CHAPTER 1

Ir-Catalyzed Asymmetric Allylic Alkylation of Dialkyl Malonates Enabling the Construction of Enantioenriched All-Carbon Quaternary Centers[†]

1.1 INTRODUCTION

The enantioselective construction of acyclic all-carbon quaternary centers is a challenging problem in synthetic organic chemistry.[1] Ir-catalyzed asymmetric allylic alkylation has emerged as a powerful methodology for the formation of acyclic stereogenic centers, owing to its exquisite branched regioselectivity.[2] While the enantioselective construction of tertiary stereocenters by virtue of this methodology is well-precedented,[3] the generation of enantioenriched all-carbon quaternary centers by Ir-catalysis remains underexplored.

Expanding on prior reports,[4] Carreira and coworkers disclosed an Ir-catalyzed process that forges enantioenriched quaternary products from silyl ketene acetal nucleophiles and tertiary allenylic alcohol electrophiles (Figure 1.1A).[5] In contrast, our group has most recently utilized linear trisubstituted electrophiles in concert with masked acyl cyanide[6] (Figure 1.1B, R = OMOM) and substituted malononitrile[7] nucleophiles (Figure 1B, R = alkyl) for the formation of all-carbon quaternary centers.

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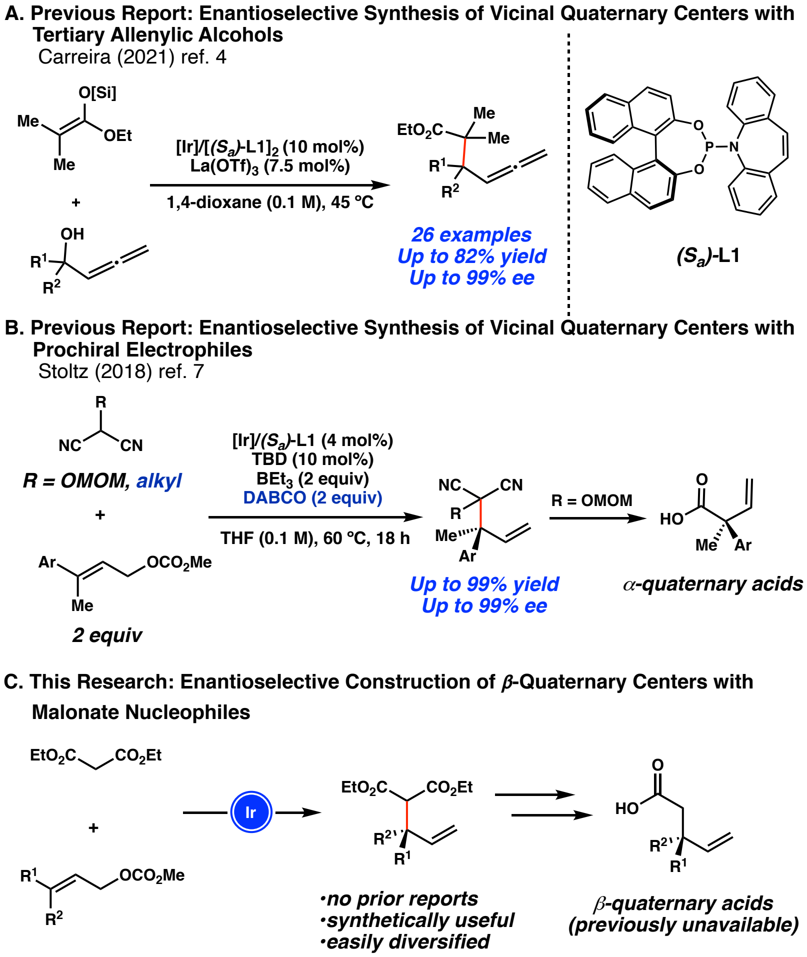
Figure 1.1. *Construction of All-Carbon Quaternary Centers via Ir-Catalyzed Allylic Alkylation*

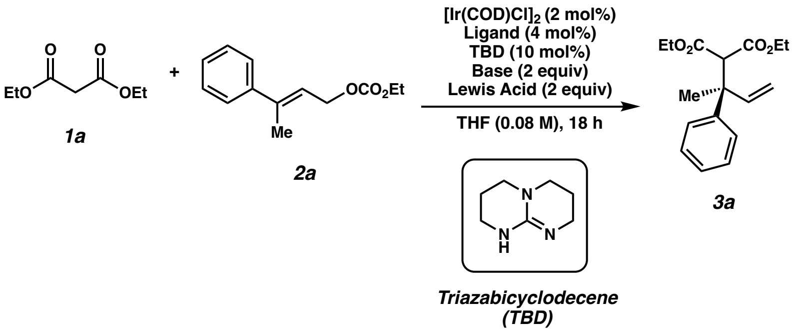


Inspired by these efforts, we aimed to expand the scope of this reaction to include malonate nucleophiles, allowing the formation of β-quaternary 1,3-dicarbonyl compounds (Figure 1.1C). These products could be converted to β-quaternary carboxylic acids, providing a functional handle for further diversification. While malonates have historically served as archetypal nucleophiles in allylic substitution reactions,[8] their application to the enantioselective construction of β-quaternary centers remains unaddressed.[9] Herein, we report the reaction of malonates with 1,1',2-trisubstituted allylic electrophiles to form acyclic quaternary centers in high levels of enantioselectivity.

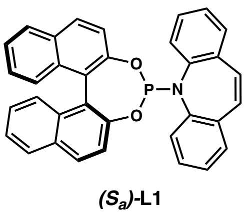
1.2 OPTIMIZATION EFFORTS

Applying our previously successful conditions for malononitrile nucleophiles to this reaction was unsuccessful (Table 1.1, entry 1). Instead, using LiO*t*-Bu as base provided a 23% yield of **3a** when ***(S$_a$)***-**L1** was utilized (entry 2), whereas ***(S$_a$, R)***-**L2**[10] and ***(S$_a$, S, S)***-**L3**[11] performed poorly (entries 3 and 4). While NaOMe failed to improve conversion, employing LiHMDS as the base increased the yield to 46% (entries 5 and 6). Replacement of BEt_3 with commonly employed lithium salts[12] such as LiBr did not lead to appreciable product formation (entry 7). Likewise, employment of $Yb(OTf)_3$ led to minimal yield (entry 8). However, we were pleased that ZnI_2, in concert with LiO*t*-Bu, resulted in an elevated 50% yield (entry 9). Zinc salt additives have indeed proven beneficial to reactivity and selectivity in many related Ir-catalyzed allylic alkylations.[13] Combination of ZnI_2 with HMDS-derived bases resulted in up to 83% yield and 86% ee (entries 10–12). Finally, decreasing the reaction temperature to ambient 21 °C increased the enantiomeric excess to 97%, delivering the desired product in 83% isolated yield, with no detectable linear alkylation product (entry 14). Interestingly, alternative Zn^{2+} sources performed poorly (entries 15–17). VCD was utilized to determine the absolute stereochemistry of this model product (see Experimental Section).

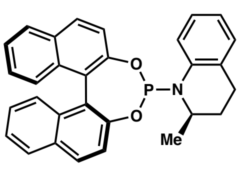
Table 1.1. *Optimization Studies*[a, b, c]



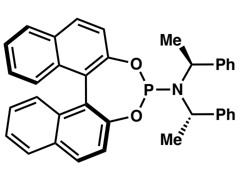
Entry	Ligand	Base	Lewis Acid	Temp.	Yield (%)[a]	ee (%)[b]
1	(S_a)-L1	DABCO	BEt_3	60 °C	0	–
2	(S_a)-L1	LiO*t*-Bu	BEt_3	60 °C	23	–
3	(S_a,R)-L2	LiO*t*-Bu	BEt_3	60 °C	0	–
4	(S_a,S,S)-L3	LiO*t*-Bu	BEt_3	60 °C	<5	–
5	(S_a)-L1	NaOMe	BEt_3	60 °C	10	–
6	(S_a)-L1	LiHMDS	BEt_3	60 °C	46	–
7	(S_a)-L1	LiO*t*-Bu	LiBr	60 °C	<5	–
8	(S_a)-L1	LiO*t*-Bu	$Yb(OTf)_3$	60 °C	14	–
9	(S_a)-L1	LiO*t*-Bu	ZnI_2	60 °C	50	–
10	(S_a)-L1	KHMDS	ZnI_2	60 °C	28	–
11	(S_a)-L1	LiHMDS	ZnI_2	60 °C	80	75
12	(S_a)-L1	NaHMDS	ZnI_2	60 °C	88[c]	86
13	(S_a)-L1	NaHMDS	ZnI_2	40 °C	86	93
14	(S_a)-L1	NaHMDS	ZnI_2	21 °C	83	97
15	(S_a)-L1	NaHMDS	$ZnBr_2$	21 °C	14	–
16	(S_a)-L1	NaHMDS	$Zn(OTf)_2$	21 °C	0	–
17	(S_a)-L1	NaHMDS	$Zn(OAc)_2$	21 °C	83	79



(S_a)-L1



(S_a,R)-L2



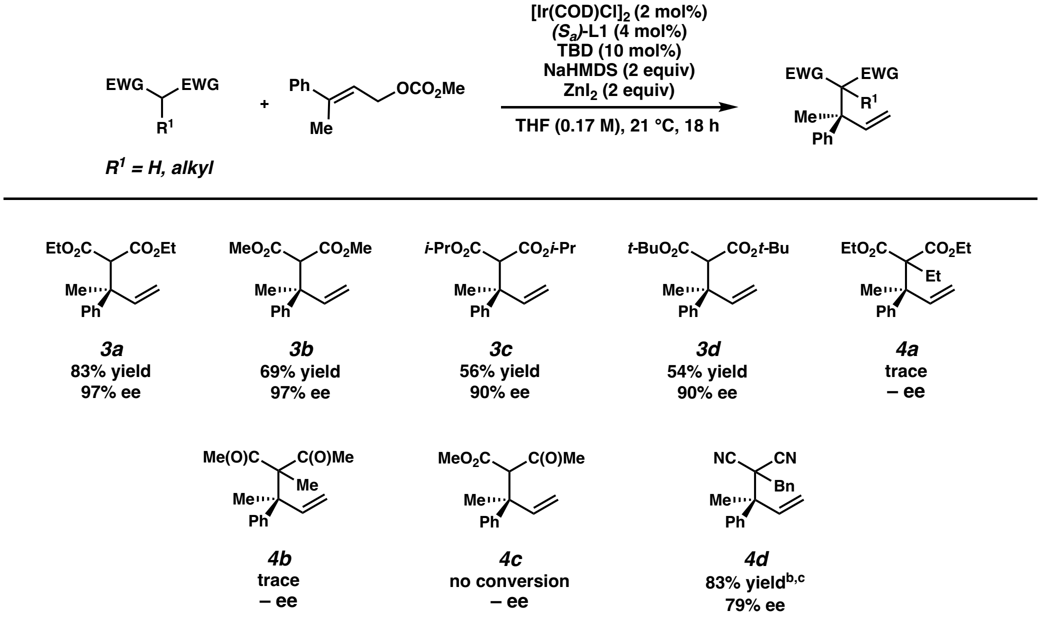
(S_a,S,S)-L3

[a] Yields determined by ^1H NMR relative to a CH_2Br_2 internal standard. Reactions conducted at 0.05 mmol scale, utilizing a 1:1 stoichiometry of **1a**:**2a**. [b] Determined by chiral SFC. [c] Average from two experiments.

1.3 SUBSTRATE SCOPE

With optimized reaction conditions in hand, the efficacy of other malonates was explored (Scheme 1.1A). The reaction utilizing dimethyl malonate afforded product **3b** in an identical 97% ee but decreased 69% yield. Use of *i*-Pr (**3c**) or *t*-Bu (**3d**) malonates resulted in diminished 54–56% yields and 90% ee. Unfortunately, substituted malonate **4a**, as well as other stabilized carbon nucleophiles (**4b, 4c**) were unsuccessful under these conditions. Intriguingly, allylic alkylation product **4d** from our prior report[7] could be synthesized in 83% yield but a diminished 79% ee. With diethyl malonate as the optimal nucleophile, we looked to elaborate the electrophile scope.

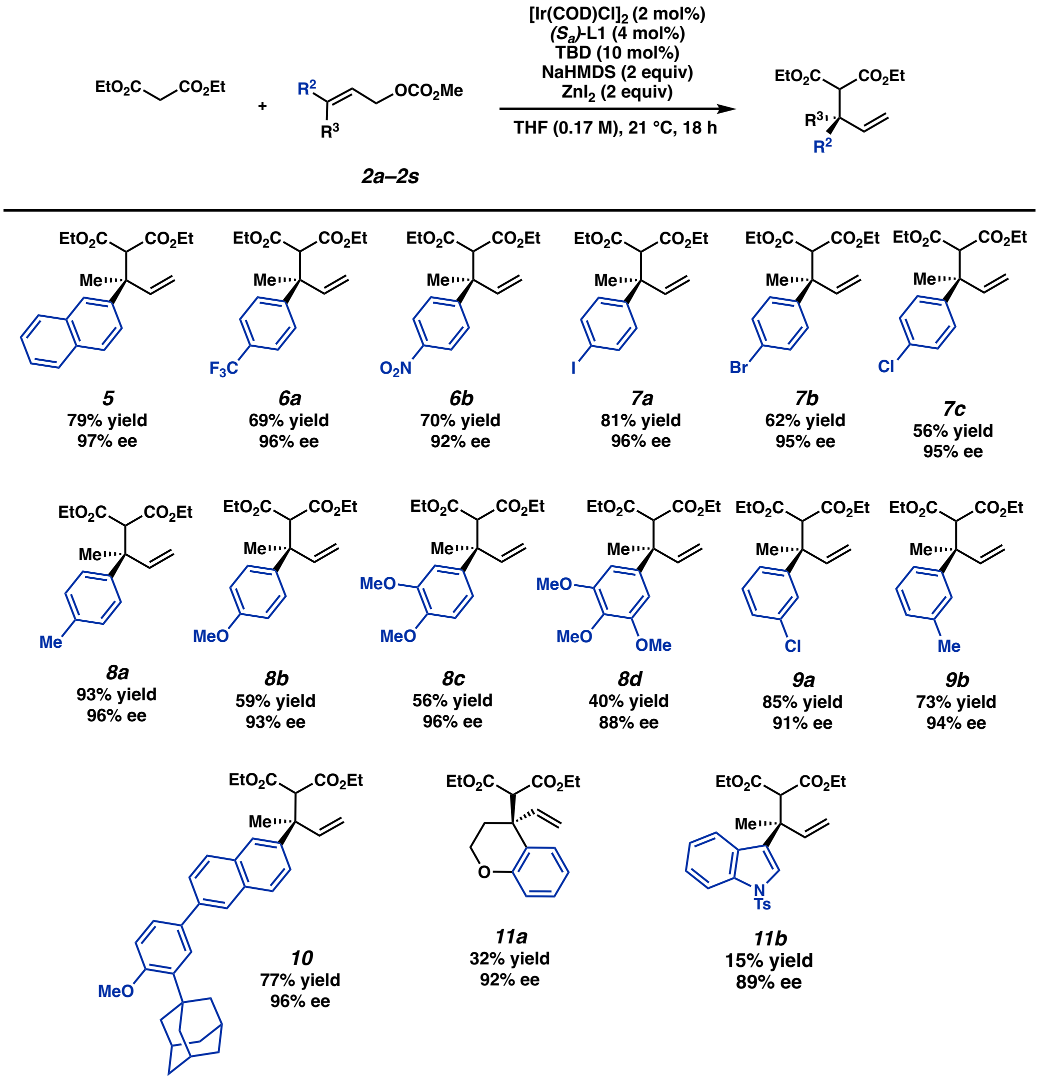
Scheme 1.1. *Nucleophile Investigation*[a,b,c]



[a]Reactions conducted at 0.1 mmol scale, with 1 equiv of both nucleophile and electrophile. [b]Yield determined by ^{1}H NMR relative to a CH_2Br_2 internal standard. [c]Reaction performed at 65 °C.

The alkylation protocol accommodated a range of aryl electrophiles (Scheme 1.2). The 2-naphthyl substituted electrophile underwent the alkylation process in 97% ee (**5**). Electron-withdrawing -CF_3 and -NO_2 substituents at the *para*-position led to the desired products in high yield and ee (**6a, 6b**). Electron-donating *para*-substituents also resulted in

Scheme 1.2. *Electrophile Scope*[a]

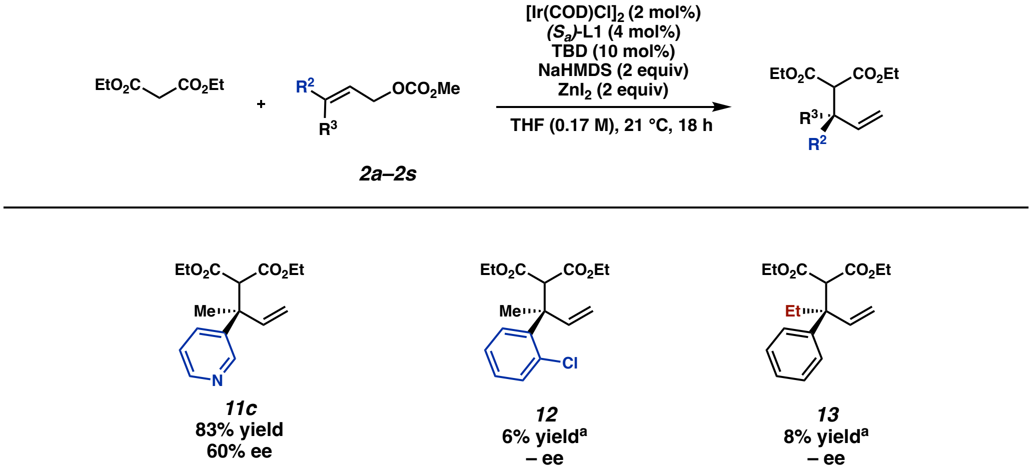


[a] Reactions conducted at 0.1 mmol scale, with 1 equiv of both nucleophile and electrophile.

moderate to high yields and excellent enantioselectivity (**8a, 8d**). *Meta*-substitution was well-tolerated (**9a, 9b**). Heterocyclic scaffolds bearing chromanone and indole-derived fragments proved compatible, (**11a, 11b**), though the 3-pyridyl suffered from poor enantioselectivity (**11c**). Exploring more structurally complex targets, we found that adapalene[14] could be converted to the corresponding allylic methyl carbonate, which underwent the allylic alkylation to yield **10** in 77% yield and 96% ee.

Similar to the limitations of our previous research,[6,7] *ortho*-substitution was not tolerated, possibly indicative of challenges related to oxidative addition (Scheme 1.3, **12**). Furthermore, replacement of the methyl substituent of the electrophile with an ethyl group dramatically decreased the yield to 8%. (**13**). Yield was somewhat recovered when this substituent was constrained in cyclic form, resulting in the

Scheme 1.3. *Electrophile Limitations*[a]

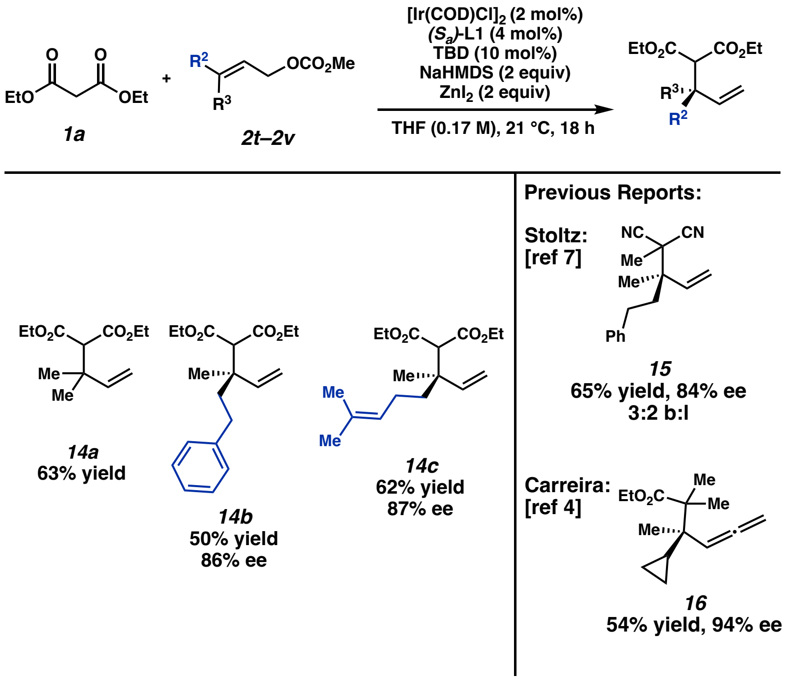


[a]Yields determined by CH_2Br_2 ^{1}H NMR standard. Reactions performed at 0.1 mmol scale.

formation of product **11a** in 32% yield and 92% ee. Additionally, other electrophile isomers led to poor conversion or poor enantioselectivity (see Experimental Section).

We then turned our attention to the historically challenging alkyl substituted electrophiles (**2t–2v**). Gratifyingly, the corresponding products could be formed in up to 63% yield (Scheme 1.4). Phenethyl-substituted compound **14b** and geranyl methyl carbonate-derived product **14c** were synthesized in 86% and 87% ee, respectively. To the best of our knowledge, the enantiomeric excess and branched-selectivity obtained in this study are among the highest reported for alkyl-substituted electrophiles. In our group's previous investigation, 2-methyl malononitrile reacted with the phenethyl

Scheme 1.4. *Fully-Alkyl Electrophiles: Novel Selectivity and Reactivity*[a]



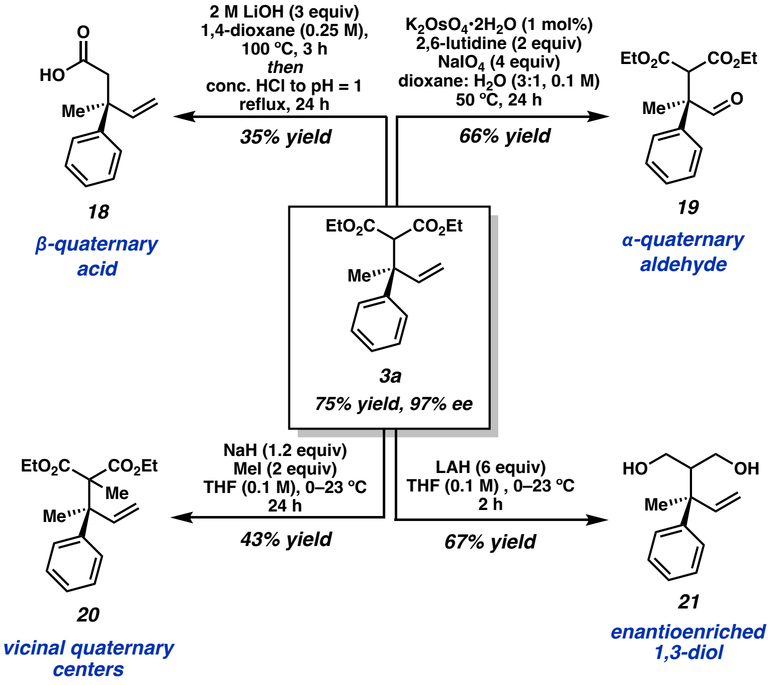
[a]Yields determined by CH_2Br_2 ^1H NMR standard. Reactions performed at 0.1 mmol scale.

methyl carbonate to form vicinal quaternary product **15** in a 65% yield and 84% ee, albeit as an inseparable mixture of constitutional isomers.[7] The Carreira group reported the substitution of a silyl ketene acetal with a cyclopropyl-substituted allenylic electrophile to form allene **16** in 94% ee,[4] but it is worth noting that the cyclopropyl substituent exhibits substantial sp^2 character and that the allenylic systems do not entail the same rationale for branched/linear selectivity.

1.4 DERIVATIZATIONS AND CONCLUSION

To explore the synthetic utility of this technology, **3a** and **8b** were prepared on a 1 mmol scale, the former in 75% yield and 97% ee and the latter in 59% yield and 96%

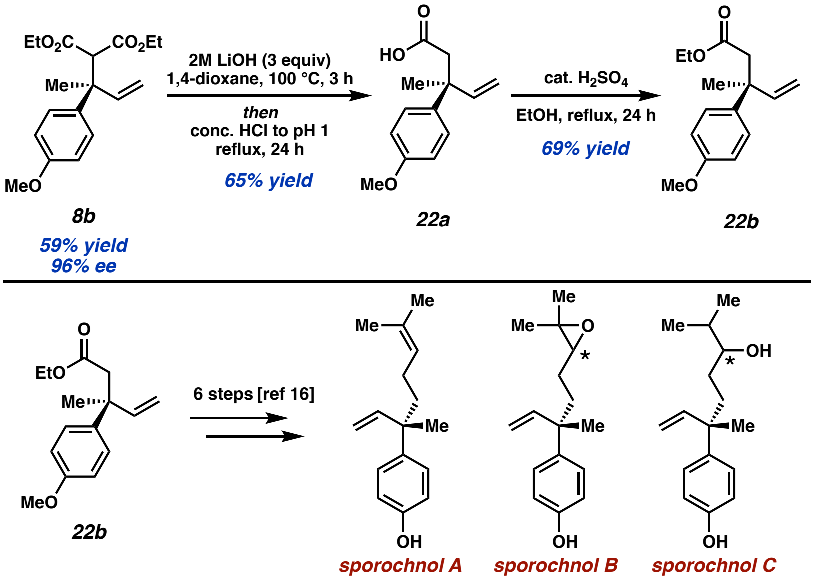
Scheme 1.5. *Product Diversification*



ee. A saponification-decarboxylation sequence furnished β-quaternary acid **18** in moderate yield (Scheme 1.5). Lemieux–Johnson oxidation[15] provided α-quaternary aldehyde **19** in 66% yield. Methylation of **3a** generated vicinal quaternary species **20** in 43% yield. Exhaustive reduction of the diester with lithium aluminum hydride afforded 1,3-diol **21** in 67% yield.

Utilizing the established saponification-decarboxylation, **8b** was converted to β-quaternary acid **22a** in 65% yield (Scheme 1.6). Subsequent Fischer esterification generated the desired ethyl ester **22b** in 69% yield. **22b** was previously prepared in racemic form by Prasad and coworkers in their formal synthesis of sporochnols A–C,[16,17] By accessing **22b** in enantioenriched form, we achieved an asymmetric formal synthesis of these sporochnol natural products.

Scheme 1.6. *Formal Asymmetric Synthesis of Sporochnols A–C*



In summary, we have developed a novel method for the synthesis of highly enantioenriched, acyclic β-quaternary carbonyl compounds via an Ir-catalyzed allylic alkylation. This transformation proceeds under mild conditions, and a broad range of allylic electrophiles, including fully alkyl-substituted substrates, are well-tolerated. Further exploration of the reaction mechanism is currently underway.

1.5 EXPERIMENTAL SECTION

1.5.1 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.[18] 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) was used for flash chromatography. ^1H NMR spectra were recorded on Varian Inova 500 MHz and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 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 $CHCl_3$ (δ 77.16 ppm). Data for ^1H 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

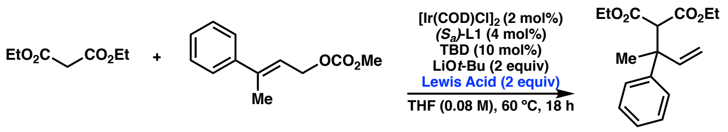
D-line (589 nm), using a 100 mm path-length cell. Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing Chiralpak (AD-H, AS-H or IC) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing Chiralpak (IH) or Chiralcel (OD-H) columns (4.6 mm x 25 cm) both 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+). Absolute configuration of **3a** was determined by vibrational circular dichroism, and all other products are assigned by analogy. Reagents were purchased from commercial sources and used as received unless otherwise stated. Ligand ***(S_a)-L1*** was prepared according to a literature procedure.[11]

List of Abbreviations:

ee – enantiomeric excess, SFC – supercritical fluid chromatography, HPLC – high-performance liquid chromatography, TLC – thin-layer chromatography, TBD – 1,5,7-triazabicyclo[4.4.0]dec-5-ene, COD – *cis,cis*-1,5-cyclooctadiene, COE – *cis*-cyclooctene, DIBAL – diisobutylaluminum hydride, LAH – lithium aluminum hydride, NaHMDS – sodium bis(trimethylsilyl)amide, IPA – isopropanol, EtOAc – ethyl acetate, Dr – dram

1.5.2 EXPERIMENTAL PROCEDURES AND SPECTROSCOPIC DATA

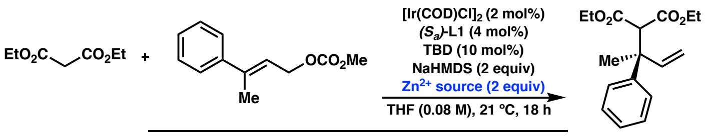
Table 1.2. *Evaluation of Additional Lewis Acids*



Entry	Lewis Acid	Yield[a]
1	BEt_3	23%
2	BPh_3	23%
3	CPh_3BF_4	0
4	$Yb(OTf)_3$	14%
5	$ZrCl_4$	trace
6	$Sc(OTf)_3$	0
7	La(O*i*-Pr)$_3$	0
8	ZnI_2	50%

[a]determined by ^{1}H NMR with CH_2Br_2 as internal standard.

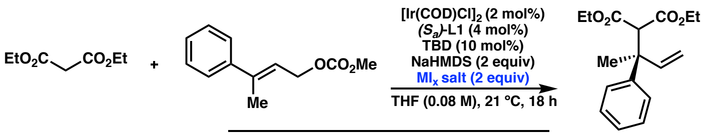
Table 1.3. *Evaluation of Other Zn(II) Sources*



Entry	Zn^{2+} source	Yield[a]	ee[b]
1	ZnI_2	83%	97%
2	$Zn(OTf)_2$	0	n.d.
3	$ZnBr_2$	14%	n.d.
4	$ZnCl_2$	17%	n.d.
5	ZnF_2	0	n.d.
6	$Zn(OAc)_2$	83%	79%

[a]determined by ^{1}H NMR with CH_2Br_2 as internal standard. [b]determined by chiral SFC.

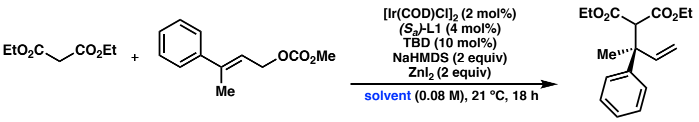
Table 1.4. *Evaluation of other I^- Sources*



Entry	I^- salt	Zn additive	Yield[a]
1	TBAI	$ZnCl_2$	9%
2	NaI	$ZnCl_2$	17%
3	CuI	none	19%

[a]determined by ^{1}H NMR with CH_2Br_2 as internal standard.

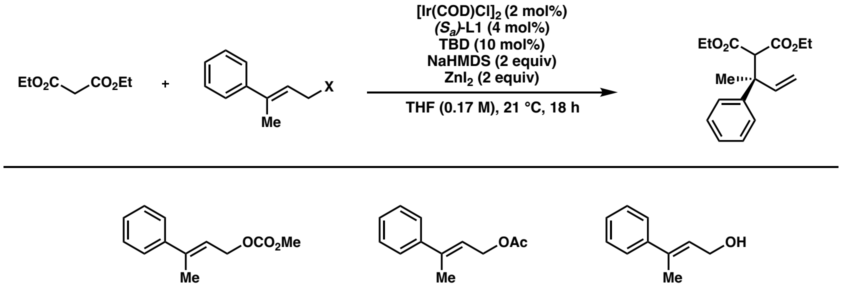
Table 1.5. *Evaluation of Solvents*



Entry	Solvent	Yield[a]	ee[b]
1	THF	83%	97%
2	Et$_2$O	0	n.d.
3	MTBE	trace	n.d.
4	1,4-dioxane	trace	n.d.
5	PhMe	trace	n.d.
6	2-Me-THF	68%	90%

[a]isolated yields. [b]determined by chiral SFC.

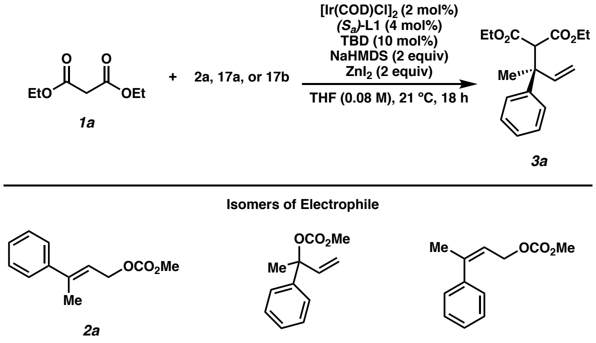
Scheme 1.7. *Evaluation of Other Leaving Groups*



2a	2aa	2ab
83% yield, 97% ee	no conversion	18% yield[a]

[a]yield determined by ^{1}H NMR internal standard

Scheme 1.8. *Isomers of Model Electrophile*

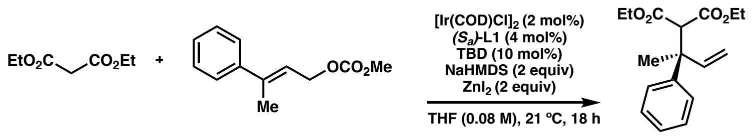


1a

3a

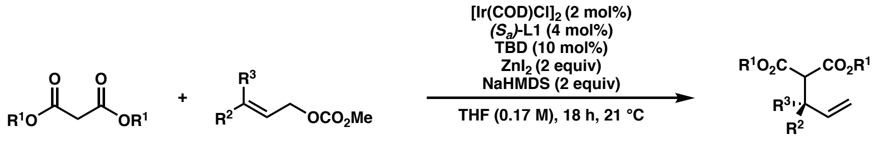
2a	*17a*	*17b*
83% yield 97% ee	87% yield 0% ee	14% yield[a] – ee

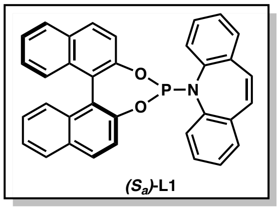
Table 1.6. Control Studies



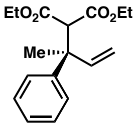
Entry	Deviation from Standard	Result[ab]
1	No TBD	trace
2	No Catalyst	no conversion
3	No NaHMDS	no conversion
4	No ZnI_2	no conversion
5	1 equiv NaHMDS	13% yield
6	1 equiv ZnI_2	86% yield, 90% ee
7	8 mol% *(S$_a$)*-L1	trace
8	$[Ir(COE)Cl]_2$	trace

Iridium-Catalyzed Allylic Alkylation Reactions: General Procedure A



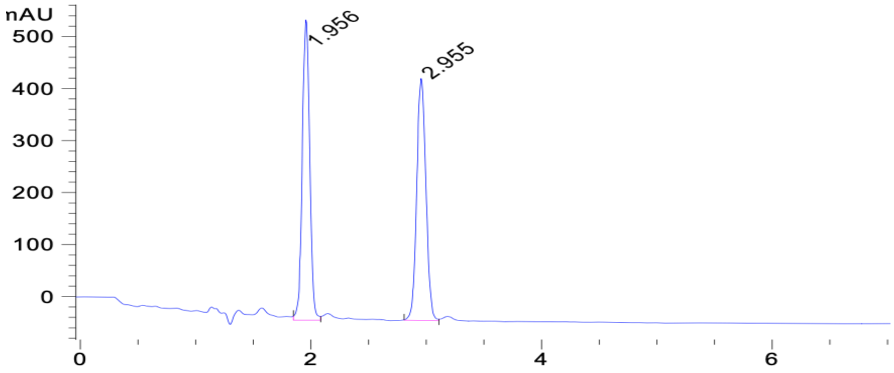

(S$_a$)-L1

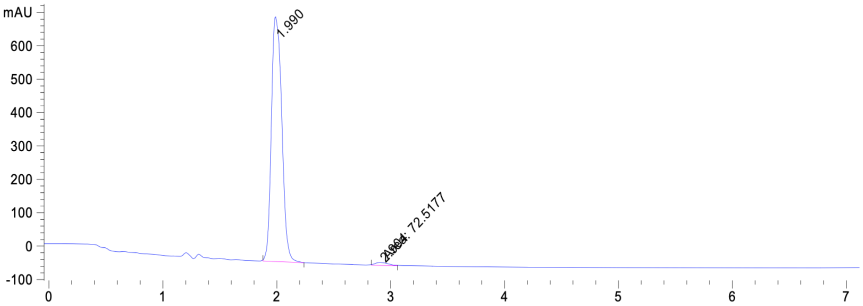
In a nitrogen-filled glovebox, a catalyst solution of $[Ir(COD)Cl]_2$ (6.5 mg/mL), ***(S$_a$)-L1*** (10 mg/mL), and TBD (7 mg/mL) in THF was stirred for 20 min at 25 °C. In separate vials, solutions of *(E)*-allylic carbonate (0.5 mmol/mL) and of malonate nucleophile (0.5 mmol/mL) were prepared in THF. During that time, the reaction vial was charged with ZnI_2 (63.8 mg, 0.2 mmol, 2.0 equiv) and NaHMDS (36.7 mg, 0.2 mmol, 2.0 equiv). 0.2 mL of the nucleophile solution (0.1 mmol, 1.0 equiv) was added to the reaction vial and stirred for 5 min, followed by 0.2 mL of catalyst solution, and finally 0.2 mL of allylic carbonate solution (0.1 mmol, 1.0 equiv). The vial was sealed with a Teflon-lined cap, removed from the glovebox, and stirred at 21 °C for 18 h unless noted otherwise. After 18 h, 3 mL 0.5 M HCl was added to the crude reaction mixture, which was then extracted three times with ethyl acetate, dried over $MgSO_4$, concentrated, and purified by silica gel flash chromatography or preparatory TLC to provide the desired alkylation product.



Diethyl (*R*)-2-(2-phenylbut-3-en-2-yl)malonate (3a)

Prepared according to general procedure A using carbonate **2a** (20.6 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) to provide a colorless oil (24.1 mg, 83% yield, 97% ee). The general procedure using carbonate **2a** (206.1mg, 1.0 mmol) and diethyl malonate (160.2 mg, 1.0 mmol). Purification by column chromatography (10% EtOAc in hexanes) provided a light orange oil (217 mg, 75% yield, 97% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 4H), 7.21 – 7.17 (m, 1H), 6.59 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.25 (dd, *J* = 10.8, 1.0 Hz, 1H), 5.12 (dd, *J* = 17.5, 1.0 Hz, 1H), 4.10 – 4.00 (m, 5H), 1.68 (s, 3H), 1.13 (td, *J* = 7.1, 5.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 145.6, 128.2, 126.3, 114.4, 61.1, 61.0, 60.9, 46.3, 23.6, 14.0, 13.9; IR (Neat Film, NaCl) 3055, 2981, 1755, 1731, 1599, 1493, 1444, 1413, 1368, 1320, 1268, 1230, 1133, 1096, 1037, 919, 761, 700 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{17}H_{22}O_4$: 290.1513, found 290.1527; $[\alpha]_D^{25}$ –7.4 (*c* 1.0, $CHCl_3$); SFC Conditions: 5% MeOH, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 1.99, minor = 2.90.





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Peak RetTime Type  Width     Area       Height      Area
  #   [min]        [min]   [mAU*s]      [mAU]        %
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   2   2.904 MM    0.1309   72.51768    9.23042   1.5316
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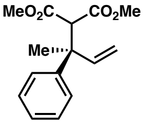
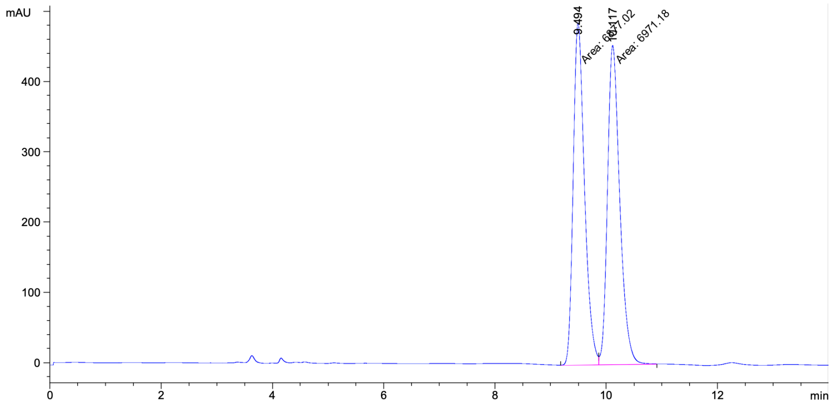
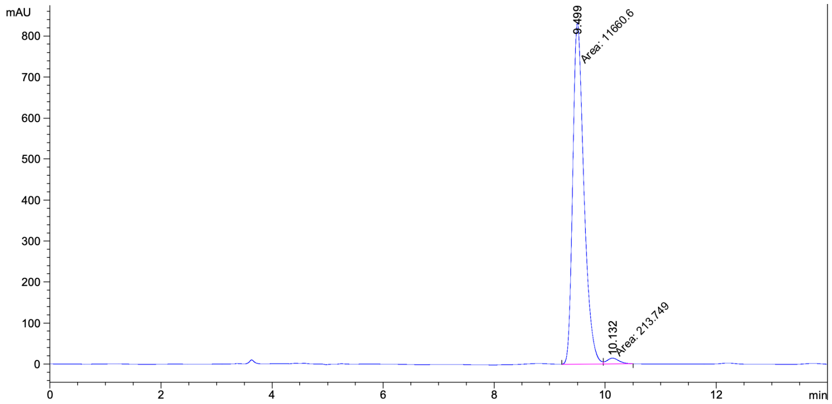


Dimethyl (*R*)-2-(2-phenylbut-3-en-2-yl)malonate (3b)

Prepared according to general procedure A using carbonate **2a** (20.6 mg, 0.1 mmol) and dimethyl malonate (13.2 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (18.0 mg, 69% yield, 97% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 4H), 7.20 (ddt, *J* = 7.1, 6.1, 1.9 Hz, 1H), 6.58 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.26 (dd, *J* = 10.8, 1.0 Hz, 1H), 5.12 (dd, *J* = 17.5, 1.0 Hz, 1H), 4.08 (s, 1H), 3.59 (d, *J* = 1.1 Hz, 6H), 1.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 168.2, 145.5, 142.7, 128.4, 126.6, 126.3, 114.6, 60.9, 52.3, 52.2, 46.4, 23.7; IR (Neat Film, NaCl) 2951, 1758, 1735, 1433, 1321, 1231, 1133, 1029, 925 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{15}H_{18}O_4$: 262.1110 found 262.1214; $[\alpha]_D^{25}$ +15.8 (*c* 1.0, $CHCl_3$); HPLC Conditions: 2% IPA, 1.0 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 9.50, minor = 10.13.





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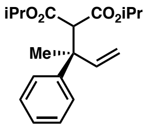
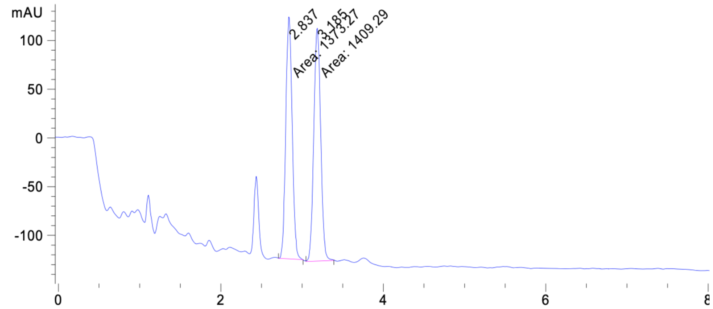
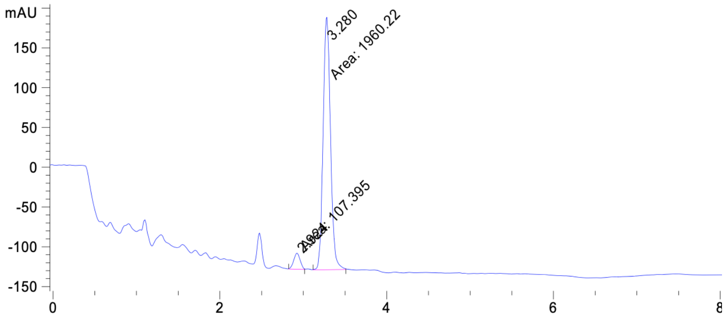


Diisopropyl (*R*)-2-(2-phenylbut-3-en-2-yl)malonate (3c)

Prepared according to general procedure A using carbonate **2a** (20.6 mg, 0.1 mmol) and diisopropyl malonate (18.8 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (17.9 mg, 56% yield, 90% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 4H), 7.18 (ddt, *J* = 7.7, 6.6, 1.4 Hz, 1H), 6.59 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.25 (dd, *J* = 10.8, 1.1 Hz, 1H), 5.11 (dd, *J* = 17.5, 1.1 Hz, 1H), 4.91 (dp, *J* = 10.6, 6.2 Hz, 2H), 3.99 (s, 1H), 1.67 (s, 3H), 1.18 – 1.06 (m, 12H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.4, 146.0, 142.9, 128.3, 126.4, 126.4, 114.5, 68.8, 68.6, 61.3, 46.3, 24.0, 21.7, 21.7, 21.5. IR (Neat Film, NaCl) 2980, 2938, 1754, 1728, 1446, 1374, 1315, 1276, 1232, 1140, 1102, 1028, 913 cm^{-1}; HRMS (FI+) *m/z* calc'd for C$_{19}$H$_{26}$O$_4$: 318.1826, found 318.1843; $[\alpha]_D^{25}$ +12.0 (*c* 1.0, CHCl$_3$); SFC Conditions: 5% IPA, 2.5 mL/min, Chiralpak IC column, λ = 210 nm, t_R (min): minor = 2.92, major = 3.28.





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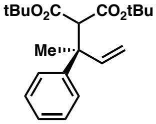
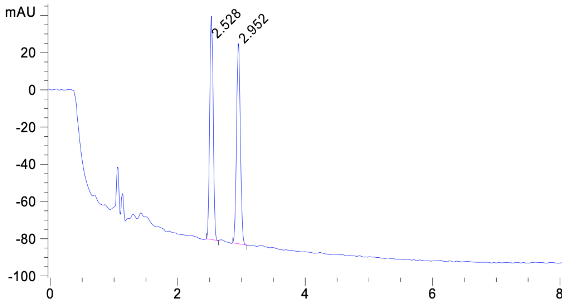
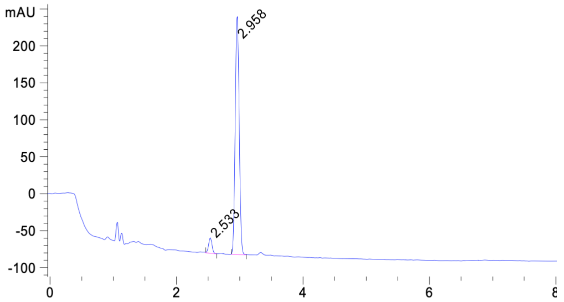


Di-*tert*-butyl (*R*)-2-(2-phenylbut-3-en-2-yl)malonate (3d)

Prepared according to general procedure A using carbonate **2a** (20.6 mg, 0.1 mmol) and di-*tert*-butyl malonate (21.6 mg, 0.1 mmol). Purification by preparative TLC (5% EtOAc in hexanes) provided a colorless oil (18.6 mg, 54% yield, 90% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 4H), 7.22 – 7.14 (m, 1H), 6.58 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.25 (dd, *J* = 10.7, 1.2 Hz, 1H), 5.11 (dd, *J* = 17.6, 1.2 Hz, 1H), 3.87 (s, 1H), 1.65 (s, 3H), 1.34 (s, 9H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 167.3, 146.4, 143.1, 128.2, 126.4, 126.3, 114.3, 81.7, 81.5, 62.7, 46.3, 27.9, 27.8, 24.1; IR (Neat Film, NaCl) 2976, 1727, 1455, 1392, 1367, 1317, 1246, 1123, 972, 914, 845, 746, 699, 668 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{21}H_{30}O_4$: 346.2139 found 346.2151; $[\alpha]_D^{25}$ –6.5 (*c* 1.0, $CHCl_3$); SFC Conditions: 5% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): minor = 2.53, major = 2.95.





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Peak RetTime Type  Width     Area      Height     Area
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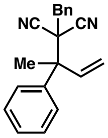
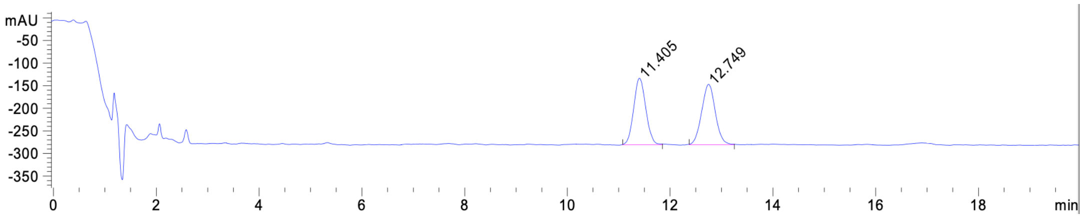
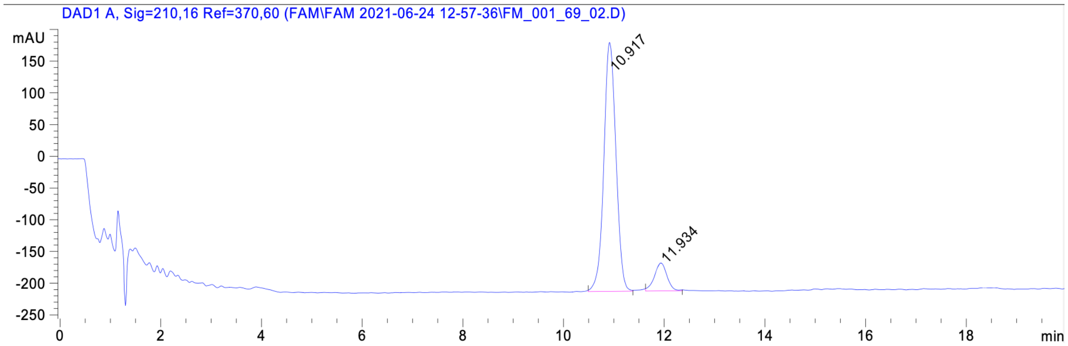


2-Benzyl-2-(2-phenylbut-3-en-2-yl)malononitrile[19] (4d)

Prepared according to general procedure A using carbonate **2a** (20.6 mg, 0.1 mmol) and benzyl malononitrile (15.6 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) afforded a colorless oil (83% yield, 79% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.60 (m, 2H), 7.48 – 7.29 (m, 8H), 6.64 (dd, *J* = 17.3, 10.9 Hz, 1H), 5.60 (d, *J* = 11.0 Hz, 1H), 5.46 (d, *J* = 17.3 Hz, 1H), 3.01 (d, *J* = 13.5 Hz, 1H), 2.94 (d, *J* = 13.4 Hz, 1H), 1.93 (s, 3H). All characterization data matched those reported in the literature.





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Peak RetTime Type  Width     Area      Height     Area
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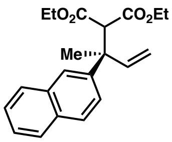
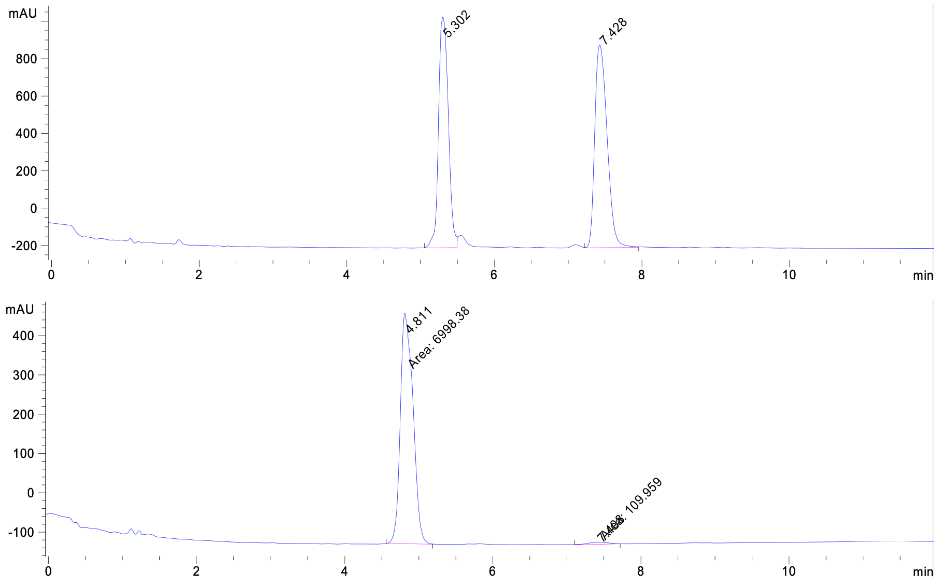


Diethyl (*R*)-2-(2-(naphthalen-2-yl)but-3-en-2-yl)malonate (5)

Prepared according to general procedure A using carbonate **2b** (25.6 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (26.8 mg, 79% yield, 97% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.68 (m, 4H), 7.46 (dtd, *J* = 14.5, 7.9, 3.6 Hz, 3H), 6.69 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.32 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.17 (dd, *J* = 17.6, 1.0 Hz, 1H), 4.18 (s, 1H), 4.04 (qd, *J* = 7.1, 2.1 Hz, 4H), 1.78 (s, 3H), 1.08 (td, *J* = 7.1, 4.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 167.8, 143.0, 142.8, 133.4, 132.1, 128.2, 127.9, 127.5, 126.1, 125.9, 125.2, 124.8, 114.8, 61.3, 61.2, 60.8, 46.6, 23.8, 14.0, 14.0; IR (Neat Film, NaCl) 2977, 1754, 1728, 1367, 1314, 1229, 1131, 1034, 921, 749, cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{21}H_{24}O_4$: 340.1669 found 340.1695; $[\alpha]_D^{25}$ +18.5 (*c* 1.0, $CHCl_3$); SFC Conditions: 5% MeOH, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): minor = 5.21, major = 5.92.



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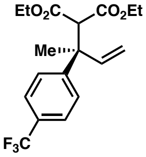
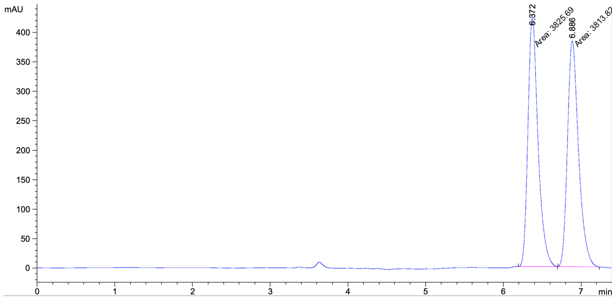
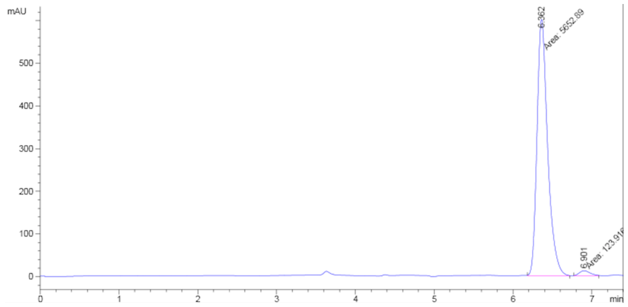


Diethyl (*R*)-2-(2-(4-(trifluoromethyl)phenyl)but-3-en-2-yl)malonate (6a)

Prepared according to general procedure A using carbonate **2c** (27.4 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a pale yellow oil (24.6 mg, 69% yield, 96% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 – 7.52 (m, 2H), 7.48 – 7.42 (m, 2H), 6.57 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.30 (dd, *J* = 10.9, 0.8 Hz, 1H), 5.14 (dd, *J* = 17.5, 0.8 Hz, 1H), 4.10 – 4.04 (m, 4H), 4.04 (s, 1H), 1.68 (s, 3H), 1.14 (td, *J* = 7.1, 5.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 167.4, 149.8, 149.8, 141.9, 129.2, 128.9, 128.5, 128.2, 126.7, 125.2, 125.2, 125.1, 125.1, 115.3, 61.3, 61.2, 60.6, 46.3, 23.8, 13.9, 13.9, the splitting pattern between 128–129 ppm is caused by ^{19}F and also present in the parent carbonate; ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.5; IR (Neat Film, NaCl) 2983, 1756, 1731, 1617, 1447, 1414, 1369, 1328, 1232, 1169, 1125, 1080, 1056, 1037, 1014, 925, 843, 675 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{18}H_{21}O_4F_3$: 358.1387, found 358.1403; $[\alpha]_D^{25}$ –5.6 (*c* 0.5, $CHCl_3$); HPLC Conditions: 2% IPA, 1.0 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 6.36, minor = 6.90.





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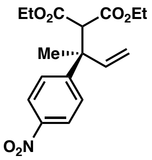
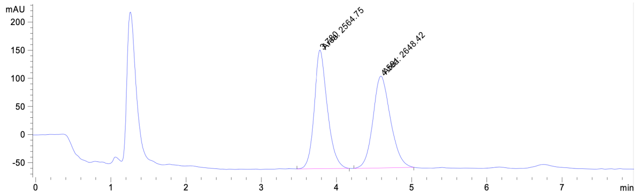
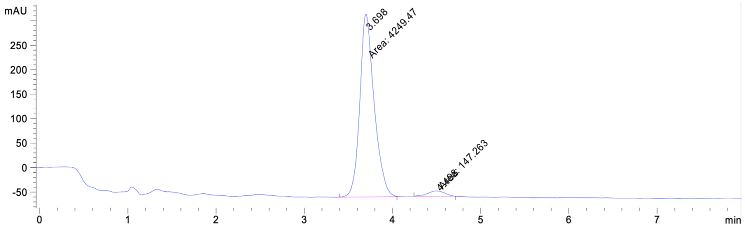


Diethyl (*R*)-2-(2-(4-nitrophenyl)but-3-en-2-yl)malonate (6b)

Prepared according to general procedure A using carbonate **2d** (25.1 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a pale yellow oil (23.6 mg, 70% yield, 92% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 9.0 Hz, 2H), 7.50 (d, J = 8.9 Hz, 2H), 6.56 (dd, J = 17.5, 10.8 Hz, 1H), 5.34 (dd, J = 10.8, 0.7 Hz, 1H), 5.16 (dd, J = 17.5, 0.7 Hz, 1H), 4.14 – 4.01 (m, 5H), 1.68 (s, 3H), 1.16 (dt, J = 8.3, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 167.3, 153.6, 146.5, 141.4, 127.4, 123.6, 116.0, 61.6, 61.5, 60.7, 46.6, 24.1, 14.1, 14.1; IR (Neat Film, NaCl) 2981, 1731, 1595, 1520, 1347, 1367, 1347, 1231, 1135, 1038, 931, 851, 698 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{17}H_{21}NO_6$: 335.1363, found 335.1375; $[\alpha]_D^{25}$ +9.5 (*c* 0.5, $CHCl_3$); SFC Conditions: 5% IPA, 2.5 mL/min, Chiralcel OB-H column, λ = 210 nm, t_R (min): major = 3.70, minor = 4.50.





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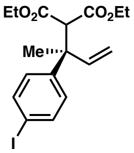
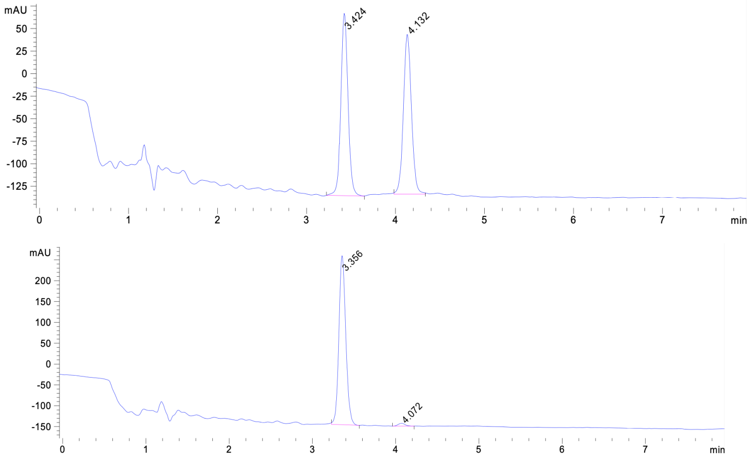


Diethyl (*R*)-2-(2-(4-iodophenyl)but-3-en-2-yl)malonate (7a)

Prepared according to general procedure A using carbonate **2e** (33.2 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a light yellow oil (33.7 mg, 81% yield, 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.52 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.25 (dd, *J* = 10.8, 0.9 Hz, 1H), 5.10 (dd, *J* = 17.6, 0.9 Hz, 1H), 4.06 (q, *J* = 7.1 Hz, 4H), 3.97 (s, 1H), 1.63 (s, 3H), 1.14 (td, *J* = 7.1, 1.3 Hz, 6H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 167.2, 145.3, 141.9, 137.0, 128.3, 114.7, 91.8, 61.1, 61.0, 60.4, 45.8, 23.4, 13.8, 13.7; IR (Neat Film, NaCl) 2980, 1755, 1730, 1486, 1465, 1412, 1392, 1367, 1322, 1264, 1231, 1133, 1095, 1078, 1037, 1003, 923, 860, 822 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{29}H_{30}O_4I$: 416.0479, found 416.0472; $[\alpha]_D^{25}$ +12.9 (*c* 1.0,

$CHCl_3$); SFC Conditions: 5% IPA, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 3.36, major = 4.07.



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Peak RetTime Type  Width     Area      Height     Area
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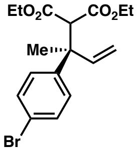
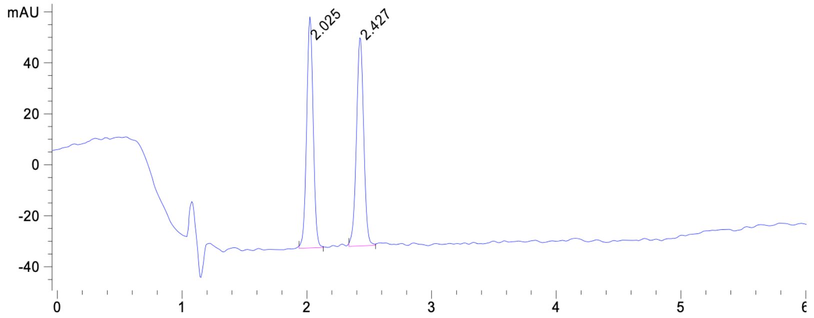
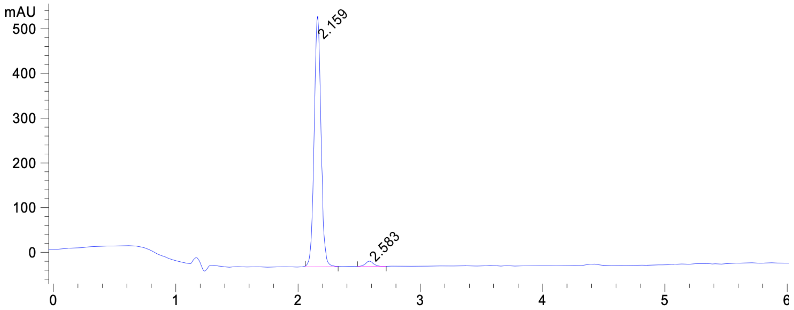


Diethyl (*R*)-2-(2-(4-bromophenyl)but-3-en-2-yl)malonate (7b)

Prepared according to general procedure A using carbonate **2f** (28.5 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a pale yellow oil (22.7 mg, 62% yield, 95% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 6.53 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.26 (dd, *J* = 10.8, 0.9 Hz, 1H), 5.10 (dd, *J* = 17.5, 0.9 Hz, 1H), 4.06 (q, *J* = 7.1 Hz, 4H), 3.97 (s, 1H), 1.64 (s, 3H), 1.14 (td, *J* = 7.1, 1.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 167.6, 144.9, 142.3, 131.4, 128.3, 120.6, 115.0, 61.4, 61.3, 60.8, 46.1, 23.8, 14.1, 14.1; IR (Neat Film, NaCl) 2981, 1755, 1731, 1488, 1394, 1367, 1321, 1268, 1229, 1133, 1095, 1081, 1038, 1008, 925, 812 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{17}H_{21}O_4Br$: 368.0617, found 368.0638; $[\alpha]_D^{25}$ +4.5 (*c* 1.0, $CHCl_3$); SFC Conditions: 10% MeOH, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 2.16, minor = 2.58.





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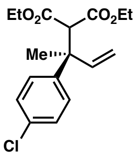
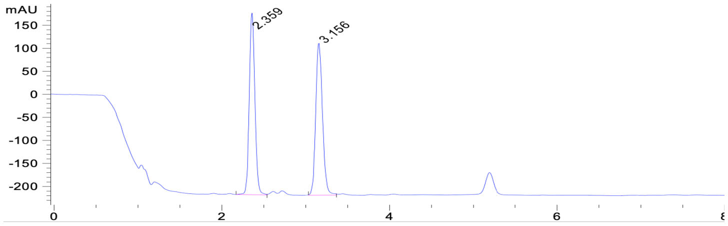
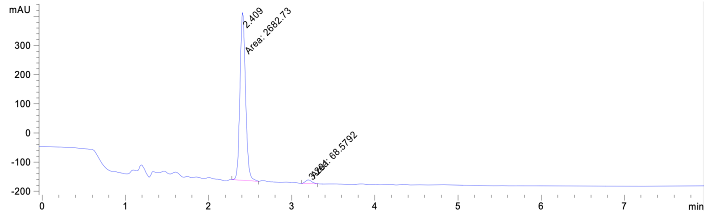


Diethyl (*R*)-2-(2-(4-chlorophenyl)but-3-en-2-yl)malonate (7c)

Prepared according to general procedure A using carbonate **2g** (12.0 mg, 0.05 mmol) and diethyl malonate (8.0 mg, 0.05 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a light yellow oil (9.0 mg, 56% yield, 95% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (m, 4H), 6.54 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.26 (dd, *J* = 10.8, 0.9 Hz, 1H), 5.11 (dd, *J* = 17.5, 0.9 Hz, 1H), 4.07 (q, *J* = 7.1 Hz, 4H), 3.98 (s, 1H), 1.65 (s, 3H), 1.15 (td, *J* = 7.1, 1.7 Hz, 6H). The aromatic protons are tightly spaced underneath the residual chloroform signal, but are clearly present (see HSQC spectrum); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 167.6, 144.3, 142.4, 132.4, 128.4, 127.9, 115.0, 61.4, 61.3, 60.9, 46.0, 23.9, 14.1, 14.1; IR (Neat Film, NaCl) 2980, 1755, 1730, 1486, 1392, 1367, 1322, 1231, 1132, 1037, 1003, 923, 822 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{17}H_{21}O_4Cl$: 324.1123, found 324.1142; $[\alpha]_D^{25}$ +4.2 (*c* 0.5, $CHCl_3$); SFC Conditions: 10% IPA, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 2.41, minor = 3.20.





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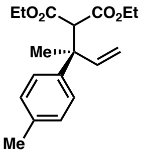
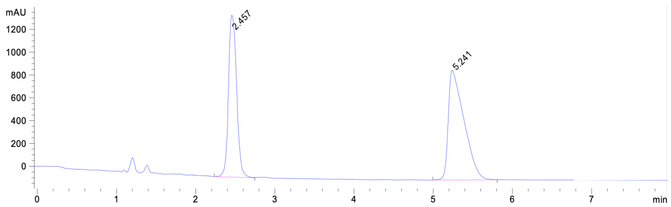
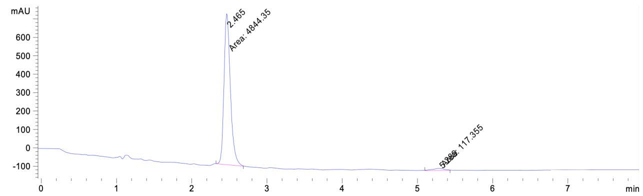


Diethyl (*R*)-2-(2-(*p*-tolyl)but-3-en-2-yl)malonate (8a)

Prepared according to general procedure A using carbonate **2h** (22.0 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (28.3 mg, 93% yield, 96% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.3 Hz, 2H), 7.12 – 7.07 (m, 2H), 6.57 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.23 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.10 (dd, *J* = 17.6, 1.1 Hz, 1H), 4.06 (qd, *J* = 7.1, 1.4 Hz, 4H), 4.02 (s, 1H), 2.30 (s, 3H), 1.65 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 167.8, 143.0, 142.7, 136.0, 129.0, 126.2, 114.2, 61.2, 61.1, 61.0, 46.0, 23.7, 21.0, 14.1, 14.0; IR (Neat Film, NaCl) 2980, 1757, 1729, 1691, 1444, 1367, 1316, 1228, 1132, 1038, 922, 817 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{18}H_{24}O_4$: 304.1667 found 304.1686; $[\alpha]_D^{25}$ –1.1 (*c* 1.0, $CHCl_3$); SFC Conditions: 2% MeOH, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 2.47, minor = 5.29.





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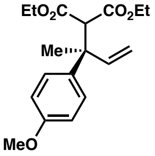
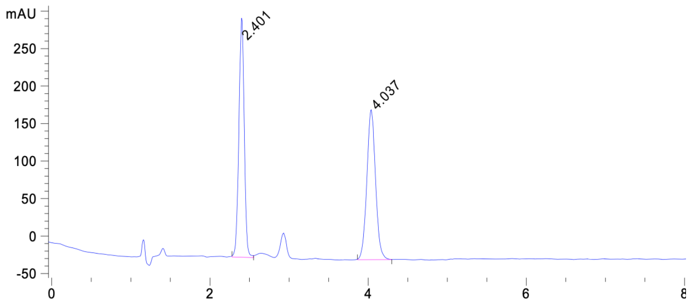
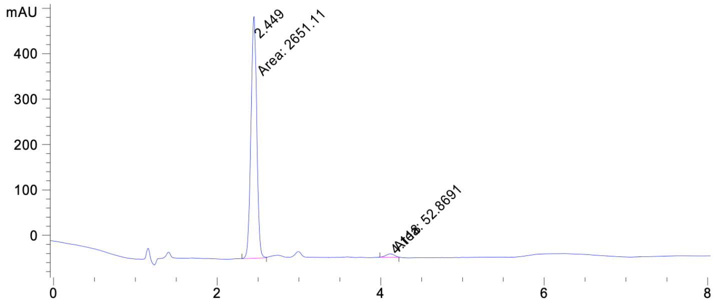


Diethyl (*R*)-2-(2-(4-methoxyphenyl)but-3-en-2-yl)malonate (8b)

Prepared according to general procedure A using carbonate **2i** (23.6 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (17.9 mg, 56% yield, 96% ee). Prepared by the general procedure using carbonate **2i** (236.3 mg, 1.0 mmol) and diethyl malonate (160.2 mg, 1.0 mmol). Purification by column chromatography (10% EtOAc in hexanes) provided a light orange oil (166.4 mg, 52% yield, 96% ee); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.24 (d, *J* = 9.0 Hz, 3H), 6.82 (d, *J* = 9.0 Hz, 2H), 6.55 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.22 (dd, *J* = 10.8, 1.0 Hz, 1H), 5.08 (dd, *J* = 17.5, 1.0 Hz, 1H), 4.05 (qd, *J* = 7.1, 5.3 Hz, 4H), 3.98 (s, 1H), 3.78 (s, 3H), 1.65 (s, 3H), 1.13 (td, *J* = 7.1, 3.1 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.7, 167.7, 158.0, 143.0, 137.5, 127.4, 114.0, 113.5, 61.1, 61.0, 61.0, 55.2, 45.7, 23.6, 14.0, 14.0; IR (Neat Film, NaCl) 2981, 1709, 1621, 1368, 1280, 1231, 1168, 1042, 854, 816, 750 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{18}H_{24}O_5$: 320.1618, found 320.1635; $[\alpha]_D^{25}$ +1.6 (*c* 0.5, CHCl$_3$); SFC Conditions: 10% IPA, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 2.45, minor = 4.12.





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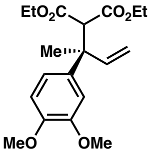
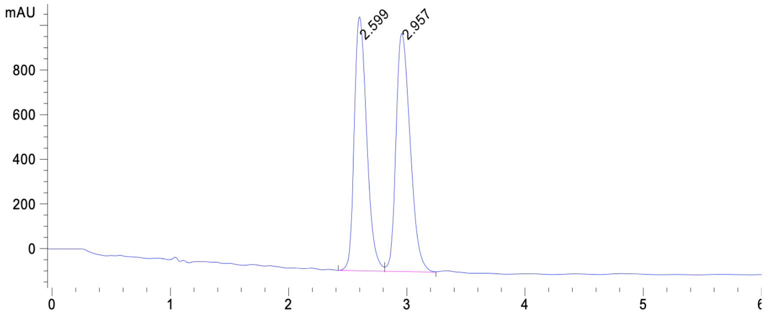
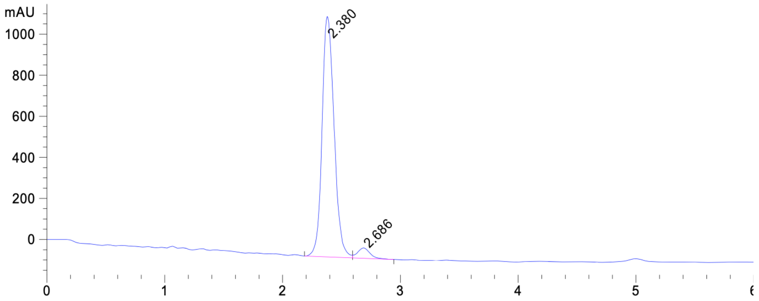


Diethyl (*R*)-2-(2-(3,4-dimethoxyphenyl)but-3-en-2-yl)malonate (8c)

Prepared according to general procedure A using carbonate **2j** (26.6 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (20.5 mg, 59% yield, 93% ee); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.88 – 6.83 (m, 2H), 6.80 – 6.76 (m, 1H), 6.56 (dd, J = 17.5, 10.8 Hz, 1H), 5.23 (dd, J = 10.8, 1.0 Hz, 1H), 5.10 (dd, J = 17.5, 1.1 Hz, 1H), 4.05 (qd, J = 7.1, 1.5 Hz, 4H), 3.99 (s, 1H), 3.85 (d, J = 5.1 Hz, 6H), 1.65 (s, 3H), 1.13 (td, J = 7.1, 0.9 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.8, 167.8, 148.6, 147.6, 143.0, 138.2, 118.6, 114.3, 110.8, 110.2, 61.2, 61.1, 61.1, 56.0, 55.9, 46.1, 24.0, 14.1, 14.1; IR (Neat Film, NaCl) 2980, 1756, 1730, 1588, 1518, 1460, 1412, 1366, 1322, 1258, 1149, 1029, 922, 866 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{19}H_{26}O_6$: 350.1724 found 350.1730; $[\alpha]_D^{25}$ +2.6 (*c* 1.0, CHCl$_3$); SFC Conditions: 2% MeOH, 2.5 mL/min, Chiralpak OJ-H column, λ = 210 nm, t_R (min): major = 2.38, major = 2.69.





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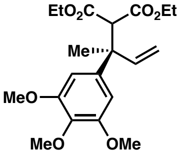
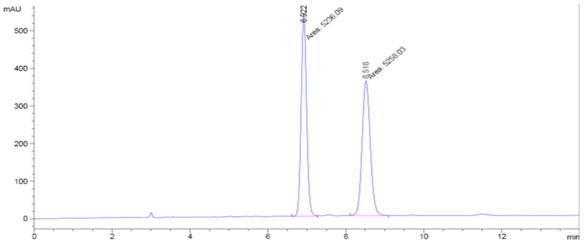
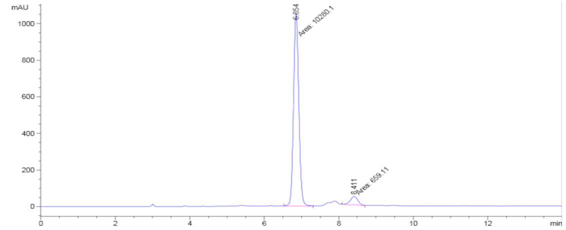


Diethyl (*R*)-2-(2-(3,4,5-trimethoxyphenyl)but-3-en-2-yl)malonate (8d)

Prepared according to general procedure A using carbonate **2k** (29.6 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (20% EtOAc in hexanes) provided a light orange oil (15.0 mg, 40% yield, 88% ee); ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.58 (dd, *J* = 17.5, 10.8 Hz, 1H), 6.53 (s, 2H), 5.27 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.14 (dd, *J* = 17.6, 1.1 Hz, 1H), 4.13 – 4.03 (m, 4H), 4.01 (s, 1H), 3.84 (s, 6H), 3.81 (s, 3H), 1.66 (s, 3H), 1.15 (dt, *J* = 11.3, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.8, 167.7, 152.9, 142.5, 141.5, 136.7, 114.7, 103.9, 61.4, 61.2, 61.1, 60.9, 56.2, 46.7, 24.2, 14.1, 14.1; IR (Neat Film, NaCl) 2979, 1730, 1586, 1512, 1456, 1413, 1367, 1321, 1231, 1125, 1036 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{20}H_{28}O_7$: 380.1829 found 380.1855; $[\alpha]_D^{25}$ +1.7 (*c* 0.5, CHCl$_3$); HPLC Conditions: 5% IPA, 1.0 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 6.85, minor = 8.41.





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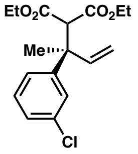
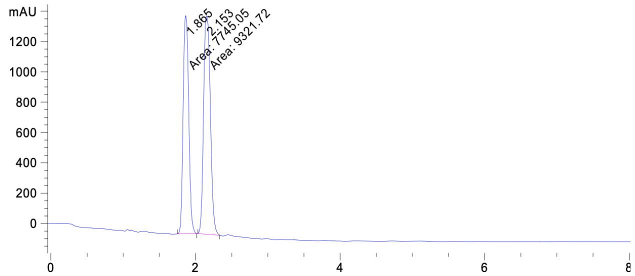
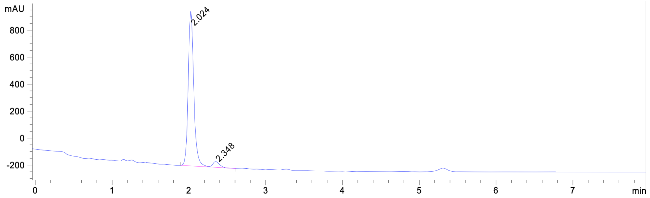


Diethyl (*R*)-2-(2-(3-chlorophenyl)but-3-en-2-yl)malonate (9a)

Prepared according to general procedure A using carbonate **2l** (24.0 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (27.6 mg, 85% yield, 91% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.23 (m, 1H), 7.17 – 7.08 (m, 3H), 6.46 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.21 (dd, *J* = 10.9, 0.9 Hz, 1H), 5.05 (dd, *J* = 17.5, 0.9 Hz, 1H), 4.07 – 3.95 (m, 4H), 3.92 (s, 1H), 1.58 (s, 3H), 1.07 (td, *J* = 7.1, 3.5 Hz, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 167.5, 148.0, 142.1, 134.3, 129.6, 126.9, 126.7, 124.6, 115.2, 61.4, 61.3, 60.8, 46.3, 23.8, 14.1, 14.0; IR (Neat Film, NaCl) 2981, 2937, 1755, 1730, 1593, 1571, 1465, 1445, 1415, 1367, 1322, 1267, 1232, 1134, 1097, 1037, 924, 861, 785, 740 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{17}H_{21}O_4Cl$: 324.1123 found 324.1136; $[\alpha]_D^{25}$ –1.0 (*c* 1.0, $CHCl_3$); SFC

Conditions: 2% MeOH, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 2.02, minor = 2.35.





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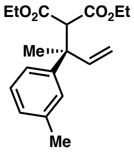
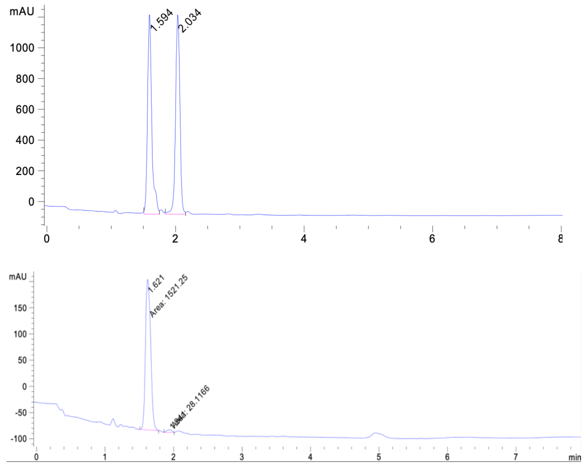


Diethyl (*R*)-2-(2-(*m*-tolyl)but-3-en-2-yl)malonate (9b)

Prepared according to general procedure A using carbonate **2m** (22.0 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (22.3 mg, 73% yield, 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 – 7.02 (m, 3H), 6.94 – 6.91 (m, 1H), 6.51 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.17 (dd, *J* = 10.9, 1.1 Hz, 1H), 5.04 (dd, *J* = 17.6, 1.1 Hz, 1H), 4.06 – 3.91 (m, 5H), 2.25 (s, 3H), 1.58 (s, 3H), 1.05 (td, *J* = 7.1, 5.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 145.6, 142.8, 137.6, 128.1, 127.1, 127.0, 123.2, 114.3, 61.1, 61.0, 60.9, 46.2, 23.7, 21.7, 14.0, 13.9; IR (Neat Film, NaCl) 2981, 1757, 1730, 1605, 1447, 1367, 1321, 1224, 1132, 1097, 1038, 924, 705 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{18}H_{24}O_4$: 304.1669 found 304.1669; $[\alpha]_D^{25}$ –4.9 (*c* 1.0, $CHCl_3$); SFC Conditions: 5% MeOH, 2.5 mL/min, Chiralcel OJ-H column, λ = 210 nm, t_R (min): major = 1.62, minor = 1.94.



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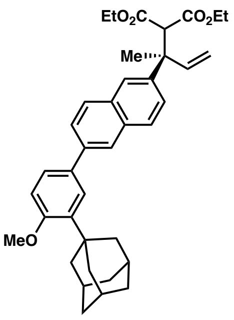
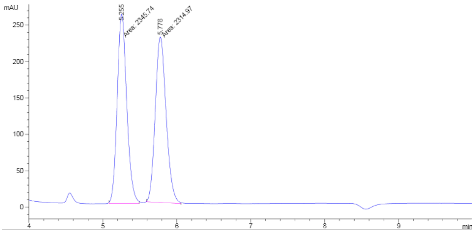
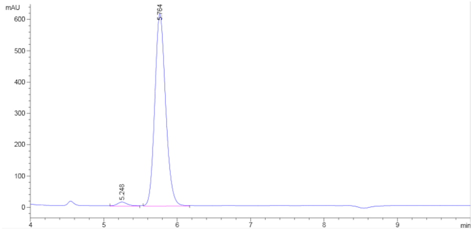


Diethyl 2-((2*R*)-2-(6-(3-((1*S*,3*S*)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)but-3-en-2-yl)malonate (10)

Prepared according to general procedure A using carbonate **2n** (49.6 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil which slowly solidified on standing to a white amorphous solid (44.7 mg, 77% yield, 92% ee); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.95 (d, *J* = 1.8 Hz, 1H), 7.84 (dd, *J* = 8.7, 3.3 Hz, 2H), 7.79 (d, *J* = 2.0 Hz, 1H), 7.73 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.60 (d, *J* = 2.3 Hz, 1H), 7.56 – 7.49 (m, 2H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.72 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.34 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.19 (dd, *J* = 17.6, 1.1 Hz, 1H), 4.20 (s, 1H), 4.06 (qd, *J* = 7.1, 3.3 Hz, 4H), 3.90 (s, 3H), 2.23 – 2.19 (m, 6H), 2.18 (s, 1H), 2.15 – 2.09 (m, 4H), 1.85 – 1.79 (m, 8H), 1.11 (td, *J* = 7.1, 5.5 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.8, 167.8, 158.6, 142.8, 142.6, 138.9, 138.9, 133.2, 132.5, 132.1, 128.5, 128.0, 125.9, 125.6, 125.1, 124.9, 124.5, 114.8, 112.2, 61.2, 61.1, 60.8, 55.2, 46.6, 40.7, 37.3, 37.2, 31.0, 29.2, 23.7, 14.0, 14.0; IR (Neat Film, NaCl) 2904, 1755, 1731, 1603, 1462, 1368, 1235, 1133, 1031, 883, 810 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{38}H_{34}O_5$: 580.3183 found 580.3188;); $[\alpha]_D^{25}$ +23.2 (*c* 1.0, CHCl$_3$); HPLC Conditions: 10% IPA, 1.0 mL/min, Chiralcel OB-H column, λ = 210 nm, t_R (min): minor = 5.25, major = 5.76.





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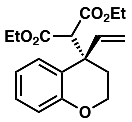
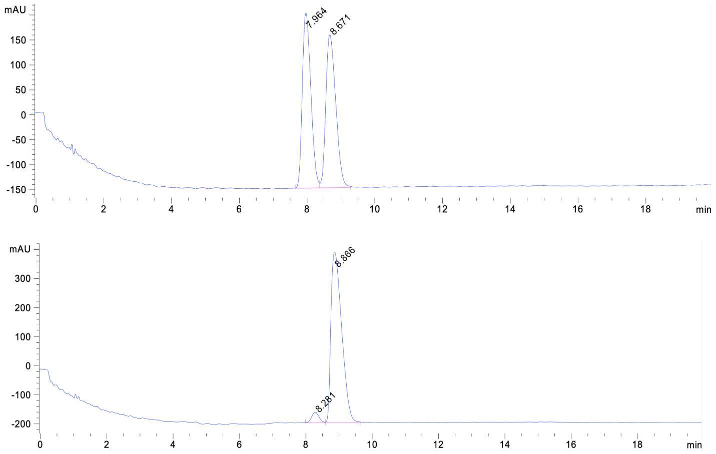


Diethyl (*R*)-2-(2-(naphthalen-2-yl)but-3-en-2-yl)malonate (11a)

Prepared according to general procedure A using carbonate **2o** (23.4 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (10.1 mg, 32% yield, 92% ee); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.13 – 7.07 (m, 2H), 6.88 – 6.78 (m, 2H), 6.22 (ddd, *J* = 17.1, 10.5, 1.7 Hz, 1H), 5.24 (ddd, *J* = 10.5, 2.1, 1.0 Hz, 1H), 4.76 (ddd, *J* = 17.1, 2.0, 0.9 Hz, 1H), 4.23 (tdd, *J* = 7.1, 5.2, 1.8 Hz, 3H), 4.08 (d, *J* = 1.7 Hz, 1H), 4.01 – 3.87 (m, 3H), 2.91 (dddd, *J* = 14.2, 12.4, 4.0, 1.7 Hz, 1H), 2.03 (ddt, *J* = 14.1, 3.1, 1.9 Hz, 1H), 1.28 (td, *J* = 7.1, 1.7 Hz, 3H), 0.97 (td, *J* = 7.1, 1.7 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.8, 167.3, 155.6, 143.3, 128.6, 128.2, 123.6, 120.1, 117.6, 117.4, 62.6, 61.6, 61.2, 59.2, 43.3, 29.0, 14.2, 13.8; IR (Neat Film, NaCl) 2981, 1749, 1732, 1489, 1449, 1366, 1304, 1226, 1169, 1031, 931 cm^{-1}; HRMS (FD+) *m/z* calc'd for $C_{18}H_{22}O_5$ [M]$^+$: 318.1462 found 318.1469; $[\alpha]_D^{25}$ +2.5 (*c* 0.5, CHCl$_3$); SFC Conditions: 2% MeOH, 2.5 mL/min, Chiralpak IC column, λ = 210 nm, t$_R$ (min): minor = 8.28, major = 8.87.



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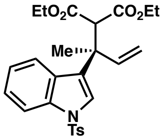
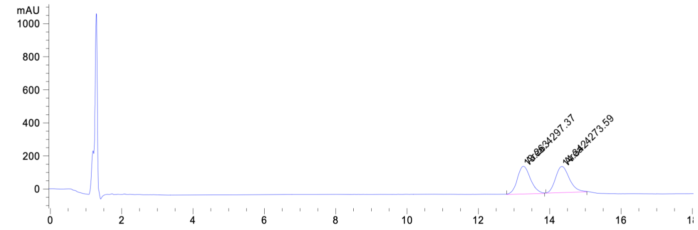
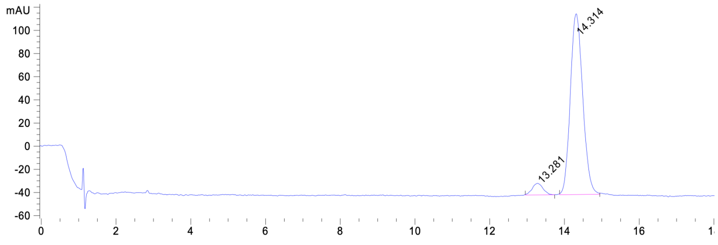


Diethyl (*R*)-2-(2-(1-tosyl-1H-indol-3-yl)but-3-en-2-yl)malonate (11b)

Prepared according to general procedure A using carbonate **2p** (39.9 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (100% CH_2Cl_2) provided a light yellow oil (7.1 mg, 15% yield, 89% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (dt, *J* = 8.4, 0.9 Hz, 1H), 7.76 – 7.70 (m, 2H), 7.59 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.43 (s, 1H), 7.28 – 7.17 (m, 4H), 6.54 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.20 (dd, *J* = 10.7, 0.9 Hz, 1H), 5.03 (dd, *J* = 17.4, 0.9 Hz, 1H), 4.20 (s, 1H), 4.07 – 3.96 (m, 2H), 3.89 – 3.74 (m, 2H), 2.34 (s, 3H), 1.80 (s, 3H), 1.05 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 167.3, 144.9, 141.2, 135.8, 135.3, 129.9, 128.9, 127.0, 126.6, 124.4, 124.4, 122.9, 122.1, 115.2, 114.0, 61.2, 61.0, 58.6, 43.3, 22.4, 21.7, 14.0, 13.7; IR (Neat Film, NaCl) 2982, 1731, 1446, 1369, 1298, 1225, 1174, 1136, 1091, 1037, 959, 809, 753, 687 cm^{-1}; HRMS (ESI +) *m/z* calc'd for $C_{26}H_{29}NO_6S$ $[M+NH_4]^+$: 501.2054 found 501.2077; $[\alpha]_D^{25}$ +10.4 (*c* 0.3, $CHCl_3$); SFC Conditions: 10% IPA, 2.5 mL/min, Chiralpak IC column, λ = 210 nm, t_R (min): minor = 13.28, major = 14.31.





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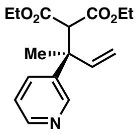
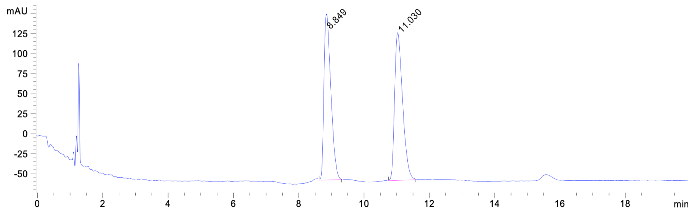
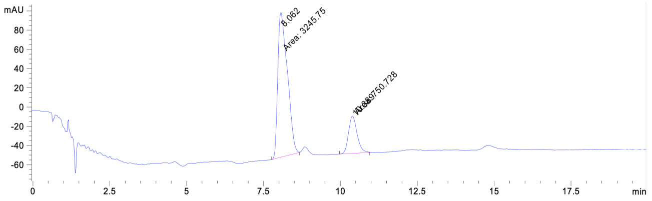


Diethyl (*R*)-2-(2-(pyridin-3-yl)but-3-en-2-yl)malonate (11c)

Prepared according to general procedure A using carbonate **2q** (20.7 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (24.3 mg, 83% yield, 63% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.68 (m, 4H), 7.46 (dtd, *J* = 14.5, 7.9, 3.6 Hz, 3H), 6.69 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.32 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.17 (dd, *J* = 17.6, 1.0 Hz, 1H), 4.18 (s, 1H), 4.04 (qd, *J* = 7.1, 2.1 Hz, 4H), 1.78 (s, 3H), 1.08 (td, *J* = 7.1, 4.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 167.3, 148.2, 147.5, 141.6, 141.5, 135.3, 123.4, 115.7, 61.5, 61.5, 60.5, 45.1, 23.7, 14.1, 14.0; $[\alpha]_D^{25}$ –0.6 (*c* 1.0, $CHCl_3$) SFC Conditions: 5% MeOH, 2.5 mL/min, Chiralpak IC column, λ = 210 nm, t_R (min): major = 8.06, minor = 10.39.





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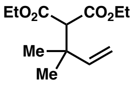
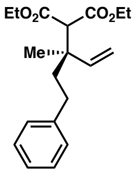


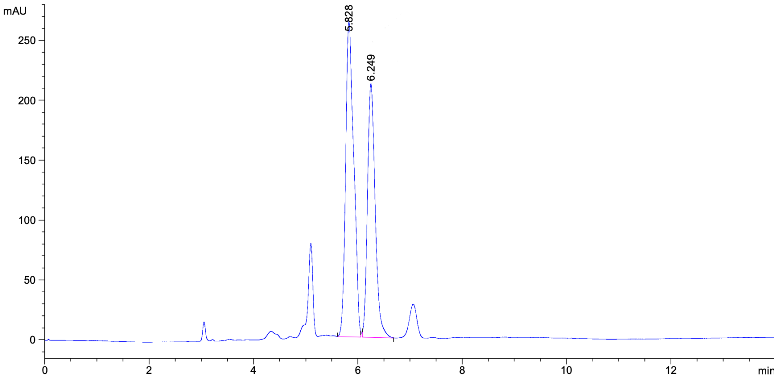
Diethyl 2-(2-methylbut-3-en-2-yl)malonate[20] (14a)

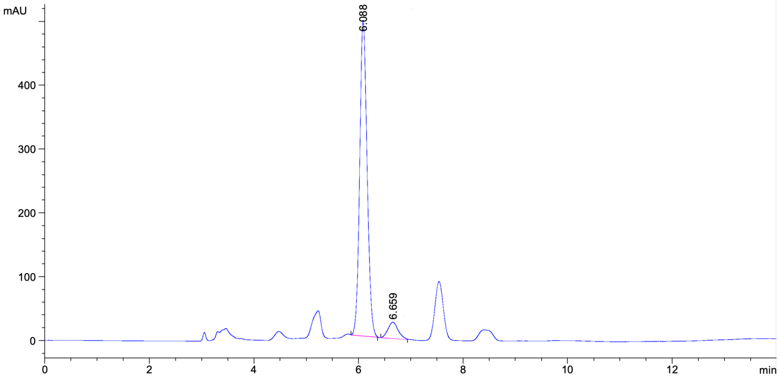
Prepared according to general procedure A using carbonate **2t** (14.4 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (10% EtOAc in hexanes) provided a colorless oil (14.3 mg, 63% yield); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.06 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.11 – 4.94 (m, 2H), 4.16 (q, *J* = 7.1 Hz, 4H), 3.32 (s, 1H), 1.32 – 1.19 (m, 12H).



Diethyl (*R*)-2-(3-methyl-5-phenylpent-1-en-3-yl)malonate (14b)

Prepared according to general procedure A using carbonate **2u** (23.4 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (5% EtOAc in hexanes, eluted twice) provided 16.0 mg of a colorless oil. Small amounts of unidentified impurity persisted despite extensive attempts to further purify the title compound. This impurity did not affect product assignment or assignment of enantiomers, but as a result, the yield is reported by NMR relative to an internal (CH$_2$Br$_2$) standard (50% yield by ^{1}H NMR, 86% ee); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.32 – 7.16 (m, 5H), 6.12 – 6.01 (m, 1H), 5.17 (dt, *J* = 10.8, 0.9 Hz, 1H), 5.08 (dt, *J* = 17.5, 0.9 Hz, 1H), 4.25 – 4.09 (m, 4H), 3.47 (s, 1H), 2.60 – 2.50 (m, 2H), 1.96 – 1.76 (m, 2H), 1.35 (s, 3H), 1.25 (tdd, *J* = 7.1, 3.5, 0.8 Hz, 6H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 168.0, 167.9, 143.1, 142.6, 128.5, 128.5, 128.4, 128.4, 125.9, 125.9, 114.2, 61.2, 61.1, 60.1, 42.3, 41.4, 30.6, 20.1, 14.3, 14.2; IR (Neat Film, NaCl) 2970, 1729, 1470, 1167, 1040, 851 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{19}H_{26}O_4$: 318.1826 found 318.1846; $[\alpha]_D^{25}$ +1.3 (*c* 0.5, $CHCl_3$); HPLC Conditions: 0.07% IPA, 1.0 mL/min, Chiralpak IH column, λ = 210 nm, t_R (min): major = 6.09, minor = 6.66.





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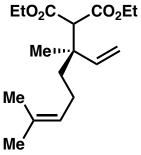
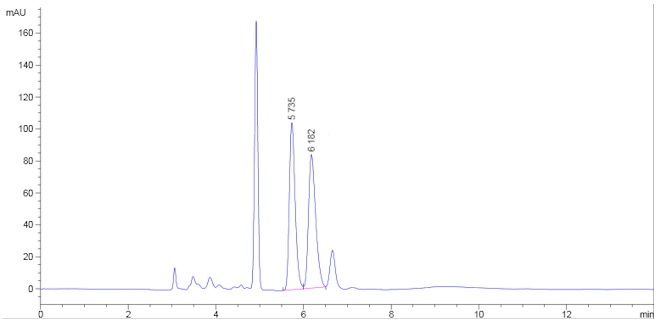
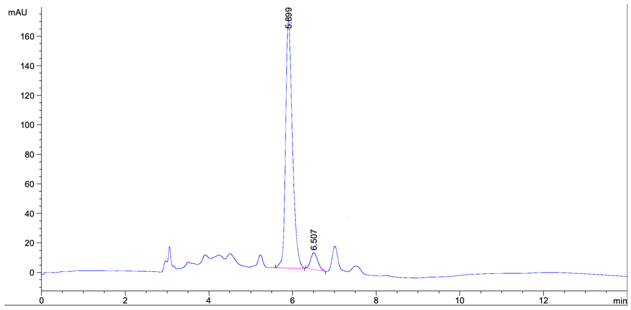


Diethyl (*R*)-2-(3,7-dimethylocta-1,6-dien-3-yl)malonate (14c)

Prepared according to general procedure A using carbonate **2v** (21.2 mg, 0.1 mmol) and diethyl malonate (16.0 mg, 0.1 mmol). Purification by preparative TLC (5% EtOAc in hexanes, eluted twice) provided 18.3 mg of a colorless oil. Small amounts of unidentified impurity persisted despite extensive attempts to further purify the title compound. This impurity did not affect product assignment or assignment of enantiomers, but as a result, the yield is reported by NMR relative to an internal (CH_2Br_2) standard (63% yield by ^{1}H NMR, 87% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.14 – 4.95 (m, 3H), 4.16 (dq, *J* = 8.5, 7.1 Hz, 4H), 3.41 (s, 1H), 1.94 – 1.85 (m, 2H), 1.66 (d, *J* = 1.4 Hz, 3H), 1.57 (d, *J* = 1.2 Hz, 4H), 1.32 – 1.18 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 168.0, 143.3, 131.7, 124.3, 113.8, 61.1, 61.1, 60.2, 42.2, 39.3, 25.8, 22.8, 20.0, 17.7, 14.3, 14.2; IR (Neat Film, NaCl) 2985, 1982, 1755, 1736, 1444, 1166, 1035, 912, 681 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{17}H_{28}O_4$: 296.1982 found 296.2001; $[\alpha]_D^{25}$ +1.1 (*c* 1.0, $CHCl_3$); HPLC Conditions: 0.06% IPA, 1.0 mL/min, Chiralpak IH column, λ = 210 nm, t_R (min): major = 5.90, minor = 6.50.





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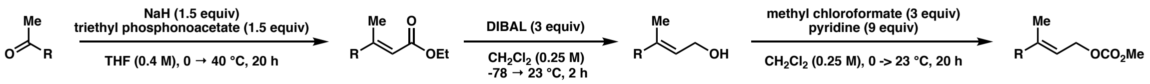
Synthesis of Allylic Carbonate Electrophiles: General Procedure B



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 nitrogen. 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 21 °C then heated to 40 °C using a metal heating block or oil bath. A solution of ketone (1.0 equiv, 1.0 M in THF) was added slowly to the reaction mixture and allowed to stir overnight. After stirring for ~20h, the mixture was cooled to 0 °C, diluted with Et_2O and quenched with water. The layers were separated and extracted three times with EtOAc (75 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue showed 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*)-products.

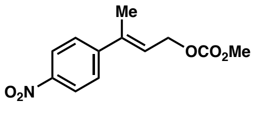
To a flame-dried round bottom flask was added the (*E*)-alkene (1.0 equiv) and CH_2Cl_2 (0.25 M), and the solution was cooled to –78 °C. DIBAL (3 equiv) was added neat dropwise. The solution was stirred at –78 °C for 1h, before warming to room temperature and stirring for an additional hour. Upon completion as determined by TLC analysis, the reaction was quenched with EtOAc and diluted twofold with Et_2O. A large excess of a saturated

Rochelle's salt solution was added and allowed to stir until two clear layers had formed. The layers were separated and extracted three times with Et_2O (75 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude allylic alcohol products were used directly in the subsequent step without further purification.

To a flame-dried round bottom flask was added crude allylic alcohol (1.0 equiv) followed by dichloromethane (0.25 M) and pyridine (9.0 equiv), and the resulting mixture stirred at 0 °C for 5 min. Methyl chloroformate (3 equiv) was added dropwise (neat). The reaction mixture was then allowed to stir and gradually reach 23 °C overnight. After stirring for 20h the crude reaction mixture was diluted with and equal volume of Et_2O and quenched with 1N HCl (8 equiv). The layers were separated, and the aqueous layer was extracted three times with EtOAc (70 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography to afford the desired allylic carbonate. Yields reported refer to the formation of the allylic carbonate from the corresponding ester unless otherwise stated.

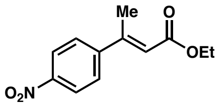
Spectroscopic Data for the Synthesis of New Allylic Carbonate Electrophiles

Note: ^1H NMR spectral data for the corresponding *(E)*-ester intermediate for each carbonate is also included.



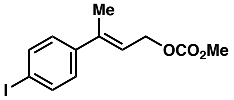
(*E*)-methyl (3-(4-nitrophenyl)but-2-en-1-yl) carbonate (2d)

Prepared from ethyl (*E*)-3-(4-nitrophenyl)but-2-enoate according to general procedure B. Purified by column chromatography (5% EtOAc in hexanes) to provide the title compound product as a light orange amorphous solid (195.3 mg, 39% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.8 Hz, 2H), 6.05 (dd, *J* = 7.5, 5.9 Hz, 1H), 4.88 (d, *J* = 6.7 Hz, 2H), 3.82 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 148.9, 147.3, 138.9, 126.8, 124.6, 123.8, 64.7, 55.1, 16.4; IR (Neat Film, NaCl) 2961, 1742, 1592, 1515, 1438, 1345, 1271, 968, 860, 792, 744 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{12}H_{13}NO_5$: 251.0788, found 251.0796.



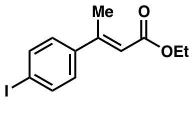
Ethyl (*E*)-3-(4-nitrophenyl)but-2-enoate[21] (2da)

Prepared according to general procedure B; reaction did not achieve full conversion. *E:Z* (3:1) by crude ^{1}H NMR. Purified by silica gel chromatography (10% EtOAc in hexanes) to afford a white solid (505 mg, 27% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.8 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 6.18 (q, *J* = 1.4 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 3H), 2.59 (d, *J* = 1.4 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). All characterization data matched those reported in the literature.



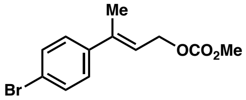
(*E*)-3-(4-iodophenyl)but-2-en-1-yl methyl carbonate (2e)

Prepared from ethyl (*E*)-3-(4-iodophenyl)but-2-enoate according to general procedure B. Purified by column chromatography (10% EtOAc in hexanes) to provide the title compound as a yellow solid (165 mg, 57% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.5 Hz, 2H), 5.91 (tq, *J* = 6.9, 1.4 Hz, 1H), 4.83 (dd, *J* = 6.9, 0.9 Hz, 2H), 3.80 (s, 3H), 2.09 (dt, *J* = 1.5, 0.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 142.0, 140.1, 137.5, 127.9, 121.4, 93.3, 64.9, 55.0, 16.2; IR (Neat Film, NaCl) 2955, 1744, 1687, 1582, 1483, 1442, 1392, 1262, 1125, 1073, 1004, 945, 849, 818, 793, 742 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{12}H_{13}O_3I$: 331.9904, found 331.9922.



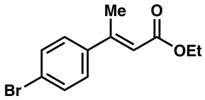
Ethyl (*E*)-3-(4-iodophenyl)but-2-enoate[22] (2ea)

Prepared according to general procedure B; the reaction did not achieve full conversion. *E*:*Z* (>10:1) by crude ^{1}H NMR. Purified by silica gel chromatography (5% EtOAc in hexanes) to afford a light yellow oil (521 mg, 25% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 2H), 6.11 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.54 (d, *J* = 1.4 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). All characterization data matched those reported in the literature.



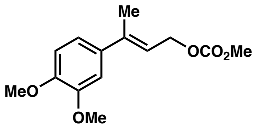
(*E*)-3-(4-bromophenyl)but-2-en-1-yl methyl carbonate (2f)

Prepared from ethyl (*E*)-3-(4-bromophenyl)but-2-enoate according to general procedure B. Purified with a short silica plug eluting with 5% EtOAc in hexanes to provide the title compound as a white amorphous solid (1.04 g, 50% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 2H), 7.30 – 7.24 (m, 2H), 5.91 (td, *J* = 6.7, 3.3 Hz, 1H), 4.84 (d, *J* = 6.9 Hz, 2H), 3.81 (d, *J* = 1.3 Hz, 3H), 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 141.4, 140.0, 131.5, 127.7, 121.8, 121.4, 64.9, 55.0, 16.3; IR (Neat Film, NaCl) 2954, 1744, 1442, 1262, 940, 791 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{12}H_{13}O_3$: 284.0042, found 284.0056.



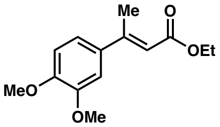
Ethyl (*E*)-3-(4-bromophenyl)but-2-enoate[23] (2fa)

Prepared according to general procedure B, *E:Z* (9:1) by crude ^{1}H NMR. Purified by silica gel chromatography (10% EtOAc in hexanes) to afford the product as a white solid (1.38 g, 60% yield). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 6.11 (s, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.55 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). All characterization data matched those reported in the literature.



(*E*)-3-(3,4-dimethoxyphenyl)but-2-en-1-yl methyl carbonate (2j)

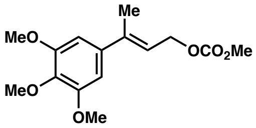
Prepared from ethyl (*E*)-3-(3,4-dimethoxyphenyl)but-2-enoate according to general procedure B. Purification by silica gel chromatography (10% EtOAc in hexanes) afforded the title compound as a colorless oil (224 mg, 84% yield); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.01 – 6.92 (m, 2H), 6.83 (d, *J* = 8.3 Hz, 2H), 5.88 (ddt, *J* = 7.1, 5.7, 1.3 Hz, 1H), 4.85 (dq, *J* = 7.1, 0.7 Hz, 2H), 3.90 (s, 3H), 3.89 (s, 3H), 3.80 (s, 3H), 2.14 – 2.10 (m, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 156.0, 149.0, 148.8, 140.9, 135.4, 119.4, 118.5, 110.9, 109.3, 65.2, 56.1, 56.1, 55.0, 16.5; (Neat Film, NaCl) 2954, 2856, 1746, 1601, 1583, 1517, 1444, 1416, 1376, 1340, 1255, 1174, 1149, 1026, 944, 905, 860, 792, 767 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{14}H_{18}O_5$: 266.1149, found 266.1173.



Ethyl (*E*)-3-(3,4-dimethoxyphenyl)but-2-enoate[24] (2ja)

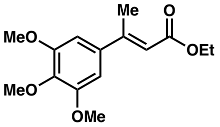
Prepared according to general procedure B; the reaction did not achieve full conversion. *E:Z* (6.3:1) by crude ^{1}H NMR. Purified by silica gel chromatography (5% EtOAc in hexanes) to afford a colorless oil (236 mg, 35% yield). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.10 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.01 (d, *J* = 2.2 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.11 (q, *J* =

1.3 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.91 (d, *J* = 4.6 Hz, 6H), 2.57 (d, *J* = 1.3 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). All characterization data matched those reported in the literature.



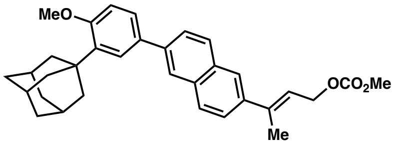
(*E*)-methyl (3-(3,4,5-trimethoxyphenyl)but-2-en-1-yl) carbonate (2k)

Prepared from ethyl (*E*)-3-(3,4,5-trimethoxyphenyl)but-2-enoate according to general procedure B. Purification by silica gel chromatography (10 → 20% EtOAc in hexanes) afforded the title compound as a colorless oil (692 mg, 39% yield); ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.60 (s, 2H), 5.87 (tq, *J* = 7.0, 1.4 Hz, 1H), 4.84 (dd, *J* = 7.0, 0.9 Hz, 2H), 3.87 (s, 6H), 3.85 (s, 3H), 3.80 (s, 3H), 2.11 (dd, *J* = 1.4, 0.7 Hz, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 155.8, 153.0, 141.1, 138.4, 137.8, 120.5, 103.3, 64.9, 60.9, 56.2, 54.9, 16.6. IR (Neat Film, NaCl) 3478, 2968, 1500, 2160, 2020, 1954, 1754, 1584, 1412, 1253, 1122, 943, 794 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{15}H_{20}O_6$: 296.1254, found 296.1277.



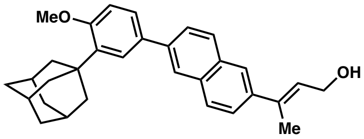
Ethyl (*E*)-3-(3,4,5-trimethoxyphenyl)but-2-enoate[25] (2ka)

Prepared according to general procedure B. *E*:*Z* (14:1) by crude ^{1}H NMR. Purified by silica gel chromatography (5% EtOAc in hexanes) to afford a colorless oil (845 mg, 30% yield). ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.68 (s, 2H), 6.10 (d, *J* = 1.3 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 6H), 3.87 (s, 3H), 2.56 (d, *J* = 1.3 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). All characterization data matched those reported in the literature.



(*E*)-3-(6-(3-((1*s*,3*s*)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)but-2-en-1-yl methyl carbonate (2n)

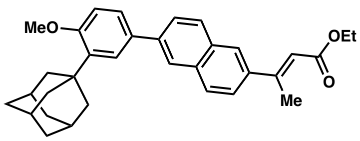
Compound **10d** was treated with methyl chloroformate according to general procedure B. Purification by silica gel chromatography (15% EtOAc in hexanes) afforded the title compound as an amorphous white solid (557 mg, 90% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.8 Hz, 1H), 7.90 – 7.80 (m, 3H), 7.73 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.59 (td, *J* = 4.1, 1.8 Hz, 2H), 7.53 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.11 (tt, *J* = 5.6, 1.3 Hz, 1H), 4.93 (dd, *J* = 7.0, 0.9 Hz, 2H), 3.90 (s, 3H), 3.83 (s, 3H), 2.25 (d, *J* = 1.3 Hz, 3H), 2.19 (d, *J* = 3.0 Hz, 6H), 2.10 (t, *J* = 3.3 Hz, 3H), 1.81 (d, *J* = 2.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 155.9, 140.8, 139.1, 139.1, 138.9, 133.2, 133.1, 132.1, 128.6, 128.0, 126.1, 125.9, 125.6, 124.6, 124.5, 124.4, 121.0, 112.1, 65.1, 55.2, 54.9, 40.6, 37.2, 37.2, 29.1, 16.3; IR (neat film, NaCl) 2903, 1746, 1443, 1266, 948, 813; HMRS (FD+) *m/z* calc'd for $C_{33}H_{36}O_4$: 496.2608, found 496.2634.



(*E*)-3-(6-(3-((1*s*,3*s*)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)but-2-en-1-ol (10d)

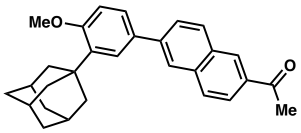
Compound **10c** was reduced as outlined in general procedure B, extracting with dichloromethane instead of Et_2O, affording the title compound as a white powder (560 mg, quantitative) which was used without further purification; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 1.8 Hz, 1H), 7.90 – 7.80 (m, 3H), 7.73 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.65 – 7.57

(m, 2H), 7.53 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.17 (tq, *J* = 6.7, 1.3 Hz, 1H), 4.48 – 4.41 (m, 2H), 3.90 (s, 3H), 2.24 – 2.15 (m, 9H), 2.14 – 2.08 (m, 3H), 1.81 (d, *J* = 3.1 Hz, 6H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 158.7, 139.7, 139.1, 139.0, 137.8, 133.2, 133.2, 132.3, 128.6, 128.5, 128.1, 126.9, 126.1, 126.0, 125.7, 124.8, 124.6, 124.4, 112.2, 60.3, 55.3, 40.8, 37.3, 37.3, 29.3, 16.2; IR (neat film, NaCl) 2901, 2846, 1601, 1452, 1235, 1180, 1138, 1025, 881, 807, 738; HMRS (FD+) *m/z* calc'd for $C_{31}H_{34}O_2$: 438.2553, found 438.2574.



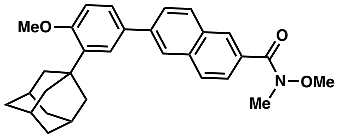
Ethyl (*E*)-3-(6-(3-((1*s*,3*s*)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)but-2-enoate (10c)

1-(6-(3-((1*s*,3*s*)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)ethan-1-one was subjected to Horner-Wadsworth-Emmons conditions as detailed in general procedure B. *E:Z* (2.5:1) by crude ^{1}H NMR. Purification of the crude material by silica gel chromatography (0 → 5% EtOAc in hexanes followed by 5 → 20% followed by 100% EtOAc in hexanes) afforded the title compound as a white powder (619 mg, 38%, mixed fractions containing both geometric olefin isomers were not collected). ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.00 – 7.94 (m, 2H), 7.89 (dd, *J* = 11.7, 8.6 Hz, 2H), 7.76 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.54 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.32 (q, *J* = 1.3 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 3H), 2.71 (d, *J* = 1.3 Hz, 3H), 2.19 (d, *J* = 3.1 Hz, 6H), 2.11 (br t, *J* = 3.2 Hz, 3H), 1.81 (d, *J* = 3.2 Hz, 6H), 1.35 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 167.1, 158.9, 155.4, 140.0, 139.1, 139.0, 134.0, 133.0, 132.0, 129.0, 128.4, 126.4, 126.0, 125.9, 125.7, 124.8, 124.4, 117.4, 112.2, 60.0, 55.3, 40.8, 37.3, 37.3, 29.3, 18.0, 14.5; IR (neat film, NaCl) 2904, 2848, 1710, 1620, 1475, 1367, 1341, 1265, 1238, 1156, 1041, 873, 812, 737, 660; HMRS (FD+) *m/z* calc'd for $C_{33}H_{36}O_3$: 480.2659, found 480.2668.



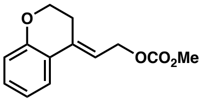
1-(6-(3-((1*s*,3*s*)-adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)ethan-1-one (10b)

To a flame-dried flask was added compound **10a** (1.83 g, 4.02 mmol, 1.0 equiv). The reaction vessel was purged and backfilled. THF (20 mL) was added and the solution was stirred and cooled to 0 °C. MeMgBr (3.0 M in Et_2O, 2.0 mL, 6.03 mmol, 1.5 equiv) was added dropwise to the stirred solution. The solution was stirred at 0 °C for 40 min. Then saturated aqueous NH_4Cl was added. CH_2Cl_2 was added, the layers were partitioned, and the aqueous layer was extracted four times with CH_2Cl_2. The combined extracts were dried over Na_2SO_4 and concentrated. The title compound was afforded relatively cleanly by NMR and was used without further purification (1.40 g, 85% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 1.7 Hz, 1H), 8.08 – 7.97 (m, 3H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.81 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.55 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 3.91 (s, 3H), 2.74 (s, 3H), 2.19 (d, *J* = 3.1 Hz, 6H), 2.15 – 2.08 (m, 3H), 1.81 (t, *J* = 3.1 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 159.1, 141.8, 139.2, 136.2, 134.2, 132.6, 131.4, 130.1, 130.1, 128.6, 126.7, 126.1, 125.9, 124.9, 124.4, 112.2, 55.3, 40.7, 37.3, 37.3, 29.2, 26.8; IR (neat film, NaCl) 2901, 2845, 1676, 1624, 1472, 1285, 1237, 1138, 1029, 878, 819; HMRS (FD+) *m/z* calc'd for $C_{29}H_{30}O_2$: 410.2240, found 410.2259.



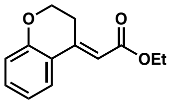
6-(3-((1*s*,3*s*)-adamantan-1-yl)-4-methoxyphenyl)-*N*-methoxy-*N*-methyl-2-naphthamide (10a)[26]

Prepared by the literature procedure of Lu and coworkers. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.28 – 8.21 (m, 1H), 8.00 (d, *J* = 1.8 Hz, 1H), 7.92 (dd, *J* = 17.4, 8.6 Hz, 2H), 7.77 (ddd, *J* = 8.5, 3.0, 1.8 Hz, 2H), 7.59 (d, *J* = 2.4 Hz, 1H), 7.54 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 3.91 (s, 3H), 3.59 (s, 3H), 3.43 (s, 3H), 2.19 (d, *J* = 3.0 Hz, 6H), 2.10 (s, 3H), 1.81 (d, *J* = 3.1 Hz, 6H).



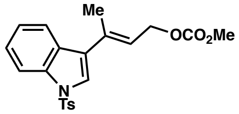
(*E*)-2-(chroman-4-ylidene)ethyl methyl carbonate (2o)

Prepared from ethyl (*E*)-2-(chroman-4-ylidene)acetate according to general procedure B. Purified by column chromatography (10% EtOAc in hexanes) to provide the title compound as a colorless oil (514 mg, 80% yield); ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.58 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.21 (ddd, *J* = 8.5, 7.2, 1.6 Hz, 1H), 6.93 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 6.88 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.20 (tt, *J* = 7.3, 1.7 Hz, 1H), 4.87 (d, *J* = 7.3 Hz, 2H), 4.29 – 4.24 (m, 2H), 3.83 (s, 3H), 2.83 – 2.77 (m, 2H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 156.0, 155.1, 134.7, 129.9, 124.4, 121.5, 121.0, 117.8, 114.3, 66.0, 64.0, 55.0, 26.0; IR (Neat Film, NaCl) 2957, 1744, 1650, 1605, 1575, 1484, 1454, 1375, 1351, 1264, 1119, 1051, 939 cm^{-1}; HRMS (FD+) *m/z* calc'd for $C_{13}H_{14}O_4$: 234.0887, found 234.0888.



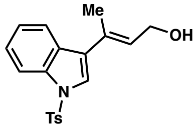
Ethyl (*E*)-2-(chroman-4-ylidene)acetate[27] (2oa)

Prepared according to general procedure B. Purified by silica gel chromatography to afford a white solid (1.30 g, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.00 – 6.81 (m, 2H), 6.35 (t, *J* = 1.7 Hz, 1H), 4.32 – 4.13 (m, 4H), 3.40 (ddd, *J* = 7.2, 5.5, 1.8 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). All characterization data matched those reported in the literature.



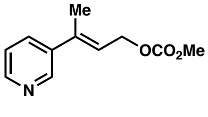
(*E*)-methyl (3-(1-tosyl-1*H*-indol-3-yl)but-2-en-1-yl) carbonate (2p)

Prepared from (*E*)-3-(1-tosyl-1*H*-indol-3-yl)but-2-en-1-ol according to general procedure B. Purified by silica gel chromatography (35% EtOAc in hexanes) afforded the title compound as a colorless oil (278 mg, 69% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.80 – 7.70 (m, 3H), 7.32 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.32 – 7.17 (m, 3H), 6.13 (ddt, *J* = 8.4, 7.1, 1.4 Hz, 1H), 4.89 (dd, *J* = 7.0, 0.8 Hz, 2H), 3.80 (s, 3H), 2.33 (s, 3H), 2.19 – 2.11 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 145.2, 135.6, 135.2, 133.8, 130.1, 128.7, 126.9, 125.0, 124.8, 123.8, 123.6, 121.6, 121.3, 113.9, 64.6, 55.0, 21.7, 17.1. IR (neat film, NaCl) 3136, 2956, 1748, 1648, 1596, 1446, 1372, 1268, 1176, 1140, 1092, 1055, 940, 812, 792, 747, 703, 669, 622, 603 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{21}H_{21}NO_5S$ $[M+H]^+$: 400.1140, found 400.1204.



(*E*)-3-(1-tosyl-1*H*-indol-3-yl)but-2-en-1-ol (2pb)

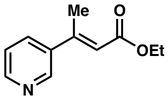
To a flame dried 40 mL vial was added lithium aluminum hydride. The vial was cooled to 0 °C and THF (3.0 mL) was added. Ethyl (*E*)-3-(1-tosyl-1*H*-indol-3-yl)but-2-enoate[28] (520 mg, 1.36 mmol, 1.0 equiv) was dissolved in THF (2.0 mL), and this solution was slowly added to the stirring lithium aluminum hydride suspension using additional THF (0.4 mL) to complete the transfer. After 20 minutes, saturated aqueous NH_4Cl (10 mL) was slowly added at 0 °C. Then saturated aqueous sodium potassium tartrate (100 mL) was added and stirred at 23 °C. The layers were separated and extracted three times with EtOAc (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by automated silica gel flash chromatography (Teledyne ISCO, 0 → 100% EtOAc in hexanes) to afford the title compound as a colorless oil (341 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.82 – 7.69 (m, 3H), 7.54 (s, 1H), 7.32 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.28 – 7.16 (m, 3H), 6.17 (ddt, *J* = 6.7, 5.3, 1.4 Hz, 1H), 4.41 (d, *J* = 6.7 Hz, 2H), 2.33 (d, *J* = 1.0 Hz, 3H), 2.10 (dd, *J* = 1.4, 0.8 Hz, 3H), 1.55 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 135.6, 135.2, 130.6, 130.0, 128.9, 127.6, 127.0, 125.3, 124.9, 123.6, 123.5, 121.3, 113.9, 59.7, 21.7, 16.9. IR (neat film, NaCl) 3353, 2924, 1597, 1446, 1370, 1276, 1174, 1139, 1092, 985, 812, 746, 670; HRMS (ESI+) *m/z* calc'd for $C_{19}H_{19}NO_3S$ $[M+H]^+$: 342.1158, found 342.1159.



(*E*)-methyl (3-(pyridin-3-yl)but-2-en-1-yl) carbonate (2q)

Prepared from compound **2qa** according to general procedure B. Purification by silica gel chromatography (0 → 100% EtOAc in hexanes) afforded the title compound as a colorless oil (564 mg, 30% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.60 (m, 1H), 8.48 (dd, *J* =

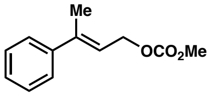
4.8, 1.6 Hz, 1H), 7.65 (ddd, *J* = 8.0, 2.3, 1.6 Hz, 1H), 7.22 (ddd, *J* = 8.0, 4.8, 0.9 Hz, 1H), 5.92 (tq, *J* = 6.9, 1.5 Hz, 1H), 4.83 (dd, *J* = 6.8, 0.9 Hz, 2H), 3.77 (s, 3H), 2.11 (dt, *J* = 1.5, 0.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 148.9, 147.4, 138.0, 137.8, 133.2, 123.2, 122.5, 64.6, 54.9, 16.1. IR (neat film, NaCl) 2957, 1748, 1568, 1444, 1415, 1378, 1327, 1263, 1129, 1022, 944, 792, 711, 624; HRMS (ESI+) *m/z* calc'd for $C_{11}H_{13}NO_3$ $[M+H]^+$: 208.0968, found 208.0972.



Ethyl (*E*)-3-(pyridin-3-yl)but-2-enoate[29] (2qa)

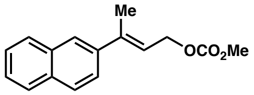
Prepared according to general procedure B. *E:*Z (3.3:1) by crude ^{1}H NMR. Purified by silica gel chromatography to afford a light yellow oil (2.24 g, 67% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (dd, *J* = 2.5, 0.9 Hz, 1H), 8.59 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.75 (ddd, *J* = 8.0, 2.4, 1.6 Hz, 1H), 7.31 (ddd, *J* = 8.0, 4.8, 0.9 Hz, 1H), 6.14 (q, *J* = 1.4 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.58 (d, *J* = 1.4 Hz, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). All characterization data matched those reported in the literature.

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



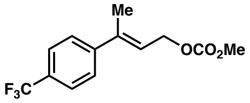
(*E*)-methyl (3-phenylbut-2-en-1-yl) carbonate (2a)[30]

Prepared according to general procedure B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 7.2 Hz, 1H), 5.93 (td, *J* = 7.0, 1.5 Hz, 1H), 4.86 (d, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 2.14 (s, 3H). All characterization data matched those reported in the literature.



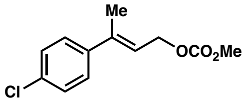
(*E*)-methyl (3-(naphthalen-2-yl)but-2-en-1-yl) carbonate (2b)[31]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.76 (m, 4H), 7.58 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.51 – 7.43 (m, 2H), 6.08 (tq, *J* = 7.0, 1.3 Hz, 1H), 4.92 (dt, *J* = 7.0, 0.7 Hz, 2H), 3.82 (s, 3H), 2.24 (dt, *J* = 1.4, 0.7 Hz, 3H). All characterization data matched those reported in the literature.



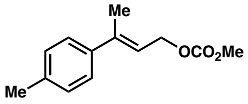
(*E*)-methyl (3-(4-(trifluoromethyl)phenyl)but-2-en-1-yl) carbonate (2c)[32]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.54 (m, 2H), 7.53 – 7.45 (m, 2H), 6.02 – 5.93 (m, 1H), 4.86 (dd, *J* = 6.8, 0.9 Hz, 2H), 3.81 (s, 3H), 2.14 (dt, *J* = 1.5, 0.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 145.9, 145.9, 139.7, 130.1, 129.8, 129.4, 129.1, 126.2, 125.3, 125.3, 122.8, 64.7, 54.9, 16.2. All characterization data matched those reported in the literature.



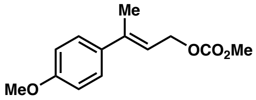
(*E*)-3-(4-chlorophenyl)but-2-en-1-yl methyl carbonate (2g)[32]

Prepared according to general procedure B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 4H), 5.91 (dd, *J* = 7.8, 6.1 Hz, 1H), 4.84 (d, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 2.11 (s, 3H). All characterization data matched those reported in the literature.



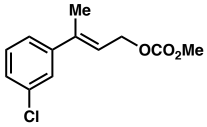
(*E*)-methyl (3-(*p*-tolyl)but-2-en-1-yl) carbonate (2h)[32]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.18 – 7.09 (m, 2H), 5.90 (tq, *J* = 7.1, 1.3 Hz, 1H), 4.84 (dd, *J* = 7.1, 0.8 Hz, 2H), 3.80 (s, 3H), 2.34 (s, 3H), 2.11 (dd, *J* = 1.4, 0.8 Hz, 3H). All characterization data matched those reported in the literature.



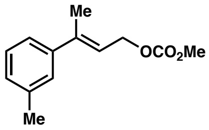
(*E*)-3-(4-methoxyphenyl)but-2-en-1-yl methyl carbonate (2i)[19]

Prepared according to general procedure B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 2H), 6.89 – 6.83 (m, 2H), 5.87 (t, *J* = 7.1 Hz, 1H), 4.84 (d, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.80 (s, 3H), 2.11 (s, 3H). All characterization data matched those reported in the literature.



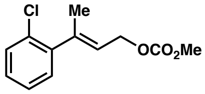
(*E*)-3-(3-chlorophenyl)but-2-en-1-yl methyl carbonate (2l)[19]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (q, *J* = 1.5 Hz, 1H), 7.29 – 7.23 (m, 3H), 5.92 (tq, *J* = 7.0, 1.4 Hz, 1H), 4.84 (dq, *J* = 6.9, 0.9 Hz, 2H), 3.81 (s, 3H), 2.10 (dt, *J* = 1.4, 0.8 Hz, 3H). All characterization data matched those reported in the literature.



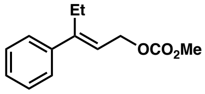
(*E*)-methyl (3-(*m*-tolyl)but-2-en-1-yl) carbonate (2m)[32]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.25 – 7.18 (m, 3H), 7.11 – 7.08 (m, 1H), 5.95 – 5.86 (m, 1H), 4.85 (dq, *J* = 7.0, 0.7 Hz, 2H), 3.80 (s, 3H), 2.36 (d, *J* = 0.8 Hz, 3H), 2.12 (dt, *J* = 1.3, 0.7 Hz, 3H). All characterization data matched those reported in the literature.



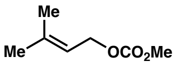
(*E*)-3-(2-chlorophenyl)but-2-en-1-yl methyl carbonate (2r)[32]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40 – 7.27 (m, 5H), 5.78 (t, *J* = 7.0 Hz, 1H), 4.85 (d, *J* = 7.1 Hz, 2H), 3.80 (s, 3H), 2.64 – 2.53 (m, 2H), 1.55 (s, 1H), 1.00 (t, *J* = 7.5 Hz, 3H). All characterization data matched those reported in the literature.



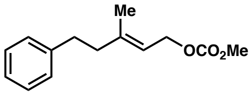
(*E*)-methyl (3-phenylpent-2-en-1-yl) carbonate (2s)[32]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.40 – 7.30 (m, 1H), 7.24 – 7.15 (m, 3H), 5.59 (ddt, *J* = 6.9, 5.4, 1.5 Hz, 1H), 4.83 (dq, *J* = 6.9, 0.8 Hz, 2H), 3.81 (s, 3H), 2.07 (dt, *J* = 1.5, 0.8 Hz, 3H). All characterization data matched those reported in the literature.



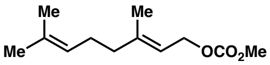
Methyl (3-methylbut-2-en-1-yl) carbonate (2t)[33]

Prepared according to general procedure B from 3-methyl-2-buten-1-ol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (ddq, *J* = 8.7, 5.9, 1.4 Hz, 1H), 4.63 (dp, *J* = 7.3, 0.8 Hz, 2H), 3.77 (s, 3H), 1.76 (dd, *J* = 1.4, 0.8 Hz, 3H), 1.74 – 1.71 (m, 3H). All characterization data matched those reported in the literature.



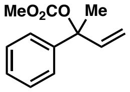
(*E*)-methyl (3-methyl-5-phenylpent-2-en-1-yl) carbonate (2u)[32]

Prepared according to general procedure B. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2H), 7.22 – 7.15 (m, 3H), 5.40 (tq, *J* = 7.1, 1.3 Hz, 1H), 4.69 – 4.62 (m, 2H), 3.78 (s, 3H), 2.78 – 2.69 (m, 2H), 2.39 – 2.30 (m, 2H), 1.78 – 1.76 (m, 3H). All characterization data matched those reported in the literature.



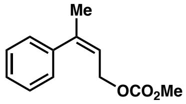
(*E*)-3,7-dimethylocta-2,6-dien-1-yl methyl carbonate (2v)[33]

Prepared according to general procedure B from geraniol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (ddq, *J* = 7.2, 5.7, 1.3 Hz, 1H), 5.07 (dddd, *J* = 6.8, 5.4, 2.9, 1.4 Hz, 1H), 4.65 (dq, *J* = 7.2, 0.7 Hz, 2H), 3.77 (s, 3H), 2.15 – 1.99 (m, 4H), 1.73 – 1.71 (m, 3H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H). All characterization data matched those reported in the literature.



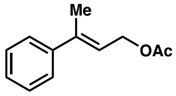
Methyl (2-phenylbut-3-en-2-yl) carbonate (17a)[34]

Prepared according to a literature procedure from 2-phenylbut-3-en-2-ol. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.42 – 7.27 (m, 5H), 6.29 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.37 – 5.25 (m, 2H), 3.70 (s, 3H), 1.92 (s, 3H). All characterization data matched those reported in the literature.



(*Z*)-methyl (3-phenylbut-2-en-1-yl) carbonate (17b)[31]

Prepared according to general procedure B from ethyl (*Z*)-3-phenylbut-2-enoate. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.38 – 7.33 (m, 2H), 7.31 – 7.27 (m, 1H), 7.20 – 7.16 (m, 2H), 5.70 (td, *J* = 7.3, 1.6 Hz, 1H), 4.56 (dt, *J* = 7.2, 1.1 Hz, 2H), 3.77 (d, *J* = 0.8 Hz, 3H), 2.11 (t, *J* = 1.3 Hz, 3H). All characterization data matched those reported in the literature.

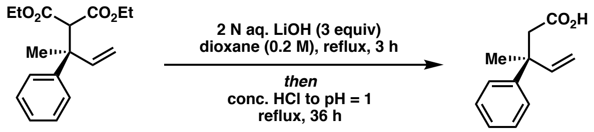


(*E*)-3-phenylbut-2-en-1-yl acetate (2aa)[35]

Prepared according to a literature procedure from the corresponding allylic alcohol. ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.43 – 7.39 (m, 2H), 7.36 – 7.26 (m, 3H), 5.90 (tq, *J* = 6.9, 1.4 Hz, 1H), 4.79 (dq, *J* = 7.1, 0.8 Hz, 2H), 2.12 (dt, *J* = 1.5, 0.8 Hz, 3H), 2.09 (s, 3H). All characterization data matched those reported in the literature.

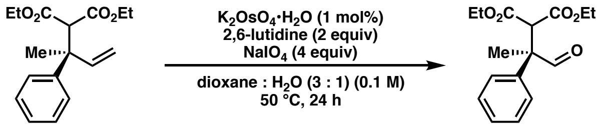
Derivatization of Alkylation Products

Note: Derivatization procedures are unoptimized.



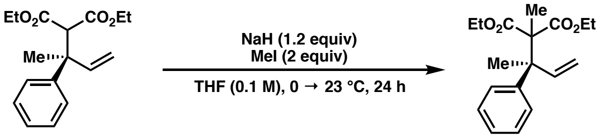
(*S*)-3-methyl-3-phenylpent-4-enoic acid (18)

To a round bottom flask with stir bar and reflux condenser was added diester **3a** (145 mg, 0.5 mmol, 1.0 equiv) in dioxane (2.5 mL). 2 N aq. LiOH (0.75 mL) was added, and the mixture was heated to reflux. After 3h, TLC analysis indicated full consumption of the starting material. The solution was allowed to cool to room temperature, then concentrated HCl was added until the solution reached a pH of 1. The reaction mixture was then heated to reflux and periodically monitored by LC/MS. After 36h, although full conversion of the diacid to the decarboxylated product was not entirely complete, ethyl acetate was added, and the layers were partitioned and extracted three times with ethyl acetate (5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel chromatography (20% EtOAc, 1% AcOH in hexanes) to afford a yellow oil (33.0 mg, 35% yield); $[\alpha]_D^{25}$ –4.5 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 4H), 7.21 (ddt, J = 6.1, 5.4, 2.6 Hz, 1H), 6.15 (dd, J = 17.4, 10.7 Hz, 1H), 5.16 (dd, J = 10.6, 0.9 Hz, 1H), 5.09 (dd, J = 17.4, 0.9 Hz, 1H), [2.83, 2.82] (ABq, 2H, J_{AB} = 14.5 Hz), 1.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 145.9, 145.2, 128.4, 126.5, 126.4, 112.9, 45.4, 43.4, 25.6. HRMS (FI+) *m/z* calc'd for $C_{12}H_{14}O_2$: 190.0984, found 190.0988.



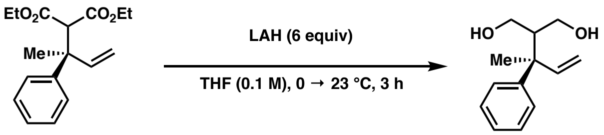
Diethyl (*R*)-2-(1-oxo-2-phenylpropan-2-yl)malonate (19)

To a flame-dried 1 Dr vial with stir bar was added the malonate product **3a** (29.0 mg, 0.1 mmol, 1.0 equiv) and K_2OsO_4•$2H_2O$ (0.4 mg, 0.001 mmol, 1 mol %). 2,6 lutidine (21.4 mg, 0.2 mmol, 2.0 equiv) was added as a solution in dioxane:H_2O (1.0 mL). To the stirring mixture was then added $NaIO_4$ (86 mg, 0.4 mmol, 4.0 equiv). The reaction vial was then heated to 50 °C for 24 h. After 24 h, the starting material had been consumed by TLC. The reaction mixture was cooled to room temperature and filtered through a pad of celite, eluting with dichloromethane (10 mL) and EtOAc (5 mL). Water was then added, and the layers were separated and extracted three times with dichloromethane. The combined organic layers were washed with brine, then dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by silica gel flash chromatography (10% EtOAc in hexanes) to afford the product as a colorless oil (19.0 mg, 67% yield); $[\alpha]_D^{25}$ +0.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H), 7.38 – 7.27 (m, 5H), 4.35 (s, 1H), 4.19 (qd, *J* = 7.2, 2.7 Hz, 2H), 3.96 (q, *J* = 7.1 Hz, 2H), 1.88 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 167.6, 167.5, 136.7, 129.0, 128.1, 127.6, 61.8, 61.4, 57.3, 54.6, 16.0, 14.1, 13.9; IR (Neat Film, NaCl) 2982, 1728, 1446, 1368, 1310, 1232, 1164, 1078, 1029 cm^{-1}; HRMS (FI+) ionization resulted in decomposition of product; *m/z* calc'd for $C_{16}H_{20}O_5$ $[M+Na]^+$: 315.1209, found 315.1203.



Diethyl (*S*)-2-methyl-2-(2-phenylbut-3-en-2-yl)malonate (20)

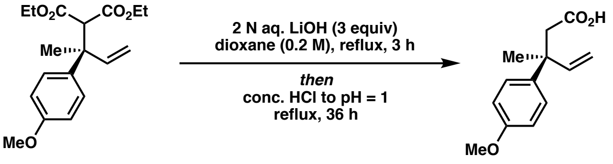
Sodium hydride (60 % dispersion in mineral oil, 0.12 mmol) was added to a 1 Dr vial. The vessel was purged and backfilled three times with nitrogen. THF (0.25 mL) was added and the suspension was cooled to 0°C. Diester **3a** (29.0 mg, 0.1 mmol, 1.0 equiv) was added as a solution in THF (0.25 mL). The solution was allowed to warm to 23°C over the course of one hour. Methyl iodide (0.2 mmol) in THF (0.5 mL) was then added dropwise to the stirred solution. After 24 hours the crude reaction mixture was diluted with ethyl acetate, then water was added and the mixture was stirred for 10 minutes. The layers were separated and extracted three times with EtOAc (20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was purified by silica gel flash chromatography (2% to 10% EtOAc in hexanes; 2% increments, 50 mL each) to afford a colorless oil (13.0 mg, 43% yield); $[\alpha]_D^{25}$ +15.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 2H), 7.25 – 7.16 (m, 2H), 6.90 (dd, *J* = 17.5, 11.0 Hz, 1H), 5.21 (dd, *J* = 11.0, 1.1 Hz, 1H), 5.02 (dd, *J* = 17.5, 1.2 Hz, 1H), 4.12 – 4.02 (m, 4H), 1.72 (s, 3H), 1.49 (s, 3H), 1.17 (dt, *J* = 14.5, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 171.4, 144.6, 144.2, 128.9, 127.4, 126.5, 114.4, 61.3, 61.2, 61.1, 49.1, 23.2, 19.8, 14.0, 14.0; IR (Neat Film, NaCl) 2981, 1729, 1445, 1381, 1254, 1026, 917, 753, 702 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{18}H_{24}O_4$: 304.1669, found 304.1683.



(*R*)-2-(2-phenylbut-3-en-2-yl)propane-1,3-diol (21)

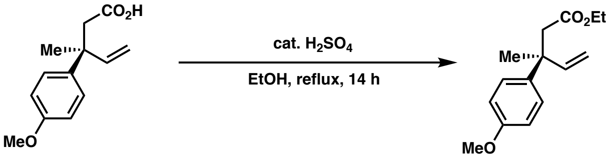
LAH (0.6 mmol, 6.0 equiv) was added to a flame dried 1 Dr vial fitted with septum. The vial was cooled to 0 °C and 0.5 mL THF was added. The diester **3a** (29.0 mg, 0.1 mmol, 1.0 equiv) was dissolved in 0.5 mL THF and added to the stirred LAH suspension. After stirring for 3 h, the reaction was cooled to 0 °C. 0.5 mL EtOAc was added to quench the reaction, which was then diluted with Et_2O followed by addition of a twofold excess of saturated potassium sodium tartrate. The layers were partitioned, the aqueous layer was extracted three times with ethyl acetate (10 mL), washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by preparative TLC (50 % EtOAc in hexanes) affording a colorless oil (13.8 mg, 67%); $[\alpha]_D^{25}$ +4.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 4H), 7.20 (ddt, *J* = 6.6, 5.6, 2.3 Hz, 1H), 6.13 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.19 (dd, *J* = 10.8, 1.0 Hz, 1H), 5.11 (dd, *J* = 17.5, 1.0 Hz, 1H), 3.85 (ddd, *J* = 10.7, 3.3, 1.4 Hz, 1H), 3.77 – 3.64 (m, 3H), 2.61 (br s, 1H), 2.51 (br s, 1H), 2.40 (tdd, *J* = 8.6, 4.1, 3.2 Hz, 1H), 1.37 (s, 3H; ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.5, 144.3, 128.6, 126.4, 126.3, 113.6, 64.9, 64.9, 50.1, 45.4, 21.7; IR (Neat Film, NaCl)

3304 (br), 2935, 1599, 1444, 1066, 1009, 919, 763, 730, 702 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{13}H_{18}O_2$: 206.1301, found 206.1315.



(*S*)-3-(4-methoxyphenyl)-3-methylpent-4-enoic acid (22a)

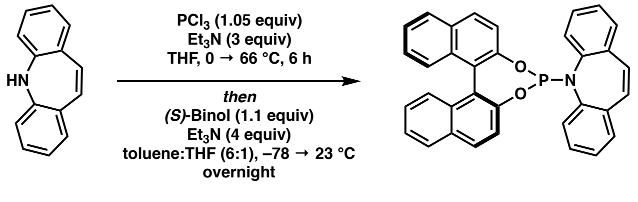
To a round bottom flask with stir bar and reflux condenser was added diester **7b** (246 mg, 0.77 mmol) in dioxane (3 mL). 2 N aq. LiOH (1.15 mL) was added, and the mixture was heated to reflux. After 3h, TLC analysis indicated full consumption of the starting material. The solution was allowed to cool to room temperature, then concentrated HCl was added until the solution reached a pH of 1. The reaction mixture was then heated to reflux and periodically monitored by LC/MS until consumption of the diacid was observed. After 36h, ethyl acetate was added, the layers were partitioned and extracted three times with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was re-dissolved in a minimal amount of ethyl acetate (0.1 mL), 2 M K_2CO_3 (5 mL) was added and the solution was stirred vigorously for 2h. The layers were separated and concentrated HCl was added until the solution reached a pH of 1. The aqueous layer was extracted four times with ethyl acetate (5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated to afford an oil that solidified to an off-white amorphous solid (110 mg, 65% yield); $[\alpha]_D^{25}$ –5.5 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 2H), 6.89 – 6.79 (m, 2H), 6.12 (dd, J = 17.4, 10.7 Hz, 1H), 5.22 – 5.01 (m, 2H), 3.79 (s, 3H), [2.81, 2.78] (ABq, 2H, J_{AB} = 14.3 Hz), 1.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 158.1, 145.6, 137.9, 127.5, 113.7, 112.5, 55.3, 45.5, 42.8, 25.7; IR (Neat Film, NaCl) 2929, 1706, 1609, 1581, 1512, 1462, 1413, 1294, 1248, 1182, 1163, 1034, 921, 827 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{13}H_{16}O_3$: 220.1094, found 220.1108.



Ethyl (*S*)-3-(4-methoxyphenyl)-3-methylpent-4-enoate (22b)

To a flame-dried round bottom 5 mL flask with stir bar and reflux condenser was added the β-quaternary acid **22a** (20 mg, 0.09 mmol) in ethanol (1 mL). Catalytic H_2SO_4 (0.05 mL) was added, and the mixture was heated to reflux. After 14h, TLC and LC/MS analysis indicated full consumption of the starting material. The solution was allowed to cool to room temperature, then neutralized with $NaHCO_3$, extracted 3x with ethyl acetate, washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The product was purified by preparative TLC (20% ethyl acetate in hexanes) affording a colorless oil (15.3 mg, 69% yield); $[\alpha]_D^{25}$ –6.9 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.22 (m, 2H), 6.87 – 6.81 (m, 2H), 6.13 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.15 – 5.02 (m, 2H), 4.00 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), [2.77, 2.72] (ABq, 2H, J_{AB} = 13.9 Hz), 1.55 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 158.0, 146.0, 138.2, 127.6, 113.6, 112.1, 60.2, 55.4, 46.0, 43.0, 25.7, 14.3; IR (Neat Film, NaCl) 2976, 2834, 1733, 1609, 1512, 1462, 1366, 1296, 1251, 1183, 1034, 911, 861, 831 cm^{-1}; HRMS (FI+) *m/z* calc'd for $C_{15}H_{20}O_3$: 248.1407, found 248.1424.

Ligand Synthesis



5-((11b*S*)-dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]dioxaphosphepin-4-yl)-5*H*-dibenzo[*b*,*f*]azepine ((*S*$_a$)-L1)[36]

The ligand was prepared according to a modified procedure disclosed by You and coworkers;[11] A flame-dried 250 mL 3-necked round bottomed flask equipped with a reflux condenser and addition funnel was charged with PCl_3 (504 mg (0.32 mL), 3.68 mmol, 1.05 equiv) and THF (5 mL). The solution was cooled to 0 ºC. Iminostilbene (676 mg, 3.0 mmol, 1 equiv) and Et_3N (1.06 g (1.46 mL), 10.5 mmol, 3 equiv) in THF (12 mL) were added dropwise. After the addition was complete, the solution was warmed to 23 °C then heated to reflux for 6 h. After TLC indicated consumption of the amine, the solution was cooled to –78 °C. A solution of *(S)*-Binol (1.10 g, 3.85 mmol, 1.1 equiv) and Et_3N (1.42 g (1.95 mL), 14 mmol, 4 equiv) in THF (10 mL) in toluene (60 mL) was added dropwise. After addition the solution was allowed to warm to 23 °C and stir overnight. The solution was then filtered over celite and silica eluting with ethyl acetate. The crude reaction mixture was concentrated and purified by silica gel chromatography (25% → 50% toluene in hexanes) to afford the desired ligand as a white solid (600 mg, 34% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.78 – 7.73 (m, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.45 – 7.32 (m, 3H), 7.30 – 7.07 (m, 9H), 7.02 – 6.89 (m, 3H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.53 (td, *J* = 7.6, 1.6 Hz, 1H). All characterization data matched those reported in the literature.

1.5.3 DETERMINATION OF ABSOLUTE CONFIGURATION OF 3a VIA VIBRATIONAL CIRCULAR DICHROISM (VCD)

Experimental Protocol. A solution of **3a** (50 mg/mL) in $CDCl_3$ was loaded into a front-loading SL-4 cell (International Crystal Laboratories) possessing BaF_2 windows and a 100 mm path length. Infrared (IR) and VCD spectra were acquired on a BioTools ChiralIR-2X VCD spectrometer as a set of 24 one-hour blocks (24 blocks, 3120 scans per block) in dual PEM mode. A 15-minute acquisition of neat (+)-α-pinene control yielded a VCD spectrum in agreement with literature spectra. IR and VCD spectra were background corrected using a 30-minute block IR acquisition of the empty instrument chamber under gentle N_2 purge, and were solvent corrected using a 16-hour (16 blocks, 3120 scans per block) IR/VCD acquisition of $CDCl_3$ in the same 100 μm BaF2 cell. The reported spectra represent the result of block averaging.

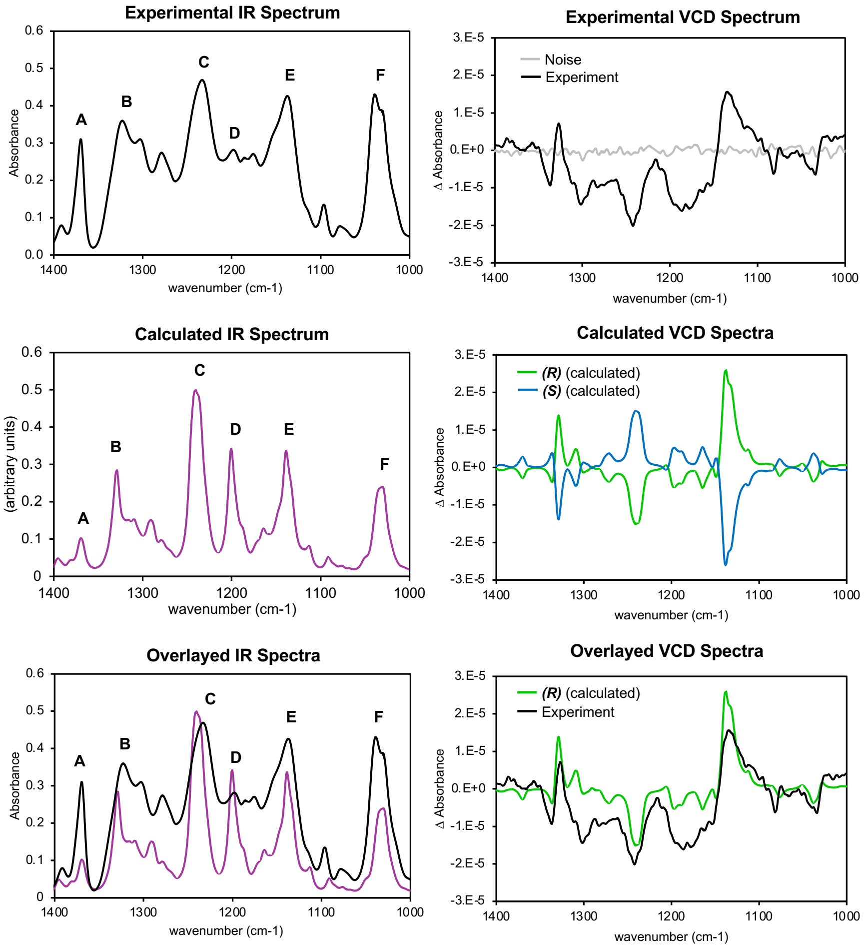
Computational Protocol. The arbitrarily chosen *(S)* enantiomer of compound **3a** was subjected to an exhaustive initial molecular mechanics-based conformational search (OPLS_2005 force field, $CHCl_3$ solvent, 10.0 kcal/mol cutoff, "Enhanced" torsional sampling) as implemented in MacroModel program.[37] The resulting ensemble containing 202 conformers was iteratively refined using the CENSO program of the Grimme group, interfaced to the Orca program of Neese, et. al. The refinement procedure includes the following steps:

1. Single point calculations with the B97-3c method. To these electronic energies are added thermochemical contributions calculated at the GFN2-xTB semi-empirical level of theory. 174 conformers remain within an energy window of 4.0 kcal/mol.
2. The conformer geometries are then optimized at the B97-3c level of theory employing a batchwise optimization procedure searching for parallel potential energy surfaces (default parameters in CENSO). 99 unique conformers remain.
3. Free energies are derived from adding thermochemical contributions calculated at the GFN2-xTB level of theory to the final electronic energies (B97-3c) from the optimizations. The 76 lowest energy conformers account for 99% of the Boltzmann population of conformers at 298.15 K (see table below).

ΔG (kcal/mol)	# conformers	Sum(Boltzmann_Pop)
0.0 – 0.5	17	64%
0.0 – 1.0	26	78%
0.0 – 1.5	46	93%

0.0 – 2.0	56	96%
0.0 – 2.5	**76**	**99%**
0.0 – 3.0	92	>99%
0.0 – 3.5	95	>99%
0.0 – 4.0	96	>99%
0.0 – 4.5	99	100%

The 76 lowest energy conformers are subsequently optimized using the B3PW91 functional, cc-pVTZ(-f) basis, and implicit PBF solvation model for chloroform using the Jaguar program. [38] Harmonic frequencies computed at the B3PW91/cc-pVTZ(-f)/PBF(chloroform) level were scaled by 0.98. The resultant 55 structurally unique conformers possessing all positive Hessian eigenvalues were Boltzmann weighted by relative free energy at 298.15 K. The predicted IR and VCD frequencies and intensities of the retained conformers were convolved using Lorentzian line shapes (γ = 4 cm^{-1}) and summed using the respective Boltzmann weights to yield the final predicted IR and VCD spectra of the *(S)* enantiomer of **3a**. The predicted VCD of the corresponding *(R)* enantiomer was generated by inversion of sign. From the reasonable agreement between the predicted and measured IR and VCD spectra in the useful range (1000–1400 cm^{-1}, see below), the absolute configuration of **3a** was assigned as *(R)*.



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