide (L22)

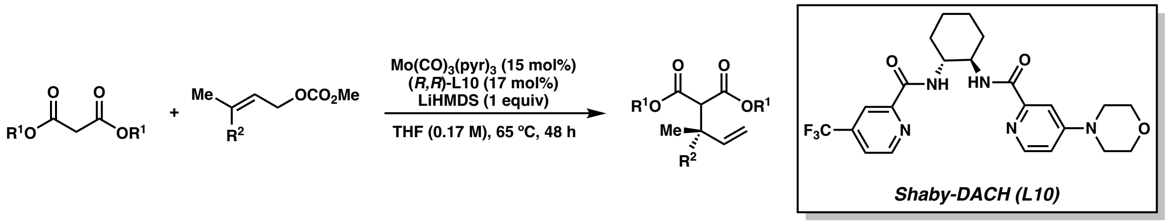
Prepared according to General Procedure B and purified by silica gel chromatography (100% EtOAc) to afford **L22** as a yellow solid (132 mg, 0.28 mmol, 55% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.26 (d, *J* = 7.9 Hz, 1H), 8.20 (d, *J* = 5.8 Hz, 1H), 8.04 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.92 (d, *J* = 7.1 Hz, 1H), 7.46 (dd, *J* = 8.2, 4.0 Hz, 2H), 6.67 (dd, *J* = 5.9, 2.7 Hz, 1H), 4.09 – 3.91 (m, 2H), 3.87 – 3.73 (m, 4H), 3.36 – 3.25 (m, 4H), 2.36 – 2.08 (m, 2H), 1.91 – 1.72 (m, 2H), 1.55 – 1.35 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 163.7, 156.2, 150.6 (q, *J* = 30.0 Hz), 149.8, 149.0, 136.0, 135.9, 125.8 (q, *J* = 34.3 Hz), 125.0, 121.6, 109.8, 106.6, 66.5, 54.5, 52.8, 46.3, 32.8, 32.4, 25.0, 24.8 ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.4. IR (thin film, NaCl) 3302, 2933, 2857, 2245, 1663, 1599, 1517, 1444, 1373, 1314, 1258, 1156, 1120, 1032, 992, 912, 894, 819, 730, 637 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{23}H_{26}F_3N_5O_3$ $[M]^{+\bullet}$: 477.1982, found 477.1960.



N-(2-(4-morpholinopicolinamido)cyclohexyl)pyrimidine-4-carboxamide (L23)

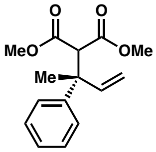
Prepared according to General Procedure B and purified by silica gel chromatography (100% CH_2Cl_2 to 1/10/89 Et_3N/MeOH/CH_2Cl_2) to afford **L23** as a yellow solid (142 mg, 0.35 mmol, 60% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 9.23 (t, *J* = 1.4 Hz, 1H), 8.87 (dd, *J* = 5.0, 1.4 Hz, 1H), 8.34 (d, *J* = 8.3 Hz, 1H), 8.21 – 8.12 (m, 2H), 8.00 (dt, *J* = 5.1, 1.4 Hz, 1H), 7.50 (dd, *J* = 2.8, 1.3 Hz, 1H), 6.66 (ddd, *J* = 5.9, 2.8, 1.2 Hz, 1H), 4.15 – 3.90 (m, 2H), 3.86 – 3.76 (m, 4H), 3.35 – 3.25 (m, 4H), 2.34 – 2.07 (m, 2H), 1.84 (s, 2H), 1.56 – 1.34 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 162.8, 158.9, 157.8, 156.4, 156.0, 150.3, 148.8, 118.5, 109.6, 106.6, 66.3, 54.5, 52.4, 46.1, 32.5, 32.3, 24.9, 24.6. IR (thin film, NaCl) 3348, 2934, 2856, 2245, 1667, 1599, 1523, 1449, 1385, 1267, 1256, 1146, 1122, 1068, 993, 912, 734 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{21}H_{26}N_6O_3$ $[M]^{+\bullet}$: 410.2061, found 410.2041.

Mo-catalyzed Allylic Alkylation: General Procedure C (0.1 mmol scale)



In a nitrogen-filled glovebox, a catalyst solution of $Mo(CO)_3(pyr)_3$ (6.3 mg, 0.015 mmol, 0.15 equiv) and *(R,R)*-ShabyDACH (8.0 mg , 0.017 mmol, 0.17 equiv) in THF (0.2 mL) was stirred for 20 min at 40 °C. In a separate vial, a stock solution of malonate nucleophile (0.5 mmol/mL) in THF was prepared and subsequently LiHMDS (0.5 mmol/mL) was added. In a separate vial, a stock solution of the (*E*)-allylic carbonate (0.5 mmol/mL) in THF was prepared. After the catalyst pre-stir was complete, the malonate stock solution

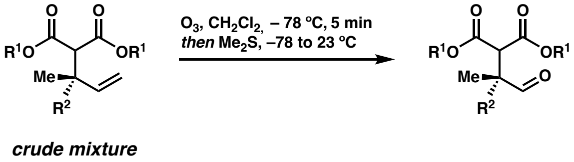
(0.23 mL, 0.1 mmol, 1 equiv) was added to the catalyst solution, followed by the allylic carbonate stock solution (0.22 mL, 0.1 mmol, 1 equiv). The reaction vessel was sealed with a Teflon-lined cap, removed from the glovebox, and stirred at 65 °C in a metal heating block for 48 h, unless noted otherwise. After 48 h, 0.5 M aq. HCl (1 mL) was added to the crude reaction mixture, which was then extracted three times with ethyl acetate, dried over Na_2SO_4, filtered, and concentrated. The residue was then run through a plug of silica gel (50% EtOAc/Hexanes) to remove polar impurities.



Dimethyl (*S*)-2-(2-phenylbut-3-en-2-yl)malonate (ent–3b)

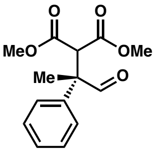
Prepared according to General Procedure C and purified by three preparative TLC elutions (10% EtOAc/Hexanes) affording a colorless oil (11.0 mg, 0.042 mmol, 42% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 4H), 7.20 (ddt, *J* = 7.1, 5.8, 2.1 Hz, 1H), 6.58 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.26 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.11 (dd, *J* = 17.5, 1.0 Hz, 1H), 4.07 (s, 1H), 3.58 (d, *J* = 1.4 Hz, 6H), 1.66 (s, 3H). $[\alpha]_D^{23}$ +5.58 (*c* 0.5, $CHCl_3$). Characterization data was in agreement with the literature.[8]

Ozonolysis: General Procedure D (0.1 mmol scale)



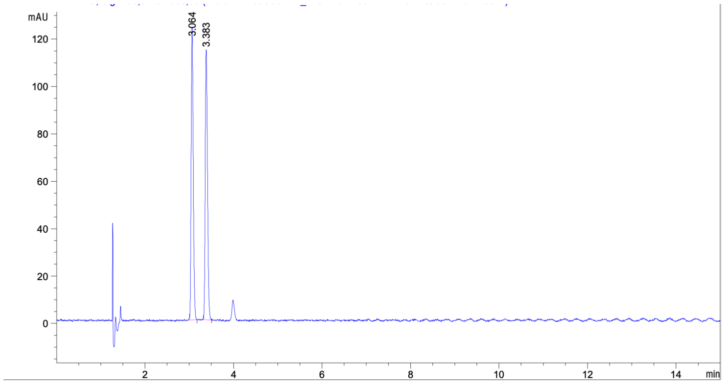
The crude mixture isolated following General Procedure C was dissolved in CH_2Cl_2 (20 mL, 0.05 M), and a pipette tip of Sudan III was added. The flask was cooled to –78 ºC and O_2 gas was bubbled through the solution using a gas diffuser. After 5 min of vigorous O_2 flow, a VMUS-4 Ozone Generator was turned to the lowest ozone output setting. After 3–

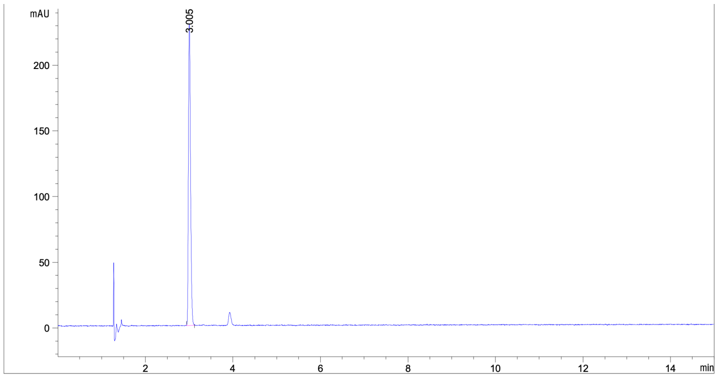
4 minutes, the color of the solution was observed to change from a vibrant red to a pale orange/brown color, and the ozonator was turned off. O_2 was bubbled through the solution for an additional 5 minutes, then the diffuser was removed. A stir bar was added to the flask, and a septum with an Ar balloon was affixed to the flask. The reaction was quenched with Me_2S (80 equiv, 0.4 mL), and the mixture was allowed to stir at –78 ºC for 1 h, then stirred at 23 °C for an additional 2 h. The solvent and Me_2S were then removed by rotatory evaporation. The residue was purified by preparatory TLC (20% EtOAc/Hexanes) to afford the desired α-quaternary aldehyde.



Dimethyl (*S*)-2-(1-oxo-2-phenylpropan-2-yl)malonate (55)

Prepared according to General Procedures C and D and isolated as a yellow oil (13.0 mg, 0.050 mmol, 50% yield over 2 steps, >99% ee). At 2 mmol scale, General Procedures C and D were scaled accordingly, and silica gel chromatography (20% EtOAc/Hexanes) delivered **6** (241 mg, 0.94 mmol, 47% overall yield, >99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.40 – 7.27 (m, 5H), 4.37 (s, 1H), 3.72 (s, 3H), 3.48 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.9, 168.02, 167.96, 136.4, 129.1, 128.2, 127.5, 56.9, 54.7, 52.8, 52.4, 15.9. IR (thin film, NaCl) 3451, 3059, 3002, 2953, 2847, 2712, 2361, 1738, 1731, 1599, 1495, 1434, 1376, 1326, 1236, 1202, 1155, 1078, 1025, 913, 850, 763, 736, 700, 678, 642 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{14}H_{17}O_5$ $[M+H]^+$: 265.1071, found 294.1062. $[\alpha]_D^{23}$ +154.06 (*c* 1.0, $CHCl_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 3.01, minor = 3.38.





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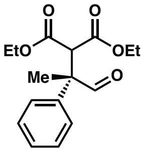
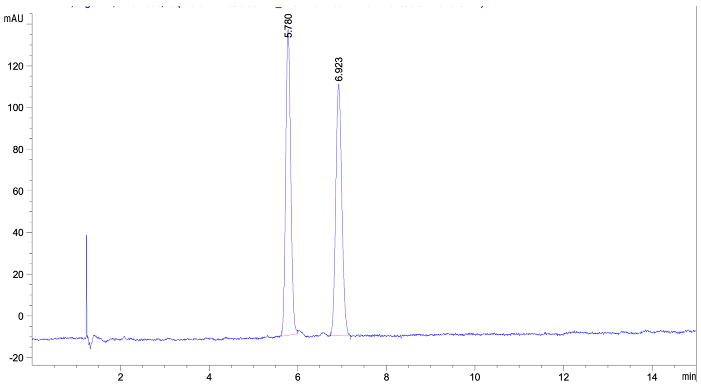
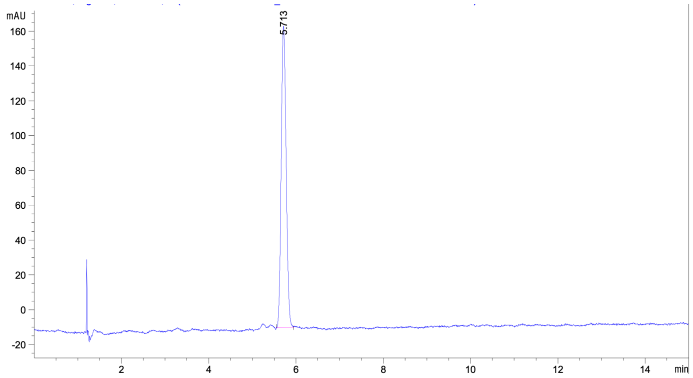


Diethyl (*S*)-2-(1-oxo-2-phenylpropan-2-yl)malonate (ent–19)

Prepared according to General Procedures C and D and isolated as a clear oil (9.9 mg, 0.034 mmol, 34% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.56 (s, 1H), 7.39 – 7.27 (m, 5H), 4.35 (s, 1H), 4.18 (qd, *J* = 7.1, 1.7 Hz, 2H), 3.95 (q, *J* = 7.1 Hz, 2H), 1.87 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H). $[\alpha]_D^{23}$ +115.94 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel IC-3 column, λ = 210.8 nm, t_R

(min): major = 5.71, minor = 6.92. Characterization data was in agreement with the literature.[8]





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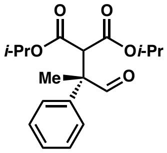
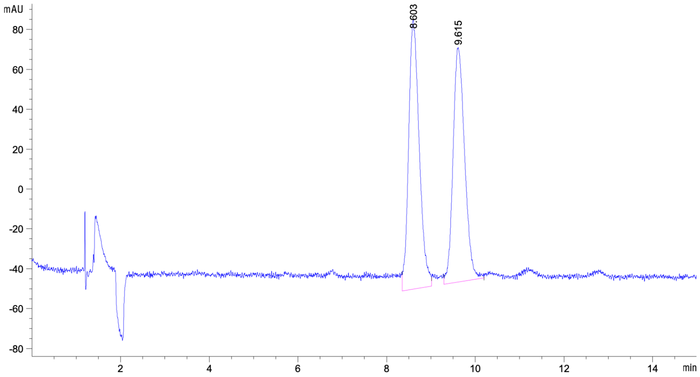
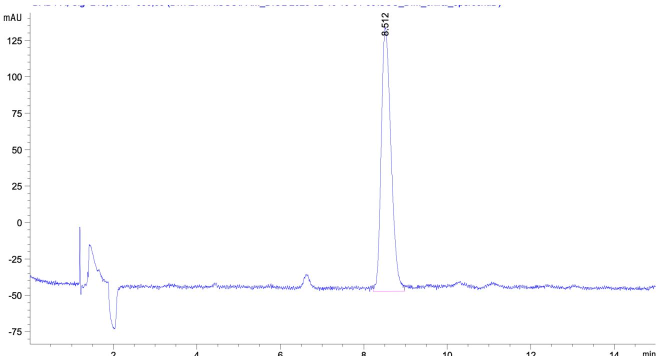


Diisopropyl (*S*)-2-(1-oxo-2-phenylpropan-2-yl)malonate (56)

Prepared according to General Procedures C and D and isolated as a clear oil (11.0 mg, 0.034 mmol, 34% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.59 (s, 1H), 7.38 – 7.27 (m, 5H), 5.03 (sept, *J* = 6.3 Hz, 1H), 4.82 (sept, *J* = 6.3 Hz, 1H), 4.31 (s, 1H), 1.85 (s, 3H), 1.22 (dd, *J* = 12.3, 6.3 Hz, 6H), 1.01 (dd, *J* = 55.8, 6.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 167.5, 167.3, 137.2, 129.3, 128.3, 127.9, 69.9, 69.3, 58.0, 54.8, 22.02, 21.97, 21.8, 21.7, 16.5. IR (thin film, NaCl) 2981, 2935, 1726, 1493, 1466, 1374, 1354, 1313, 1279, 1236, 1181, 1101, 1011, 903, 762, 698, 676 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{18}H_{25}O_5$ [M+H]$^+$: 321.1697, found 321.1698. $[\alpha]_D^{23}$ +42.44 (*c* 1.0, $CHCl_3$). SFC Conditions: 3% IPA, 2.5 mL/min, Chiralcel IC-3 column, λ = 210.8 nm, t_R (min): major = 8.51, minor = 9.62.





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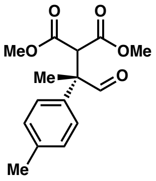
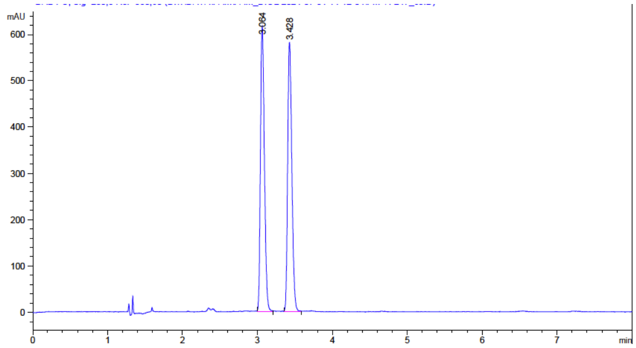
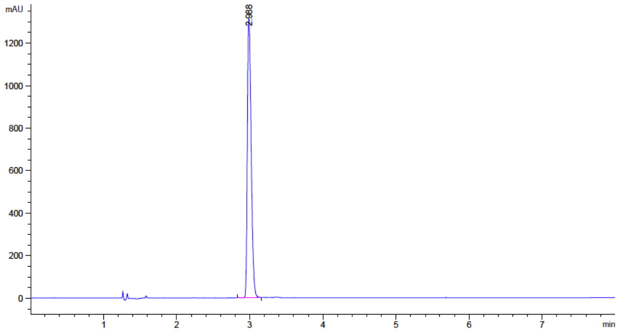
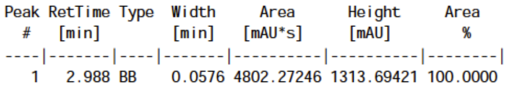


Dimethyl (*S*)-2-(1-oxo-2-(*p*-tolyl)propan-2-yl)malonate (58)

Prepared according to General Procedures C and D and isolated as a yellow oil (13.6 mg, 0.049 mmol, 49% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.48 (s, 1H), 7.16 (s, 4H), 4.35 (s, 1H), 3.72 (s, 3H), 3.50 (s, 3H), 2.32 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.9, 168.1, 168.0, 138.0, 133.3, 129.8, 127.4, 56.8, 54.4, 52.7, 52.4, 21.1, 15.9. IR (thin film, NaCl) 2924, 1738, 1434, 1320, 1239, 1038, 813 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{15}H_{18}O_5$ $[M]^{+\bullet}$: 278.1149, found 278.1141. $[\alpha]_D^{23}$ +149.00 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 2.99, minor = 3.43.







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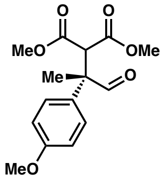
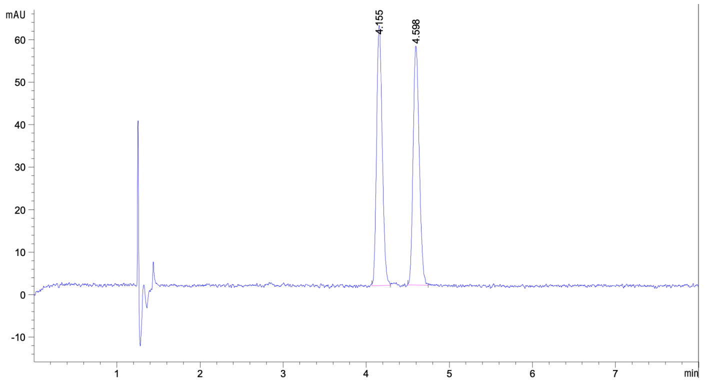
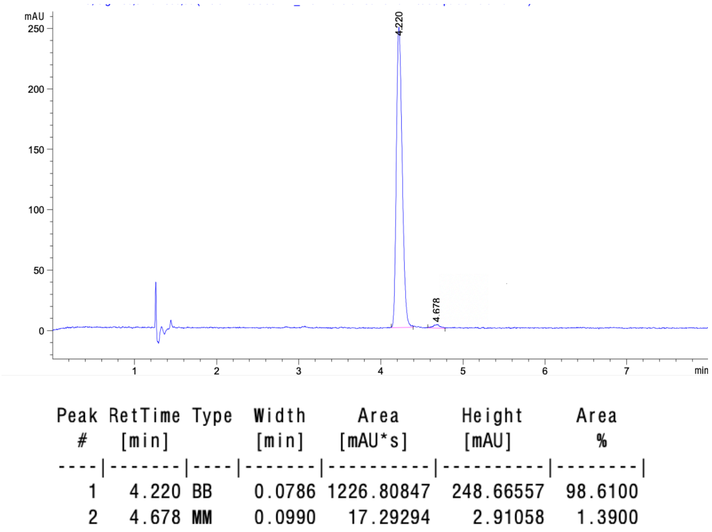


Dimethyl (*S*)-2-(2-(4-methoxyphenyl)-1-oxopropan-2-yl)malonate (59)

Prepared according to General Procedures C and D and isolated as a yellow oil (14.5 mg, 50% yield over 2 steps, 97% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.45 (s, 1H), 7.22 – 7.17 (m, 2H), 6.91 – 6.86 (m, 2H), 4.34 (s, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.49 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.8, 168.10, 168.07, 159.4, 128.8, 127.9, 114.5, 56.8, 55.4, 54.0, 52.8, 52.5, 15.8. IR (thin film, NaCl) 3441, 2955, 2844, 2722, 1735, 1606, 1450, 1255, 1078, 1033, 908, 833, 681 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{15}H_{18}O_6$ [M]$^{+\bullet}$: 294.1098, found 294.1092. $[\alpha]_D^{23}$ +150.80 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 4.22, minor = 4.68.





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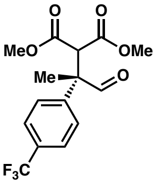
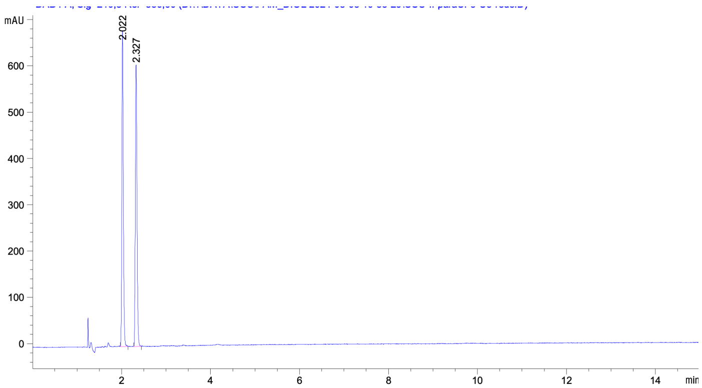
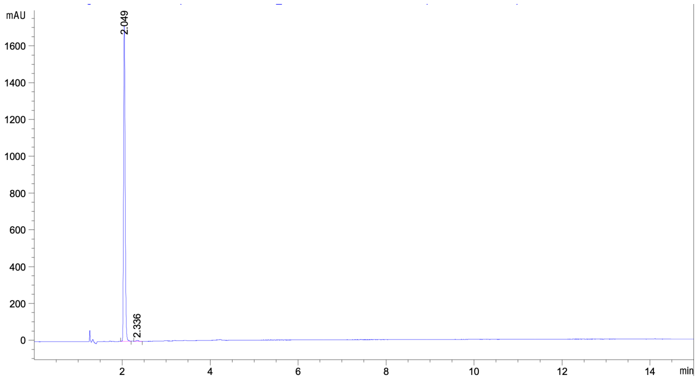


Dimethyl (*S*)-2-(1-oxo-2-(4-(trifluoromethyl)phenyl)propan-2-yl)malonate (60)

Prepared according to General Procedures C and D and isolated as a yellow oil (10.5 mg, 0.032 mmol, 32% yield over 2 steps, 99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.59 (s, 1H), 7.67 – 7.60 (m, 2H), 7.46 – 7.40 (m, 2H), 4.37 (s, 1H), 3.73 (s, 3H), 3.52 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.4, 167.4, 167.3, 140.6, 130.3, 129.9, 127.7, 125.6 (q, *J* = 3.7 Hz), 56.7, 54.3, 52.7, 52.3, 16.2. ^{19}F NMR (376 MHz, CDCl$_3$) δ -62.7. IR (thin film, NaCl) 2955, 2848, 1734, 1617, 1436, 1412, 1327, 1240, 1169, 1125, 1082, 1066, 1015, 913, 836, 709 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{15}H_{16}O_5F_3$ [M+H]$^+$: 333.0944, found 333.0934. $[\alpha]_D^{23}$ +74.03 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 210.8 nm, t_R (min): major = 2.05, minor = 2.34.





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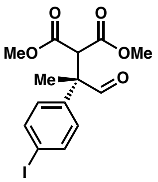
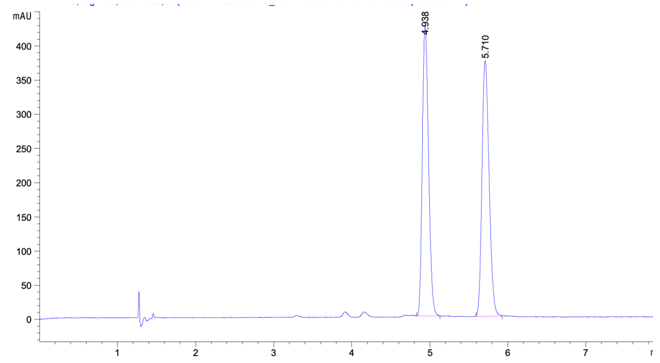
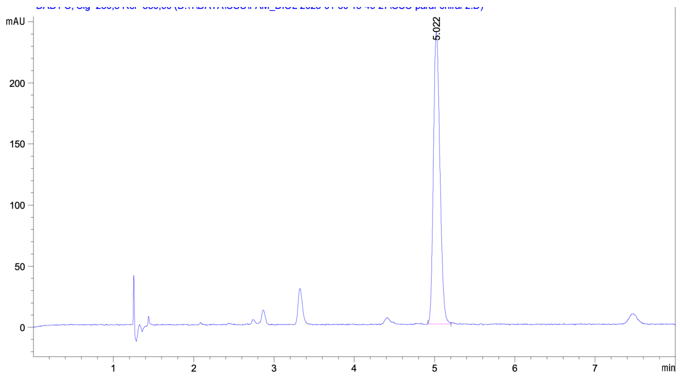


Dimethyl (*S*)-2-(2-(4-iodophenyl)-1-oxopropan-2-yl)malonate (62)

Prepared according to General Procedures C and D and isolated as a yellow oil (15.5 mg, 0.040 mmol, 40% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.72 – 7.66 (m, 2H), 7.06 – 7.00 (m, 2H), 4.32 (s, 1H), 3.72 (s, 3H), 3.53 (s, 3H), 1.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 167.8, 167.7, 138.2, 136.4, 129.4, 94.3, 56.8, 54.4, 52.9, 52.6, 16.1. IR (thin film, NaCl) 3453, 2952, 2845, 1738, 1731, 1582, 1488, 1434, 1395, 1328, 1237, 1203, 1155, 1079, 1027, 1004, 914, 850, 816, 765, 700, 679 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{14}H_{15}O_5I$ [M]$^{+•}$: 389.9959, found 389.9972. $[\alpha]_D^{23}$ +81.59 (*c* 1.0, $CHCl_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 5.02, minor = 5.71.





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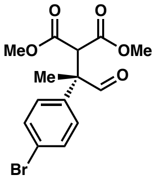
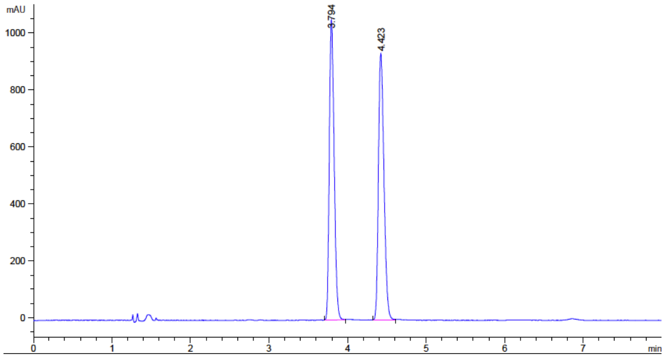
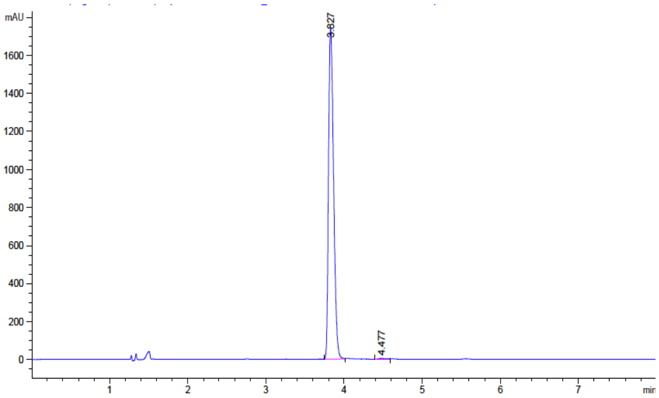


Dimethyl (*S*)-2-(2-(4-bromophenyl)-1-oxopropan-2-yl)malonate (63)

Prepared according to General Procedures C and D and isolated as a colorless oil (17.4 mg, 0.051 mmol, 51% yield over 2 steps, 99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.52 – 7.46 (m, 2H), 7.20 – 7.13 (m, 2H), 4.32 (s, 1H), 3.72 (s, 3H), 3.52 (s, 3H), 1.84 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 167.81, 167.75 135.7, 132.2, 129.3, 122.6, 56.8, 54.3, 52.9, 52.6, 16.2. IR (thin film, NaCl) 2956, 2925, 2360, 1731, 1491, 1435, 1329, 1243, 1157, 1082, 1024, 1008, 910, 820 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{14}H_{16}O_5Br$ [M+H]$^+$: 343.0176, found 343.0167. $[\alpha]_D^{23}$ +115.94 (*c* 1.0, $CHCl_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 3.83, minor = 4.48.





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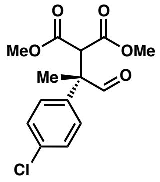
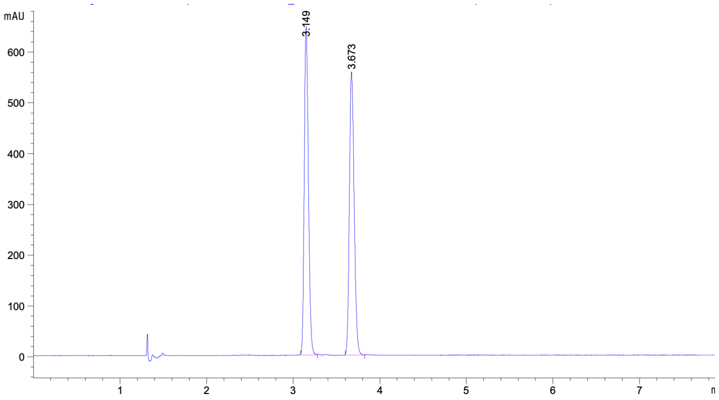
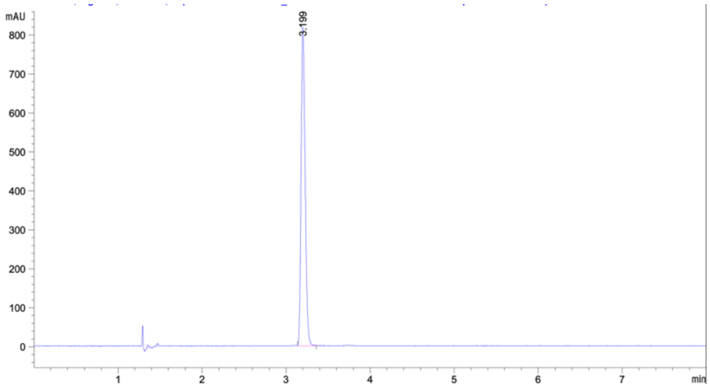


Dimethyl (*S*)-2-(2-(4-chlorophenyl)-1-oxopropan-2-yl)malonate (64)

Prepared according to General Procedures C and D and isolated as a yellow oil (16.0 mg, 0.053 mmol, 53% overall yield, >99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 7.37 – 7.31 (m, 2H), 7.25 – 7.20 (m, 2H), 4.33 (s, 1H), 3.72 (s, 3H), 3.52 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 167.83, 167.78, 135.1, 134.4, 129.2, 129.0, 56.9, 54.2, 52.9, 52.6, 16.2. IR (thin film, NaCl) 2952, 2850, 1731, 1493, 1434, 1403, 1310, 1239, 1154, 1097, 1012, 912, 825, 711 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{14}H_{15}O_5Cl$ $[M]^{+\bullet}$: 298.0603, found 298.0606. $[\alpha]_D^{23}$ +137.23 (*c* 1.0, $CHCl_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 3.20, minor = 3.67.





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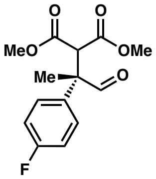
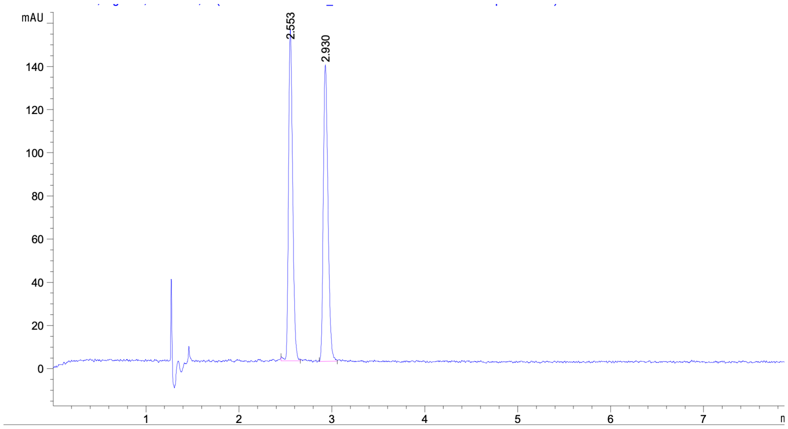
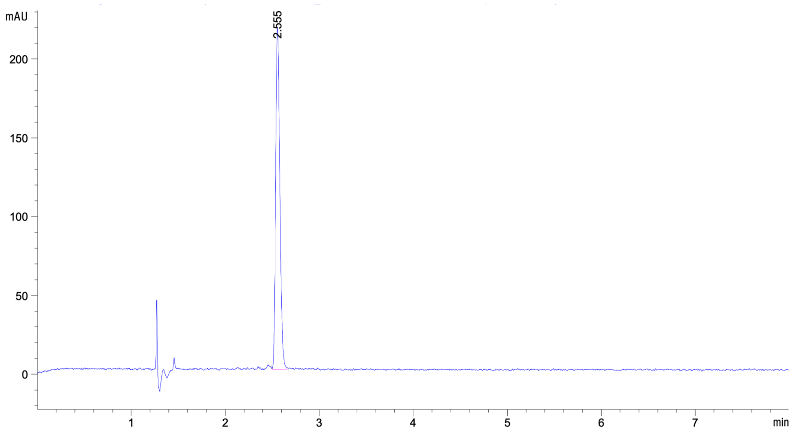


Dimethyl (*S*)-2-(2-(4-fluorophenyl)-1-oxopropan-2-yl)malonate (65)

Prepared according to General Procedures C and D and isolated as a yellow oil (11.0 mg, 0.039 mmol, 39% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.51 (s, 1H), 7.30 – 7.24 (m, 2H), 7.09 – 7.02 (m, 2H), 4.33 (s, 1H), 3.72 (s, 3H), 3.50 (s, 3H), 1.87 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 199.1, 168.2, 164.0, 161.6, 132.5 (d, *J* = 3.5 Hz), 129.7 (d, *J* = 8.2 Hz), 116.4 (d, *J* = 21.6 Hz), 57.3, 54.4, 53.2, 52.8, 16.5. ^{19}F NMR (376 MHz, CDCl$_3$) δ -113.7 (tt, *J* = 8.2, 5.1 Hz). IR (thin film, NaCl) 3450, 2955, 2848, 1738, 1731, 1602, 1512, 1434, 1372, 1331, 1282, 1240, 1198, 1169, 1075, 1029, 909, 835 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{14}H_{16}O_5F$ [M+H]$^+$: 283.0976, found 283.0982. $[\alpha]_D^{23}$ +97.74 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 2.56, minor = 2.93.





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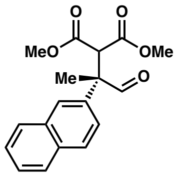
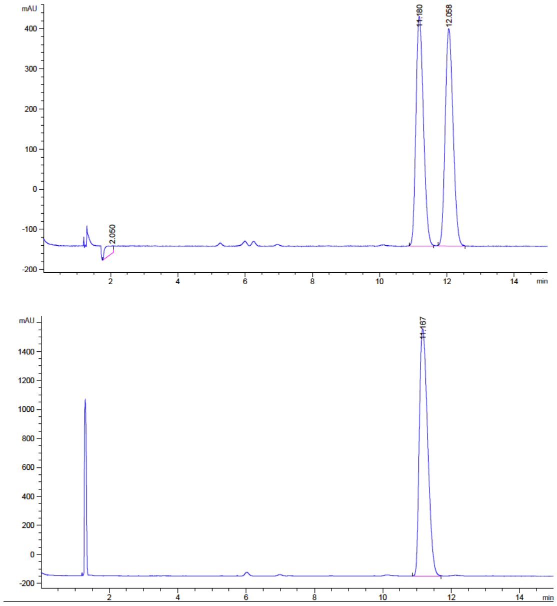


Dimethyl (*S*)-2-(2-(naphthalen-2-yl)but-3-en-2-yl)malonate (66)

Prepared according to General Procedures C and D and isolated as a clear oil (13.4 mg, 0.043 mmol, 43% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.59 (s, 1H), 7.88 – 7.77 (m, 3H), 7.75 (d, *J* = 2.1 Hz, 1H), 7.50 (dt, *J* = 6.3, 3.5 Hz, 2H), 7.40 (dd, *J* = 8.7, 2.1 Hz, 1H), 4.51 (s, 1H), 3.74 (s, 3H), 3.43 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.9, 168.1, 168.0, 133.8, 133.4, 132.7, 128.8, 128.4, 127.6, 127.2, 126.9, 126.6, 124.6, 56.8, 54.8, 52.8, 52.5, 16.1. IR (thin film, NaCl) 2955, 2848, 1731, 1434, 1322, 1234, 1018, 911, 818, 751 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{18}H_{18}O_5$ [M]$^{+\bullet}$: 314.1149, found 314.1164. [α]$_D^{23}$ +172.90 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel IC-3 column, λ = 230.8 nm, t$_R$ (min): major = 11.17, minor = 12.06.



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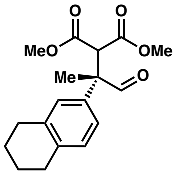
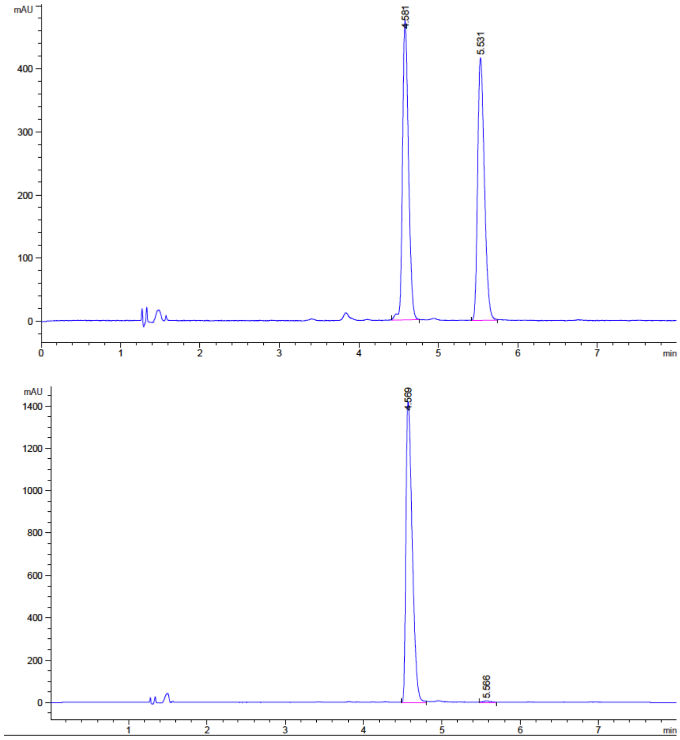


Dimethyl (*S*)-2-(2-(5,6,7,8-tetrahydronaphthalen-2-yl)but-3-en-2-yl)malonate (67)

Prepared according to General Procedures C and D and isolated as a clear oil (16.8 mg, 0.053 mmol, 53% yield over 2 steps, 99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.47 (s, 1H), 7.04 (d, *J* = 8.1 Hz, 1H), 6.97 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.93 (d, *J* = 2.2 Hz, 1H), 4.34 (s, 1H), 3.73 (s, 3H), 3.53 (s, 3H), 2.77 – 2.68 (m, 4H), 1.82 (s, 3H), 1.77 (dq, *J* = 6.6, 3.2 Hz, 4H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.9, 168.2, 168.0, 137.9, 137.3, 133.2, 129.8, 128.1, 124.3, 56.7, 54.5, 52.7, 52.4, 29.6, 29.0, 23.2, 23.1, 15.9. IR (thin film, NaCl) 2924, 1737, 1433, 1322, 1238, 1026 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{18}H_{22}O_5$ [M]$^{+\bullet}$: 318.1462, found 318.1453. $[\alpha]_D^{23}$ +118.45 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 4.57, minor = 5.57.



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Peak RetTime Type  Width     Area      Height     Area
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   2   5.566 BB    0.0747   32.14148    5.62010  0.4044
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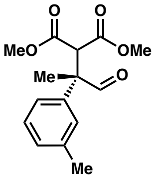
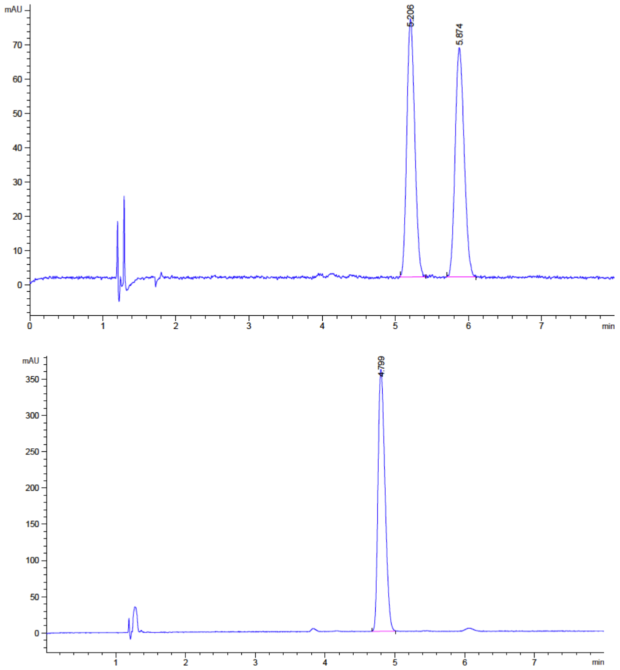


Dimethyl (*S*)-2-(2-(*m*-tolyl)but-3-en-2-yl)malonate (68)

Prepared according to General Procedures C and D and isolated as a yellow oil (13.7 mg, 0.050 mmol, 50% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.51 (s, 1H), 7.30–7.21 (m, 1H), 7.14 – 7.03 (m, 3H), 4.36 (s, 1H), 3.73 (s, 3H), 3.50 (s, 3H), 2.34 (s, 3H), 1.86 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.9, 168.1, 168.0, 138.8, 136.4, 128.9, 128.1, 124.4, 56.8, 54.6, 52.8, 52.4, 21.7, 15.9. IR (thin film, NaCl) 2925, 2332, 1737, 1443, 1316, 1226, 1152, 1026 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{15}H_{18}O_5$ $[M]^{+\bullet}$: 278.1149, found 278.1138. $[\alpha]_D^{23}$ +133.04 (*c* 1.0, $CHCl_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel IC-3 column, λ = 230.8 nm, t_R (min): major = 4.80, minor = 5.88.



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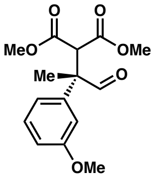
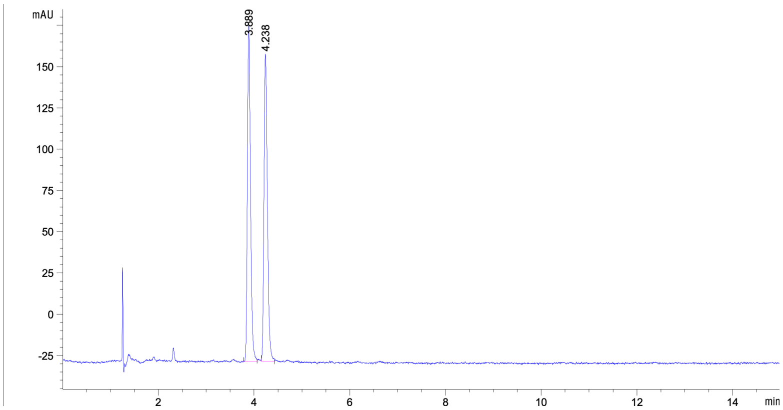
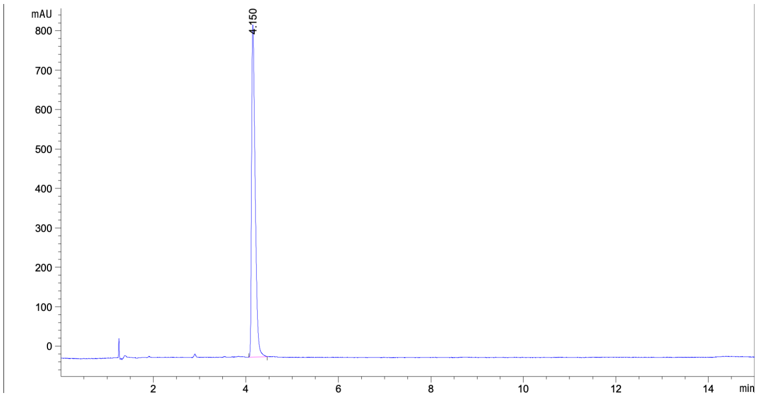


Dimethyl (*S*)-2-(2-(3-methoxyphenyl)-1-oxopropan-2-yl)malonate (69)

Prepared according to General Procedures C and D and isolated as a yellow oil (10.0 mg, 0.034 mmol, 34% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.52 (s, 1H), 7.31 – 7.27 (m, 1H), 6.88 – 6.79 (m, 3H), 4.36 (s, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.51 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.6, 167.9, 167.8, 160.0, 138.0, 129.9, 119.6, 113.6, 113.1, 56.7, 55.3, 54.5, 52.7, 52.4, 15.9. IR (thin film, NaCl) 2951, 2916, 2847, 1734, 1599, 1582, 1490, 1432, 1292, 1230, 1030, 891, 785, 698 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{15}H_{18}O_6$ $[M]^{+\bullet}$: 294.1098, found 294.1091. $[\alpha]_D^{23}$ +120.12 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel ID-3 column, λ = 210.8 nm, t_R (min): major = 4.15, minor = 3.89.





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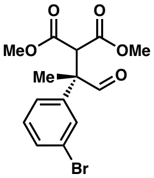
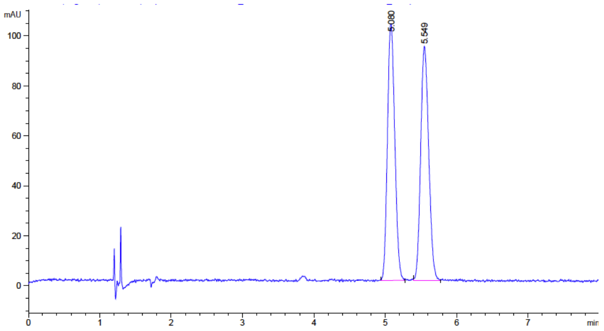
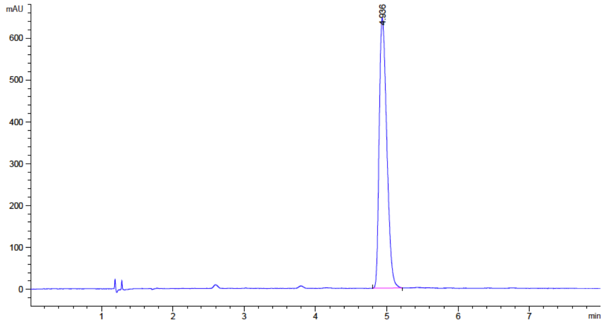
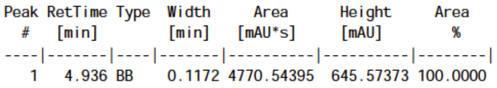


Dimethyl (*S*)-2-(2-(3-bromophenyl)but-3-en-2-yl)malonate (70)

Prepared according to General Procedures C and D and isolated as a yellow oil (12.9 mg, 0.038 mmol, 38% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.53 (s, 1H), 7.44 (dd, *J* = 6.1, 1.7 Hz, 2H), 7.29 – 7.18 (m, 2H), 4.32 (s, 1H), 3.72 (s, 3H), 3.53 (s, 3H), 1.84 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 198.6, 167.8, 167.7, 139.1, 131.4, 130.7, 130.5, 126.2, 123.3, 56.9, 54.4, 52.9, 52.6, 16.2. IR (thin film, NaCl) 3444, 2955, 2926, 2916, 2848, 1731, 1568, 1436, 1236, 1026, 908, 789 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{14}H_{16}O_5Br$ [M+H]$^+$: 343.0176, found 343.0191. $[\alpha]_D^{23}$ +106.01 (*c* 1.0, CHCl$_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel IC-3 column, λ = 230.8 nm, t_R (min): major = 4.94, minor = 5.55.







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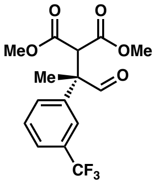
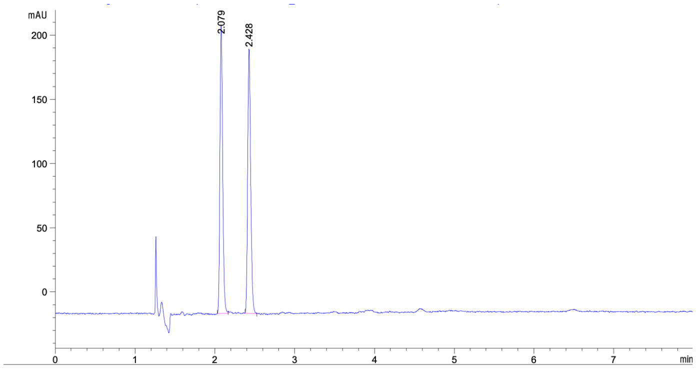
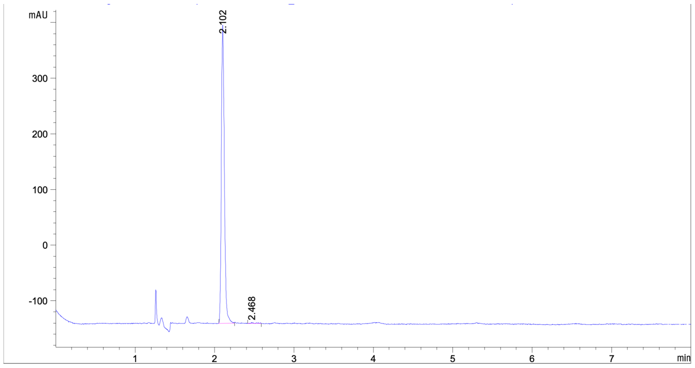


Dimethyl (*S*)-2-(1-oxo-2-(3-(trifluoromethyl)phenyl)propan-2-yl)malonate (71)

Prepared according to General Procedures C and D and isolated as a yellow oil (7.0 mg, 0.021 mmol, 21% yield over 2 steps, 99% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 7.62 – 7.54 (m, 2H), 7.52 – 7.48 (m, 2H), 4.35 (s, 1H), 3.73 (s, 3H), 3.51 (s, 3H), 1.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 167.4, 167.3, 137.7, 131.0 (q, *J* = 32.5 Hz), 130.8, 129.2, 124.7 (q, *J* = 4.2 Hz), 123.9 (q, *J* = 3.6 Hz), 56.8, 54.2, 52.6, 52.3, 29.5, 16.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5. IR (thin film, NaCl) 2915, 1733, 1434, 1327, 1123 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{15}H_{16}O_5F_3$ $[M+H]^+$: 333.0944, found 333.0958. $[\alpha]_D^{23}$ +67.22 (*c* 1.0, $CHCl_3$). SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 210.8 nm, t_R (min): major = 2.10, minor = 2.47.





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Peak RetTime Type  Width     Area       Height     Area
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  2   2.468 BB    0.0447    4.99526    1.39721   0.3538
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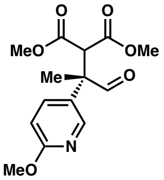
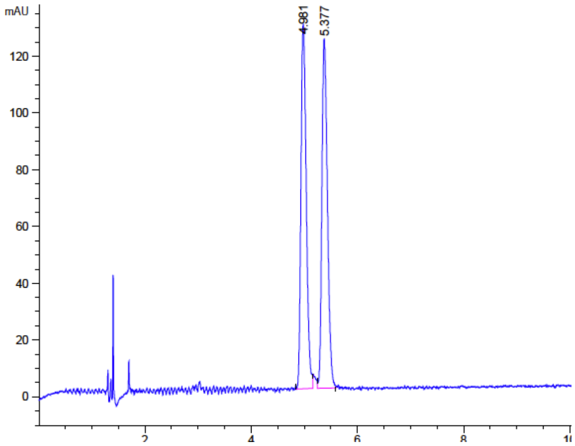
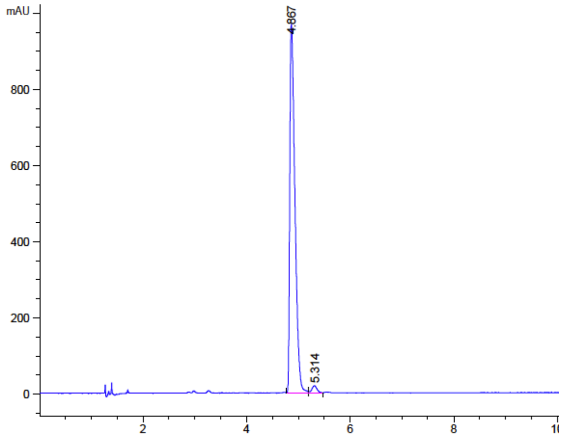


Dimethyl (*S*)-2-(2-(6-methoxypyridin-3-yl)but-3-en-2-yl)malonate (72)

Prepared according to General Procedures C and D and isolated as an orange oil (14.5 mg, 0.049 mmol, 49% yield over 2 steps, 96% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.51 (s, 1H), 8.10 (d, *J* = 2.7 Hz, 1H), 7.50 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 1H), 4.31 (s, 1H), 3.92 (s, 3H), 3.73 (s, 3H), 3.55 (s, 3H), 1.85 (s, 3H).^{13}C NMR (100 MHz, CDCl$_3$) δ 198.6, 167.82, 167.77, 163.9, 146.3, 138.0, 124.8, 111.2, 56.7, 53.7, 52.9, 52.6, 16.1. IR (thin film, NaCl) 2951, 1732, 1603, 1496, 1383, 1295, 1026 cm^{-1}. $[\alpha]_D^{23}$ +197.7 (*c* 1.0, CHCl$_3$). HRMS (MM:FD+) m/z calc'd for $C_{14}H_{17}NO_6$ $[M]^{+\bullet}$: 295.1050, found 295.1036. SFC Conditions: 3% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 4.87, minor = 5.31.





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  #   [min]        [min]   [mAU*s]     [mAU]       %
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   2   5.314 BB    0.1033  124.25487   18.29177   1.8091
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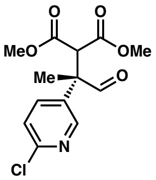
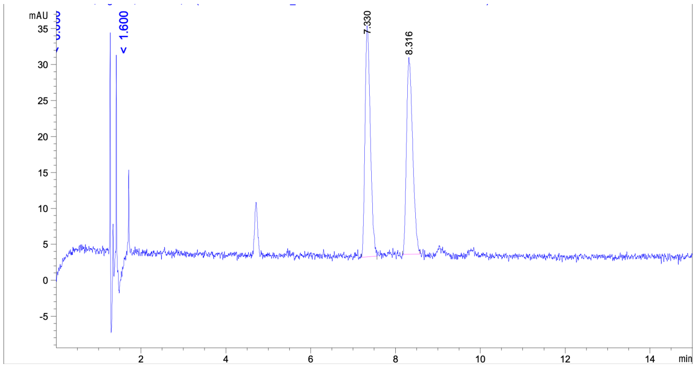
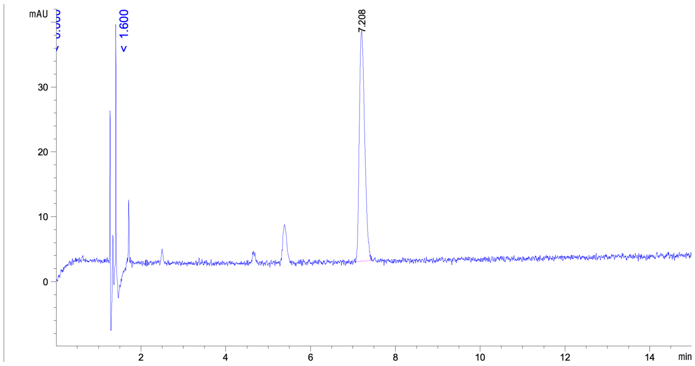


Dimethyl (*S*)-2-(2-(6-chloropyridin-3-yl)but-3-en-2-yl)malonate (73)

Prepared according to General Procedures C and D and isolated as a clear oil (16 mg, 0.053 mmol, 53% yield over 2 steps, >99% ee). ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.62 (s, 1H), 8.39

– 8.21 (m, 1H), 7.62 (dd, *J* = 8.5, 2.8 Hz, 1H), 7.33 (dd, *J* = 8.5, 0.7 Hz, 1H), 4.30 (s, 1H), 3.73 (s, 3H), 3.58 (s, 3H), 1.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 167.4, 167.3, 151.4, 148.9, 138.2, 131.7, 124.3, 56.9, 53.0, 52.7, 52.6, 16.7. IR (thin film, NaCl) 2952, 1731, 1465, 1163, 1017 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{13}H_{15}O_5NCl$ $[M+H]^+$: 300.0633, found 333.0619. $[\alpha]_D^{23}$ +38.92 (*c* 0.5, $CHCl_3$). SFC Conditions: 3% IPA, 2.5 mL/min, Chiralcel OD-3 column, λ = 230.8 nm, t_R (min): major = 7.21, minor = 8.32.





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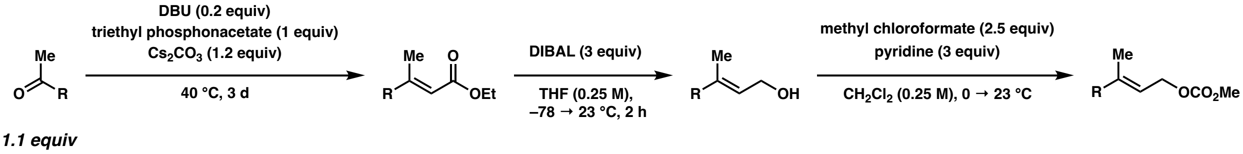
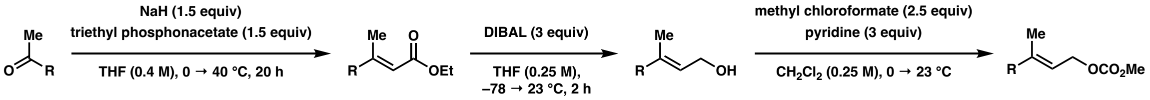
Synthesis of Allylic Electrophiles: General Procedure E



Method A: In accordance with a literature protocol,[37] a highly (*E*)-selective Horner-Wadsworth-Emmons reaction was utilized in the synthesis of the linear electrophiles. To a flame dried flask equipped with a large stir bar was added Cs_2CO_3 (1.2 equiv) and the acetophenone derivative (if solid, 1.1 equiv). The flask was purged and backfilled with N_2, at which point triethyl phosphonoacetate (1 equiv) was added via syringe, followed by DBU (20 mol%) and the acetophenone derivative (if liquid, 1.1 equiv). The mixture was heated to 40 ºC and stirred for 3 days. Minimal THF was used to rinse the sides of the flask and ensure even stirring over the course of the reaction, if necessary. After 3 days, the reaction mixture was diluted with water and ethyl acetate. Three extractions were performed with ethyl acetate, then the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The crude extract was purified by silica gel chromatography to afford the desired (*E*)-esters.

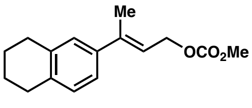
The purified ester was dissolved in THF (0.25 M) and transferred to a flame-dried flask, equipped with a stir bar under N_2 atmosphere. The flask was cooled to –78 ºC, then DIBAL-H (3 equiv) was added dropwise via syringe. The reaction was allowed to stir at 23 °C and monitored by TLC. Upon completion (typically 2 h), the reaction was quenched and concentrated following the Fieser protocol.[38] No further purification was needed.

The crude alcohol was dissolved in CH_2Cl_2 (0.25 M) and transferred to a flame-dried flask containing a stir bar under N_2 atmosphere. Freshly distilled pyridine (3 equiv) was added via syringe. The mixture was cooled to 0 ºC, and then methyl chloroformate (2.5 equiv) was added dropwise via syringe. The solution was observed to become radiantly yellow or orange during the addition of this reagent. The reaction was stirred at 23 °C and monitored by TLC. Upon completion (typically 2 h), the reaction was quenched with 1 M aq. HCl, and three extractions were performed with CH_2Cl_2. The combined organic layers were washed with saturated aq. $NaHCO_3$ solution, then dried with Na_2SO_4, filtered, and concentrated. The residue was purified via silica gel chromatography to deliver the desired allylic methyl carbonate.



Method B[8]: To a flame-dried round bottom flask was added NaH (60% dispersion in mineral oil, 1.5 equiv). The flask was purged and backfilled three times with N_2. Then THF (0.4 M) was added, and the resulting gray suspension was cooled to 0 °C and stirred. To the cooled suspension was added neat triethyl phosphonoacetate (1.5 equiv) dropwise, causing rapid gas evolution, and stirred for 30 minutes, during which time the solution became clear. The solution was allowed to warm to 23 °C, then heated to 40 °C using a metal heating block or oil bath. A solution of the acetophenone derivative (1.0 equiv, 1.0 M in THF) was added slowly to the reaction mixture. After stirring for 20 h, the mixture was cooled to 0 °C, diluted with Et_2O and quenched with water. The layers were separated and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude residue contained the desired (*E*)-alkene product in ratios ranging from 2:1 to 10:1 depending on the substrate. These geometric isomers were separated by silica gel flash column chromatography to afford the desired (*E*)-ester products.

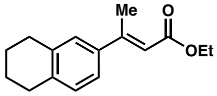
Subsequent synthetic steps performed in analogy to Method A.



(*E*)-methyl (3-(5,6,7,8-tetrahydronaphthalen-2-yl)but-2-en-1-yl) carbonate (67a)

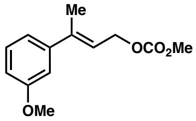
Prepared from **67b** according to General Procedure E and purified by silica gel chromatography (0–15% EtOAc/Hexanes) to afford **67a** as a clear oil (536 mg, 2.06 mmol, 41% yield over 3 steps). ^1H NMR (500 MHz, $CDCl_3$) δ 7.14 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.11 (d, *J* = 2.0 Hz, 1H), 7.03 (d, *J* = 7.9 Hz, 1H), 5.88 (td, *J* = 7.0, 1.5 Hz, 1H), 4.84 (d, *J* = 7.0

Hz, 2H), 3.80 (s, 3H), 2.77 (d, *J* = 5.3 Hz, 4H), 2.11 (d, *J* = 1.3 Hz, 3H), 1.80 (p, *J* = 3.3 Hz, 4H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 156.0, 141.3, 139.8, 137.1, 137.0, 129.2, 126.7, 123.2, 119.8, 65.2, 54.9, 29.6, 29.3, 23.4, 23.3, 16.4. IR (thin film, NaCl) 2925, 2355, 1747, 1442, 1267, 938, 826 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{16}H_{20}O_3$ [M]$^{+\bullet}$: 260.1407, found 260.1404.



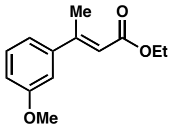
Ethyl (*E*)-3-(5,6,7,8-tetrahydronaphthalen-2-yl)but-2-enoate (67b)

Prepared via Method A of General Procedure E. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.22 (dd, *J* = 7.9, 2.1 Hz, 1H), 7.19 (d, *J* = 2.0 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 6.12 (d, *J* = 1.4 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.81 – 2.75 (m, 4H), 2.56 (s, 3H), 1.81 (p, *J* = 3.3 Hz, 4H), 1.32 (t, *J* = 7.1 Hz, 3H). Characterization data was in agreement with the literature.[39]



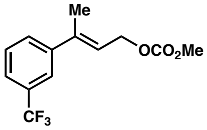
(*E*)-3-(3-methoxyphenyl)but-2-en-1-yl methyl carbonate (69a)

Prepared from **69b** according to General Procedure E and purified by silica gel chromatography (10% EtOAc/Hexanes) to afford **69a** as a clear oil (733 mg, 3.10 mmol, 62% yield over 3 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.27 – 7.22 (m, 1H), 7.00 (ddd, *J* = 7.7, 1.7, 0.9 Hz, 1H), 6.93 (t, *J* = 2.1 Hz, 1H), 6.83 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 5.93 (td, *J* = 7.0, 1.5 Hz, 1H), 4.85 (d, *J* = 7.0 Hz, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.7, 156.0, 144.1, 141.0, 129.4, 121.0, 118.6, 113.1, 111.9, 65.1, 55.4, 55.0, 16.5. IR (thin film, NaCl) 2954, 2348, 1747, 1578, 1440, 1256, 1045, 948 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{13}H_{16}O_4$ [M]$^{+\bullet}$: 236.1043, found 236.1044.



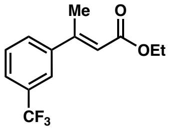
Ethyl (*E*)-3-(3-methoxyphenyl)but-2-enoate (69b)

Prepared via Method A of General Procedure E. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.29 (t, *J* = 8.0 Hz, 1H), 7.06 (ddd, *J* = 7.7, 1.7, 0.9 Hz, 1H), 6.99 (dd, *J* = 2.5, 1.7 Hz, 1H), 6.90 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.13 (q, *J* = 1.3 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 2.57 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). Characterization data was in agreement with the literature.[40]



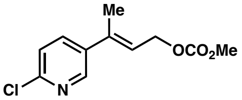
(*E*)-methyl (3-(3-(trifluoromethyl)phenyl)but-2-en-1-yl) carbonate (71a)

Prepared from **71b** according to General Procedure E and purified by silica gel chromatography (10% EtOAc/Hexanes) to afford **71a** as a clear oil (0.777 g, 2.83 mmol, 57% yield over 3 steps). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.70 – 7.33 (m, 4H), 5.98 (tt, *J* = 6.9, 1.3 Hz, 1H), 4.88 (d, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 155.8, 143.2, 139.6, 130.6 (q, *J* = 32.1 Hz), 129.2 (d, *J* = 1.5 Hz), 128.8, 124.3 (q, *J* = 3.8 Hz), 124.2 (q, *J* = 272.4 Hz), 122.7 (q, *J* = 3.9 Hz), 122.4, 64.7, 54.9, 16.2. ^{19}F NMR (376 MHz, CDCl$_3$) δ -62.5. IR (thin film, NaCl) 2959, 2357, 1746, 1444, 1380, 1328, 1265, 1119, 944, 797 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{13}H_{13}O_3F_3$ [M]$^{+\bullet}$: 274.0811, found 274.0816.



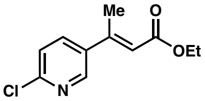
Ethyl (*E*)-3-(3-(trifluoromethyl)phenyl)but-2-enoate (71b)

Prepared via Method A of General Procedure E. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.70 (d, *J* = 1.8 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 6.15 (q, *J* = 1.3 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.60 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.6, 153.8, 143.2, 131.0 (q, *J* = 32.5 Hz), 129.72, 129.70, 129.2, 125.7 (q, *J* = 3.7 Hz) , 123.3 (q, *J* = 3.9 Hz), 118.8, 60.2, 18.1, 14.5. ^{19}F NMR (376 MHz, CDCl$_3$) δ -62.6. IR (thin film, NaCl) 3411, 2983, 1905, 1713, 1632, 1434, 1368, 1330, 1259, 1165, 1133,1073, 1043, 904, 874, 827,803, 728, 698, 658 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{13}H_{13}O_2F_3$ $[M]^{+\bullet}$: 258.0862, found 258.0873.



(*E*)-3-(6-chloropyridin-3-yl)but-2-en-1-yl methyl carbonate (73a)

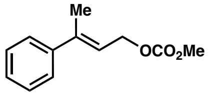
Prepared from **72b** according to General Procedure E and purified by silica gel chromatography (10–20% EtOAc/Hexanes) to afford **72a** as a clear solid (86 mg, 0.36 mmol, 18% yield over 3 steps). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.42 (d, *J* = 1.9 Hz, 1H), 7.65 (dd, *J* = 8.4, 2.6 Hz, 1H), 7.29 (dd, *J* = 8.4, 0.7 Hz, 1H), 5.95 (tq, *J* = 6.9, 1.4 Hz, 1H), 4.85 (d, *J* = 6.8 Hz, 2H), 3.81 (s, 3H), 2.12 (s, 3H).^{13}C NMR (100 MHz, CDCl$_3$) δ 155.8, 150.5, 147.1, 136.7, 136.0, 123.8, 123.1, 64.4, 55.0, 16.1. IR (thin film, NaCl) 1747, 1458, 1262, 1169, 942 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{11}H_{12}NO_3Cl$ $[M]^{+\bullet}$: 241.0500, found 241.0491.



Ethyl (*E*)-3-(6-chloropyridin-3-yl)but-2-enoate (73b)

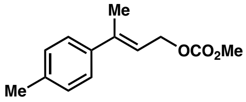
Prepared via Method A of General Procedure E. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.49 (dd, *J* = 2.7, 0.7 Hz, 1H), 7.72 (dd, *J* = 8.4, 2.6 Hz, 1H), 7.34 (dd, *J* = 8.4, 0.7 Hz, 1H), 6.13 (q, *J* = 1.4 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.56 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 166.2, 151.9, 150.6, 147.5, 136.7, 136.5, 124.2, 119.2, 60.4, 17.8, 14.4. IR (thin film, NaCl) 2980, 1713, 1630, 1458, 1276, 1168, 1109, 1041, 822 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{11}H_{12}NO_2Cl$ $[M]^{+\bullet}$: 225.0551, found 225.0541.

^{1}H NMR Data of Previously Synthesized Allylic Carbonate Electrophiles



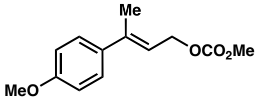
(*E*)-methyl (3-phenylbut-2-en-1-yl) carbonate (2a)

Prepared via Method A of General Procedure E (5.389 g, 26.1 mmol, 66% yield over 3 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 – 7.37 (m, 2H), 7.35 – 7.31 (m, 2H), 7.30 – 7.27 (m, 1H), 5.93 (tq, *J* = 7.0, 1.3 Hz, 1H), 4.86 (dd, *J* = 6.9, 0.9 Hz, 2H), 3.81 (s, 3H), 2.14 (s, 3H). Characterization data was in agreement with the literature.[8]



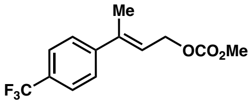
(*E*)-methyl (3-(p-tolyl)but-2-en-1-yl) carbonate (2h)

Prepared via Method B of General Procedure E. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.31 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 5.90 (tq, *J* = 7.1, 1.4 Hz, 1H), 4.85 (d, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 2.35 (s, 3H), 2.12 (s, 3H). Characterization data was in agreement with the literature.[8]



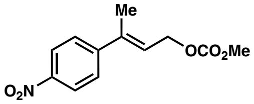
(*E*)-3-(4-methoxyphenyl)but-2-en-1-yl methyl carbonate (2i)

Prepared via Method B of General Procedure E. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.87 (td, *J* = 7.1, 1.4 Hz, 1H), 4.84 (d, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.80 (s, 3H), 2.11 (s, 3H). Characterization data was in agreement with the literature.[8]



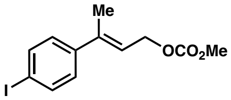
(*E*)-methyl (3-(4-(trifluoromethyl)phenyl)but-2-en-1-yl) carbonate (2c)

Prepared via Method A of General Procedure E (0.418 g, 1.52 mmol, 28% yield over 3 steps). ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.54 (dd, *J* = 52.4, 8.2 Hz, 4H), 5.97 (ddt, *J* = 6.9, 5.5, 1.4 Hz, 1H), 4.86 (d, *J* = 6.8 Hz, 2H), 3.81 (s, 3H), 2.14 (s, 3H). Characterization data was in agreement with the literature.[8]



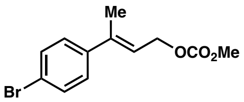
(*E*)-methyl (3-(4-nitrophenyl)but-2-en-1-yl) carbonate (2d)

Prepared via Method A of General Procedure E (0.601 g, 2.39 mmol, 48% yield over 3 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.19 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.9 Hz, 2H), 6.05 (tq, *J* = 6.8, 1.4 Hz, 1H), 4.88 (dd, *J* = 6.8, 1.0 Hz, 2H), 3.82 (s, 3H), 2.17 (s, 3H). Characterization data was in agreement with the literature.[8]



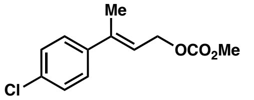
(*E*)-3-(4-iodophenyl)but-2-en-1-yl methyl carbonate (2e)

Prepared via Method A of General Procedure E (0.520 g, 1.57 mmol, 28% yield over 3 steps). ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.70 – 7.50 (m, 2H), 7.18 – 7.02 (m, 2H), 5.91 (tq, *J* = 6.9, 1.3 Hz, 1H), 4.83 (d, *J* = 6.9 Hz, 2H), 3.80 (s, 3H), 2.09 (s, 3H). Characterization data was in agreement with the literature.[8]



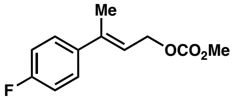
(*E*)-3-(4-bromophenyl)but-2-en-1-yl methyl carbonate (2f)

Prepared via Method B of General Procedure E. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 5.94 – 5.88 (m, 1H), 4.84 (d, *J* = 6.9 Hz, 2H), 3.81 (s, 3H), 2.11 (s, 3H). Characterization data was in agreement with the literature.[8]



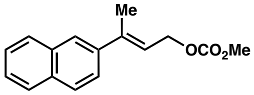
(*E*)-3-(4-chlorophenyl)but-2-en-1-yl methyl carbonate (2g)

Prepared via Method A of General Procedure E (0.385 g, 1.60 mmol, 29% yield over 3 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 4H), 5.90 (tq, *J* = 7.0, 1.4 Hz, 1H), 4.84 (d, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 2.10 (s, 3H). Characterization data was in agreement with the literature.[8]



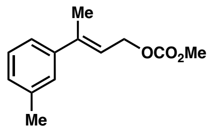
(*E*)-3-(4-fluorophenyl)but-2-en-1-yl methyl carbonate (65a)

Prepared via Method A of General Procedure E (0.435 g, 1.94 mmol, 39% yield over 3 steps). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.04 – 6.96 (m, 2H), 5.87 (td, *J* = 7.0, 1.5 Hz, 1H), 4.84 (d, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 2.11 (s, 3H). Characterization data was in agreement with the literature.[41]



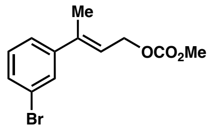
(*E*)-methyl (3-(naphthalen-2-yl)but-2-en-1-yl) carbonate (2b)

Prepared via Method B of General Procedure E. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 4H), 7.58 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.49 (tt, *J* = 6.9, 5.2 Hz, 2H), 6.08 (td, *J* = 7.0, 1.5 Hz, 1H), 4.92 (d, *J* = 7.0 Hz, 2H), 3.83 (s, 3H), 2.25 (s, 3H). Characterization data was in agreement with the literature.[8]



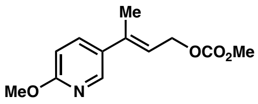
(*E*)-methyl (3-(m-tolyl)but-2-en-1-yl) carbonate (2m)

Prepared via Method A of General Procedure E (626 mg, 2.84 mmol, 57% yield over 3 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.25 – 7.17 (m, 2H), 7.13 – 7.07 (m, 2H), 5.91 (tt, *J* = 6.9, 1.4 Hz, 1H), 4.85 (d, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 2.36 (s, 3H), 2.13 (s, 3H). Characterization data was in agreement with the literature.[8]



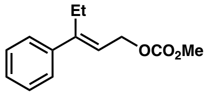
(*E*)-3-(3-bromophenyl)but-2-en-1-yl methyl carbonate (70a)

Prepared via Method A of General Procedure E (1.16 g, 4.07 mmol, 81% yield over 3 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.54 (t, *J* = 1.9 Hz, 1H), 7.40 (ddd, *J* = 7.9, 2.0, 1.0 Hz, 1H), 7.32 (ddd, *J* = 7.8, 1.8, 1.0 Hz, 1H), 7.20 (t, *J* = 7.9 Hz, 1H), 5.91 (tt, *J* = 6.9, 1.3 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 2H), 3.81 (s, 3H), 2.11 (s, 3H). Characterization data was in agreement with the literature.[41]



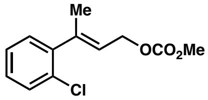
(*E*)-3-(6-methoxypyridin-3-yl)but-2-en-1-yl methyl carbonate (72a)

Prepared via Method A of General Procedure E (484 mg, 2.04 mmol, 41% yield over 3 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.24 – 8.10 (m, 1H), 7.62 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.70 (d, *J* = 8.6 Hz, 1H), 5.86 (tq, *J* = 7.0, 1.3 Hz, 1H), 4.83 (d, *J* = 7.0 Hz, 2H), 3.93 (s, 3H), 3.80 (s, 3H), 2.11 (s, 3H). Characterization data was in agreement with the literature.[42]



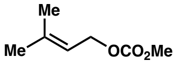
(*E*)-methyl (3-phenylpent-2-en-1-yl) carbonate (2s)

Prepared via Method B of General Procedure E. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.39 – 7.35 (m, 2H), 7.35 – 7.30 (m, 2H), 7.30 – 7.26 (m, 1H), 5.79 (t, *J* = 7.0 Hz, 1H), 4.85 (d, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 2.59 (q, *J* = 7.6 Hz, 2H), 1.01 (t, *J* = 7.5 Hz, 3H). Characterization data was in agreement with the literature.[8]



(*E*)-3-(2-chlorophenyl)but-2-en-1-yl methyl carbonate (2r)

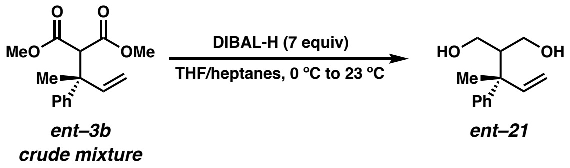
Prepared via Method B of General Procedure E. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38 – 7.31 (m, 1H), 7.25 – 7.14 (m, 3H), 5.60 (tt, *J* = 5.5, 1.5 Hz, 1H), 4.83 (d, *J* = 6.8 Hz, 2H), 3.81 (s, 3H), 2.08 (s, 3H). Characterization data was in agreement with the literature.[8]



Methyl (3-methylbut-2-en-1-yl) carbonate (2t)

Synthesized from prenol according to the final step in General Procedure E Method A (1.44 g, 10 mmol, quant.). ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.38 (tp, *J* = 7.2, 1.4 Hz, 1H), 4.63 (d, *J* = 7.3 Hz, 2H), 3.78 (s, 3H), 1.77 (s, 3H), 1.73 (s, 3H). Characterization data was in agreement with the literature.[8]

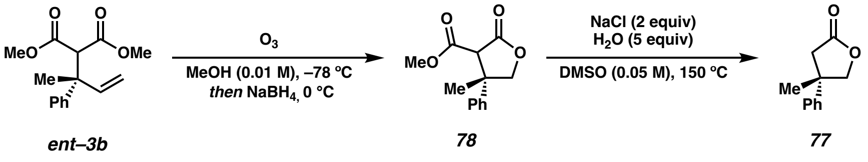
Derivatization of Allylic Alkylation Products



2-(2-phenylbut-3-en-2-yl)propane-1,3-diol (29)

Following General Procedure C, the crude mixture containing **ent–3b** was dissolved in THF (1 mL, 0.1 M) under N_2, and the vial was cooled to 0 ºC. DIBAL-H in heptanes (0.7 mL 1.0 M solution, 7 equiv) was added, and the reaction was allowed to warm to 23 °C. After stirring for 18 h, the reaction was quenched via the Fieser method.[10] The mixture was filtered, and concentrated. The crude residue was purified by preparatory TLC (100% EtOAc) to deliver **ent–21** as a clear oil (7.6 mg, 0.037 mmol, 37% over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 – 7.22 (m, 4H), 7.17 – 7.10 (m, 1H), 6.06 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.18 – 4.96 (m, 2H), 3.79 (ddd, *J* = 10.7, 3.3, 1.5 Hz, 1H), 3.73 – 3.58 (m, 3H), 2.62 – 2.18 (m, 3H), 1.31 (s, 3H). $[\alpha]_D^{23}$ 48.23 (*c* 0.3, $CHCl_3$).

Characterization data was in agreement with the literature.[8]



ent–3b
crude mixture

78

77

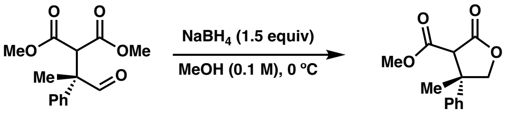
4-methyl-4-phenyldihydrofuran-2(3H)-one (77)

Following General Procedure C, the crude mixture containing **ent–3b** (0.2 mmol scale) was dissolved in MeOH (20 mL, 0.01 M) and a pipette tip of Sudan III was added. The flask was cooled to –78 ºC and O_2 gas was bubbled through the solution using a gas diffuser. After 5 min of vigorous O_2 flow, a VMUS-4 Ozone Generator was turned to the lowest ozone output setting. After 3 minutes, the color of the solution was observed to change from a vibrant red to a pale orange/brown color, and the ozonator was turned off. O_2 was bubbled through the solution for an additional 5 minutes, then the diffuser was removed. A stir bar was added to the flask, and a septum with an Ar balloon was affixed to the flask. The reaction was moved to a 0 °C bath and $NaBH_4$ (22.7 mg, 0.6 mmol, 3 equiv) was added slowly. The mixture was stirred at 0 ºC for 20 min. The reaction was quenched with NH_4Cl (6 mL) at 0 °C and then warmed to 23 ºC. Three extractions with CH_2Cl_2 were performed, and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated.

Purification by silica gel chromatography (20% EtOAc/Hexanes) afforded **31** as a clear oil (23 mg, 0.098 mmol 49% yield over 2 steps). ^{1}H NMR was consistent with that obtained for **78**.

To a flame-dried microwave vial equipped with a stir bar, was added lactone **78** (23 mg, 0.098 mmol, 1 equiv) and sodium chloride (11.4 mg, 0.196 mmol, 2 equiv), followed by water (8 μL, 0.49 mmol, 5 equiv) and DMSO (1.82 mL). The microwave vial was sealed then heated to 150 °C for 18 hours. The reaction was then cooled to 23 °C and diluted with water (3 mL) and brine (3 mL). The mixture was extracted three times with ethyl acetate, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. Purification by silica gel column chromatography (20% EtOAc/Hexanes) afforded **77** as a clear oil (13 mg, 0.074 mmol, 76% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.33 (m, 2H), 7.33 – 7.27 (m, 1H), 7.23 – 7.15 (m, 2H), 4.47 – 4.37 (m, 2H), 2.92 (d, *J* = 16.8 Hz, 1H), 2.68 (d, *J* = 17.5 Hz, 1H), 1.53 (s, 3H). $[\alpha]_D^{23}$ –16.30 (*c* 1.0, $CHCl_3$).

Characterization data was in agreement with the literature.[43]

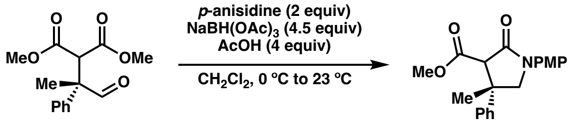


55 *78*

Methyl (4*S*)-4-methyl-2-oxo-4-phenyltetrahydrofuran-3-carboxylate (78)

To a flame-dried one-dram vial equipped with a stir bar and septum was added aldehyde **55** (26.5 mg, 0.1 mmol, 1 equiv) and MeOH (1 mL, 0.1 M) under N_2 atmosphere. The solution was cooled to 0 ºC. $NaBH_4$ (6 mg, 0.15 mmol, 1.5 equiv) was then added in a single portion, and the reaction was stirred at 0 °C for 20 minutes and monitored by TLC. Upon completion, the reaction was quenched with 1 mL sat. aq. NH_4Cl solution, and the mixture warmed to 23 °C. Three extractions with EtOAc were performed, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The material was purified via preparatory TLC (20% EtOAc/Hexanes) to afford **78** as a clear oil (17.4

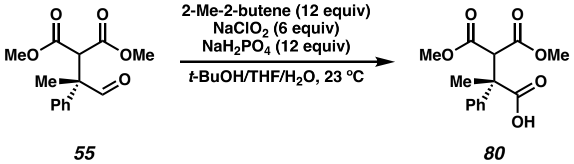
mg, 0.074 mmol, 74% yield, 1.2:1 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.27 (m, 4H), 7.15 – 7.09 (m, 1H), 5.08 (d, *J* = 8.3 Hz, 0.6H), 4.53 – 4.39 (m, 1.6H), 3.89 (s, 0.5H), 3.84 (s, 1.5H), 3.66 (s, 0.5H), 3.43 (s, 1.6H), 1.57 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 171.92, 171.87 167.4, 166.8, 143.2, 141.1, 129.3, 129.0, 127.8, 127.6, 125.5, 125.3, 77.8, 76.8, 59.1, 57.0, 52.9, 52.6, 48.5, 48.1, 29.9, 23.3. IR (thin film, NaCl) 2961, 2354, 1778, 1445, 1139, 1021, 763, 697 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{13}H_{14}O_4$ $[M]^{+\bullet}$: 234.0887, found 234.0886. $[\alpha]_D^{23}$ –21.48 (*c* 1.0, $CHCl_3$).



55 **79**

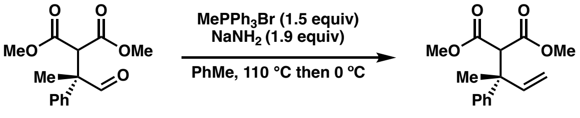
Methyl (4*S*)-1-(4-methoxyphenyl)-4-methyl-2-oxo-4-phenylpyrrolidine-3-carboxylate (79)

To a flame-dried one-dram vial equipped with a stir bar and septum was added aldehyde **55** (26.5 mg, 0.1 mmol, 1 equiv) and CH_2Cl_2 (0.5 mL, 0.2 M) under N_2 atmosphere. The solution was cooled to 0 ºC. AcOH (12 μL, 0.2 mmol, 2 equiv), *p*-anisidine (24.6 mg, 0.2 mmol, 2 equiv), and $NaBH(OAc)_3$ (53 mg, 0.25 mmol, 2.5 equiv) were then added successively to the reaction. The reaction was then slowly warmed to 23 °C and was monitored by LCMS. After 3.5 h, additional $NaBH(OAc)_3$ (42 mg, 0.2 mmol, 2 equiv) and AcOH (10 μL, 0.17 mmol, 1.7 equiv) were added. The reaction was stirred at 23 °C for an additional 18.5 h and monitored by LCMS. Upon completion, the reaction was quenched with H_2O. Three extractions with EtOAc were performed, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The material was purified via preparatory TLC (40% EtOAc/Hexanes) to afford **79** as a pale yellow oil (25.8 mg, 0.076 mmol, 76% yield, 1.7:1 dr). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.39 (m, 2H), 7.36 – 7.10 (m, 5H), 6.91 – 6.80 (m, 2H), 4.68 (d, *J* = 8.8 Hz, 0.6H), 4.09 – 3.89 (m, 0.7H), 3.87 (s, 0.4H), 3.74 (s, 3H), 3.73 – 3.70 (m, 1.7H), 3.66 (s, 0.6H), 3.33 (d, *J* = 0.7 Hz, 1.9H), 1.51 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 169.2, 168.8, 168.48, 168.45, 157.3, 157.2, 145.5, 143.1, 132.2, 131.9, 129.1, 128.8, 127.3, 127.1, 125.5, 125.4, 122.7, 122.2, 114.33, 114.29, 62.6, 60.8, 60.6, 58.9, 55.63, 55.61, 52.5, 52.2, 44.4, 43.7, 31.5, 24.4. IR (thin film, NaCl) 2953, 2340, 1738, 1695, 1514, 1322, 1297, 1248, 1032, 831 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{20}H_{21}NO_4$ $[M]^{+\bullet}$: 339.1465, found 339.1477. $[\alpha]_D^{23}$ –87.15 (*c* 1.0, CHCl$_3$).



(*S*)-4-methoxy-3-(methoxycarbonyl)-2-methyl-4-oxo-2-phenylbutanoic acid (80)

To a flame-dried one-dram vial equipped with a stir bar and septum was added aldehyde **55** (26.5 mg, 0.1 mmol, 1 equiv) and 2-Me-2-butene (127 μL, 1.2 mmol, 12 equiv) in *t*-BuOH (0.5 mL, 0.2 M) and THF (1 mL, 0.1 M) under N$_2$ atmosphere. To this mixture was added a solution of NaClO$_2$ (54 mg, 0.6 mmol, 6 equiv) and NaH$_2$PO$_4$ (144 mg, 1.2 mmol, 12 equiv) in H$_2$O (0.5 mL, 0.4 M) dropwise. The reaction was stirred at 23 °C for 6.5 h and monitored by LCMS. Upon completion, the reaction was quenched with 1 mL 1 M aq. HCl. The mixture was extracted with EtOAc three times, and the combined organic layers were washed with a sat. aq. Na$_2$SO$_3$ then dried with Na$_2$SO$_4$, filtered, and concentrated. The material was purified by preparatory TLC (0.5% AcOH/5% MeOH/94.5% CH$_2$Cl$_2$) to afford **80** as a white solid (16.4 mg, 0.059 mmol, 59% yield). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.41 – 7.33 (m, 2H), 7.30 – 7.16 (m, 3H), 4.46 (s, 1H), 3.66 (s, 3H), 3.36 (s, 3H), 1.88 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 179.5, 168.4, 167.9, 139.0, 128.7, 128.0, 126.5, 58.5, 52.8, 52.4, 51.0, 17.7. IR (thin film, NaCl) 2953, 1737, 1436, 1236, 1026 cm^{-1}. HRMS (MM:FD+) m/z calc'd for $C_{14}H_{17}O_6$ $[M+H]^+$: 281.1020, found 281.1007. $[\alpha]_D^{23}$ +134.17 (*c* 1.0, CHCl$_3$).

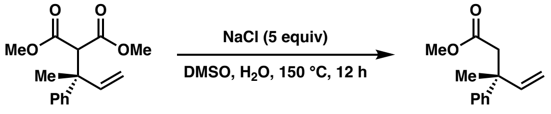


55 *5*

Dimethyl (*S*)-2-(2-phenylbut-3-en-2-yl)malonate (ent–3b)

In accordance with a literature protocol,[44] an oven dried two-neck conical flask equipped with a stir bar and reflux condenser was charged with $MePPh_3Br$ (536 mg, 15 equiv, 1.5 mmol) and $NaNH_2$ (146 mg, 18.8 equiv, 1.88 mmol) in toluene (5 mL) under N_2 atmosphere. After 2 h, the resulting yellow suspension was cooled to 23 °C, and the solids were allowed to settle to the bottom of the flask over 16 h. To a separate flame-dried 25 mL flask equipped with a stir bar, was added aldehyde **55** (26.5 mg, 0.1 mmol, 1 equiv) in PhMe (2 mL, 0.05 M) under N_2 atmosphere. The solution was then cooled to 0 ºC. To this mixture was added the methylene ylide solution (0.2 mL, 0.6 mmol, 6 equiv) (no solids) dropwise. The reaction was stirred at 0 ºC for 5 h and monitored by TLC. Upon completion, the reaction was diluted with Et_2O (10 mL) and quenched with sat. aq. NaCl (10 mL). The aqueous phase was extracted three times with Et_2O, and the combined organics were dried with Na_2SO_4, filtered, and concentrated. The material was purified by silica gel chromatography (0–10% EtOAc/Hexanes) to afford **ent–3b** as a clear oil (13 mg, 0.05 mmol, 50% yield). Characterization was in agreement with the literature.[8]

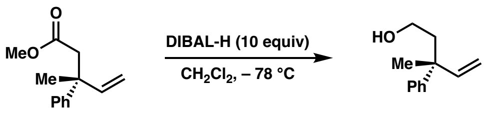
Synthetic Sequence toward Pharmaceutically Relevant Enantioenriched Azepane Motif (81)



ent–3b *81*

Methyl (*R*)-3-methyl-3-phenylpent-4-enoate (81)

To a flame-dried microwave vial equipped with a stir bar was added NaCl (13 mg, 0.22 mmol, 5 equiv). A solution of **ent–3b** (11 mg, 0.042 mmol, 1 equiv) in DMSO (0.8 mL, 0.05 M) was introduced, followed by H_2O (8 µL, 0.44 mmol, 10 equiv). The reaction was sealed and heated to 150 ºC for 12 h. The reaction was then cooled to 23 °C and diluted with water (2 mL) and brine (2 mL). Three extractions were performed with Et_2O, then the organic phase was washed two times with brine in an effort to remove residual DMSO. The residue was purified by preparatory TLC (20% EtOAc/Hexanes) to afford ester **81** as a clear, volatile liquid (8.6 mg, 0.042 mmol, quant.). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 4H), 7.16 (ddd, *J* = 8.5, 5.9, 2.4 Hz, 1H), 6.10 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.19 – 5.04 (m, 2H), 3.48 (s, 3H), 2.78 – 2.71 (m, 2H), 1.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 146.2, 145.5, 128.4, 128.3, 126.5, 126.4, 126.4, 112.6, 51.4, 45.6, 43.5, 25.6. IR (thin film, NaCl) 2361, 1732, 822 cm^{-1}. HRMS (MM:FI+) m/z calc'd for $C_{13}H_{16}O_2$ $[M]^{+\bullet}$: 204.1145, found 204.1136. $[\alpha]_D^{23}$ -56.14 (*c* 1.0, $CHCl_3$).

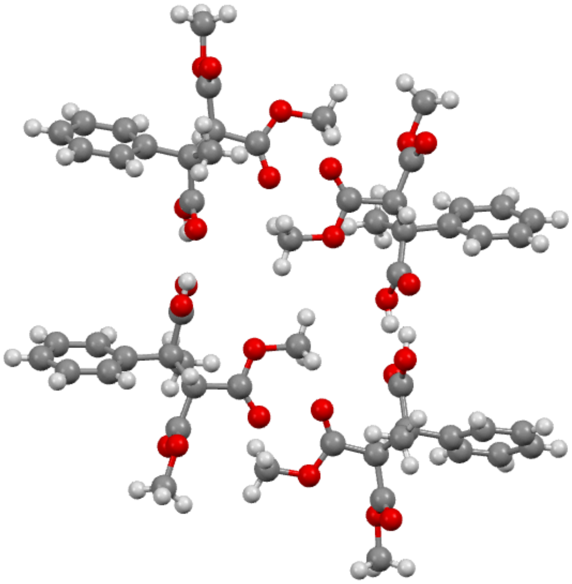


81 *82*

(*R*)-3-methyl-3-phenylpent-4-en-1-ol (82)

To a flame-dried 10 mL round bottom flask and stir bar was added ester **81** (4.3 mg, 0.02 mmol) in CH_2Cl_2 (1 mL, 0.02 M) under N_2 atmosphere. The flask was cooled to –78 ºC and then DIBAL-H (0.04 mL, 0.2 mmol, 10 equiv) was added dropwise via syringe. The mixture was then slowly warmed to 23 ºC. The reaction was stirred at 23 °C for 2 h and monitored by TLC. Upon completion, the reaction was quenched following the Fieser protocol,[10] and the resultant solution was filtered, and concentrated. The residue was purified by preparatory TLC (50% EtOAc/Hexanes) to deliver alcohol **82** as a clear oil (2.9 mg, 0.016 mmol, 82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 4H), 7.24 – 7.17 (m, 1H), 6.06 (dd, *J* = 17.5, 10.7 Hz, 1H), 5.17 – 5.07 (m, 2H), 3.74 – 3.53 (m, 2H), 2.11 (dddd, *J* = 38.5, 13.8, 8.6, 6.1 Hz, 2H), 1.43 (s, 3H). $[\alpha]_D^{23}$ -10.00. (*c* 0.1, $CHCl_3$). Characterization data was in agreement with the literature.[23]

2.5.3 CRYSTAL STRUCTURE ANALYSIS OF (*S*)-4-METHOXY-3-(METHOXYCARBONYL)-2-METHYL-4-OXO-2-PHENYLBUTANOIC ACID (CSD2414384)



Compound **80** was crystallized by rotary evaporation of the sample in $CDCl_3$, followed by further drying under vacuum to provide crystals suitable for X-ray analsysis. Compound V24319_t4 (CSD2414384) crystallizes in the triclinic space group P1 with four molecules in the asymmetric unit.

Table 2.9. *Crystal data and structure refinement for V24319_t4.*

Identification code	V24319_t4
Empirical formula	C14 H16 O6
Formula weight	280.27
Temperature	100(2) K
Wavelength	1.54178 Å

Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 6.0838(4) Å	a= 96.716(4)°.
	b = 14.8985(11) Å	b= 90.717(8)°.
	c = 15.1604(7) Å	g = 95.622(6)°.
Volume	1357.74(15) Å3	
Z	4	
Density (calculated)	1.371 Mg/m3	
Absorption coefficient	0.911 mm-1	
F(000)	592	
Crystal size	0.200 x 0.200 x 0.150 mm3	
Theta range for data collection	2.936 to 74.534°.	
Index ranges	?<=h<=?, ?<=k<=?, ?<=l<=?	
Reflections collected	10269	
Independent reflections	10269 [R(int) = ?]	
Completeness to theta = 67.679°	99.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.753817 and 0.646780	
Refinement method	Full-matrix least-squares on F2	
Data / restraints / parameters	10269 / 7 / 745	
Goodness-of-fit on F2	1.043	
Final R indices [I>2sigma(I)]	R1 = 0.0299, wR2 = 0.0765	
R indices (all data)	R1 = 0.0318, wR2 = 0.0775	
Absolute structure parameter	0.01(6)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.169 and -0.202 e.Å-3	

Table 2.10. *Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103)for V24319_t4. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.*

	x	y	z	U(eq)
C(1)	8567(4)	2133(1)	2127(2)	16(1)
C(2)	10400(4)	2172(2)	1587(2)	22(1)
C(3)	10249(5)	1787(2)	705(2)	28(1)
C(4)	8267(5)	1348(2)	346(2)	28(1)
C(5)	6445(5)	1302(2)	878(2)	31(1)
C(6)	6576(4)	1699(2)	1757(2)	23(1)
C(7)	8735(3)	2621(1)	3086(2)	14(1)
C(9)	11025(3)	2611(2)	3517(2)	18(1)
C(10)	8349(4)	3608(2)	2964(2)	14(1)
O(1)	9872(2)	4209(1)	2979(1)	17(1)
O(2)	6279(2)	3720(1)	2783(1)	18(1)
C(8)	6882(3)	2218(1)	3665(1)	13(1)
C(11)	6812(4)	1186(1)	3640(1)	14(1)
O(3)	8385(3)	764(1)	3669(1)	20(1)
O(4)	4705(2)	821(1)	3592(1)	17(1)
C(12)	4373(4)	-158(2)	3596(2)	22(1)
C(13)	7059(3)	2629(2)	4636(2)	16(1)
O(5)	6987(3)	2197(1)	5259(1)	20(1)
O(6)	7232(3)	3535(1)	4694(1)	21(1)
C(14)	7369(5)	4010(2)	5593(2)	29(1)
C(21)	7416(3)	6612(1)	944(1)	13(1)
C(22)	5656(4)	6175(2)	414(2)	21(1)
C(23)	5901(4)	5924(2)	-489(2)	26(1)
C(24)	7921(4)	6105(2)	-878(2)	22(1)
C(25)	9695(4)	6531(2)	-357(2)	22(1)
C(26)	9451(4)	6780(2)	547(2)	18(1)
C(27)	7123(3)	6834(1)	1955(1)	12(1)

C(29)	4786(3)	7096(2)	2172(2)	15(1)
O(21)	5920(2)	5409(1)	2506(1)	16(1)
O(22)	9550(2)	5780(1)	2384(1)	14(1)
C(30)	7468(3)	5944(1)	2331(1)	12(1)
C(28)	8916(3)	7582(1)	2363(1)	13(1)
C(31)	8951(4)	8468(2)	1949(1)	14(1)
O(23)	7366(3)	8826(1)	1749(1)	20(1)
O(24)	11055(3)	8804(1)	1852(1)	21(1)
C(32)	11309(5)	9695(2)	1544(2)	30(1)
C(33)	8684(3)	7755(1)	3369(2)	13(1)
O(25)	8216(3)	7167(1)	3833(1)	18(1)
O(26)	9119(3)	8634(1)	3656(1)	16(1)
C(34)	8950(4)	8884(2)	4604(2)	18(1)
C(41)	1603(4)	3539(1)	9069(2)	15(1)
C(42)	77(4)	4003(2)	9579(2)	20(1)
C(43)	520(4)	4305(2)	10476(2)	25(1)
C(44)	2469(4)	4143(2)	10877(2)	25(1)
C(45)	4000(4)	3682(2)	10382(2)	23(1)
C(46)	3571(4)	3385(2)	9483(2)	18(1)
C(47)	1145(3)	3281(1)	8062(1)	13(1)
C(49)	-1335(3)	3043(2)	7837(2)	16(1)
O(41)	4106(3)	4310(1)	7610(1)	18(1)
O(42)	650(3)	4686(1)	7488(1)	19(1)
C(50)	2055(4)	4144(1)	7671(1)	13(1)
C(48)	2501(3)	2510(1)	7680(1)	13(1)
C(51)	2075(4)	1643(1)	8120(1)	15(1)
O(43)	304(3)	1302(1)	8315(1)	24(1)
O(44)	3992(3)	1293(1)	8249(1)	21(1)
C(52)	3754(5)	419(2)	8585(2)	30(1)
C(53)	2141(3)	2313(1)	6674(2)	13(1)
O(45)	1952(3)	2892(1)	6195(1)	20(1)
O(46)	2118(3)	1432(1)	6404(1)	16(1)
C(54)	1860(4)	1172(2)	5454(2)	19(1)
C(61)	5859(4)	7874(1)	7801(2)	15(1)

C(62)	7906(4)	8327(2)	8083(2)	23(1)
C(63)	8221(4)	8770(2)	8945(2)	29(1)
C(64)	6521(5)	8762(2)	9541(2)	25(1)
C(65)	4457(5)	8333(2)	9262(2)	25(1)
C(66)	4133(4)	7900(2)	8401(2)	20(1)
C(67)	5487(3)	7353(1)	6860(1)	14(1)
C(69)	7644(3)	7275(2)	6357(2)	17(1)
O(61)	2430(3)	6269(1)	7148(1)	19(1)
O(62)	5792(3)	5787(1)	7014(1)	18(1)
C(70)	4455(3)	6399(2)	7005(1)	13(1)
C(68)	3751(3)	7805(1)	6336(2)	13(1)
C(71)	4067(4)	8842(2)	6409(1)	15(1)
O(63)	2544(3)	9297(1)	6485(1)	23(1)
O(64)	6178(3)	9164(1)	6369(1)	17(1)
C(72)	6668(4)	10145(2)	6446(2)	23(1)
C(73)	3548(3)	7428(2)	5356(2)	14(1)
O(65)	3637(3)	7885(1)	4750(1)	19(1)
O(66)	3200(3)	6524(1)	5266(1)	19(1)
C(74)	2981(5)	6078(2)	4360(2)	25(1)

Table 2.11. *Bond lengths [Å] and angles [°] for V24319_t4.*

C(1)-C(2)	1.393(3)
C(1)-C(6)	1.394(3)
C(1)-C(7)	1.545(3)
C(2)-C(3)	1.390(4)
C(2)-H(2)	0.9500
C(3)-C(4)	1.387(4)
C(3)-H(3)	0.9500
C(4)-C(5)	1.380(4)
C(4)-H(4)	0.9500
C(5)-C(6)	1.391(4)
C(5)-H(5)	0.9500
C(6)-H(6)	0.9500
C(7)-C(9)	1.534(3)
C(7)-C(10)	1.542(3)
C(7)-C(8)	1.556(3)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-O(1)	1.222(3)
C(10)-O(2)	1.316(3)
O(2)-H(2O)	0.83(2)
C(8)-C(13)	1.525(3)
C(8)-C(11)	1.529(3)
C(8)-H(8)	1.0000
C(11)-O(3)	1.199(3)
C(11)-O(4)	1.340(3)
O(4)-C(12)	1.452(3)
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-O(5)	1.202(3)

C(13)-O(6)	1.335(3)
O(6)-C(14)	1.458(3)
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(21)-C(22)	1.391(3)
C(21)-C(26)	1.397(3)
C(21)-C(27)	1.545(3)
C(22)-C(23)	1.390(3)
C(22)-H(22)	0.9500
C(23)-C(24)	1.386(4)
C(23)-H(23)	0.9500
C(24)-C(25)	1.385(4)
C(24)-H(24)	0.9500
C(25)-C(26)	1.391(3)
C(25)-H(25)	0.9500
C(26)-H(26)	0.9500
C(27)-C(30)	1.535(3)
C(27)-C(29)	1.540(3)
C(27)-C(28)	1.549(3)
C(29)-H(29A)	0.9800
C(29)-H(29B)	0.9800
C(29)-H(29C)	0.9800
O(21)-C(30)	1.225(3)
O(22)-C(30)	1.317(3)
O(22)-H(22O)	0.86(2)
C(28)-C(31)	1.525(3)
C(28)-C(33)	1.527(3)
C(28)-H(28)	1.0000
C(31)-O(23)	1.199(3)
C(31)-O(24)	1.344(3)
O(24)-C(32)	1.452(3)
C(32)-H(32A)	0.9800
C(32)-H(32B)	0.9800

C(32)-H(32C)	0.9800
C(33)-O(25)	1.202(3)
C(33)-O(26)	1.331(3)
O(26)-C(34)	1.450(3)
C(34)-H(34A)	0.9800
C(34)-H(34B)	0.9800
C(34)-H(34C)	0.9800
C(41)-C(46)	1.396(3)
C(41)-C(42)	1.399(3)
C(41)-C(47)	1.545(3)
C(42)-C(43)	1.395(3)
C(42)-H(42)	0.9500
C(43)-C(44)	1.381(4)
C(43)-H(43)	0.9500
C(44)-C(45)	1.388(4)
C(44)-H(44)	0.9500
C(45)-C(46)	1.396(3)
C(45)-H(45)	0.9500
C(46)-H(46)	0.9500
C(47)-C(50)	1.535(3)
C(47)-C(49)	1.540(3)
C(47)-C(48)	1.541(3)
C(49)-H(49A)	0.9800
C(49)-H(49B)	0.9800
C(49)-H(49C)	0.9800
O(41)-C(50)	1.255(3)
O(42)-C(50)	1.282(3)
O(42)-H(42O)	0.85(2)
C(48)-C(51)	1.524(3)
C(48)-C(53)	1.528(3)
C(48)-H(48)	1.0000
C(51)-O(43)	1.201(3)
C(51)-O(44)	1.345(3)
O(44)-C(52)	1.448(3)

C(52)-H(52A)	0.9800
C(52)-H(52B)	0.9800
C(52)-H(52C)	0.9800
C(53)-O(45)	1.203(3)
C(53)-O(46)	1.327(3)
O(46)-C(54)	1.450(3)
C(54)-H(54A)	0.9800
C(54)-H(54B)	0.9800
C(54)-H(54C)	0.9800
C(61)-C(62)	1.394(3)
C(61)-C(66)	1.398(3)
C(61)-C(67)	1.546(3)
C(62)-C(63)	1.396(4)
C(62)-H(62)	0.9500
C(63)-C(64)	1.381(4)
C(63)-H(63)	0.9500
C(64)-C(65)	1.389(4)
C(64)-H(64)	0.9500
C(65)-C(66)	1.390(3)
C(65)-H(65)	0.9500
C(66)-H(66)	0.9500
C(67)-C(69)	1.534(3)
C(67)-C(70)	1.537(3)
C(67)-C(68)	1.563(3)
C(69)-H(69A)	0.9800
C(69)-H(69B)	0.9800
C(69)-H(69C)	0.9800
O(61)-C(70)	1.254(3)
O(62)-C(70)	1.282(3)
O(62)-H(62O)	0.87(2)
C(68)-C(73)	1.525(3)
C(68)-C(71)	1.528(3)
C(68)-H(68)	1.0000
C(71)-O(63)	1.200(3)

C(71)-O(64)	1.331(3)
O(64)-C(72)	1.453(3)
C(72)-H(72A)	0.9800
C(72)-H(72B)	0.9800
C(72)-H(72C)	0.9800
C(73)-O(65)	1.205(3)
C(73)-O(66)	1.333(3)
O(66)-C(74)	1.453(3)
C(74)-H(74A)	0.9800
C(74)-H(74B)	0.9800
C(74)-H(74C)	0.9800
C(2)-C(1)-C(6)	118.1(2)
C(2)-C(1)-C(7)	120.0(2)
C(6)-C(1)-C(7)	121.85(19)
C(3)-C(2)-C(1)	120.9(2)
C(3)-C(2)-H(2)	119.5
C(1)-C(2)-H(2)	119.5
C(4)-C(3)-C(2)	120.5(2)
C(4)-C(3)-H(3)	119.7
C(2)-C(3)-H(3)	119.7
C(5)-C(4)-C(3)	118.9(2)
C(5)-C(4)-H(4)	120.5
C(3)-C(4)-H(4)	120.5
C(4)-C(5)-C(6)	120.8(3)
C(4)-C(5)-H(5)	119.6
C(6)-C(5)-H(5)	119.6
C(5)-C(6)-C(1)	120.7(2)
C(5)-C(6)-H(6)	119.6
C(1)-C(6)-H(6)	119.6
C(9)-C(7)-C(10)	109.25(18)
C(9)-C(7)-C(1)	112.38(17)
C(10)-C(7)-C(1)	103.34(17)
C(9)-C(7)-C(8)	111.27(17)

C(10)-C(7)-C(8)	109.38(16)
C(1)-C(7)-C(8)	110.90(17)
C(7)-C(9)-H(9A)	109.5
C(7)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(7)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
O(1)-C(10)-O(2)	123.9(2)
O(1)-C(10)-C(7)	121.99(19)
O(2)-C(10)-C(7)	113.97(18)
C(10)-O(2)-H(2O)	110(2)
C(13)-C(8)-C(11)	107.93(17)
C(13)-C(8)-C(7)	113.25(17)
C(11)-C(8)-C(7)	112.77(17)
C(13)-C(8)-H(8)	107.5
C(11)-C(8)-H(8)	107.5
C(7)-C(8)-H(8)	107.5
O(3)-C(11)-O(4)	124.8(2)
O(3)-C(11)-C(8)	125.8(2)
O(4)-C(11)-C(8)	109.47(17)
C(11)-O(4)-C(12)	115.77(17)
O(4)-C(12)-H(12A)	109.5
O(4)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
O(4)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
O(5)-C(13)-O(6)	125.1(2)
O(5)-C(13)-C(8)	124.6(2)
O(6)-C(13)-C(8)	110.27(18)
C(13)-O(6)-C(14)	115.53(19)
O(6)-C(14)-H(14A)	109.5
O(6)-C(14)-H(14B)	109.5

H(14A)-C(14)-H(14B)	109.5
O(6)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(22)-C(21)-C(26)	118.2(2)
C(22)-C(21)-C(27)	119.74(19)
C(26)-C(21)-C(27)	121.93(19)
C(23)-C(22)-C(21)	121.1(2)
C(23)-C(22)-H(22)	119.5
C(21)-C(22)-H(22)	119.5
C(24)-C(23)-C(22)	120.2(2)
C(24)-C(23)-H(23)	119.9
C(22)-C(23)-H(23)	119.9
C(25)-C(24)-C(23)	119.4(2)
C(25)-C(24)-H(24)	120.3
C(23)-C(24)-H(24)	120.3
C(24)-C(25)-C(26)	120.4(2)
C(24)-C(25)-H(25)	119.8
C(26)-C(25)-H(25)	119.8
C(25)-C(26)-C(21)	120.7(2)
C(25)-C(26)-H(26)	119.6
C(21)-C(26)-H(26)	119.6
C(30)-C(27)-C(29)	109.43(17)
C(30)-C(27)-C(21)	104.16(16)
C(29)-C(27)-C(21)	111.82(17)
C(30)-C(27)-C(28)	108.77(17)
C(29)-C(27)-C(28)	111.18(16)
C(21)-C(27)-C(28)	111.20(16)
C(27)-C(29)-H(29A)	109.5
C(27)-C(29)-H(29B)	109.5
H(29A)-C(29)-H(29B)	109.5
C(27)-C(29)-H(29C)	109.5
H(29A)-C(29)-H(29C)	109.5
H(29B)-C(29)-H(29C)	109.5

C(30)-O(22)-H(22O)	111(2)
O(21)-C(30)-O(22)	123.39(19)
O(21)-C(30)-C(27)	122.31(18)
O(22)-C(30)-C(27)	114.11(18)
C(31)-C(28)-C(33)	110.65(17)
C(31)-C(28)-C(27)	113.89(17)
C(33)-C(28)-C(27)	110.52(17)
C(31)-C(28)-H(28)	107.1
C(33)-C(28)-H(28)	107.1
C(27)-C(28)-H(28)	107.1
O(23)-C(31)-O(24)	124.4(2)
O(23)-C(31)-C(28)	126.0(2)
O(24)-C(31)-C(28)	109.51(18)
C(31)-O(24)-C(32)	114.69(19)
O(24)-C(32)-H(32A)	109.5
O(24)-C(32)-H(32B)	109.5
H(32A)-C(32)-H(32B)	109.5
O(24)-C(32)-H(32C)	109.5
H(32A)-C(32)-H(32C)	109.5
H(32B)-C(32)-H(32C)	109.5
O(25)-C(33)-O(26)	125.2(2)
O(25)-C(33)-C(28)	123.88(19)
O(26)-C(33)-C(28)	110.87(17)
C(33)-O(26)-C(34)	115.96(17)
O(26)-C(34)-H(34A)	109.5
O(26)-C(34)-H(34B)	109.5
H(34A)-C(34)-H(34B)	109.5
O(26)-C(34)-H(34C)	109.5
H(34A)-C(34)-H(34C)	109.5
H(34B)-C(34)-H(34C)	109.5
C(46)-C(41)-C(42)	118.1(2)
C(46)-C(41)-C(47)	122.27(18)
C(42)-C(41)-C(47)	119.4(2)
C(43)-C(42)-C(41)	120.7(2)

C(43)-C(42)-H(42)	119.6
C(41)-C(42)-H(42)	119.6
C(44)-C(43)-C(42)	120.5(2)
C(44)-C(43)-H(43)	119.8
C(42)-C(43)-H(43)	119.8
C(43)-C(44)-C(45)	119.6(2)
C(43)-C(44)-H(44)	120.2
C(45)-C(44)-H(44)	120.2
C(44)-C(45)-C(46)	120.1(2)
C(44)-C(45)-H(45)	119.9
C(46)-C(45)-H(45)	119.9
C(45)-C(46)-C(41)	120.9(2)
C(45)-C(46)-H(46)	119.5
C(41)-C(46)-H(46)	119.5
C(50)-C(47)-C(49)	111.39(18)
C(50)-C(47)-C(48)	107.21(16)
C(49)-C(47)-C(48)	111.19(17)
C(50)-C(47)-C(41)	102.71(16)
C(49)-C(47)-C(41)	112.27(17)
C(48)-C(47)-C(41)	111.68(17)
C(47)-C(49)-H(49A)	109.5
C(47)-C(49)-H(49B)	109.5
H(49A)-C(49)-H(49B)	109.5
C(47)-C(49)-H(49C)	109.5
H(49A)-C(49)-H(49C)	109.5
H(49B)-C(49)-H(49C)	109.5
C(50)-O(42)-H(42O)	114(2)
O(41)-C(50)-O(42)	123.9(2)
O(41)-C(50)-C(47)	119.05(19)
O(42)-C(50)-C(47)	116.81(19)
C(51)-C(48)-C(53)	110.79(17)
C(51)-C(48)-C(47)	113.91(17)
C(53)-C(48)-C(47)	110.62(17)
C(51)-C(48)-H(48)	107.1

C(53)-C(48)-H(48)	107.1
C(47)-C(48)-H(48)	107.1
O(43)-C(51)-O(44)	124.0(2)
O(43)-C(51)-C(48)	126.1(2)
O(44)-C(51)-C(48)	109.91(18)
C(51)-O(44)-C(52)	114.4(2)
O(44)-C(52)-H(52A)	109.5
O(44)-C(52)-H(52B)	109.5
H(52A)-C(52)-H(52B)	109.5
O(44)-C(52)-H(52C)	109.5
H(52A)-C(52)-H(52C)	109.5
H(52B)-C(52)-H(52C)	109.5
O(45)-C(53)-O(46)	125.1(2)
O(45)-C(53)-C(48)	123.67(19)
O(46)-C(53)-C(48)	111.20(18)
C(53)-O(46)-C(54)	115.81(17)
O(46)-C(54)-H(54A)	109.5
O(46)-C(54)-H(54B)	109.5
H(54A)-C(54)-H(54B)	109.5
O(46)-C(54)-H(54C)	109.5
H(54A)-C(54)-H(54C)	109.5
H(54B)-C(54)-H(54C)	109.5
C(62)-C(61)-C(66)	117.9(2)
C(62)-C(61)-C(67)	121.66(19)
C(66)-C(61)-C(67)	120.5(2)
C(61)-C(62)-C(63)	120.6(2)
C(61)-C(62)-H(62)	119.7
C(63)-C(62)-H(62)	119.7
C(64)-C(63)-C(62)	120.8(2)
C(64)-C(63)-H(63)	119.6
C(62)-C(63)-H(63)	119.6
C(63)-C(64)-C(65)	119.1(2)
C(63)-C(64)-H(64)	120.4
C(65)-C(64)-H(64)	120.4

C(64)-C(65)-C(66)	120.1(2)
C(64)-C(65)-H(65)	119.9
C(66)-C(65)-H(65)	119.9
C(65)-C(66)-C(61)	121.3(2)
C(65)-C(66)-H(66)	119.3
C(61)-C(66)-H(66)	119.3
C(69)-C(67)-C(70)	109.39(17)
C(69)-C(67)-C(61)	112.62(18)
C(70)-C(67)-C(61)	105.25(17)
C(69)-C(67)-C(68)	112.17(18)
C(70)-C(67)-C(68)	107.62(17)
C(61)-C(67)-C(68)	109.45(17)
C(67)-C(69)-H(69A)	109.5
C(67)-C(69)-H(69B)	109.5
H(69A)-C(69)-H(69B)	109.5
C(67)-C(69)-H(69C)	109.5
H(69A)-C(69)-H(69C)	109.5
H(69B)-C(69)-H(69C)	109.5
C(70)-O(62)-H(62O)	112(2)
O(61)-C(70)-O(62)	123.8(2)
O(61)-C(70)-C(67)	119.88(19)
O(62)-C(70)-C(67)	116.21(18)
C(73)-C(68)-C(71)	108.71(17)
C(73)-C(68)-C(67)	112.87(17)
C(71)-C(68)-C(67)	115.66(17)
C(73)-C(68)-H(68)	106.3
C(71)-C(68)-H(68)	106.3
C(67)-C(68)-H(68)	106.3
O(63)-C(71)-O(64)	125.1(2)
O(63)-C(71)-C(68)	122.34(19)
O(64)-C(71)-C(68)	112.61(18)
C(71)-O(64)-C(72)	117.15(18)
O(64)-C(72)-H(72A)	109.5
O(64)-C(72)-H(72B)	109.5

H(72A)-C(72)-H(72B)	109.5
O(64)-C(72)-H(72C)	109.5
H(72A)-C(72)-H(72C)	109.5
H(72B)-C(72)-H(72C)	109.5
O(65)-C(73)-O(66)	124.9(2)
O(65)-C(73)-C(68)	124.6(2)
O(66)-C(73)-C(68)	110.42(18)
C(73)-O(66)-C(74)	115.95(18)
O(66)-C(74)-H(74A)	109.5
O(66)-C(74)-H(74B)	109.5
H(74A)-C(74)-H(74B)	109.5
O(66)-C(74)-H(74C)	109.5
H(74A)-C(74)-H(74C)	109.5
H(74B)-C(74)-H(74C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 2.12. *Anisotropic displacement parameters (Å2x 103) for V24319_t4. The anisotropic displacement factor exponent takes the form: -2p2[h2 a*2U11 + ... + 2 h k a* b* U12]*

	U11	U22	U33	U23	U13	U12
C(1)	18(1)	13(1)	17(1)	7(1)	2(1)	4(1)
C(2)	22(1)	17(1)	27(1)	4(1)	8(1)	-1(1)
C(3)	35(1)	23(1)	26(1)	3(1)	15(1)	0(1)
C(4)	42(2)	24(1)	18(1)	2(1)	6(1)	-1(1)
C(5)	35(1)	35(1)	20(1)	3(1)	-2(1)	-7(1)
C(6)	20(1)	30(1)	19(1)	4(1)	3(1)	-2(1)
C(7)	12(1)	13(1)	19(1)	6(1)	1(1)	2(1)
C(9)	11(1)	17(1)	26(1)	8(1)	0(1)	2(1)
C(10)	14(1)	15(1)	14(1)	4(1)	1(1)	2(1)
O(1)	14(1)	15(1)	23(1)	6(1)	-2(1)	1(1)
O(2)	13(1)	13(1)	28(1)	8(1)	-2(1)	2(1)
C(8)	11(1)	13(1)	16(1)	4(1)	1(1)	2(1)
C(11)	16(1)	14(1)	13(1)	4(1)	1(1)	0(1)
O(3)	16(1)	16(1)	30(1)	7(1)	1(1)	4(1)
O(4)	14(1)	14(1)	22(1)	2(1)	0(1)	-1(1)
C(12)	22(1)	14(1)	29(1)	2(1)	1(1)	-4(1)
C(13)	11(1)	16(1)	21(1)	3(1)	2(1)	2(1)
O(5)	24(1)	20(1)	18(1)	6(1)	1(1)	1(1)
O(6)	30(1)	14(1)	18(1)	0(1)	2(1)	4(1)
C(14)	44(2)	21(1)	21(1)	-4(1)	2(1)	5(1)
C(21)	17(1)	10(1)	14(1)	3(1)	-1(1)	3(1)
C(22)	18(1)	21(1)	22(1)	-1(1)	-2(1)	1(1)
C(23)	26(1)	27(1)	22(1)	-5(1)	-8(1)	3(1)
C(24)	32(1)	22(1)	14(1)	0(1)	-2(1)	9(1)
C(25)	25(1)	24(1)	18(1)	4(1)	5(1)	3(1)
C(26)	18(1)	19(1)	17(1)	1(1)	-1(1)	1(1)
C(27)	11(1)	11(1)	13(1)	2(1)	-1(1)	1(1)

C(29)	13(1)	15(1)	19(1)	2(1)	0(1)	3(1)
O(21)	13(1)	13(1)	22(1)	5(1)	0(1)	0(1)
O(22)	12(1)	12(1)	19(1)	6(1)	0(1)	2(1)
C(30)	14(1)	12(1)	10(1)	-1(1)	0(1)	2(1)
C(28)	12(1)	12(1)	14(1)	2(1)	-1(1)	0(1)
C(31)	19(1)	12(1)	11(1)	0(1)	1(1)	-1(1)
O(23)	23(1)	16(1)	21(1)	6(1)	-3(1)	2(1)
O(24)	20(1)	16(1)	26(1)	7(1)	2(1)	-4(1)
C(32)	36(1)	21(1)	34(1)	14(1)	-1(1)	-9(1)
C(33)	10(1)	12(1)	16(1)	2(1)	-1(1)	2(1)
O(25)	24(1)	15(1)	15(1)	4(1)	1(1)	0(1)
O(26)	21(1)	11(1)	13(1)	0(1)	0(1)	-1(1)
C(34)	24(1)	16(1)	12(1)	-1(1)	-2(1)	1(1)
C(41)	19(1)	11(1)	14(1)	3(1)	3(1)	-1(1)
C(42)	23(1)	18(1)	19(1)	1(1)	2(1)	6(1)
C(43)	30(1)	21(1)	22(1)	-3(1)	7(1)	3(1)
C(44)	34(1)	22(1)	15(1)	-2(1)	2(1)	-7(1)
C(45)	20(1)	28(1)	20(1)	3(1)	-2(1)	-4(1)
C(46)	16(1)	19(1)	16(1)	1(1)	2(1)	-1(1)
C(47)	14(1)	11(1)	14(1)	1(1)	1(1)	1(1)
C(49)	13(1)	16(1)	19(1)	2(1)	2(1)	1(1)
O(41)	16(1)	16(1)	22(1)	3(1)	2(1)	-2(1)
O(42)	21(1)	13(1)	24(1)	6(1)	-1(1)	3(1)
C(50)	15(1)	12(1)	11(1)	-2(1)	-1(1)	2(1)
C(48)	13(1)	13(1)	13(1)	1(1)	0(1)	1(1)
C(51)	22(1)	12(1)	12(1)	0(1)	1(1)	4(1)
O(43)	28(1)	19(1)	27(1)	6(1)	10(1)	2(1)
O(44)	26(1)	16(1)	24(1)	6(1)	-5(1)	6(1)
C(52)	50(2)	17(1)	26(1)	7(1)	-8(1)	10(1)
C(53)	11(1)	12(1)	16(1)	1(1)	2(1)	0(1)
O(45)	27(1)	15(1)	17(1)	4(1)	1(1)	2(1)
O(46)	22(1)	12(1)	14(1)	0(1)	1(1)	2(1)
C(54)	24(1)	17(1)	14(1)	-2(1)	0(1)	0(1)
C(61)	18(1)	12(1)	16(1)	6(1)	-2(1)	2(1)

C(62)	19(1)	28(1)	22(1)	1(1)	-2(1)	1(1)
C(63)	24(1)	31(1)	29(1)	-2(1)	-11(1)	1(1)
C(64)	38(1)	21(1)	16(1)	2(1)	-8(1)	6(1)
C(65)	34(1)	22(1)	18(1)	3(1)	4(1)	0(1)
C(66)	22(1)	18(1)	21(1)	2(1)	2(1)	-2(1)
C(67)	13(1)	14(1)	15(1)	4(1)	-1(1)	2(1)
C(69)	13(1)	18(1)	20(1)	6(1)	1(1)	2(1)
O(61)	15(1)	16(1)	25(1)	5(1)	2(1)	-1(1)
O(62)	20(1)	14(1)	21(1)	5(1)	2(1)	3(1)
C(70)	14(1)	15(1)	11(1)	2(1)	-1(1)	2(1)
C(68)	11(1)	13(1)	16(1)	3(1)	0(1)	1(1)
C(71)	18(1)	15(1)	11(1)	2(1)	0(1)	1(1)
O(63)	20(1)	17(1)	33(1)	2(1)	1(1)	7(1)
O(64)	17(1)	12(1)	22(1)	4(1)	2(1)	-1(1)
C(72)	28(1)	13(1)	26(1)	1(1)	5(1)	-3(1)
C(73)	12(1)	14(1)	17(1)	2(1)	-1(1)	1(1)
O(65)	22(1)	19(1)	17(1)	5(1)	0(1)	1(1)
O(66)	25(1)	14(1)	18(1)	1(1)	-3(1)	0(1)
C(74)	34(1)	20(1)	19(1)	-4(1)	-5(1)	3(1)

Table 2.13. *Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 10 3)for V24319_t4.*

	x	y	z	U(eq)
H(2)	11773	2466	1824	27
H(3)	11513	1826	344	33
H(4)	8165	1083	-256	34
H(5)	5085	996	641	37
H(6)	5295	1675	2109	28
H(9A)	12125	2971	3202	27
H(9B)	11404	1983	3483	27
H(9C)	11009	2871	4141	27
H(2O)	6160(50)	4262(16)	2720(20)	26
H(8)	5436	2355	3419	16
H(12A)	5192	-454	3110	33
H(12B)	2796	-363	3514	33
H(12C)	4908	-317	4164	33
H(14A)	6049	3822	5915	43
H(14B)	7467	4666	5566	43
H(14C)	8686	3860	5901	43
H(22)	4264	6046	673	25
H(23)	4680	5627	-841	31
H(24)	8087	5939	-1496	27
H(25)	11087	6653	-619	27
H(26)	10682	7069	898	22
H(29A)	3709	6564	2025	23
H(29B)	4440	7580	1822	23
H(29C)	4723	7311	2806	23
H(22O)	9670(50)	5290(17)	2620(20)	21
H(28)	10381	7345	2252	15
H(32A)	10687	9654	940	45

H(32B)	12881	9915	1546	45
H(32C)	10530	10119	1940	45
H(34A)	7576	8585	4811	26
H(34B)	8947	9544	4729	26
H(34C)	10213	8690	4915	26
H(42)	-1276	4114	9313	24
H(43)	-527	4624	10812	30
H(44)	2760	4347	11489	30
H(45)	5343	3568	10655	28
H(46)	4633	3073	9148	21
H(49A)	-2121	3580	7994	24
H(49B)	-1922	2554	8175	24
H(49C)	-1539	2843	7200	24
H(42O)	1230(50)	5203(17)	7390(20)	29
H(48)	4095	2735	7791	16
H(52A)	3122	485	9178	45
H(52B)	5206	191	8621	45
H(52C)	2773	-10	8184	45
H(54A)	418	1320	5251	28
H(54B)	1956	517	5322	28
H(54C)	3033	1503	5149	28
H(62)	9098	8335	7684	28
H(63)	9623	9080	9125	35
H(64)	6761	9046	10133	30
H(65)	3265	8337	9661	30
H(66)	2710	7615	8216	24
H(69A)	8677	6984	6705	25
H(69B)	8300	7882	6262	25
H(69C)	7332	6907	5781	25
H(62O)	5190(50)	5306(18)	7220(20)	27
H(68)	2286	7643	6598	16
H(72A)	6356	10359	5875	34
H(72B)	8231	10307	6611	34
H(72C)	5749	10429	6903	34

H(74A)	1775	6312	4050	37
H(74B)	2656	5422	4368	37
H(74C)	4364	6200	4051	37

Table 2.14. *Torsion angles [°] for V24319_t4.*

C(6)-C(1)-C(2)-C(3)	-0.2(3)
C(7)-C(1)-C(2)-C(3)	-175.9(2)
C(1)-C(2)-C(3)-C(4)	-0.6(4)
C(2)-C(3)-C(4)-C(5)	0.3(4)
C(3)-C(4)-C(5)-C(6)	0.8(4)
C(4)-C(5)-C(6)-C(1)	-1.7(4)
C(2)-C(1)-C(6)-C(5)	1.3(4)
C(7)-C(1)-C(6)-C(5)	176.9(2)
C(2)-C(1)-C(7)-C(9)	-34.2(3)
C(6)-C(1)-C(7)-C(9)	150.4(2)
C(2)-C(1)-C(7)-C(10)	83.5(2)
C(6)-C(1)-C(7)-C(10)	-92.0(2)
C(2)-C(1)-C(7)-C(8)	-159.40(19)
C(6)-C(1)-C(7)-C(8)	25.1(3)
C(9)-C(7)-C(10)-O(1)	18.6(3)
C(1)-C(7)-C(10)-O(1)	-101.2(2)
C(8)-C(7)-C(10)-O(1)	140.6(2)
C(9)-C(7)-C(10)-O(2)	-165.94(18)
C(1)-C(7)-C(10)-O(2)	74.2(2)
C(8)-C(7)-C(10)-O(2)	-43.9(2)
C(9)-C(7)-C(8)-C(13)	50.2(2)
C(10)-C(7)-C(8)-C(13)	-70.6(2)
C(1)-C(7)-C(8)-C(13)	176.03(17)
C(9)-C(7)-C(8)-C(11)	-72.8(2)
C(10)-C(7)-C(8)-C(11)	166.43(18)
C(1)-C(7)-C(8)-C(11)	53.1(2)
C(13)-C(8)-C(11)-O(3)	-84.0(3)
C(7)-C(8)-C(11)-O(3)	41.9(3)
C(13)-C(8)-C(11)-O(4)	95.1(2)
C(7)-C(8)-C(11)-O(4)	-139.06(18)
O(3)-C(11)-O(4)-C(12)	1.2(3)

C(8)-C(11)-O(4)-C(12)	-177.85(19)
C(11)-C(8)-C(13)-O(5)	-5.0(3)
C(7)-C(8)-C(13)-O(5)	-130.6(2)
C(11)-C(8)-C(13)-O(6)	177.08(17)
C(7)-C(8)-C(13)-O(6)	51.5(2)
O(5)-C(13)-O(6)-C(14)	0.9(3)
C(8)-C(13)-O(6)-C(14)	178.84(19)
C(26)-C(21)-C(22)-C(23)	-0.9(3)
C(27)-C(21)-C(22)-C(23)	-176.6(2)
C(21)-C(22)-C(23)-C(24)	0.1(4)
C(22)-C(23)-C(24)-C(25)	0.6(4)
C(23)-C(24)-C(25)-C(26)	-0.4(4)
C(24)-C(25)-C(26)-C(21)	-0.4(4)
C(22)-C(21)-C(26)-C(25)	1.1(3)
C(27)-C(21)-C(26)-C(25)	176.7(2)
C(22)-C(21)-C(27)-C(30)	82.3(2)
C(26)-C(21)-C(27)-C(30)	-93.3(2)
C(22)-C(21)-C(27)-C(29)	-35.8(3)
C(26)-C(21)-C(27)-C(29)	148.6(2)
C(22)-C(21)-C(27)-C(28)	-160.76(19)
C(26)-C(21)-C(27)-C(28)	23.7(3)
C(29)-C(27)-C(30)-O(21)	21.2(3)
C(21)-C(27)-C(30)-O(21)	-98.5(2)
C(28)-C(27)-C(30)-O(21)	142.8(2)
C(29)-C(27)-C(30)-O(22)	-163.64(18)
C(21)-C(27)-C(30)-O(22)	76.7(2)
C(28)-C(27)-C(30)-O(22)	-42.0(2)
C(30)-C(27)-C(28)-C(31)	172.09(17)
C(29)-C(27)-C(28)-C(31)	-67.4(2)
C(21)-C(27)-C(28)-C(31)	58.0(2)
C(30)-C(27)-C(28)-C(33)	-62.6(2)
C(29)-C(27)-C(28)-C(33)	57.9(2)
C(21)-C(27)-C(28)-C(33)	-176.76(16)
C(33)-C(28)-C(31)-O(23)	-83.6(3)

C(27)-C(28)-C(31)-O(23)	41.6(3)
C(33)-C(28)-C(31)-O(24)	95.4(2)
C(27)-C(28)-C(31)-O(24)	-139.40(18)
O(23)-C(31)-O(24)-C(32)	4.8(3)
C(28)-C(31)-O(24)-C(32)	-174.1(2)
C(31)-C(28)-C(33)-O(25)	166.0(2)
C(27)-C(28)-C(33)-O(25)	38.9(3)
C(31)-C(28)-C(33)-O(26)	-15.5(2)
C(27)-C(28)-C(33)-O(26)	-142.58(17)
O(25)-C(33)-O(26)-C(34)	-1.6(3)
C(28)-C(33)-O(26)-C(34)	179.94(17)
C(46)-C(41)-C(42)-C(43)	0.3(3)
C(47)-C(41)-C(42)-C(43)	-175.2(2)
C(41)-C(42)-C(43)-C(44)	-0.6(4)
C(42)-C(43)-C(44)-C(45)	0.4(4)
C(43)-C(44)-C(45)-C(46)	0.1(4)
C(44)-C(45)-C(46)-C(41)	-0.4(4)
C(42)-C(41)-C(46)-C(45)	0.2(3)
C(47)-C(41)-C(46)-C(45)	175.6(2)
C(46)-C(41)-C(47)-C(50)	-89.9(2)
C(42)-C(41)-C(47)-C(50)	85.4(2)
C(46)-C(41)-C(47)-C(49)	150.3(2)
C(42)-C(41)-C(47)-C(49)	-34.4(3)
C(46)-C(41)-C(47)-C(48)	24.7(3)
C(42)-C(41)-C(47)-C(48)	-160.06(19)
C(49)-C(47)-C(50)-O(41)	-163.29(19)
C(48)-C(47)-C(50)-O(41)	-41.4(3)
C(41)-C(47)-C(50)-O(41)	76.3(2)
C(49)-C(47)-C(50)-O(42)	21.7(3)
C(48)-C(47)-C(50)-O(42)	143.59(19)
C(41)-C(47)-C(50)-O(42)	-98.6(2)
C(50)-C(47)-C(48)-C(51)	170.13(18)
C(49)-C(47)-C(48)-C(51)	-67.9(2)
C(41)-C(47)-C(48)-C(51)	58.4(2)

C(50)-C(47)-C(48)-C(53)	-64.3(2)
C(49)-C(47)-C(48)-C(53)	57.7(2)
C(41)-C(47)-C(48)-C(53)	-176.06(17)
C(53)-C(48)-C(51)-O(43)	-82.8(3)
C(47)-C(48)-C(51)-O(43)	42.7(3)
C(53)-C(48)-C(51)-O(44)	96.2(2)
C(47)-C(48)-C(51)-O(44)	-138.35(19)
O(43)-C(51)-O(44)-C(52)	4.7(3)
C(48)-C(51)-O(44)-C(52)	-174.30(19)
C(51)-C(48)-C(53)-O(45)	165.2(2)
C(47)-C(48)-C(53)-O(45)	37.8(3)
C(51)-C(48)-C(53)-O(46)	-16.3(2)
C(47)-C(48)-C(53)-O(46)	-143.57(17)
O(45)-C(53)-O(46)-C(54)	0.5(3)
C(48)-C(53)-O(46)-C(54)	-178.02(17)
C(66)-C(61)-C(62)-C(63)	1.7(4)
C(67)-C(61)-C(62)-C(63)	-178.0(2)
C(61)-C(62)-C(63)-C(64)	0.6(4)
C(62)-C(63)-C(64)-C(65)	-2.3(4)
C(63)-C(64)-C(65)-C(66)	1.6(4)
C(64)-C(65)-C(66)-C(61)	0.7(4)
C(62)-C(61)-C(66)-C(65)	-2.3(3)
C(67)-C(61)-C(66)-C(65)	177.4(2)
C(62)-C(61)-C(67)-C(69)	8.9(3)
C(66)-C(61)-C(67)-C(69)	-170.8(2)
C(62)-C(61)-C(67)-C(70)	128.0(2)
C(66)-C(61)-C(67)-C(70)	-51.7(2)
C(62)-C(61)-C(67)-C(68)	-116.6(2)
C(66)-C(61)-C(67)-C(68)	63.7(2)
C(69)-C(67)-C(70)-O(61)	-158.2(2)
C(61)-C(67)-C(70)-O(61)	80.6(2)
C(68)-C(67)-C(70)-O(61)	-36.1(3)
C(69)-C(67)-C(70)-O(62)	25.2(3)
C(61)-C(67)-C(70)-O(62)	-96.0(2)

C(68)-C(67)-C(70)-O(62)	147.31(19)
C(69)-C(67)-C(68)-C(73)	45.3(2)
C(70)-C(67)-C(68)-C(73)	-75.1(2)
C(61)-C(67)-C(68)-C(73)	171.05(16)
C(69)-C(67)-C(68)-C(71)	-80.8(2)
C(70)-C(67)-C(68)-C(71)	158.84(17)
C(61)-C(67)-C(68)-C(71)	45.0(2)
C(73)-C(68)-C(71)-O(63)	92.3(2)
C(67)-C(68)-C(71)-O(63)	-139.5(2)
C(73)-C(68)-C(71)-O(64)	-87.1(2)
C(67)-C(68)-C(71)-O(64)	41.1(3)
O(63)-C(71)-O(64)-C(72)	1.5(3)
C(68)-C(71)-O(64)-C(72)	-179.10(19)
C(71)-C(68)-C(73)-O(65)	0.3(3)
C(67)-C(68)-C(73)-O(65)	-129.4(2)
C(71)-C(68)-C(73)-O(66)	-178.04(17)
C(67)-C(68)-C(73)-O(66)	52.2(2)
O(65)-C(73)-O(66)-C(74)	1.8(3)
C(68)-C(73)-O(66)-C(74)	-179.86(18)

Symmetry transformations used to generate equivalent atoms:

Table 2.15. *Hydrogen bonds for V24319_t4 [Å and °].*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(12)-H(12A)...O(23)#1	0.98	2.64	3.622(3)	176.7
C(12)-H(12B)...O(26)#2	0.98	2.59	3.519(3)	158.0
C(14)-H(14C)...O(45)#3	0.98	2.63	3.547(3)	155.9
O(22)-H(22O)...O(1)	0.86(2)	1.78(2)	2.628(2)	173(3)
C(34)-H(34A)...O(64)	0.98	2.60	3.188(3)	118.6
C(34)-H(34A)...O(65)	0.98	2.51	3.444(3)	158.3
C(34)-H(34B)...O(3)#4	0.98	2.61	3.329(3)	130.6
C(34)-H(34C)...O(65)#3	0.98	2.50	3.359(3)	145.6
O(42)-H(42O)...O(61)	0.85(2)	1.76(2)	2.606(2)	178(3)
C(52)-H(52C)...O(63)#1	0.98	2.66	3.454(3)	138.6
C(54)-H(54A)...O(5)#5	0.98	2.57	3.491(3)	156.7
C(54)-H(54C)...O(5)	0.98	2.52	3.368(3)	144.9
O(62)-H(62O)...O(41)	0.87(2)	1.73(2)	2.599(2)	177(3)
C(72)-H(72C)...O(44)#4	0.98	2.58	3.552(3)	169.7
C(74)-H(74A)...O(25)#5	0.98	2.65	3.583(3)	158.5

Symmetry transformations used to generate equivalent atoms:
#1 x,y-1,z #2 x-1,y-1,z #3 x+1,y,z #4 x,y+1,z
#5 x-1,y,z

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