Asymmetric additions of thioglycolates and N-Boc aldimines catalyzed by a bifunctional tertiary-amine squaramide

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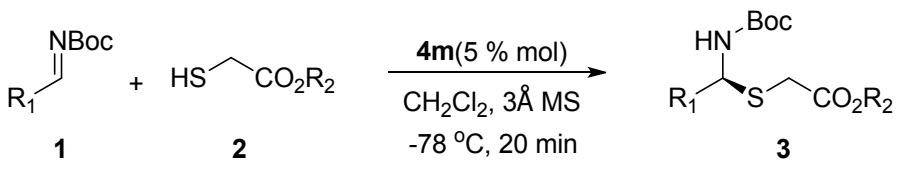
Table of Contents

General Information

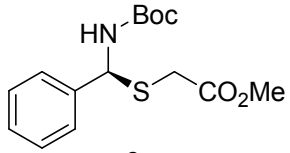
Commercial reagents were used as received, unless otherwise stated. ^{1}H and ^{13}C NMR were recorded on 400 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard. The following abbreviations were used to designate chemical shift mutiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m). Mass spectra were obtained using electrospray ionization (ESI) or electron impact ionization (EI) mass spectrometer. In each case, enantiomeric ratio was determined by chiral HPLC analysis on Chiralcel column in comparison with authentic racemates. N-Boc aldimines **1a-o** were prepared according to previously reported procedures.[1]

General experimental reaction procedure:



1 **2** **3**

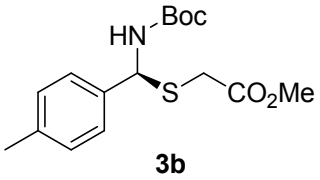
To a 10-mL test-tube were sequentially added catalyst (0.005 equiv), CH_2Cl_2 (2.0 mL), 80mg 3Å molecular sieves and the Boc-protected imine **1** (1.0 equiv). The mixture was cooled to -78 °C and stirred for 30 min. Alkyl thioglycolate (0.24 mmol) was then added. The reaction mixture was stirred at -78 °C and monitored by TLC. Upon completion, the residual was purified by silica gel flash chromatography (petroleum ether: ethyl acetate, 5:1) to afford the desired product.



3a

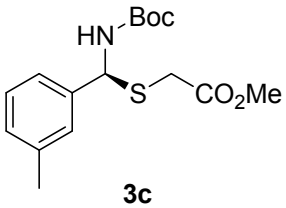
The title compound was prepared according to general procedure to get colorless oil (57.9 mg, 93%). $[\alpha]^{25}D$ = -5.4 (c = 1.00, $CHCl_3$); ^{1}H

NMR (400 MHz, Chloroform-d) δ 7.41 (d, J = 7.0 Hz, 2H), 7.37 – 7.33 (m, 2H), 7.31 – 7.26 (m, 1H), 6.14 (d, J = 9.8 Hz, 1H), 5.65 (d, J = 9.8 Hz, 1H), 3.74 (s, 3H), 3.32 (dd, J = 15.9 Hz, 2H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.23, 154.54, 138.58, 128.70, 128.26, 126.51, 80.30, 59.05, 52.63, 32.79, 28.29. HRMS (ESI) Exact mass calcd for $C_{15}H_{21}NO_4S$ $[M+Na]^+$: 334.1089, found 334.1079. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 3:97),1.0 mL/min; t_R = 12.4 min (minor), 13.4 min (major).



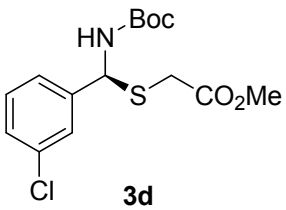
3b

The title compound was prepared according to general procedure to get yellow oil (68.3 mg, 97%). $[\alpha]^{25}D$ = -3.8 (c = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, Chloroform-d) δ 7.21 (d, J = 7.9 Hz, 2H), 7.07 (d, J = 7.8 Hz, 2H), 6.02 (d, J = 9.8 Hz, 1H), 5.56 (d, J = 9.9 Hz, 1H), 3.66 (s, 3H), 3.31 – 3.15 (dd, 2H), 2.25 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.31, 154.55, 138.07, 135.61, 129.44, 126.49, 80.21, 58.88, 52.72, 32.83, 28.35, 21.21. HRMS (ESI) Exact mass calcd for $C_{16}H_{23}NO_4S$ $[M+ Na]^+$: 348.1245, found 348.1239. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 3:97),1.0mL/min; t_R=11.9min(minor), 9.5 min (major).



3c

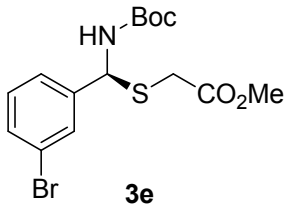
The title compound was prepared according to general procedure to get yellow oil (62.4 mg, 96%). $[\alpha]^{25}D$ = 1.0 (c = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, Chloroform-d) δ 7.28 – 7.18 (m, 3H), 7.12 – 7.08 (m, 1H), 6.09 (d, J = 9.8 Hz, 1H), 5.60 (d, J = 9.8 Hz, 1H), 3.75 (s, 3H), 3.43 – 3.25 (dd, 2H), 2.35 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.24, 154.54, 138.48, 135.28, 129.06, 128.60, 127.17, 123.48, 80.26, 59.07, 52.62, 32.89, 28.29, 21.42. HRMS (ESI) Exact mass calcd for $C_{16}H_{23}NO_4S$ $[M+Na]^+$: 348.1245, found 348.1239. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 1:19), 1.0 mL/min; t_R = 8.6 min (minor), 7.4 min (major).



3d

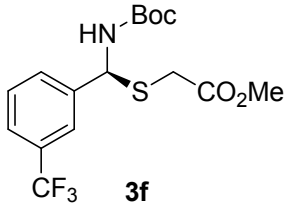
The title compound was prepared according to general procedure to

get colorless oil (63.5 mg, 92%). $[\alpha]^{25}D$ = -3.8 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 7.41 (d, J = 2.1 Hz, 1H), 7.30 – 7.25 (m, 3H), 6.10 (d, J = 9.6 Hz, 1H), 5.77 (d, J = 9.6 Hz, 1H), 3.75 (s, 3H), 3.38 – 3.25 (dd, 2H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.17, 154.54, 140.68, 134.57, 129.97, 128.40, 126.75, 124.84, 80.55, 58.35, 52.74, 32.72, 28.28. HRMS (ESI) Exact mass calcd for $C_{15}H_{20}ClNO_4S$ $[M+Na]^+$: 368.0699, found 368.0696. Enantiomeric excess was determined by HPLC with an AD-H column at 210 nm (2-propanol: hexane = 1:19), 1.0 mL/min; t_R = 11.1 min (minor), 11.8 min (major).



3e

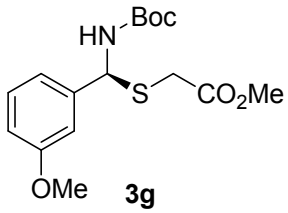
The title compound was prepared according to general procedure to get yellow oil (52.6 mg, 91%). $[\alpha]^{25}D$ = -6.6 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 7.49 (t, J = 1.9 Hz, 1H), 7.34 (dt, J = 7.9, 1.4 Hz, 1H), 7.27 (dt, J = 7.9, 1.2 Hz, 1H), 7.14 (t, J = 7.8 Hz, 1H), 6.01 (d, J = 9.6 Hz, 1H), 5.67 (d, J = 9.7 Hz, 1H), 3.68 (s, 3H), 3.31 – 3.14 (dd, 2H), 1.38 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.17, 154.52, 140.89, 131.41, 130.30, 129.68, 125.32, 122.72, 80.56, 58.27, 52.86, 32.74, 28.33. HRMS (ESI) Exact mass calcd for $C_{15}H_{20}BrNO_4S$ $[M+NH_4]^+$: 407.0640, found 407.0626. Enantiomeric excess was determined by HPLC with an AD-H column at 210 nm (2-propanol: hexane = 1:9),1.0 mL/min; t_R = 7.7 min (minor), 8.2 min (major).



3f

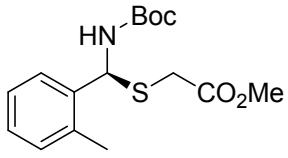
The title compound was prepared according to general procedure to get colorless oil (69.0 mg, 91%). $[\alpha]^{25}D$ = -3.6 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 7.67 (s, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.48 (t, J = 7.7 Hz, 1H), 6.17 (d, J = 9.5 Hz, 1H), 5.77 (d, J = 9.5 Hz, 1H), 3.76 (s, 3H), 3.32 (dd, J = 3.9 Hz, 2H), 1.46 (s, 9H). ^{13}C NMR

(100 MHz, Chloroform-d) δ 171.13, 154.59, 139.76, 130.89, 130.09, 129.24, 125.11, 123.36, 122.51, 80.71, 58.45, 52.80, 32.77, 28.26. HRMS (ESI) Exact mass calcd for $C_{16}H_{20}F_3NO_4S$ [M+Na]$^+$: 402.0963, found 402.0958. Enantiomeric excess was determined by HPLC with an AD-H column at 210 nm (2-propanol: hexane = 3:97), 1.0 mL/min; t_R = 10.8 min (minor), 11.9 min (major).



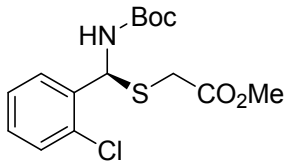
3g

The title compound was prepared according to general procedure to get colorless oil (64.8 mg, 95%). [α]^{25}D = 3.6 (c = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, Chloroform-d) δ 7.22 – 7.14 (m, 1H), 6.95 – 6.89 (m, 1H), 6.87 (t, J = 2.1 Hz, 1H), 6.75 (dd, J = 8.2, 2.6 Hz, 1H), 6.02 (d, J = 9.8 Hz, 1H), 5.64 (d, J = 9.8 Hz, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 3.25 (dd, J = 15.9 Hz, 2H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.28, 159.78, 154.57, 140.11, 129.77, 118.77, 113.84, 112.15, 80.29, 58.97, 55.28, 52.65, 32.80, 28.30.HRMS (ESI) Exact mass calcd for $C_{16}H_{23}NO_5S$ [M+Na]$^+$: 364.1195, found 364.1194. Enantiomeric excess was determined by HPLC with an AD-H column at 210 nm (2-propanol: hexane = 1:9), 1.0 mL/min; t_R = 11.8 min (minor), 14.8 min (major).



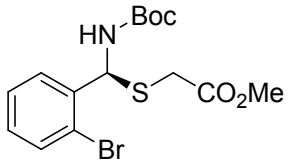
3h

The title compound was prepared according to general procedure to get white solid (57.2 mg, 88%). [α]^{25}D = -13.4 (c = 0.50, $CHCl_3$); ^{1}H NMR (400 MHz, Chloroform-d) δ 7.29 – 7.25 (m, 1H), 7.16 – 7.04 (m, 3H), 6.17 (d, J = 9.7 Hz, 1H), 5.65 (d, J = 9.7 Hz, 1H), 3.68 (s, 3H), 3.37 – 3.14 (dd, 2H), 2.39 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.24, 154.59, 136.82, 135.21, 130.90, 128.22, 126.24, 125.55, 80.22, 55.91, 52.64, 32.94, 28.31, 19.07. HRMS (ESI) Exact mass calcd for $C_{16}H_{23}NO_4S$ [M+Na]$^+$: 348.1245, found 348.1242. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 1:9), 1.0 mL/min; t_R = 7.0 min (minor), 6.4 min (major).



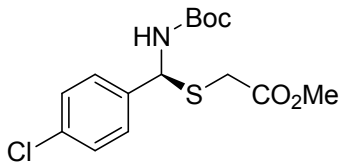
3i

The title compound was prepared according to general procedure to get yellow oil (64.2 mg, 93%). $[\alpha]^{25}$D = 7.4 (c = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, Chloroform-d) δ 7.44 (d, J = 7.4 Hz, 1H), 7.38 (dd, J = 7.3, 1.8 Hz, 1H), 7.26 (qd, J = 7.1, 2.1 Hz, 2H), 6.39 (d, J = 9.3 Hz, 1H), 5.93 (d, J = 9.4 Hz, 1H), 3.76 (s, 3H), 3.48 – 3.27 (dd, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.24, 154.38, 136.28, 132.44, 130.24, 129.46, 127.77, 127.05, 80.41, 56.60, 52.75, 33.18, 28.29. HRMS (ESI) Exact mass calcd for $C_{15}H_{20}ClNO_4S$ $[M+Na]^+$: 368.0699, found 368.0696. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 1:4), 1.0 mL/min; t_R = 6.0 min (minor), 5.5 min (major).



3j

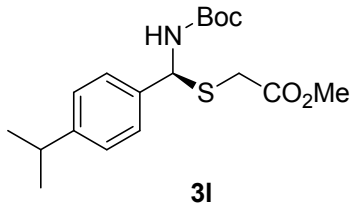
The title compound was prepared according to general procedure to get white solid (73.1 mg, 94%). $[\alpha]^{25}$D = 5.8 (c = 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, Chloroform-d) δ 7.57 (dd, J = 8.0, 1.2 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.32 (td, J = 7.6, 1.2 Hz, 1H), 7.16 (td, J = 7.7, 1.7 Hz, 1H), 6.35 (d, J = 9.2 Hz, 1H), 5.88 (d, J = 9.2 Hz, 1H), 3.77 (s, 3H), 3.37 (dd, J = 6.3 Hz, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.22, 154.30, 137.94, 133.56, 129.69, 127.84, 122.65, 80.45, 59.02, 52.75, 33.25, 29.70, 28.29. HRMS (ESI) Exact mass calcd for $C_{15}H_{20}BrNO_4S$ $[M+Na]^+$: 412.0194, found 412.0184. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 1:4), 1.0 mL/min; t_R = 6.9 min (minor), 6.0 min (major).



3k

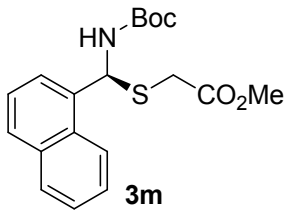
The title compound was prepared according to general procedure

to get colorless oil (62.1 mg, 90%). $[\alpha]^{25}D$ = 6.0 (c = 0.50, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 7.37 – 7.30 (m, 4H), 6.10 (d, J = 9.6 Hz, 1H), 5.71 (d, J = 9.7 Hz, 1H), 3.75 (s, 3H), 3.37 – 3.20 (dd, 2H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.25, 154.52, 137.18, 134.02, 128.84, 127.96, 80.52, 58.33, 52.75, 32.69, 28.29. HRMS (ESI) Exact mass calcd for $C_{15}H_{20}ClNO_4S$ $[M+Na]^+$: 368.0699, found 368.0696. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 3:97), 1.0 mL/min; t_R = 10.7 min (minor), 9.7 min (major).



3l

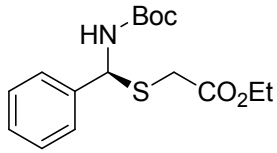
The title compound was prepared according to general procedure to get colorless oil (66.4 mg, 94%). $[\alpha]^{25}D$ = -2.4 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 7.44 (d, J = 7.4 Hz, 1H), 7.38 (dd, J = 7.3, 1.8 Hz, 1H), 7.26 (qd, J = 7.1, 2.1 Hz, 2H), 6.39 (d, J = 9.3 Hz, 1H), 5.93 (d, J = 9.4 Hz, 1H), 3.76 (s, 3H), 3.44 – 3.27 (dd, 2H), 1.44 (s, 9H).^{13}C NMR (100 MHz, Chloroform-d) δ 171.29, 154.55, 149.03, 135.94, 126.78, 126.46, 80.22, 58.95, 52.63, 33.82, 32.89, 28.31, 23.92. HRMS (ESI) Exact mass calcd for $C_{18}H_{27}NO_4S$ $[M+Na]^+$: 376.1558, found 376.1555. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 3:97), 1.0 mL/min; t_R = 9.0 min (minor), 7.7 min (major).



3m

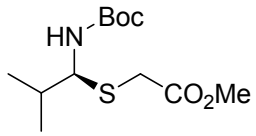
The title compound was prepared according to general procedure to get yellow oil (69.3 mg, 96%). $[\alpha]^{25}D$ = -1.2 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 8.30 (d, J = 8.6 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.79 (d, J = 8.2 Hz, 1H), 7.57 (t, J = 8.2 Hz, 2H), 7.49 (t, J = 7.5 Hz, 1H), 7.42 (t, J = 7.7 Hz, 1H), 6.87 (d, J = 9.6 Hz, 1H), 5.95 (d, J = 9.6 Hz, 1H), 3.75 (s, 3H), 3.35 (dd, J = 16.2 Hz, 2H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.36, 154.69, 134.18, 133.93, 129.80, 129.22, 128.82, 126.66, 126.10, 125.02, 124.05, 123.48, 80.39,

55.91, 52.73, 33.06, 28.34. HRMS (ESI) Exact mass calcd for $C_{19}H_{23}NO_4S$ $[M+Na]^+$: 384.1245, found 384.1242. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 3:97), 1.0 mL/min; t_R = 15.3 min (minor), 18.4 min (major).



3n

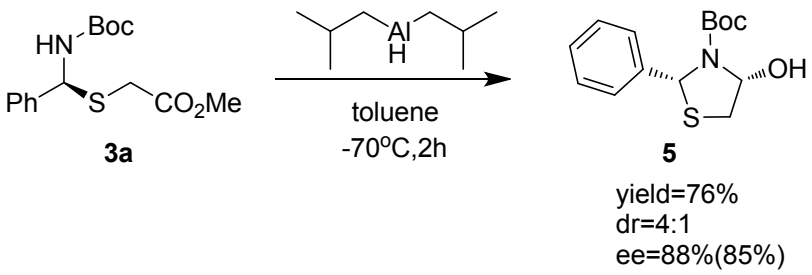
The title compound was prepared according to general procedure to get colorless oil (68.2 mg, 98%). $[\alpha]^{25}D$ = -1.2 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 7.37 – 7.29 (m, 2H), 7.24 – 7.15 (m, 2H), 6.11 (d, J = 9.8 Hz, 1H), 5.61 (d, J = 9.9 Hz, 1H), 3.74 (s, 3H), 3.42 – 3.22 (dd, 2H), 2.95 – 2.81 (m, 1H), 1.44 (s, 9H), 1.23 (d, J = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-d) δ 170.82, 154.57, 138.61, 128.68, 128.21, 126.54, 80.24, 61.69, 58.92, 32.93, 28.31, 14.14. HRMS (ESI) Exact mass calcd for $C_{16}H_{23}NO_4S$ $[M+Na]^+$: 348.1245 found 348.1240. Enantiomeric excess was determined by HPLC with an OD-H column at 210 nm (2-propanol: hexane = 3:97), 1.0 mL/min; t_R = 19.7 min (minor), 18.6 min (major).



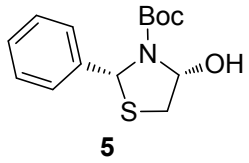
3o

The title compound was prepared according to general procedure to get colorless oil (51.5 mg, 93%). $[\alpha]^{25}D$ = -22.0 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 4.88 (s, 2H), 3.74 (s, 3H), 3.53 – 3.21 (dd, 2H), 1.98 (s, 1H), 1.45 (s, 9H), 1.00 (d, J = 6.7 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-d) δ 171.01, 155.27, 79.85, 63.02, 52.46, 33.72, 32.47, 28.24, 19.30, 18.27. HRMS (ESI) Exact mass calcd for $C_{12}H_{23}NO_4S$ $[M+Na]^+$: 300.1240, found 300.1245. Enantiomeric excess was determined by HPLC with an AD-H column at 210 nm (2-propanol: hexane = 1:19), 1.0 mL/min; t_R = 7.9 min (minor), 8.9 min (major).

Cyclization of compound **3a** into compound **5**.[2]



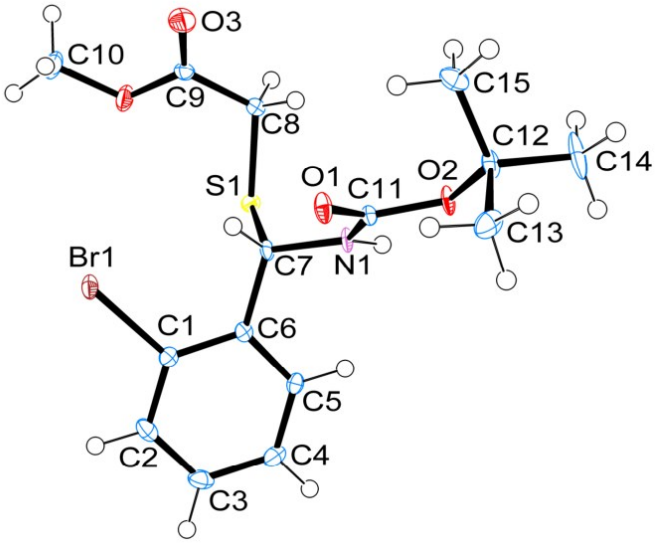
To the solution of the compound **3a** (622 mg) in dry toluene (12 ml), diisobutylaluminum hydride (1.01 N toluene solution; 2 ml) was slowly added at -70 °C. The mixture was stirred for 2 hours. A saturated aqueous solution of sodium sulfate was added to the reaction mixture, and then the mixture was filtrated at room temperature. The filtrate was concentrated in vacuo, the residue was purified by flash column chromatography (silica gel, ethyl acetate/petroleum ether 1:5) to give **5** (828mg, 76% yield, 88% ee) as a colorless oil.



5

The title compound was prepared according to general procedure to get olorless oil (828 mg, 76%). $[\alpha]^{25}D$ = -186.0 (c = 1.00, $CHCl_3$); ^1H NMR (400 MHz, Chloroform-d) δ 7.44 (dd, J = 7.2, 1.9 Hz, 2H), 7.32 (dd, J = 8.2, 6.4 Hz, 2H), 7.28 – 7.25 (m, 1H), 5.93 (d, J = 59.9 Hz, 2H), 4.18 (s, 1H), 3.29 (dd, J = 12.0, 4.9 Hz, 1H), 3.09 (dd, J = 12.0, 3.3 Hz, 1H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-d) δ 153.37, 141.80, 128.34, 127.73, 126.40, 84.59, 81.49, 65.02, 36.84, 27.98. HRMS (ESI) Exact mass calcd for $C_{14}H_{19}NO_3S$ $[M+Na]^+$: 304.0983, found 304.0975. Enantiomeric excess was determined by HPLC with an AD-H column at 210 nm (2-propanol: hexane = 3:97), 1.0 mL/min; t_R = 11.2 min (minor), 14.3 min (major).

ORTEP Drawing of Compound 3j:

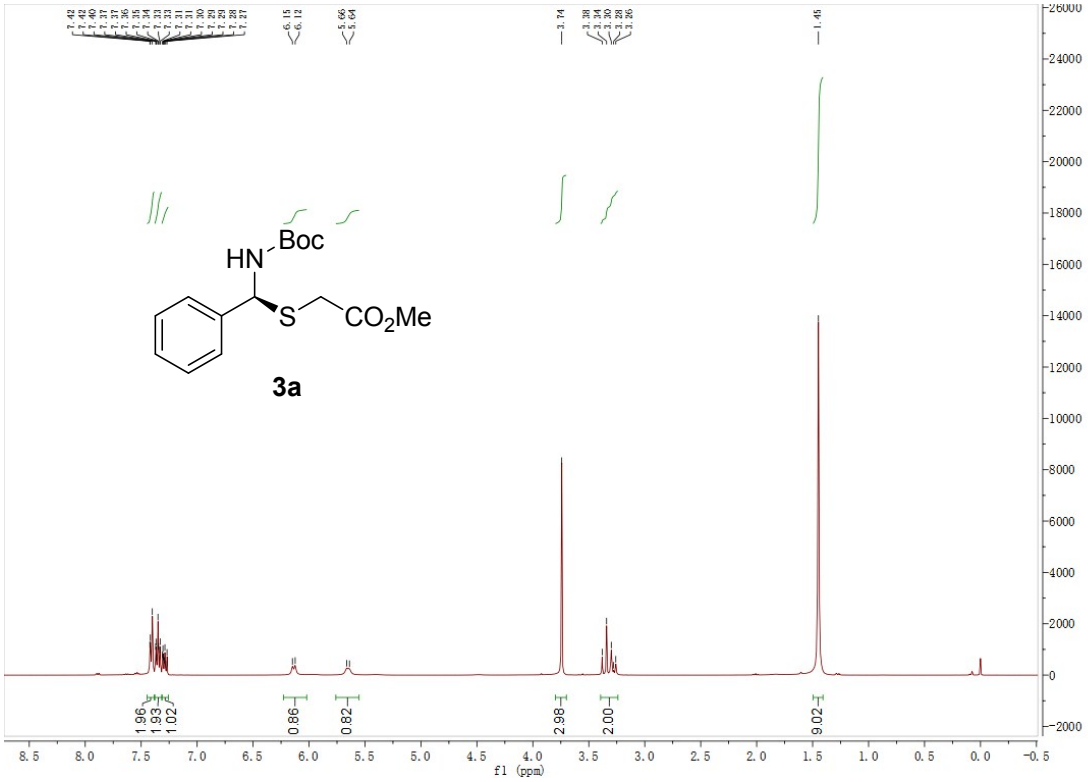


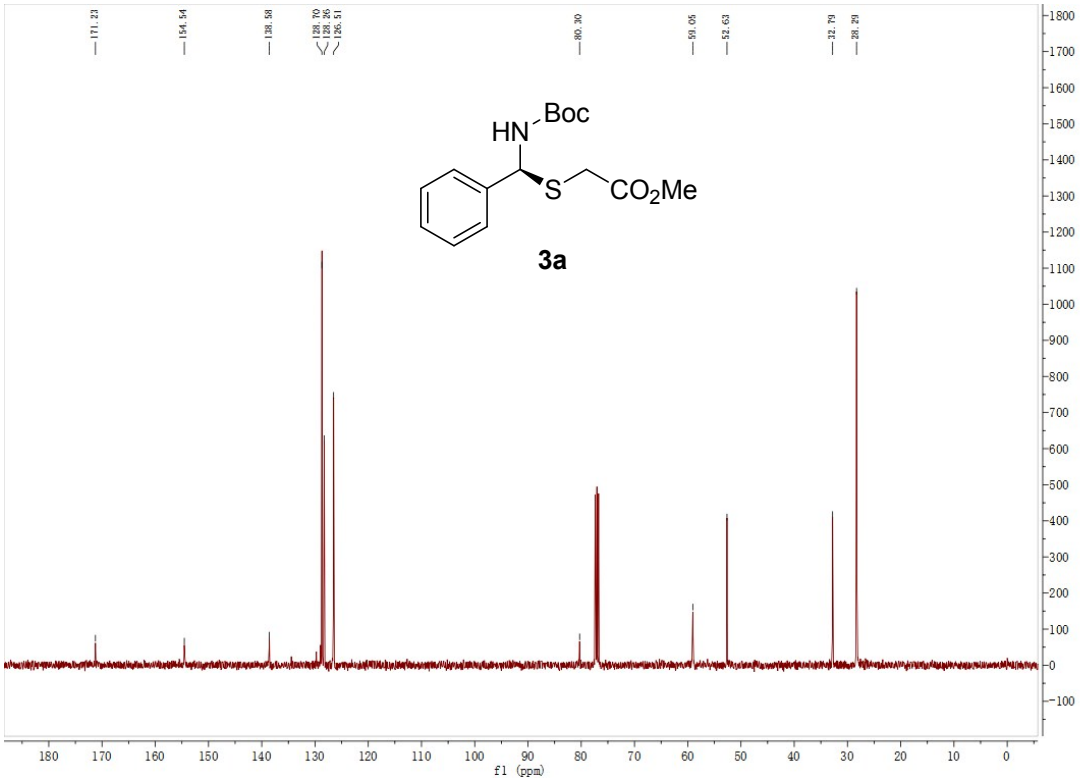
Crystal data and structure refinement for 3j

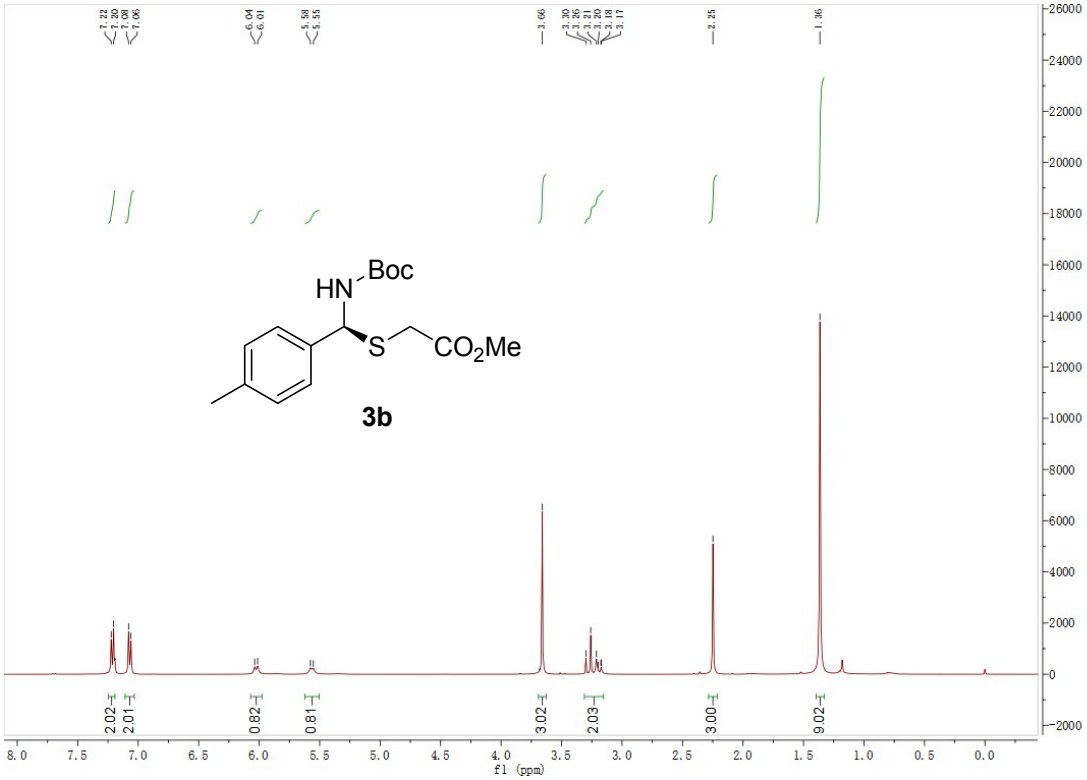
Identification code	shelx
Empirical formula	C15 H20 Br N O4 S
Formula weight	390.29
Temperature	113(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 5.1680(5) A alpha = 90 deg. b = 10.0269(12) A beta = 90 deg. c = 32.073(4) A gamma = 90 deg.
Volume	1662.0(3) A^3
Z, Calculated density	4, 1.560 Mg/m^3
Absorption coefficient	2.615 mm^-1
F(000)	800
Crystal size	0.20 x 0.18 x 0.12 mm
Theta range for data collection	3.25 to 27.49 deg.
Limiting indices	-6<=h<=6, -13<=k<=12, -41<=l<=41
Reflections collected / unique	16927 / 3804 [R(int) = 0.0424]
Completeness to theta = 27.49	99.8 %

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7443 and 0.6228
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3804 / 1 / 207
Goodness-of-fit on F^2	1.024
Final R indices [I>2sigma(I)]	R1 = 0.0186, wR2 = 0.0443
R indices (all data)	R1 = 0.0198, wR2 = 0.0444
Absolute structure parameter	0.007(5)
Largest diff. peak and hole	0.264 and -0.621 e.A^-3

NMR Spectra (^{1}H NMR, ^{13}C NMR)



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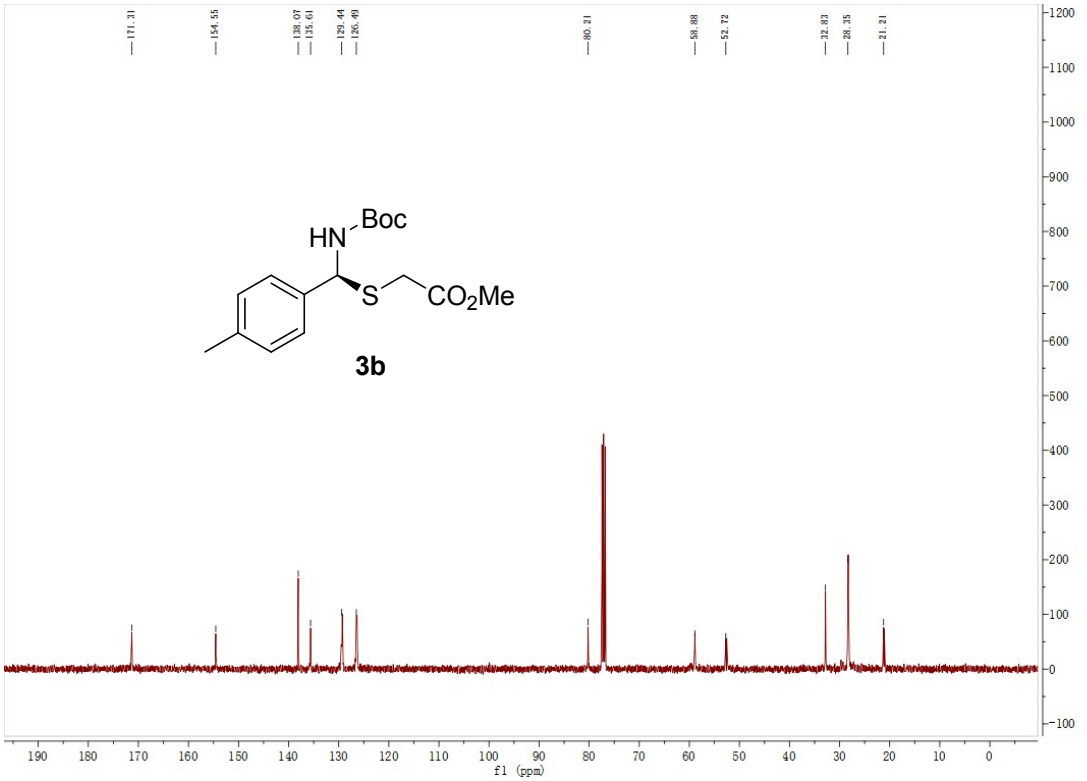
S
CO2Me
3b
f1 (ppm)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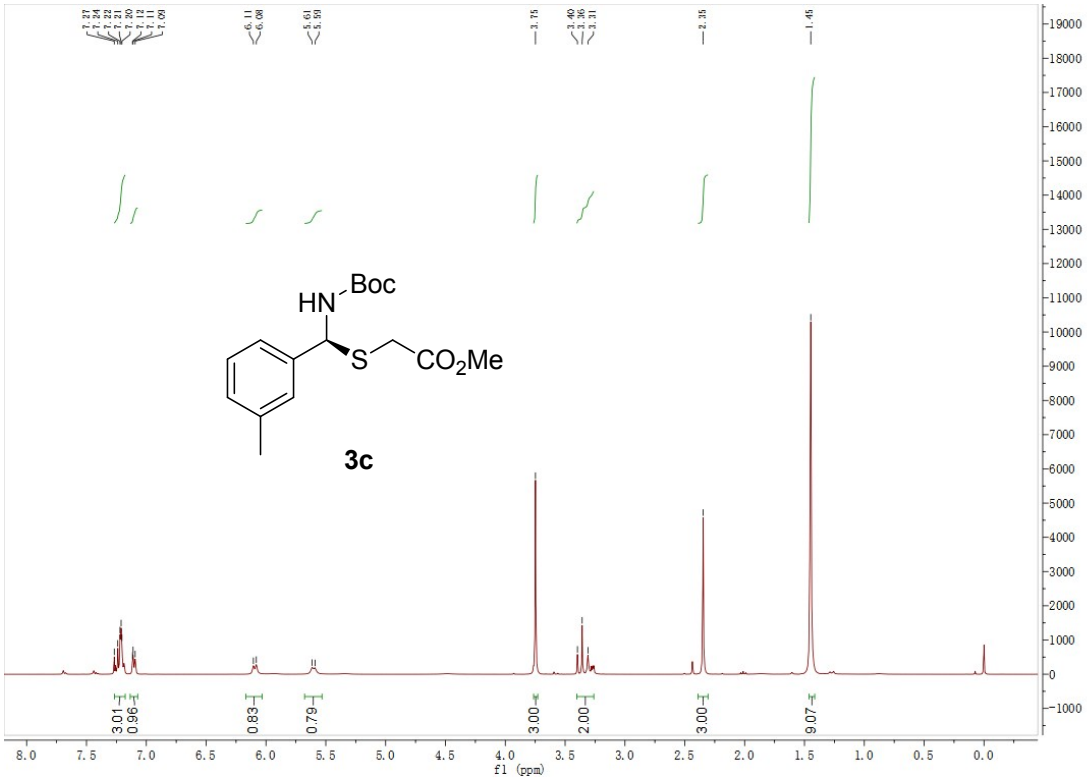
CO2Me
3b
f1 (ppm)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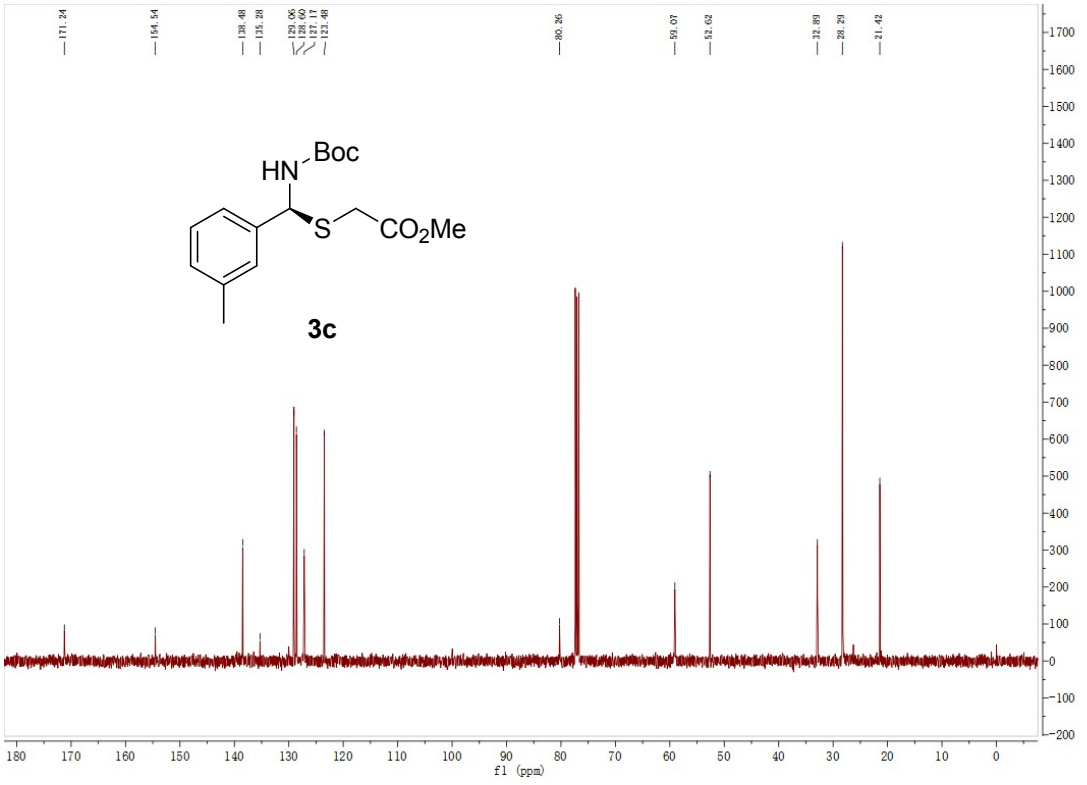
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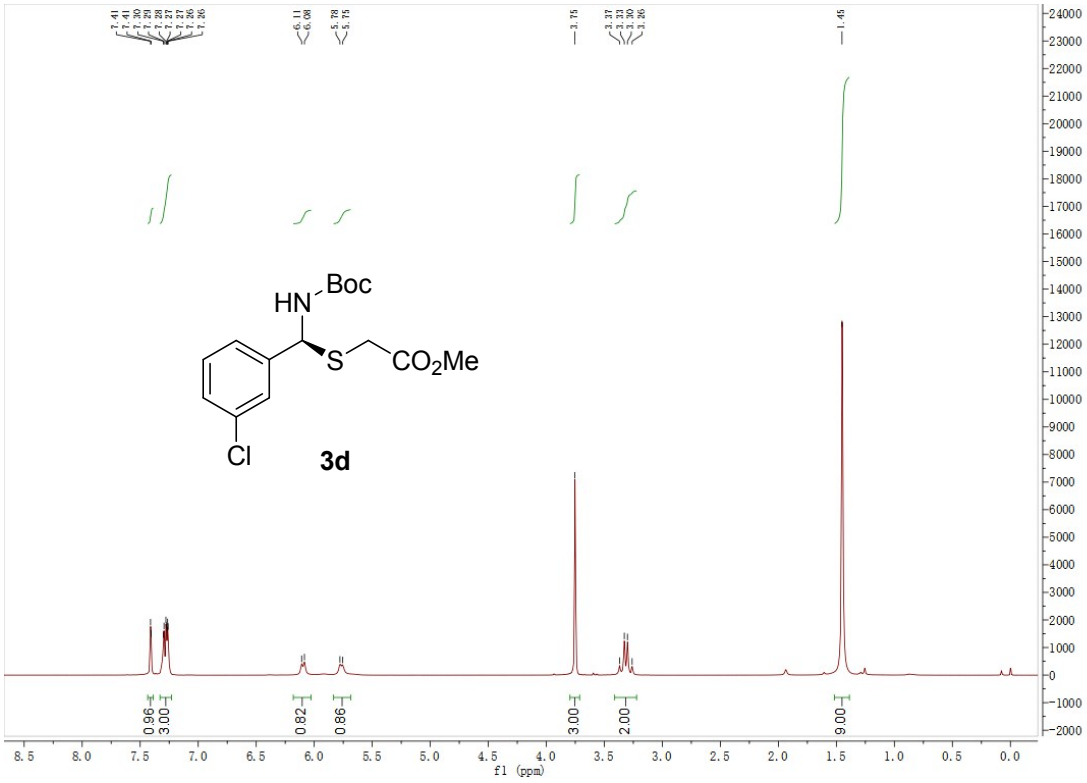
CO2Me
3c
f1 (ppm)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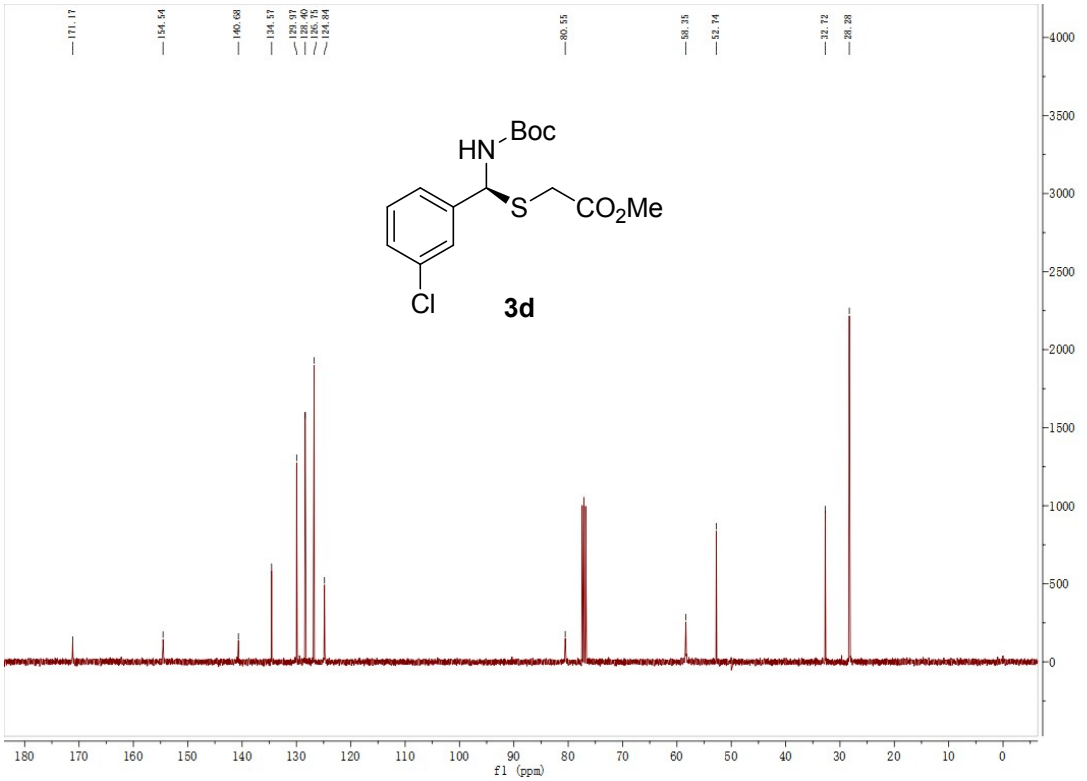
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CO2Me
Cl
3d
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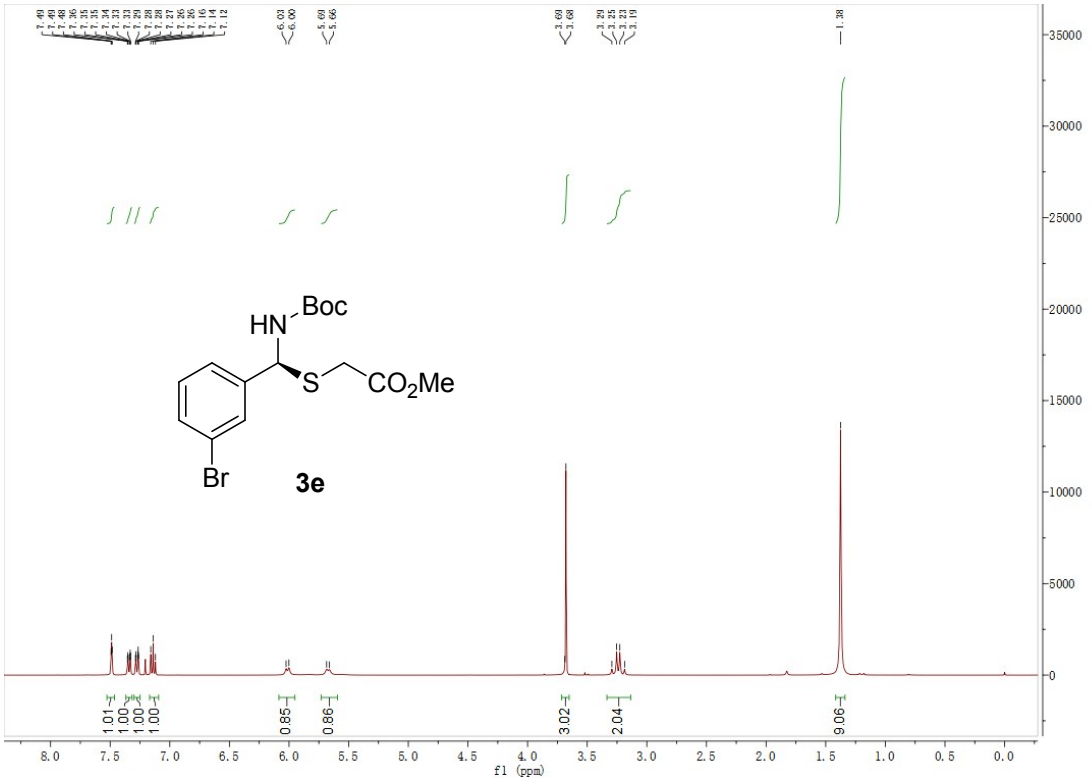
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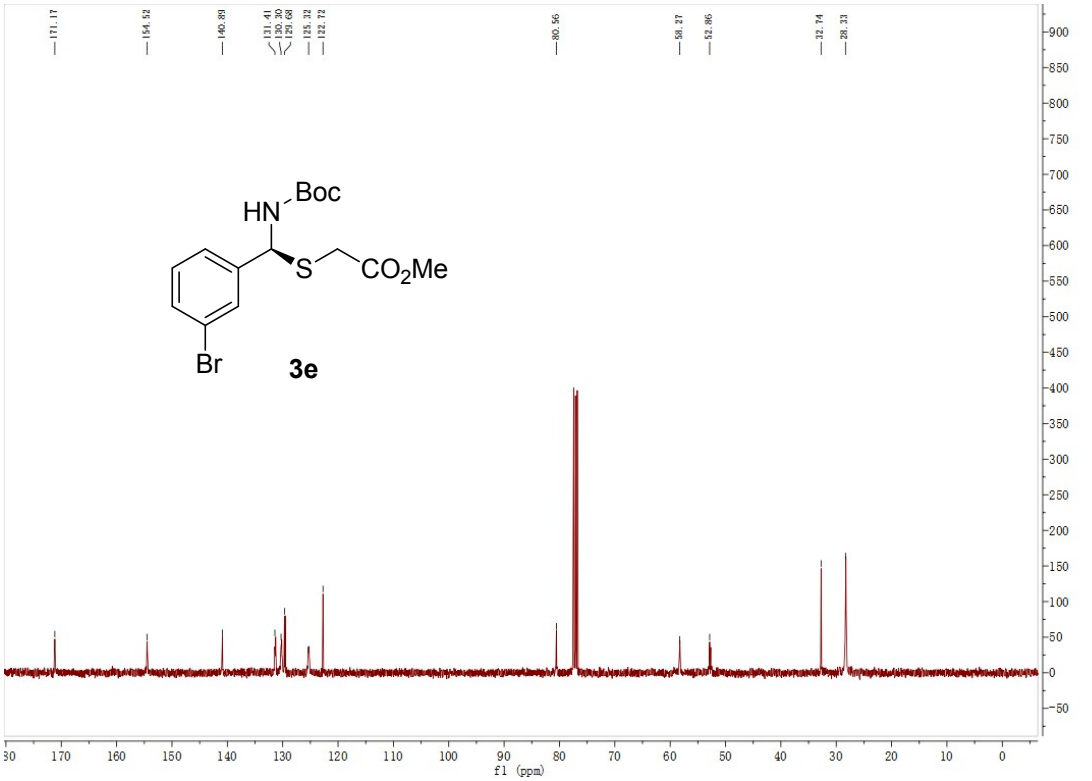
CO2Me
Br
3e
f1 (ppm)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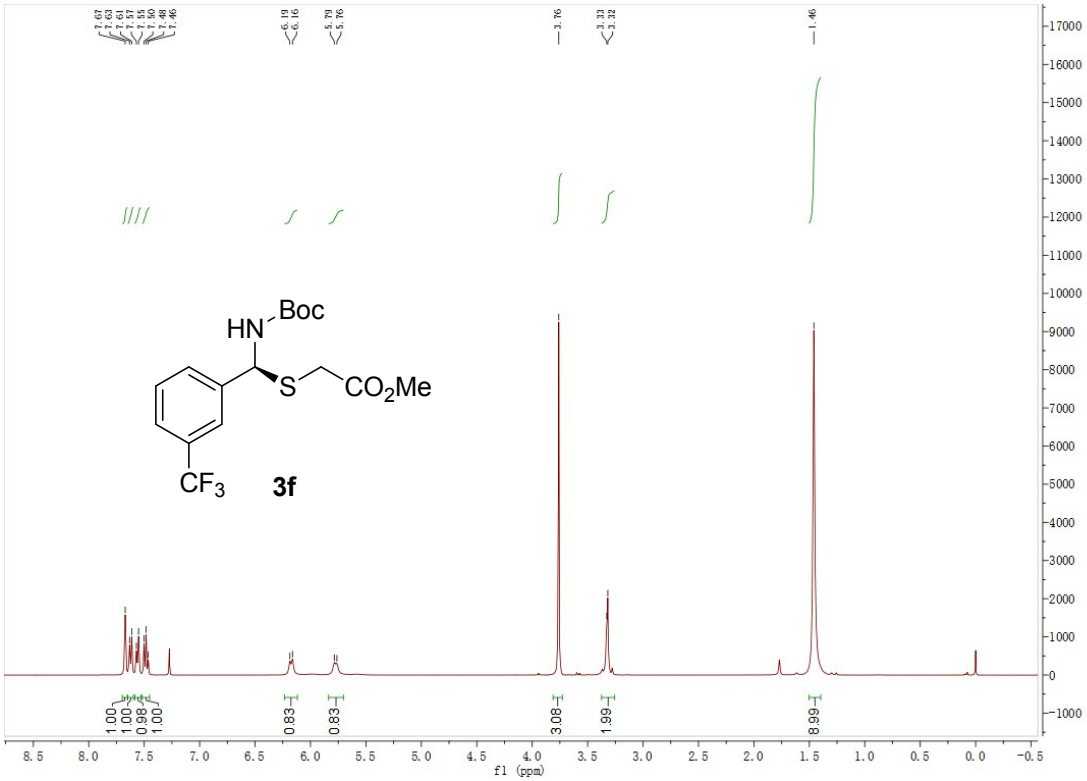
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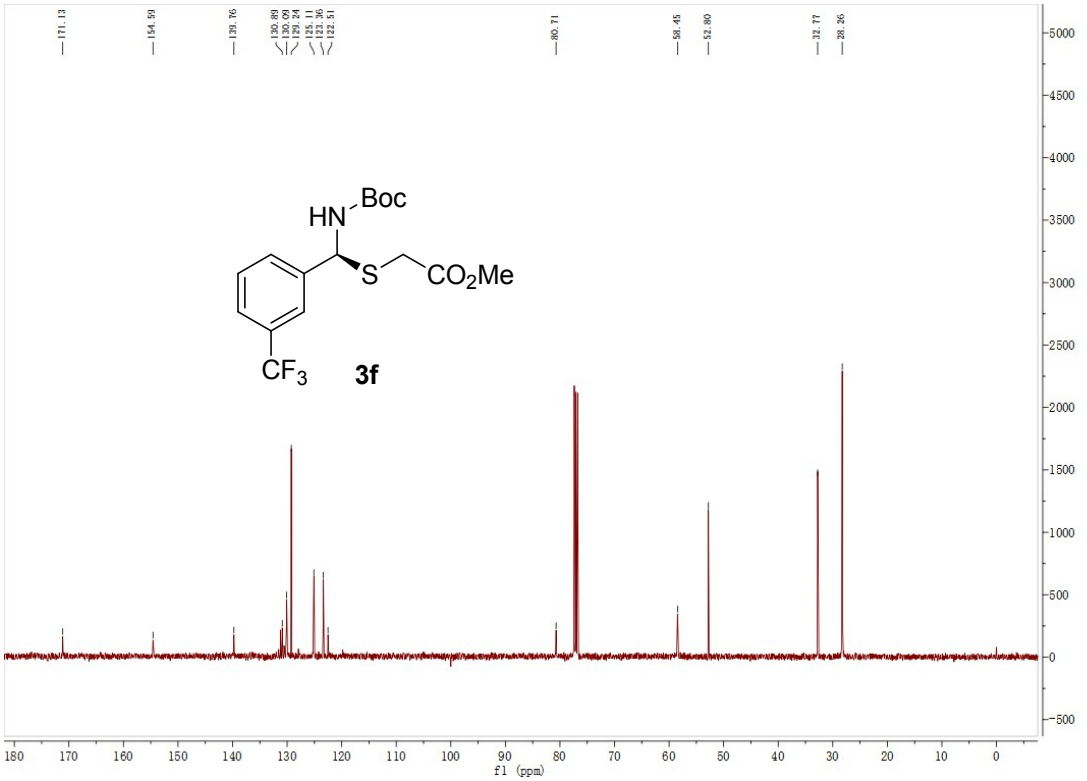
CO2Me
CF3
3f
fl (ppm)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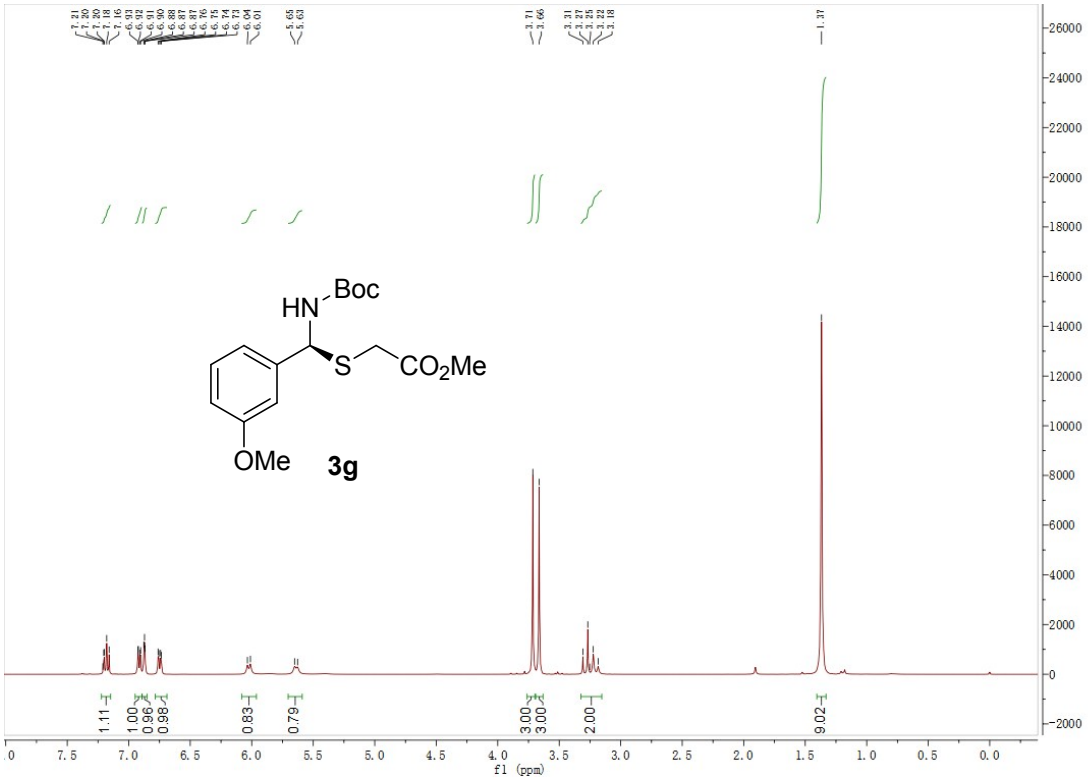
S
CO2Me
CF3
3f
fl (ppm)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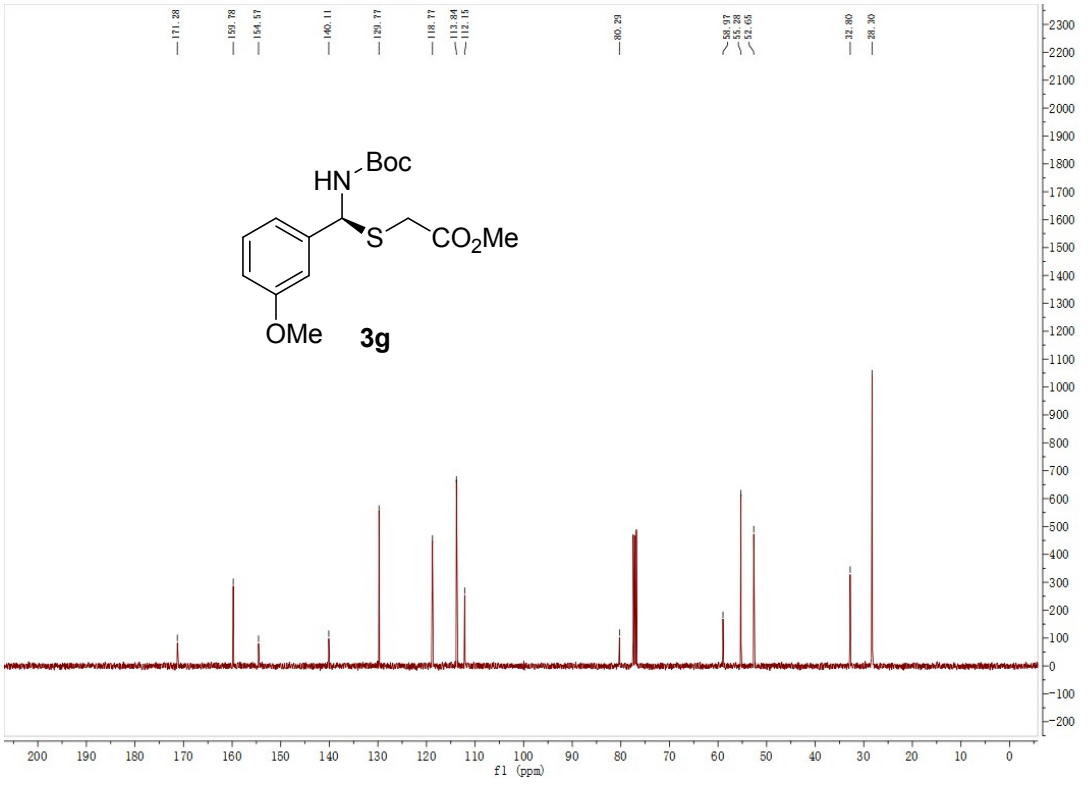
CO2Me
OMe
3g
f1 (ppm)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Boc
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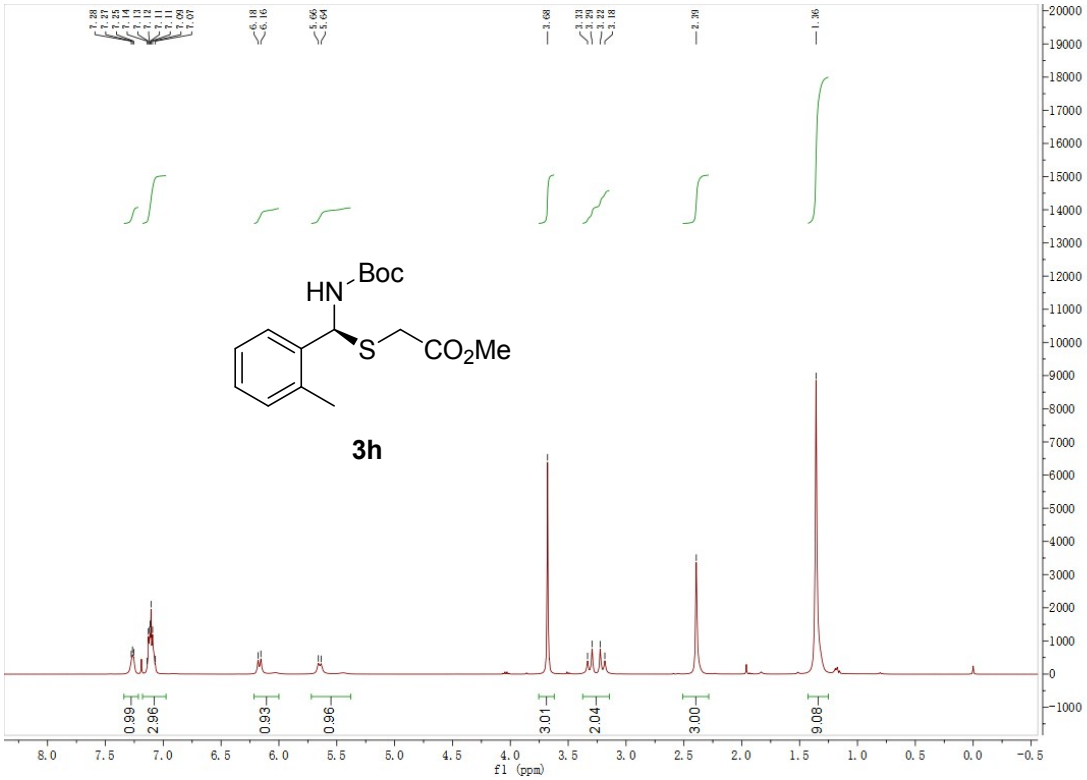
CO2Me
OMe
3g
f1 (ppm)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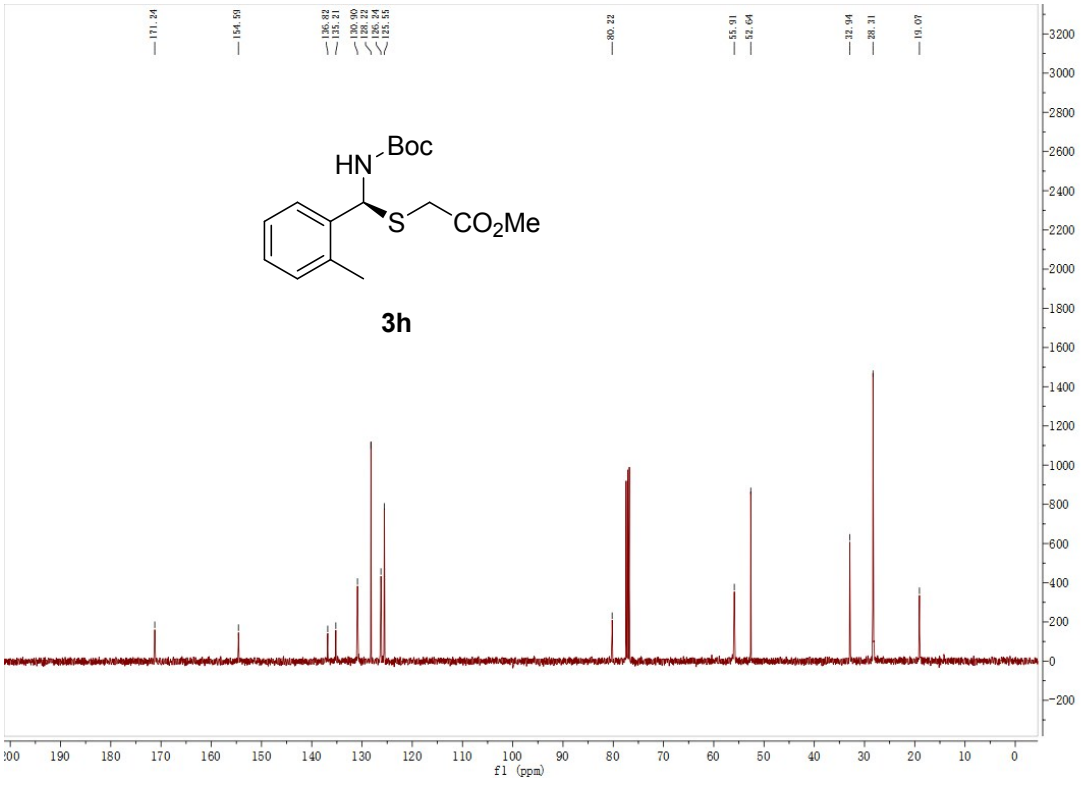
0.93
0.96
3.01
2.04
3.00
9.08
f1 (ppm)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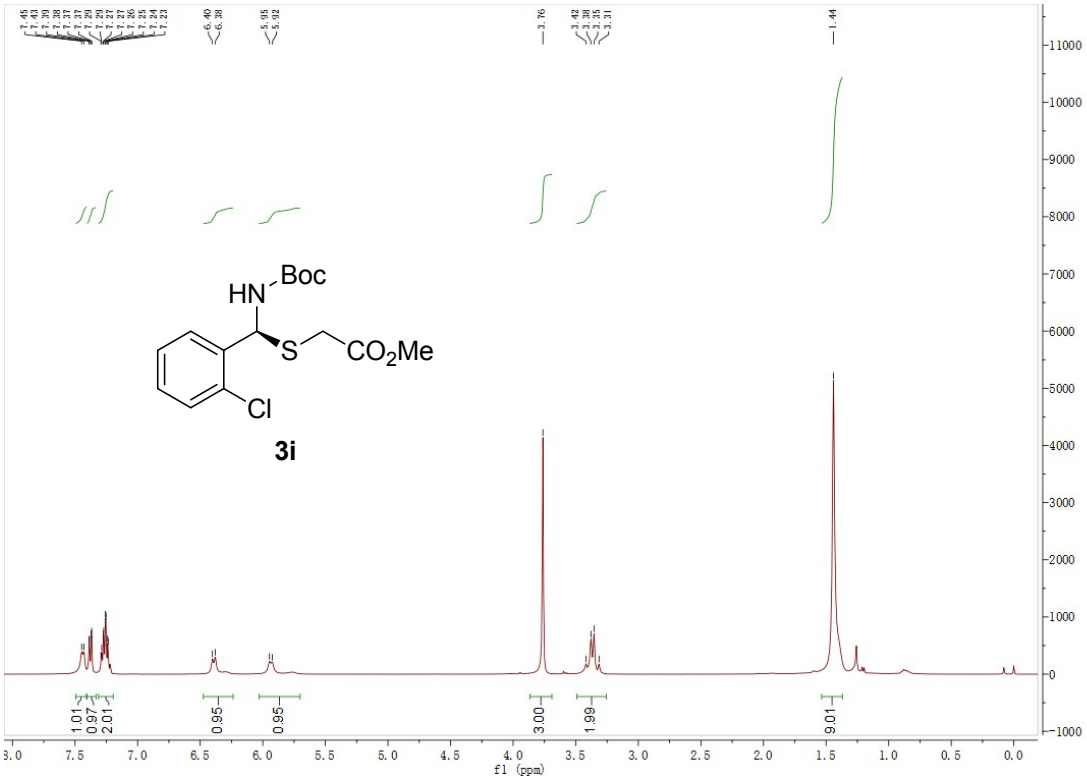
Boc
S
CO2Me
3h
f1 (ppm)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Cl
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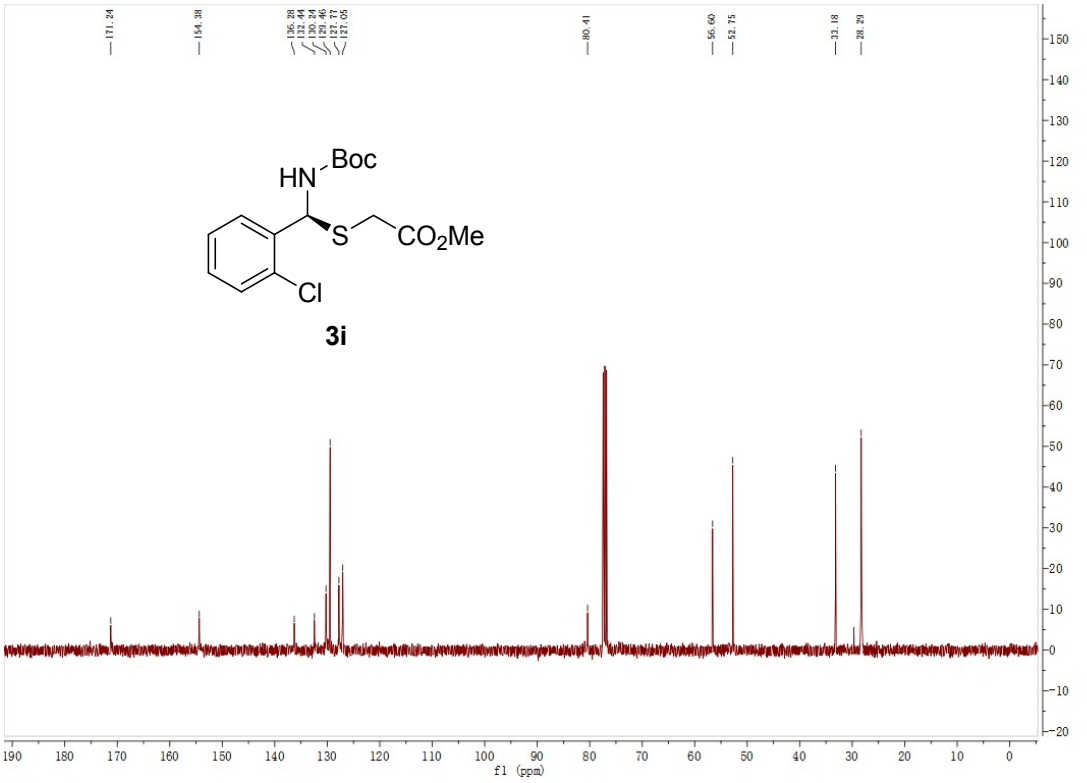
f1 (ppm)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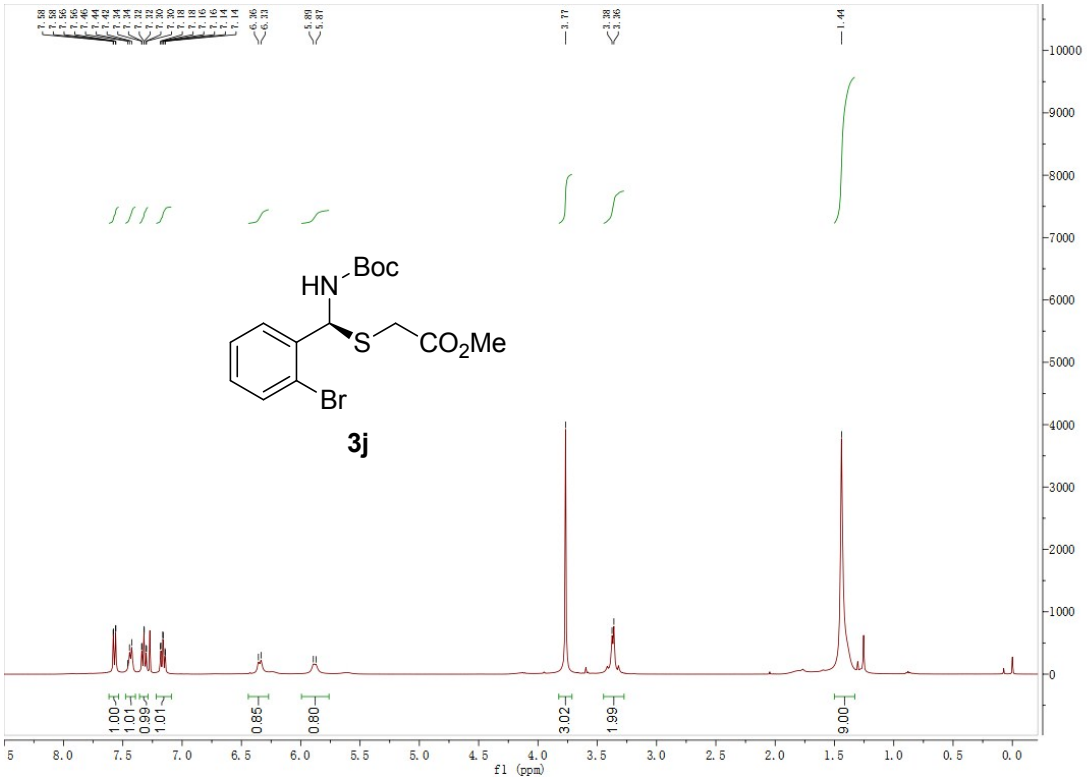
CO2Me
Cl
3i
f1 (ppm)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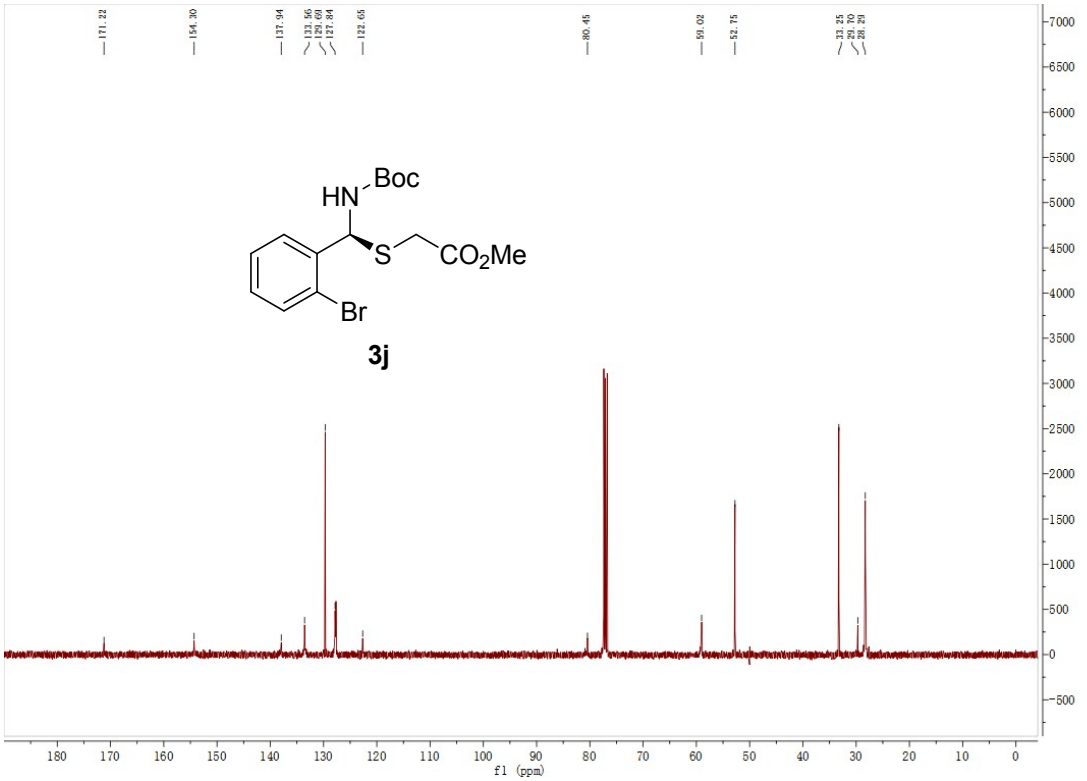
Br
3j
f1 (ppm)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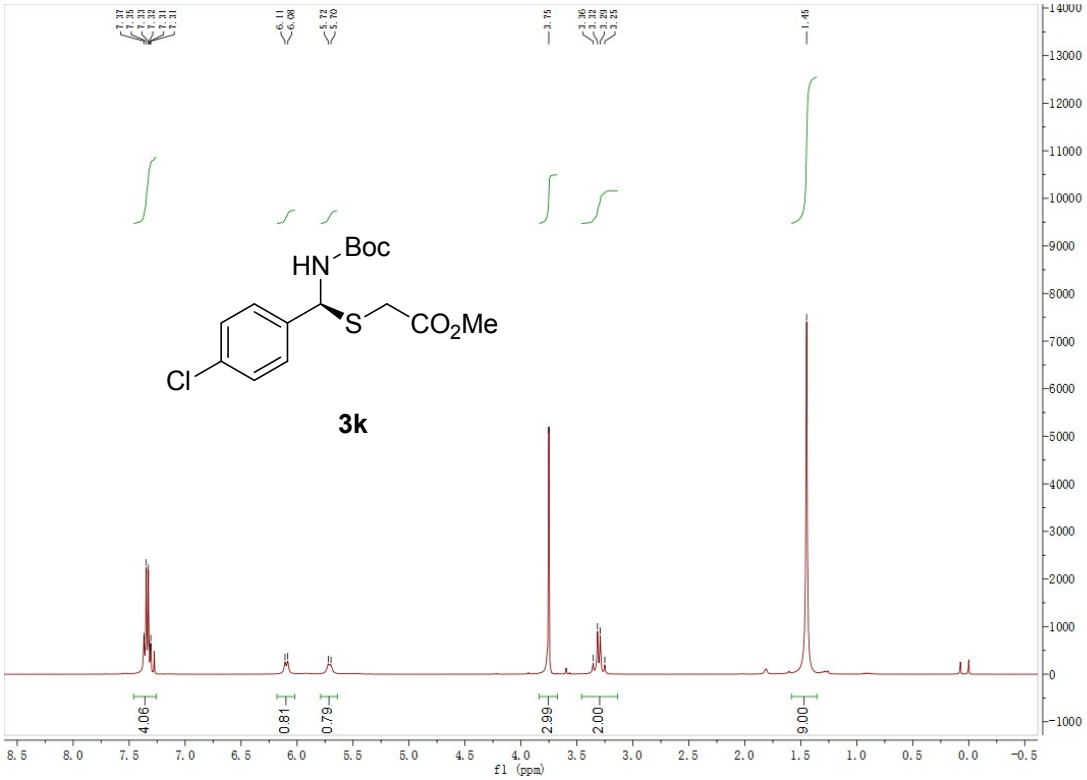
Boc
S
CO2Me
Br
3j
f1 (ppm)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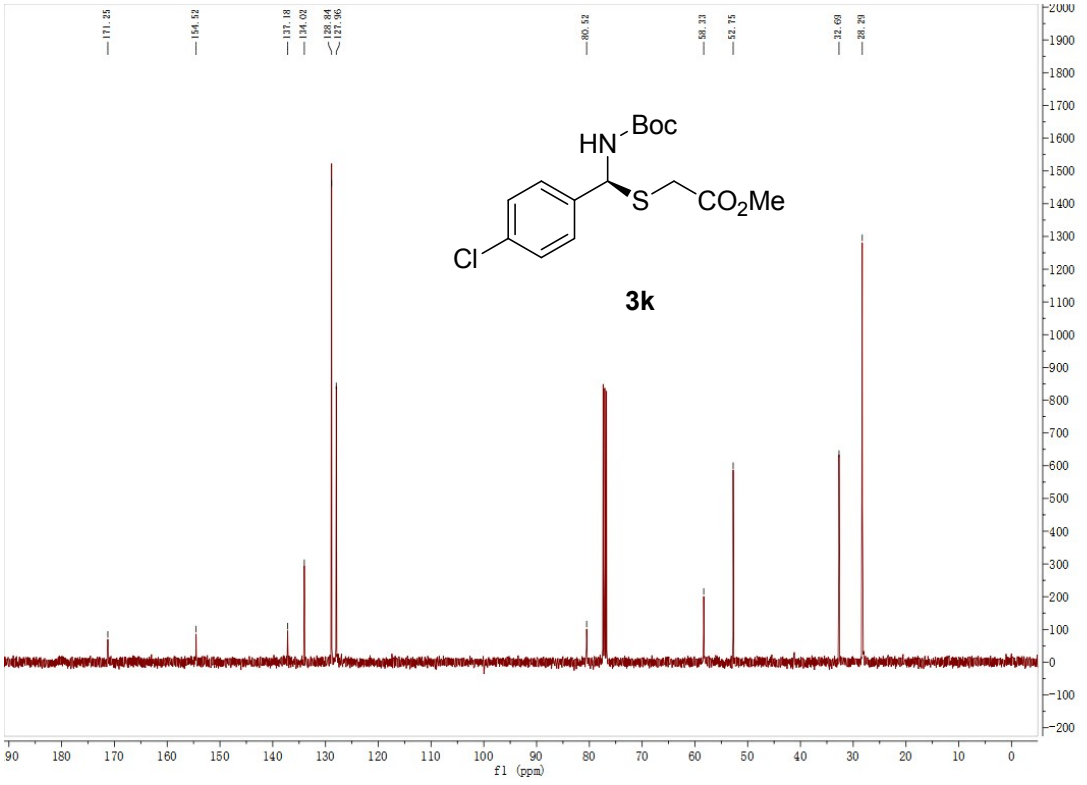
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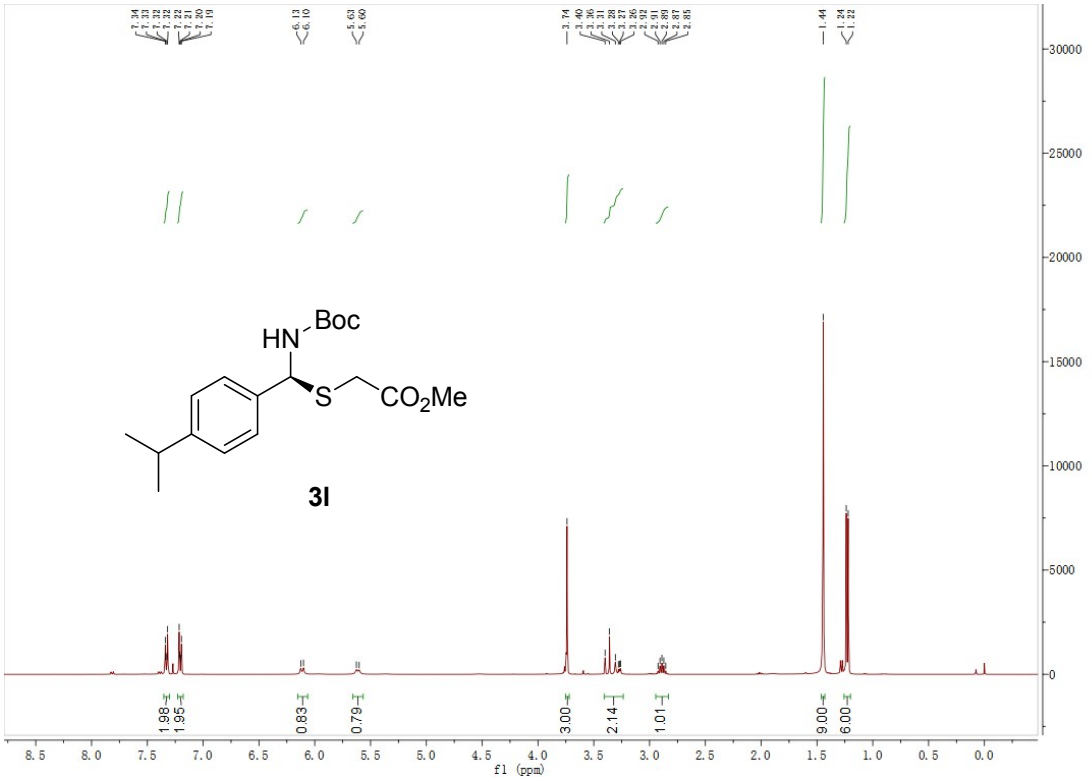
Boc
S
CO2Me
Cl
3k
f1 (ppm)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CO2Me
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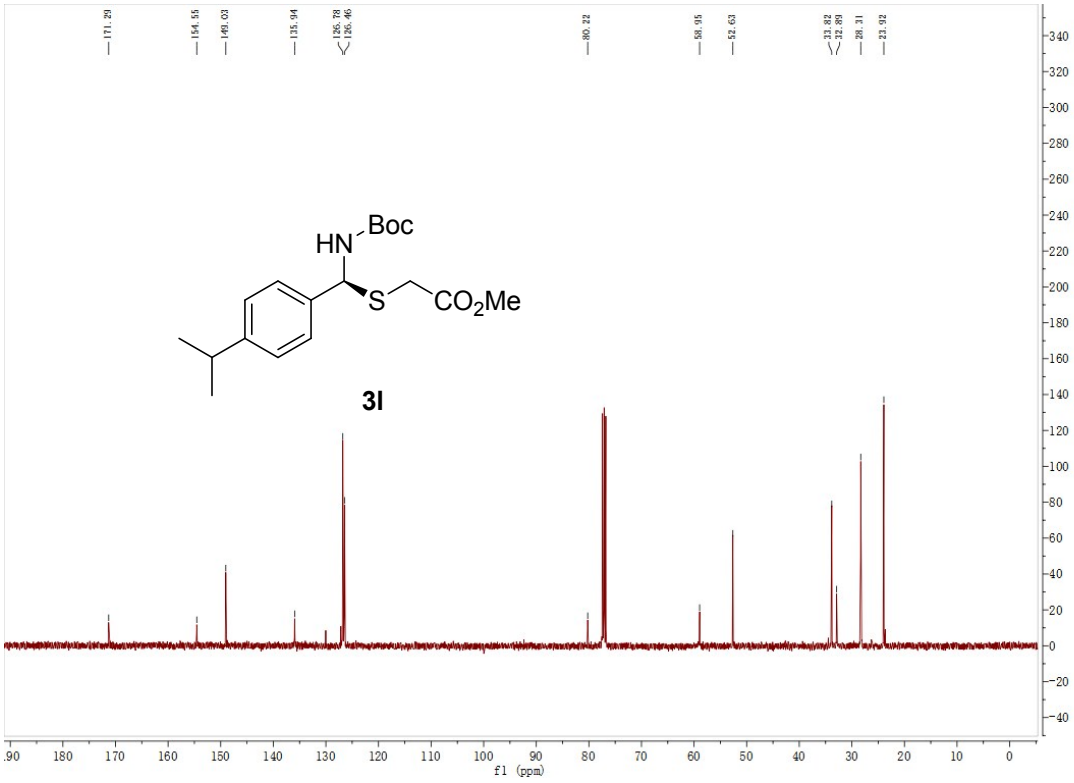
f1 (ppm)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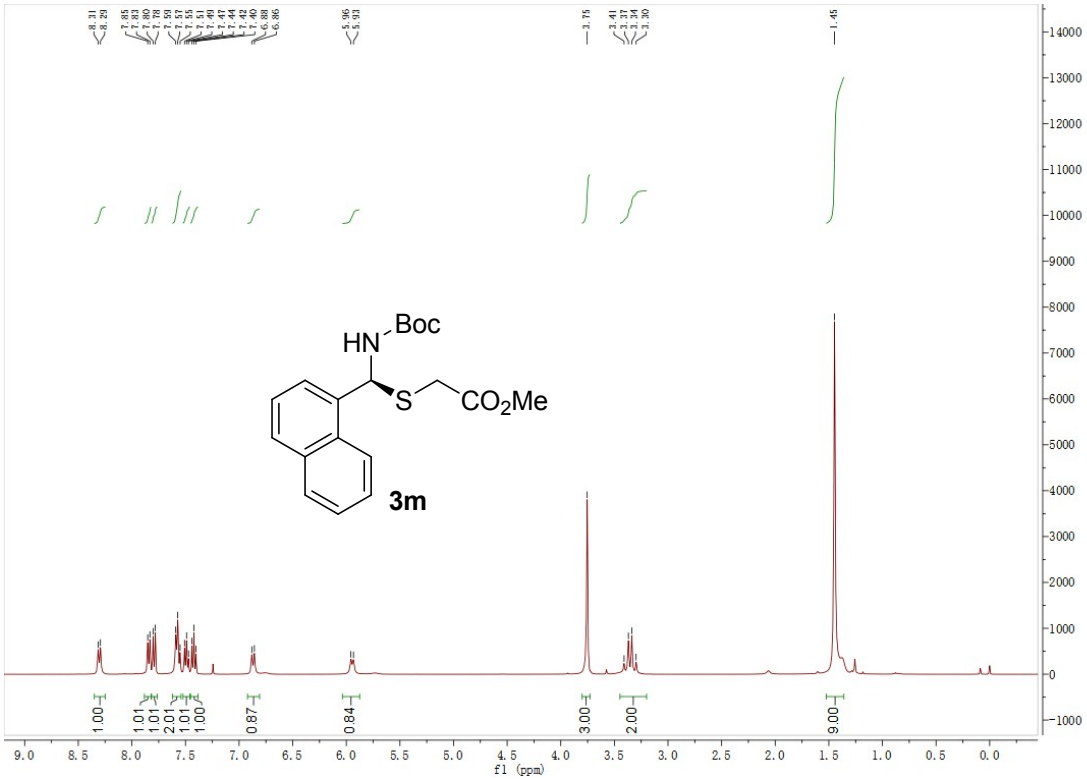
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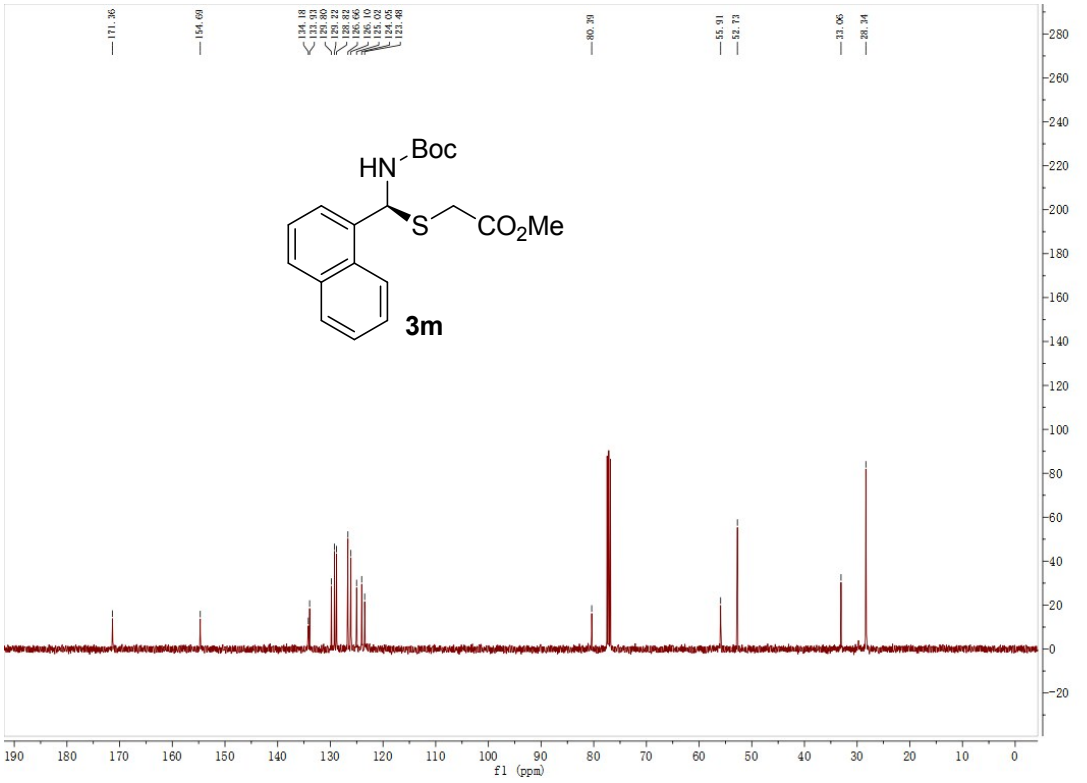
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S
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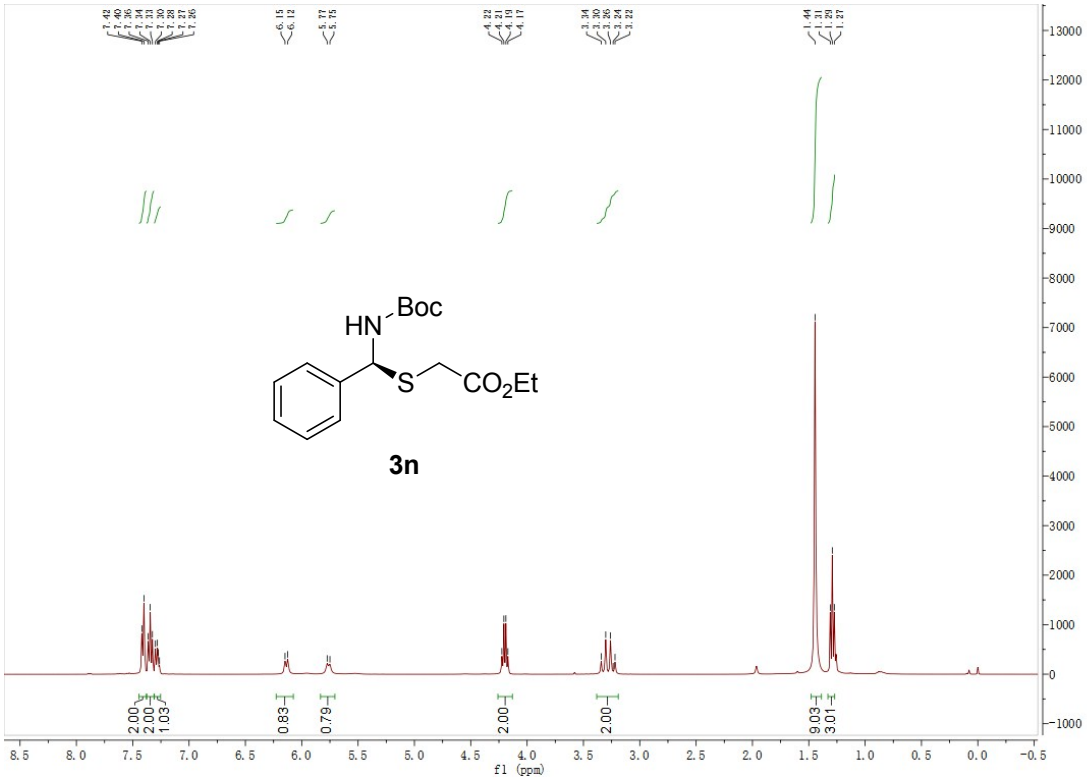
HN
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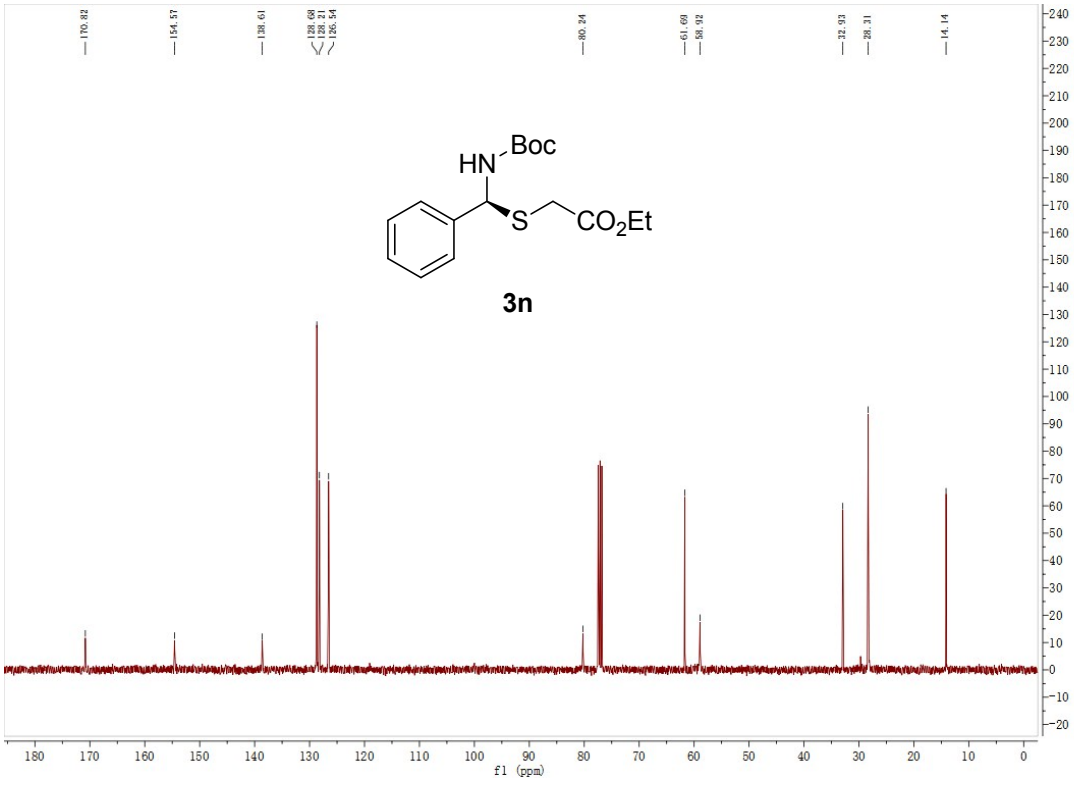
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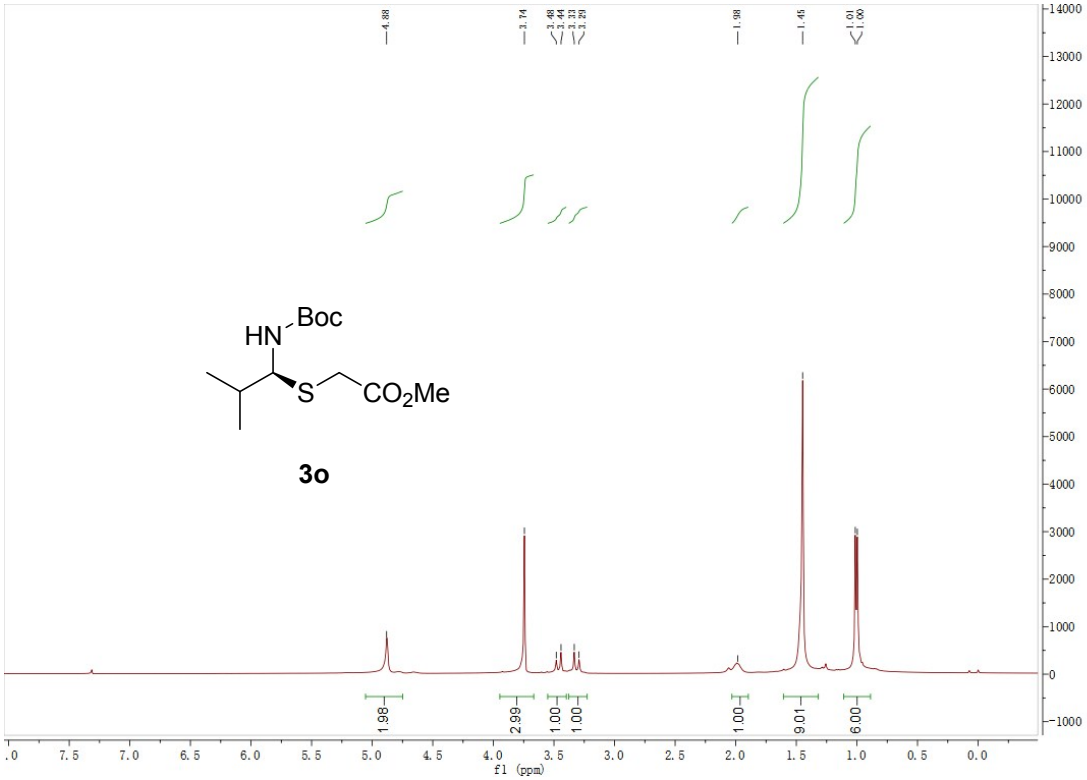
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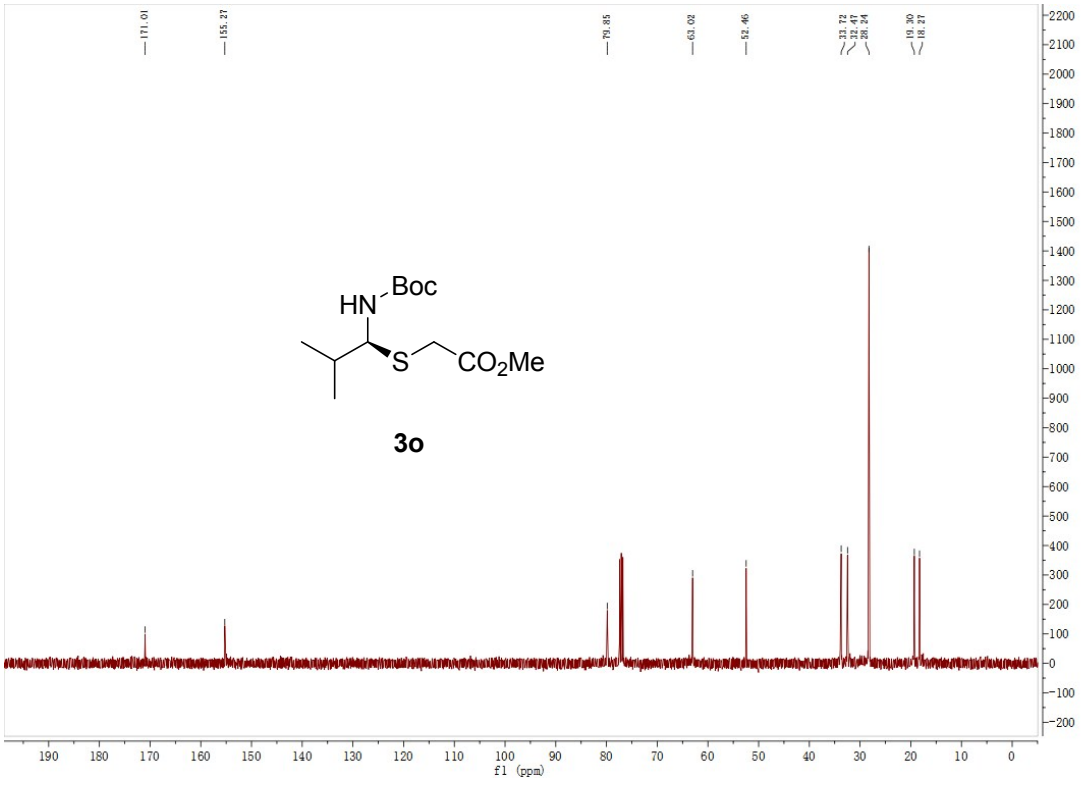
3o
f1 (ppm)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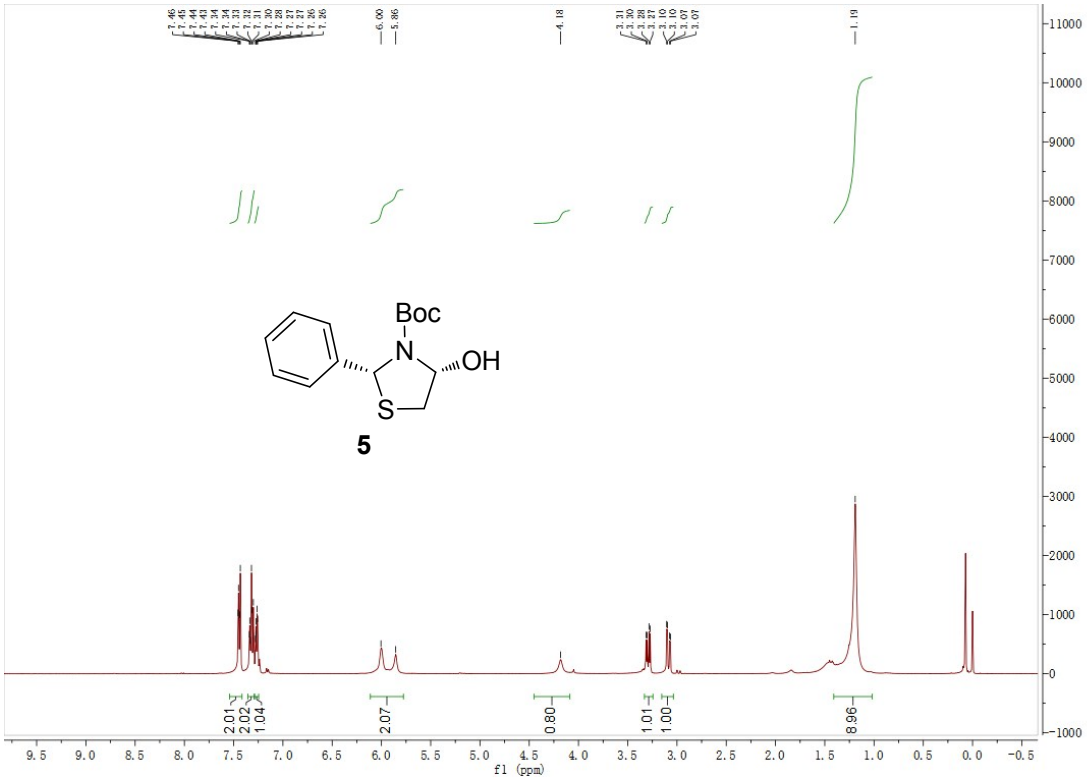
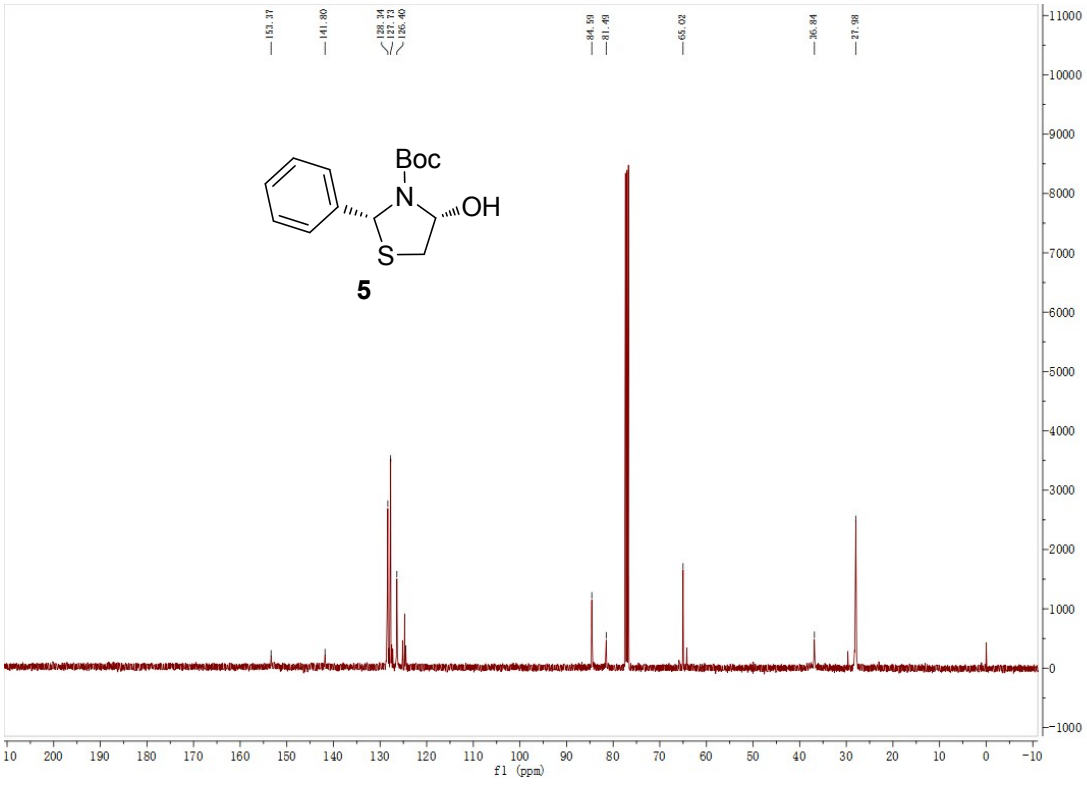
f1 (ppm)


Boc
N
OH
S
5
f1 (ppm)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OH
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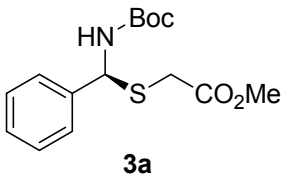
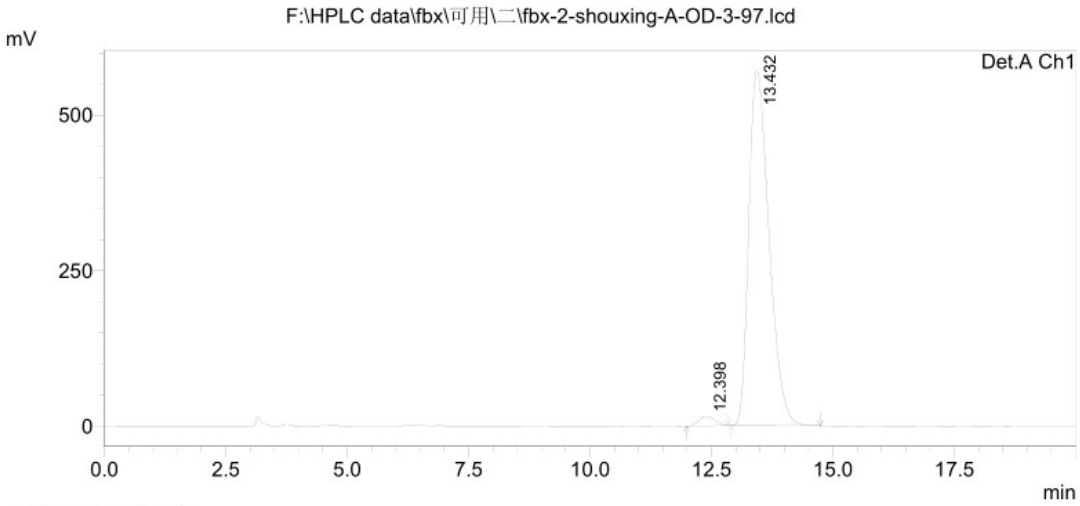
f1 (ppm)

HPLC Spectrum



3a

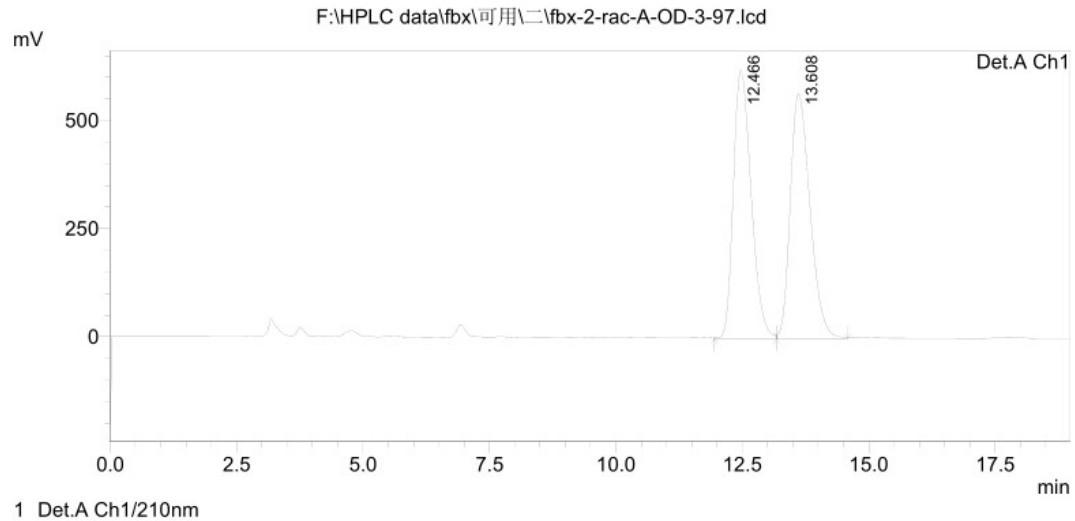


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.398	358940	15596	2.120	2.657
2	13.432	16572879	571360	97.880	97.343
Total		16931818	586957	100.000	100.000

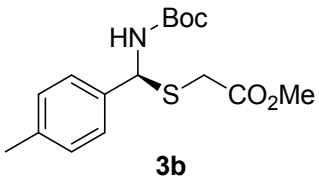


1 Det.A Ch1/210nm

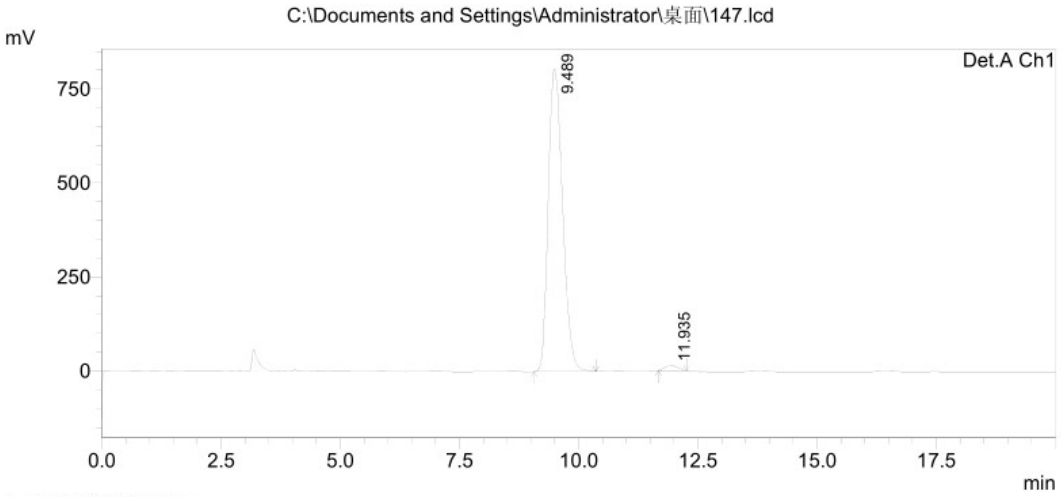
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.466	15159157	620136	49.705	52.282
2	13.608	15338844	566003	50.295	47.718
Total		30498001	1186140	100.000	100.000



3b

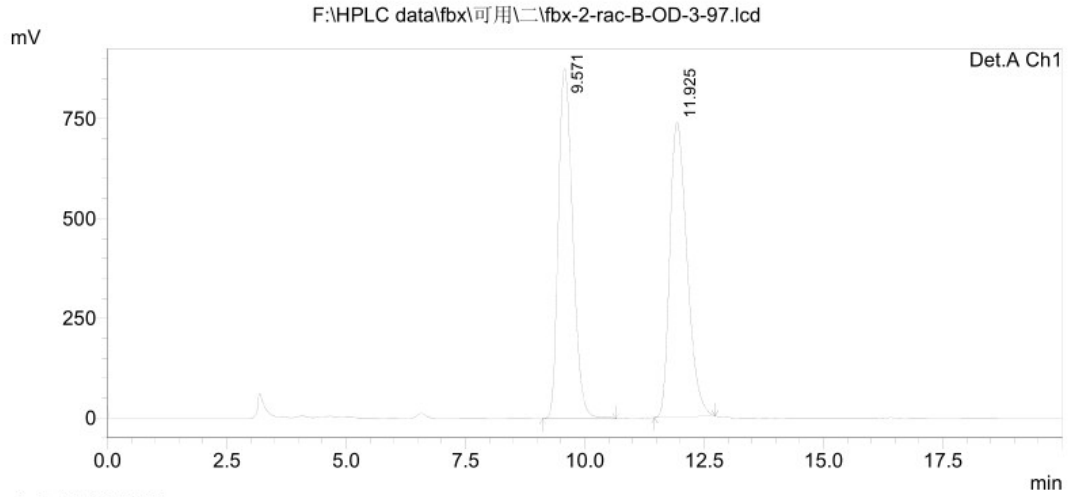


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.489	16873514	806390	98.554	98.450
2	11.935	247594	12697	1.446	1.550
Total		17121108	819088	100.000	100.000

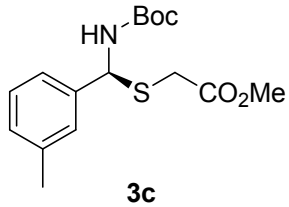


1 Det.A Ch1/210nm

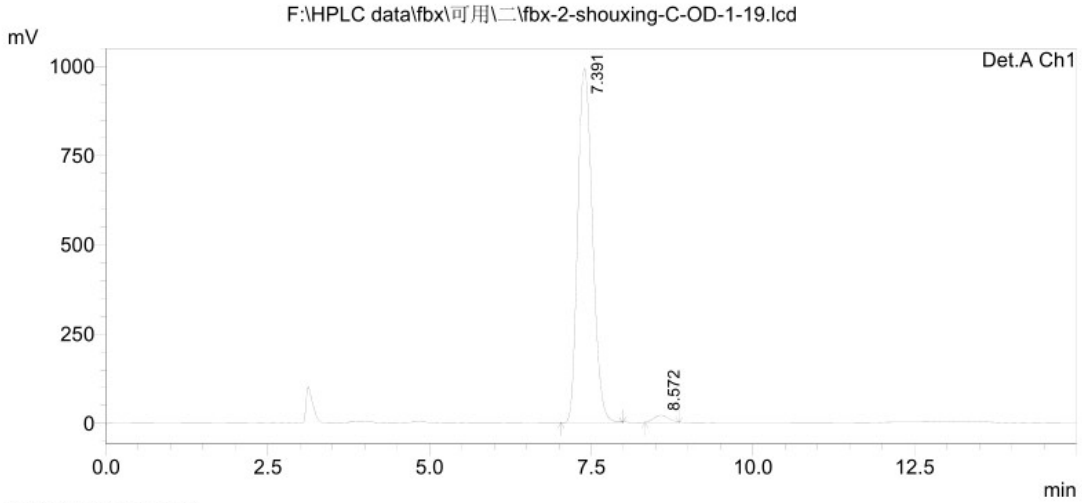
PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.571	18461390	878979	49.877	54.324
2	11.925	18552728	739065	50.123	45.676
Total		37014118	1618043	100.000	100.000



3c

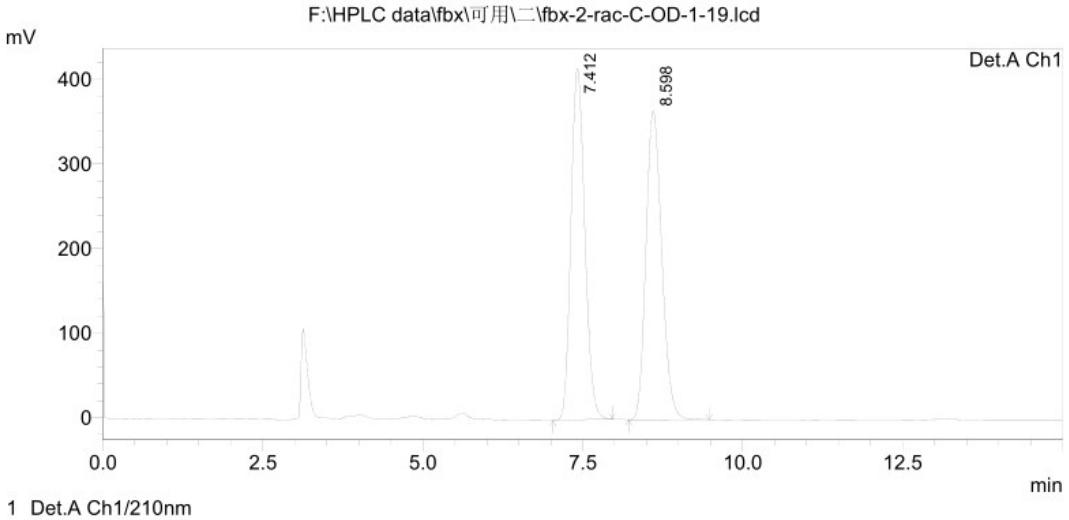


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.391	15772184	992955	97.804	97.936
2	8.572	354146	20929	2.196	2.064
Total		16126330	1013884	100.000	100.000

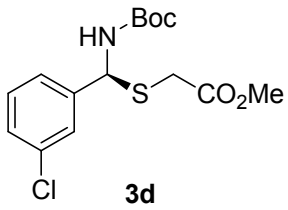


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.412	6242313	415950	49.868	53.239
2	8.598	6275242	365340	50.132	46.761
Total		12517555	781290	100.000	100.000



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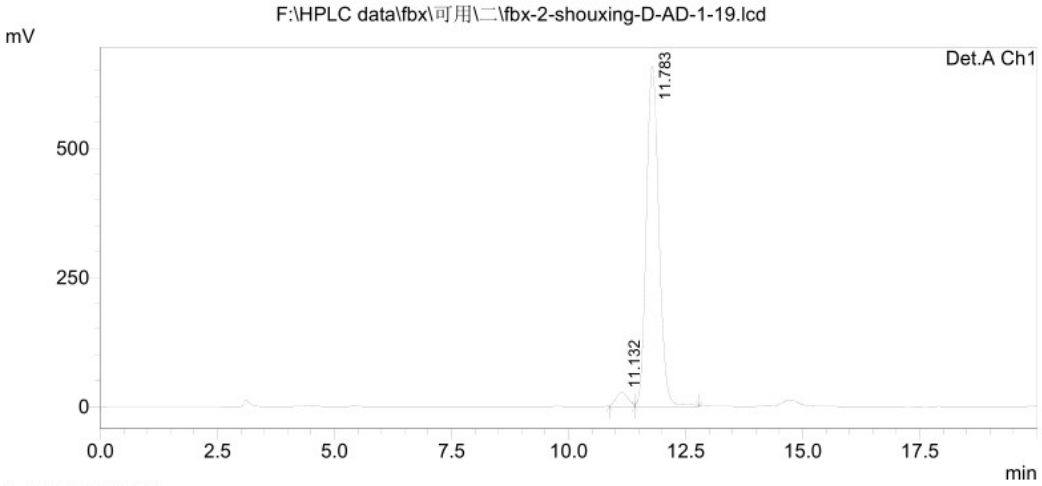
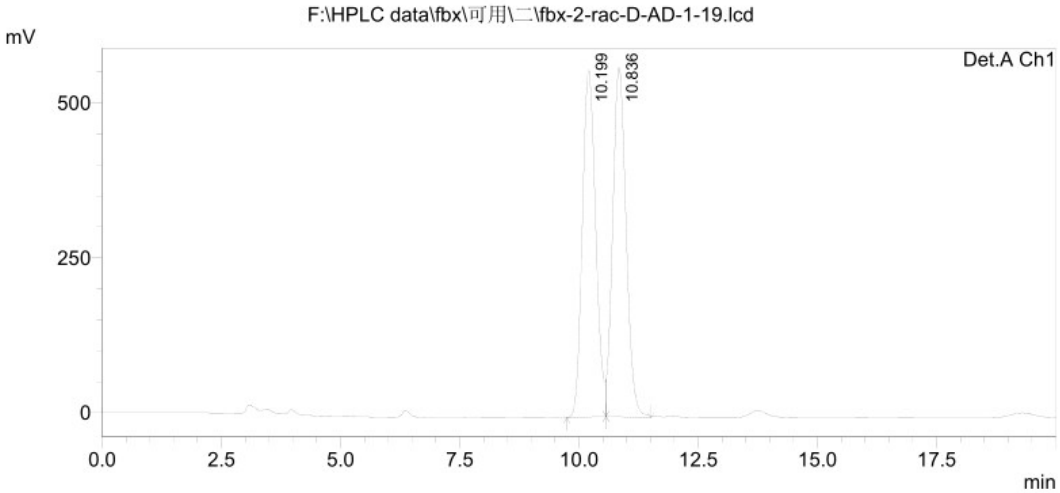


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.132	494796	27280	3.882	3.980
2	11.783	12250737	658221	96.118	96.020
Total		12745533	685501	100.000	100.000

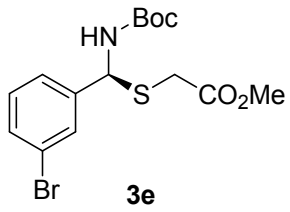


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.199	10954622	559384	49.868	49.824
2	10.836	11012692	563338	50.132	50.176
Total		21967314	1122722	100.000	100.000



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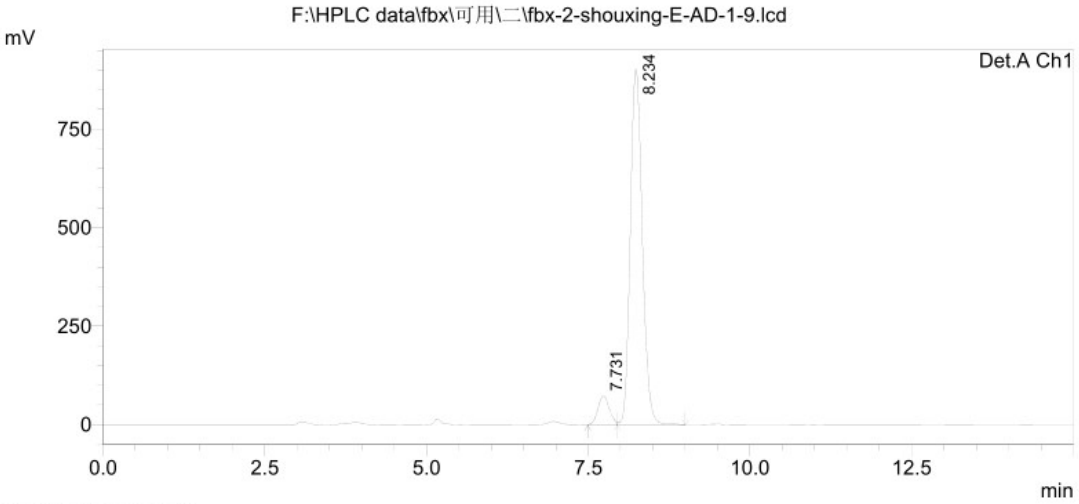
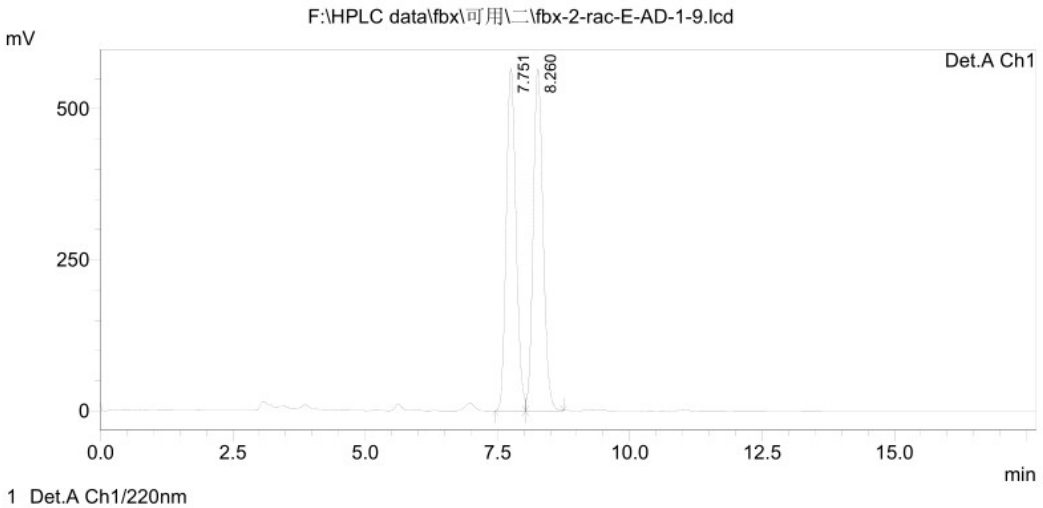


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.731	933782	74500	7.393	7.619
2	8.234	11696425	903318	92.607	92.381
Total		12630206	977819	100.000	100.000

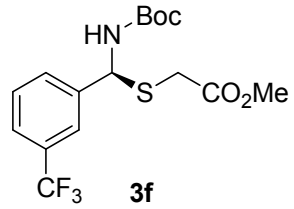


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.751	7246100	566503	49.700	50.026
2	8.260	7333606	565924	50.300	49.974
Total		14579706	1132427	100.000	100.000



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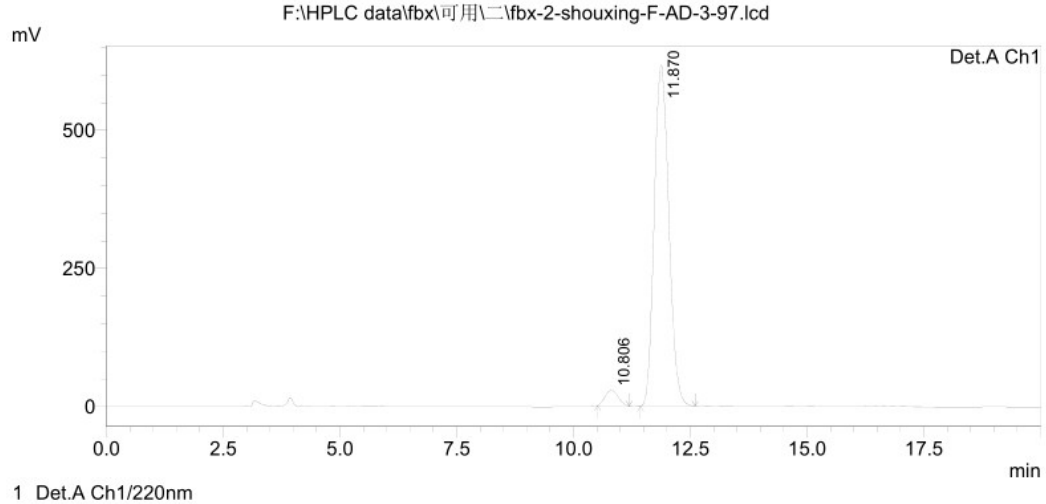
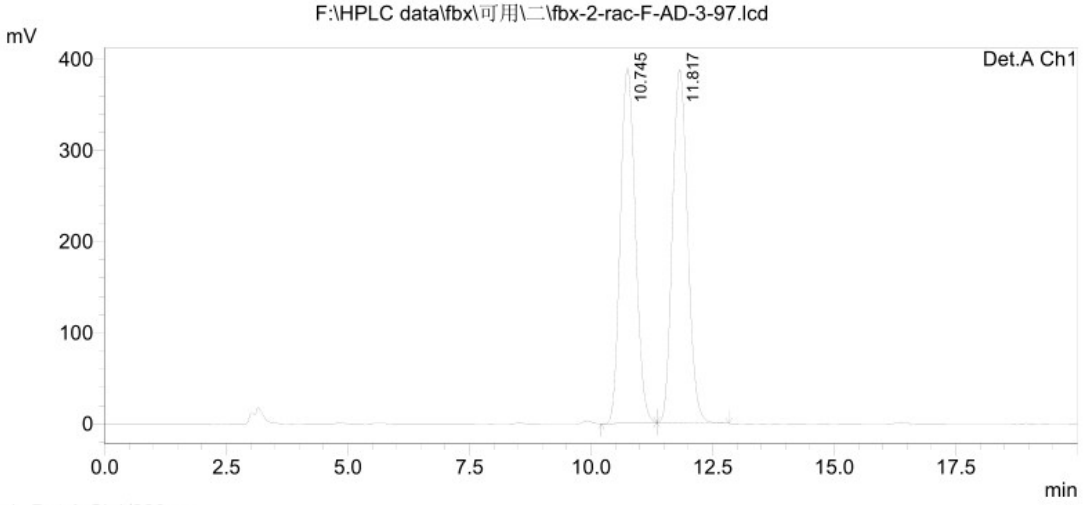


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.806	545498	27965	3.893	4.334
2	11.870	13467767	617240	96.107	95.666
Total		14013265	645205	100.000	100.000

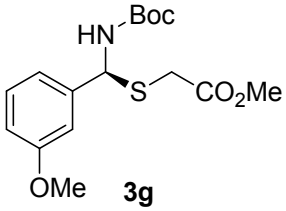


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.745	8368135	390132	49.860	50.199
2	11.817	8415110	387046	50.140	49.801
Total		16783245	777177	100.000	100.000



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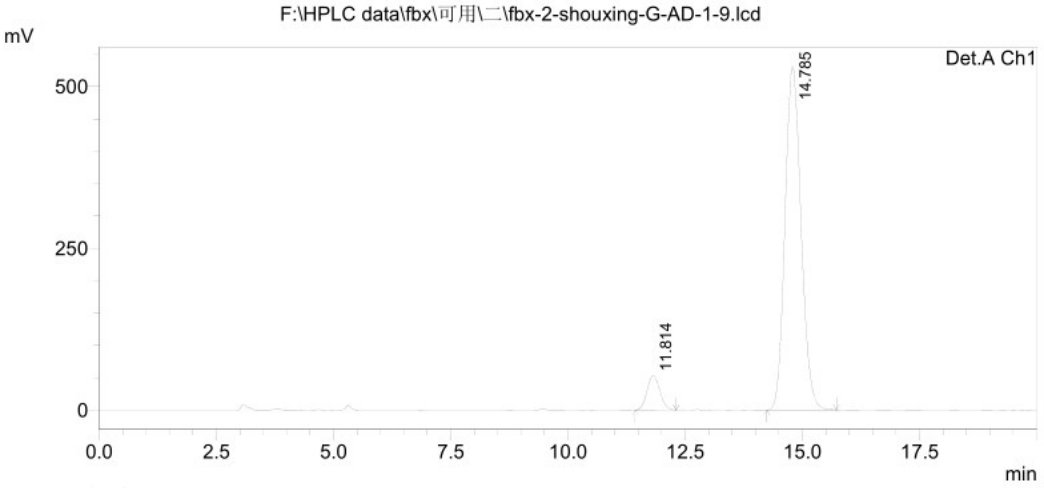
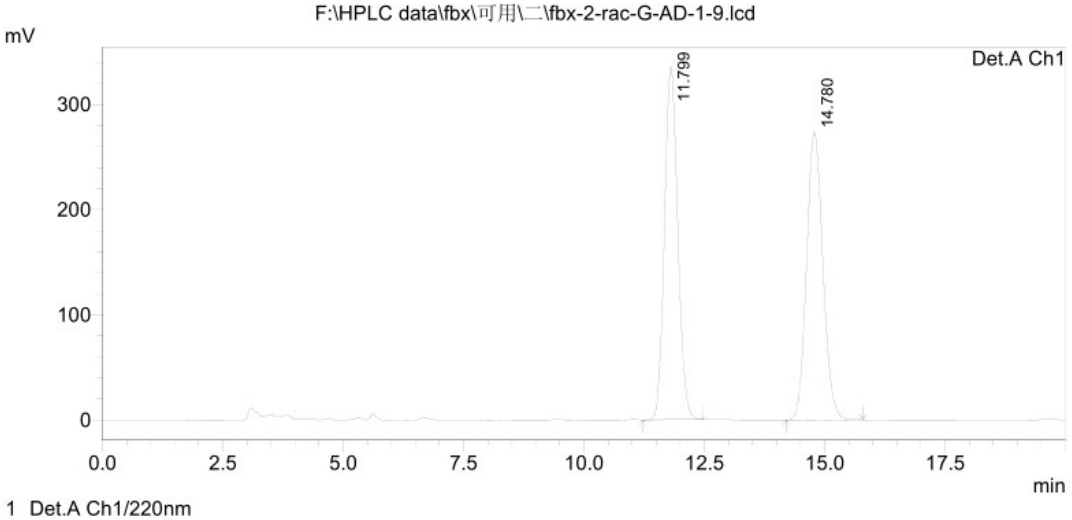


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.814	1016972	53476	7.438	9.150
2	14.785	12655640	530950	92.562	90.850
Total		13672612	584426	100.000	100.000

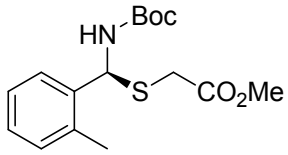


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.799	6443518	335387	49.957	55.064
2	14.780	6454734	273699	50.043	44.936
Total		12898252	609086	100.000	100.000



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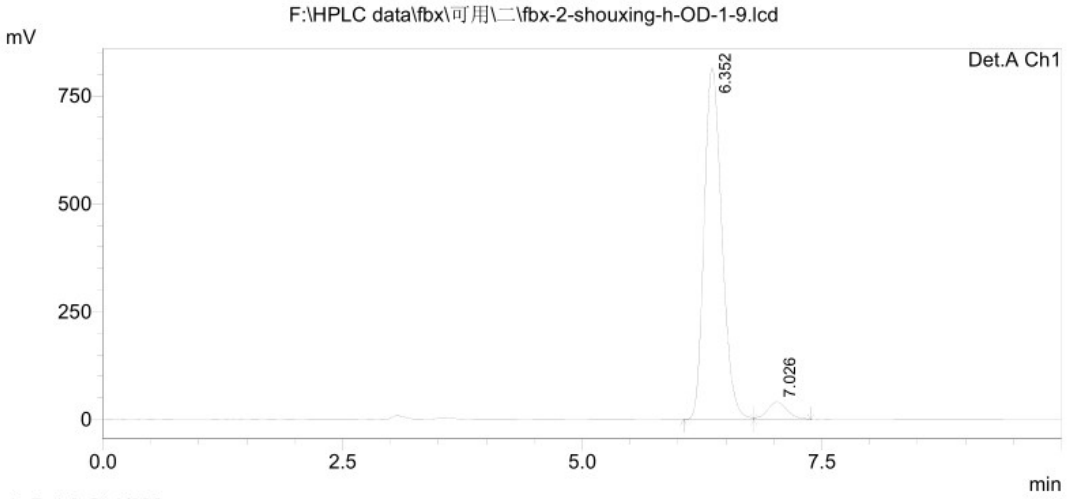
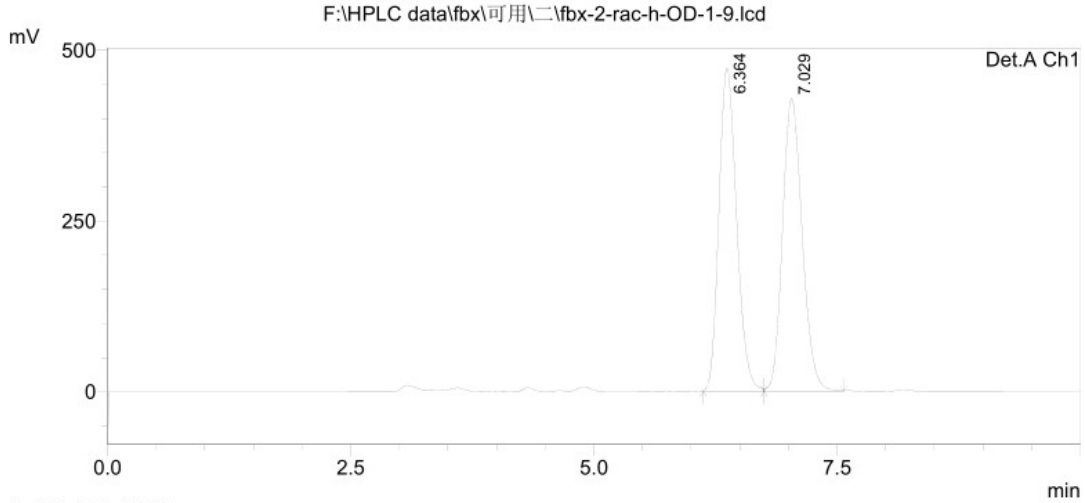


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.352	10523686	814814	94.563	95.242
2	7.026	605129	40703	5.437	4.758
Total		11128815	855517	100.000	100.000

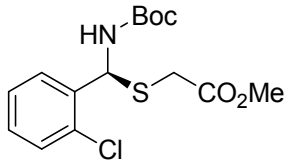


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.364	5988616	473118	49.851	52.437
2	7.029	6024488	429146	50.149	47.563
Total		12013104	902264	100.000	100.000



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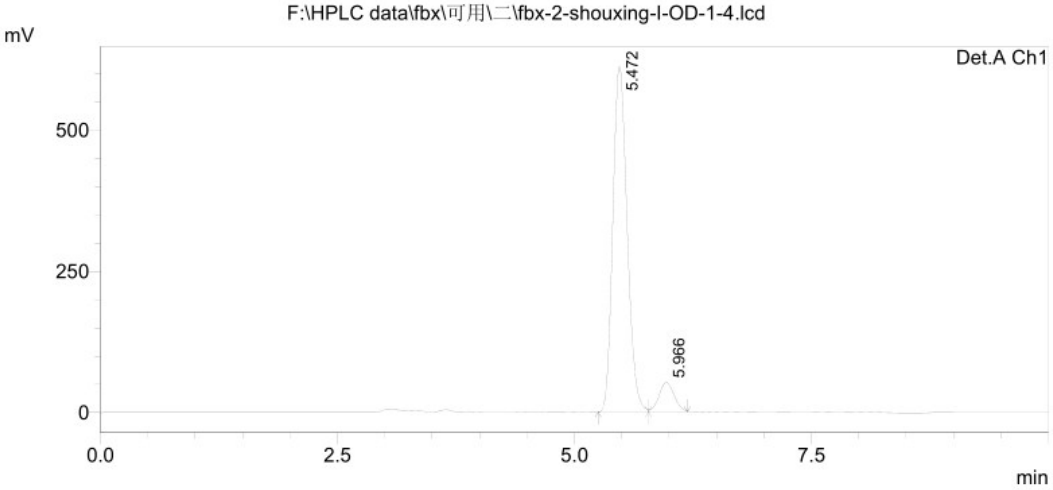
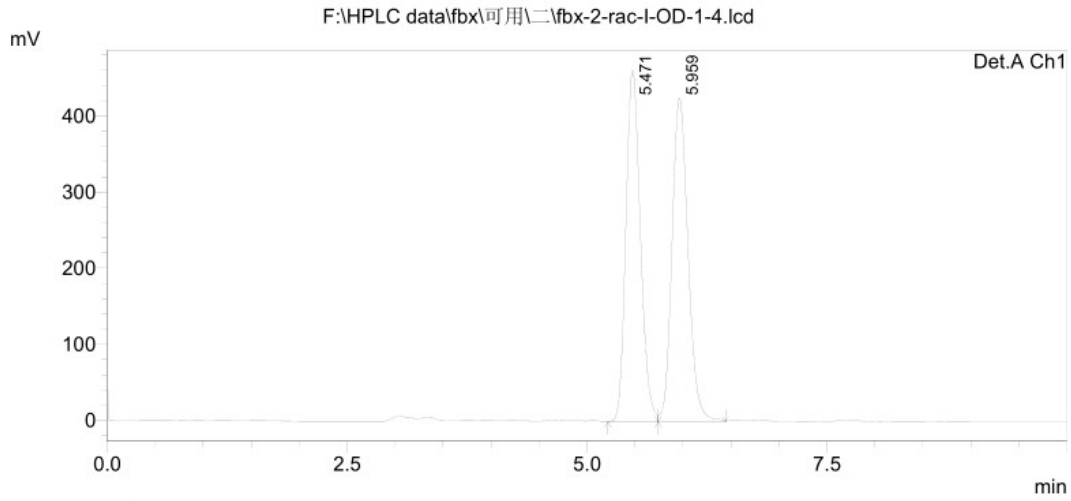


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.472	6421760	613251	91.598	92.152
2	5.966	589086	52224	8.402	7.848
Total		7010846	665475	100.000	100.000

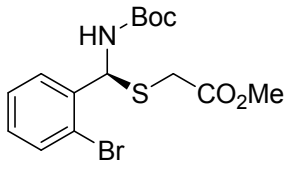


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.471	4875175	462733	49.555	52.077
2	5.959	4962753	425815	50.445	47.923
Total		9837929	888548	100.000	100.000



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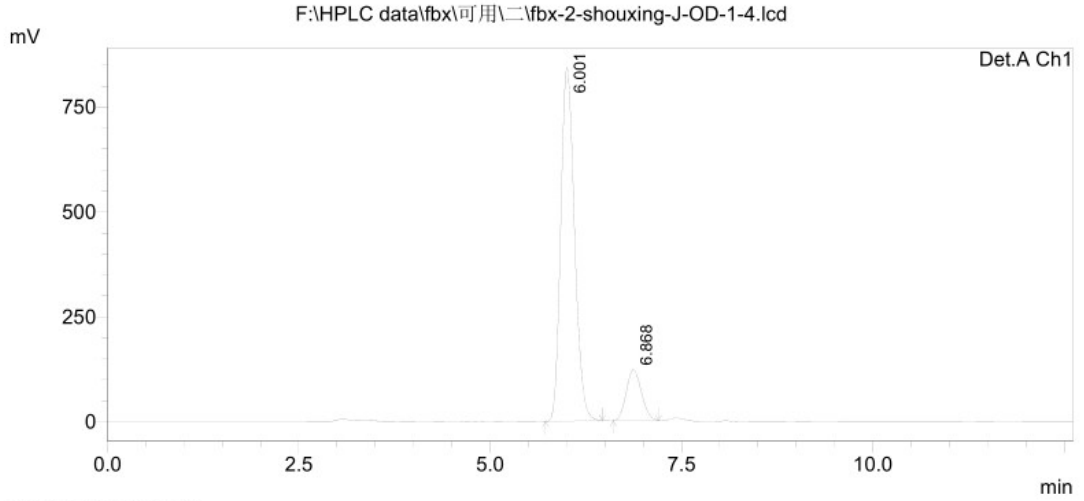
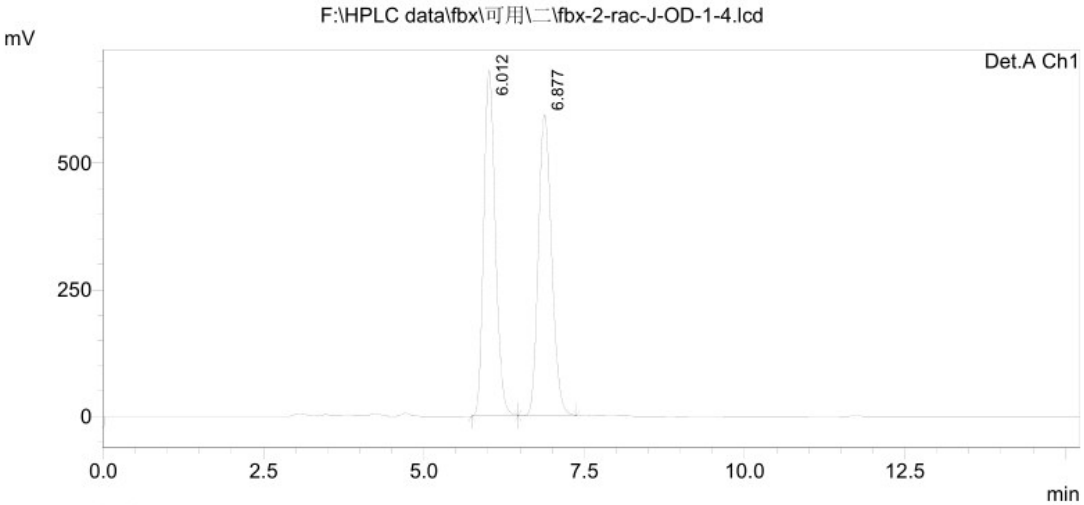


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.001	10539502	842170	86.273	87.435
2	6.868	1676899	121029	13.727	12.565
Total		12216401	963199	100.000	100.000

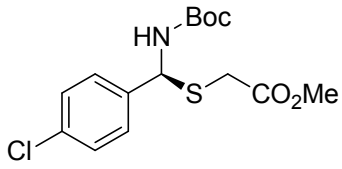


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.012	8564059	683079	49.816	53.456
2	6.877	8627344	594747	50.184	46.544
Total		17191403	1277827	100.000	100.000



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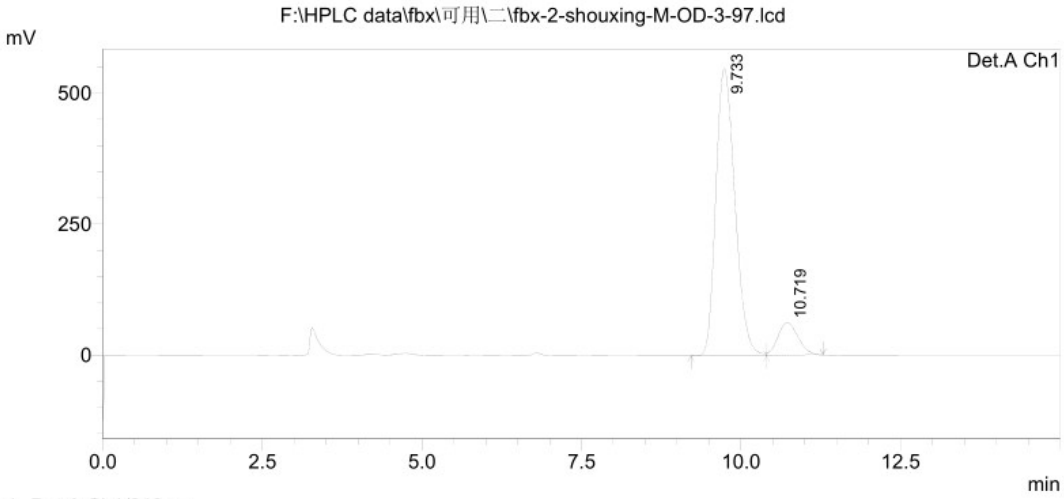
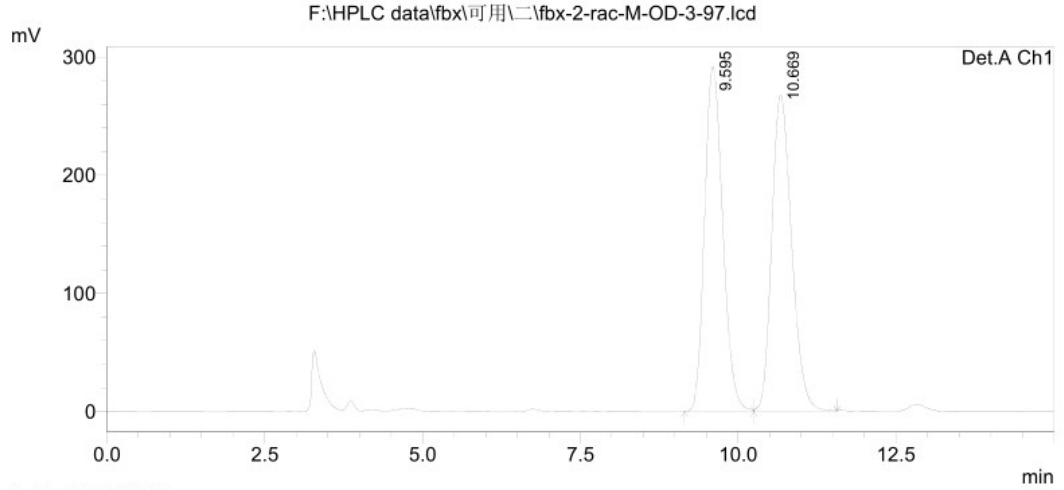


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.733	11458288	548714	89.260	89.728
2	10.719	1378631	62818	10.740	10.272
Total		12836919	611532	100.000	100.000

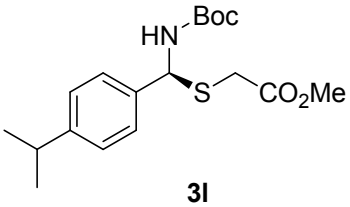


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.595	5848522	292260	49.895	52.212
2	10.669	5873144	267493	50.105	47.788
Total		11721666	559752	100.000	100.000



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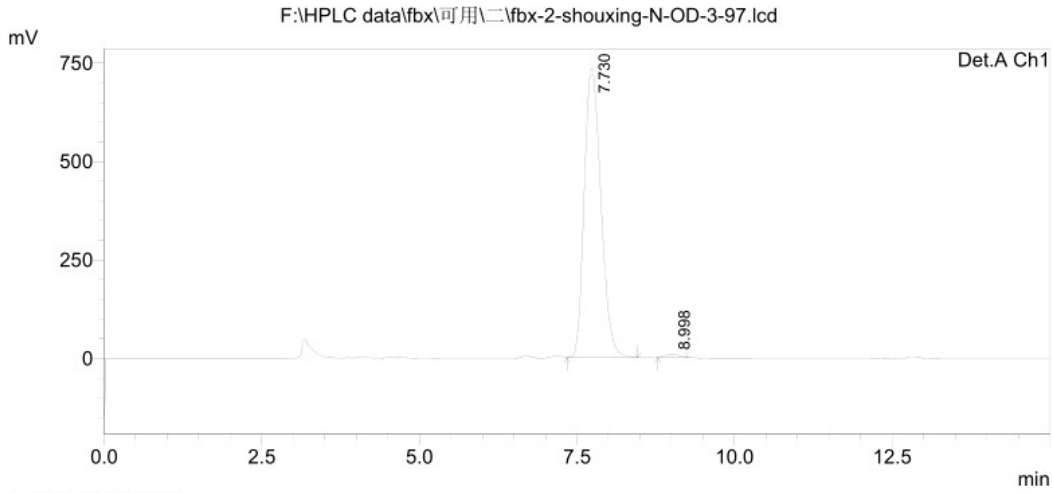
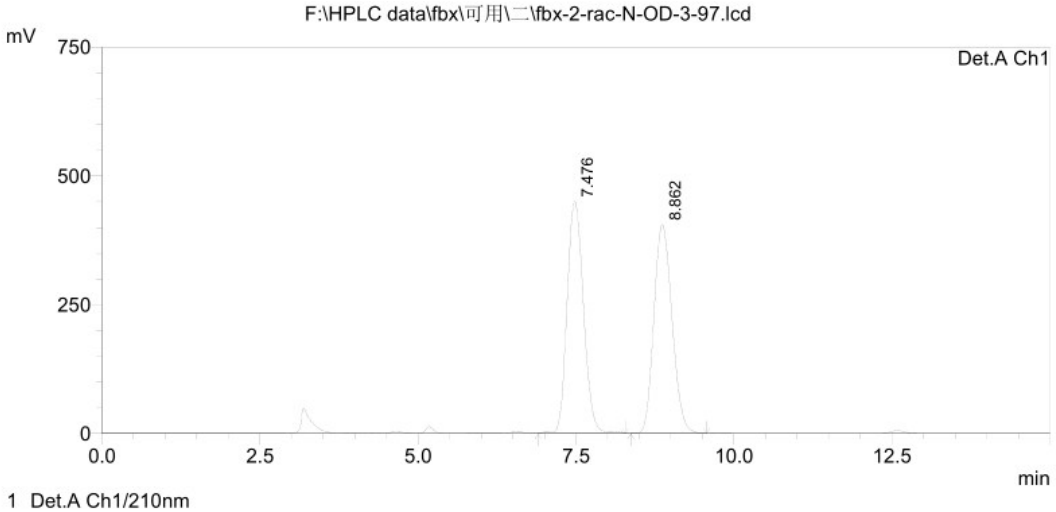


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.730	13598600	735174	98.769	98.758
2	8.998	151387	8507	1.100	1.143
3	16.785	18087	742	0.131	0.100
Total		13768075	744423	100.000	100.000

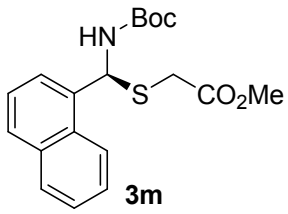


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.476	8199286	450831	50.198	52.623
2	8.862	8134621	405892	49.802	47.377
Total		16333907	856722	100.000	100.000



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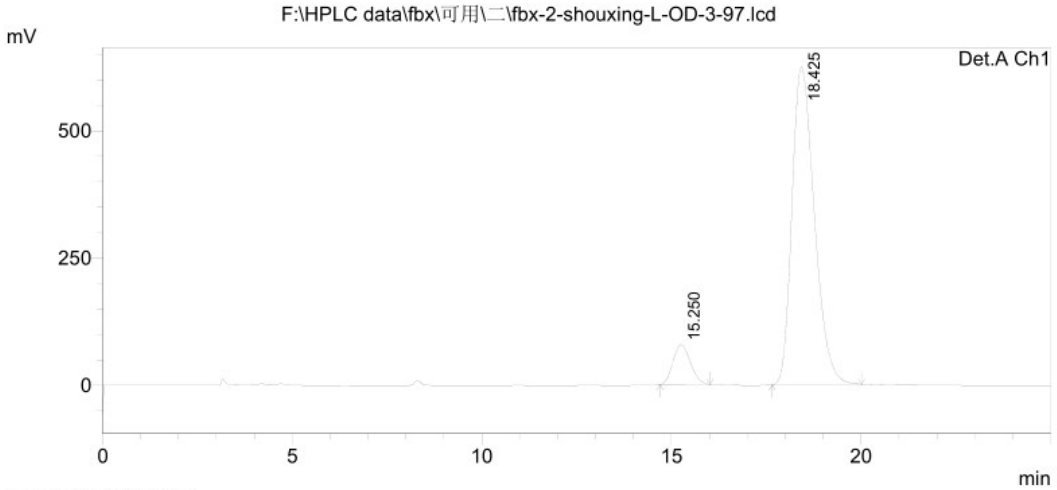
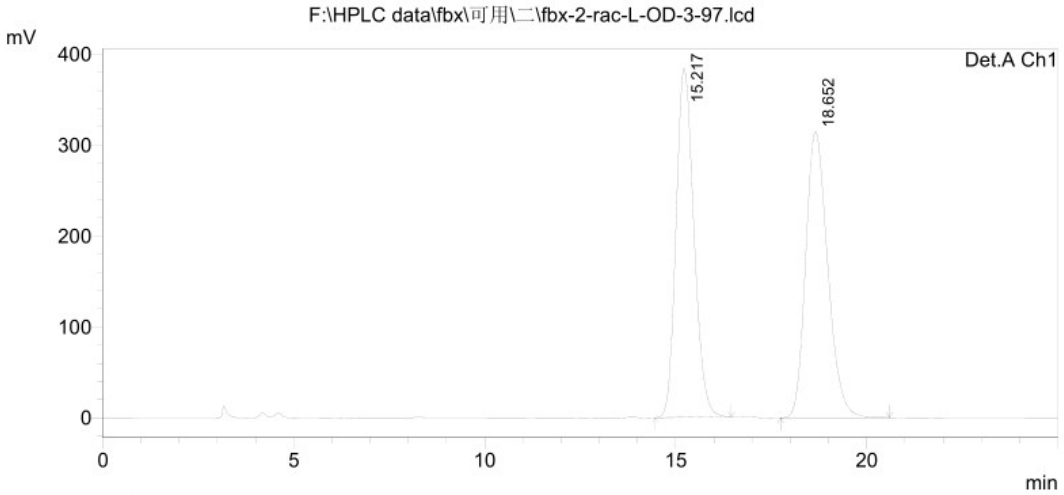


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.250	2519766	78292	8.945	11.145
2	18.425	25649980	624165	91.055	88.855
Total		28169747	702457	100.000	100.000

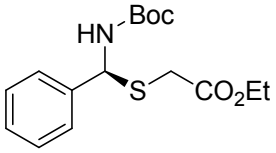


1 Det.A Ch1/220nm

PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.217	12483193	384020	49.724	54.978
2	18.652	12621669	314473	50.276	45.022
Total		25104862	698493	100.000	100.000



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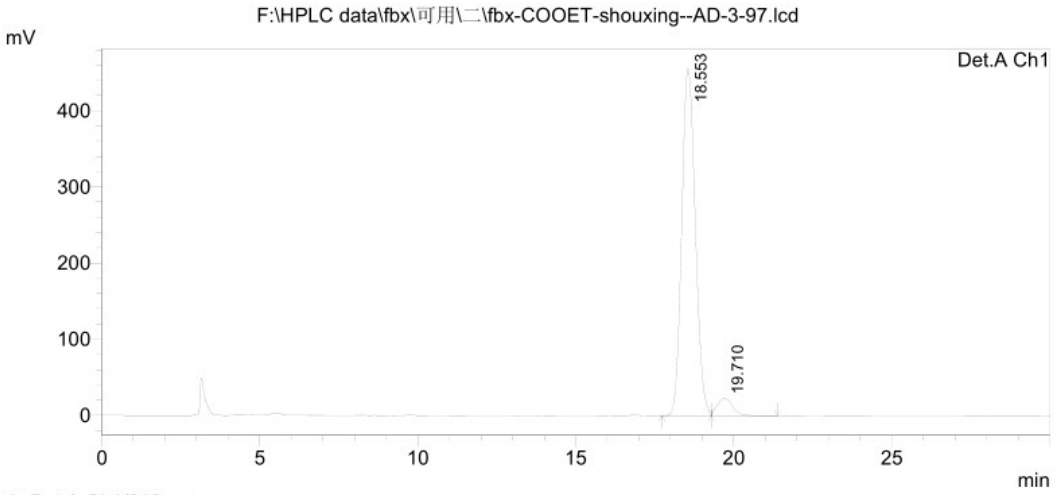

1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.553	13620660	456348	94.535	95.192
2	19.710	787469	23047	5.465	4.808
Total		14408130	479395	100.000	100.000

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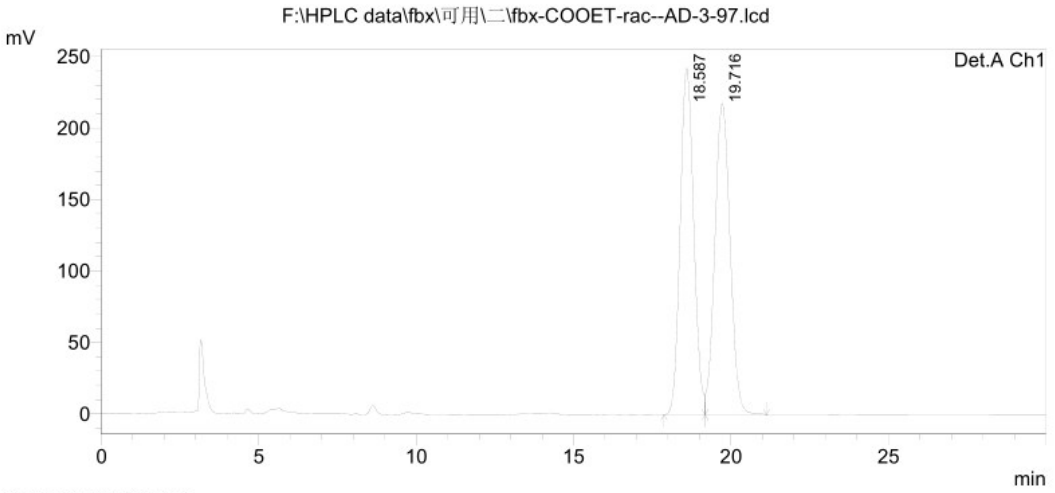
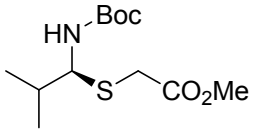


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.587	7228979	242268	49.566	52.675
2	19.716	7355482	217659	50.434	47.325
Total		14584461	459927	100.000	100.000



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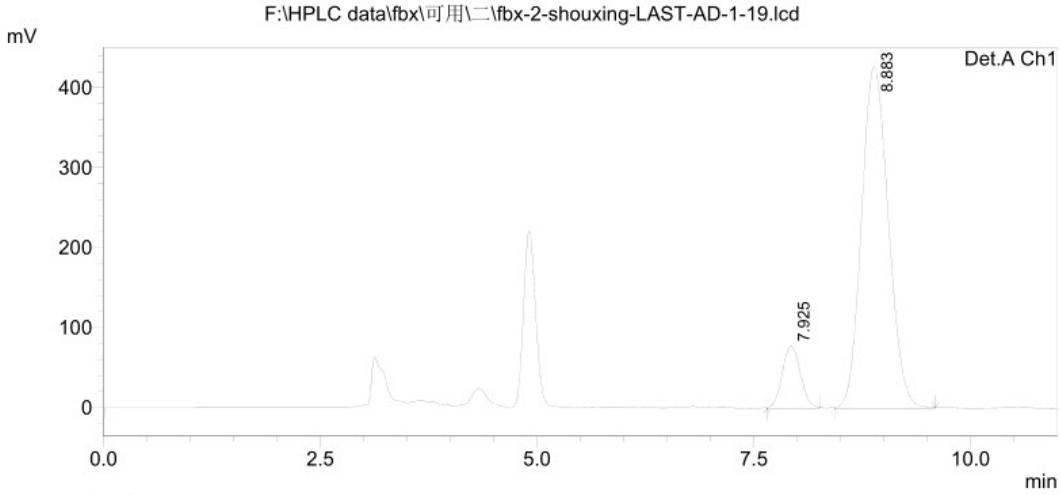
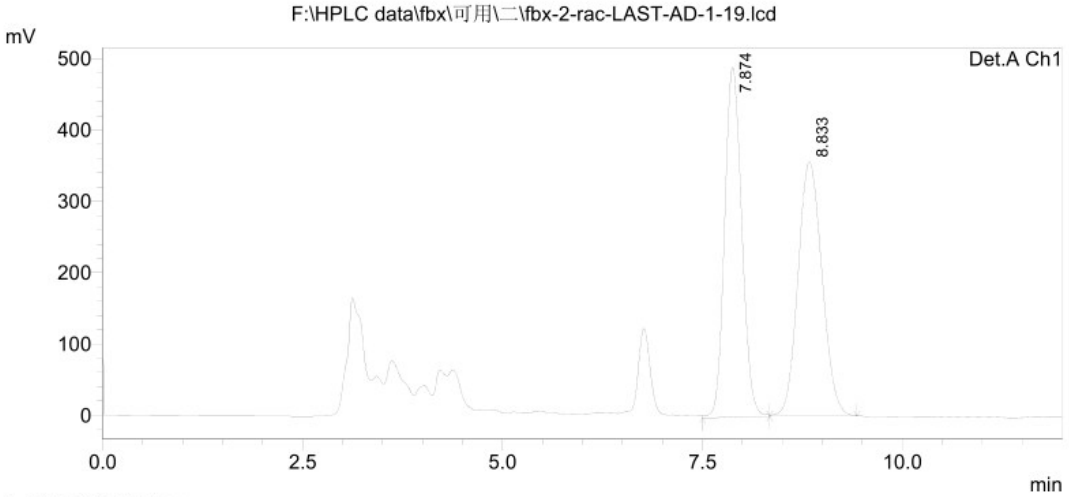


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.925	1130359	77420	10.967	15.372
2	8.883	9176955	426220	89.033	84.628
Total		10307314	503640	100.000	100.000

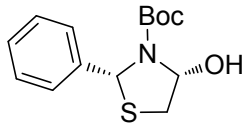


1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.874	7318932	490418	49.465	57.903
2	8.833	7477149	356553	50.535	42.097
Total		14796081	846971	100.000	100.000



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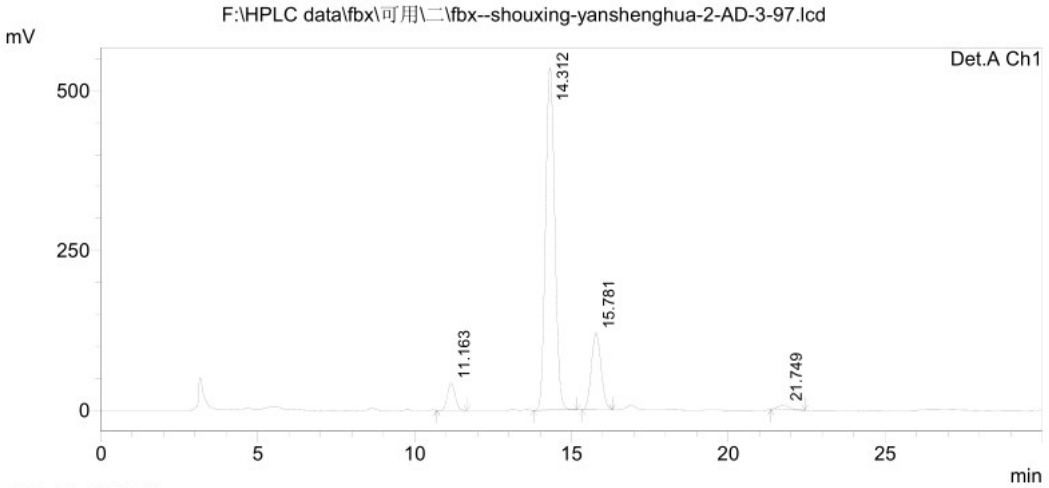


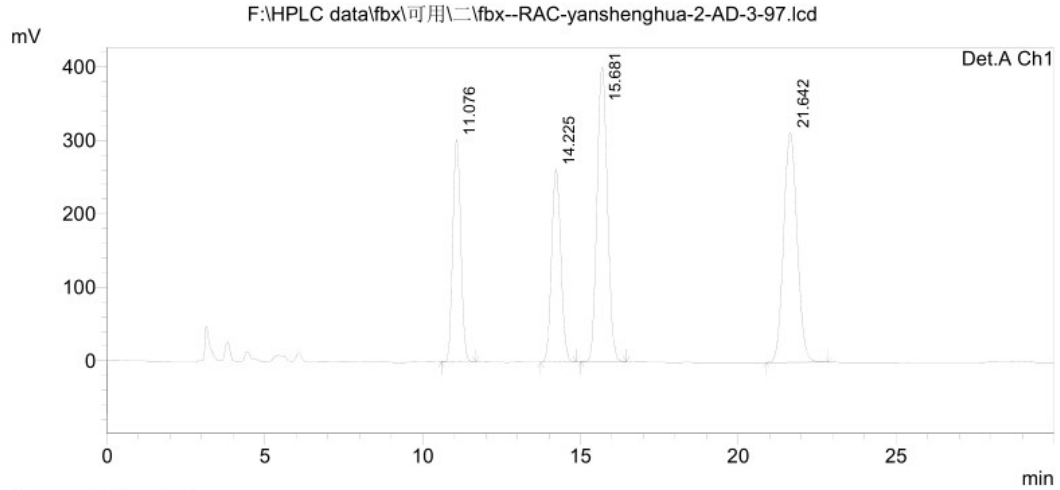
1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.163	729463	42647	5.048	6.043
2	14.312	10962528	536552	75.863	76.029
3	15.781	2573054	120023	17.806	17.007
4	21.749	185362	6494	1.283	0.920
Total		14450407	705716	100.000	100.000

<Chromatogram>



1 Det.A Ch1/210nm

PeakTable

Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.076	5344028	302971	18.303	23.675
2	14.225	5356087	262405	18.345	20.505
3	15.681	9179643	401294	31.440	31.358
4	21.642	9317322	313059	31.912	24.463
Total		29197081	1279728	100.000	100.000

Reference

1. The synthesis procedure of **1a-o,** see: (*a*) Q. Wang, M. van Gemmeren and B. List, *Angew. Chem. Int. Ed.*, 2014, **53**, 13592; (*b*) C. R. Jones, G. Dan Pantoş, A. J. Morrison and M. D. Smith, *Angew. Chem. Int. Ed.*, 2009, **48**, 7391; (*c*) A. J. Neuvonen and P. M. Pihko, *Org. Lett.*, 2014, **16**, 5152.
2. The synthesis procedure of **5,** see: N. Hisao, K. Takashi and Y. Susumu, EP1535906 A1, 2005.