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Highly Enantio- and Diastereoselective Allylic Alkylation of Morita–Baylis–Hillman Carbonates with Allyl Ketones

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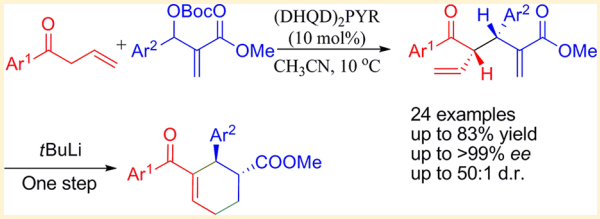
Supporting Information

ABSTRACT: The asymmetric allylic alkylation of Morita–Baylis–Hillman (MBH) carbonates with allyl ketones has been developed. The α-regioselective alkylation adducts, containing a hexa-1,5-diene framework with important synthetic value, were achieved in up to 83% yield, >99% *ee*, and 50:1 dr by using a commercially available *Cinchona* alkaloid as the catalyst. From the allylic alkylation adduct, a cyclohexene bearing two adjacent chiral centers was readily prepared.



In recent years, allyl ketones, involving an allyl group and ketone moieties, have been widely employed as valuable intermediates in organic synthesis of natural and non-natural products.[1−4] For example, allyl phenyl ketone was utilized as an important precursor to prepare the natural products including (−)-lobeline,[1] (−)-sedamine[1] and (−)-allosedamine.[2] Furthermore, Δ^2-isoxazolines could be readily prepared from allyl ketones through a tandem oximation–cyclization protocol.[3,4] However, to date to the best of our knowledge, no example has been reported on their application in asymmetric catalysis. It is thus our goal to develop some efficient organocatalytic variants to allow easy access to various chiral biologically interesting molecules from allyl ketones.[5]

As much effort has been devoted to asymmetric Morita–Baylis–Hillman (MBH) reactions,[6] recently, there has been an increasing interest focused on the enantioselective transformation of MBH products. In particular, by converting the hydroxy group into a leaving group, the MBH adducts, such as acetates and carbonates, can undergo the asymmetric allylic alkylation with various nucleophiles by the metal-free catalysis of tertiary amines and phosphines,[7,8] to access substantial *C*-,[9−20] *N*-,[21−26] *O*-,[27−31] *P*-,[32−34] and *S*-allylic[35] and spirocyclic[36−38] compounds. Since 2011, our group has successively established the allylic alkylation of bis(phenylsulfonyl)methane (BSM),[18] fluoro-bis(phenylsulfonyl)methane (FBSM),[18] *N*-itaconimides[20] and water[31] with MBH carbonates by using modified *Cinchona* alkaloids as the catalyst. Inspired by these progresses and extending our research interest, we wondered if such an activation strategy could be applied to the fascinating allyl ketones.

As Figure 1 shows, under a Lewis base catalyst, *tert*-butoxide would be derived from the expulsion of MBH carbonate, which then gets rid of an α-proton of electron-withdrawing group (EWG)-activated allyl to generate a EWG-stabilized allylic anion. It is easy to find that α-, proton-shifted α- and γ-selective adducts should be the feasible products. At the same time, both α- and γ-selective adducts contain a hexa-1,5-diene framework, which has been recognized as an important structural feature in many bioactive natural products.[39−44] Therefore, it is valuable to investigate the asymmetric allylic alkylation of MBH carbonates with EWG-activated ally compounds. In 2011, Chen and co-workers presented an allylic alkylation of MBH carbonates with allylic sulfones (EWG = sulfone). The γ-regioselective alkylation products were obtained with good to excellent enantioselectivities catalyzed by $(DHQD)_2AQN$ (Figure 1).[17] When they increased the reaction temperature to 50 °C and utilized $(DHQD)_2PYR$ as the catalyst, the α-selective product could be produced; however, the yield, enantio- and diastereoselectivity were not satisfactory (48% yield, 82% *ee*, 3.5:1 dr).[17] Herein, we wish to report the first allylic alkylation of MBH carbonates with allyl ketones (EWG = ketone) in excellent enantio- and diastereoselectivities with special α-regioselectivity, furnishing synthetically valuable chiral hexa-1,5-diene compounds as products. Most importantly, a cyclohexene, containing two adjacent chiral centers, could be synthesized conveniently from the α-selective allylic alkylation adduct (Figure 1).

As an initial study, we examined with allyl phenyl ketone **1a** and MBH carbonate **2a** as the model substrates in the presence of DABCO in CH_2Cl_2 at 25 °C. The α-regioselective adduct

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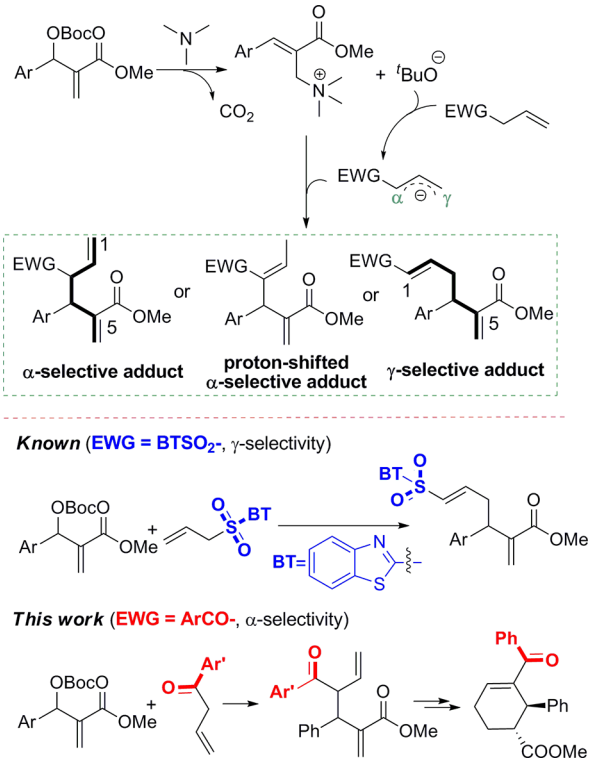
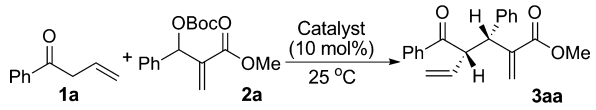


Figure 1. Two regioselective protocols of allylic alkylations of MBH carbonates with different EWG-activated allyl compounds.

3aa was delighted to be achieved with 100% conversion and 6:1 dr in 12 h. Encouraged by the results, we examined the stereoselective variant of the reaction between **1a** and **2a** in the presence of several commercially available *Cinchona* alkaloids as Lewis base catalysts at 25 °C (Table 1). Quinidine and hydroquinine showed the low reactivities and poor enantio- and diastereoselectivities (Table 1, entries 1−2). Then, a series of C_2-symmetric (bis)cinchona alkaloids, which contain rigid enzyme-like pockets,[45] was screened under the same conditions (Table 1, entries 3−8). $(DHQD)_2PYR$ showed good catalytic activity; **3aa** was achieved in 41% yield with good enantioselectivity (84% *ee*) and moderate diastereoselectivity (80:20 dr) (Table 1, entry 3). Next, we investigated the effects of solvent (Table 1, entries 9−12). The best-performing solvent with regard to reactivity and yield was acetonitrile, giving **3aa** in 67% yield with 92% *ee* and 95:5 dr in 24 h (Table 1, entry 10). Lowering the temperature to 10 °C increased *ee* to 95% and dr to 95:5 in a reasonable reaction time (Table 1, entry 13). Higher enantio- and diastereoselectivities could be obtained when the reaction temperature was decreased to 0 °C, but the reaction rate became sluggish (Table 1, entry 14).

With the optimized conditions established (10 mol % $(DHQD)_2PYR$ as catalyst in CH_3CN at 10 °C), we first evaluated the performance of the reactions between allyl phenyl ketone **1a** and various MBH carbonates **2**, and the results are summarized in Table 2. The corresponding allylic alkylation adducts were obtained in 68−82% yields with 90−95% *ee* and a dr of 13:1 to 50:1. The results showed that introducing various aryl substituents onto MBH carbonates did not affect the ee value (Table 2, entries 1−12). Also, excellent ee value could be obtained when the phenyl group of MBH carbonate was replaced with hetereoaromatic group, such as thiophene (Table 2, entry 13).

Table 1. Optimization of the Reaction Conditions[a]



entry	catalyst	solvent	*t* (h)	yield (%)[b]	*ee* (%)[c]	dr[d]
1	QD	CH_2Cl_2	48	26	51	73:27
2	HQN	CH_2Cl_2	48	32	17	41:59
3	$(DHQD)_2PYR$	CH_2Cl_2	48	41	84	80:20
4	$(DHQ)_2PYR$	CH_2Cl_2	48	44	−39	88:12
5	$(DHQD)_2AQN$	CH_2Cl_2	48	52	79	70:30
6	$(DHQ)_2PHAL$	CH_2Cl_2	48	38	70	65:35
7	$(DHQD)_2PHAL$	CH_2Cl_2	48	49	7	65:35
8	$(DHQ)_2AQN$	CH_2Cl_2	48	41	−15	72:28
9	$(DHQD)_2PYR$	acetone	24	76	86	88:12
10	$(DHQD)_2PYR$	CH_3CN	24	67	92	95:5
11	$(DHQD)_2PYR$	DMF	24	55	76	94:6
12	$(DHQD)_2PYR$	CH_3OH	24	38	87	79:21
13[e]	$(DHQD)_2PYR$	CH_3CN	67	72	95	95:5[f]
14[g]	$(DHQD)_2PYR$	CH_3CN	96	44	96	97:3

[a]Unless otherwise noted, the reaction was carried out with 0.15 mmol of **1a**, 0.05 mmol of **2a** and 0.005 mmol of catalyst in 0.5 mL of solvent. [b]Isolated yield. [c]*ee* of major diastereomer was determined by Chiral HPLC. [d]Determined by HPLC. [e]The reaction was conducted at 10 °C, 1.0 mmol scale in 1.0 mL of solvent. [f]16:1 dr was determined by crude ^1H NMR. [g]The reaction was conducted at 0 °C. QD = quinidine, HQN = hydroquinine, $(DHQD)_2PYR$ = hydroquinidine-2,5-diphenyl-4,6-pyrimidinediyl diether, $(DHQ)_2PYR$ = hydroquinine-2,5-diphenyl-4,6-pyrimidinediyl diether, $(DHQD)_2AQN$ = hydroquinidine (anthraquinone-1,4-diyl) diether, $(DHQ)_2PHAL$ = hydroquinine 1,4-phthalazinediyl diether, $(DHQD)_2PHAL$ = hydroquinidine 1,4-phthalazinediyl diether, $(DHQ)_2AQN$ = hydroquinine anthraquinone-1,4-diyl diether.

Subsequently, the scope of the allylic alkylation reaction with respect to various allyl ketones **1** and MBH carbonate **2a** was examined (Table 3, entries 1−6). In all the example studies, the desired α-regioselective allylic alkylation adducts were achieved in excellent results (up to >99% *ee* and 33:1 dr) with the exception of **3fa** (97% *ee* but 3:1 dr), indicating that the ortho-substitutent of allyl ketones **1** should decrease the reaction diastereoselectivity. The absolute configurations of the allylic alkylation adducts were assigned on the basis of X-ray crystallographic analysis of a single crystal of **3ga**.[46] Excellent enantioselectivities and diastereoselectivities were also observed for the reactions between some allyl ketones **1** and MBH carbonates **2** bearing different aryl substituents, which gave corresponding adducts **3eh**, **3ej**, **3hj** and **3hl** with up to 98% *ee* and 50:1 dr (Table 3, entries 7−10).

As Scheme 1 shows, in the presence of 10 equiv of *tert*-butyl lithium in THF at 50 °C, the α-selective allylic alkylation adduct **3aa** could be transformed to the desired chiral cyclohexene **4** with 51% yield in 10 min and without compromising *ee*. In this context, the allylic alkylation described here provides an unprecedent and efficient protocol to furnish the asymmetric synthesis of biologically important cyclohexenes with two adjacent chiral centers.[47−50]

In summary, we have developed the first highly enantio- and diastereoselective allylic alkylation of allyl ketones with MBH carbonates catalyzed by a commercially available *Cinchona* alkaloid. Several α-regioselective alkylation adducts, containing a hexa-1,5-diene framework with important synthetic value,

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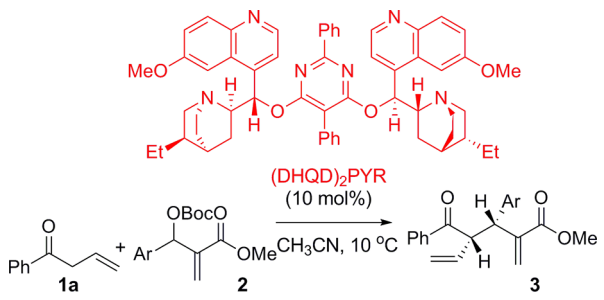
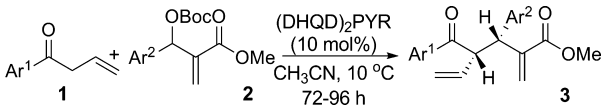
Table 2. Allylic Alkylation of Allyl Phenyl Ketone 1a with MBH Carbonates 2[a]



entry	2 Ar	t (h)	3	yield (%)[b]	ee (%)[c]	dr[d]
1	**2b**, 4-FC_6H_4	96	**3ab**	77	93	20:1
2	**2c**, 4-ClC_6H_4	72	**3ac**	75	92	20:1
3	**2d**, 4-BrC_6H_4	72	**3ad**	80	92	20:1
4	**2e**, 2,4-$Cl_2C_6H_3$	96	**3ae**	82	91	20:1
5	**2f**, 3-FC_6H_4	96	**3af**	73	93	14:1
6	**2g**, 3-ClC_6H_4	96	**3ag**	71	93	25:1
7	**2h**, 3-BrC_6H_4	96	**3ah**	70	94	25:1
8	**2i**, 2-FC_6H_4	72	**3ai**	72	94	25:1
9	**2j**, 2-ClC_6H_4	60	**3aj**	70	94	50:1
10	**2k**, 4-$CH_3C_6H_4$	96	**3ak**	68	93	14:1
11	**2l**, 3-$CH_3OC_6H_4$	96	**3al**	70	95	25:1
12	**2m**, 2-naphthyl	96	**3am**	72	91	25:1
13	**2n**, 2-thienyl	72	**3an**	79	90	13:1

[a]The reaction was carried out with 0.3 mmol of **1a**, 0.1 mmol of **2** and 0.01 mmol of $(DHQD)_2PYR$ in 1.0 mL of CH_3CN. [b]Isolated yield. [c]*ee* values were determined by chiral HPLC analysis. [d]Determined by crude ^1H NMR.

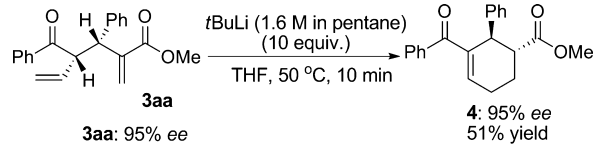
Table 3. Allylic Alkylation between β,γ-Unsaturated Ketones 1 and MBH Carbonates 2[a]



entry	1, Ar^1	2	3	yield (%)[b]	ee (%)[c]	dr[d]
1	**1b**, 2-FC_6H_4	**2a**	**3ba**	68	>99	20:1
2	**1c**, 4-ClC_6H_4	**2a**	**3ca**	71	90	20:1
3	**1d**, 4-$MeOC_6H_4$	**2a**	**3da**	77	92	33:1
4	**1e**, 3-$MeOC_6H_4$	**2a**	**3ea**	68	94	33:1
5	**1f**, 2-$MeOC_6H_4$	**2a**	**3fa**	67	97	3:1
6	**1g**, 2-thienyl	**2a**	**3ga**	83	98	20:1
7	**1e**, 3-$MeOC_6H_4$	**2h**	**3eh**	65	96	13:1
8	**1e**, 3-$MeOC_6H_4$	**2j**	**3ej**	71	96	50:1
9	**1h**, 3-BrC_6H_4	**2j**	**3hj**	72	92	25:1
10	**1h**, 3-BrC_6H_4	**2l**	**3hl**	53	96	13:1

[a]The reaction was carried out with 0.3 mmol of **1**, 0.1 mmol of **2** and 0.01 mmol of $(DHQD)_2PYR$ in 1.0 mL of CH_3CN. [b]Isolated yield. [c]*ee* values were determined by chiral HPLC analysis. [d]Determined by crude ^1H NMR.

Scheme 1. Preparation of Chiral Cyclohexene 4 from Allylic Alkylation Adduct 3aa



were obtained in 53−83% yields with 90 to >99% *ee* and a dr of 3:1 to 50:1. The synthetic method reported provides easy access to a biologically important cyclohexene bearing two adjacent chiral centers.

EXPERIMENTAL SECTION

General Procedure. MBH carbonate **2** (0.1 mmol, 1.0 equiv) and $(DHQD)_2PYR$ (8.8 mg, 0.01 mmol, 0.1 equiv) were dissolved in acetonitrile (1.0 mL) in 4 mL sample vials and stirred at 10 °C for 30 min. Then allylic ketone **1** (0.3 mmol, 3.0 equiv) was added. The reaction mixtures were stirred and maintained at 10 °C, and the reaction progress was monitored by TLC. Upon complete consumption of **2**, the reaction mixtures were loaded onto a short silica gel column, followed by separation with flash chromatography using gradient elution with petroleum ether/ethyl acetate (10:1 to 5:1). After removal of solvent under a vacuum, the corresponding adducts **3** were obtained.

3aa, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-2-methylene-3-phenylhex-5-enoate. Yellow wax: 23 mg (0.1 mmol), 72% yield; 95% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −219.68 (*c* 0.40, $CHCl_3$); ^1H NMR (400 MHz, CDCl3) δ 8.03 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 4.2 Hz, 4H), 7.21 (m, 1H), 6.14 (s, 1H), 5.61 (m, 2H), 5.05−4.94 (m, 2H), 4.84 (dd, *J* = 11.3, 8.7 Hz, 1H), 4.61 (d, *J* = 11.3 Hz, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 166.7, 142.3, 139.8, 136.9, 135.1, 133.2, 129.0, 128.7, 128.5, 128.4, 128.2, 126.8, 123.8, 119.9, 55.0, 51.9, 48.7; HRMS (ESI) *m*/*z* 321.1487 (M + H^+), calc. for $C_{21}H_{21}O_3$ 321.1491. The *ee* was determined by HPLC analysis: AMYLOSE-2 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 230 nm; retention time 9.8 min (major) and 12.6 min (minor).

3ab, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-3-(4-fluorophenyl)-2-methylenehex-5-enoate. Yellow oil: 26 mg (0.1 mmol), 77% yield; 93% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −238.69 (*c* 0.26, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 6.97 (t, *J* = 8.7 Hz, 2H), 6.14 (s, 1H), 5.66−5.51 (m, 2H), 5.01 (dd, *J* = 13.6, 7.9 Hz, 2H), 4.78 (dd, *J* = 11.3, 8.8 Hz, 1H), 4.59 (d, *J* = 11.3 Hz, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.9, 166.6, 162.9, 160.5, 142.1, 136.7, 135.6, 135.0, 133.3, 130.5, 130.4, 128.7, 128.4, 123.9, 120.2, 115.2, 115.0, 55.1, 51.9, 48.0; HRMS (ESI) *m*/*z* 361.1208 (M + Na^+), calc. for $C_{21}H_{19}FO_3Na$ 361.1210. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.5 min (major) and 13.9 min (minor).

3ac, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-3-(4-chlorophenyl)-2-methylenehex-5-enoate. Yellow oil: 27 mg (0.1 mmol), 75% yield; 92% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −188.92 (*c* 0.27, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.9 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.26−7.15 (m, 4H), 6.14 (s, 1H), 5.65−5.50 (m, 2H), 5.01 (dd, *J* = 13.8, 7.0 Hz, 2H), 4.83−4.71 (m, 1H), 4.58 (d, *J* = 11.4 Hz, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 166.5, 141.9, 138.5, 136.7, 134.8, 133.3, 132.6, 130.4, 128.8, 128.7, 128.6, 128.4, 128.4, 124.1, 120.3, 54.9, 51.9, 48.2; HRMS (ESI) *m*/*z* 377.0927 (M + Na^+), calc. for $C_{21}H_{19}ClO_3Na$ 377.0920. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.9 min (major) and 12.5 min (minor).

3ad, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-3-(4-bromophenyl)-2-methylenehex-5-enoate. Yellow oil: 32 mg (0.1 mmol), 80% yield; 92% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −267.33 (*c* 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 6.14 (s, 1H), 5.65−5.50 (m, 2H), 5.02 (dd, *J* = 13.7, 7.9 Hz, 2H), 4.84−4.73 (m, 1H), 4.56 (d, *J* = 11.3 Hz, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 166.5, 141.8, 139.0, 136.7, 134.8, 133.3, 131.4, 130.8, 128.7, 128.6, 128.4, 124.2, 120.7, 120.4, 54.8, 52.0, 48.3; HRMS (ESI) *m*/*z* 421.0417 (M + Na^+), calc. for $C_{21}H_{19}BrO_3Na$ 421.0415. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 10.2 min (major) and 14.1 min (minor).

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3ae, (3*S*,4*S*)-(−)-Methyl 4-benzoyl-3-(2,4-dichlorophenyl)-2-methylenehex-5-enoate. Pale yellow oil: 32 mg (0.1 mmol), 82% yield; 91% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −278.56 (*c* 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05−7.99 (m, 2H), 7.62−7.55 (m, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 2.1 Hz, 1H), 7.28 (s, 1H), 7.19 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.23 (s, 1H), 5.71−5.58 (m, 2H), 5.20 (d, *J* = 11.3 Hz, 1H), 5.01 (dd, *J* = 13.7, 3.0 Hz, 2H), 4.83 (s, 1H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 166.3, 136.5, 136.2, 135.9, 133.8, 133.4, 132.9, 129.4, 128.7, 128.4, 127.0, 126.0, 120.7, 51.9; HRMS (ESI) *m*/*z* 411.0529 (M + Na^+), calc. for $C_{21}H_{18}Cl_2O_3Na$ 411.0531. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 7.7 min (minor) and 8.6 min (major).

3af, (3*R*,4*S*)-Methyl 4-benzoyl-3-(3-fluorophenyl)-2-methylenehex-5-enoate. Yellow oil: 25 mg (0.1 mmol), 73% yield; 93% *ee*; dr = 14:1; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 5.4 Hz, 2H), 7.62−7.54 (m, 1H), 7.52−7.44 (m, 2H), 7.25 (d, *J* = 2.2 Hz, 1H), 7.07 (d, *J* = 6.1 Hz, 1H), 6.99 (d, *J* = 10.0 Hz, 1H), 6.89 (dd, *J* = 11.8, 4.8 Hz, 1H), 6.16 (d, *J* = 4.0 Hz, 1H), 5.67−5.50 (m, 2H), 5.01 (dd, *J* = 10.5, 7.2 Hz, 2H), 4.78 (t, *J* = 8.3 Hz, 1H), 4.60 (d, *J* = 9.3 Hz, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.7, 166.5, 164.0, 142.6, 141.8, 136.7, 134.8, 133.3, 129.7, 129.6, 128.7, 128.6, 128.4, 124.9, 124.3, 120.3, 115.8, 115.6, 113.9, 113.7, 55.0, 52.0, 48.5; HRMS (ESI) *m*/*z* 361.1215 (M + Na^+), calc. for $C_{21}H_{19}FO_3Na$ 361.1216. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.3 min (major) and 12.3 min (minor).

3ag, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-3-(3-chlorophenyl)-2-methylenehex-5-enoate. Yellow oil: 25 mg (0.1 mmol), 71% yield; 93% *ee*; dr = 25:1; $[\alpha]_D^{22}$ −205.49 (*c* 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.20 (m, 4H), 6.17 (s, 1H), 5.69−5.49 (m, 2H), 5.02 (dd, *J* = 13.6, 6.6 Hz, 2H), 4.84−4.71 (m, 1H), 4.58 (d, *J* = 11.4 Hz, 1H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 166.4, 142.1, 141.6, 136.6, 134.7, 134.0, 133.3, 129.5, 128.8, 128.7, 128.6, 128.4, 127.6, 127.0, 124.3, 120.4, 54.9, 52.0, 48.3; HRMS (ESI) *m*/*z* 377.0919 (M + Na^+), calc. for $C_{21}H_{19}ClO_3Na$ 377.0920. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.5 min (major) and 10.5 min (minor).

3ah, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-3-(3-bromophenyl)-2-methylenehex-5-enoate. Pale yellow oil: 28 mg (0.1 mmol), 70% yield; 94% *ee*; dr = 25:1; $[\alpha]_D^{22}$ −249.32 (*c* 1.70, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06−7.99 (m, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 1.6 Hz, 1H), 7.37−7.31 (m, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.17 (s, 1H), 5.65−5.51 (m, 2H), 5.03 (dd, *J* = 13.7, 8.1 Hz, 2H), 4.77 (dd, *J* = 11.4, 8.7 Hz, 1H), 4.57 (d, *J* = 11.4 Hz, 1H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 166.4, 142.4, 141.6, 136.7, 134.7, 133.3, 131.7, 130.0, 129.8, 128.7, 128.4, 128.1, 124.4, 122.3, 120.4, 54.9, 52.0, 48.4; HRMS (ESI) *m*/*z* 399.0599 (M + H^+), calc. for $C_{21}H_{20}O_3Br$ 399.0596. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.2 min (major) and 10.0 min (minor).

3ai, (3*S*,4*S*)-(−)-Methyl 4-benzoyl-3-(2-fluorophenyl)-2-methylenehex-5-enoate. Pale yellow wax: 24 mg (0.1 mmol), 72% yield; 94% *ee*; dr = 25:1; $[\alpha]_D^{22}$ −228.01 (*c* 1.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.32 (td, *J* = 7.6, 1.5 Hz, 1H), 7.19 (td, *J* = 7.3, 1.5 Hz, 1H), 7.07 (t, *J* = 7.4 Hz, 1H), 7.04−6.95 (m, 1H), 6.20 (s, 1H), 5.74−5.56 (m, 2H), 5.13−4.88 (m, 4H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 166.6, 162.5, 160.1, 140.6, 136.7, 134.7, 133.3, 130.6, 130.6, 128.7, 128.5, 128.4, 128.4, 127.2, 127.0, 125.0, 123.9, 123.9, 120.2, 115.6, 115.4, 54.1, 51.9, 42.3; HRMS (ESI) *m*/*z* 361.1217 (M + Na^+), calc. for $C_{21}H_{19}FO_3Na$ 361.1216. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.6 min (minor) and 11.8 min (major).

3aj, (3*S*,4*S*)-(−)-Methyl 4-benzoyl-3-(2-chlorophenyl)-2-methylenehex-5-enoate. Pale yellow wax: 25 mg (0.1 mmol), 70% yield; 94% *ee*; dr = 50:1; $[\alpha]_D^{22}$ −252.98 (*c* 1.90, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.14 (t, *J* = 7.1 Hz, 1H), 6.22 (s, 1H), 5.78−5.57 (m, 2H), 5.26 (d, *J* = 11.2 Hz, 1H), 5.05−4.92 (m, 2H), 4.86 (s, 1H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 166.6, 162.6, 160.1, 140.6, 136.7, 134.7, 133.3, 130.6, 130.6, 128.7, 128.5, 128.4, 128.4, 127.0, 125.0, 123.9, 123.9, 120.2, 115.6, 115.4, 54.1, 51.9, 42.3; HRMS (ESI) *m*/*z* 377.0919 (M + Na^+), calc. for $C_{21}H_{19}ClO_3Na$ 377.0920. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 230 nm; retention time 8.3 min (minor) and 9.9 min (major).

3ak, (3*R*,4*S*)-Methyl 4-benzoyl-2-methylene-3-*p*-tolylhex-5-enoate. Yellow oil: 23 mg (0.1 mmol), 68% yield; 93% *ee*; dr = 14:1; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 2H), 6.11 (s, 1H), 5.69−5.52 (m, 2H), 5.05−4.94 (m, 2H), 4.83 (dd, *J* = 11.2, 8.7 Hz, 1H), 4.57 (d, *J* = 11.2 Hz, 1H), 3.63 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.2, 166.7, 142.5, 136.9, 136.8, 136.3, 135.2, 133.1, 129.0, 128.9, 128.7, 128.4, 123.6, 119.8, 55.0, 51.9, 48.4, 21.1; HRMS (ESI) *m*/*z* 357.1464 (M + Na^+), calc. for $C_{22}H_{22}O_3Na$ 357.1467. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 230 nm; retention time 9.2 min (major) and 13.2 min (minor).

3al, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-3-(3-methoxyphenyl)-2-methylenehex-5-enoate. Yellow foam: 25 mg (0.1 mmol), 70% yield; 95% *ee*; dr = 25:1; $[\alpha]_D^{22}$ −267.40 (*c* 1.90, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.9 Hz, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.84 (s, 1H), 6.75 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.13 (s, 1H), 5.69−5.54 (m, 2H), 5.06−4.96 (m, 2H), 4.81 (dd, *J* = 11.3, 8.7 Hz, 1H), 4.57 (d, *J* = 11.3 Hz, 1H), 3.80 (s, 3H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 166.7, 159.4, 142.2, 141.5, 136.8, 135.1, 133.2, 129.2, 128.7, 128.3, 123.9, 121.5, 119.9, 115.1, 111.7, 55.2, 55.0, 51.9, 48.7; HRMS (ESI) *m*/*z* 373.1418 (M + Na^+), calc. for $C_{22}H_{22}O_4Na$ 373.1416. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 13.1 min (major) and 15.4 min (minor).

3am, (3*R*,4*S*)-(−)-Methyl 4-benzoyl-2-methylene-3-(naphthalen-2-yl)hex-5-enoate. Colorless foam: 27 mg (0.1 mmol), 72% yield; 91% *ee*; dr = 25:1; $[\alpha]_D^{22}$ −275.77 (*c* 0.60, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09−8.03 (m, 2H), 7.78 (m, 4H), 7.62−7.56 (m, 1H), 7.53−7.41 (m, 5H), 6.18 (s, 1H), 5.70−5.57 (m, 2H), 5.04−4.87 (m, 3H), 4.79 (d, *J* = 11.5 Hz, 1H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.8, 168.4, 143.3, 139.2, 138.2, 131.4, 128.8, 128.6, 128.5, 127.6, 127.5, 127.1, 126.4, 124.7, 123.0, 108.7, 54.4, 44.1, 43.2, 26.5; HRMS (ESI) *m*/*z* 371.1646 (M + H^+), calc. for $C_{25}H_{23}O_3$ 371.1647. The *ee* was determined by HPLC analysis: AD-H; hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time 8.2 min (minor) and 9.1 min (major).

3an, (3*S*,4*S*)-Methyl 4-benzoyl-2-methylene-3-(thiophen-2-yl)hex-5-enoate. Dark yellow oil: 26 mg (0.1 mmol), 79% yield; 90% *ee*; dr = 13:1; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05−8.00 (m, 2H), 7.57 (m, 1H), 7.47 (dd, *J* = 10.4, 4.7 Hz, 3H), 7.17 (dd, *J* = 5.0, 1.3 Hz, 1H), 6.92 (m, 2H), 6.14 (s, 1H), 5.78−5.63 (m, 2H), 5.15−5.06 (m, 2H), 4.91−4.87 (m, 2H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 166.5, 143.6, 142.0, 136.5, 134.8, 133.3, 128.7, 128.5, 128.5, 126.6, 126.3, 124.8, 124.4, 120.3, 56.0, 52.0, 44.3; HRMS (ESI) *m*/*z* 327.1056 (M + H^+), calc. for $C_{19}H_{19}O_3S$ 327.1055. The *ee* was determined by HPLC analysis: AD-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time 6.1 min (minor) and 6.9 min (major).

3ba, (3*R*,4*S*)-(−)-Methyl 4-(2-fluorobenzoyl)-2-methylene-3-phenylhex-5-enoate. Yellow oil: 23 mg (0.1 mmol), 68% yield; >99% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −198.76 (*c* 1.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (td, *J* = 7.7, 1.8 Hz, 1H), 7.52 (m, 1H), 7.29−7.26 (m, 4H), 7.23−7.11 (m, 3H), 6.19 (s, 1H), 5.70 (s, 1H), 5.62−5.44 (m, 1H), 4.99 (t, *J* = 12.7 Hz, 2H), 4.78 (dd, *J* = 11.4, 8.7 Hz, 1H), 4.59 (dd, *J* = 11.4, 1.8 Hz, 1H), 3.65 (s, 3H); ^{13}C NMR (100

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MHz, $CDCl_3$) δ 197.7, 197.6, 166.8, 162.6, 160.0, 142.6, 139.9, 134.6, 134.5, 134.4, 131.3, 131.3, 129.0, 128.2, 126.7, 124.6, 124.6, 123.7, 120.1, 116.8, 116.6, 59.3, 59.2, 51.9, 48.3; HRMS (ESI) m/z 339.1400 (M + H^+), calc. for $C_{21}H_{20}FO_3$ 339.1396. The *ee* was determined by HPLC analysis: AD-H; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 13.4 min (minor) and 14.9 min (major).

3ca, (3*R*,4*S*)-Methyl 4-(4-chlorobenzoyl)-2-methylene-3-phenylhex-5-enoate. Colorless solid: mp 135.5−137.9 °C; 25 mg (0.1 mmol), 71% yield; 90% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −263.58 (*c* 2.50, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.30−7.27 (m, 4H), 7.23−7.17 (m, 1H), 6.13 (s, 1H), 5.64−5.52 (m, 2H), 4.99 (t, *J* = 12.9 Hz, 2H), 4.79 (dd, *J* = 11.3, 8.7 Hz, 1H), 4.57 (d, *J* = 11.3 Hz, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1, 166.8, 142.4, 139.9, 139.8, 135.2, 135.0, 130.0, 129.2, 129.1, 128.5, 127.0, 124.1, 120.3, 55.2, 52.1, 49.0; HRMS (ESI) m/z 355.1108 (M + H^+), calc. for $C_{21}H_{20}O_3Cl$ 355.1101. The *ee* was determined by HPLC analysis: AD-H; hexane/2-propanol = 95/05; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.2 min (minor) and 10.2 min (major).

3da, (3*R*,4*S*)-(−)-Methyl 4-(4-methoxybenzoyl)-2-methylene-3-phenylhex-5-enoate. Yellow oil: 27 mg (0.1 mmol), 77% yield; 92% *ee*; dr = 33:1; $[\alpha]_D^{22}$ −112.37 (*c* 0.71, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.9 Hz, 2H), 7.28 (d, *J* = 4.3 Hz, 4H), 7.20 (m, 1H), 6.95 (d, *J* = 8.9 Hz, 2H), 6.13 (s, 1H), 5.66−5.52 (m, 2H), 5.01−4.90 (m, 2H), 4.77 (dd, *J* = 11.5, 8.7 Hz, 1H), 4.59 (d, *J* = 11.5 Hz, 1H), 3.87 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 166.7, 163.6, 142.3, 140.0, 135.5, 130.7, 129.8, 129.1, 128.2, 126.7, 123.7, 119.6, 113.9, 55.5, 54.7, 51.9, 48.6; HRMS (ESI) m/z 351.1597 (M + H^+), calc. for $C_{22}H_{23}O_4$ 351.1596. The *ee* was determined by HPLC analysis: IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 85/15; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time 7.0 min (minor) and 7.8 min (major).

3ea, (3*R*,4*S*)-(−)-Methyl 4-(3-methoxybenzoyl)-2-methylene-3-phenylhex-5-enoate. Yellow oil: 24 mg (0.1 mmol), 68% yield; 94% *ee*; dr = 33:1; $[\alpha]_D^{22}$ −241.11 (*c* 0.82, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.7 Hz, 1H), 7.54 (s, 1H), 7.36 (m, 4H), 7.20 (dd, *J* = 10.8, 4.2 Hz, 1H), 7.16−7.09 (m, 2H), 6.23 (s, 1H), 5.74−5.61 (m, 2H), 5.26 (d, *J* = 11.2 Hz, 1H), 4.98 (dd, *J* = 13.6, 3.0 Hz, 2H), 4.82 (s, 1H), 3.85 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 166.5, 159.9, 140.7, 138.1, 137.5, 135.3, 134.2, 129.7, 129.7, 127.9, 126.6, 125.6, 120.9, 120.3, 119.7, 112.8, 55.4, 51.9; HRMS (ESI) m/z 351.1592 (M + H^+), calc. for $C_{22}H_{23}O_4$ 351.1596. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 8.7 min (minor) and 10.0 min (major).

3fa, (3*R*,4*S*)-Methyl 4-(2-methoxybenzoyl)-2-methylene-3-phenylhex-5-enoate. Yellow wax: 23 mg (0.1 mmol), 67% yield; 97% *ee*; dr = 3:1; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.49−7.42 (m, 1H), 7.26 (s, 1H), 7.25 (s, 2H), 7.20−7.14 (m, 1H), 7.14−7.05 (m, 1H), 7.02−6.96 (m, 2H), 6.20 (s, 1H), 5.76 (s, 1H), 5.55 (m, 1H), 5.01−4.86 (m, 3H), 4.56 (d, *J* = 11.4 Hz, 1H), 3.94 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 201.3, 166.6, 158.1, 142.6, 140.4, 135.4, 133.5, 131.3, 129.1, 128.8, 128.3, 128.1, 128.0, 126.5, 124.1, 120.8, 119.2, 111.7, 59.0, 55.5, 51.8, 48.6; HRMS (ESI) m/z 351.1600 (M + H^+), calc. for $C_{22}H_{23}O_4$ 351.1596. The *ee* was determined by HPLC analysis: CHIRALCEL IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 27.5 min (minor) and 31.2 min (major).

3ga, (3*R*,4*S*)-(−)-Methyl 2-methylene-3-phenyl-4-(thiophene-2-carbonyl)hex-5-enoate. Yellow solid: mp 138.5−140.2 °C; 27 mg (0.1 mmol), 83% yield; 98% *ee*; dr = 20:1; $[\alpha]_D^{22}$ −244.87 (*c* 1.20, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.67 (dd, *J* = 4.9, 1.1 Hz, 1H), 7.28 (d, *J* = 4.4 Hz, 4H), 7.18 (m, 2H), 6.17 (s, 1H), 5.72 (s, 1H), 5.68−5.54 (m, 1H), 5.07−4.94 (m, 2H), 4.61 (m, 2H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 166.6, 144.0, 141.9, 139.6, 135.1, 134.2, 132.1, 129.0, 128.3, 126.8, 124.1, 119.9, 57.0, 51.9, 48.4; HRMS (ESI) m/z 327.1050 (M + H^+), calc. for $C_{19}H_{19}O_3S$ 327.1055. The *ee* was determined by HPLC analysis: AD-H; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time 5.3 min (minor) and 6.6 min (major).

3eh, (3*R*,4*S*)-Methyl 3-(3-bromophenyl)-4-(3-methoxybenzoyl)-2-methylenehex-5-enoate. Yellow oil: 28 mg (0.1 mmol), 65% yield; 96% *ee*; dr = 13:1; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.7 Hz, 1H), 7.51 (dd, *J* = 2.4, 1.7 Hz, 1H), 7.42−7.36 (m, 2H), 7.36−7.32 (m, 1H), 7.24−7.13 (m, 3H), 6.17 (s, 1H), 5.64−5.51 (m, 2H), 5.02 (dd, *J* = 13.6, 10.1 Hz, 2H), 4.73 (dd, *J* = 11.4, 8.7 Hz, 1H), 4.56 (d, *J* = 11.4 Hz, 1H), 3.85 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 166.4, 159.9, 142.3, 141.6, 138.0, 134.7, 131.7, 130.0, 129.8, 129.7, 128.0, 124.4, 122.3, 120.9, 120.4, 119.8, 112.8, 55.4, 55.0, 52.0, 48.3; HRMS (ESI) m/z 429.0702 (M + H^+), calc. for $C_{22}H_{22}O_4Br$ 429.0701. The *ee* was determined by HPLC analysis: AD-H; hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time 6.2 min (minor) and 8.1 min (major).

3ej, (3*S*,4*S*)-(−)-Methyl 3-(2-chlorophenyl)-4-(3-methoxybenzoyl)-2-methylenehex-5-enoate. Yellow oil: 27 mg (0.1 mmol), 71% yield; 96% *ee*; dr = 50:1; $[\alpha]_D^{22}$ −281.75 (*c* 1.71, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.7 Hz, 1H), 7.53 (dd, *J* = 2.4, 1.7 Hz, 1H), 7.43−7.29 (m, 3H), 7.20 (td, *J* = 7.5, 1.4 Hz, 1H), 7.17−7.07 (m, 2H), 6.23 (s, 1H), 5.75−5.60 (m, 2H), 5.26 (d, *J* = 11.2 Hz, 1H), 4.98 (dd, *J* = 13.9, 3.0 Hz, H), 4.82 (s, 1H), 3.85 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 166.5, 159.9, 140.7, 138.0, 137.4, 135.3, 134.1, 129.7, 129.7, 127.9, 126.6, 125.6, 120.9, 120.3, 119.7, 112.8, 55.4, 51.9; HRMS (ESI) m/z 385.1212 (M + H^+), calc. for $C_{22}H_{22}O_4Cl$ 385.1207. The *ee* was determined by HPLC analysis: AD-H; hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 210 nm; retention time 6.6 min (minor) and 9.7 min (major).

3hj, (3*S*,4*S*)-(−)-Methyl 4-(3-bromobenzoyl)-3-(2-chlorophenyl)-2-methylenehex-5-enoate. Colorless oil: 31 mg (0.1 mmol), 72% yield; 92% *ee*; dr = 25:1; $[\alpha]_D^{22}$ −132.32 (*c* 1.70, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (t, *J* = 1.7 Hz, 1H), 8.06−7.93 (m, 1H), 7.70 (m, 1H), 7.40−7.31 (m, 3H), 7.21 (m, 1H), 7.17−7.09 (m, 1H), 6.23 (s, 1H), 5.72−5.59 (m, 2H), 5.23 (d, *J* = 11.5 Hz, 1H), 5.04−4.94 (m, 2H), 4.81 (s, 1H), 3.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 166.5, 138.4, 137.1, 136.1, 135.2, 133.7, 131.4, 130.3, 129.7, 128.7, 128.4, 128.0, 126.9, 126.7, 126.6, 125.8, 123.1, 120.8, 51.9; HRMS (ESI) m/z 433.0203 (M + H^+), calc. for $C_{21}H_{19}O_3ClBr$ 433.0206. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 7.2 min (minor) and 8.2 min (major).

3hl, (3*R*,4*S*)-Methyl 4-(3-bromobenzoyl)-3-(3-methoxyphenyl)-2-methylenehex-5-enoate. Yellow oil: 28 mg (0.1 mmol), 53% yield; 96% *ee*; dr = 13:1; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (t, *J* = 1.7 Hz, 1H), 7.96 (m, 1H), 7.69 (m, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.21 (t, *J* = 7.9 Hz, 1H), 6.91−6.80 (m, 2H), 6.79−6.71 (m, 1H), 6.14 (s, 1H), 5.66−5.53 (m, 2H), 5.02 (t, *J* = 13.3 Hz, 2H), 4.74 (dd, *J* = 11.4, 8.6 Hz, 1H), 4.53 (d, *J* = 11.4 Hz, 1H), 3.80 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.8, 166.6, 159.5, 142.1, 141.2, 138.6, 136.0, 134.6, 131.4, 130.3, 129.2, 128.7, 128.4, 126.9, 124.0, 123.1, 121.4, 120.3, 115.1, 111.8, 55.2, 55.1, 52.0, 48.8; HRMS (ESI) m/z 429.0695 (M + H^+), calc. for $C_{22}H_{22}O_4Br$ 429.0701. The *ee* was determined by HPLC analysis: AMYLOSE-2; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 10.0 min (major) and 13.5 min (minor).

4, (1*R*,2*R*)-(−)-Methyl 3-benzoyl-2-phenylcyclohex-3-enecarboxylate. 0.63 mL of *t*BuLi solution (1.6 M in pentane) (10 equiv) was added dropwise into a solution of **3aa** (0.1 mmol) in 5 mL of dry THF at −78 °C. After being stirred for 10 min at that temperature, the mixture was slowly warmed up to 50 °C and stirred for 10 min. Then the mixture was cooled to 0 °C, quenched by NH_4Cl (Sat.) solution, extracted by ethyl acetate, dried over Na_2SO_4, and purified by flash chromatography using gradient elution with petroleum ether/ethyl acetate (20:1 to 10:1) to afford **4**, 16 mg (0.1 mmol), 51% yield as a colorless foam: 95% *ee*; $[\alpha]_D^{22}$ −97.94 (*c* 0.25, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) 7.61 (d, *J* = 7.9 Hz, 2H), 7.44 (dt, *J* = 14.2, 7.5 Hz, 4H), 7.23−7.12 (m, 4H), 6.77 (s, 1H), 4.76 (d, *J* = 4.9 Hz, 1H), 3.56 (s, 3H), 2.97−2.87 (m, 1H), 2.67−2.60 (m, 1H), 2.43−2.29 (m, 1H), 2.04−1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 173.5,

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143.0, 139.5, 139.0, 138.4, 131.6, 129.2, 129.1, 128.1, 128.1, 127.1, 120.0, 51.3, 44.6, 40.6, 29.7, 25.5; HRMS (ESI) *m/z* 321.1491 (M + H^+), calc. for $C_{21}H_{21}O_3$ 321.1492. The *ee* was determined by HPLC analysis: AD-H; hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time 7.4 min (minor) and 9.6 min (major).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General information, HPLC spectra of chiral products, crystallographic data of **3ga**, and NMR spectra of the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ NOTE ADDED AFTER ASAP PUBLICATION

Reference 5 was corrected and reposted on April 30, 2013. All graphics contained errors and were replaced on May 7, 2013.