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Enantioselective α-Functionalization of 1, 3-Dithianes by an Iridium Catalyzed Allylic Substitution

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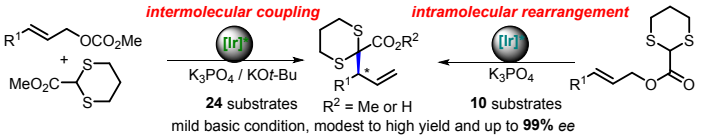
Supporting Information Placeholder



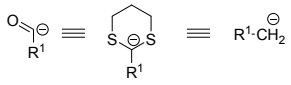
ABSTRACT: An iridium-catalyzed asymmetric allylic substitution reaction with 2-alkoxy carbonyl-1,3-dithianes has been achieved with high regio- and enantio-selectivities. The transformation provides a new method for the enantioselective α-functionalization of dithianes. The corresponding dithiane-containing products are easily converted into many other derivatives with high yields and enantioselectivities.

▪ INTRODUCTION

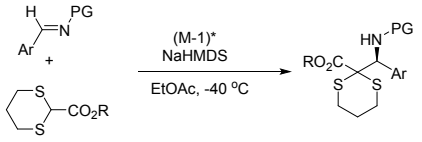
1,3-Dithiane derivatives are considered as useful acyl anion equivalents, which have been widely used as masked nucleophilic acylating agents, since the pioneering work of Corey and Seebach.[1] On the other hand, the 1,3-dithiane unit was also used as the mask of methylene and difluoromethylene groups due to its variability under a reductive or an oxidative condition (Scheme 1a).[2] The application of 1,3-dithiane was further explored in total syntheses of natural products, known as the anion relay reaction.[3] Therefore, 1,3-dithianes are found to be versatile building blocks for the formation of many important organic compounds and natural products.[4,5] However, the catalytic enantioselective addition reactions of 1,3-dithianes are still largely unexplored due to they are incompatibility with other catalytic reaction system. So far, only a few papers reported the enantioselective addition reaction of 1,3-dithianes with different electrophiles in a catalytic manner.[6] Especially, the Terada group successfully performed the asymmetric 2-alkoxycarbonyl-1,3-dithiane addition of imines assisted by bis(guanidino)amino-phosphorane with excellent enantioselectivity and good yields. (Scheme 1b).[6a] Zhang reported 2-phenyl-1,3-dithiane's asymmetric allylic substitution with 1,3-diphenylallyl pivalate (Scheme 1c).[6b] Previous strategies can only synthesis of specific dithiane containing products due to the limitation of electrophiles. New methods are still needed to prepare optically active α-functionalized 1,3-dithiane derivatives, which are known as versatile starting materials for further synthetic transformations. The iridium-catalyzed asymmetric allylic substitution reaction has attracted considerable attentions due to the wide functional-group tolerance and powerful efficiency for constructing a chiral center with high regio- and enantio-selectivities.[7] And it was widely used in the synthesis of natural products and

Scheme 1. Representative forms of enantioselective α-functionalization of dithianes

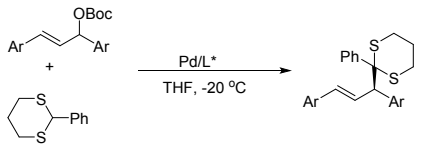
a). 1,3-dithiane synthon



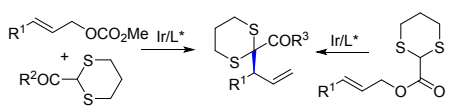
b). Terada's work: chiral super base catalyzed asymmetric dithiane addition



c). Zhang's work: palladium catalyzed asymmetric dithiane substitution



d). This work: iridium catalyzed asymmetric allylic dithiane substitution



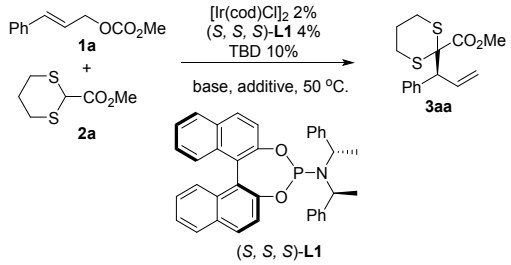
pharmaceutical molecules.[8] On the other hand, the Li group recently reported dithiane-directed C−H borylation via iridium catalysis.[9] They observed a strong coordination 1,3-dithiane group with an iridium metal catalyst[9, 10] and other transition metals.[11] Inspired by these works, we herein report a new method to prepare optically active α-functionalized 1,3-dithiane derivatives by using iridium catalyzed intermolecular and intramolecular allylic substitution methods (Scheme 1d).

▪ RESULTS AND DISCUSSION

Initially, allylic ester **1a** and 1,3-dithiane derivative **2a** were used as the model substrate. The reaction was carried out by using a common Ir-catalytic system consisting of $[Ir(cod)Cl]_2$ and a chiral ligand with a variety of bases[13] under an argon atmosphere in THF at 50 ℃ for 6 h. First, the effect of the ligand on the reaction was examined.[7d, e, f] **L1** was found to be a suitable ligand obtaining the desired coupling product **3a** with 27% yield and 95% ee (Table 1, entry 1). The low yield could attribute to the decomposition of ester **1a** and the formation of a hydrolysis byproduct with 1.5 equivalents *t*-BuOK as a base. Other strong bases did not improve the yield (Table 1, entries 2-7). However, a clean reaction was obtained by using K_3PO_4 as the base, giving **3a** in 41% yield together with 55% recovered **1a** (Table 1, entry 8). Prolonging the reaction time and increasing the amount of K_3PO_4 or adding additives, such as 4ÅMS, 18-crown-6, CsF, or LiCl, did not give any positive result (Table 1, entries 9-12). Further experiments revealed that the choice of a suitable mixture of bases was important for the allylic substitution reaction. To our delight, the desired product was obtained with 78% yield by using a mixture of 3.0 equiv. K_3PO_4 and 0.2 equiv. *t*-BuOK as combined bases (Table 1, entry 13). The mixture of bases might provide a buffer system to accelerate the reaction and lower down the hydrolysis of the dithiane ester. After an extensive screening process, the reaction conditions were optimized as follows: the coupling reaction was performed with 3.0 equivalent K_3PO_4, 0.2 equivalent *t*-BuOK, 2 mol% $[Ir(cod)Cl]_2$, 4 mol% (*S, S, S*)-**L1** and 10 mol% TBD in THF at 50 ℃ for 6 h. Besides, no linear product was observed in this reaction system. The coordination of 1,3-dithiane motif with the iridium catalyst might help explain the observed excellent regioselectivity.

With the optimized conditions in hand, the scope of aryl allylic esters was investigated. First, *ortho*-, *meta*-, and *para*-aryl esters were tested, and the corresponding products **3b-3d** were obtained with high yields and high enantioselectivities. Esters with an electron-donating group, such as a methyl and a methoxy group, or an electron-withdrawing group, such as a floro, a chloro, or a bromo group, smoothly underwent the reaction to produce products **3d-3f** with high yields and excellent enantioselectivities. The steric hindering substituent on the aromatic ring, such as an *i*-Pr or a *t*-Bu group at the *para* position proceeded without any problems. The naphthyl or the benzo-furanyl ring showed little influence on this reaction, affording the corresponding products **3g**, **3h**, and **3i** with high yields and high enantioselectivities, respectively. More importantly, heteroaromatic esters were also found to be tolerant in this reaction. Furyl and thionyl esters were found to be compatible with the reaction conditions and produced the products **3j** and **3p-3r** with excellent yields. The substitution of 1,3-dithianes also exerted little influence on this reaction. Particularly, the proton of 2-acetyl 1,3-dithiane also did not show any impact on this allylic substitution, affording the product **3x** with excellent regioselectivity. Fortunately, a crystal of **3x** was obtained, which further confirmed the absolute configuration of the stereocenters in the products depicted in Table 2.

Table 1. Optimization of reaction conditions[a]

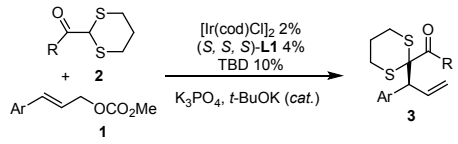


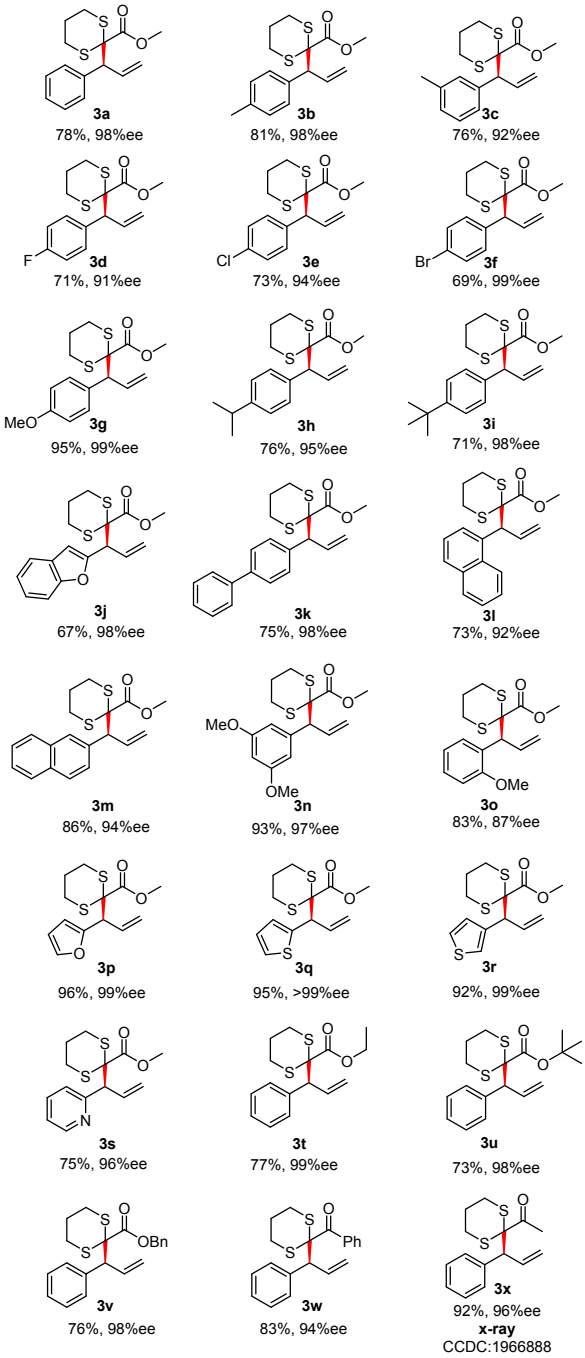
entry	bases	additive	yield[b]	ee[c]
1	*t*-BuOK		27	95
2	*t*-BuOLi		25	94
3	*t*-BuONa		22	95
4	LiHMDS		11	94
5	DBU		10	96
6[f]	*t*-BuOK		23	94
7[g]	*t*-BuOK		15	95
8[d]	K_3PO_4		41	94
9	K_3PO_4	LiCl	37	95
10	K_3PO_4	18-crown-6	31	95
11	K_3PO_4	CsF	33	93
12	K_3PO_4	4ÅMS	29	98
13	K_3PO_4	*t*-BuOK	78	98
14[e]	K_3PO_4	*t*-BuOK	76	98

[a]Unless otherwise noted, the reaction of **1a** (0.1 mmol) with **2a** (0.15 mmol) was carried out by using a catalytic system consisting of $[Ir(cod)Cl]_2$ (2 mol%) and (*S, S, S*)-**L1** (4 mol%) and 10 mol% TBD under an Ar atmosphere in the presence of a base (0.11 mmol) and an additive (0.02 mmol) in THF (2 mL) at 50 ℃ for 6 h. TBD=1, 5, 7-Triazabicyclo[4. 4. 0] dec-5-ene. [b]Isolated yields. [c]Determined by HPLC using a chiral Daicel OD-H column. [d]K_3PO_4 (3.0 equiv.) was used with 55% recovery of starting material **1a**. [e]At room temperature for 14 h. [f]DCM was used as solvent. [g]DMSO was used as solvent.

The intramolecular reaction of **4a** was also examined in the presence of 2 mol% $[Ir(cod)Cl]_2$, 4 mol% (*R, R, R*)-**L1** and 10 mol% TBD, with K_3PO_4 as a base, which provided the acid **5a** as the sole product in 62% yield (condition optimization see SI). It seems that ester hydrolysis is a more favorable process to form a dithiane-containing acid than five-membered cyclic ester formation. The substrate scope of the Ir-catalyzed intramolecular rearrangement reaction of dithianes **4** was investigated under the optimized reaction conditions (Table 3). The reaction proceeded well in all cases, yielding dithiane-containing acid **5a-5d** with moderate yields and high enantioselectivities. Substitution on the aryl group of substrates exerted little influence on the intramolecular allylic substitution reactions. Most importantly, the reaction also proceeded well for alkyl-substituted allylic ester **4e**, providing the corresponding product **5e** with excellent ee and moderate yield.

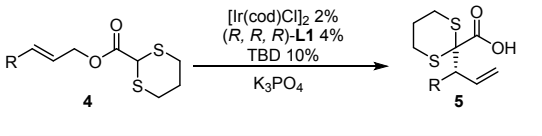
Table 2. Scope of the intermolecular enantioselective α-functionalization of dithianes[a]

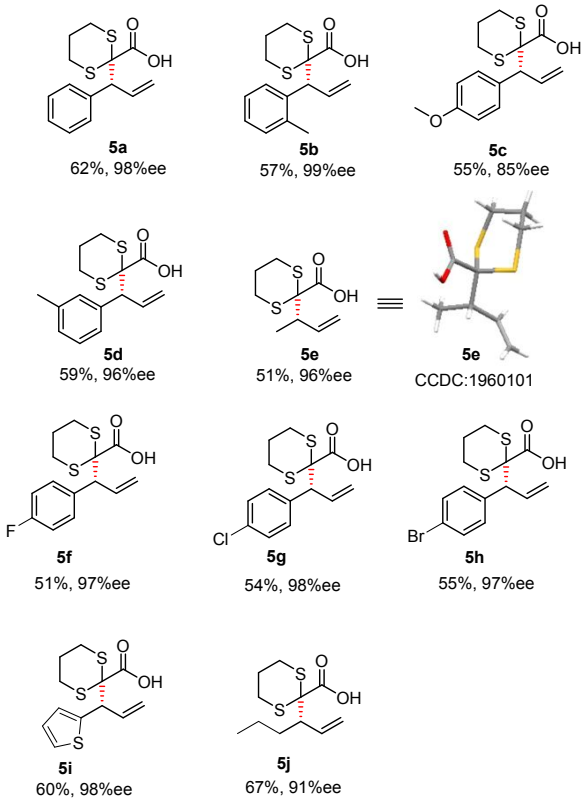




[a]The reaction of **1** (0.1 mmol) with **2** (0.15 mmol) was carried out by using a catalytic system consisting of $[Ir(cod)Cl]_2$ (2 mol%) and (*S, S, S*)-**L1** (4 mol%) under an Ar atmosphere in the presence of K_3PO_4 (0.30 mmol) and *t*-BuOK (0.02 mmol) in THF (2 mL) at 50 °C for 6 h. Isolated products; ee values were determined by HPLC using chiral Daicel columns.

Table 3. Scope of the intramolecular enantioselective α-functionalization of dithianes[a]

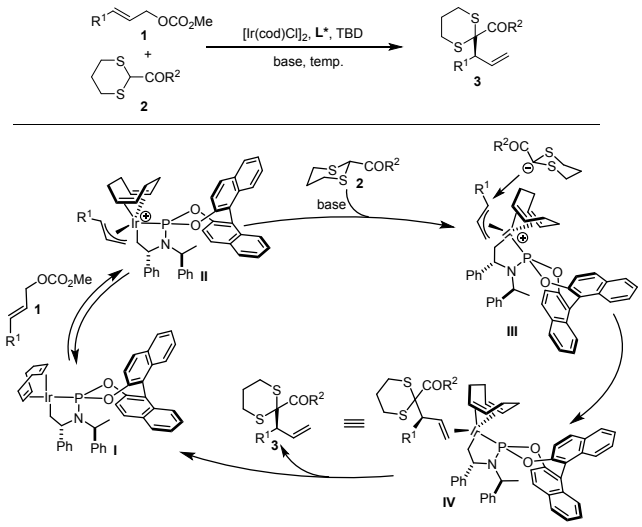




[a]The reaction of **4** (0.1 mmol) was carried out by using a catalytic system consisting of $[Ir(cod)Cl]_2$ (2 mol%) and (*R, R, R*)-**L1** (4 mol%) under an Ar atmosphere in the presence of a base (0.15 mmol) in THF (2 mL) at 50 °C for 6 h. Isolated products; ee values were determined by HPLC using chiral Daicel columns.

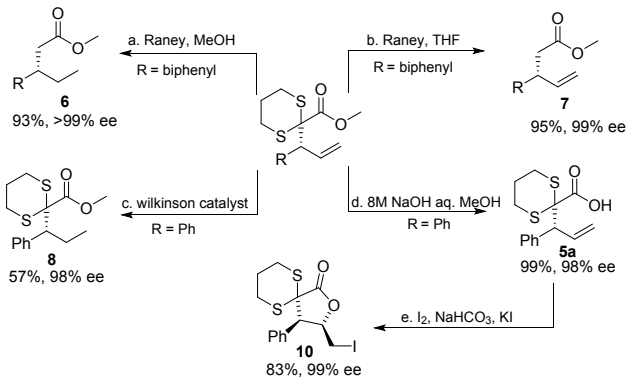
The absolute configuration of the stereocenters in the products showed in Table 2 was also confirmed through the single-crystal X-ray diffraction analysis of **5e**. Furthermore, the absolute configurations of the stereocenters in **5a-5d** in Table 2 were also indirectly confirmed via comparing the optical rotation of acid derivative of **3a** and **5a**. The stereocenter's absolute configuration of **5a-5d** was conforms to the general rule of the iridium-catalytic system.

Scheme 2. Mechanisms of the iridium catalyzed enantioselective dithaine allylic substitution reaction.



Based on the initial studies of Hartwig and previous literature[7], a plausible reaction pathway was proposed (Scheme 2). Allylic ester **1** coordinates to a chiral Ir catalyst **I** to give the intermediate **II**.[7] Owing to the coordination of dithiane with the iridium catalyst,[9] 2-alkoxycarbonyl-1, 3-dithiane anion and cationic Ir intermediate **II** might form a complex transition state **III**. Then, a nucleophilic allylic substitution reaction occurs between the α-position of the dithiane derivative and the allylic cation, in which the stereo-chemical outcome is controlled by the chiral ligand of iridium in an enantio- and regioselective manner.[12]

Scheme 3. Transformation of enantioenriched α-functionalized 1,3-dithianes[a]



[a]General reaction conditions: a) Raney-Ni, MeOH, 50 ℃; b) Raney-Ni, THF, 50 ℃; c) Wilkinson catalyst (5%), H_2, THF, RT; d) NaOH (4.0 equiv, 4 M aq.), MeOH, reflux; e) I_2 (1.3 equiv), $NaHCO_3$ (1.4 equiv), KI (1.3 equiv), MeCN/H_2O (1:1), RT.

Finally, the derivative transformations of the optically dithiane-containing products were performed (Scheme 3). First, the selective reduction of the 1,3-dithiane and alkene moiety was investigated. The reduction of the alkene moiety of **3k** with Raney-Ni in MeOH yielded enantioenriched ester **6**. Pleasingly, the selective removal of the 1,3-dithiane moiety was achieved with Raney-Ni in THF to produce ester **7** in high yield. Moreover, the hydrogenative of the double bond moiety of (*S*)-**4a** by using the Wilkinson catalyst yielded (*S*)-**8** in good enantioselectivity. The hydrolysis of (*S*)-**4a** under basic condition was smoothly carried out to produce **5a** in good yield with high enantioselectivity. More importantly, enantio-rich acid **5a** could further transformed into lactone **10** in high yield via intramolecular esterification.

In conclusion, we have developed a catalytic enantioselective α-functionalization of 1,3-dithianes by using an iridium catalyzed allylic substitution. The allylic substitution has proceeded in a highly enantioselective manner to produce optically active dithiane-containing compounds, which are known as valuable versatile building blocks in organic synthesis. Ongoing studies are focused on the development of novel enantioselective transformations for the synthesis of dithiane-containing compounds.

▪ EXPERIMENTAL SECTION

General Information ^{1}H NMR spectra were recorded on a Bruker Mercury 400, 600MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The data are reported as (s = single, d = double, t = triple, q = quartet, m = multiple or unresolved, and br = broad). ^{13}C NMR spectra were recorded on a Bruker 100 MHz spectrometer in $CDCl_3$. Chemical shifts are reported in ppm. Commercially available reagents were used without further purification. All reactions were monitored by TLC with silica gel plates. Enantiomeric ratios were determined by HPLC, using a CHIRALPAK AD-H And OD-H with hexane and *i*-PrOH as solvents. HRMS was tested by a Bruker Daltonics Apex II 47e Specifications. The mass analyzer type Q-TOF used for the HRMS measurements. The melting points were determined in glass capillary tubes using WRS-2U melting point apparatus (Shanghai precision Instrument Co. Ltd. Shanghai, China) and are uncorrected. The crystal date structure was obtained at room temperature using Mo Kα radiation on a Bruker APEXII diffractometer X-ray diffraction data were collected on Agilent SuperNova Eos diffractometer. 1,3-dithiane derivatives (**1**(Methyl ester)[16d], **1t**[16c], **1u**[16a],**1v**[6a], **1w**[6b] and **1x**[16b]) were reported in the literatures.

General produces for the preparation of compound 1

To a stirred suspension of NaH (60% w/w in mineral oil, 2.0 equiv.) in THF (1.0 M) was added triethylphosphonoacetate (1.5 equiv.) at 0 ºC and was stirred for 20 min before being added with the appropriate aldehyde (1.0 equiv.) and was allowed to warm to room temperature. After cooling to 0 ºC the reaction was carefully quenched with H_2O and extracted with EtOAc. The organic layer was separated, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in Et_2O (1.0 M) and was stirred at -78 ºC when DIBAL-H (1.0 M toluene, 2.5 equiv.) was added dropwise. The solution was allowed to warm to room temperature and was stirred for 3-5 h before being quenched with sat. Rochelle's salts very slowly followed by H_2O, diluted with EtOAc and was stirred overnight. The organic layer was separated and dried over anhydrous Na_2SO_4. After the solvent was removed *in vacuo*, the crude product was purified by column chromatography (silica gel, hexane/EtOAc) to give the corresponding allylic alcohol. Finally, the residue was dissolved in dichloromethane (0.5 M), added with DMAP (0.20 equiv.) and pyridine (3.0 equiv.) and was stirred at 0 ºC for 20 min before methyl chloroformate (1.5 equiv.) was added dropwise over 10 min. Then the reaction mixture was allowed to warm to room temperature and was stirred overnight. The reaction was quenched with aq. NH_4Cl and was poured into EtOAc. The organic layer was separated and dried over anhydrous Na_2SO_4. After the solvent was

removed *in vacuo*, the crude product was purified by column chromatography (silica gel, Petroleum ether /EtOAc) to give the corresponding allylic carbonates.

Allylic carbonates **1a-1b**[15a], **1c**[15c], **1d-1g**[15a], **1j-1k**[15e], **1l**[15c], 1m-**1o**[15a], **1p**[15c], **1q**[15b], **1r**[15d] and **1s**[15c] were reported in the literatures.

Compound 1h. Petroleum ether/ethyl acetate (10:1) as the eluent; colorless oil (starting from 10 mmol of cuminaldehyde, 1.7 g, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 6.67 (dd, J = 15.8 Hz, 1.4 Hz, 1H), 6.25 (dt, J = 15.8, 6.5 Hz, 1H), 4.78 (dd, J = 6.4, 1.4 Hz, 2H), 3.80 (s, 3H), 2.93–2.86 (m, J = 6.9 Hz, 1H), 1.24 (d, J = 6.9 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.7, 149.1, 134.9, 133.6, 126.7, 126.7, 121.4, 68.6, 54.8, 33.9, 23.9; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{14}H_{18}NaO_3$ 257.1148; found 257.1147.

Compound 1i. Petroleum ether/ethyl acetate (10:1) as the eluent; colorless oil (starting from 10 mmol of 4-tert-Butylbenzaldehyde, 2.0 g, 81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.30 (m, 4H), 6.66 (dt, J = 15.9, 1.3 Hz, 1H), 6.25 (dt, J = 15.9, 6.5 Hz, 1H), 4.77 (dd, J = 6.6, 1.3 Hz, 2H), 3.79 (s, 3H), 1.31 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.6, 151.3, 134.6, 133.2, 126.4, 125.5, 121.5, 68.5, 54.7, 34.5, 31.2; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{15}H_{20}NaO_3$ 271.1305; found 271.1301.

Gram-Scale Synthesis.

In a 100 mL schlenk flask $[Ir(cod)Cl]_2$ (0.1 mmol), chiral phosphoramidite (0.2 mmol), and TBD (0.5 mmol) were dissolved in THF (20 mL) under an Ar atmosphere. The reaction vessel was sealed with a screw cap and the mixture heated at 50 ℃ (oil bath) for 30 min to allow the formation of the active catalyst species (the solution turns from orange to yellow). After this time, **1a** (5 mmol), **2a** (7.5 mmol), K_3PO_4 (10 mmol), *t*-BuOK (1 mmol) and THF (20 mL) were then added and the resulting mixture was heated at 50 ℃. Upon completion, the solvent evaporated. The mixture was then purified by flash chromatography to afford the product **3a** (1.02g, 72%).

General produces for the preparation of compound 3.

In a reaction vessel $[Ir(cod)Cl]_2$ (0.002 mmol), chiral phosphoramidite (0.004 mmol), and TBD (0.01 mmol) were dissolved in THF (0.5 mL) under an Ar atmosphere. The reaction vessel was sealed with a screw cap and the mixture heated at 50 ℃ (oil bath) for 30 min to allow the formation of the active catalyst species (the solution turns from orange to yellow). After this time, the allylic carbonate (0.1 mmol), the nucleophile (0.15 mmol), K_3PO_4 (0.2 mmol), *t*-BuOK (0.02 mmol) and THF (1.5 mL) were then added and the resulting mixture was heated at 50 ℃ (oil bath). Upon completion, the solvent evaporated. The mixture was then purified by flash chromatography to afford the product.

Preparation of Racemic Standards Racemic samples were obtained by using the above-mentioned procedure, however racemic ligand was used (*S*, *S, S*)-Ligand and (*R*, *R, R*)-Ligand at the ratio of 1:1.

Compound 3a. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (22 mg, 78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5H), 6.46 (ddd, J = 16.9, 10.1, 8.8 Hz, 1H), 5.22 (dd, J = 16.9, 10.1 Hz, 2H), 4.05 (d, J = 8.8 Hz, 1H), 3.73 (s, 3H), 3.16–3.05 (m, 2H), 2.72–2.66 (m, 2H), 2.06–2.01 (m, 1H), 1.86–1.79 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.7, 138.1, 135.7, 129.6, 128.0, 127.6, 118.7, 60.4, 57.5, 52.9, 28.5, 28.2, 24.2; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98% with Rt = 8.6 min (major) and Rt = 9.0 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +45.4 (c 0.79, CH_2Cl_2). HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{19}O_2S_2$ 295.0821; found 295.0826.

Compound 3b. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (24.9 mg, 81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.22 (m, 2H), 7.09 (d, J = 8.0 Hz, 2H), 6.46 (ddd, J = 16.9, 10.2, 8.8 Hz, 1H), 5.21 (dd, J = 16.9, 10.2 Hz, 2H), 4.01 (d, J = 8.8 Hz, 1H), 3.73 (s, 3H), 3.08 (ddd, J = 15.2, 12.9, 2.8 Hz, 2H), 2.73–2.65 (m, 2H), 2.31 (s, 3H), 2.06–2.01 (m, 1H), 1.80 (qt, J = 13.0, 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.8, 137.3, 135.8, 135.0, 129.4, 128.8, 118.5, 60.6, 57.1, 52.9, 28.5, 28.3, 24.3, 21.1; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98% with Rt = 8.1 min (minor) and Rt = 8.7 min (major) [1.0% *i*-PrOH in hexanes, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D +56.1 (*c* 0.49, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{16}H_{21}O_2S_2$ 309.0977; found 309.0981.

Compound 3c. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (23.4 mg, 76%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20–7.13 (m, 3H), 7.06 (dd, J = 6.9, 1.8 Hz, 1H), 6.46 (ddd, J = 16.9, 10.2, 9.1 Hz, 1H), 5.20 (dd, J = 16.9, 10.2 Hz, 2H), 4.01 (d, J = 9.1 Hz, 1H), 3.74 (s, 3H), 3.14–3.04 (m, 2H), 2.73–2.65 (m, 2H), 2.33 (s, 3H), 2.07–2.03 (m, 1H), 1.87–1.77 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9, 138.1, 137.6, 135.8, 130.5, 128.5, 128.0, 126.6, 118.7, 60.6, 57.6, 53.0, 28.6, 28.4, 24.4, 21.6; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 92% with Rt = 18.2 min (major) and Rt = 20.8 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +17.3 (*c* 0.52, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{16}H_{21}O_2S_2$ 309.0977; found 309.0981.

Compound 3d. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (22 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.32 (m, 2H), 7.01–6.96 (m, 2H), 6.42 (ddd, J = 16.9, 10.2, 8.7 Hz, 1H), 5.19 (dd, J = 16.9, 10.2 Hz, 2H), 4.05 (d, J = 8.7 Hz, 1H), 3.74 (s, 3H), 3.11 (ddd, J = 14.2, 11.4, 2.8 Hz, 2H), 2.74–2.66 (m, 2H), 2.05 (dtt, J = 14.1, 4.3, 2.8 Hz, 1H), 1.86–1.76 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.7, 135.5, 133.8, 131.3, 118.8, 115.0, 114.7, 60.2, 56.6, 53.0, 28.4, 28.2, 24.2; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 91% with Rt = 15.8 min (minor) and Rt = 16.9 min (major) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +4.1 (*c* 0.5, CH_2Cl_2); ^{19}F NMR (282 MHz, $CDCl_3$): δ –115.2; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{18}FO_2S_2$ 313.0727; found 313.0729.

Compound 3e. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (23.9 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.25 (m, 4H), 6.41 (ddd, J = 16.9, 10.2, 8.7 Hz, 1H), 5.20 (dd, J = 16.9, 10.2 Hz, 2H), 4.04 (d, J = 8.7 Hz, 1H), 3.74 (s, 3H), 3.12 (ddd, J = 14.2, 12.4, 2.8 Hz, 2H), 2.73–2.66 (m, 2H), 2.08–2.03 (m, 1H), 1.80 (dtt, J = 13.8, 12.6, 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.7, 136.6, 135.3, 133.5, 131.1, 128.2, 119.1, 59.9, 56.7, 53.0, 28.4, 28.2, 24.2; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 94% with Rt = 21.3 min (minor) and Rt = 22.8 min (major) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D –6.5 (*c* 0.31, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{18}ClO_2S_2$ 329.0431; found 329.0435.

Compound 3f. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (25.6 mg, 69%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.41 (m, 2H), 7.27–7.24 (m, 2H), 6.40 (ddd, J = 16.9, 10.2, 8.7 Hz, 1H), 5.20 (dd, J = 16.9, 10.2 Hz, 1H), 4.03 (d, J = 8.7 Hz, 1H), 3.74 (s, 3H), 3.12 (ddd, J = 14.2, 12.5, 2.8 Hz, 2H), 2.76–2.62 (m, 2H), 2.08–2.03 (m, 1H), 1.80 (dtt, J = 13.9, 12.6, 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.6, 137.1, 135.2, 131.4, 131.1, 121.7, 119.1, 59.8, 58.5, 56.7, 28.2, 24.2, 18.4; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 99% with Rt = 18.5 min (minor) and Rt = 19.8 min

(major) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +5 (*c* 0.2, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{18}BrO_2S_2$ 372.9926; found 372.9930.

Compound 3g. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (30.8 mg, 95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2H), 6.85–6.81 (m, 2H), 6.44 (ddd, *J* = 16.9, 10.1, 8.7 Hz, 1H), 5.18 (dd, *J* = 16.9, 10.1 Hz, 2H), 4.01 (d, *J* = 8.7 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 3.10 (ddd, *J* = 14.3, 12.5, 2.8 Hz, 2H), 2.70 (ddd, *J* = 12.7, 2.4 Hz, 2H), 2.07–2.02 (m, 1H), 1.81 (dtt, *J* = 13.9, 12.5, 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.8, 158.9, 135.9, 135.9, 130.7, 118.4, 113.4, 60.7, 56.7, 55.1, 52.9, 28.5, 28.2, 24.3; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 99% with Rt = 12.8 min (major) and Rt = 14.9 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +45.4 (*c* 0.22, CH_2Cl_2). HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{16}H_{21}O_3S_2$ 325.0927; found 325.0930.

Compound 3h. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (25 mg, 76%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.25 (m, 2H), 7.16–7.14 (m, 2H), 6.46 (ddd, *J* = 16.9, 10.1, 9.0 Hz, 1H), 5.20 (dd, *J* = 16.9, 10.1 Hz, 2H), 4.01 (d, *J* = 9.0 Hz, 1H), 3.73 (s, 3H), 3.10 (ddd, *J* = 14.2, 12.6, 2.8 Hz, 2H), 2.90–2.83 (m, 1H), 2.74–2.67 (m, 2H), 2.11–2.01 (m, 1H), 1.82 (dtt, *J* = 13.7, 12.6, 3.4 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 6H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 170.8, 148.0, 135.8, 135.3, 129.4, 126.1, 118.5, 60.6, 57.3, 52.9, 33.6, 28.6, 28.3, 24.3, 23.9; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 95% with Rt = 8.9 min (minor) and Rt = 9.6 min (major) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +9.2 (*c* 0.32, CH_2Cl_2). HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{18}H_{25}O_2S_2$ 337.1290; found 337.1293.

Compound 3i. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (25 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.25 (m, 4H), 6.47 (ddd, *J* = 16.9, 10.1, 9.2 Hz, 1H), 5.20 (dd, *J* = 16.9, 10.1 Hz, 2H), 4.01 (d, *J* = 9.2 Hz, 1H), 3.73 (s, 3H), 3.17–3.03 (m, 2H), 2.70 (dq, *J* = 13.6, 4.3 Hz, 2H), 2.05 (dtd, *J* = 13.4, 4.0, 1.9 Hz, 1H), 1.87–1.77 (m, 1H), 1.29 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.7, 150.2, 135.8, 134.9, 129.1, 125.0, 118.5, 60.5, 57.2, 52.9, 34.4, 31.3, 28.5, 28.2, 24.3; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98% with Rt = 6.9 min (minor) and Rt = 7.4 min (major) [1.0% *i*-PrOH in hexanes, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D −14.3 (*c* 0.84, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{19}H_{27}O_2S_2$ 351.1447; found 351.1451.

Compound 3j. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (22 mg, 67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51–7.49 (m, 1H), 7.42–7.41 (m, 1H), 7.20 (dtd, *J* = 20.1, 7.3, 1.3 Hz, 2H), 6.67 (s, 1H), 6.35 (ddd, *J* = 17.0, 10.1, 8.9 Hz, 1H), 5.35 (dd, *J* = 17.0, 10.1 Hz, 2H), 4.39 (d, *J* = 8.9 Hz, 1H), 3.85 (s, 3H), 3.39–3.28 (m, 1H), 3.12 (ddd, *J* = 14.9, 12.6, 2.6 Hz, 1H), 2.74–2.67 (m, 2H), 2.11–2.07 (m, 1H), 1.88–1.78 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.7, 154.5, 132.7, 128.1, 123.9, 122.7, 120.9, 120.3, 111.1, 105.8, 57.6, 53.1, 51.5, 28.2, 28.1, 24.2; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98%with Rt = 9.2 min (major) and Rt = 9.9 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +65 (*c* 0.2, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{19}O_3S_2$ 335.0770; found 335.0773.

Compound 3k. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (28 mg, 75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.52 (m, 4H), 7.44–7.40 (m, 4H), 7.35–7.30 (m, 1H), 6.50 (ddd, *J* = 16.9, 10.1, 8.9 Hz, 1H), 5.24 (dd, *J* = 16.9, 10.1 Hz, 2H), 4.10 (d, *J* = 8.9 Hz, 1H), 3.76 (s, 3H), 3.13 (ddd, *J* = 14.2, 12.5, 2.8 Hz, 2H), 2.75–2.68 (m, 2H), 2.08–2.04 (m, 1H), 1.89–1.78 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.7, 140.6, 140.3, 137.1, 135.6, 129.9, 128.7, 127.2, 127.0, 126.7, 118.8, 60.3, 57.2, 53.0, 28.5, 28.3, 24.3; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98% with Rt = 11.2 min (major) and Rt = 12.1 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −4.2 (*c* 0.24, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{21}H_{23}O_2S_2$ 371.1134; found 371.1140.

Compound 3l. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (25 mg, 73%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.6 Hz, 1H), 7.85 (dd, *J* = 12.4, 7.7 Hz, 2H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.56–7.52 (m, 1H), 7.47 (td, *J* = 7.5, 4.0 Hz, 2H), 6.56–6.48 (m, 1H), 5.26–5.00 (m, 3H), 3.50 (d, *J* = 1.0 Hz, 3H), 3.18–3.12 (m, 2H), 2.74–2.67 (m, 2H), 2.04 (dt, *J* = 13.7, 3.6 Hz, 1H), 1.83 (dt, *J* = 12.7, 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9, 136.1, 134.6, 133.8, 132.2, 128.9, 128.1, 126.8, 125.9, 125.4, 125.0, 123.4, 118.5, 61.3, 52.9, 51.0, 28.9, 28.3, 24.2; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 92% with Rt = 6.0 min (major) and Rt =7.3 min (minor) [2.0% *i*-PrOH in hexanes, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D +87.3 (*c* 0.24, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{19}H_{21}O_2S_2$ 345.0933; found 345.0939.

Compound 3m. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (29 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.76 (m, 4H), 7.52 (dd, *J* = 8.5, 1.9 Hz, 1H), 7.47–7.41 (m, 2H), 6.57 (ddd, *J* = 16.9, 10.2, 8.7 Hz, 1H), 5.20 (d, *J* = 16.9, 10.2 Hz, 2H), 4.24 (d, *J* = 8.7 Hz, 1H), 3.73 (s, 3H), 3.11 (ddd, *J* = 14.3, 12.5, 2.8 Hz, 2H), 2.76–2.64 (m, 2H), 2.04 (dtt, *J* = 14.1, 4.2, 2.8 Hz, 1H), 1.81 (dtt, *J* = 13.8, 12.6, 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.8, 135.6, 135.6, 133.0, 132.7, 128.8, 128.0, 127.5, 127.4, 127.5, 126.0, 125.9, 118.9, 60.4, 57.5, 53.0, 28.5, 28.2, 24.3. The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 94% with Rt = 9.8 min (major) and Rt = 11.2 min (minor) [2.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +21.7 (*c* 0.42, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{19}H_{21}O_2S_2$ 345.0933; found 345.0939.

Compound 3n. Petroleum ether/ethyl acetate (10:1) as the eluent; colorless oil (32 mg, 93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.51 (d, *J* = 2.3 Hz, 2H), 6.46–6.37 (m, 1H), 6.36 (t, *J* = 2.3 Hz, 1H), 5.28–5.17 (m, 2H), 3.98 (d, *J* = 9.1 Hz, 1H), 3.77 (d, *J* = 3.7 Hz, 9H), 3.11 (ddd, *J* = 15.0, 12.6, 2.7 Hz, 2H), 2.75–2.66 (m, 2H), 2.04–2.08 (m, 1H), 1.87–1.77 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.7, 160.2, 140.2, 135.4, 118.8, 107.7, 99.3, 60.1, 57.6, 55.2, 53.0, 28.6, 28.3, 24.3; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 97% with Rt =11.9 min (major) and Rt = 15.0 min (minor) [2.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −16 (*c* 0.13, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{17}H_{23}O_4S_2$ 355.1032; found 355.1036.

Compound 3o. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (27 mg, 83%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50–7.49 (m, 1H), 7.27–7.22 (m, 1H), 6.93 (t, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.44–6.34 (m, 1H), 5.15 (dd, *J* = 16.9, 10.1 Hz, 2H), 4.72 (d, *J* = 8.6 Hz, 1H), 3.84 (d, *J* = 1.7 Hz, 3H), 3.72 (d, *J* = 1.7 Hz, 3H), 3.14 (tt, *J* = 12.4, 2.3 Hz, 1H), 3.01 (tt, *J* = 12.4, 2.3 Hz, 1H), 2.73–2.67 (m, 2H), 2.02 (dtd, *J* = 13.7, 4.7, 2.1 Hz, 1H), 1.82 (q, *J* = 13.3 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9, 157.2, 135.8, 130.0, 128.5, 126.8, 120.1, 118.1, 110.7, 61.4, 55.6, 53.0, 48.7, 28.7, 28.3, 24.3; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 87% with Rt = 12.8 min (major) and Rt = 14.2 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +53.5 (*c* 0.54, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. For $C_{16}H_{21}O_3S_2$ 325.0927; found 325.0931.

Compound 3p. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (27 mg, 96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.34 (m, 1H), 6.31–6.20 (m, 3H), 5.31–5.23 (m, 2H), 4.25 (d, *J* = 8.9 Hz, 1H), 3.81 (s, 3H), 3.29 (ddd, *J* = 14.1, 12.7, 2.9 Hz, 1H),

3.08 (ddd, J = 14.3, 12.5, 2.7 Hz, 1H), 2.73–2.61 (m, 2H), 2.09–2.04 (m, 1H), 1.86–1.75 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.8, 151.5, 142.0, 133.0, 119.7, 110.2, 108.8, 58.0, 53.0, 51.0, 28.1, 28.1, 24.3; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 99% with Rt = 8.2 min (major) and Rt = 8.6 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +72.5 (c 0.51, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{13}H_{17}O_3S_2$ 285.0614; found 285.0616.

Compound 3q. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (28 mg, 95%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 5.1 Hz, 1H), 7.01 (d, J = 2.8 Hz, 1H), 6.94 (dd, J = 5.0, 3.7 Hz, 1H), 6.35 (ddd, J = 16.6, 10.1, 8.7 Hz, 1H), 5.20 (d, J = 16.6, 10.1 Hz, 1H), 4.42 (d, J = 8.7 Hz, 1H), 3.80 (s, 3H), 3.19 (ddd, J = 14.0, 12.6, 2.9 Hz, 2H), 2.77–2.65 (m, 2H), 2.13–2.04 (m, 1H), 1.89–1.76 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.6, 140.2, 135.5, 127.3, 126.2, 125.2, 118.9, 58.7, 52.8, 52.6, 28.3, 28.1, 24.2; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 99% with Rt = 9.3 min (minor) and Rt = 9.9 min (major) [2.0% *i*-PrOH in hexanes, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D +5.9 (c 0.34, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{13}H_{17}O_2S_3$ 301.0385; found 301.0388.

Compound 3r. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (28 mg, 92%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26–7.21 (m, 2H), 7.10 (dd, J = 5.0, 1.4 Hz, 1H), 6.37 (ddd, J = 16.9, 10.1, 8.7 Hz, 1H), 5.20 (d, J = 16.9, 10.1 Hz, 2H), 4.23 (d, J = 8.7 Hz, 1H), 3.76 (s, 3H), 3.24–3.07 (m, 2H), 2.73–2.67 (m, 2H), 2.10–2.05 (m, 1H), 1.88–1.76 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.9, 138.2, 135.5, 128.5, 124.8, 123.7, 118.6, 59.4, 52.9, 52.8, 28.4, 28.2, 24.3; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 99% with Rt = 8.2 min (major) and Rt = 8.7 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +50.0 (c 0.4, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{13}H_{17}O_2S_3$ 301.0385; found 301.0388.

Compound 3s. Petroleum ether/ethyl acetate (30:1) as the eluent; colorless oil (22 mg, 75%); ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 2.3 Hz, 1H), 8.51–8.50 (m, 1H), 7.77 (dt, J = 8.0, 2.0 Hz, 1H), 7.21 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 6.40 (ddd, J = 17.0, 10.2, 8.5 Hz, 1H), 5.21 (d, J = 17.0, 10.2 Hz, 1H), 4.08 (d, J = 8.5 Hz, 1H), 3.73 (s, 3H), 3.19–3.11 (m, 2H), 2.74–2.66 (m, 2H), 2.03 (dtt, J = 14.2, 4.4, 2.8 Hz, 1H), 1.84–1.74 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.5, 151.0, 148.8, 137.1, 134.7, 133.9, 122.8, 119.6, 59.3, 54.6, 53.0, 28.0, 24.0, 18.4; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 96% with Rt = 21.5 min (major) and Rt = 24.1 min (minor) [5.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +13.7 (c 0.44, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{14}H_{18}NO_2S_2$ 296.0773; found 296.0778.

Compound 3t. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (24 mg, 77%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.38 (m, 2H), 7.32–7.22 (m, 3H), 6.47 (ddd, J = 16.9, 10.1, 8.7 Hz, 1H), 5.18 (dd, J = 16.9, 10.1 Hz, 2H), 4.18 (qd, J = 6.9, 1.7 Hz, 2H), 4.05 (d, J = 8.7 Hz, 1H), 3.14 (ddd, J = 14.2, 12.6, 2.9 Hz, 2H), 2.75–2.64 (m, 2H), 2.09–2.00 (m, 1H), 1.89–1.75 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.2, 138.3, 135.9, 129.7, 127.9, 127.5, 118.6, 62.2, 59.9, 57.4, 28.5, 28.2, 24.3, 14.1; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 99% with Rt = 10.3 min (major) and Rt = 10.9 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +6.1 (c 0.33, CH_2Cl_2). HRMS (ESI) m/z: $[M+H]^+$ calcd. For $C_{16}H_{21}O_2S_2$ 309.0977; found 309.0980.

Compound 3u. Petroleum ether/ethyl acetate (60:1) as the eluent; colorless oil (24 mg, 73%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.42 (m, 2H), 7.30–7.24 (m, 3H), 6.45 (ddd, J = 16.9, 10.1, 8.3 Hz, 1H), 5.16 (dd, J = 16.9, 10.1, 2H), 3.99 (d, J = 8.3 Hz, 1H), 3.30–3.09 (m, 2H), 2.73–2.61 (m, 2H), 2.10–2.01 (m, 1H), 1.87–1.75 (m, 1H), 1.37 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz，$CDCl_3$) δ 168.9, 138.7, 136.4, 129.9, 127.9, 127.3, 118.2, 82.6, 59.9, 57.4, 28.4, 28.0, 27.8, 24.4; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98% with Rt = 18.3 min (major) and Rt = 20.2 min (minor) [1.0% i-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −21.7 (c 0.41, CH_2Cl_2). HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{18}H_{25}O_2S_2$ 337.1290; found 337.1293.

Compound 3uu. In a 4-dram vial equipped with a magnetic stir bar were added **3u** (24 mg, 0.07 mmol,) and anhydrous THF (2 mL). After this time, $LiAlH_4$ (3.8 mg, 0.10 mmol, 1.50 equiv) was added at 0 ℃. The vial was sealed with a cap containing PTFE/silicone septa. The reaction mixture was stirred at rt for 2 h. The mixture was quenched with aqueous HCl (1 M, 5 mL) at 0 ℃, and was stirred at rt for 30 min until all the solids were dissolved. The mixture was extracted with Et_2O (3 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4. After removal of solvent under vacuum, the crude mixture was purified by column chromatography (EA/PE 1:10). colorless oil (starting from 0.07 mmol of **3uu**; 12.1 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.38 (m, 2H), 7.33–7.26 (m, 3H), 6.52 (dt, J = 16.9, 9.7 Hz, 1H), 5.22–5.13 (m, 2H), 3.85–3.77 (m, 2H), 3.59 (d, J = 12.0 Hz, 1H), 2.87 (ddd, J = 14.9, 12.5, 2.8 Hz, 2H), 2.64–2.55 (m, 2H), 2.08–2.01 (m, 1H), 1.80 (dtt, J = 13.8, 12.5, 3.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.5, 136.3, 129.8, 127.9, 127.3, 118.3, 60.8, 58.2, 55.4, 26.0, 25.7, 24.4; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98% with Rt = 18.3 min (major) and Rt = 20.2 min (minor) [1.0% i-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −32.3 (c 0.13, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{14}H_{19}OS_2$ 267.0872; found 267.0873.

Compound 3v. Petroleum ether/ethyl acetate (80:1) as the eluent; colorless oil (28 mg, 76%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.22 (m, 10H), 6.44 (ddd, J = 16.9, 10.1, 8.8 Hz, 1H), 5.22 (m, 4H), 4.06 (d, J = 8.8 Hz, 1H), 3.05 (ddd, J = 14.2, 12.5, 2.8 Hz, 2H), 2.67–2.61 (m, 2H), 1.99 (dtt, J = 14.1, 4.3, 2.8 Hz, 1H), 1.79 (dtt, J = 13.7, 12.5, 3.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.1, 138.1, 135.8, 135.4, 129.7, 128.5, 128.5, 128.4, 128.0, 127.5, 118.7, 67.8, 60.0, 57.4, 28.4, 28.1, 24.2; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 98% with Rt = 18.4 min (major) and Rt = 20.2 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −40.1 (c 0.57, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{21}H_{23}O_2S_2$ 371.1134; found 371.1137.

Compound 3vv. In a 4-dram vial equipped with a magnetic stir bar were added **3v** (28 mg, 0.076 mmol,) and anhydrous THF (2 mL). After this time, $LiAlH_4$ (4.2 mg, 0.110 mmol, 1.50 equiv) was added at 0 ℃. The vial was sealed with a cap containing PTFE/silicone septa. The reaction mixture was stirred at rt for 2 h. The mixture was quenched with aqueous HCl (1 M, 5 mL) at 0 ℃, and was stirred at rt for 30 min until all the solids were dissolved. The mixture was extracted with Et_2O (3 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4. After removal of solvent under vacuum, the crude mixture was purified by column chromatography (EA/PE 1:10).

colorless oil (starting from 0.076 mmol of **3v**, 14.3 mg, 71%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.38 (m, 2H), 7.33–7.26 (m, 3H), 6.52 (dt, J = 16.9, 9.7 Hz, 1H), 5.22–5.13 (m, 2H), 3.85–3.77 (m, 2H), 3.59 (d, J = 12.0 Hz, 1H), 2.87 (ddd, J = 14.9, 12.5, 2.8 Hz, 2H), 2.64–2.55 (m, 2H), 2.08–2.01 (m, 1H), 1.80 (dtt, J = 13.8, 12.5, 3.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.5, 136.3 129.8, 127.9, 127.3, 118.3, 60.8, 58.2, 55.4, 26.0, 25.7, 24.4; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H

column to be 98% with Rt = 18.4 min (major) and Rt = 20.2 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −29.6 (*c* 0.13, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{14}H_{19}OS_2$ 267.0872; found 267.0873.

Compound 3w. Petroleum ether/ethyl acetate (40:1) as the eluent; colorless oil (28 mg, 83%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.97 (m, 2H), 7.48–7.44(m, 1H), 7.33 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.17 (tdd, *J* = 5.3, 3.6, 2.7 Hz, 5H), 6.45 (ddd, *J* = 17.0, 10.1, 8.0 Hz, 1H), 5.17 (d, *J* = 10.1, 1H), 4.85 (d, *J* = 17.0, 1H), 4.24 (d, *J* = 8.0 Hz, 1H), 3.29 (ddd, *J* = 13.9, 12.8, 2.9 Hz, 1H), 3.13 (ddd, *J* = 14.1, 12.6, 2.8 Hz, 1H), 2.75–2.67 (m, 2H), 2.06–2.01 (m, 1H), 1.89–1.77 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.5, 138.0, 137.8, 135.8, 131.6, 129.9, 129.8, 127.8, 127.9, 127.3, 118.4, 65.3, 56.9, 28.2, 28.1, 24.0; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 94% with Rt = 8.9 min (major) and Rt = 10.2 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −40.9 (*c* 0.22, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$calcd. for $C_{20}H_{21}OS_2$ 341.1028; found 341.1027.

Compound 3x. Petroleum ether/ethyl acetate (40:1) as the eluent; White solid: 26 mg, 92%; mp 87–92 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.36 (m, 2H), 7.33–7.27 (m, 3H), 6.45 (ddd, *J* = 16.9, 10.2, 8.1 Hz, 1H), 5.24 (d, *J* = 10.2, 1H), 5.08 (d, *J* = 16.9, 1H), 3.85 (d, *J* = 8.1 Hz, 1H), 3.05–2.84 (m, 2H), 2.70–2.59 (m, 2H), 2.32 (d, *J* = 0.7 Hz, 3H), 2.03–1.93 (m, 1H), 1.84–1.68 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 201.2, 137.7, 135.6, 129.5, 128.2, 127.7, 118.5, 67.5, 56.6, 28.0, 27.8, 25.7, 24.1; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 96% with Rt = 9.9 min (minor) and Rt = 11.2 min (major) [AD-H, 1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D 3.9 (*c* 0.26, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{19}OS_2$ 279.0872; found 279.0873.

General produces for the preparation of compound 4. To a solution of 2-carboxy-1,3-dithiane (0.8 g, 5 mmol) in CH_2Cl_2 (10 mL) was added allylic alcohols (0.6 mL, 6 mmol) and DMAP (0.49 g, 4.0 mmol). After cooled to 0 ℃, *N*, *N*′- dicyclohexylcarbodiimide (DCC) (1.15 g, 5.5 mmol) was added portionwise. The reaction mixture was stirred at 0 ℃ for a few minutes and then warmed to room temperature. After stirring for 15 h, the reaction mixture was washed with sat. NH_4Cl aq. (×3) and sat. $NaHCO_3$ aq. (×1) and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/AcOEt = 13/1) to give **4.**

Compound 4a. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.32 g, 94%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.38 (m, 2H), 7.34–7.31 (m, 2H), 7.28–7.24 (m, 1H), 6.73–6.68 (m, 1H), 6.30 (dt, *J* = 15.9, 6.4 Hz, 1H), 4.83 (dd, *J* = 6.4, 1.4 Hz, 2H), 4.22 (s, 1H), 3.43 (ddd, *J* = 14.2, 11.5, 2.8 Hz, 2H), 2.63–2.57 (m, 2H), 2.17–1.98 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 136.0, 134.6, 128.6, 128.1, 126.6, 122.4, 66.1, 39.8, 25.9, 24.9; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{17}O_2S_2$ 281.0664; found 281.0661.

Compound 4b. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.3 g, 90%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.42 (m, 1H), 7.19–7.13 (m, 3H), 6.92 (dt, *J* = 15.7, 1.4 Hz, 1H), 6.22–6.15 (m, 1H), 4.86 (dd, *J* = 6.3, 1.4 Hz, 2H), 4.22 (s, 1H), 3.44 (ddd, *J* = 14.2, 11.5, 2.7 Hz, 2H), 2.64–2.58 (m, 2H), 2.35 (s, 3H), 2.16–1.99 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.4, 135.6, 135.1, 132.2, 130.2, 127.9, 126.0, 125.7, 123.7, 66.1, 39.8, 25.8, 24.9, 19.7; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{19}O_2S_2$ 295.0821; found 295.0817.

Compound 4c. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.26 g, 81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.32 (m, 2H), 6.87–6.85 (m, 2H), 6.65 (dd, *J* = 15.7, 1.3 Hz, 1H), 6.17 (dt, *J* = 15.8, 6.6 Hz, 1H), 4.81 (dd, *J* = 6.7, 1.3 Hz, 2H), 4.21 (s, 1H), 3.81 (s, 3H), 3.43 (ddd, *J* = 14.2, 11.4, 2.7 Hz, 2H), 2.63–2.57 (m, 2H), 2.18–1.98 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.6, 159.6, 134.5, 128.8, 127.9, 120.0, 114.0, 66.4, 55.2, 39.9, 25.9, 25.0; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{19}O_3S_2$ 311.0770; found 311.0765.

Compound 4d. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.36 g, 93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.19 (m, 3H), 7.09–7.08 (m, 1H), 6.68 (dd, *J* = 15.9, 1.4 Hz, 1H), 6.29 (dt, *J* = 15.9, 6.5 Hz, 1H), 4.83 (dd, *J* = 6.5, 1.3 Hz, 2H), 4.22 (s, 1H), 3.43 (ddd, *J* = 14.2, 11.5, 2.7 Hz, 2H), 2.64–2.58 (m, 2H), 2.35 (s, 3H), 2.18–2.01 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.6, 138.1, 136.0, 134.8, 128.9, 128.5, 127.3, 123.8, 122.1, 66.2, 39.9, 25.9, 25.0, 21.3; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{19}O_2S_2$ 295.0821; found 295.0817.

Compound 4e. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.05 g, 96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (dqt, *J* = 15.5, 6.5, 1.2 Hz, 1H), 5.62 (dtq, *J* = 14.9, 6.6, 1.7 Hz, 1H), 4.60 (dp, *J* = 6.6, 1.1 Hz, 2H), 4.18 (s, 1H), 3.42 (ddd, *J* = 14.2, 11.5, 2.7 Hz, 2H), 2.64–2.58 (m, 2H), 2.18–2.01 (m, 2H), 1.74 (dq, *J* = 6.6, 1.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 132.0, 124.4, 66.2, 39.9, 25.9, 25.0, 17.8; HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_9H_{15}O_2S_2$ 219.0508; found 219.0504.

Compound 4f. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.37 g, 92%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.34 (m, 2H), 7.04–6.99 (m, 2H), 6.67 (d, *J* = 15.8 Hz, 1H), 6.22 (dt, *J* = 15.9, 6.4 Hz, 1H), 4.82 (d, *J* = 6.3 Hz, 2H), 4.22 (s, 1H), 3.46–3.39 (m, 1H), 2.64–2.58 (m, 1H), 2.19–1.99 (m, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 133.5, 128.3, 128.2, 122.2, 115.6, 115.4, 65.9, 39.9, 25.9, 25.0; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{14}H_{15}FNaO_2S_2$ 321.0390; found 321.0393.

Compound 4g. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.49 g, 95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 4H), 6.66 (d, *J* = 15.9 Hz, 1H), 6.27 (dt, *J* = 15.9, 6.3 Hz, 1H), 4.82 (dd, *J* = 6.3, 1.4 Hz, 2H), 4.22 (s, 1H), 3.46–3.39 (m, 2H), 2.64–2.59 (m, 2H), 2.18–2.02 (m, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 134.5, 133.8, 133.2, 128.8, 127.8, 123.1, 65.8, 39.9, 25.9, 25.0; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{14}H_{15}ClNaO_2S_2$ 337.0094; found 337.0096.

Compound 4h. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.38 g, 93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.64 (d, *J* = 15.8 Hz, 1H), 6.29 (dt, *J* = 15.9, 6.3 Hz, 1H), 4.82 (dd, *J* = 6.3, 1.4 Hz, 2H), 4.22 (s, 1H), 3.42 (ddd, *J* = 14.2, 11.5, 2.7 Hz, 2H), 2.64–2.58 (m, 2H), 2.19–1.96 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.4, 134.9, 133.2, 131.7, 128.1, 123.2, 122.0, 65.7, 39.8, 25.9, 24.9; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{14}H_{15}BrNaO_2S_2$ 380.9589; found 380.9593.

Compound 4i. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.30 g, 91%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 5.0 Hz, 1H), 7.01–6.96 (m, 2H), 6.83 (d, *J* = 15.7 Hz, 1H), 6.13 (dt, *J* = 15.7, 6.5 Hz, 1H), 4.79 (dd, *J* = 6.5, 1.4 Hz, 2H), 4.21 (s, 1H), 3.42 (ddd, *J* = 14.2, 11.4, 2.7 Hz, 2H), 2.63–2.58 (m, 2H), 2.23–1.94 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 141.0, 127.9, 127.4, 126.7, 125.1, 121.8, 65.8, 39.9, 25.9, 25.0; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{12}H_{14}NaO_2S_3$ 309.0048; found 309.0056.

Compound 4j. Petroleum ether/ethyl acetate (20:1) as the eluent; colorless oil (starting from 5 mmol of 2-carboxy-1,3-dithiane, 1.11 g, 90%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (dt, *J* = 15.2, 6.8 Hz, 1H), 5.63–5.56 (m, 1H), 4.62 (d, *J* = 6.5 Hz, 2H), 4.18 (s, 1H), 3.42

(ddd, J = 14.2, 11.5, 2.7 Hz, 2H), 2.63–2.58 (m, 2H), 2.17–2.03 (m, 4H), 1.42 (q, J = 7.4 Hz, 2H), 0.90 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 169.5, 137.0, 123.2, 66.2, 39.9, 34.2, 25.8, 24.9, 21.9, 13.5; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{11}H_{18}NaO_2S_2$ 269.0640; found 269.0640.

General produces for the preparation of compound 5. In a reaction vessel $[Ir(cod)Cl]_2$ (0.002 mmol), chiral phosphoramidite (0.004 mmol), and TBD (0.01 mmol) were dissolved in THF (0.5 mL) under Ar atmosphere. The reaction vessel was sealed with a screw cap and the mixture heated at 50 ℃ (oil bath) for 30 min to allow the formation of the active catalyst species (the solution turns from orange to yellow). After this time, K_3PO_4 (0.15 mmol) and **4** (0.1 mmol) were added and the resulting mixture was heated at 50 ℃ (oil bath). Upon completion, the reaction was then quenched by 1N HCl and diluted with ethyl acetate. The organic phases were separated and the aqueous phase was extracted with ethyl acetate (3x). The combined organic phase was dried over Na_2SO_4, filtered and concentrated under vacuum. The mixture was then purified by flash chromatography affording the product.

Compound 5a. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (17 mg, 62%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.39 (m, 2H), 7.30–7.26 (m, 3H), 6.46 (ddd, J = 16.9, 10.1, 9.0 Hz, 1H), 5.25 (dd, J = 16.9, 10.1 Hz, 2H), 4.05 (d, J = 9.0 Hz, 1H), 3.13 (ddd, J = 15.2, 12.7, 2.9 Hz, 2H), 2.75–2.68 (m, 2H), 2.07 (ddt, J = 11.2, 4.2, 2.7 Hz, 1H), 1.82 (qt, J = 12.7, 3.4 Hz, 1H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 174.3, 137.7, 135.2, 129.8, 128.1, 127.8, 119.2, 60.4, 57.4, 28.5, 28.2, 24.1; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 98% with Rt = 6.0 min (major) and Rt = 7.5 min (minor) [15% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/min, 210 nm, 25 ℃]; [α]25 D –8.3 (c 0.24, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{14}H_{17}O_2S_2$ 281.0664; found 281.0667.

Compound 5b. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (16.7 mg, 57%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.64(m, 1H), 7.18–7.16 (m, 3H), 6.31 (ddd, J = 16.9, 10.1, 8.1 Hz, 1H), 5.21 (d, J = 10.1, 1H), 5.09 (d, J = 16.9, 1H), 4.37 (d, J = 8.1 Hz, 1H), 3.15 (ddd, J = 14.9, 12.8, 2.8 Hz, 2H), 2.75–2.69 (m, 2H), 2.42 (s, 3H), 2.11–2.05 (m, 1H), 1.91–1.80 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 173.5, 137.1, 136.4, 135.5, 130.6, 128.5, 127.4, 125.9, 118.7, 61.3, 52.6, 28.7, 28.2, 24.0, 20.4; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 99% with Rt = 9.5 min (major) and Rt = 10.0 min (minor) [15% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/min, 210 nm, 25 ℃]; [α]25 D –15.8 (c 0.38, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{19}O_2S_2$ 295.0821; found 295.0818.

Compound 5c. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (17 mg, 55%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 2H), 6.85–6.83 (m, 2H), 6.44 (ddd, J = 16.9, 10.1, 8.9 Hz, 1H), 5.22 (dd, J = 16.9 Hz, 10.1 Hz, 2H), 4.02 (d, J = 8.9 Hz, 1H), 3.78 (s, 3H), 3.13 (ddd, J = 14.9, 12.6, 2.7 Hz, 2H), 2.77–2.65 (m, 2H), 2.08 (dtt, J = 14.0, 4.6, 2.8 Hz, 1H), 1.88–1.76 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.1, 159.0, 135.4, 130.8, 129.6, 118.9, 113.5, 60.2, 56.6, 55.1, 28.4, 28.2, 24.1; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 85% with Rt =12.8 min (major) and Rt = 13.9 min (minor) [10% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/min, 210 nm, 25 ℃]; [α]25 D–11.1 (c 0.18, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{19}O_3S_2$ 311.0770; found 311.0768.

Compound 5d. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (17.3 mg, 59%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.20–7.17 (m, 3H), 7.09–7.07 (m, 1H), 6.45 (ddd, J = 16.8, 10.1, 9.1 Hz, 1H), 5.24 (d, J = 16.8, 10.1 Hz, 1H), 4.02 (d, J = 9.1 Hz, 1H), 3.21–3.07 (m, 2H), 2.77–2.66 (m, 2H), 2.33 (s, 3H), 2.08 (dtd, J = 14.0, 4.3, 2.2 Hz, 1H), 1.88–1.77 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.0, 137.7, 137.5, 135.3, 130.5, 128.5, 128.0, 126.6, 119.1, 60.1, 57.4, 28.4, 28.2, 24.0, 21.5; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 96% with Rt = 6.4 min (major) and Rt = 8.2 min (minor) [10% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/min, 210 nm, 25 ℃]; [α]25 D –10.8 (c 0.37, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{19}O_2S_2$ 295.0821; found 295.0818.

Compound 5e. Petroleum ether/ethyl acetate (5:1) as the eluent; white solid (11.1 mg, 51%); mp 102–107 ℃; ^1H NMR (400 MHz, $CDCl_3$) δ 6.01 (ddd, J = 17.1, 10.2, 8.4 Hz, 1H), 5.23–5.14 (m, 2H), 3.24 (ddd, J = 15.4, 12.7, 2.7 Hz, 2H), 2.98–2.88 (m, 1H), 2.75–2.70 (m, 2H), 2.17–2.11 (m, 1H), 1.91–1.80 (m, 1H), 1.29 (d, J = 6.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.6, 137.4, 117.6, 58.6, 45.7, 28.0, 27.9, 24.4, 16.0; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 96% with Rt = 6.6 min (minor) and Rt = 6.9 min (major) [8.0% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D –11.8 (c 0.17, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_9H_{15}O_2S_2$ 219.0508; found 219.0509.

Compound 5f. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (15.2 mg, 51%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, J = 8.7, 5.4 Hz, 2H), 6.99 (t, J = 8.7 Hz, 2H), 6.42 (ddd, J = 16.9, 10.2, 8.7 Hz, 1H), 5.29–5.17 (m, 2H), 4.06 (d, J = 8.7 Hz, 1H), 3.18–3.11 (m, 2H), 2.75–2.69 (m, 2H), 2.12–2.06 (m, 1H), 1.86– 1.77 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.6, 135.0, 133.4, 131.5, 119.4, 115.1, 114.8, 59.5, 56.3, 28.3, 28.1, 23.9; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 97% with Rt = 8.9 min (major) and Rt = 10.9 min (minor) [8.0% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D –54.12 (c 0.85, CH_2Cl_2); ^{19}F NMR (282 MHz, $CDCl_3$): δ –114.6; HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{14}H_{15}FNaO_2S_2$ 321.0390; found 321.0393.

Compound 5g. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (16.9 mg, 54%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.35 (m, 2H), 7.29–7.26 (m, 2H), 6.41 (ddd, J = 16.9, 10.2, 8.7 Hz, 1H), 5.32–5.13 (m, 2H), 4.05 (d, J = 8.7 Hz, 1H), 3.15 (ddd, J = 14.3, 12.7, 2.8 Hz, 2H), 2.75–2.69 (m, 2H), 2.12–2.05 (m, 1H), 1.86–1.76 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.2, 136.2, 134.8, 133.7, 131.2, 128.2, 119.6, 59.3, 56.5, 28.3, 28.1, 23.9; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 98% with Rt = 10.2 min (major) and Rt = 11.9 min (minor) [8.0% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D –46.67 (c 0.9, CH_2Cl_2); HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{14}H_{15}ClNaO_2S_2$ 337.0094; found 337.0096.

Compound 5h. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (19.7 mg, 55%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.42 (m, 2H), 7.31–7.26 (m, 2H), 6.41 (ddd, J = 16.9, 10.1, 8.7 Hz, 1H), 5.29–5.17 (m, 2H), 4.03 (d, J = 8.7 Hz, 1H), 3.15 (ddd, J = 14.3, 12.6, 2.7 Hz, 2H), 2.76–2.68 (m, 2H), 2.12–2.06 (m, 1H), 1.87–1.75 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 175.0, 136.7, 134.7, 131.6, 131.2, 121.9, 119.6, 59.3, 56.5, 28.3, 28.1, 23.9; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 97% with Rt = 10.8 min (major) and Rt = 12.7 min (minor) [8.0% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D –50 (c 0.5, CH_2Cl_2); HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{14}H_{15}BrNaO_2S_2$ 380.9589; found 380.9593.

Compound 5i. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (17.2 mg, 60%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, J = 5.1, 1.2 Hz, 1H), 7.07–7.05 (m, 1H), 6.96 (dd, J = 5.2, 3.5 Hz, 1H), 6.35 (ddd, J = 16.9, 10.1, 8.7 Hz, 1H), 5.30–5.24 (m, 2H), 4.44 (d, J = 8.7 Hz, 1H), 3.30–3.19 (m, 2H), 2.75–2.68 (m, 2H), 2.13–2.09 (m, 1H), 1.87–1.78 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 176.3, 139.8, 135.2, 127.6, 126.2, 125.4, 119.3, 57.8,

52.5, 28.2, 28.0, 23.9; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 98% with Rt = 14.2 min (major) and Rt = 15.1 min (minor) [8.0% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D −38 (*c* 0.5, CH_2Cl_2);
HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{12}H_{14}NaO_2S_3$ 309.0048; found 309.0054.

Compound 5j. Petroleum ether/ethyl acetate (5:1) as the eluent; colorless oil (16.5 mg, 67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87−5.78 (m, 1H), 5.24−5.15 (m, 2H), 3.32−3.18 (m, 2H), 2.74−2.64 (m, 3H), 2.15−2.11 (m, 1H), 1.92−1.81 (m, 1H), 1.70−1.64 (m, 1H), 1.56−1.38 (m, 2H), 1.25−1.18 (m, 1H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 175.8, 135.8, 119.5, 58.7, 51.9, 31.9, 28.0, 24.5, 20.7, 13.7; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 91% with Rt = 7.1 min (minor) and Rt = 7.7 min (major) [8.0% *i*-PrOH in hexanes, 1/1000TFA, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D +5 (*c* 0.2, CH_2Cl_2); HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{11}H_{18}NaO_2S_2$ 269.0640; found 269.0647.

Compound 6. To a solution of **3k** (74 mg, 0.2 mmol) in absolute MeOH (10 mL), Raney-nickel (1 g, Aldrich- 2800 50% slurry in water) was added. The reaction mixture was stirred at 50 ℃ (oil bath) for 12 h, then was filtered through a Celite pad and washed with absolute THF. The organic solution was dried over $MgSO_4$ and concentrated in vacuum to afford a crude residue that was purified by flash column chromatography (EA/PE 1:40) to give the colorless oil compound **6** (50 mg, 93% yield).
colorless oil (50 mg, 93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.58 (m, 2H), 7.54−7.52 (m, 2H), 7.42 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.34−7.30 (m, 1H), 7.26−7.24 (m, 2H), 3.60 (s, 3H), 3.06 (qd, *J* = 7.9, 5.5 Hz, 1H), 2.71−2.58 (m, 2H), 1.77−1.58 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.0, 143.0, 140.9, 139.2, 128.7, 127.9, 127.1, 127.1, 126.9, 51.5, 43.5, 41.2, 29.1, 11.9; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be >99% with Rt = 11.2 min (major) and Rt = 11.5 min (minor) [0.5% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −2.8 (*c* 0.36, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{18}H_{21}O_2$ 269.1536; found 269.1540.

Compound 7. To a solution of **3k** (74 mg, 0.2 mmol) in absolute THF (10 mL), Raney-nickel (1 g, Aldrich-2800 50% slurry in water) was added. The reaction mixture was stirred at 50 ℃ (oil bath) for 12 h, then was filtered through a Celite pad and washed with absolute MeOH. The organic solution was dried over $MgSO_4$ and concentrated in vacuum to afford a crude residue that was purified by flash column chromatography (EA/PE 1:40) to give the colorless oil compound (51 mg, 95% yield).
colorless oil (51 mg, 95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.53 (m, 4H), 7.42 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.35−7.28 (m, 3H), 6.01 (ddd, *J* = 17.3, 10.5, 7.2 Hz, 1H), 5.11 (dd, *J* = 17.3, 10.5 Hz, 2H), 3.92 (q, *J* = 7.2 Hz, 1H), 3.64 (s, 3H), 2.84−2.72 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.3, 141.5, 140.8, 140.1, 139.6, 128.7, 127.9, 127.3, 127.2, 127.0, 115.0, 51.6, 45.2, 40.0; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 99% with Rt = 8.9 min (major) and Rt = 9.5 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D −2.4 (*c* 0.84, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{18}H_{19}O_2$ 267.1380; found 267.1382.

Compound 8. To a solution of substrate **3a** in degassed solvent (THF, 0.2 M) and saturated by hydrogen was added 10% Wilkinson's catalyst. The solution was stirred under a hydrogen atmosphere at room temperature. When the hydrogenation was deemed complete by TLC, the reaction mixture was filtered through a short pad of alumina and washed thoroughly with diethyl ether. Purification by flash chromatography (EA/PE 1:50) on silica gel provided the saturated product **8**.
colorless oil (16.8 mg, 57%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.26 (m, 5H), 3.71 (s, 3H), 3.21−3.02 (m, 3H), 2.74−2.62 (m, 2H), 2.12−1.99 (m, 3H), 1.79 (dtt, *J* = 13.9, 12.6, 3.4 Hz, 1H), 0.73 (t, *J* = 7.3 Hz, 3H); ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 171.2, 138.0, 130.0, 127.8, 127.5, 61.9, 55.7, 52.9, 28.7, 28.2, 24.5, 24.0, 12.7; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 98% with Rt = 6.5 min (major) and Rt = 7.6 min (minor) [1.0% *i*-PrOH in hexanes, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D −4.5 (*c* 0.2, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{15}H_{21}O_2S_2$ 297.0977; found 297.0982.

Compound 5a. A 1-dram vial containing a magnetic stir bar was charged with **3a** (29.4 mg, 0.1 mmol, 1.0 equiv), NaOH (8 M aqueous solution, 0.24 mL, 1.92 mmol, 20 equiv), and MeOH (0.5 mL). The vial was sealed with a cap containing PTFE/silicone septa. The reaction mixture was stirred at 80 ℃ (oil bath) for 6 h. The mixture was acidified with aqueous HCl solution (1 M, 5 mL) and the resulting mixture was extracted with Et_2O (3 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4. After removal of solvent under vacuum, the title compound was obtained without further purification.
colorless oil (28 mg, 99%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.39 (m, 2H), 7.30−7.26 (m, 3H), 6.46 (ddd, *J* = 16.9, 10.1, 9.0 Hz, 1H), 5.25 (dd, *J* = 16.9, 10.1 Hz, 1H), 4.05 (d, *J* = 9.0 Hz, 1H), 3.13 (ddd, *J* = 15.2, 12.7, 2.9 Hz, 2H), 2.75−2.68 (m, 2H), 2.07 (ddt, *J* = 11.2, 4.2, 2.7 Hz, 1H), 1.82 (qt, *J* = 12.7, 3.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 174.3, 137.7, 135.2, 129.8, 128.1, 127.8, 119.2, 60.4, 57.4, 28.5, 28.2, 24.1; The enantiomeric excess was isolated: HPLC Daicel Chiralpak AD-H column to be 98% with Rt = 6.0 min (major) and Rt = 7.5 min (minor) [15% *i*-PrOH in hexanes, 1 mL/ min, 210 nm, 25 ℃]; [α]25 D −8.3 (*c* 0.24, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{14}H_{17}O_2S_2$ 281.0664; found 281.0667.

Compound 10. A 1-dram vial containing a magnetic stir bar was charged with carboxylic acid **5a** (28 mg, 0.1 mmol, 1.0 equiv), sodium bicarbonate ($NaHCO_3$, 11.8 mg, 0.14 mmol, 1.4 equiv), acetonitrile (1.0 mL), and water (1.0 mL). The mixture was stirred at rt until the carboxylic acid was completely dissolved. After this time, potassium iodide (KI, 21.6 mg, 0.130 mmol, 1.30 equiv) and iodine (I_2, 33.0 mg, 0.13 mmol, 1.3 equiv) were added into the mixture. The reaction mixture was stirred at rt for 2 h. The reaction mixture was quenched with a saturated aqueous sodium thiosulfate (Na_2SO_4) solution dropwise until the yellow color disappeared. After this time, 5 mL of water was added into the mixture. The mixture was extracted with EtOAc (3 x 5 mL). The organic layer was dried over anhydrous Na_2SO_4. After removal of solvent under vacuum, the crude mixture was purified by column chromatography (EA/PE 1:10).
colorless oil (33.8 mg, 83%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.31 (m, 3H), 7.23−7.21 (m, 2H), 5.30 (ddd, *J* = 8.9, 6.1, 5.1 Hz, 1H), 3.88 (ddd, *J* = 13.9, 13.1, 2.7 Hz, 1H), 3.69 (d, *J* = 5.1 Hz, 1H), 3.34−3.26 (m, 2H), 2.82−2.72 (m, 2H), 2.56−2.51 (m, 1H), 2.22−2.15 (m, 1H), 1.88 (dtt, *J* = 14.0, 12.9, 3.1 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.5, 130.4, 130.2, 129.0, 128.3, 79.6, 58.1, 52.1, 27.2, 27.1, 24.5, 0.1; The enantiomeric excess was isolated: HPLC Daicel Chiralpak OD-H column to be 99% with Rt = 14.8 min (major) and Rt = 16.1 min (minor) [2.0% *i*-PrOH in hexanes, 1 mL/min, 210 nm, 25 ℃]; [α]25 D +31.5 (*c* 0.24, CH_2Cl_2); HRMS (ESI) m/z: $[M+H]^+$ calcd. for $C_{14}H_{16}IO_2S_2$ 406.9631; found 406.9635.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:.
Experimental procedures, characterization data, NMR spectra, and X-ray analysis (PDF)

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Notes

The authors declare no competing financial interest.

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