Supporting Information

Lewis Base-Catalyzed Asymmetric Sulfenylation of Alkenes: Construction of Sulfenylated Lactones and Application to the Formal Syntheses of (-) -Nicotlactone B and (-) -Galbacin

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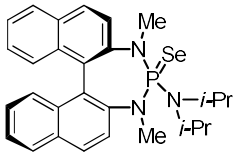
General Considerations:

All reactions were performed using oven-dried or flame-dried glassware equipped with a magnetic stir bar under an atmosphere of argon unless otherwise noted. All reagents were purchased from commercial suppliers and used without further purification. In addition to commercially available extra dry solvents, all solvents were purified by standard operating method. Toluene, tetrahydrofuran (THF), diethyl ether (Et_2O) and benzene were distilled from sodium; Dichloromethane (DCM) was distilled from calcium hydride. Thin-layer chromatography was performed with EMD silica gel 60 F254 plates eluting with solvents indicated, visualized by a 254 nm UV lamp and stained with phosphomolybdic acid (PMA). ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were obtained on Bruker AM-400 and Bruker AM-500. Chemical shifts (δ) were quoted in ppm relative to tetramethylsilane or residual protio solvent as internal standard ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR), multiplicities are as indicated: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Infrared (IR) spectra were recorded on a Fourier transform infrared spectromete. High-resolution mass spectral analysis (HRMS) data were measured on an APEXII 47e FT-ICR spectrometer by means of the ESI technique. Optical rotations were detected on RUDOLPH A21202-J APTV/GW. The enantiomeric excesses (ee) of the products were determined by high performance liquid chromatography (HPLC) analysis employing Daicel Chiralpak OJ-H, Daicel Chiralpak IC, Chiralcel OD-H Columns. Melting points were measured on a melting point apparatus and were uncorrected.

Catalysts and Substrate Preparation

1.1 Procedures for the synthesis of catalysts according to the literature procedure.[1]

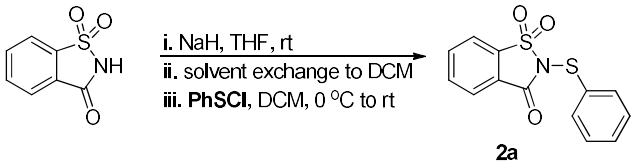
Figure S1. catalysts screened



(*S*)-Cat. 4a

(*S*)-Cat. 4a is known compounds and the analytical data (^{1}H-NMR and ^{13}C-NMR) match with the literature.[1]

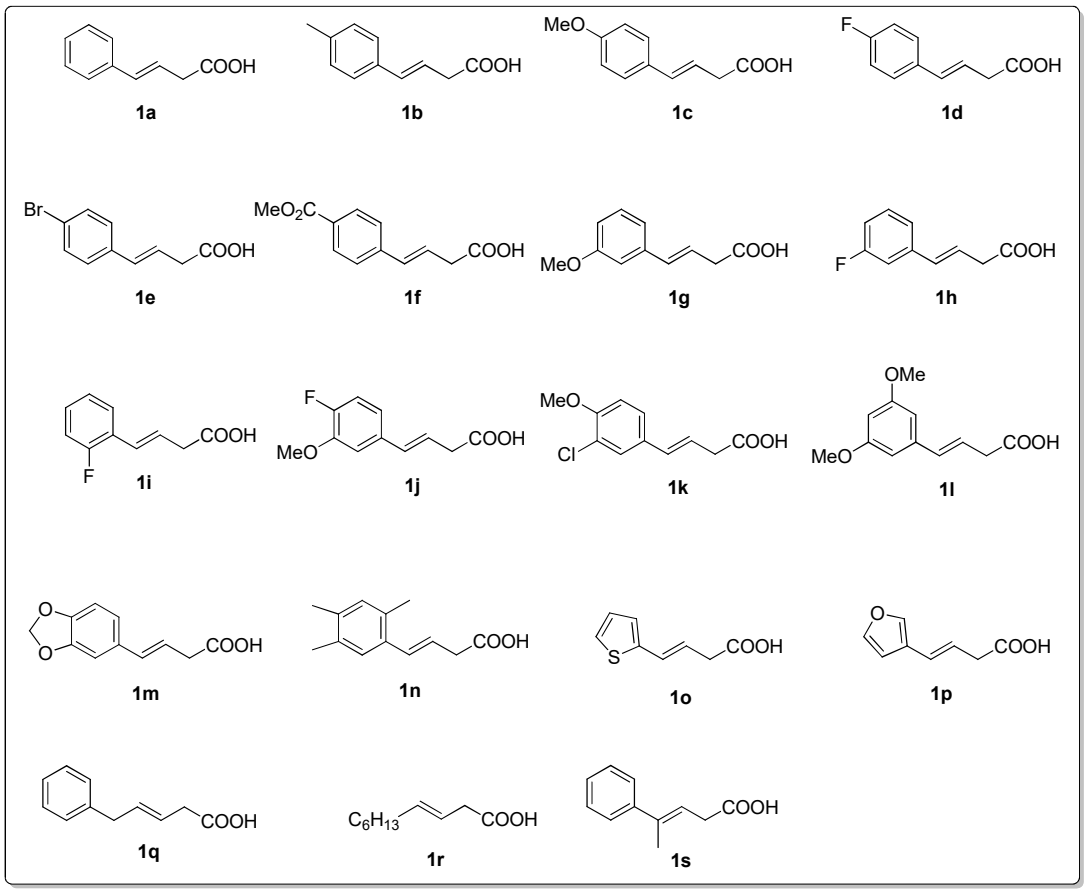
1.2 The compound **2b** was purchased from commercial suppliers (TCI) and used without further purification. The analytical data (^{1}H-NMR and ^{13}C-NMR) of compound **2a** match with the literature.[1]

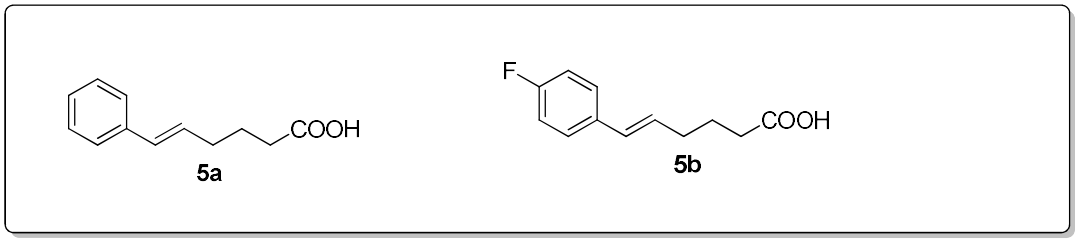


2a

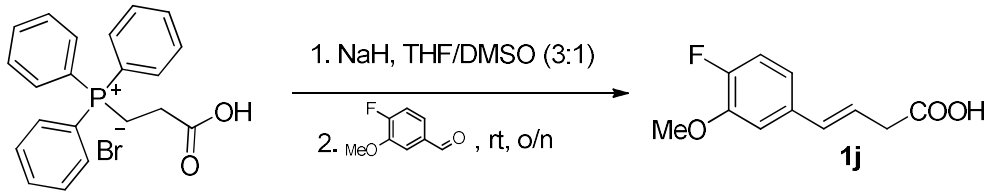
2.1 The substrates **1a**[2], **1f-1g**[2], **1m**[2], **1i**[3], **1b-1e**[4], **1n**[4], **1h**[5], **1l**[6], **1p**[7], **1q**[8] , **5a**[9] and **5b**[10] are known compound. Analytical data (^{1}H-NMR and ^{13}C-NMR) match with the literature.

Figure S2. The substrates examined in this manuscript





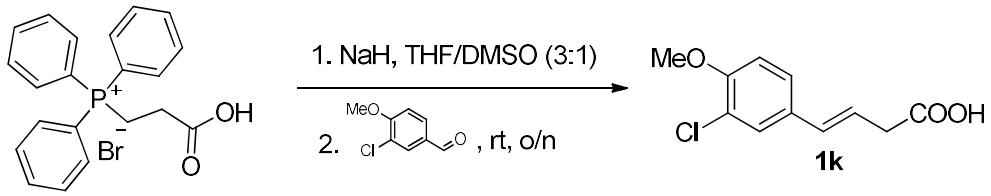
Synthesis of **1j, 1k** and **1p**



To a suspension of of (2-carboxyethyl)triphenylphosphonium bromide (2.28 g, 5.5 mmol, 1.1 equiv) in anhydrous THF/DMSO (15 mL: 5 mL) was added sodium hydride (0.264 g, 11 mmol, 2.2 equiv) at room temperature under argon atmosphere. 5 mins later,

4-fluoro-3-methoxybenzaldehyde (0.770 g, 5.0 mmol, 1.0 equiv) was added. The mixture was stirred at room temperature overnight and monitored by TLC analysis and after completion of the reaction THF was evaporated. H_2O（90 mL）and DCM（90 mL）was added. Aqueous layer was separated and acidified with HCl (1 M) up to pH = 2. Et_2O（90 mL）was added. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 90 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed in vacuum (35 °C). After flash chromatography on silica gel (1:2 EtOAc:petroleum ether) gave the compound **1j** as a white solid (480 mg, 46% yield), R_f = 0.15 (2:1 EtOAc:petroleum ether).

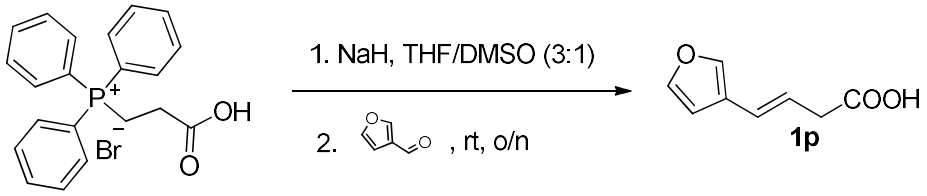
Data for **1j**: **Mp**: 64.2 ~65.1 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.11 – 6.93 (m, 2H), 6.88 (ddd, J = 8.1, 4.2, 1.9 Hz, 1H), 6.46 (d, J = 15.8 Hz, 1H), 6.28 – 6.05 (m, 1H), 3.90 (s, 3H), 3.29 (d, J = 7.1 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 177.51, 152.31 (d, J = 247.0 Hz), 147.80 (d, J = 11.0 Hz), 133.30, 120.81 (d, J = 2.3 Hz), 119.37 (d, J = 6.8 Hz), 116.18 (d, J = 18.7 Hz), 111.11 (d, J = 1.7 Hz), 56.37, 37.98; **^{19}F NMR** (376 MHz, $CDCl_3$, ppm): δ -136.31; **HRMS** (ESI) m/z calcd. for $C_{11}H_{10}FO_3$ $(M-H)^-$: 209.0595, found: 209.0591.



The same procedure as used for the synthesis of **1j** (above) was followed using (2-carboxyethyl)triphenylphosphonium bromide (2.28 g, 5.5 mmol, 1.1 equiv) in anhydrous THF/DMSO (15 mL: 5 mL), sodium hydride (264 mg, 11 mmol, 2.2 equiv), and 4-chloro-3-methoxybenzaldehyde (0.853 g, 5.0 mmol, 1.0 equiv). The alkenoic acid was purified over silica gel (1:2 EtOAc:petroleum ether) gave the compound **1k** as a white solid (450 mg, 40% yield), R_f = 0.2 (1:2 EtOAc:petroleum ether).

Data for **1k**: **Mp**: 89.7 ~91.6 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.41 (d, J = 2.1 Hz, 1H), 7.21 (dd, J = 8.5, 2.1 Hz, 1H), 6.86 (d, J = 8.5 Hz, 1H), 6.40 (d, J = 15.9 Hz, 1H), 6.16 (dt, J = 15.8, 7.1 Hz, 1H), 3.90 (s, 3H), 3.28 (dd, J = 7.1, 1.1 Hz, 2H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 177.28, 154.66, 132.38, 130.56, 128.02, 126.00, 122.83, 120.24, 112.12, 56.35, 37.97;

HRMS (ESI) m/z calcd. for $C_{11}H_{10}ClO_3$ $(M-H)^-$: 225.0318, found: 225.0327 .



The same procedure as used for the synthesis of **1j** (above) was followed using (2-carboxyethyl)triphenylphosphonium bromide (2.28 g, 5.5 mmol, 1.1 equiv) in anhydrous THF/DMSO (15 mL: 5 mL), sodium hydride (264 mg, 11 mmol, 2.2 equiv), and 3-furaldehyde (0.481 g, 5.0 mmol, 1.0 equiv). The alkenoic acid was purified over silica gel (1:2 EtOAc:petroleum ether) gave the compound **1p** as a light yellow solid (450 mg, 54% yield), R_f = 0.2 (1:2 EtOAc:petroleum ether).

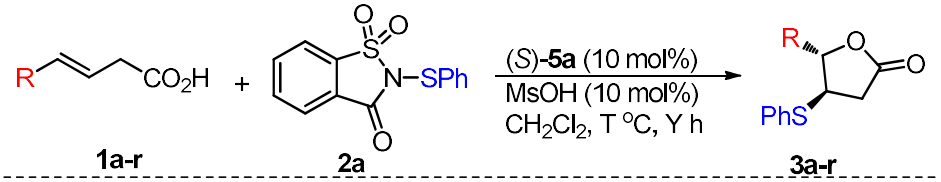
Data for **1p**: **Mp**: 75.8 ~77.1 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.46 – 7.30 (m, 2H), 6.54 (dd, J = 1.0, 0.5 Hz, 1H), 6.38 (d, J = 15.8 Hz, 1H), 6.00 (m, 1H), 3.24 (dd, J = 7.2, 1.3 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 178.03, 143.70, 140.52, 123.92, 123.78, 120.43, 107.62, 38.04; **HRMS** (ESI) m/z calcd. for $C_8H_7O_3$ $(M-H)^-$: 151.0376, found: 151.0375.

Product Purification/Characterization Data

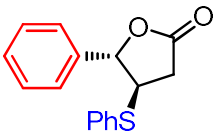
3.1 General procedure for the enantioselective *5-endo* thiolactonization (procedure A):

In a dry tube, unsaturated carboxylic acids **1a-r** (0.1 mmol, 1.0 equiv) and sulfenylating agent **2a** (0.12 mmol, 1.2 equiv), (*S*)-Cat. **4a** (0.01 mmol, 0.1 equiv) were added in DCM (1.0 mL) under argon atmosphere. After stirred for 5 min at corresponding temperature, methanesulfonic acid (0.1 mmol, 1.0 equiv) were added in one portion. The resulting mixture was stirred for another 15 h to 3 d at corresponding temperature. After the reaction was complete (monitored by TLC), the solvent was concentrated under reduced pressure, and the resulting residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc) to give the corresponding sulfenylated lactones.

The synthesis of *5-endo* racemic sample was followed using unsaturated carboxylic acids **1** (0.1 mmol, 1.0 equiv) and sulfenylating agent **2a** (0.12 mmol, 1.2 equiv), methanesulfonic acid (0.1 mmol, 1.0 equiv) were added in DCM (1.0 mL) under argon atmosphere at room temperature for overnight.



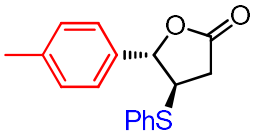
(4*R*, 5*S*)-5-phenyl-4-(phenylthio)dihydrofuran-2(3H)-one (**3a**):



General procedure A was followed using (*E*)-4-phenylbut-3-enoic acid (**1a**, 16.2 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12

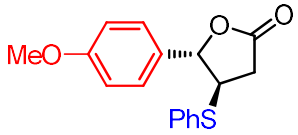
mmol, 1.2 equiv) stirred for 24 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:20 EtOAc:petroleum ether) to afford product **3a** as a colorless oil (26.0 mg, 96% yield), R_f = 0.6 (1:5 EtOAc:petroleum ether). **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.39 (m, 8H), 7.31 – 7.25 (m, 2H), 5.37 (d, J = 5.8 Hz, 1H), 3.84 (ddd, J = 8.1, 7.0, 5.8 Hz, 1H), 3.05 (dd, J = 18.0, 8.2 Hz, 1H), 2.68 (dd, J = 18.0, 7.0 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 174.36, 137.52, 133.57, 131.88, 129.56, 128.98, 128.95, 128.73, 125.57, 85.30, 50.09, 35.57; **IR** (neat): 1787, 1479, 1439, 1261, 1223, 1164, 1141, 1025, 1001, 802, 749, 695 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{16}H_{14}O_2S$ $(M+Na)^+$: 293.0612, found: 293.0611; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 16.04 min, minor retention time: 20.23 min, er = 96:4; $[\alpha]_D^{20}$ = -35.2 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-4-(phenylthio)-5-(p-tolyl)dihydrofuran-2(3H)-one (**3b**):



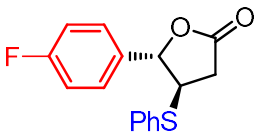
General procedure A was followed using (*E*)-4-(p-tolyl)but-3-enoic acid (**1b**, 17.6 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 16 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:25 EtOAc:petroleum ether) to afford product **3b** as a colorless oil (26.0 mg, 92% yield), R_f = 0.5 (1:7 EtOAc:petroleum ether). **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.43 – 7.37 (m, 2H), 7.36 – 7.29 (m, 3H), 7.20 – 7.12 (m, 4H), 5.30 (t, J = 4.6 Hz, 1H), 3.80 (ddd, J = 8.0, 7.0, 5.9 Hz, 1H), 3.02 (dd, J = 18.0, 8.2 Hz, 1H), 2.64 (dd, J = 18.0, 7.0 Hz, 1H), 2.35 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.46, 138.94, 134.49, 133.56, 131.94, 129.61, 129.55, 128.68, 125.60, 85.34, 50.06, 35.69, 21.30; **IR** (neat): 2923, 1787, 1439, 1261, 1165, 1141, 1024, 800, 748, 692 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{16}NaO_2S$ $(M+Na)^+$: 307.0769, found: 307.0766; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 14.52 min, minor retention time: 17.74 min, er = 95.5:4.5; $[\alpha]_D^{20}$ = -44.2 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-5-(4-methoxyphenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3c**):



General procedure A was followed using (*E*)-4-(4-methoxyphenyl)but-3-enoic acid (**1c**, 19.2 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 25 h at -10 °C. The crude mixture was purified by silica gel flash chromatography (1:10 EtOAc:petroleum ether) to afford product **3c** as a white solid (23.0 mg, 77% yield), R_f = 0.4 (1:5 EtOAc:petroleum ether). **Mp**: 80.8 ~ 82.5 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): 7.52 – 7.40 (m, 2H), 7.40 – 7.32 (m, 3H), 7.29 (dd, J = 10.6, 5.3 Hz, 1H), 6.94 – 6.82 (m, 2H), 6.77 (d, J = 1.8 Hz, 1H), 5.34 (d, J = 5.5 Hz, 1H), 3.84 (ddd, J = 8.2, 6.6, 5.7 Hz, 1H), 3.80 (s, 3H), 3.04 (dd, J = 18.0, 8.2 Hz, 1H), 2.66 (dd, J = 18.0, 6.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.41, 160.04, 139.18, 133.62, 131.94, 130.10, 129.59, 128.77, 117.64, 114.46, 111.00, 85.13, 55.44, 50.05, 35.42; **IR** (neat): 2961, 2925, 1787, 1603, 1439, 1291, 1263, 1142, 800, 748, 692 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{16}NaO_3S$ $(M+Na)^+$: 323.0718, found:323.0716; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 16.82 min, minor retention time: 30.81 min, er = 95.5:4.5; $[\alpha]_D^{20}$ = -40.2 (c = 1.0, $CHCl_3$).

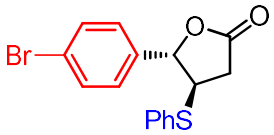
(4*R*, 5*S*)-5-(4-fluorophenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3d**):



General procedure A was followed using (*E*)-4-(4-fluorophenyl)but-3-enoic acid (**1d**, 18.0 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 33 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:12 EtOAc:petroleum ether) to afford product **3d** as a colorless oil (24.0 mg, 83% yield), R_f = 0.5 (1:5 EtOAc:petroleum ether). **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.47 – 7.37 (m, 2H), 7.34 (dd, J = 5.0, 1.8 Hz, 3H), 7.30 – 7.22 (m, 2H), 7.07 (t, J = 8.6 Hz, 2H),

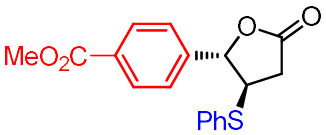
5.32 (d, J = 6.5 Hz, 1H), 3.78 (td, J = 8.0, 6.6 Hz, 1H), 3.04 (dd, J = 18.0, 8.2 Hz, 1H), 2.69 (dd, J = 18.0, 7.9 Hz, 1H); **^{13}C NMR** (126MHz, $CDCl_3$, ppm): δ 173.99, 163.01 (d, J = 248.1 Hz), 133.64, 133.21 (d, J = 3.2 Hz), 131.61, 129.60, 128.85, 127.63 (d, J = 8.4 Hz), 115.94 (d, J = 21.8 Hz), 84.85, 50.19, 35.76; **^{19}F NMR** (471 MHz, $CDCl_3$, ppm): δ -112.50; **IR** (neat): 1789, 1607, 1512, 1228, 1158, 1142, 1025, 1001, 853, 837, 748, 692 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{16}H_{13}FNaO_2S$ $(M+Na)^+$: 311.0518, found 311.0511; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 21.81 min, minor retention time: 27.29 min, er = 95: 5; $[\alpha]_D^{20}$ = -18.6 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-5-(4-bromophenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3e**):



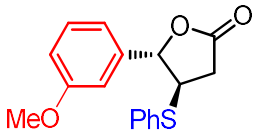
General procedure A was followed using (*E*)-4-(4-bromophenyl)but-3-enoic acid (**1e**, 24.1 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 28 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:20 EtOAc:petroleum ether) to afford product **3e** as a white solid (21.0 mg, 61% yield), R_f = 0.2 (1:20 EtOAc:petroleum ether). **Mp**: 63.8 ~65.7 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.52 – 7.44 (m, 2H), 7.43 – 7.36 (m, 2H), 7.37 – 7.29 (m, 3H), 7.20 – 7.09 (m, 2H), 5.26 (d, J = 6.3 Hz, 1H), 3.74 (td, J = 7.9, 6.4 Hz, 1H), 3.00 (dd, J = 18.0, 8.2 Hz, 1H), 2.66 (dd, J = 18.0, 7.7 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 173.89, 136.47, 133.64, 132.03, 131.49, 129.59, 128.85, 127.31, 123.00, 84.58, 50.01, 35.59; **IR** (neat): 2962, 2925, 2854, 1789, 1261, 1094, 1022, 800 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{16}H_{13}BrNaO_2S$ $(M+Na)^+$: 370.9717, found: 370.9712; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 27.20 min, minor retention time: 31.40 min, er = 94.5:5.5; $[\alpha]_D^{20}$ = -47.0 (c = 1.0, $CHCl_3$).

Methyl 4-((2*S*, 3*R*)-5-oxo-3-(phenylthio)tetrahydrofuran-2-yl)benzoate (**3f**):



General procedure A was followed using (*E*)-4-(4-(methoxycarbonyl)phenyl)but-3-enoic acid (**1f**, 22.0 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 3 d at 0 °C. The crude mixture was purified by silica gel flash chromatography (1:25 EtOAc:petroleum ether) to afford product **3f** as a white solid (15.0 mg, 46% yield), R_f = 0.6 (1:5 EtOAc:petroleum ether). **Mp**: 73.6 ~75.1 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 8.21 – 7.82 (m, 2H), 7.40 (d, J = 3.6 Hz, 2H), 7.37 – 7.29 (m, 5H), 5.37 (d, J = 6.0 Hz, 1H), 3.92 (s, 3H), 3.77 (ddd, J = 8.2, 7.3, 6.0 Hz, 1H), 3.01 (dd, J = 18.0, 8.3 Hz, 1H), 2.67 (dd, J = 18.0, 7.2 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 173.97, 166.53, 142.43, 133.77, 131.54, 130.74, 130.20, 129.67, 128.99, 125.53, 84.66, 52.39, 50.14, 35.50; **IR** (neat): 2923, 1789, 1722, 1613, 1437, 1281, 1183, 1111, 1002, 750, 693 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{18}H_{16}NaO_4S$ $(M+Na)^+$: 351.0667, found: 351.0679; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 88:12, 1 mL/min, major retention time: 32.00 min, minor retention time: 38.99 min, er = 94.5:5.5; $[\alpha]_D^{20}$ = -30.6 (c = 1.0, $CHCl_3$).

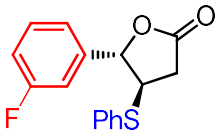
(4*R*, 5*S*)-5-(3-methoxyphenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3g**):



General procedure A was followed using (*E*)-4-(3-methoxyphenyl)but-3-enoic acid (**1g**, 19.2 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 24 h at -40 °C. The crude mixture was purified by silica gel flash chromatography (1:15 EtOAc:petroleum ether) to afford product **3g** as a white solid (28.5 mg, 95% yield), R_f = 0.5 (1:5 EtOAc:petroleum ether). **Mp**: 91.1 ~93.5 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.32 (dd, J = 6.7, 3.5 Hz, 3H), 7.23 – 7.13 (m, 2H), 6.97 – 6.78 (m, 2H), 5.28 (d, J = 6.3 Hz, 1H), 3.98 – 3.39 (m, 4H), 3.02 (dd, J = 17.9, 8.1 Hz,

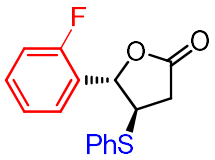
1H), 2.65 (dd, J = 17.9, 7.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.33, 160.16, 133.53, 131.90, 129.53, 129.29, 128.66, 127.22, 114.32, 85.37, 55.48, 50.04, 35.89; **IR** (neat): 1786, 1613, 1516, 1252, 1226, 1176, 1141, 1028, 803 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{16}NaO_3S$ $(M+Na)^+$: 323.0718, found: 323.0715; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 88:12, 1 mL/min, major retention time: 24.18 min, minor retention time: 27.29 min, er = 96:4; $[\alpha]_D^{20}$ = -46.8 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-5-(3-fluorophenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3h**):



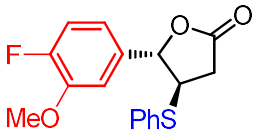
General procedure A was followed using (*E*)-4-(3-fluorophenyl)but-3-enoic acid (**1h**, 18.0 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 41 h at 5 °C. The crude mixture was purified by silica gel flash chromatography (1:10 EtOAc:petroleum ether) to afford product **3h** as a white solid (23.0 mg, 80% yield), R_f = 0.4 (1:5 EtOAc:petroleum ether). **Mp**: 86.8 ~88.9 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.48 – 7.44 (m, 2H), 7.35 (m, 4H), 7.29 – 7.24 (m, 1H), 7.16 (t, J = 7.6 Hz, 1H), 7.12 – 7.05 (m, 1H), 5.58 (d, J = 5.3 Hz, 1H), 3.97 (dt, J = 8.0, 5.9 Hz, 1H), 3.06 (dd, J = 18.0, 8.2 Hz, 1H), 2.66 (dd, J = 18.0, 6.4 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.36, 160.22 (d, J = 248.5 Hz), 133.97, 131.37, 130.95 (d, J = 8.3 Hz), 129.47, 128.86, 127.67 (d, J = 3.5 Hz), 124.81 (d, J = 12.5 Hz), 124.64 (d, J = 3.6 Hz), 116.14 (d, J = 21.0 Hz), 81.10 (d, J = 2.0 Hz), 48.68, 35.27; **^{19}F NMR** (471 MHz, $CDCl_3$, ppm): δ -116.47; **IR** (neat): 1789, 1586, 1492, 1459, 1440, 1238, 1222, 1183, 1143, 1025, 1001, 758, 692 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{16}H_{13}FNaO_2S$ $(M+Na)^+$: 311.0518, found: 311.0526; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 15.67 min, minor retention time: 18.43 min, er = 95.5:4.5; $[\alpha]_D^{20}$ = -34.4 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-5-(2-fluorophenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3i**):



General procedure A was followed using (*E*)-4-(2-fluorophenyl)but-3-enoic acid (**1i**, 18.0 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 41 h at 5 °C. The crude mixture was purified by silica gel flash chromatography (1:12 EtOAc:petroleum ether) to afford product **3i** as a colorless oil (27.0 mg, 94% yield), R_f = 0.5 (1:5 EtOAc:petroleum ether). **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.42 (dd, J = 6.5, 3.0 Hz, 2H), 7.39 – 7.29 (m, 4H), 7.11 – 7.00 (m, 2H), 6.96 (dd, J = 9.5, 1.8 Hz, 1H), 5.31 (d, J = 5.9 Hz, 1H), 3.77 (td, J = 7.3, 6.1 Hz, 1H), 3.01 (dd, J = 18.0, 8.2 Hz, 1H), 2.66 (dd, J = 18.0, 7.2 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 173.98, 163.00 (d, J = 247.6 Hz), 140.10 (d, J = 7.1 Hz), 133.77, 131.55, 130.66 (d, J = 8.3 Hz), 129.66 (s), 128.97, 121.19 (d, J = 3.0 Hz), 115.94 (d, J = 21.0 Hz), 112.73 (d, J = 22.9 Hz), 84.46 (d, J = 1.9 Hz), 50.08, 35.45; **^{19}F NMR** (471 MHz, $CDCl_3$, ppm): δ -111.54; **IR** (neat): 2924, 1789, 1592, 1453, 1261, 1139, 1025, 800, 748, 691 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{16}H_{13}FNaO_2S$ $(M+Na)^+$: 311.0518, found : 311.0524; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 19.11 min, minor retention time: 22.53 min, er = 94.5:5.5; $[\alpha]_D^{20}$ = -36.8 (c = 1.0, $CHCl_3$).

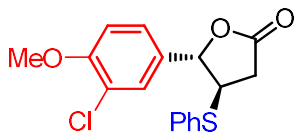
(4*R*, 5*S*)-5-(4-fluoro-3-methoxyphenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3j**):



General procedure A was followed using (*E*)-4-(4-fluoro-3-methoxyphenyl)but-3-enoic acid (**1j**, 21.0 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 24 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:10 EtOAc:petroleum ether) to afford product **3j** as a colorless oil (24.0 mg, 76% yield), R_f = 0.4 (1:5 EtOAc:petroleum ether). **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.44 – 7.36 (m, 2H), 7.37 – 7.28 (m, 3H), 7.04 (dd, J = 10.9, 8.3 Hz, 1H),

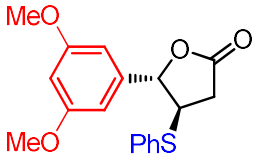
6.80 (ddd, J = 12.5, 6.9, 2.0 Hz, 2H), 5.29 (d, J = 6.3 Hz, 1H), 3.84 (s, 3H), 3.77 (td, J = 7.9, 6.4 Hz, 1H), 3.03 (dd, J = 18.0, 8.3 Hz, 1H), 2.67 (dd, J = 18.0, 7.7 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 173.98, 163.00 (d, J = 247.6 Hz), 140.10 (d, J = 7.1 Hz), 133.77, 131.55, 130.66 (d, J = 8.3 Hz), 129.66, 128.97, 121.19 (d, J = 3.0 Hz), 115.94 (d, J = 21.0 Hz), 112.73 (d, J = 22.9 Hz), 84.46 (d, J = 1.9 Hz), 50.08, 35.45; **^{19}F NMR** (471 MHz, $CDCl_3$, ppm): δ -134.48; **IR** (neat): 1789, 1520, 1466, 1283, 1263, 1215, 1164, 1142, 1121, 1091, 1028, 808, 746, 693cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{15}FNaO_3S$ $(M+Na)^+$: 341.0624, found: 341.0627; separation of enantiomers by HPLC, Chiralcel® Column OJ-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, minor retention time: 66.86 min, major retention time: 70.33 min, er = 3.5:96.5; $[\alpha]_D^{20}$ = -29.8 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-5-(3-chloro-4-methoxyphenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3k**):



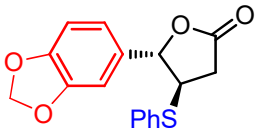
General procedure A was followed using (*E*)-4-(3-chloro-4-methoxyphenyl)but-3-enoic acid (**1k**, 22.7 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 24 h at -20 °C. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product **3k** as a white solid (30.0 mg, 90% yield), R_f = 0.3 (1:5 EtOAc:petroleum ether). **Mp**: 62.9 ~64.7 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.44 – 7.36 (m, 2H), 7.33 (dd, J = 4.2, 2.4 Hz, 3H), 7.28 – 7.22 (m, 1H), 7.17 – 7.06 (m, 1H), 6.89 (d, J = 8.5 Hz, 1H), 5.23 (d, J = 6.5 Hz, 1H), 3.90 (s, 3H), 3.76 (dd, J = 8.0, 1.5 Hz, 1H), 3.02 (dd, J = 18.0, 8.2 Hz, 1H), 2.66 (dd, J = 18.0, 7.9 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 173.95, 155.53, 133.73, 131.56, 130.38, 129.61, 128.90, 127.81, 125.41, 123.09, 112.18, 84.64, 56.39, 50.03, 35.78. **IR** (neat): 1787, 1607, 1505, 1440, 1297, 1221, 1182, 1137, 1065, 1023, 806, 748, 692 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{15}ClNaO_3S$ $(M+Na)^+$: 357.0328, found: 357.0331; separation of enantiomers by HPLC, Chiralcel® Column IC, 30 °C, n-hexane: *i*-PrOH = 88:12, 1 mL/min, minor retention time: 29.36 min, major retention time: 38.76 min, er = 5:95; $[\alpha]_D^{20}$ = -43.2 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-5-(3, 5-dimethoxyphenyl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3l**):



General procedure A was followed using (*E*)-4-(3,5-dimethoxyphenyl)but-3-enoic acid (**1l**, 22.2 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 45 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product **3l** as a white solid (18.0 mg, 55% yield), R_f = 0.3 (1:5 EtOAc:petroleum ether). **Mp**: 80.8 ~81.6 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.48 – 7.41 (m, 2H), 7.34 (dd, J = 5.0, 1.8 Hz, 3H), 6.40 (t, J = 2.2 Hz, 1H), 6.35 (d, J = 2.0 Hz, 2H), 5.29 (d, J = 5.2 Hz, 1H), 3.86 – 3.78 (m, 1H), 3.75 (s, 6H), 3.01 (dd, J = 18.1, 8.3 Hz, 1H), 2.62 (dd, J = 18.1, 6.3 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$, ppm): δ 174.45, 161.30, 140.07, 133.68, 132.03, 129.61, 128.80, 103.29, 100.69, 85.16, 55.57, 50.02, 35.29; **IR** (neat): 2962, 1788, 1599, 1465, 1431, 1261, 1206, 1157, 1092, 1064, 1024, 802, 693 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{18}H_{18}NaO_4S$ $(M+Na)^+$: 353.0823, found: 353.0821; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 70:30, 1 mL/min, major retention time: 11.51 min, minor retention time: 22.71 min, er = 95.5:4.5; $[\alpha]_D^{20}$ = -39.0 (c = 1.0, $CHCl_3$).

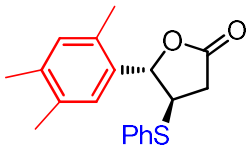
(4*R*, 5*S*)-5-(benzo[d][1,3]dioxol-5-yl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3m**):



General procedure A was followed using (*E*)-4-(benzo[*d*][1,3]dioxol-5-yl)but-3-enoic acid (**1m**, 20.6 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 15 h at -45 °C. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product **3m** as a white solid (31.0 mg, 99% yield), R_f = 0.3 (1:5 EtOAc:petroleum ether). **Mp**: 70.9 ~72.5 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.39 (m, 2H), 7.35 – 7.28 (m, 3H), 6.83 – 6.55 (m, 3H),

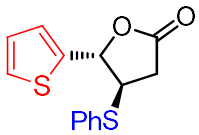
5.97 (s, 2H), 5.22 (d, J = 6.3 Hz, 1H), 3.76 (td, J = 7.9, 6.3 Hz, 1H), 3.01 (dd, J = 17.9, 8.2 Hz, 1H), 2.64 (dd, J = 17.9, 7.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.14, 148.26, 148.23, 131.77, 131.08, 129.56, 128.75, 119.73, 108.52, 106.13, 101.51, 85.40, 50.09, 35.79; **IR** (neat): 2918, 1787, 1504, 1448, 1253, 1142, 1038, 934, 804, 748, 692cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{14}NaO_4S$ $(M+Na)^+$: 337.0510, found: 337.0509; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 29.18 min, minor retention time: 34.48 min, er = 93.5:6.5; $[\alpha]_D^{20}$ = -51.2 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-4-(phenylthio)-5-(2,4,5-trimethylphenyl)dihydrofuran-2(3H)-one(**3n**):



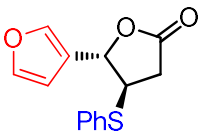
General procedure A was followed using (*E*)-4-(2,4,5-trimethylphenyl)but-3-enoic acid (**1n**, 20.4 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 24 h at -20 °C. The crude mixture was purified by silica gel flash chromatography (1:35 EtOAc:petroleum ether) to afford product **3n** as a yellow solid (29.0 mg, 93% yield), R_f = 0.6 (1:5 EtOAc:petroleum ether). **Mp**: 84.7 ~86.4 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.40 (m, J = 6.6, 3.0 Hz, 2H), 7.35 – 7.27 (m, 3H), 6.95 (d, J = 8.5 Hz, 2H), 5.57 (d, J = 4.4 Hz, 1H), 3.83 (dt, J = 7.9, 4.8 Hz, 1H), 3.03 (dd, J = 18.0, 7.9 Hz, 1H), 2.63 (dd, J = 18.0, 5.1 Hz, 1H), 2.21 (d, J = 2.2 Hz, 6H), 2.17 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 175.10, 137.27, 134.68, 133.48, 132.84, 132.51, 132.45, 132.23, 129.47, 128.62, 125.91, 82.94, 49.23, 35.65, 19.49, 19.42, 18.60; **IR** (neat): 3445, 2921, 1786, 1773, 1632, 1166, 1046, 748, 693 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{19}H_{20}NaO_2S$ $(M+Na)^+$: 335.1082, found: 335.1077; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 95:5, 1 mL/min, minor retention time: 17.43 min, major retention time: 21.66 min, er = 6.5:93.5; $[\alpha]_D^{20}$ = -51.0 (c = 1.0, $CHCl_3$).

(4*R*, 5*R*)-4-(phenylthio)-5-(thiophen-2-yl)dihydrofuran-2(3H)-one (**3o**):



General procedure A was followed using (*E*)-4-(thiophen-2-yl)but-3-enoic acid (**1o**, 16.8 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 11 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product **3o** as a colorless oil (27.0 mg, 98% yield), R_f = 0.3 (1:5 EtOAc:petroleum ether). **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.46 – 7.37 (m, 2H), 7.38 – 7.30 (m, 4H), 7.05 (d, J = 3.5 Hz, 1H), 6.99 (dd, J = 5.0, 3.6 Hz, 1H), 5.54 (d, J = 6.2 Hz, 1H), 3.94 (td, J = 7.8, 6.2 Hz, 1H), 3.08 (dd, J = 18.0, 8.1 Hz, 1H), 2.66 (dd, J = 18.0, 7.5 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 173.51, 139.84, 133.74, 131.38, 129.61, 128.88, 127.24, 126.62, 126.54, 81.82, 49.94, 35.68; **IR** (neat): 2922, 1788, 1476, 1439, 1213, 1135, 983, 748, 705, 692 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{14}H_{12}NaO_2S_2$ $(M+Na)^+$: 299.0176, found: 299.0173; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 93:7, 1 mL/min, major retention time: 27.21 min, minor retention time: 34.88 min, er = 95:5; $[\alpha]_D^{20}$ = -35.5 (c = 0.4, $CHCl_3$).

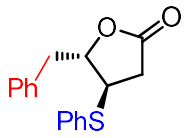
(4*R*, 5*S*)-5-(furan-3-yl)-4-(phenylthio)dihydrofuran-2(3H)-one (**3p**):



General procedure A was followed using (*E*)-4-(furan-3-yl)but-3-enoic acid (**1p**, 15.2 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 24 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product **3p** as a white solid (20.0 mg, 77% yield), R_f = 0.5 (1:5 EtOAc:petroleum ether). **Mp**: 85.8 ~87.2 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.50 – 7.38 (m, 4H), 7.39 – 7.29 (m, 3H), 6.34 (d, J = 0.8 Hz, 1H), 5.29 (d, J = 6.3 Hz, 1H), 3.81 (td, J = 7.9, 6.4 Hz, 1H), 3.02 (dd, J = 17.9, 8.2 Hz, 1H), 2.64 (dd, J = 17.9, 7.6 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 173.95, 144.30, 140.28, 133.70, 131.55,

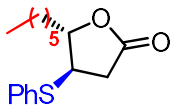
129.61, 128.88, 122.74, 108.08, 79.33, 48.58, 35.69; **IR** (neat): 2963, 1786, 1261, 1162, 1092, 1024, 956, 875, 801, 747, 692, 601 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{14}H_{12}NaO_3S$ $(M+Na)^+$: 283.0405, found: 283.0405; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 85:15, 1 mL/min, major retention time: 13.54 min, minor retention time: 18.69 min, er = 93.5:6.5; $[\alpha]_D^{20}$ = -19.4 (c = 1.0, $CHCl_3$).

(4*R*, 5*S*)-5-benzyl-4-(phenylthio)dihydrofuran-2(3H)-one (**3q**):



General procedure A was followed using (*E*)-5-phenylpent-3-enoic acid (**1q**, 17.6 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 24 h at room temperature. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product **3q** as a white solid (28.0 mg, 99% yield), R_f = 0.5 (1:5 EtOAc:petroleum ether). **Mp**: 82.0 ~83.1 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.43 – 7.22 (m, 8H), 7.19 – 7.05 (m, 2H), 4.59 (dd, J = 11.0, 6.0 Hz, 1H), 3.60 (ddd, J = 8.3, 7.1, 6.0 Hz, 1H), 3.06 (dd, J = 14.5, 4.9 Hz, 1H), 2.93 (dd, J = 14.5, 6.2 Hz, 1H), 2.71 (dd, J = 18.0, 8.4 Hz, 1H), 2.48 (dd, J = 18.0, 7.1 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.28, 135.32, 133.52, 131.82, 129.76, 129.61, 128.86, 128.70, 127.31, 84.93, 45.31, 39.52, 35.7; **IR** (neat): 2960, 2924, 1800, 1482, 1261, 1174, 1033, 1003, 802, 734, 700, 691 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{16}NaO_2S$ $(M+Na)^+$: 307.0769, found: 307.0766; separation of enantiomers by HPLC, Chiralcel® Column OJ-H, 30 °C, n-hexane: *i*-PrOH = 88:12, 1 mL/min, minor retention time: 32.95 min, major retention time: 39.47 min, er = 5:95; $[\alpha]_D^{20}$ = -29.4 (c = 1.0, $CHCl_3$).

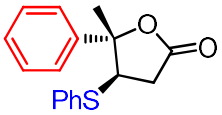
(4*R*, 5*S*)-5-hexyl-4-(phenylthio)dihydrofuran-2(3H)-one (**3r**):



General procedure A was followed using (*E*)-dec-3-enoic acid (**1r**, 17.0 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2

equiv) stirred for 24 h at 0 °C. The crude mixture was purified by silica gel flash chromatography (1:1 EtOAc:petroleum ether) to afford product **3r** as a yellow oil (23.0 mg, 83% yield), R_f = 0.5 (1:1 EtOAc:petroleum ether). **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.46 (dd, J = 5.6, 2.0 Hz, 2H), 7.42 – 7.31 (m, 3H), 4.35 (ddd, J = 7.9, 6.2, 3.0 Hz, 1H), 3.57 (td, J = 8.1, 1.7 Hz, 1H), 2.95 (ddd, J = 18.0, 8.3, 1.7 Hz, 1H), 2.58 (ddd, J = 18.0, 7.6, 1.8 Hz, 1H), 1.83 – 1.68 (m, 1H), 1.69 – 1.56 (m, 1H), 1.52 – 1.35 (m, 2H), 1.34 – 1.19 (m, 5H), 0.90 (dd, J = 6.9, 5.2 Hz, 4H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.50, 133.53, 132.10, 129.56, 128.68, 85.17, 46.82, 36.16, 34.17, 31.44, 25.13, 22.54, 14.07; **IR** (neat): 2959, 2929, 2858, 1783, 1439, 1261, 1773, 1094, 1024, 802, 748, 692 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{16}H_{23}O_2S$ $(M+H)^+$: 279.1438, found: 279.1423; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 88:12, 1 mL/min, major retention time: 10.25 min, minor retention time: 11.87 min, er = 97:3; $[\alpha]_D^{20}$ = -49.8 (c = 1.0, $CHCl_3$).

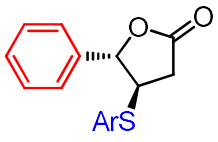
(4*R*, 5*S*)-4-(argiothio)-5-phenyldihydrofuran-2(3H)-one (**3s**):



General procedure A was followed using (*E*)-4-phenylpent-3-enoic acid (**1s**, 17.6 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) using (R)-CPA (Cas: 39648-67-4) as the acid under $CDCl_3$ stirred for 20 h at -20 °C. The crude mixture was purified by silica gel flash chromatography (1:20 EtOAc:petroleum ether) to afford product **3s** as a white solid (26.5 mg, 93% yield), R_f = 0.4 (8:1 EtOAc:petroleum ether). **Mp**: 145.7 ~147.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.54 – 7.41 (m, 2H), 7.42 – 7.17 (m, 8H), 4.04 (t, J = 7.5 Hz, 1H), 2.90 (dd, J = 17.8, 7.8 Hz, 1H), 2.73 (dd, J = 17.9, 7.2 Hz, 1H), 1.83 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 173.86, 143.44, 133.31, 132.25, 129.51, 128.81, 128.22, 128.10, 124.33, 88.76, 54.13, 37.43, 24.48; **IR** (neat): 3445, 2925, 1782, 1441, 1230, 1135, 934, 766, 748, 699 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{17}H_{17}O_2S$ $(M+H)^+$: 285.0950, found: 285.0945; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time:

12.60 min, minor retention time: 14.77 min, er = 88.5:11.5; $[\alpha]_D^{20}$ = -14.0 (c = 1.0, $CHCl_3$).

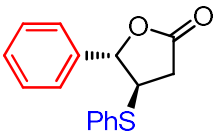
(4*R*, 5*R*)-4-(2-ethylbenzyl)-5-phenyldihydrofuran-2(3H)-one (**3t**):



Ar = 2-EtC_6H_4

General procedure A was followed using (*E*)-4-phenylbut-3-enoic acid (**1t**, 16.2 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 35 mg, 0.12 mmol, 1.2 equiv) stirred for 24 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:8 EtOAc:petroleum ether) to afford product **3t** as a colorless oil (23.0 mg, 77% yield), R_f = 0.7 (5:1 EtOAc:petroleum ether). **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.44 – 7.32 (m, 4H), 7.31 – 7.22 (m, 4H), 7.21 – 7.12 (m, 1H), 5.37 (d, J = 5.2 Hz, 1H), 3.84 (dt, J = 8.0, 6.0 Hz, 1H), 3.06 (dd, J = 18.0, 8.0 Hz, 1H), 2.86 – 2.73 (m, 2H), 2.66 (dd, J = 18.0, 6.2 Hz, 1H), 1.21 (t, J = 7.5 Hz, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 174.68, 146.77, 137.65, 133.52, 131.15, 129.47, 128.96, 128.87, 126.92, 125.44, 85.13, 49.97, 35.63, 27.40, 15.41; **IR** (neat): 2965, 1788, 1469, 1164, 1026, 1002, 755, 699 cm^{-1}; **HRMS** (ESI) *m/z* calcd. for $C_{18}H_{18}NaO_2S$ $(M+Na)^+$: 321.0925, found: 321.0923; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 85:15, 1 mL/min, major retention time: 10.23 min, minor retention time: 16.73 min, er = 97:3; $[\alpha]_D^{20}$ = -32.5 (c = 0.4, $CHCl_3$).

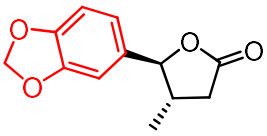
5-*endo* cyclization of **1a** for the formation of **3a** on a gram-scale:



A dried round bottom flask was charged with (*E*)-4-phenylbut-3-enoic acid (**1a**, 1.00 g, 6.17 mmol, 1.0 equiv) and 2-(phenylthio)benzo[*d*]isothiazol-3(2H)-one 1,1-dioxide (**2a**, 2.16 g, 7.40 mmol, 1.2 equiv) stirred for 24 h at -5 °C. The crude mixture was purified by silica gel flash chromatography (1:20 EtOAc:petroleum ether) to afford product **3a** as a colorless oil (1.53 g, 92% yield), R_f = 0.6 (1:5 EtOAc:petroleum ether). Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time:

16.37 min, minor retention time: 20.38 min, er = 94.5:5.5.

(4*S*, 5*S*)-5-(benzo[d][1,3]dioxol-5-yl)-4-methyldihydrofuran-2(3H)-one (**8**):



Procedures for the synthesis of **7** according to the literature procedure.[11] A solution of (4S,5R)-5-(benzo[d][1,3]dioxol-5-yl)-4-(phenylthio)dihydrofuran-2(3H)-one (*ent*-**3m**, 104.0 mg, 0.33 mmol, 1.0 equiv) and MeOH (6.9 mL), H_2O (2.7 mL) stirred at room temperature. Sodium periodate (77.8 mg, 0.36 mmol, 1.1 equiv) was added as a solid, resulting in a heterogeneous solution. The mixture was stirred at room temperature for 24 h. The reaction was quenched by water (10 mL). The aqueous layer was extracted with DCM (2 × 30 mL). The organic layers were combined, washed with brine (15 mL), dried over Na_2SO_4, filtered, concentration and carry out the next step without purification.

In a dry tube, the solution of sulfoxide intermediate and toluene (2 mL) was refluxed at 115 °C for 3 h. After the reaction was complete (TLC), the flask was removed from the oil bath and allowed to cool to rt. The solution was concentrated by rotary evaporation. Purification by silica gel flash column chromatography (5:1 EtOAc:petroleum ether) afforded 49.5 mg (73%) of **7** as a light brown solid. R_f = 0.3 (5:1 EtOAc:petroleum ether).

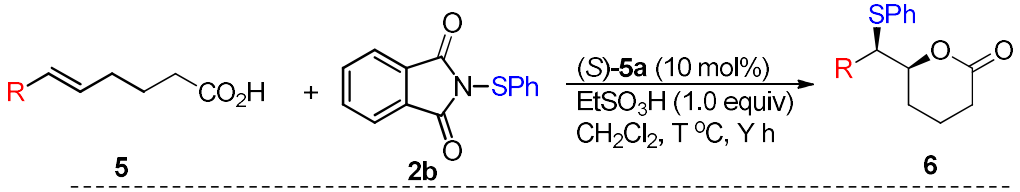
Under anhydrous anaerobic conditions, cuprous iodide (140 mg, 0.74 mmol, 10.0 equiv) was dissolves in anhydrous ether, methyllithium (1.6 M solution in diethyl ether, 0.92 mL, 1.47 mmol, 20.0 equiv) was added in the mixture at -38 °C, then stirred at 0 °C for 45 min. After this, the mixture was cooled to -78 °C stirred for 15 min, **7** (15 mg, 0.074 mmol, 1.0 equiv) was dissolved in ether (4 mL) and added dropwise to the reaction system at -78 °C. The reaction system stirred for 4 h at -78 °C. The reaction was quenched by saturated ammonium chloride solution (15 mL). The aqueous layer was extracted with DCM (2 × 20 mL). The organic layers were combined, washed with brine (15 mL), dried over Na_2SO_4, filtered, concentration and purification by silica gel flash column chromatography (8:1 EtOAc:petroleum ether) afforded 12.6 mg (78%) of **8** as a fuchsia liquid. R_f = 0.6 (2:1 EtOAc:petroleum ether). **^{1}H NMR** (400

MHz, $CDCl_3$, ppm): δ 6.81 (m, 3H), 5.98 (s, 2H), 4.84 (d, J = 8.6 Hz, 1H), 2.78 (dd, J = 16.8, 7.5 Hz, 1H), 2.55 – 2.40 (m, 1H), 2.32 (dd, J = 16.8, 10.8 Hz, 1H), 1.16 (d, J = 6.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 176.06, 148.28, 148.18, 131.64, 120.18, 108.38, 106.52, 101.48, 88.37, 39.96, 37.48, 16.45; **IR** (neat): 3445, 2962, 2925, 1778, 1636, 1260, 1097, 1038, 803 cm^{-1}; **HRMS** (ESI) m/z calcd. for $C_{12}H_{12}NaO_4$ $(M+Na)^+$: 243.0633, found: 243.0630 ; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 70:30, 1 mL/min, minor retention time: 8.17 min, major retention time: 8.58 min, er = 1.5:98.5; $[\alpha]_D^{20}$ = +6.0 (c = 0.2, $CHCl_3$).

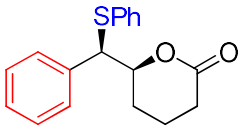
3.2 General procedure for the enantioselective *6-exo* thiolactonization (procedure B):

In a dry tube, unsaturated carboxylic acids **5** (0.1 mmol, 1.0 equiv) and sulfenylating agent **2b** (0.12 mmol, 1.2 equiv), (*S*)-Cat. **4a** (0.1 mmol, 1.0 equiv) were added in DCM (1.0 mL) under argon atmosphere. After stirred for 5 min at corresponding temperature, ethanesulfonic acid (0.1 mmol, 1.0 equiv) were added in one portion. The resulting mixture was stirred for another 36 h to 72 h at corresponding temperature. After the reaction was complete (monitored by TLC), the solvent was concentrated under reduced pressure, and the resulting residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc) to give the corresponding sulfenylated lactones.

The synthesis of *6-exo* racemic sample was followed using unsaturated carboxylic acids **5** (0.1 mmol, 1.0 equiv) and sulfenylating agent **2b** (0.12 mmol, 1.2 equiv), racemic-Cat. **4a** (0.01 mmol, 0.1 equiv) and ethanesulfonic acid (0.1 mmol, 1.0 equiv) were added in DCM (1.0 mL) under argon atmosphere at room temperature for overnight.

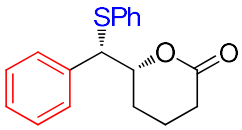


(*S*)-6-((*R*)-phenyl(phenylthio)methyl)tetrahydro-2H-pyran-2-one (**6a**)



General procedure B was followed using (*E*)-6-phenylhex-5-enoic acid (**5a**, 19.0 mg (*E:Z* = 9:1), 0.1 mmol, 1.0 equiv) and 2-(phenylthio)isoindoline-1,3-dione (**2b**, 30.6 mg, 0.12 mmol, 1.2 equiv) stirred for 36 h at -10 °C. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product **6a** as a white solid (25.0 mg, 84% yield), R_f = 0.2 (5:1 EtOAc:petroleum ether). **Mp**: 125.5 ~127.6 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, ppm): δ 7.39 – 7.35 (m, 2H), 7.34 – 7.29 (m, 4H), 7.27 – 7.24 (m, 1H), 7.23 – 7.16 (m, 3H), 4.75 – 4.65 (m, 1H), 4.33 (d, J = 4.8 Hz, 1H), 2.56 (m, 1H), 2.44 – 2.25 (m, 1H), 2.10 – 1.96 (m, 1H), 1.93 – 1.83 (m, 1H), 1.77 (m, 1H), 1.60 – 1.51 (m, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$, ppm): δ 170.86, 137.87, 134.53, 132.51, 129.18, 129.04, 128.61, 127.92, 127.59, 82.11, 58.54, 29.69, 25.68, 18.60; **IR** (neat): 2917, 1726, 1580, 1480, 1438, 1368, 1232, 1166, 1057, 938, 744, 703, 692, 513 cm^{-1}; **HRMS** (ESI) m/z calcd. for $C_{18}H_{18}NaO_2S$ $(M+Na)^+$: 321.0925, found: 321.0927; separation of enantiomers by HPLC, Chiralcel® Column AD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min, major retention time: 12.51 min, minor retention time: 13.94 min, er = 97.5:2.5; $[\alpha]_D^{20}$ = -113.2 (c = 1.0, $CHCl_3$).

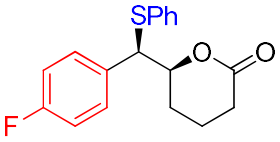
(*R*)-6-((*S*)-phenyl(phenylthio)methyl)tetrahydro-2H-pyran-2-one (*ent*-**6a**)



General procedure B was followed using (*E*)-6-phenylhex-5-enoic acid (**5a**, 19.0 mg (*E:Z* = 9:1), 0.1 mmol, 1.0 equiv) and 2-(phenylthio)isoindoline-1,3-dione (**2b**, 30.6 mg, 0.12 mmol, 1.2 equiv) stirred for 66 h at -10 °C. The crude mixture was purified by silica gel flash chromatography (1:5 EtOAc:petroleum ether) to afford product *ent*-**6a** as a white solid (24.0 mg, 80% yield), R_f = 0.2 (5:1 EtOAc:petroleum ether). **Mp**: 93.8~95.4 °C. Separation of enantiomers by HPLC, Chiralcel® Column AD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min,

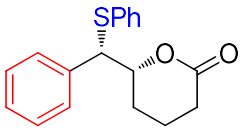
minor retention time: 12.04 min, major retention time: 13.38 min, er = 2.5:97.5; $[\alpha]_D^{20}$ = +101.8 (c = 1.0, $CHCl_3$).

(*S*)-6-((*R*)-(4-fluorophenyl)(phenylthio)methyl)tetrahydro-2H-pyran-2-one (**6b**)



General procedure B was followed using (*E*)-6-(4-fluorophenyl)hex -5-enoic acid (**5b**, 20.8 mg, 0.1 mmol, 1.0 equiv) and 2-(phenylthio)isoindoline-1,3-dione (**2b**, 30.6 mg, 0.12 mmol, 1.2 equiv) stirred for 72 h at -10 °C. The crude mixture was purified by silica gel flash chromatography (1:4 EtOAc:petroleum ether) to afford product **6b** as a colorless oil (34.0 mg, 95% yield), R_f = 0.2 (5:1 EtOAc:petroleum ether). **^{1}H NMR** (400 MHz, $CDCl_3$, ppm): δ 7.30 (m, 4H), 7.21 (dd, J = 6.5, 2.7 Hz, 3H), 7.05 – 6.85 (m, 2H), 4.66 (ddd, J = 11.3, 4.9, 3.3 Hz, 1H), 4.28 (d, J = 5.0 Hz, 1H), 2.57 (m, 1H), 2.43 – 2.26 (m, 1H), 2.03 (ddd, J = 12.4, 7.3, 3.5 Hz, 1H), 1.95 – 1.69 (m, 2H), 1.52 (dtd, J = 13.8, 11.3, 5.4 Hz, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$, ppm): δ 170.75, 162.32 (d, J = 246.7 Hz), 133.97, 133.59 (d, J = 3.3 Hz), 132.77, 130.80 (d, J = 8.1 Hz), 129.10, 127.82, 115.47 (d, J = 21.5 Hz), 81.82, 57.67, 29.61, 25.91, 18.52; **^{19}F NMR** (376 MHz, $CDCl_3$): δ -114.35; **IR** (neat): 2956, 1737, 1604, 1508, 1439, 1233, 1159, 1053, 839, 743, 692, 529 cm^{-1}; **HRMS** (ESI) m/z calcd. for $C_{18}H_{17}FNaO_2S$ $(M+Na)^+$: 339.0831, found: 339.0833; separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 70:30, 1 mL/min, major retention time: 7.27 min, minor retention time: 11.84 min, er = 92:8; $[\alpha]_D^{20}$ = -68.42 (c = 1.0, $CHCl_3$).

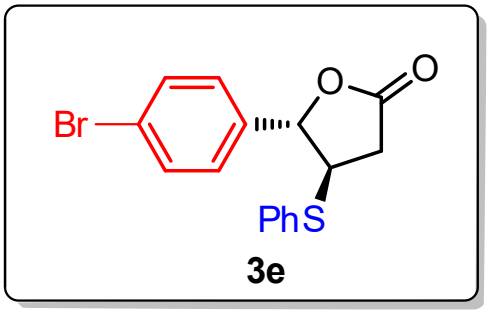
6-exo cyclization of **5a** for the formation of *ent*-**6a** on a gram-scale:



A dried round bottom flask was charged with (*E*)-6-phenylhex-5-enoic acid (**5a**, 1.141 g (*E:Z* = 4:1), 6.0 mmol, 1.0 equiv) and 2-(phenylthio)isoindoline-1,3-dione (**2b**, 1.838 g, 7.2 mmol, 1.2 equiv) stirred for 66 h at -10 °C. The crude mixture was purified by silica gel flash

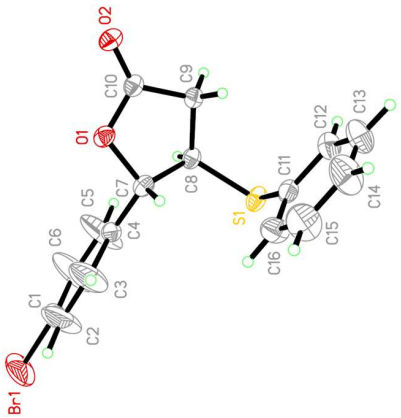
chromatography (1:8 EtOAc:petroleum ether) to afford product *ent*-**6a** as a white solid (1.350 g, 75% yield), R_f = 0.2 (5:1 EtOAc:petroleum ether) , and recycling raw materials *Z*-**5a** (180 mg, 10%). Separation of enantiomers by HPLC, Chiralcel® Column AD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min, minor retention time: 12.28 min, major retention time: 13.58 min, er =4:96.

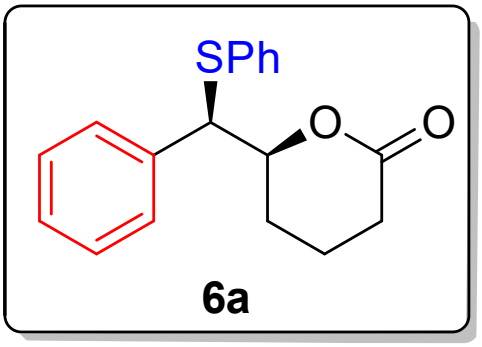
Crystals 3e and 6a



3e

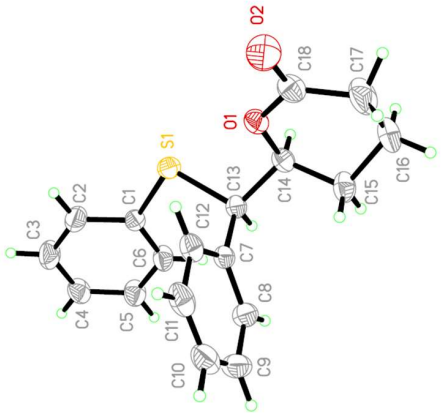
CCDC 1899806



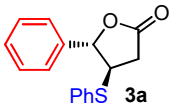
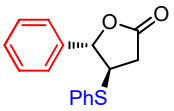
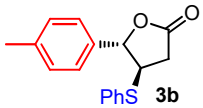
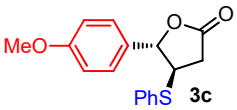
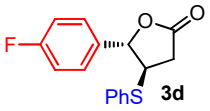
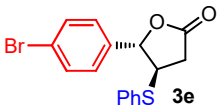
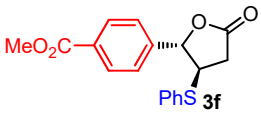
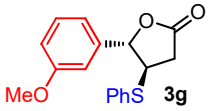
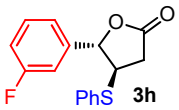
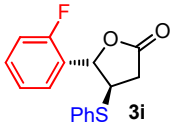


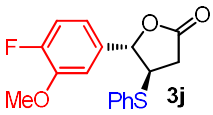
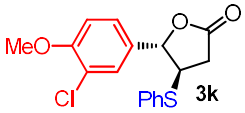
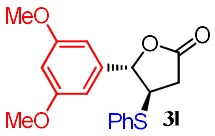
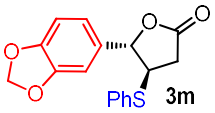
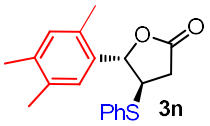
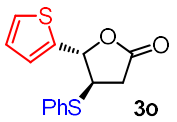
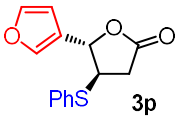
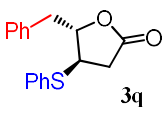
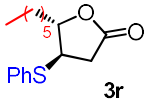
6a

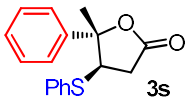
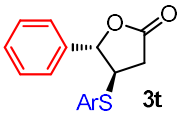
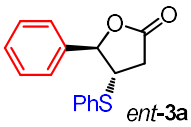
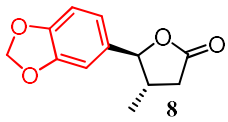
CCDC 1938651



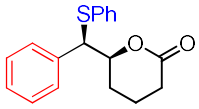
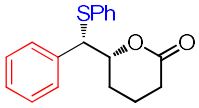
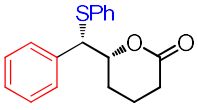
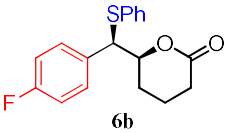
HPLC list of products *5-endo*

Compounds	Chiral column	Eluent ratio, flow rate, retention time	ee
 **3a**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 20.23 min; major isomer: tr = 16.04 min	92%
 **3a-gram-scale**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 20.38 min; major isomer: tr = 16.37 min	89%
 **3b**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 17.74 min; major isomer: tr = 14.52 min	91%
 **3c**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 30.81 min; major isomer: tr = 16.82 min	91%
 **3d**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 27.29 min; major isomer: tr = 21.81 min	90%
 **3e**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 31.40 min; major isomer: tr = 27.20 min	89%
 **3f**	Chiralpak OD-H	Hexane/Isopropanol 88/12, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 38.99 min; major isomer: tr = 32.00 min	89%
 **3g**	Chiralpak OD-H	Hexane/Isopropanol 88/12, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 27.29 min; major isomer: tr = 24.18 min	92%
 **3h**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 18.43 min; major isomer: tr = 15.67 min	90%
 **3i**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 22.53 min; major isomer: tr = 19.11 min	89%

 **3j**	Chiralpak OJ-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 66.86 min; major isomer: tr = 70.33 min	93%
 **3k**	Chiralpak IC	Hexane/Isopropanol 88/12, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 29.36 min; major isomer: tr = 38.76 min	90%
 **3l**	Chiralpak OD-H	Hexane/Isopropanol 70/30, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 22.71 min; major isomer: tr = 11.51 min	91%
 **3m**	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 34.48 min; major isomer: tr = 29.18 min	87%
 **3n**	Chiralpak OD-H	Hexane/Isopropanol 93/7, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 17.43 min; major isomer: tr = 21.66 min	87%
 **3o**	Chiralpak OD-H	Hexane/Isopropanol 93/7, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 34.88 min; major isomer: tr = 27.21 min	90%
 **3p**	Chiralpak OD-H	Hexane/Isopropanol 85/15, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 18.69 min; major isomer: tr = 13.54 min	87%
 **3q**	Chiralpak OJ-H	Hexane/Isopropanol 88/12, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 32.95 min; major isomer: tr = 39.47 min	90%
 **3r**	Chiralpak OD-H	Hexane/Isopropanol 88/12, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 11.87 min; major isomer: tr = 10.25 min	94%

 3s	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 14.77 min; major isomer: tr = 12.60 min	77%
 3t	Chiralpak OD-H	Hexane/Isopropanol 85/15, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 16.73 min; major isomer: tr = 10.23 min	94%
 *ent*-3a	Chiralpak OD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 17.95 min; major isomer: tr = 21.56 min	91%
 8	Chiralpak OD-H	Hexane/Isopropanol 70/30, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 8.17 min; major isomer: tr = 8.58 min	97%

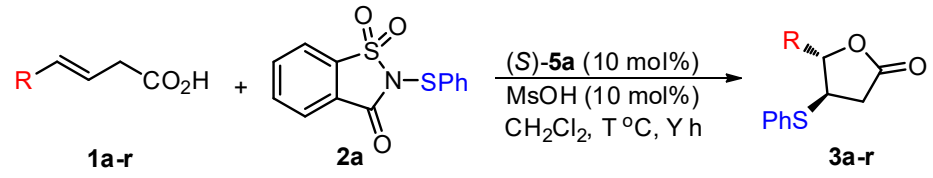
HPLC list of products *6-exo*

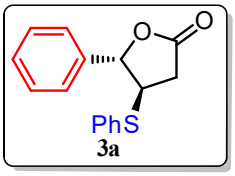
Compounds	Chiral column	Eluent ratio, flow rate, retention time	ee
 **6a**	Chiralpak AD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 13.94 min; major isomer: tr = 12.51 min	95%
 *ent*-**6a**	Chiralpak AD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 12.04 min; major isomer: tr = 13.38 min	95%
 *ent*-**6a-gram-scale**	Chiralpak AD-H	Hexane/Isopropanol 90/10, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 12.28 min; major isomer: tr = 13.58 min	92%
 **6b**	Chiralpak OD-H	Hexane/Isopropanol 70/30, flow rate = 1.0 mL/min, 254 nm minor isomer: tr = 11.84 min; major isomer: tr = 7.27 min	84%

References

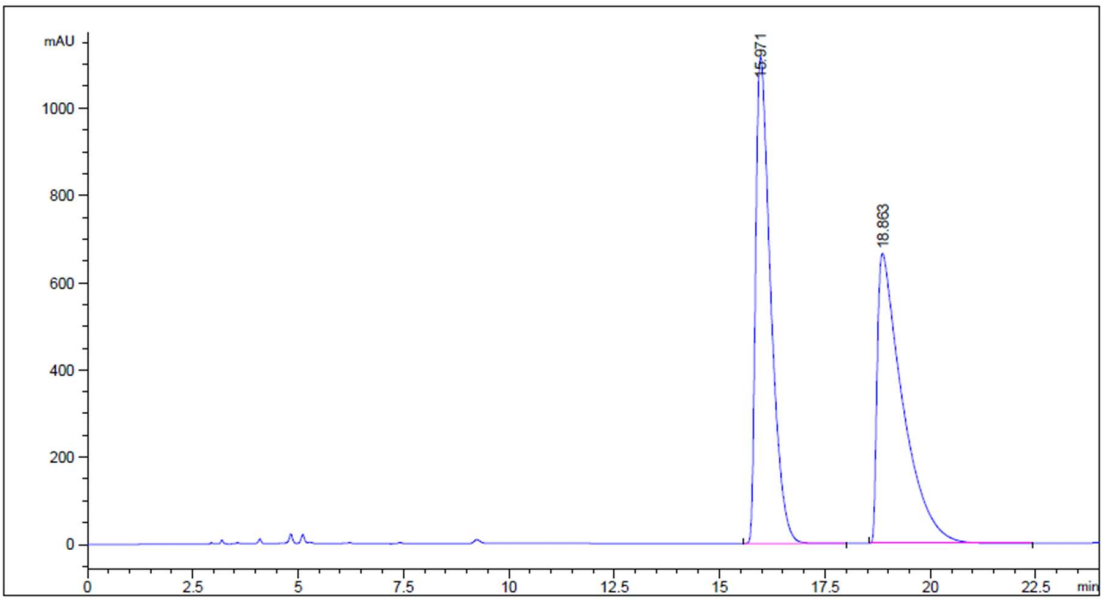
1. S. E. Denmark, S. Rossi, M. P. Webster and H. Wang, *J. Am. Chem. Soc.,* 2014, **136**, 13016.
2. Y. Sato, T. Mita and K. Michigami, *J. Am. Chem. Soc.,* 2017, **139**, 6094.
3. F. Kouser, V. K. Sharma, M. Rizvi, S. Sultan, N. Chalotra, V. K. Gupta, U. Utpal Nandi and B. AliShah, *Tetrahedron Letters*. , 2018, **59**, 2261.
4. X. F. Wu, J. B. Peng, F. P. Wu, L. Y. Fu and X.- X. Qi, *Org. Lett.,* 2017, **19**, 5474.
5. Y. Fu, R. Shang, M. C. Fu and W. M. Cheng, *Chem. Eur. J.,* 2017, **23**, 8818.
6. R. Beugelmans, J. Chastanet, H. Ginsburg, L. Q. Cortes and G. Roussi, *J. Org. Chem.,* 1985, **50**, 4933.
7. C. H. Tan, J. M. Wang, J. Chen and C. W. Kee, *Angew. Chem. Int. Ed*., 2012, **51**, 2382.
8. W. B. Motherwell, S. Desrat, P. J. Gray and M. R. Penny, *Chem. Eur. J*., 2014, **20**, 8918.
9. Y. Yamamoto, K. Tomioka, Y. Nakanishi and K. Yamada, *Tetrahedron*., 2018, **74**, 5309.
10. G. D. Abigail, R. Tomislav, E. S. Erin and B. E. Alyssa, *ACS Catal*., 2018, **8**, 11134.
11. S. E. Denmark and D. J. P. Kornfilt, *J. Org. Chem.,* 2017, **82**, 3192.

Copies of HPLC :



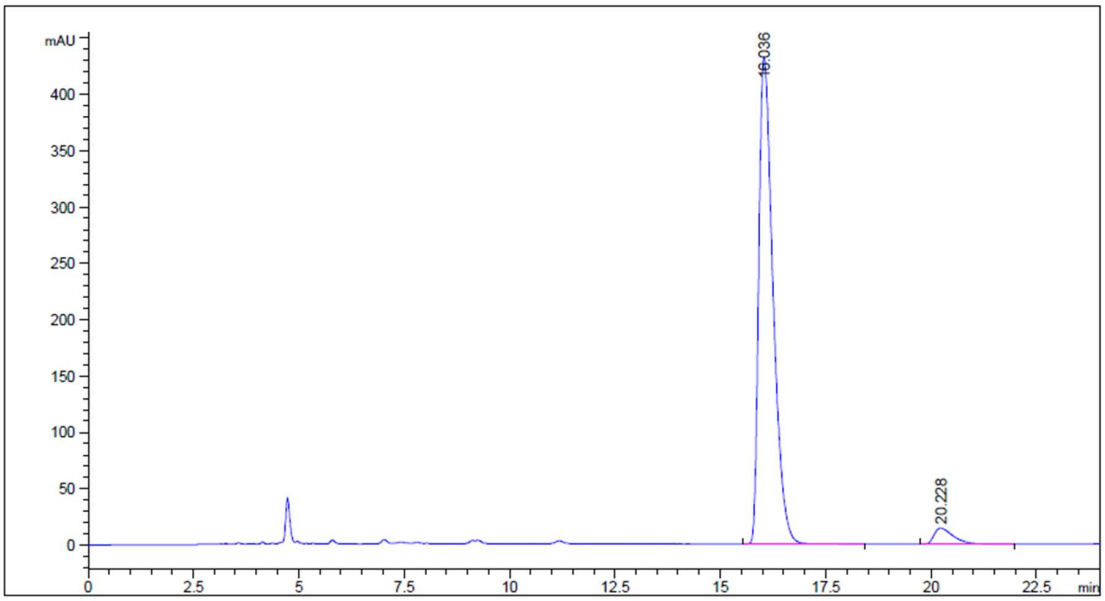


Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.971	BB	0.3740	2.77293e4	1115.50098	49.9959
2	18.863	BB	0.5885	2.77338e4	665.02350	50.0041

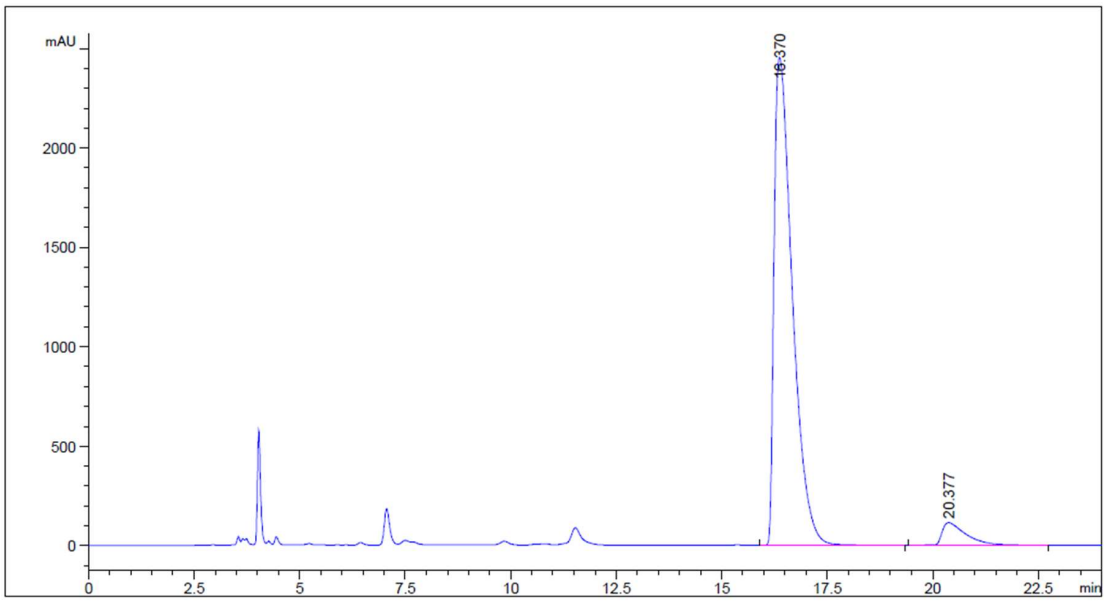


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.036	BB	0.3597	1.01376e4	432.13904	95.8079
2	20.228	BB	0.4735	443.57434	14.16008	4.1921

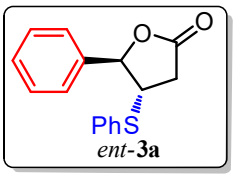
1 gram-scale 6-endo lactoniaton of **3a**

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



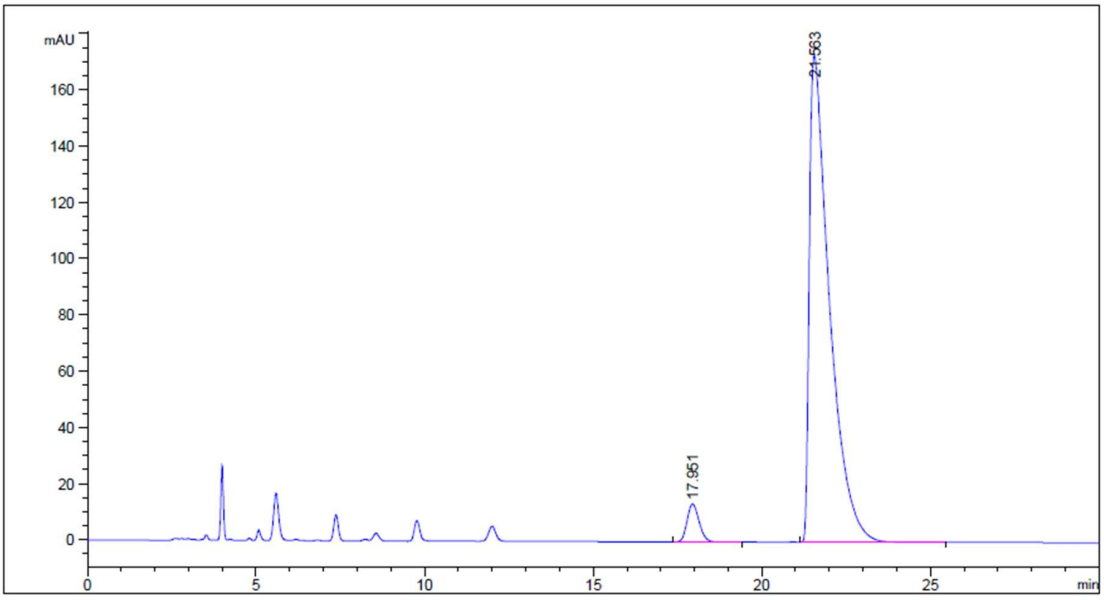
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.370	BB	0.4582	7.36245e4	2452.57861	94.4120
2	20.377	BB	0.5689	4357.65527	112.74175	5.5880



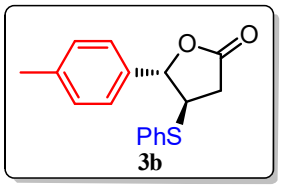
ent-**3a**

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



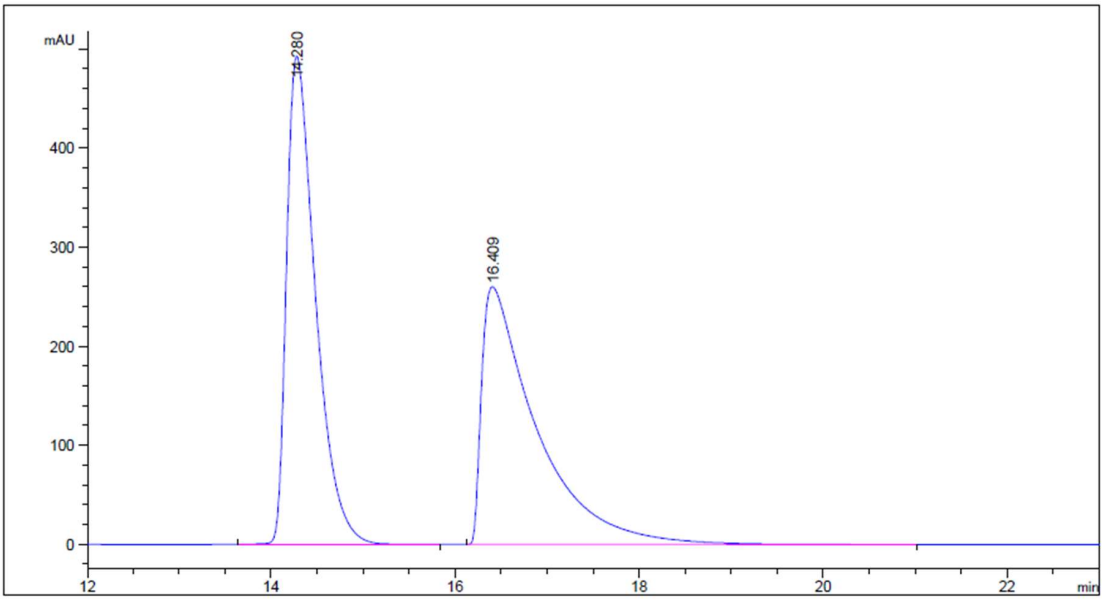
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.951	BB	0.3821	332.87674	13.57563	4.4315
2	21.563	BB	0.6023	7178.75195	172.93964	95.5685



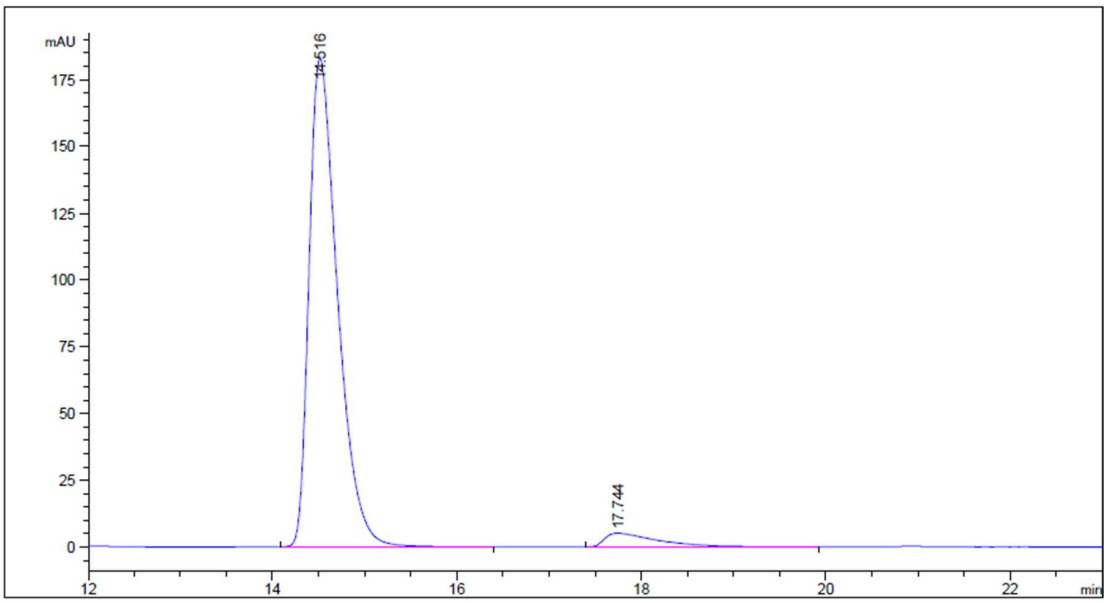
3b

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



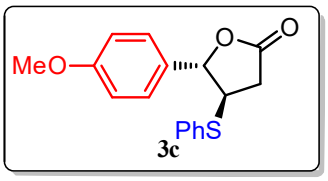
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.280	BB	0.3307	1.07522e4	492.56180	49.9477
2	16.409	BB	0.5817	1.07747e4	259.88947	50.0523



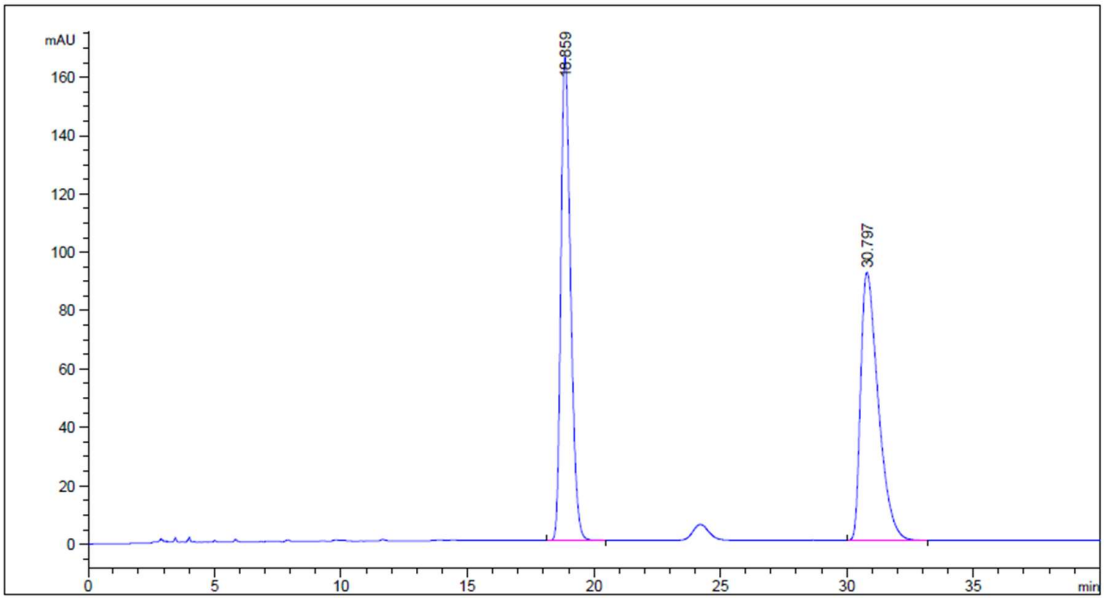
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.516	BB	0.3289	3933.89844	182.92715	95.3111
2	17.744	BB	0.5235	193.53072	5.00104	4.6889



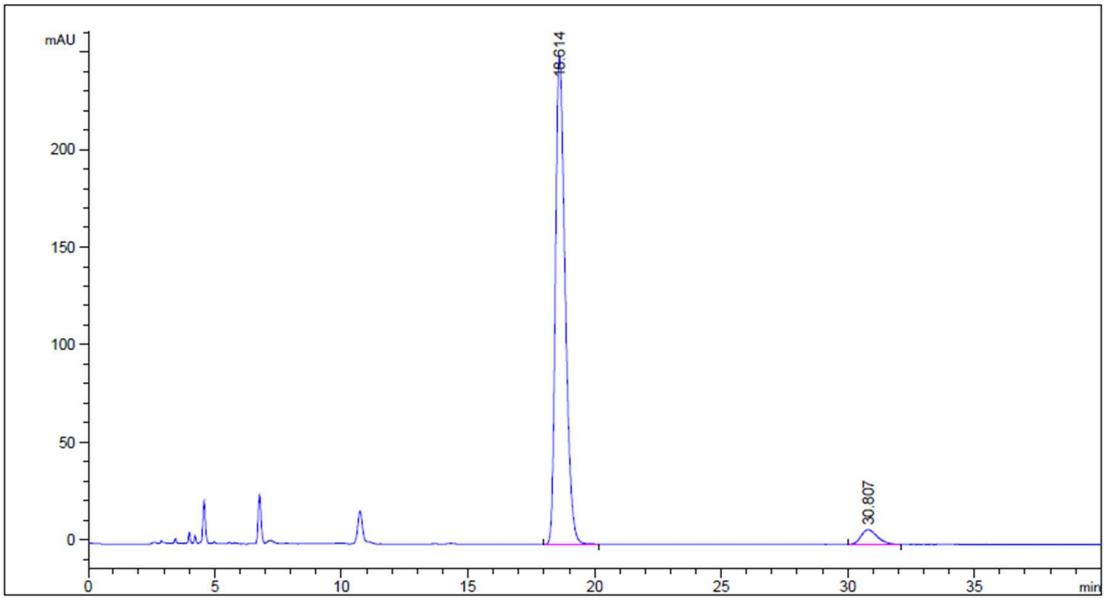
3c

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



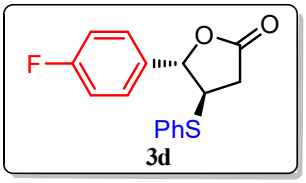
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.859	BB	0.4128	4447.25830	165.88283	50.0988
2	30.797	BB	0.7230	4429.71826	91.78625	49.9012



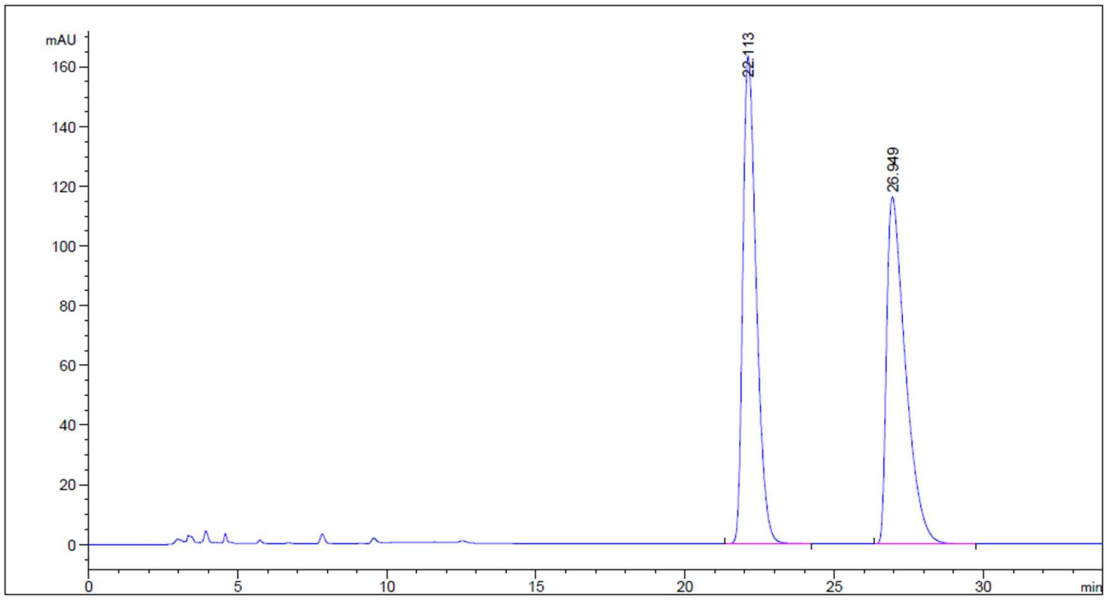
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.614	BB	0.4104	6655.21191	250.10754	95.3000
2	30.807	BB	0.5808	328.22467	7.43790	4.7000



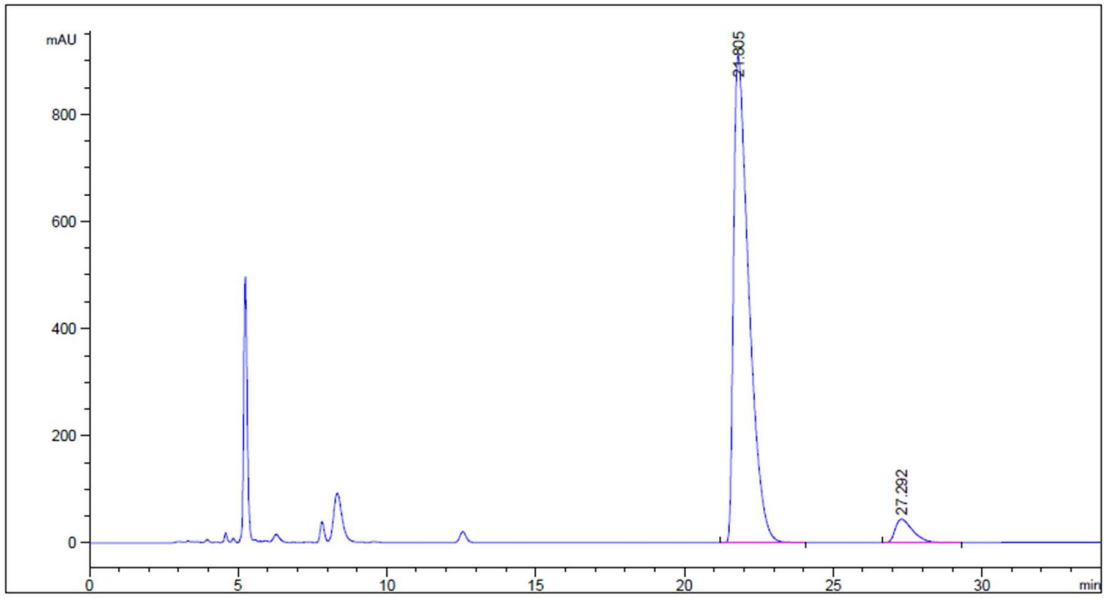
3d

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



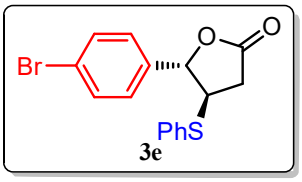
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.113	BB	0.4784	5106.16113	163.47510	50.0370
2	26.949	BB	0.6557	5098.60107	116.23823	49.9630



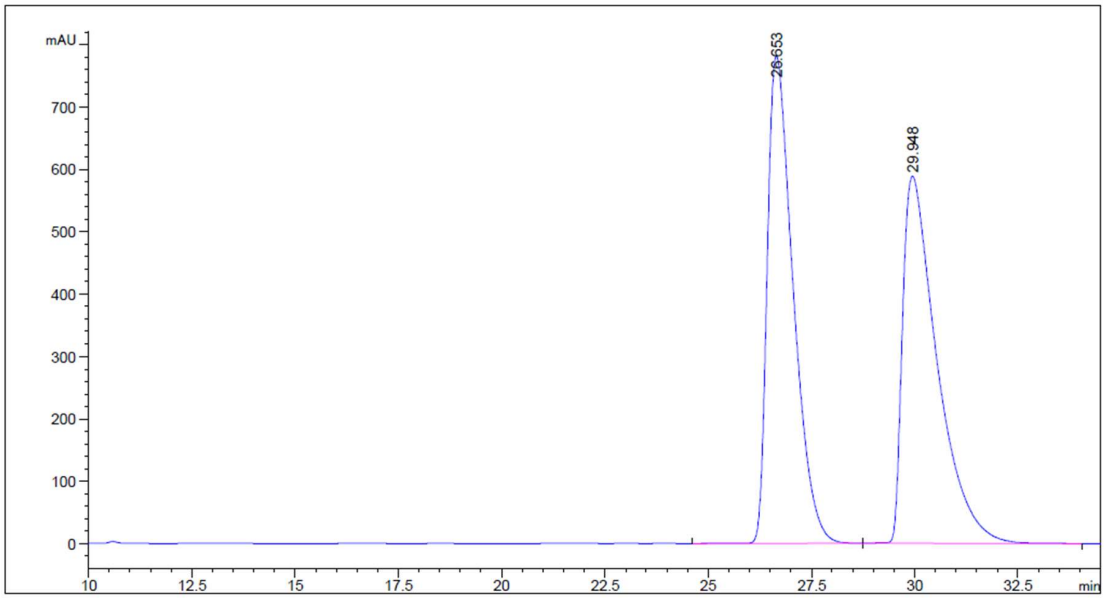
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.805	BB	0.5333	3.24043e4	910.21326	94.7526
2	27.292	BB	0.6185	1794.56860	43.75899	5.2474



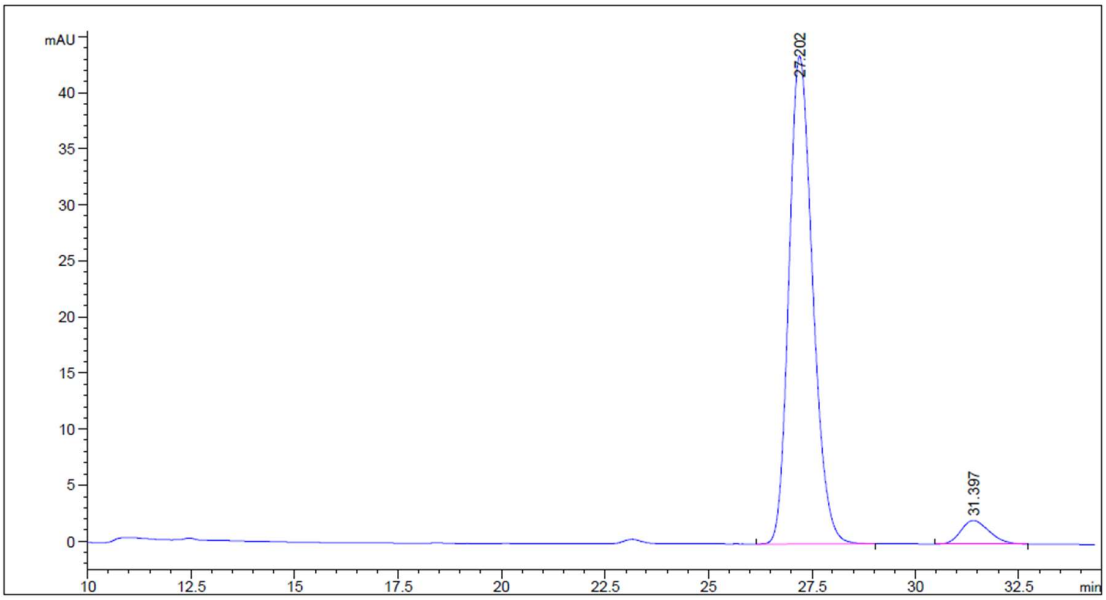
3e

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



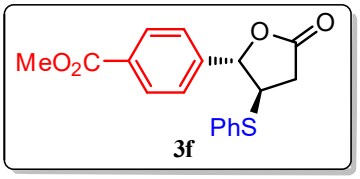
Signal 1: VWD1 B, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.653	VB R	0.6582	3.39251e4	781.93158	49.8886
2	29.948	BB	0.8631	3.40766e4	588.91351	50.1114



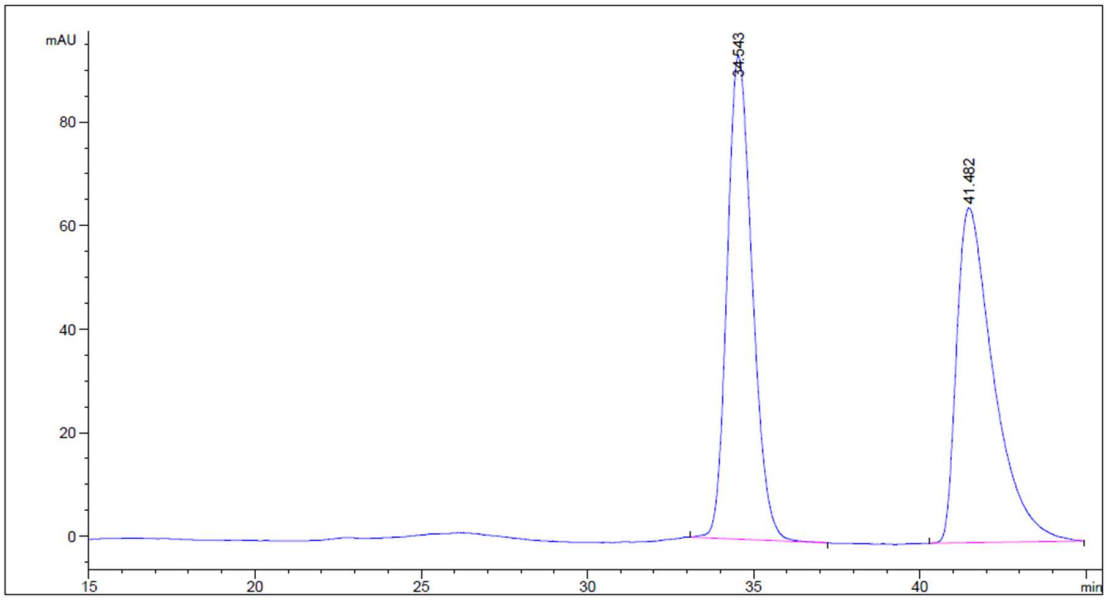
Signal 1: VWD1 B, Wavelength=230 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.202	BB	0.6172	1734.94409	43.51159	94.5100
2	31.397	BB	0.7287	100.78227	2.11197	5.4900



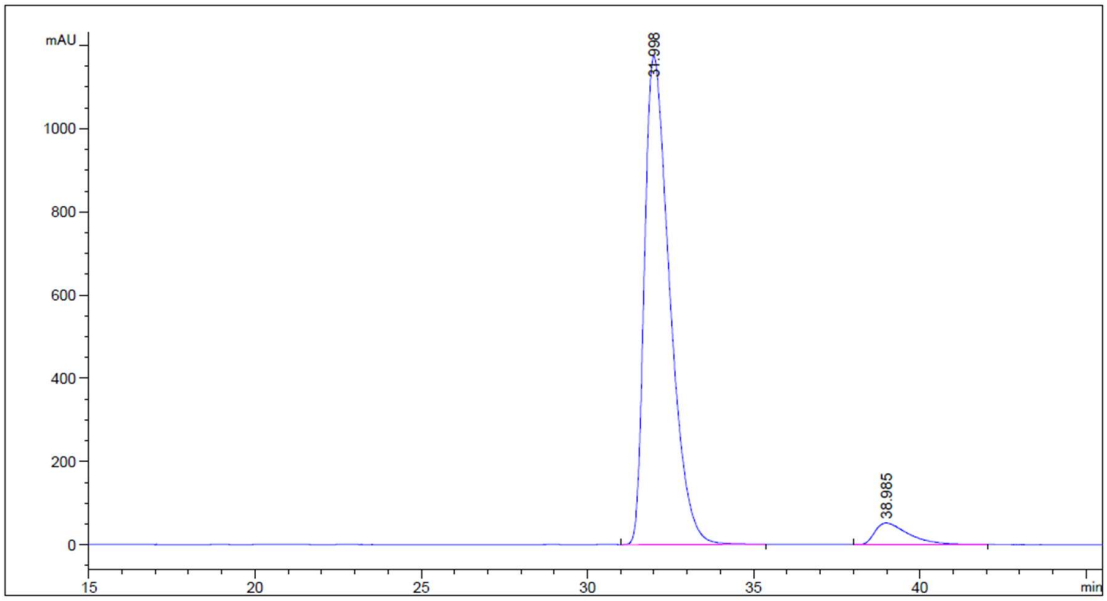
3f

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 88:12, 1 mL/min.



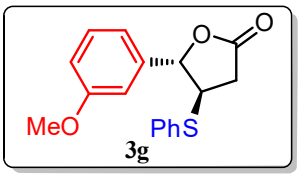
Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.543	BB	0.8110	4906.02002	93.36728	49.4981
2	41.482	BBA	1.1028	5005.51709	64.68230	50.5019



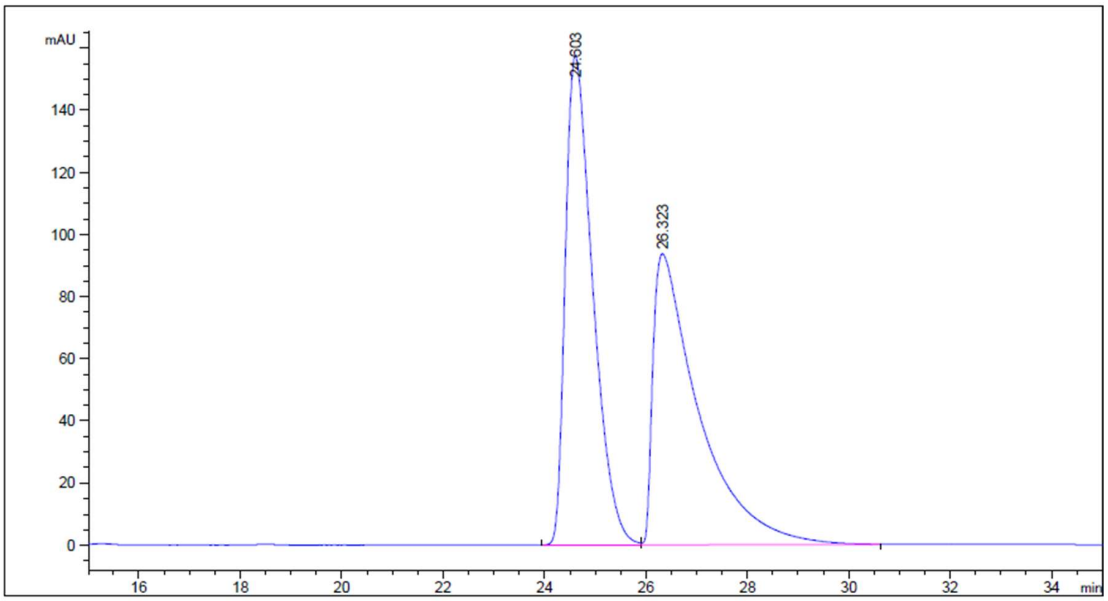
Signal 1: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.998	BB	0.8011	6.16932e4	1173.95630	94.5029
2	38.985	BB	1.0014	3588.60474	51.47446	5.4971



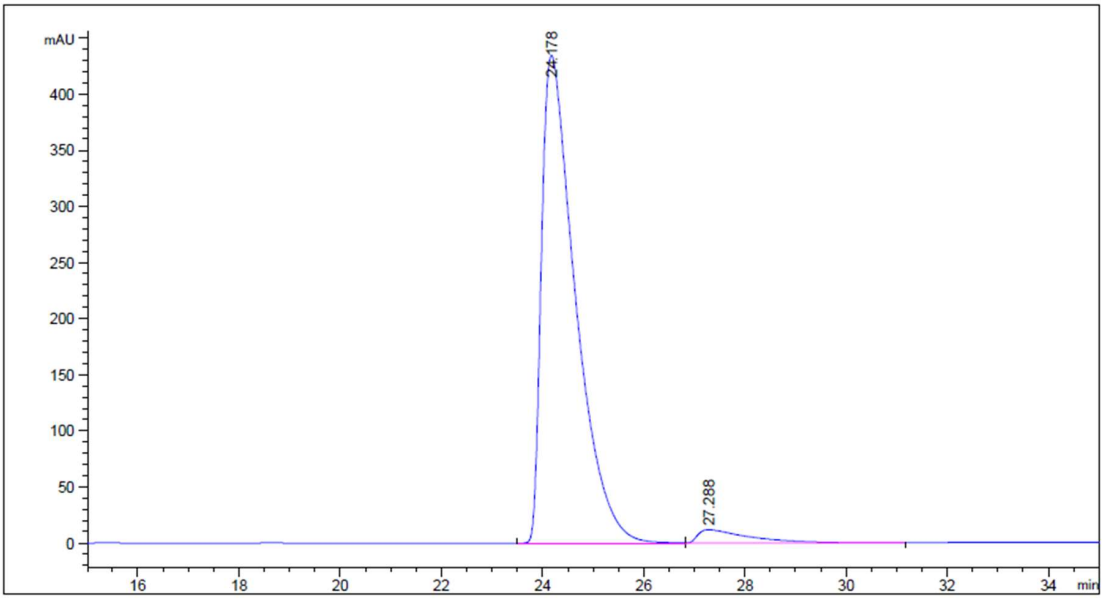
3g

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 88:12, 1 mL/min.



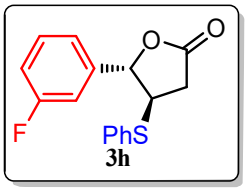
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.603	BV	0.5760	5906.83496	157.32224	50.1124
2	26.323	VB	0.8747	5880.33008	93.63766	49.8876



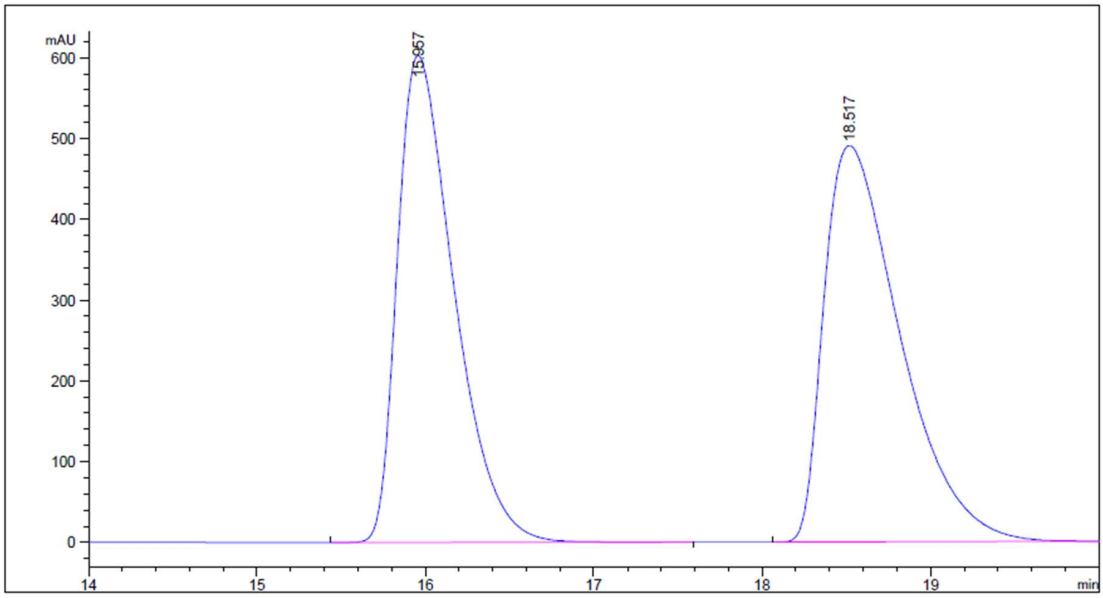
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.178	BV	0.6978	2.01802e4	434.50961	96.0997
2	27.288	VB	0.9837	819.02258	11.71386	3.9003



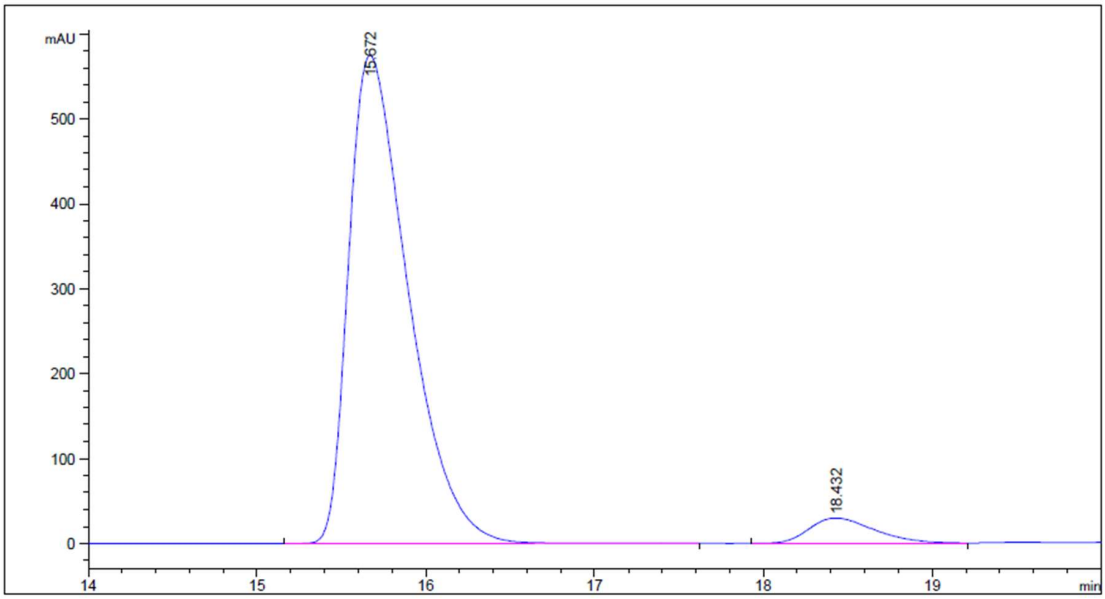
3h

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



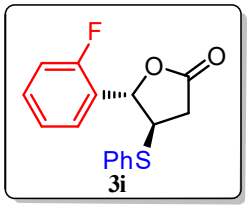
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.957	BB	0.3590	1.40995e4	602.54376	47.7291
2	18.517	BB	0.4852	1.54412e4	490.65820	52.2709



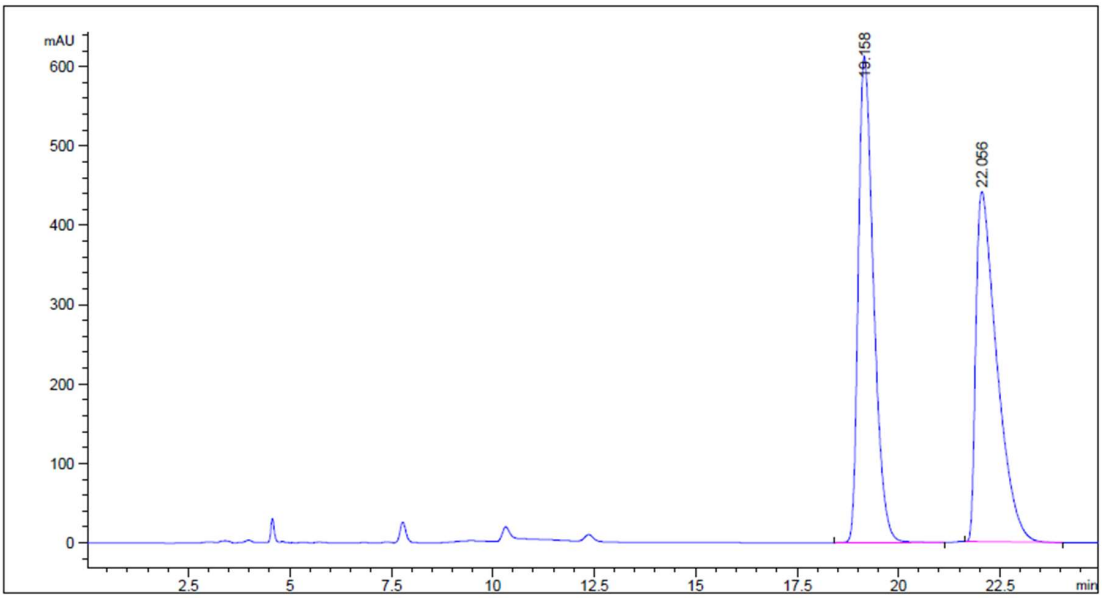
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.672	BB	0.3736	1.40755e4	574.90918	94.6450
2	18.432	BB	0.4128	796.39716	29.70049	5.3550



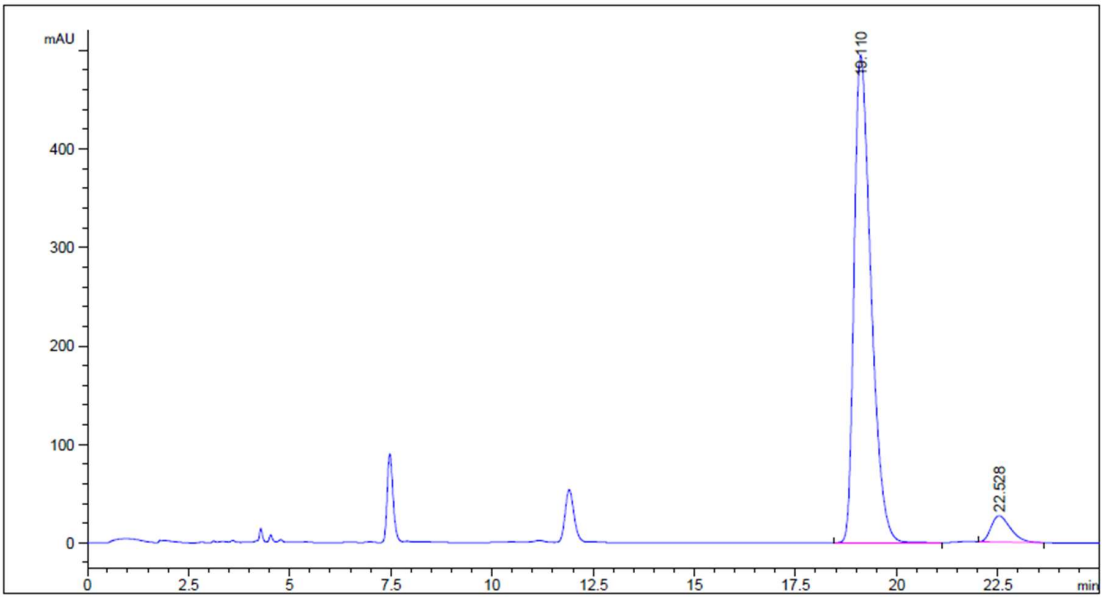
3i

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



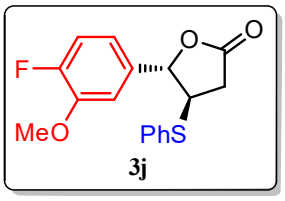
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.158	BB	0.3997	1.59506e4	612.67273	50.2153
2	22.056	BBA	0.5322	1.58138e4	441.18546	49.7847



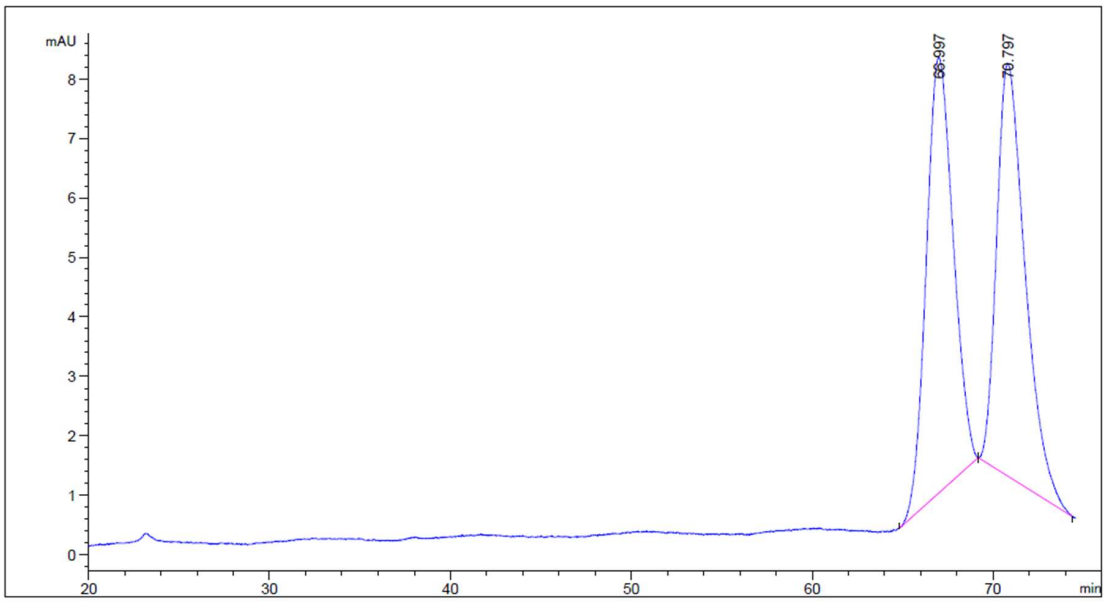
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.110	BB	0.4450	1.43845e4	495.04242	94.2553
2	22.528	BB	0.5085	876.71429	26.59950	5.7447



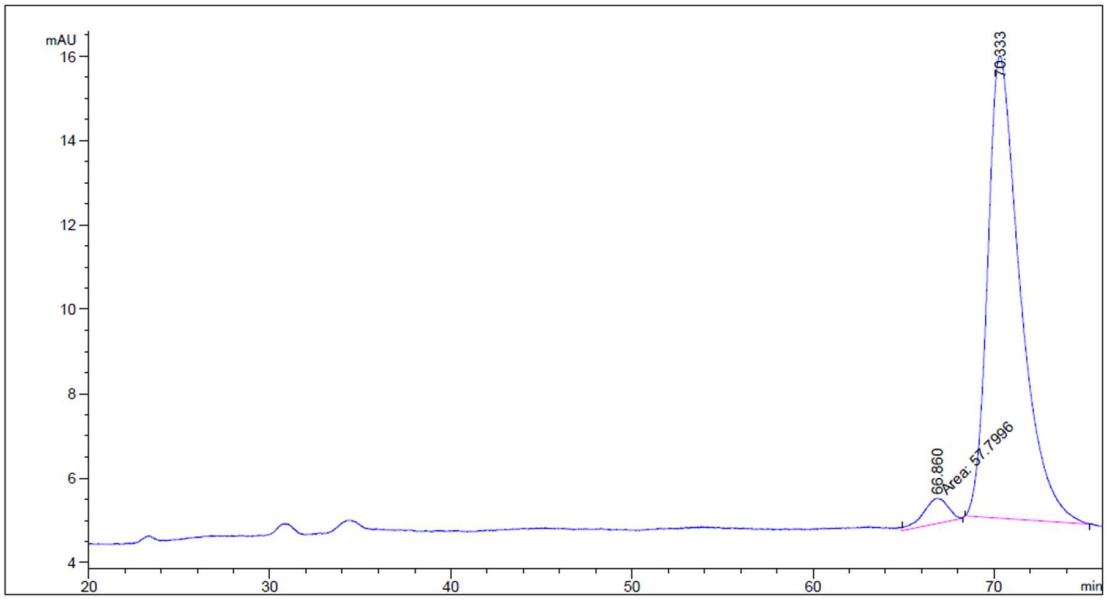
3j

Separation of enantiomers by HPLC, Chiralcel® Column OJ-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



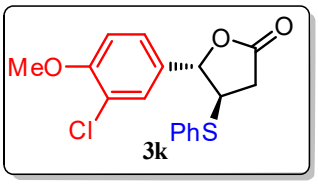
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	66.997	BB	1.2220	758.53436	7.32588	49.9175
2	70.797	BB	1.2858	761.04199	6.93786	50.0825



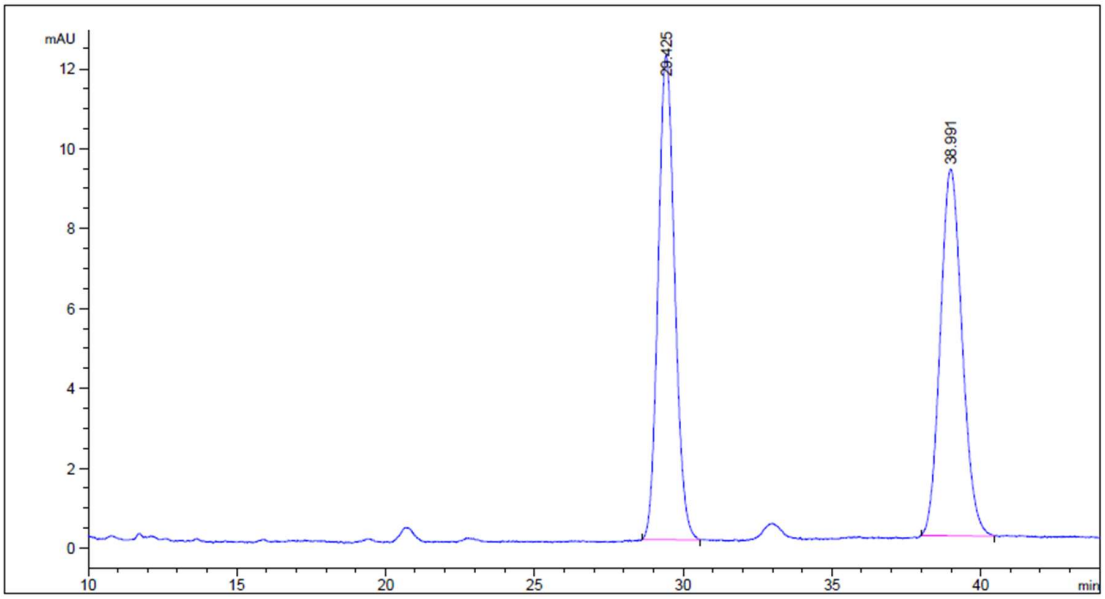
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	66.860	MM	1.4970	52.20176	5.81198e-1	3.6597
2	70.333	BB	1.5235	1374.19189	10.95499	96.3403



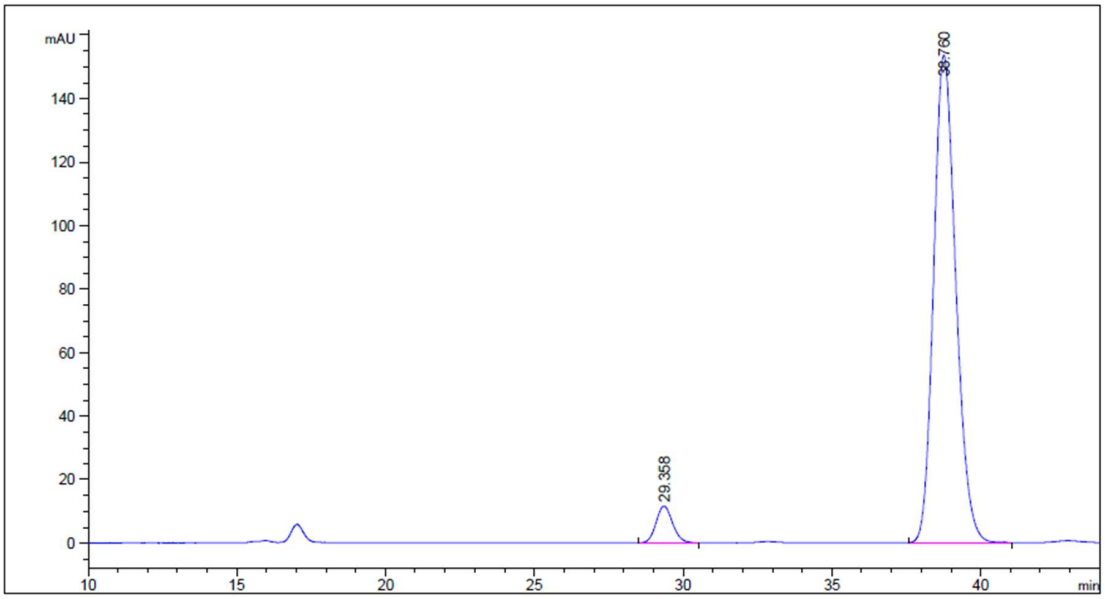
3k

Separation of enantiomers by HPLC, Chiralcel® Column IC, 30 °C, n-hexane: *i*-PrOH = 88:12, 1 mL/min.



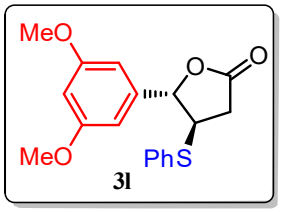
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.425	BB	0.5835	469.42480	12.13025	50.0686
2	38.991	BB	0.6672	468.13934	9.17569	49.9314



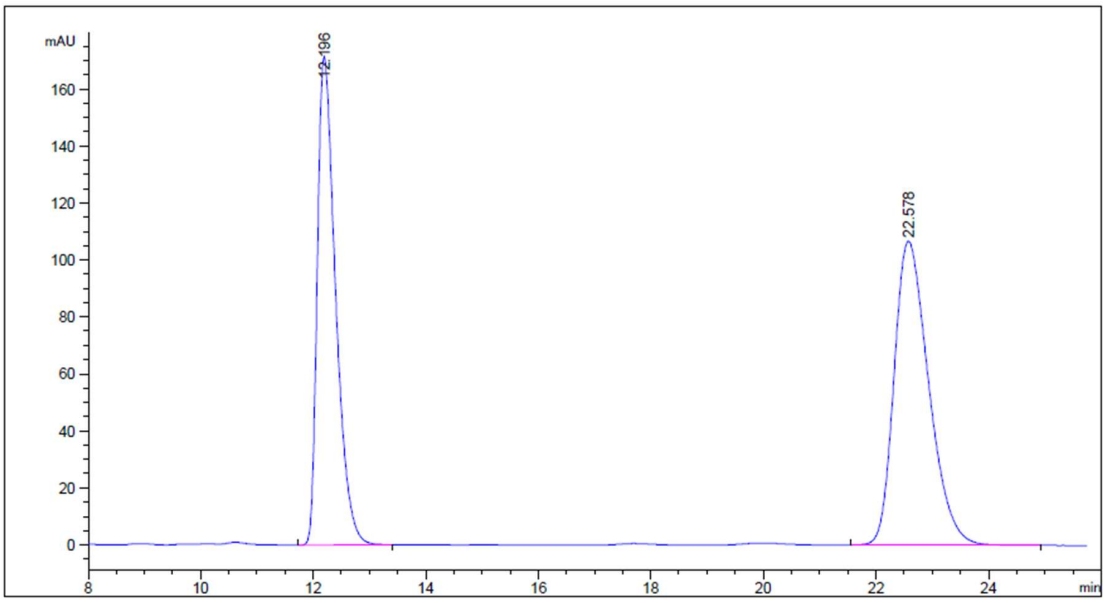
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.358	BB	0.5679	445.59506	11.55458	5.3099
2	38.760	BB	0.8002	7946.19775	153.44635	94.6901



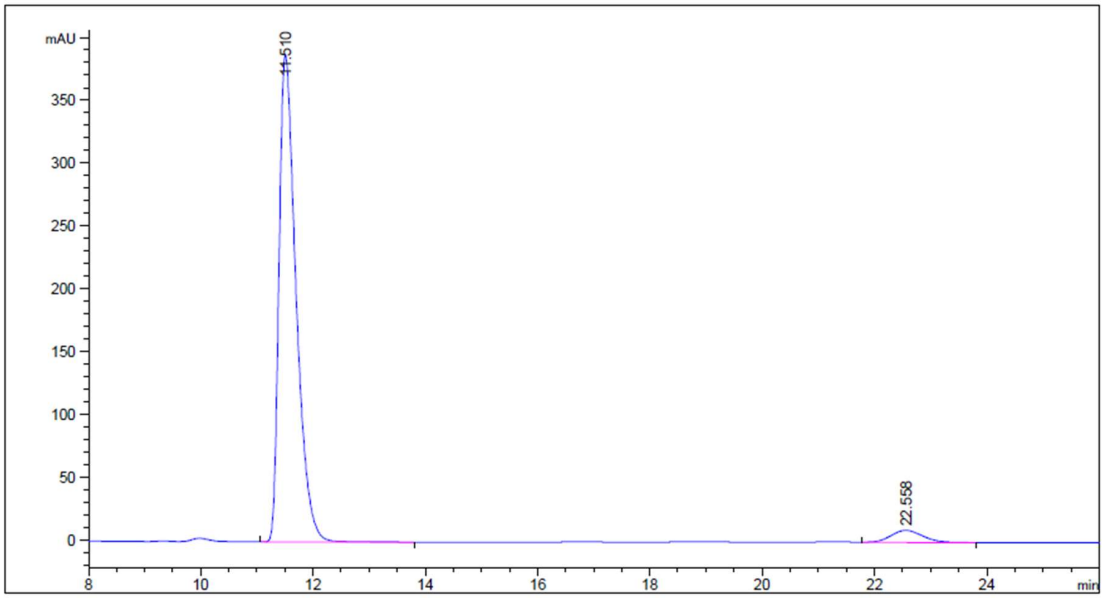
3l

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 70:30, 1 mL/min.



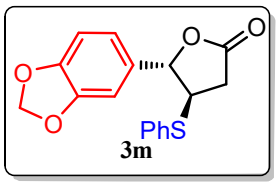
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.196	BB	0.3445	3855.86377	171.35959	45.8891
2	22.578	BB	0.6551	4546.70801	106.69806	54.1109



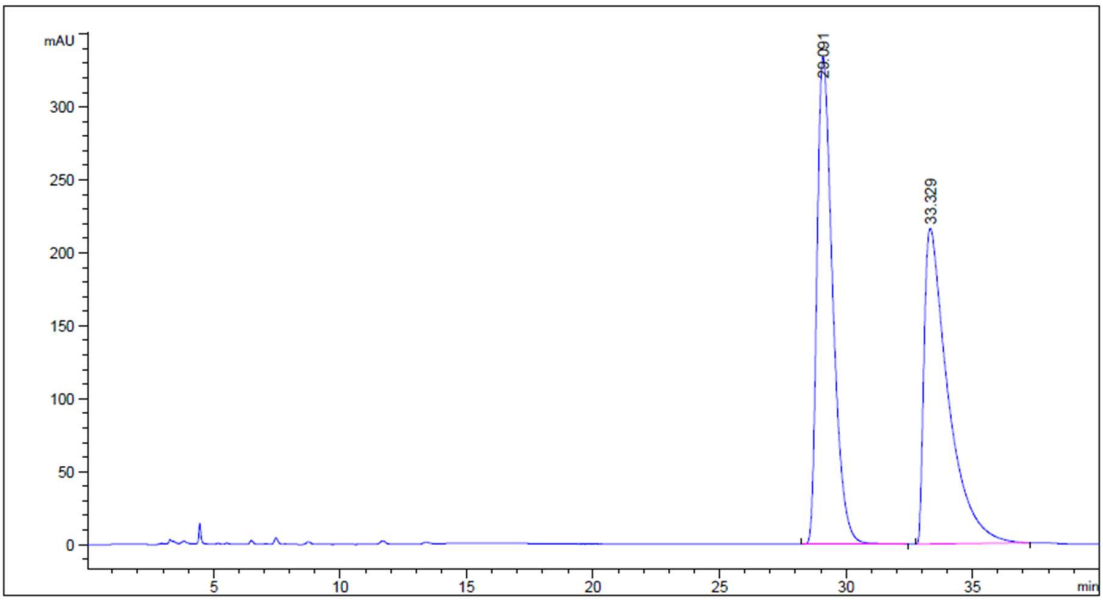
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.510	BB	0.3196	8158.76367	387.51880	95.6536
2	22.558	BB	0.6049	370.72568	9.54942	4.3464



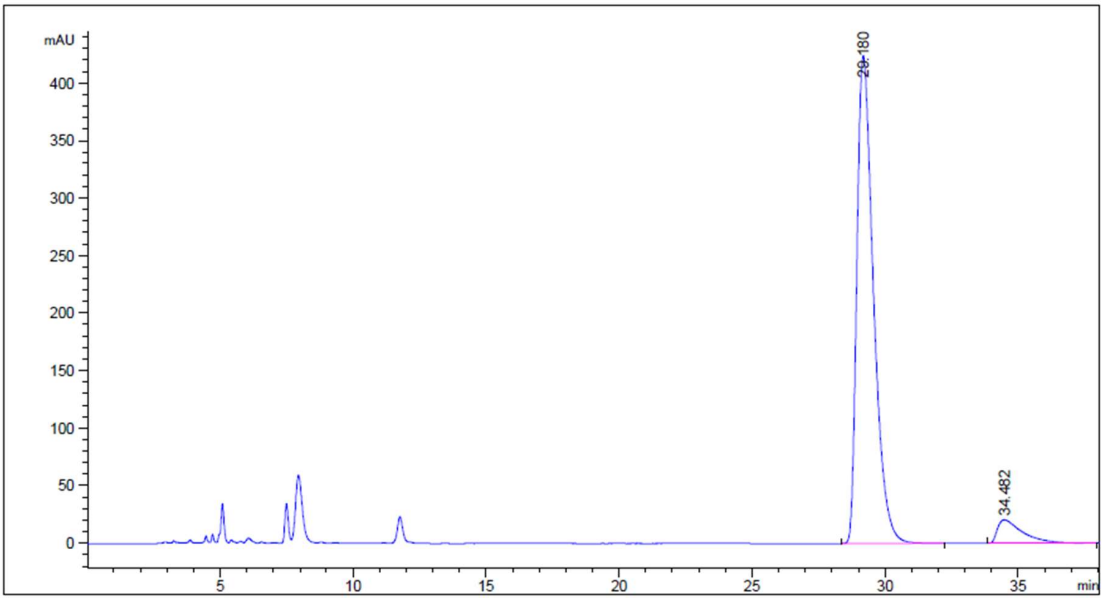
3m

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



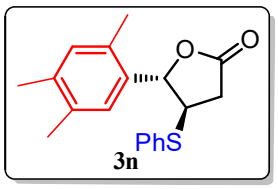
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.091	BB	0.6611	1.44138e4	334.25522	50.3234
2	33.329	BB	0.9558	1.42285e4	216.20981	49.6766



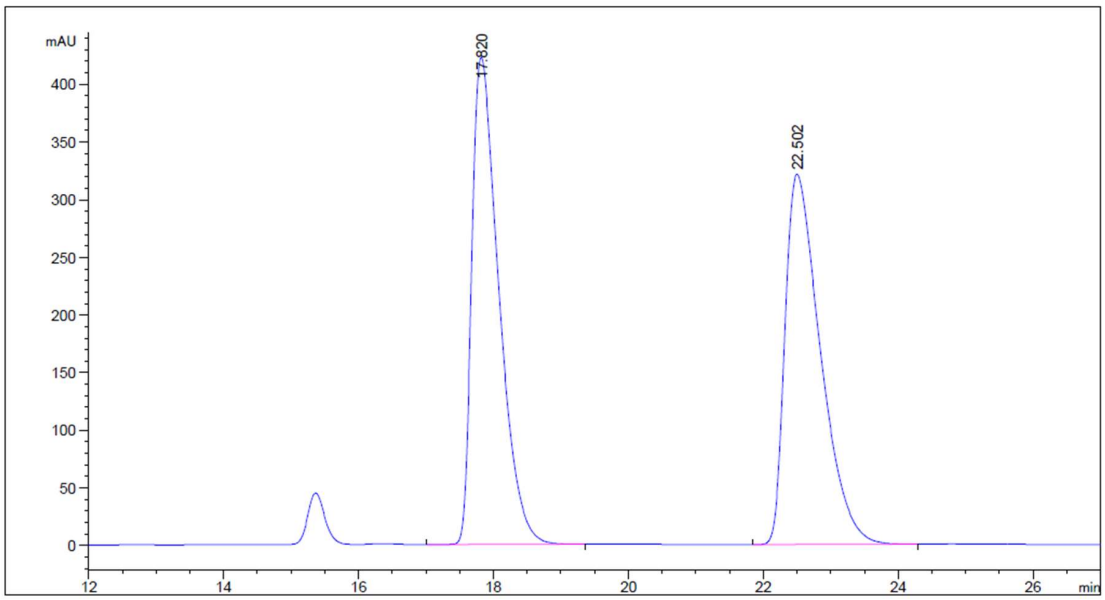
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.180	BB	0.6628	1.83387e4	423.87427	93.2330
2	34.482	BB	0.9296	1331.05591	20.28225	6.7670



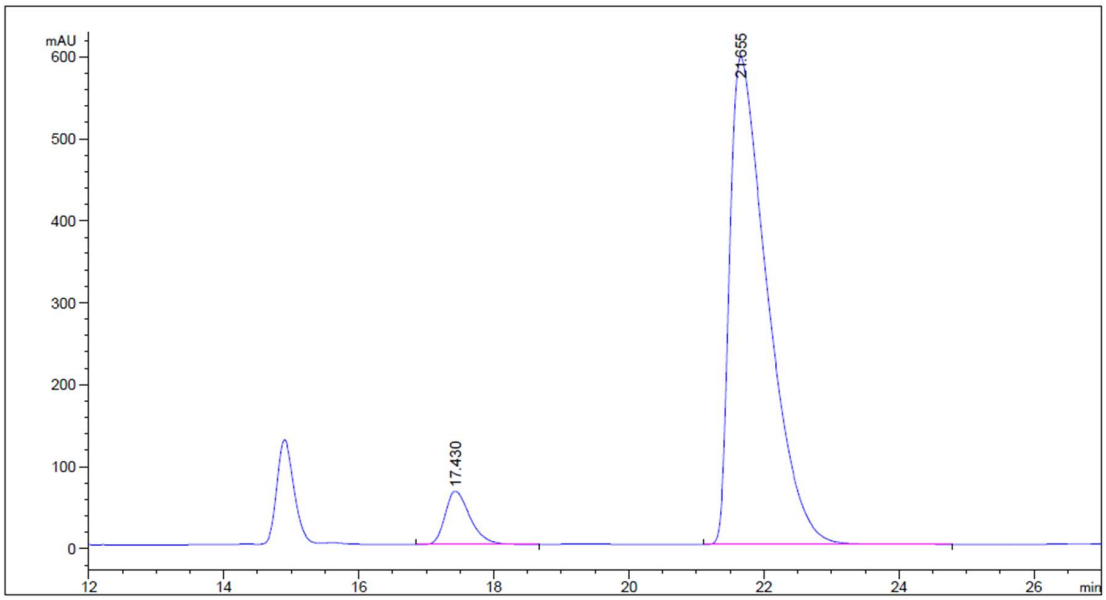
3n

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 93:7, 1 mL/min.



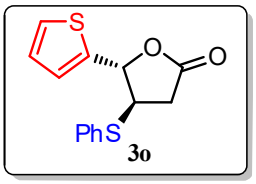
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.820	BB	0.4222	1.17413e4	422.51422	50.1121
2	22.502	BB	0.5566	1.16888e4	321.16843	49.8879



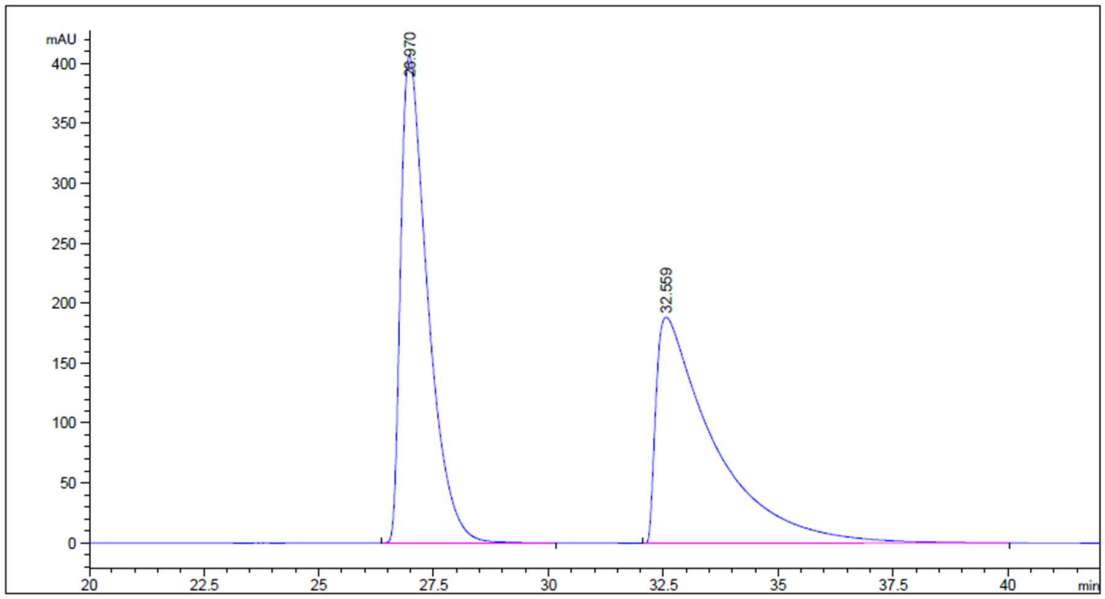
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.430	BB	0.3931	1669.38037	65.11443	6.7542
2	21.655	BB	0.5819	2.30470e4	595.02740	93.2458



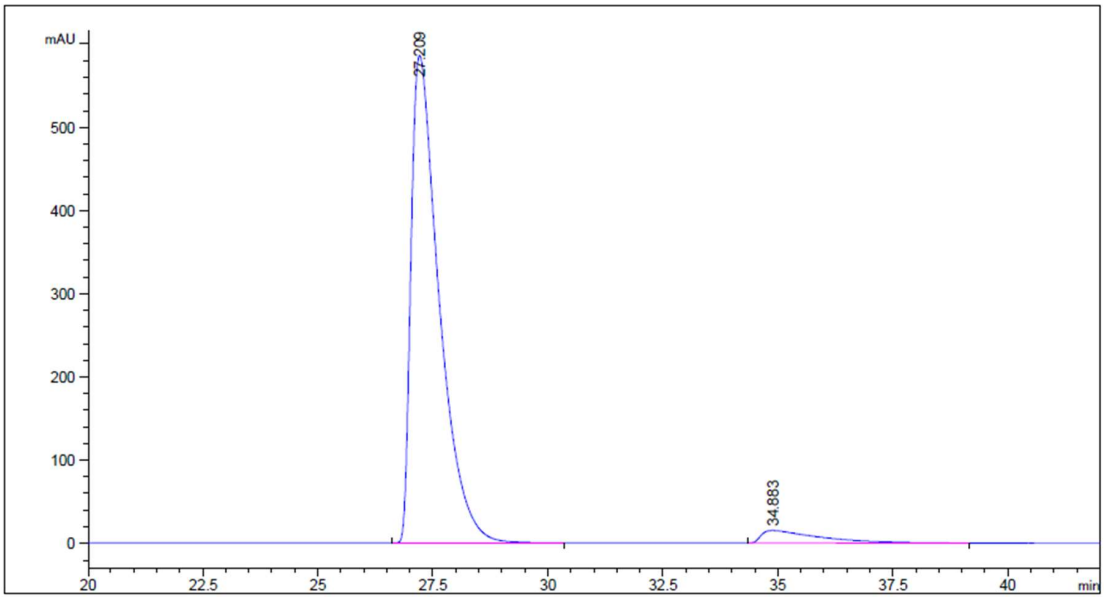
3o

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 93:7, 1 mL/min.



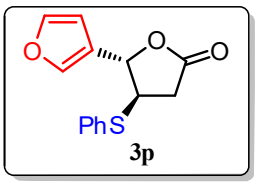
Signal 1: DAD1 D, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.970	BB	0.6144	1.66014e4	406.52188	50.0735
2	32.559	BB	1.2008	1.65526e4	188.44669	49.9265



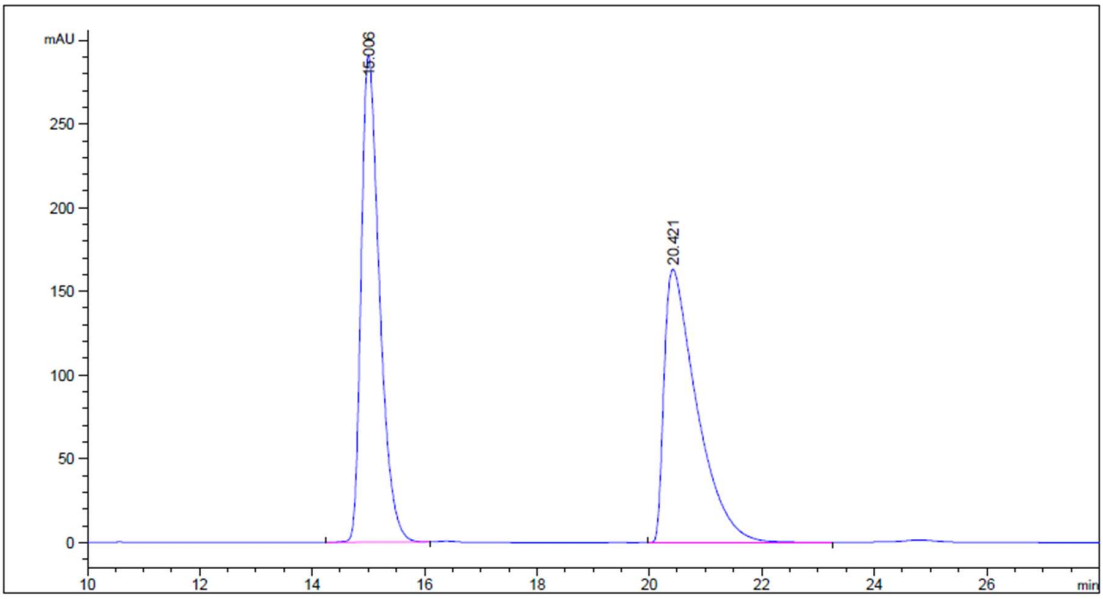
Signal 1: DAD1 D, Sig=230,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.209	BB	0.6343	2.49081e4	585.56464	95.0757
2	34.883	BB	1.1412	1290.06580	14.91418	4.9243



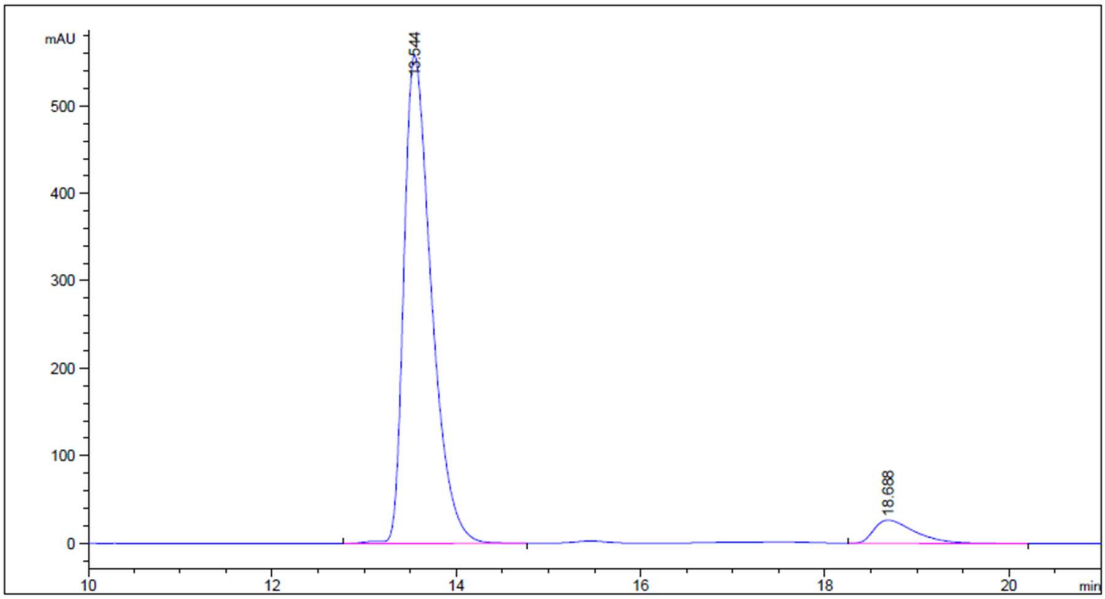
3p

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 85:15, 1 mL/min.



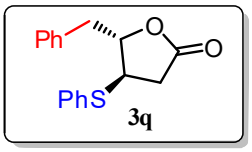
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.006	BB	0.3462	6587.55664	290.92068	49.9737
2	20.421	BB	0.5956	6594.47852	163.13556	50.0263



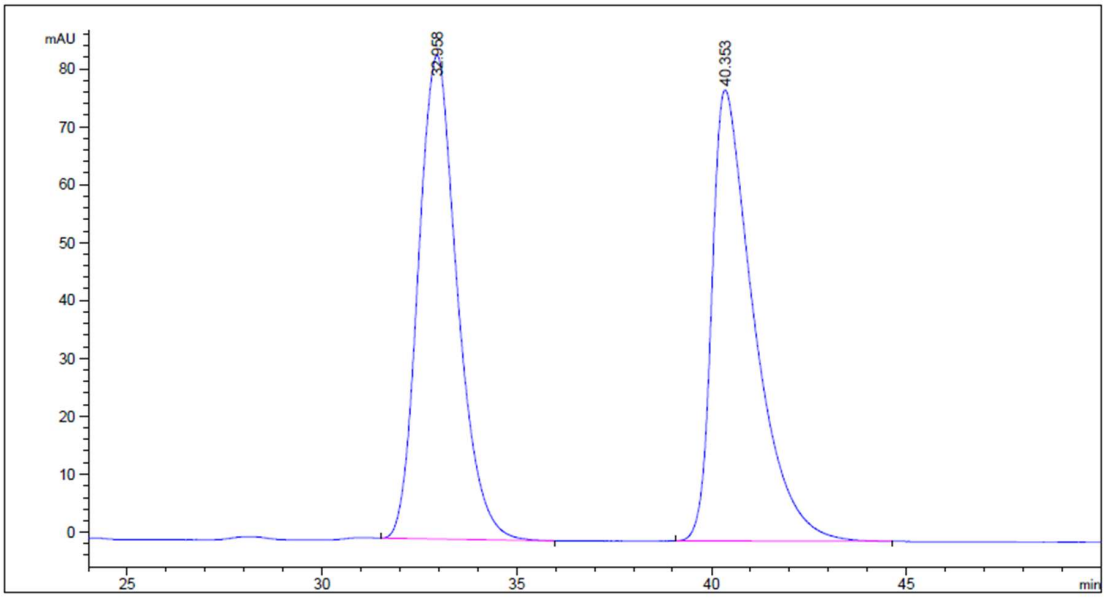
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.544	VB R	0.3174	1.15855e4	558.35229	93.4226
2	18.688	BB	0.4541	815.68005	26.57772	6.5774



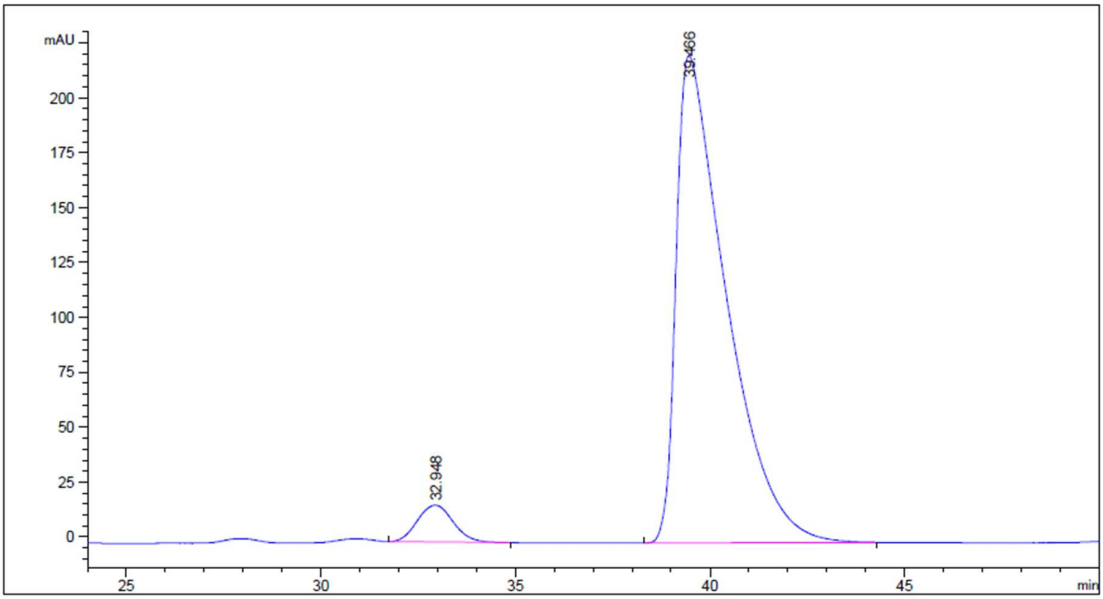
3q

Separation of enantiomers by HPLC, Chiralcel® Column OJ-H, 30 °C, n-hexane: *i*-PrOH = 88:12, 1 mL/min.



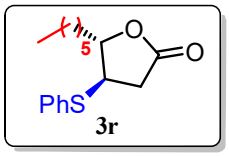
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.958	BB	1.0461	5801.50586	83.54620	49.8464
2	40.353	BB	1.0742	5837.24854	77.90540	50.1536



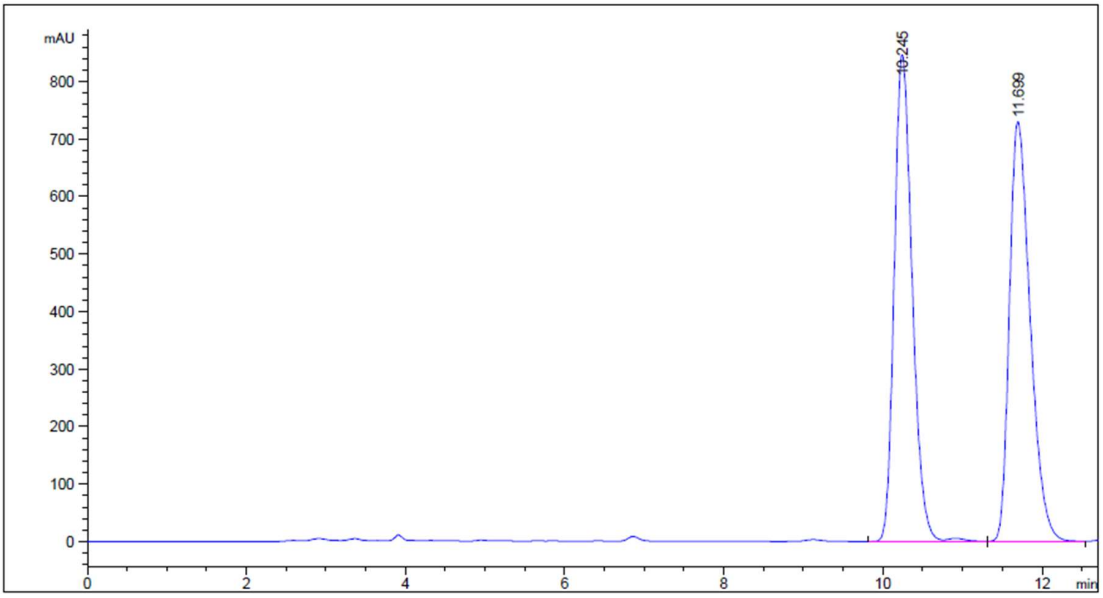
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.948	BB	0.9516	1080.20691	16.81145	5.1548
2	39.466	BB	1.2718	1.98753e4	221.72658	94.8452



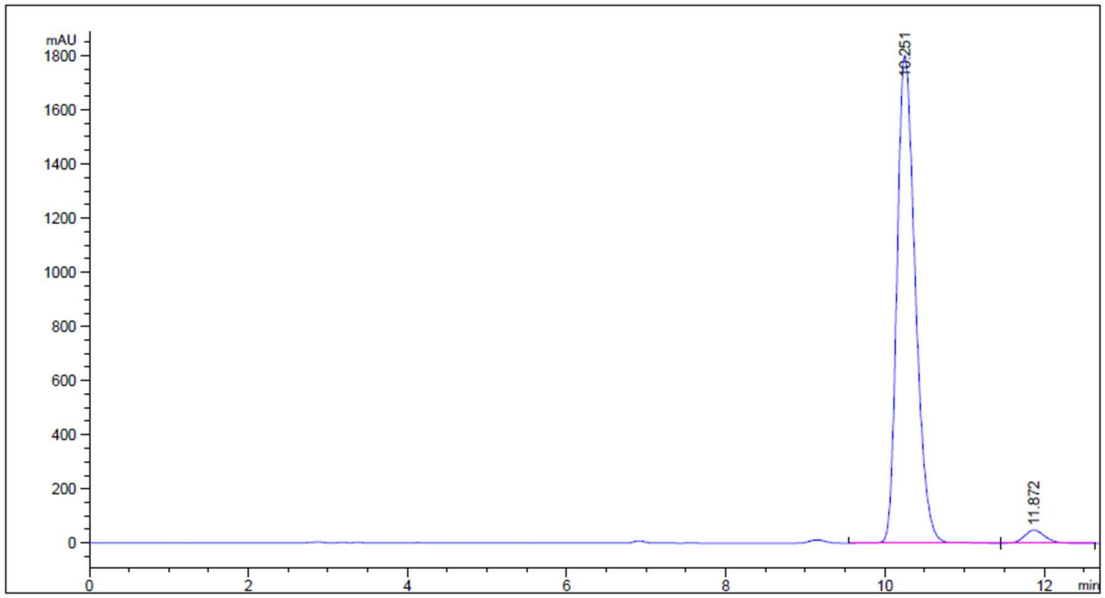
3r

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 88:12, 1 mL/min.



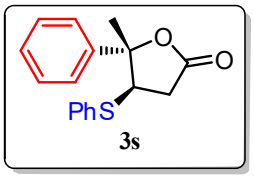
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.245	BV R	0.2419	1.32836e4	846.80975	50.0915
2	11.699	BB	0.2796	1.32350e4	729.85736	49.9085



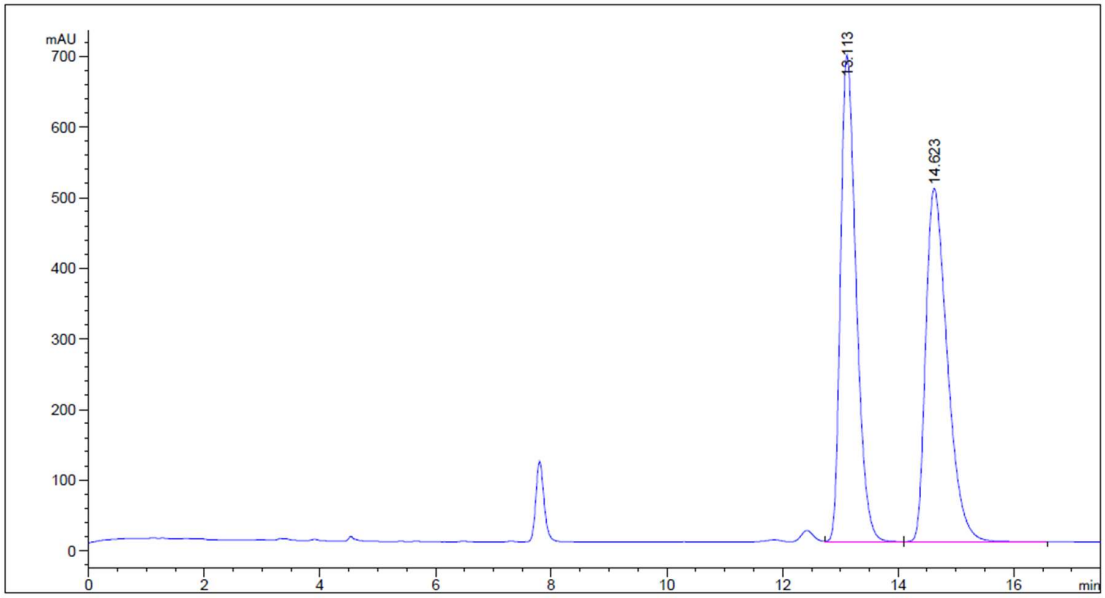
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.251	BV R	0.2478	2.87464e4	1801.26587	97.1136
2	11.872	VB	0.2757	854.40991	47.99118	2.8864



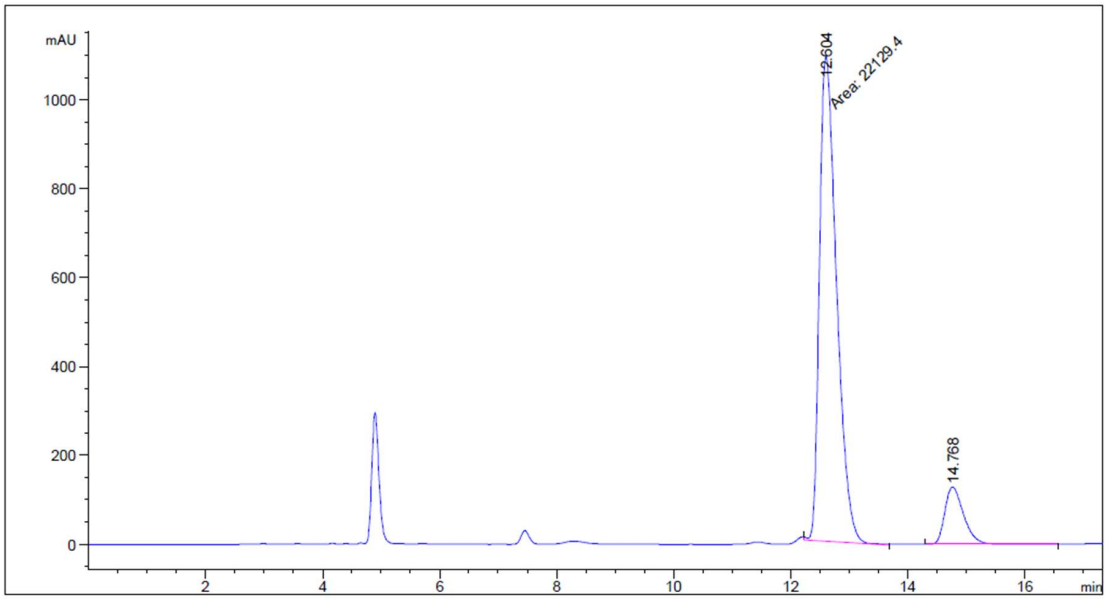
3s

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



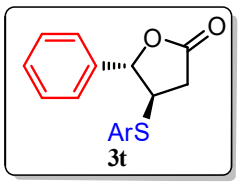
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.113	VB	0.2890	1.29319e4	688.93884	50.0455
2	14.623	BB	0.3992	1.29083e4	499.95743	49.9545



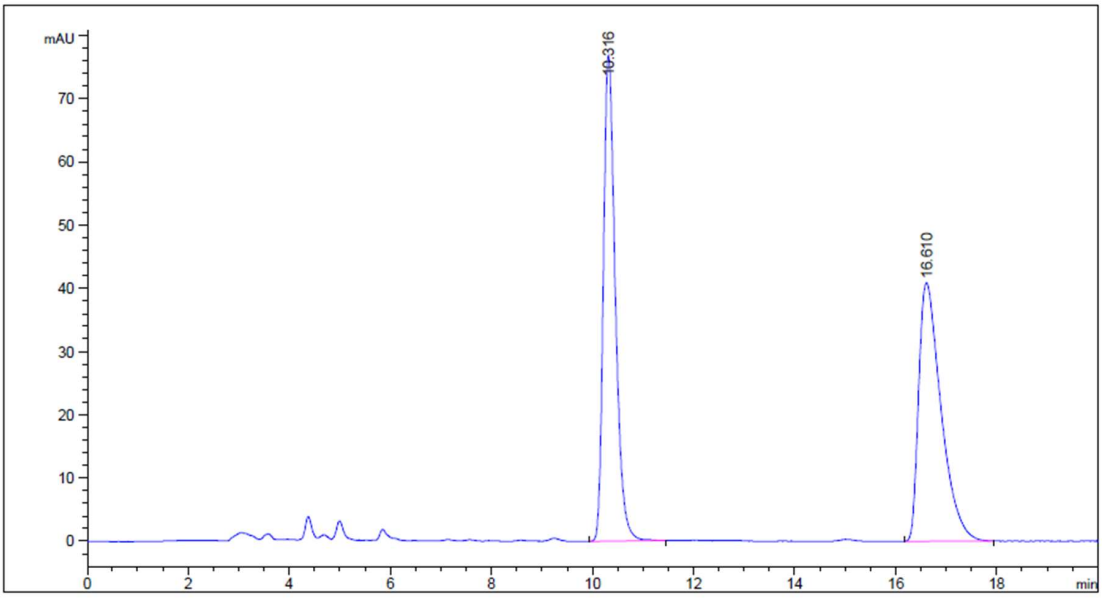
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.604	MM	0.3379	2.21294e4	1091.43079	88.6130
2	14.768	BB	0.3400	2843.69189	128.58479	11.3870



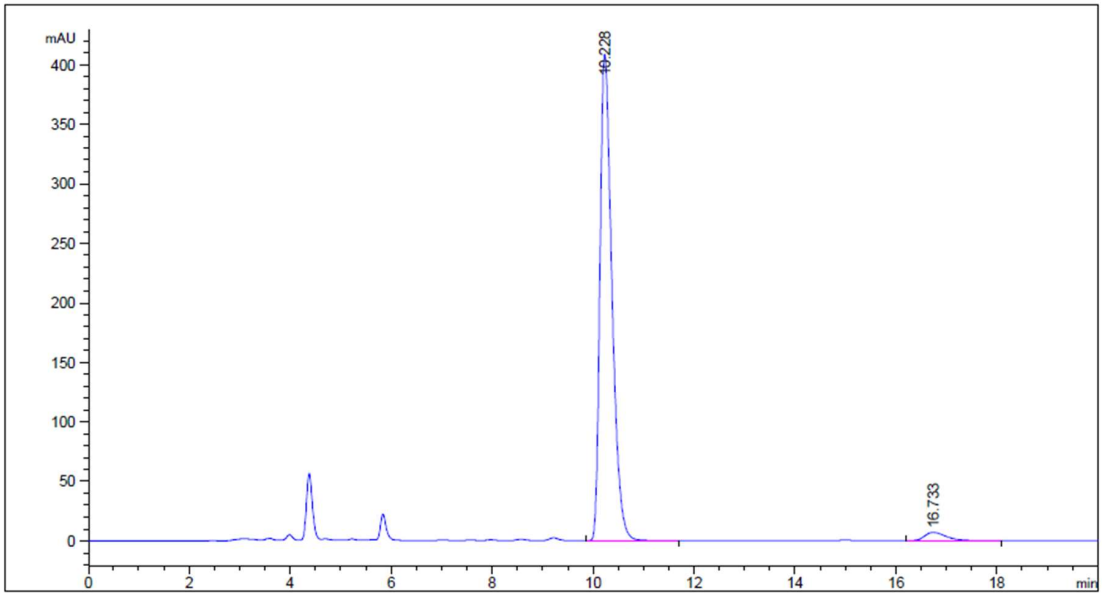
3t

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 ºC, n-hexane: *i*-PrOH = 85:15, 1 mL/min.



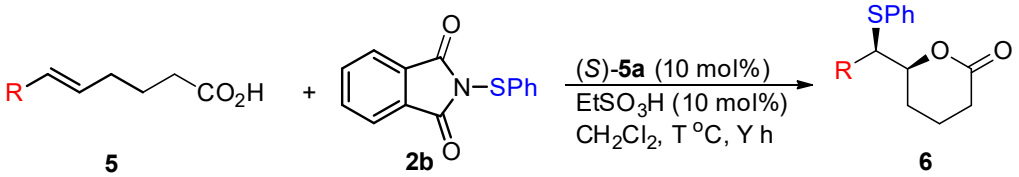
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.316	BB	0.2515	1263.07629	76.93445	50.1662
2	16.610	BB	0.4596	1254.70691	40.93485	49.8338

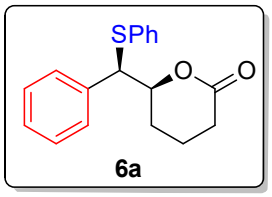


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.228	BB	0.2520	6725.42480	408.56396	97.0449
2	16.733	BB	0.4206	204.79640	6.97314	2.9551

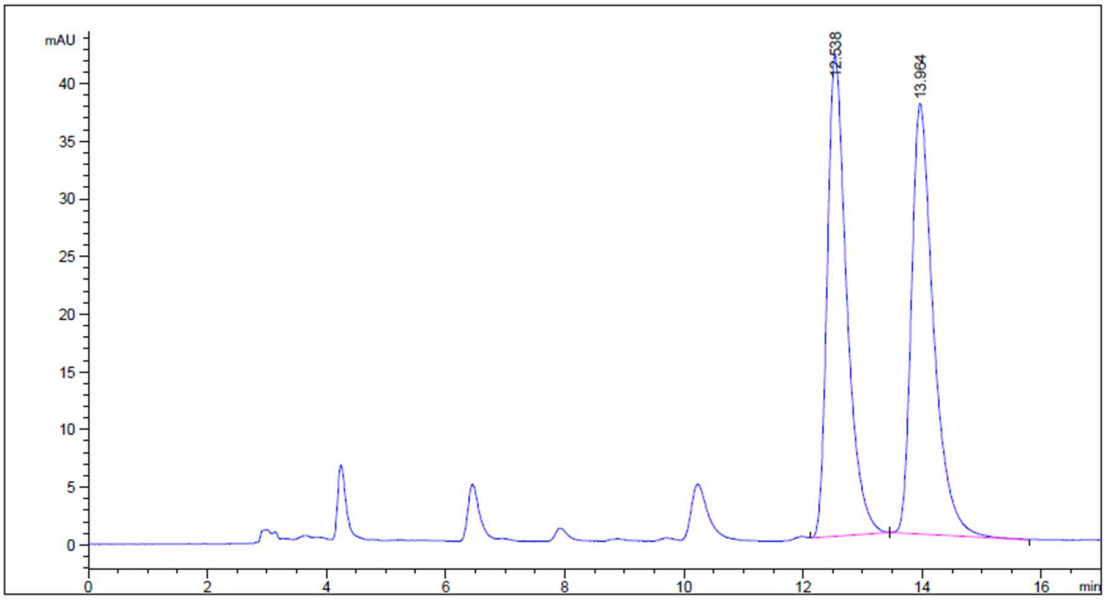


5 2b 6



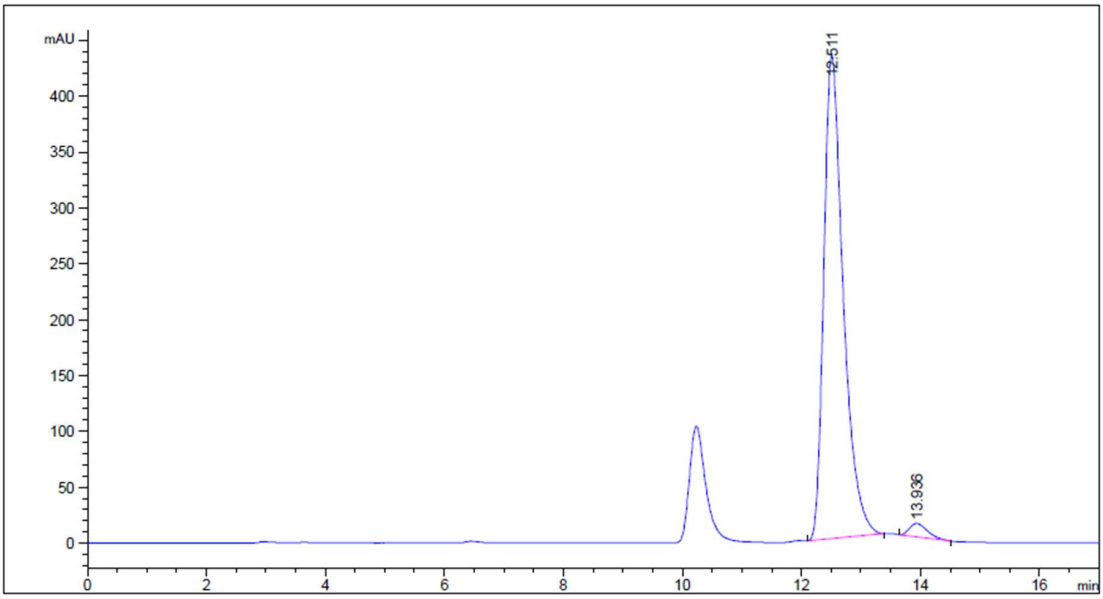
6a

Separation of enantiomers by HPLC, Chiralcel® Column AD-H, 30 °C, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



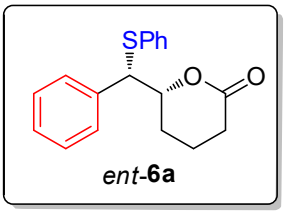
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.538	BB	0.3410	946.40668	41.67130	49.7658
2	13.964	BB	0.3827	955.31482	37.31761	50.2342



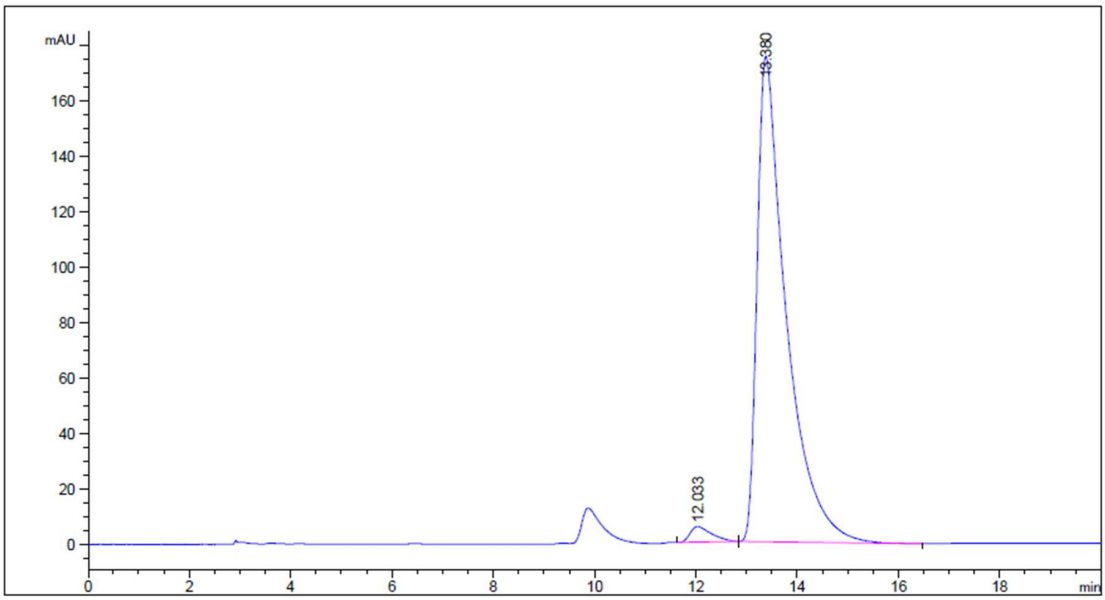
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.511	BB	0.3431	9833.28223	432.72348	97.5254
2	13.936	BB	0.3228	249.50914	11.89124	2.4746



ent-**6a**

Separation of enantiomers by HPLC, Chiralcel® Column AD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min.

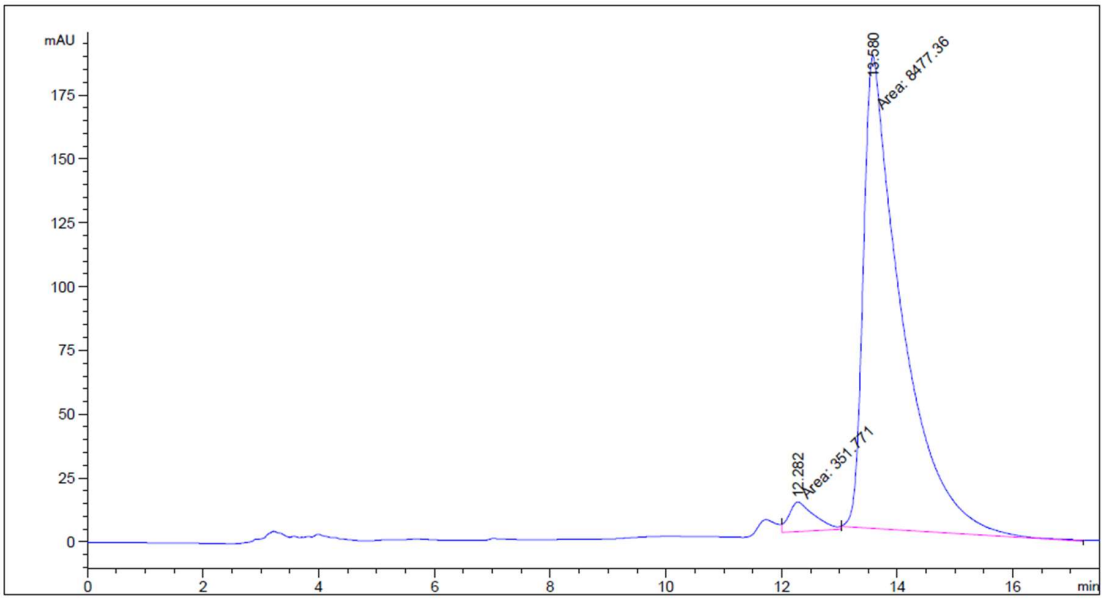


Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.033	BB	0.4106	165.28850	5.66151	2.3057
2	13.380	BB	0.5624	7003.54492	175.19321	97.6943

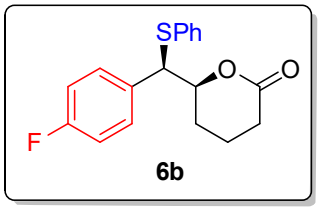
1 gram-scale 6-*exo* lactoniaton of *ent*-**6a**

Separation of enantiomers by HPLC, Chiralcel® Column AD-H, 30 ºC, n-hexane: *i*-PrOH = 90:10, 1 mL/min.



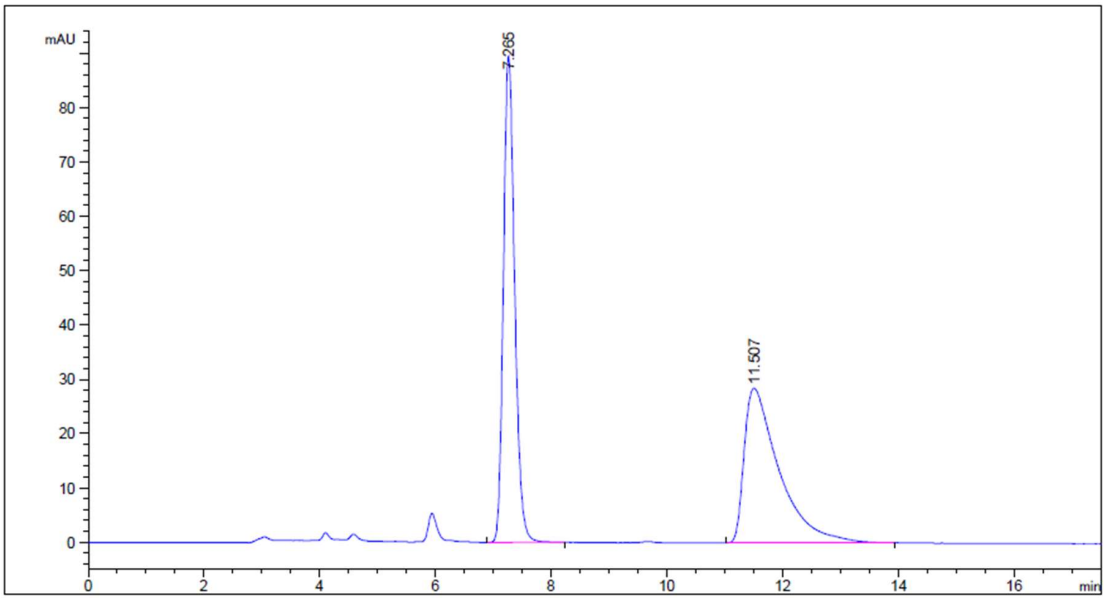
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.282	MM	0.5096	351.77063	11.50445	3.9842
2	13.580	MM	0.7645	8477.36230	184.82449	96.0158



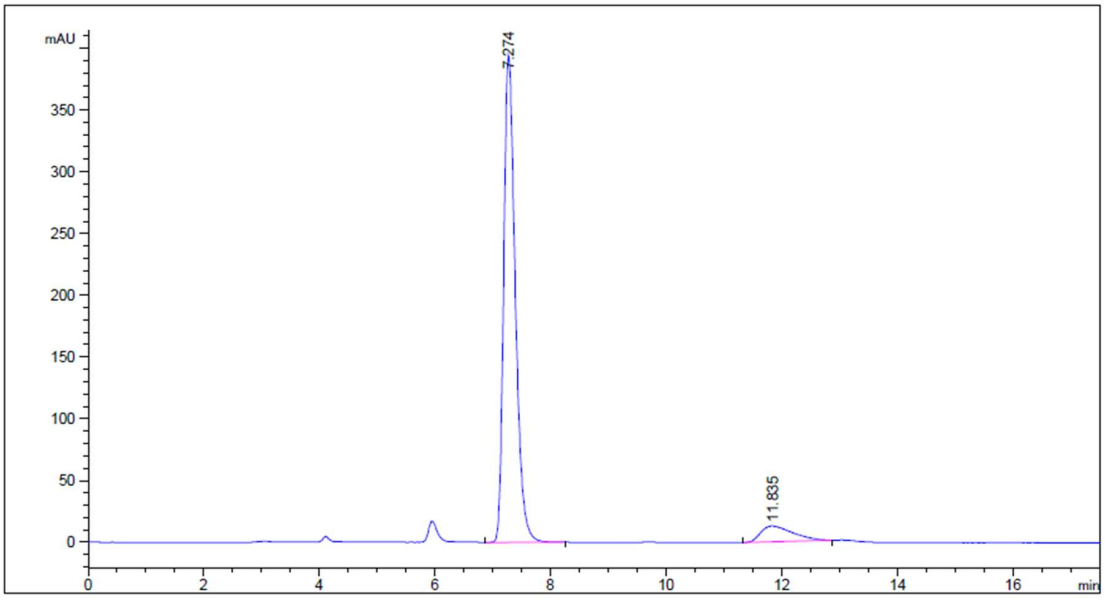
6b

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 70:30, 1 mL/min.



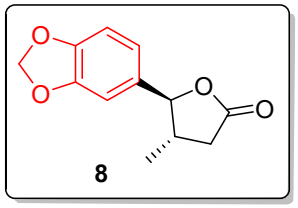
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.265	BB	0.2095	1210.16602	89.61892	50.3423
2	11.507	BB	0.6053	1193.71045	28.45974	49.6577



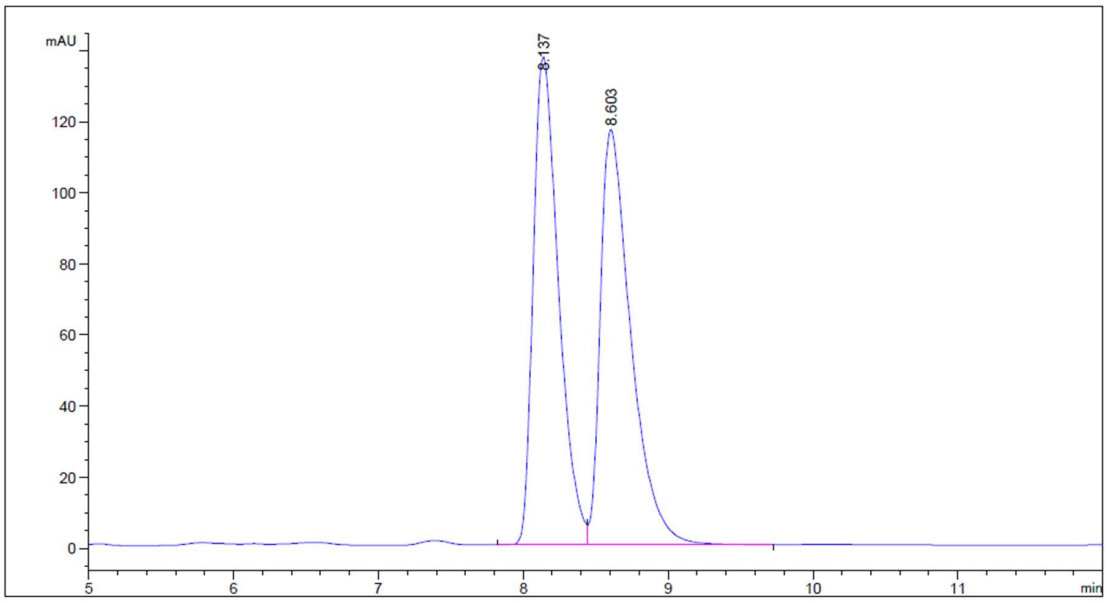
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.274	BB	0.2145	5494.76367	394.58136	91.8150
2	11.835	BB	0.5474	489.84109	12.77272	8.1850



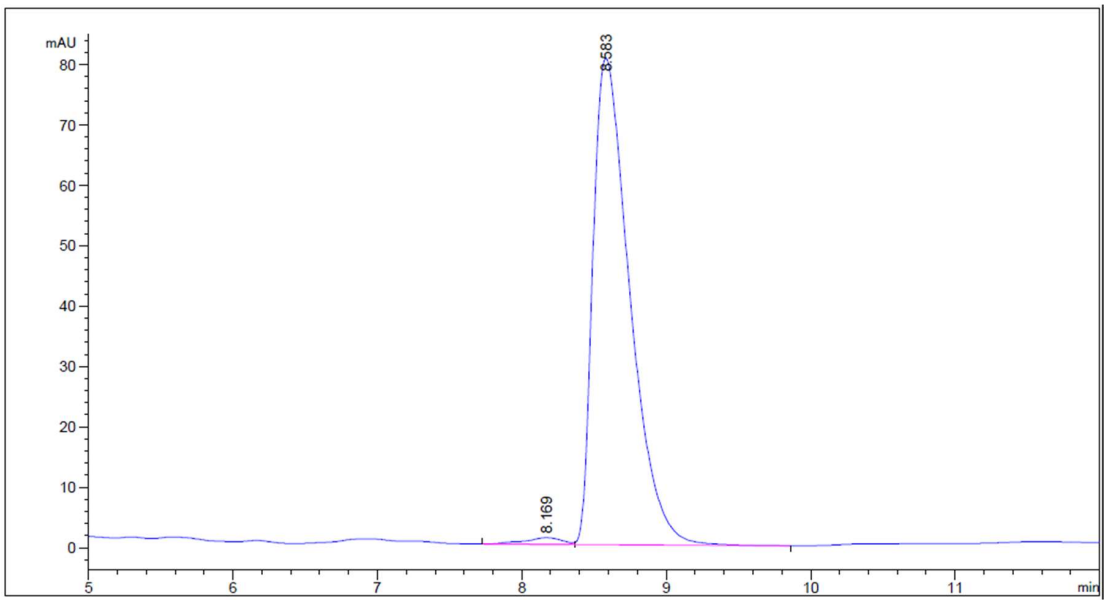
8

Separation of enantiomers by HPLC, Chiralcel® Column OD-H, 30 °C, n-hexane: *i*-PrOH = 70:30, 1 mL/min.



Signal 1: DAD1 B, Sig=254,4 Ref=off

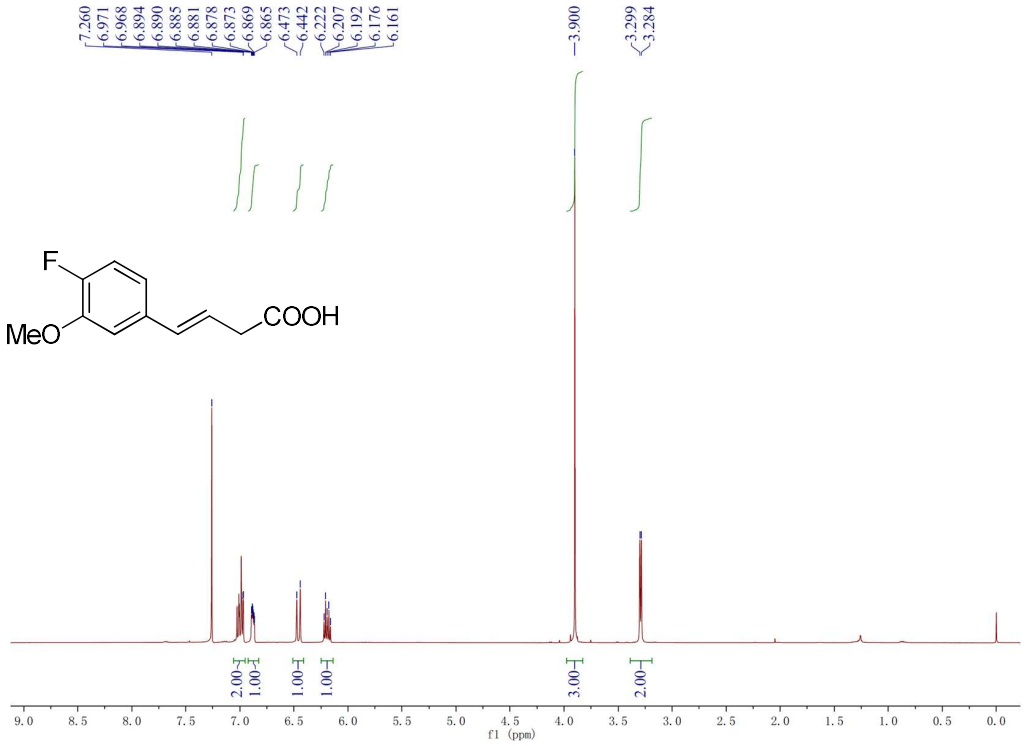
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.137	BV	0.1880	1668.77979	137.12631	49.3328
2	8.603	VB	0.2212	1713.91809	116.77088	50.6672

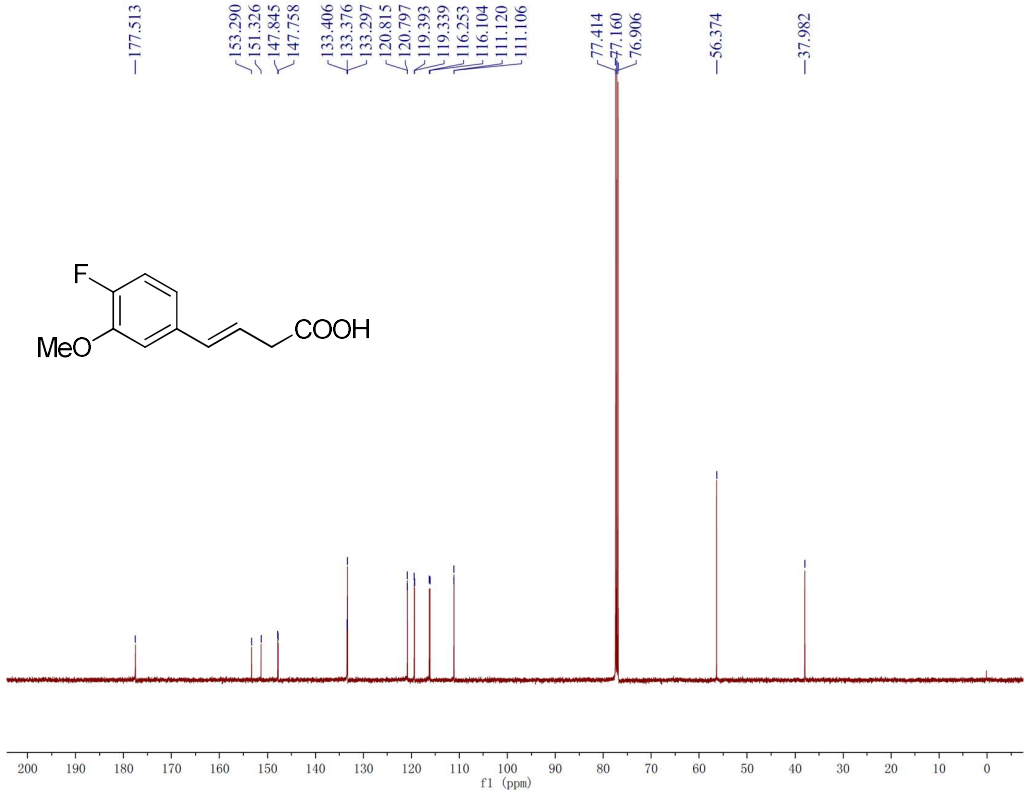


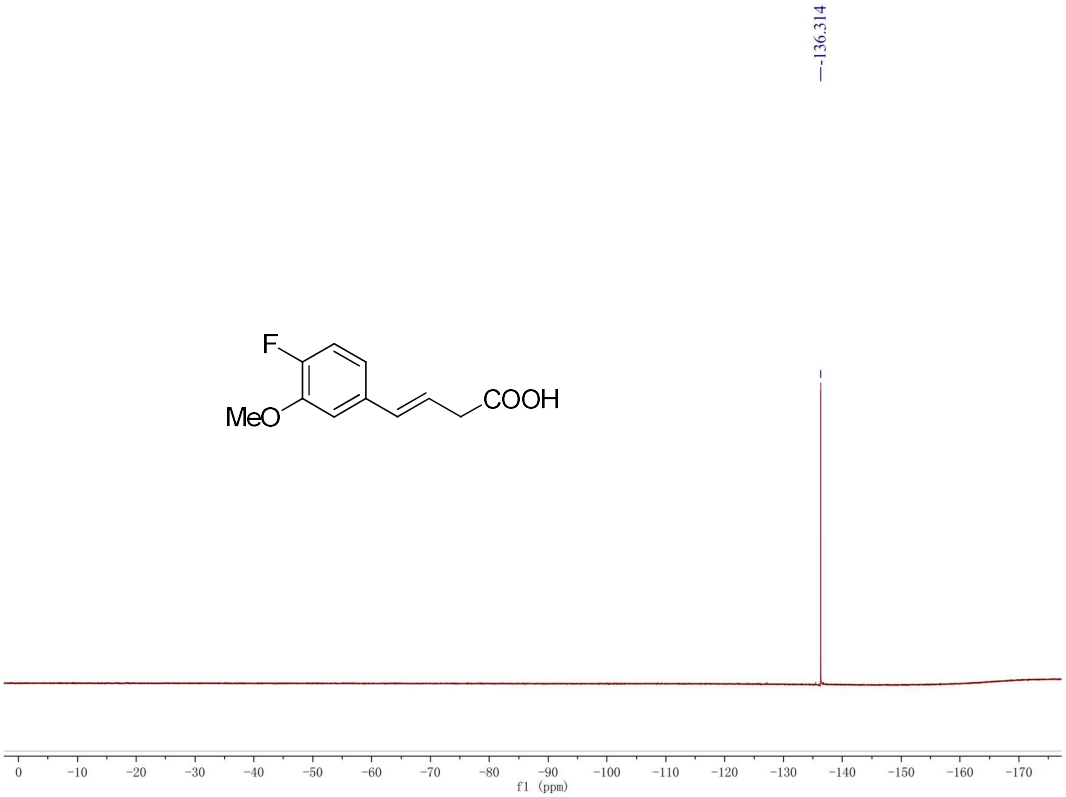
Signal 1: DAD1 B, Sig=254,4 Ref=off

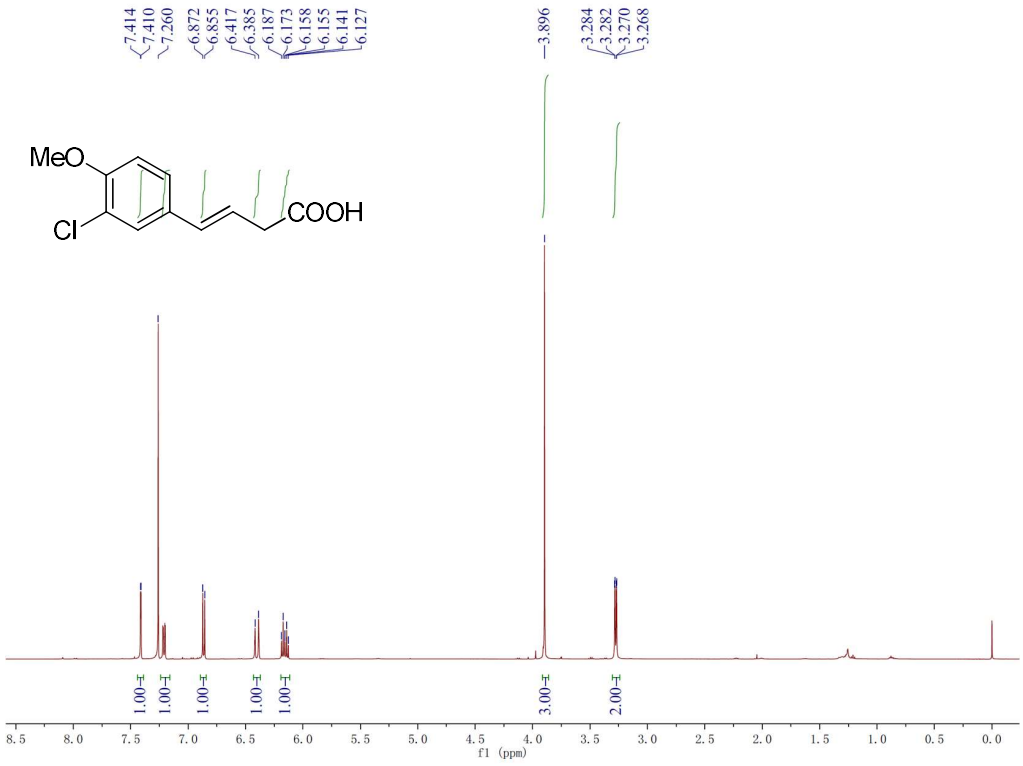
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.169	BV E	0.2588	19.85062	1.10901	1.3746
2	8.583	VB R	0.2743	1424.21106	80.52248	98.6254

Copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra






-136.314
F
MeO
COOH
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
f1 (ppm)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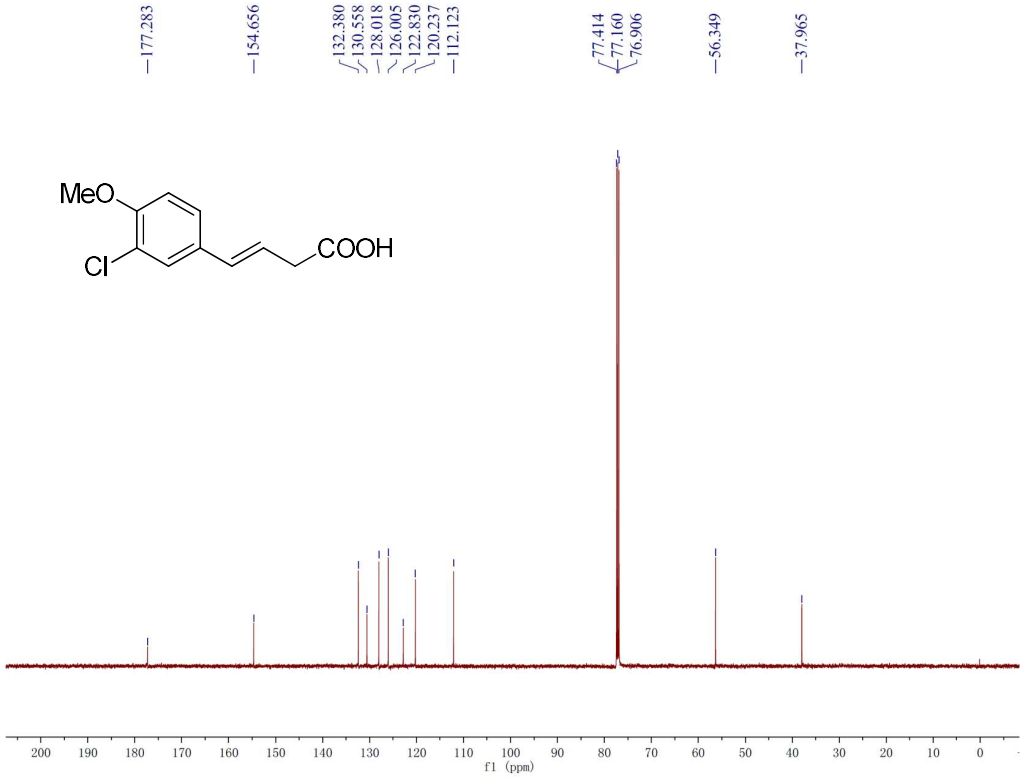
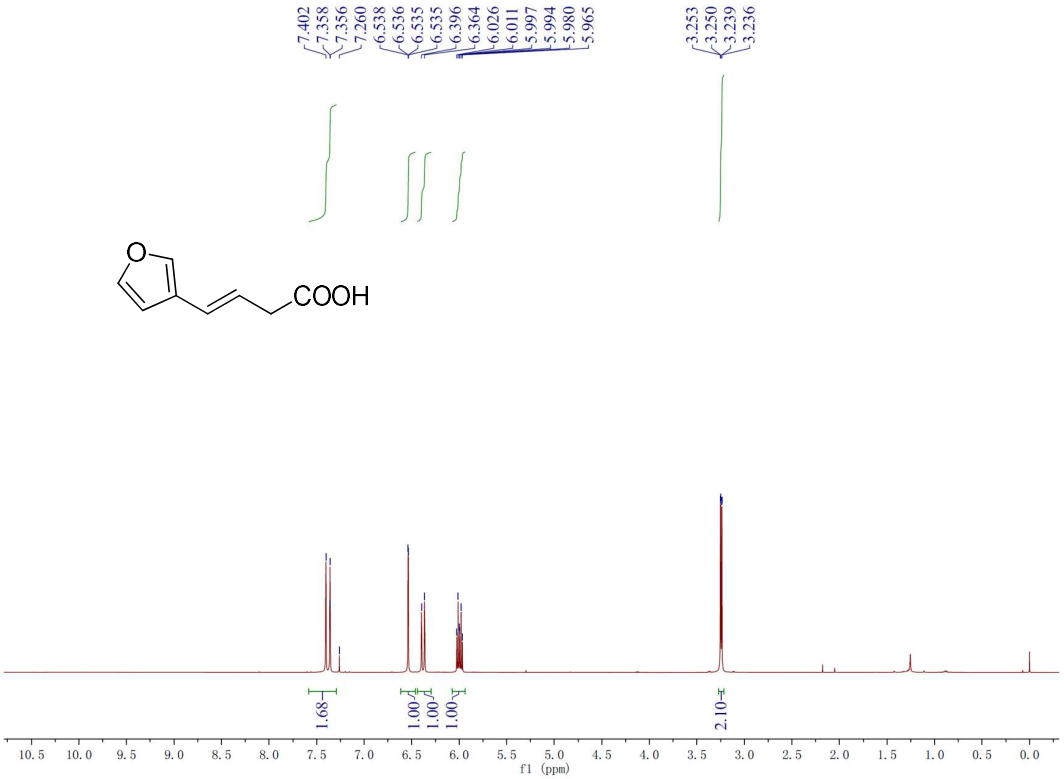
7.410
7.260
6.872
6.855
6.417
6.385
6.187
6.173
6.158
6.155
6.141
6.127
3.896
3.284
3.282
3.270
3.268
MeO
Cl
COOH
1.00
1.00
1.00
1.00
1.00
3.00
2.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


177.283
154.656
132.380
130.558
128.018
126.005
122.830
120.237
112.123
77.414
77.160
76.906
56.349
37.965
MeO
Cl
COOH
f1 (ppm)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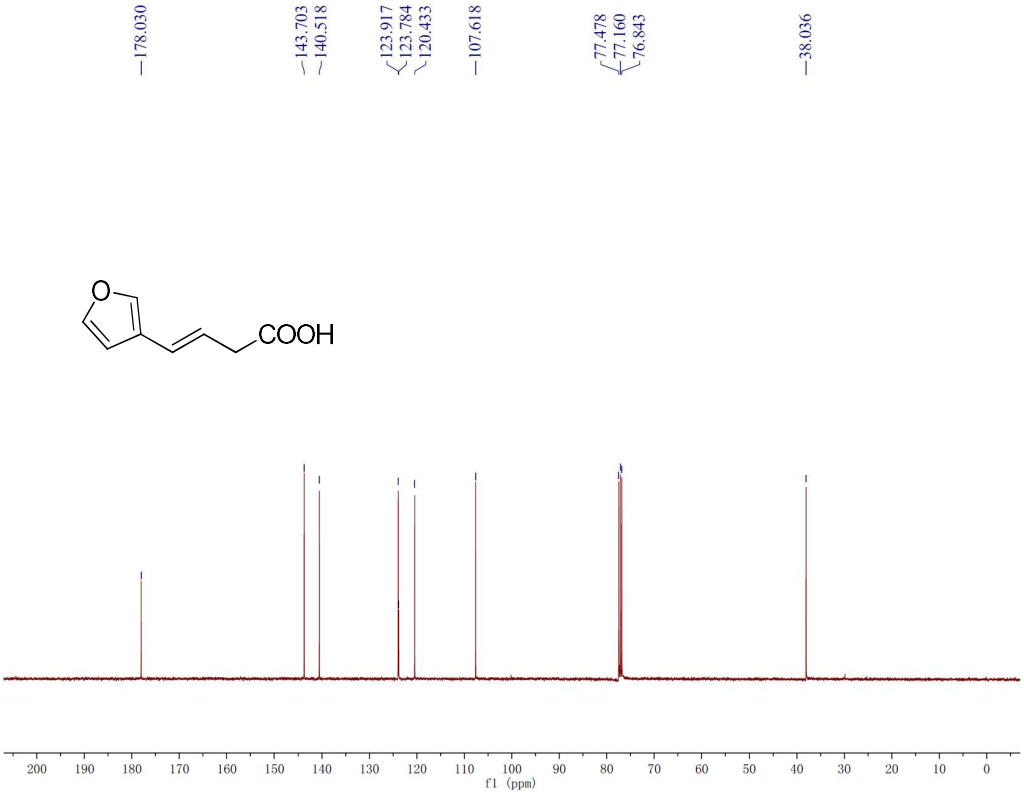
7.358
7.356
7.260
6.538
6.536
6.535
6.535
6.396
6.364
6.026
6.011
5.997
5.994
5.980
5.965
3.253
3.250
3.239
3.236
O
COOH
1.68
1.00
1.00
1.00
2.10
f1 (ppm)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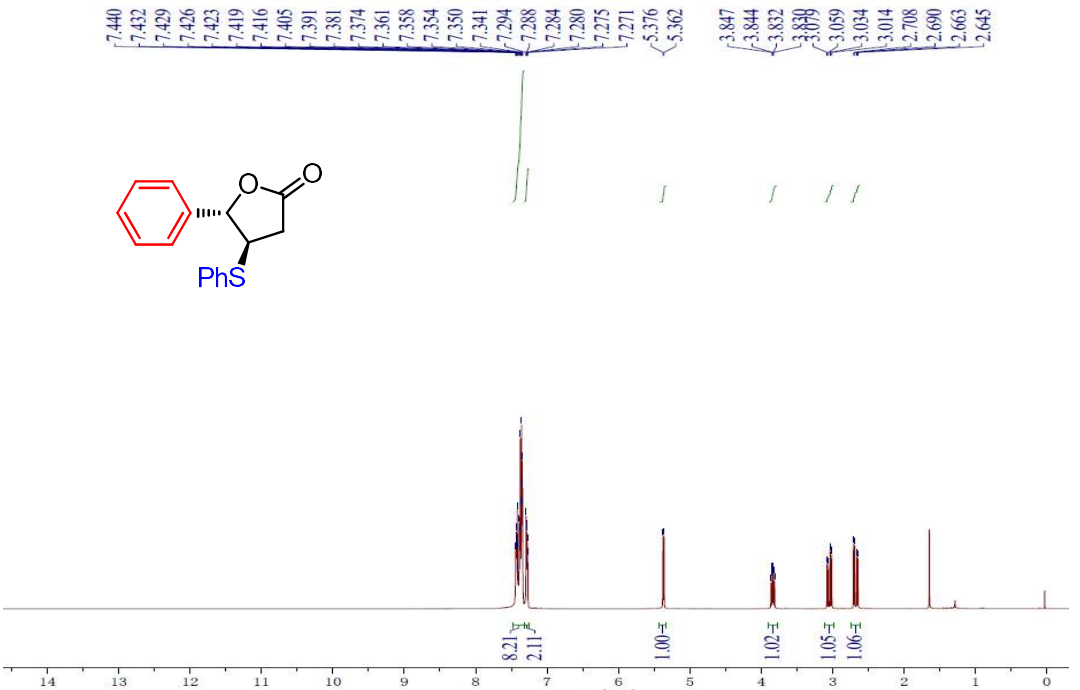
143.703
140.518
123.917
123.784
120.433
107.618
77.478
77.160
76.843
38.036
O
COOH
f1 (ppm)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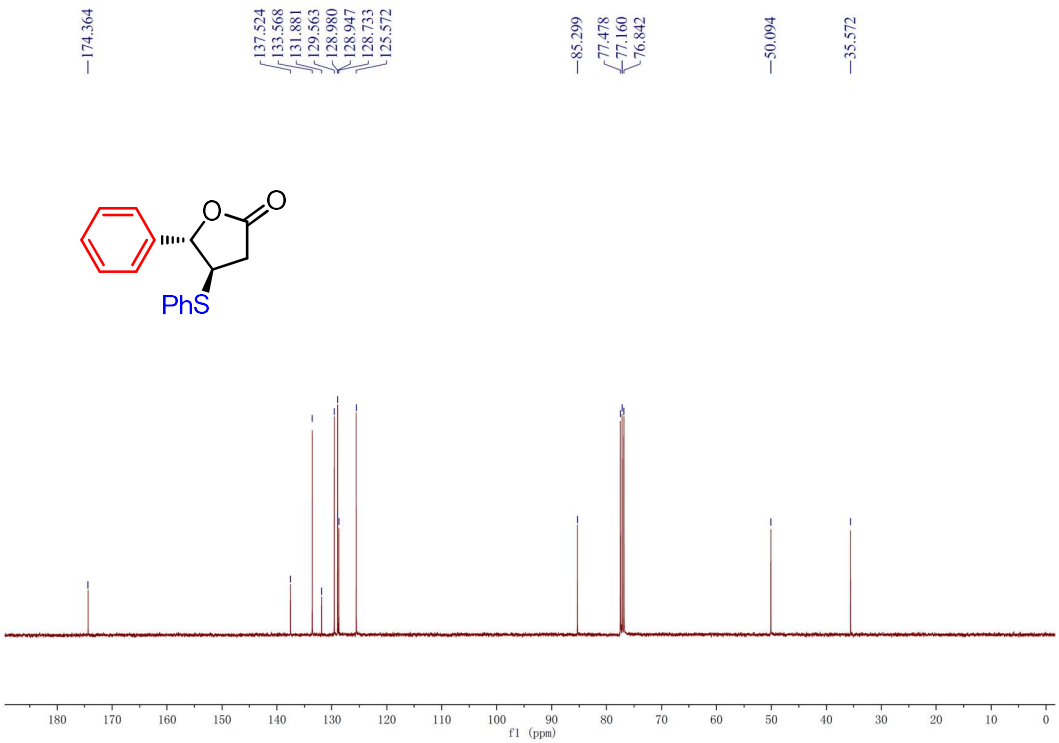
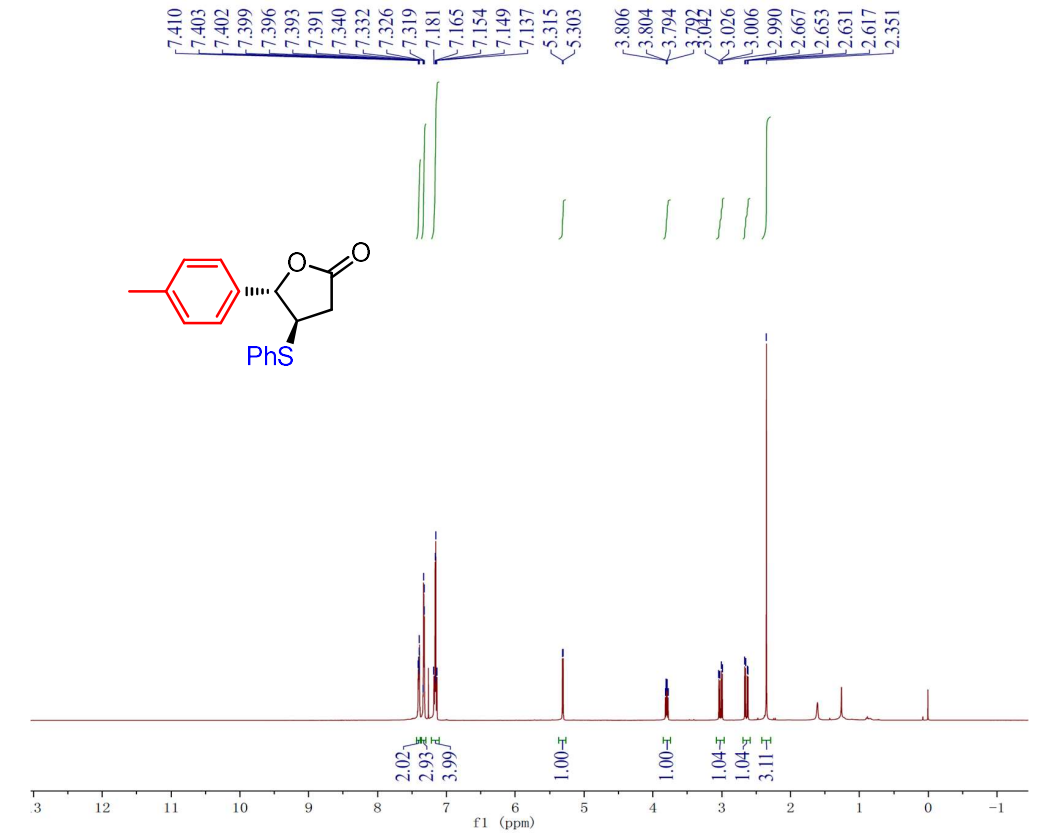
7.429
7.426
7.423
7.419
7.416
7.405
7.391
7.381
7.374
7.361
7.358
7.354
7.350
7.341
7.294
7.288
7.284
7.280
7.275
7.271
5.376
5.362
3.847
3.844
3.832
3.059
3.034
3.014
2.708
2.690
2.663
2.645
O
O
PhS
8.21
2.11
1.00
1.02
1.05
1.06
f1 (ppm)


174.364
137.524
133.568
131.881
129.563
128.980
128.947
128.733
125.572
85.299
77.478
77.160
76.842
50.094
35.572
PhS
f1 (ppm)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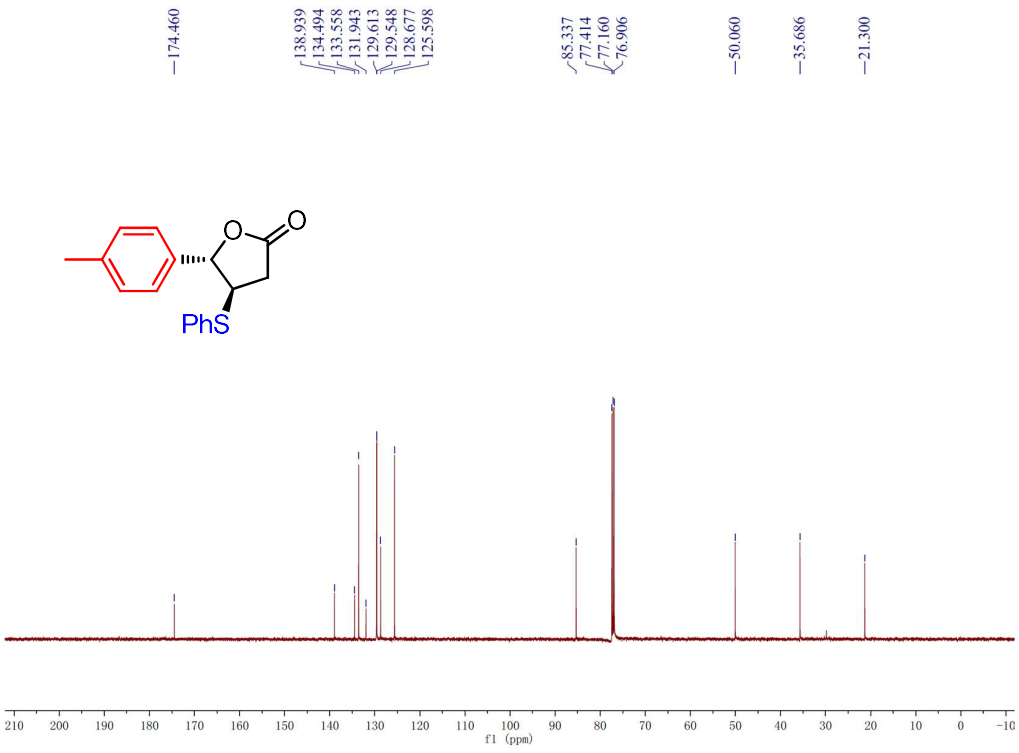
7.403
7.402
7.399
7.396
7.393
7.391
7.340
7.332
7.326
7.319
7.181
7.165
7.154
7.149
7.137
5.315
5.303
3.806
3.804
3.794
3.792
3.042
3.026
3.006
2.990
2.667
2.653
2.631
2.617
2.351
PhS
2.02
2.93
3.99
1.00
1.00
1.04
1.04
3.11
f1 (ppm)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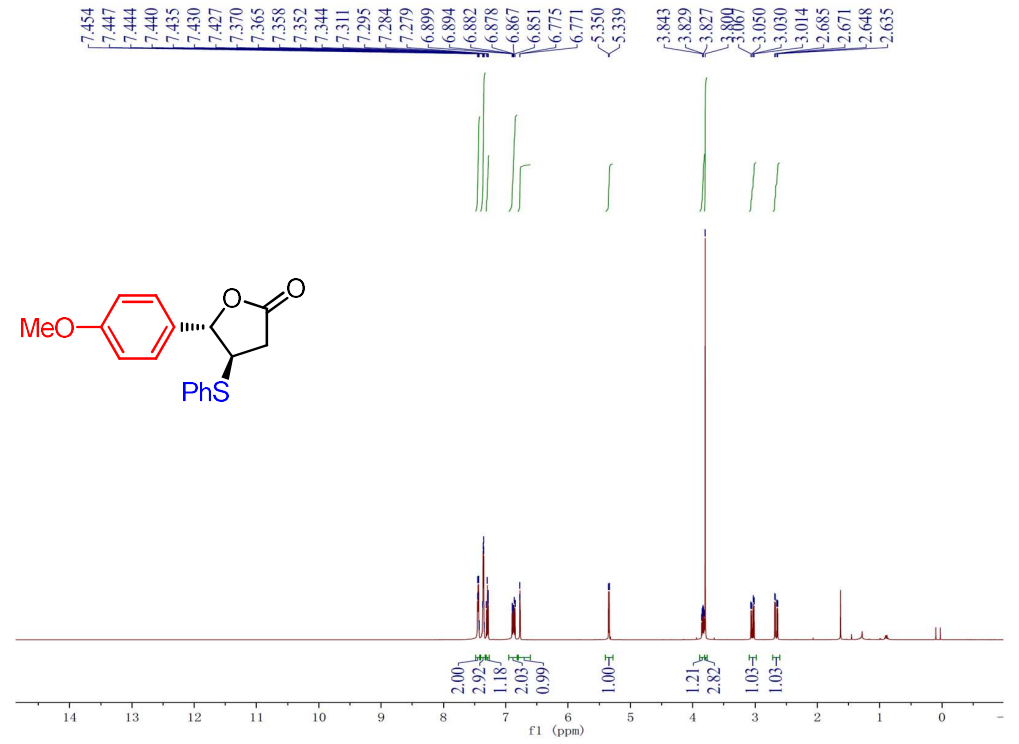
138.939
134.494
133.558
131.943
129.613
129.548
128.677
125.598
85.337
77.414
77.160
76.906
50.060
35.686
21.300
O
O
PhS
f1 (ppm)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7.447
7.444
7.440
7.435
7.430
7.427
7.370
7.365
7.358
7.352
7.344
7.311
7.295
7.284
7.279
6.899
6.894
6.882
6.878
6.867
6.851
6.775
6.771
5.350
5.339
3.843
3.829
3.827
3.809
3.067
3.050
3.030
3.014
2.685
2.671
2.648
2.635
MeO
O
O
PhS
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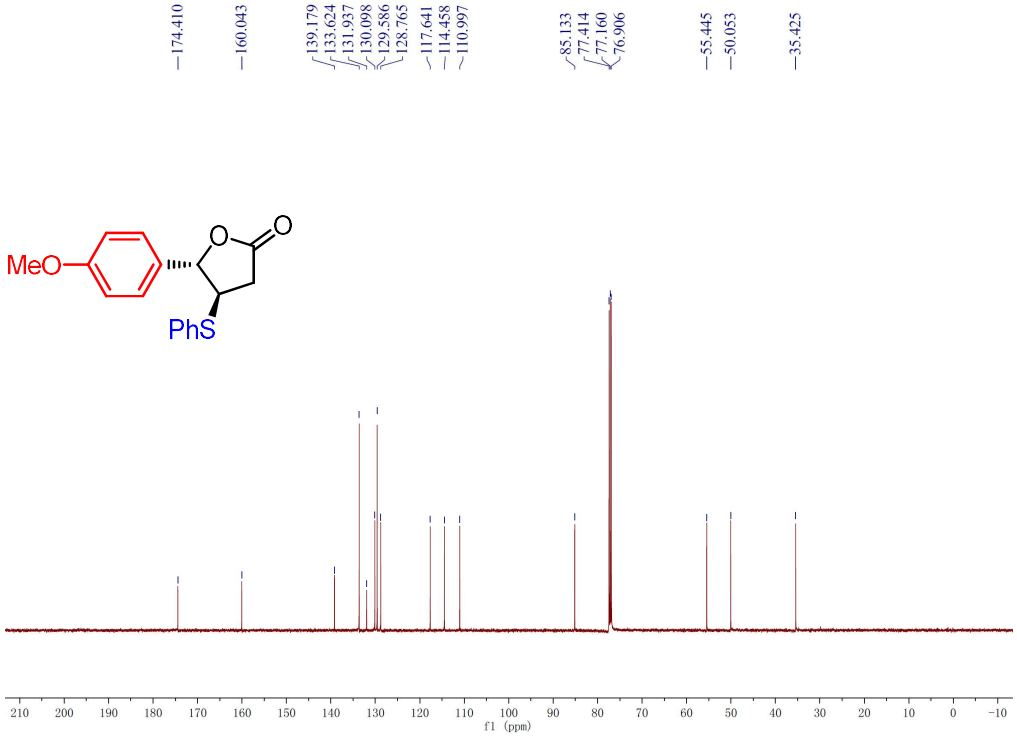
1.18
2.03
0.99
1.00
1.21
2.82
1.03
1.03
f1 (ppm)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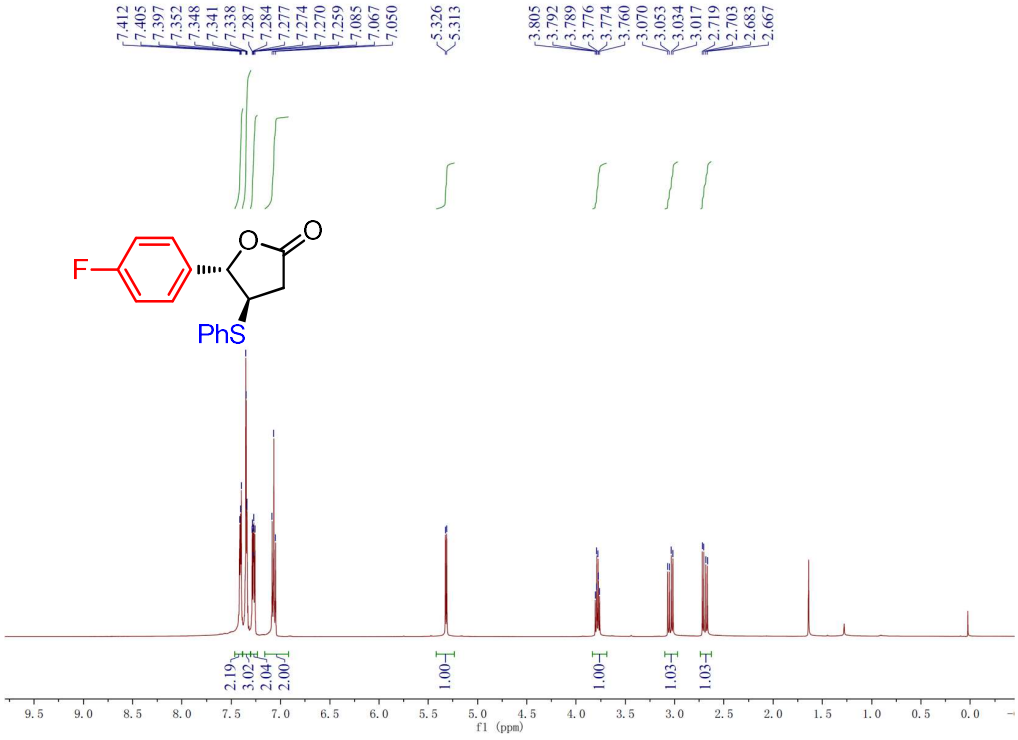
160.043
139.179
133.624
131.937
130.098
129.586
128.765
117.641
114.458
110.997
85.133
77.414
77.160
76.906
55.445
50.053
35.425
MeO
O
O
PhS
f1 (ppm)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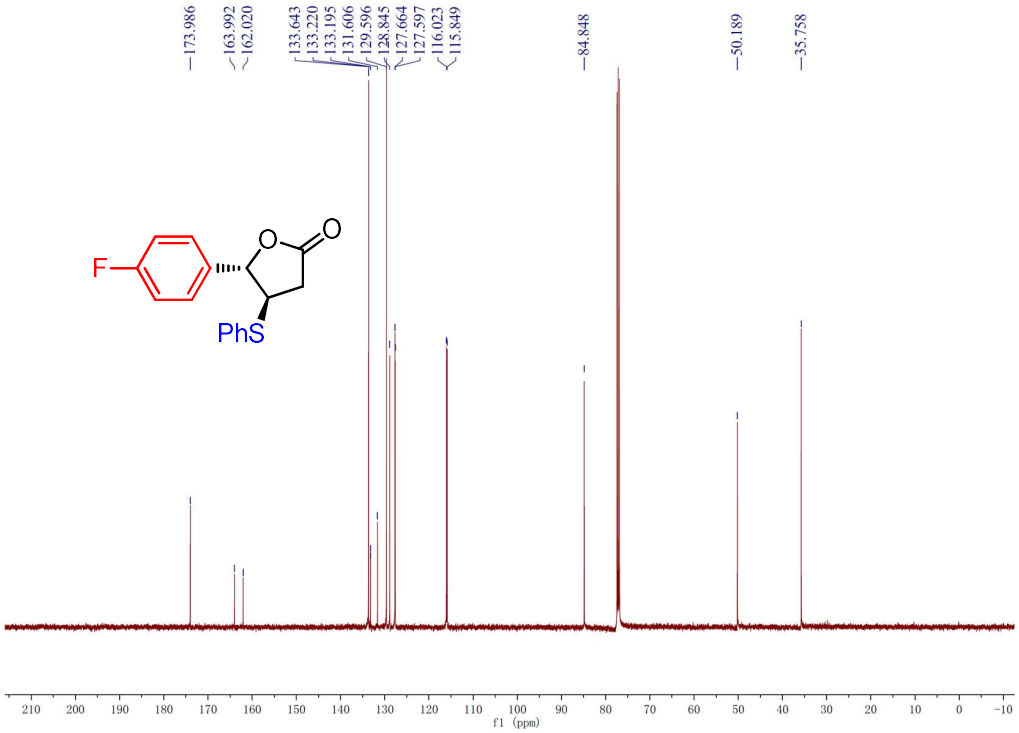
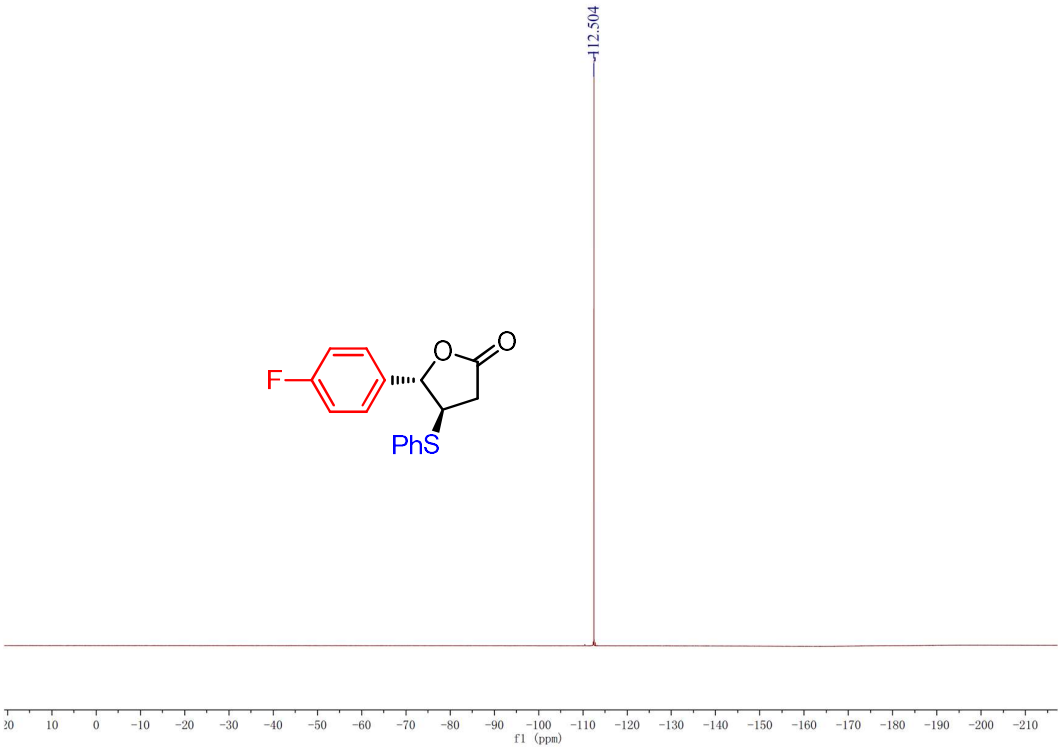
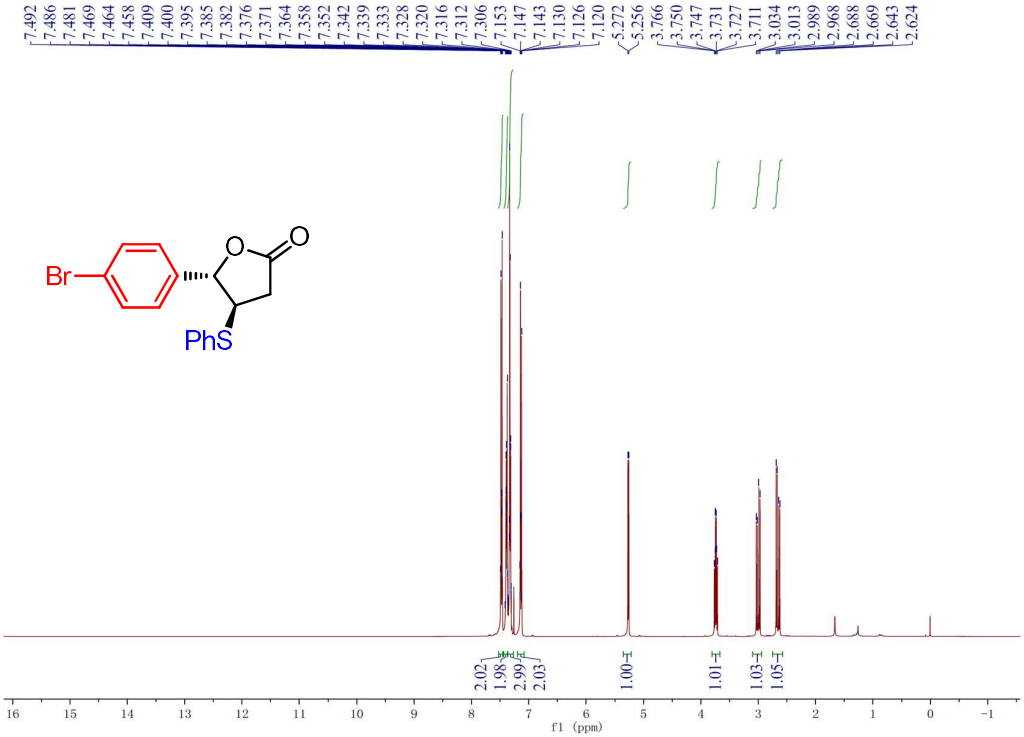
7.405
7.397
7.352
7.348
7.341
7.338
7.287
7.284
7.277
7.274
7.270
7.259
7.085
7.067
7.050
5.326
5.313
3.805
3.792
3.789
3.776
3.774
3.760
3.070
3.053
3.034
3.017
2.719
2.703
2.683
2.667
F
O
O
PhS
2.19
3.02
2.04
2.00
1.00
1.00
1.03
1.03
f1 (ppm)


173.986
163.992
162.020
133.643
133.220
133.195
131.606
129.596
128.845
127.664
127.597
116.023
115.849
84.848
50.189
35.758
F
O
O
PhS
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


−112.504
F
O
O
PhS
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)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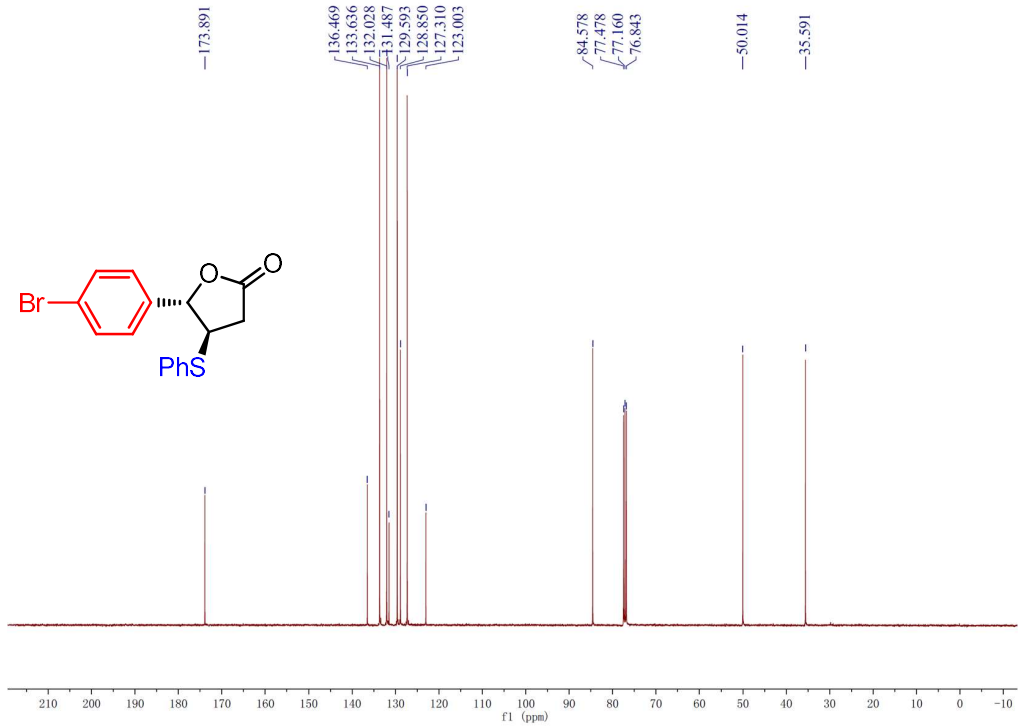
7.486
7.481
7.469
7.464
7.458
7.409
7.400
7.395
7.385
7.382
7.376
7.371
7.364
7.358
7.352
7.342
7.339
7.333
7.328
7.320
7.316
7.312
7.306
7.153
7.147
7.143
7.130
7.126
7.120
5.272
5.256
3.766
3.750
3.747
3.731
3.727
3.711
3.034
3.013
2.989
2.968
2.688
2.669
2.643
2.624
Br
O
O
PhS
2.02
1.98
2.99
2.03
1.00
1.01
1.03
1.05
f1 (ppm)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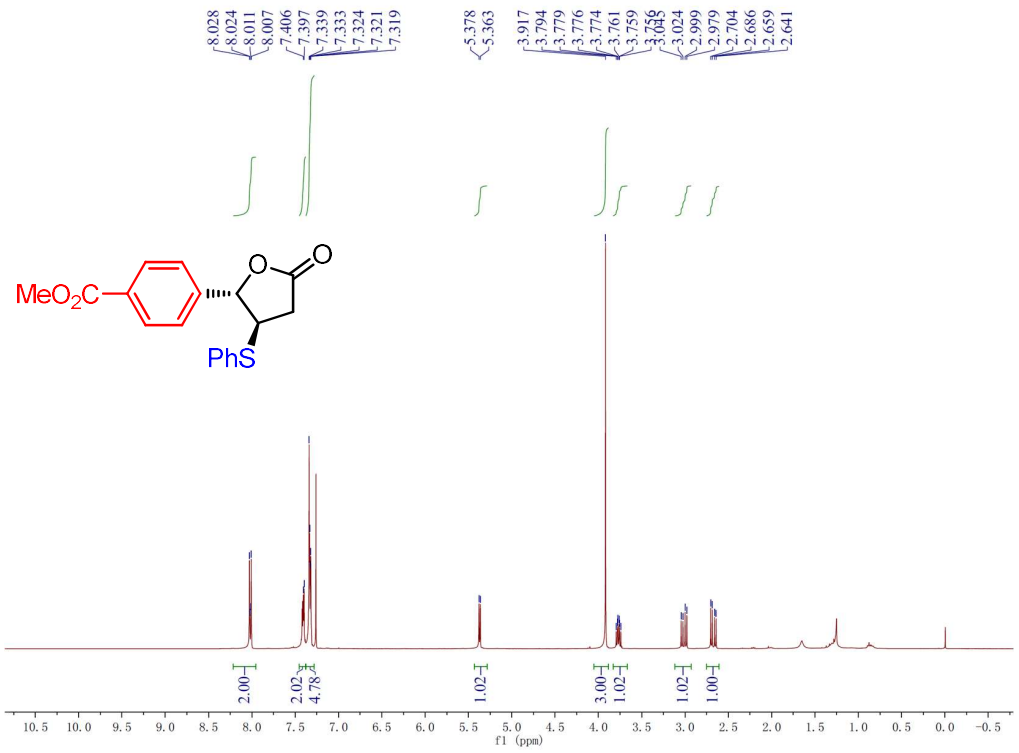
131.487
129.593
128.850
127.310
123.003
84.578
77.478
77.160
76.843
50.014
35.591
Br
O
O
PhS
f1 (ppm)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8.024
8.011
8.007
7.406
7.397
7.339
7.333
7.324
7.321
7.319
5.378
5.363
3.917
3.794
3.779
3.776
3.774
3.761
3.759
3.756
3.045
3.024
2.999
2.979
2.704
2.686
2.659
2.641
MeO2C
O
O
PhS
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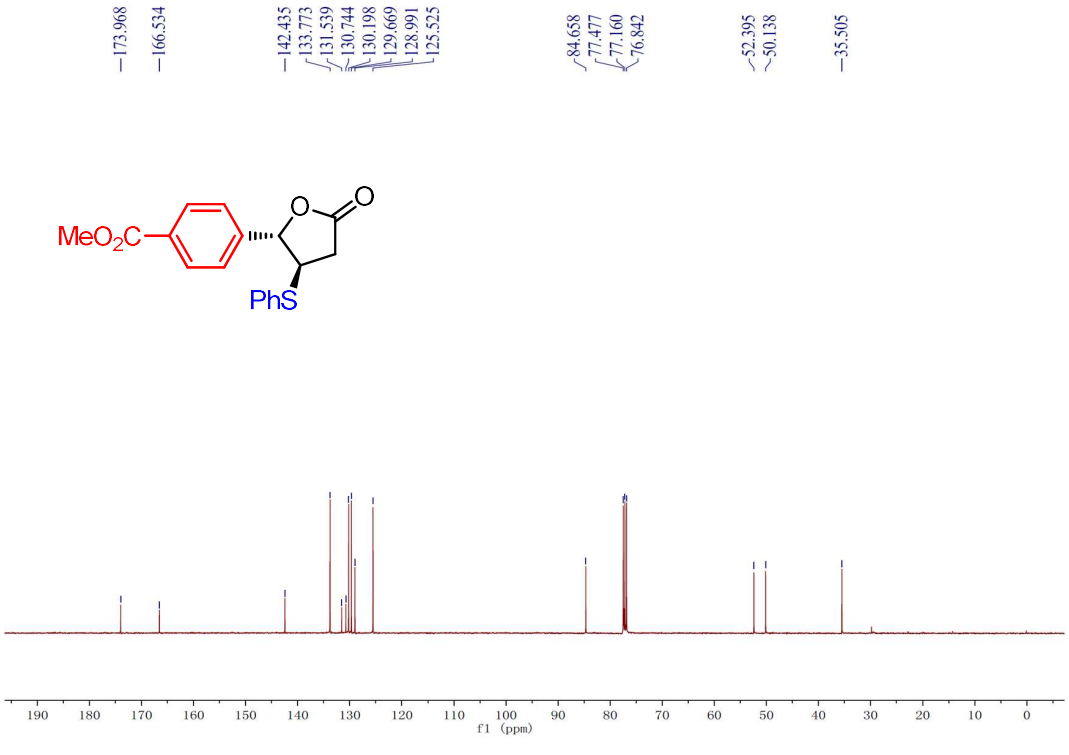
2.02
4.78
1.02
3.00
1.02
1.02
1.00
f1 (ppm)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133.773
131.539
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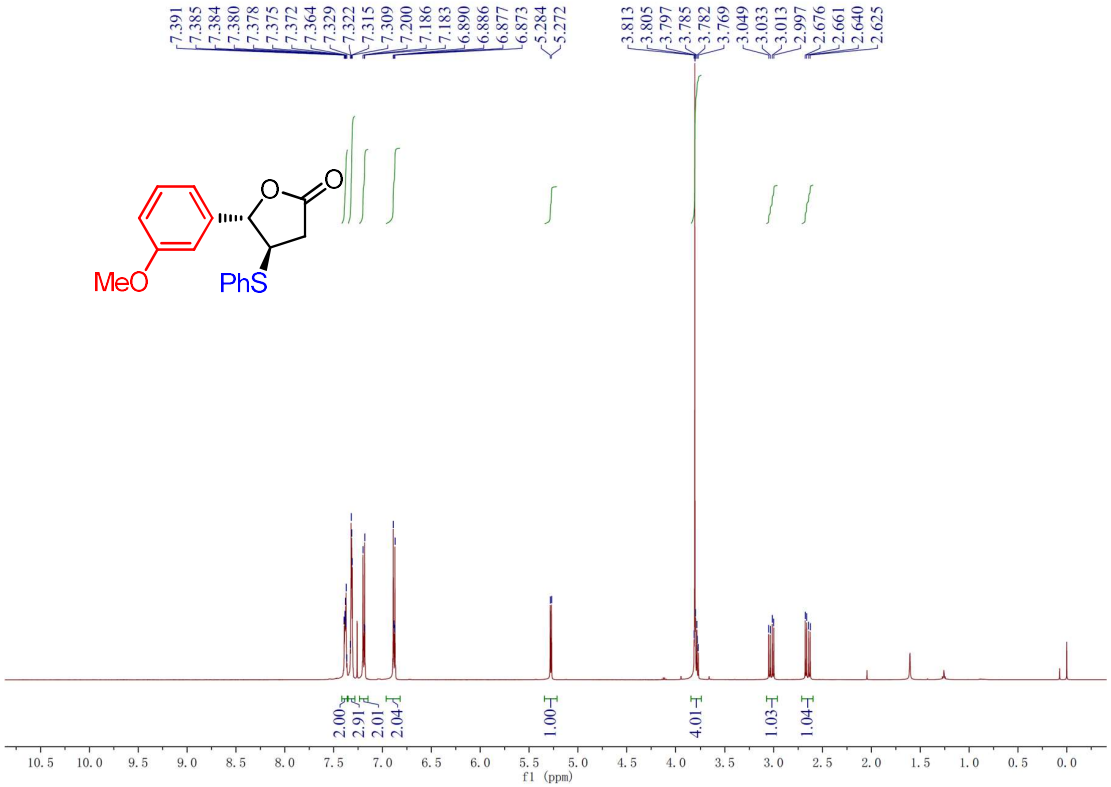
130.198
129.669
128.991
125.525
84.658
77.477
77.160
76.842
52.395
50.138
35.505
MeO2C
O
O
PhS
f1 (ppm)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7.372
7.364
7.329
7.322
7.315
7.309
7.200
7.186
7.183
6.890
6.886
6.877
6.873
5.284
5.272
3.813
3.805
3.797
3.785
3.782
3.769
3.049
3.033
3.013
2.997
2.676
2.661
2.640
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MeO
PhS
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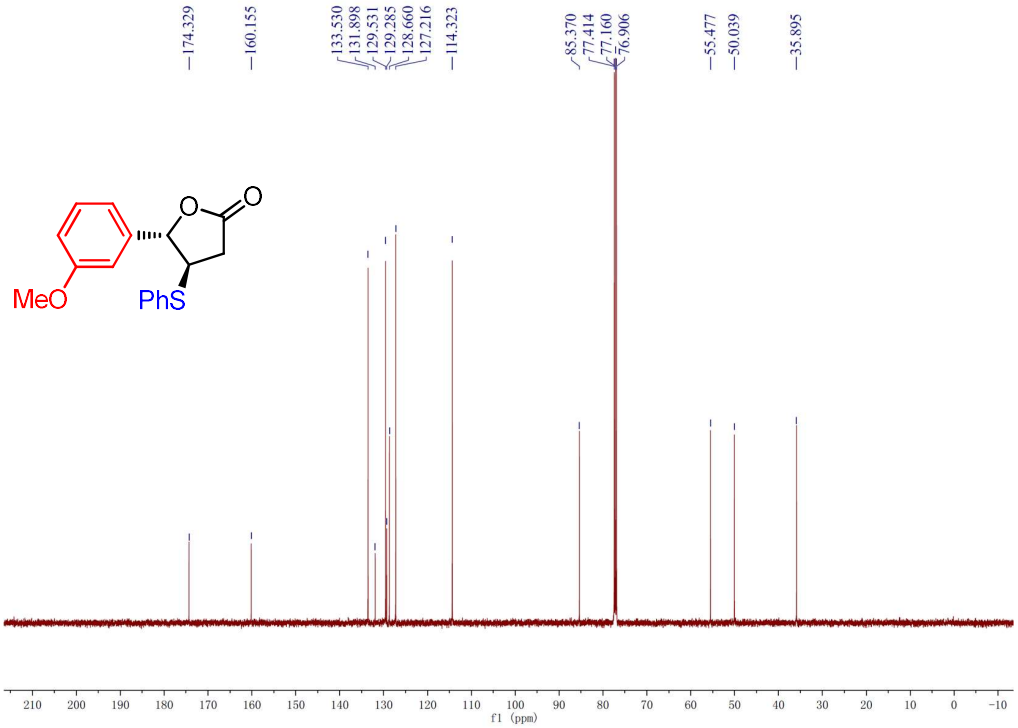
2.01
2.04
1.00
4.01
1.03
1.04
f1 (ppm)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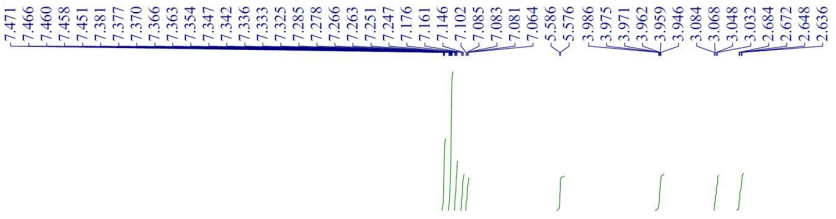
133.530
131.898
129.531
129.285
128.660
127.216
114.323
85.370
77.414
77.160
76.906
55.477
50.039
35.895
MeO
PhS
f1 (ppm)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7.370
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7.342
7.336
7.333
7.325
7.285
7.278
7.266
7.263
7.251
7.247
7.176
7.161
7.146
7.102
7.085
7.083
7.081
7.064
5.586
5.576
3.986
3.975
3.971
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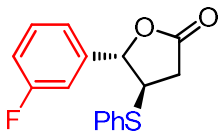
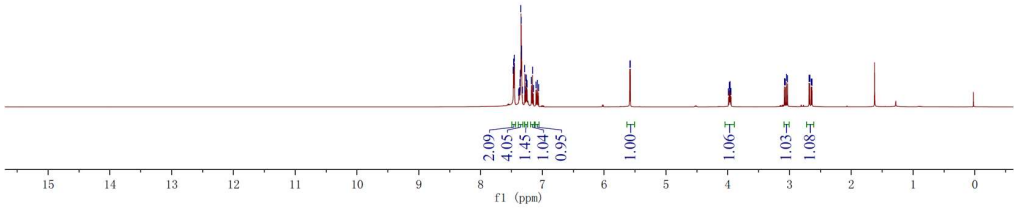
2.672
2.648
2.636


O
O
F
PhS


2.09
4.05
1.45
1.04
0.95
1.00
1.06
1.03
1.08
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


174.365
161.210
159.234
133.975
130.981
129.472
128.861
127.686
127.658
124.650
124.622
116.223
116.056
81.111
81.096
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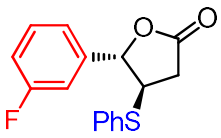
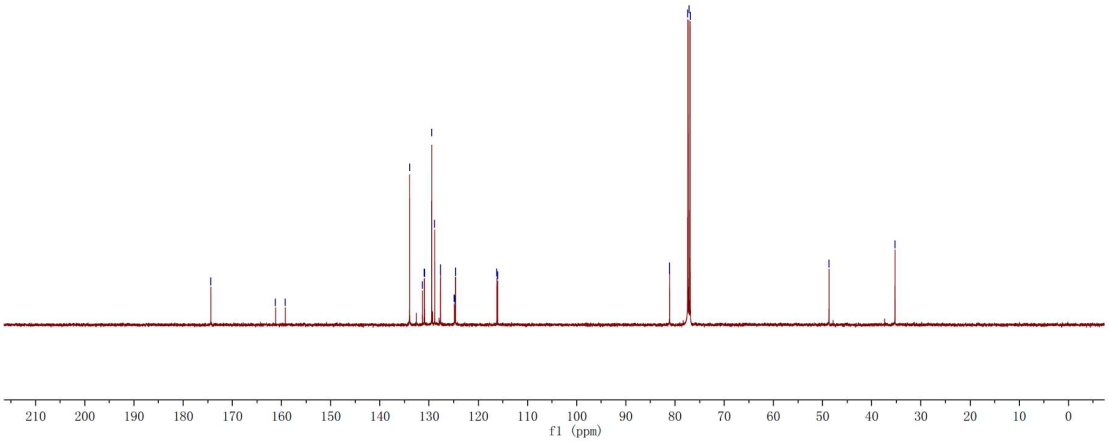
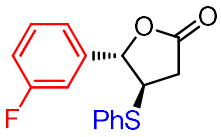
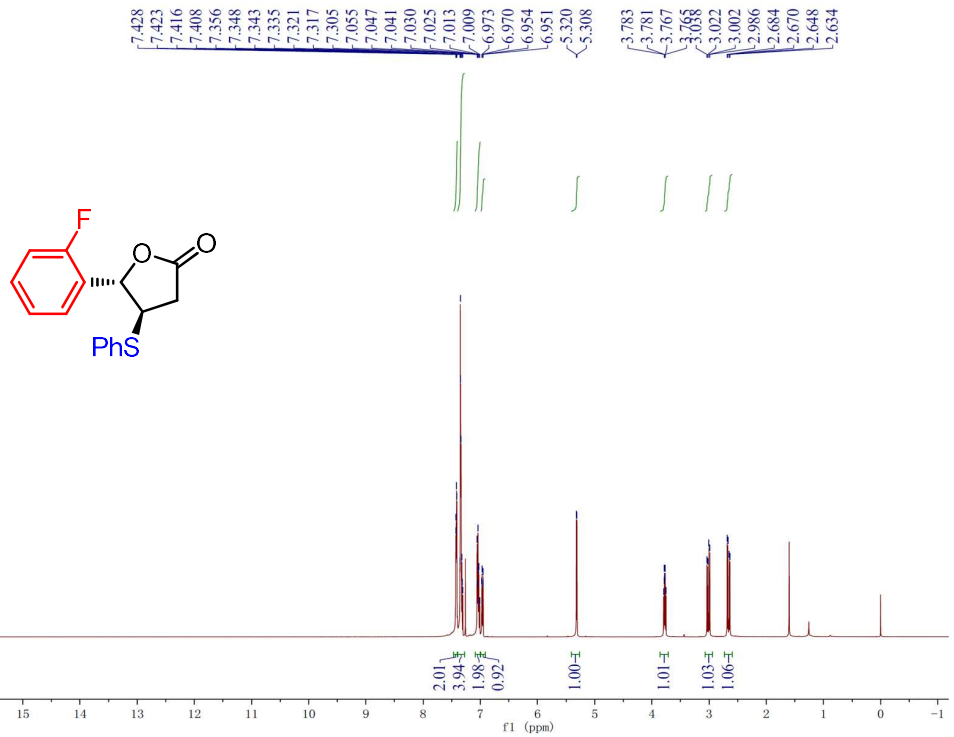
77.160
76.905
48.680
35.269

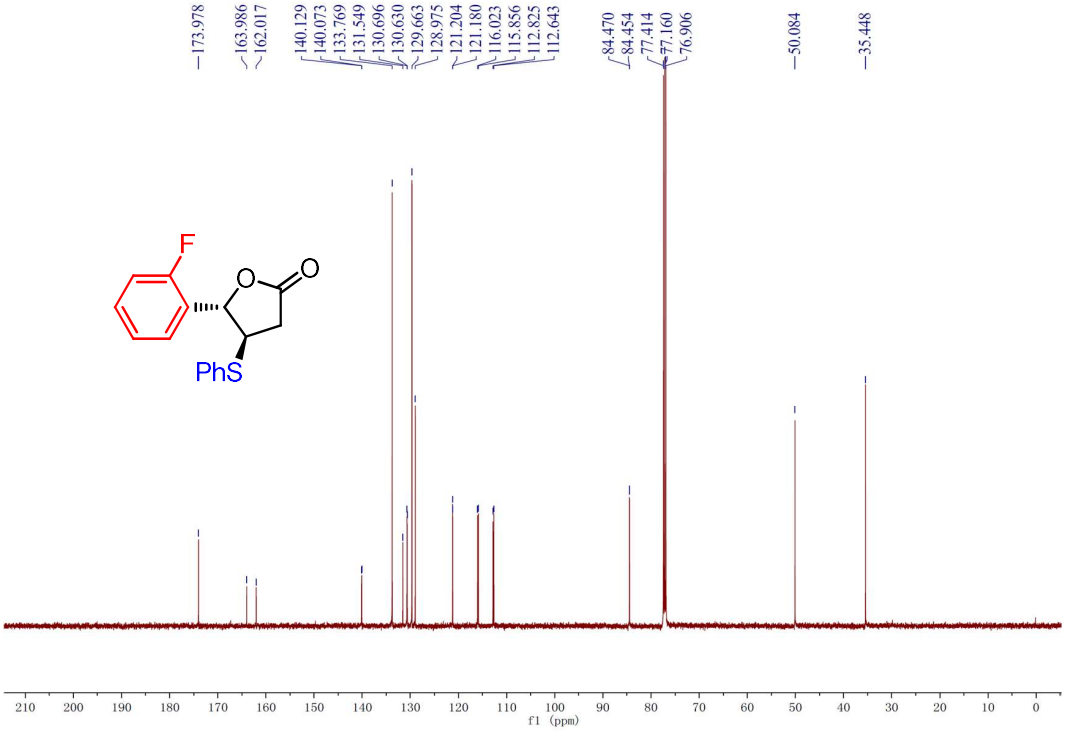

O
O
F
PhS


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


F
O
O
PhS

-116.472
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


7.428
7.423
7.416
7.408
7.356
7.348
7.343
7.335
7.321
7.317
7.305
7.055
7.047
7.041
7.030
7.025
7.013
7.009
6.973
6.970
6.954
6.951
5.320
5.308
3.783
3.781
3.767
3.765
3.038
3.022
3.002
2.986
2.684
2.670
2.648
2.634
F
O
O
PhS
2.01
3.94
1.98
0.92
1.00
1.01
1.03
1.06
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)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162.017
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131.549
130.696
130.630
129.663
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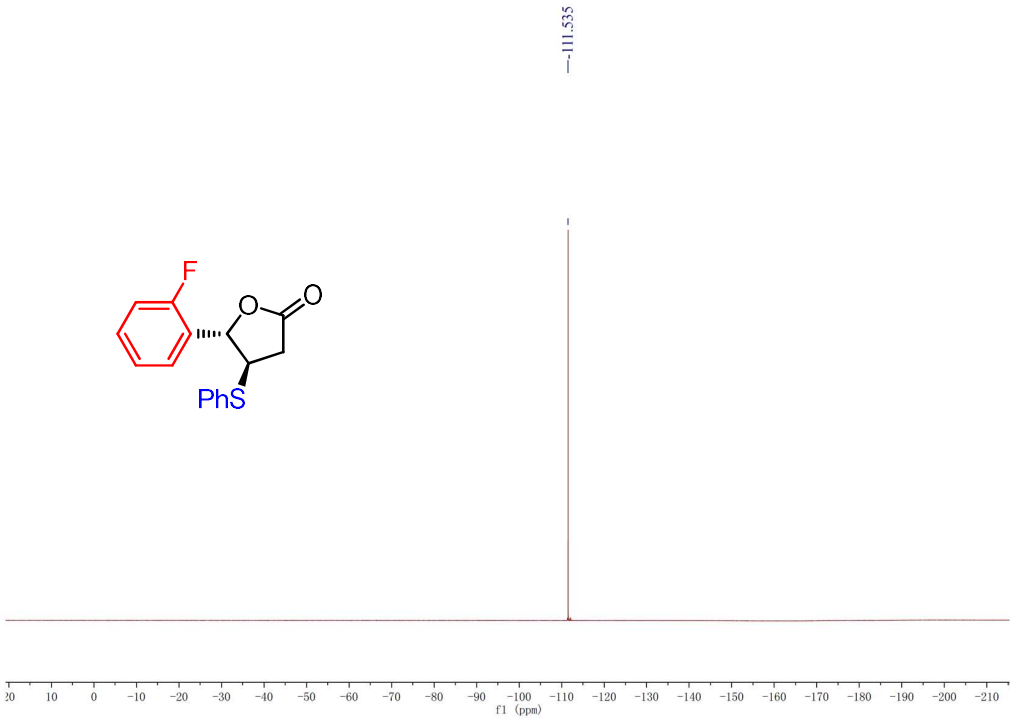
121.204
121.180
116.023
115.856
112.825
112.643
84.470
84.454
77.414
77.160
76.906
50.084
35.448
F
O
O
PhS
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-111.535
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O
O
PhS
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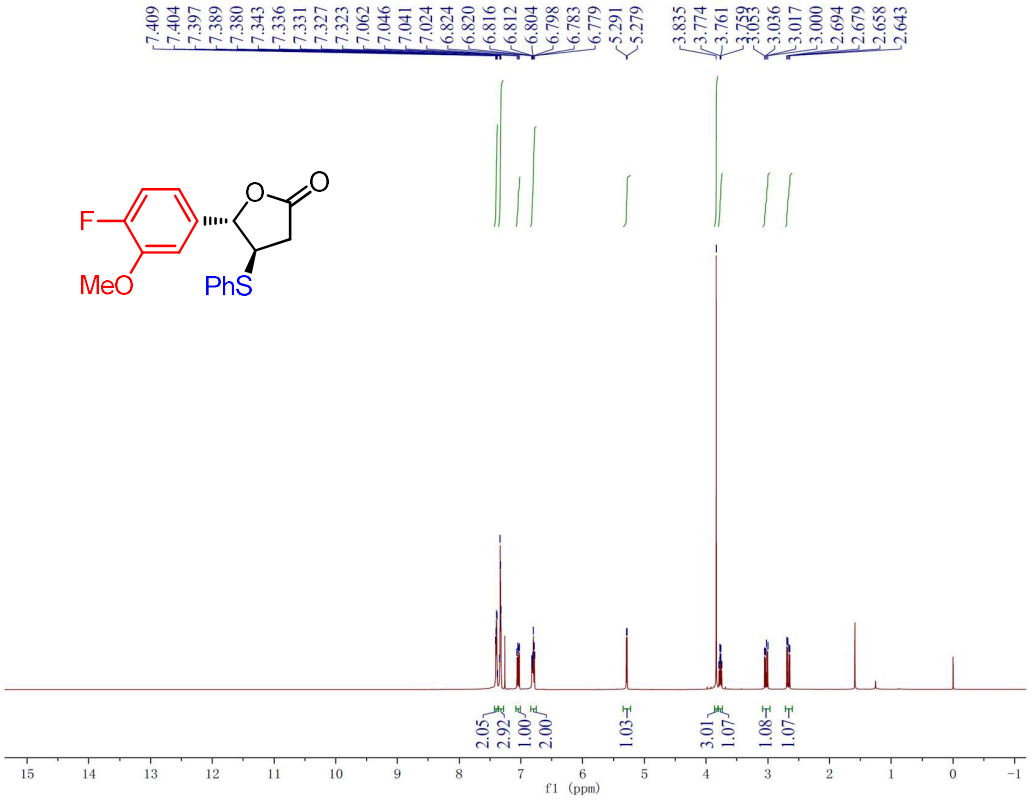
f1 (ppm)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7.323
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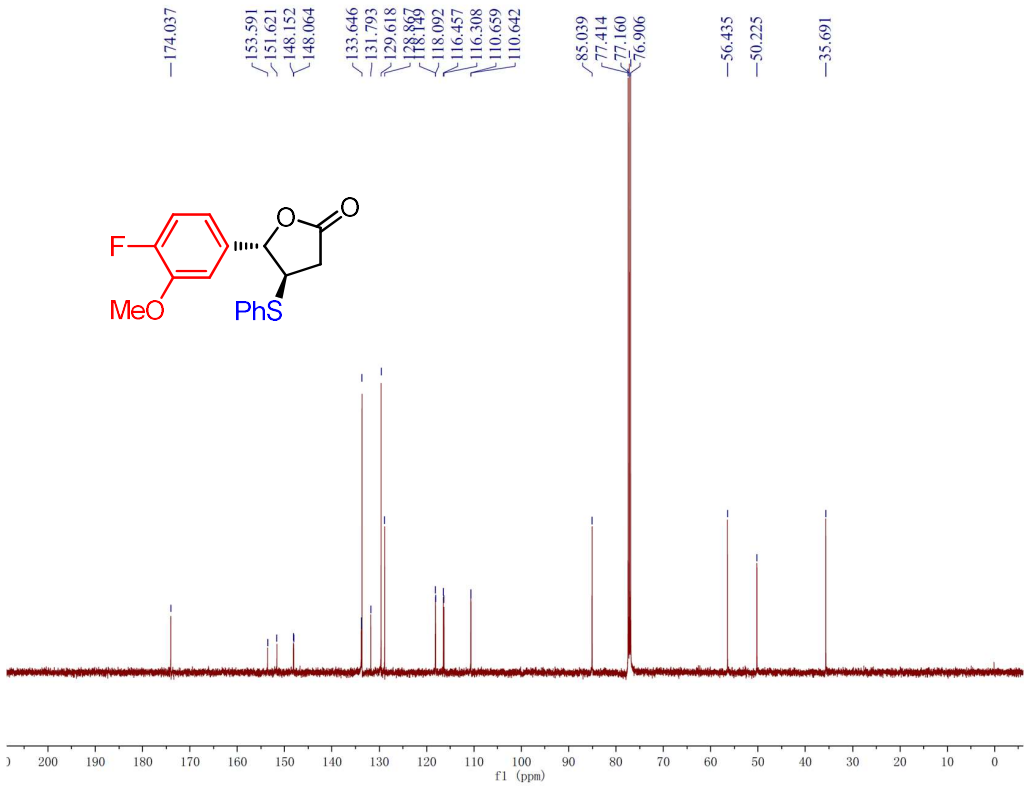
7.041
7.024
6.824
6.820
6.816
6.812
6.804
6.798
6.783
6.779
5.291
5.279
3.835
3.774
3.761
3.759
3.053
3.036
3.017
3.000
2.694
2.679
2.658
2.643
F
MeO
PhS
O
O
2.05
2.92
1.00
2.00
1.03
3.01
1.07
1.08
1.07
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)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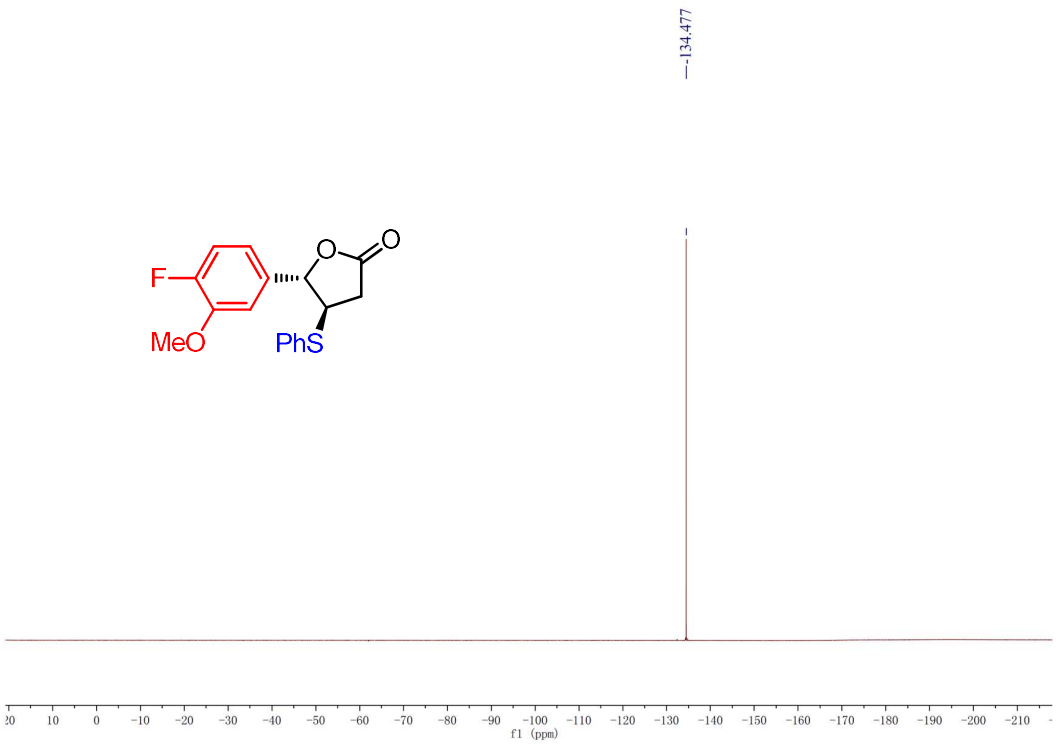
116.308
110.659
110.642
85.039
77.414
77.160
76.906
56.435
50.225
35.691
F
MeO
PhS
O
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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F
MeO
PhS
O
O
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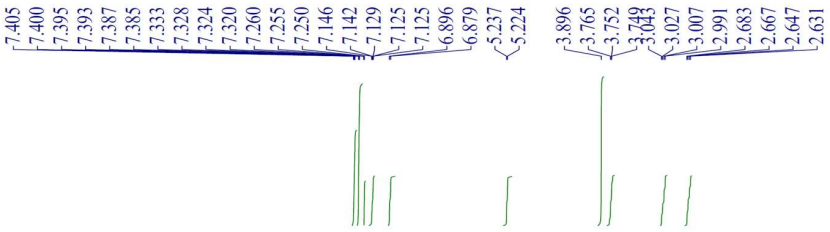
f1 (ppm)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7.328
7.324
7.320
7.260
7.255
7.250
7.146
7.142
7.129
7.125
7.125
6.896
6.879
5.237
5.224
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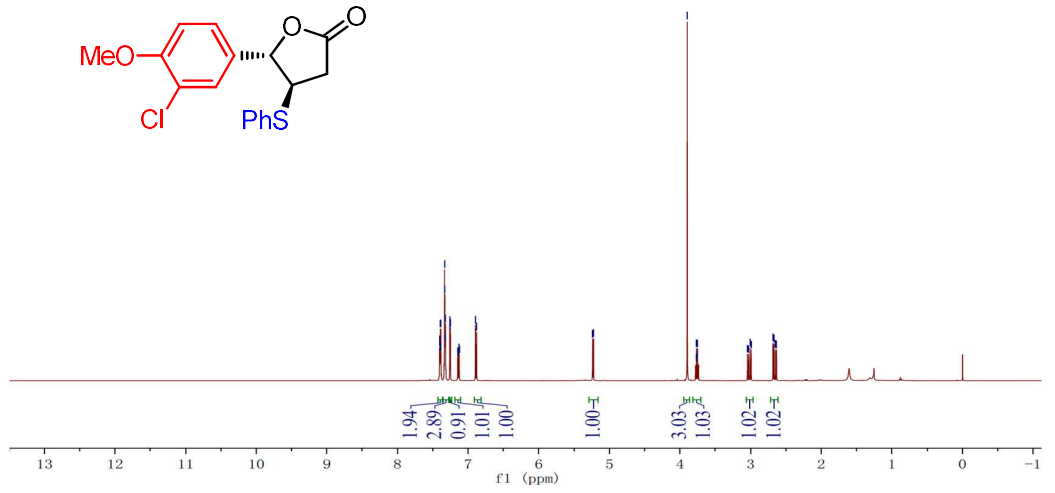
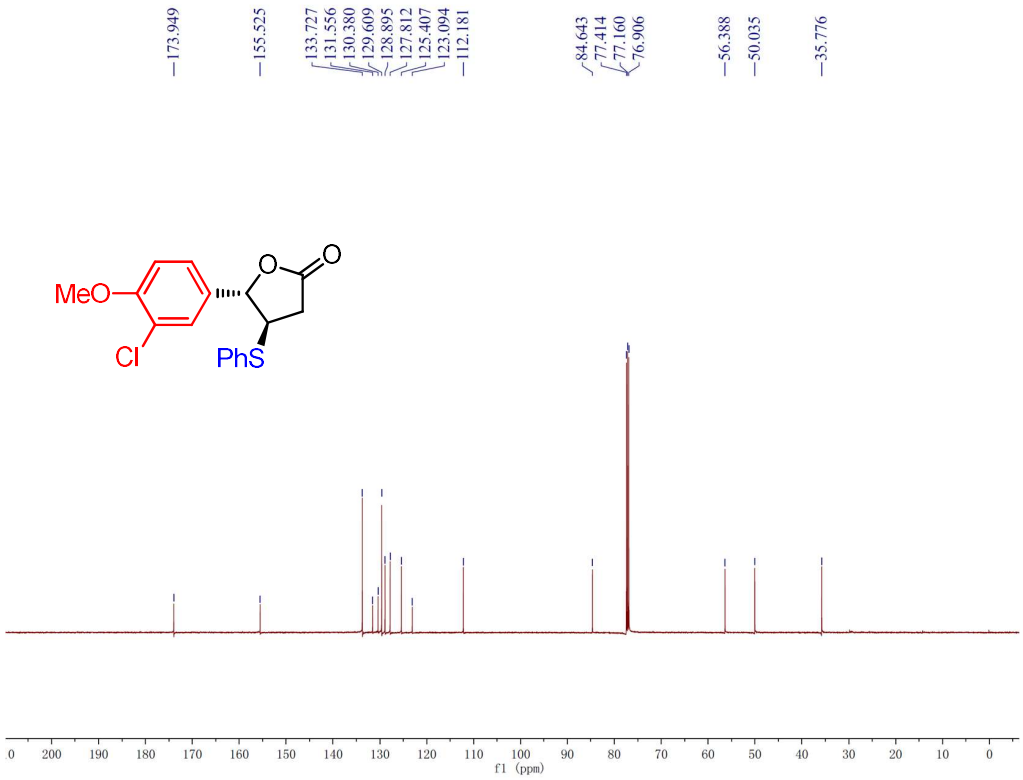
3.752
3.749
3.043
3.027
3.007
2.991
2.683
2.667
2.647
2.631


MeO
Cl
PhS
O
O
1.94
2.89
0.91
1.01
1.00
1.00
3.03
1.03
1.02
1.02
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)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129.609
128.895
127.812
125.407
123.094
112.181
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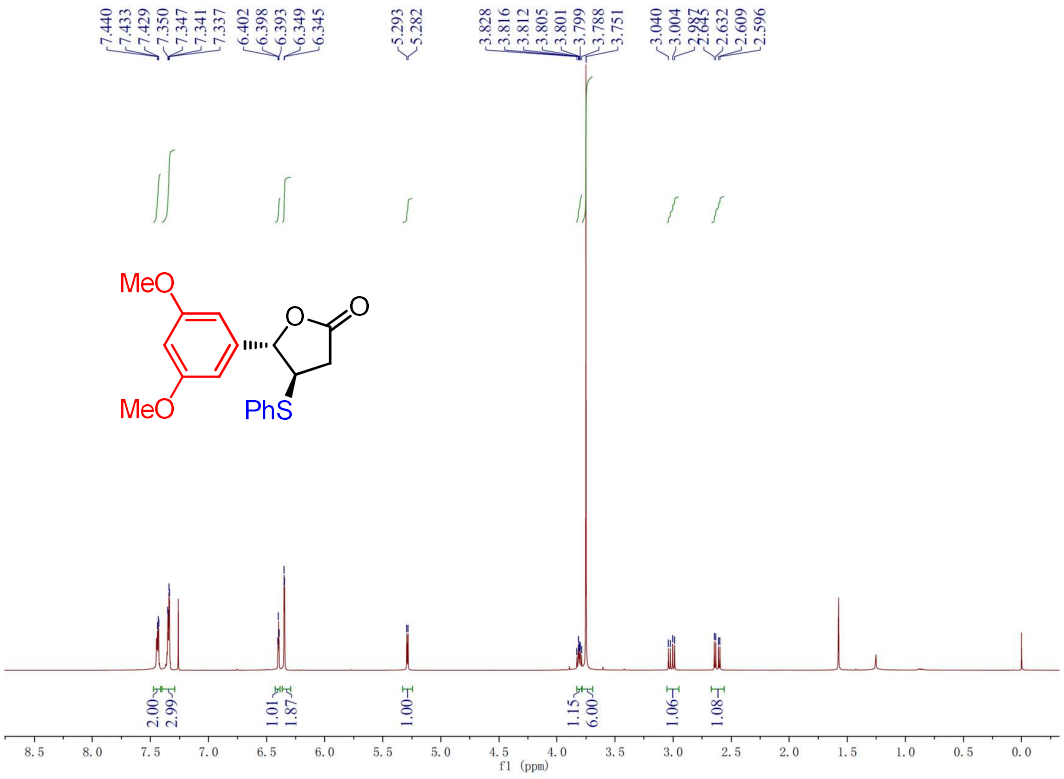
77.414
77.160
76.906
56.388
50.035
35.776
MeO
Cl
O
O
PhS
f1 (ppm)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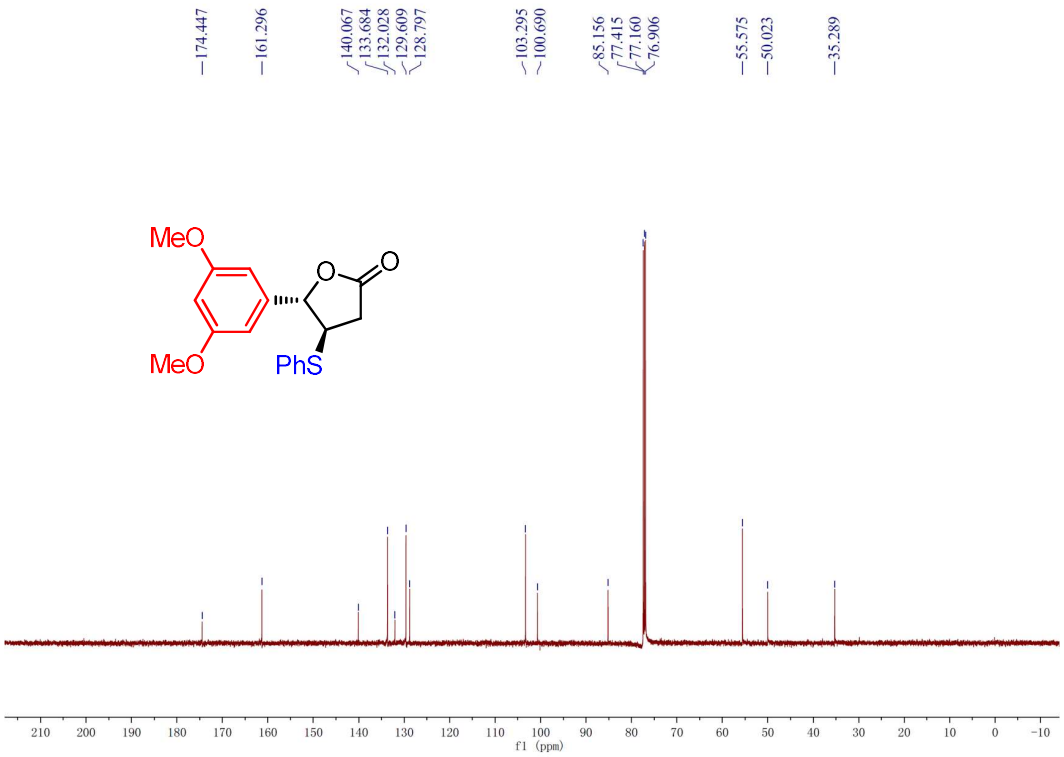
7.433
7.429
7.350
7.347
7.341
7.337
6.402
6.398
6.393
6.349
6.345
5.293
5.282
3.828
3.816
3.812
3.805
3.801
3.799
3.788
3.751
3.040
3.004
2.632
2.609
2.596
MeO
MeO
O
O
PhS
2.00
2.99
1.01
1.87
1.00
1.15
6.00
1.06
1.08
f1 (ppm)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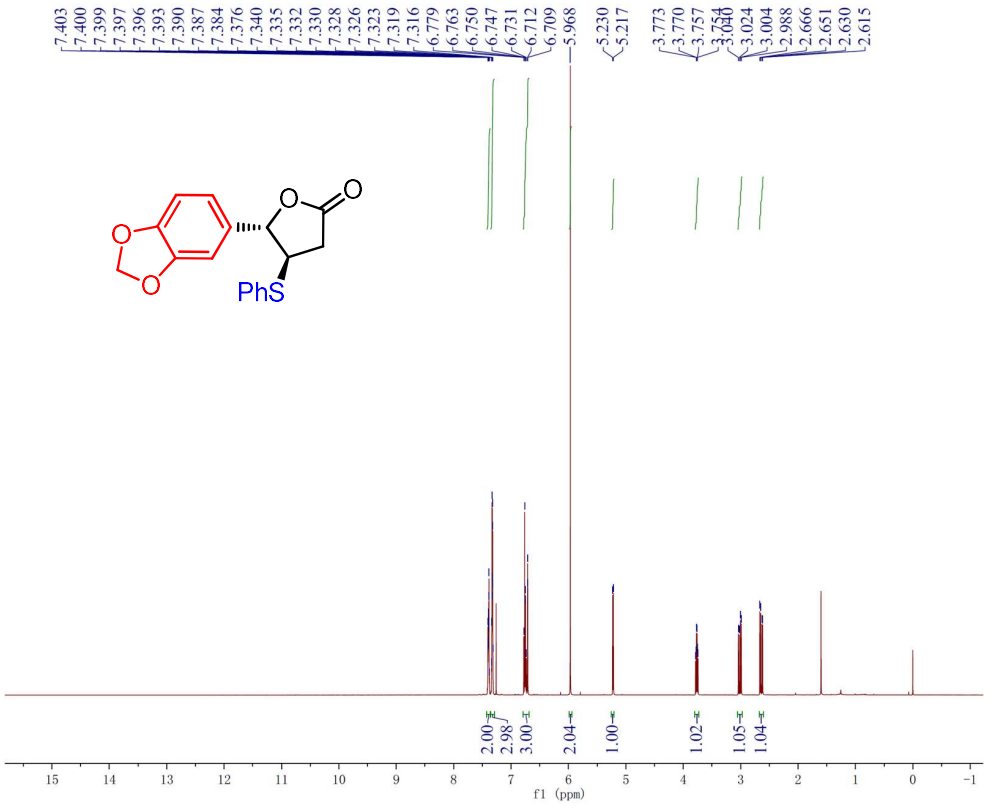
140.067
133.684
132.028
129.609
128.797
103.295
100.690
85.156
77.415
77.160
76.906
55.575
50.023
35.289
MeO
MeO
O
O
PhS
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)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7.399
7.397
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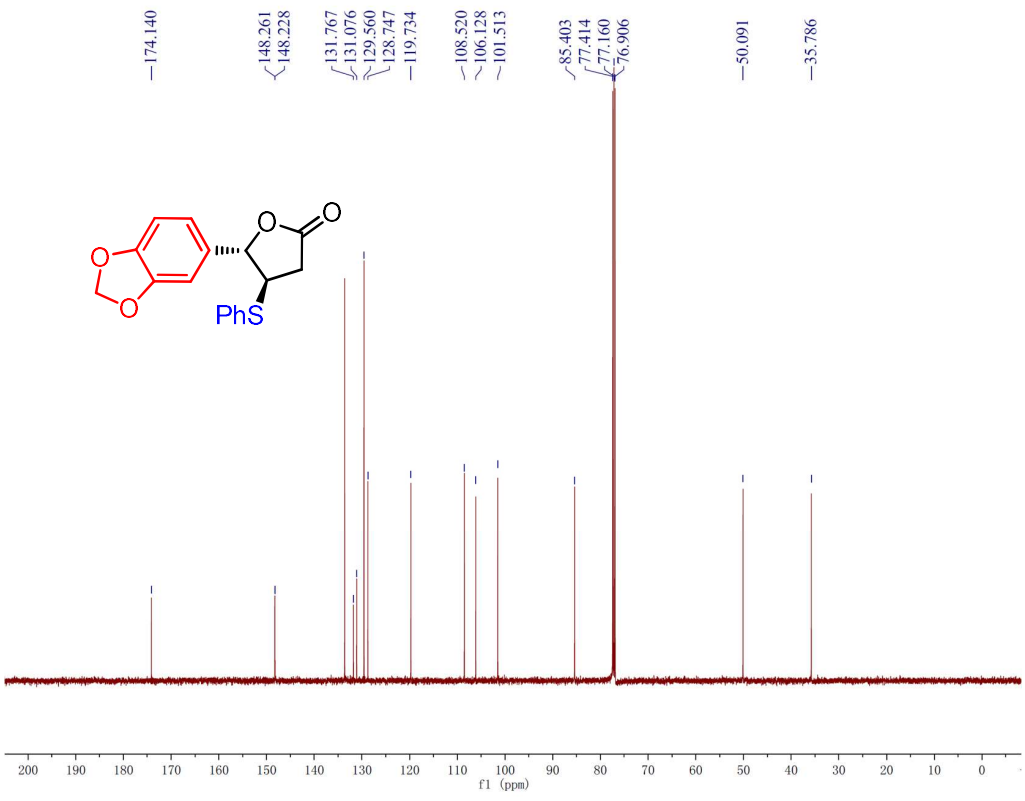
7.393
7.390
7.387
7.384
7.376
7.340
7.335
7.332
7.330
7.328
7.326
7.323
7.319
7.316
6.779
6.763
6.750
6.747
6.731
6.712
6.709
5.968
5.230
5.217
3.773
3.770
3.757
3.754
3.040
3.024
3.004
2.988
2.666
2.651
2.630
2.615
O
O
O
O
PhS
2.00
2.98
3.00
2.04
1.00
1.02
1.05
1.04
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1
f1 (ppm)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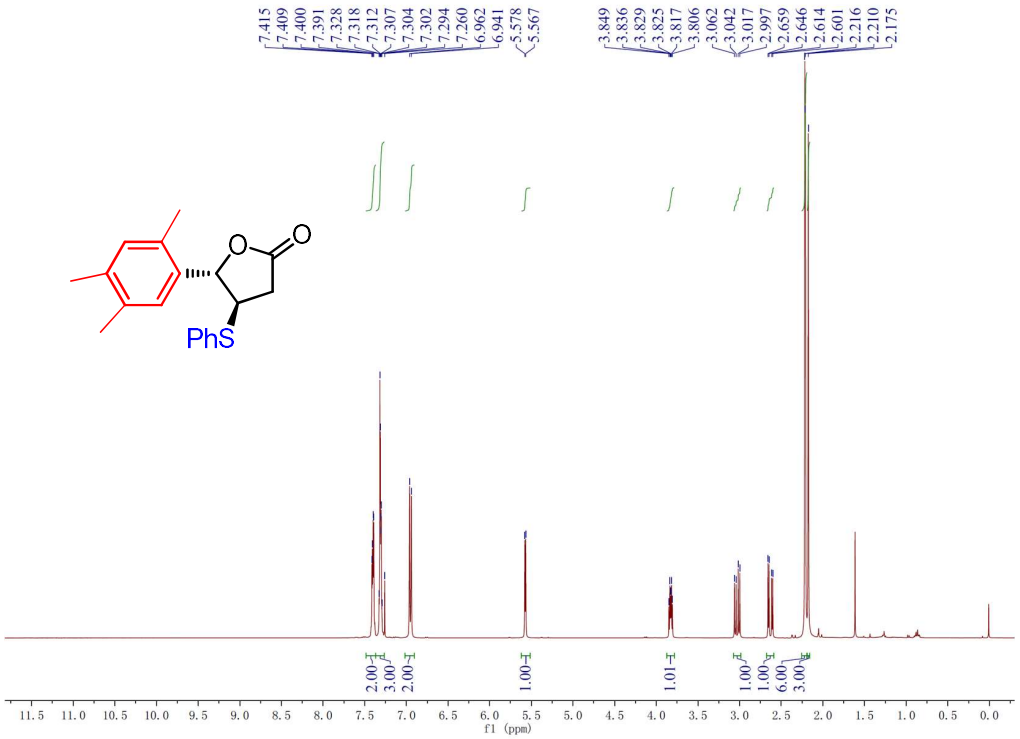
148.228
131.767
131.076
129.560
128.747
119.734
108.520
106.128
101.513
85.403
77.414
77.160
76.906
50.091
35.786
O
O
O
O
PhS
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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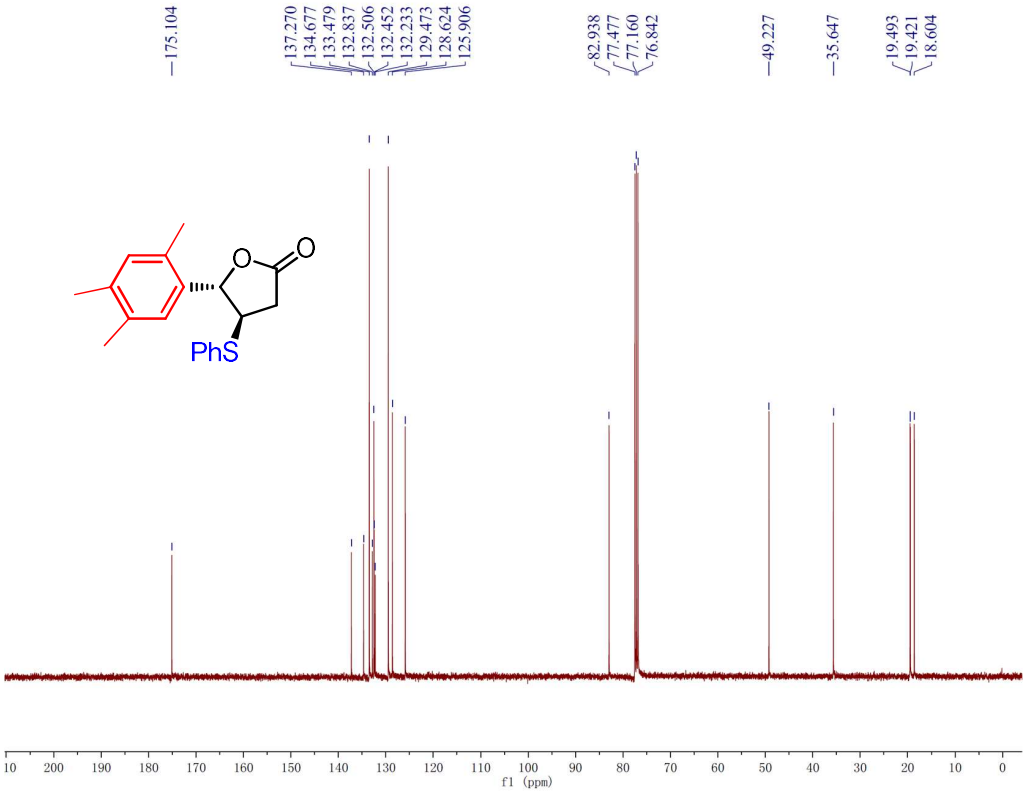
7.400
7.391
7.328
7.318
7.312
7.307
7.304
7.302
7.294
7.260
6.962
6.941
5.578
5.567
3.849
3.836
3.829
3.825
3.817
3.806
3.062
3.042
3.017
2.997
2.659
2.646
2.614
2.601
2.216
2.210
2.175
O
O
PhS
2.00
3.00
2.00
1.00
1.01
1.00
1.00
6.00
3.00
f1 (ppm)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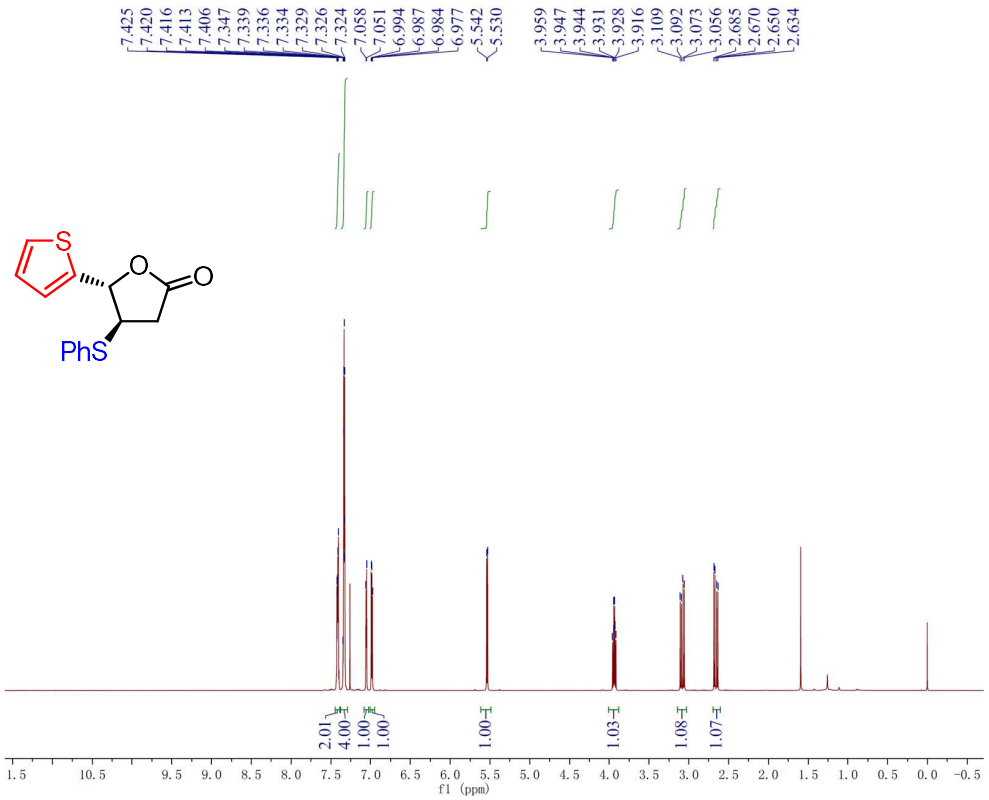
133.479
132.837
132.506
132.452
132.233
129.473
128.624
125.906
82.938
77.477
77.160
76.842
49.227
35.647
19.493
19.421
18.604
O
O
PhS
f1 (ppm)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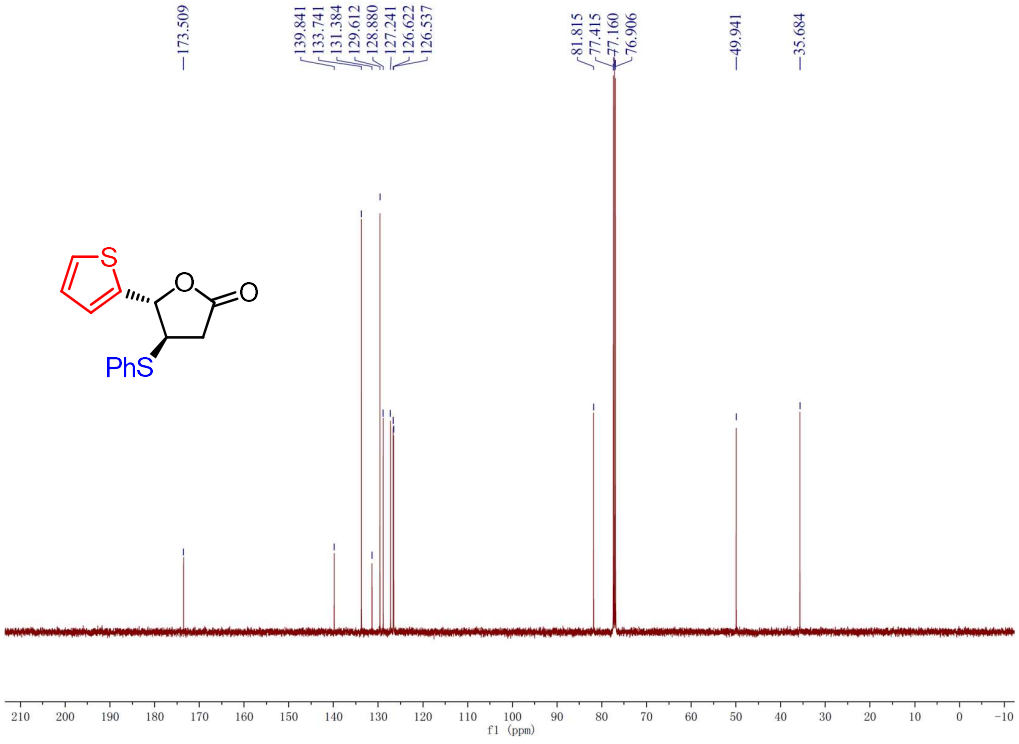
7.420
7.416
7.413
7.406
7.347
7.339
7.336
7.334
7.329
7.326
7.324
7.058
7.051
6.994
6.987
6.984
6.977
5.542
5.530
3.959
3.947
3.944
3.931
3.928
3.916
3.109
3.092
3.073
3.056
2.685
2.670
2.650
2.634
S
O
O
PhS
2.01
4.00
1.00
1.00
1.00
1.03
1.08
1.07
f1 (ppm)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128.880
127.241
126.622
126.537
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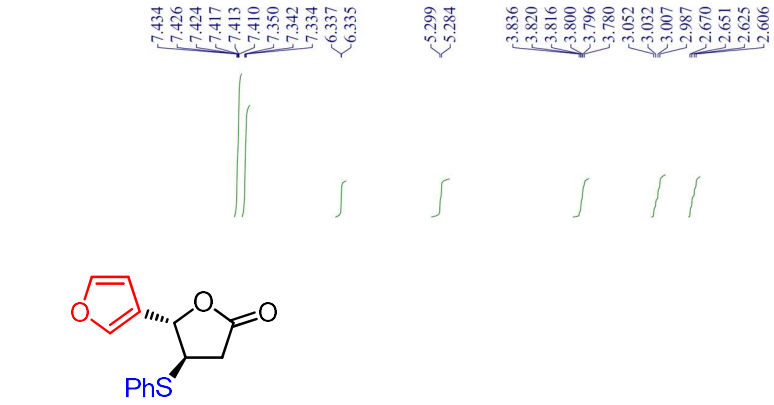
77.415
77.160
76.906
49.941
35.684
S
O
O
PhS
f1 (ppm)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7.342
7.334
6.337
6.335
5.299
5.284
3.836
3.820
3.816
3.800
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3.032
3.007
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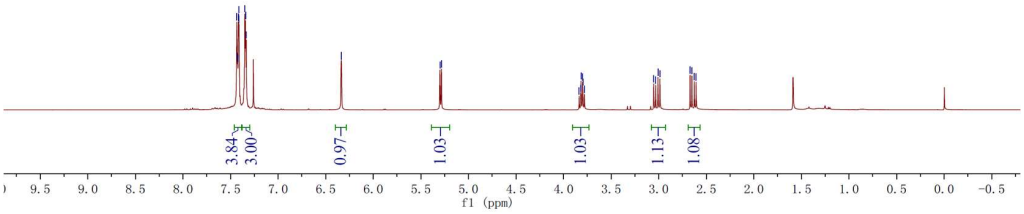
2.651
2.625
2.606
O
O
O
PhS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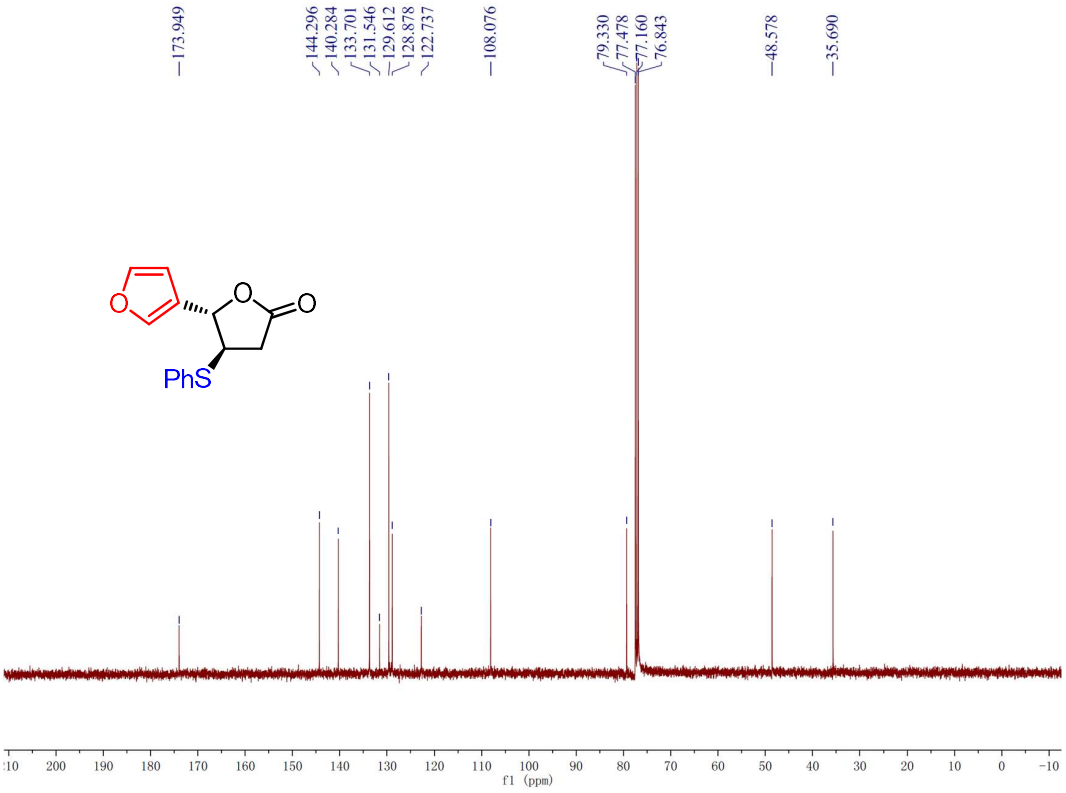
1.03
1.13
1.08
f1 (ppm)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128.878
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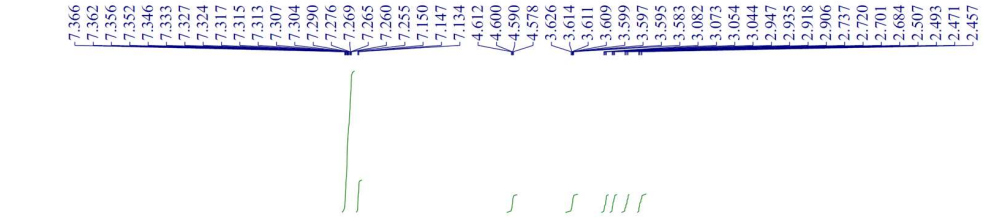
77.478
77.160
76.843
48.578
35.690
O
O
O
PhS
f1 (ppm)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7.327
7.324
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7.315
7.313
7.307
7.304
7.290
7.276
7.269
7.265
7.260
7.255
7.150
7.147
7.134
4.612
4.600
4.590
4.578
3.626
3.614
3.611
3.609
3.599
3.597
3.595
3.583
3.082
3.073
3.054
3.044
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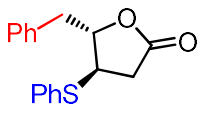
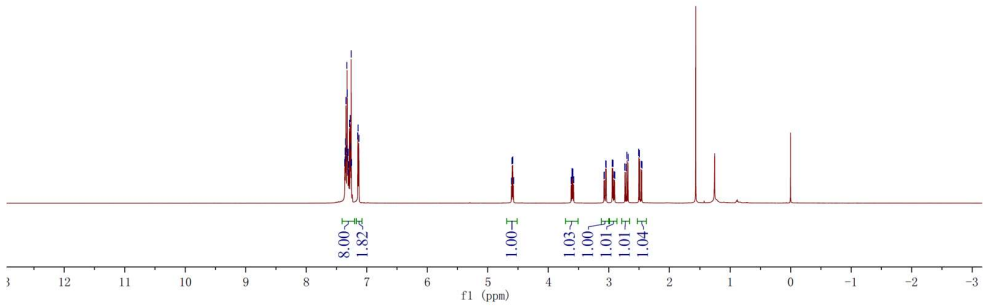
2.457


Ph
O
O
PhS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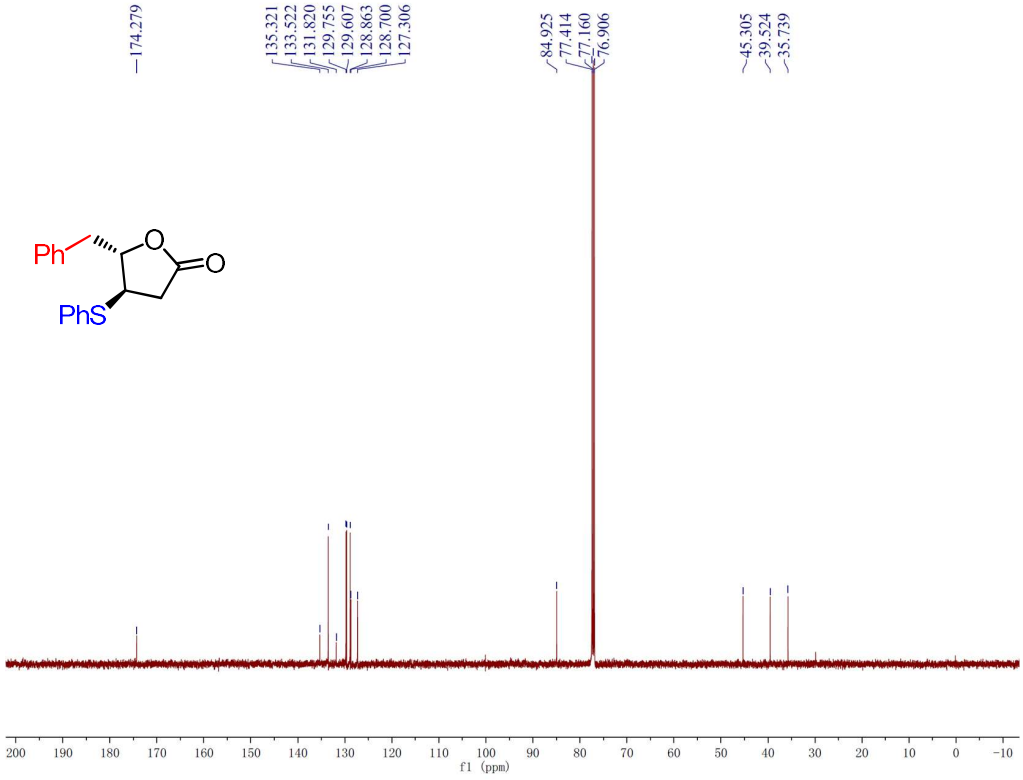
1.82
1.00
1.03
1.00
1.01
1.01
1.04
f1 (ppm)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129.755
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128.700
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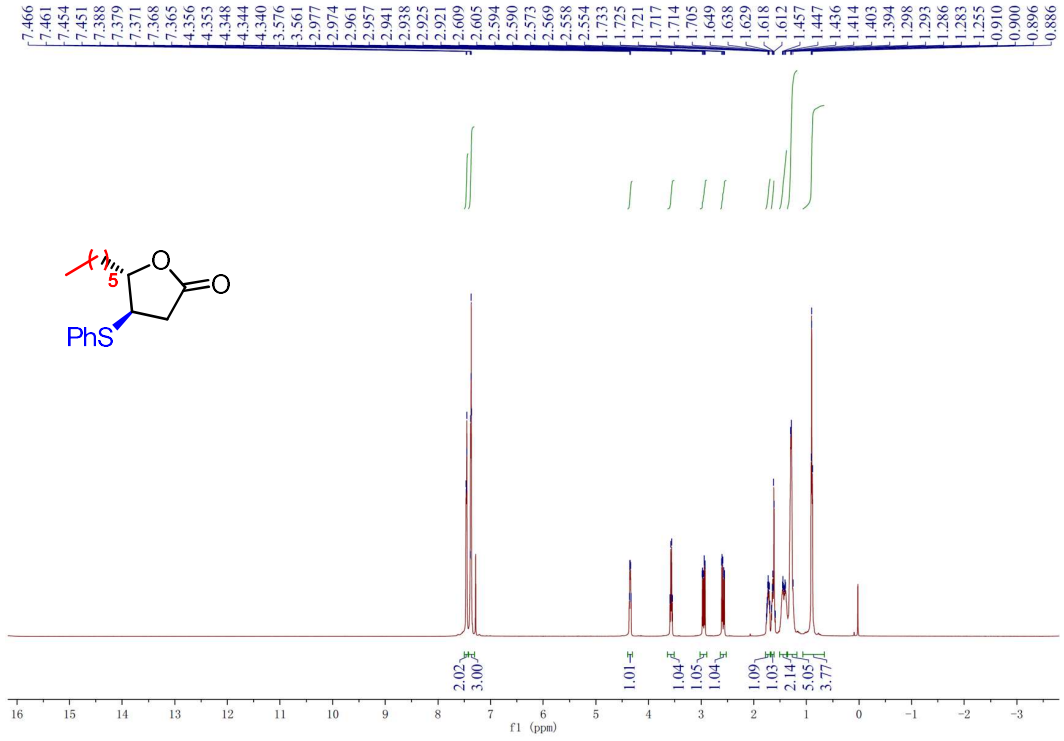
77.414
77.160
76.906
45.305
39.524
35.739
f1 (ppm)

Ph
O
O
PhS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4.348
4.344
4.340
3.576
3.561
2.977
2.974
2.961
2.957
2.941
2.938
2.925
2.921
2.609
2.605
2.594
2.590
2.573
2.569
2.558
2.554
1.733
1.725
1.721
1.717
1.714
1.705
1.649
1.638
1.629
1.618
1.612
1.457
1.447
1.436
1.414
1.403
1.394
1.298
1.293
1.286
1.283
1.255
0.910
0.900
0.896
0.886
O
O
5
PhS
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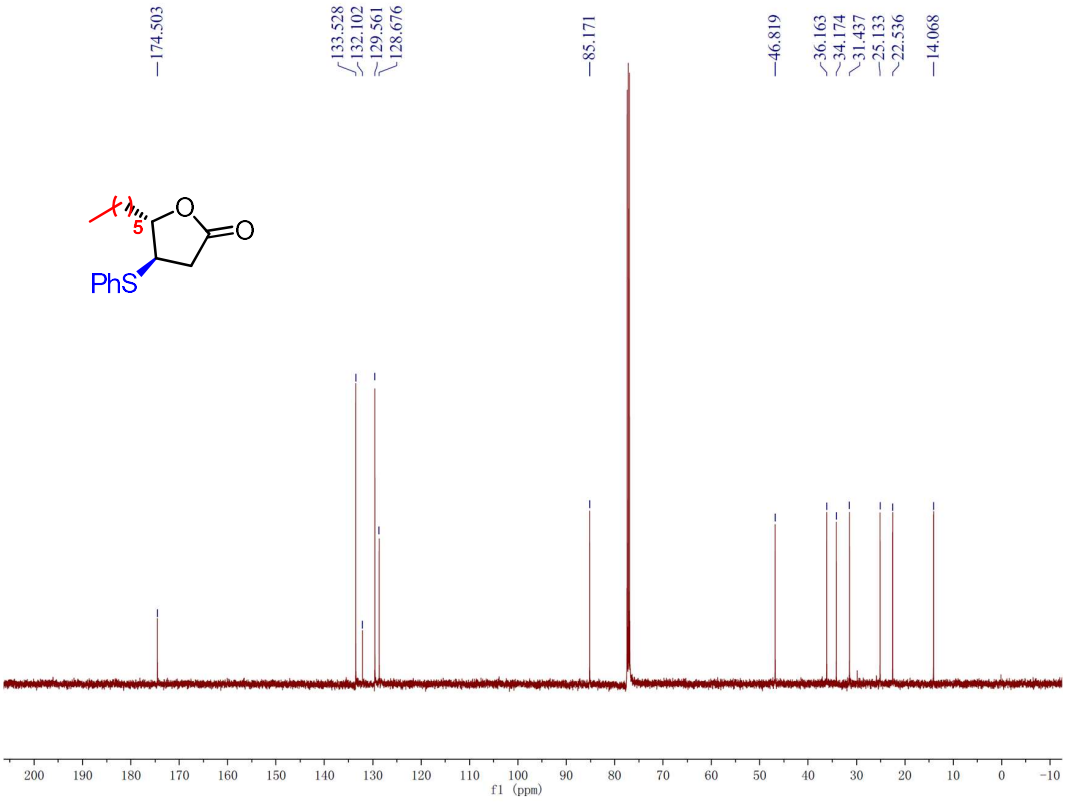
3.00
1.01
1.04
1.05
1.04
1.09
1.03
2.14
5.05
3.77
f1 (ppm)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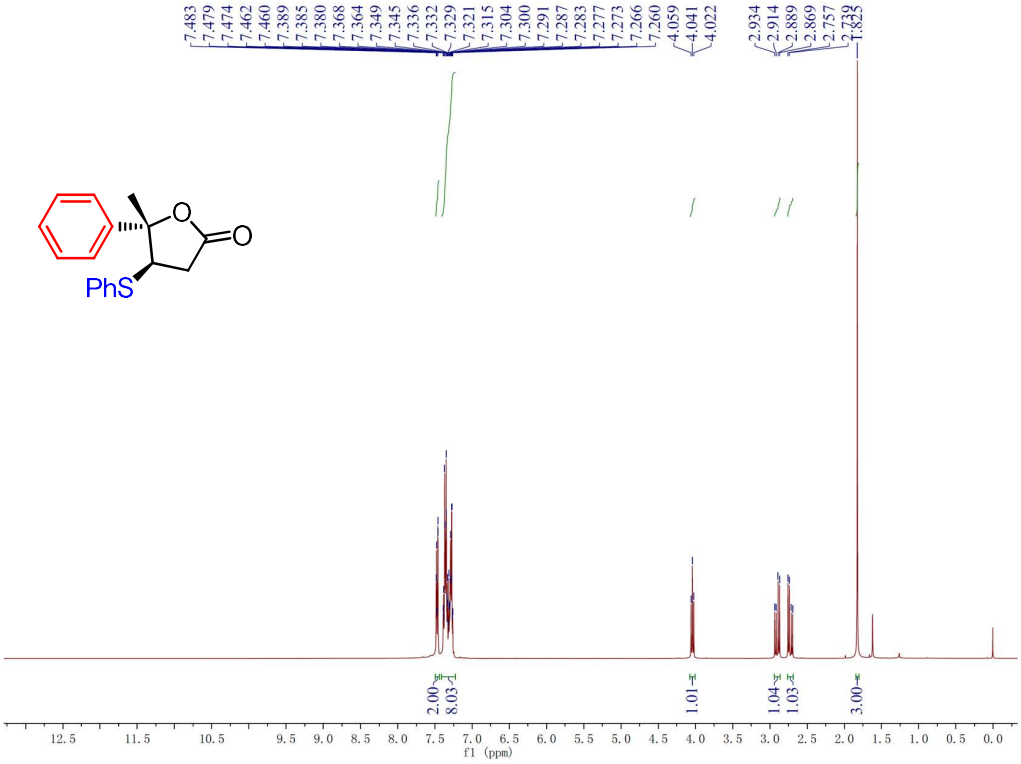
36.163
34.174
31.437
25.133
22.536
14.068
O
O
5
PhS
f1 (ppm)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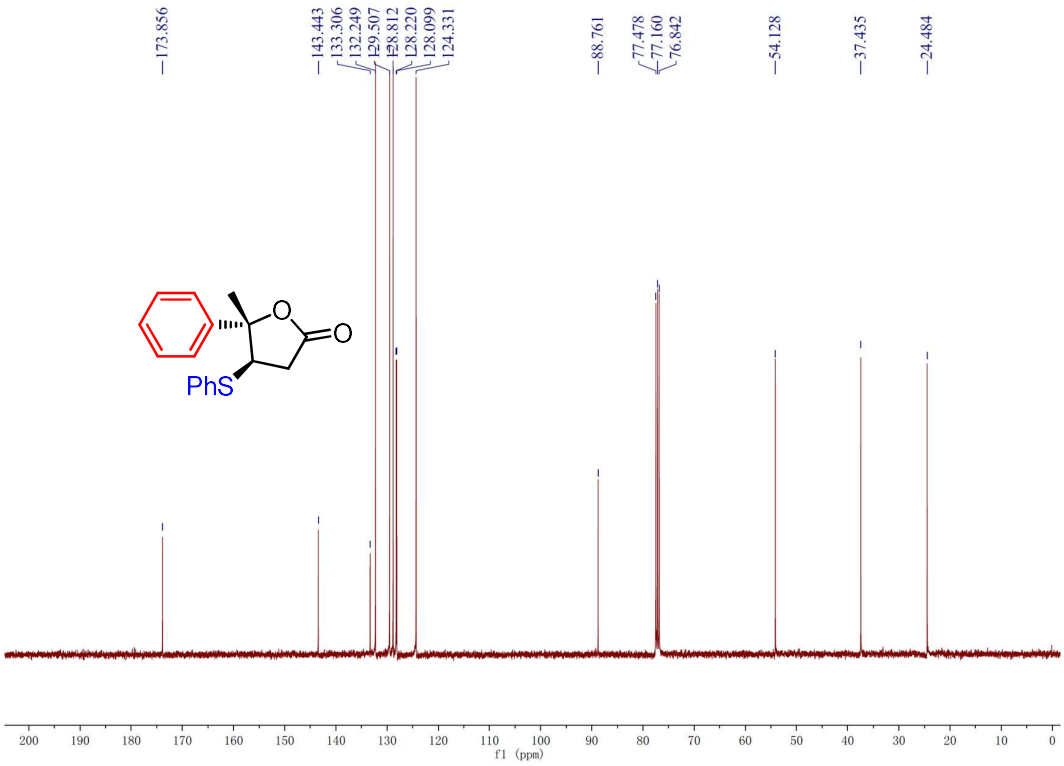
7.364
7.349
7.345
7.336
7.332
7.329
7.321
7.315
7.304
7.300
7.291
7.287
7.283
7.277
7.273
7.266
7.260
4.059
4.041
4.022
2.934
2.914
2.889
2.869
2.757
2.739
1.823
PhS
2.00
8.03
1.01
1.04
1.03
3.00
f1 (ppm)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132.249
129.507
128.812
128.220
128.099
124.331
88.761
77.478
77.160
76.842
54.128
37.435
24.484
PhS
f1 (ppm)


7.407
7.399
7.394
7.385
7.368
7.352
7.332
7.309
7.285
7.276
7.257
7.252
7.238
7.190
7.180
7.170
7.160
7.148
5.374
5.361
3.861
3.846
3.841
3.833
3.827
3.813
3.047
3.027
2.817
2.798
2.692
2.677
2.647
2.632
1.226
1.208
1.189
O
O
ArS
4.02
4.36
1.02
1.03
1.05
1.02
2.00
1.06
3.00
f1 (ppm)
174.677
146.773
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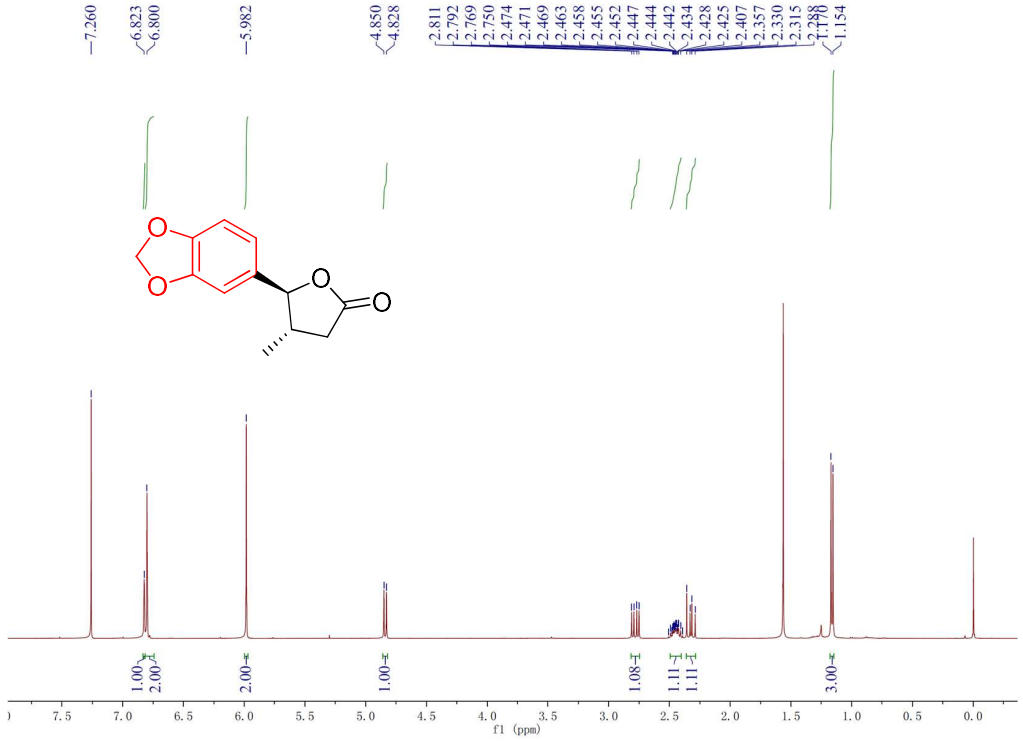
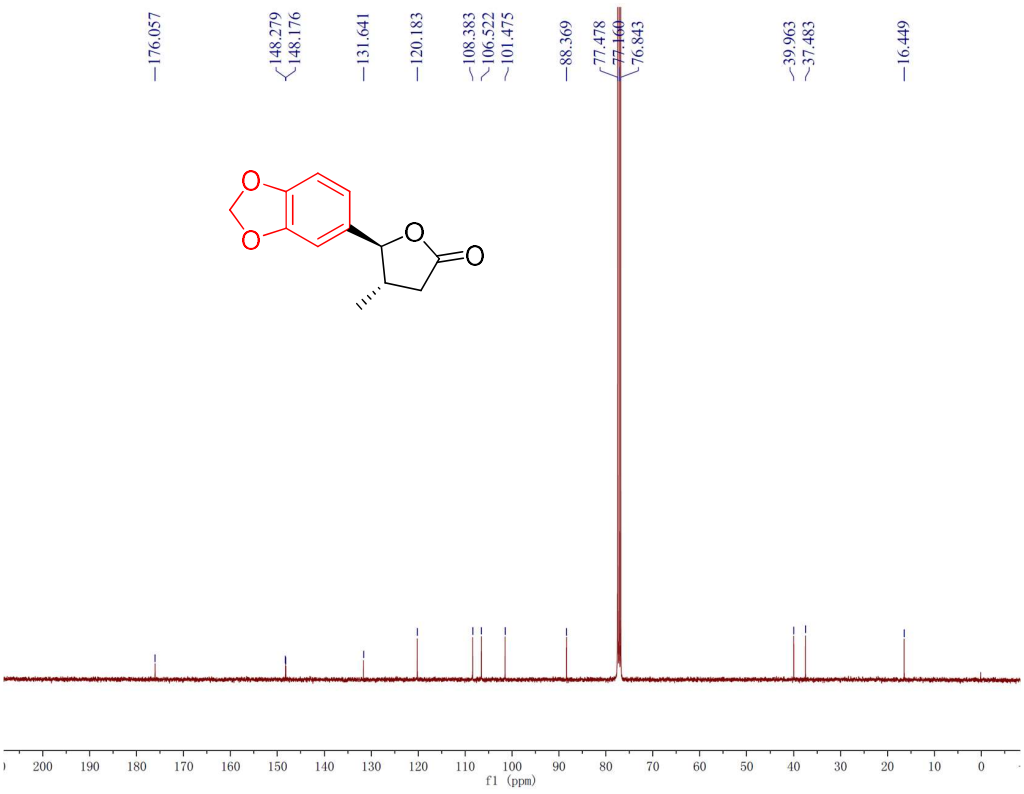
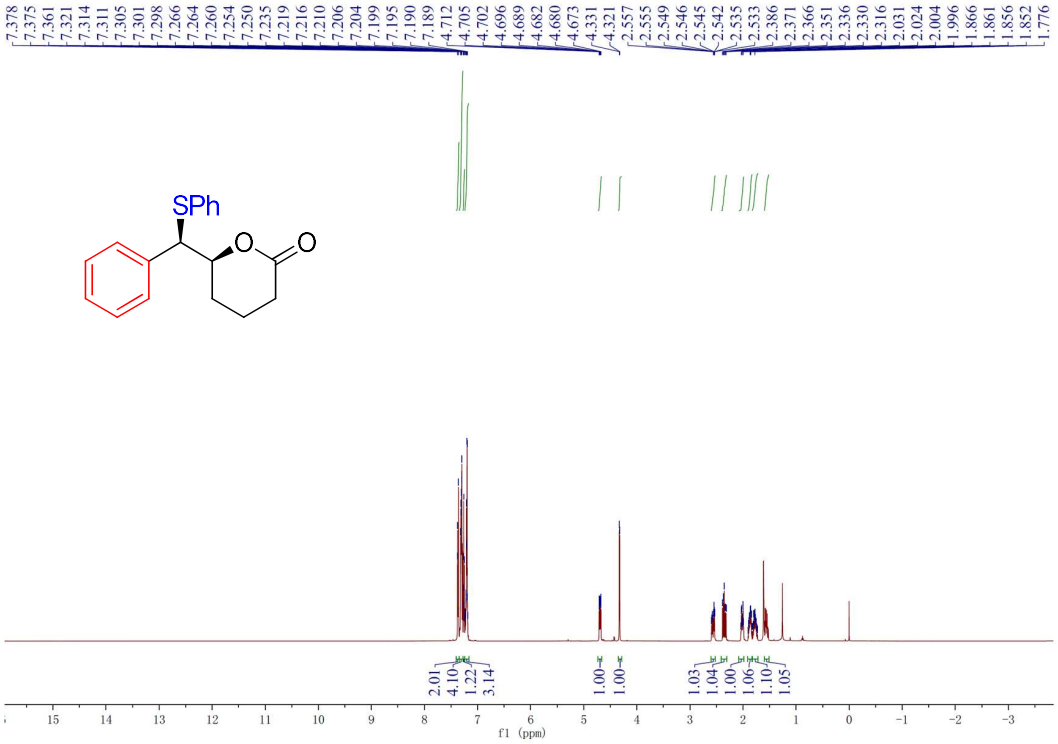
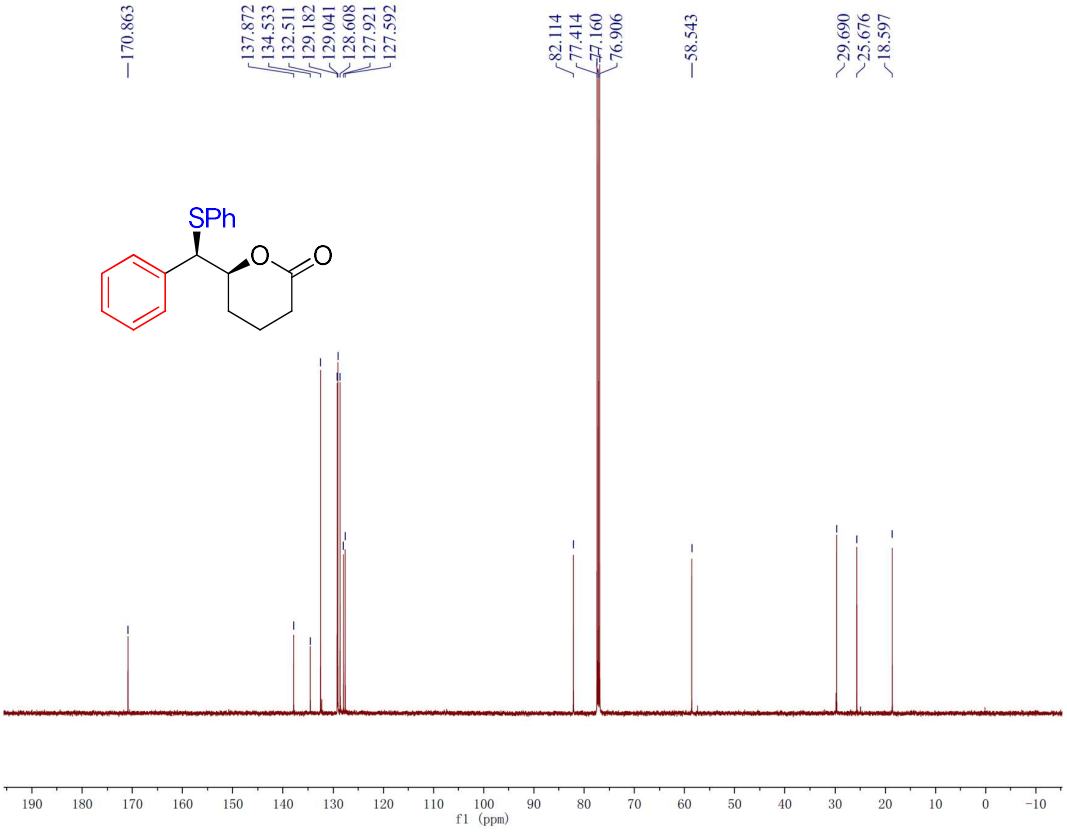
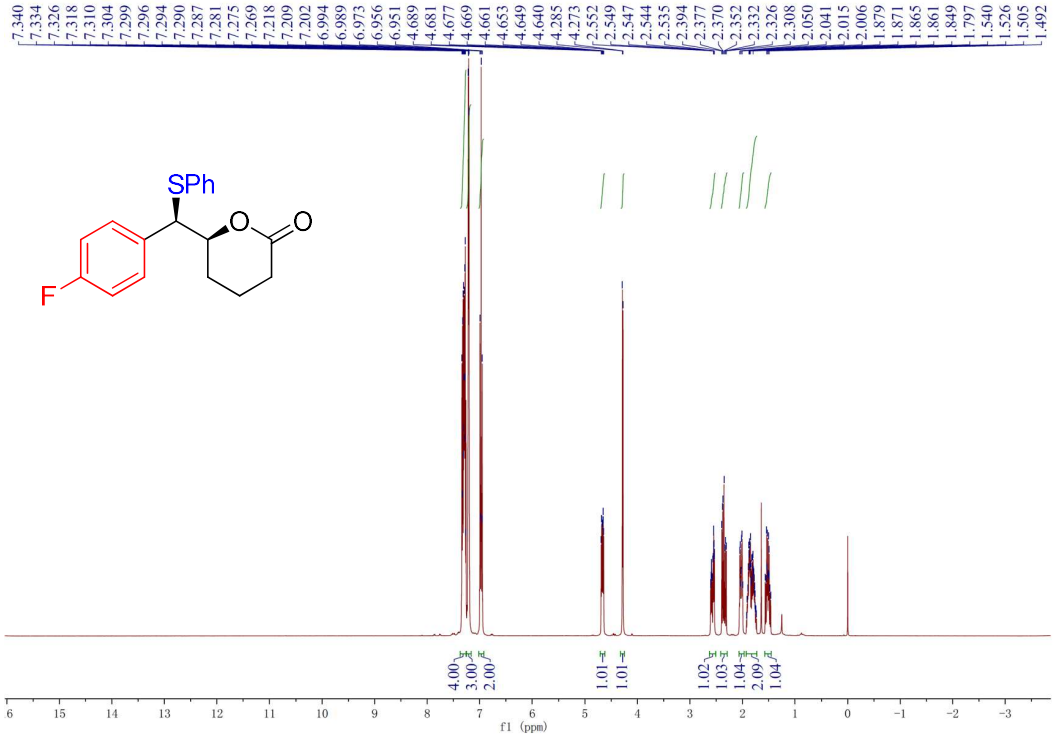
133.524
131.154
129.472
128.958
128.874
126.919
125.438
85.132
49.967
35.628
27.404
15.406
O
O
ArS
f1 (ppm)


7.260
6.823
6.800
5.982
4.850
4.828
2.811
2.792
2.769
2.750
2.474
2.471
2.469
2.463
2.458
2.455
2.452
2.447
2.444
2.442
2.434
2.428
2.425
2.407
2.357
2.330
2.315
1.170
1.154
1.00
2.00
2.00
1.00
1.08
1.11
1.11
3.00
f1 (ppm)

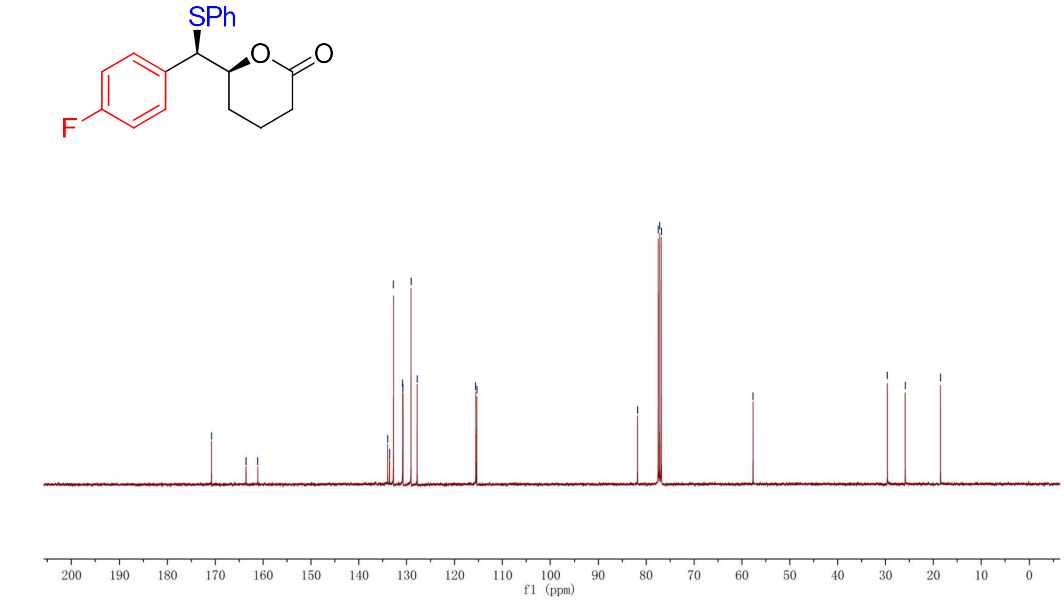

176.057
148.279
148.176
131.641
120.183
108.383
106.522
101.475
88.369
77.478
77.160
76.843
39.963
37.483
16.449
f1 (ppm)

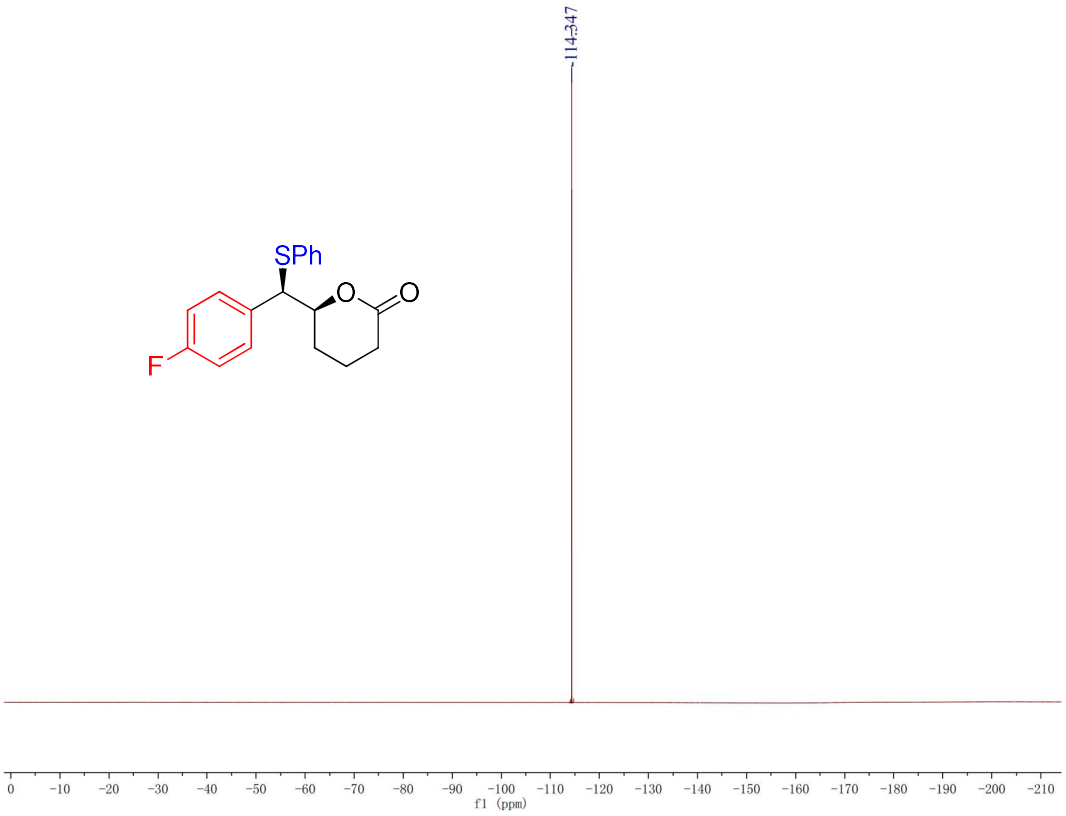

7.378
7.375
7.361
7.321
7.314
7.311
7.305
7.301
7.298
7.266
7.264
7.260
7.254
7.250
7.235
7.219
7.216
7.210
7.206
7.204
7.199
7.195
7.190
7.189
4.712
4.705
4.702
4.696
4.689
4.682
4.680
4.673
4.331
4.321
2.557
2.555
2.549
2.546
2.545
2.542
2.535
2.533
2.386
2.371
2.366
2.351
2.336
2.330
2.316
2.031
2.024
2.004
1.996
1.866
1.861
1.856
1.852
1.776
SPh
O
O
2.01
4.10
1.22
3.14
1.00
1.00
1.03
1.04
1.00
1.06
1.10
1.05
f1 (ppm)


170.863
137.872
134.533
132.511
129.182
129.041
128.608
127.921
127.592
82.114
77.414
77.160
76.906
58.543
29.690
25.676
18.597
SPh
O
O
f1 (ppm)


7.340
7.334
7.326
7.318
7.310
7.304
7.299
7.296
7.294
7.290
7.287
7.281
7.275
7.269
7.218
7.209
7.202
6.994
6.989
6.973
6.956
6.951
4.689
4.681
4.677
4.669
4.661
4.653
4.649
4.640
4.285
4.273
2.552
2.549
2.547
2.544
2.535
2.394
2.377
2.370
2.352
2.332
2.326
2.308
2.050
2.041
2.015
2.006
1.879
1.871
1.865
1.861
1.849
1.797
1.540
1.526
1.505
1.492
SPh
O
O
F
4.00
3.00
2.00
1.01
1.01
1.02
1.03
1.04
2.09
1.04
f1 (ppm)


170.755
163.546
161.094
133.967
133.605
133.572
132.770
130.844
130.763
129.096
127.825
115.574
115.360
81.816
77.478
77.160
76.843
57.671
29.612
25.915
18.524


SPh
O
O
F
f1 (ppm)


-114.347
SPh
O
O
F
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)