Supplementary information for

Bifunctional Iminophosphorane Catalyzed Enantioselective Sulfa-Michael Addition to Unactivated α-Substituted Acrylate Esters

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1. Supplementary Methods

1.1 General information

Solvents and Reagents

Concentration under reduced pressure was performed by rotary evaporation at the appropriate pressure and temperature. Reagents used were obtained from commercial suppliers or purified according to standard procedures. Petroleum ether refers to distilled light petroleum of fraction 30 - 40 °C. Anhydrous toluene, tetrahydrofuran, dichloromethane and diethyl ether were dried by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic, Sigma-Aldrich) columns. Dimethyl sulfoxide and dimethylformamide were used as supplied. Deuterated solvents were used as supplied.

Chromatography

Reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F_{254} plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained with potassium permanganate solution. Flash column chromatography (FCC) was performed on VWR 60 silica gel 40 - 63 μm using technical grade solvents that were used as supplied.

Instrumentation

Melting points were obtained on a Leica Galen III Hot-stage melting point apparatus and microscope and on a Kofler hot block and are reported uncorrected. NMR spectra were recorded on a Bruker Spectrospin spectrometer operating at 200, 400 or 500 MHz (^{1}H acquisitions), 50, 100 or 125 MHz (^{13}C acquisitions),. Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard (e.g. Chloroform δ 7.27 ppm for ^{1}H and 77.0 ppm for ^{13}C). Coupling constants (*J*) are reported in hertz (Hz), and rounded to the nearest 0.5 Hz. Data are reported as follows: multiplicity [s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublets of doublets, td = triplet of doublets, m = multiplet, br = broad], coupling constants in Hz, integration. Two-dimensional spectroscopy (COSY, HSQC and HMBC) was used to assist in the assignment and the data is not reported. High-resolution mass spectra (ESI) were recorded on Bruker μTOF mass spectrometer. Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer as a thin film. Only selected maximum absorbances are reported. Optical rotations were recorded using a Perkin Elmer 341 polarimeter; $[\alpha]_D^T$ values are reported in 10^{-1} deg cm^2 g^{-1}; concentrations (c) are quoted in g/100 mL; D refers to the D-line of sodium (589 nm); temperatures (T) are given in degrees Celsius (°C). (+) and (–) compound number prefixes indicate the sign of

the optical rotation. The enantiomeric excesses were determined by HPLC analysis on an Agilent 1200 Series instrument or by GC analysis on an Agilent 7820A instrument employing a chiral stationary phase column specified in the individual experiment and by comparing the samples with the appropriate racemic mixtures.

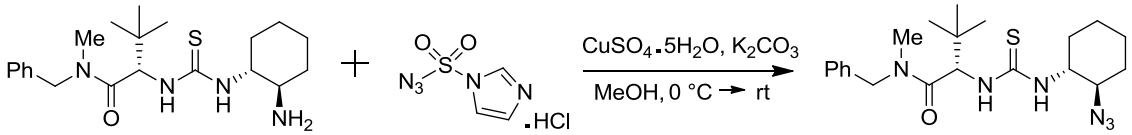
1.2 Synthesis and Characterization of Catalysts 1a – m Precursors

Catalysts **1a – g** were prepared using the methods reported previously in the literature.[1] In the preparation of catalyst **1h**, the primary amine intermediate **6** was synthesized according to a literature procedure.[2]

Unless otherwise stated, all synthesized azides were concentrated under reduced pressure by rotary evaporation inside a fume cupboard behind a blast shield at T < 25 ºC.

1.2.1 Synthesis of Catalyst 1h Precursor

(2*S*)-2-({[(1*R*,2*R*)-2-Azidocyclohexyl]carbamothioyl}amino)-*N*-benzyl-*N*,3,3-trimethylbutanamide (7)



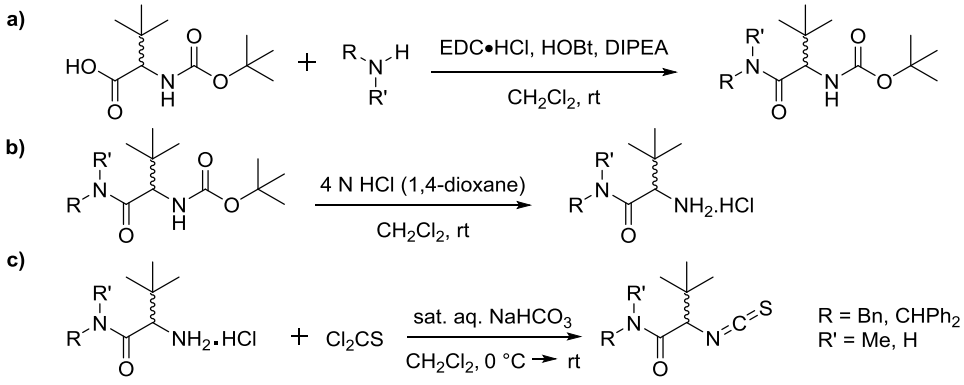
To a solution of (2*S*)-2-({[(1*R*,2*R*)-2-aminocyclohexyl]carbamothioyl}amino)-*N*-benzyl-*N*,3,3-trimethylbutanamide[2] (**6**) (100 mg, 0.266 mmol, 1.00 eq), copper sulfate pentahydrate (1 mg, 0.004 mmol, 1 mol%) and potassium carbonate (63 mg, 0.45 mmol, 1.7 eq) in MeOH (2.0 mL) under an Ar atmosphere at 0 °C was added 1*H*-imidazole-1-sulfonyl azide hydrochloride [3,4] (55 mg, 0.32 mmol, 1.2 eq), and the reaction mixture was warmed to rt and stirred for 15 h. The volatiles were removed under a stream of N_2 and the resulting crude mixture dissolved in H_2O/Et_2O (1:1 v/v, 10 mL). The organic phase was extracted using Et_2O (2 x 10 mL), washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The reaction was purified by FCC (petroleum ether/Et_2O = 4/1 to 1/1) to afford the title compound **7** as a colorless solid in 45% yield (48 mg).

$[\alpha]_D^{20}$ = -17.4 (*c* 1.21, $CHCl_3$); **MP** 154-158 °C; **IR** (film) ν_{max}/cm^{-1}: 3282 (thiourea NH), 2938, 2094, 1622 (C=O), 1535 (C=S), 1451, 1416, 1260, 756, 701; **^{1}H NMR** ($CDCl_3$, 400 MHz, compound exists as ~4.1:1 mixture of rotamers, major rotamer identified by *) δ (ppm): 7.44 - 7.19 (m, 5 H, ArH* and ArH), 7.12 (d, *J* = 7.5 Hz, 1 H, one of NH*C(=S)NH or NHC(=S)NH*), 7.00 (d,

J = 9.0 Hz, 1 H, one of NHC(=S)NH or NHC(=S)NH), 6.56 (d, *J* = 7.5 Hz, 1 H, one of NH*C(=S)NH or NHC(=S)NH*), 6.45 (d, *J* = 8.0 Hz, 1 H, one of NHC(=S)NH or NHC(=S)NH), 5.85 (d, *J* = 8.0 Hz, 1 H, C(=O)CH(^{t}Bu)), 5.68 (d, *J* = 9.5 Hz, 1 H, C(=O)CH*(^{t}Bu)), 5.02 (d, *J* = 15.5 Hz, 1 H, PhCH$_A$H$_B$N), 4.87 (d, *J* = 14.5 Hz, 1 H, PhCH$_A$*H$_B$N), 4.60 (d, *J* = 15.5 Hz, 1 H, PhCH$_A$H$_B$N), 4.34 (d, *J* = 14.5 Hz, 1 H, PhCH$_A$H$_B$*N), 3.27 - 3.17 (m, 4 H, PhCH$_2$N(CH$_3$*), CH*N$_3$ and CHN$_3$), 2.86 (s, 3 H, PhCH$_2$N(CH$_3$)), 2.17 - 1.93 (m, 2 H, CH*NHC(=S), CHNHC(=S) and 1 H* of cyclohexane), 1.83 - 1.56 (m, 3 H, 3 H*/3 H of cyclohexane), 1.53 - 1.14 (m, 5 H, 5 H*/5 H of cyclohexane), 1.10 (s, 9 H, C(CH$_3$*)$_3$), 1.07 (s, 9 H, C(CH$_3$)$_3$); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ (ppm): 181.9 (C*=S and C=S), 172.2 (C*=O and C=O), 136.7 (ArC*), 136.1 (ArC), 128.7, 128.7 (ArC*H and ArCH), 128.1 (ArCH), 128.0 (ArC*H), 127.8 (ArCH), 127.5 (ArC*H), 65.4 (CHN$_3$), 65.2 (C*HN$_3$), 60.8 (C*H(^{t}Bu)), 60.7 (CH(^{t}Bu)), 56.9 (C*(CH$_3$)$_3$), 56.8 (C(CH$_3$)$_3$), 54.4 (PhCH$_2$N), 51.4 (PhC*H$_2$N), 36.5 (CHNH(=S), 36.3 (C*HNH(=S)), 36.2 (PhCH$_2$N(C*H$_3$)), 33.4 (PhCH$_2$N(CH$_3$)), 32.0 (1 C of cyclohexane), 31.9 (1 C* of cyclohexane), 30.7 (1 C of cyclohexane), 30.6 (1 C* of cyclohexane), 26.8 (C(CH$_3$)$_3$), 26.8 (C(C*H$_3$)$_3$), 24.1 (1 C of cyclohexane), 24.1 (1 C* of cyclohexane), 23.8 (1 C of cyclohexane), 23.7 (1 C* of cyclohexane); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{21}H_{32}N_6NaOS$) requires *m/z* 439.2251, found *m/z* 439.2233.

1.2.3 Synthesis of Isothiocyanate Precursors to Catalysts 1j-m

General Procedure A for Synthesis of Isothiocyanates:



According to a literature procedure,[2]

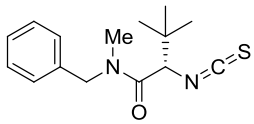
a) To a stirred solution of EDC hydrochloride (421 mg, 2.20 mmol, 1.10 eq) and 1-hydroxybenzotriazole hydrate (298 mg, 2.20 mmol, 1.10 eq) in CH_2Cl_2 (10 mL) under a N_2 atmosphere at rt was added *N*,*N*-diisopropylethylamine (0.52 mL, 3.0 mmol, 1.5 eq) and the corresponding *amine* (2.20 mmol, 1.10 eq) sequentially. Boc-L-*tert*-leucine (463 mg, 2.00 mmol, 1.00 eq) was added in one portion and the reaction mixture was stirred for 20 h. The reaction was diluted with Et_2O (10 mL), washed with 0.5 N HCl (2 x 10 mL) and the organic phase extracted

with Et_2O (5 mL). The combined organic was washed with sat. aq. $NaHCO_3$ (10 mL) and brine (10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford the product, which was used crude without further purification.

b) To a vigorously stirred solution of the crude product in CH_2Cl_2 (5.0 mL) under a N_2 atmosphere at rt was added 4 N HCl in 1,4-dioxane (4.8 mL, 19 mmol, 9.6 eq) over 5 min. The reaction mixture was stirred for 3.5 h and concentrated *in vacuo* to afford the product which was used crude without further purification.

c) To a vigorously stirred solution of the crude product in CH_2Cl_2 (20 mL) under a N_2 atmosphere at 0 °C was added sat. aq. $NaHCO_3$ (20 mL), and the biphasic mixture was stirred for 20 min. Stirring was stopped and thiophosgene (153 μL, 2.00 mmol, 1.00 eq) was added to the organic layer. Immediately, vigorous stirring was restored and the mixture allowed to warm to rt over 30 min. The organic phase was extracted with CH_2Cl_2 (2 x 20 mL), washed with brine (20 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to afford the crude product.

(2*S*)-*N*-Benzyl-2-isothiocyanato-*N*,3,3-trimethylbutanamide (8)



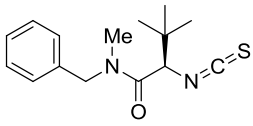
N-Boc-L-*tert*-leucine (463 mg, 2.00 mmol, 1.00 eq) was reacted with *N*-benzylmethylamine (284 μL, 2.20 mmol, 1.10 eq) according to general procedure **A** to afford the title compound **8** as a yellow oil in 56% yield (312 mg).

$[\alpha]_D^{20}$ = +155.2 (*c* 0.61, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2967, 2080 (NCS), 1656 (C=O), 1369, 1094, 769, 701; **^{1}H NMR** ($CDCl_3$, 400 MHz, compound exists as ~1.9:1 mixture of rotamers, major rotamer identified by *) δ (ppm): 7.45 - 7.25 (m, 4 H, Ar<u>H*</u> and Ar<u>H</u>), 7.19 - 7.14 (m, 1 H, Ar<u>H*</u> and Ar<u>H</u>), 4.79 (d, *J* = 14.0 Hz, 1 H, PhC<u>H_A*</u>H_BN), 4.75 (d, *J* = 16.0 Hz, 1 H, PhC<u>H_A</u>H_BN), 4.49 (d, *J* = 14.5 Hz, 1 H, PhCH_A<u>H_B*</u>N), 4.45 (d, *J* = 16.0 Hz, 1 H, PhCH_A<u>H_B</u>N), 4.28 (s, 1 H, C<u>H*</u>(^{t}Bu)), 4.22 (s, 1 H, C<u>H</u>(^{t}Bu)), 3.01 (s, 3 H, PhCH_2N(C<u>H_3</u>)), 2.99 (s, 3 H, PhCH_2N(C<u>H_3*</u>)), 1.12 (s, 9 H, C(C<u>H_3*</u>)$_3$), 1.11 (s, 9 H, C(C<u>H_3</u>)$_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz, major rotamer identified by *)[i] δ (ppm): 166.9 (<u>C</u>=O), 166.5 (<u>C*</u>=O), 136.6 (Ar<u>C*</u>), 135.6 (Ar<u>C</u>), 129.2 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 128.8 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 128.4 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 128.1 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 127.8 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 126.3 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 64.2 (<u>C</u>H(^{t}Bu)), 64.1 (<u>C*</u>H(^{t}Bu)), 54.0 (Ph<u>C</u>H_2N), 51.7 (Ph<u>C*</u>H_2N), 37.7 (CH<u>C*</u>(CH_3)$_3$), 37.5 (CH<u>C</u>(CH_3)$_3$), 35.7 (PhCH_2N(<u>C*</u>H_3)),

[i] Quaternary carbon N<u>C</u>S not found in spectrum.

34.9 ($PhCH_2N(\underline{C}H_3)$), 26.5 ($C(\underline{C}^*H_3)_3$ and $C(\underline{C}H_3)_3$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{20}N_2NaOS$) requires *m/z* 299.1189, found *m/z* 299.1175.

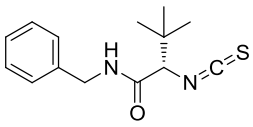
(2*R*)-*N*-Benzyl-2-isothiocyanato-*N*,3,3-trimethylbutanamide (9)



N-Boc-D-*tert*-leucine (980 mg, 4.24 mmol, 1.00 eq) was reacted with *N*-benzylmethylamine (0.94 mL, 4.66 mmol, 1.10 eq) according to general procedure **A** to afford the title compound **9** as an orange oil in 67% yield (787 mg).

$[\alpha]_D^{20}$ = -107.2 (*c* 2.14, $CHCl_3$). All other characterisation data agree with the enantiomer **8**.

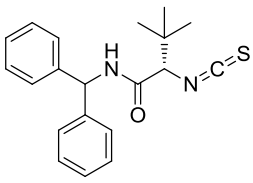
(2*S*)-*N*-Benzyl-2-isothiocyanato-3,3-dimethylbutanamide (10)



N-Boc-L-*tert*-leucine (600 mg, 2.59 mmol, 1.00 eq) was reacted with benzylamine (311 μL, 2.85 mmol, 1.10 eq) according to general procedure **A** to afford the title compound **10** as a yellow solid in 61% yield (412 mg).

$[\alpha]_D^{24}$ = +15.4 (*c* 1.51, $CHCl_3$); **MP** 106-109 °C; **IR** (film) ν_{max}/cm^{-1}: 3392 (NH), 2968, 2074 (NCS), 1658 (C=O), 1549, 1370, 1305, 1247, 750, 698; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.40 - 7.28 (m, 5 H, Ar$\underline{H}$), 6.30 (br s, 1 H, N$\underline{H}$), 4.53 (dd, *J* = 15.0, 6.0 Hz, 1 H, $PhC\underline{H}_AH_BNH$), 4.44 (dd, *J* = 15.0, 5.5 Hz, 1 H, $PhCH_A\underline{H}_BNH$), 4.09 (s, 1 H, $C\underline{H}(^tBu)$), 1.10 (s, 9 H, $C(C\underline{H}_3)_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz)[ii] δ (ppm): 166.1 ($\underline{C}$=O), 137.4 (Ar$\underline{C}$), 128.9 (Ar$\underline{C}$H), 127.9 (Ar$\underline{C}$H), 127.9 (Ar$\underline{C}$H), 71.0 ($\underline{C}H(^tBu)$), 43.9 ($Ph\underline{C}H_2NH$), 37.0 ($\underline{C}(CH_3)_3$), 26.7 ($C(\underline{C}H_3)_3$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{18}N_2NaOS$) requires *m/z* 285.1032, found *m/z* 285.1022.

(2*S*)-*N*-(Diphenylmethyl)-2-isothiocyanato-3,3-dimethylbutanamide (11)



N-Boc-L-*tert*-leucine (1.00 g, 4.32 mmol, 1.00 eq) was reacted with benzhydrylamine (0.82 mL, 4.76 mmol, 1.10 eq) according to general procedure **A** to afford the title compound **11** as a pale yellow solid in 84% yield (1.23 g).

$[\alpha]_D^{20}$ = +47.5 (*c* 0.72, $CHCl_3$); **MP** 162-166 °C; **IR** (film) ν_{max}/cm^{-1}: 3297 (NH), 2965, 2117 (NCS), 1658 (C=O), 1526, 1452, 1237, 753, 699; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.41 - 7.28 (m, 6 H, Ar$\underline{H}$), 7.28 - 7.21 (m, 4 H, Ar$\underline{H}$), 6.64 (d, *J* = 8.0 Hz, 1 H, N$\underline{H}$), 6.25 (d, *J* = 8.0 Hz, 1 H,

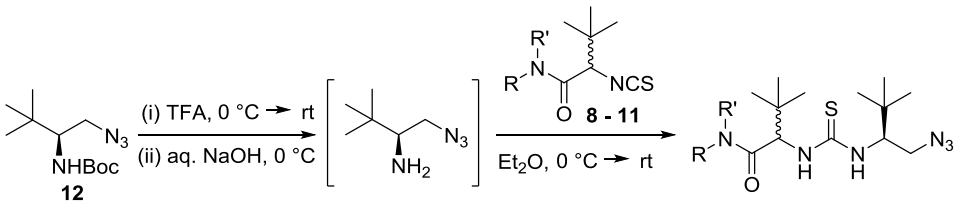
[ii] Quaternary carbon N$\underline{C}$S not found in spectrum.

$Ph_2C\underline{H}NH$), 4.09 (s, 1 H, $C\underline{H}(^tBu)$), 1.08 (s, 9 H, $C(C\underline{H_3})_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz)[iii] δ (ppm): 165.4 ($\underline{C}$=O), 140.8 (Ar$\underline{C}$), 140.5 (Ar$\underline{C}$), 128.8 (Ar$\underline{C}$H), 128.8 (Ar$\underline{C}$H), 127.8 (Ar$\underline{C}$H), 127.7(Ar$\underline{C}$H), 127.5 (Ar$\underline{C}$H), 127.3 (Ar$\underline{C}$H), 70.9 ($\underline{C}H(^tBu)$), 57.2 ($Ph_2\underline{C}HNH$), 37.1 ($\underline{C}(CH_3)_3$), 26.7 ($C(\underline{C}H_3)_3$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{20}H_{22}N_2NaOS$) requires *m/z* 361.1345, found *m/z* 361.1328.

1.2.3 Synthesis of Azide Precursors to Catalysts 1j – m

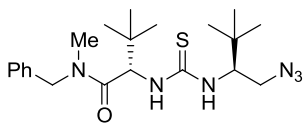
The *N*-Boc protected amino azide **12** was synthesised on a 9.35 mmol scale in 89% yield (affording 2.01 g of **12**) according to a literature procedure.[1]

General Procedure B for synthesis of azide precursors to catalysts 1j - m:



To compound **12** (80 mg, 0.33 mmol, 1.0 eq) at 0 °C was added trifluoroacetic acid (0.24 mL, 3.1 mmol, 9.4 eq) dropwise. The reaction mixture was warmed to rt and stirred for 2 h, and the volatiles removed by N_2 stream. The crude material was dissolved in Et_2O/H_2O (1:1 v/v, 4 mL) and adjusted to pH 14 by the addition of sodium hydroxide at 0 °C. The organic phase was extracted using Et_2O (2 x 2 mL), washed with brine (5 mL), dried ($MgSO_4$), filtered, and concentrated to 2 mL under a N_2 stream. The solution was cooled to 0 °C and the corresponding *isothiocyanate* **8 - 11** (0.35 mmol, 1.1 eq) added. The reaction mixture was then warmed to rt and stirred for 24 h. Volatiles were removed by N_2 stream and the crude product was purified by FCC to afford the corresponding azide.

(2*S*)-2-({[(2*S*)-1-Azido-3,3-dimethylbutan-2-yl]carbamothioyl}amino)-*N*-benzyl-*N*,3,3-trimethylbutanamide (13)

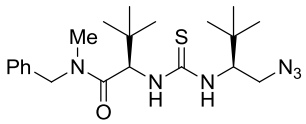


Azide **12** (80 mg, 0.33 mmol, 1.0 eq) was reacted with isothiocyanate **8** (96 mg, 0.35 mmol, 1.1 eq) according to the general procedure **B**. The reaction mixture was purified by FCC (petroleum ether/EtOAc = 9/1 to 4/1) to afford the title compound **13** as a colorless foam in 59% yield (82 mg).

[iii] Quaternary carbon N$\underline{C}$S not found in spectrum

$[\alpha]_D^{20}$ = -33.1 (*c* 1.20, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 3293 (thiourea NH), 2963, 2097, 1618 (C=O), 1534 (C=S), 1302, 1086, 739; **^{1}H NMR** (MeOD-d_4, 500 MHz, compound exists as ~4.4:1 mixture of rotamers, major rotamer identified by *) δ (ppm): 7.41 - 7.38 (m, 1 H, Ar<u>H*</u> and Ar<u>H</u>), 7.35 - 7.21 (m, 4 H, Ar<u>H*</u> and Ar<u>H</u>), 5.87 (s, 1 H, C(=O)C<u>H</u>(^{t}Bu)), 5.57 (s, 1 H, C(=O)C<u>H*</u>(^{t}Bu)), 5.17 (d, *J* = 15.0 Hz, 1 H, PhC<u>H_A</u>H_BN), 4.76 (d, *J* = 15.0 Hz, 1 H, PhC<u>H_A</u>*H_BN), 4.65 (dd, *J* = 8.0, 3.5 Hz, 1 H, C<u>H*</u>CH_2N_3 and C<u>H</u>CH_2N_3), 4.61 (d, *J* = 15.0 Hz, 1 H, PhCH_A<u>H_B</u>N), 4.49 (d, *J* = 15.0 Hz, 1 H, PhCH_A<u>H_B*</u>N), 3.52 (dd, *J* = 12.5, 3.5 Hz, 1 H, CHC<u>H_A*</u>$H_B N_3$ and CHC<u>H_A</u>$H_B N_3$), 3.35 - 3.29 (m[iv], 1 H, CHCH_A<u>H_B*</u>N_3 and CHCH_A<u>H_B</u>N_3), 3.28 (s, 3 H, PhCH_2N(C<u>H_3*</u>)), 2.81 (s, 3 H, PhCH_2N(C<u>H_3</u>)), 1.07 (s, 9 H, one of C(=O)CHC(C<u>H_3*</u>)$_3$ or NHCHC(C<u>H_3*</u>)$_3$), 1.03 (s, 9 H, one of C(=O)CHC(C<u>H_3</u>)$_3$ or NHCHC(C<u>H_3</u>)$_3$), 1.01 (s, 9 H, one of C(=O)CHC(C<u>H_3</u>)$_3$ or NHCHC(C<u>H_3</u>)$_3$), 1.00 (s, 9 H, one of C(=O)CHC(C<u>H_3*</u>)$_3$ or NHCHC(C<u>H_3*</u>)$_3$); **^{13}C NMR** (MeOD-d_4, 125 MHz, major rotamer identified by *) δ (ppm): 186.0 (<u>C*</u>=S), 185.8 (<u>C</u>=S), 174.6 (<u>C*</u>=O and <u>C</u>=O), 138.3 (Ar<u>C*</u>), 138.1 (Ar<u>C</u>), 129.8 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 129.7 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 129.7 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 129.5 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 129.0 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 128.5 (one of Ar<u>C*</u>H or Ar<u>C</u>H), 63.6 (<u>C*</u>HCH_2N_3 and <u>C</u>HCH_2N_3), 61.6 (C(=O)<u>C*</u>H(^{t}Bu)), 61.1 (C(=O)<u>C</u>H(^{t}Bu)), 55.5 (Ph<u>C</u>H_2N), 53.1 (CH<u>C*</u>H_2N_3 and CH<u>C</u>H_2N_3), 52.3 (Ph<u>C*</u>H_2N), 37.5 (one of C(=O)CH<u>C</u>$(CH_3)_3$ or NHCH<u>C</u>$(CH_3)_3$), 37.1 (PhCH_2N(<u>C*</u>H_3)), 36.6 (one of C(=O)CH<u>C*</u>$(CH_3)_3$ or NHCH<u>C*</u>$(CH_3)_3$), 35.8 (either C(=O)CH<u>C*</u>$(CH_3)_3$ and C(=O)CH<u>C</u>$(CH_3)_3$, or NHCH<u>C*</u>$(CH_3)_3$ and NHCH<u>C</u>$(CH_3)_3$), 33.9 (PhCH_2N(<u>C</u>H_3)), 27.4 (one of C(=O)CHC(<u>C</u>$H_3)_3$ or NHCHC(<u>C</u>$H_3)_3$), 27.3 (one of C(=O)CHC(<u>C*</u>$H_3)_3$ or NHCHC(<u>C*</u>$H_3)_3$), 27.3 (either C(=O)CHC(<u>C*</u>$H_3)_3$ and C(=O)CHC(<u>C</u>$H_3)_3$, or NHCHC(<u>C*</u>$H_3)_3$ and NHCHC(<u>C</u>$H_3)_3$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{21}H_{36}NaOS$) requires *m/z* 441.2407, found *m/z* 441.2386.

(2*R*)-2-({[(2*S*)-1-Azido-3,3-dimethylbutan-2-yl]carbamothioyl}amino)-*N*-benzyl-*N*,3,3-trimethylbutanamide (14)



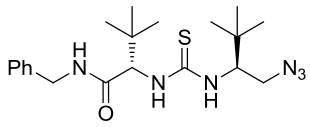
Azide **12** (120 mg, 0.500 mmol, 1.00 eq) was reacted with isothiocyanate **9** (144 mg, 0.520 mmol, 1.05 eq) according to the general procedure **B**. The reaction mixture was purified by FCC (petroleum ether/EtOAc = 9/1 to 4/1) to afford the title compound **14** as a colorless foam in 74% yield (153 mg).

$[\alpha]_D^{20}$ = -19.2 (*c* 1.00, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 3326 (thiourea NH), 2963, 2095, 1618 (C=O), 1527 (C=S), 1275, 1085, 701; **^{1}H NMR** (MeOD-d_4, 400 MHz, compound exists as ~3.4:1 mixture of rotamers, major rotamer identified by *) δ (ppm): 7.43 - 7.39 (m, 1 H, Ar<u>H*</u> and Ar<u>H</u>), 7.35 -

[iv] Multiplet beneath solvent peak identified by 2D COSY and HSQC NMR. Integration assumed.

7.21 (m, 4 H, ArH* and ArH), 5.88 (s, 1 H, C(=O)CH(ᵗBu)), 5.65 (s, 1 H, C(=O)CH*(ᵗBu)), 5.08 (d, *J* = 15.5 Hz, 1 H, PhCH$_A$H$_B$N), 4.73 - 4.60 (m, 3 H, PhCH$_A$*H$_B$N, PhCH$_A$H$_B$N, CH*CH$_2$N$_3$ and CHCH$_2$N$_3$), 4.54 (d, *J* = 15.0 Hz, 1 H, PhCH$_A$H$_B$*N), 3.54 (dd, *J* = 12.5, 4.0 Hz, 1 H, CHCH$_A$*H$_B$N$_3$ and CHCH$_A$H$_B$N$_3$), 3.36 - 3.33 (m, 1 H, CHCH$_A$H$_B$*N$_3$ and CHCH$_A$H$_B$N$_3$), 3.25 (s, 3 H, PhCH$_2$N(CH$_3$*)), 2.80 (s, 3 H, PhCH$_2$N(CH$_3$)), 1.06 (s, 9 H, one of C(=O)CHC(CH$_3$*)$_3$ or NHCHC(CH$_3$*)$_3$), 1.04 (s, 9 H, one of C(=O)CHC(CH$_3$)$_3$ or NHCHC(CH$_3$)$_3$), 1.00 (s, 9 H, one of C(=O)CHC(CH$_3$)$_3$ or NHCHC(CH$_3$)$_3$), 0.99 (s, 9 H, one of C(=O)CHC(CH$_3$*)$_3$ or NHCHC(CH$_3$*)$_3$); **^{13}C NMR** (MeOD-d$_4$, 125 MHz, major rotamer identified by *) δ (ppm): 186.0 (C*=S and C=S), 174.3 (C*=O and C=O), 138.3 (ArC*), 138.2 (ArC), 129.8 (one of ArC*H or ArCH), 129.7 (one of ArC*H or ArCH), 129.4 (one of ArC*H or ArCH), 129.1 (one of ArC*H or ArCH), 128.9 (one of ArC*H or ArCH), 128.5 (one of ArC*H or ArCH), 63.3 (CHCH$_2$N$_3$), 63.2 (C*HCH$_2$N$_3$), 61.3 (C(=O)C*H(ᵗBu)), 60.8 (C(=O)CH(ᵗBu)), 55.4 (PhCH$_2$N), 53.1 (CHC*H$_2$N$_3$), 53.0 (CHCH$_2$N$_3$), 52.2 (PhC*H$_2$N), 37.6 (one of C(=O)CHC(CH$_3$)$_3$ or NHCHC(CH$_3$)$_3$), 37.0 (PhCH$_2$N(C*H$_3$)), 35.9 (one of C(=O)CHC*(CH$_3$)$_3$ or NHCHC*(CH$_3$)$_3$), 35.8 (either C(=O)CHC*(CH$_3$)$_3$ and C(=O)CHC(CH$_3$)$_3$, or NHCHC*(CH$_3$)$_3$ and NHCHC(CH$_3$)$_3$), 34.1 (PhCH$_2$N(CH$_3$)), 27.4 (one of C(=O)CHC(CH$_3$)$_3$ or NHCHC(CH$_3$)$_3$), 27.3 (one of C(=O)CHC(C*H$_3$)$_3$ or NHCHC(C*H$_3$)$_3$), 27.3 (either C(=O)CHC(C*H$_3$)$_3$ and C(=O)CHC(CH$_3$)$_3$, or NHCHC(C*H$_3$)$_3$ and NHCHC(CH$_3$)$_3$); **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ (C$_{21}$H$_{34}$N$_6$NaOS) requires *m/z* 441.2407, found *m/z* 441.2392.

(2*S*)-2-({[(2*S*)-1-Azido-3,3-dimethylbutan-2-yl]carbamothioyl}amino)-*N*-benzyl-3,3-dimethylbutanamide (15)



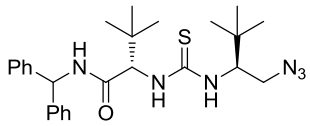
Azide **12** (50 mg, 0.21 mmol, 1.0 eq) was reacted with isothiocyanate **10** (57 mg, 0.22 mmol, 1.1 eq) according to the general procedure **B**. The reaction mixture was purified by FCC (petroleum ether/EtOAc = 4/1 to 1/1) to afford the title compound **15** as a colorless solid in 57% yield (47 mg).

[α]$_D^{20}$ = -69.9 (*c* 0.49, CHCl$_3$); **MP** 181-183 °C; **IR** (film) ν$_{max}$/cm^{-1}: 3288 (thiourea/amide NH), 2964, 2098, 1649 (C=O), 1533 (C=S), 1353, 699; **^{1}H NMR** (MeOD-d$_4$, 400 MHz) δ (ppm): 7.32 - 7.15 (m, 5 H, ArH), 4.91 (s, 1 H, C(=O)CH(ᵗBu)), 4.61 (dd, *J* = 8.0, 3.5 Hz, 1 H, CHCH$_2$N$_3$), 4.36 (s, 2 H, PhCH$_2$NH), 3.49 (dd, *J* = 13.0, 4.0 Hz, 1 H, CHCH$_A$H$_B$N$_3$), 3.31 - 3.24 (m[v], 1 H, CHCH$_A$H$_B$N$_3$), 1.00 (s, 9 H, one of C(=O)CHC(CH$_3$)$_3$ or NHCHC(CH$_3$)$_3$), 0.95 (s, 9 H, one of C(=O)CHC(CH$_3$)$_3$ or NHCHC(CH$_3$)$_3$); **^{13}C NMR** (MeOD-d$_4$, 125 MHz) δ (ppm): 186.1 (C=S),

[v] Multiplet beneath solvent peak identified by 2D COSY and HSQC NMR. Integration assumed.

173.6 (C=O), 140.0 (ArC), 129.6 (ArCH), 128.8 (ArCH), 128.2 (ArCH), 67.0 (C(=O)CH(^{t}Bu)), 63.5 ($\underline{C}HCH_2N_3$), 53.1 ($CH\underline{C}H_2N_3$), 44.1 ($Ph\underline{C}H_2NH$), 35.7, 35.7 ($C(=O)CH\underline{C}(CH_3)_3$ and $NHCH\underline{C}(CH_3)_3$), 27.5, 27.4 ($C(=O)CHC(\underline{C}H_3)_3$ and $NHCHC(\underline{C}H_3)_3$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{20}H_{32}N_6NaOS$) requires *m/z* 427.2251, found *m/z* 427.2237.

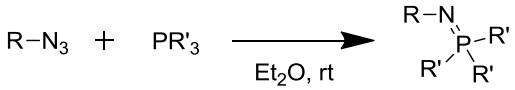
(2*S*)-2-({[(2*S*)-1-Azido-3,3-dimethylbutan-2-yl]carbamothioyl}amino)-*N*-(diphenylmethyl)-3,3-dimethylbutanamide (16)



Azide **12** (409 mg, 1.69 mmol, 1.10 eq) was reacted with isothiocyanate **11** (520 mg, 1.54 mmol, 1.00 eq) according to a modified general procedure **B**. The reaction mixture was purified by FCC (petroleum ether/EtOAc = 4/1 to 3/2) to afford the title compound **16** as a colorless solid in 90% yield (661 mg).

$[\alpha]_D^{20}$ = -33.4 (*c* 0.54, $CHCl_3$); **MP** 200-202 °C; **IR** (film) ν_{max}/cm^{-1}: (thiourea/amide NH), 2963, 2098, 1649 (C=O), 1529 (C=S), 1348, 752, 699; **^{1}H NMR** (MeOD-d_4, 500 MHz) δ (ppm): 7.35 - 7.19 (m, 10 H, ArH), 6.18 (s, 1 H, $Ph_2C\underline{H}NH$), 5.02 (s, 1 H, C(=O)CH(^{t}Bu)), 4.67 (dd, *J* = 8.0, 3.5 Hz, 1 H, $C\underline{H}CH_2N_3$), 3.52 (dd, *J* = 13.0, 3.5 Hz, 1 H, $CHC\underline{H}_AH_BN_3$), 3.35 - 3.28 (m[vi], 1 H, $CHCH_A\underline{H}_BN_3$), 1.01 (s, 9 H, one of $C(=O)CHC(C\underline{H}_3)_3$ or $NHCHC(C\underline{H}_3)_3$), 0.98 (s, 9 H, one of $C(=O)CHC(C\underline{H}_3)_3$ or $NHCHC(C\underline{H}_3)_3$); **^{13}C NMR** (MeOD-$d_4$, 125 MHz) δ (ppm): 186.1 (C=S), 172.9 (C=O), 143.2 (ArC), 142.9 (ArC), 129.7 (ArCH), 129.5 (ArCH), 129.4 (ArCH), 128.7 (ArCH), 128.6 (ArCH), 128.2 (ArCH), 66.7 (C(=O)CH(^{t}Bu)), 63.5 ($\underline{C}HCH_2N_3$), 58.5 ($Ph_2\underline{C}HNH$), 53.1 ($CH\underline{C}H_2N_3$), 35.7, 35.7 ($C(=O)CH\underline{C}(CH_3)_3$ and $NHCH\underline{C}(CH_3)_3$), 27.5, 27.4 ($C(=O)CHC(\underline{C}H_3)_3$ and $NHCHC(\underline{C}H_3)_3$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{26}H_{36}N_6NaOS$) requires *m/z* 503.2564, found *m/z* 503.2552.

General Procedure C for the *in situ* Generation of Iminophosphorane Catalysts



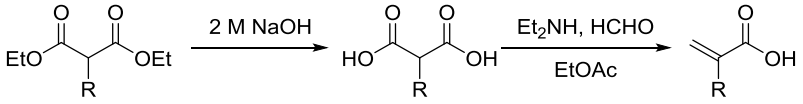
To the corresponding *organoazide* (0.020 mmol, 1.0 eq) and *phosphine* (0.020 mmol, 1.0 eq) under an Ar atmosphere was added Et_2O (0.1 mL), and the reaction mixture was stirred at rt for 24 h. The iminophosphorane product was confirmed by LRMS and TLC, and the volatiles were removed by a N_2 stream to yield the crude product, which was used as a catalyst without further purification.

[vi]Multiplet beneath solvent peak identified by 2D COSY and HSQC NMR. Integration assumed.

1.3 Synthesis of α-Substituted Acrylate Esters

Methacrylate esters **2a**, **2c** – **f** and dimethyl itaconate (**2h**) are commercially available and were used as supplied. α-Substituted α,β-unsaturated esters **2b**,[5] **2i**,[6] **2j**[6] and **2r**[7] were synthesised according to literature procedures and their physical and chemical properties are in agreement with those reported.

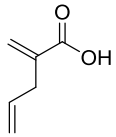
General procedure D for the Synthesis of Aliphatic α-Substituted Acrylate Acids



According to a modified literature procedure,[8] to the substituted malonate (synthesised by the treatment of diethylmalonate with NaH and the corresponding alkyl bromide in DMF) was added 2 M NaOH (2.67 eq), and the resulting mixture was stirred vigorously and refluxed for 2 h. The resulting solution was cooled to rt and extracted with hexane (2x) and the aqueous layer was then acidified to pH 1 with aq HCl. The resulting solution was then extracted with EtOAc (3x), the combined organics washed with brine, dried ($MgSO_4$) and the volatiles removed *in vacuo* to afford the corresponding diacid which was used crude in the next step.

The crude diacid was dissolved in EtOAc (0.75 M) and the resulting solution was cooled to 0 °C, followed by the dropwise addition of diethylamine (1.01 eq) and subsequent addition of *p*-formaldehyde (1.5 eq). The resulting suspension was refluxed for 2 hours and then the reaction mixture was cooled to 0 °C, diluted with H_2O (0.6 mL/mmol diacid) and acidified to pH 1 with concentrated HCl. The aqueous layer was then extracted with EtOAc (3x) and the combined organics washed with brine, dried ($MgSO_4$) and the volatiles removed *in vacuo* to afford the crude acid which was purified by FCC (petroleum ether/Et_2O).

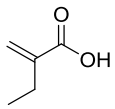
2-Methylidenepent-4-enoic acid (17)



Synthesised from 1,3-diethyl 2-(prop-2-en-1-yl)propanedioate on a 62.4 mmol scale to afford the title compound **17** as a colorless oil in 68% yield over two steps (4.17 g).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 6.36 (d, *J* = 1.0 Hz, 1 H, C$\underline{H_A}H_BC$), 5.96 - 5.80 (m, 1 H, $CH_AH_BC\underline{H}$), 5.71 ('q', *J* = 1.0 Hz, 1 H, $CH_A\underline{H_B}C$), 5.16 - 5.11 (m, 1 H, C$\underline{H_A}H_BCH$), 5.11 - 5.08 (m, 1 H, $CH_A\underline{H_B}CH$), 3.11 - 3.01 (m, 2 H, $CH_AH_BC\underline{H_2}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm) 172.7 ($\underline{C}$=O), 138.9 ($CH_AH_B\underline{C}$), 135.1 ($CH_AH_B\underline{C}H$), 128.1 ($\underline{C}H_AH_BC$), 117.0 ($\underline{C}H_AH_BCH$), 35.8 ($\underline{C}H_2$). Data consistent with that given in the literature.[9]

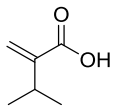
2-Methylidenebutanoic acid (18)



Synthesised from 1,3-diethyl 2-ethylpropanedioate on a 55.4 mmol scale to afford the title compound **18** as a colorless oil in 76% yield over two steps (4.20 g).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.29 ('s', 1 H $C\underline{H_A}H_BC$), 5.66 ('s', 1 H, $CH_A\underline{H_B}C$), 2.33 (q, *J* = 7.5 Hz, 2 H, $C\underline{H_2}CH_3$), 1.10 (t, *J* = 7.5 Hz, 3 H, $CH_2C\underline{H_3}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 173.3 ($\underline{C}$=O), 141.8 ($CH_A\underline{H_B}\underline{C}$), 126.2 ($\underline{C}H_AH_BC$), 24.5 ($\underline{C}H_2CH_3$), 12.8 ($CH_2\underline{C}H_3$). Data consistent with that given in the literature.[10]

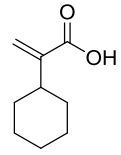
3-Methyl-2-methylidenebutanoic acid (19)



Synthesised from 1,3-diethyl 2-(propan-2-yl)propanedioate on a 54.4 mmol scale to afford the title compound **19** as a colorless oil in 61% yield over two steps (3.80 g).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.30 (s, 1 H, $C\underline{H_A}H_BC$), 5.66 (s, 1 H, $CH_A\underline{H_B}C$), 2.81 (spt, *J* = 7.0 Hz, 1 H, $C\underline{H}(CH_3)_2$), 1.12 (d, *J* = 7.0 Hz, 6 H, $CH(C\underline{H_3})_2$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 173.0 ($\underline{C}$=O), 146.3 ($CH_A\underline{H_B}\underline{C}$), 124.2 ($\underline{C}H_AH_BC$), 29.0 ($\underline{C}H(CH_3)_2$), 21.8 ($CH(\underline{C}H_3)_2$). Data consistent with that given in the literature.[11]

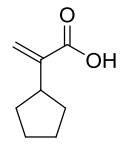
2-Cyclohexylprop-2-enoic acid (20)



Synthesised from 1,3-diethyl 2-cyclohexylpropanedioate on a 14.5 mmol scale to afford the title compound **20** as a colorless oil in 19% yield over two steps (417 mg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.28 ('s', 1 H, $C\underline{H_A}H_BC$), 5.60 ('s', 1 H, $CH_A\underline{H_B}C$), 2.50 - 2.38 (m, 1 H, $CH_2C\underline{H}CH_2$), 1.95 - 1.64 (m, 5 H, 5 of $C_6\underline{H_{11}}$), 1.46 - 1.27 (m, 2 H, 2 of $C_6\underline{H_{11}}$), 1.25 - 1.07 (m, 3 H, 3 of $C_6\underline{H_{11}}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 172.8 ($\underline{C}$=O), 145.7 ($CH_A\underline{H_B}\underline{C}$), 124.8 ($\underline{C}H_AH_BC$), 38.9 ($CH_2\underline{C}HCH_2$), 32.6, 26.7, 26.3 ($\underline{C}H_2\underline{C}H_2\underline{C}H_2CH$). Data consistent with that given in the literature.[12]

2-Cyclopentylprop-2-enoic acid (21)

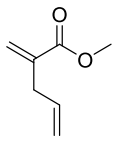


Synthesised from 1,3-diethyl 2-cyclopentylpropanedioate on a 6.58 mmol scale to afford the title compound **21** as a colorless oil in 49% yield over two steps (449 mg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm); 11.50 (br. s, 1 H, (C=O)O$\underline{H}$), 6.29 ('s', 1 H, $C\underline{H_A}H_BC$), 5.67 ('t', *J* = 1.5 Hz, 1 H, $CH_A\underline{H_B}C$), 2.86 (quin, *J* = 8.5 Hz, 1 H, $CH_2C\underline{H}CH_2$), 2.00 – 1.89 (m, 2 H, $C\underline{H_A}H_BCHC\underline{H_A}H_B$), 1.78 - 1.56 (m, 4 H, $C\underline{H_2}CH_2CHCH_2C\underline{H_2}$), 1.50 - 1.36 (m, 2 H, $CH_A\underline{H_B}CHCH_A\underline{H_B}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm) 173.3 ($\underline{C}$=O), 143.8 ($CH_A\underline{H_B}\underline{C}$), 124.3 ($\underline{C}H_AH_BC$), 41.0 ($CH_2\underline{C}HCH_2$), 31.9 ($\underline{C}H_2CH\underline{C}H_2$), 24.9 ($\underline{C}H_2CH_2CHCH_2\underline{C}H_2$). Data is consistent with that given in the literature.[13]

Synthesis of α-Substituted Acrylate Esters

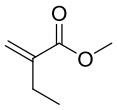
Methyl 2-methylidenepent-4-enoate (2g)



To a solution of MeOH (20 mL) at 0 °C was added thionyl chloride (1.64 mL, 22.4 mmol, 2.50 eq) dropwise followed by acid **17** (1.00 g, 8.93 mmol, 1.00 eq). The reaction mixture was refluxed for 2 h, then cooled to 0 °C, diluted with pentane (40mL), and aq K_2CO_3 was added until pH to 9-10. The aqueous layer was then extracted with pentane (2x 30 mL), the combined organics were washed with brine, dried ($MgSO_4$) and the volatiles were removed under a stream of nitrogen to afford the crude product **2g** in 54% yield (612 mg) as a colorless oil which was used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.15 ('s', 1 H, $C\underline{H_A}H_BC$), 5.89 - 5.73 (m, 1 H, $CH_AH_BC\underline{H}CH_2$), 5.53 (d, *J* = 1.5 Hz, 1 H, $CH_A\underline{H_B}C$), 5.06 (dd, *J* = 6.5, 1.5 Hz, 1 H, $C\underline{H_A}H_BCHCH_2$), 5.03 ('s', 1 H, $CH_A\underline{H_B}CHCH_2$), 3.71 (s, 3 H, $OC\underline{H_3}$), 3.02 (d, *J* = 6.5 Hz, 2 H, $CH_AH_BCHC\underline{H_2}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 167.2 ($\underline{C}$=O), 138.8 ($CH_AH_B\underline{C}$), 134.9 ($CH_AH_B\underline{C}HCH_2$), 125.3 ($\underline{C}H_AH_BC$), 116.7 ($\underline{C}H_AH_BCHCH_2$), 51.7 ($O\underline{C}H_3$), 35.7 ($CH_AH_BCH\underline{C}H_2$). Data is consistent with that given in the literature.[14]

Methyl 2-methylidenebutanoate (2k)



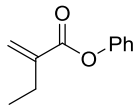
To a solution of MeOH (12 mL) at 0 °C was added thionyl chloride (1.10 mL, 15.0 mmol, 2.50 eq) dropwise followed by acid **18** (600 mg, 6.00 mmol, 1.00 eq). The reaction mixture was refluxed for 2 h, then cooled to 0 °C, diluted with pentane (30 mL), and aq K_2CO_3 was added until pH to 9-10. The aqueous layer was then extracted with pentane (2 x 20 mL), the combined organics were washed with brine, dried ($MgSO_4$) and the volatiles were removed under a stream of nitrogen to afford the crude product **2k** in 50% yield (340 mg) as a colorless oil which was used without further purification.

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 6.13 ('s', 1 H, $C\underline{H_A}H_BC$), 5.53 (d, *J* = 1.0 Hz, 1 H, $CH_A\underline{H_B}C$), 3.75 (s, 3 H, $OC\underline{H_3}$), 2.32 (q, *J* = 7.5 Hz, 2 H, $C\underline{H_2}CH_3$), 1.07 (t, *J* = 7.5 Hz, 3 H, $CH_2C\underline{H_3}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 168.0 ($\underline{C}$=O), 142.3 ($CH_AH_B\underline{C}$), 123.7 ($\underline{C}H_AH_BC$), 51.9 ($O\underline{C}H_3$), 24.9 ($\underline{C}H_2CH_3$), 12.8 ($CH_2\underline{C}H_3$). Data is consistent with that given in the literature.[15]

General procedure E for the Synthesis of α-Substituted Acrylate Phenolic Esters

To a solution of the acid **18** – **21** in CH_2Cl_2 (0.3 M) was added PhOH (1 eq), DIEA (1 eq), DMAP (0.2 eq) followed by EDCI (1 eq) at room temperature and stirring was maintained overnight, whereupon the volatiles were removed *in vacuo*. The crude mixtures were purified by FCC (Petroleum ether/Et_2O = 19/1) to afford the desired phenolic ester.

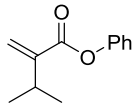
Phenyl 2-methylidenebutanoate (2l)



Synthesised on a 3.00 mmol scale of acid **18** according to general procedure **E** to afford the title compound **2l** as a colorless oil in 75% yield (398 mg).

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.46 - 7.34 (m, 2 H, ArC$\underline{H}$), 7.30 - 7.20 (m, 1 H, ArC$\underline{H}$), 7.13 (d, *J* = 8.0 Hz, 2 H, ArC$\underline{H}$), 6.40 (‘s’, 1 H, C$\underline{H_A}H_BC$), 5.73 (d, *J* = 1.0 Hz, 1 H, $CH_A\underline{H_B}C$), 2.46 (q, *J* = 7.5 Hz, 2 H, C$\underline{H_2}CH_3$), 1.17 (t, *J* = 7.5 Hz, 3 H, $CH_2C\underline{H_3}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 165.9 (C$\underline{=}$O), 151.0 (Ar$\underline{C}$), 141.9 ($CH_A\underline{H_B}C$), 129.5 (Ar$\underline{C}$H), 125.8 (Ar$\underline{C}$H), 125.5 ($\underline{C}H_AH_BC$), 121.8 (Ar$\underline{C}$H), 25.0 ($\underline{C}H_2CH_3$), 12.8 ($CH_2\underline{C}H_3$). Data consistent with that given in the literature.[16]

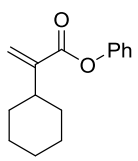
Phenyl 3-methyl-2-methylidenebutanoate (2m)



Synthesised on a 4.38 mmol scale of acid **19** according to general procedure **E** to afford the title compound **2m** as a colorless oil in 98% yield (805 mg).

IR: 2955 (C-H), 1733 (C=O), 1498, 1197 (C-O), 1110; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.44 - 7.36 (m, 2 H, ArC$\underline{H}$), 7.28 - 7.21 (m, 1 H, ArC$\underline{H}$), 7.16 - 7.10 (m, 2 H, ArC$\underline{H}$), 6.39 (br s, 1 H, C$\underline{H_A}H_BC$), 5.72 (‘t’, *J* = 1.0 Hz, 1 H, $CH_A\underline{H_B}C$), 2.92 (sptd, *J* = 7.0, 1.0 Hz, 1 H, $(CH_3)_2C\underline{H}$), 1.18 (d, *J* = 7.0 Hz, 6 H, $(C\underline{H_3})_2CH$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 166.0 (C$\underline{=}$O), 151.1 (Ar$\underline{C}$), 146.8 ($CH_A\underline{H_B}C$), 129.5 (Ar$\underline{C}$H), 125.8 (Ar$\underline{C}$H), 123.8, ($\underline{C}H_AH_BC$), 121.8 (Ar$\underline{C}$H), 29.7 ($(CH_3)_2\underline{C}H$), 22.0 ($(\underline{C}H_3)_2CH$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{12}H_{14}NaO_2$) requires *m/z* 213.0886, found *m/z* 213.0883.

Phenyl 2-cyclohexylprop-2-enoate (2n)

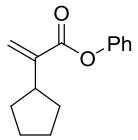


Synthesised on a 1.95 mmol scale of acid **20** according to general procedure **E** to afford the title compound **2n** as a colorless solid in 75% yield (336 mg).

MP: 27-29 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.45 - 7.36 (m, 2 H, Ar$\underline{H}$), 7.29 - 7.20 (m, 1 H, Ar$\underline{H}$), 7.13 (d, *J* = 7.5 Hz, 2 H, Ar$\underline{H}$), 6.38 (‘s’, 1 H, C$\underline{H_A}H_BC$), 5.68 (‘s’, 1 H, $CH_A\underline{H_B}C$), 2.61 – 2.51 (m, 1 H, $CH_2C\underline{H}CH_2$), 1.92 (‘d’, *J* = 12.0 Hz, 2 H, 2 of $C_6\underline{H_{11}}$), 1.87 - 1.78 (m, 2 H, 2 of $C_6\underline{H_{11}}$), 1.78 - 1.69 (m, 1 H, 1 of $C_6\underline{H_{11}}$), 1.47 - 1.14 (m, 5 H, 5 of $C_6\underline{H_{11}}$); **^{13}C NMR**

($CDCl_3$, 100 MHz) δ (ppm): 166.1 (C=O), 151.1 (ArC), 146.0 (CH_AH_BC), 129.5 (ArCH), 125.8 (ArCH), 124.1 (CH_AH_BC), 121.8 (ArCH), 39.4 (CH_2CHCH_2), 32.7, 26.7, 26.3 (3 of C_6H_{11}). Data consistent with that given in the literature.[17]

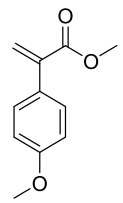
Phenyl 2-cyclopentylprop-2-enoate (2o)



Synthesised on a 2.85 mmol scale of acid **21** according to general procedure **E** to afford the title compound **2o** as a colorless oil in 89% yield (546 mg).

IR (film) ν_{max}/cm^{-1}: 2953 (C-H), 1734 (C=O), 1492, 1196 (C-O), 1110; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.45 - 7.35 (m, 2 H, ArH), 7.28 - 7.20 (m, 1 H, ArH), 7.13 (d, *J* = 8.0 Hz, 2 H, ArH), 6.37 ('s', 1 H, CH_AH_BC), 5.73 ('s', 1 H, CH_AH_BC), 2.97 (quin, *J* = 8.5 Hz, 1 H, CH_2CHCH_2), 2.10 - 1.94 (m, 2 H, 2 of C_5H_9), 1.82 - 1.59 (m, 4 H, 4 of C_5H_9), 1.56 - 1.42 (m, 2 H, 2 of C_5H_9); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 166.2 (C=O), 151.1 (ArC), 144.2 (CH_AH_BC), 129.5 (ArCH), 125.8 (ArCH), 123.8 (CH_AH_BC), 121.8 (ArCH), 41.7 (CH_2CHCH_2), 32.0 ($CHCH_2$), 25.1 ($CHCH_2CH_2$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{16}NaO_2$) requires *m/z* 239.1043, found *m/z* 239.1038.

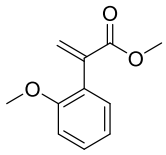
Methyl 2-(4-methoxyphenyl)prop-2-enoate (2p)



To a solution of MeOH (44 mL) at 0 °C was added thionyl chloride (1.41 mL, 19.5 mmol, 2.2 eq) dropwise and to the resulting solution was added ethyl 2-(4-methoxyphenyl)prop-2-enoate[18] (1.70 g, 8.25 mmol, 1.0 eq). The reaction mixture was refluxed for 14 h and the reaction mixture was cooled to 0 °C, diluted with pentane (100 mL) and aq K_2CO_3 until pH to 9-10. The aqueous layer was then extracted with pentane (2 x 40 mL), the combined organics were washed with brine, dried ($MgSO_4$) and the volatiles were removed *in vacuo* to afford the crude product which was purified by FCC (Petrol/Et_2O 9/1) to afford the title compound **2p** in 78% yield (1.23 g) as a pale yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.42 - 7.34 (m, 2 H, ArH), 6.93 - 6.87 (m, 2 H, ArH), 6.28 (d, *J* = 1.0 Hz, 1 H, CH_AH_BC), 5.84 (d, *J* = 1.0 Hz, 1 H, CH_AH_BC), 3.83 ('s', 6 H, $ArOCH_3$ and $C(=O)OCH_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 167.5 (C=O), 159.6 ($ArCOCH_3$), 140.6 (CH_AH_BC), 129.5 (ArCH), 129.1 (ArC), 125.4 (CH_AH_BC), 113.5 (ArCH), 55.2 ($ArCOCH_3$), 52.1 ($C(=O)OCH_3$). Data is consistent with that given in the literature.[6]

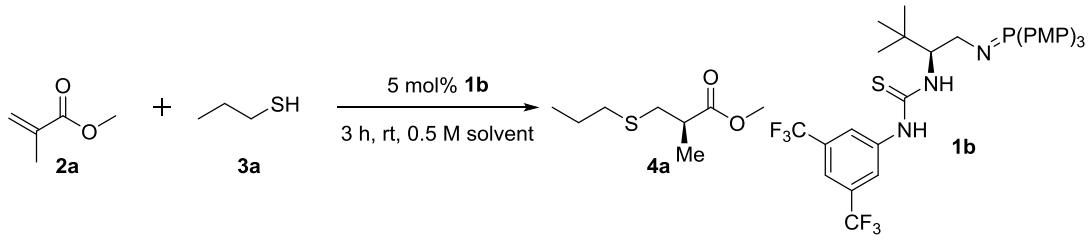
Methyl 2-(2-methoxyphenyl)prop-2-enoate (2q)



To a solution of MeOH (10 mL) at 0 °C was added thionyl chloride (0.32 mL, 4.3 mmol, 2.2 eq) dropwise and to the resulting solution was added ethyl 2-(2-methoxyphenyl)prop-2-enoate[18] (300 mg, 1.97 mmol, 1.0 eq). The reaction mixture was refluxed for 14 h and the reaction mixture was cooled to 0 °C, diluted with pentane (20 mL) and aq K_2CO_3 until pH to 9-10. The aqueous layer was then extracted with pentane (2x 10 mL), the combined organics were washed with brine, dried ($MgSO_4$) and the volatiles were removed *in vacuo* to afford the crude product **2q** in 61% yield (234 mg) as a pale yellow oil which was used without further purification.

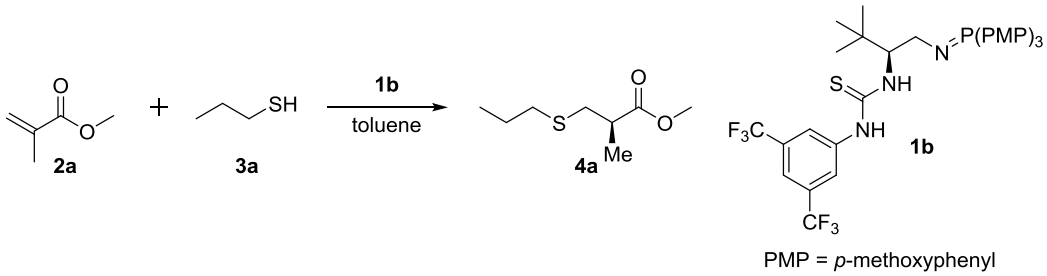
^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.38 - 7.30 (m, 1 H, Ar$\underline{H}$), 7.22 (dd, *J* = 7.5, 1.5 Hz, 1 H, Ar$\underline{H}$), 6.97 ('td', *J* = 7.5, 1.0 Hz, 1 H, Ar$\underline{H}$), 6.90 (d, *J* = 8.5 Hz, 1 H, Ar$\underline{H}$), 6.29 (d, *J* = 1.5 Hz, 1 H, C$\underline{H_A}H_BC$), 5.74 (d, *J* = 1.5 Hz, 1 H, $CH_A\underline{H_B}C$), 3.80 (s, 3 H, ArCOC$\underline{H_3}$), 3.76 (s, 3 H, C(=O)OC$\underline{H_3}$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 168.1 ($\underline{C}$=O), 157.0 (Ar$\underline{C}$OCH$_3$), 140.0 ($CH_AH_B\underline{C}$), 130.2 (Ar$\underline{C}$H), 130.0 (Ar$\underline{C}$H), 127.2 (Ar$\underline{C}$), 126.6 ($\underline{C}H_AH_BC$), 120.8 (Ar$\underline{C}$H), 110.9 (Ar$\underline{C}$H), 55.8 (ArCO$\underline{C}$H$_3$), 52.2 (C(=O)O$\underline{C}$H$_3$). Data is consistent with that given in the literature.[19]

1.4 Optimization of Conditions for the Sulfa-Michael Addition



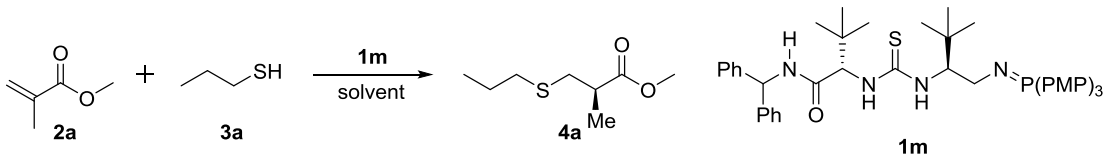
Entry	Solvent	Yield /	ee / %	Entry	Solvent	Yield /	ee / %
1	MeOH	>99	0	7	$CHCl_3$	57	57
2	DMF	85	19	8	TBME	74	70
3	EtOAc	71	67	9	Toluene	>99	72
4	THF	80	65	10	Benzene	88	70
5	CH_2Cl_2	51	61	11	Cyclohexane	74	71
6	Et_2O	82	71	12	Hexane	88	73

Table SI.1: Solvent optimization for the sulfa-Michael addition of 1-propanethiol **3a** (0.2 mmol) to methyl methacrylate **2a** (1.0 mmol), with 5 mol% catalyst **1b**.



Entry	Temp. / °C	Catalyst Loading / mol%	Concentration / M (toluene)	Time / h	Yield / %	ee / %
1	–40	5	0.5	24	88	72
2	–20	10	0.5	6	>99	74
3	0	10	0.5	6	>99	74
4	rt	10	0.5	3	>99	72
5	50	10	0.5	1	>99	68
6	rt	1	0.5	21	94	72
7[a]	rt	0.05	0.5	96	70	73
8	rt	10	0.05	27	92	74

Table SI.2: Optimization of conditions for the sulfa-Michael addition of 1-propanethiol **3a** (0.2 mmol) to methyl methacrylate **2a** (1.0 mmol), with catalyst **1a**. [a]Reaction performed on a 20 mmol scale.



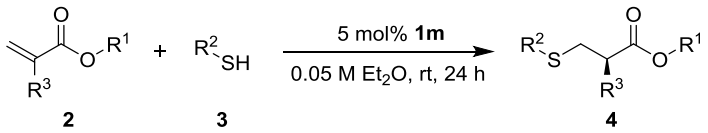
PMP = *p*-methoxyphenyl

Entry	Temp / °C	Catalyst / mol%	Solvent	Concentration / M	Time / h	Yield / %	ee / %
1	–20	5	Toluene	0.5	5	>99	82
2	0	5	Toluene	0.5	5	>99	83
3	rt	5	Toluene	0.5	3	>99	87
4	50	5	Toluene	0.5	1	>99	86
5	rt	1	Toluene	0.5	3	96	86
6	rt	5	TBME	0.5	3	94	87
7	rt	5	$PhCF_3$	0.5	3	74	87
8	rt	5	Hexane	0.5	3	>99	85
9	rt	5	Et_2O	0.5	3	86	89
10	rt	5	Toluene	0.05	6	74	91
11	rt	5	Toluene	0.01	24	14	91
12	rt	5	Et_2O	0.05	24	97	94

Table SI.3: Reoptimization of conditions for the sulfa-Michael addition of 1-propanethiol **3a** (0.2 mmol) to methyl methacrylate **2a** (1.0 mmol), with catalyst **1m**.

1.5 Synthesis and Characterization of α-Substituted, β-Mercaptoesters 4

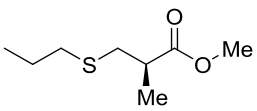
General procedure F for the Enantioselective Sulfa-Michael Addition of Alkyl Thiols to α-Substituted Acrylate esters.[vii]



2 3 4

Azide **16** (4.8 mg, 0.010 mmol, 0.05 eq) and tris(4-methoxyphenyl)phosphine (3.5 mg, 0.010 mmol, 0.05 eq) were stirred in diethyl ether (0.2 mL) under an argon atmosphere in a sealed vial at room temperature for 24 h. The *in situ* generated catalyst was then transferred with washings (3.8 mL Et_2O) to a flask containing the *α-substituted acrylate ester* **2** (0.40 or 1.0 mmol, 2.0 eq or 5.0 eq), and the desired *thiol* **3** (0.20 mmol, 1.0 eq) was then added *via* syringe. The reaction mixture was stirred for 24 h and then quenched with 1.0 M AcOH (in CH_2Cl_2, 0.1 mL). The volatiles were removed under a stream of N_2 and the reaction mixture was purified by flash column chromatography to afford the product **4**.

Methyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (4a)



4a

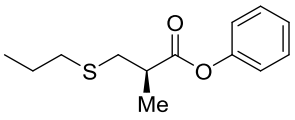
Methyl methacrylate **2a** (110 μL, 1.0 mmol, 5.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4a** as a pale yellow oil in 97% yield (34 mg) and 94% ee [determined by HPLC, chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min, λ = 230 nm, t (major) = 5.32 min, t (minor) = 5.91 min].

$[\alpha]_D^{20}$ = +27.3 (*c* 1.09, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2962, 1736 (C=O), 1458, 1435, 1375, 1208 (C-O), 1161 (C-O), 986, 826; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 3.70 (s, 3 H, $OC\underline{H}_3$), 2.83 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SC\underline{H}_AH_BCH(CH_3)$), 2.68 ('sxt', *J* = 7.0 Hz, 1 H, $C\underline{H}(CH_3)C{=}O$), 2.57 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SCH_A\underline{H}_BCH(CH_3)$), 2.49 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2C\underline{H}_2S$), 1.60 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3C\underline{H}_2CH_2S$), 1.25 (d, *J* = 7.0 Hz, 3 H, $CH(C\underline{H}_3)C{=}O$), 0.98 (t, *J* = 7.5 Hz, 3 H,

[vii] Racemic products for HPLC/GC analysis were formed using a modification of general procedure **F**, with 10 mol% BEMP (2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine) in 0.5 M toluene, and left until completion.

$C\underline{H_3}CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.7 ($\underline{C}$=O), 51.8 (O$\underline{C}H_3$), 40.2 ($\underline{C}H(CH_3)C$=O), 35.4 (S$\underline{C}H_2CH(CH_3)$), 34.7 ($CH_3CH_2\underline{C}H_2S$), 22.9 ($CH_3\underline{C}H_2CH_2S$), 16.8 (CH($\underline{C}H_3$)C=O), 13.4 ($\underline{C}H_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_8H_{16}NaO_2S$) requires *m/z* 199.0763, found *m/z* 199.0758.

Phenyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (4b)

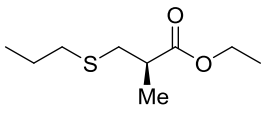


4b

Phenyl methacrylate **2b** (65 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4b** as a colorless oil in >99% yield (48 mg) and 95% ee [determined by HPLC, chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min, λ = 230 nm, t (major) = 7.13 min, t (minor) = 7.64 min].

$[\alpha]_D^{20}$ = +44.2 (*c* 0.65, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2963, 1757 (C=O), 1594, 1493, 1457, 1192 (C-O), 1162, 1136 (C-O), 748, 690; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.41 - 7.35 (m, 2 H, Ar$\underline{H}$), 7.27 - 7.20 (m, 1 H, Ar$\underline{H}$), 7.13 - 7.08 (m, 2 H, Ar$\underline{H}$), 2.99 - 2.88 (m, 2 H, S$\underline{H_A}H_BCH(CH_3)$ and $C\underline{H}(CH_3)$C=O), 2.77 - 2.68 (m, 1 H, $SCH_A\underline{H_B}CH(CH_3)$), 2.57 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2C\underline{H_2}S$), 1.64 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3C\underline{H_2}CH_2S$), 1.40 (d, *J* = 7.0 Hz, 3 H, CH($C\underline{H_3}$)C=O), 1.00 (t, *J* = 7.5 Hz, 3 H, $C\underline{H_3}CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 173.7 ($\underline{C}$=O), 150.7 (Ar$\underline{C}$), 129.4 (Ar$\underline{C}H$), 125.8 (Ar$\underline{C}H$), 121.5 (Ar$\underline{C}H$), 40.5 ($\underline{C}H(CH_3)$C=O), 35.4 (S$\underline{C}H_2CH(CH_3)$), 34.7 ($CH_3CH_2\underline{C}H_2SH$), 22.9 ($CH_3\underline{C}H_2CH_2SH$), 16.9 (CH($\underline{C}H_3$)C=O), 13.4 ($\underline{C}H_3CH_2CH_2SH$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{13}H_{18}NaO_2S$) requires *m/z* 261.0920, found *m/z* 261.0908.

Ethyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (4c)

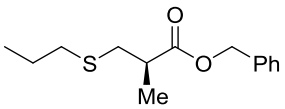


4c

Ethyl methacrylate **2c** (124 μL, 1.00 mmol, 5.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 19/1) to afford the title compound **4c** as a colorless oil in 87% yield (33 mg) and 92% ee [determined by GC, Supelco β-dex^{TM} 325, 30 m, 0.25 mm, 0.25 μm, carrier gas He (flow rate 30 cm/s); column temperature 80 ℃ ramp 1 ℃/min to 90 ℃ then 90 ℃ t (minor) = 62.70 min, t (major) = 63.21 min].

$[\alpha]_D^{24}$ = +15.8 (*c* 0.66, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2964, 1732 (C=O), 1458, 1375, 1340, 1204, 1159 (C-O), 1117, 1030, 862; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 4.16 (q, *J* = 7.0 Hz, 2 H, $OC\underline{H}_2CH_3$), 2.83 (dd, *J* = 12.5, 7.0 Hz, 1 H, $SC\underline{H}_AH_BCH(CH_3)$), 2.65 ('sxt', *J* = 7.0 Hz, 1 H, $C\underline{H}(CH_3)C=O$), 2.56 (dd, *J* = 12.5, 7.0 Hz, 1 H, $SCH_A\underline{H}_BCH(CH_3)$), 2.50 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2C\underline{H}_2S$), 1.60 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3C\underline{H}_2CH_2S$), 1.27 (t, *J* = 7.0 Hz, 3 H, $OCH_2C\underline{H}_3$), 1.25 (d, *J* = 7.0 Hz, 3 H, $CH(C\underline{H}_3)C=O$), 0.98 ppm (t, *J* = 7.5 Hz, 3 H, $C\underline{H}_3CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.2 ($\underline{C}=O$), 60.5 ($O\underline{C}H_2CH_3$), 40.3 ($\underline{C}H(CH_3)C=O$), 35.4 ($S\underline{C}H_2CH(CH_3)$), 34.7 ($CH_3CH_2\underline{C}H_2S$), 22.9 ($CH_3\underline{C}H_2CH_2S$), 16.8 ($CH(\underline{C}H_3)C=O$), 14.2 ($OCH_2\underline{C}H_3$), 13.4 ($\underline{C}H_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_9H_{18}NaO_2S$) requires *m/z* 213.0920, found *m/z* 213.0916.

Benzyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (4d)

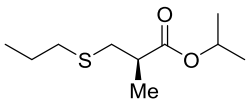


4d

Benzyl methacrylate **2d** (68 μL, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4d** as a colorless oil in 78% yield (39 mg) and 89% ee [determined by HPLC, chiralcel OD, hexane/isopropanol = 99/1, 1 mL/min, λ = 210 nm, t (minor) = 7.49 min, t (major) = 8.31 min].

$[\alpha]_D^{20}$ = +18.8 (*c* 0.73, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2962, 2361, 1735 (C=O), 1456, 1240 (C-O), 1157 (C-O), 1028, 751, 697; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.41 - 7.30 (m, 5 H, $Ar\underline{H}$), 5.15 (s, 2 H, $OC\underline{H}_2Ph$), 2.86 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SC\underline{H}_AH_BCH(CH_3)$), 2.74 ('sxt', *J* = 7.0 Hz, 1 H, $C\underline{H}(CH_3)C=O$), 2.60 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SCH_A\underline{H}_BCH(CH_3)$), 2.49 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2C\underline{H}_2S$), 1.67 - 1.52 (m, 2 H, $CH_3C\underline{H}_2CH_2S$), 1.28 (d, *J* = 7.0 Hz, 3 H, $CH(C\underline{H}_3)C=O$), 0.97 (t, *J* = 7.5 Hz, 3 H, $C\underline{H}_3CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.0 ($\underline{C}=O$), 135.9 ($Ar\underline{C}$), 128.5 ($Ar\underline{C}H$), 128.2 ($Ar\underline{C}H$), 128.1 ($Ar\underline{C}H$), 66.4 ($O\underline{C}H_2Ph$), 40.3 ($\underline{C}H(CH_3)C=O$), 35.4 ($S\underline{C}H_2CH(CH_3)$), 34.7 ($CH_3CH_2\underline{C}H_2S$), 22.9 ($CH_3\underline{C}H_2CH_2S$), 16.8 ($CH(\underline{C}H_3)C=O$), 13.4 ($\underline{C}H_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{20}NaO_2S$) requires *m/z* 275.1076, found *m/z* 275.1081.

Propan-2-yl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (4e)

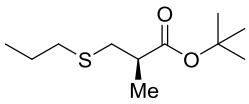


4e

Isopropyl methacrylate **2e** (144 µL, 1.00 mmol, 5.0 eq) was reacted with 1-propanethiol **3a** (18 µL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 19/1) to afford the title compound **4e** as a colorless oil in 71% yield (29 mg) and 93% ee [determined by HPLC, chiralcel OD, hexane/isopropanol = 99.5/0.5, 1 mL/min, λ = 220 nm, t (minor) = 6.32 min, t (major) = 7.25 min].

$[\alpha]_D^{23}$ = +22.3 (*c* 0.39, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2972, 1731 (C=O), 1457, 1375, 1208, 1169 (C-O), 1109; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 5.02 (spt, *J* = 6.5 Hz, 1 H, OC<u>H</u>$(CH_3)_2$), 2.85 - 2.78 (m, 1 H, SC<u>H$_A$</u>H$_B$CH(CH_3)), 2.67 - 2.45 (m, 4 H, SCH$_A$<u>H$_B$</u>CH(CH_3), C<u>H</u>(CH_3)C=O and CH_3CH_2C<u>H$_2$</u>S), 1.60 ('sxt', *J* = 7.5 Hz, 2 H, CH_3C<u>H$_2$</u>CH_3S), 1.28 - 1.20 (m, 9 H, CH(C<u>H$_3$</u>)C=O and OCH(C<u>H$_3$</u>)$_2$), 0.98 (t, *J* = 7.5 Hz, 3 H, C<u>H$_3$</u>CH_2CH_2S); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.3 (<u>C</u>=O), 68.3 (O<u>C</u>H$(CH_3)_2$), 40.9 (<u>C</u>H(CH_3)C=O), 35.9 (S<u>C</u>H_2CH(CH_3)), 35.1 (CH_3CH_2<u>C</u>H_2S), 23.4 (CH_3<u>C</u>H_2CH_2S), 22.3 (one of OCH(<u>C</u>$H_3)_2$), 22.2 (one of CH(<u>C</u>$H_3)_2$), 17.3 (CH(<u>C</u>H_3)C=O), 13.9 (<u>C</u>$H_3CH_2CH_2$S); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{10}H_{20}NaO_2S$) requires *m/z* 227.1076, found *m/z* 227.1074.

***tert*-Butyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (4f)**



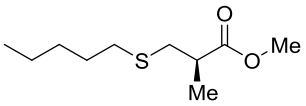
4f

tert-Butyl methacrylate **2f** (163 µL, 1.00 mmol, 5.0 eq) was reacted with 1-propanethiol **3a** (18 µL, 0.20 mmol, 1.0 eq) according to the general procedure **F** stirring for 48 h. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 19/1) to afford the title compound **4f** as a colorless oil in 37% yield (16 mg) and 96% ee [determined by GC, Supelco β-dex^{TM} 325, 30 m, 0.25 mm, 0.25 µm, carrier gas He (flow rate 30 cm/s); column temperature 80 ℃ ramp 1 ℃/min to 90 ℃ then 90 ℃ t (major) = 81.36 min, t (minor) = 82.60 min].

$[\alpha]_D^{23}$ = +19.2 (*c* 0.63, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2969, 1728 (C=O), 1458, 1367, 1252, 1148 (C-O), 848; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 2.80 (s, 1 H, SC<u>H$_A$</u>H$_B$CH(CH_3)), 2.60 - 2.47 (m, 4 H, SCH$_A$<u>H$_B$</u>CH(CH_3), C<u>H</u>(CH_3)C=O and CH_3CH_2C<u>H$_2$</u>S), 1.61 ('sxt', *J* = 7.5 Hz, 2 H, CH_3C<u>H$_2$</u>CH_2S), 1.46 (s, 9 H, OC(C<u>H$_3$</u>)$_3$), 1.21 (d, *J* = 7.0 Hz, 3 H, CH(C<u>H$_3$</u>)C=O), 0.99 ppm (t, *J* = 7.5 Hz, 3 H, C<u>H$_3$</u>CH_2CH_2S); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 174.6 (<u>C</u>=O), 80.4 (O<u>C</u>$(CH_3)_3$), 41.1 (<u>C</u>H(CH_3)C=O), 35.6 (S<u>C</u>H_2CH(CH_3)), 34.7 (CH_3CH_2<u>C</u>H_2S), 28.0 (OC(<u>C</u>$H_3)_3$),

22.9 ($CH_3\underline{C}H_2CH_2S$), 16.9 ($CH(\underline{C}H_3)C=O$), 13.4 ($\underline{C}H_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{11}H_{22}NaO_2S$) requires *m/z* 241.1233, found *m/z* 241.1240.

Methyl (2*R*)-2-methyl-3-(pentylsulfanyl)propanoate (4g)

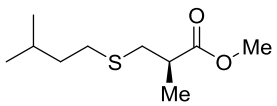


4g

Methyl methacrylate **2a** (110 µL, 1.0 mmol, 5.0 eq) was reacted with 1-pentanethiol **3b** (25 µL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4g** as a yellow oil in >99% yield (41 mg) and 93% ee [determined by HPLC, chiralpak AD-H, hexane/isopropanol = 99/1, 1 mL/min, λ = 230 nm, t (major) = 4.71 min, t (minor) = 5.04 min].

$[\alpha]_D^{20}$ = +24.9 (*c* 1.21, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2928, 1738 (C=O), 1459, 1209 (C-O), 1162 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 3.70 (s, 3 H, $OC\underline{H}_3$), 2.83 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SC\underline{H}_AH_BCH(CH_3)$), 2.68 ('sxt', *J* = 7.0 Hz, 1 H, $C\underline{H}(CH_3)C=O$), 2.57 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SCH_A\underline{H}_BCH(CH_3)$), 2.51 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2CH_2CH_2C\underline{H}_2S$), 1.57 ('quin', *J* = 7.5 Hz, 2 H, $CH_3CH_2CH_2C\underline{H}_2CH_2S$), 1.41 - 1.28 (m, 4 H, $CH_3C\underline{H}_2CH_2CH_2CH_2S$ and $CH_3CH_2C\underline{H}_2CH_2CH_2S$), 1.25 (d, *J* = 7.0 Hz, 3 H, $CH(C\underline{H}_3)C=O$), 0.90 (t, *J* = 7.0 Hz, 3 H, $C\underline{H}_3CH_2CH_2CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.7 ($\underline{C}=O$), 51.8 ($O\underline{C}H_3$), 40.2 ($\underline{C}H(CH_3)C=O$), 35.5 ($S\underline{C}H_2CH(CH_3)$), 32.6 ($CH_3CH_2CH_2CH_2\underline{C}H_2S$), 31.0 ($CH_3CH_2\underline{C}H_2CH_2CH_2S$), 29.3 ($CH_3CH_2CH_2\underline{C}H_2CH_2S$), 22.3 ($CH_3\underline{C}H_2CH_2CH_2CH_2S$), 16.8 ($CH(\underline{C}H_3)C=O$), 13.9 ($\underline{C}H_3CH_2CH_2CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{10}H_{20}NaO_2S$) requires *m/z* 227.1076, found *m/z* 227.1082.

Methyl (2*R*)-2-methyl-3-[(3-methylbutyl)sulfanyl]propanoate (4h)

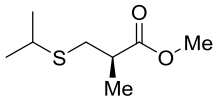


4h

Methyl methacrylate **2a** (0.107 mL, 1.00 mmol, 5.0 eq) was reacted with isopentylmercaptan **3c** (25 µL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether to petroleum ether/Et_2O 49/1) to afford the title compound **4h** as a colorless oil in 86% yield (35 mg) and 92% ee [determined by GC, Supelco β-dex^{TM} 325, 30 m, 0.25 mm, 0.25 µm, carrier gas He (flow rate 40 cm/s); column temperature 80 ℃ ramp 1 ℃/min to 120 ℃ then 10 ℃/min to 220 ℃, t (minor) = 89.56 min, t (major) = 90.27 min].

$[\alpha]_D^{25}$ = +14.2 (*c* 0.51, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2955, 1740 (C=O), 1460, 1163 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 3.69 (s, 3 H, $OC\underline{H}_3$), 2.82 (dd, *J* = 13.0 Hz, 7.0 Hz, 1 H, $SC\underline{H}_AH_BCH(CH_3)$), 2.67 ('sxt', *J* = 7.0 Hz, 1 H, $C\underline{H}(CH_3)C=O$), 2.56 (dd, J = 13.0, 7.0 Hz, 1 H, $SCH_A\underline{H}_BCH(CH_3)$), 2.53 - 2.45 (m, 2 H, $CH_2C\underline{H}_2S$), 1.72 - 1.57 (m, 1 H, $C\underline{H}(CH_3)_2$), 1.50 - 1.38 (m, 2 H, $C\underline{H}_2CH_2S$), 1.24 (d, *J* = 7.0 Hz, 3 H, $CH(C\underline{H}_3)C=O$), 0.88 (d, *J* = 6.5 Hz, 6 H, $CH(C\underline{H}_3)_2$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.7 ($\underline{C}=O$), 51.8 ($O\underline{C}H_3$) 40.1 ($\underline{C}H(CH_3)C=O$), 38.5 ($\underline{C}H_2CH_2S$), 35.4 ($CH_2\underline{C}H_2S$), 30.6 ($S\underline{C}H_2CH(CH_3)$), 27.4 ($\underline{C}H(CH_3)_2$), 22.2 ($CH(\underline{C}H_3)_2$), 16.8 ($CH(\underline{C}H_3)C=O$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{10}H_{20}NaO_2S$) requires *m/z* 227.1076, found *m/z* 227.1072.

Methyl (2*R*)-2-methyl-3-(propan-2-ylsulfanyl)propanoate (4i)

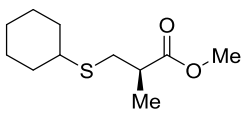


4i

Methyl methacrylate **2a** (110 µL, 1.0 mmol, 5.0 eq) was reacted with 2-propanethiol **3d** (19 µL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4i** as a colorless oil in >99% yield (36 mg) and 92% ee [determined by GC, Supelco β-dex^{TM} 325, 30 m, 0.25 mm, 0.25 µm, carrier gas He (flow rate 30 cm/s); column temperature 80℃ ramp 1 ℃/min to 90 ℃ then 90 ℃ t (minor) = 31.11 min, t (major) = 31.45 min].

$[\alpha]_D^{20}$ = +23.1 (*c* 0.79, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2959, 2360, 1739 (C=O), 1460, 1210 (C-O), 1164 (C-O), 772; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 3.70 (s, 3 H, $OC\underline{H}_3$), 2.91 (spt, *J* = 7.0 Hz, 1 H, $(CH_3)_2C\underline{H}S$), 2.85 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SC\underline{H}_AH_BCH(CH_3)$), 2.66 ('sxt', *J* = 7.0 Hz, 1 H, $C\underline{H}(CH_3)C=O$), 2.59 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SCH_A\underline{H}_BCH(CH_3)$), 1.30 - 1.23 (m, 9 H, $(C\underline{H}_3)_2CHS$ and $CH(C\underline{H}_3)C=O$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.7 ($\underline{C}=O$), 51.8 ($O\underline{C}H_3$), 40.3 ($\underline{C}H(CH_3)C=O$), 35.3 ($(CH_3)_2\underline{C}HS$), 33.8 ($S\underline{C}H_2CH(CH_3)$), 23.4 ($\underline{C}H_3CHCH_3$), 23.3 ($CH_3CH\underline{C}H_3$), 16.9 ($CH(\underline{C}H_3)C=O$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_8H_{16}NaO_2S$) requires *m/z* 199.0763, found *m/z* 199.0755.

Methyl (2*R*)-3-(cyclohexylsulfanyl)-2-methylpropanoate (4j)



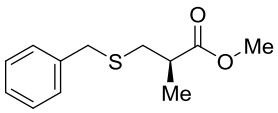
4j

Methyl methacrylate **2a** (110 µL, 1.0 mmol, 5.0 eq) was reacted with cyclohexanethiol **3e** (24 µL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4j** as a colorless oil in 81% yield (35 mg) and 90% ee

[determined by HPLC, chiralpak AS-H, hexane/isopropanol = 99.5/0.5, 1 mL/min, λ = 210 nm, t (major) = 13.52 min, t (minor) = 15.05 min].

$[\alpha]_D^{20}$ = +21.2 (*c* 0.79, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2929, 2852, 1738 (C=O), 1449, 1262, 1206 (C-O), 1162 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 3.70 (s, 3 H, OCH_3), 2.86 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SCH_AH_BCH(CH_3)$), 2.71 - 2.56 (m, 3 H, CHS, $SCH_AH_BCH(CH_3)$ and $CH(CH_3)C=O$), 2.02 - 1.89 (m, 2 H, 2 H of C_6H_{11}), 1.84 - 1.69 (m, 2 H, 2 H of C_6H_{11}), 1.66 - 1.55 (m, 1 H, 1 H of C_6H_{11}), 1.35 - 1.23 (m, 5 H, 5 H of C_6H_{11}), 1.25 (d, *J* = 7.0 Hz, 3 H, $CH(CH_3)C=O$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.7 (C=O), 51.8 (OCH_3), 44.0 (either CHS or $CH(CH_3)C=O$), 40.5 (either CHS or $CH(CH_3)C=O$), 33.7 (1 C of C_6H_{11}), 33.6 (1 C of C_6H_{11}), 33.4 ($SCH_2CH(CH_3)$), 26.1 (1 C of C_6H_{11}), 26.1 (1 C of C_6H_{11}), 25.8 (1 C of C_6H_{11}), 16.9 ($CH(CH_3)C=O$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{11}H_{20}NaO_2S$) requires *m/z* 239.1076, found *m/z* 239.1073.

Methyl (2*R*)-3-(benzylsulfanyl)-2-methylpropanoate (4k)

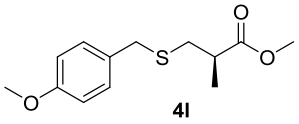


4k

Methyl methacrylate **2a** (110 μL, 1.0 mmol, 5.0 eq) was reacted with benzyl mercaptan **3f** (24 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4k** as a pale yellow oil in 85% yield (38 mg) and 90% ee [determined by HPLC, chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min, λ = 230 nm, t (major) = 7.58 min, t (minor) = 8.10 min].

$[\alpha]_D^{20}$ = +30.5 (*c* 0.69, $CHCl_3$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.31 - 7.25 (m, 4 H, ArH), 7.25 - 7.18 (m, 1 H, ArH), 3.68 (s, 2 H, $PhCH_2S$), 3.65 (s, 3 H, OCH_3), 2.71 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SCH_AH_BCH(CH_3)$), 2.60 ('sxt', *J* = 7.0 Hz, 1 H, $CH(CH_3)C=O$), 2.43 (dd, *J* = 13.0, 6.5 Hz, 1 H, $SCH_AH_BCH(CH_3)$), 1.17 (d, *J* = 7.0 Hz, 3 H, $CH(CH_3)C=O$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.2 (C=O), 137.8 (ArC), 128.5 (ArCH), 128.2 (ArCH), 126.7 (ArCH), 51.5 (OCH_3), 39.5 ($CH(CH_3)C=O$), 36.3 ($PhCH_2S$), 34.2 ($SCH_2CH(CH_3)$), 16.5 ($CH(CH_3)C=O$); **LRMS** (ES+) mass calculated for $[M+Na]^+$ ($C_{12}H_{16}NaO_2S$) requires *m/z* 247.1, found *m/z* 247.1. All characterisation data agree with those published in the literature.[20]

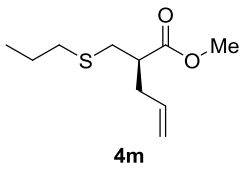
Methyl (2*R*)-3-[(4-methoxybenzyl)sulfanyl]-2-methylpropanoate (4l)



Methyl methacrylate (110 µL, 1.0 mmol, 5.0 eq) was reacted with 4-methoxybenzyl mercaptan **3g** (28 µL, 0.20 mmol, 1.0 eq) according to general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 4/1) to afford the title compound **4l** as a colourless oil in 89% yield (45 mg) and 89% ee [determined by HPLC, Chiralcel OD, hexane/isopropanol = 98/2, 1 mL/min, λ = 220 nm, t (minor) = 9.52 min, t (major) = 10.53 min].

$[\alpha]_D^{22}$ = +25.2 (*c* 1.00, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2952, 2836, 1735 (C=O), 1511, 1248, 1212 (C-O), 1174 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.26 - 7.20 (m, 2 H, Ar$\underline{H}$), 6.89 - 6.82 (m, 2 H, Ar$\underline{H}$), 3.81 (s, 3 H, ArOC$\underline{H_3}$), 3.70 (s, 3 H, C(O)C$\underline{H_3}$), 3.68 (s, 2 H, ArC$\underline{H_2}$S), 2.74 (dd, *J* = 13.0, 7.0 Hz, 1 H, SC$\underline{H_A}H_BCH(CH_3)$), 2.65 ('sxt', *J* = 7.0 Hz, 1 H, $SCH_AH_BC\underline{H}(CH_3)$), 2.46 (dd, *J* = 13.0, 7.0 Hz, 1 H, $SCH_A\underline{H_B}CH(CH_3)$), 1.21 (d, *J* = 7.0 Hz, 3 H, $SCH_AH_BCH(C\underline{H_3})$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.6 ($\underline{C}$=O), 158.6 (ArC), 130.0 (Ar$\underline{C}$), 129.9 (Ar$\underline{C}$H), 113.9 (Ar$\underline{C}$H), 55.3 (ArO$\underline{C}H_3$), 51.8 (C(O)$\underline{C}H_3$), 39.8 ($SCH_AH_BC\underline{H}(CH_3)$), 36.0 (Ar$\underline{C}H_2$S), 34.4 (S$\underline{C}H_AH_BCH(CH_3)$), 16.9 ($SCH_AH_BCH(\underline{C}H_3)$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{13}H_{18}NaO_3S$) requires *m/z* 277.0869, found *m/z* 277.0868.

Methyl (2*R*)-2-[(propylsulfanyl)methyl]pent-4-enoate (4m)

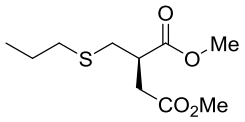


Ester **2g** (50 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 µL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether to petroleum ether/Et_2O 49/1) to afford the title compound **4m** as a colorless oil in 94% yield (38 mg) and 93% ee [determined by HPLC, chiralpak AS-H, hexane/isopropanol = 99.5/0.5, 1 mL/min, λ = 220 nm, t (major) = 12.62 min, t (minor) = 14.42 min].

$[\alpha]_D^{24}$ = +23.0 (*c* 0.32, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2959, 1739 (C=O), 1438, 1218; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 5.70 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1 H, C$\underline{H}$=CH_AH_B), 5.12 - 4.97 (m, 2 H, CH=C$\underline{H_A}H_B$ and CH=$CH_A\underline{H_B}$), 3.67 (s, 3 H, OC$\underline{H_3}$), 2.80 - 2.70 (m, 1 H, SC$\underline{H_A}H_BCH(CH_2CH=CH_2)$), 2.69 - 2.57 (m, 2 H, $SCH_A\underline{H_B}CH(CH_2CH=CH_2)$ and C$\underline{H}$($CH_2CH=CH_2$)C=O), 2.46 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2C\underline{H_2}S$), 2.31 - 2.41 (m, 2 H, C$\underline{H_2}$CH=CH_2), 1.57 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3C\underline{H_2}CH_2S$), 0.95 (t, *J* = 7.5 Hz, 3 H, C$\underline{H_3}CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 174.5 ($\underline{C}$=O), 134.5 ($\underline{C}$H=CH_AH_B), 117.4 (CH=$\underline{C}H_AH_B$), 51.6 (O$\underline{C}H_3$), 45.7 ($SCH_2\underline{C}HC$=O), 35.8 ($\underline{C}H_2CH=CH_2$), 34.5 ($SCH_3CH_2\underline{C}H_2S$),

33.2 (S<u>C</u>H$_2$CHC=O), 22.8 (CH$_3$<u>C</u>H$_2$CH$_2$S) 13.3 (<u>C</u>H$_3$CH$_2$CH$_2$S); **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{10}H_{18}NaO_2S$) requires *m/z* 225.0920, found *m/z* 225.0916.

Dimethyl (2*R*)-2-((propylsulfanyl)methyl)succinate (4n)

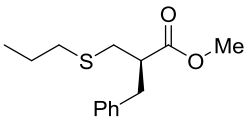


4n

Dimethyl itaconate **2h** (63 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/EtOAc/EtOH = 94/4.5/1.5) to afford the title compound **4n** as a colorless oil in 85% yield (40 mg) and 90% ee [determined by HPLC, chiralpak AS-H, hexane/isopropanol = 99/1, 1 mL/min, λ = 220 nm, t (minor) = 10.90 min, t (major) = 11.76 min].

[α]$_D^{20}$ = +7.0 (*c* 0.63, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2957, 1737 (C=O), 1437, 1201 (C-O), 1166 (C-O), 1035; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ (ppm): 3.73 (s, 3 H, one of OC<u>H$_3$</u>), 3.70 (s, 3 H, one of OC<u>H$_3$</u>), 3.07 (tt, *J* = 8.0, 6.0 Hz, 1 H, C<u>H</u>(CH$_2$CO$_2$Me)C=O), 2.89 (dd, *J* = 13.5, 6.0 Hz, 1 H, either SC<u>H$_A$</u>H$_B$CH(CH$_2$CO$_2$Me) or CH(C<u>H$_A$</u>H$_B$CO$_2$Me)C=O), 2.79 (dd, *J* = 17.0, 8.0 Hz, 1 H, either SC<u>H$_A$</u>H$_B$CH(CH$_2$CO$_2$Me) or CH(C<u>H$_A$</u>H$_B$CO$_2$Me)C=O), 2.73 (dd, *J* = 17.0, 5.5 Hz, 1 H, either SCH$_A$<u>H$_B$</u>CH(CH$_2$CO$_2$Me) or CH(CH$_A$<u>H$_B$</u>CO$_2$Me)C=O), 2.67 (dd, *J* = 13.5, 8.0 Hz, 1 H, either SCH$_A$<u>H$_B$</u>CH(CH$_2$CO$_2$Me) or CH(CH$_A$<u>H$_B$</u>CO$_2$Me)C=O), 2.50 (t, *J* = 7.5 Hz, 2 H, CH$_3$CH$_2$C<u>H$_2$</u>S), 1.66 - 1.56 (m, 2 H, CH$_3$C<u>H$_2$</u>CH$_2$S), 0.99 (t, *J* = 7.5 Hz, 3 H, C<u>H$_3$</u>CH$_2$CH$_2$S); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ (ppm): 173.8 (one of <u>C</u>=O), 172.2 (one of <u>C</u>=O), 52.1 (one of O<u>C</u>H$_3$), 51.9 (one of O<u>C</u>H$_3$), 41.4 (<u>C</u>H(CH$_2$CO$_2$Me)C=O), 34.7 (either S<u>C</u>H$_2$CH(CH$_2$CO$_2$Me) or CH(<u>C</u>H$_2$CO$_2$Me)C=O), 34.4 (CH$_3$CH$_2$<u>C</u>H$_2$S), 33.4 (either S<u>C</u>H$_2$CH(CH$_2$CO$_2$Me) or CH(<u>C</u>H$_2$CO$_2$Me)C=O), 22.7 (CH$_3$<u>C</u>H$_2$CH$_2$S), 13.4 (<u>C</u>H$_3$CH$_2$CH$_2$S); **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{10}H_{18}NaO_4S$) requires *m/z* 257.0818, found *m/z* 257.0825.

Methyl (2*R*)-2-benzyl-3-(propylsulfanyl)propanoate (4o)

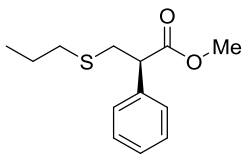


4o

Methyl 2-benzylprop-2-enoate[6] **2i** (70 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to a modified general procedure **F** stirring for 48 h. The reaction mixture was purified by FCC (petroleum ether/Et$_2$O = 99/1 to 49/1) to afford the title compound **4o** as a pale yellow oil in 99% yield (50 mg) and 86% ee [determined by HPLC, chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min, λ = 230 nm, t (major) = 7.36 min, t (minor) = 7.92 min].

$[\alpha]_D^{20}$ = +86.0 (*c* 1.01, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2959, 1735 (C=O), 1495, 1435, 1369, 1214 (C-O), 1162 (C-O), 1029, 745, 700; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.30 - 7.24 (m, 2 H, ArH), 7.23 - 7.12 (m, 3 H, ArH), 3.62 (s, 3 H, OCH_3), 3.01 - 2.83 (m, 3 H, $CH(CH_2Ph)C{=}O$ and either $CH(CH_2Ph)C{=}O$ or $SCH_2C(CH_2Ph)$), 2.76 (dd, *J* = 13.0, 8.0 Hz, 1 H, either $SCH_AH_BCH(CH_2Ph)$ or $CH(CH_AH_BPh)C{=}O$), 2.62 (dd, *J* = 13.0, 5.5 Hz, 1 H, either $SCH_AH_BCH(CH_2Ph)$ or $CH(CH_AH_BPh)C{=}O$), 2.45 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2CH_2S$), 1.54 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3CH_2CH_2S$), 0.94 (t, *J* = 7.5 Hz, 3 H, $CH_3CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 174.5 (C=O), 138.5 (ArC), 128.8 (ArCH), 128.5 (ArCH), 126.5 (ArCH)), 51.7 (OCH_3), 48.0 ($CH(CH_2Ph)C{=}O$), 37.7 (either $SCH_2CH(CH_2Ph)$ or $CH(CH_2Ph)C{=}O$), 34.5 ($CH_3CH_2CH_2S$), 33.2 (either $SCH_2CH(CH_2Ph)$ or $CH(CH_2Ph)C{=}O$), 22.8 ($CH_3CH_2CH_2S$), 13.4 ($CH_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{20}NaO_2S$) requires *m/z* 275.1076, found *m/z* 275.1075.

Methyl (2*R*)-2-phenyl-3-(propylsulfanyl)propanoate (4p)

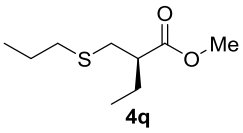


4p

Methyl 2-phenylprop-2-enoate[6] **2j** (65 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1) to afford the title compound **4p** as a colorless oil in 84% yield (40 mg) and 83% ee [determined by HPLC, chiralpak AS-H, hexane/isopropanol = 99/1, 1 mL/min, λ = 230 nm, t (major) = 6.49 min, t (minor) = 7.15 min].

$[\alpha]_D^{20}$ = -86.6 (*c* 0.58, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2958, 1736 (C=O), 1454, 1435, 1369, 1213 (C-O), 1156 (C-O), 728, 698; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.32 - 7.20 (m, 5 H, ArH), 3.74 (dd, *J* = 9.5, 6.0 Hz, 1 H, CH(Ph)C=O), 3.64 (s, 3 H, OCH_3), 3.15 (dd, *J* = 13.0, 9.5 Hz, 1 H, $SCH_AH_BCH(Ph)$), 2.80 (dd, *J* = 13.0, 6.0 Hz, 1 H, $SCH_AH_BCH(Ph)$), 2.43 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2CH_2S$), 1.54 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3CH_2CH_2S$), 0.91 (t, *J* = 7.5 Hz, 3 H, $CH_3CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 173.2 (C=O), 137.9 (ArC), 128.8 (ArCH), 127.8 (ArCH), 127.7 (ArCH), 52.3, 52.2 (CH(Ph)C=O and OCH_3), 35.2 ($SCH_2CH(Ph)$), 34.7 ($CH_3CH_2CH_2S$), 22.9 ($CH_3CH_2CH_2S$), 13.4 ($CH_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{13}H_{18}NaO_2S$) requires *m/z* 261.0920, found *m/z* 261.0908.

Methyl (2*R*)-2-[(propylsulfanyl)methyl]butanoate (4q)

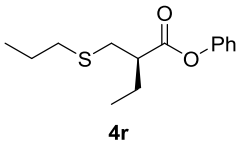


4q

Methyl 2-methylidenebutanoate **2k** (46 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol (18 μL, 0.20 mmol, 1.0 eq) according to a modified general procedure **F** stirring for 48 h. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4q** as a colorless oil in 47% yield (18 mg) and 92% ee [determined by HPLC, chiralpak AD-H, hexane/isopropanol = 99/1, 1 mL/min, λ = 230 nm, t (major) = 11.53 min, t (minor) = 12.59 min].

$[\alpha]_D^{20}$ = +27.1 (*c* 0.72, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2963, 1737 (C=O), 1460, 1263, 1202 (C-O), 1160 (C-O), 797; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 3.72 (s, 3 H, OC$\underline{H}_3$), 2.77 (dd, *J* = 13.5, 8.5 Hz, 1 H, SC$\underline{H}_A$$H_B$CH($CH_2CH_3$)), 2.63 (dd, *J* = 13.0, 6.0 Hz, 1 H, SC$\underline{H}_A$$H_B$CH($CH_2CH_3$)), 2.58 - 2.50 (m, 1 H, C$\underline{H}$(CH_2CH_3)C=O), 2.49 (t, *J* = 7.5 Hz, 1 H, $CH_3CH_2C\underline{H}_2S$), 1.71 - 1.63 (m, 2 H, CH(C$\underline{H}_2CH_3$)C=O), 1.63 - 1.55 (m, 2 H, $CH_3C\underline{H}_2CH_2S$), 0.98 (t, *J* = 7.5 Hz, 3 H, C$\underline{H}_3CH_2CH_2S$), 0.92 ppm (t, *J* = 7.5 Hz, 3 H, CH($CH_2C\underline{H}_3$)C=O); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 175.2 (C=O), 51.6 (O$\underline{C}H_3$), 47.6 ($\underline{C}$H(CH_2CH_3)C=O), 34.6 ($CH_3CH_2\underline{C}H_2S$), 33.6 (S$\underline{C}H_2$CH($CH_2CH_3$)), 25.1 (CH($\underline{C}H_2CH_3$)C=O), 22.9 ($CH_3\underline{C}H_2CH_2S$), 13.4 ($\underline{C}H_3CH_2CH_2S$), 11.6 (CH($CH_2\underline{C}H_3$)C=O); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_9H_{18}NaO_2S$) requires *m/z* 213.0920, found *m/z* 213.0916.

Phenyl (2*R*)-2-[(propylsulfanyl)methyl]butanoate (4r)



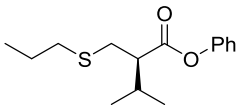
4r

Ester **2l** (70 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4r** as a colorless oil in 85% yield (43 mg) and 92% ee [determined by HPLC, chiralcel AS-H, hexane/isopropanol = 98/2, 1 mL/min, λ = 220 nm, t (major) = 6.10 min, t (minor) = 6.43 min].

$[\alpha]_D^{24}$ = +40.7 (*c* 0.82, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2969, 1754 (C=O), 1457, 1197 (C-O), 1133 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.44 - 7.34 (m, 2 H, Ar$\underline{H}$), 7.26 - 7.20 (m, 1 H, Ar$\underline{H}$), 7.15 - 7.08 (m, 2 H, Ar$\underline{H}$), 2.95 - 2.84 (m, 1 H, SC$\underline{H}_A$$H_B$CH), 2.83 - 2.73 (m, 2 H, SC$H_A\underline{H}_B$CH and C$\underline{H}$(CH_2CH_3)C=O), 2.57 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2C\underline{H}_2S$), 1.91 - 1.74 (m, 2 H, CH(C$\underline{H}_2CH_3$)C=O), 1.64 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3C\underline{H}_2CH_2S$), 1.06 (3 H, t, *J* = 7.5 Hz, CH($CH_2C\underline{H}_3$)C=O), 1.00 (3 H, t, *J* = 7.5 Hz, C$\underline{H}_3CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ

(ppm): 173.4 (C=O), 150.9 (ArC), 129.5 (ArCH), 125.9 (ArCH), 121.8 (ArCH), 47.9 ($CH(CH_2CH_3)C=O$), 34.7 ($CH_3CH_2CH_2S$), 33.8 (SCH_2CH), 25.4 ($CH(CH_2CH_3)C=O$), 23.0 ($CH_3CH_2CH_2S$), 13.6 ($CH(CH_2CH_3)C=O$), 11.8 ($CH_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{20}NaO_2S$) requires *m/z* 275.1076, found *m/z* 275.1070.

Phenyl (2*R*)-3-methyl-2-[(propylsulfanyl)methyl]butanoate (4s)

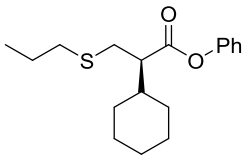


4s

Ester **2m** (76 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **D**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4s** as a colorless oil in 98% yield (52 mg) and 88% ee [determined by HPLC, chiralcel OD, hexane/isopropanol = 99/1, 1 mL/min, λ = 220 nm, t (minor) = 7.60 min, t (major) = 8.03 min].

$[\alpha]_D^{24}$ = +52.8 (*c* 1.06, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2963, 1756 (C=O), 1492, 1194 (C-O), 1121 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.43 - 7.34 (m, 2 H, ArH), 7.25 – 7.21 (m, 1 H, ArH), 7.16 - 7.09 (m, 2 H, ArH), 2.84 ('d', *J* = 7.5 Hz, 2 H, SCH_AH_BCH and SCH_AH_BCH), 2.65 ('q', *J* = 7.5 Hz, 1 H, SCH_AH_BCH), 2.57 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2CH_2S$), 2.15 - 2.03 (m, 1 H, CH_3CHCH_3), 1.69 - 1.59 (m, 2 H, $CH_3CH_2CH_2S$), 1.08 (d, *J* = 7.0 Hz, 3 H, one of CH_3CHCH_3), 1.08 (d, *J* = 7.0 Hz, 3 H, one of CH_3CHCH_3), 1.01 (t, *J* = 7.5 Hz, 3 H, $CH_3CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 172.9 (C=O), 150.9 (ArC), 129.5 (ArCH), 125.9 (ArCH), 121.8 (ArCH), 53.3 (SCH_2CH), 34.6 ($CH_3CH_2CH_2S$), 32.0 (SCH_2CH), 31.1 (CH_3CHCH_3), 23.0 ($CH_3CH_2CH_2S$), 20.5 (one of CH_3CHCH_3), 20.4 (one of CH_3CHCH_3), 13.6 ($CH_3CH_2CH_3S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{15}H_{22}NaO_2S$) requires *m/z* 289.1233, found *m/z* 289.1226.

Phenyl (2*R*)-2-cyclohexyl-3-(propylsulfanyl)propanoate (4t)

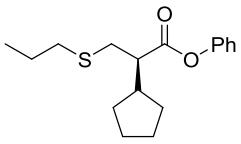


4t

Ester **2n** (92 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4t** as a colorless oil in 93% yield (57 mg) and 85% ee [determined by HPLC, chiralcel AD-H, hexane/isopropanol = 98/2, 1 mL/min, λ = 220 nm, t (major) = 9.91 min, t (minor) = 10.55 min].

$[\alpha]_D^{24}$ = +40.5 (*c* 0.50, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2928, 1740 (C=O), 1366, 1216 (C-O), 1129 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.44 - 7.32 (m, 2 H, Ar<u>H</u>), 7.25 - 7.19 (m, 1 H, Ar<u>H</u>), 7.17 - 7.09 (m, 2 H, Ar<u>H</u>), 2.87 (dd, *J* = 13.0, 5.0 Hz, 1 H, SC<u>H_A</u>H_BCH), 2.81 (dd, *J* = 13.0, 10.5 Hz, 1 H, SCH_A<u>H_B</u>CH), 2.67 (ddd, *J* = 10.5, 7.5, 5.0 Hz, 1 H, SC$H_A$$H_B$C<u>H</u>), 2.56 (t, *J* = 7.0 Hz, 2 H, CH_3CH_2C<u>H_2</u>S), 1.96 -1.84 (m, 1 H, one of C_6<u>H_{11}</u>), 1.84 - 1.55 (m, 7 H, CH_3C<u>H_2</u>CH_2S and 5 of C_6<u>H_{11}</u>), 1.37 - 1.04 (m, 5 H, 5 of C_6<u>H_{11}</u>), 1.00 (t, *J* = 7.5 Hz, 3 H, C<u>H_3</u>CH_2CH_2S). **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 173.0 (<u>C</u>=O), 150.9 (Ar<u>C</u>), 129.5 (Ar<u>C</u>H), 125.9 (Ar<u>C</u>H), 121.9 (Ar<u>C</u>H), 52.6 (SC$H_A$$H_B$<u>C</u>H), 40.6 (SC$H_A$$H_B$CH<u>C</u>H), 34.6 ($CH_3CH_2$<u>C</u>$H_2$S), 31.8 (S<u>C</u>$H_A$$H_B$CH), 30.9, 30.9, 26.4, 26.3, 26.3 (CH(<u>C</u>H_2)$_5$), 23.0 (CH_3<u>C</u>H_2CH_2S), 13.6 (<u>C</u>$H_3CH_2CH_2$S); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{18}H_{26}NaO_2S$) requires *m/z* 329.1546, found *m/z* 329.1538.

Phenyl (2*R*)-2-cyclopentyl-3-(propylsulfanyl)propanoate (4u)

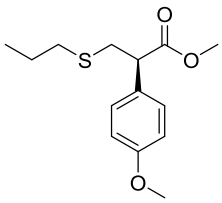


4u

Ester **2o** (86 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 49/1) to afford the title compound **4u** as a colorless oil in 96% yield (56 mg) and 90% ee [determined by HPLC, chiralcel AS-H, hexane/isopropanol = 99.5/0.5, 0.5 mL/min, λ = 210 nm, t (major) = 29.47 min, t (minor) = 35.51 min].

$[\alpha]_D^{24}$ = +53.8 (*c* 1.12, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2958, 1756 (C=O), 1493, 1194 (C-O), 1125 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.42 - 7.34 (m, 2 H, Ar<u>H</u>), 7.25 - 7.19 (m, 1 H, Ar<u>H</u>), 7.15 - 7.09 (m, 2 H, Ar<u>H</u>), 2.87 - 2.82 (m, 2 H, SC<u>$H_A$$H_B$</u>CH), 2.72 - 2.63 (m, 1 H, SC$H_A$$H_B$C<u>H</u>), 2.57 (t, *J* = 7.0 Hz, 2 H, CH_3CH_2C<u>H_2</u>S), 2.23 - 2.09 (m, 1 H, SC$H_A$$H_B$CHC<u>H</u>), 1.98 - 1.81 (m, 2 H, 2 of C<u>H_A</u>H_BCHC<u>H_A</u>H_B), 1.76 - 1.55 (m, 6 H, CH_3C<u>H_2</u>CH_2S and CH_2C<u>H_2</u>C<u>H_2</u>CH_2), 1.50 - 1.36 (m, 1 H, CH_A<u>H_B</u>CHC$H_A$$H_B$), 1.33 - 1.18 (m, 1 H, C$H_A$$H_BCHCH_A$<u>$H_B$</u>), 1.00 (t, *J* = 7.5 Hz, 3 H, C<u>H_3</u>CH_2CH_2S); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 173.2 (<u>C</u>=O), 151.0 (Ar<u>C</u>), 129.5 (Ar<u>C</u>H), 125.9 (Ar<u>C</u>H), 121.9 (Ar<u>C</u>H), 52.2 (SCH_2<u>C</u>H), 43.1 (SCH_2CH<u>C</u>H), 34.6 (S<u>C</u>H_2CH), 33.4 (CH_3CH_2<u>C</u>H_2S), 31.0 (one of <u>C</u>H_2CH<u>C</u>H_2), 30.9 (one of <u>C</u>H_2CH<u>C</u>H_2), 25.2 (one of CH_2<u>C</u>H_2<u>C</u>H_2CH_2), 25.1 (one of CH_2<u>C</u>H_2<u>C</u>H_2CH_2), 23.0 (CH_3<u>C</u>H_2CH_2S), 13.6 (<u>C</u>$H_3CH_2CH_2$S); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{17}H_{24}NaO_2S$) requires *m/z* 315.1389, found *m/z* 315.1380.

Methyl (2*R*)-2-(4-methoxyphenyl)-3-(propylsulfanyl)propanoate (4v)

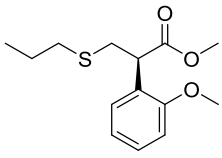


4v

Ester **2p** (38.4 mg, 0.20 mmol, 1.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to a modified general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 19/1) to afford the title compound **4u** as a colorless oil in 94% yield (49 mg) and 86% ee [determined by HPLC, chiralcel OD-H, hexane/isopropanol = 99/1, 1 mL/min, λ = 220 nm, t (major) = 10.30 min, t (minor) = 12.39 min].

$[\alpha]_D^{23}$ = -48.4 (*c* 0.86, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2959, 1735 (C=O), 1511, 1250 (C-O), 1155 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.26 - 7.18 (m, 2 H, Ar<u>H</u>), 6.91 - 6.80 (m, 2 H, Ar<u>H</u>), 3.78 (s, 3 H, ArCOC<u>H</u>$_3$), 3.74 (dd, *J* = 9.5, 6.5 Hz, 1 H, SCH$_A$H$_B$C<u>H</u>), 3.68 (3 H, s, C(=O)OC<u>H</u>$_3$), 3.16 (1 H, dd, *J* = 13.0, 9.5 Hz, SC<u>H</u>$_A$H$_B$CH), 2.82 (dd, *J* = 13.0, 6.5 Hz, 1 H, SCH$_A$<u>H</u>$_B$CH), 2.50 - 2.43 (m, 2 H, CH$_3$CH$_2$C<u>H</u>$_2$S), 1.58 ('sxt', *J* = 7.5 Hz, 2 H, CH$_3$C<u>H</u>$_2$CH$_2$S), 0.96 (t, *J* = 7.5 Hz, 3 H, C<u>H</u>$_3$CH$_2$CH$_2$S); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 173.6 (<u>C</u>=O), 159.2 (Ar<u>C</u>OCH$_3$), 130.1 (Ar<u>C</u>), 128.9 (Ar<u>C</u>H), 114.2 (Ar<u>C</u>H), 55.3 (ArCO<u>C</u>H$_3$), 52.3 (C(=O)O<u>C</u>H$_3$), 51.4 (SCH$_A$H$_B$<u>C</u>H), 35.4 (S<u>C</u>H$_A$H$_B$CH), 34.7 (CH$_3$CH$_2$<u>C</u>H$_2$S), 23.0 (CH$_3$<u>C</u>H$_2$CH$_2$S), 13.5 (<u>C</u>H$_3$CH$_2$CH$_2$S); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{14}H_{20}NaO_3S$) requires *m/z* 291.1025, found *m/z* 291.1020.

Methyl (2*R*)-2-(2-methoxyphenyl)-3-(propylsulfanyl)propanoate (4w)



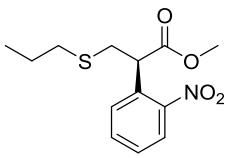
4w

Ester **2q** (77 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et_2O = 99/1 to 19/1) to afford the title compound **4w** as a colorless oil in 89% yield (47 mg) and 94% ee [determined by HPLC, chiralcel IB, hexane/isopropanol = 99/1, 1 mL/min, λ = 220 nm, t (major) = 6.96 min, t (minor) = 7.65 min].

$[\alpha]_D^{23}$ = -67.2 (*c* 0.18, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2960, 1737 (C=O), 1494, 1247 (C-O), 1156 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.30 - 7.21 (m, 2 H, Ar<u>H</u>), 6.94 (ddd, *J* = 7.5, 1.0 Hz, 1 H, Ar<u>H</u>), 6.89 (d, *J* = 8.0 Hz, 1 H, Ar<u>H</u>), 4.26 (dd, *J* = 9.0, 6.0 Hz, 1 H, SCH$_A$H$_B$C<u>H</u>), 3.84 (s, 3 H, ArOC<u>H</u>$_3$), 3.70 (s, 3 H, C(=O)OC<u>H</u>$_3$), 3.14 (dd, *J* = 13.5, 9.0 Hz, 1 H, SC<u>H</u>$_A$H$_B$CH), 2.80 (dd, *J* = 13.5, 6.0 Hz, 1 H, SCH$_A$<u>H</u>$_B$CH), 2.50 (t, *J* = 7.5 Hz, 2 H, CH$_3$CH$_2$C<u>H</u>$_2$S), 1.60 ('sxt', *J* = 7.5 Hz, 2 H, CH$_3$C<u>H</u>$_2$CH$_2$S), 0.97 (t, *J* = 7.5 Hz, 3 H, C<u>H</u>$_3$CH$_2$CH$_2$S); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ

(ppm): 173.6 (C=O), 156.6 (ArCOCH$_3$), 128.6 (ArCH), 128.3 (ArCH), 126.6 (ArC), 120.7 (ArCH), 110.8 (ArCH), 55.5 (ArOCH$_3$), 52.0 (C(=O)OCH$_3$), 45.3 (SCH$_2$CH), 34.4 (CH$_3$CH$_2$CH$_2$S), 34.0 (SCH$_2$CH), 22.8 (CH$_2$CH$_2$CH$_3$S), 13.4 (CH$_3$CH$_2$CH$_2$S); **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{14}H_{20}NaO_3S$) requires *m/z* 291.1025, found *m/z* 291.1020.

Methyl (2*R*)-2-(2-nitrophenyl)-3-(propylsulfanyl)propanoate (4x)

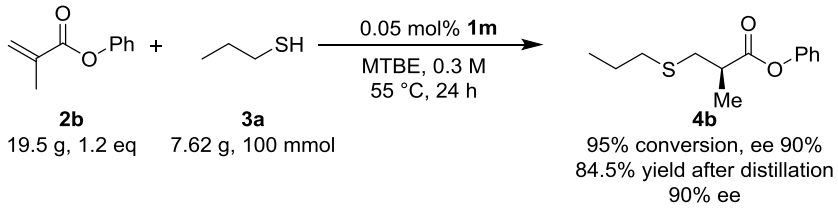


4x

Methyl 2-(2-nitrophenyl)prop-2-enoate[7] **2r** (63 mg, 0.40 mmol, 2.0 eq) was reacted with 1-propanethiol **3a** (18 μL, 0.20 mmol, 1.0 eq) according to the general procedure **F**. The reaction mixture was purified by FCC (petroleum ether/Et$_2$O = 99/1 to 19/1) to afford the title compound **4x** as a colorless oil in 98% yield (56 mg) and 84% ee [determined by HPLC, chiralcel IA, hexane/isopropanol = 98/2, 1 mL/min, λ = 220 nm, t (minor) = 10.20 min, t (major) = 10.96 min].

[α]$_D^{25}$ = -137.3 (*c* 0.64, CHCl$_3$); **IR** (film) ν_{max}/cm^{-1}: 3016, 2970, 1739 (C=O), 1527 (NO$_2$), 1435 (C-O), 1368, 1216; **^{1}H NMR** (CDCl$_3$, 400 MHz) δ (ppm): 7.91 (dd, *J* = 8.0, 1.0 Hz, 1 H, ArH), 7.61 - 7.54 (m, 2 H, ArH), 7.49 - 7.38 (m, 1 H, ArH), 4.46 (dd, *J* = 8.0, 6.5 Hz, 1 H, SCH$_A$H$_B$CH), 3.69 (s, 3 H, OCH$_3$), 3.24 (dd, *J* = 13.5, 8.0 Hz, 1 H, SCH$_A$H$_B$CH), 2.95 (dd, *J* = 13.5, 6.5 Hz, 1 H, SCH$_A$CH$_B$CH), 2.53 - 2.47 (m, 2 H, CH$_3$CH$_2$CH$_2$S), 1.63 - 1.54 (m, 2 H, CH$_3$CH$_2$CH$_2$S), 1.18 (t, *J* = 7.5 Hz, 3 H, CH$_3$CH$_2$CH$_2$S); **^{13}C NMR** (CDCl$_3$, 100 MHz) δ (ppm): 172.1 (C=O), 149.3 (ArC), 133.4 (ArC), 132.3 (ArCH), 130.2 (ArCH), 128.7 (ArCH), 125.0 (ArCH), 52.6 (OCH$_3$), 47.4 (SCH$_2$CH), 34.8 (SCH$_2$CH), 34.6 (CH$_3$CH$_2$CH$_2$S), 23.0 (CH$_3$CH$_2$CH$_2$S), 13.5 (CH$_3$CH$_2$CH$_2$S); **HRMS** (ES+) exact mass calculated for [M+Na]$^+$ ($C_{13}H_{17}NNaO_4S$) requires *m/z* 306.0771, found *m/z* 306.0763.

1.6 Preparative scale synthesis of 4b



2b 19.5 g, 1.2 eq

3a 7.62 g, 100 mmol

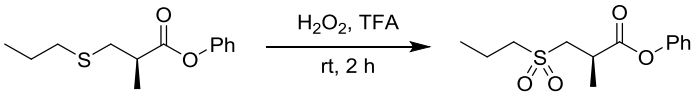
4b 95% conversion, ee 90%, 84.5% yield after distillation, 90% ee

Under an argon atmosphere, azide **16** (24 mg, 0.05 mmol, 0.0005 eq) and tris(4-methoxyphenyl)phosphine (18 mg, 0.05 mmol, 0.0005 eq) were stirred in diethyl ether (0.5 mL) at room temperature for 24 h.

To a two-necked 500 mL R.B. was charged phenyl methacrylate **2b** (19.5 g, 120 mmol, 1.2 eq), freshly distilled MTBE (330 mL) and distilled 1-propanethiol **3a** (9.05 mL, 100 mmol, 1.00 eq) under an argon atmosphere at room temperature. The *in situ* generated catalyst was then transferred with washings (3 mL MTBE) to the flask and the reaction mixture was stirred at reflux for 24 h (an aliquot taken after 22 h showed 95% conversion by ^{1}H NMR and an ee of 90%) whereupon it was quenched by the addition of 1 M AcOH in CH_2Cl_2 (2 mL). The solvent was removed *in vacuo* and the crude product was purified by distillation [120°C, 0.7 mmHg] to afford the pure title compound as a colorless oil in 84.5% yield (20.1 g)[viii] and 90% ee [determined by HPLC, chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min, λ = 220 nm, t (major) = 8.68 min, t (minor) = 9.25 min]. $[\alpha]_D^{23}$ = +47.3 (*c* 0.99, $CHCl_3$); all other spectroscopic data was in accordance to that reported in section 1.5.

1.7 Derivatization of 4b

Phenyl (2*R*)-2-methyl-3-(propane-1-sulfonyl)propanoate (5a)



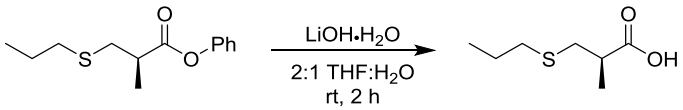
According to a modified literature procedure,[21] to a solution of **4b** (119 mg, 0.500 mmol, 90% ee) in trifluoroacetic acid (5 mL) was added 30% H_2O_2 (5 mL). The reaction mixture was stirred at room temperature for 4 hours whereupon it was diluted with water (30 mL) and extracted with CH_2Cl_2 (2 x 30 mL). The combined organics were washed (brine), dried ($MgSO_4$) and the volatiles were removed *in vacuo*. The crude product was purified by FCC (petroleum ether to petroleum ether/Et_2O 4/1) to afford the title compound **5a** as a pale yellow oil in >99% yield (135 mg) and

[viii] The isolated yield of title compound **4b** is lower than the conversion due to the occurrence of mixed distillates between **2b** and **4b.**

89% ee [determined by HPLC, chiralpak IB, hexane/isopropanol = 90/10, 1 mL/min, λ = 220 nm, t (major) = 21.91 min, t (minor) = 25.29 min].

$[\alpha]_D^{22}$ = +27.7 (*c* 0.93, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2979, 2940, 2356, 1757 (C=O), 1382, 1253 (S=O), 1131 (S=O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.43 - 7.36 (m, 2 H, Ar<u>H</u>), 7.27 - 7.22 (m, 1 H, Ar<u>H</u>), 7.14 - 7.09 (m, 2 H, Ar<u>H</u>), 3.66 (dd, *J* = 14.0, 8.0 Hz, 1 H, SC<u>H</u>$_A$H$_B$CH(CH_3)), 3.47 - 3.37 (m, 1 H, C<u>H</u>(CH_3)C=O), 3.05 (dd, *J* = 14.0, 5.0 Hz, 1 H, SCH$_A$<u>H</u>$_B$CH(CH_3)), 3.04 - 2.99 (m, 2 H, $CH_3CH_2C\underline{H}_2S$), 1.97 - 1.87 (m, 2 H, $CH_3C\underline{H}_2CH_2S$), 1.55 (d, *J* = 7.0 Hz, 3 H, CH(C<u>H</u>$_3$)C=O), 1.09 (t, *J* = 7.5 Hz, 3 H, C<u>H</u>$_3$$CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 172.7 (<u>C</u>=O), 150.4 (Ar<u>C</u>), 129.4 (Ar<u>C</u>H), 126.1 (Ar<u>C</u>H), 121.3 (Ar<u>C</u>H), 55.8 ($CH_3CH_2\underline{C}H_2S$), 55.1 (S<u>C</u>$H_2$CH($CH_3$)), 34.2 (<u>C</u>H($CH_3$)C=O), 17.8 (CH(<u>C</u>$H_3$)C=O), 15.7 ($CH_3\underline{C}H_2CH_2S$), 13.0 (<u>C</u>$H_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_{13}H_{18}NaO_4S$) requires *m/z* 293.0818, found *m/z* 293.0810.

(2*R*)-2-Methyl-3-(propylsulfanyl)propanoic acid (5b)

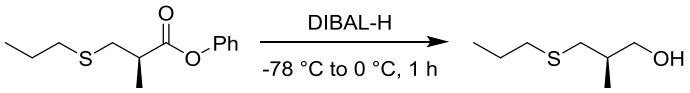


To a solution of **4b** (238 mg, 1.00 mmol, 1.00 eq, 90% ee) in THF (6.0 mL) at rt was added LiOH•H_2O (210 mg, 5.00 mmol, 5.00 eq) in H_2O (3.0 mL). Stirring was maintained for 2 h whereupon the reaction mixture was diluted with H_2O (10 mL) and extracted with Et_2O (2 x 10 mL). The aqueous layer was acidified to pH 2 using 1 M HCl (aq) and extracted with CH_2Cl_2 (4 x 10 mL). The organics were washed with brine, dried ($MgSO_4$) and the volatiles removed *in vacuo.* The crude product was purified by FCC (petroleum ether/Et_2O 9/1 to Et_2O) to yield the title compound **5b** as a pale yellow oil in 82% yield (133 mgs) and 86% ee.

[The ee was determined by treating **5b** in CH_2Cl_2/MeOH (4/1) with 1.0 eq of (trimethylsilyl)diazomethane (2.0 mL in hexanes) to afford **4a** in 86% ee and 89% yield]
$[\alpha]_D^{22}$ = +24.3 (*c* 1.22, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 2964, 2934 (O-H), 1706 (C=O), 1462, 1234, 932; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 2.85 (dd, *J* = 13.0, 7.0 Hz, 1 H, SC<u>H</u>$_A$H$_B$CH(CH_3)), 2.70 ('sxt', *J* = 7.0 Hz, 1 H, SCH$_A$H$_B$C<u>H</u>(CH_3)), 2.58 (dd, *J* = 13.0, 7.0 Hz, 1 H, SCH$_A$<u>H</u>$_B$CH(CH_3)), 2.51 (t, *J* = 7.5 Hz, 2 H, $CH_3CH_2C\underline{H}_2S$), 1.61 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3C\underline{H}_2CH_2S$), 1.29 (d, *J* = 7.0 Hz, 3 H, CH(C<u>H</u>$_3$)), 0.98 (t, *J* = 7.5 Hz, 3 H, C<u>H</u>$_3$$CH_2CH_2S$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 181.6 (<u>C</u>=O), 40.3 (SCH$_A$H$_B$<u>C</u>H(CH_3)), 35.2

($S\underline{C}H_AH_BCH(CH_3)$), 34.9 ($CH_3CH_2\underline{C}H_2S$), 23.0 ($CH_3\underline{C}H_2CH_2S$), 16.8 ($SCH_AH_BCH(\underline{C}H_3)$), 13.6 ($\underline{C}H_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+Na]^+$ ($C_7H_{14}NaO_2S$) requires *m/z* 185.0607, found *m/z* 185.0608

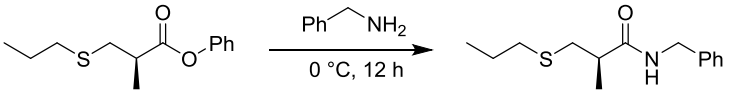
(2*R*)-2-methyl-3-(propylsulfanyl)propan-1-ol (5c)



To a solution of **4b** (119 mg, 0.500 mmol, 1.00 eq, 90% ee) in THF (2.5 mL) at –78 °C was added DIBAL-H (1.10 mL, 1.10 mmol, 2.20 eq) dropwise. Upon complete addition the reaction mixture was allowed to warm to 0℃ whereupon stirring was maintained for 20 mins. The reaction mixture was quenched by the addition of saturated aq NH_4Cl (5 mL) and extracted with Et_2O (3 x 10 mL). The combined organics were washed with brine, dried ($MgSO_4$), the volatiles *in vacuo* and purification by FCC (petroleum ether/Et_2O 9/1 to Et_2O) to afford the title compound **5c** as a pale yellow oil in 64% yield (47 mg) and 90% ee. [determined by HPLC, chiralpak IA, hexane/isopropanol = 95/5, 1 mL/min, λ = 210 nm, t (major) = 8.12 min, t (minor) = 9.15 min].

$[\alpha]_D^{22}$ = -3.1 (*c* 0.66, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 3354 (O-H), 2960 (C-H), 2930, 2872, 1457 (C-O), 1033 (C-O); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 3.52 (d, *J* = 6.0 Hz, 2 H, $C\underline{H_2}OH$), 2.53 (dd, *J* = 12.5, 7.0 Hz, 1 H, $SC\underline{H_A}H_BCH(CH_3)$), 2.47 - 2.37 (m, 3 H, $SCH_A\underline{H_B}CH(CH_3)$ and $CH_3CH_2C\underline{H_2}S$), 1.98 (br s, 1 H, O<u>H</u>), 1.91 - 1.77 (m, 1 H, $SCH_AH_BC\underline{H}(CH_3)$), 1.55 ('sxt', *J* = 7.5 Hz, 2 H, $CH_3C\underline{H_2}CH_2S$), 0.97 - 0.87 (m, 6 H, $C\underline{H_3}CH_2CH_2S$ and $CH(C\underline{H_3})$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 67.4 ($\underline{C}H_2OH$), 36.3 ($S\underline{C}H_AH_BCH(CH_3)$), 35.6 ($SCH_AH_B\underline{C}H(CH_3)$), 34.8 ($CH_3CH_2\underline{C}H_2S$), 22.9 ($CH_3\underline{C}H_2CH_2S$), 16.6 ($SCH_AH_BCH(\underline{C}H_3)$), 13.4 ($\underline{C}H_3CH_2CH_2S$); **HRMS** (ES+) exact mass calculated for $[M+H]^+$ ($C_7H_{17}OS$) requires *m/z* 149.0995, found *m/z* 149.0996.

(2*R*)-*N*-Benzyl-2-methyl-3-(propylsulfanyl)propanamide (5d)

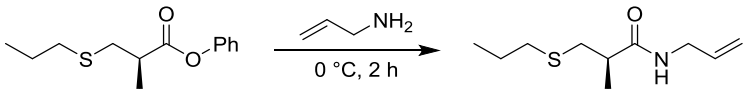


To a vial containing **4b** (119 mg, 0.500 mmol, 1.00 eq, 90% ee) at 0 °C was added benzylamine (164 µL, 1.50 mmol, 3.00 eq) and the reaction mixture was stirred for 12 hours whereupon it was purified by FCC (petroleum ether to petroleum ether/Et_2O 1/1) to yield the title compound **5d** as a

colorless oil in 99% yield (125 mg) and 89% ee [determined by HPLC, chiralpak AD, hexane/isopropanol = 90/10, 1 mL/min, λ = 220 nm, t (major) = 9.24 min, t (minor) = 10.60 min].

$[\alpha]_D^{22}$ = +5.3 (*c* 1.28, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 3284 (N-H), 2963, 2930, 1645 (C=O), 1548, 1239 (C-N); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 7.37 - 7.22 (m, 5 H, Ar<u>H</u>), 6.32 (br. s., 1 H, N<u>H</u>CH_2), 4.50 - 4.37 (m, 2 H, NHC<u>H_2</u>), 2.82 (dd, *J* = 13.0, 8.0 Hz, 1 H, SC<u>H_A</u>H_BCH(CH_3)), 2.56 (dd, *J* = 13.0, 6.0 Hz, 1 H, SCH_A<u>H_B</u>CH(CH_3)), 2.51 - 2.38 (m, 3 H, SCH_AH_BC<u>H</u>(CH_3) and CH_3CH_2C<u>H_2</u>S), 1.58 ('sxt', *J* = 7.5 Hz, 2 H, CH_3C<u>H_2</u>CH_2S), 1.23 (d, *J* = 7.0 Hz, 3 H, CH(C<u>H_3</u>)), 0.96 (t, *J* = 7.5 Hz, 3 H, C<u>H_3</u>CH_2CH_2S); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 174.7 (<u>C</u>=O), 138.2 (Ar<u>C</u>), 128.5 (Ar<u>C</u>H), 127.6 (Ar<u>C</u>H), 127.3 (Ar<u>C</u>H), 43.4 (NH<u>C</u>H_2), 41.9 ($SCH_A$$H_B$<u>C</u>H($CH_3$)), 35.9 (S<u>C</u>$H_A$$H_B$CH($CH_3$)), 34.8 ($CH_3CH_2$<u>C</u>$H_2$S), 22.8 ($CH_3$<u>C</u>$H_2CH_2$S), 17.6 ($SCH_A$$H_B$CH(<u>C</u>$H_3$)), 13.3 (<u>C</u>$H_3CH_2CH_2$S); **HRMS** (ES+) exact mass calculated for $[M+H]^+$ ($C_{14}H_{22}NOS$) requires *m/z* 252.1417, found *m/z* 252.1418.

(2*R*)-2-Methyl-*N*-(prop-2-en-1-yl)-3-(propylsulfanyl)propanamide (5e)

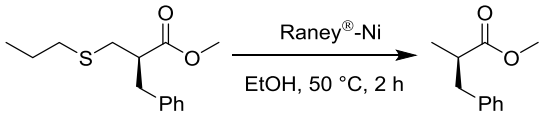


To a vial containing **4b** (119 mg, 0.500 mmol, 1.00 eq, 90% ee) at 0℃ was added allylamine (113 µL, 1.50 mmol, 3.00 eq) and the reaction mixture was stirred for 2 hours whereupon it was purified by FCC (petroleum ether to petroleum ether/Et_2O 1/1) to yield the title compound **5e** as a colorless oil in 99% yield (107 mg) and 91% ee [determined by HPLC, chiralpak AD, hexane/isopropanol = 97/3, 1 mL/min, λ = 220 nm, t (major) = 18.67 min, t (minor) = 20.16 min].

$[\alpha]_D^{22}$ = +9.9 (*c* 0.82, $CHCl_3$); **IR** (film) ν_{max}/cm^{-1}: 3289 (N-H), 2964, 1642 (C=O), 1548, 1248 (C-N); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ (ppm): 6.11 (br. s, 1 H, N<u>H</u>CH_2), 5.89 - 5.73 (m, 1 H, $CH_A$$H_B$C<u>H</u>$CH_2$NH), 5.18 (dd, *J* = 17.0, 1.5 Hz, 1 H, C<u>H_A</u>$H_B$$CHCH_2$NH), 5.09 (dd, *J* = 10.0, 1.5 Hz, 1 H, CH_A<u>H_B</u>$CHCH_2$NH), 3.85 (ddd, *J* = 7.0, 4.0, 2.0 Hz, 2 H, CHC<u>H_2</u>NH), 2.78 (dd, *J* = 13.0, 8.0 Hz, 1 H, SC<u>H_A</u>H_BCH(CH_3)), 2.53 (dd, *J* = 13.0, 6.0 Hz, 1 H, SCH_A<u>H_B</u>CH(CH_3)), 2.49 - 2.35 (m, 3 H, SCH_AH_BC<u>H</u>(CH_3) and CH_3CH_2C<u>H_2</u>S), 1.56 ('sxt', *J* = 7.5 Hz, 2 H, CH_3C<u>H_2</u>CH_2S), 1.19 (d, *J* = 7.0 Hz, 3 H, CH(C<u>H_3</u>)), 0.93 (t, *J* = 7.5 Hz, 3 H, C<u>H_3</u>CH_2CH_2S); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 174.7 (<u>C</u>=O), 134.1 ($CH_A$$H_B$<u>C</u>H$CH_2$NH), 116.1 (<u>C</u>$H_A$$H_B$$CHCH_2$NH), 41.8 ($SCH_A$$H_B$<u>C</u>H($CH_3$)), 41.7 (CH<u>C</u>$H_2$NH), 35.9 (S<u>C</u>$H_A$$H_B$CH($CH_3$)), 34.8 ($CH_3CH_2$<u>C</u>$H_2$S), 22.8 ($CH_3$<u>C</u>$H_2CH_2$S), 17.6 ($SCH_A$$H_B$CH(<u>C</u>$H_3$)), 13.3 (<u>C</u>$H_3CH_2CH_2$S); **HRMS** (ES+) exact mass calculated for $[M+H]^+$ ($C_{10}H_{20}NOS$) requires *m/z* 202.1260, found *m/z* 202.1260.

1.8 Determination of Absolute Configuration

Methyl (2*R*)-2-methyl-3-phenylpropanoate (22)



Raney®-Nickel (approximately 300 mg wet) was weighed into a round bottom flask under an argon atmosphere and the water was decanted with washings (3 x 2 mL EtOH). The activated catalyst was suspended in 2 mL EtOH and a solution of **4o** (20 mg, 0.079 mmol, 86% ee) in 0.5 mL EtOH was added and the reaction mixture placed under a hydrogen atmosphere. The reaction mixture was warmed to 50 ℃ and stirring was maintained for 2 h whereupon the reaction mixture was cooled to rt, filtered through a pad of silica washing with CH_2Cl_2 and MeOH, and the volatiles were removed *in vacuo*. The crude product was purified by FCC (petroleum ether to petroleum ether/Et_2O 19/1) to afford the title compound **22** as a colorless oil in 86% yield (12 mg) and 83% ee. [determined by GC, Supelco β-dex^{TM} 325, 30 m, 0.25 mm, 0.25 µm, carrier gas He (flow rate 30 cm/s); column temperature 80 ℃ ramp 1 ℃/min to 90 ℃ then 90 ℃ t (major) = 72.96 min, t (minor) = 73.82 min].

$[\alpha]_D^{21}$ = -27.2 (*c* 0.6, $CHCl_3$), [lit.[22] $[\alpha]_D$ = -35.3, (*c* 0.5, $CHCl_3$)], [lit.[23] $[\alpha]_D^{25}$ = -33.7, (*c* 1, $CHCl_3$)]. From the optical rotation, the absolute configuration was determined to be (*R*). [22,23]

^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.34 - 7.11 (m, 5 H, Ar$\underline{H}$), 3.65 (s, 3 H, O$C\underline{H}_3$), 3.04 (dd, *J* = 13.0, 6.5 Hz, 1 H, PhC$\underline{H}_A$$H_B$CH($CH_3$)), 2.83 - 2.61 (m, 2 H, PhC$H_A\underline{H}_B$CH(CH_3) and C$\underline{H}$(CH_3)C=O), 1.17 (d, *J* = 7.0 Hz, 3 H, CHC$\underline{H}_3$); **^{13}C NMR** ($CDCl_3$, 100 MHz) δ (ppm): 176.5 ($\underline{C}$=O), 139.4 (Ar$\underline{C}$), 128.9 (Ar$\underline{C}$H), 128.3 (Ar$\underline{C}$H), 126.3 (Ar$\underline{C}$H), 51.6 (O$\underline{C}H_3$), 41.4 ($\underline{C}$H(CH_3)C=O), 39.7 (Ph$\underline{C}$$H_A$$H_B$CH($CH_3$)), 16.7 (CH$\underline{C}H_3$). Data is consistent with that given in the literature.[22]

2. References

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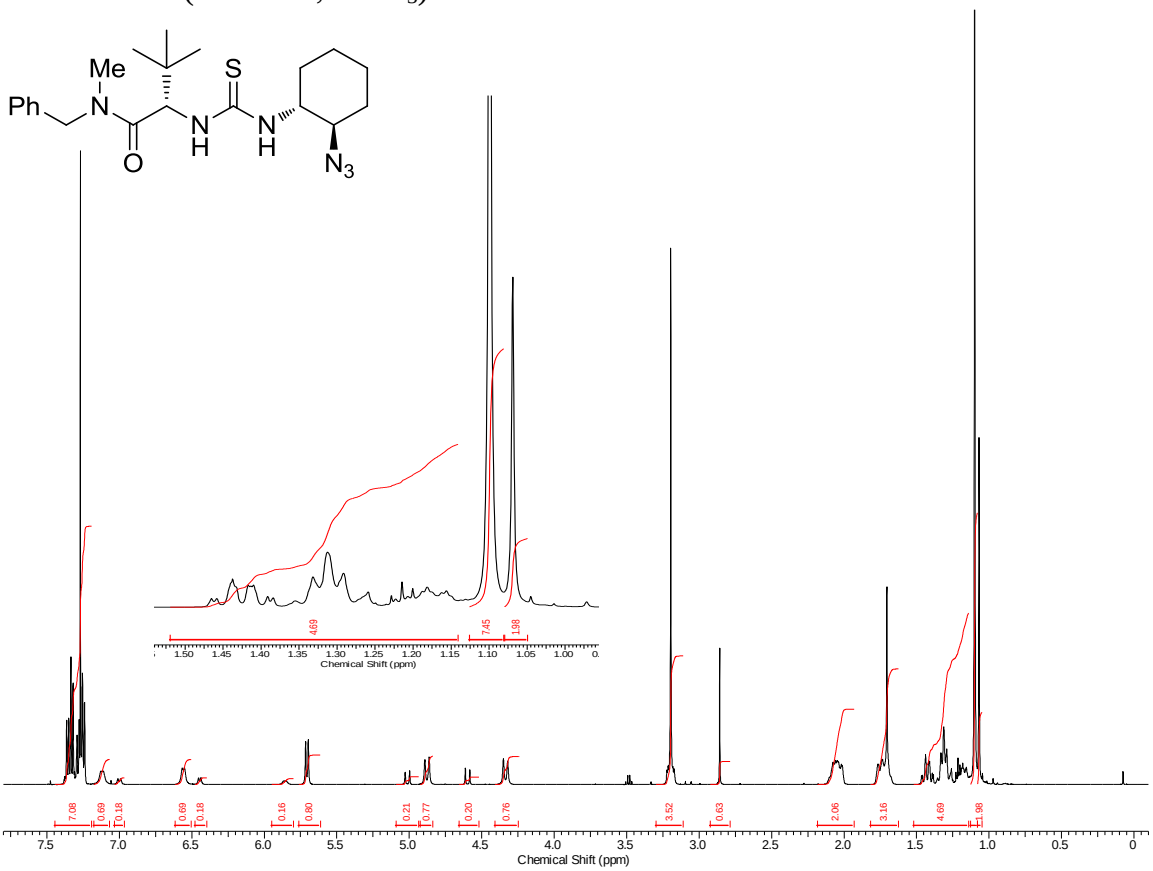
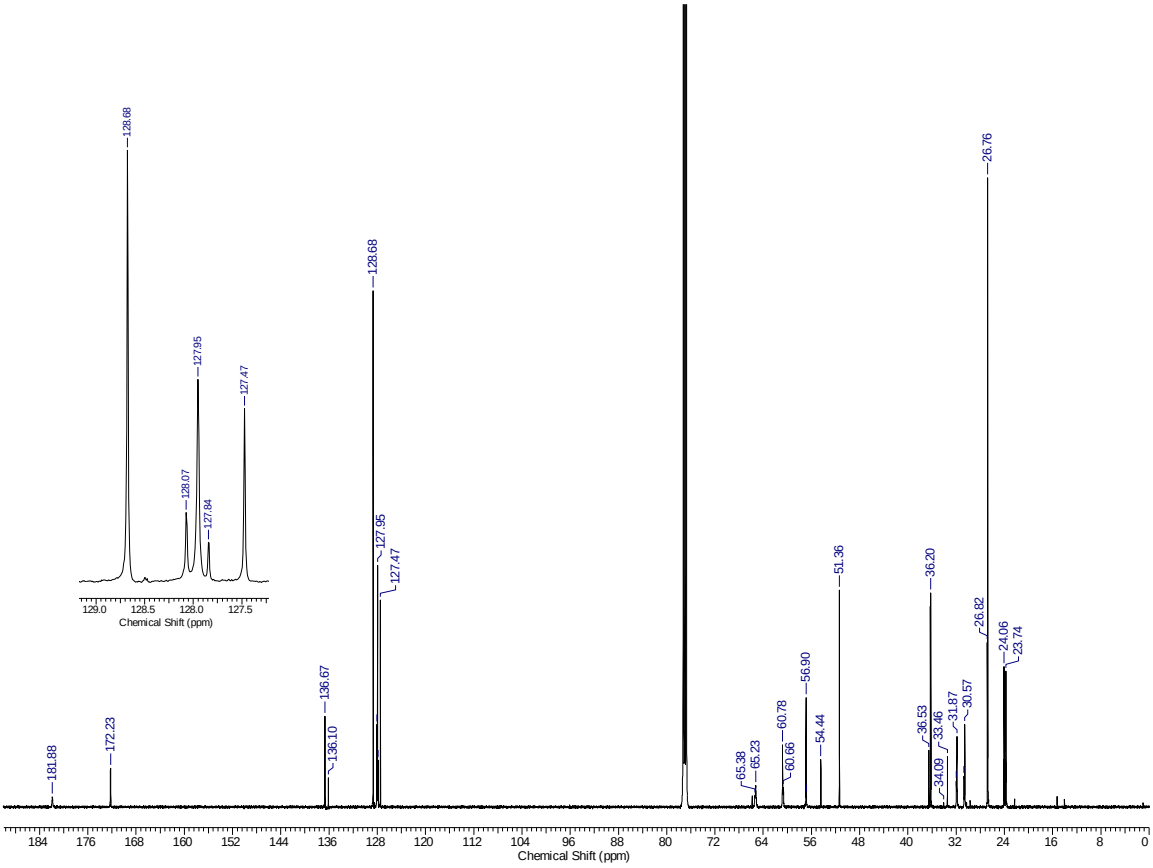
3 Supplementary Data

3.1 Copies of NMR spectra

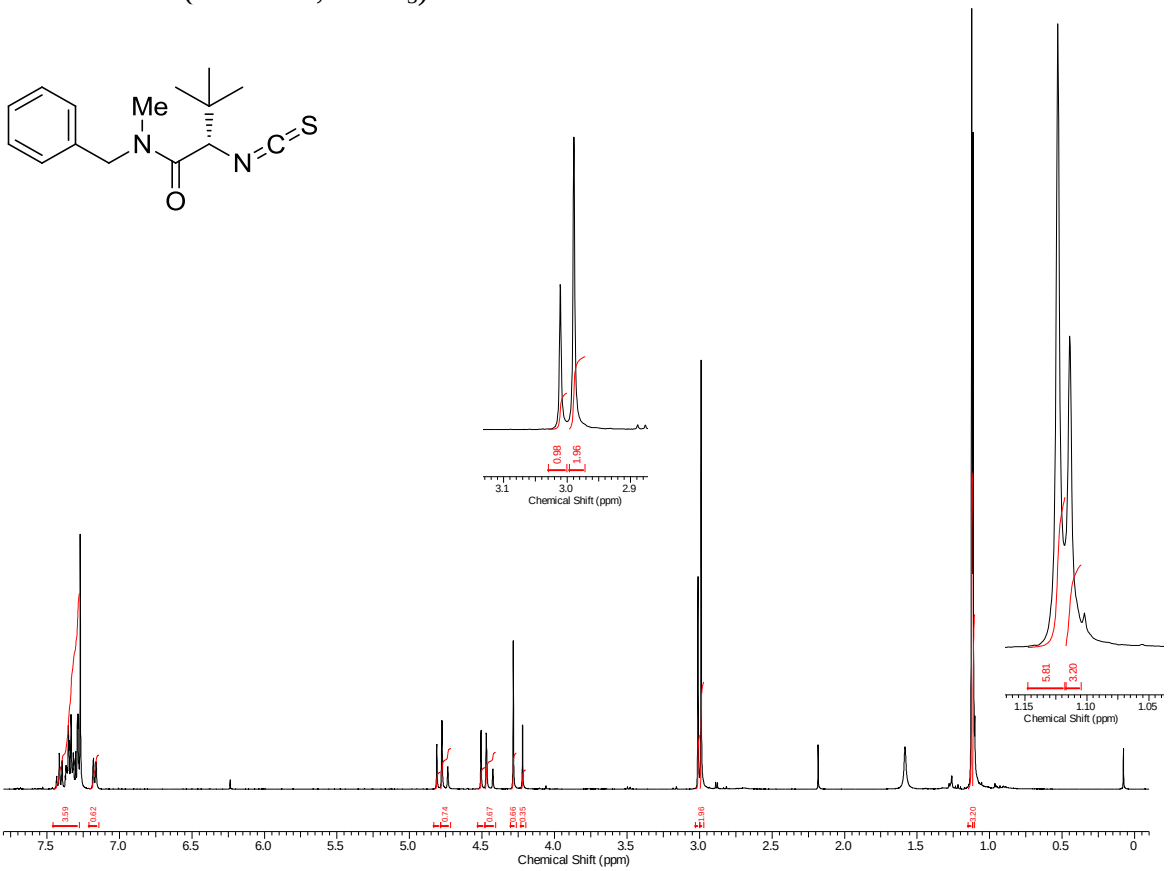
^{1}H NMR of **7** (400 MHz, $CDCl_3$)



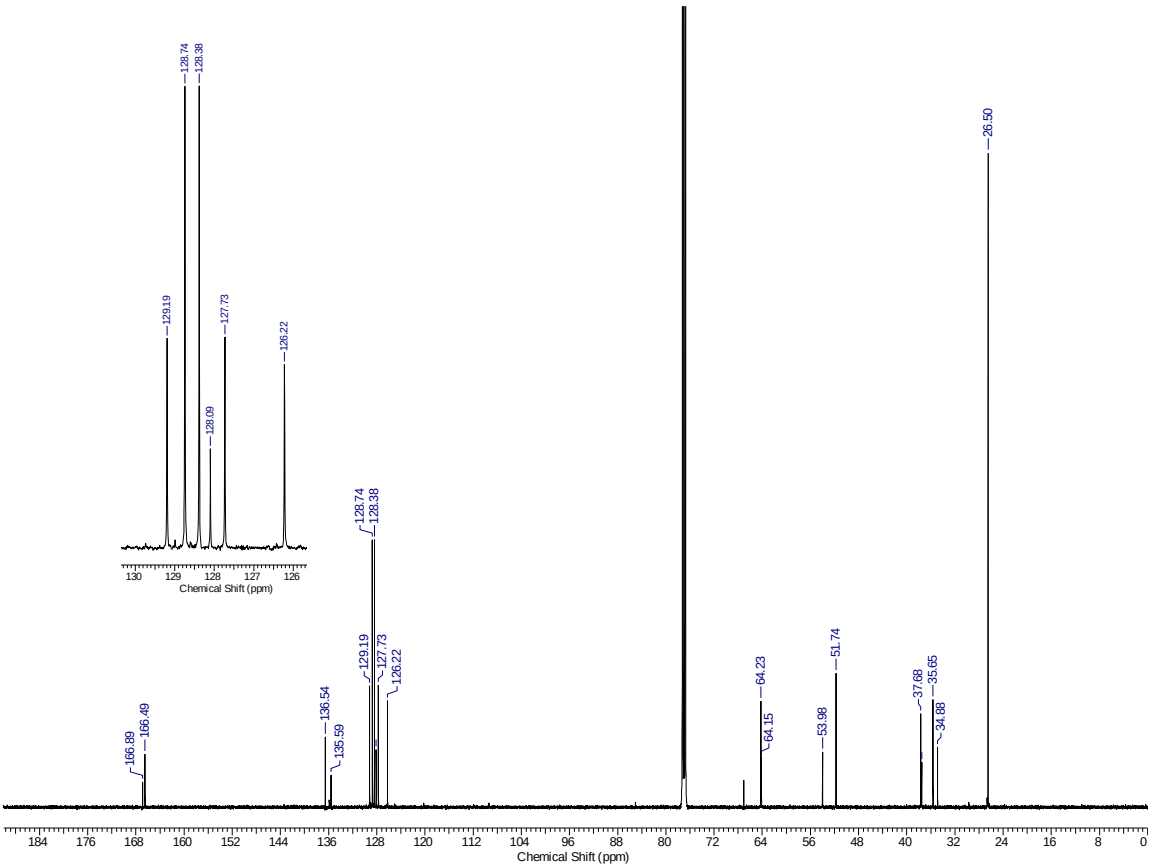
^{13}C NMR of **7** (125 MHz, $CDCl_3$)



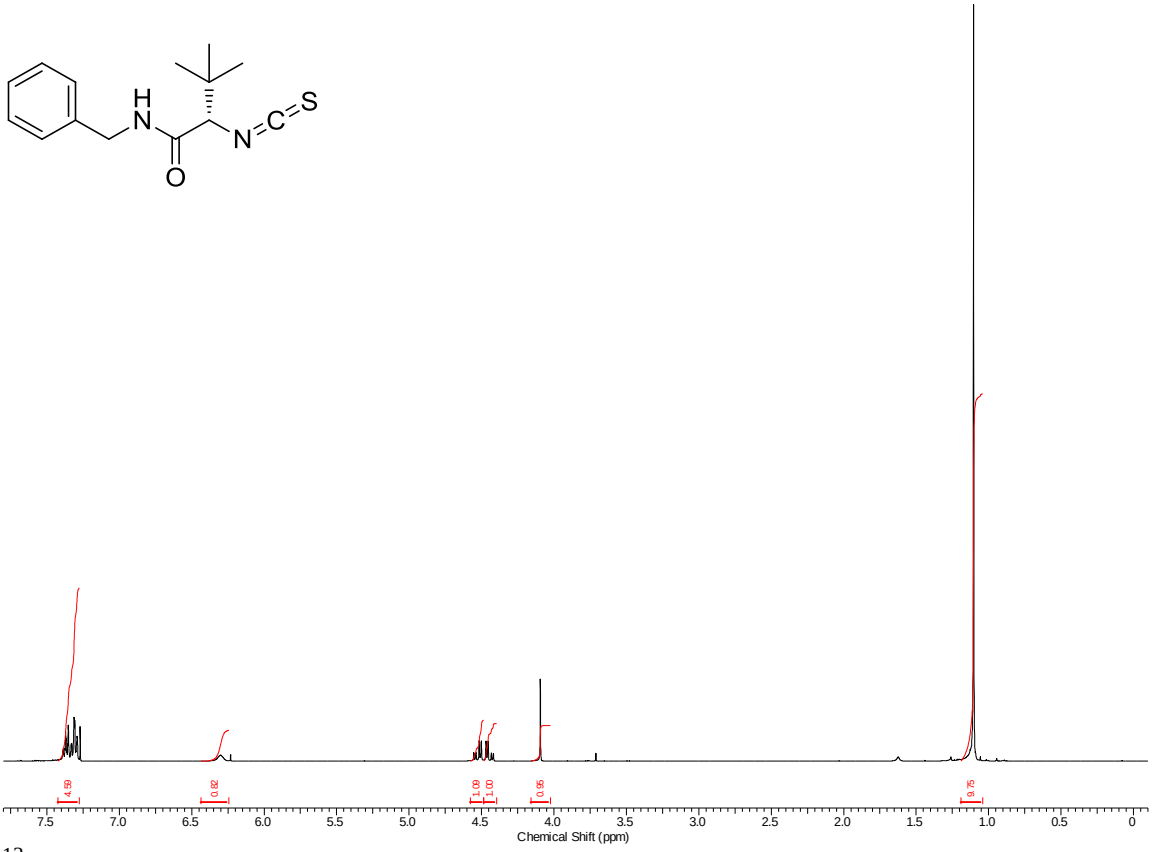
^{1}H NMR of **8** (400 MHz, $CDCl_3$)



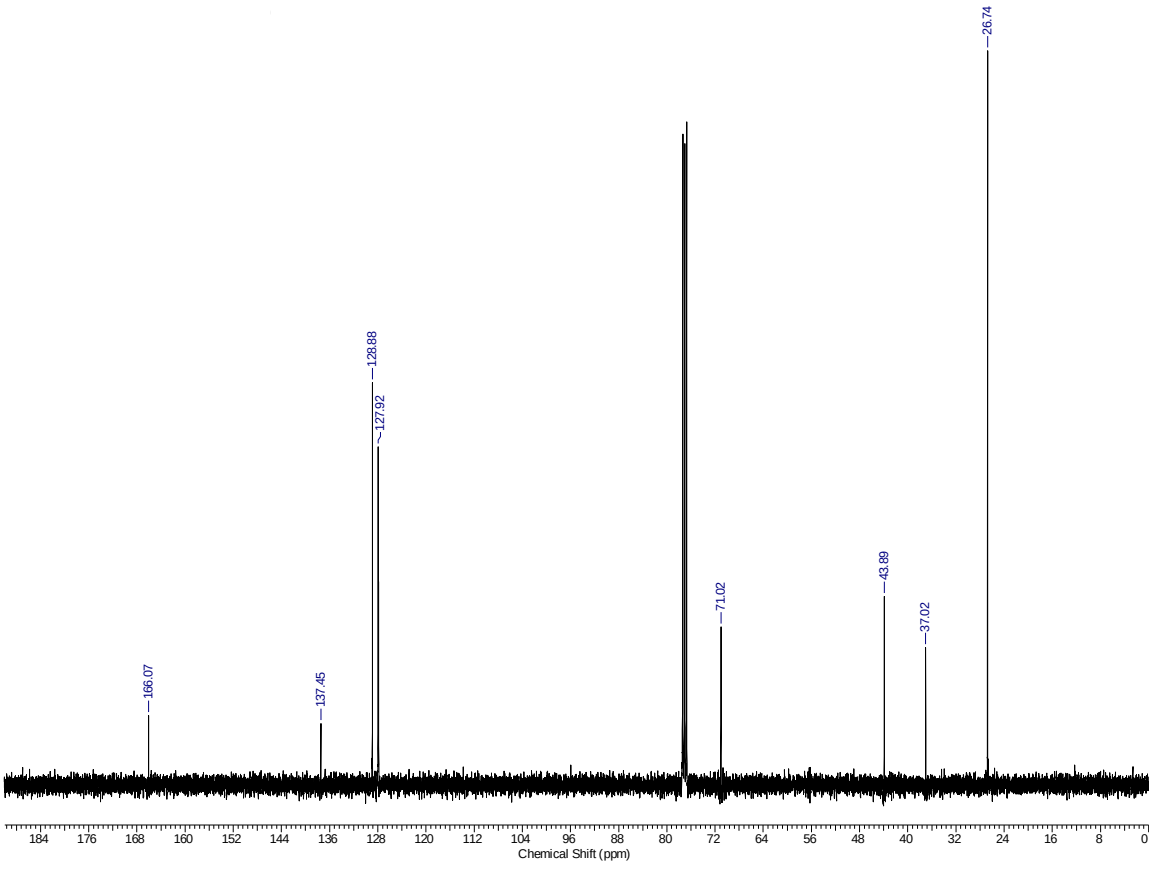
^{13}C NMR of **8** (125 MHz, $CDCl_3$)



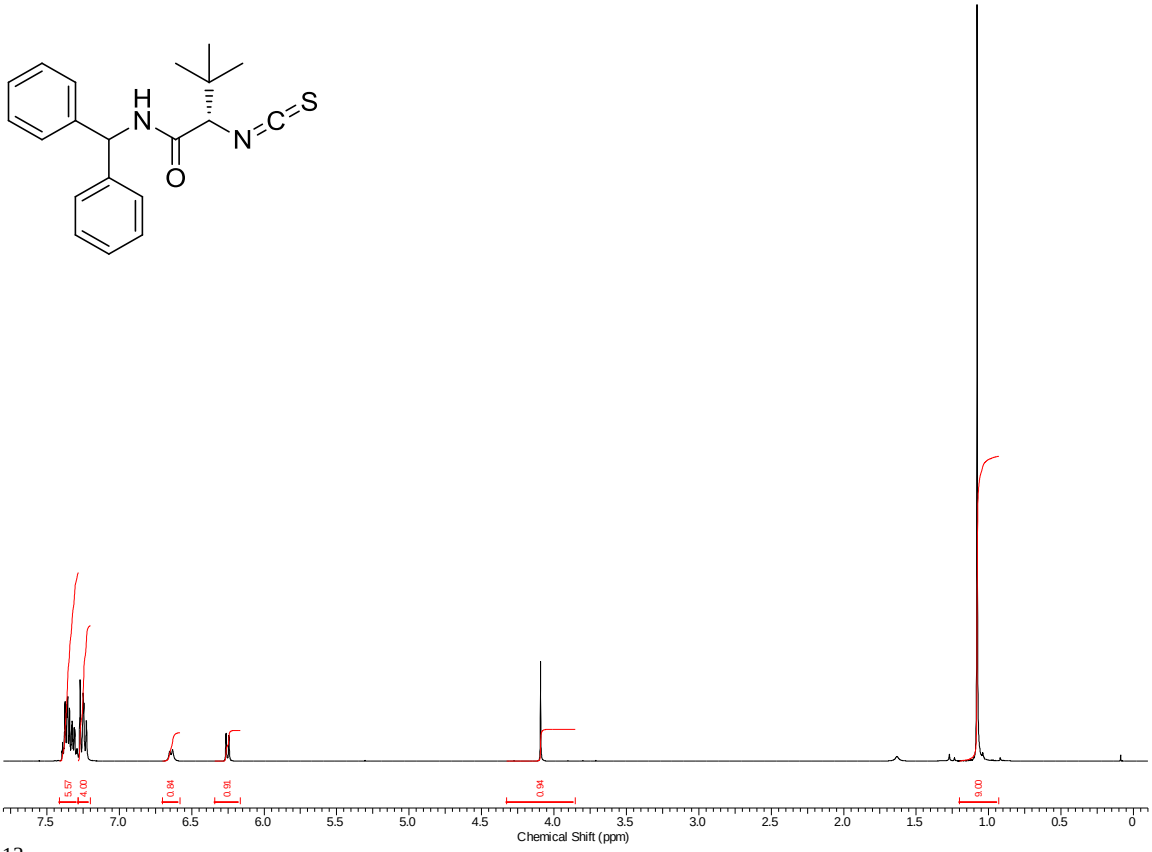
^{1}H NMR of **10** (400 MHz, $CDCl_3$)



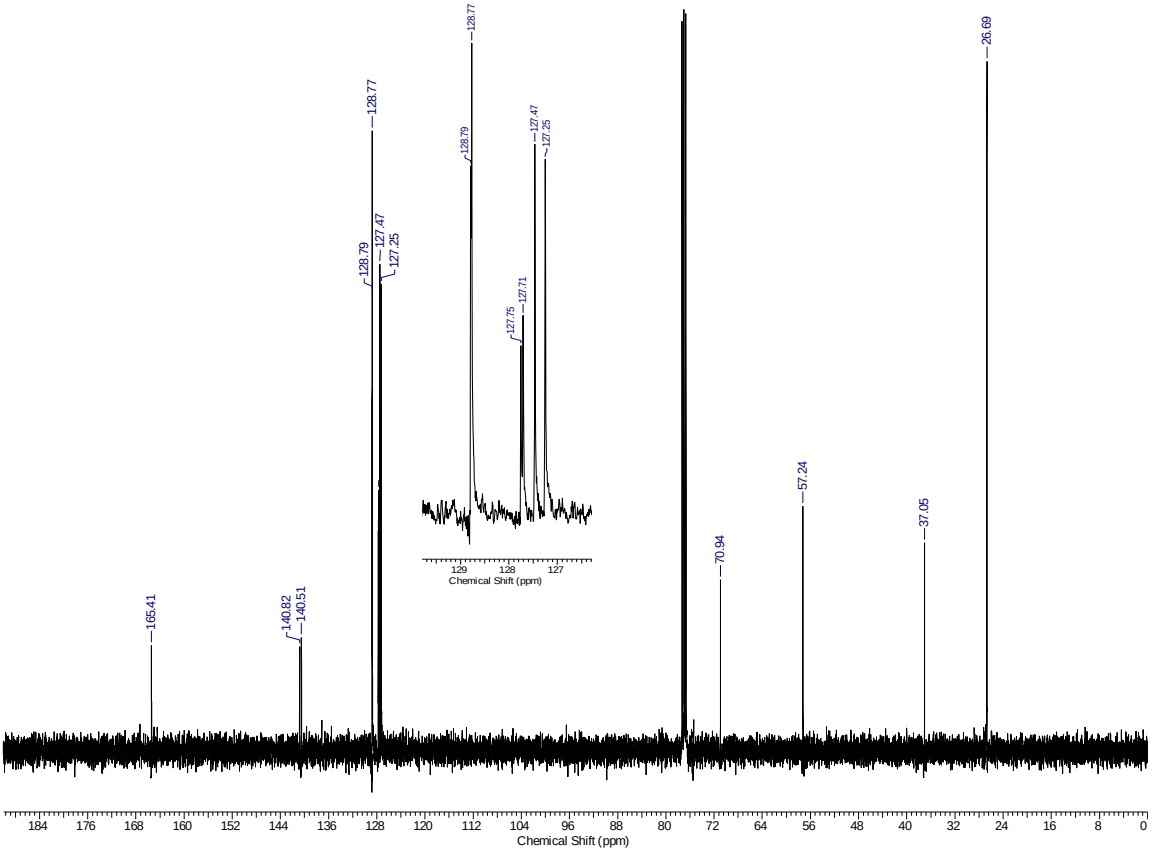
^{13}C NMR of **10** (100 MHz, $CDCl_3$)



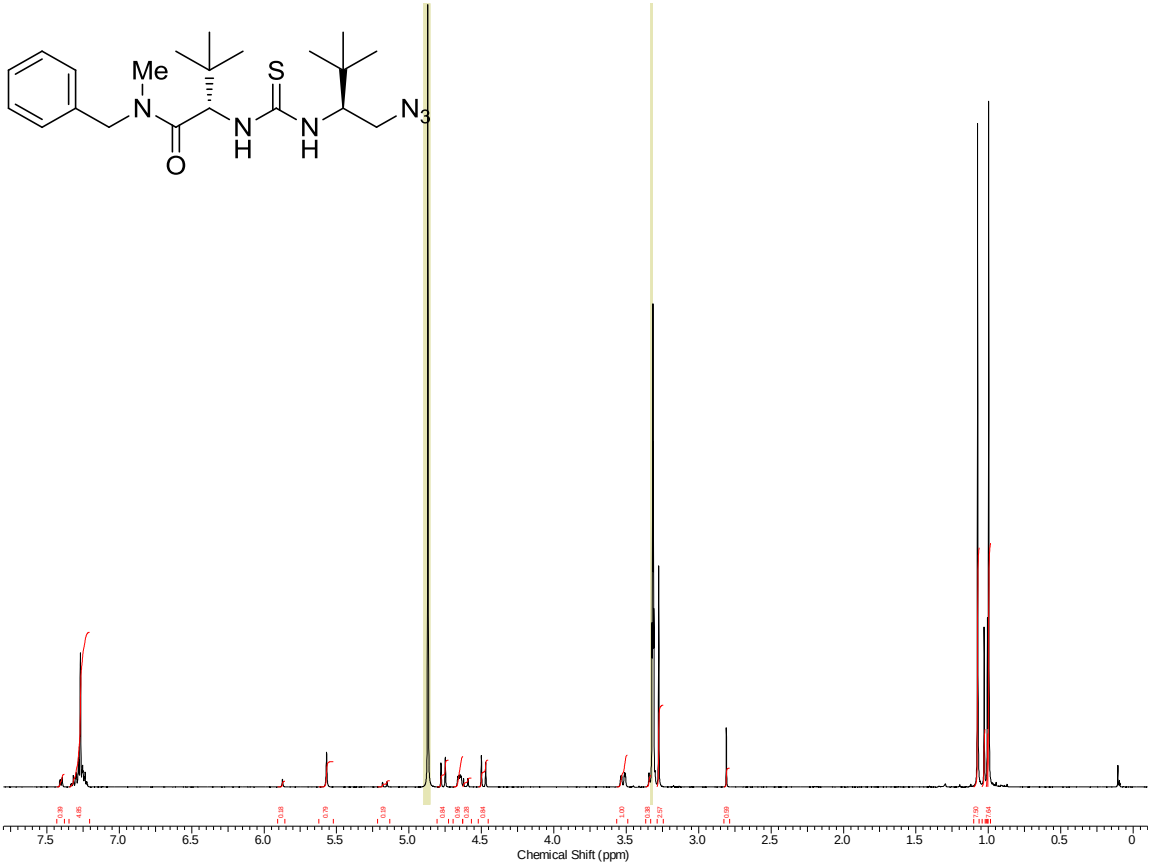
^{1}H NMR of **11** (400 MHz, $CDCl_3$)



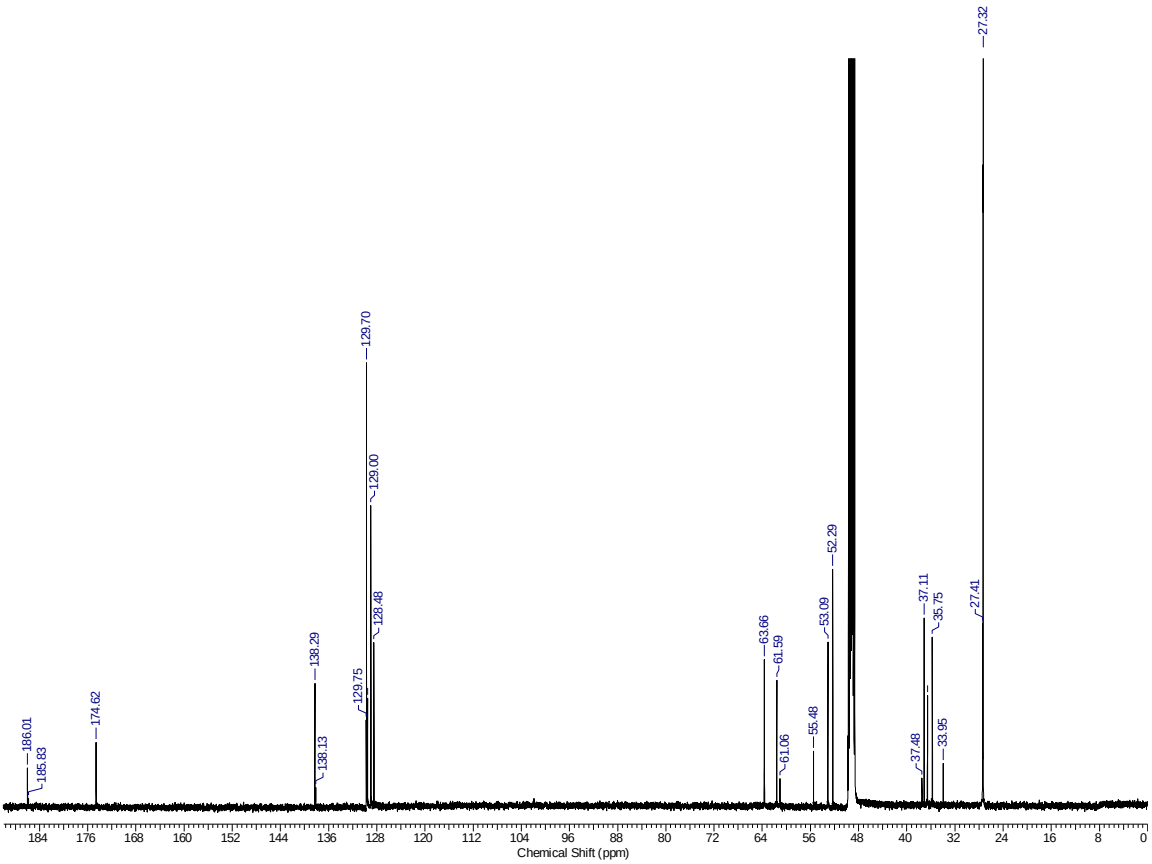
^{13}C NMR of **11** (100 MHz, $CDCl_3$)



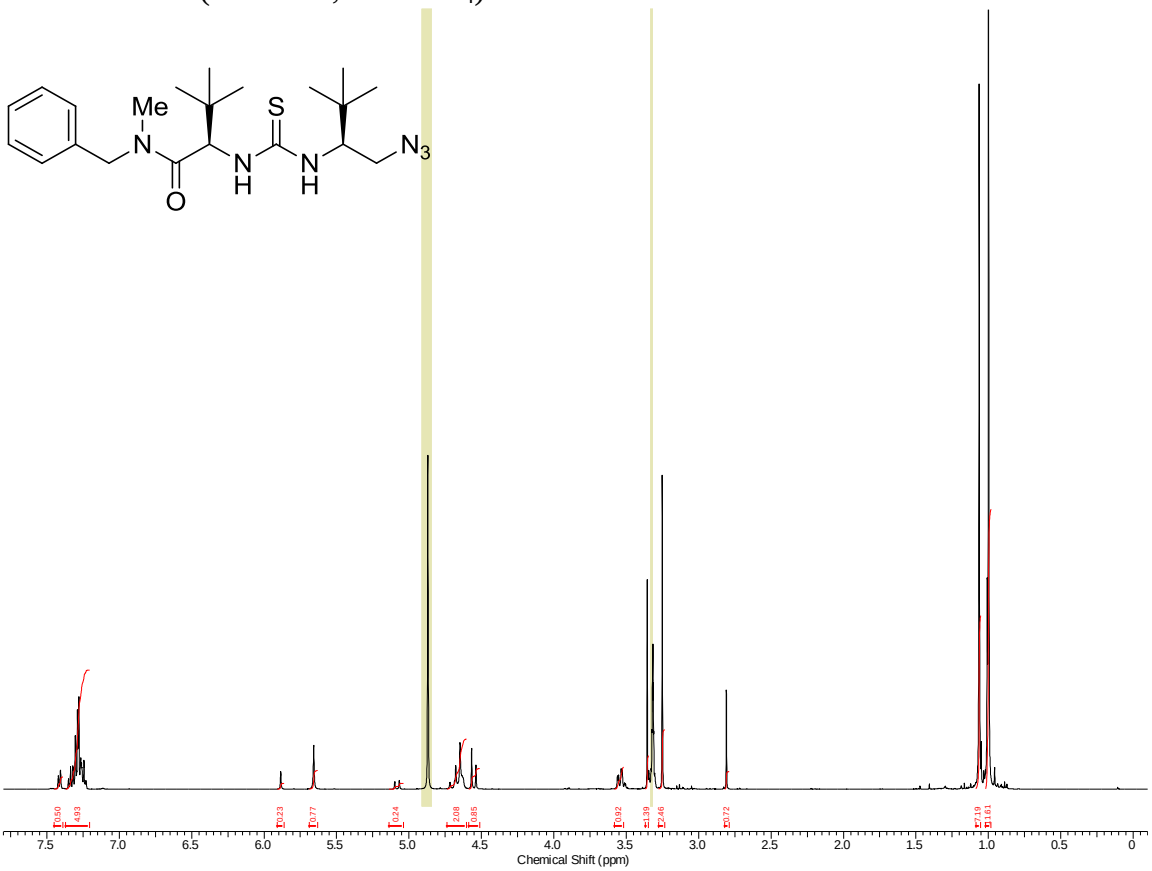
^{1}H NMR of **13** (500 MHz, MeOD-d_4)



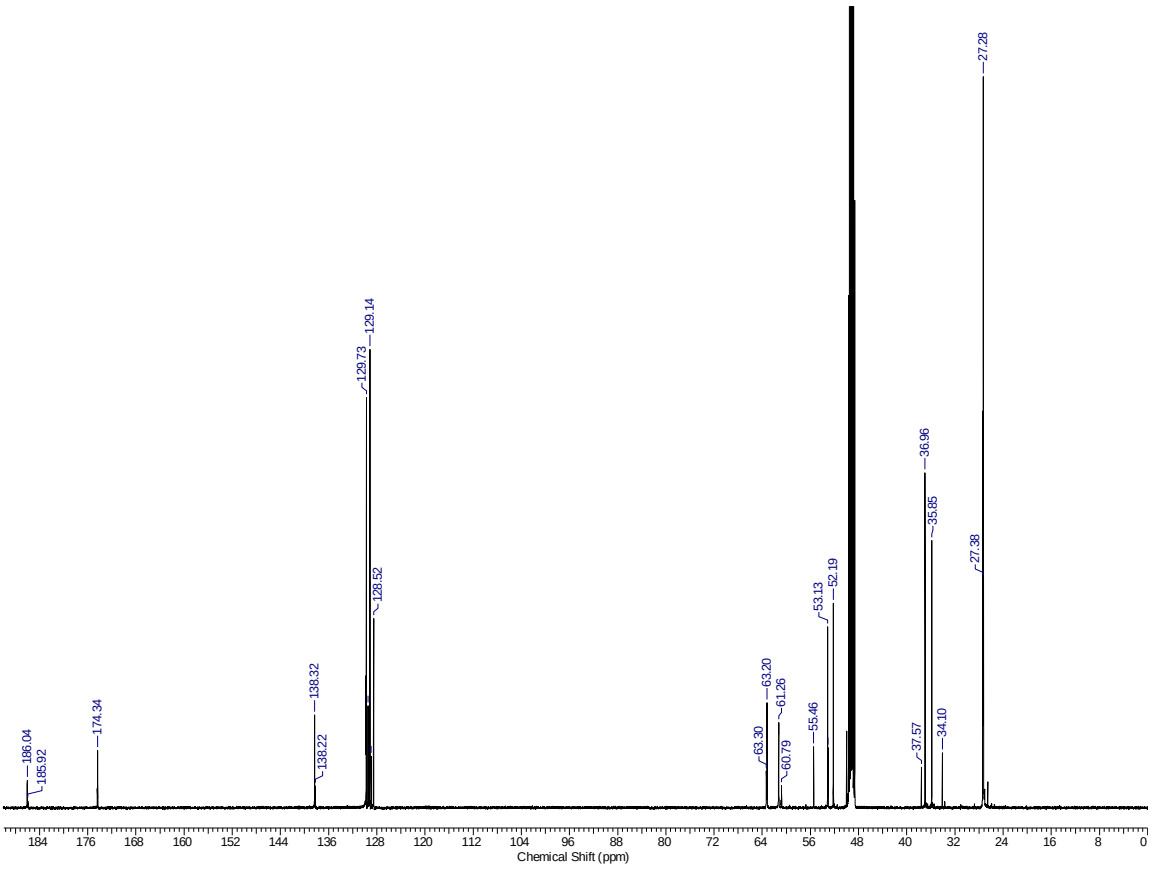
^{13}C NMR of **13** (125 MHz, MeOD-d_4)



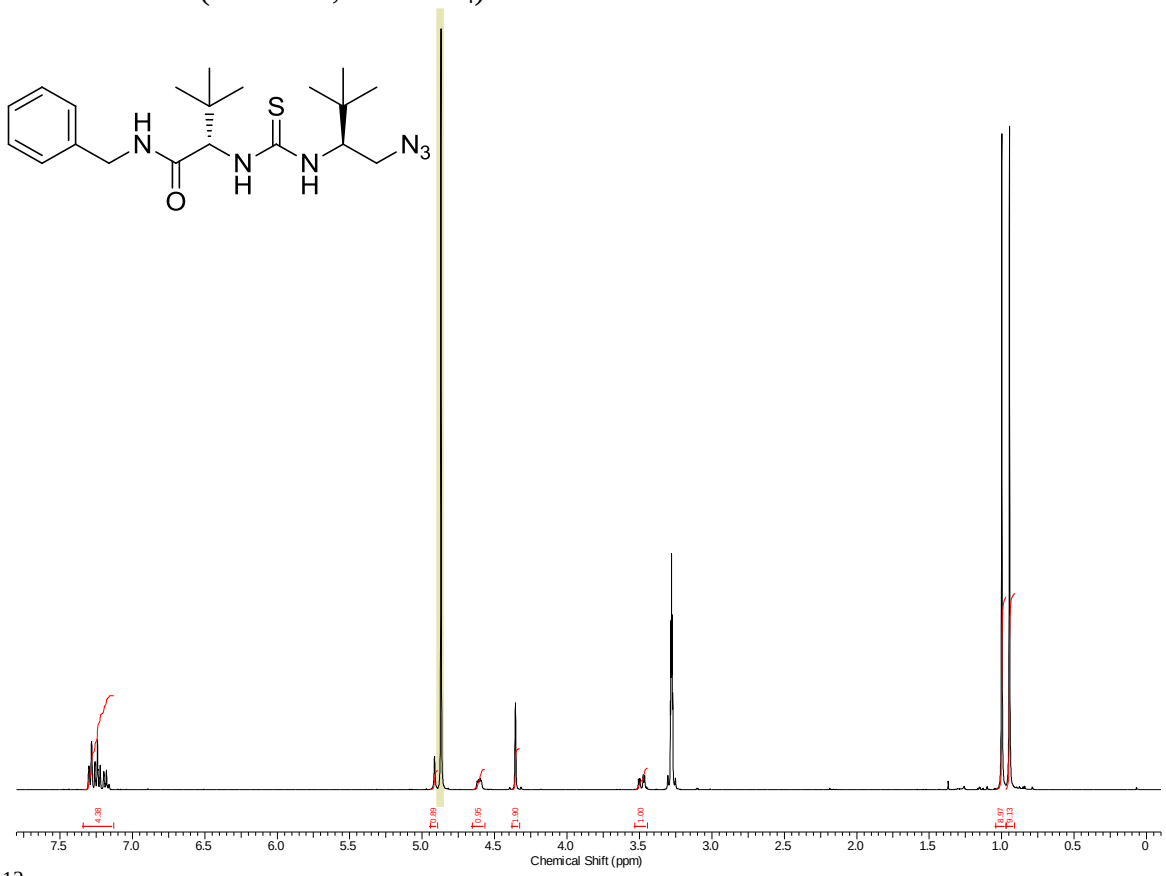
^{1}H NMR of **14** (500 MHz, MeOD-d_4)



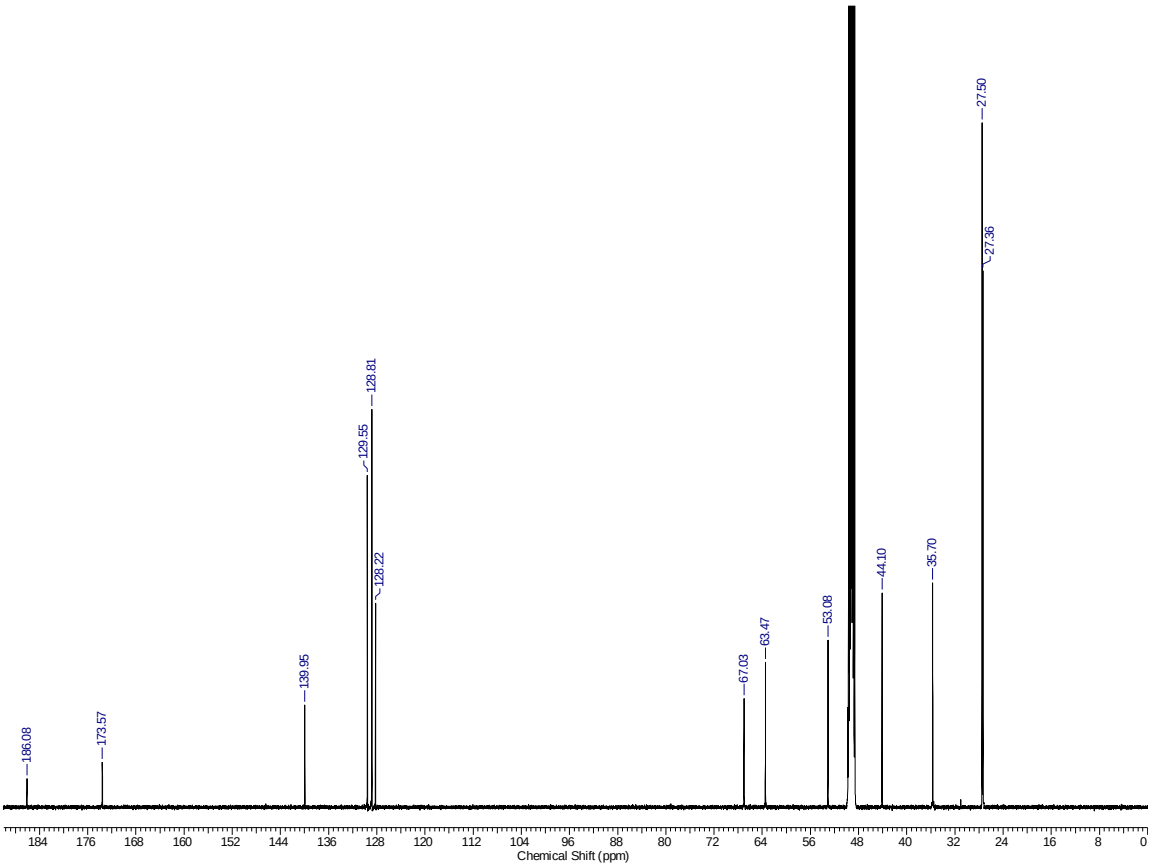
^{13}C NMR of **14** (125 MHz, MeOD-d_4)



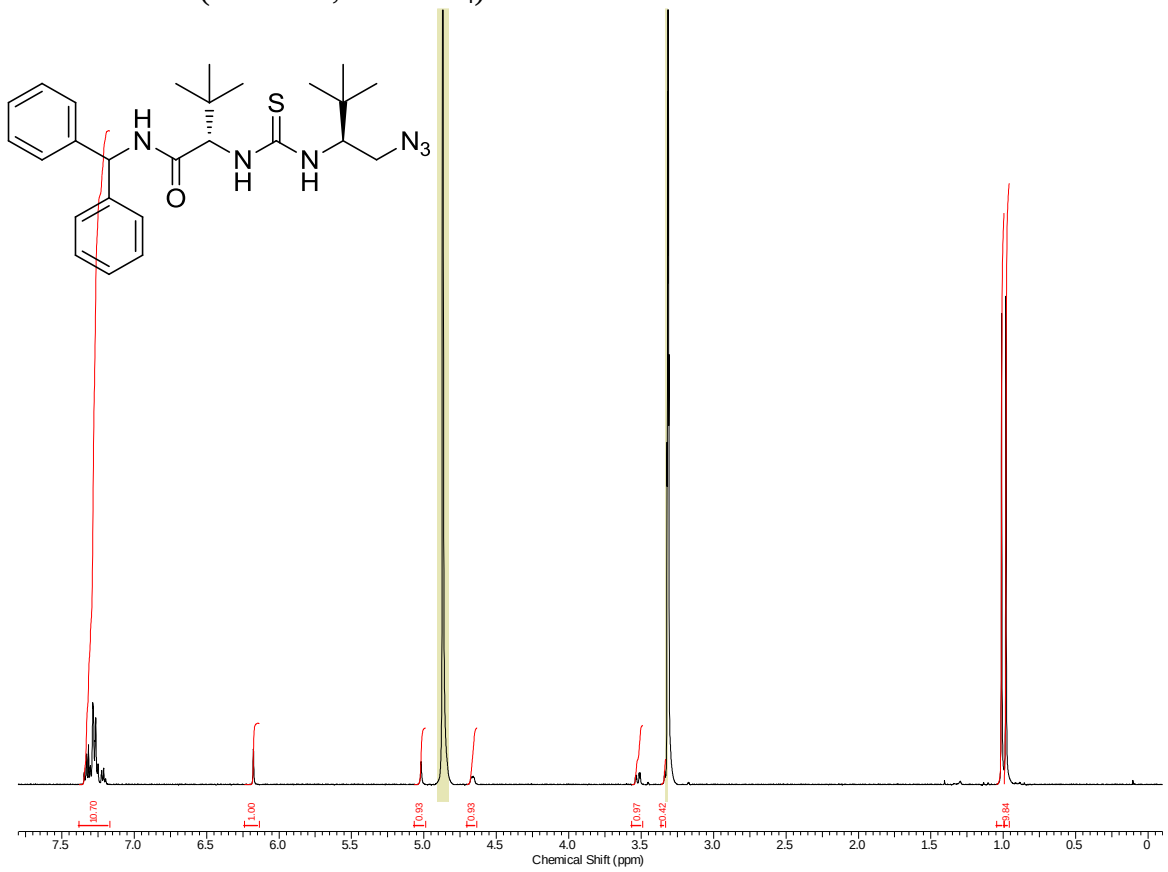
^{1}H NMR of **15** (400 MHz, MeOD-d_4)



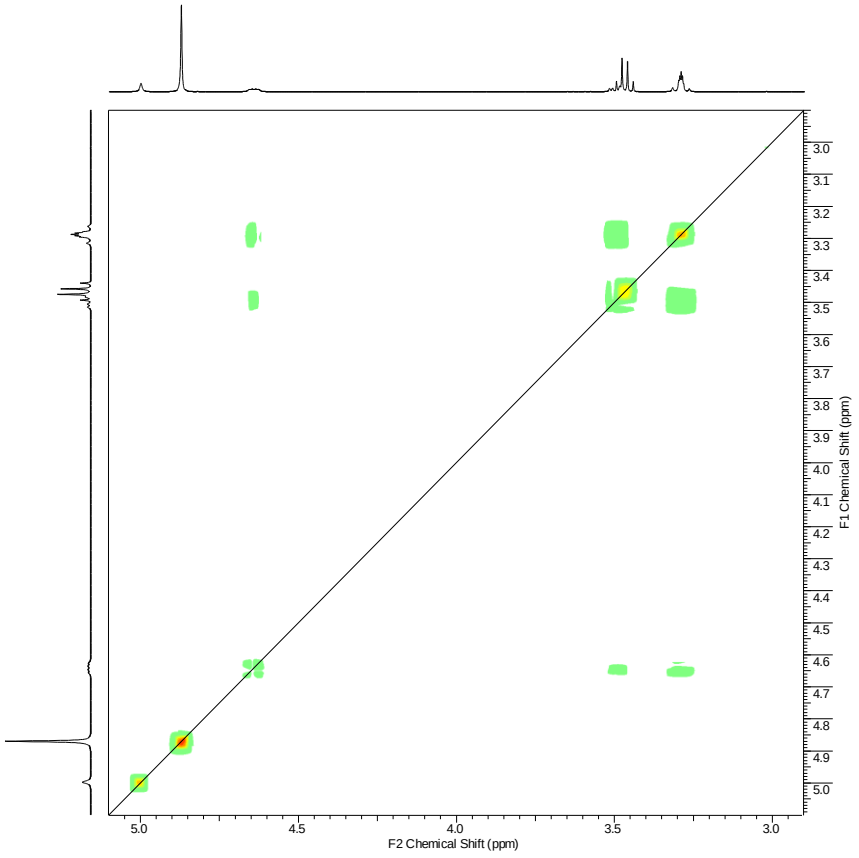
^{13}C NMR of **15** (125 MHz, MeOD-d_4)



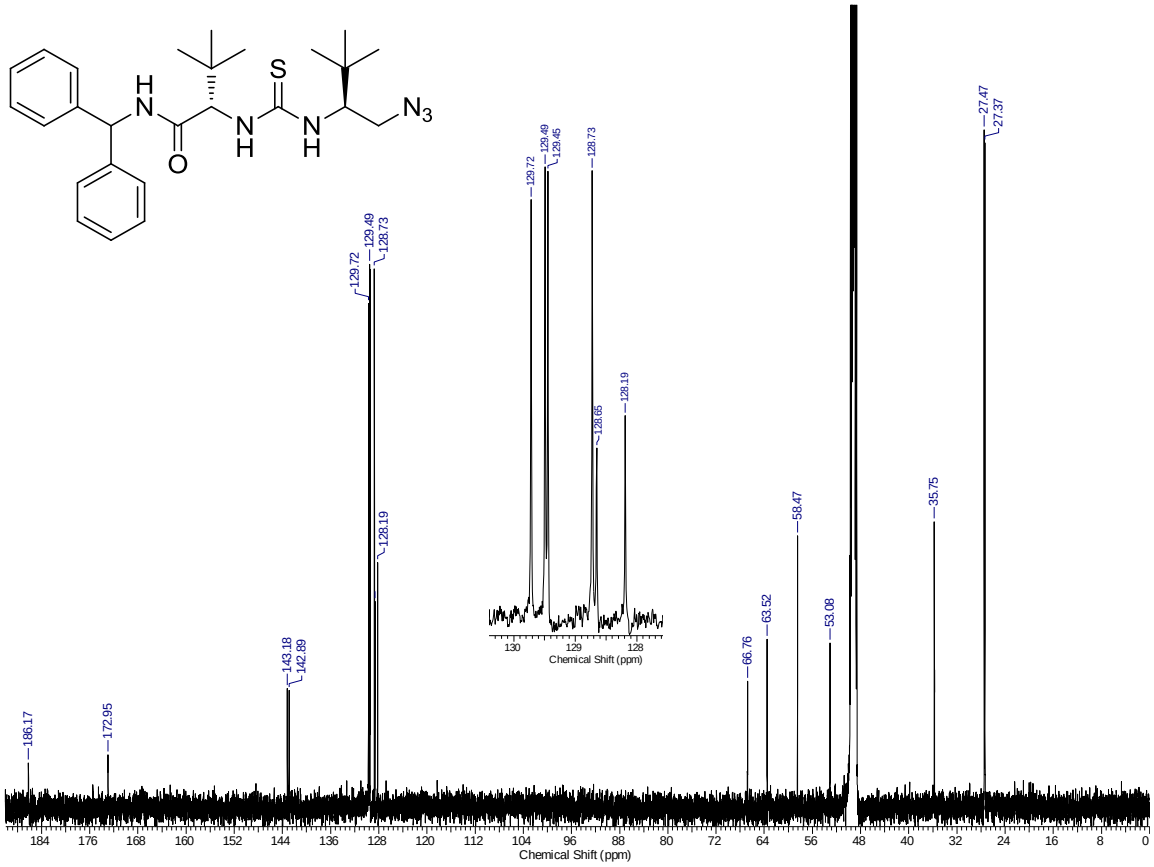
^{1}H NMR of **16** (500 MHz, MeOD-d_4)



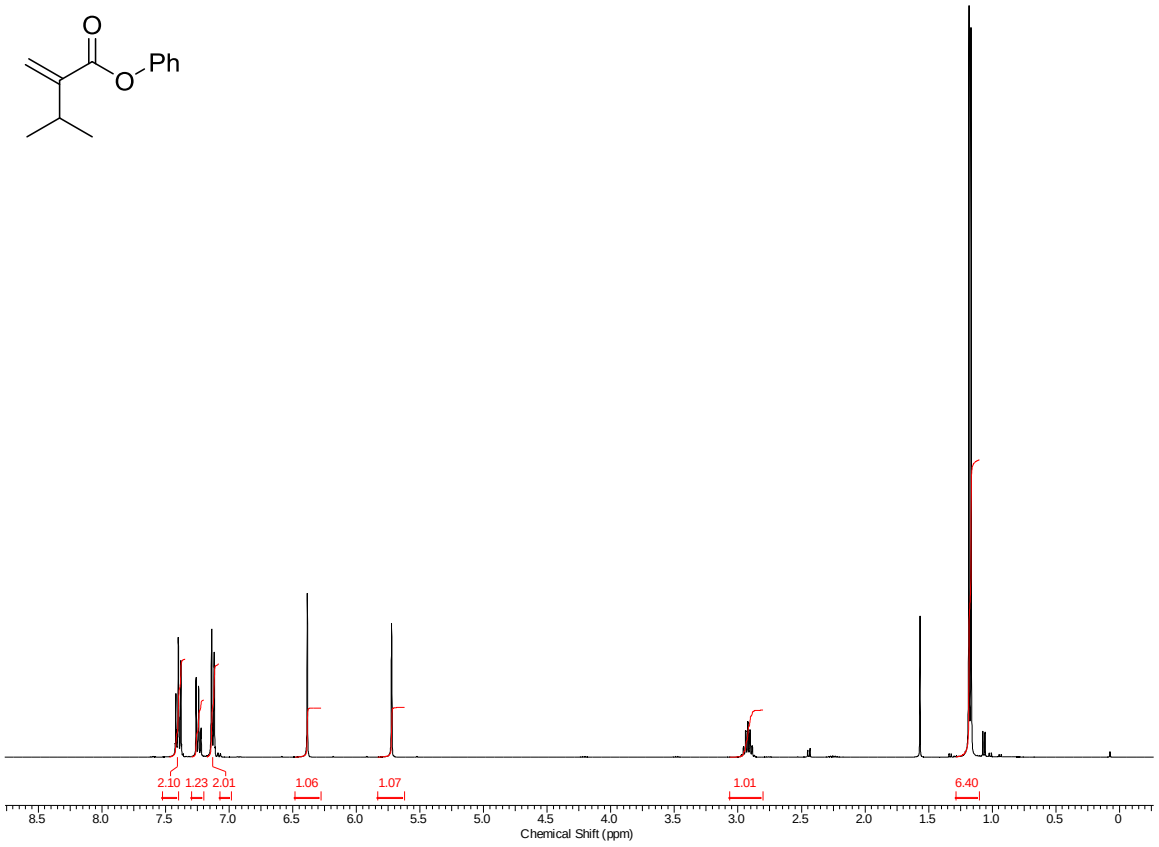
COSY NMR of **16** (400 MHz, MeOD-d_4) – Identification of multiplet beneath solvent peak.



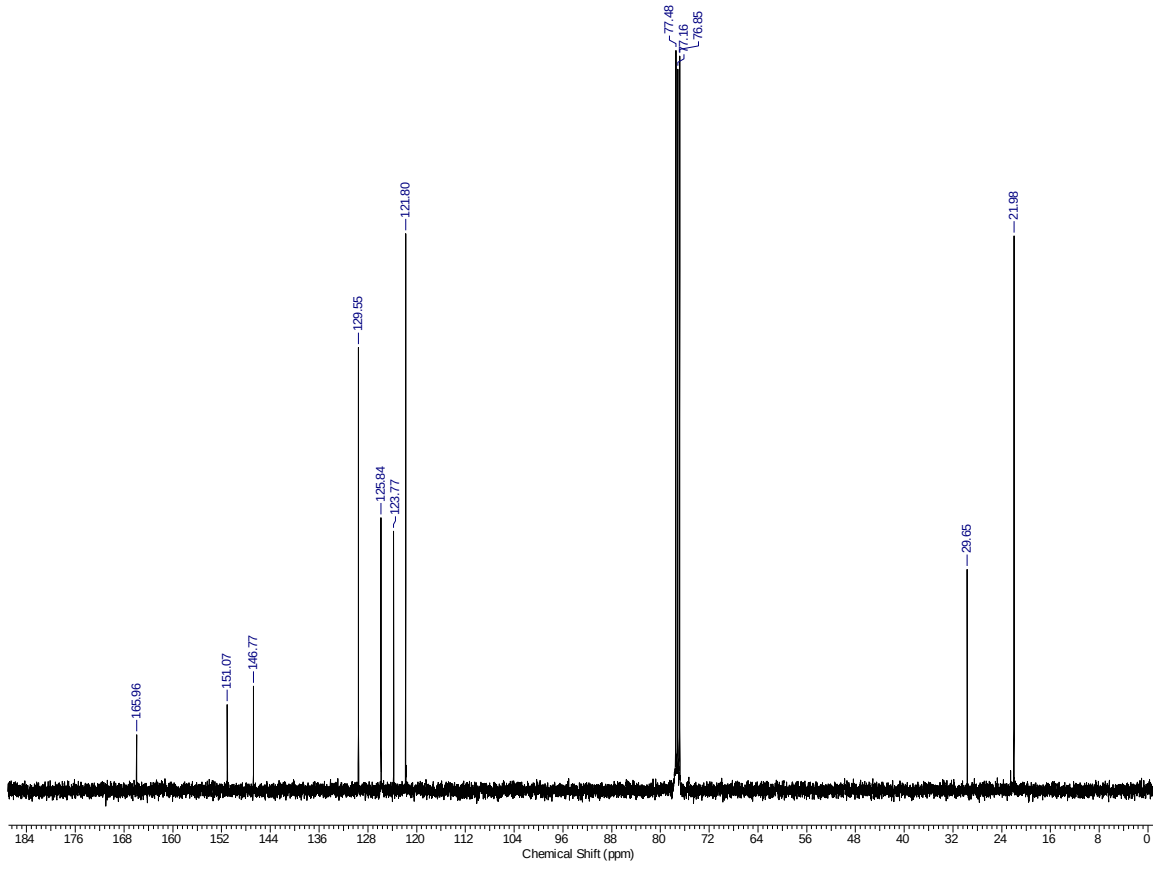
^{13}C NMR of **16** (125 MHz, MeOD-d_4)



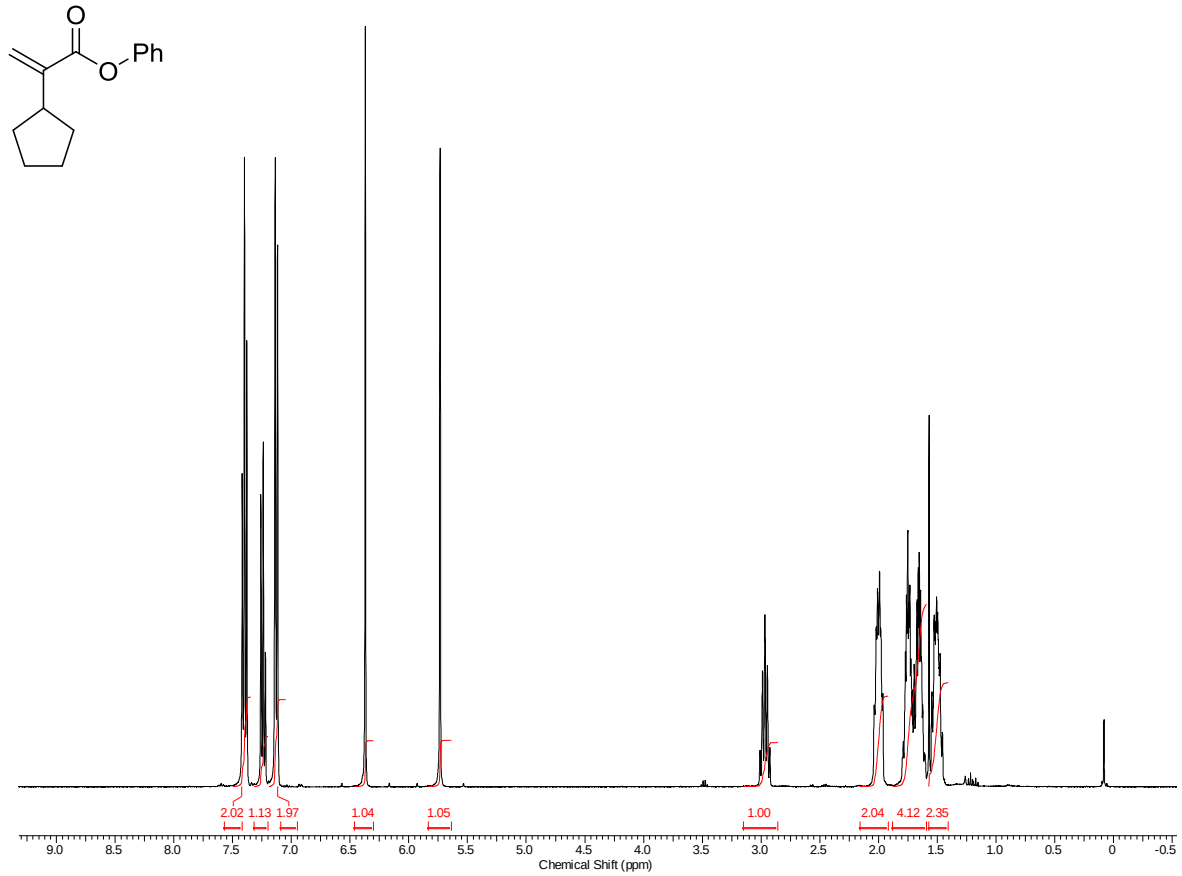
^{1}H NMR of **2l** (400 MHz, $CDCl_3$)



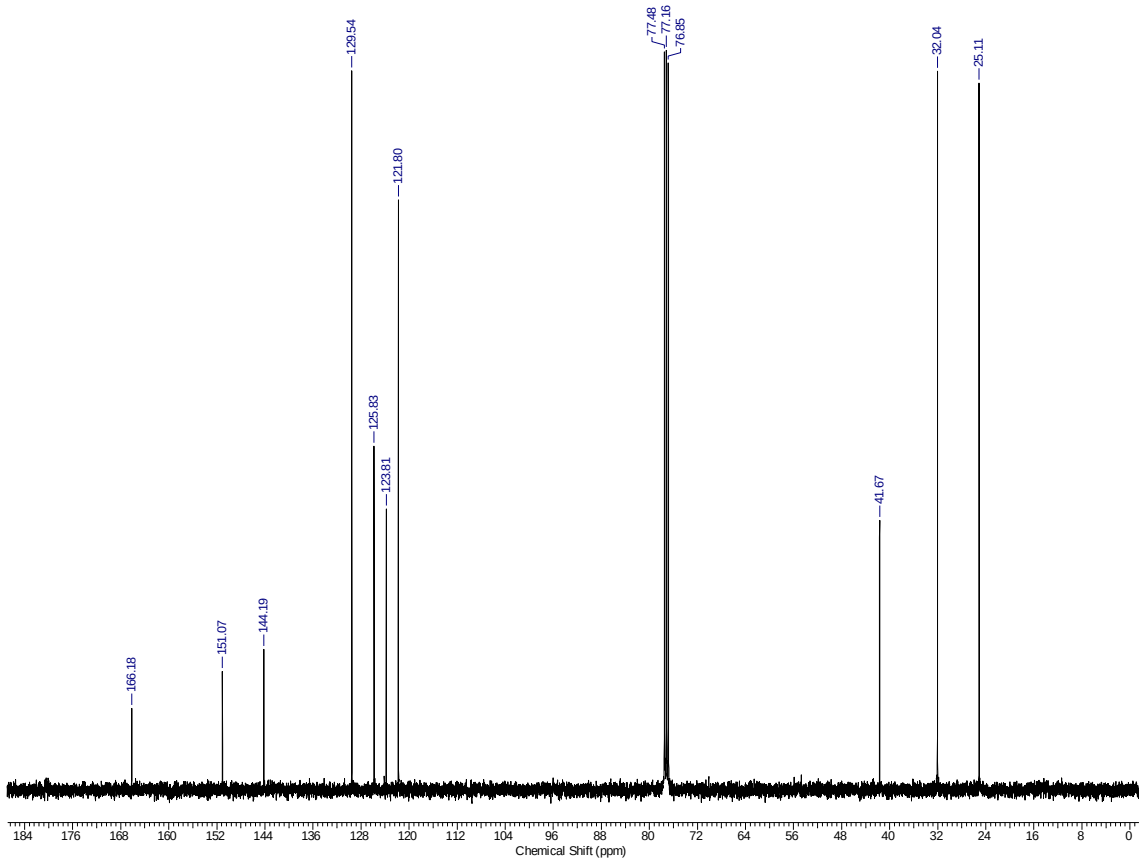
^{13}C NMR of **2l** (100 MHz, $CDCl_3$)



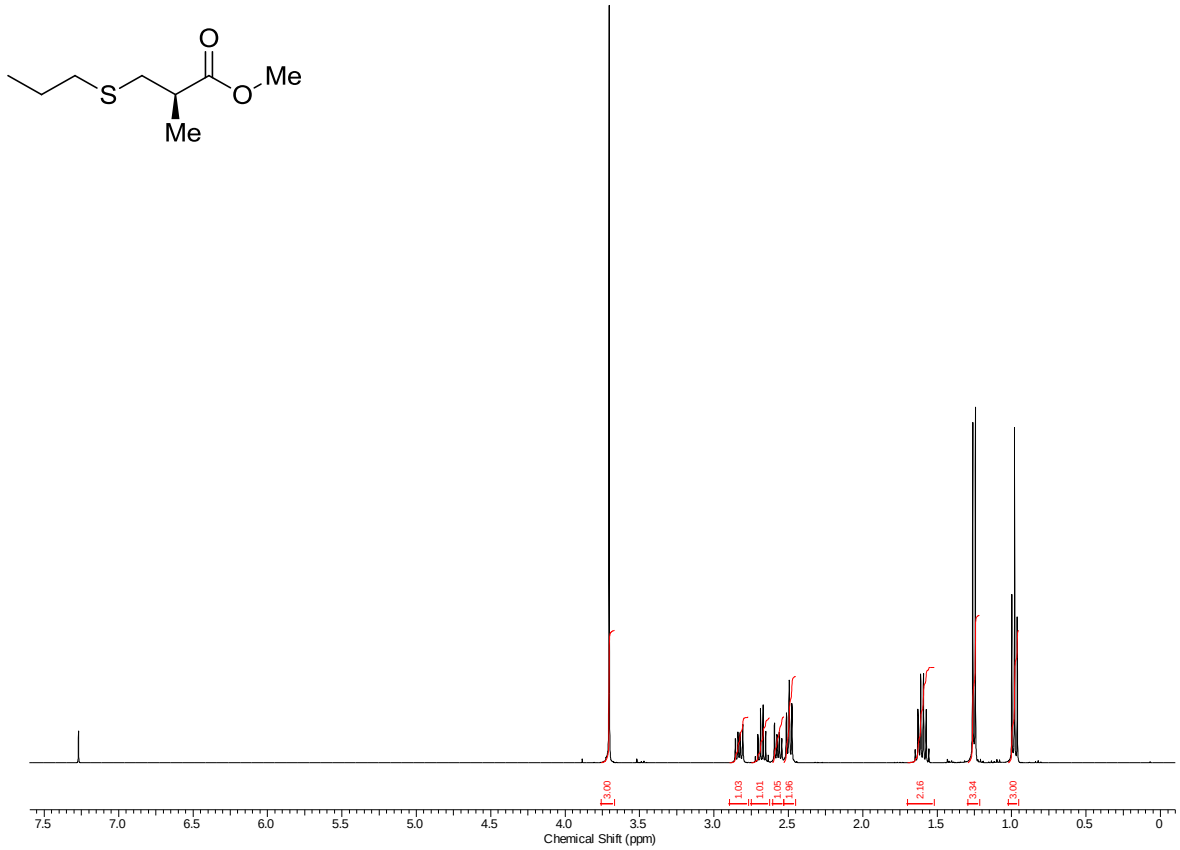
^{1}H NMR of **2n** (400 MHz, $CDCl_3$)



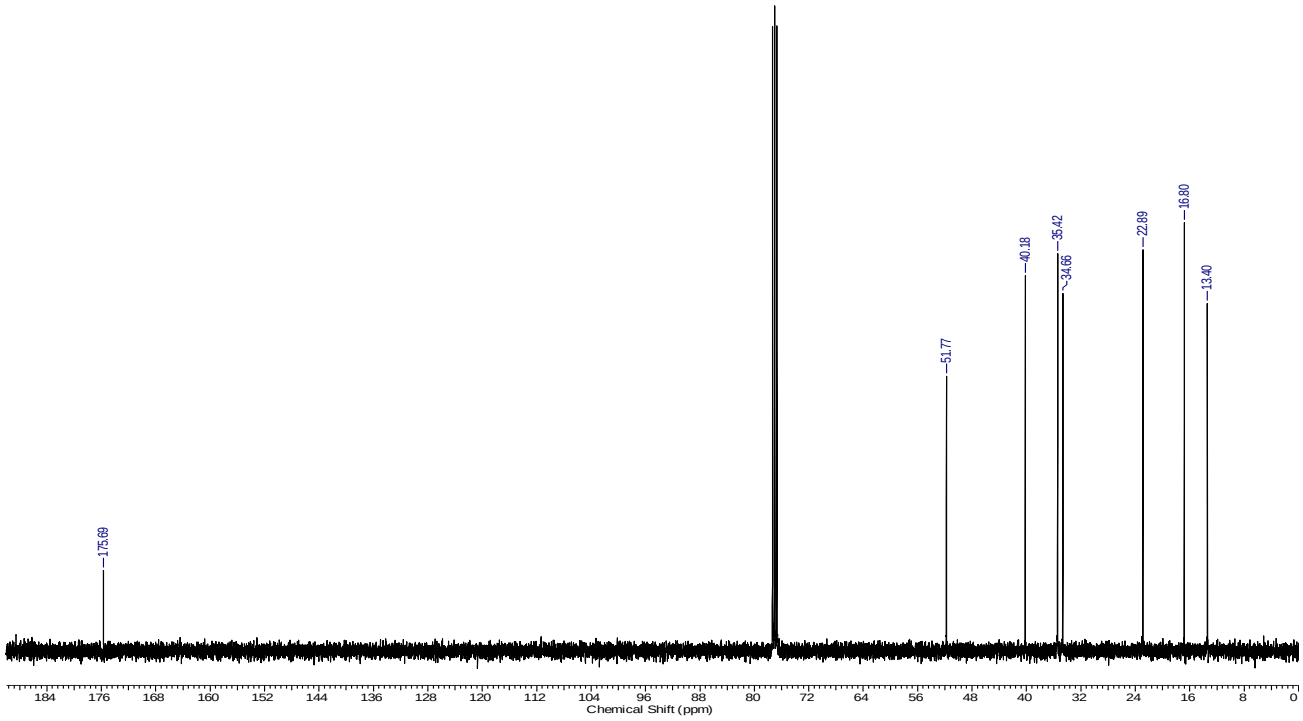
^{13}C NMR of **2n** (100 MHz, $CDCl_3$)



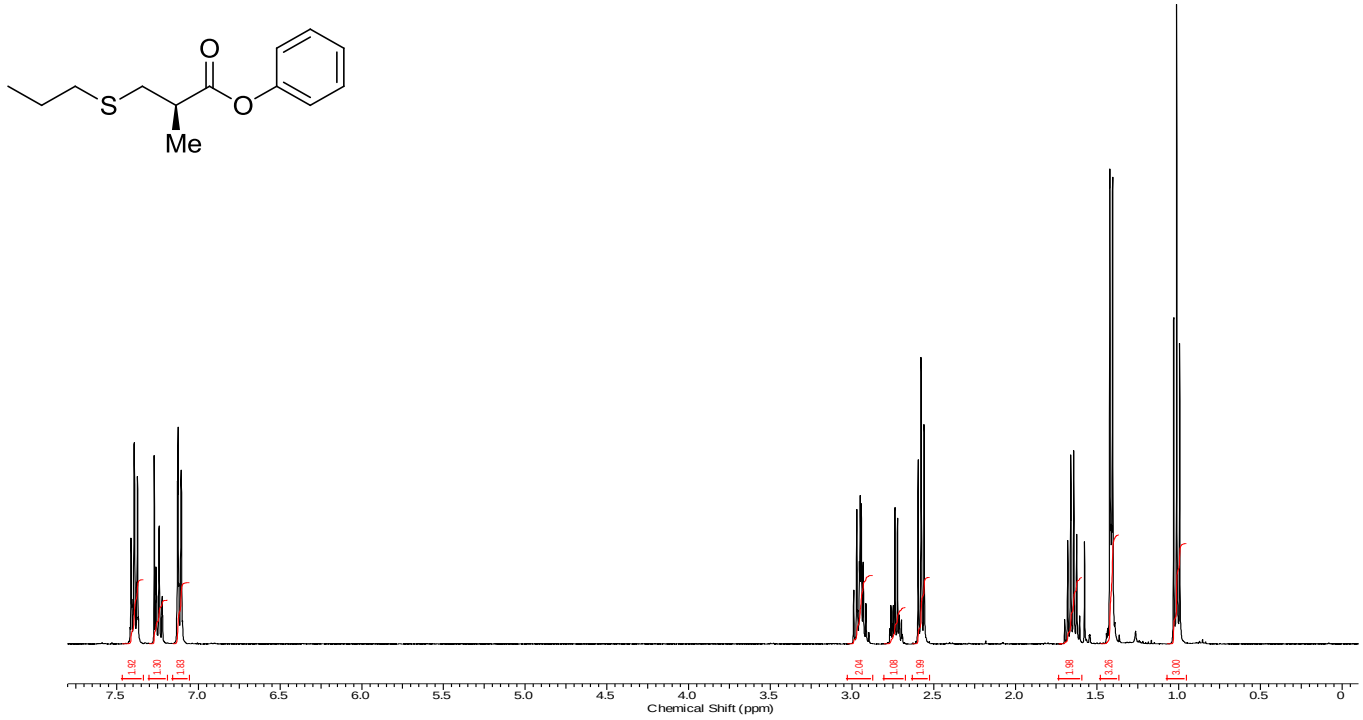
^{1}H NMR of **4a** (400 MHz, $CDCl_3$)



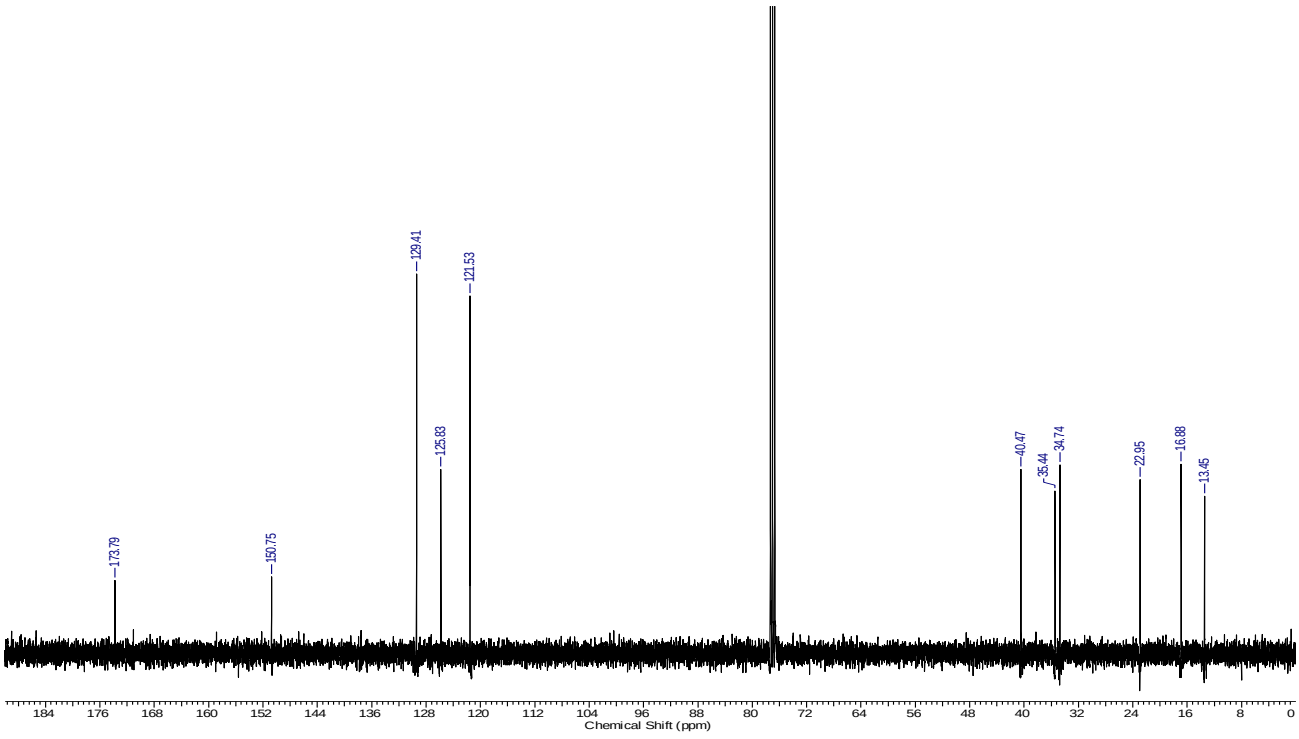
^{13}C NMR of **4a** (100 MHz, $CDCl_3$)



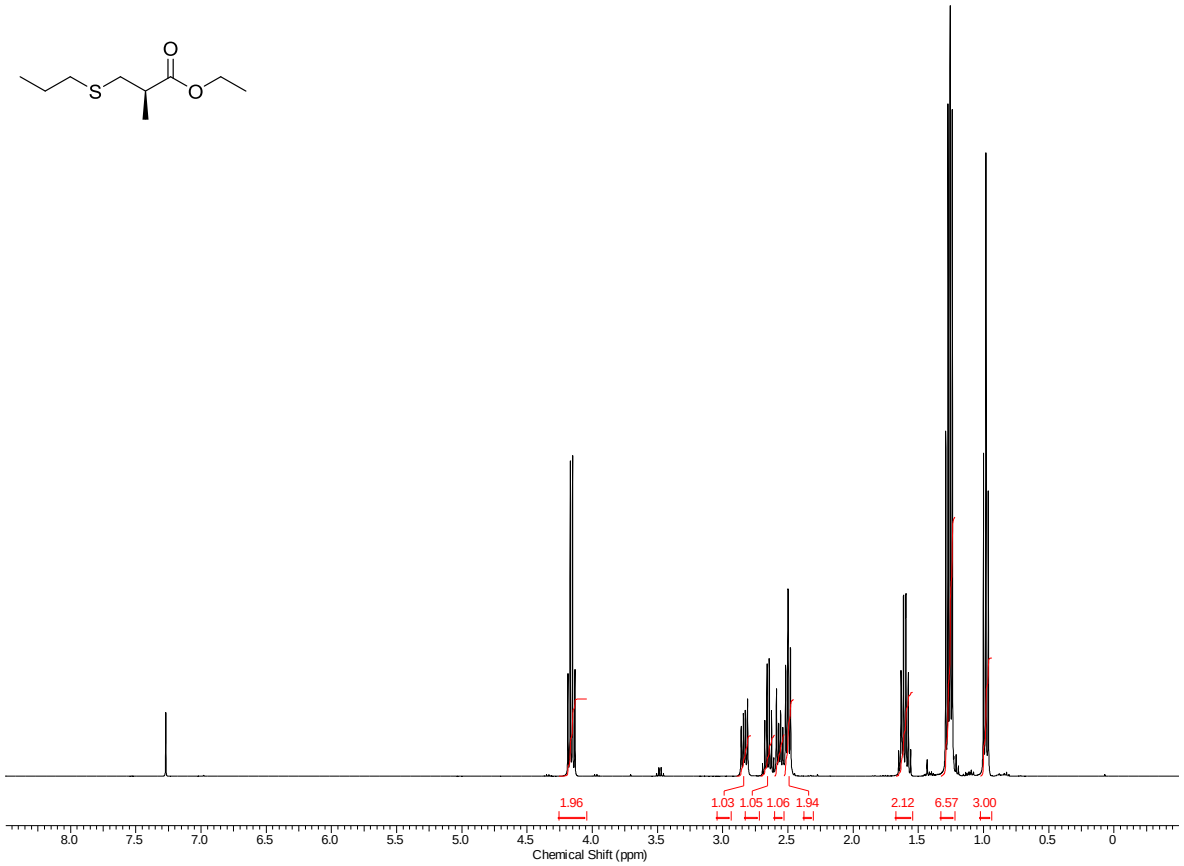
^{1}H NMR of **4b** (400 MHz, $CDCl_3$)



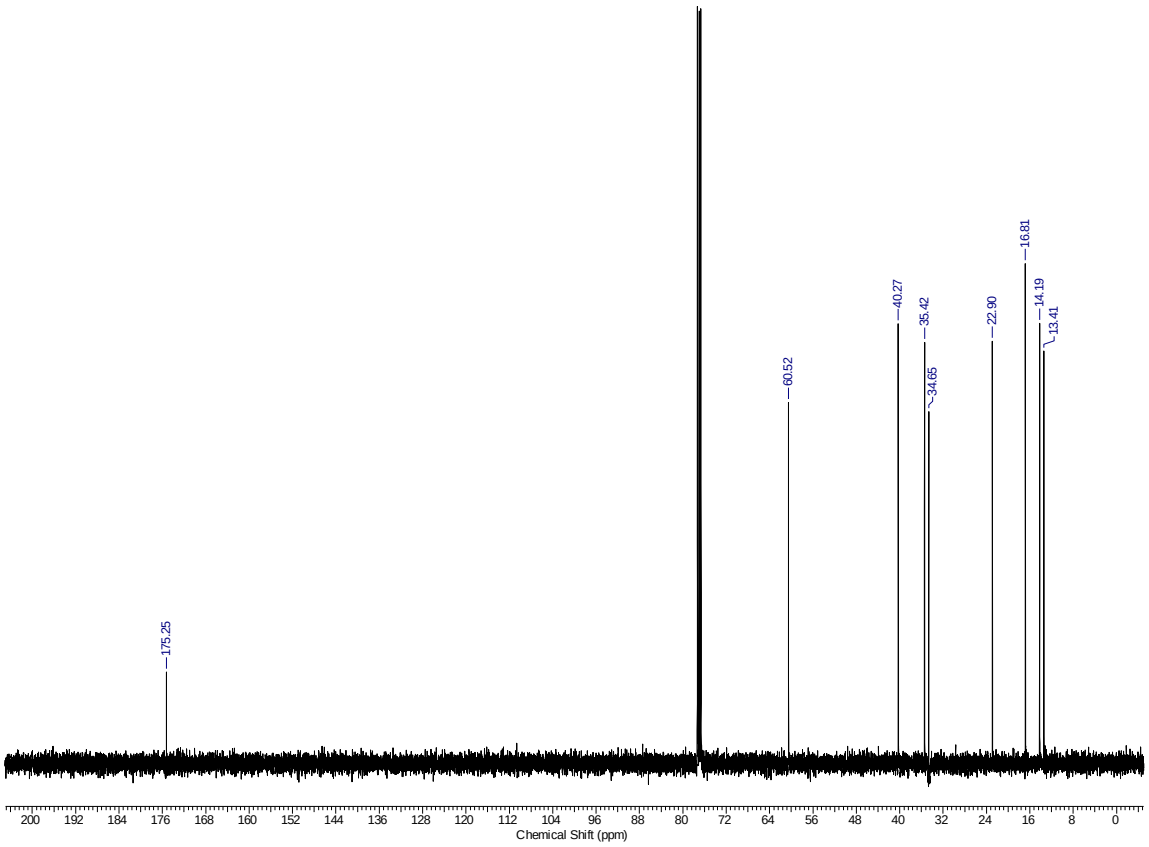
^{13}C NMR of **4b** (100 MHz, $CDCl_3$)



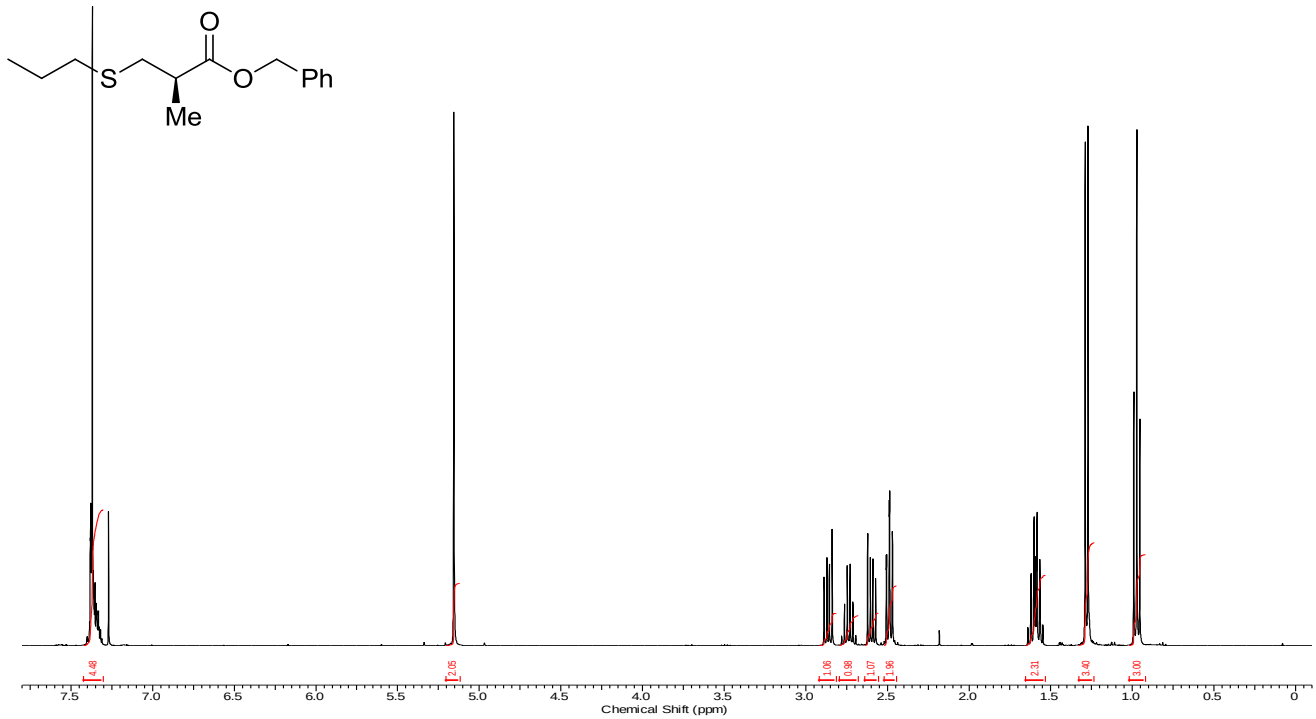
^{1}H NMR of **4c** (400 MHz, $CDCl_3$)



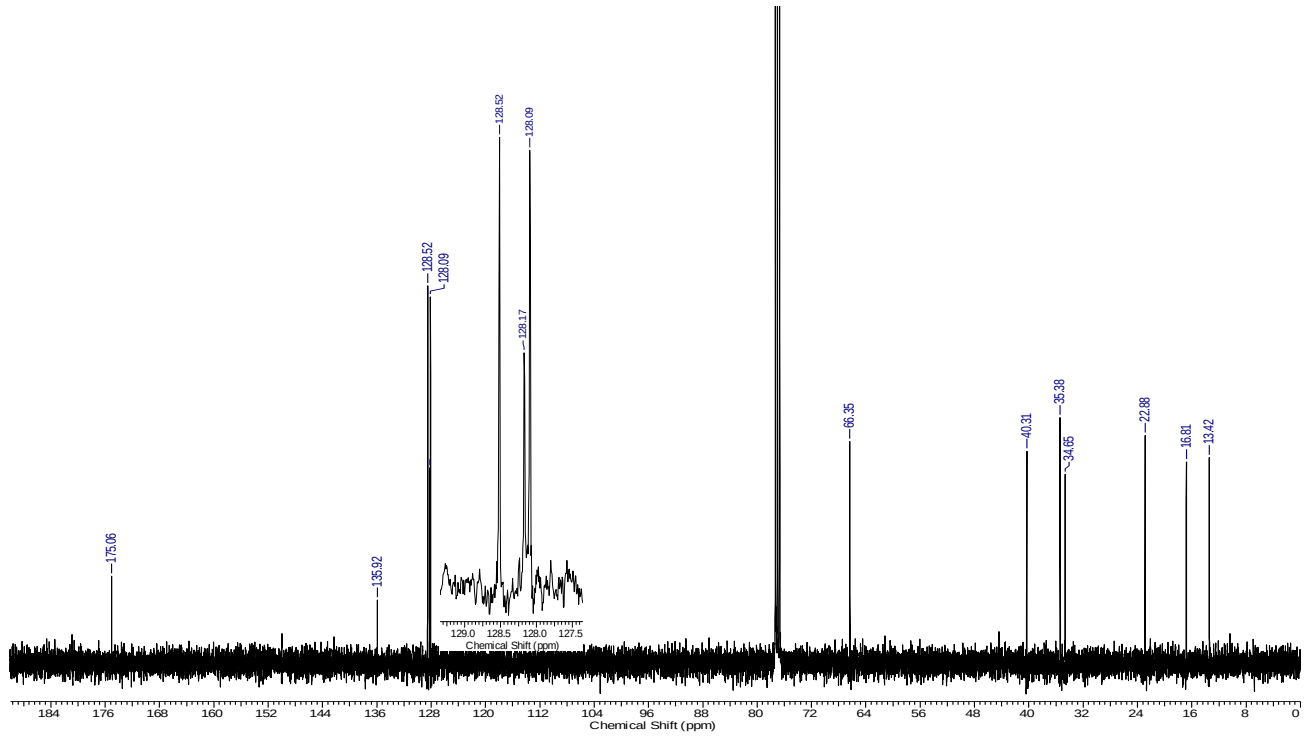
^{13}C NMR of **4c** (100 MHz, $CDCl_3$)



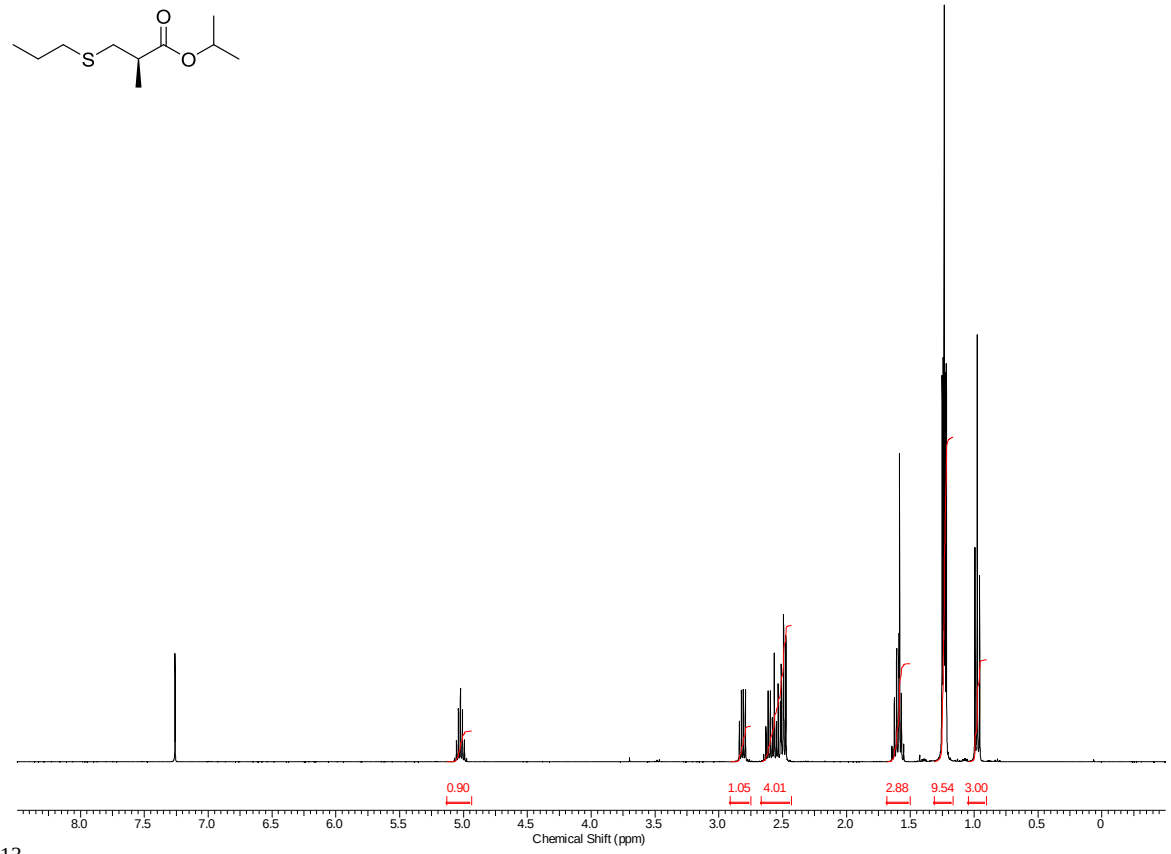
^{1}H NMR of **4d** (400 MHz, $CDCl_3$)



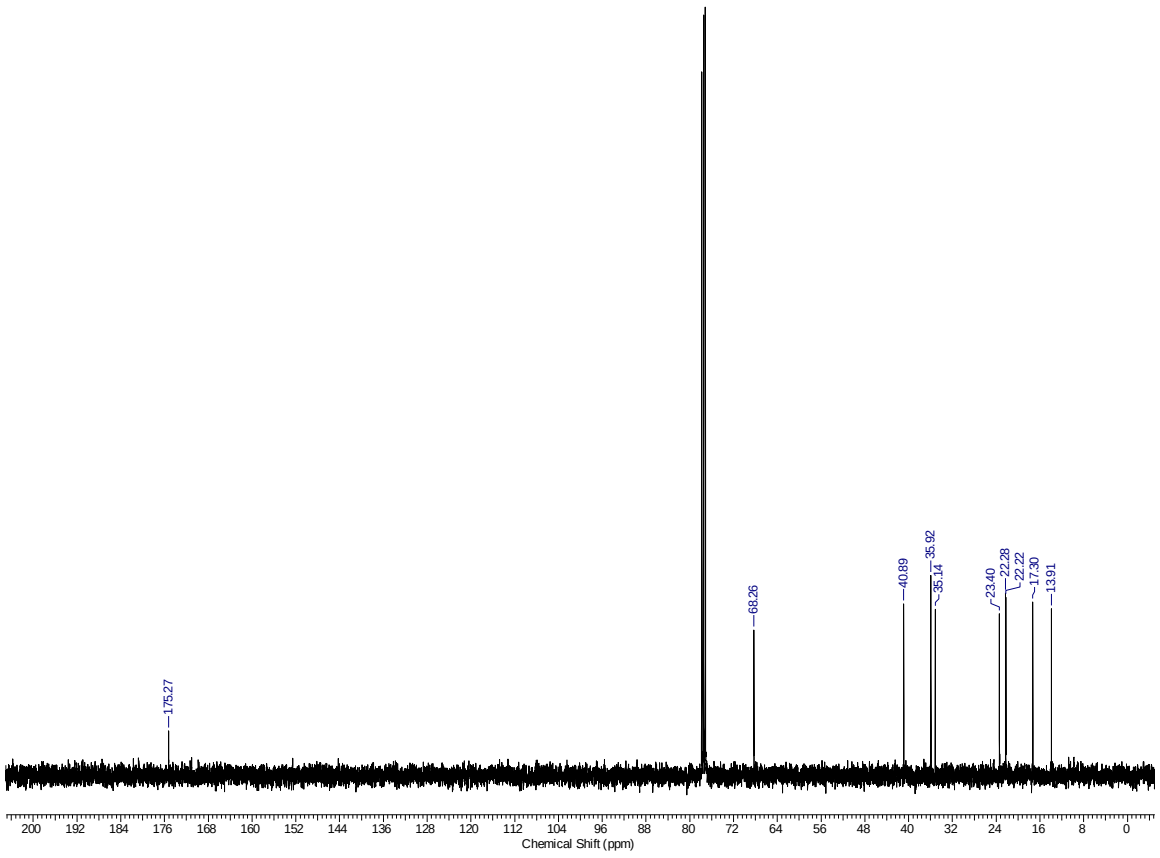
^{13}C NMR of **4d** (100 MHz, $CDCl_3$)



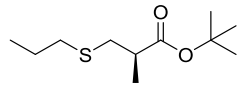
^{1}H NMR of **4e** (400 MHz, $CDCl_3$)



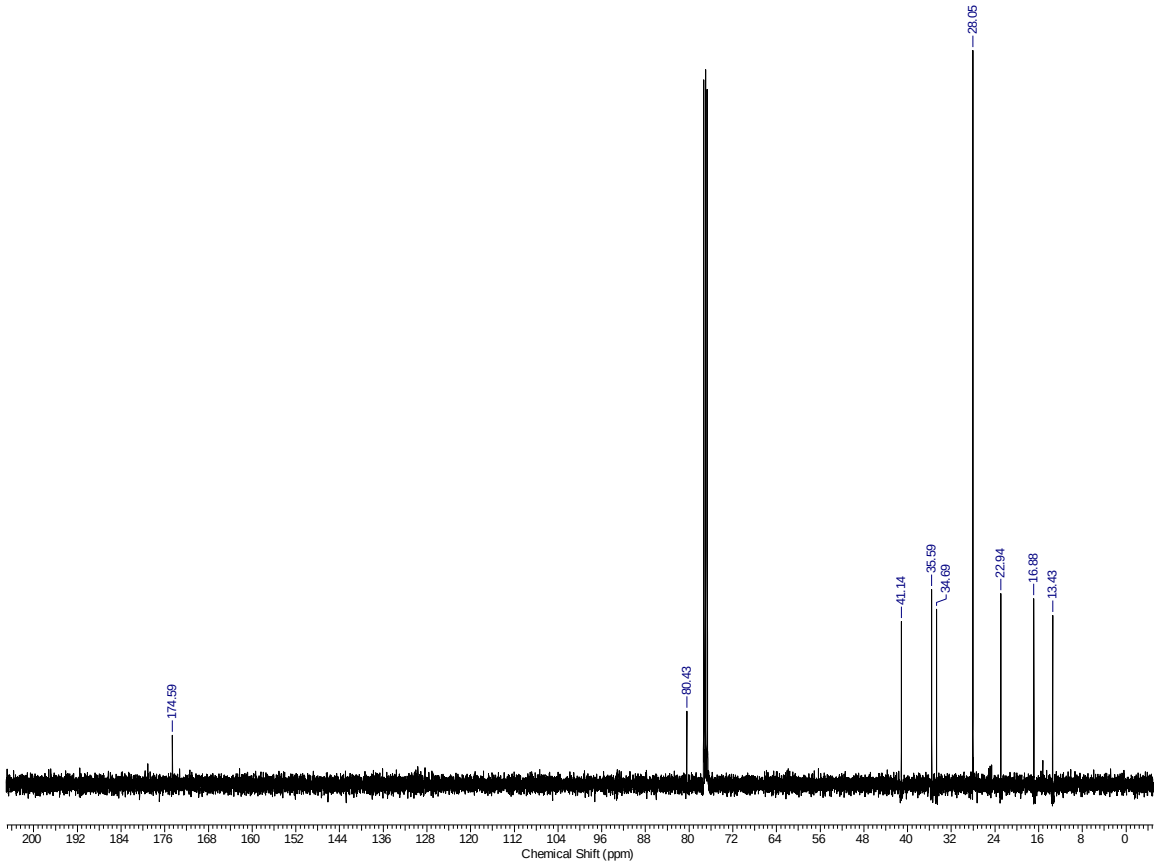
^{13}C NMR of **4e** (100 MHz, $CDCl_3$)



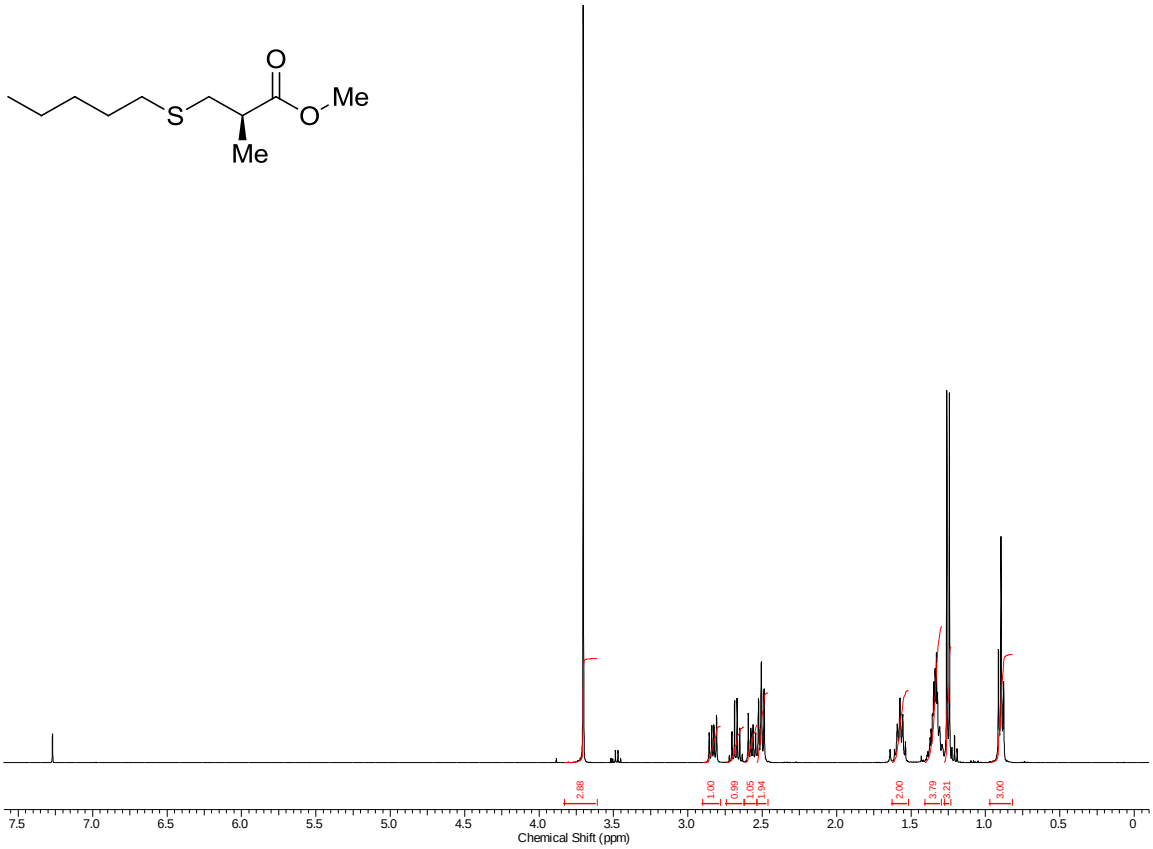
^{1}H NMR of **4f** (400 MHz, $CDCl_3$)



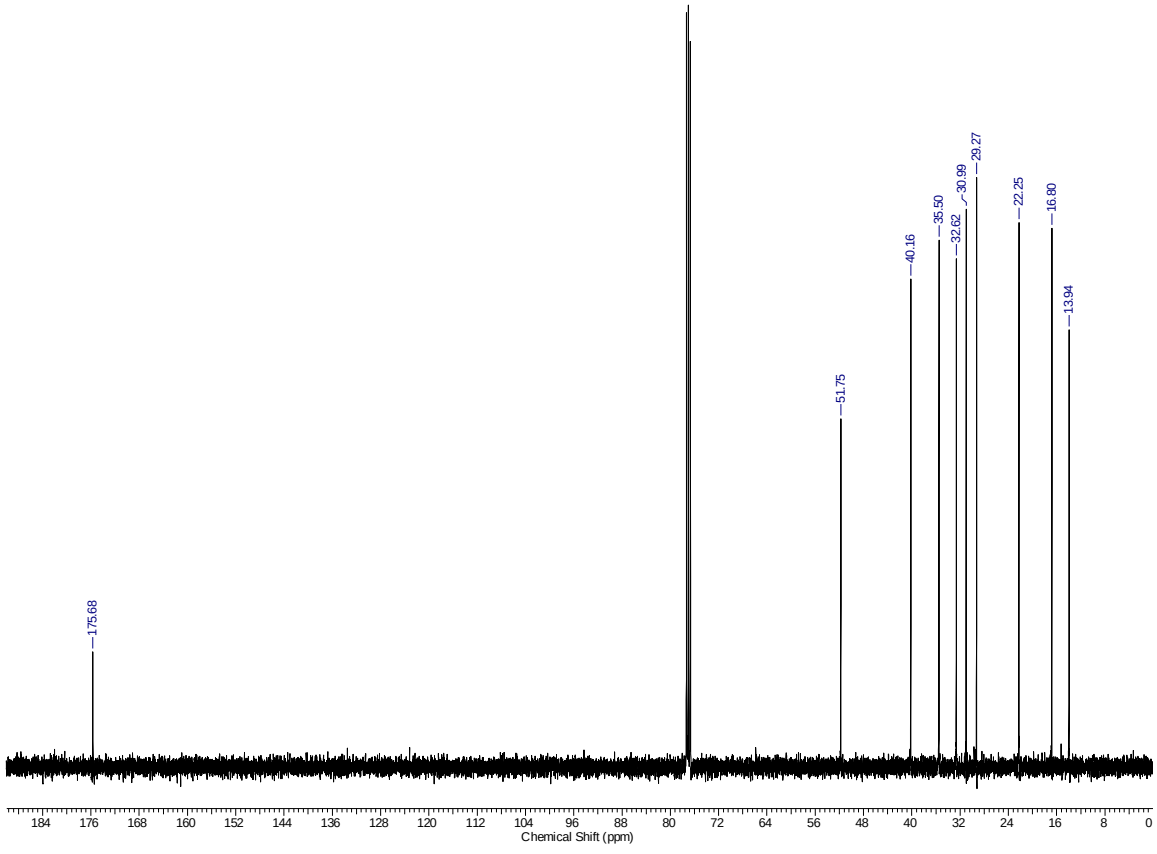
^{13}C NMR of **4f** (100 MHz, $CDCl_3$)



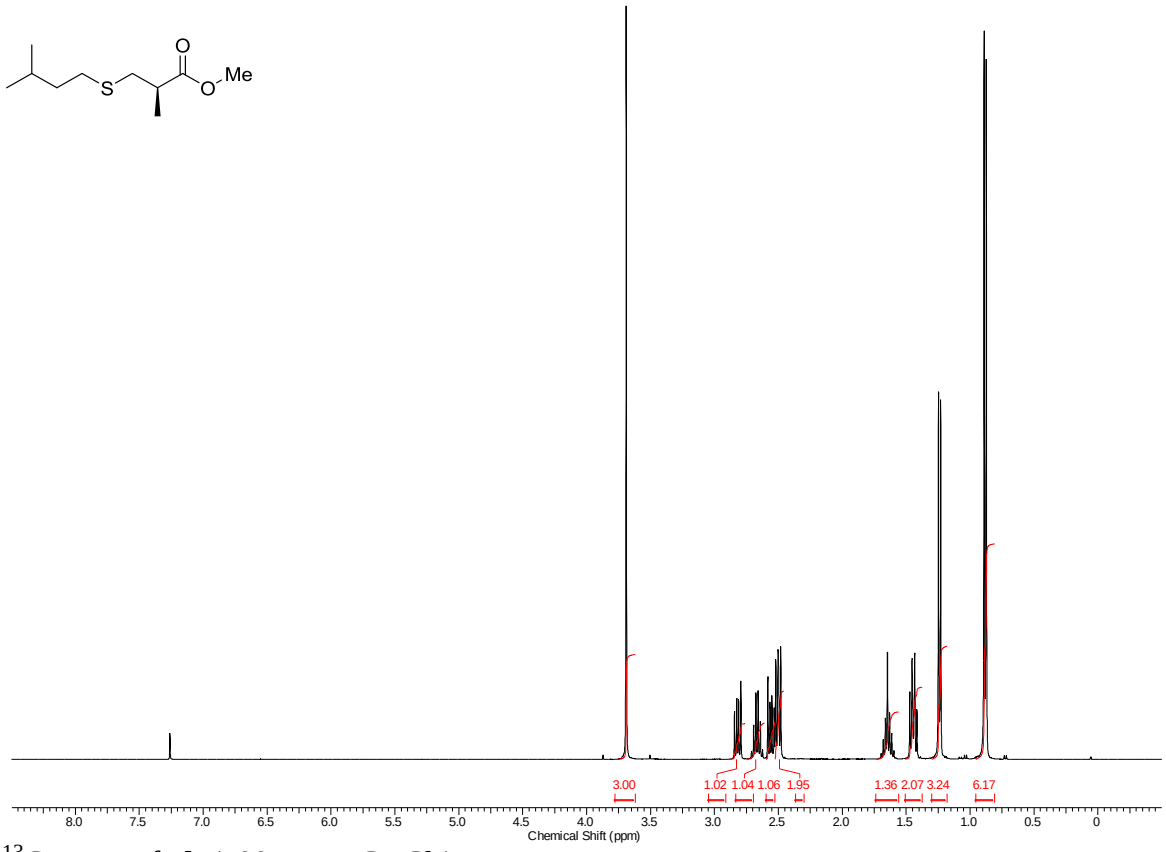
^{1}H NMR of **4g** (400 MHz, $CDCl_3$)



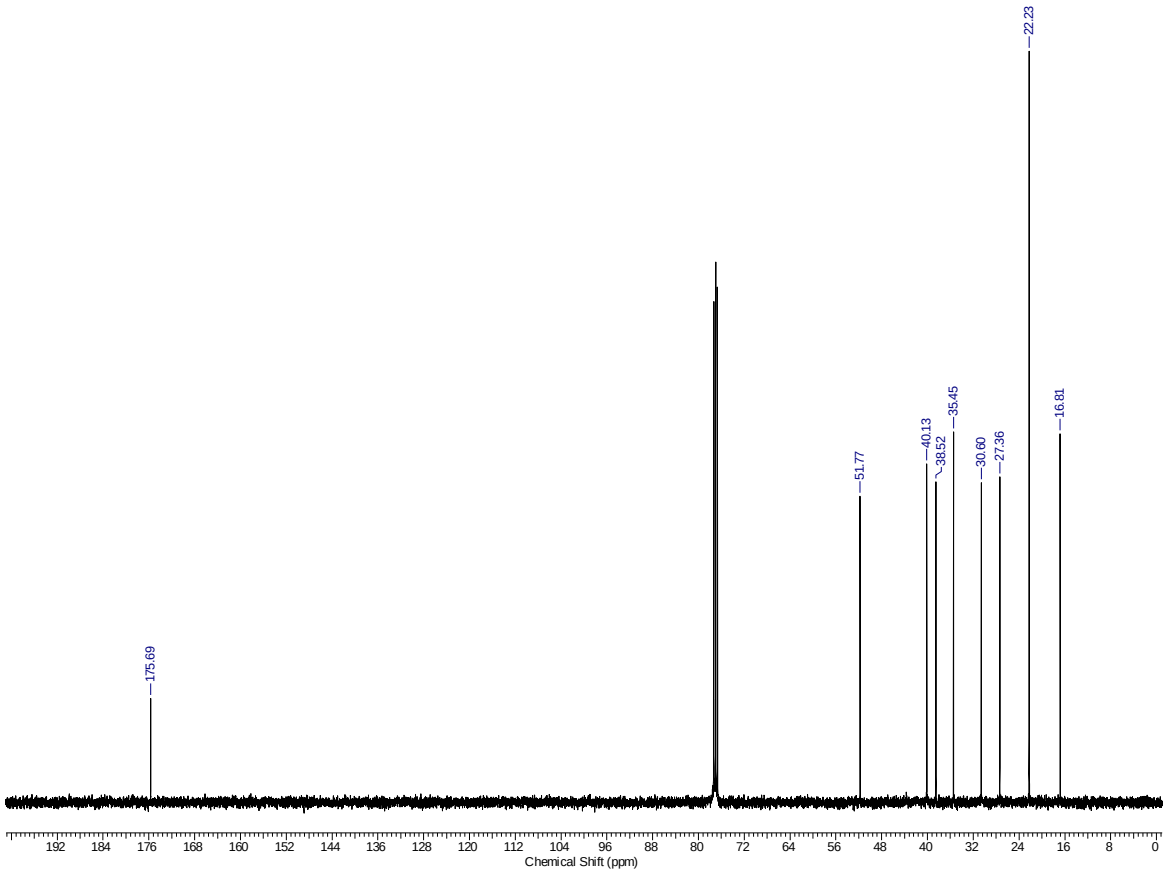
^{13}C NMR of **4g** (100 MHz, $CDCl_3$)



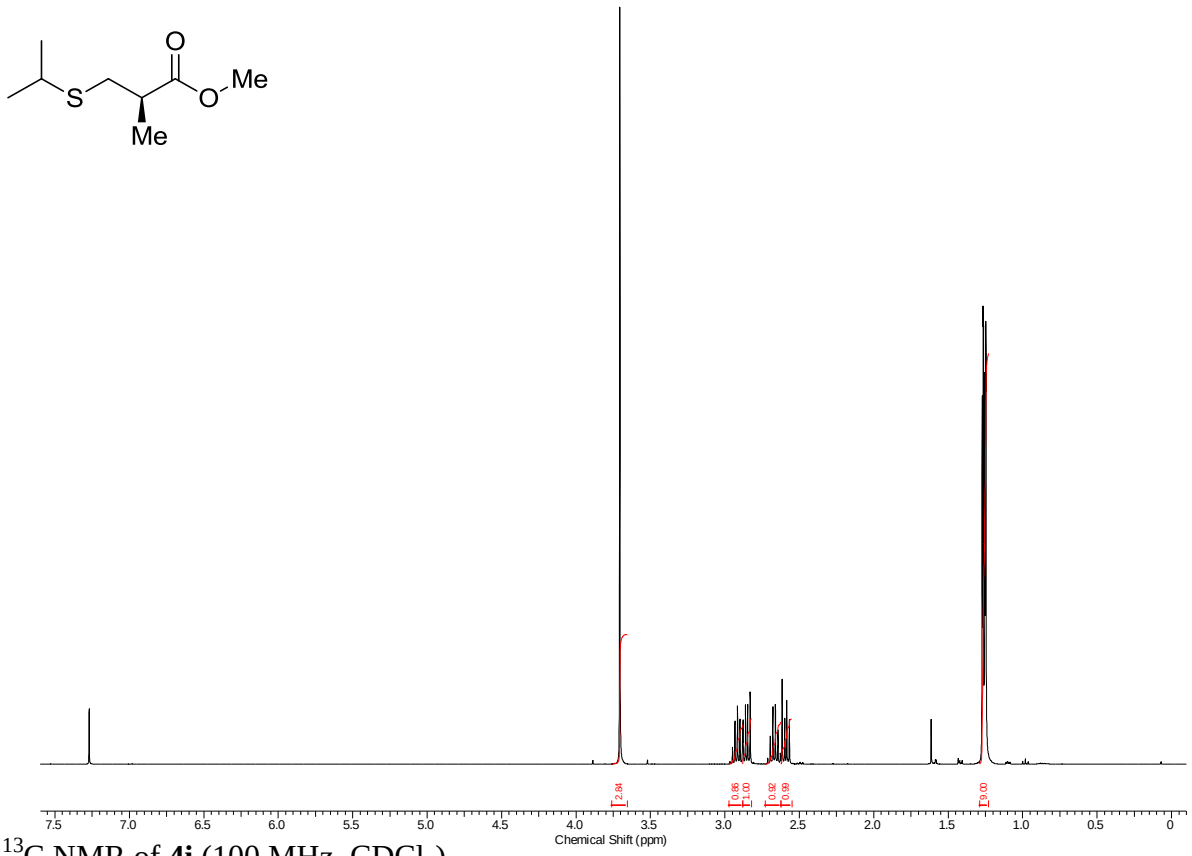
^{1}H NMR of **4h** (400 MHz, $CDCl_3$)



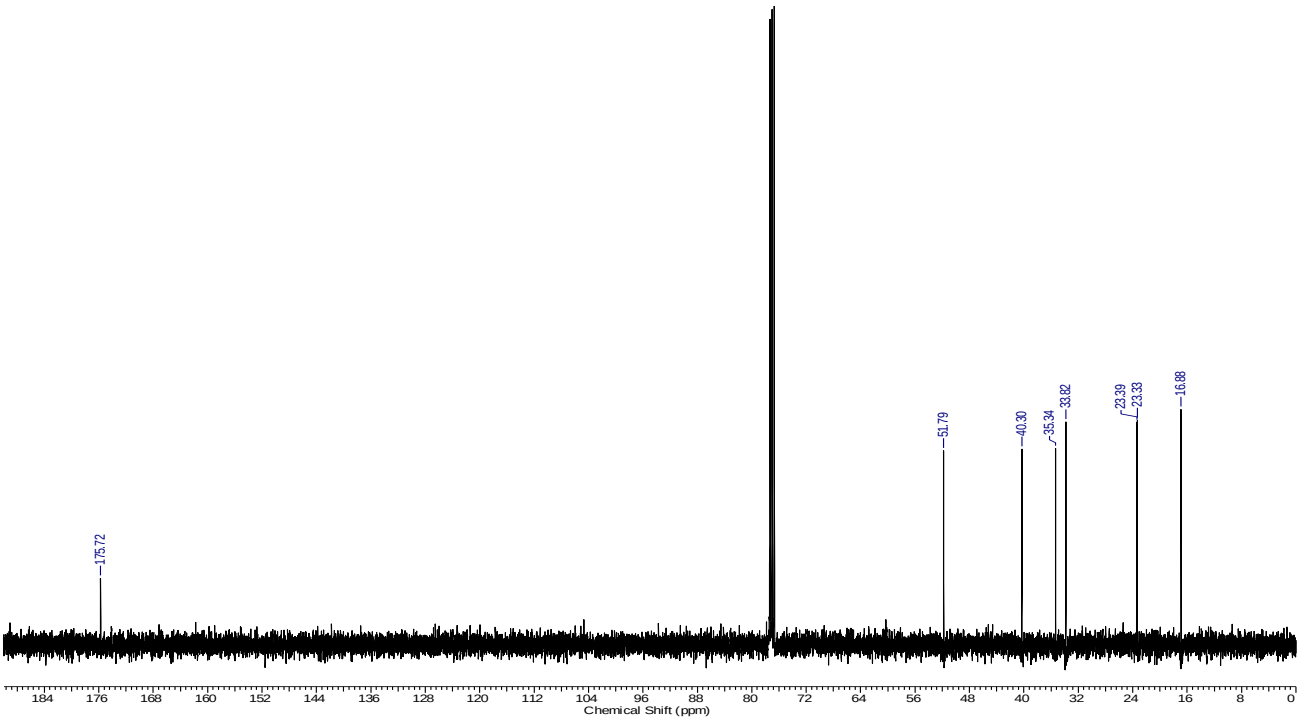
^{13}C NMR of **4h** (100 MHz, $CDCl_3$)



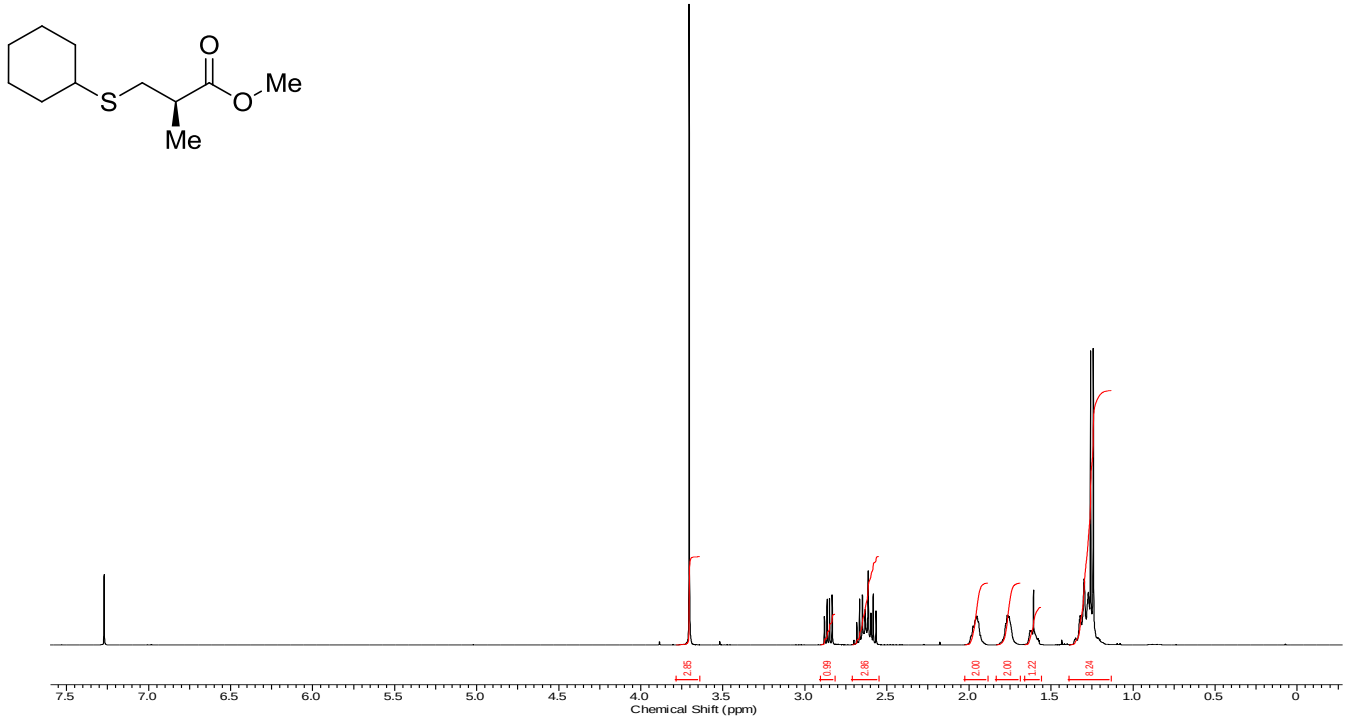
^{1}H NMR of **4i** (400 MHz, $CDCl_3$)



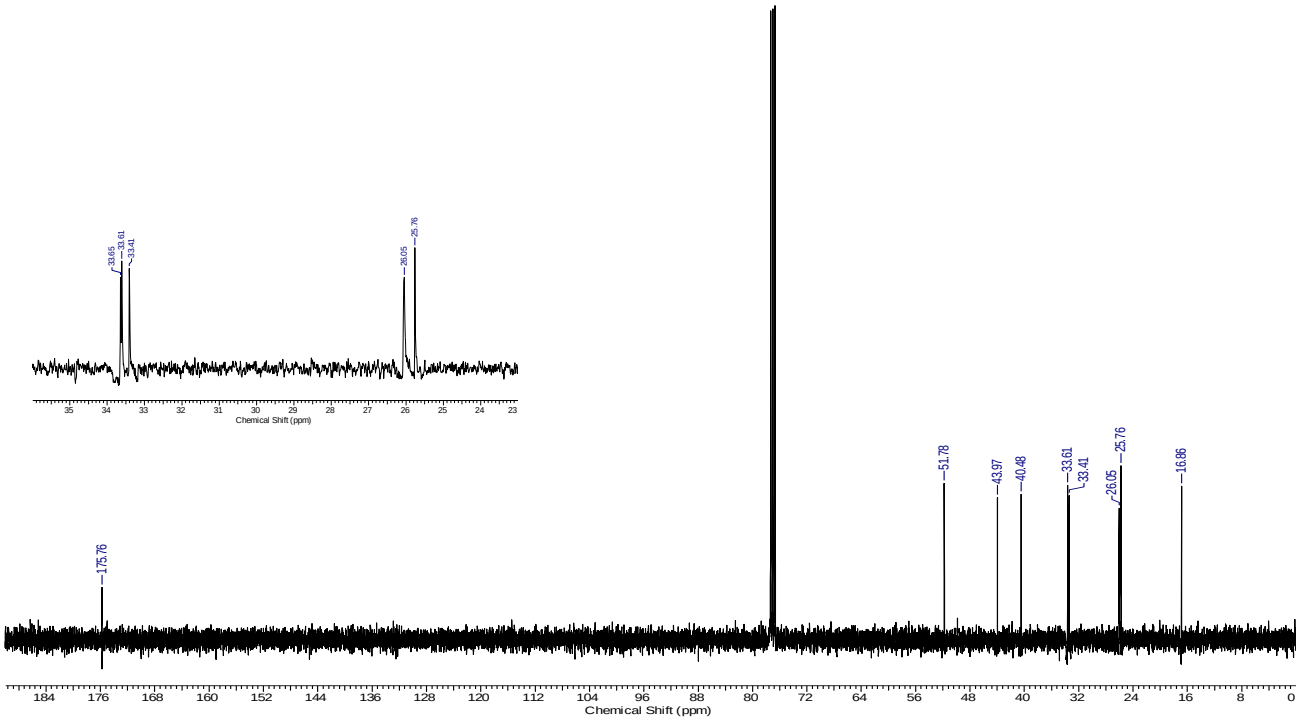
^{13}C NMR of **4i** (100 MHz, $CDCl_3$)



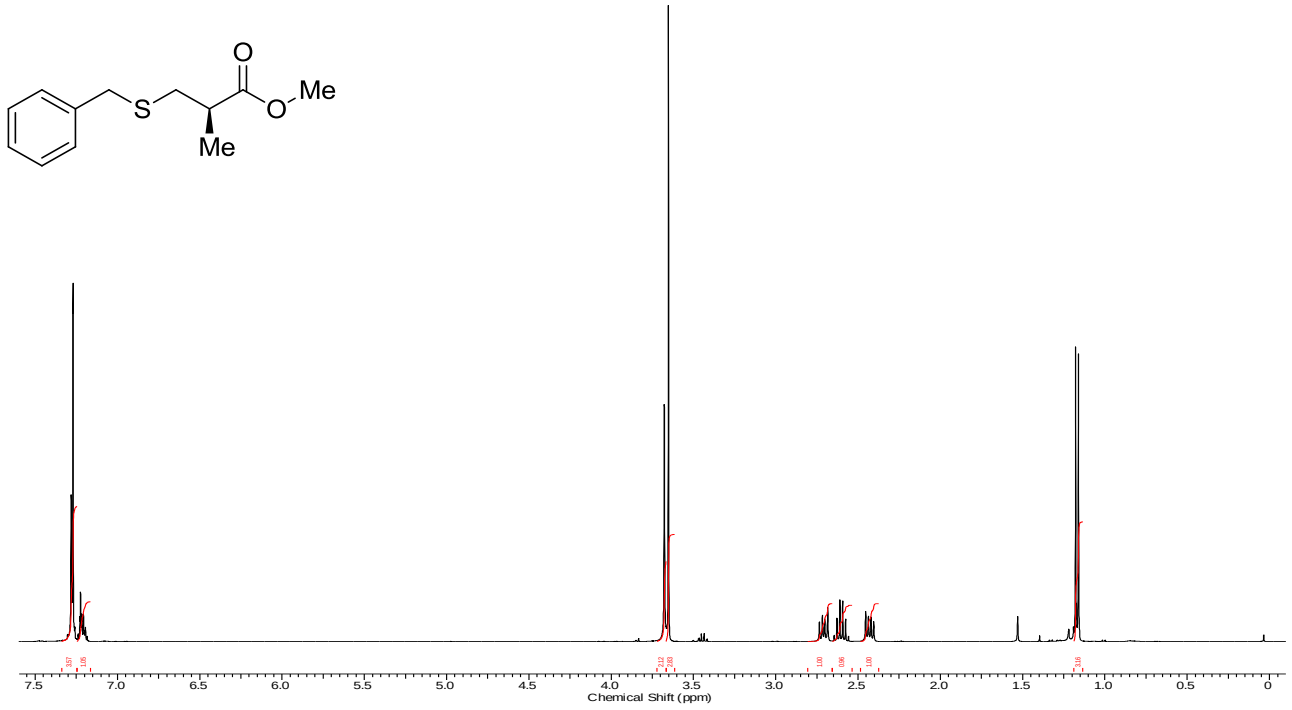
^{1}H NMR of **4j** (400 MHz, $CDCl_3$)



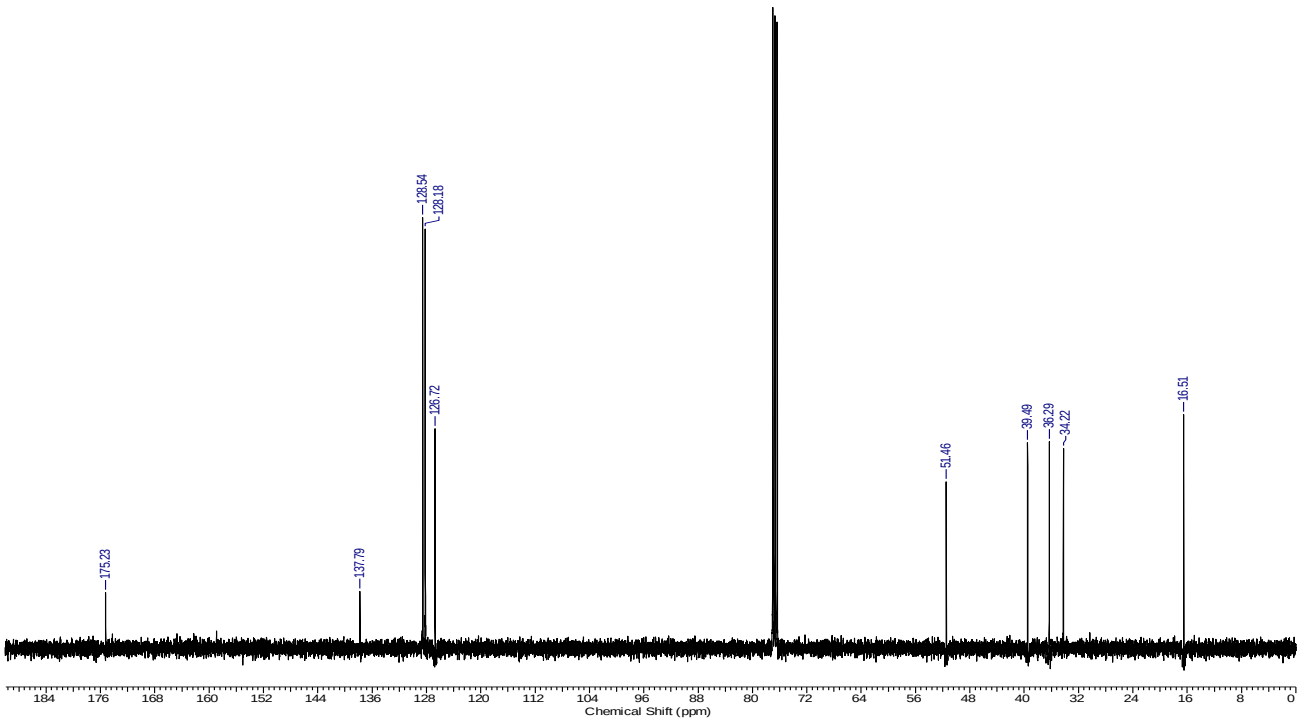
^{13}C NMR of **4j** (100 MHz, $CDCl_3$)



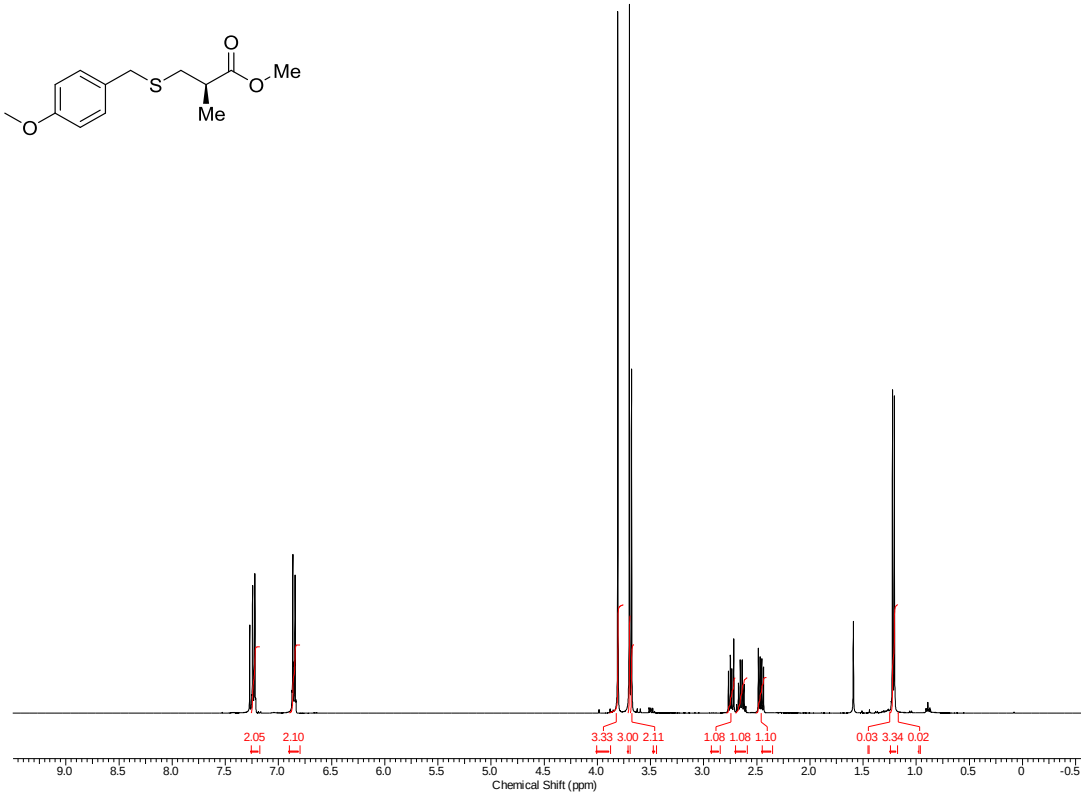
^{1}H NMR of **4k** (400 MHz, $CDCl_3$)



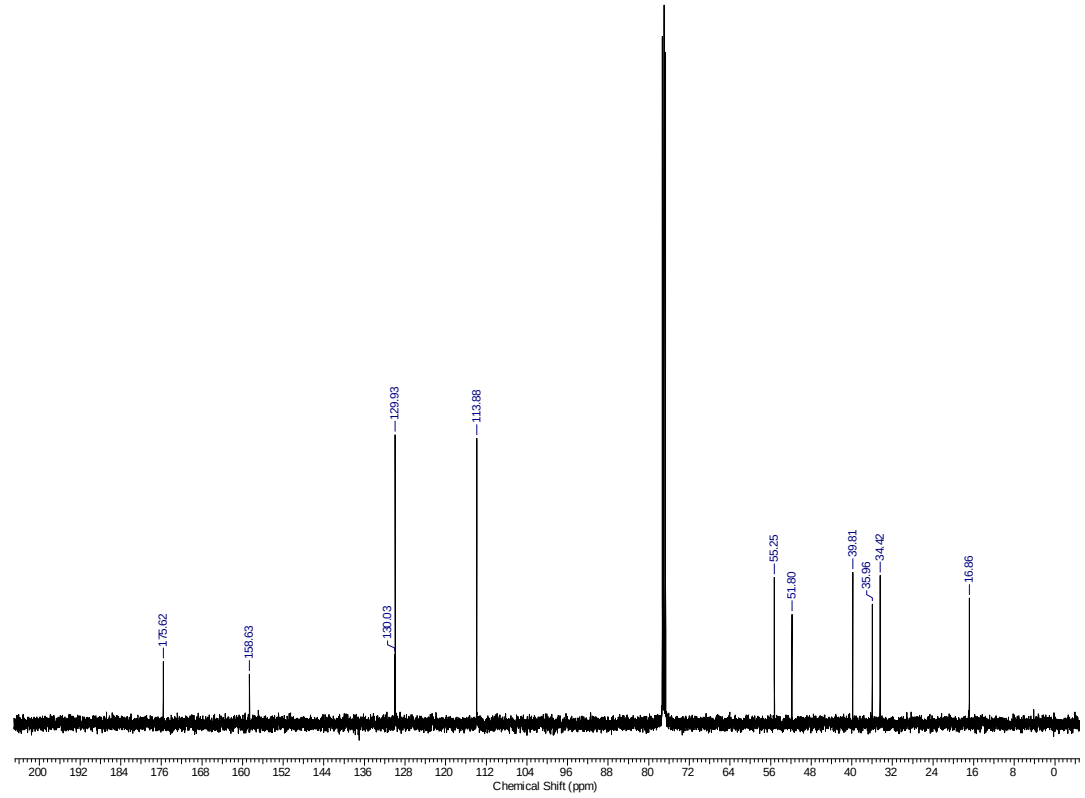
^{13}C NMR of **4k** (100 MHz, $CDCl_3$)



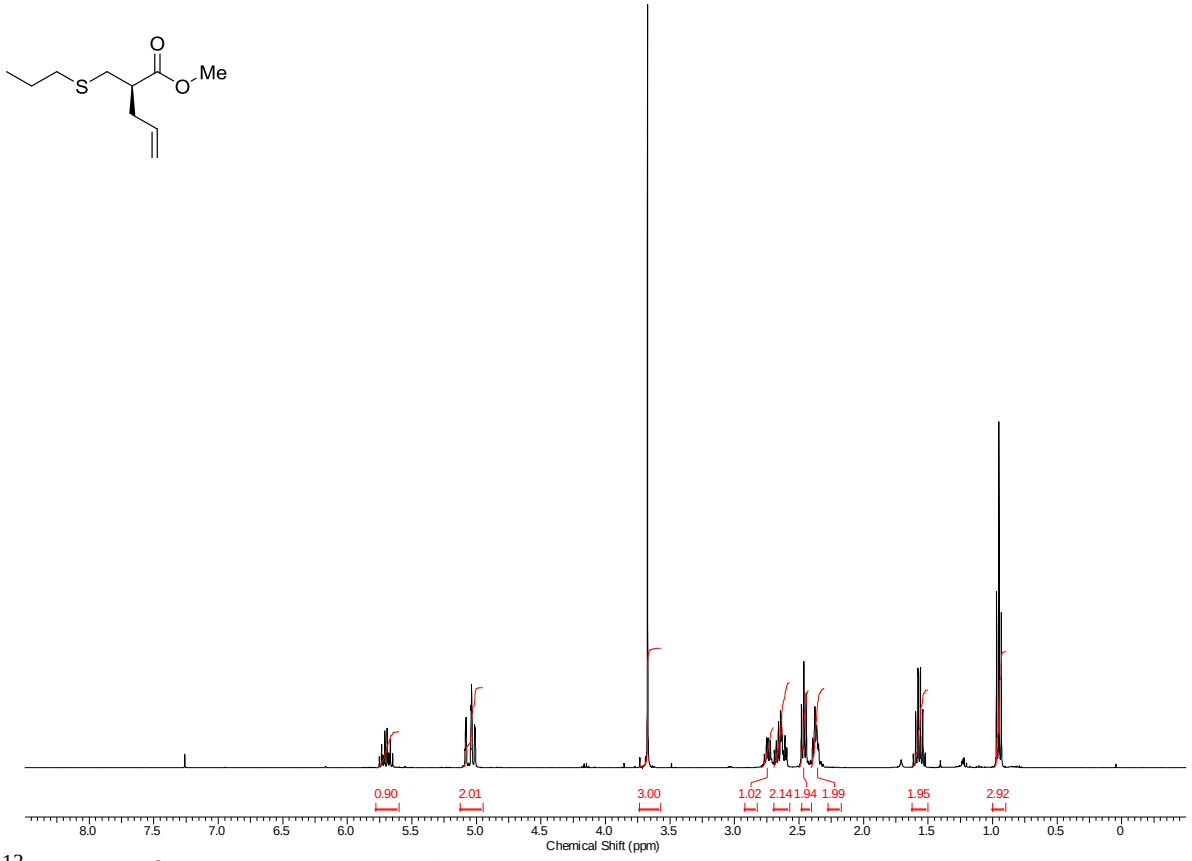
^{1}H NMR of **4l** (400 MHz, $CDCl_3$)



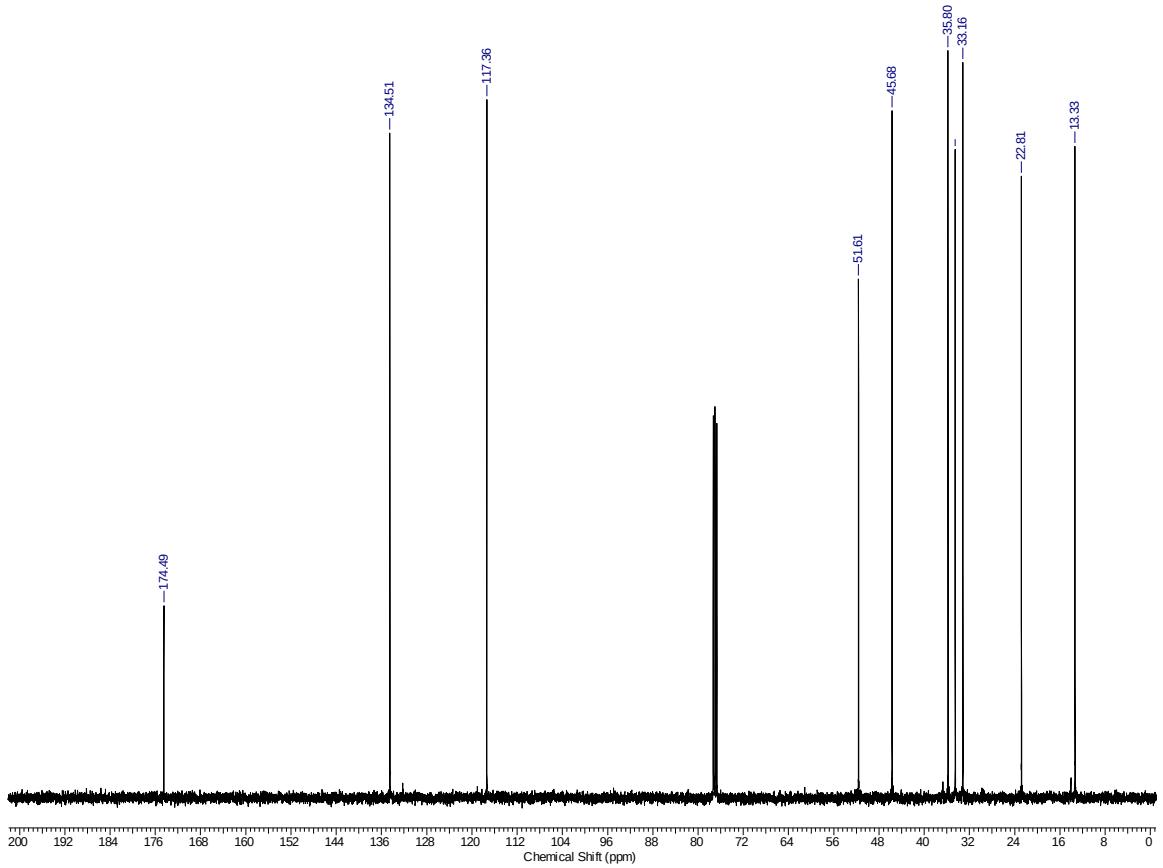
^{13}C NMR of **4l** (100 MHz, $CDCl_3$)



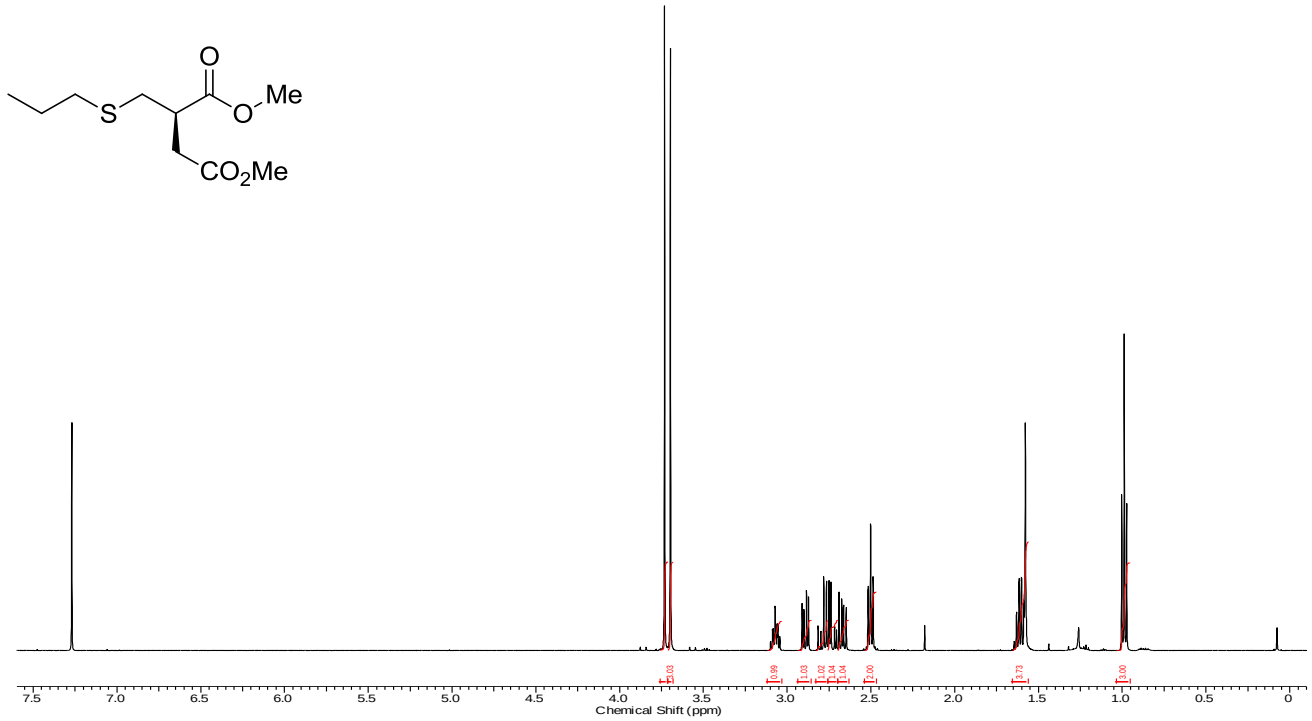
^{1}H NMR of **4m** (400 MHz, $CDCl_3$)



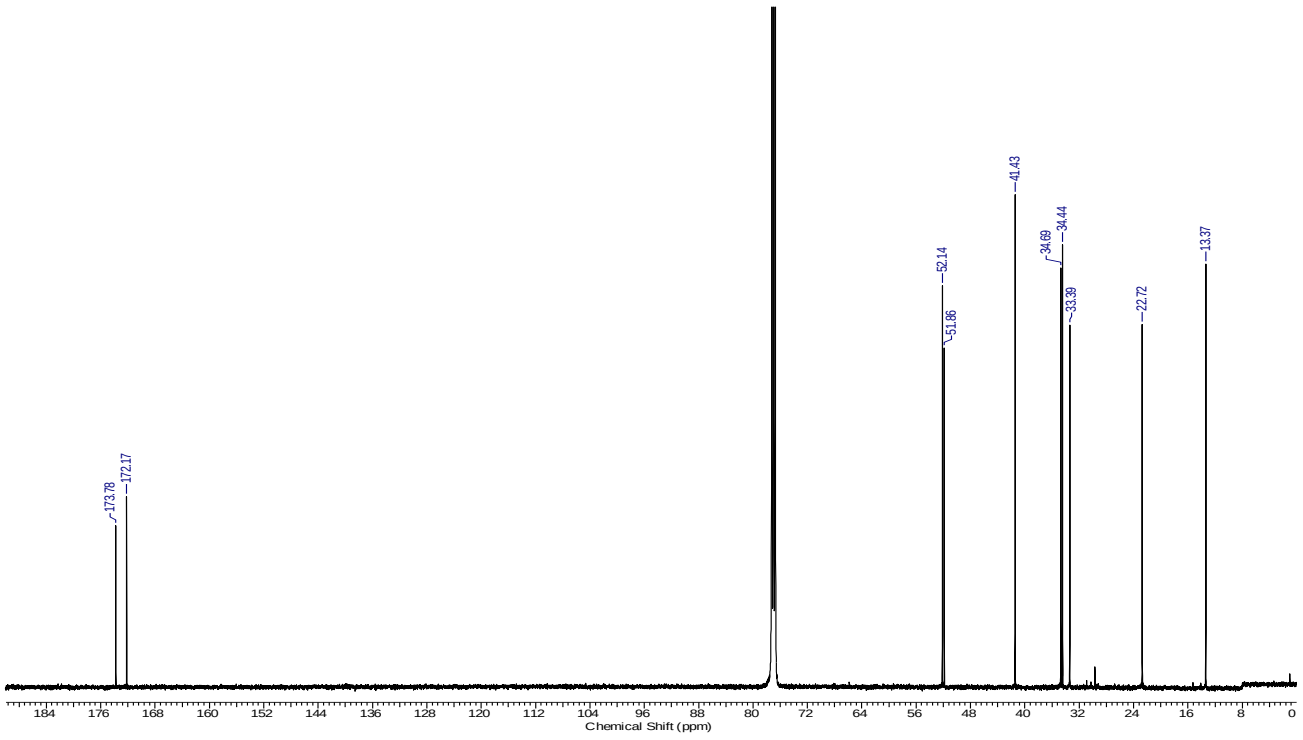
^{13}C NMR of **4m** (100 MHz, $CDCl_3$)



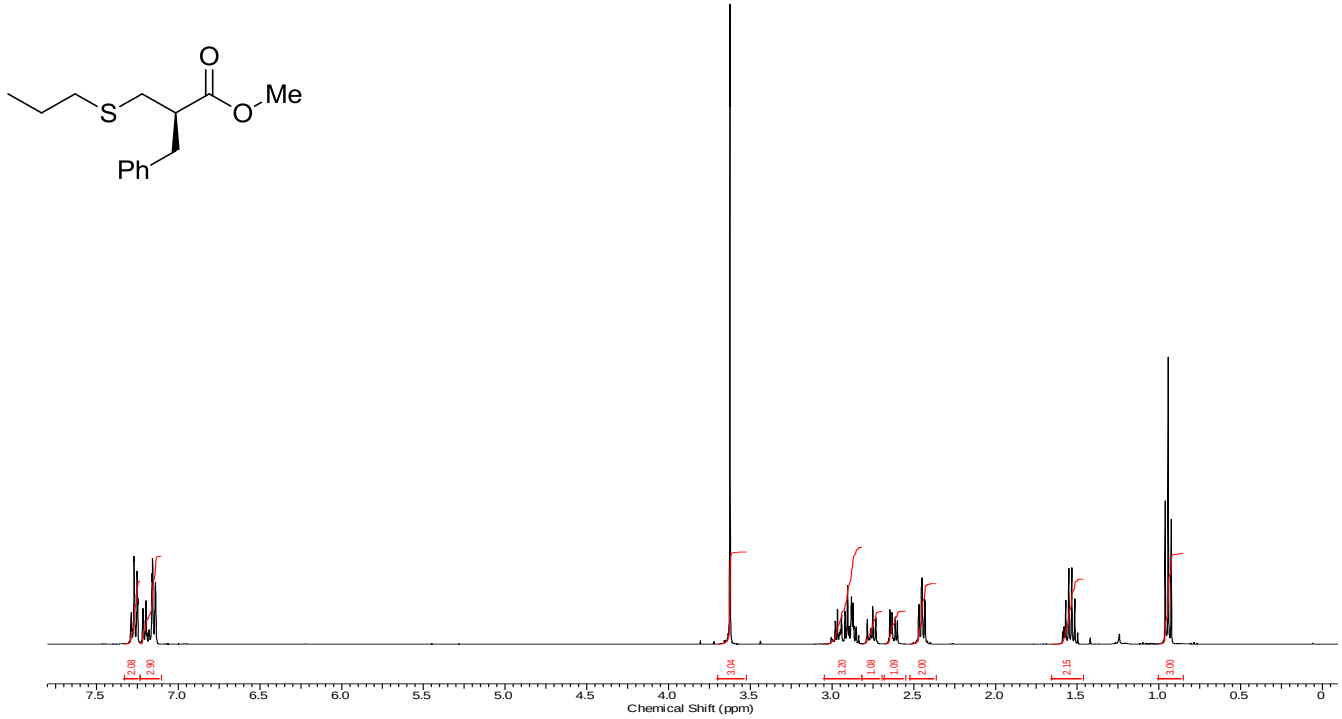
^{1}H NMR of **4n** (500 MHz, $CDCl_3$)



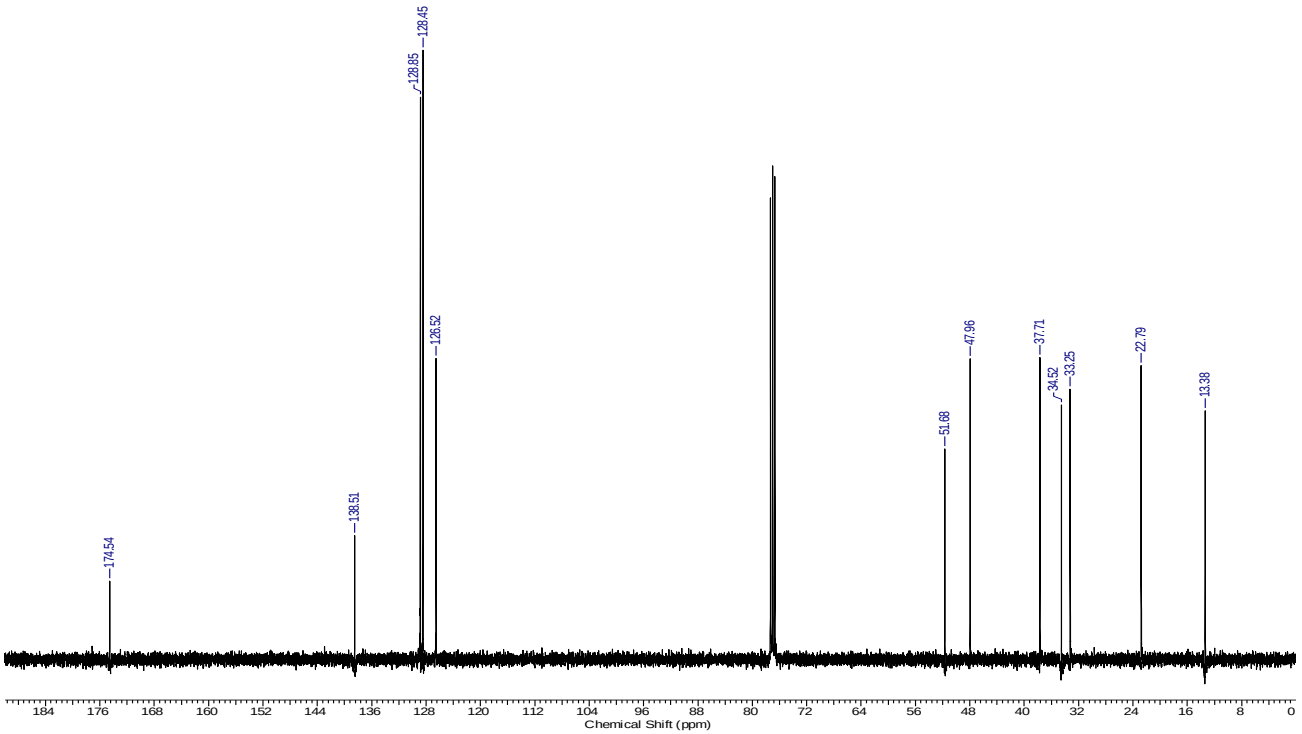
^{13}C NMR of **4n** (125 MHz, $CDCl_3$)



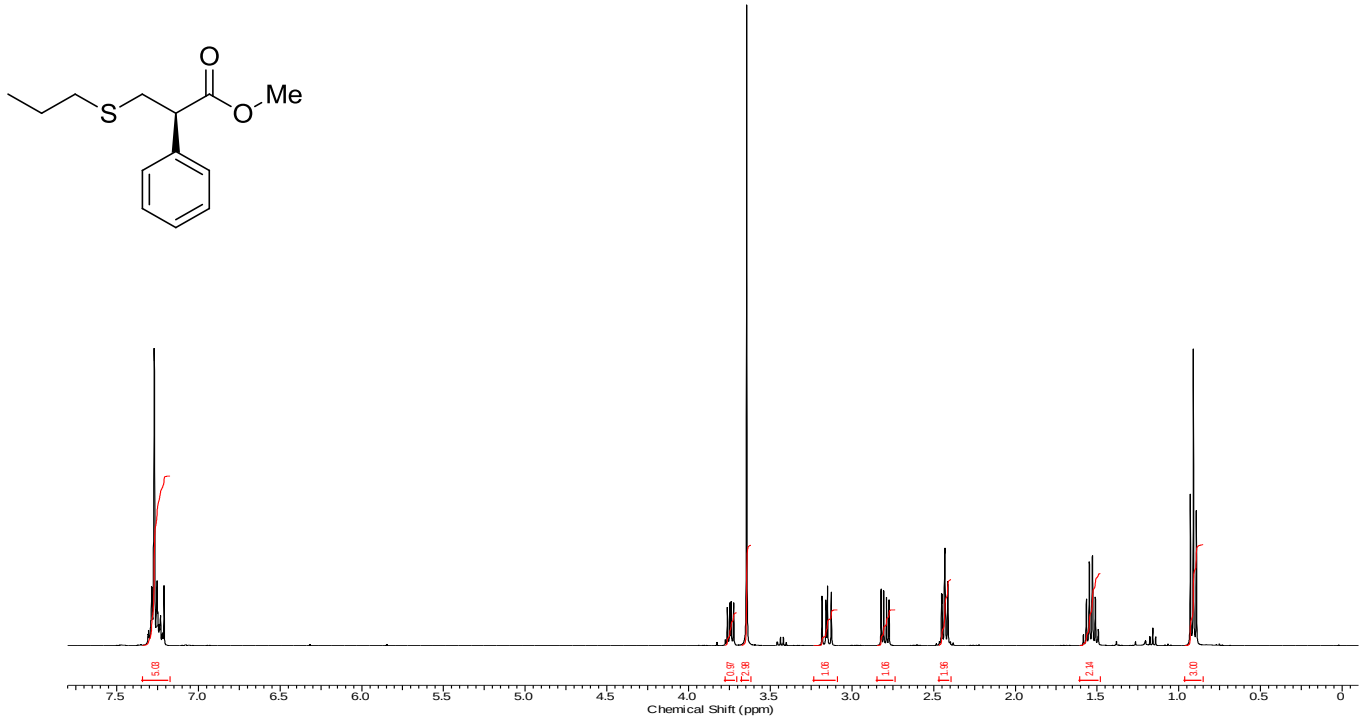
^{1}H NMR of **4o** (400 MHz, $CDCl_3$)



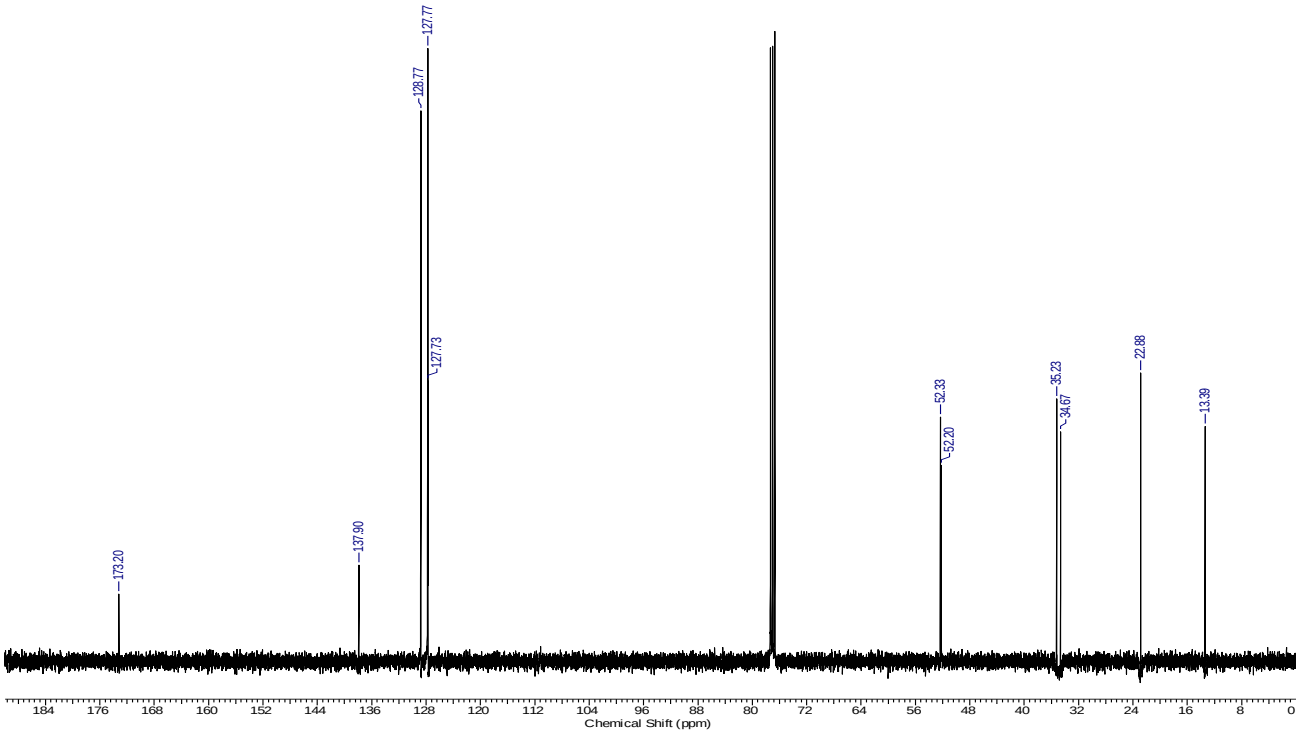
^{13}C NMR of **4o** (100 MHz, $CDCl_3$)



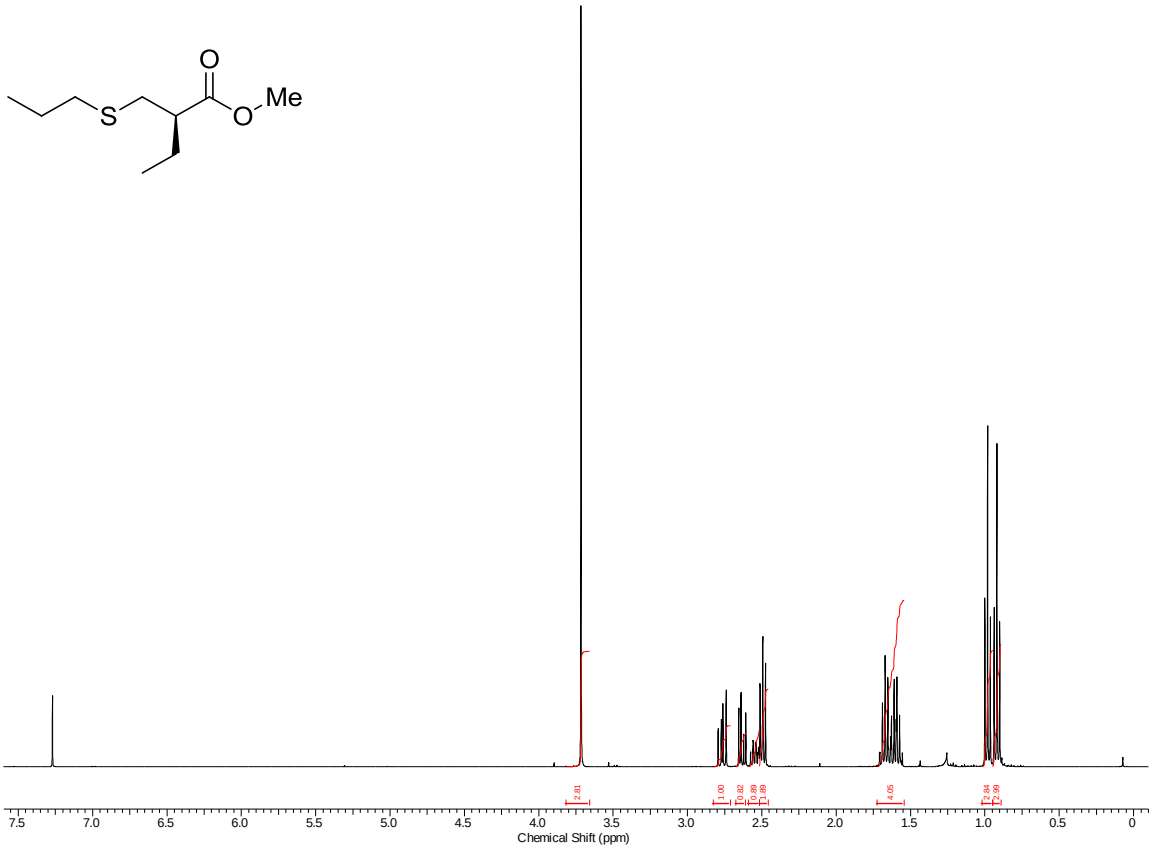
^{1}H NMR of **4p** (400 MHz, $CDCl_3$)



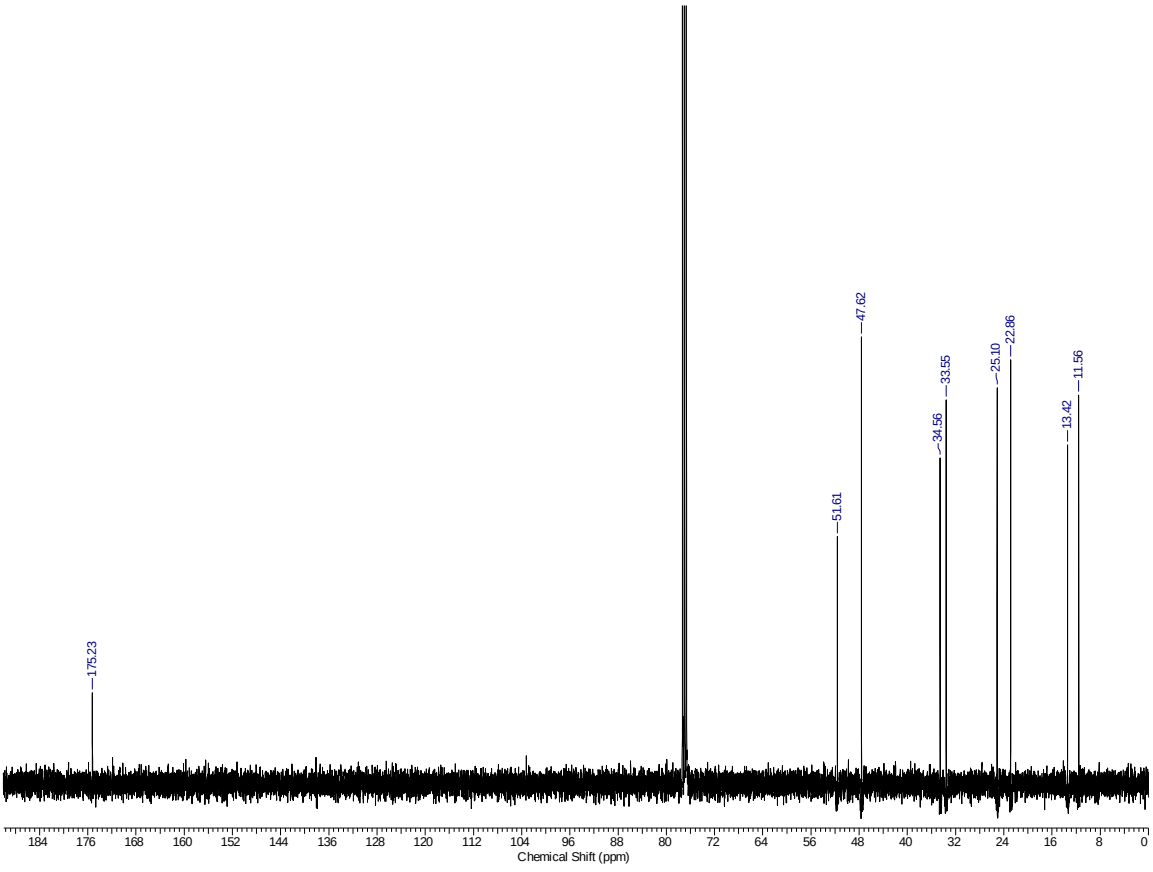
^{13}C NMR of **4p** (100 MHz, $CDCl_3$)



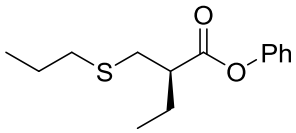
^{1}H NMR of **4q** (400 MHz, $CDCl_3$)



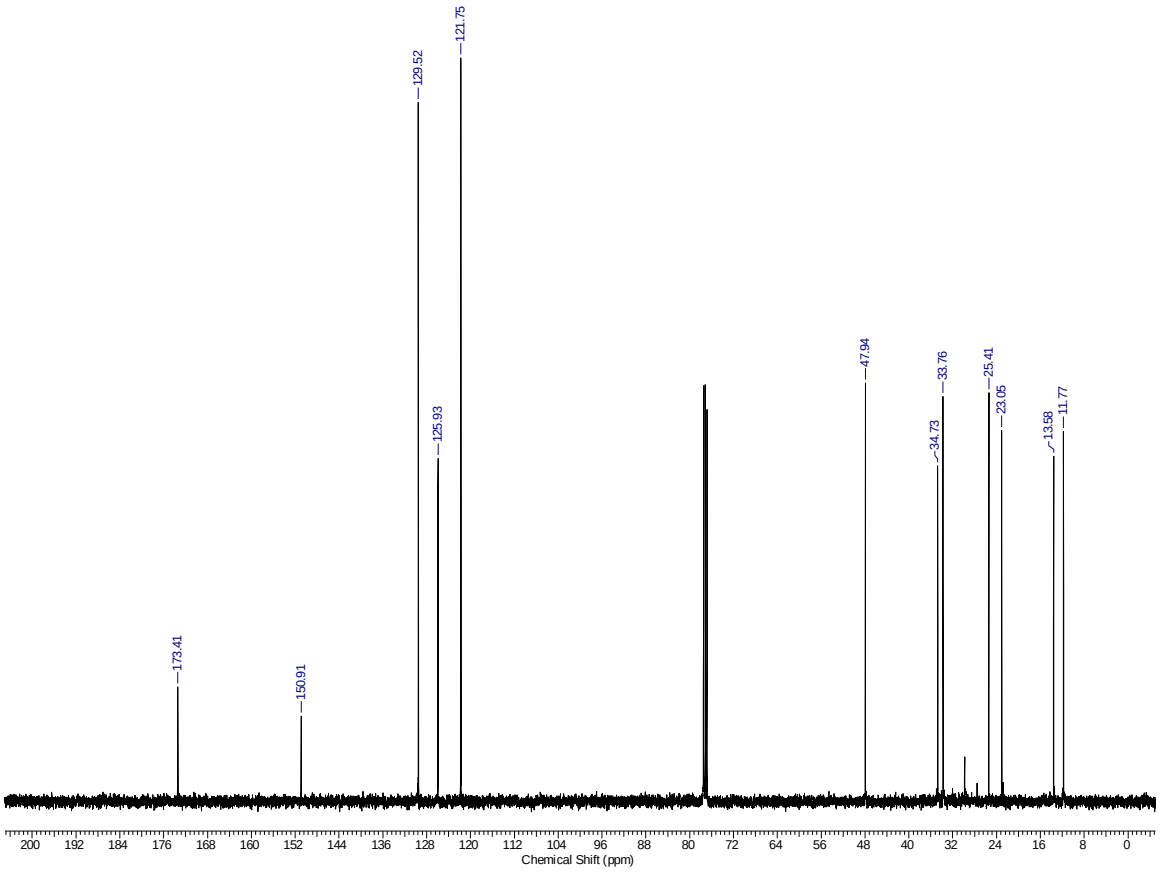
^{13}C NMR of **4q** (100 MHz, $CDCl_3$)



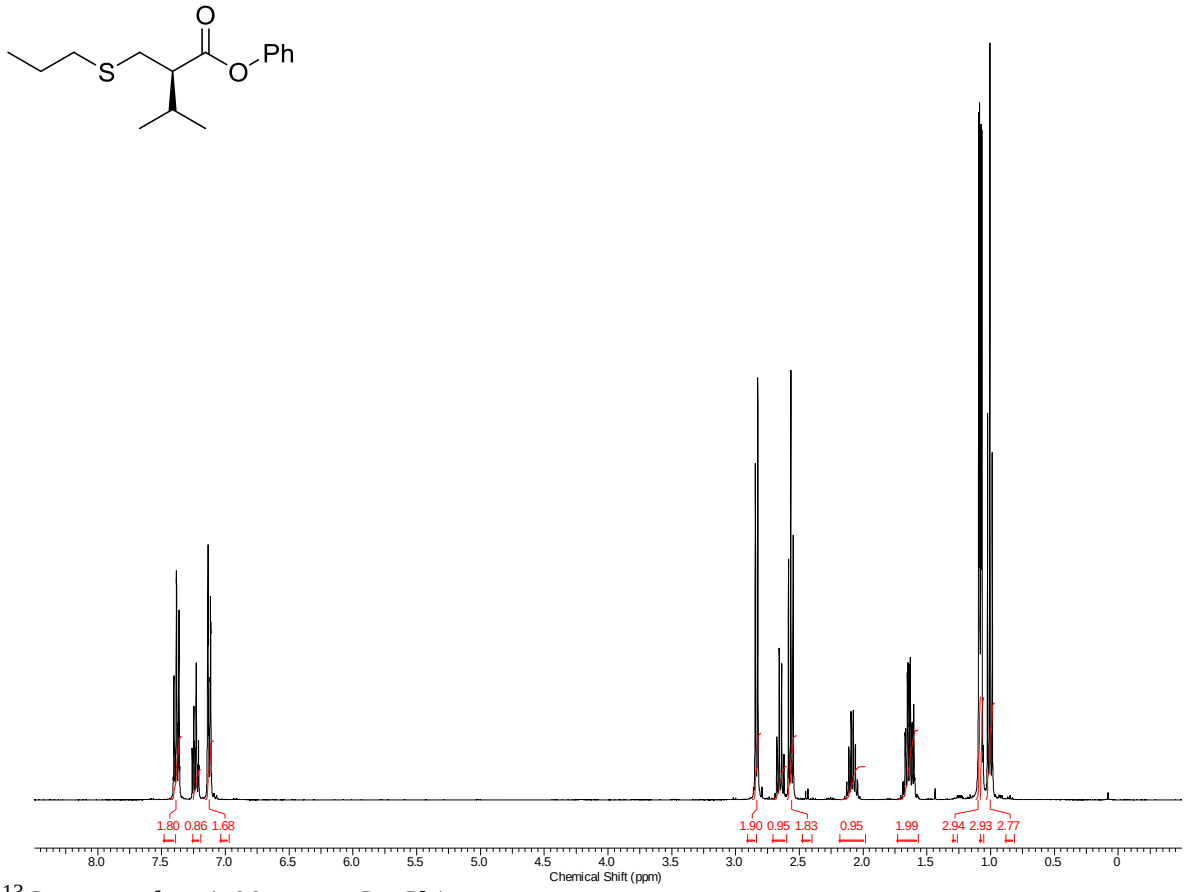
^{1}H NMR of **4r** (400 MHz, $CDCl_3$)



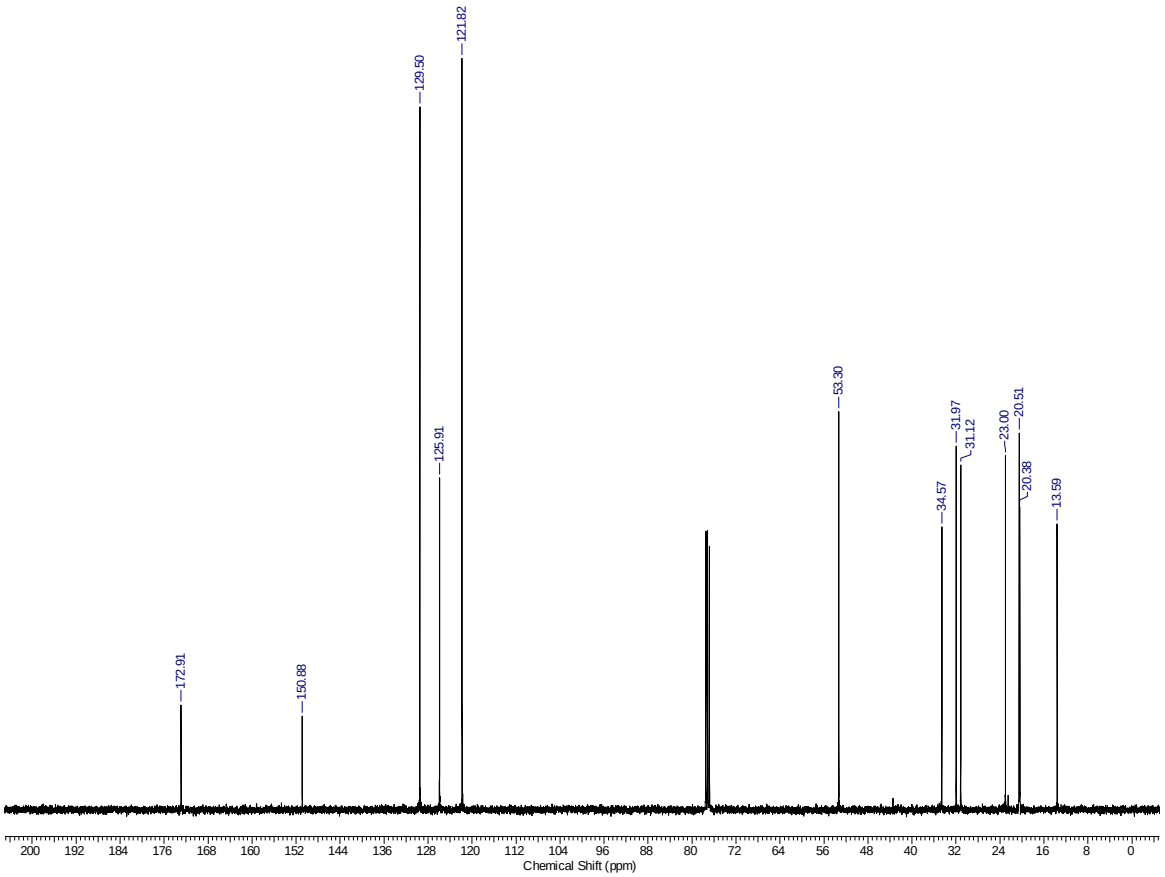
^{13}C NMR of **4r** (100 MHz, $CDCl_3$)



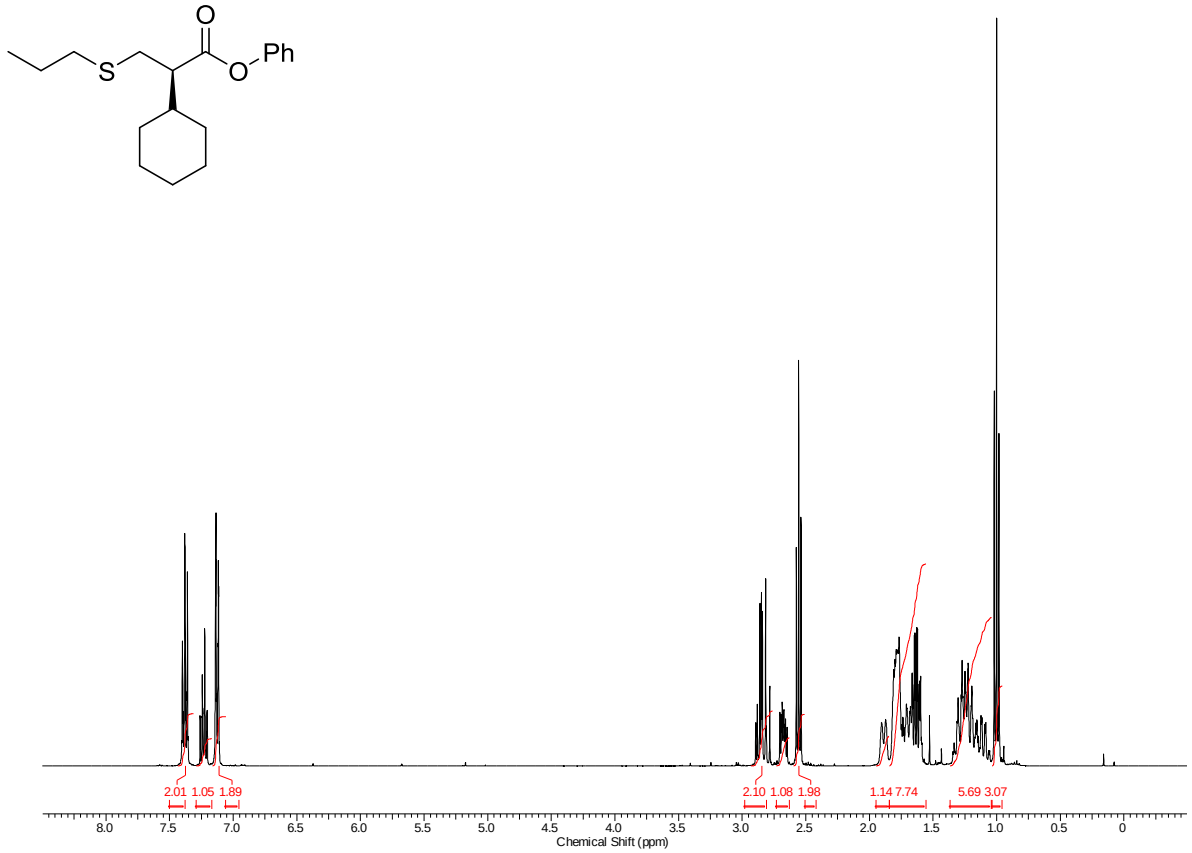
^{1}H NMR of **4s** (400 MHz, $CDCl_3$)



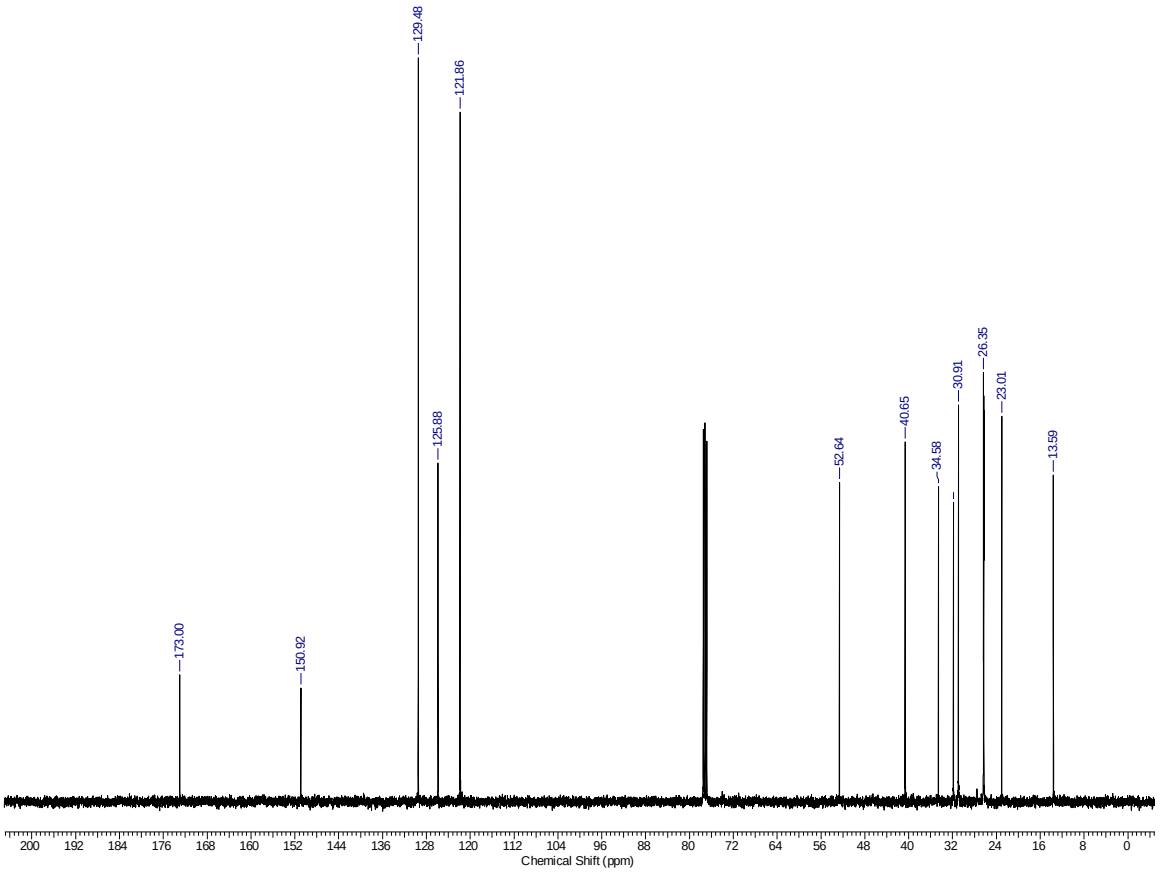
^{13}C NMR of **4s** (100 MHz, $CDCl_3$)



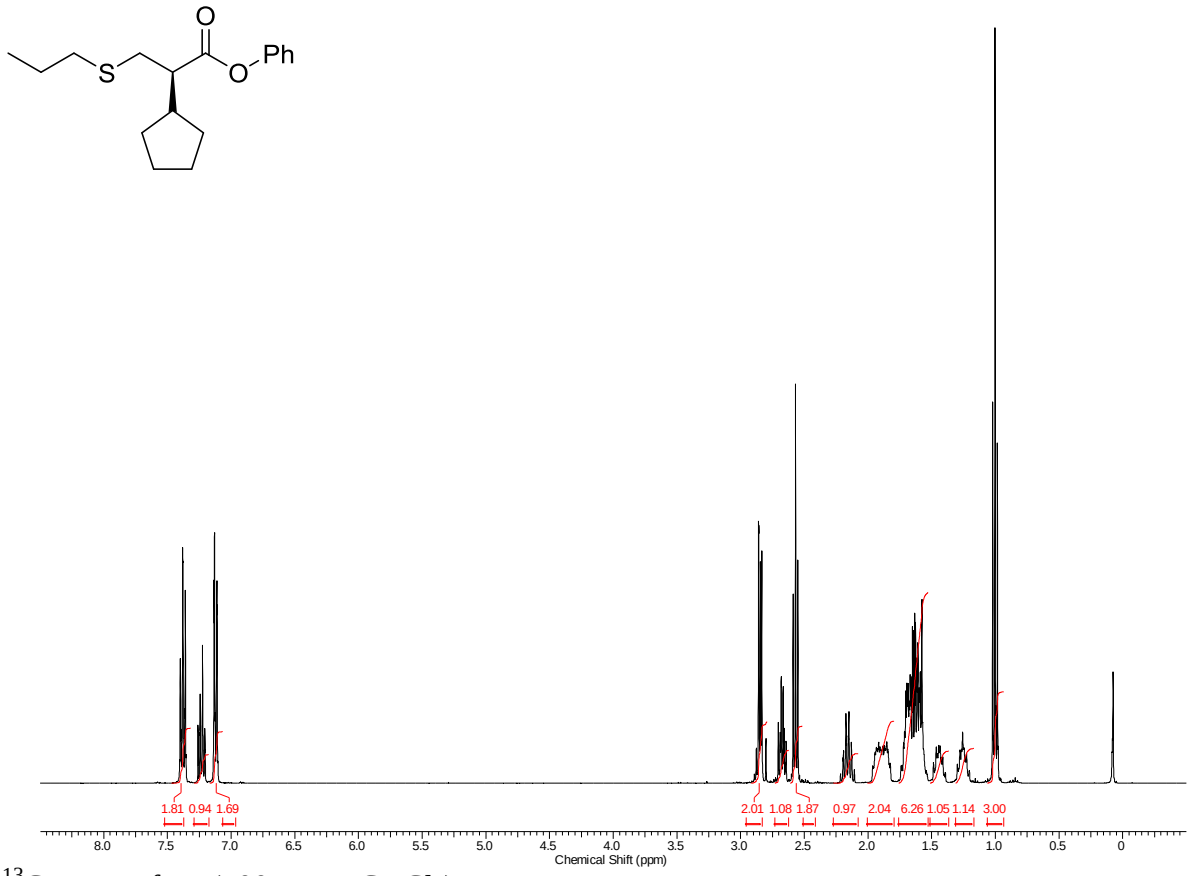
^{1}H NMR of **4t** (400 MHz, $CDCl_3$)



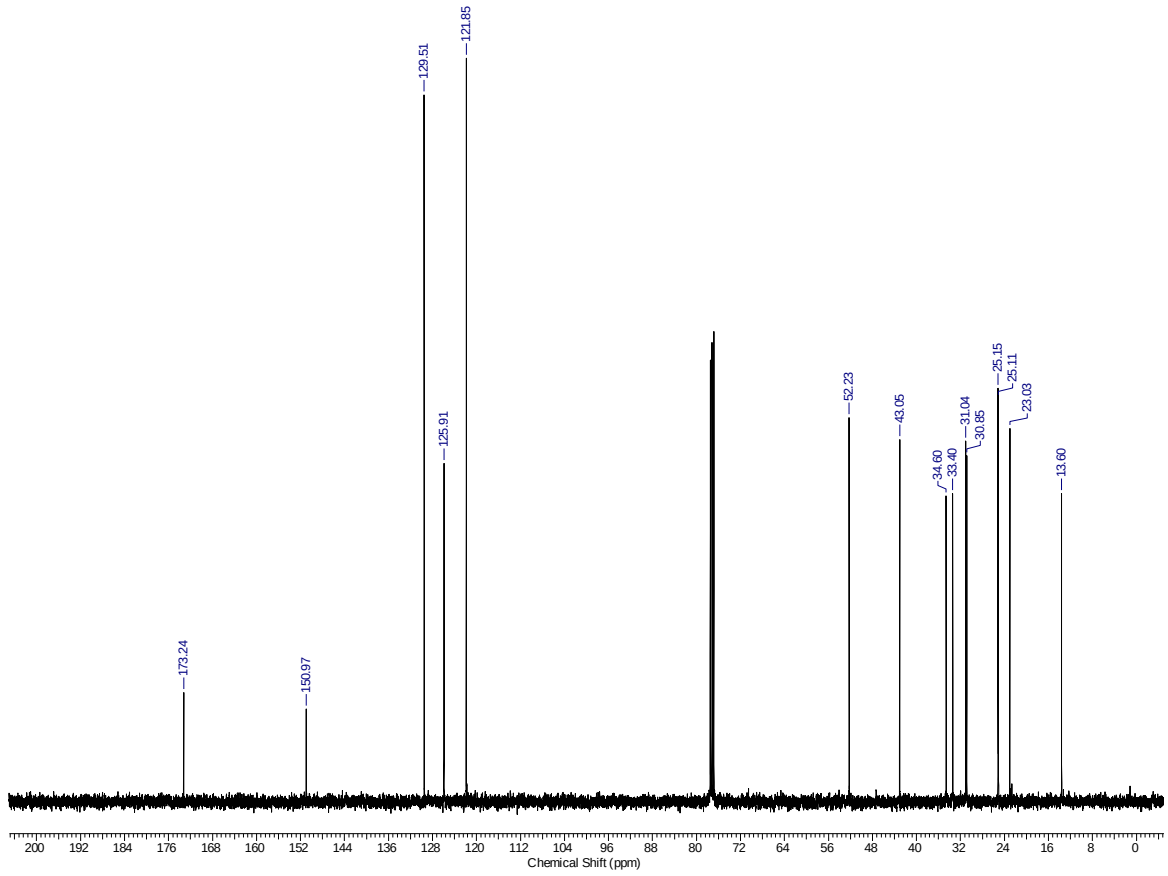
^{13}C NMR of **4t** (100 MHz, $CDCl_3$)



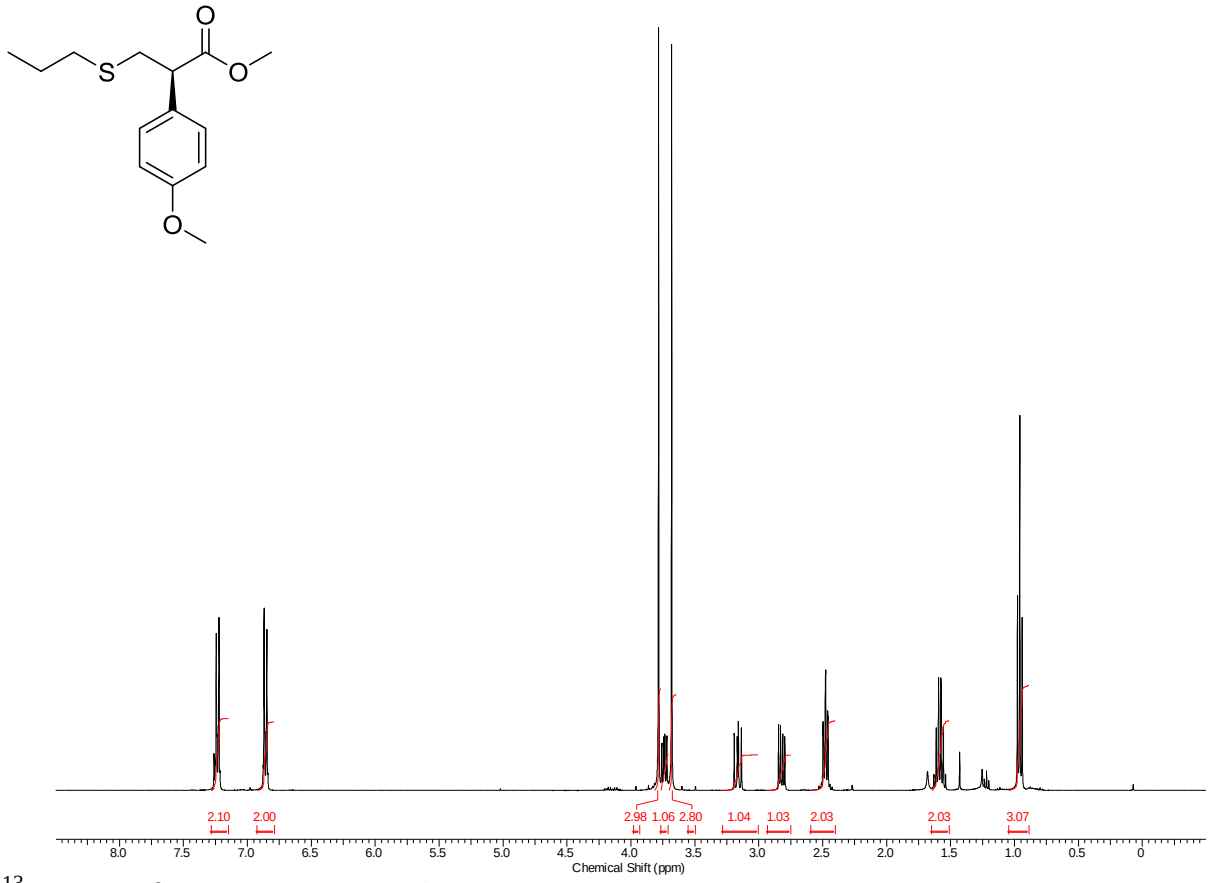
^{1}H NMR of **4u** (400 MHz, $CDCl_3$)



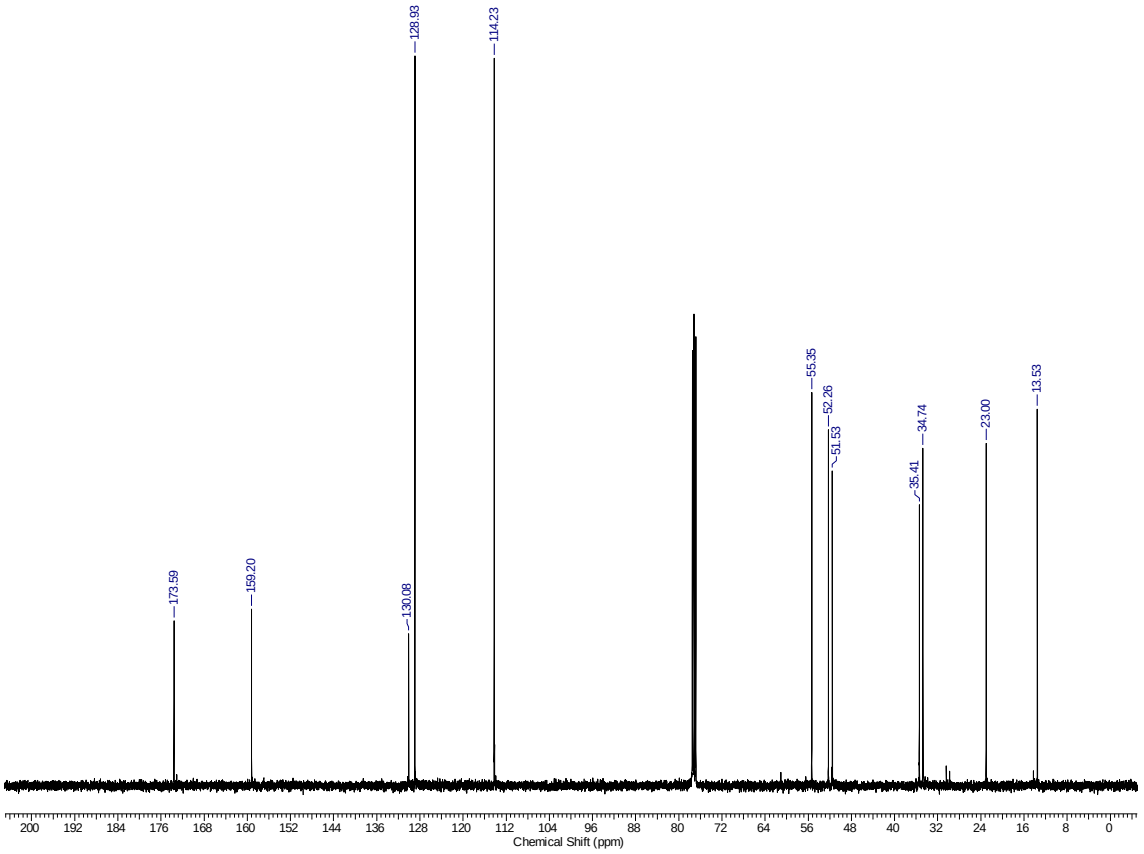
^{13}C NMR of **4u** (100 MHz, $CDCl_3$)



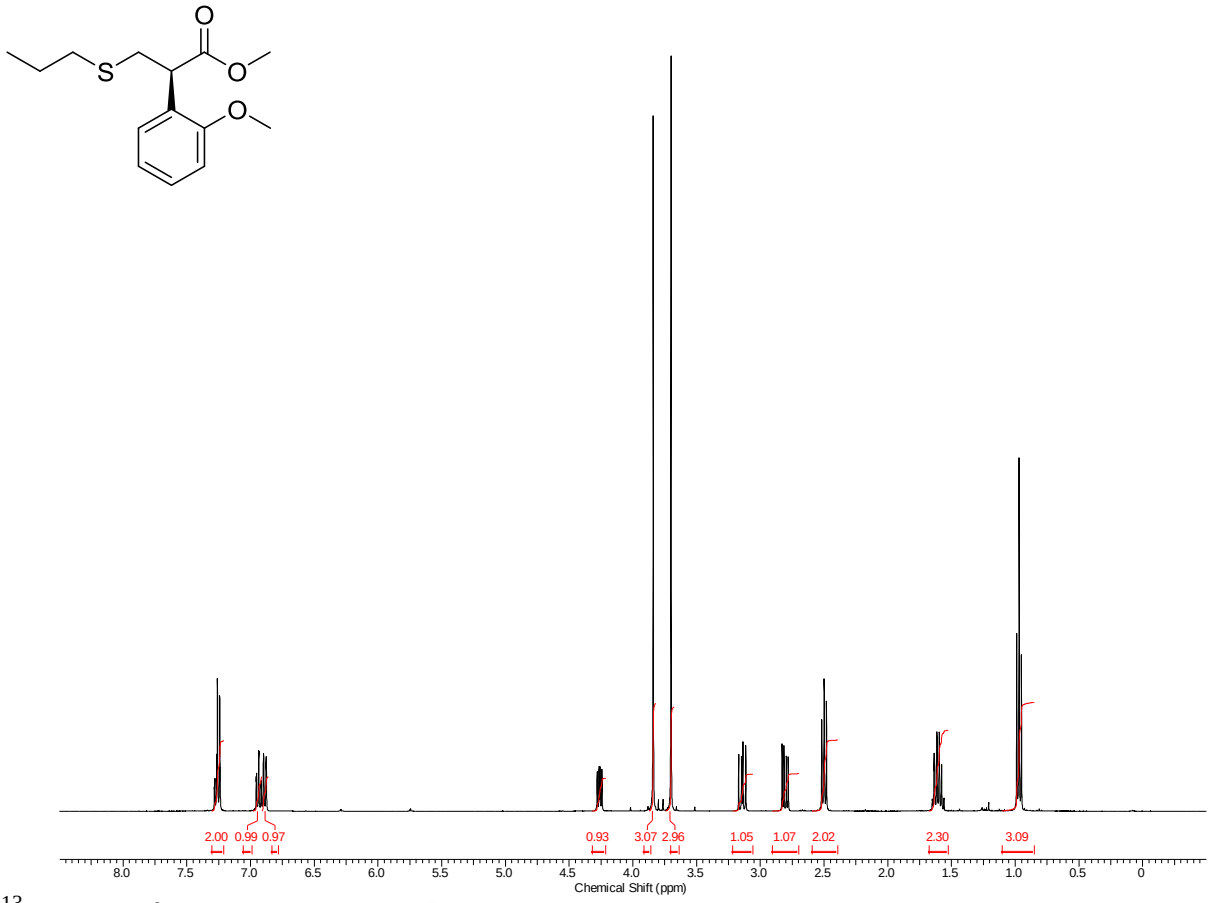
^{1}H NMR of **4v** (400 MHz, $CDCl_3$)



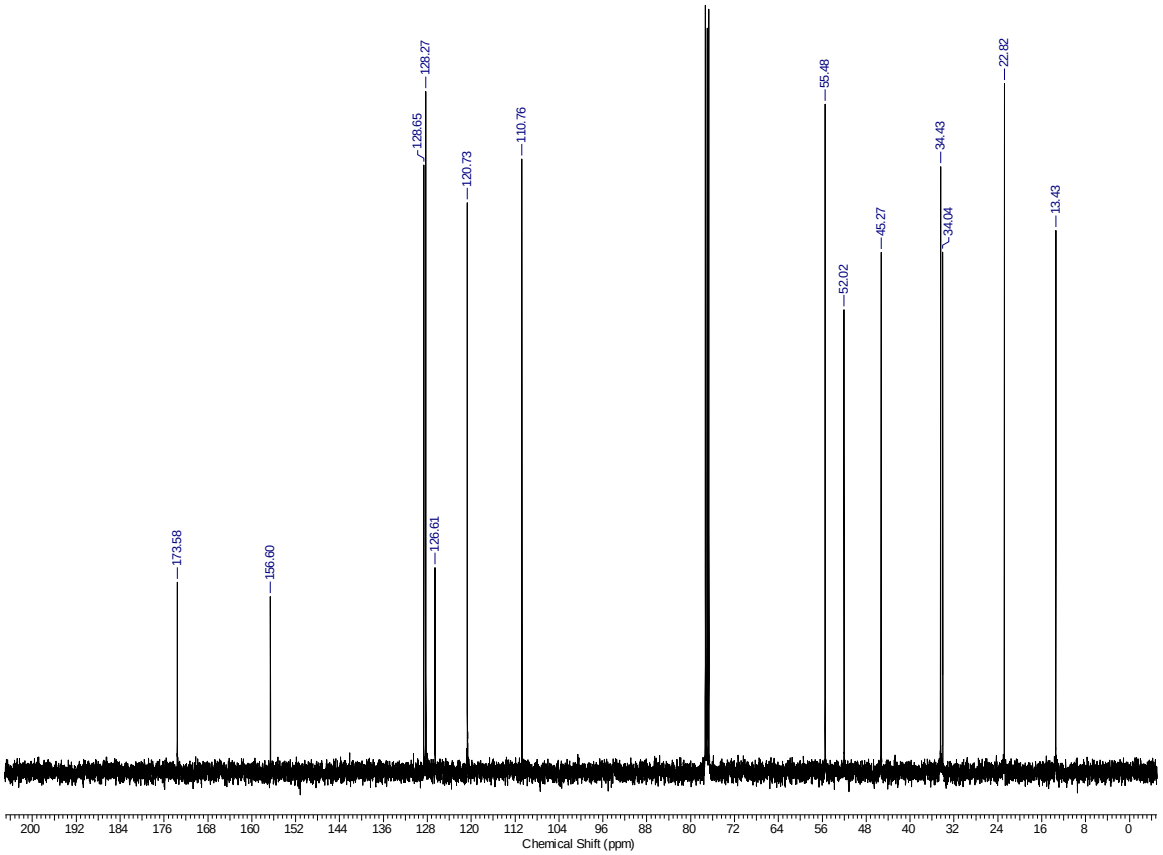
^{13}C NMR of **4v** (100 MHz, $CDCl_3$)



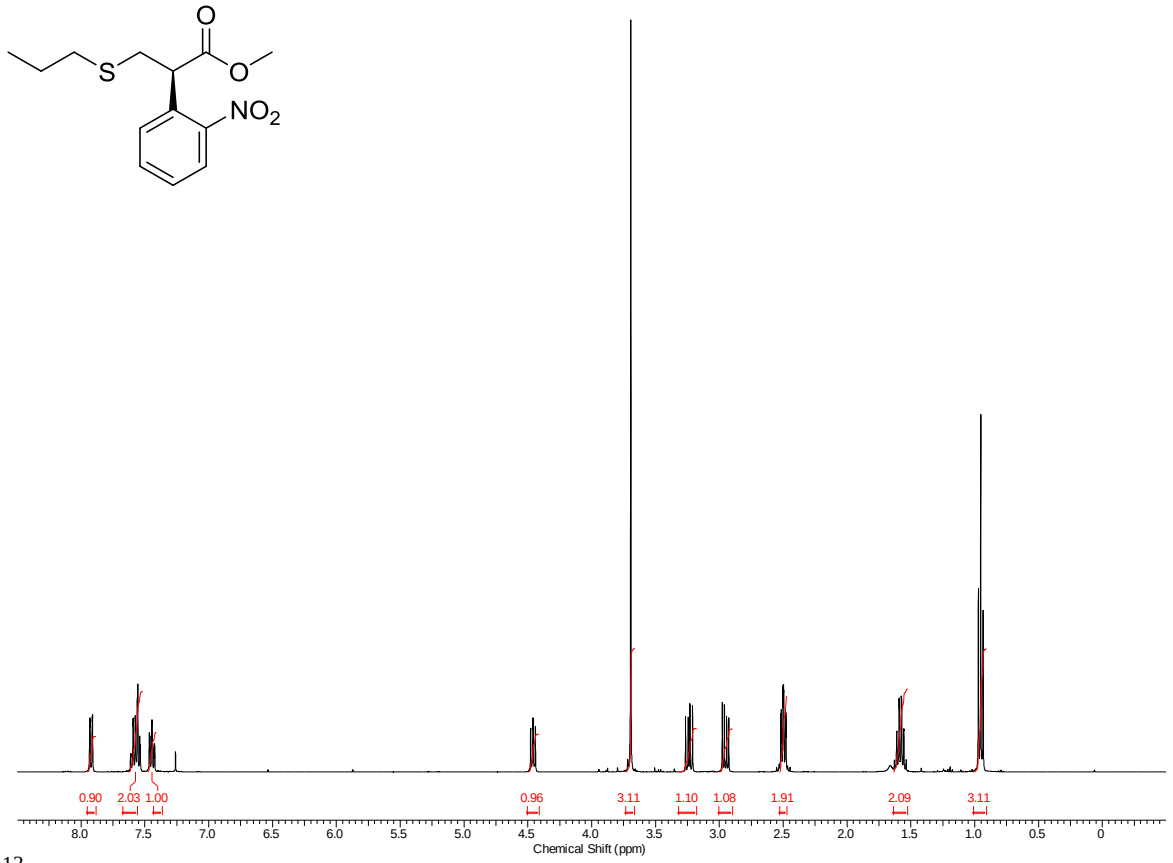
^{1}H NMR of **4w** (400 MHz, $CDCl_3$)



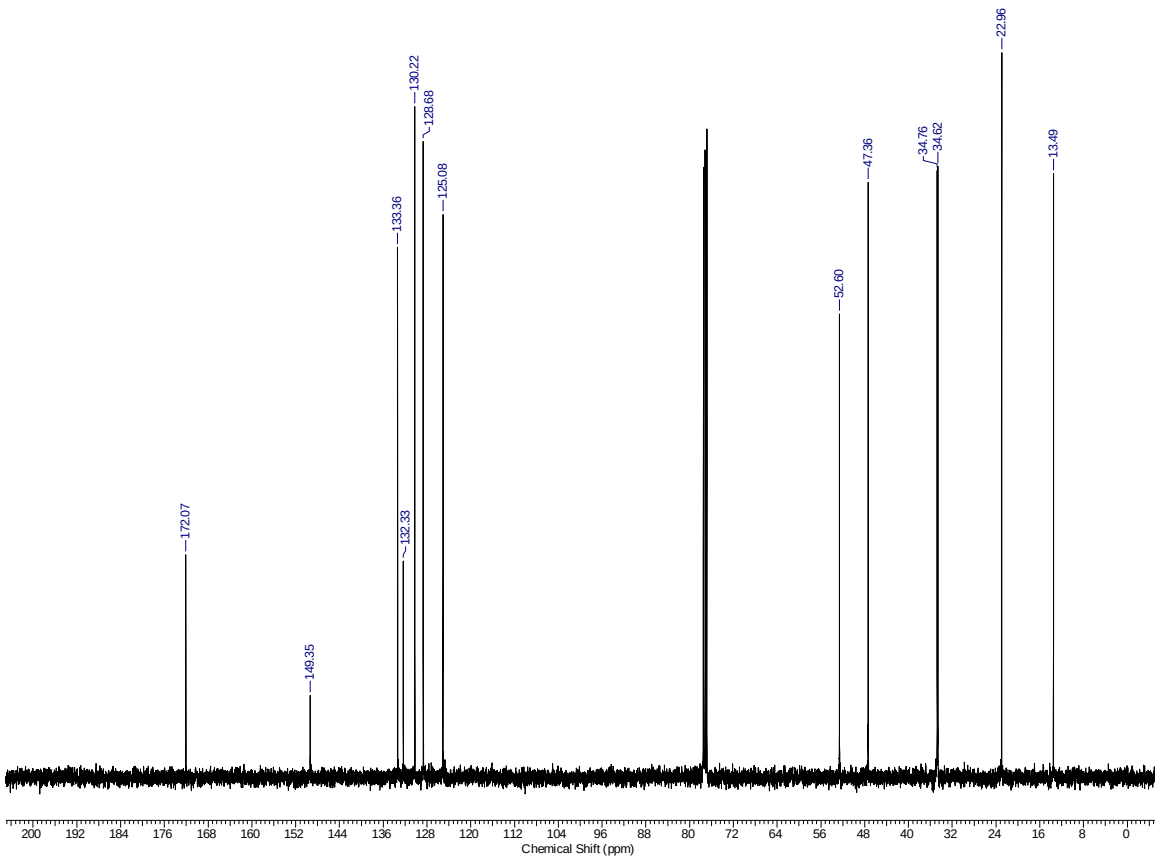
^{13}C NMR of **4w** (100 MHz, $CDCl_3$)



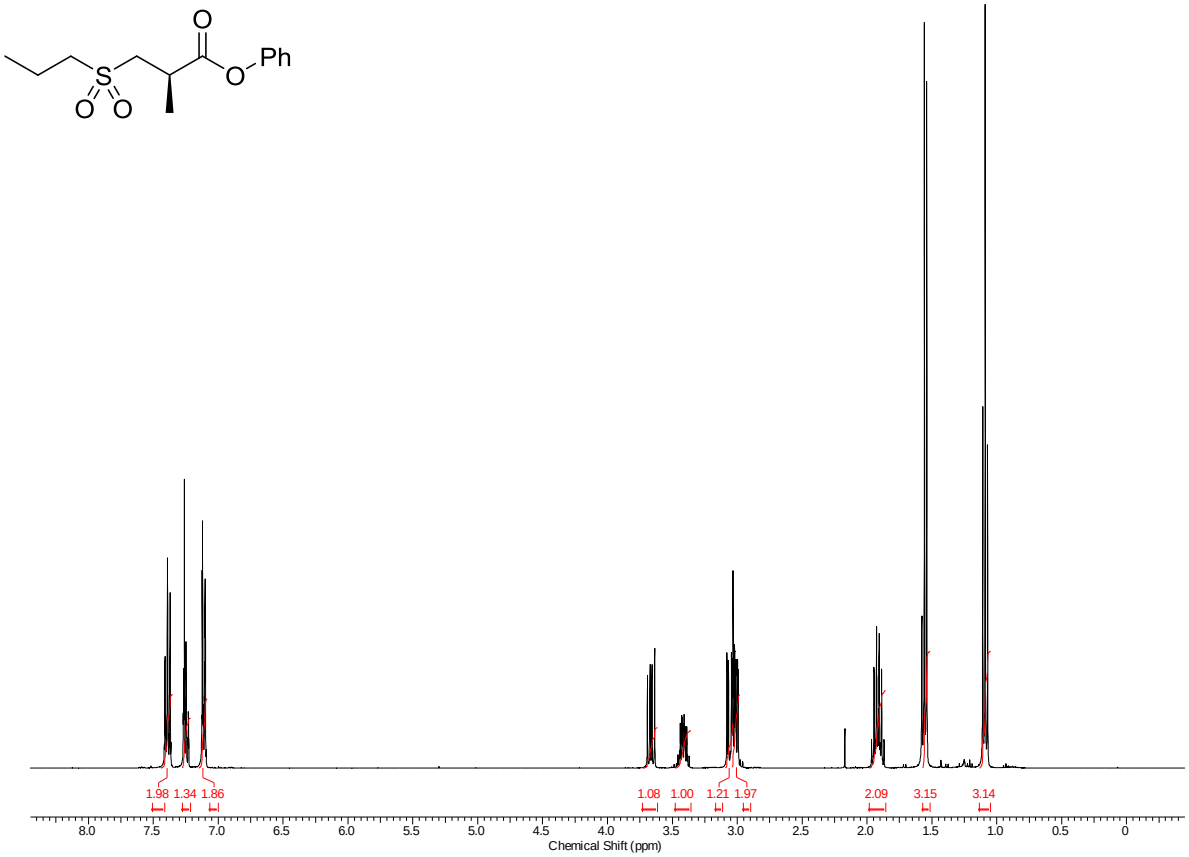
^{1}H NMR of **4x** (400 MHz, $CDCl_3$)



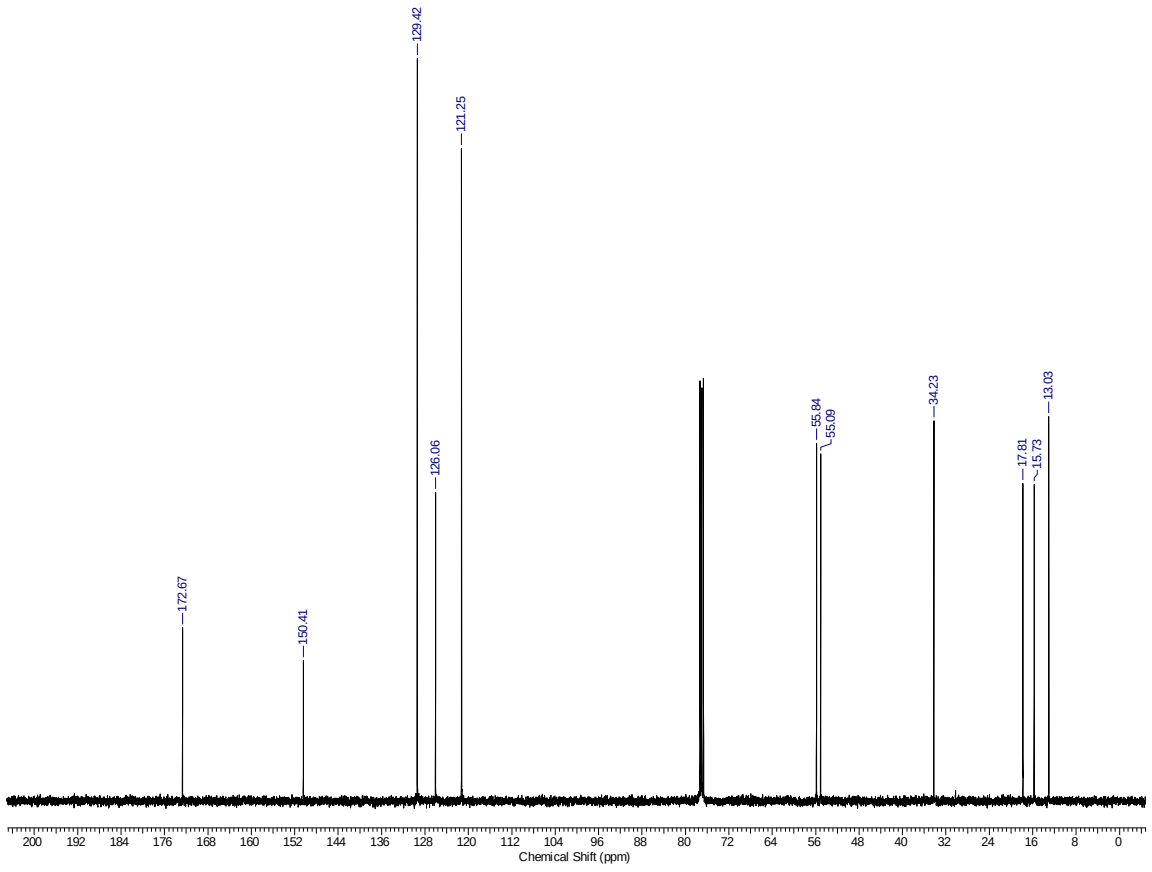
^{13}C NMR of **4x** (100 MHz, $CDCl_3$)



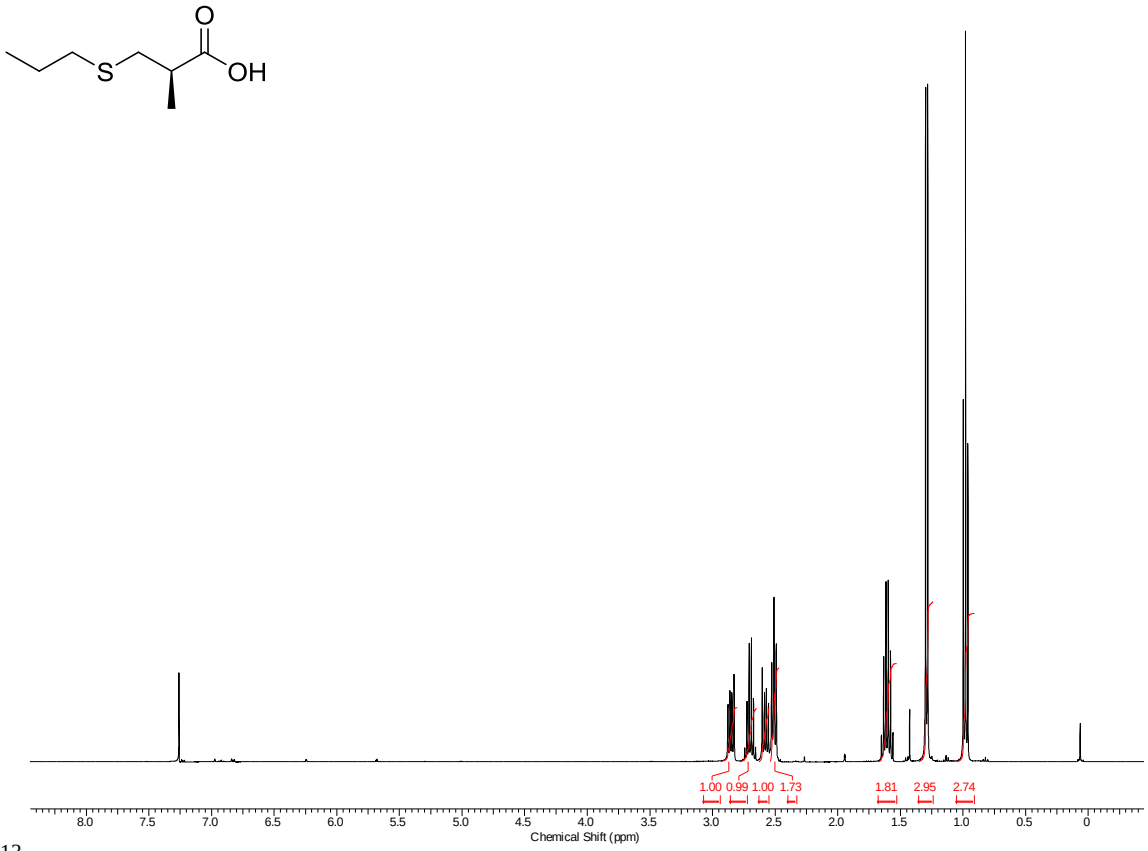
^{1}H NMR of **5a** (400 MHz, $CDCl_3$)



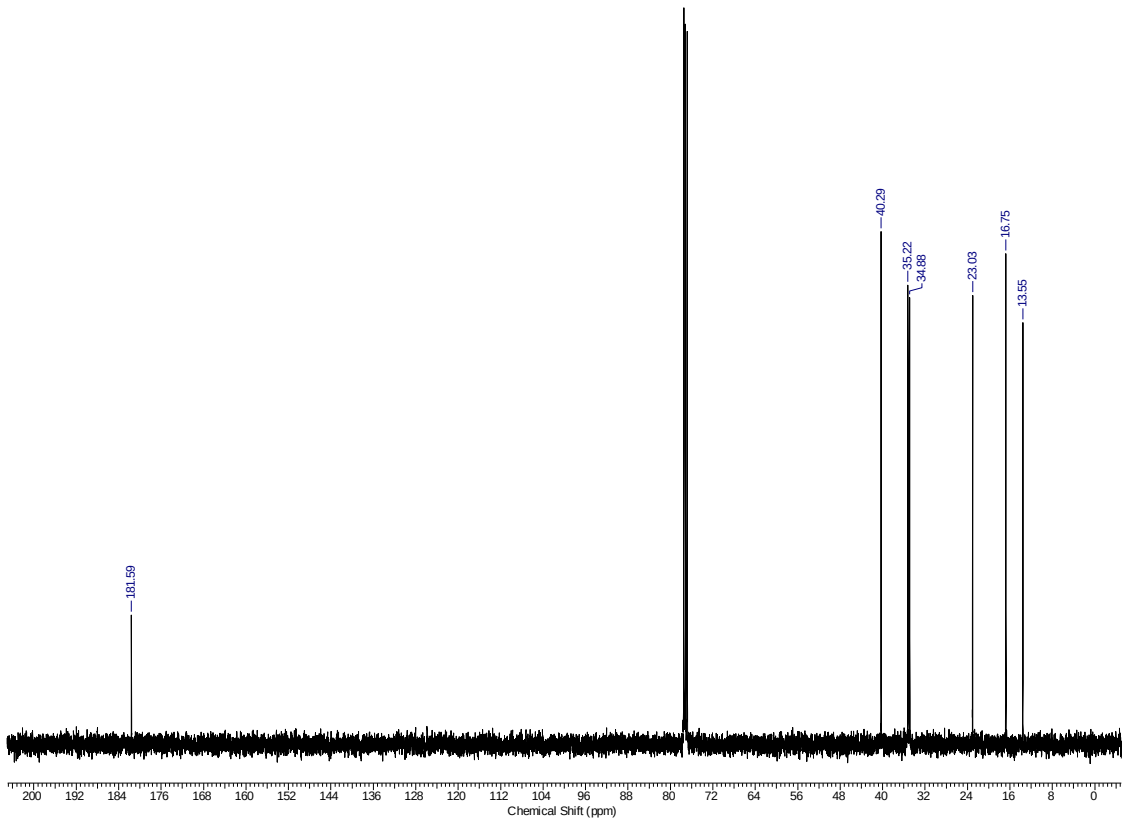
^{13}C NMR of **5a** (100 MHz, $CDCl_3$)



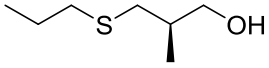
^{1}H NMR of **5b** (400 MHz, $CDCl_3$)



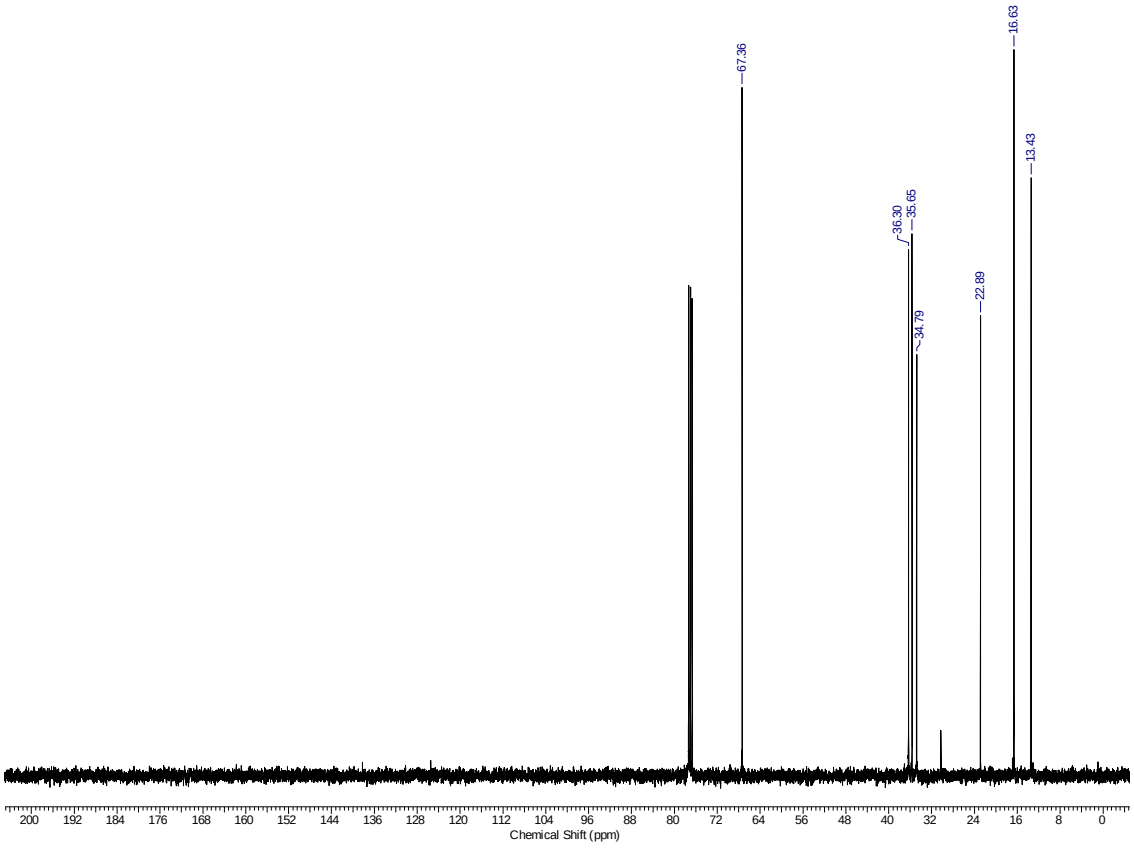
^{13}C NMR of **5b** (100 MHz, $CDCl_3$)



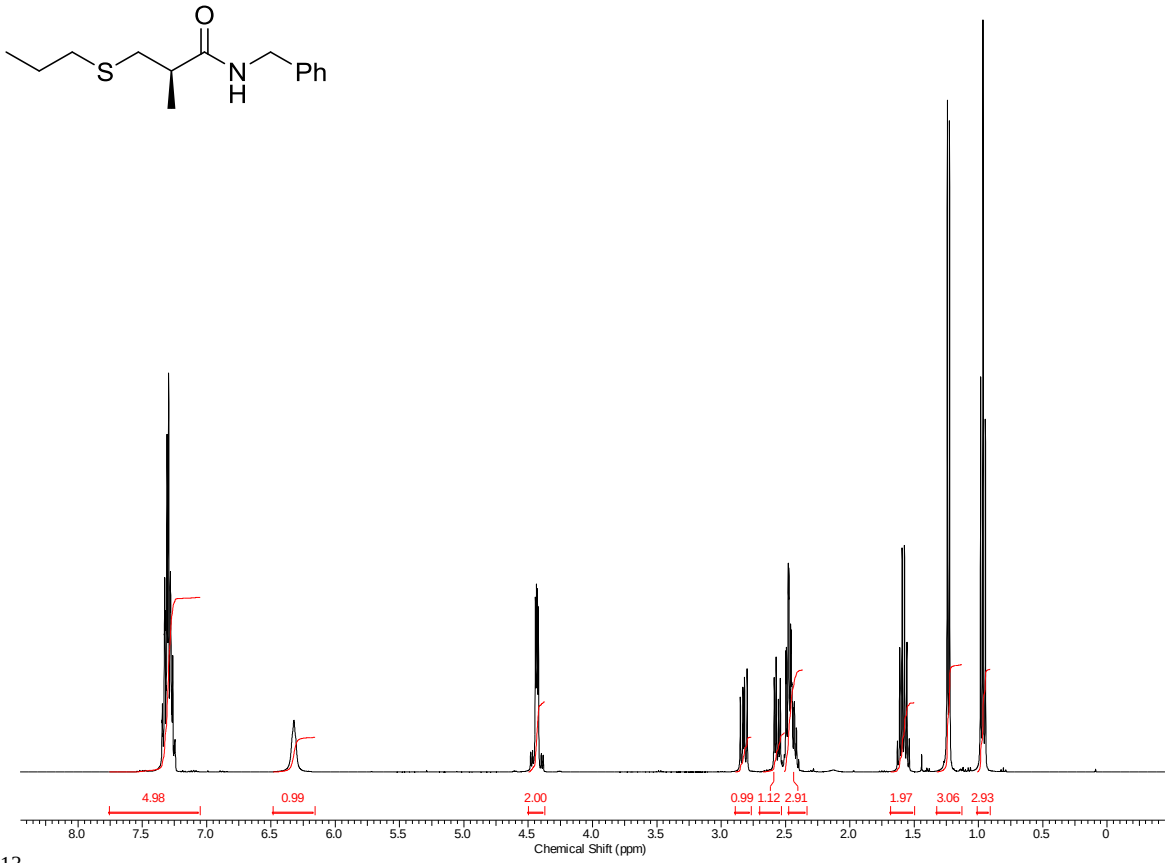
^{1}H NMR of **5c** (400 MHz, $CDCl_3$)



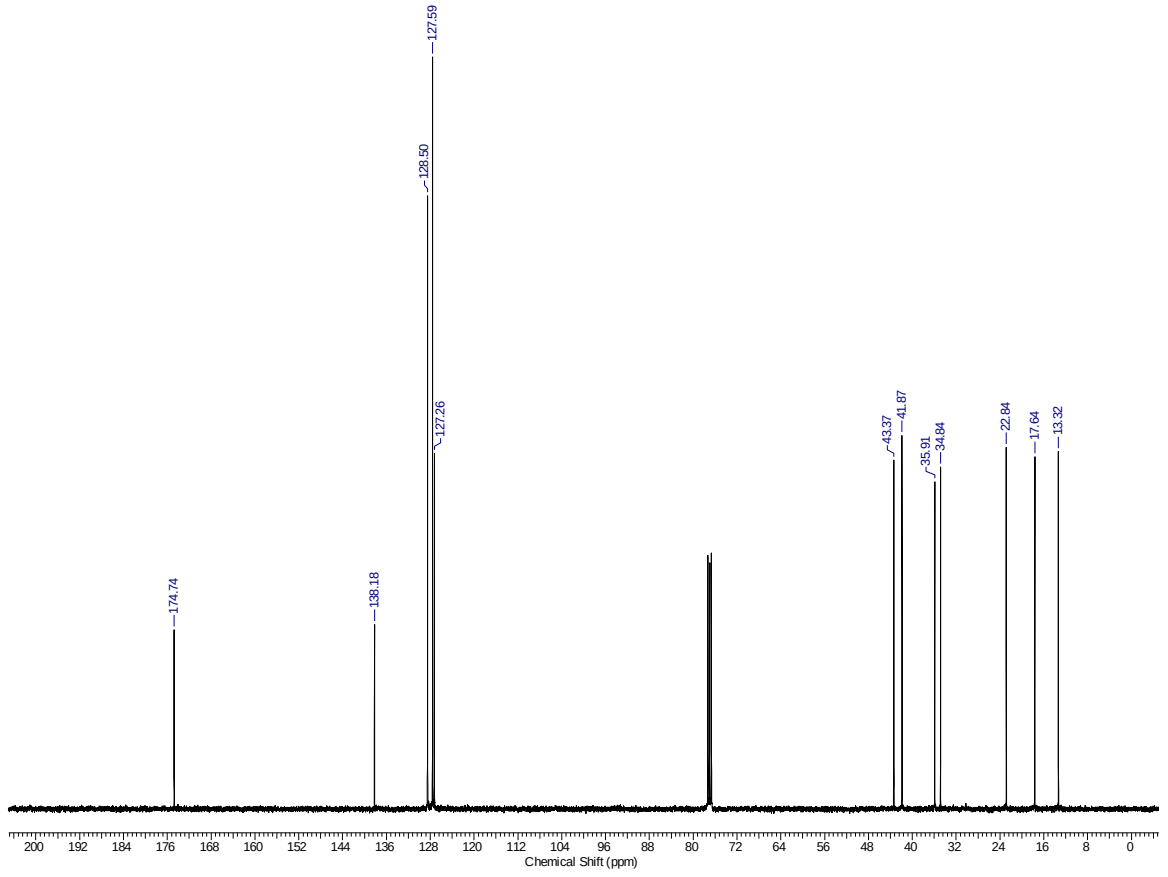
^{13}C NMR of **5c** (100 MHz, $CDCl_3$)



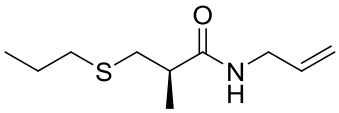
^{1}H NMR of **5d** (400 MHz, $CDCl_3$)



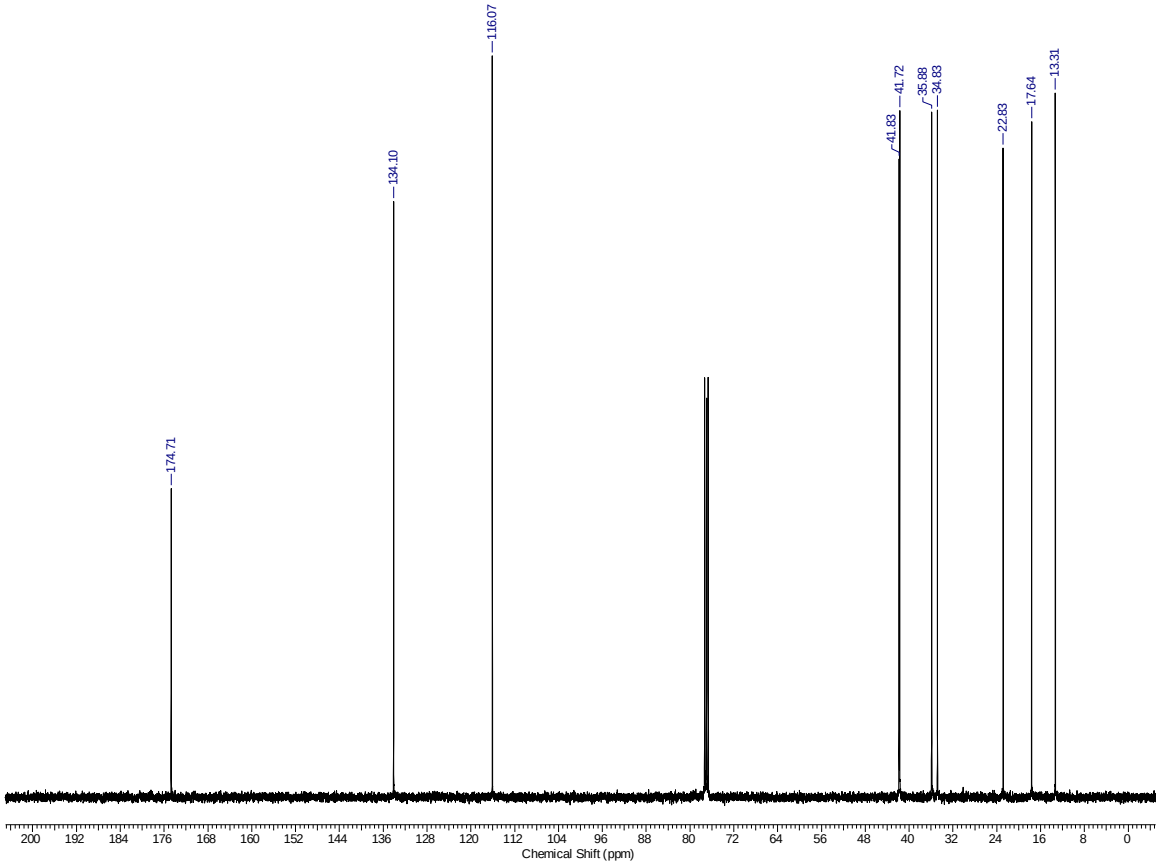
^{13}C NMR of **5d** (100 MHz, $CDCl_3$)



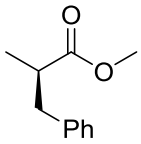
^{1}H NMR of **5e** (400 MHz, $CDCl_3$)



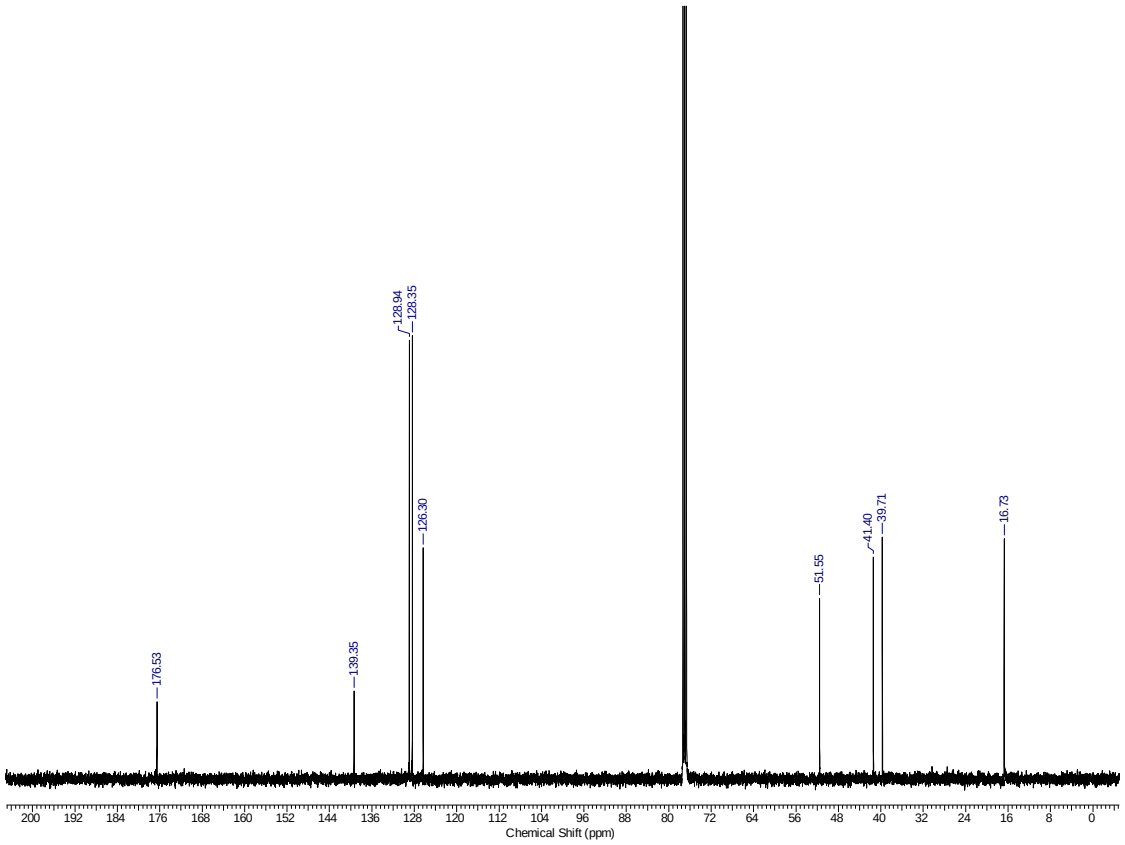
^{13}C NMR of **5e** (100 MHz, $CDCl_3$)



^{1}H NMR of **22** (400 MHz, $CDCl_3$)



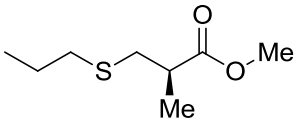
^{13}C NMR of **22** (100 MHz, $CDCl_3$)



3.2 Copies of HPLC and GC traces

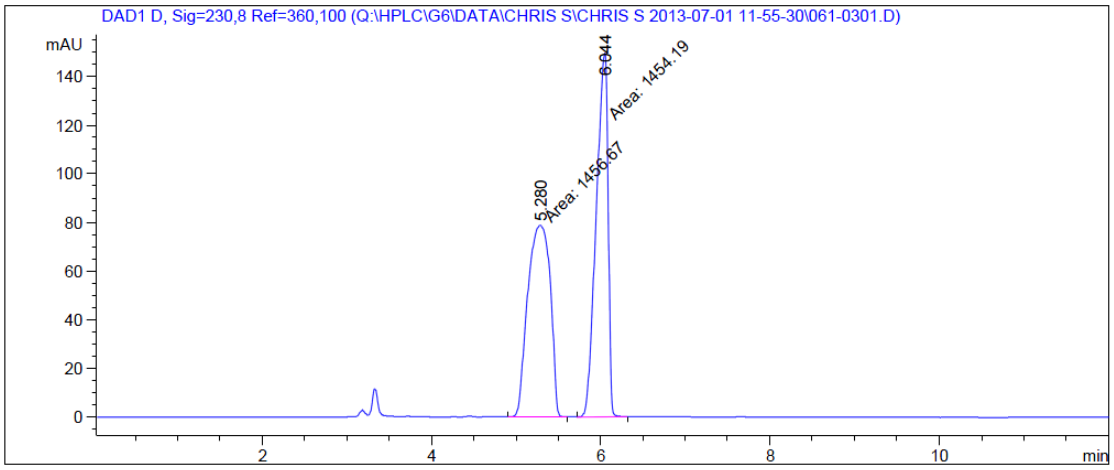
HPLC and GC chromatograms of β-mercaptoesters 4 (Section 1.5)

Methyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate **(4a)**



(Chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min)

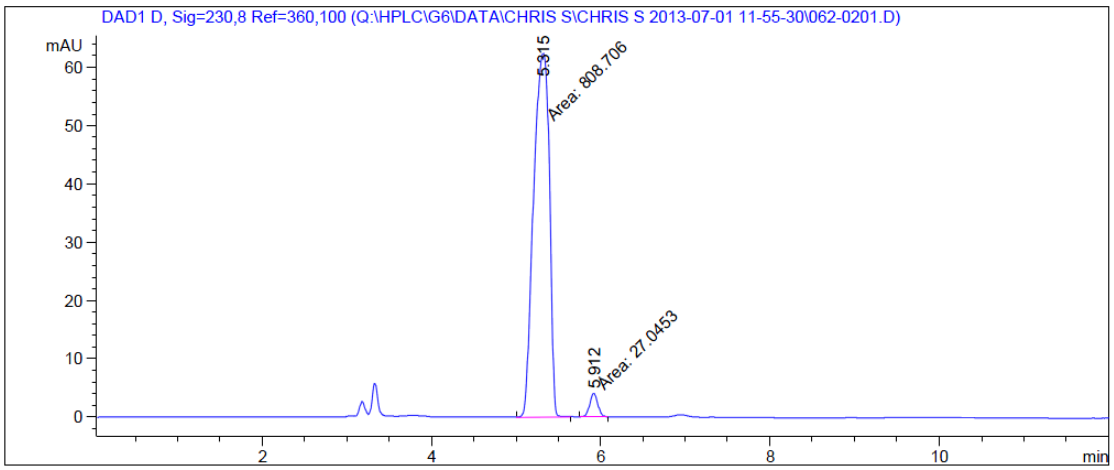
Racemic



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.280	MM	0.3085	1456.66736	78.68633	50.0426
2	6.044	MM	0.1619	1454.18616	149.72061	49.9574

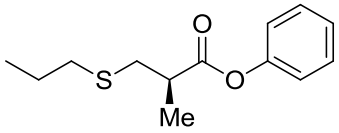
Enantiomerically enriched (94% ee)



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

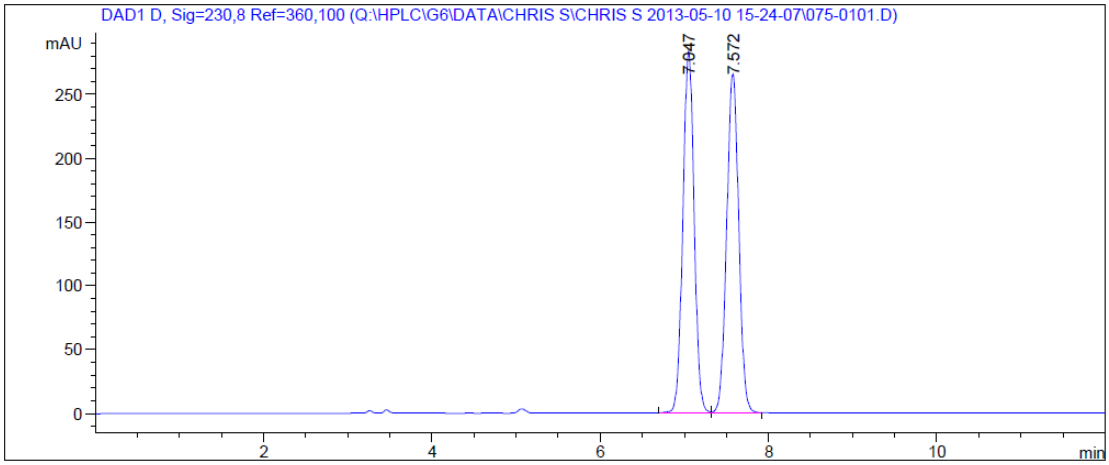
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.315	MM	0.2162	808.70642	62.34639	96.7640
2	5.912	MM	0.1128	27.04533	3.99533	3.2360

Phenyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate **(4b)**



(Chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min)

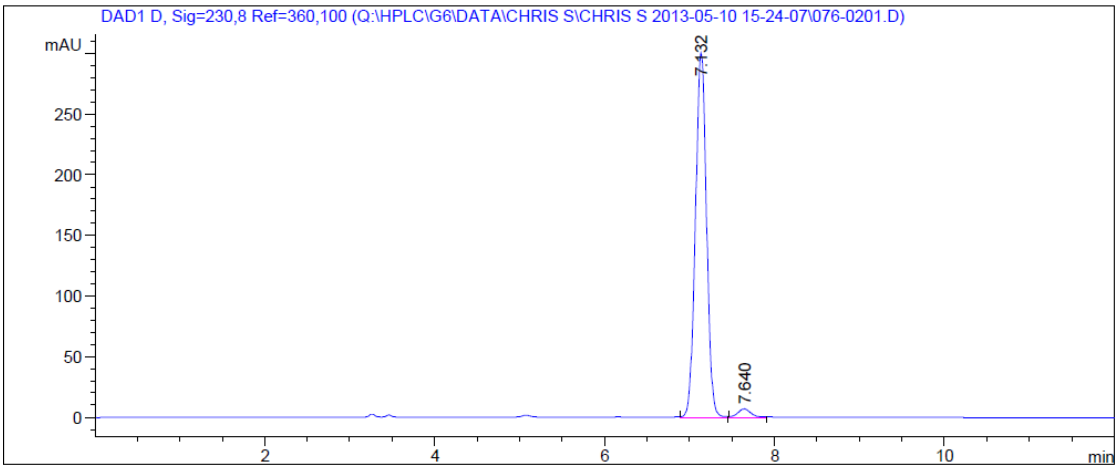
Racemic



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.047	BV	0.1449	2647.44263	283.67178	49.9519
2	7.572	VB	0.1546	2652.54224	265.50064	50.0481

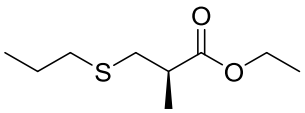
Enantiomerically enriched (95% ee)



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

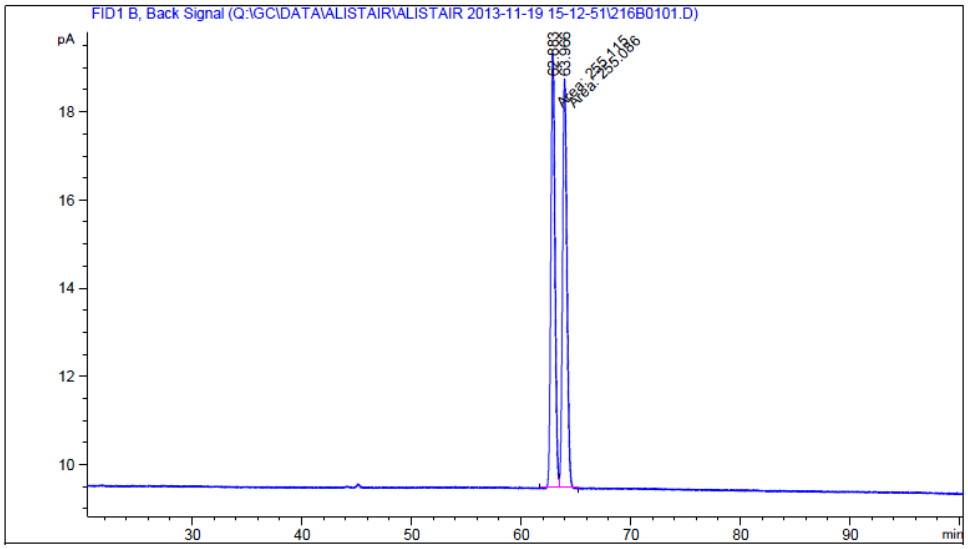
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.132	BB	0.1398	2723.80737	300.43539	97.5049
2	7.640	BB	0.1574	69.69989	6.80795	2.4951

Ethyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (**4c**)



(Supelco β-dex™ 325)

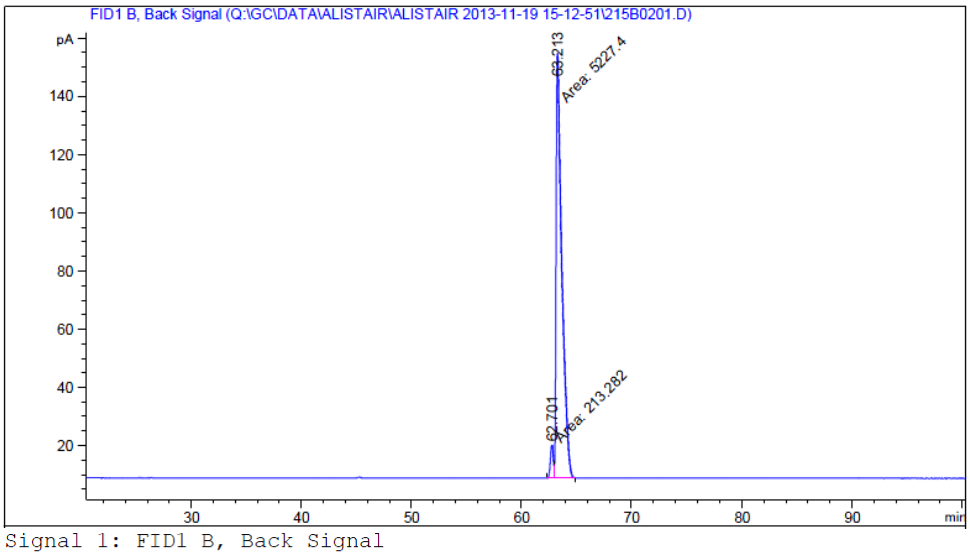
Racemic



Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.883	MF	0.4323	255.11453	9.83584	50.00283
2	63.966	FM	0.4598	255.08565	9.24577	49.99717

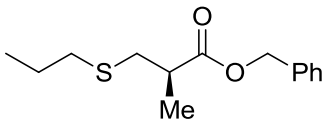
Enantiomerically enriched (92% ee)



Signal 1: FID1 B, Back Signal

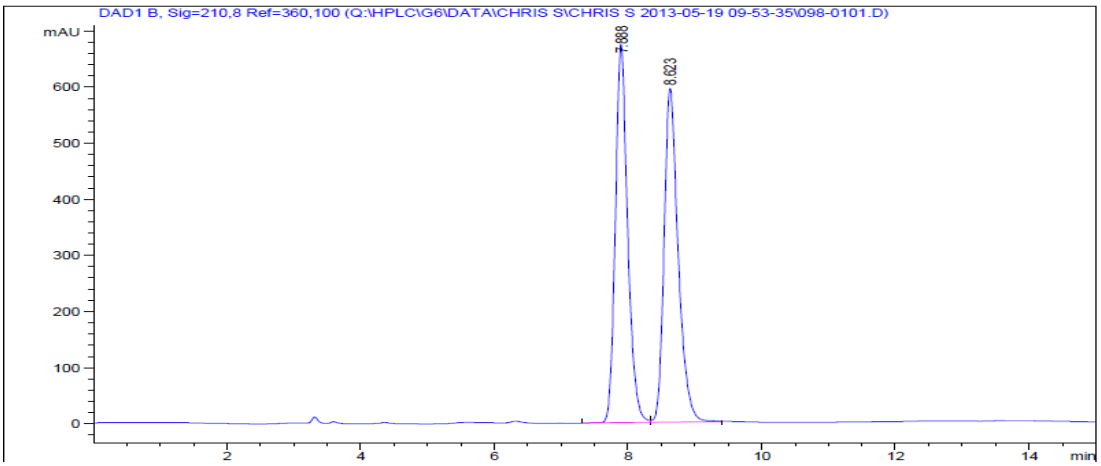
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	62.701	MF	0.3156	213.28198	11.26455	3.92013
2	63.213	FM	0.5964	5227.39844	146.08598	96.07987

Benzyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate **(4d)**



(Chiralcel OD, hexane/isopropanol = 99/1, 1 mL/min)

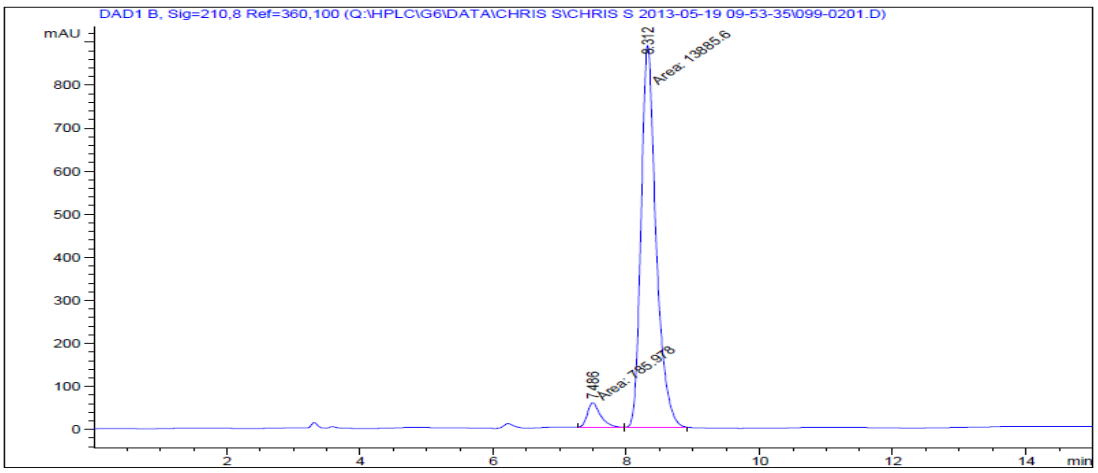
Racemic



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.888	BV	0.1892	8618.42187	673.91217	49.8298
2	8.623	VB	0.2182	8677.30273	594.64294	50.1702

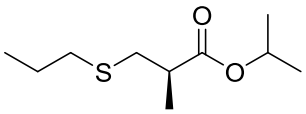
Enantiomerically enriched (89% ee)



Signal 1: DAD1 B, Sig=210,8 Ref=360,100

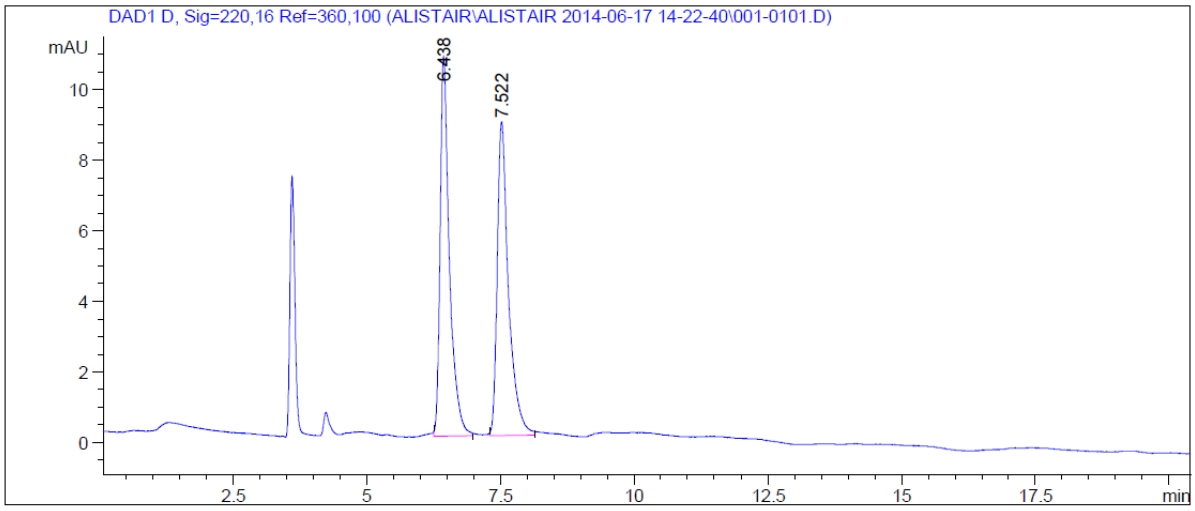
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.486	MF	0.2283	785.97778	57.37785	5.3571
2	8.312	FM	0.2610	1.38856e4	886.62372	94.6429

Propan-2-yl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (**4e**)



(Chiralpak OD, hexane/isopropanol = 99.5/0.5, 1.0 mL/min)

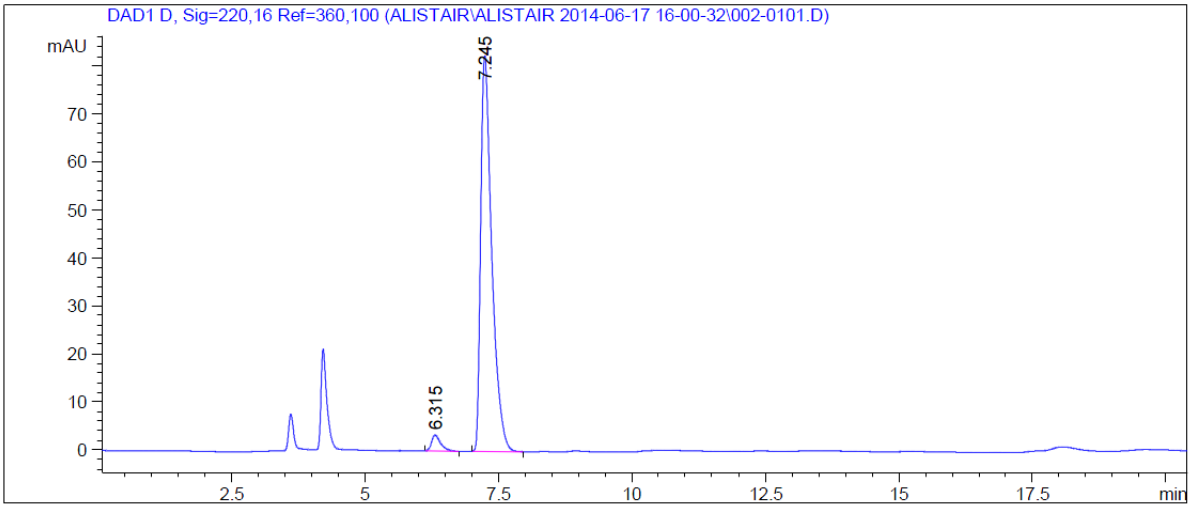
Racemic



Signal 4: DAD1 D, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.438	BB	0.1818	130.72006	10.75590	50.0501
2	7.522	BB	0.2195	130.45824	8.87627	49.9499

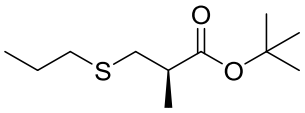
Enantiomerically enriched (93%)



Signal 4: DAD1 D, Sig=220,16 Ref=360,100

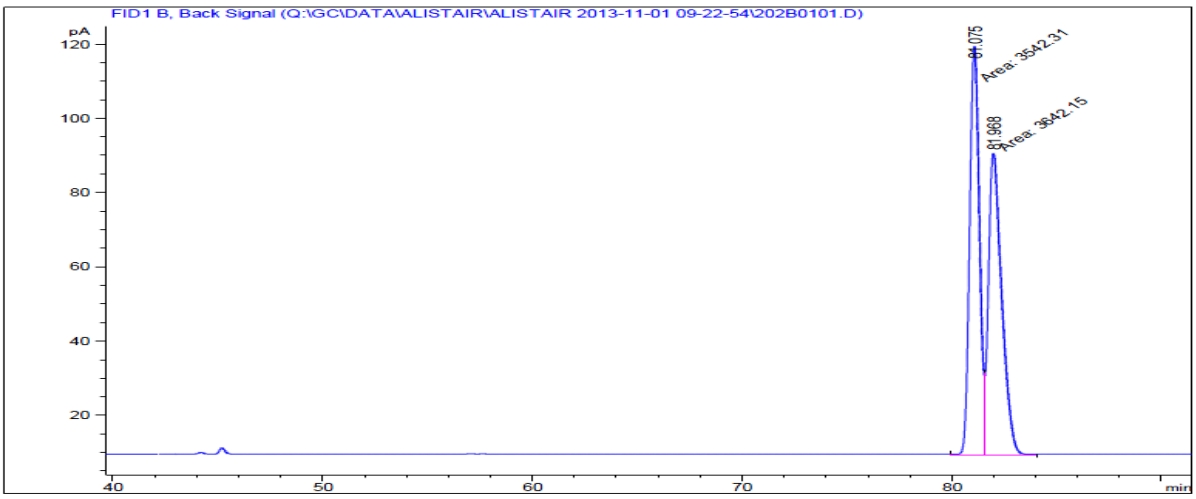
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.315	BB	0.1795	40.37839	3.37741	3.2833
2	7.245	BB	0.2204	1189.41528	82.40891	96.7167

tert-Butyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate (**4f**)



(Supelco β-dex™ 325)

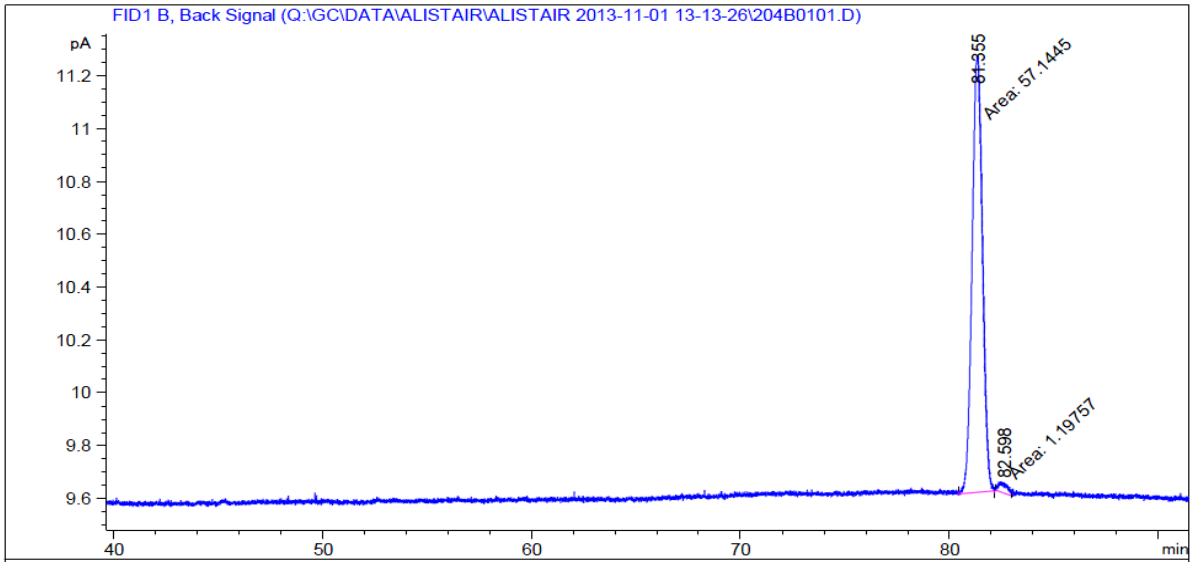
Racemic



Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	81.075	MF	0.5355	3542.30542	110.24638	49.30510
2	81.968	FM	0.7452	3642.15454	81.45321	50.69490

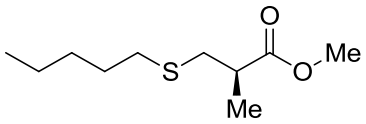
Enantiomerically enriched (96% ee)



Signal 1: FID1 B, Back Signal

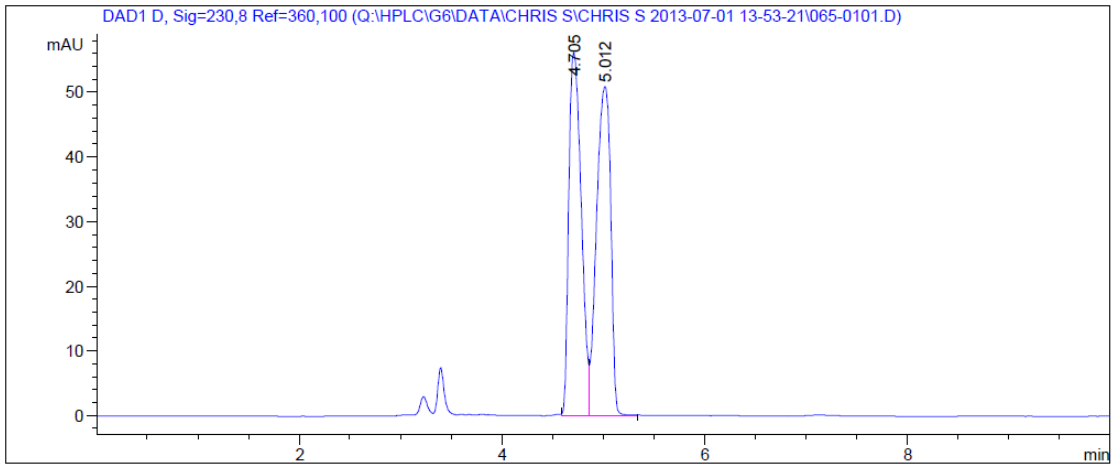
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	81.355	MM	0.5771	57.14455	1.65046	97.94734
2	82.598	MM	0.4826	1.19757	4.13613e-2	2.05266

Methyl (2*R*)-2-methyl-3-(pentylsulfanyl)propanoate **(4g)**



(Chiralpak AD-H, hexane/isopropanol = 99/1, 1 mL/min)

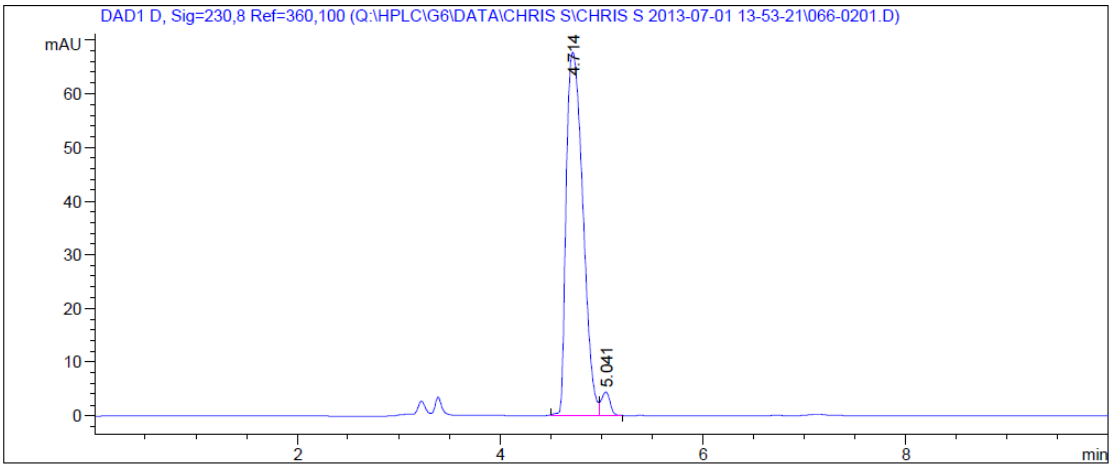
Racemic



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.705	BV	0.1393	477.95306	56.14232	49.2024
2	5.012	VB	0.1612	493.44904	50.87218	50.7976

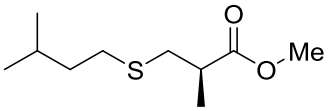
Enantiomerically enriched (93% ee)



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

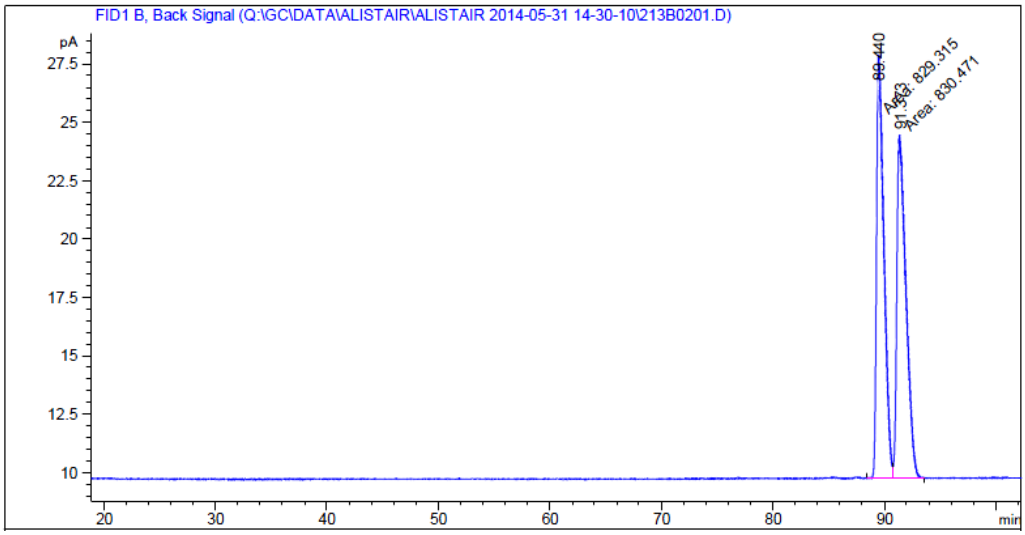
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.714	BV	0.1868	770.71606	67.71148	96.5997
2	5.041	VB	0.0937	27.12885	4.41509	3.4003

Methyl (2*R*)-2-methyl-3-[(3-methylbutyl)sulfanyl]propanoate (**4h**)



(Supelco β-dex^{TM} 325)

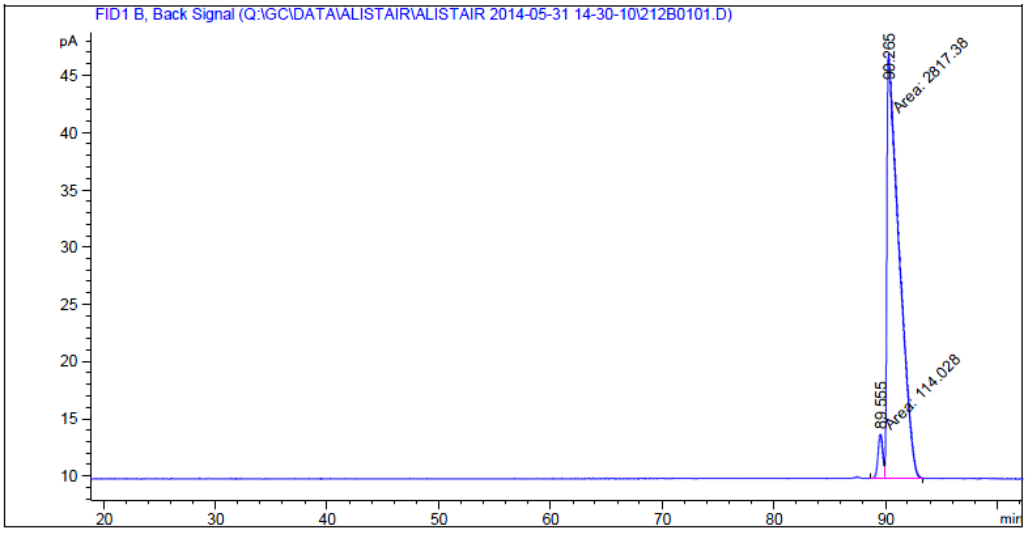
Racemic



Signal 1: FID1 B, Back Signal

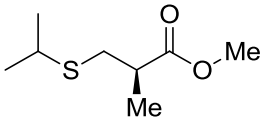
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	89.440	MF	0.7608	829.31500	18.16733	49.96517
2	91.373	FM	0.9396	830.47137	14.73161	50.03483

Enantiomerically enriched (92% ee)



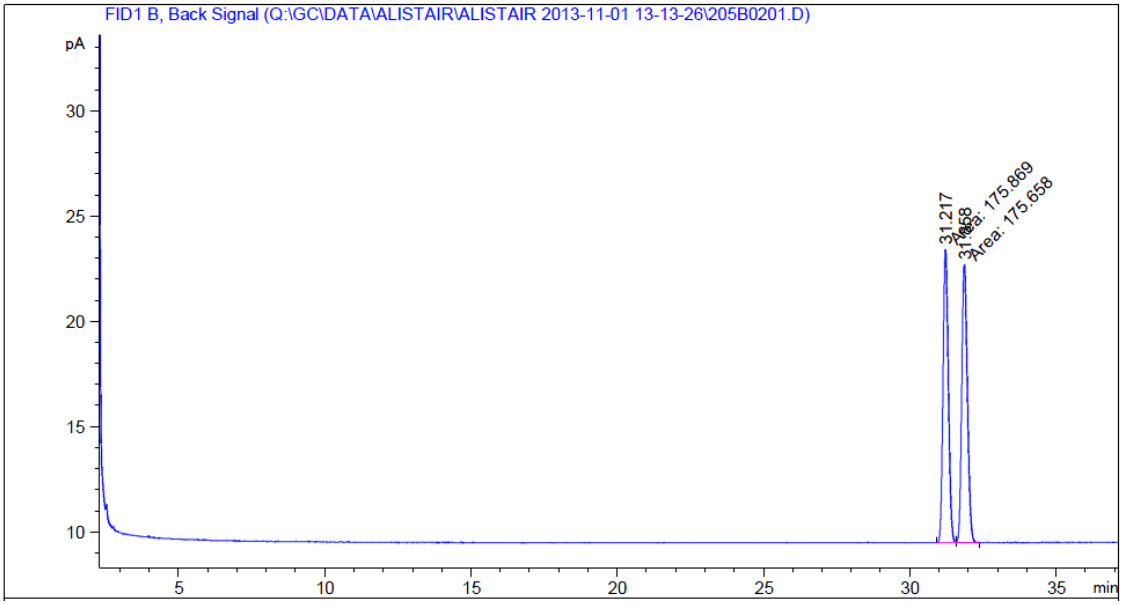
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	89.555	MF	0.4822	114.02778	3.94152	3.88987
2	90.265	FM	1.2641	2817.37817	37.14605	96.11013

Methyl (2*R*)-2-methyl-3-(propan-2-ylsulfanyl)propanoate (**4i**)



(Supelco β-dex™ 325)

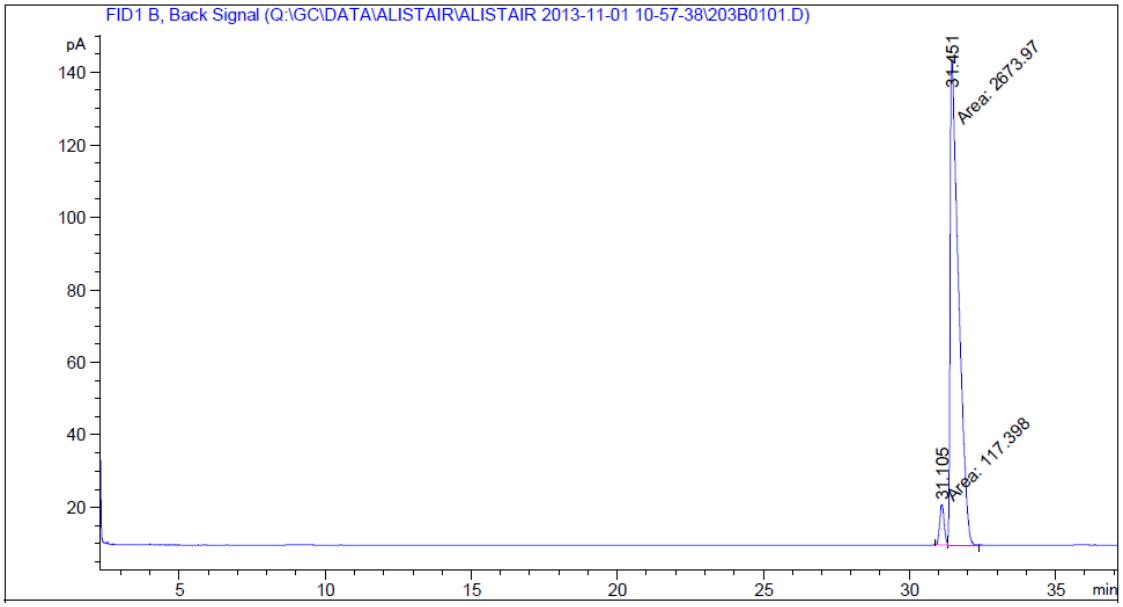
Racemic



Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	31.217	MM	0.2104	175.86888	13.93414	50.02993
2	31.858	MM	0.2217	175.65843	13.20288	49.97007

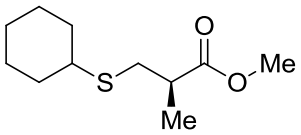
Enantiomerically enriched (92%)



Signal 1: FID1 B, Back Signal

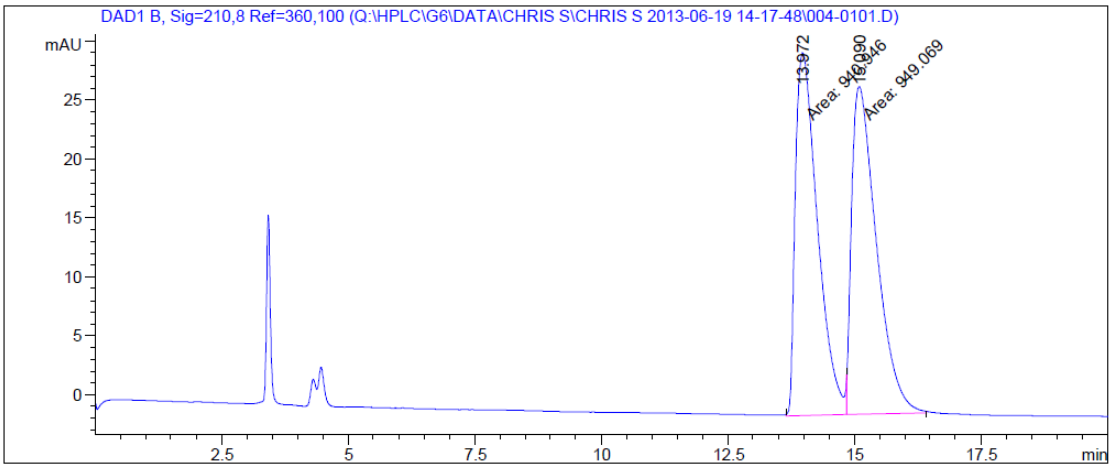
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	31.105	MF	0.1763	117.39832	11.10104	4.20576
2	31.451	FM	0.3324	2673.96851	134.06290	95.79424

Methyl (2*R*)-3-(cyclohexylsulfanyl)-2-methylpropanoate **(4j)**



(Chiralpak AS-H, hexane/isopropanol = 99.5/0.5, 1 mL/min)

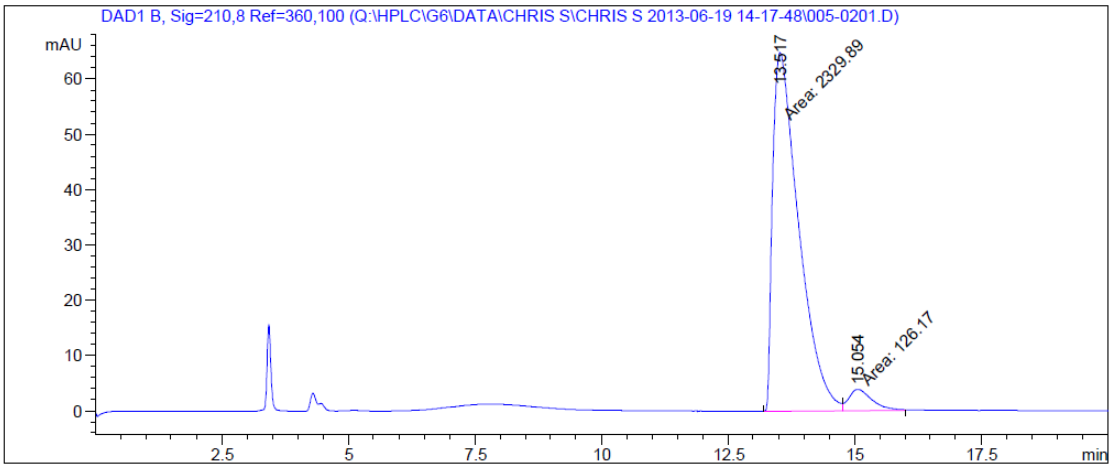
Racemic



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.972	MF	0.5093	940.94623	30.79462	49.7851
2	15.090	FM	0.5686	949.06946	27.81937	50.2149

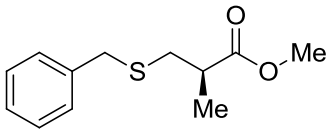
Enantiomerically enriched (90% ee)



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

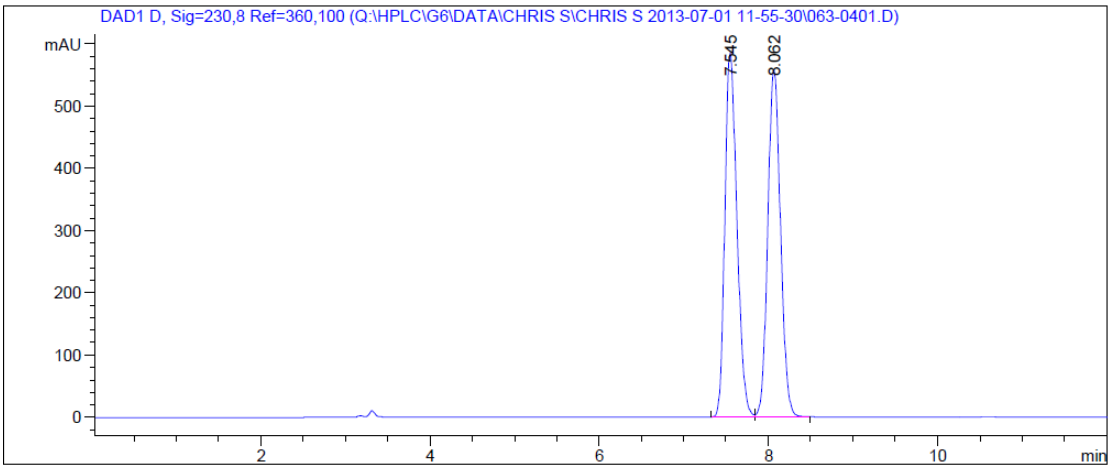
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.517	MF	0.5986	2329.89282	64.87470	94.8629
2	15.054	FM	0.5391	126.17004	3.90040	5.1371

Methyl (2*R*)-3-(benzylsulfanyl)-2-methylpropanoate **(4k)**



(Chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min)

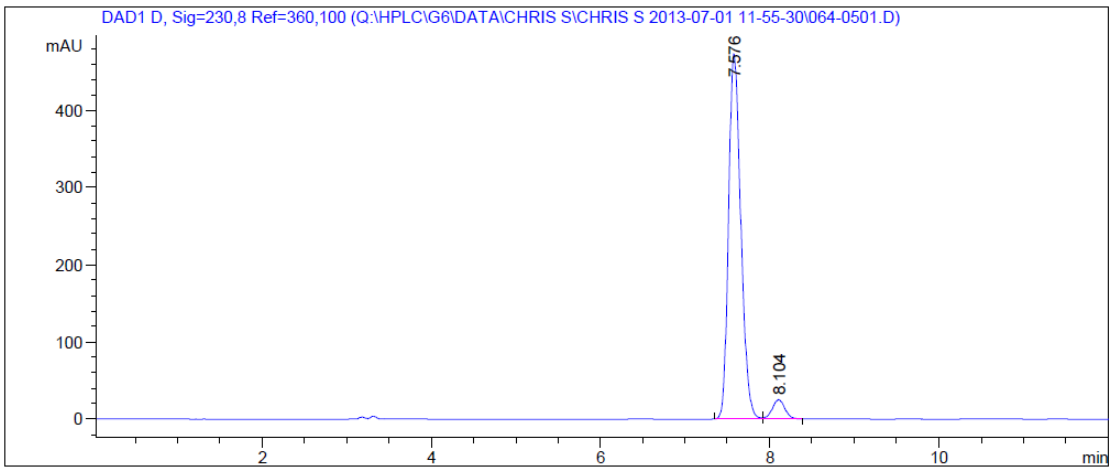
Racemic



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.545	BV	0.1539	5810.33789	584.95789	49.8945
2	8.062	VB	0.1621	5834.91846	557.43646	50.1055

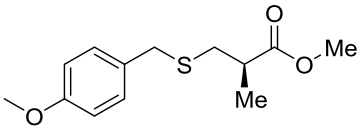
Enantiomerically enriched (90% ee)



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

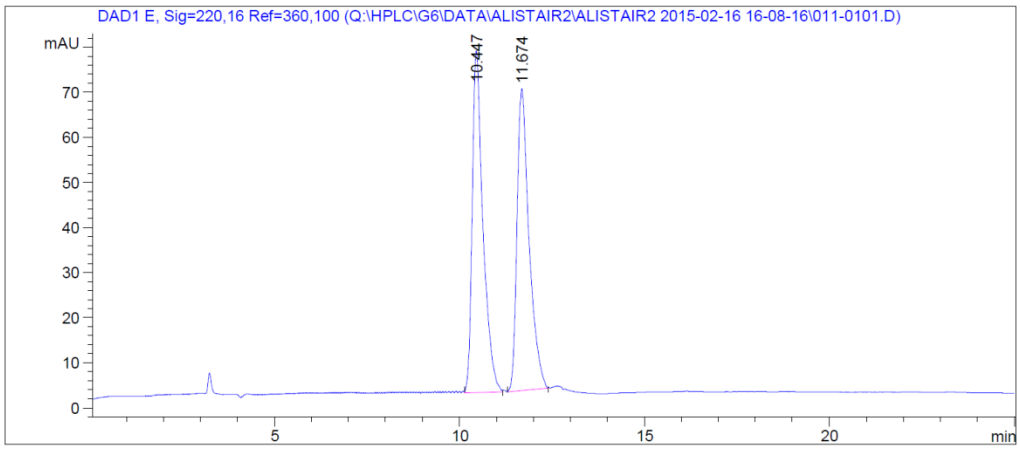
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.576	BV	0.1555	4766.79053	473.45972	94.8092
2	8.104	VB	0.1617	260.97916	25.02822	5.1908

Methyl (2*R*)-3-[(4-methoxybenzyl)sulfanyl]-2-methylpropanoate (**4l)**



(Chiralcel OD, hexane/isopropanol = 98/2, 1 mL/min)

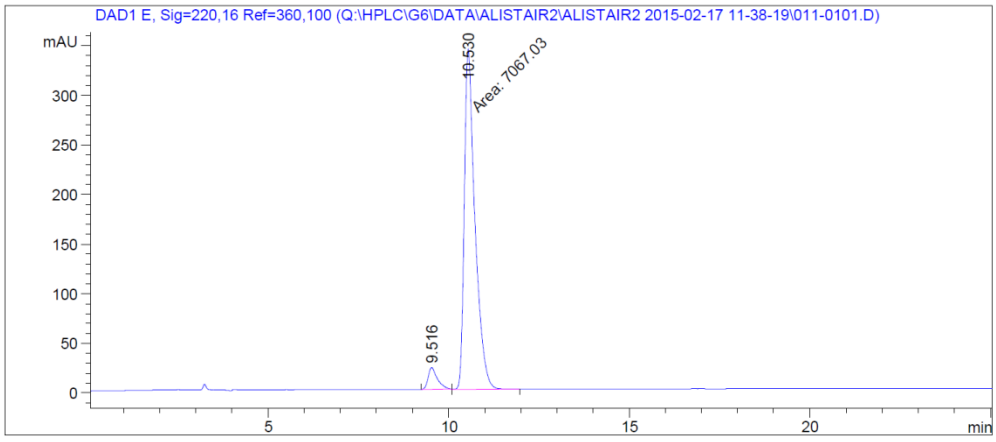
Racemic



Signal 5: DAD1 E, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.447	VB	0.2948	1537.60645	75.76772	50.5296
2	11.674	BB	0.3302	1505.37317	66.98518	49.4704
Totals :				3042.97961	142.75291	

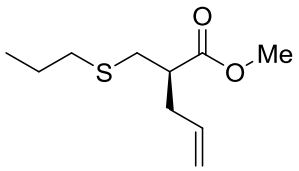
Enantiomerically enriched (89% ee)



Signal 5: DAD1 E, Sig=220,16 Ref=360,100

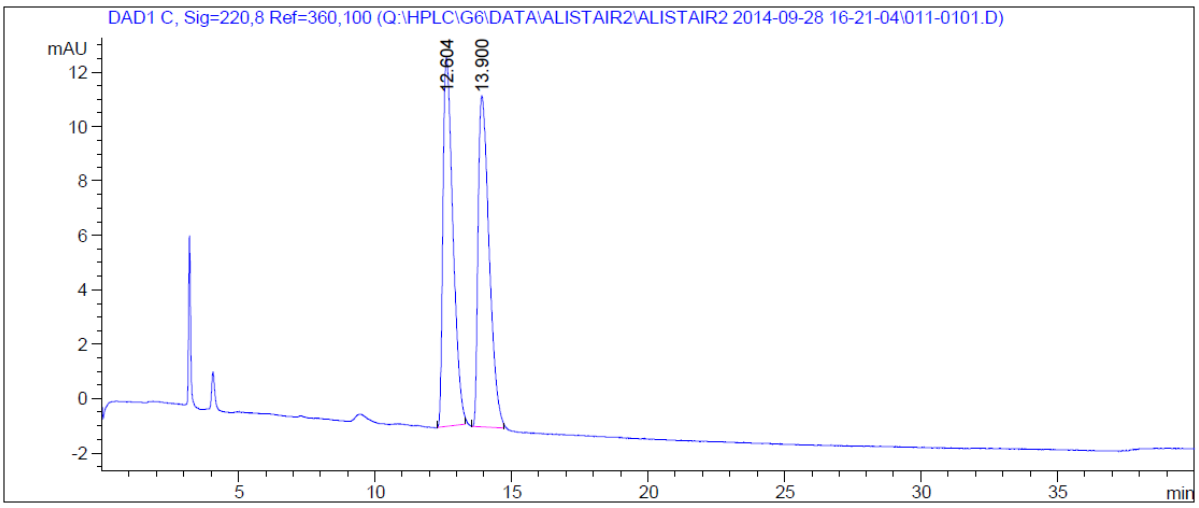
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.516	BB	0.2655	392.99472	21.88272	5.2680
2	10.530	MM	0.3437	7067.02783	342.68033	94.7320
Totals :				7460.02255	364.56305	

Methyl (2*R*)-2-[(propylsulfanyl)methyl]pent-4-enoate (**4m**)



(Chiralpak AS-H, hexane/isopropanol = 99.5/0.5, 1 mL/min)

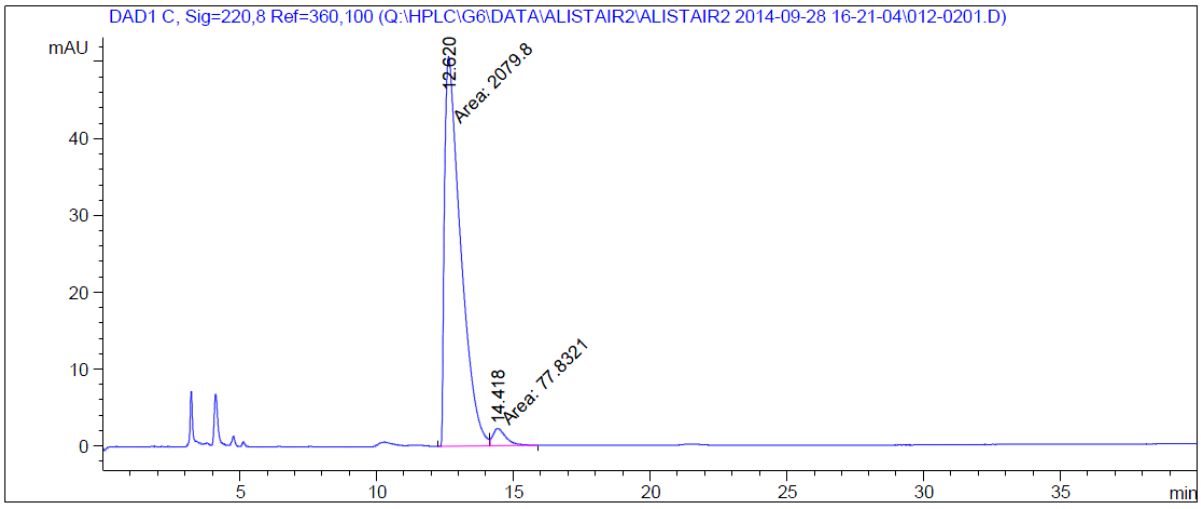
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.604	BB	0.3970	345.13492	13.55909	50.0633
2	13.900	BB	0.4339	344.26236	12.17460	49.9367

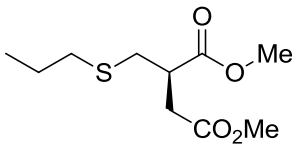
Enantiomerically enriched (93%)



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

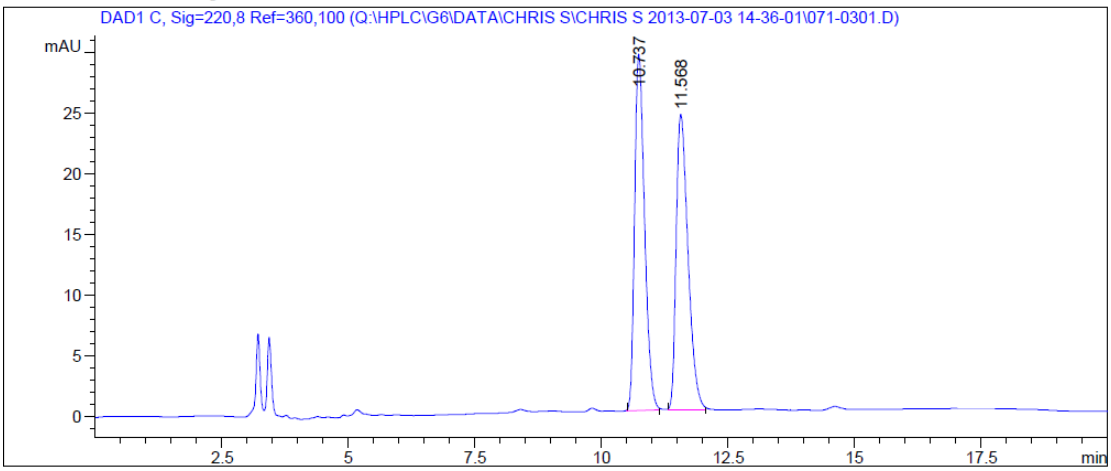
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.620	MF	0.6822	2079.80347	50.80854	96.3927
2	14.418	FM	0.5757	77.83212	2.25308	3.6073

Dimethyl (2*R*)-2-((propylsulfanyl)methyl)succinate **(4n)**



(Chiralpak AS-H, hexane/isopropanol = 99/1, 1 mL/min)

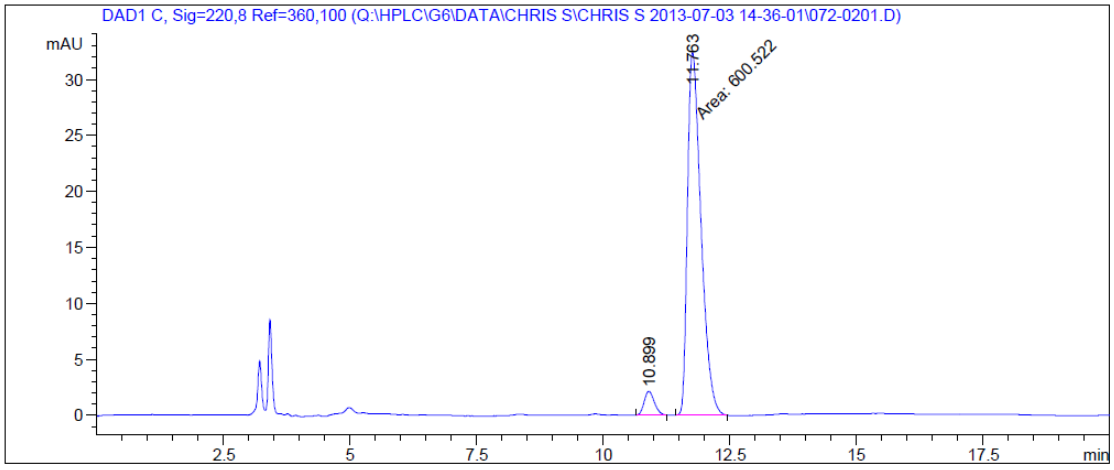
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.737	BB	0.2092	400.63760	29.36786	50.3664
2	11.568	BB	0.2513	394.80865	24.32895	49.6336

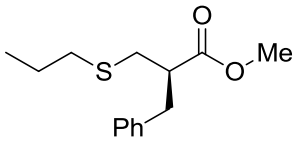
Enantiomerically enriched (90% ee)



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

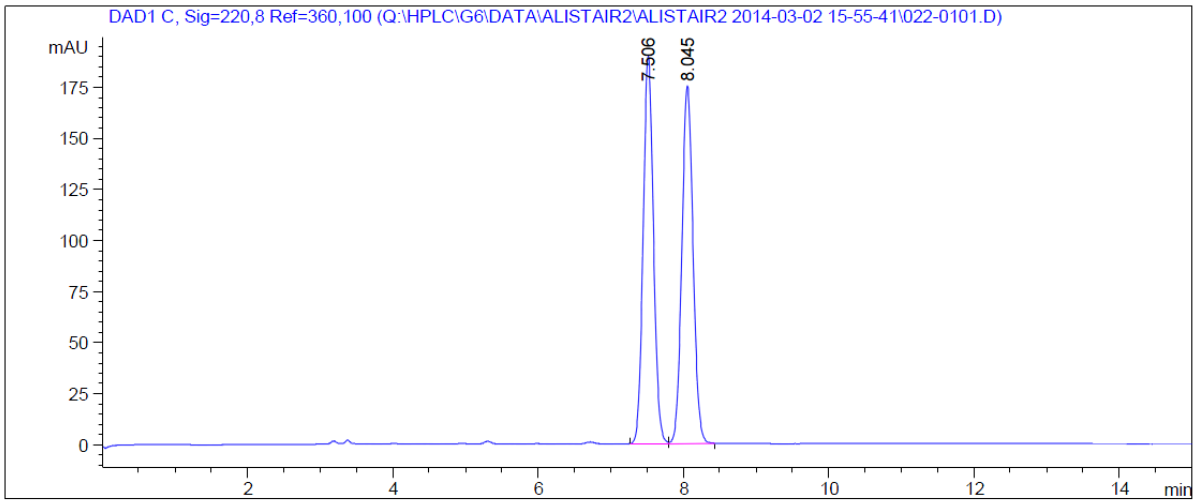
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.899	BB	0.2159	30.13931	2.14517	4.7790
2	11.763	MM	0.3089	600.52203	32.40231	95.2210

Methyl (2*R*)-2-benzyl-3-(propylsulfanyl)propanoate **(4o)**



(Chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min)

Racemic

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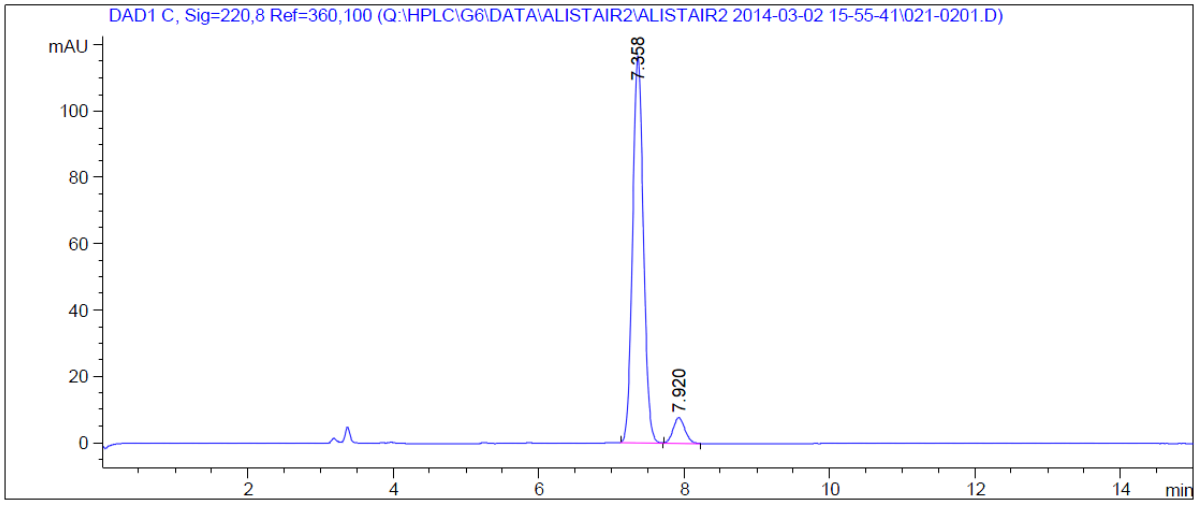
Signal 3: DAD1 C, Sig=220,8 Ref=360,100
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.506 BV    0.1532 1873.53467  189.73610  49.9760
   2   8.045 VB    0.1648 1875.33740  175.27962  50.0240
```

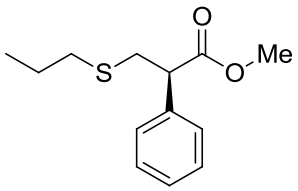
Enantiomerically enriched (86% ee)




```
Signal 3: DAD1 C, Sig=220,8 Ref=360,100

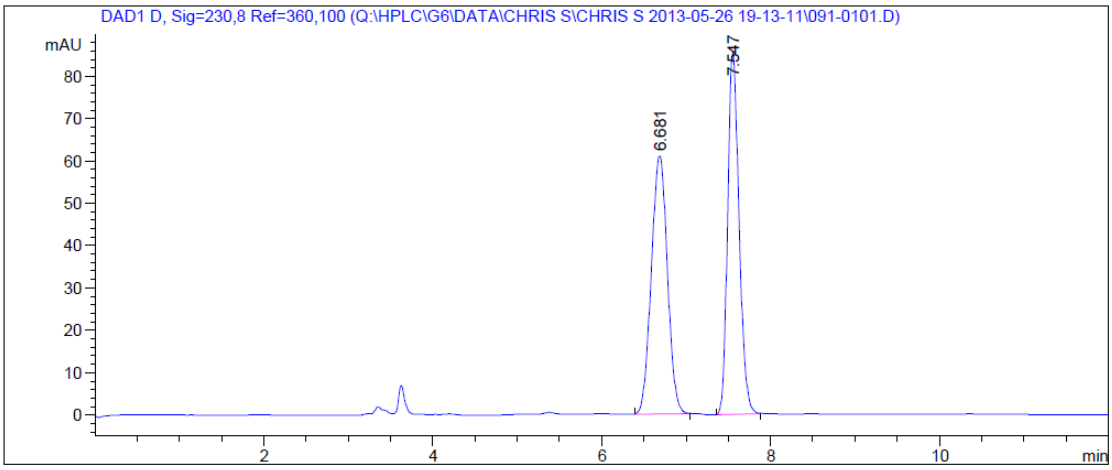
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.358 BB    0.1601 1203.97400  116.93714  93.2219
   2   7.920 BB    0.1738   87.54045    7.74973   6.7781
```

Methyl (2*R*)-2-phenyl-3-(propylsulfanyl)propanoate **(4p)**



(Chiralpak AS-H, hexane/isopropanol = 99/1, 1 mL/min)

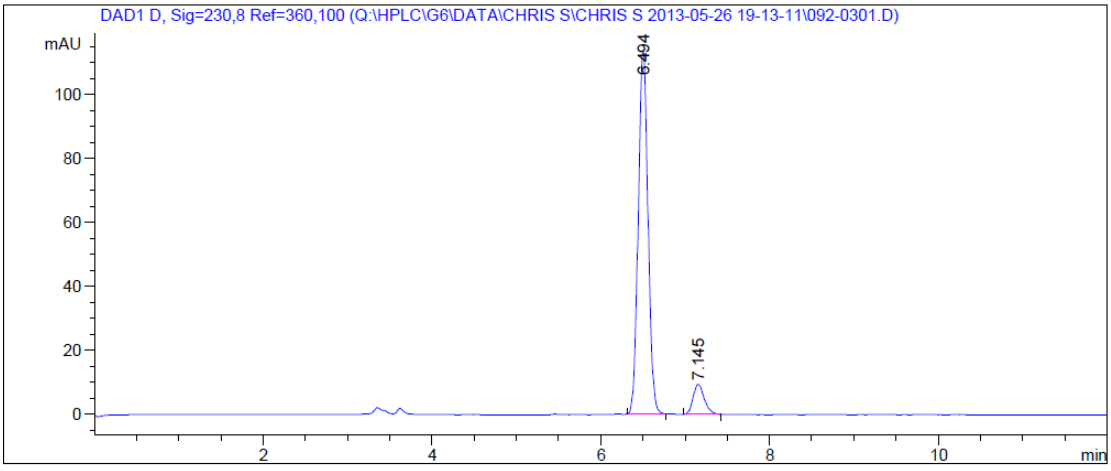
Racemic



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.681	BB	0.2062	806.50073	61.01258	50.0591
2	7.547	BB	0.1460	804.59601	85.37467	49.9409

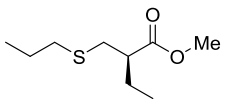
Enantiomerically enriched (83% ee)



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

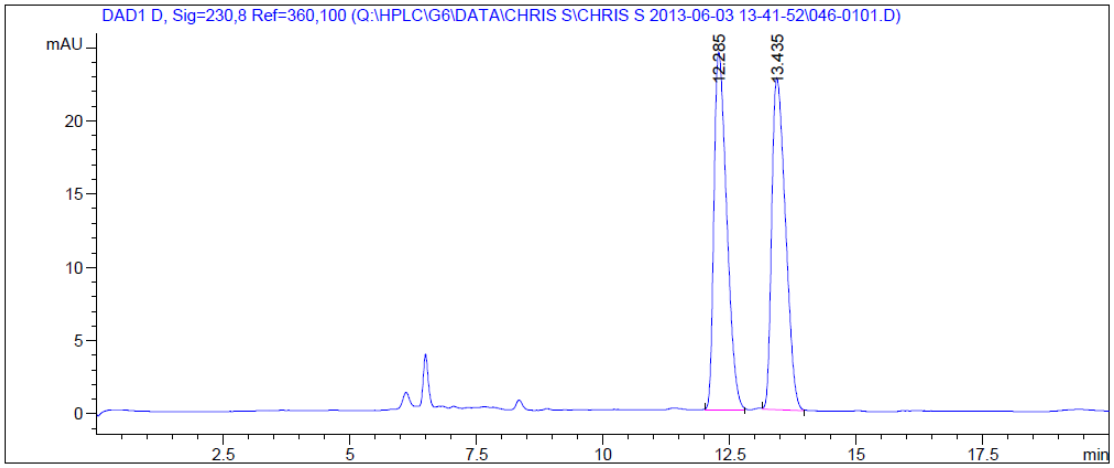
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.494	BB	0.1262	913.99115	113.20681	91.3142
2	7.145	BB	0.1418	86.93851	9.40499	8.6858

Methyl (2*R*)-2-[(propylsulfanyl)methyl]butanoate **(4q)**



(Chiralpak AD-H, hexane/isopropanol = 99/1, 1 mL/min)

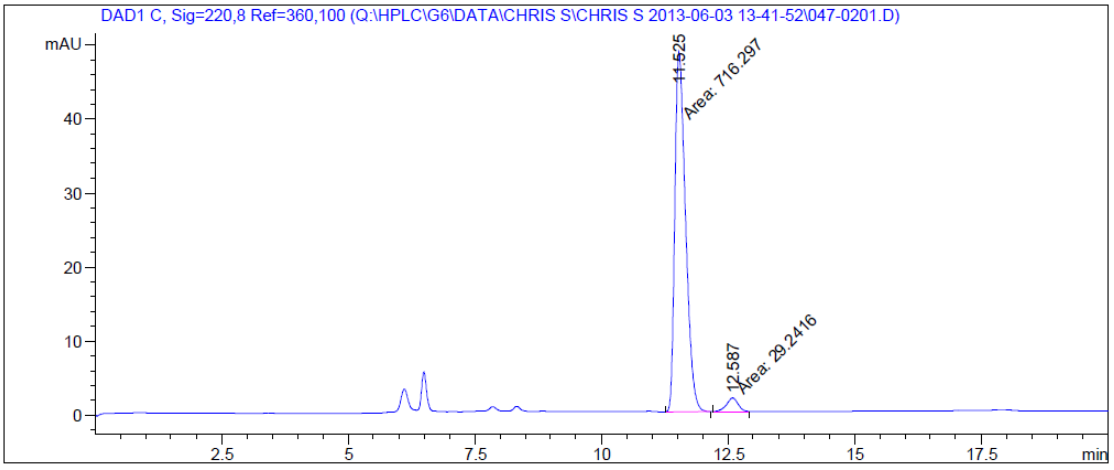
Racemic



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.285	BB	0.2721	427.06357	24.40928	50.0434
2	13.435	BB	0.2997	426.32278	22.64250	49.9566

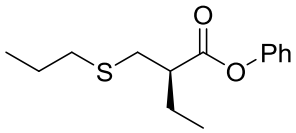
Enantiomerically enriched (92% ee)



Signal 4: DAD1 D, Sig=230,8 Ref=360,100

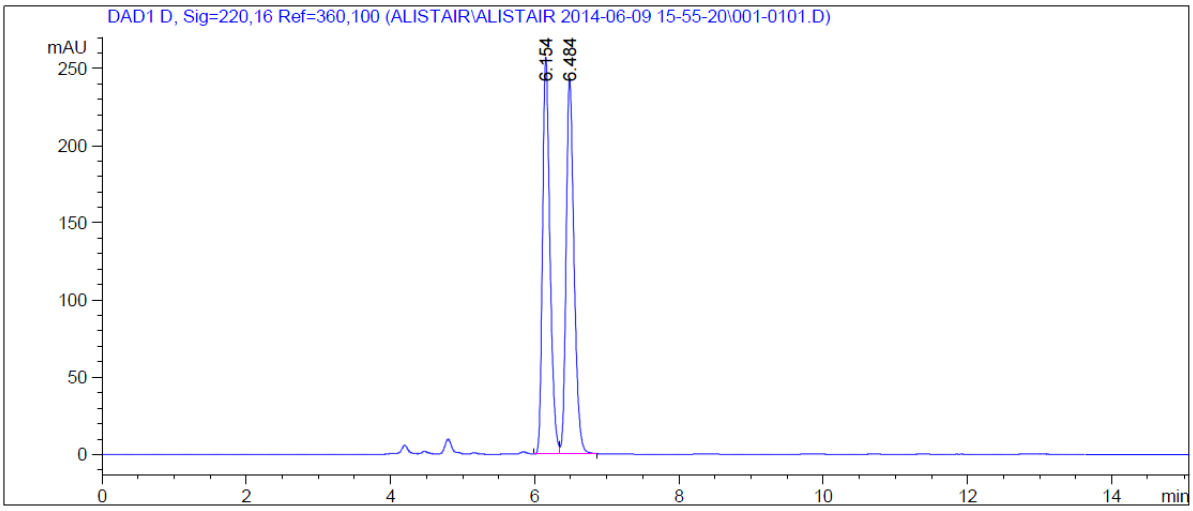
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.525	MM	0.2452	299.25372	20.34108	96.1102
2	12.586	MM	0.2660	12.11155	7.58927e-1	3.8898

Phenyl (2*R*)-2-[(propylsulfanyl)methyl]butanoate (**4r**)



(Chiralpak AS-H, hexane/isopropanol = 98/2, 1.0 mL/min)

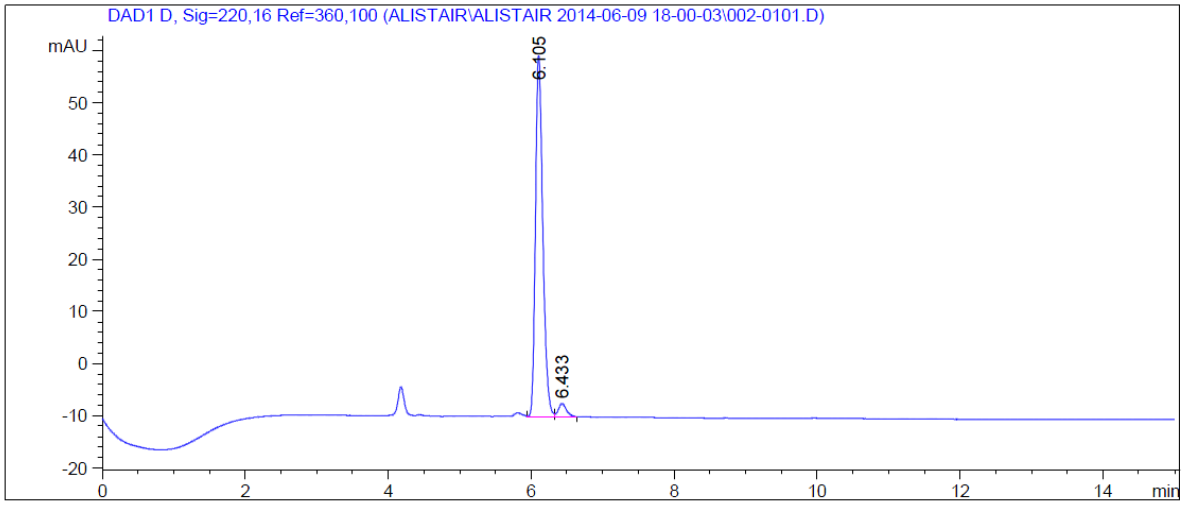
Racemic



Signal 4: DAD1 D, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.154	VV	0.1084	1840.41077	257.30743	49.7020
2	6.484	VB	0.1162	1862.47742	243.59578	50.2980

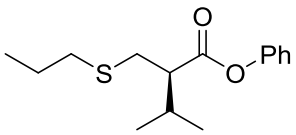
Enantiomerically enriched (92%)



Signal 4: DAD1 D, Sig=220,16 Ref=360,100

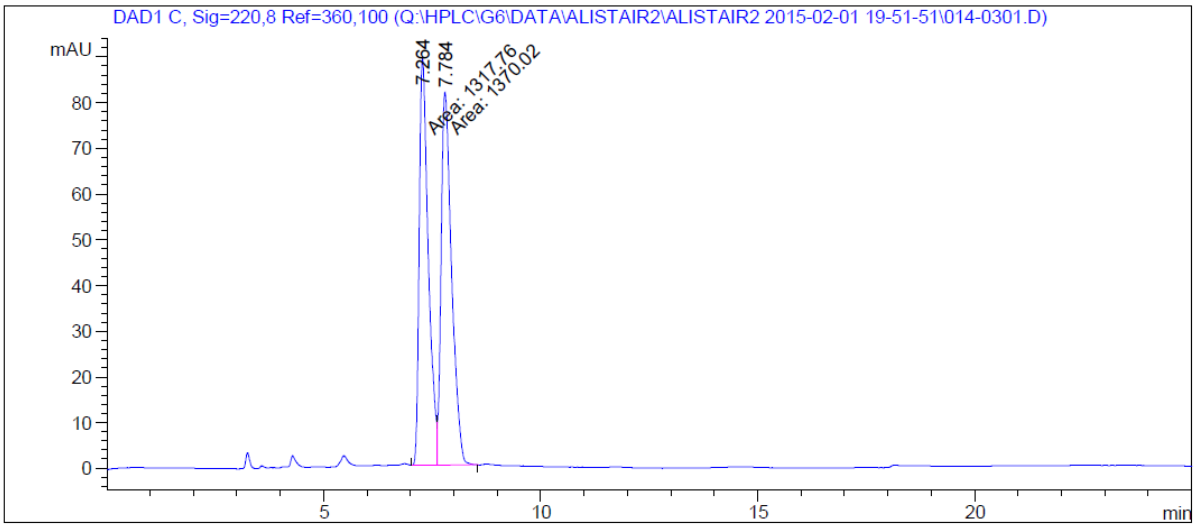
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.105	VV	0.1085	495.96350	69.29136	96.1828
2	6.433	VB	0.1174	19.68319	2.51145	3.8172

Phenyl (2*R*)-3-methyl-2-[(propylsulfanyl)methyl]butanoate (**4s**)



(Chiralpak OD, hexane/isopropanol = 99/1, 1.0 mL/min)

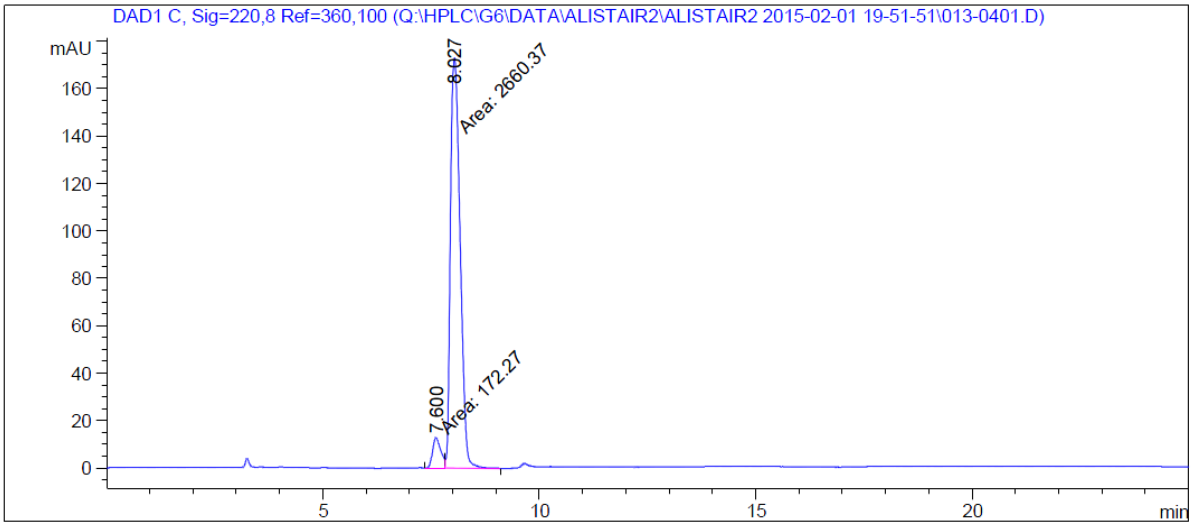
Racemic




```
Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.264 MF    0.2471 1317.76428   88.87209  49.0279
   2   7.784 FM    0.2802 1370.02136   81.49705  50.9721
```

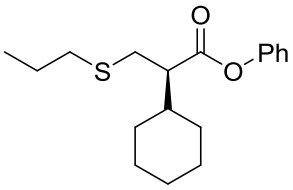
Enantiomerically enriched (88%)




```
Signal 3: DAD1 C, Sig=220,8 Ref=360,100

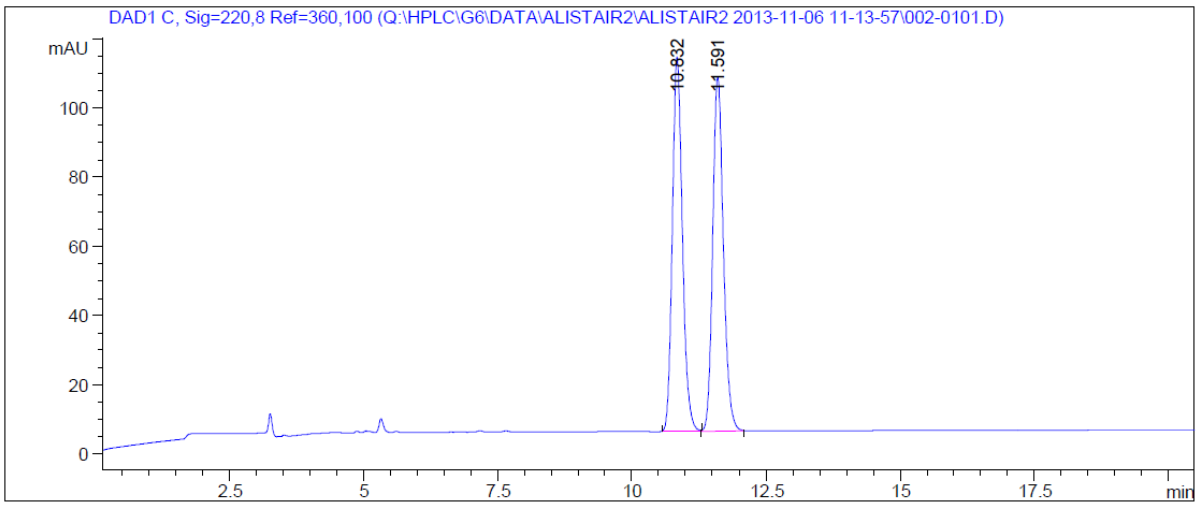
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   7.600 MF    0.2244  172.26961   12.79431   6.0816
   2   8.027 FM    0.2562 2660.36572  173.09555  93.9184
```

Phenyl (2*R*)-2-cyclohexyl-3-(propylsulfanyl)propanoate (**4t**)



(Chiralpak AD-H, hexane/isopropanol = 98/2, 1.0 mL/min)

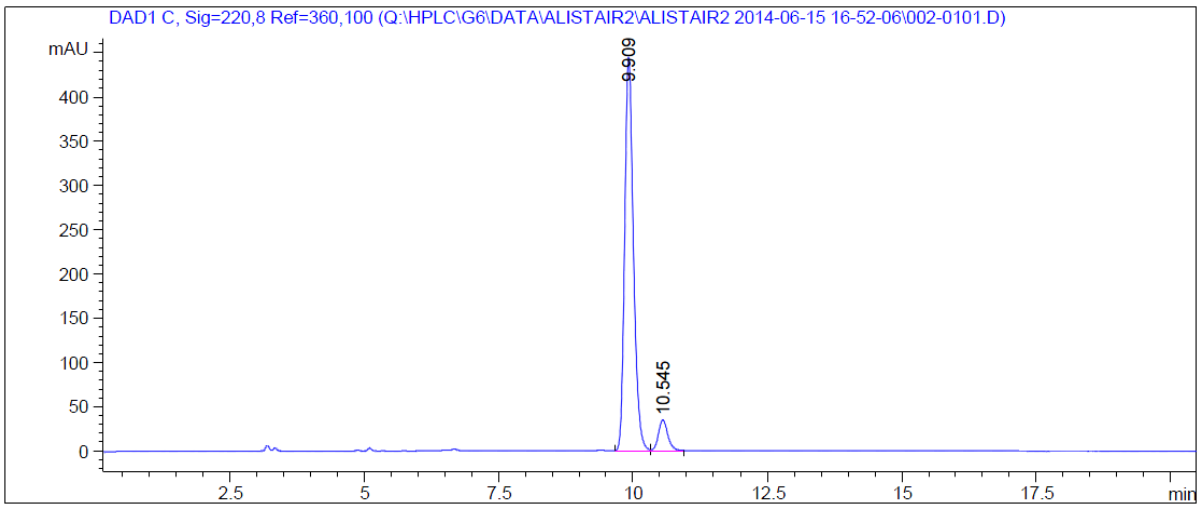
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.832	BB	0.2002	1410.52246	108.15060	49.9585
2	11.591	BB	0.2131	1412.86523	102.28801	50.0415

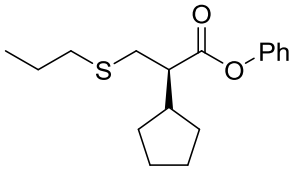
Enantiomerically enriched (85% ee)



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

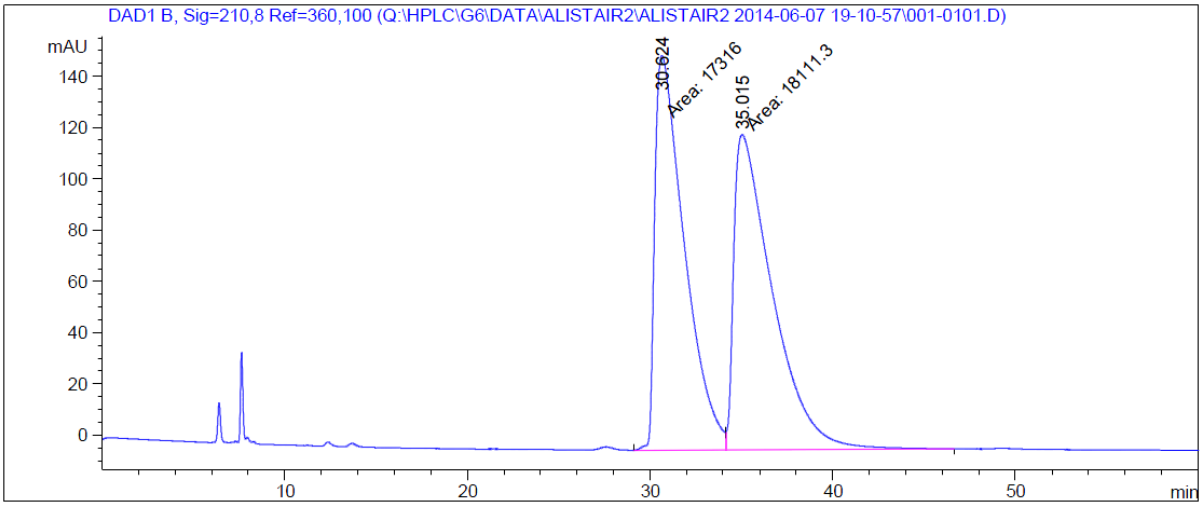
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.909	BV	0.1719	5028.43066	444.81497	92.3139
2	10.545	VB	0.1846	418.67212	34.74311	7.6861

Phenyl (2*R*)-2-cyclopentyl-3-(propylsulfanyl)propanoate (**4u**)



(Chiralpak AS-H, hexane/isopropanol = 99.5/0.5, 0.5 mL/min)

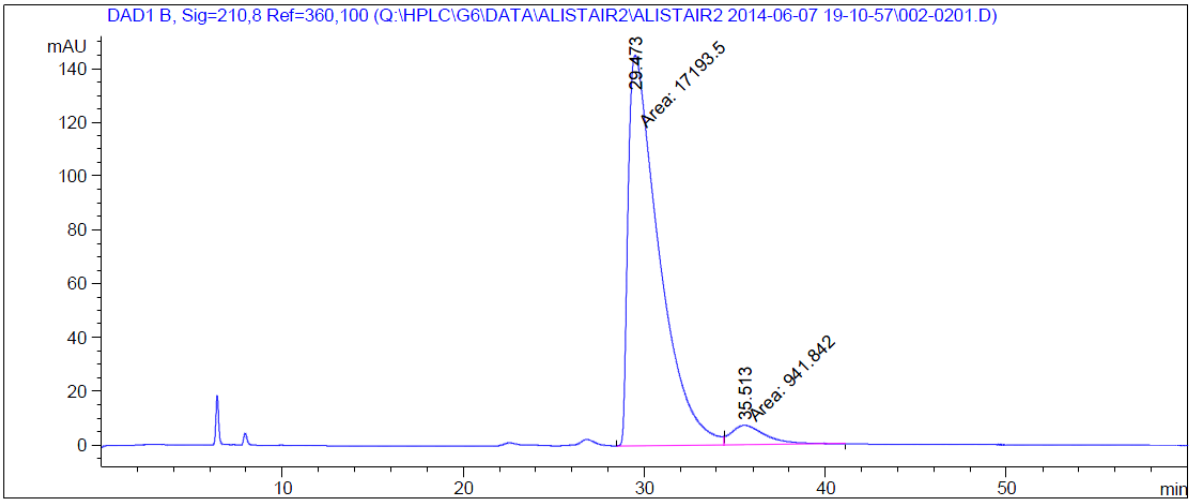
Racemic



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.624	MF	1.8754	1.73160e4	153.88661	48.8774
2	35.015	FM	2.4557	1.81113e4	122.92086	51.1226

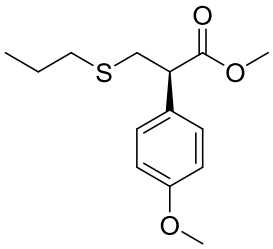
Enantiomerically enriched (90%)



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

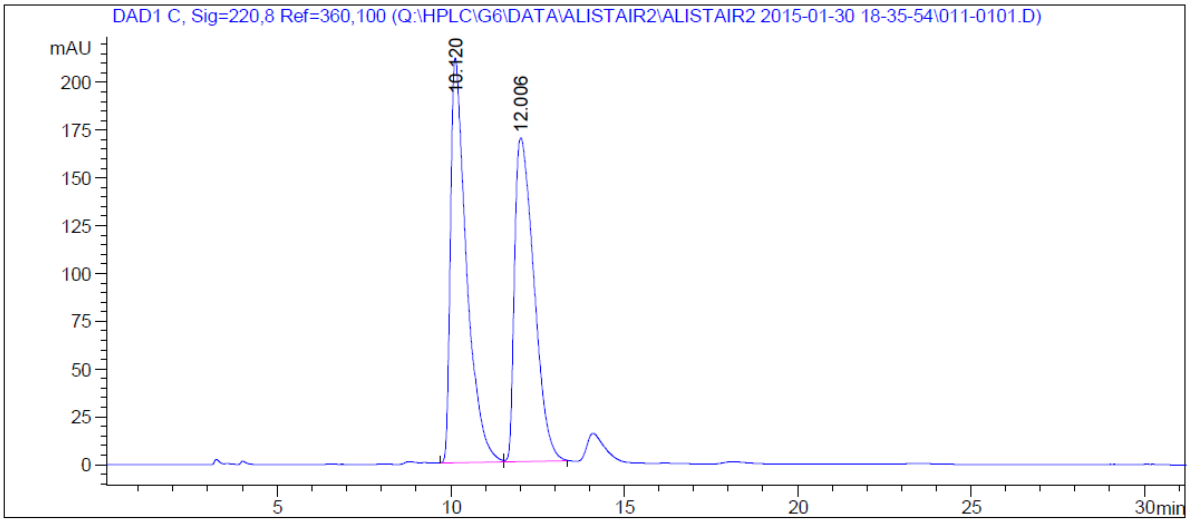
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.473	MF	1.9725	1.71935e4	145.27318	94.8066
2	35.513	FM	2.1852	941.84216	7.18352	5.1934

Methyl (2*R*)-2-(4-methoxyphenyl)-3-(propylsulfanyl)propanoate (**4v**)



(Chiralpak OD-H, hexane/isopropanol = 99/1, 1.0 mL/min)

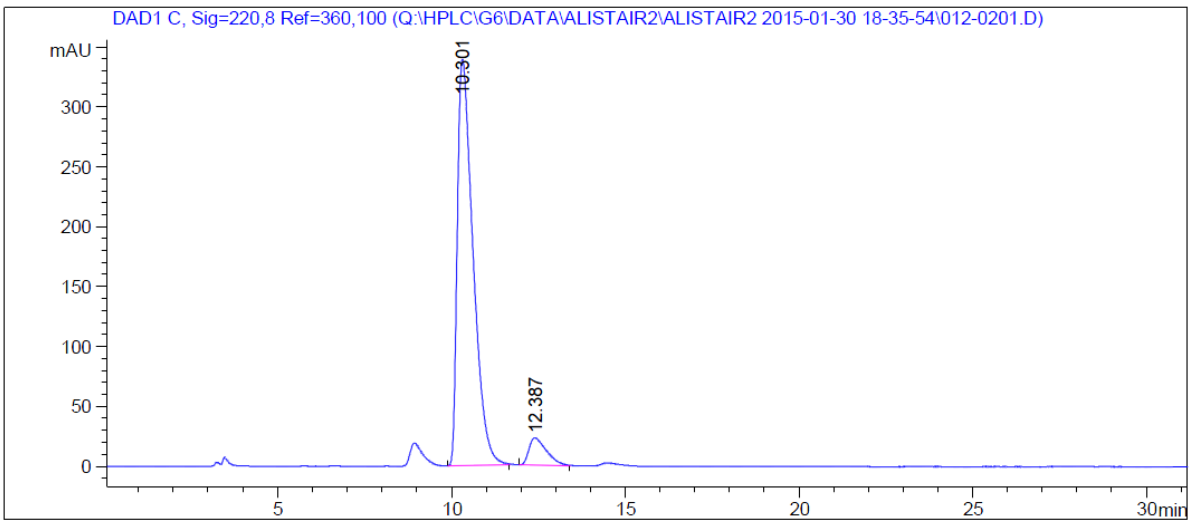
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.120	BB	0.4642	6802.02002	212.07251	50.7977
2	12.006	BB	0.6272	6588.38330	169.62158	49.2023

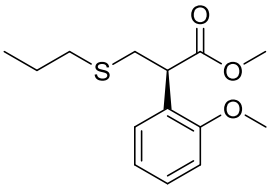
Enantiomerically enriched (86%)



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

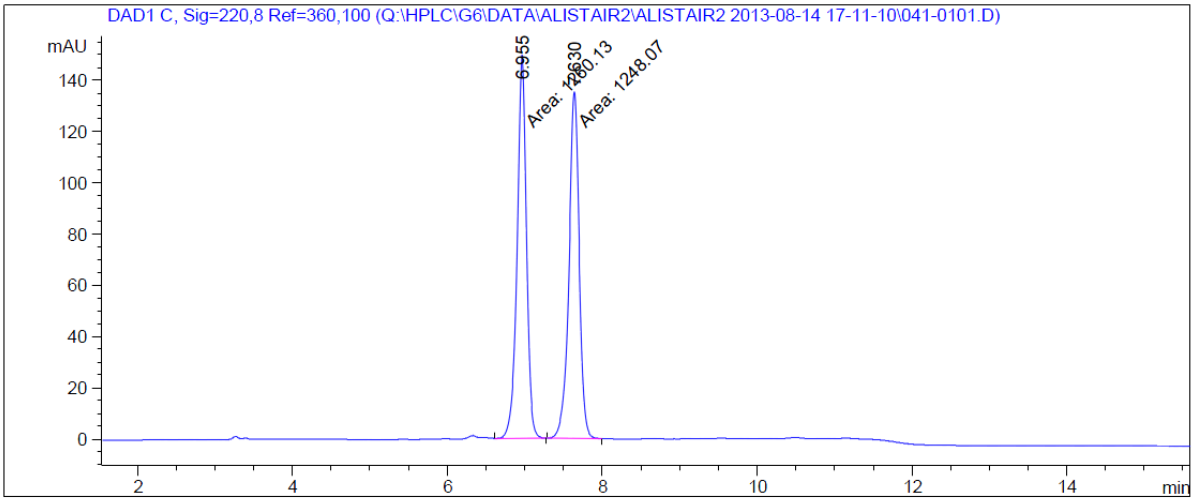
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.301	BB	0.4715	1.06304e4	339.33075	93.0338
2	12.387	BB	0.5106	795.98358	22.72938	6.9662

Methyl (2*R*)-2-(2-methoxyphenyl)-3-(propylsulfanyl)propanoate (**4w**)



(Chiralpak IB, hexane/isopropanol = 99/1, 1.0 mL/min)

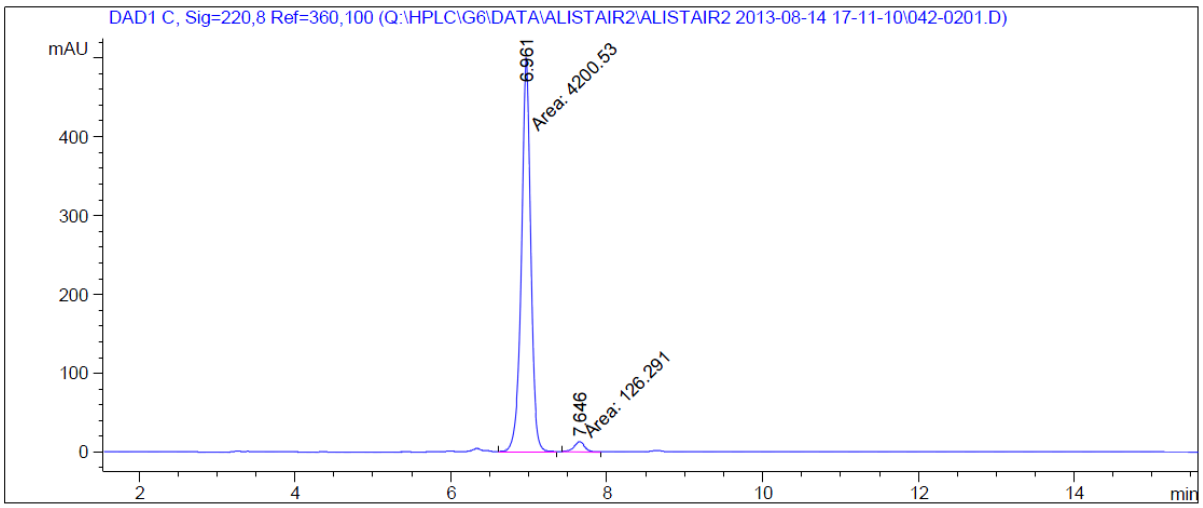
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.955	MM	0.1400	1260.12524	149.98210	50.2404
2	7.630	MM	0.1535	1248.06775	135.50911	49.7596

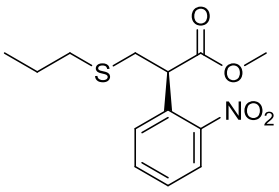
Enantiomerically enriched (94% ee)



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

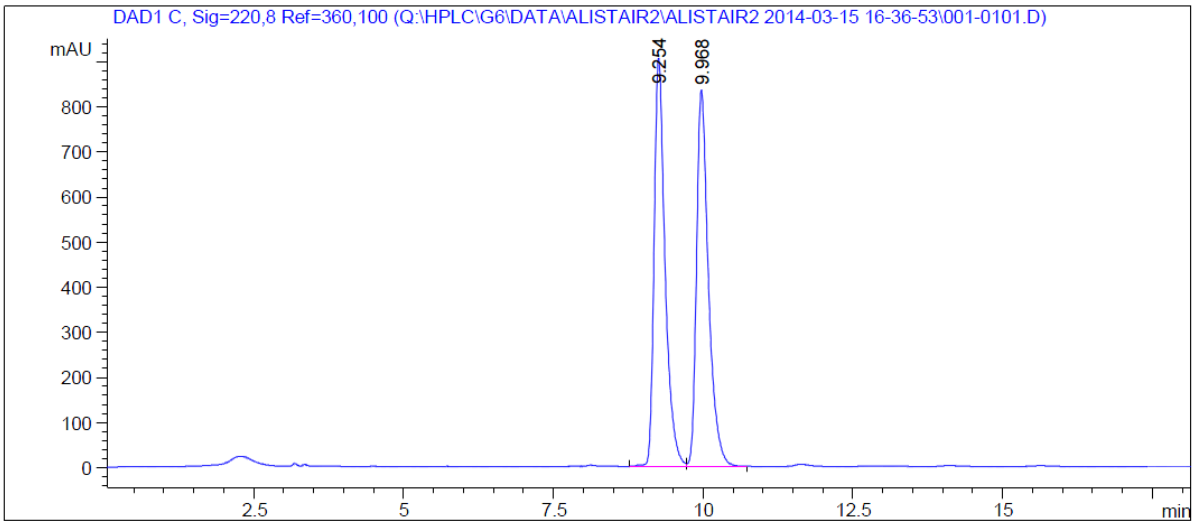
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.961	MM	0.1396	4200.53467	501.45319	97.0812
2	7.646	MM	0.1619	126.29069	13.00457	2.9188

Methyl (2*R*)-2-(2-nitrophenyl)-3-(propylsulfanyl)propanoate (**4x**)



(Chiralpak IA, hexane/isopropanol = 98/2, 1.0 mL/min)

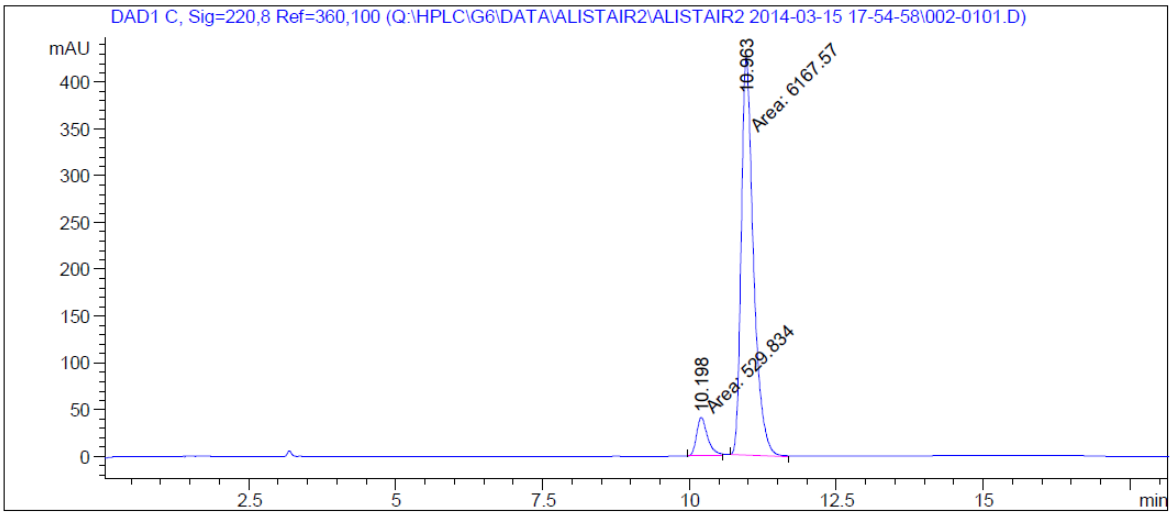
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.254	BV	0.1908	1.15519e4	905.70245	50.0205
2	9.968	VB	0.2094	1.15425e4	834.54340	49.9795

Enantiomerically enriched (84% ee)

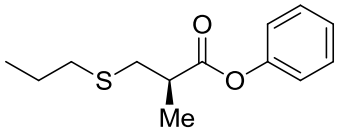


Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.198	MM	0.2162	529.83405	40.83569	7.9110
2	10.963	MM	0.2420	6167.56885	424.79129	92.0890

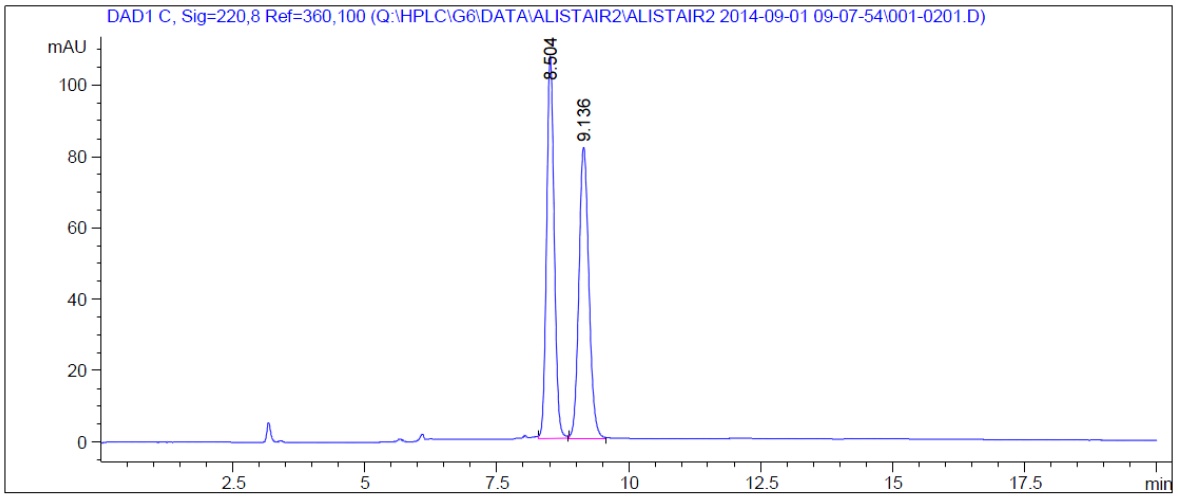
HPLC chromatrogram of 4b (Section 1.6)

Phenyl (2*R*)-2-methyl-3-(propylsulfanyl)propanoate **(4b)**



(Chiralpak AD, hexane/isopropanol = 99/1, 1 mL/min)

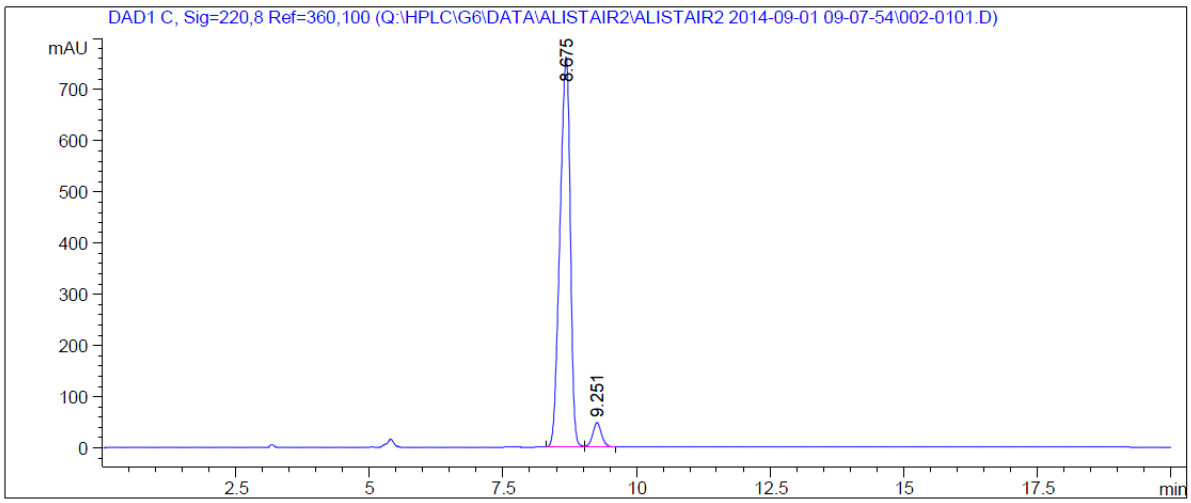
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.504	BB	0.1547	1074.35620	107.35939	50.0898
2	9.136	BB	0.2029	1070.50500	81.68515	49.9102

Enantiomerically enriched (90% ee)

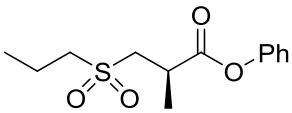


Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.675	BV	0.2164	1.02101e4	761.59033	94.9238
2	9.251	VB	0.1762	545.99976	47.47775	5.0762

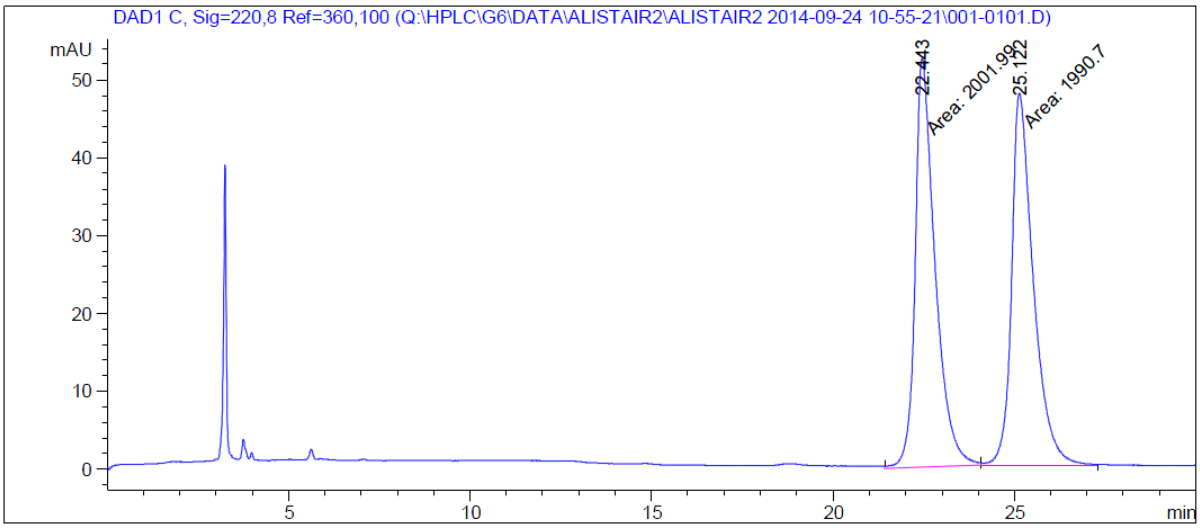
HPLC chromatrograms of derivitization products (Section 1.7)

Phenyl (2*R*)-2-methyl-3-(propane-1-sulfonyl)propanoate (**5a**)



(Chiralpak IB, hexane/isopropanol = 90/10, 1.0 mL/min)

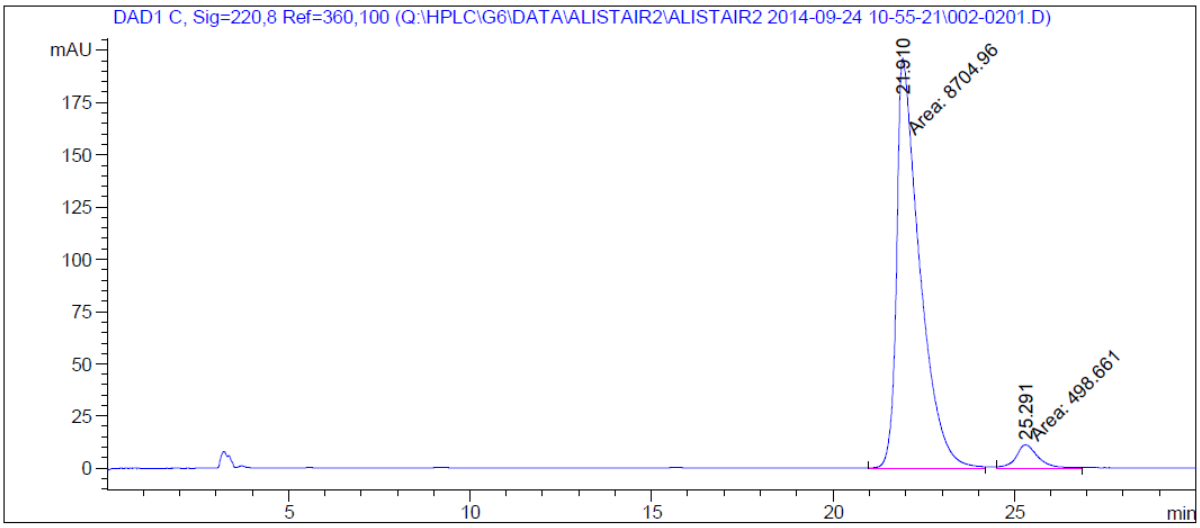
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.443	MM	0.6364	2001.98889	52.43082	50.1414
2	25.122	MM	0.6943	1990.69836	47.78539	49.8586

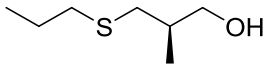
Enantiomerically enriched (89% ee)



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

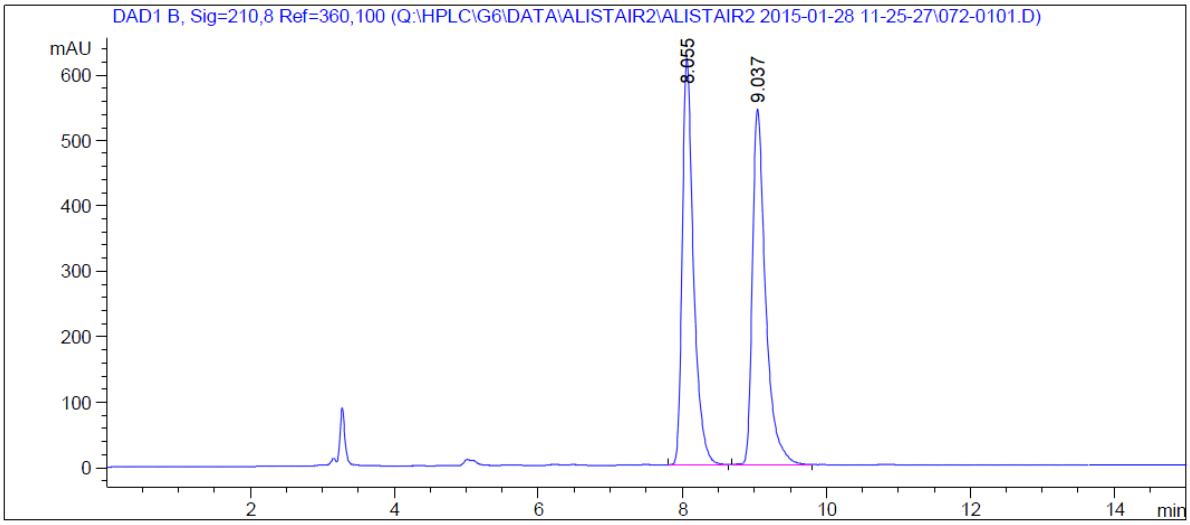
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.910	MM	0.7391	8704.96289	196.28937	94.5819
2	25.291	MM	0.7326	498.66055	11.34513	5.4181

(2*R*)-2-Methyl-3-(propylsulfanyl)propan-1-ol (**5c**)



(Chiralpak IA, hexane/isopropanol = 95/5, 1.0 mL/min)

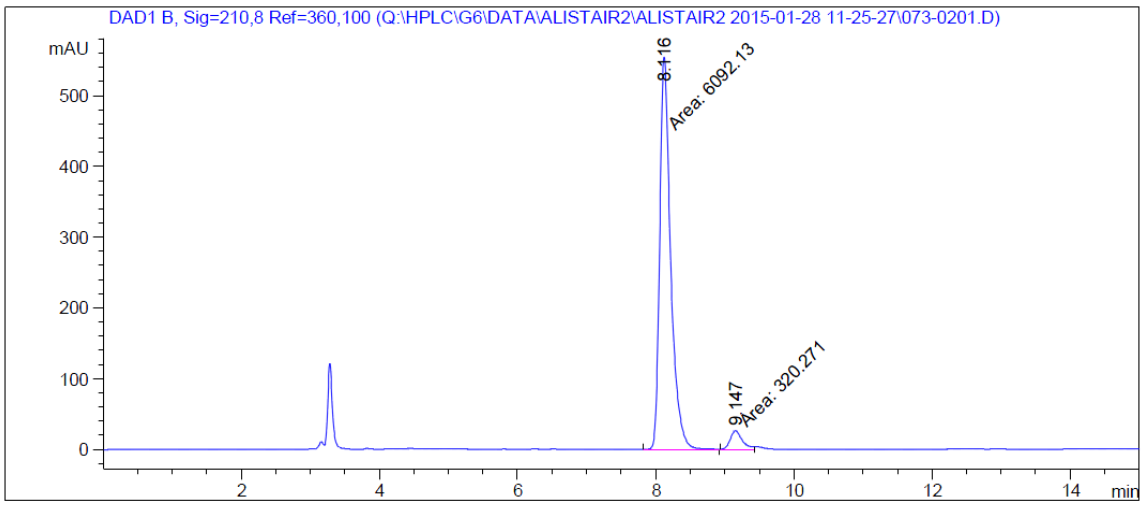
Racemic



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.055	BB	0.1628	6770.53906	622.91791	49.4841
2	9.037	BB	0.1878	6911.72168	545.50507	50.5159

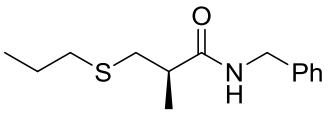
Enantiomerically enriched (90% ee)



Signal 2: DAD1 B, Sig=210,8 Ref=360,100

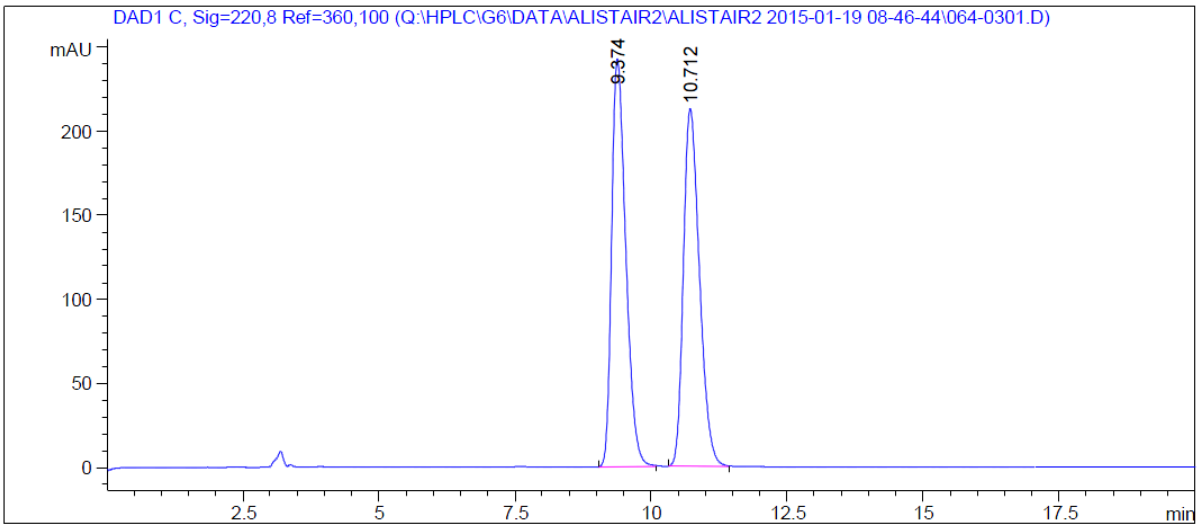
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.116	MM	0.1829	6092.12598	555.17358	95.0054
2	9.147	MF	0.2041	320.27051	26.15010	4.9946

(2*R*)-*N*-Benzyl-2-methyl-3-(propylsulfanyl)propanamide (**5d**)



(Chiralpak AD, hexane/isopropanol = 90/10, 1.0 mL/min)

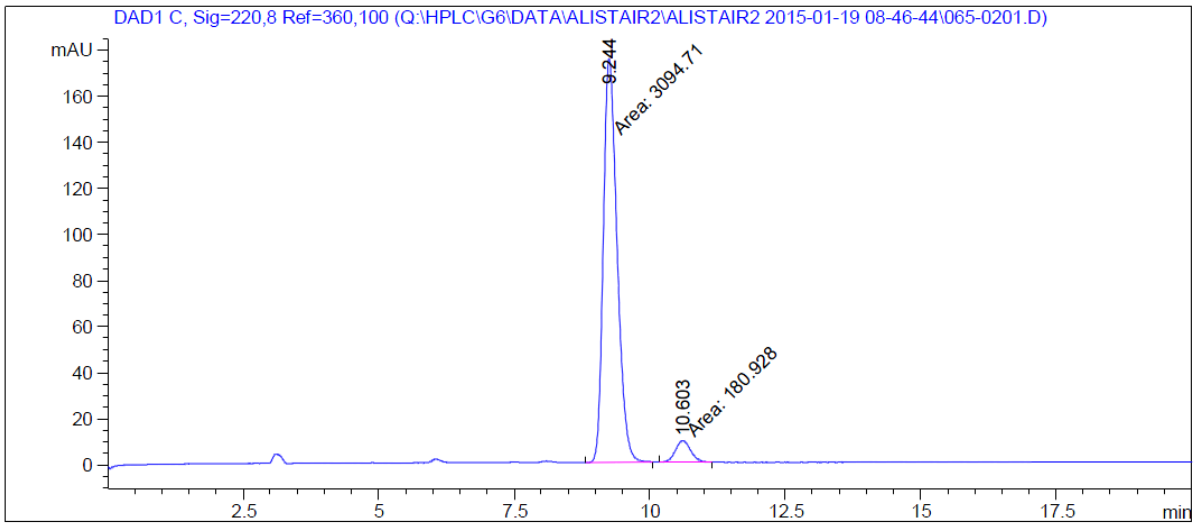
Racemic



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.374	BB	0.2788	4383.32178	242.61737	50.1229
2	10.712	BB	0.3174	4361.82031	212.56367	49.8771

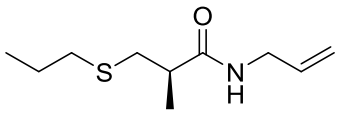
Enantiomerically enriched (89% ee)



Signal 3: DAD1 C, Sig=220,8 Ref=360,100

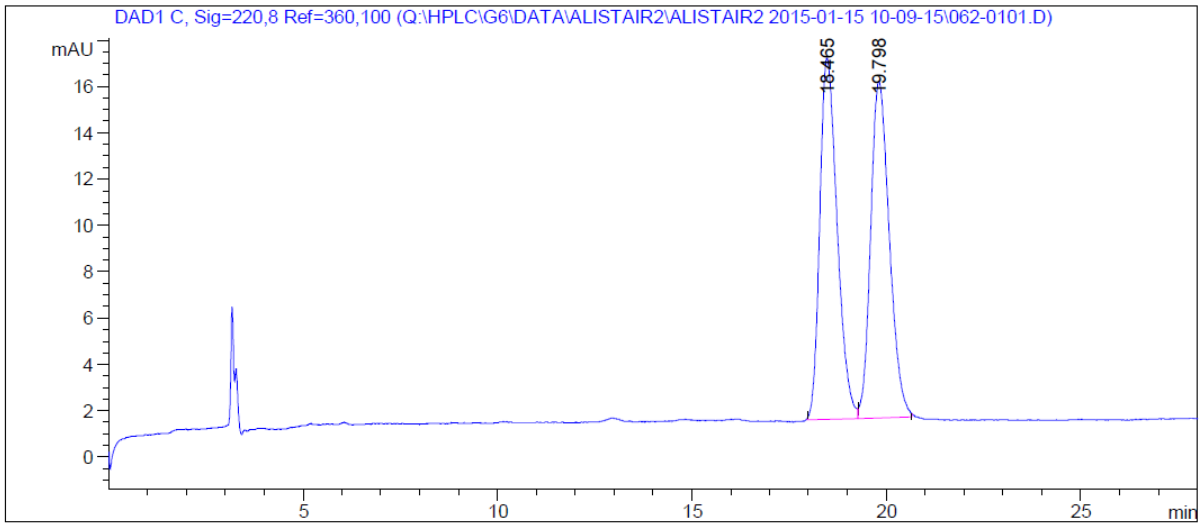
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.244	MM	0.2943	3094.70923	175.23845	94.4766
2	10.603	MM	0.3242	180.92786	9.30256	5.5234

(2*R*)-2-Methyl-*N*-(prop-2-en-1-yl)-3-(propylsulfanyl)propanamide (**5e**)



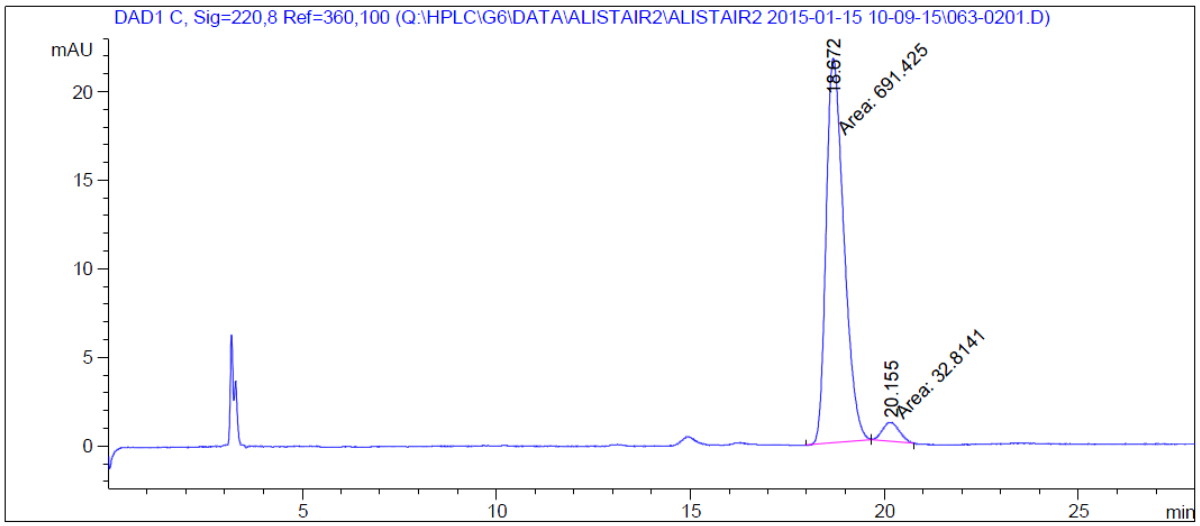
(Chiralpak AD, hexane/isopropanol = 97/3, 1.0 mL/min)

Racemic



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.465	BB	0.4786	484.76907	15.59776	50.0089
2	19.798	BB	0.5053	484.59735	14.52420	49.9911

Enantiomerically enriched (91% ee)

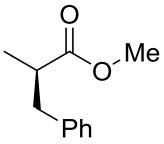


Signal 3: DAD1 C, Sig=220,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.672	MM	0.5312	691.42468	21.69448	95.4692
2	20.155	MM	0.5071	32.81410	1.07847	4.5308

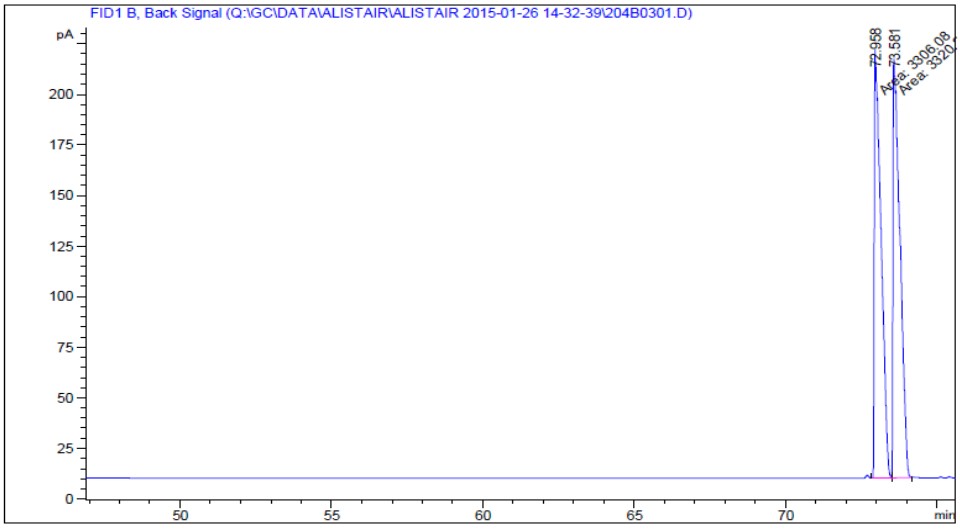
GC chromatrograms of derivitization products (Section 1.8)

Methyl (2*R*)-2-methyl-3-phenylpropanoate **22**



(Supelco β-dex™ 325)

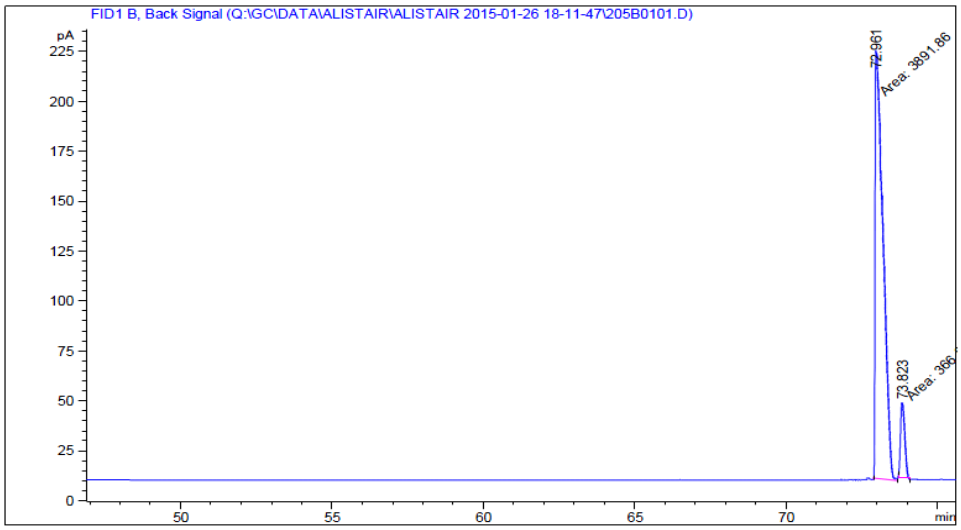
Racemic



Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	72.958	MF	0.2598	3306.08081	212.09502	49.89289
2	73.581	FM	0.2671	3320.27515	207.15094	50.10711

Enantiomerically enriched (83%)



Signal 1: FID1 B, Back Signal

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	72.961	MM	0.3023	3891.86060	214.58572	91.38650
2	73.823	MM	0.1630	366.82138	37.51637	8.61350