Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Mono-selective β-C–H arylation of *N*-methylated amino acids and peptides promoted by 2-(methylthio)aniline directing group

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Supporting Information

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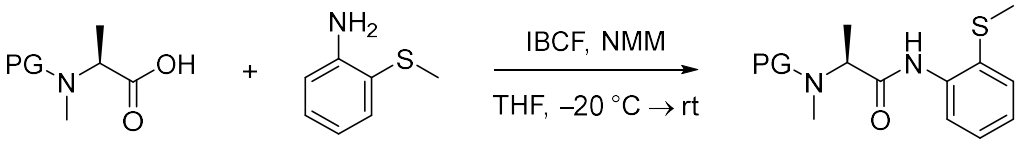
General Information

All air and moisture sensitive reactions were carried out in dried glassware (> 100 °C) under nitrogen or argon atmosphere. THF was dried over sodium and distilled before use. The products were purified by column chromatography on silica gel columns (Machery-Nagel 60, 0.04–0.063 mm). Mixtures of ethyl acetate (EtOAc) and petroleum ether (PE, 40–60 °C fraction) or CH_2Cl_2 and Et_2O were generally used as eluents. Analytical TLC was performed on pre-coated silica gel plates (Machery-Nagel, Polygram Sil G/UV_{254}). Detection was accomplished with UV light (254 nm), $KMnO_4$ solution or ceric ammonium sulfate solution. Melting points were detected with a MEL-TEMP II (Laboratory devices) apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded with a Bruker AV400 [400 MHz (^1H) and 100 MHz (^{13}C)] or a Bruker AV500 [500 MHz (^1H) and 125 MHz (^{13}C)] spectrometer. Chemical shifts are reported in ppm relative to TMS or internal solvent signal. Mass spectra were recorded with a Finnigan MAT 95 spectrometer (quadropole) using the CI technique. Optical rotations were measured with a Perkin-Elmer polarimeter (model 341) in a thermostated (20 °C ± 0.1 °C) cuvette, using a sodium vapour lamp (λ = 589 nm) as radiation source. The concentrations are given in g per 100 mL. HPLC analysis was performed on a Merck Hitachi D-7000 system with diode array detector L-7455.

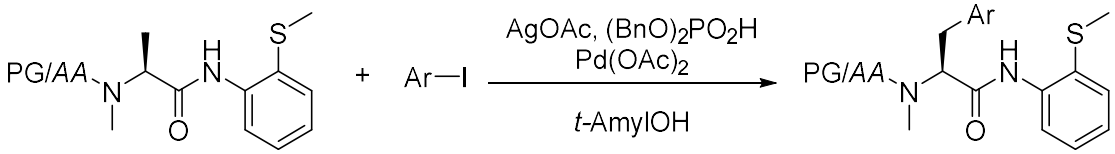
General Procedures (GP)

GP1: IBCF-mediated coupling of amino acids with 2-(methylthio)aniline (MTA)



To a solution of the amino acid (1.0 equiv) in anhydrous THF (6 mL/mmol) were added 1.1 equiv NMM and 1.0 equiv IBCF drop wise at –20 °C. After stirring for 20 min a solution of 1.1 equiv 2-(methylthio)aniline in anhydrous THF (1 mL/mmol) was slowly added at –20 °C and the reaction mixture was allowed to warm to room temperature overnight. The mixture was diluted with EtOAc, washed with 1 M $KHSO_4$ solution (3x), sat. aq. $NaHCO_3$ (1x) and brine (1x). The organic phase was dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified by column chromatography.

GP2: C-H activation of *N*-Methyl amino acids and peptides



A 4 mL glass vial with PTFE lined cap or a schlenk tube was charged with the amino acid or peptide compound, 2.0 equiv AgOAc, 20 mol% $(BnO)_2PO_2H$, 10 mol% $Pd(OAc)_2$ and 2.0 equiv of the electrophile. The reactants were suspended in *tert*-Amyl alcohol (2.5 mL/mmol), a magnetic stirring

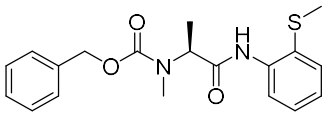
bar was added and the vial or schlenk tube was sealed under air atmosphere unless otherwise noted. The reaction mixture was stirred at given temperature for 2 – 3 days. After cooling to room temperature, the mixture was diluted with CH_2Cl_2 and filtered through a pad of Celite (rinsed with CH_2Cl_2). The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography.

Synthesis of Compounds

Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)carbamate (1a)

According to **GP1** 2.70 g (11.4 mmol, 1.0 equiv) *N*-((benzyloxy)carbonyl)-*N*-methyl-*L*-alanine, 1.74 g (12.5 mmol, 1.1 equiv) 2-(methylthio)aniline, 1.38 mL (12.5 mmol, 1.1 equiv) NMM and 1.48 mL (11.4 mmol, 1.0 equiv) IBCF were reacted. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **1a** (3.87 g, 10.8 mmol, 95%, > 99% ee) was obtained as colourless oil.

R_f (1a) = 0.20 (PE/EtOAc 8:2)



1a

^{1}H NMR (400 MHz, $CDCl_3$): 8.90 (bs, 1 H), 8.31 (d, *J* = 7.8 Hz, 1 H), 7.45 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.23–7.43 (m, 6 H), 7.06 (td, *J* = 7.6, 1.3 Hz), 5.15–5.30 (m, 2 H), 5.08 and 4.88 (rotamers, bs, bs, 1 H), 2.96 (s, 3 H), 2.23 (s, 3 H), 1.48 (d, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 13.3, 18.5, 29.7, 55.4, 67.6, 120.2, 124.3, 125.5, 127.8, 128.0, 128.4, 128.7, 132.7, 136.1, 137.8, 156.6, 169.3.

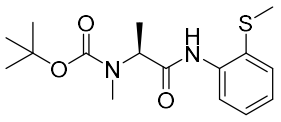
Optical rotation: $[\alpha]_D^{20}$ = -67.1 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{19}H_{22}N_2O_3S$ $[M]^+$	358.1346	358.1349

tert-Butyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)carbamate (1b)

According to **GP1** 2.28 g (9.62 mmol, 1.0 equiv) *N*-(*tert*-butoxycarbonyl)-*N*-methyl-*L*-alanine, 1.47 g (10.6 mmol, 1.1 equiv) 2-(methylthio)aniline, 1.16 mL (10.6 mmol, 1.1 equiv) NMM and 1.25 mL (9.62 mmol, 1.0 equiv) IBCF were reacted. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **1b** (2.73 g, 8.42 mmol, 88%) was obtained as colourless oil.

R_f (1b) = 0.55 (PE/EtOAc 1:1)



1b

^{1}H NMR (400 MHz, $CDCl_3$): 8.97 (bs, 1 H), 8.35 (d, *J* = 8.1 Hz, 1 H), 7.58 (d, *J* = 7.7 Hz, 1 H), 7.30 (t, *J* = 7.6 Hz, 1 H), 7.06 (t, *J* = 7.5 Hz, 1 H), 5.05 and 4.74 (rotamers, bs, bs, 1 H), 2.87 (bs, 3 H), 2.36 (s, 3 H), 1.50 (s, 9 H), 1.45 (d, *J* = 7.1 Hz, 3 H).

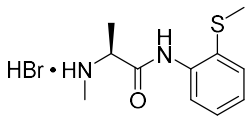
^{13}C NMR (100 MHz, $CDCl_3$): 13.5, 18.8, 28.3, 29.9, 54.5, 70.9, 80.7, 120.0, 124.2, 125.3, 128.8, 132.8, 138.1, 156.1, 169.9.

Optical rotation: $[\alpha]_D^{20}$ = -66.2 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{16}H_{25}N_2O_3S$ $[M+H]^+$	325.1580	325.1571

(*S*)-2-(Methylamino)-N-(2-(methylthio)phenyl)propanamide hydrobromide (9)[a]

2.10 g (5.86 mmol, 1.0 equiv) **1a** were suspended in 7.18 g (29.3 mmol, 5.0 equiv) HBr in AcOH (33 w%) at 0 °C. The reaction mixture was stirred for 3 hours at room temperature before adding Et_2O to precipitate the hydrobromide from the solution as orange solid. The solvent was removed by decanting and the solid was washed two more times with Et_2O. The residue was dried *in vacuo* to obtain the hydrobromide **9** (1.71 g, 5.51 mmol, 94%) as a white solid.



9

^{1}H NMR (400 MHz, MeOH-d_4): 7.39–7.47 (m, 2 H), 7.32 (td, *J* = 7.5, 1.0 Hz, 1 H), 7.24 (td, *J* = 7.7 Hz, 1.1 Hz, 1 H), 4.13 (q, *J* = 7.0 Hz, 1 H), 2.77 (s, 3 H), 2.47 (s, 3 H), 1.69 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, MeOH-d_4): 16.3, 16.7, 32.1, 58.9, 127.1, 127.7, 128.9, 129.0, 135.2, 136.0, 169.5.

Melting point: 160–162 °C

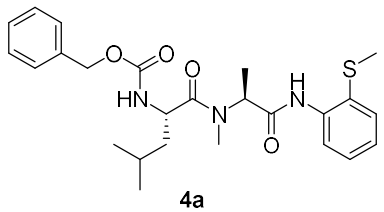
Benzyl ((*S*)-4-methyl-1-(methyl((S)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)amino)-1-oxopentan-2-yl)carbamate (4a)

To a solution of 1.48 g (4.85 mmol, 1.0 equiv) **9** in 32 mL dry DMF were added 1.93 g (7.27 mmol, 1.5 equiv) *N*-((benzyloxy)carbonyl)-*L*-leucine, 1.11 g (7.27 mmol, 1.5 equiv) HOBt, 1.39 g (7.27 mmol, 1.5 equiv) EDC·HCl and 1.33 mL (12.1 mmol, 2.5 equiv) NMM at 0 °C. The reaction mixture was allowed to warm to room temperature overnight and concentrated under reduced pressure. The residue was taken up in EtOAc and washed with 1 M $KHSO_4$ (x2), sat. aq. $NaHCO_3$ (x1) and brine (x1). After drying

[a] An attempt to remove the Cbz protecting group by hydrogenation (Pd/C, H_2, MeOH) failed. We assume, that the catalyst is inactivated by the thioether functionality of the directing group.

over Na_2SO_4 the mixture was filtrated and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) to obtain the dipeptide **4a** (2.10 g, 4.45 mmol, 92%) as colourless oil.

R_f (4a) = 0.42 (PE/EtOAc 1:1)



4a

The Leu-Ala dipeptide as well as the derived β-functionalized products show significant rotamers in the NMR spectra (e.g. see also compound **5ac**), which was verified by high temperature (373 K) NMR spectroscopy.

^{1}H NMR (400 MHz, $CDCl_3$): 8.99 and 8.64 (rotamers), 8.26 and 8.01 (rotamers, d, *J* = 8.2 Hz, d, *J* = 7.8 Hz, 1 H), 7.21–7.46 (m, 7 H), 7.05–7.15 (m, 1 H), 5.55 (d, *J* = 8.9 Hz, 1 H), 5.41 and 5.29 (rotamers, q, *J* = 6.9 Hz, bs, 1 H), 4.97–5.14 (m, 2 H), 4.57–4.81 (m, 1 H), 3.06 and 2.94 (rotamers, s, s, 3 H), 1.74–1.85 (m, 1 H), 1.51–1.64 (m, 2 H), 1.45 (d, *J* = 7.1 Hz, 3 H), 1.02 (d, *J* = 6.4 Hz, 3 H), 0.93 (d, *J* = 6.7 Hz, 3 H).

^{1}H NMR (500 MHz, DMSO-d_6, 373 K): 8.83 (s, 1 H), 7.73 (d, *J* = 7.8 Hz, 1 H), 7.43 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.28–7.37 (m, 5 H), 7.23 (td, *J* = 7.6, 1.5 Hz, 1 H), 7.17 (td, *J* = 7.6, 1.5 Hz, 1 H), 7.09 (bs, 1 H), 5.14 (bs, 1 H), 5.04 (m, 2 H), 4.57 (td, *J* = 8.7, 4.5 Hz, 1 H), 2.97–3.00 (m, 4 H), 2.39 (s, 3 H), 1.67–1.76 (m, 1 H), 1.48–1.62 (m, 2 H), 1.37 (d, *J* = 6.7 Hz, 3 H), 0.93 (d, *J* = 6.7 Hz, 3 H), 0.91 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 13.3, 18.6, 21.4, 23.5, 24.6, 30.5, 42.6, 49.7, 53.3, 66.9, 120.7, 124.7, 125.9, 128.0, 128.1, 128.5, 132.3, 136.3, 137.6, 156.2, 169.0, 173.8.

^{13}C NMR (125 MHz, DMSO-d_6, 373 K): 16.2, 21.1, 22.5, 23.8, 49.3, 65.2, 123.1, 125.0, 126.1, 127.0, 127.1, 127.7, 129.1, 136.1, 136.6, 155.4, 168.9, 172.3.

Optical rotation: $[\alpha]_D^{20}$ = -86.4 [$CHCl_3$, c = 1.00]

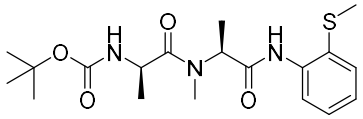
HRMS (CI):	Calculated	Found
$C_{25}H_{33}N_3O_4S$ $[M]^+$	471.2186	471.2187

tert-Butyl ((*R*)-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)amino)-1-oxopropan-2-yl)carbamate (4b)

2.07 g (6.38 mmol, 1.0 equiv) **1b** were dissolved in 6.0 mL dry CH_2Cl_2 and cooled to 0 °C before adding 15.9 mL (63.8 mmol, 10 equiv, 4 M) hydrogen chloride in 1,4-dioxane. The reaction mixture was stirred for 2 hours at room temperature. The solvent was removed *in vacuo* and the hydrochloride was obtained as a white solid, which was used directly for the next step. Therefore, it was dissolved in 42 mL anhydrous DMF and 1.45 g (7.67 mmol, 1.2 equiv) (*tert*-butoxycarbonyl)-*D*-alanine, 1.17 g (7.67 mmol, 1.2 equiv) HOBt, 1.47 g (7.67 mmol, 1.2 equiv) EDC·HCl and 1.58 mL (14.4 mmol, 2.25

equiv) NMM were added at 0 °C. The reaction mixture was allowed to warm to room temperature overnight and concentrated under reduced pressure. The residue was taken up in EtOAc and washed with 1 M $KHSO_4$ (x2), sat. aq. $NaHCO_3$ (x1) and brine (x1). After drying over Na_2SO_4 the mixture was filtrated and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO_2, PE/EtOAc 1:1) to obtain the dipeptide **4b** (2.32 g, 5.88 mmol, 92%) as colourless oil.

R_f (4b) = 0.33 (PE/EtOAc 1:1)



4b

^{1}H NMR (400 MHz, $CDCl_3$): 8.83 (bs, 1 H), 8.20 (d, *J* = 8.1 Hz, 1 H), 7.44 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.27 (m, 1 H), 7.08 (td, *J* = 7.6, 1.1 Hz, 1 H), 5.52 (d, *J* = 7.6 Hz, 1 H), 5.41 (q, *J* = 7.1 Hz, 1 H), 4.74 (quint, *J* = 7.1 Hz, 1 H), 3.06 (s, 3 H), 2.34 (s, 3 H), 1.45 (d, *J* = 7.1 Hz, 1 H), 1.41 (s, 9 H), 1.36 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): 13.3, 18.5, 19.0, 28.3, 30.6, 46.7, 53.3, 79.7, 121.1, 124.8, 126.6, 128.5, 132.4, 137.7, 155.0, 168.8, 174.2.

Optical rotation: $[\alpha]_D^{20}$ = -113.0 [$CHCl_3$, c = 1.00]

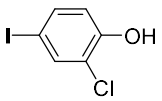
HRMS (CI):	Calculated	Found
$C_{19}H_{30}N_3O_4S$ $[M+H]^+$	396.1952	396.1945

2-Chloro-4-iodophenol (10a)

Compound **10a** was synthesized according to a modified procedure of S. N. Georgiades and J. Clardy.[3]

5.50 g (25.0 mmol, 1.0 equiv) 4-iodophenol were dissolved in 139 mL toluene under N_2 atmosphere. 36.0 µL (250 µmol, 0.01 equiv) diisopropylamine were added and the solution was warmed to 70 °C, before 2.03 mL (25.0 mmol, 1.0 equiv) sulfuryl chloride were slowly syringed in. After stirring for 1 h at 70 °C, the reaction mixture was cooled to room temperature, diluted with diethyl ether and washed once with sat. aq. $NaHCO_3$, H_2O and brine. After drying over Na_2SO_4, the solvent was removed *in vacuo* and the crude product was purified by column chromatography (SiO_2, PE/Et_2O 8:2) giving access to **10a** (5.66 g, 22.3 mmol, 89%) as white solid.

R_f (10a) = 0.23 (PE/Et_2O 8:2)



10a

^{1}H NMR (400 MHz, $CDCl_3$): 7.62 (d, *J* = 2.1 Hz, 1 H), 7.46 (dd, *J* = 8.6, 2.1 Hz, 1 H), 6.78 (d, *J* = 8.7 Hz, 1 H), 5.52 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): 151.4, 137.3, 136.9, 121.1, 118.2, 81.5.

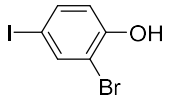
Melting point: 53 °C

2-Bromo-4-iodophenol (10b)

Compound **10b** was synthesized according to a modified procedure of S. N. Georgiades and J. Clardy.[3]

4.25 g (19.3 mmol, 1.0 equiv) 4-iodophenol were dissolved in 26 mL MeOH and cooled to 0 °C. 1.09 mL (21.2 mmol, 1.1 equiv) Br_2 were added drop wise under vigorous stirring and the reaction was allowed to proceed for 1 h at 0 °C. The reaction was quenched by addition of sat. aq. $Na_2S_2O_3$ and diluted with Et_2O. The phases were separated and the aqueous phase was extracted with Et_2O. The combined organic phase was washed once with H_2O and brine, dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was redissolved in CH_2Cl_2 and purified by column chromatography (SiO_2, 100% CH_2Cl_2) to obtain **10b** (3.69 g, 12.3 mmol, 64%) as white solid.

R_f (10b) = 0.53 (CH_2Cl_2)



10b

^{1}H NMR (400 MHz, $CDCl_3$): 7.76 (d, *J* = 2.0 Hz, 1 H), 7.49 (dd, *J* = 8.6, 2.1 Hz, 1 H), 6.79 (d, *J* = 8.7 Hz, 1 H), 5.49 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): 152.3, 139.6, 138.0, 118.1, 111.3, 82.0.

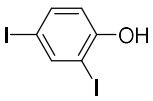
Melting point: 50 °C

2,4-Diiodophenol (10c)

Compound **10c** was synthesized according to a modified procedure of K. J. Edgar and S. N. Falling.[2]

4.50 g (20.4 mmol, 1.0 equiv) 2-iodophenol, 3.07 g (20.4 mmol, 1.0 equiv) NaI and 818 mg NaOH (20.4 mmol, 1.0 equiv) were dissolved in 51 mL MeOH. The solution was cooled to 0 °C and 24.1 g (19.43 mmol, 0.95 equiv, 6% aq. solution) NaOCl were added via dropping funnel over 1.5 h. After stirring for another hour at 0 °C, the reaction was quenched b the addition of sat. aq. $Na_2S_2O_3$ and acidified to pH 7 using 1 M aq. HCl. The mixture was diluted with CH_2Cl_2, the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (x2). The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, PE/EtOAc 9:1) to obtain compound **10c** as white solid.

R_f (10c) = 0.35 (PE/EtOAc 7:3)



10c

^{1}H NMR (400 MHz, $CDCl_3$): 7.93 (d, *J* = 2.1 Hz, 1 H), 7.51 (dd, *J* = 8.6, 2.1 Hz, 1 H), 6.76 (d, *J* = 8.6 Hz, 1 H), 5.28 (s, 1 H).

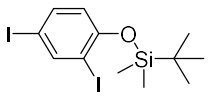
^{13}C NMR (100 MHz, $CDCl_3$): 154.8, 145.3, 138.9, 117.0, 86.9, 82.8.

Melting point: 73 °C

***tert*-Butyl(2,4-diiodophenoxy)dimethylsilane (10d)**

To a solution of 2.99 g (8.64 mmol, 1.0 equiv) **10c** and 1.18 g (17.3 mmol, 2.0 equiv) imidazole in dry DMF 1.43 g (9.51 mmol, 1.1 equiv) *tert*-butylchlorodimethylsilane was added at 0 °C in portions. The reaction mixture was stirred at room temperature for 3 h. EtOAc was added and the mixture was washed with sat. aq. NH_4Cl (x2) and brine, dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 9:1) to obtain compound **10d** (3.97 g, 8.63 mmol, 100%) as a colourless liquid.

R_f (10d) = 0.61 (PE/EtOAc 9:1)



10d

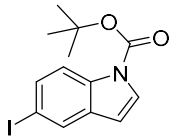
^{1}H NMR (400 MHz, $CDCl_3$): 8.03 (d, *J* = 2.2 Hz, 1 H), 7.46 (dd, *J* = 8.6, 2.2 Hz, 1 H), 6.57 (d, *J* = 8.4 Hz, 1 H), 1.05 (s, 9 H), 0.26 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): -4.1, 18.3, 25.8, 83.7, 92.1, 120.2, 138.0, 146.8, 155.3.

***tert*-Butyl 5-iodo-1*H*-indole-1-carboxylate (11a)**

To a solution of 1.35 g (5.55 mmol, 1.0 equiv) 5-iodoindol in CH_2Cl_2 were added 34.0 mg (278 µmol, 0.05 equiv) 4-DMAP, 2.32 mL (16.7 mmol, 3.0 equiv) triethylamine and 1.42 mL (6.11 mmol, 1.1 equiv) di-*tert*-butyl dicarbonate. The reaction mixture was stirred at room temperature for 1 h and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 95:5) to obtain the product **11a** (1.90 g, 5.54 mmol, 100%) as an orange oil.

R_f (11a) = 0.75 (CH_2Cl_2/Et_2O 9:1)



11a

^{1}H NMR (400 MHz, $CDCl_3$): 7.92 (bs, 1 H), 7.89 (d, *J* = 1.6 Hz, 1 H), 7.75 (dd, *J* = 8.8, 1.7 Hz, 1 H), 7.54 (d, *J* = 3.5 Hz, 1 H), 6.48 (d, *J* = 3.8 Hz, 1 H), 1.66 (s, 9 H).

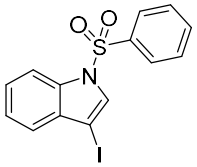
^{13}C NMR (100 MHz, $CDCl_3$): 28.1, 84.1, 86.6, 106.2, 117.0, 126.6, 129.7, 132.6, 132.8, 134.5, 149.4.

3-Iodo-1-(phenylsulfonyl)-1*H*-indole (11b)

The intermediate 3-iodoindole was synthesized according to a modified procedure of Palla *et al.*[4]

To a solution of 2.80 g (23.9 mmol, 1.0 equiv) 1*H*-indole in DMF were added 3.35 g (59.8 mmol, 2.5 equiv) KOH and 12.1 g (47.8 mmol, 2.0 equiv) iodine. The reaction mixture was stirred for 15 min before being poured into ice water. The precipitating solid was collected by filtration, washed with water and dried *in vacuo*. The crude 3-iodo-1*H*-indole was added to a solution of 12.4 g (311 mmol, 13 equiv) NaOH and 1.16 g (3.59 mmol, 0.15 equiv) tetrabutylammonium bromide in 29 mL water at 0 °C, before a solution of 4.31 mL (33.5 mmol, 1.4 equiv) benzenesulfonyl chloride in 50 mL THF was added drop wise. The reaction mixture was stirred at room temperature for 3 h, extracted with EtOAc (x3), dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 8:2) to obtain the product **11b** (7.70 g, 20.1 mmol, 84%) as a brown solid.

R_f (11b) = 0.42 (PE/EtOAc 7:3)



11b

^{1}H NMR (400 MHz, $CDCl_3$): 7.94–7.99 (m, 1 H), 7.87–7.92 (m, 2 H), 7.70 (s, 1 H), 7.52–7.58 (m, 1 H), 7.43–7.48 (m, 2 H), 7.35–7.40 (m, 2 H), 7.28–7.33 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): 67.1, 113.3, 122.0, 124.0, 125.7, 126.9, 129.4, 129.7, 132.4, 134.1, 134.3, 137.8.

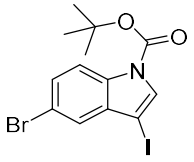
Melting point: 115–117 °C

***tert*-Butyl 5-bromo-3-iodo-1*H*-indole-1-carboxylate (11c)**

The intermediate 5-bromo-3-iodoindole was synthesized according to a modified procedure of Mori *et al.*[5]

To a solution of 175 mg (893 µmol, 1.0 equiv) 5-bromo-1*H*-indole and 35.7 mg (893 µmol, 1.0 equiv) sodium hydroxide in 9 mL methanol were added 227 mg (893 µmol, 1.0 equiv) iodine and a solution of 148 mg (893 µmol, 1.0 equiv) potassium iodide in 1.8 mL water. The reaction mixture was stirred for 3 h at room temperature before being poured into ice water. The precipitating solid was collected by filtration, washed with water and dried *in vacuo*. The crude 5-bromo-3-iodo-1*H*-indole (253 mg, 786 mmol, 88%) was directly used in the next step. Therefore, it was dissolved in 4 mL CH_2Cl_2, treated with 201 µL (865 µmol, 1.1 equiv) di-*tert*-butyl dicarbonate, 329 µL (2.36 mmol, 3 equiv) triethylamine and 4.8 mg (39 µmol, 0.05 equiv) 4-DMAP. The reaction mixture was stirred at room temperature for 3 h, diluted with CH_2Cl_2, washed with sat. aq. $Na_2S_2O_3$, dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 8:2) to obtain the product **11c** (328 mg, 777 mmol, 99%) as a brown solid.

R_f (11c) = 0.56 (PE/EtOAc 8:2)



11c

^{1}H NMR (400 MHz, $CDCl_3$): 8.01 (d, *J* = 8.7 Hz, 1 H), 7.71 (s, 1 H), 7.54 (d, *J* = 1.8 Hz, 1 H), 7.45 (dd, *J* = 8.8, 2.0 Hz, 1 H), 1.66 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 28.1, 63.9, 84.8, 116.6, 116.8, 124.3, 128.3, 131.2, 133.7, 133.9, 148.3.

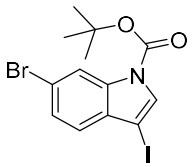
Melting point: 98–100 °C

***tert*-Butyl 6-bromo-3-iodo-1*H*-indole-1-carboxylate (11d)**

The intermediate 6-bromo-3-iodoindole was synthesized according to a modified procedure of Palla *et al.*[4]

To a solution of 932 mg (4.75 mmol, 1.0 equiv) 6-bromo-1*H*-indole and 667 mg (11.9 mmol, 2.5 equiv) potassium hydroxide in 12 mL DMF were added 2.41 g (9.51 mmol, 2.0 equiv) iodine. The reaction mixture was stirred for 15 min at room temperature before being poured into ice water. The precipitating solid was collected by filtration, washed with water and dried *in vacuo*. The crude 6-bromo-3-iodo-1*H*-indole was dissolved in 24 mL CH_2Cl_2, treated with 1.21 mL (5.23 mmol, 1.1 equiv) di-*tert*-butyl dicarbonate, 1.99 mL (14.3 mmol, 3 equiv) triethylamine and 29.0 mg (238 µmol, 0.05 equiv) 4-DMAP. The reaction mixture was stirred at room temperature for 3 h, diluted with CH_2Cl_2, washed with sat. aq. $Na_2S_2O_3$, dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 8:2) to obtain the product **11d** (1.85 g, 4.38 mmol, 92%) as a slightly brown solid.

R_f (11d) = 0.56 (PE/EtOAc 8:2)



11d

^{1}H NMR (400 MHz, $CDCl_3$): 8.36 (bs, 1 H), 7.68 (s, 1 H), 7.42 (dd, *J* = 8.4, 1.7 Hz, 1 H), 7.25 (d, *J* = 8.2 Hz, 1H), 1.67 (s, 9 H).

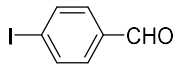
^{13}C NMR (100 MHz, $CDCl_3$): 28.1, 64.8, 84.9, 118.2, 119.3, 122.7, 126.6, 130.5, 131.0, 135.4, 148.3.

Melting point: 142–144 °C

4-Iodobenzaldehyde (12)

Compound **12** was synthesized according to a modified procedure of L. F. Tietze *et al*.[1]

2.20 g (6.67 mmol, 1.0 equiv) 1,4-diiodobenzene were dissolved in 33 mL dry Et_2O and cooled to -78 °C before adding 2.80 mL (7.00 mmol, 1.05 equiv, 2.5 M in hexanes) *n*BuLi and stirred for 20 min. Afterwards 2.58 mL (33.3 mmol, 5 equiv) dry DMF were slowly added and the solution was allowed to warm to room temperature over 2 h. The reaction was quenched by the addition of H_2O (30 mL), the phases were separated and the aqueous phase was extracted with Et_2O (x4). The combined organic phase was washed once with H_2O and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was recrystallized from EtOH/H_2O to afford **12** (1.29 g, 5.55 mmol, 83%) as slightly yellow solid.



12

^{1}H NMR (400 MHz, $CDCl_3$): 9.96 (s, 1 H), 7.92 (d, *J* = 8.3 Hz, 2 H), 7.59 (d, *J* = 8.3 Hz, 2 H).

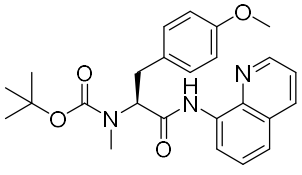
^{13}C NMR (100 MHz, $CDCl_3$): 191.4, 138.4, 130.8, 102.8.

Melting point: 78 °C

***tert*-Butyl (*S*)-(3-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)propan-2-yl)(methyl)carbamate (3dc), *tert*-Butyl (*S*)-(1,1-bis(4-methoxyphenyl)-3-oxo-3-(quinolin-8-ylamino)propan-2-yl)(methyl) carbamate (2dc)**[6]

According to **GP2** 100 mg (304 µmol, 1.0 equiv) *tert*-butyl (*S*)-methyl(1-oxo-1-(quinolin-8-ylamino)propan-2-yl)carbamate,[6] 142 mg (607 µmol, 2.0 equiv) 4-iodoanisole, 101 mg (607 µmol, 2.0 equiv) AgOAc, 16.9 mg (61 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.8 mg (34 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 50 °C for 2 days. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3dc** (72.9 mg, 167 µmol, 55%) was obtained as slightly yellow solid. The bifunctionalized compound **2dc** (38.1 mg, 70 µmol, 23%) was obtained as a white solid.

R_f (3dc) = 0.53 (PE/EtOAc 1:1)



3dc

^{1}H NMR (400 MHz, $CDCl_3$): 10.43 and 10.35 (rotamers, s, s, 1 H), 8.71–8.83 (m, 2 H), 8.09–8.18 (m, 1 H), 7.47–7.58 (m, 2 H), 7.38–7.46 (m, 1 H), 7.23(d, *J* = 8.2 Hz, 1 H), 7.18 (d, *J* = 8.3 Hz, 1 H), 6.80–6.91 (m, 2 H), 5.32 and 5.00 (rotamers, dd, *J* = 9.2, 6.4 Hz, dd, *J* = 10.0, 4.6 Hz, 1 H), 3.78 (s, 3 H), 3.43–3.54

(m, 1 H), 3.04 (dd, *J* = 14.2, 10.6 Hz, 1 H), 2.89 and 2.84 (rotamers, s, s, 3 H), 1.46 and 1.41 (rotamers, s, s, 9 H).

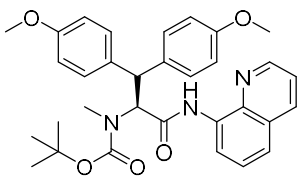
^{13}C NMR (100 MHz, $CDCl_3$): 28.1 and 28.3 (rotamers), 30.9, 33.1, 55.2, 60.6 and 62.7 (rotamers), 80.3 and 80.8 (rotamers), 113.8 and 114.0 (rotamers), 116.2 and 116.3 (rotamers), 121.6 and 121.7 (rotamers), 127.2 and 127.9 (rotamers), 129.6 and 129.9 (rotamers), 134.2 and 134.4 (rotamers), 136.0 and 136.2 (rotamers), 138.4, 148.2 and 148.3 (rotamers), 155.1, 158.3, 169.0 and 169.4 (rotamers).

Optical rotation: $[\alpha]_D^{20}$ = -72.1 [$CHCl_3$, c = 1.00]

Melting point: 83 °C

HRMS (CI):	Calculated	Found
$C_{25}H_{30}N_3O_4[M+H]^+$	436.2231	436.2265

R_f (2dc) = 0.47 (PE/EtOAc 1:1)



2dc

^{1}H NMR (400 MHz, $CDCl_3$): 10.17 and 10.10 (rotamers, s, s, 1 H), 8.76–8.80 (m, 1 H), 8.59–8.67 (m, 1 H), 8.13 and 8.08 (rotamers, d, *J* = 8.2 Hz, d, *J* = 8.2 Hz, 1 H), 7.26–7.50 (m, 7 H), 6.83 (dd, *J* = 8.6, 1.3 Hz, 2 H), 6.75 and 6.71 (rotamers, d, *J* = 8.7 Hz, d, *J* = 8.7 Hz, 2 H), 5.86 and 5.60 (rotamers, d, *J* = 11.2 Hz, d, *J* = 11.6 Hz, 1 H), 4.71 and 4.68 (rotamers, d, *J* = 11.6 Hz, d, *J* = 11.5 Hz, 1 H), 3.77 (s, 3 H), 3.66 and 3.62 (rotamers, s, s, 3 H), 2.75 and 2.71 (rotamers, s, s, 3 H), 1.70 and 1.42 (rotamers, s, s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 28.3 and 28.4 (rotamers), 48.2 and 48.6 (rotamers), 55.0 and 55.0 (rotamers), 55.2, 80.3 and 81.1 (rotamers), 113.9 and 114.0 (rotamers), 116.5, 121.5 and 121.6 (rotamers), 127.0 and 127.2 (rotamers), 128.8 and 128.9 (rotamers), 129.0 and 129.1 (rotamers), 133.2 and 133.5 (rotamers), 133.9 and 134.0 (rotamers), 134.4 and 134.6 (rotamers), 135.9 and 136.3 (rotamers), 138.2 and 138.4 (rotamers), 147.9 and 148.2 (rotamers), 154.5, 158.1 and 158.1 (rotamers), 158.1 and 158.3 (rotamers), 167.3 and 168.3 (rotamers).

Optical rotation: $[\alpha]_D^{20}$ = +25.6 [$CHCl_3$, c = 1.00]

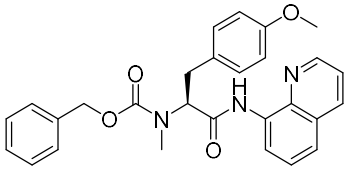
Melting point: 154 °C

HRMS (CI):	Calculated	Found
$C_{32}H_{36}N_3O_5[M+H]^+$	542.2649	542.2654

Benzyl (*S*)-(3-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)propan-2-yl)(methyl)carbamate (3cc), Benzyl (*S*)-(1,1-bis(4-methoxyphenyl)-3-oxo-3-(quinolin-8-ylamino)propan-2-yl)(methyl)carbamate (2cc)[6]

According to **GP2** 100.0 mg (275 µmol, 1.0 equiv) benzyl (*S*)-methyl(1-oxo-1-(quinolin-8-ylamino)propan-2-yl)carbamate,[6] 129 mg (550 µmol, 2.0 equiv) 4-iodoanisole, 91.9 mg (550 µmol, 2.0 equiv) AgOAc, 15.3 mg (55 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.2 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 40 °C for 24 h. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3cc** (93.8 mg, 200 µmol, 73%) was obtained as colourless oil. The bifunctionalized compound **2cc** (12.6 mg, 22 µmol, 8%) was obtained as a colourless oil.

R_f (3cc) = 0.28 (PE/EtOAc 7:3)



3cc

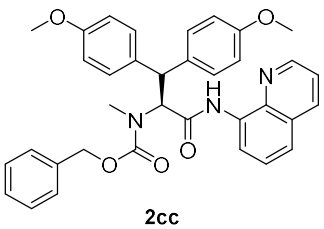
^{1}H NMR (400 MHz, $CDCl_3$): 10.33 (s, 1 H), 8.66–8.82 (m, 2 H), 8.12 (dd, *J* = 7.8, 3.3 Hz, 1 H), 7.47–7.57 (m, 2 H), 7.38–7.44 (m, 1 H), 7.08–7.32 (m, 6 H), 6.75–7.05 (m, 2 H), 5.05–5.38 (m, 3 H), 3.77 (s, 3 H), 3.43–3.54 (m, 1 H), 3.01–3.11 (m, 1 H), 2.99 and 2.97 (rotamers, s, s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 30.7 and 31.5 (rotamers), 33.3, 55.1, 61.5 and 62.5 (rotamers), 67.4 and 67.7 (rotamers), 113.9 and 114.0 (rotamers), 116.3 and 116.5 (rotamers), 121.6 and 121.8 (rotamers), 127.1, 127.5, 127.8, 128.3 and 128.4 (rotamers), 129.2 and 129.3 (rotamers), 129.9 and 129.9 (rotamers), 136.1 and 136.1 (rotamers), 136.6, 138.4 and 138.5 (rotamers), 148.4, 156.1 and 157.0 (rotamers), 158.2, 168.5 and 168.8 (rotamers).

Optical rotation: $[\alpha]_D^{20}$ = -62.9 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{28}H_{28}N_3O_4[M+H]^+$	470.2074	470.2057

R_f (2cc) = 0.19 (PE/EtOAc 7:3)



2cc

^{1}H NMR (400 MHz, $CDCl_3$): 10.08 and 10.06 (rotamers, s, s, 1 H), 8.79 and 8.66 (rotamers, dd, *J* = 4.2, 1.5 Hz, dd, *J* = 4.2, 1.5 Hz, 1 H), 8.58–8.65 (m, 1 H), 8.12 and 8.09 (rotamers, dd, *J* = 8.4, 1.2 Hz, dd, *J* = 8.3, 1.4 Hz, 1 H), 7.12–7.61 (m, 12 H), 6.68–6.83 (m, 4 H), 5.80 and 5.60 (rotamers, d, *J* = 12.0 Hz, d, *J*

= 11.7 Hz, 1 H), 5.46 and 5.21 (rotamers, d, *J* = 12.3 Hz, d, *J* = 12.4 Hz, 1 H), 5.26 and 5.09 (rotamers, d, *J* = 12.3 Hz, d, *J* = 12.4 Hz, 1 H), 4.71 and 4.70 (rotamers, d, *J* = 12.0 Hz, d, *J* = 11.8 Hz, 1 H), 3.77 and 3.75 (rotamers, s, s, 3 H), 3.61 and 3.60 (rotamers, s, s, 3 H), 2.88 and 2.86 (rotamers, s, s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 29.5, 48.5 and 48.7 (rotamers), 55.0 and 55.1 (rotamers), 67.3 and 67.8 (rotamers), 114.1 and 114.1 (rotamers), 116.7, 121.5 and 121.7 (rotamers), 127.0, 127.3, 127.9, 128.2 and 128.3 (rotamers), 128.6, 128.7 and 128.8 (rotamers), 129.0 and 129.2 (rotamers), 133.0, 1335., 134.3, 136.0, 136.7 and 136.8 (rotamers), 138.3, 148.3, 157.2, 158.2 and 158.2 (rotamers), 167.9.

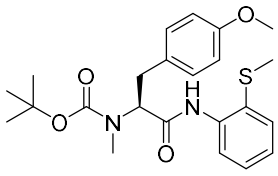
Optical rotation: $[\alpha]_D^{20}$ = +37.2 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{35}H_{35}N_3O_5$[M]	575.2420	575.2427

***tert*-Butyl (*S*)-(3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3bc)**

According to **GP2** 100 mg (308 µmol, 1.0 equiv) **1b**, 144 mg (616 µmol, 2.0 equiv) 4-iodoanisole, 103 mg (616 µmol, 2.0 equiv) AgOAc, 17.2 mg (62 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.9 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 9:1) and the product **3bc** (87.9 mg, 204 µmol, 66%) was obtained as colourless oil.

R_f (3bc) = 0.43 (PE/EtOAc 7:3)



3bc

^{1}H NMR (400 MHz, $CDCl_3$): 8.97 (s, 1 H), 8.30–8.43 (m, 1 H), 6.98–7.51 (m, 5 H), 6.84 (bs, 2 H), 4.79–5.23 (m, 1 H), 3.77 (s, 3 H), 3.44 (dd, *J* = 14.7, 5.0 Hz, 1 H), 2.91–3.00 (m, 1 H), 2.85 and 2.80 (rotamers, s, s, 3 H), 2.32 (s, 3 H), 1.42 and 1.32 (rotamers, s, s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.8, 28.0 and 28.2 (rotamers), 30.8 and 31.2 (rotamers), 32.8, 55.2, 60.5 and 63.1 (rotamers), 80.4 and 80.8 (rotamers), 113.8 and 114.0 (rotamers), 119.8 and 120.3 (rotamers), 122.2, 124.4, 125.1 and 125.5 (rotamers), 128.8 and 128.9 (rotamers), 129.3, 129.8, 129.9, 133.0, 138.0 and 138.2 (rotamers), 155.0 and 156.2 (rotamers), 158.2 and 158.3 (rotamers), 168.8 and 169.1 (rotamers).

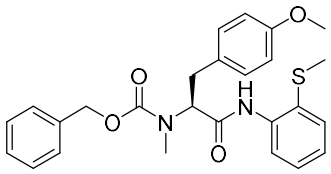
Optical rotation: $[\alpha]_D^{20}$ = -59.3 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{23}H_{31}N_2O_4S$ $[M+H]^+$	431.1999	431.2056

Benzyl (*S*)-(3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ac)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 131 mg (558 µmol, 2.0 equiv) 4-iodoanisole, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 2 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 9:1) and the product **3ac** (110 mg, 237 µmol, 85%) was obtained as colourless oil.

R_f (3ac) = 0.32 (PE/EtOAc 7:3)



3ac

^{1}H NMR (400 MHz, $CDCl_3$): 8.89 (bs, 1 H), 8.31 (m, 1 H), 7.44 (d, *J* = 7.7 Hz, 1 H), 7.00–7.37 (m, 9 H), 6.75–6.84 (m, 2 H), 4.92–5.20 (m, 2 H), 3.77 (s, 3 H), 3.44 (dd, *J* = 14.7, 6.0 Hz, 1 H), 3.00 (dd, *J* = 14.1, 10.0 Hz, 1 H), 2.93 and 2.91 (rotamers, s, s, 3 H), 2.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.7, 32.9 and 33.0 (rotamers), 55.1, 61.4 and 62.5 (rotamers), 67.5 and 67.7 (rotamers), 113.9, 120.0 and 120.5 (rotamers), 124.5, 125.8, 127.6, 128.0 and 128.0 (rotamers), 128.4, 128.7 and 128.9 (rotamers), 129.0 and 129.2 (rotamers), 129.8 and 129.8 (rotamers), 132.8 and 132.9 (rotamers), 136.3, 137.9, 157.0 and 158.2 (rotamers), 168.2 and 168.5 (rotamers).

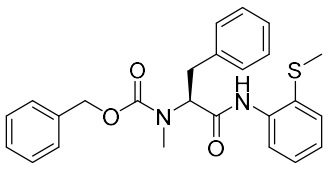
Optical rotation: $[\alpha]_D^{20}$ = -55.4 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{26}H_{29}N_2O_4S$ $[M+H]^+$	465.1843	465.1839

Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (3aa)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 62.2 µL (558 µmol, 2.0 equiv) iodobenzene, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 2 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3aa** (93.1 mg, 214 µmol, 77%) was obtained as colourless oil.

R_f (3aa) = 0.39 (PE/EtOAc 7:3)



3aa

^{1}H NMR (400 MHz, $CDCl_3$): 8.90 (bs, 1 H), 8.33 and 8.30 (rotamers, d, *J* = 8.3 Hz, d, *J* = 8.3 Hz, 1 H), 7.44 (d, *J* = 7.7 Hz, 1 H), 7.14–7.34 (m, 10 H), 7.03–7.10 (m, 1 H), 4.97–5.26 (m, 3 H), 3.51 (dd, *J* = 14.6, 6.0 Hz, 1 H), 3.06 (dd, *J* = 14.4, 10.0 Hz, 1 H), 2.93 and 2.91 (rotamers, s, s, 3 H), 2.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.7 and 31.6 (rotamers), 33.7 and 33.9 (rotamers), 61.3 and 62.4 (rotamers), 67.5 and 67.8 (rotamers), 120.0 and 120.5 (rotamers), 124.5, 126.6 and 126.6 (rotamers), 127.6, 128.0 and 128.1 (rotamers), 128.4 and 128.5 (rotamers), 128.6, 128.7, 128.8, 132.8 and 132.9 (rotamers), 135.8 and 136.3 (rotamers), 137.1 and 137.3 (rotamers), 137.7 and 137.9 (rotamers), 155.8 and 157.0 (rotamers), 168.1 and 168.4 (rotamers).

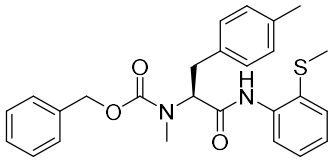
Optical rotation: $[\alpha]_D^{20}$ = -61.4 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{26}N_2O_3S$ $[M]^+$	434.1659	434.1659

Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-(*p*-tolyl)propan-2-yl)carbamate (3ab)

According to **GP2** 500 mg (1.40 mmol, 1.0 equiv) **1a**, 608 mg (2.79 mmol, 2.0 equiv) 4-iodotoluene, 466 mg (2.79 mmol, 2.0 equiv) AgOAc, 77.6 mg (279 µmol, 20 mol%) $(BnO)_2PO_2H$ and 31.3 mg (139 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 9:1) and the product **3ab** (546 mg, 1.22 mmol, 87%, > 99% ee) was obtained as colourless oil.

R_f (3ab) = 0.41 (PE/EtOAc 7:3)



3ab

^{1}H NMR (400 MHz, $CDCl_3$): 8.90 (s, 1 H), 8.31 (m, 1 H), 7.44 (d, *J* = 7.7 Hz, 1 H), 6.98–7.35 (m, 12 H), 4.95–5.24 (m, 3 H), 3.46 (dd, *J* = 14.6, 5.8 Hz, 1 H), 3.02 (dd, *J* = 14.1, 10.0 Hz, 1 H), 2.93 and 2.91 (rotamers, s, s, 3 H), 2.30 (s, 3 H), 2.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6 and 21.0 (rotamers), 30.6 and 31.55 (rotamers), 33.3 and 33.5 (rotamers), 61.2 and 62.4 (rotamers), 67.5 and 67.7 (rotamers), 120.0 and 120.5 (rotamers), 124.5, 125.3 and 125.8 (rotamers), 127.6, 128.0 and 128.0 (rotamers), 128.4, 128.7 and 128.9 (rotamers), 129.2 and 129.3 (rotamers), 132.8 and 132.9 (rotamers), 133.9 and 134.1 (rotamers), 135.9 and 136.0 (rotamers), 136.1 and 136.3 (rotamers), 137.8 and 137.9 (rotamers), 155.8 and 157.0 (rotamers), 168.3 and 168.5 (rotamers).

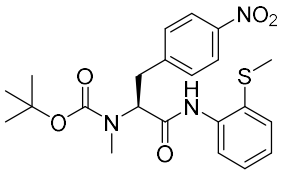
Optical rotation: $[\alpha]_D^{20}$ = -78.9 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{26}H_{29}N_2O_3S$ $[M+H]^+$	449.1893	449.1894

tert-Butyl (_S_)-methyl(1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl) carbamate (3bd)

According to **GP2** 290 mg (894 µmol, 1.0 equiv) **1b**, 445 mg (1.79 mmol, 2.0 equiv) 1-iodo-4-nitrobenzene, 298 mg (1.79 µmol, 2.0 equiv) AgOAc, 24.9 mg (89 µmol, 20 mol%) $(BnO)_2PO_2H$ and 20.1 mg (89 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 99:1) and the product 3**bd** (250 mg, 561 µmol, 63%) was obtained as slightly yellow oil.

R_f (3bd) = 0.42 (CH_2Cl_2/Et_2O 95:5)



3bd

^{1}H NMR (500 MHz, $CDCl_3$): 8.96 (s, 1H), 8.36 and 8.29 (rotamers, d, *J* = 7.9 Hz, d, *J* = 8.2 Hz, 1 H), 8.13–8.22 (m, 2 H), 7.39–7.51 (m, 3 H), 7.28–7.35 (m, 1 H), 7.06–7.13 (m, 1 H), 5.30 and 4.95 (rotamers, bs, d, *J* = 6.6 Hz, 1 H), 3.60 (dd, *J* = 14.5, 6.3 Hz, 1 H), 3.13 (dd, *J* = 14.7, 9.6 Hz, 1 H), 2.88 and 2.82 (rotamers, s, s, 3 H), 2.34 (s, 3 H), 1.42 and 1.33 (rotamers, s, s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): 18.8, 28.2, 30.7 and 31.2 (rotamers), 33.7 and 33.9 (rotamers), 59.8 and 62.4 (rotamers), 81.1 and 81.5 (rotamers), 119.9 and 120.4 (rotamers), 123.6 and 123.8 (rotamers), 124.7, 125.8, 128.8 and 129.0 (rotamers), 132.9, 137.8, 145.6, 146.8, 156.2, 168.2.

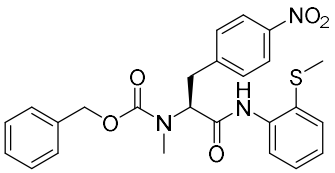
Optical rotation: $[\alpha]_D^{20}$ = -76.8 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{22}H_{28}N_3O_5S$ $[M+H]^+$	446.1744	446.1752

Benzyl (_S_)-methyl(1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl)carbamate (3ad)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 139 mg (558 µmol, 2.0 equiv) 1-iodo-4-nitrobenzene, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 2 d. After workup the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 99:1) and the product **3ad** (112 mg, 234 µmol, 84%) was obtained as colourless oil.

R_f (3ad) = 0.30 (PE/EtOAc 7:3)



3ad

^{1}H NMR (400 MHz, $CDCl_3$): 8.88 (s, 1 H), 8.27 (m, 1 H), 8.10 and 8.03 (rotamers, d, *J* = 8.3 Hz, d, *J* = 7.5 Hz, 1 H), 7.46 (d, *J* = 7.3 Hz, 1 H), 7.41 (d, *J* = 8.20 Hz, 1 H), 7.20–7.35 (m, 7 H), 4.95–4.32 (m, 3 H), 3.60 (dd, *J* = 14.7, 5.9 Hz, 1 H), 3.15 (dd, *J* = 14.6, 9.7 Hz, 1 H), 2.95 and 2.92 (rotamers, s, s, 3 H), 2.24 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.7, 33.7 and 33.9 (rotamers), 60.8, 67.9 and 68.1 (rotamers), 120.6, 123.7, 124.9, 127.9, 128.3 and 128.5 (rotamers), 128.7 and 128.9 (rotamers),129.7 and 129.8 (rotamers), 132.7, 136.0, 137.5, 145.1 and 146.8 (rotamers), 157.0, 167.7.

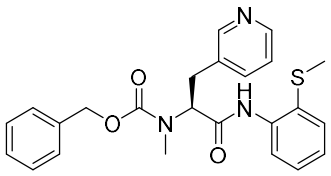
Optical rotation: $[\alpha]_D^{20}$ = -72.6 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{26}N_3O_5S$ $[M+H]^+$	480.1588	480.1556

Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-(pyridin-3-yl)propan-2-yl)carbamate (3ae)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 114 mg (558 µmol, 2.0 equiv) 4-iodopyridine, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 80 h. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3 → 1:1) and the product **3ae** (56.7 mg, 130 µmol, 47%) was obtained as slightly yellow oil.

R_f (3ae) = 0.05 (PE/EtOAc 1:1)



xx09

^{1}H NMR (400 MHz, $CDCl_3$): 8.89 and 8.86 (rotamers, s, s, 1 H), 8.45–8.55 (m, 2 H), 8.27 (d, *J* = 8.3 Hz, 1 H), 7.60 and 7.45 (rotamers, d, *J* = 7.6 Hz, d, *J* = 7.5 Hz, 2 H), 7.05–7.38 (m, 8 H), 4.99–5.27 (m, 3 H), 3.51 (dd, *J* = 14.8, 5.9 Hz, 1 H), 3.06 (dd, *J* = 15.2, 10.3 Hz, 1 H), 2.95 and 2.93 (rotamers, s, s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.6, 31.0 and 31.3 (rotamers), 60.8, 67.8 and 68.1 (rotamers), 120.6, 123.4, 124.8, 126.0, 127.8 and 128.2 (rotamers), 128.5 and 128.8 (rotamers), 132.8, 136.1 and 136.4 (rotamers), 137.7, 148.2, 150.4, 167.9.

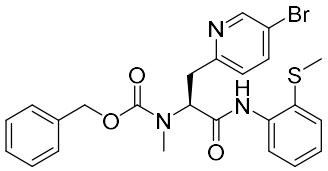
Optical rotation: $[\alpha]_D^{20}$ = -51.5 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{24}H_{26}N_3O_3S$ $[M+H]^+$	451.1686	451.1686

Benzyl (*S*)-(3-(5-bromopyridin-2-yl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3af)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 158 mg (558 µmol, 2.0 equiv) 5-bromo-2-iodopyridine, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3af** (115 mg, 224 µmol, 80%) was obtained as slightly yellow oil.

R_f (3af) = 0.48 (PE/EtOAc 1:1)



3af

^{1}H NMR (400 MHz, $CDCl_3$): 9.02 and 8.97 (rotamers, s, s, 1 H), 8.53 and 8.48 (rotamers, s, s, 1 H), 8.27 (m, 1 H), 7.61–7.69 (m, 1 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 7.24–7.37 (m, 6 H), 6.98–7.15 (m, 2 H), 5.46 and 5.38 (rotamers, t, *J* = 7.5 Hz, q, *J* = 8.6, 5.4 Hz, 1 H), 5.05–5.25 (m, 2 H), 3.60 (dd, *J* = 14.4, 6.5 Hz, 1H), 3.18 (m, 1 H), 2.97 (s, 3 H), 2.25 and 2.21 (rotamers, s, s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 31.1 and 31.8 (rotamers), 35.5 and 35.8 (rotamers), 60.0 and 60.6 (rotamers), 67.6 and 67.8 (rotamers), 118.6, 120.2 and 120.6 (rotamers), 124.6, 124.7 and 124.8 (rotamers), 125.5 and 126.0 (rotamers), 127.8, 128.1, 128.4, 128.6 and 128.8 (rotamers), 132.7 and 132.8 (rotamers), 135.9 and 136.3 (rotamers), 137.8, 138.9, 150.3, 155.8 and 156.2 (rotamers), 156.3 and 156.9 (rotamers), 168.1 and 168.3 (rotamers).

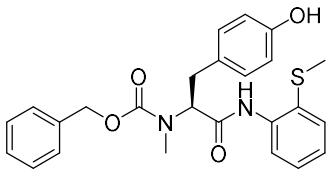
Optical rotation: $[\alpha]_D^{20}$ = -64.3 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{24}H_{25}BrN_3O_3S$ $[M+H]^+$	514.0795	514.0840

Benzyl (*S*)-(3-(4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ag)

According to **GP2** 80 mg (223 µmol, 1.0 equiv) **1a**, 98.2 mg (446 µmol, 2.0 equiv) 4-iodophenol, 74.5 mg (446 µmol, 2.0 equiv) AgOAc, 12.4 mg (45 µmol, 20 mol%) $(BnO)_2PO_2H$ and 5.0 mg (22 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3ag** (74.5 mg, 165 µmol, 74%) was obtained as colourless oil.

R_f (3ag) = 0.45 (PE/EtOAc 1:1)



3ag

^{1}H NMR (400 MHz, $CDCl_3$): 8.88 (s, 1 H), 8.30 and 8.25 (rotamers, d, *J* = 7.9 Hz, d, *J* = 7.9 Hz, 1 H), 7.44 (d, *J* = 7.0 Hz, 1 H), 6.94–6.35 (m, 9 H), 6.64–6.71 (m, 2 H), 6.26 (bs, 1 H), 4.88–5.22 (m, 3 H), 3.41 (dd, *J* = 14.2, 5.9 Hz, 1 H), 2.89–3.01 (m, 4 H), 2.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.6 and 31.9 (rotamers), 33.0, 61.5 and 62.8 (rotamers), 67.8 and 68.1 (rotamers), 115.5, 120.2 and 120.8 (rotamers), 124.8 and 126.2 (rotamers), 127.7, 128.1 and 128.2 (rotamers), 128.5, 128.7 and 128.9 (rotamers), 130.0, 132.7 and 132.9 (rotamers), 136.1, 137.7, 154.8 and 157.3 (rotamers), 168.3 and 168.6 (rotamers).

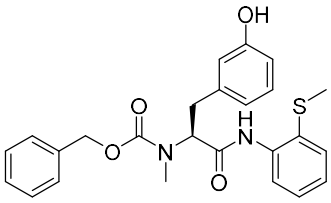
Optical rotation: $[\alpha]_D^{20}$ = -51.7 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{27}N_2O_4S$ $[M+H]^+$	451.1686	451.1686

Benzyl (*S*)-(3-(3-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ah)

According to **GP2** 80 mg (223 µmol, 1.0 equiv) **1a**, 98.2 mg (446 µmol, 2.0 equiv) 3-iodophenol, 74.5 mg (446 µmol, 2.0 equiv) AgOAc, 12.4 mg (45 µmol, 20 mol%) $(BnO)_2PO_2H$ and 5.0 mg (22 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 2 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3ah** (86.0 mg, 191 µmol, 86%) was obtained as colourless oil.

R_f (3ah) = 0.16 (PE/EtOAc 7:3)



3ah

^{1}H NMR (400 MHz, $CDCl_3$): 8.90 (bs, 1 H), 8.29 and 8.24 (rotamers, d, *J* = 7.9 Hz, d, *J* = 8.1 Hz, 1 H), 7.40–7.48 (m, 1 H), 7.18–7.36 (m, 5 H), 7.02–7.15 (m, 2 H), 6.62–6.80 (m, 3 H), 6.18 (bs, 1 H), 4.88–5.25 (m, 3 H), 3.45 (dd, *J* = 14.6, 5.8 Hz, 1 H), 3.02 (dd, *J* = 14.7, 9.9 Hz, 1 H), 2.92 and 2.91 (rotamers, s, s, 3 H), 2.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5 and 18.6 (rotamers), 30.8 and 31.9 (rotamers), 33.7, 61.1 and 62.5 (rotamers), 67.8 and 68.1 (rotamers), 113.9, 115.7 and 115.8 (rotamers), 120.2, 120.9 and 121.0 (rotamers), 124.8, 126.3, 127.7, 128.1 and 128.2 (rotamers), 128.5 and 128.6 (rotamers), 129.8,

132.6 and 132.8 (rotamers), 136.2, 137.6, 138.6 and 139.0 (rotamers), 156.2 and 157.3 (rotamers), 168.3 and 168.6 (rotamers).

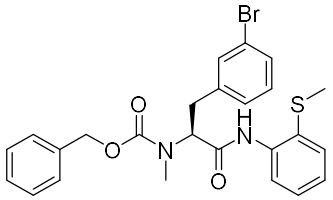
Optical rotation: $[\alpha]_D^{20}$ = -58.8 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{27}N_2O_4S$ $[M+H]^+$	451.1686	451.1686

Benzyl (*S*)-(3-(3-bromophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ai)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 158 mg (558 µmol, 2.0 equiv) 3-bromoiodobenzene, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 2 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3ai** (102 mg, 198 µmol, 71%) was obtained as colourless oil.

R_f (3ai) = 0.38 (PE/EtOAc 7:3)



3ai

^{1}H NMR (400 MHz, $CDCl_3$): 8.89 (bs, 1 H), 8.24–8.33 (m, 1 H), 7.02–7.47 (m, 12 H), 4.96–5.22 (m, 3 H), 3.48 (dd, *J* = 14.6, 5.8 Hz, 1 H), 3.02 (dd, *J* = 14.5, 9.8 Hz, 1 H) , 2.95 and 2.91 (rotamers, s, s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.7 and 31.5 (rotamers), 33.4 and 33.6 (rotamers), 61.0 and 62.0 (rotamers), 67.7 and 68.0 (rotamers), 120.0 and 120.6 (rotamers), 122.5 and 122.6 (rotamers), 124.7, 125.5 and 126.0 (rotamers), 127.5 and 127.7 (rotamers), 128.1 and 128.2 (rotamers), 128.5, 128.7 and 128.9 (rotamers), 129.8, 130.1, 131.8 and 132.0 (rotamers), 132.8 and 132.9 (rotamers), 135.7 and 136.2 (rotamers), 137.6 and 137.7 (rotamers), 139.6 and 139.8 (rotamers), 155.7 and 157.0 (rotamers), 167.7 and 168.0 (rotamers).

Optical rotation: $[\alpha]_D^{20}$ = -51.2 [$CHCl_3$, c = 1.00]

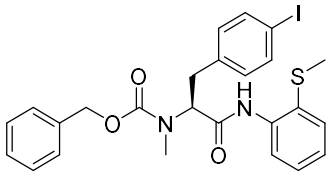
HRMS (CI):	Calculated	Found
$C_{25}H_{26}BrN_2O_3S$ $[M+H]^+$	513.0842	513.0821

Benzyl (*S*)-(3-(4-iodophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)carbamate (3aj)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 184 mg (558 µmol, 2.0 equiv) 1,4-diiodobenzene, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol,

10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 2 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3aj** (112 mg, 199 µmol, 71%) was obtained as colourless oil.

R_f (3aj) = 0.43 (PE/EtOAc 7:3)



3aj

^{1}H NMR (400 MHz, $CDCl_3$): 8.88 (s, 1 H), 8.24–8.33 (m, 1 H), 7.57 and 7.53 (rotamers, d, *J* = 7.9 Hz, d, *J* = 7.0 Hz, 1 H), 7.45 (d, *J* = 7.6 Hz, 1 H), 7.18–7.38 (m, 6 H), 6.85–7.10 (m, 3 H), 4.91–5.23 (m, 3 H), 3.44 (dd, *J* = 14.6, 6.1 Hz, 1 H), 2.99 (dd, *J* = 14.8, 9.8 Hz, 1 H), 2.93 and 2.90 (rotamers, s, s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.6 and 31.6 (rotamers), 33.3 and 33.4 (rotamers), 60.9 and 61.0 (rotamers), 67.7 and 67.9 (rotamers), 92.0, 120.8 and 120.6 (rotamers), 124.7, 125.5 and 125.9 (rotamers), 127.7, 128.1 and 128.2 (rotamers), 128.3, 128.5, 128.7 and 128.8 (rotamers), 130.8 and 130.9 (rotamers), 132.7 and 132.8 (rotamers), 135.7 and 136.6 (rotamers), 137.5 and 137.7 (rotamers), 155.7 and 157.0 (rotamers), 167.8 and 168.1 (rotamers).

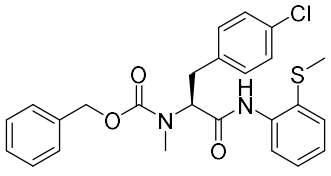
Optical rotation: $[\alpha]_D^{20}$ = -55.8 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{26}IN_2O_3S$ $[M+H]^+$	561.0703	561.0697

Benzyl (*S*)-(3-(4-chlorophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ak)

According to GP2 100 mg (279 µmol, 1.0 equiv) **1a**, 133 mg (558 µmol, 2.0 equiv) 1-chloro-4-iodobenzene, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 60 °C for 2 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3ak** (152 mg, 246 µmol, 88%) was obtained as colourless oil.

R_f (3ak) = 0.41 (PE/EtOAc 7:3)



3ak

^{1}H NMR (400 MHz, $CDCl_3$): 8.88 (s, 1 H), 8.24–8.34 (m, 1 H), 7.45 (d, *J* = 7.6 Hz, 1 H), 7.02–7.37 (m, 11 H), 4.91–5.24 (m, 3 H), 3.47 (dd, *J* = 14.5, 5.9 Hz, 1 H), 3.02 (dd, *J* = 14.7, 10.0 Hz, 1 H), 2.93 and 2.90 (rotamers, s, s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.6 and 31.5 (rotamers), 33. and 32.2 (rotamers), 61.0 and 62.2 (rotamers), 67.6 and 67.9 (rotamers), 120.1 and 120.6 (rotamers), 124.6, 125.9, 127.7, 128.1 and 128.3 (rotamers), 128.5, 128.6 and 128.7 (rotamers), 130.1 and 130.2 (rotamers), 132.4, 132.7 and 132.9 (rotamers), 135.6 and 135.7 (rotamers), 135.9 and 136.2 (rotamers), 137.6 and 137.7 (rotamers), 155.7 and 157.0 (rotamers), 167.8 and 168.1 (rotamers).

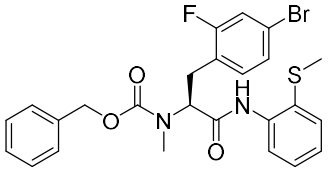
Optical rotation: $[\alpha]_D^{20}$ = -52.8 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{26}ClN_2O_3S$ $[M+H]^+$	469.1347	469.1384

Benzyl (*S*)-(3-(4-bromo-2-fluorophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3al)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 168 mg (558 µmol, 2.0 equiv) 4-bromo-2-fluoro-1-iodobenzene, 93.1 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3al** (115 mg, 217 µmol, 78%) was obtained as colourless oil.

R_f (3al) = 0.57 (PE/EtOAc 1:1)



3al

^{1}H NMR (400 MHz, $CDCl_3$): 8.88 and 8.86 (rotamers, s, s, 1 H), 8.25–8.32 (m, 1 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 6.96–7.36 (m, 10 H), 5.00–5.26 (m, 3 H), 3.37–3.48 (m, 1 H), 3.14 and 3.06 (rotamers, dd, *J* = 14.5, 10.1 Hz, dd, *J* = 15.8, 11.5 Hz, 1 H), 2.94 and 2.92 (rotamers, s, s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 26.7 and 27.4 (rotamers), 30.8 and 31.7 (rotamers), 60.0 and 60.8 (rotamers), 67.7 and 67.9 (rotamers), 119.0 (d, $^2J_{C\text{-}F}$ = 25.7 Hz), 120.1, 120.5 and 120.7 (rotamers), 123.5 and 123.6 (rotamers, d, $^3J_{C\text{-}F}$ = 15.4 Hz, d, $^3J_{C\text{-}F}$ = 15.4 Hz), 124.7, 125.4 and 125.9 (rotamers), 127.4, 127.9 (d, $^2J_{C\text{-}F}$ = 35.2 Hz), 128.5, 128.7 and 128.9 (rotamers), 132.1 and 132.2 (rotamers, d, $^3J_{C\text{-}F}$ = 14.7 Hz, d, $^3J_{C\text{-}F}$ = 14.7 Hz), 132.7 and 132.9 (rotamers), 135.7 and 136.2 (rotamers), 137.7, 155.6 and 156.9 (rotamers), 161.0 and 161.1 (rotamers, d, $^1J_{C\text{-}F}$ = 250.9 Hz, d, $^1J_{C\text{-}F}$ = 250.2 Hz), 167.6 and 167.9 (rotamers).

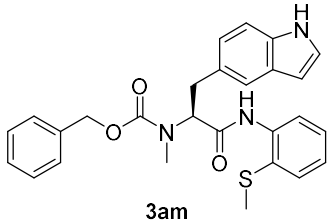
Optical rotation: $[\alpha]_D^{20}$ = -59.8 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{24}BrFN_2O_3S$ $[M]^+$	530.0670	530.0637

Benzyl (*S*)-(3-(1*H*-indol-5-yl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)carbamate (3am)

According to **GP2** 80 mg (223 µmol, 1.0 equiv) **1a**, 109 mg (446 µmol, 2.0 equiv) 5-iodoindole, 74.5 mg (446 µmol, 2.0 equiv) AgOAc, 12.4 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 100 °C for 60 h. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3am** (32.1 mg, 68 µmol, 30%) was obtained as yellow oil.

R_f (3am) = 0.16 (PE/EtOAc 7:3)



3am

^{1}H NMR (500 MHz, $CDCl_3$): 8.90 and 8.88 (rotamers, s, s, 1 H), 8.35 and 8.31 (rotamers, d, *J* = 8.2 Hz, d, *J* = 8.2 Hz, 1 H), 8.16 (bs, 1 H), 7.41–7.54 (m, 2H), 6.97–7.31 (m, 10 H), 6.49 (bs, 1 H), 4.97–5.30 (m, 3 H), 3.61 (dd, *J* = 14.5, 6.0 Hz, 1 H), 3.16 (dd, *J* = 14.5, 9.5 Hz, 1 H), 2.97 and 2.95 (rotamers, s, s, 3 H), 2.17 (s, 3 H).

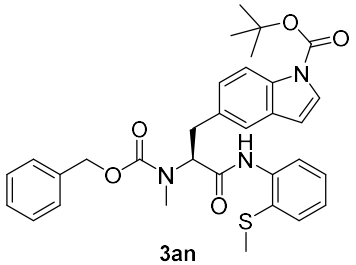
^{13}C NMR (125 MHz, $CDCl_3$): 18.7, 29.7 and 30.8 (rotamers), 31.8 and 34.0, 61.9 and 63.2 (rotamers), 67.5 and 67.8 (rotamers), 102.5, 111.1, 120.1 and 120.6 (rotamers), 120.8 and 120.8 (rotamers), 123.0 and 123.1, 124.3 and 124.5 (rotamers), 125.4 and 125.9 (rotamers), 127.7, 127.9, 128.1 and 128.2 (rotamers), 128.4, 128.8 and 129.0 (rotamers), 133.09 and 133.0 (rotamers), 134.8, 136.0 and 136.4 (rotamers), 156.0 and 157.1 (rotamers), 168.6 and 168.9.

Optical rotation:	$[\alpha]_D^{20}$ = -113.1 [$CHCl_3$, c = 0.50]	
HRMS (CI):	Calculated	Found
$C_{27}H_{28}N_3O_3S$ $[M+H]^+$	474.1846	474.1850

***tert*-Butyl (*S*)-5-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-1*H*-indole-1-carboxylate (3an)**

According to **GP2** 115 mg (321 µmol, 1.0 equiv) **1a**, 220 mg (642 µmol, 2.0 equiv) *tert*-butyl 5-iodo-1*H*-indole-1-carboxylate (**11a**), 107 mg (642 µmol, 2.0 equiv) AgOAc, 17.8 mg (64 µmol, 20 mol%) $(BnO)_2PO_2H$ and 7.2 mg (32 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 60 h. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3an** (132 mg, 229 µmol, 71%) was obtained as slightly yellow oil.

R_f (3an) = 0.29 (PE/EtOAc 7:3)



3an

^{1}H NMR (400 MHz, $CDCl_3$): 8.91 and 8.89 (rotamers, s, s, 1 H), 8.28–8.36 (m, 1 H), 8.03 (bs, 1 H), 7.57 (d, *J* = 3.3 Hz, 1 H), 7.39–7.49 (m, 2 H), 6.99–7.36 (m, 8 H), 6.45–6.52 (m, 1 H), 4.96–5.22 (m, 3 H), 3.60 (dd, *J* = 14.6, 5.8 Hz, 1 H), 3.16 (dd, *J* = 14.5, 9.7 Hz, 1 H), 2.96 and 2.93 (rotamers, s, s, 3 H), 2.20 (s, 3 H), 1.67 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6 and 18.9 (rotamers), 28.1, 30.8 and 31.8 (rotamers), 33.7 and 33.9 (rotamers), 61.6 and 62.9 (rotamers), 67.5 and 67.8 (rotamers), 83.6, 107.1, 115.2, 115.4, 120.1 and 120.6 (rotamers), 121.1, 124.5, 125.0 and 125.2 (rotamers), 125.9 and 126.1 (rotamers), 127.3 and 127.6 (rotamers), 128.0, 128.4, 128.7 and 128.9 (rotamers), 130.9, 131.3 and 131.6 (rotamers), 132.9, 134.0, 136.3, 138.0, 149.7, 155.9 and 157.0 (rotamers), 168.3 and 168.6 (rotamers).

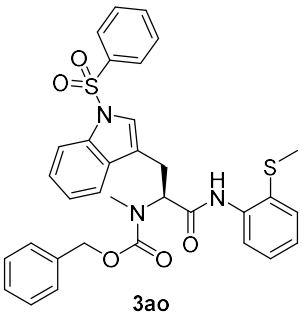
Optical rotation: $[\alpha]_D^{20}$ = -37.4 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{32}H_{36}N_3O_5S$ $[M+H]^+$	574.2370	574.2342

Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-(1-(phenylsulfonyl)-1*H*-indol-3-yl) propan-2-yl)carbamate (3ao)

According to **GP2** 100 mg (279 µmol, 1.0 equiv) **1a**, 214 mg (558 µmol, 2.0 equiv) 3-iodo-1-(phenylsulfonyl)-1*H*-indole (**11b**), 93 mg (558 µmol, 2.0 equiv) AgOAc, 15.5 mg (56 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.3 mg (28 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 99:1) and the product **3ao** (128 mg, 209 µmol, 75%) was obtained as slightly brown oil.

R_f (3ao) = 0.4 (PE/EtOAc 1:1)



3ao

^{1}H NMR (400 MHz, $CDCl_3$): 8.90 and 8.85 (rotamers, s, s, 1 H), 8.27–8.34 (m, 1 H), 7.99 (d, *J* = 8.2 Hz, 1 H), 7.77 (d, *J* = 7.0 Hz, 1 H), 7.15–7.61 (m, 13 H), 7.08 (t, *J* = 7.2 Hz, 2 H), 4.76–5.37 (m, 3 H), 3.52 (dd, *J* = 15.0, 7.0 Hz, 1 H), 3.16 (dd, *J* = 14.8, 9.4 Hz, 1 H), 2.88 (s, 3 H), 2.13 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5 and 18.9 (rotamers), 23.3 and 23.7 (rotamers), 30.5 and 31.2 (rotamers), 59.4 and 60.0 (rotamers), 66.5 and 67.9 (rotamers), 113.7 and 113.8 (rotamers), 118.4, 119.0 and 119.2 (rotamers), 120.0 and 120.6 (rotamers), 123.4, 124.0 and 124.2 (rotamers), 124.6, 124.9, 126.5, 127.8, 128.0 and 128.1 (rotamers), 128.2, 128.4 and 128.5, 128.5, 128.7 and 128.9 (rotamers), 129.0 and 129.2 (rotamers), 130.3 and 130.6 (rotamers), 132.9 and 133.0 (rotamers), 133.5, 135.1 and 135.5 (rotamers), 136.0, 137.6 and 137.8 (rotamers), 137.9, 155.6 and 157.0 (rotamers), 167.7 and 168.0 (rotamers).

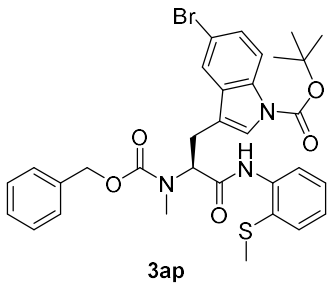
Optical rotation: $[\alpha]_D^{20}$ = -38.0 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{33}H_{32}N_3O_5S_2$ $[M+H]^+$	614.1778	614.1793

***tert*-Butyl (*S*)-3-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-5-bromo-1*H*-indole-1-carboxylate (3ap)**

According to **GP2** 50.0 mg (139 µmol, 1.0 equiv) **1a**, 118 mg (279 µmol, 2.0 equiv) *tert*-butyl 5-bromo-3-iodo-1*H*-indole-1-carboxylate (**11c**), 46.6 mg (279 µmol, 2.0 equiv) AgOAc, 7.8 mg (28 µmol, 20 mol%) $(BnO)_2PO_2H$ and 3.1 mg (14 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3ap** (60.0 mg, 92 µmol, 66%) was obtained as slightly yellow oil.

R_f (3ap) = 0.38 (PE/EtOAc 7:3)



3ap

^{1}H NMR (400 MHz, $CDCl_3$): 8.92 and 8.86 (rotamers, s, s, 1 H), 8.26–8.36 (m, 1 H), 8.02 (d, *J* = 8.3 Hz, 1 H), 7.74 and 7.70 (rotamers, s, s, 1 H), 7.39–7.51 (m, 3 H), 7.05–7.37 (m, 7 H), 4.89–5.29 (m, 3 H), 3.47–3.58 (m, 1 H), 3.13 (dd, *J* = 15.0, 9.4 Hz, 1 H), 2.99 and 2.96 (rotamers, s, s, 3 H), 2.21 and 2.17 (rotamers, s, s, 3 H), 1.64 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.7, 23.2 and 23.7 (rotamers), 28.1, 30.5, 59.6 and 60.0 (rotamers), 67.9 and 68.1 (rotamers), 84.0 and 84.2 (rotamers), 115.5 and 116.0 (rotamers), 116.7 and 116.9 (rotamers), 120.2 and 120.7 (rotamers), 121.4 and 121.5 (rotamers), 124.7 and 125.1 (rotamers), 127.4, 127.8 and 128.0 (rotamers), 128.2, 128.5, 128.8 and 129.0 (rotamers), 132.8, 134.2, 136.2, 137.8, 149.2, 157.1, 168.2.

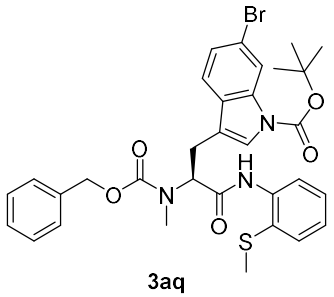
Optical rotation: $[\alpha]_D^{20}$ = -38.0 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{32}H_{35}BrN_3O_5S$ $[M+H]^+$	652.1475	652.1478

***tert*-Butyl (*S*)-3-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-6-bromo-1*H*-indole-1-carboxylate (3aq)**

According to **GP2** 115 mg (321 µmol, 1.0 equiv) **1a**, 271 mg (279 µmol, 2.0 equiv) *tert*-butyl 6-bromo-3-iodo-1*H*-indole-1-carboxylate (**11d**), 107 mg (642 µmol, 2.0 equiv) AgOAc, 17.9 mg (64 µmol, 20 mol%) $(BnO)_2PO_2H$ and 7.2 mg (32 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3aq** (133 mg, 204 µmol, 64%) was obtained as slightly yellow oil.

R_f (3aq) = 0.31 (PE/EtOAc 7:3)



3aq

^{1}H NMR (400 MHz, $CDCl_3$): 8.88 (bs, 1 H), 8.24–8.37 (m, 2 H), 7.19–7.53 (m, 9 H), 7.03–7.13 (m, 2 H), 4.93–5.35 (m, 3 H), 3.52 (dd, *J* = 15.1, 6.3 Hz, 1 H), 3.14 (dd, *J* = 15.6, 9.0 Hz, 1 H), 2.99 and 2.95 (rotamers, s, s, 3 H), 2.20 (s, 3 H), 1.66 and 1.65 (rotamers, s, s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 23.4 and 23.7 (rotamers), 28.1, 30.4 and 31.0 (rotamers), 59.5 and 60.2 (rotamers), 67.8 and 68.1 (rotamers), 84.1, 114.1, 116.0, 118.3 and 118.5 (rotamers), 119.7 and 119.9 (rotamers), 120.2 and 120.6 (rotamers), 122.3, 124.1 and 124.7 (rotamers), 125.8 and 126.0 (rotamers), 127.8, 128.0 and 128.2 (rotamers), 128.5, 128.7, 129.0, 132.8 and 133.0 (rotamers), 135.6 and 136.2 (rotamers), 137.8, 149.2, 155.8 and 157.1 (rotamers), 168.0 and 168.3 (rotamers).

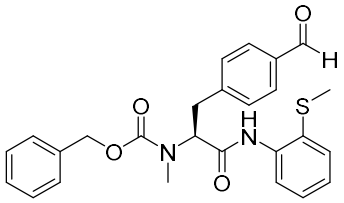
Optical rotation: $[\alpha]_D^{20}$ = -40.5 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{32}H_{35}BrN_3O_5S$ $[M+H]^+$	652.1475	652.1458

Benzyl (*S*)-(3-(4-formylphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ar)

According to **GP2** 105 mg (293 µmol, 1.0 equiv) **1a**, 136 mg (586 µmol, 2.0 equiv) 4-iodobenzaldehyde (**12**), 98.0 mg (586 µmol, 2.0 equiv) AgOAc, 16.3 mg (59 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.6 mg (29 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 2 d under argon atmosphere. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3ar** (109 mg, 235 µmol, 80%) was obtained as colourless oil.

R_f (3ar) = 0.48 (PE/EtOAc 1:1)



3ar

^{1}H NMR (400 MHz, $CDCl_3$): 9.95 (s, 1 H), 8.90 (s, 1 h), 8.26–8.33 (m, 1 H), 7.77 and 7.72 (rotamers, d, *J* = 7.7 Hz, d, *J* = 7.2 Hz, 1 H), 7.39–7.46 (m, 2H), 7.19–7.35 (m, 6 H), 7.04–7.11 (m, 1 H), 4.99–5.32 (m, 3 H), 3.58 (dd, *J* = 14.6, 5.8 Hz, 1 H), 3.14 (dd, *J* = 14.5, 10 Hz, 1 H), 2.94 and 2.92 (rotamers, s, s, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 30.6 and 31.6 (rotamers), 33.9 and 34.1 (rotamers), 60.8 and 61.9 (rotamers), 67.7 and 67.9 (rotamers), 120.1 and 120.6 (rotamers), 124.7, 125.6 and 126.0 (rotamers), 127.7, 128.1 and 128.2 (rotamers), 128.4, 128.6 and 128.8 (rotamers), 129.5, 129.9, 132.6 and 132.7 (rotamers), 135.0, 135.6 and 136.1 (rotamers), 137.5, 144.6 and 144.7 (rotamers), 155.5 and 156.9 (rotamers), 167.6 and 167.9 (rotamers), 191.6 and 191.7 (rotamers).

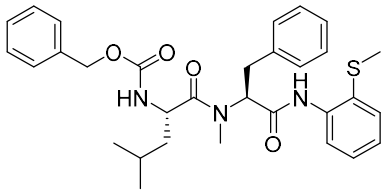
Optical rotation: $[\alpha]_D^{20}$ = -97.6 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{26}H_{27}N_2O_4S$ $[M+H]^+$	463.1686	463.1706

Benzyl ((*S*)-4-methyl-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-1-oxo-3-phenylpropan-2-yl) amino)-1-oxopentan-2-yl)carbamate (5aa)

According to **GP2** 80.0 mg (168 µmol, 1.0 equiv) **4a**, 68.5 mg (336 µmol, 2.0 equiv) iodobenzene, 56.0 mg (336 µmol, 2.0 equiv) AgOAc, 9.3 mg (34 µmol, 20 mol%) $(BnO)_2PO_2H$ and 3.8 mg (17 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 85:15) and the product **5aa** (71.6 mg, 131 µmol, 78%) was obtained as colourless oil.

R_f (5aa) = 0.56 (PE/EtOAc 1:1)



5aa

^{1}H NMR (400 MHz, $CDCl_3$): 9.06 and 8.62 (rotamers, s, s, 1 H), 8.23 and 7.91 (rotamers, d, *J* = 8.1 Hz, d, *J* = 8.1 Hz, 1 H), 7.03–7.43 (m, 13 H), 4.89–5.50 (m, 4 H), 4.66 and 4.34 (rotamers, td, *J* = 9.7, 3.6 Hz, td, *J* = 8.3, 3.3 Hz, 1 H), 3.48 (dd, *J* = 14.2, 7.1 Hz, 1 H), 2.98–3.12 (m, 4 H), 2.28 (s, 3 H), 1.62–1.77 (m, 1 H), 1.31–1.55 (m, 2 H), 0.64–0.98 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 20.8 and 21.6 (rotamers), 23.1 and 23.4 (rotamers), 24.0 and 24.6 (rotamers), 31.7, 33.8, 42.4, 48.2 and 49.5 (rotamers), 59.6, 66.9 and 67.4 (rotamers), 120.9, 124.8,

126.8, 128.0, 128.4, 128.5 and 128.5 (rotamers), 129.0 and 129.1 (rotamers), 129.5, 132.3, 136.3, 136.7, 137.6, 155.9, 167.9, 173.7.

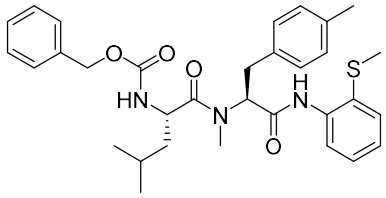
Optical rotation: $[\alpha]_D^{20}$ = -82.7 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{38}N_3O_4S$ $[M+H]^+$	548.2578	548.2574

Benzyl ((*S*)-4-methyl-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-1-oxo-3-(*p*-tolyl)propan-2-yl) amino)-1-oxopentan-2-yl)carbamate (5ab)

According to **GP2** 80.0 mg (168 µmol, 1.0 equiv) **4a**, 73.2 mg (336 µmol, 2.0 equiv) 4-iodotoluene, 56.0 mg (336 µmol, 2.0 equiv) AgOAc, 9.3 mg (34 µmol, 20 mol%) $(BnO)_2PO_2H$ and 3.8 mg (17 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 85:15) and the product **5ab** (74.1 mg, 132 µmol, 79%) was obtained as colourless oil.

R_f (5ab) = 0.57 (PE/EtOAc 1:1)



5ab

^{1}H NMR (400 MHz, $CDCl_3$): 9.06 and 8.63 (rotamers, s, s, 1 H), 8.22 and 7.89 (rotamers, d, *J* = 8.1 Hz, d, *J* = 7.8 Hz, 1 H), 6.99–7.44 (m, 12 H), 4.89–5.49 (m, 4H), 4.67 and 4.33 (rotamers, td, *J* = 9.6, 3.5 Hz, td, *J* = 11.4, 3.6 Hz, 1 H), 3.37–3.48 (m, 1 H), 2.96–3.10 (m, 4 H), 2.24–2.32 (m, 6 H), 1.65–1.82 (m, 1 H), 1.30–1.58 (m, 2 H), 0.63–0.98 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 20.7 and 21.5 (rotamers), 20.9, 23.1 and 23.3 (rotamers), 23.9 and 24.5 (rotamers), 40.8 and 42.3 (rotamers), 48.1 and 49.5 (rotamers), 56.7, 66.8 and 67.3 (rotamers), 123.6, 124.7, 125.8 and 126.2 (rotamers), 127.0, 127.9, 128.1, 128.3 and 128.4 (rotamers), 128.5, 128.8, 129.2 and 129.3 (rotamers), 129.6 and 129.8, 132.2, 133.5, 136.2 and 136.3 (rotamers), 136.5, 137.5, 156.0 and 156.7 (rotamers), 167.6 and 168.0, 173.6.

Optical rotation: $[\alpha]_D^{20}$ = -80.1 [$CHCl_3$, c = 1.00]

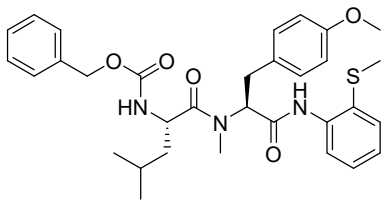
HRMS (CI):	Calculated	Found
$C_{32}H_{39}N_3O_4S$ $[M]^+$	561.2656	561.2635

Benzyl ((*S*)-1-(((*S*)-3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate(5ac)

According to **GP2** 490 mg (1.04 mmol, 1.0 equiv) **4a**, 486 mg (2.08 mmol, 2.0 equiv) 4-iodoanisole, 347 mg (2.08 mmol, 2.0 equiv) AgOAc, 57.8 mg (208 µmol, 20 mol%) $(BnO)_2PO_2H$ and 23.3 mg (104

µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 85:15 → 7:3) and the product **5ac** (518 mg, 897 µmol, 86%) was obtained as colourless oil.

R_f (5ac) = 0.43 (PE/EtOAc 1:1)



5ac

^{1}H NMR (400 MHz, $CDCl_3$): 9.04 and 8.61 (rotamers, s, s, 1 H), 8.22 and 7.91 (rotamers, d, *J* = 8.1 Hz, d, *J* = 7.8 Hz, 1 H), 7.04–7.43 (m, 10 H), 6.86 and 6.80 (rotamers, d, *J* = 8.6 Hz, d, *J* = 8.6 Hz, 1 H), 4.89–5.46 (m, 4 H), 4.67 and 4.34 (rotamers, td, *J* = 9.7, 3.6 Hz, m, 1 H), 3.77 and 3.72 (rotamers, s, s, 3 H), 3.42 (dd, *J* = 14.1, 7.9 Hz, 1 H), 3.07 and 3.05 (rotamers, s, s, 3 H), 2.99 (dd, *J* = 14.2, 8.5 Hz, 1 H), 2.28 (s, 3 H), 1.63–1.84 (m, 1 H), 1.26–1.54 (m, 2 H), 0.96 and 0.72 (rotamers, d, *J* = 6.5 Hz, d, *J* = 6.5 Hz, 3 H), 0.89 and 0.68 (rotamers, d, *J* = 6.7 Hz, d, *J* = 6.5 Hz, 3 H).

^{1}H NMR (500 MHz, DMSO-d_6, 373 K): 8.87 (s, 1 H), 7.69 (s, 1 H), 7.42 (dd, *J* = 7.5, 1.6 Hz, 1 H), 7.14–7.37 (m, 9 H), 6.83 (d, *J* = 6.6 Hz, 1 H), 5.29 (bs, 1 H), 5.00 (bs, 2 H), 4.49 (bs, 1 H), 3.31 (dd, *J* = 14.4, 5.0 Hz, 1 H), 2.94–3.05 (m, 7 H), 2.36 (s, 3 H), 1.66 (bs, 1 H), 1.50 (bs, 1 H), 1.42 (bs, 1 H), 0.87 (bs, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 20.8 and 21.6 (rotamers), 23.4, 24.1 and 24.6 (rotamers), 31.7, 33.0 and 33.3 (rotamers), 42.4, 49.5, 55.1, 59.7, 66.9 and 67.4 (rotamers), 114.0, 114.5, 120.9, 123.5, 125.8, 126.2, 127.1, 128.0, 128.1, 128.4, 128.5, 128.6, 130.0, 130.4, 132.3, 136.3, 137.6, 156.0, 158.4, 168.0, 173.7.

^{13}C NMR (125 MHz, DMSO-d_6, 373 K): 16.1, 20.9, 22.4, 23.7, 31.4, 32.4, 49.3, 54.6, 54.6, 58.9, 65.2, 113.5, 123.1, 125.0, 126.1, 127.0, 127.1, 127.7, 129.1, 129.4, 136.0, 136.5, 155.3, 157.7, 168.0, 172.5.

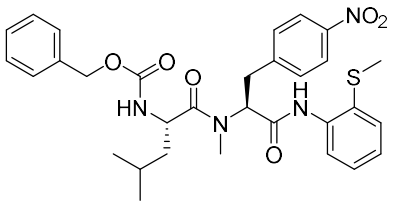
Optical rotation: $[\alpha]_D^{20}$ = -96.4 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{32}H_{40}N_3O_5S$ $[M+H]^+$	578.2683	578.2683

Benzyl ((*S*)-4-methyl-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl)amino)-1-oxopentan-2-yl)carbamate (5ad)

According to **GP2** 80.0 mg (168 µmol, 1.0 equiv) **4a**, 83.6 mg (336 µmol, 2.0 equiv) 1-iodo-4-nitrobenzene, 56.0 mg (336 µmol, 2.0 equiv) AgOAc, 9.3 mg (34 µmol, 20 mol%) $(BnO)_2PO_2H$ and 3.8 mg (17 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 9:1) and the product **5ad** (78.6 mg, 133 µmol, 79%) was obtained as colourless oil.

R_f (5ad) = 0.49 (PE/EtOAc 1:1)



5ad

^{1}H NMR (400 MHz, $CDCl_3$): 9.03 and 8.57 (rotamers, s, s, 1 H), 8.09–8.23 (m, 3 H), 7.07–7.46 (m, 10 H), 5.61 (t, *J* = 7.6 Hz, 1 H), 5.25 (d, *J* = 9.0 Hz, 1 H), 4.90–5.13 (m, 2 H), 4.65 and 4.34 (rotamers, td, *J* = 9.8, 3.5 Hz, td, *J* = 9.6, 3.8 Hz, 1 H), 3.59 (dd, *J* = 14.3, 7.0 Hz, 1 H), 3.03–3.15 (m, 4 H), 2.32 and 2.28 (rotamers, s, s, 3 H), 1.69–1.78 (m, 1 H), 1.39–1.58 (m, 2 H), 0.96 and 0.71 (rotamers, d, *J* = 6.5 Hz, d, *J* = 6.2 Hz, 3 H), 0.90 and 0.67 (rotamers, d, *J* = 6.6 Hz, d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 21.5, 23.4, 24.6, 31.3, 33.6, 42.0, 49.4, 58.6, 67.0, 121.0, 123.7 and 124.2 (rotamers), 125.1, 126.3, 128.0, 128.2, 128.4, 128.5, 130.0, 132.0, 136.1, 137.1, 144.7, 146.9, 156.0, 167.2, 174.2.

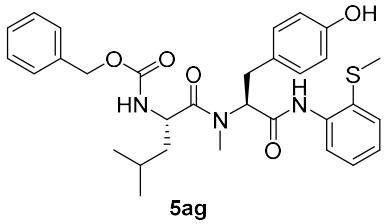
Optical rotation: $[\alpha]_D^{20}$ = -92.1 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{37}N_4O_6S$ $[M+H]^+$	593.2428	593.2439

Benzyl ((*S*)-1-(((*S*)-3-(4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) amino)-4-methyl-1-oxopentan-2-yl)carbamate (5ag)

According to **GP2** 80.0 mg (168 µmol, 1.0 equiv) **4a**, 73.9 mg (336 µmol, 2.0 equiv) 4-iodophenol, 56.0 mg (336 µmol, 2.0 equiv) AgOAc, 9.3 mg (34 µmol, 20 mol%) $(BnO)_2PO_2H$ and 3.8 mg (17 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 85:15) and the product **5ag** (54.9 mg, 97 µmol, 58%) was obtained as colourless oil.

R_f (5ag) = 0.42 (PE/EtOAc)



5ag

^{1}H NMR (400 MHz, $CDCl_3$): 9.08 and 8.59 (rotamers, s, s, 1 H), 8.21 and 7.86 (rotamers, d, *J* = 8.2 Hz, d, *J* = 7.6 Hz, 1 H), 7.00–7.45 (m, 11 H), 6.74 and 6.67 (rotamers, d, *J* = 8.4 Hz, d, *J* = 8.3 Hz, 1 H), 6.10 and 5.83 (rotamers, bs, bs, 1 H), 4.89–5.49 (m, 4 H), 4.68 and 4.37 (rotamers, td, *J* = 9.7, 3.5 Hz, m, 1 H), 3.39 (dd, *J* = 14.2, 7.5 Hz, 1 H), 3.08 and 3.05 (rotamers, s, s, 3 H), 2.94 (dd, *J* = 14.4, 8.5 Hz, 1 H), 2.28 (s, 3 H), 1.60–1.77 (m, 1 H), 1.30–1.57 (m, 2 H), 0.67–0.97 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 21.6, 23.4, 24.6, 31.6, 32.9, 42.2, 49.4, 59.6, 66.9, 115.5 and 116.0 (rotamers), 121.0, 124.9, 128.0 and 128.0 (rotamers), 128.2, 128.3, 128.4 and 128.5 (rotamers), 128.5, 130.1 and 130.5 (rotamers), 132.2, 136.3, 137.4, 154.7, 156.0, 168.0, 174.0.

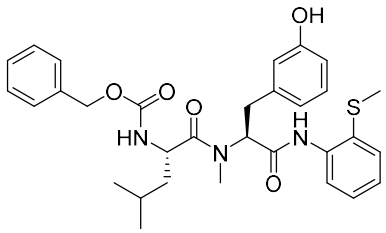
Optical rotation: $[\alpha]_D^{20}$ = -84.6 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{38}N_3O_5S$ $[M+H]^+$	564.2527	564.2534

Benzyl ((*S*)-1-(((*S*)-3-(3-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) amino)-4-methyl-1-oxopentan-2-yl)carbamate (5ah)

According to **GP2** 100.0 mg (212 µmol, 1.0 equiv) 4a, 93.3 mg (424 µmol, 2.0 equiv) 3-iodophenol, 70.8 mg (424 µmol, 2.0 equiv) AgOAc, 11.8 mg (42 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.8 mg (21 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **5ah** (76.3 mg, 135 µmol, 64%) was obtained as colourless oil.

R_f (5ah) = 0.35 (PE/EtOAc 1:1)



5ah

^{1}H NMR (400 MHz, $CDCl_3$): 9.11 and 8.68 (rotamers, s, s, 1 H), 8.20 and 7.84 (rotamers, d, *J* = 8.1 Hz, d, *J* = 7.8 Hz, 1 H), 7.05–7.43 (m, 9 H), 6.88 (bs, 1 H), 6.67–6.78 (m, 3 H), 5.56 (dd, *J* = 10.3, 5.1 Hz, 1 H), 5.43 (d, *J* = 8.2 Hz, 1 H), 5.13 and 4.97 (rotamers, d, *J* = 12.2 Hz, d, *J* = 12.1 Hz, 1 H), 5.04 and 4.90 (rotamers, d, *J* = 12.1 Hz, d, *J* = 12.1 Hz, 1 H), 4.35–4.67 (m, 1 H), 3.39 and 3.31 (rotamers, dd, *J* = 14.4, 3.5 Hz, dd, *J* = 15.5, 10.4 Hz, 1 H), 3.16 (dd, *J* = 15.7, 10.4 Hz, 1 H), 3.07 and 3.04 (rotamers, s, s, 3 H), 2.31 and 2.27 (rotamers, s, s, 3 H), 1.71–1.85 (m, 1 H), 1.43–1.63 (m, 2 H), 0.96 and 0.70 (rotamers, d, *J* = 6.5 Hz, d, *J* = 6.5 Hz, 3 H), 0.92 and 0.67 (rotamers, d, *J* = 6.6 Hz, d, *J* = 6.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.4, 21.3, 23.4, 24.7, 31.0, 32.0, 41.1, 50.2, 58.3, 67.4, 114.1, 115.0, 121.1, 121.2, 126.6, 128.0, 128.1, 128.3, 128.3, 128.4, 128.5, 131.9, 135.8, 137.4, 138.2, 156.7, 156.9, 168.3, 174.3.

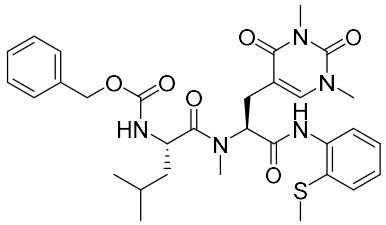
Optical rotation: $[\alpha]_D^{20}$ = -81.6 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{38}N_3O_5S$ $[M+H]^+$	564.2527	564.2532

Benzyl ((*S*)-1-(((*S*)-3-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1-((2-(methylthio) phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5as)

According to **GP2** 68.0 mg (144 µmol, 1.0 equiv) **4a**, 76.6 mg (288 µmol, 2.0 equiv) 5-iodo-1,3-dimethyluracil, 48.1 mg (288 µmol, 2.0 equiv) AgOAc, 8.0 mg (29 µmol, 20 mol%) $(BnO)_2PO_2H$ and 3.2 mg (14 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 1:1 → CH_2Cl_2/MeOH 95:5) and the product **5as** (58.6 mg, 96 µmol, 67%) was obtained as slightly yellow oil.

R_f (5as) = 0.21 (CH_2Cl_2/MeOH 95:5)



5as

^{1}H NMR (400 MHz, $CDCl_3$): 9.11 and 8.62 (rotamers, s, s, 1 H), 8.17 and 7.58 (rotamers, d, *J* = 8.1 Hz, d, *J* = 6.7 Hz, 1 H), 7.06–7.45 (m, 9 H), 5.34–5.76 (m, 2 H), 4.60–5.12 (m, 3 H), 3.34 (s, 6 H), 2.98–3.17 (m, 4 H), 2.83 (dd, *J* = 14.5, 8.3 Hz, 1 H), 2.33 and 2.31 (rotamers, s, s, 3 H), 1.71–1.81 (bs, 1 H), 1.40–1.61 (m, 2 H), 0.98 (d, *J* = 6.4 Hz, 3 H), 0.91 (d, *J* = 6.6 Hz, 3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): 18.3, 21.3, 23.4, 24.6, 25.9, 27.7 and 27.9 (rotamers), 31.9, 36.8 and 37.0 (rotamers), 42.0, 49.7, 57.4, 66.9, 101.3, 108.4, 121.1, 124.9, 126.6, 127.9 and 128.0 (rotamers), 128.1, 128.2, 128.4 and 128.5 (rotamers), 131.8, 136.2, 137.2, 141.3, 142.6, 151.6, 155.2, 163.5, 168.0, 174.0.

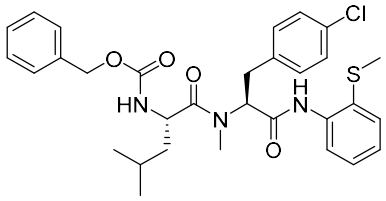
Optical rotation: $[\alpha]_D^{20}$ = -95.8 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{40}N_5O_6S$ $[M+H]^+$	610.2694	610.2699

Benzyl ((*S*)-1-(((*S*)-3-(4-chlorophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) amino)-4-methyl-1-oxopentan-2-yl)carbamate (5ak)

According to **GP2** 95.0 mg (201 µmol, 1.0 equiv) **4a**, 96.0 mg (403 µmol, 2.0 equiv) 1-chloro-4-iodobenzene, 67.2 mg (403 µmol, 2.0 equiv) AgOAc, 11.2 mg (40 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.5 mg (20 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **5ak** (90.0 mg, 155 µmol, 77%) was obtained as colourless oil.

R_f (5ak) = 0.53 (PE/EtOAc 1:1)



5ak

^{1}H NMR (400 MHz, $CDCl_3$): 9.04 and 8.59 (rotamers, s, s, 1 H), 8.21 and 7.88 (rotamers, d, *J*= 8.2 Hz, d, *J* = 8.1 Hz, 1 H), 7.06–7.45 (m, 12 H), 4.89–5.52 (m, 4 H), 4.66 and 4.30 (rotamers, td, *J* = 9.7, 3.4 Hz, m, 1 H), 3.46 (dd, *J* = 14.3, 7.1 Hz, 1 H), 3.08 and 3.04 (rotamers, s, s, 3 H), 3.00 (dd, *J* = 14.4, 8.6 Hz, 1 H), 2.30 and 2.28 (rotamers, s, s, 3 H), 1.66–1.79 (m, 1 H), 1.37–1.56 (m, 2 H), 0.66–0.98 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 20.9 and 21.5 (rotamers), 23.4, 24.6, 31.5, 33.2, 42.3, 49.4, 59.2, 67.0, 120.9, 124.9, 126.2, 128.0, 128.2, 128.4, 128.5, 128.7, 129.3, 130.4 and 130.8 (rotamers), 132.2, 132.6, 135.2, 136.3, 137.4, 156.0, 167.7, 174.0.

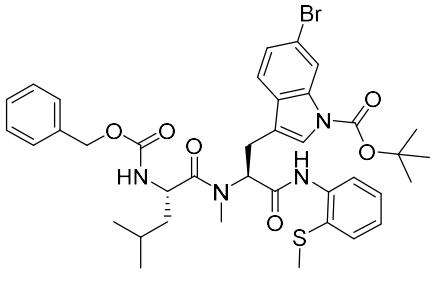
Optical rotation: $[\alpha]_D^{20}$ = -89.1 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{37}ClN_3O_4S$ $[M+H]^+$	582.2188	582.2195

***tert*-Butyl 3-((*S*)-2-((*S*)-2-(((benzyloxy)carbonyl)amino)-*N*,4-dimethylpentanamido)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-6-bromo-1*H*-indole-1-carboxylate (5aq)**

According to **GP2** 100 mg (212 µmol, 1.0 equiv) **4a**, 179 mg (424 µmol, 2.0 equiv) *tert*-butyl 6-bromo-3-iodo-1*H*-indole-1-carboxylate (**11d**), 70.8 mg (424 µmol, 2.0 equiv) AgOAc, 11.8 mg (42 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.8 mg (21 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 99:1) and the product **5aq** (98.3 mg, 128 µmol, 61%) was obtained as slightly yellow oil.

R_f (5aq) = 0.15 (PE/EtOAc 7:3)



5aq

^{1}H NMR (400 MHz, $CDCl_3$): 9.08 and 8.60 (rotamers, s, s, 1 H), 8.33 (bs, 1 H), 8.20 and 7.92 (rotamers, d, *J* = 8.1 Hz, d, *J* = 7.8 Hz, 1 H), 7.04–7.52 (m, 11 H), 5.15–5.60 (m, 2 H), 5.09 and 4.95 (rotamers, d, *J* = 12.2 Hz, d, *J* = 12.1 Hz, 1 H), 5.02 and 4.90 (rotamers, d, *J* = 12.2 Hz, d, *J* = 12.1 Hz, 1 H), 4.72 and 4.26 (rotamers, td, *J* = 9.6, 3.3 Hz, m, 1 H), 3.60 and 3.51 (rotamers, dd, *J* = 15.5, 3.5 Hz, dd, *J* = 15.0, 7.8 Hz, 1 H), 3.00–3.17 (m, 4 H), 2.29 and 2.26 (rotamers, s, s, 3 H), 1.69–1.79 (m, 1 H), 1.66 and 1.62 (rotamers, s, s, 9 H), 1.46–1.58 (m, 2 H), 0.87–0.99 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): 15.3, 18.5, 21.5, 22.8 and 23.4 (rotamers), 23.6 and 24.6 (rotamers), 28.1, 31.5, 42.4, 49.6, 57.8, 65.8, 66.9, 84.1, 115.5, 118.3, 118.5, 120.1, 121.0, 124.4, 124.9, 125.9, 126.3, 128.0, 128.1, 128.4, 128.5, 129.0, 132.1, 136.2, 137.4, 149.1, 156.0, 167.7, 173.8.

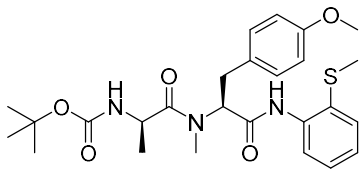
Optical rotation: $[\alpha]_D^{20}$ = -55.7 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{38}H_{46}BrN_4O_6S$ $[M+H]^+$	765.2316	765.2321

tert-Butyl ((*R*)-1-(((*S*)-3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bc)

According to **GP2** 100 mg (253 µmol, 1.0 equiv) **4b**, 118 mg (506 µmol, 2.0 equiv) 4-iodoanisole, 84.0 mg (506 µmol, 2.0 equiv) AgOAc, 14.1 mg (51 µmol, 20 mol%) $(BnO)_2PO_2H$ and 5.7 mg (25 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **5bc** (102 mg, 201 µmol, 80%) was obtained as colourless oil.

R_f (5bc) = 0.40 (PE/EtOAc 1:1)



5bc

^{1}H NMR (400 MHz, $CDCl_3$): 8.82 (s, 1 H), 8.21 (d, *J* = 8.1 Hz, 1 H), 7.44 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.27–7.31 (m, 1 H), 7.15 (d, *J* = 8.6 Hz, 2 H), 7.08 (td, *J* = 7.6, 1.3 Hz, 1 H), 6.82 (d, *J* = 8.6 Hz, 1 H), 5.66 (dd, *J* = 10.7, 5.9 Hz, 1 H), 5.40 (d, *J* = 7.9 Hz, 1 H), 4.58 (quint, *J* = 7.2 Hz, 1 H), 3.77 (s, 3 H), 3.41 (dd, *J* = 15.0, 5.9 Hz, 1 H), 3.01–3.07 (m, 1 H), 2.99 (s, 3 H), 2.31 (s, 3 H), 1.40 (s, 9 H), 0.92 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 18.6, 28.3, 30.9, 32.5, 46.5, 55.3, 58.2, 79.6, 114.0, 121.1, 124.8, 126.6, 128.5, 128.6, 129.7, 132.6, 137.7, 155.0, 158.5, 168.1.

Optical rotation: $[\alpha]_D^{20}$ = -66.6 [$CHCl_3$, c = 1.00]

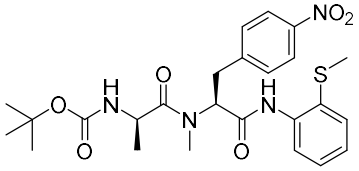
HRMS (CI):	Calculated	Found
$C_{26}H_{36}N_3O_5S$ $[M+H]^+$	502.2370	502.2378

tert-Butyl ((*R*)-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl)amino)-1-oxopropan-2-yl)carbamate (5bd)

According to **GP2** 70 mg (177 µmol, 1.0 equiv) **4b**, 88.0 mg (354 µmol, 2.0 equiv) 1-iodo-4-nitrobenzene, 59.1 mg (354 µmol, 2.0 equiv) AgOAc, 9.9 mg (35 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.0 mg (18 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was

purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **5bd** (74.0 mg, 143 µmol, 81%) was obtained as colourless oil.

R_f (5bd) = 0.38 (PE/EtOAc 1:1)



5bd

^{1}H NMR (400 MHz, $CDCl_3$): 8.76 (s, 1 H), 8.10–8.20 (m, 3 H), 7.44 (d, *J* = 8.4 Hz, 3 H), 7.27–7.31 (m, 1 H), 7.11 (td, *J* = 7.6, 1.0 Hz, 1 H), 5.76 (dd, *J* = 10.0, 6.2 Hz, 1 H), 5.32 (d, *J* = 7.9 Hz, 1 H), 4.60 (quint, *J* = 7.3 Hz, 1 H), 3.60 (dd, *J* = 15.2, 6.1 Hz, 1 H), 3.18 (dd, *J* = 15.0, 10.1 Hz, 1 H), 3.04 (s, 3 H), 2.33 (s, 3 H), 1.39 (s, 9 H), 0.98 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.4, 18.5, 28.3, 30.1, 33.4, 46.5, 57.6, 79.9, 121.4, 123.7, 125.2, 127.2, 128.3, 129.8, 132.1, 137.1, 144.7, 146.9, 155.0, 167.2, 174.9.

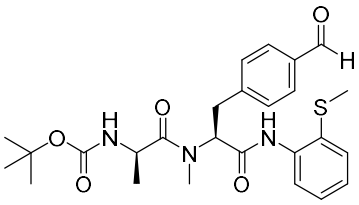
Optical rotation: $[\alpha]_D^{20}$ = -73.6 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{32}N_4O_6S$ $[M]^+$	516.2037	516.2066

***tert*-Butyl ((*R*)-1-(((*S*)-3-(4-formylphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)amino)-1-oxopropan-2-yl)carbamate (5br)**

According to **GP2** 340 mg (860 µmol, 1.0 equiv) **4b**, 399 mg (1.72 mmol, 2.0 equiv) 4-iodobenzaldehyde (**12**), 287 mg (1.72 mmol, 2.0 equiv) AgOAc, 23.9 mg (86 µmol, 20 mol%) $(BnO)_2PO_2H$ and 19.3 mg (86 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 9:1) and the product **5br** (74.0 mg, 143 µmol, 81%) was obtained as colourless oil.

R_f (5br) = 0.19 (CH_2Cl_2/Et_2O 9:1)



5br

^{1}H NMR (400 MHz, $CDCl_3$): 9.97 (s, 1 H), 8.80 (s, 1 H), 8.16 (d, *J* = 8.1 Hz, 1 H), 7.82 (d, *J* = 8.2 Hz, 1 H), 7.40–7.46 (m, 3 H), 7.25–7.31 (m, 1 H), 7.10 (td, *J* = 7.6, 1.2 Hz, 1H), 5.78 (dd, *J* = 10.5, 5.9 Hz, 1 H), 5.37 (d, *J* = 8.1 Hz, 1 H), 4.59 (quint, *J* = 7.1 Hz, 1 H), 3.57 (dd, *J* = 15.2, 5.7 Hz, 1 H), 3.18 (dd, *J* = 15.0, 10.6 Hz, 1 H), 3.02 (s, 3 H), 2.32 (s, 3 H), 1.39 (s, 9 H), 0.91 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.4, 28.3, 30.9, 33.6, 46.5, 57.7, 79.8, 121.3, 125.1, 127.0, 128.4, 129.5, 129.9, 132.3, 135.2, 137.3, 144.1, 155.0, 167.5, 174.9, 191.7.

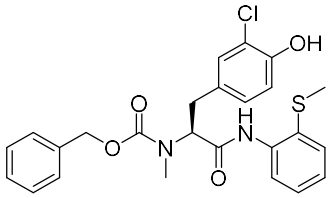
Optical rotation: $[\alpha]_D^{20}$ = -69.7 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{26}H_{34}N_3O_5S$ $[M]^+$	500.2214	500.2221

Benzyl (*S*)-(3-(3-chloro-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3at)

According to **GP2** 110 mg (307 µmol, 1.0 equiv) **1a**, 156 mg (614 µmol, 2.0 equiv) 2-chloro-4-iodophenol (**10a**), 102 mg (614 µmol, 2.0 equiv) AgOAc, 17.1 mg (61 µmol, 20 mol%) $(BnO)_2PO_2H$ and 6.9 mg (31 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3at** (80.7 mg, 166 µmol, 54%) was obtained as slightly yellow oil.

R_f (3at) = 0.47 (PE/EtOAc 1:1)



3at

^{1}H NMR (400 MHz, $CDCl_3$): 8.87 (s, 1 H), 8.29 and 8.25 (rotamers, d, *J* = 8.7 Hz, d, *J* = 8.2 Hz, 1 H), 7.45 (d, *J* = 7.5 Hz, 1 H), 7.21–7.39 (m, 9 H), 6.82–7.10 (m, 3 H), 5.90 and 5.86 (rotamers, bs, bs, 1 H), 4.68–5.21 (m, 4 H), 3.41 (dd, *J* = 14.7, 6.0 Hz, 1 H), 2.86–3.00 (m, 4 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.7 and 31.6 (rotamers), 32.8 and 32.9 (rotamers), 61.2 and 62.3 (rotamers), 67.7 and 68.1 (rotamers), 116.4, 119.8 and 119.9 (rotamers), 120.2 and 120.7 (rotamers), 124.7, 126.1, 127.7, 128.1 and 128.1 (rotamers), 128.3, 128.5, 128.5, 128.7 and 128.8 (rotamers), 129.3 and 129.4 (rotamers), 130.2, 132.7 and 132.9 (rotamers), 136.2, 136.5, 137.7, 150.2, 157.1, 168.2.

Optical rotation: $[\alpha]_D^{20}$ = -45.1 [$CHCl_3$, c = 1.00]

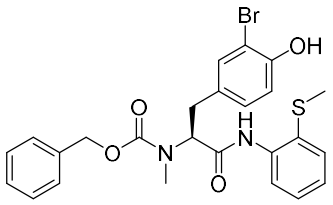
HRMS (CI):	Calculated	Found
$C_{25}H_{26}ClN_2O_4S$ $[M+H]^+$	485.1296	485.1306

Benzyl (*S*)-(3-(3-bromo-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3au)

According to **GP2** 107 mg (299 µmol, 1.0 equiv) **1a**, 178 mg (597 µmol, 2.0 equiv) 2-bromo-4-iodophenol (**10b**), 100 mg (597 µmol, 2.0 equiv) AgOAc, 16.6 mg (60 µmol, 20 mol%) $(BnO)_2PO_2H$ and

6.7 mg (30 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 75 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **3au** (88.2 mg, 167 µmol, 56%) was obtained as slightly brown oil.

R_f (3au) = 0.18 (PE/EtOAc 7:3)



3au

^{1}H NMR (400 MHz, $CDCl_3$): 8.87 (s, 1 H), 8.29 and 8.25 (rotamers, d, *J* = 8.4 Hz, d, *J* = 8.1 Hz, 1 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 7.21–7.39 (m, 7 H), 6.83–7.12 (m, 3 H), 5.77 and 5.74 (rotamers, bs, bs, 1 H), 4.91–5.21 (m, 3 H), 3.41 (dd, *J* = 14.7, 6.0 Hz, 1 H), 2.86–3.01 (m, 4 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.4 and 31.6 (rotamers), 32.7 and 32.8 (rotamers), 61.2 and 62.3 (rotamers), 67.8 and 68.1 (rotamers), 110.1, 116.2, 120.2 and 120.7 (rotamers), 124.7, 126.1, 127.7, 128.1 and 128.3 (rotamers), 128.5, 128.7 and 128.9, 129.6, 130.7, 132.2 and 132.3 (rotamers), 132.7 and 132.9 (rotamers), 136.2, 137.7, 151.1, 157.1, 168.2.

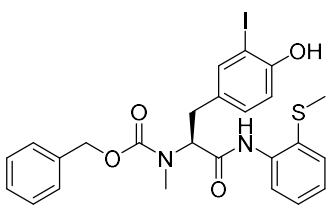
Optical rotation: $[\alpha]_D^{20}$ = -44.6 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{25}BrN_2O_4S$ $[M]^+$	528.0713	528.0720

Benzyl (*S*)-(3-(4-hydroxy-3-iodophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3av)

According to **GP2** 70.0 mg (195 µmol, 1.0 equiv) **1a**, 135 mg (391 µmol, 2.0 equiv) 2,4-diiodophenol (**10c**), 65.2 mg (391 µmol, 2.0 equiv) AgOAc, 10.9 mg (39 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.4 mg (20 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 75 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **3av** (34.6 mg, 60 µmol, 31%) was obtained as colourless oil. Additionally unreacted starting material **1a** (33.6 mg, 94 µmol, 48%) was obtained as colourless oil.

R_f (3av) = 0.18 (PE/EtOAc 7:3)



3av

^{1}H NMR (400 MHz, $CDCl_3$): 8.86 (s, 1 H), 8.30 and 8.25 (rotamers, d, *J* = 8.0, d, *J* = 7.9 Hz, 1 H), 7.57 and 7.51 (rotamers, bs, bs, 1 H), 7.45 (d, *J* = 7.6 Hz, 1 H), 7.21–7.37 (m, 7 H), 6.96–7.15 (m, 2 H), 6.85

and 6.81 (rotamers, d, *J* = 8.2 Hz, d, *J* = 8.3 Hz, 1 H), 5.63 and 5.58 (rotamers, bs, bs, 1 H), 4.61–5.22 (m, 4 H), 3.40 (dd, *J* = 14.7, 5.9 Hz, 1 H), 2.89–2.99 (m, 4 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.6, 30.8, 32.5, 61.3, 67.8 and 68.1 (rotamers), 85.5, 115.1, 120.2 and 120.7 (rotamers), 124.7, 127.8, 128.1, 128.5, 128.5, 128.7, 130.7, 131.2, 132.8, 137.7, 138.5, 153.8, 157.1, 168.2.

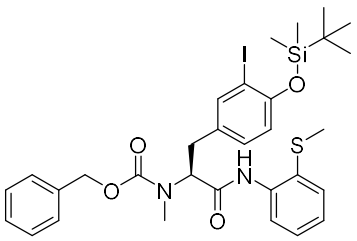
Optical rotation: $[\alpha]_D^{20}$ = -41.4 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{26}IN_2O_4S$ $[M+H]^+$	577.0652	577.0661

Benzyl (*S*)-(3-(4-((*tert*-butyldimethylsilyl)oxy)-3-iodophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)carbamate (3aw)

According to **GP2** 117 mg (326 µmol, 1.0 equiv) **1a**, 300 mg (653 µmol, 2.0 equiv) *tert*-butyl(2,4-diiodophenoxy)dimethylsilane (**10d**), 109 mg (653 µmol, 2.0 equiv) AgOAc, 18.2 mg (65 µmol, 20 mol%) $(BnO)_2PO_2H$ and 7.3 mg (33 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 75 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 85:15) and the product **3aw** (137 mg, 198 µmol, 61%) was obtained as colourless oil.

R_f (3aw) = 0.48 (PE/EtOAc 7:3)



3aw

^{1}H NMR (400 MHz, $CDCl_3$): 8.88 and 8.85 (rotamers, s, s, 3 H), 8.23–8.34 (m, 1 H), 7.67 and 7.64 (rotamers, bs, bs ,1 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 7.22–7.37 (m, 6 H), 6.94–7.12 (m, 2 H), 6.72 and 6.69 (rotamers, d, *J* = 8.2 Hz, d, *J* = 8.2 Hz, 1 H), 4.90–5.21 (m, 3 H), 3.39 (dd, *J* = 14.7, 5.9 Hz, 1 H), 2.85–2.99 (m, 3 H), 2.21 (s, 3 H), 1.06 (s, 9 H), 0.26 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): -4.1, 18.3 and 18.6 (rotamers), 25.8, 30.8, 31.5, 32.4 and 32.5 (rotamers), 61.3 and 62.2 (rotamers), 67.7 and 68.0 (rotamers), 90.4 and 90.6 (rotamers), 118.3, 120.1 and 120.6 (rotamers), 124.6, 125.4 and 125.9 (rotamers), 127.7, 128.0 and 128.1 (rotamers), 128.5, 128.7 and 128.9, 129.7, 131.6 and 131.8 (rotamers), 132.8 and 132.9 (rotamers), 135.8 and 136.2 (rotamers), 137.7 and 137.8 (rotamers), 139.6 and 139.8 (rotamers), 153.9, 157.0, 167.9 and 168.2 (rotamers).

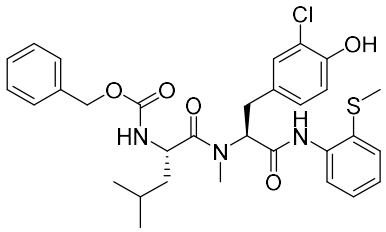
Optical rotation: $[\alpha]_D^{20}$ = -33.0 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{40}IN_2O_4SSi$ $[M+H]^+$	691.1517	691.1519

Benzyl ((*S*)-1-(((*S*)-3-(3-chloro-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5at)

According to **GP2** 100 mg (212 µmol, 1.0 equiv) **4a**, 108 mg (424 µmol, 2.0 equiv) 2-chloro-4-iodophenol (**10a**), 70.8 mg (424 µmol, 2.0 equiv) AgOAc, 11.8 mg (42 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.8 mg (21 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **5at** (70.2 mg, 117 µmol, 55%) was obtained as white solid.

R_f (5at) = 0.33 (PE/EtOAc 1:1)



5at

^{1}H NMR (400 MHz, $CDCl_3$): 9.06 and 8.60 (rotamers, s, s, 1 H), 8.20 and 7.90 (rotamers, d, *J* = 8.1 Hz, d, *J* = 7.9 Hz, 1 H), 6.86–7.45 (m, 11 H), 5.75 and 5.61 (rotamers, bs, bs, 1 H), 4.87–5.43 (m, 4 H), 4.68 and 4.38 (rotamers, td, *J* = 10.3, 2.5 Hz, m, 1 H), 3.40 (dd, *J* = 14.3, 7.1 Hz, 1 H), 3.07 and 3.04 (rotamers, s, s, 3 H), 2.96 (dd, *J* = 14.4, 8.2 Hz, 1 H), 2.30 (s, 3 H), 1.67–1.79 (m, 1 H), 1.35–1.56 (m, 2 H), 0.68–0.99 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 21.5, 23.4, 24.6, 31.8, 32.8, 42.3, 49.5, 67.0, 116.3, 119.8, 121.0, 124.9, 128.0, 128.1, 128.4, 128.5, 129.0, 129.5, 129.9, 132.2, 136.3, 137.4, 150.2, 156.0, 167.7, 173.9.

Optical rotation: $[\alpha]_D^{20}$ = -81.0 [$CHCl_3$, c = 1.00]

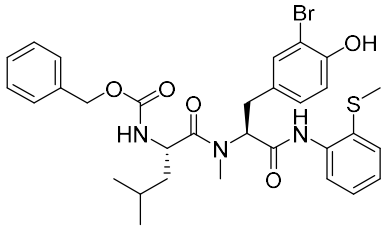
Melting point: 145–148 °C

HRMS (CI):	Calculated	Found
$C_{31}H_{36}ClN_3O_5S$ $[M]^+$	597.2059	597.2090

Benzyl ((*S*)-1-(((*S*)-3-(3-bromo-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5au)

According to **GP2** 100 mg (212 µmol, 1.0 equiv) **4a**, 127 mg (424 µmol, 2.0 equiv) 2-bromo-4-iodophenol (**10b**), 70.8 mg (424 µmol, 2.0 equiv) AgOAc, 11.8 mg (42 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.8 mg (21 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 85:15) and the product **5au** (72.1 mg, 112 µmol, 53%) was obtained as white solid.

R_f (5au) = 0.35 (PE/EtOAc 1:1)



5au

^{1}H NMR (400 MHz, $CDCl_3$): 9.06 and 8.60 (rotamers, s, s, 1 H), 8.18 and 7.84 (rotamers, d, *J* = 8.2 Hz, d, *J* = 7.8 Hz, 1 H), 7.00–7.43 (m, 10 H), 6.95 and 6.88 (rotamers, d, *J* = 8.3 Hz, d, *J* = 8.3 Hz, 1 H), 5.90 and 5.74 (rotamers, s, s, 1 H), 4.89–5.40 (m, 4 H), 4.68 and 4.38 (rotamers, td, *J* = 10.3, 3.3 Hz, m, 1 H), 3.40 (dd, *J* = 14.3, 7.3 Hz, 1 H), 3.07 and 3.04 (rotamers, s, s, 3 H), 2.96 (dd, *J* = 14.1, 7.8 Hz, 1 H), 2.30 and 2.29 (rotamers, s, s, 3 H), 1.67–1.78 (bs, 1 H), 1.33–1.56 (m, 2 H), 0.96 and 0.75 (rotamers, d, *J* = 6.4 Hz, d, *J* = 6.5 Hz, 3 H), 0.90 and 0.70 (rotamers, d, *J* = 6.6 Hz, d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 20.9 and 21.5 (rotamers), 23.1 and 23.4 (rotamers), 24.6, 31.9, 32.7, 42.3, 49.5, 59.8, 67.0, 110.1, 116.1, 121.1, 124.9, 126.4, 128.0, 128.1, 128.3 and 128.4 (rotamers), 128.5, 129.7, 130.3, 132.1, 132.6, 136.2, 137.3, 151.2, 156.1, 167.7, 173.9.

Optical rotation:	$[\alpha]_D^{20}$ = -129.6 [$CHCl_3$, c = 1.00]	
Melting point:	142–144 °C	
HRMS (CI):	Calculated	Found
$C_{31}H_{37}BrN_3O_5S$ $[M+H]^+$	642.1632	642.1639

Benzyl ((*S*)-1-(((*S*)-3-(4-hydroxy-3-iodophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5av)

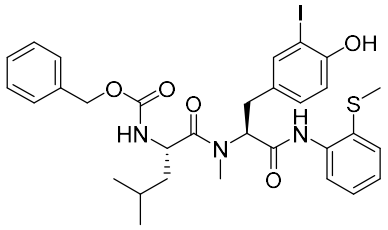
Method A) C-H activation

According to **GP2** 100 mg (212 µmol, 1.0 equiv) **4a**, 147 mg (424 µmol, 2.0 equiv) 2,4-diiodophenol (**10c**), 70.8 mg (424 µmol, 2.0 equiv) AgOAc, 11.8 mg (42 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.8 mg (21 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 75 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) and the product **5av** (62.8 mg, 91 µmol, 43%) was obtained as slightly yellow solid.

Method B) TBS deprotection

To a solution of 33.0 mg (41 µmol, 1.0 equiv) **5aw** in anhydrous THF (0.5 mL) was added 45.2 µL (45 µmol, 1.1 equiv, 1.0 M solution in THF) TBAF at 0 °C and the mixture was stirred for 30 min at room temperature. The mixture was quenched with sat. aq. NH_4Cl and the aqueous phase was extracted with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 99:1 → 95:5) and the product **5av** (26.6 mg, 39 µmol, 94%) was obtained as slightly yellow solid.

R_f (5av) = 0.38 (PE/EtOAc 1:1)



5av

^{1}H NMR (400 MHz, $CDCl_3$): 9.06 and 8.59 (rotamers, s, s, 1 H), 8.18 and 7.84 (rotamers, d, *J* = 8.2 Hz, d, *J* = 8.2 Hz, 1 H), 4.90–5.40 (m, 4 H), 4.68 and 4.37 (rotamers, td, *J* = 9.4, 3.3 Hz, m, 1 H), 3.38 (dd, *J* = 14.3, 7.3 Hz, 1 H), 3.07 and 3.04 (rotamers, s, s, 3 H), 2.94 (dd, *J* = 14.3, 7.9 Hz, 1 H), 2.29 (s, 3 H), 1.68–1.78 (bs, 1 H), 1.35–1.56 (m, 2 H), 0.68–0.99 (m, 6 H).

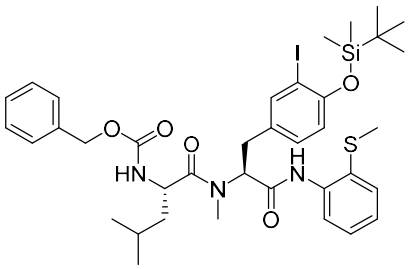
^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 21.5, 23.5, 24.6, 31.9, 32.5, 42.3, 49.6, 59.8, 67.0, 85.4, 115.0, 121.1, 124.9, 126.4, 128.0, 128.1, 128.4, 128.4, 128.5, 130.7 and 130.8 (rotamers), 132.1, 136.3, 138.6, 153.9, 156.1, 167.7, 173.9.

Optical rotation:	$[\alpha]_D^{20}$ = -65.1 [$CHCl_3$, c = 1.00]	
Melting point:	110–115 °C	
HRMS (CI):	Calculated	Found
$C_{31}H_{37}IN_3O_5S$ $[M+H]^+$	690.1493	690.1499

Benzyl ((*S*)-1-(((*S*)-3-(4-((*tert*-butyldimethylsilyl)oxy)-3-iodophenyl)-1-((2-(methylthio)phenyl) amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5aw)

According to **GP2** 75.0 mg (159 µmol, 1.0 equiv) **4a**, 146 mg (318 µmol, 2.0 equiv) *tert*-butyl(2,4-diiodophenoxy)dimethylsilane (**10d**), 53.1 mg (318 µmol, 2.0 equiv) AgOAc, 8.9 mg (32 µmol, 20 mol%) $(BnO)_2PO_2H$ and 3.6 mg (21 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 75 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 85:15) and the product **5aw** (69.0 mg, 86 µmol, 54%) was obtained as colourless oil.

R_f (5aw) = 0.34 (PE/EtOAc 7:3)



5aw

^{1}H NMR (400 MHz, $CDCl_3$): 9.06 and 8.61 (rotamers, s, s, 1 H), 8.18 and 7.84 (rotamers, d, *J* = 8.1 Hz, d, *J* = 7.5 Hz, 1 H), 7.66 and 7.63 (rotamers, d, *J* = 1.8 Hz, d, *J* = 2.1 Hz, 1 H), 6.99–7.43 (m, 8 H), 6.72 (d, *J* = 8.2 Hz, 1 H), 4.90–5.50 (m, 4 H), 4.69 and 4.40 (rotamers, td, *J* = 10.4, 3.1 Hz, m, 1 H), 3.38 (dd,

J = 14.1, 7.8 Hz, 1 H), 3.07 and 3.04 (rotamers, s, s, 3 H), 2.96 (dd, *J* = 14.1, 7.5 Hz, 1 H), 2.29 (s, 3 H), 1.68–1.78 (m, 1 H), 1.33–1.54 (m, 2 H), 1.05 and 1.03 (rotamers, s, s, 9 H), 0.72–0.98 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): -4.1, 18.3, 18.4, 21.5, 23.5, 24.6, 25.7, 25.8, 32.5, 42.3, 49.7, 66.9, 90.5, 118.3, 121.1, 124.9, 128.0, 128.1 and 128.1 (rotamers), 128.3, 128.4, 128.5, 129.9, 131.2, 132.1, 139.9, 154.1, 156.1, 167.7, 173.8.

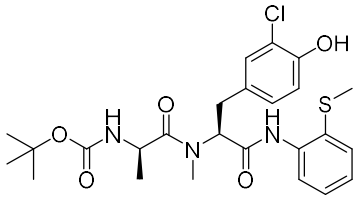
Optical rotation: $[\alpha]_D^{20}$ = -48.4 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{37}H_{51}IN_3O_5SSi$ $[M+H]^+$	804.2358	804.2361

tert-Butyl ((*R*)-1-(((*S*)-3-(3-chloro-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bt)

According to **GP2** 150 mg (379 µmol, 1.0 equiv) **4b**, 193 mg (758 µmol, 2.0 equiv) 2-chloro-4-iodophenol (**10a**), 127 mg (758 µmol, 2.0 equiv) AgOAc, 21.1 mg (76 µmol, 20 mol%) $(BnO)_2PO_2H$ and 8.5 mg (38 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **5bt** (109 mg, 208 µmol, 55%) was obtained as slightly yellow oil.

R_f (5bt) = 0.28 (PE/EtOAc 1:1)



5bt

^{1}H NMR (400 MHz, $CDCl_3$): 8.80 (s, 1 H), 8.16 (d, *J* = 7.9 Hz, 1 H), 7.44 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.27 (td, *J* = 8.7, 1.2 Hz, 1 H), 7.17 (d, *J* = 1.8 Hz, 1 H), 7.09 (td, *J* = 7.6, 1.1 Hz, 1 H), 7.02 (dd, *J* = 8.3, 1.8 Hz, 1 H), 6.91 (d, *J* = 8.3 Hz, 1H), 6.17 (bs, 1 H), 5.64 (dd, *J* = 10.6, 5.9 Hz, 1 H), 5.43 (d, *J* = 8.1 Hz, 1 H), 4.61 (quint, *J* = 7.2 Hz, 1 H), 3.38 (dd, *J* = 15.2, 5.8 Hz, 1 H), 2.95–3.08 (m, 4 H), 2.31 (s, 3 H), 1.40 (s, 9 H), 0.98 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.4, 28.3, 30.9, 32.2, 46.5, 57.8, 79.8, 116.4, 119.9, 121.3, 125.0, 127.0, 128.4, 128.6, 129.2, 129.5, 132.3, 137.4, 150.4, 155.1, 167.7, 175.0.

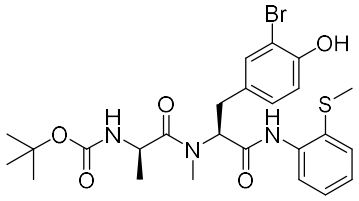
Optical rotation: $[\alpha]_D^{20}$ = -51.9 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{26}H_{27}N_2O_4S$ $[M+H]^+$	463.1686	463.1706

***tert*-Butyl ((*R*)-1-(((*S*)-3-(3-bromo-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bu)**

According to **GP2** 70 mg (177 µmol, 1.0 equiv) **4b**, 106 mg (354 µmol, 2.0 equiv) 2-bromo-4-iodophenol (**10b**), 59.1 mg (354 µmol, 2.0 equiv) AgOAc, 9.8 mg (35 µmol, 20 mol%) $(BnO)_2PO_2H$ and 4.0 mg (18 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, PE/EtOAc 8:2) and the product **5bu** (58.9 mg, 104 µmol, 59%) was obtained as slightly yellow oil.

R_f (5bu) = 0.33 (PE/EtOAc 1:1)



5bu

^{1}H NMR (400 MHz, $CDCl_3$): 8.80 (s, 1 H), 8.16 (d, *J* = 8.1 Hz, 1 H), 7.24–7.46 (m, 3 H), 7.06–7.13 (m, 2 H), 6.92 (d, *J* = 8.3 Hz, 1 H), 5.64 (dd, *J* = 10.5, 5.9 Hz, 1 H), 5.43 (d, *J* = 7.8 Hz, 1 H), 4.61 (quint, *J* = 7.1 Hz, 1 H), 3.39 (dd, *J* = 15.2, 5.9 Hz, 1 H), 2.94–3.05 (m, 4 H), 2.32 (s, 3 H), 1.40 (s, 9 H), 0.99 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.5, 28.3, 30.9, 31.2, 46.6, 57.7, 79.9, 110.0, 116.1, 121.3, 125.0, 127.0, 128.4, 129.5, 130.1, 132.0, 132.3, 137.4, 151.3, 155.1, 167.7, 175.0.

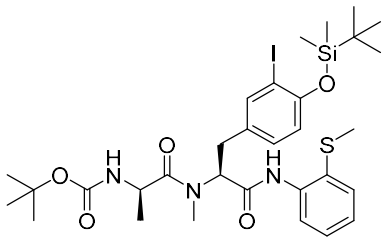
Optical rotation: $[\alpha]_D^{20}$ = -50.0 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{33}BrN_3O_5S$ $[M+H]^+$	566.1319	566.1321

***tert*-Butyl ((*R*)-1-(((*S*)-3-(4-((*tert*-butyldimethylsilyl)oxy)-3-iodophenyl)-1-((2-(methylthio) phenyl) amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bw)**

According to **GP2** 100 mg (253 µmol, 1.0 equiv) **4b**, 233 mg (506 µmol, 2.0 equiv) *tert*-butyl(2,4-diiodophenoxy)dimethylsilane (**10d**), 84.0 mg (506 µmol, 2.0 equiv) AgOAc, 14.1 mg (51 µmol, 20 mol%) $(BnO)_2PO_2H$ and 5.7 mg (25 µmol, 10 mol%) $Pd(OAc)_2$ were reacted at 65 °C for 3 d. After workup the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 99:1) and the product **5bw** (126 mg, 173 µmol, 69%) was obtained as colourless oil.

R_f (5bw) = 0.19 (PE/EtOAc 7:3)



5bw

^{1}H NMR (400 MHz, $CDCl_3$): 8.82 (s, 1 H), 8.19 (d, *J* = 8.1 Hz, 1 H), 7.6 (d, *J* = 2.0 Hz, 1 H), 7.44 (d, *J* = 7.8 Hz, 1 H), 7.25–7.31 (m, 1 H), 7.04–7.11 (m, 1 H), 6.73 (d, *J* = 8.3 Hz, 1 H), 5.65 (dd, *J* = 10.8, 5.7 Hz, 1 H), 5.43 (d, *J* = 8.1 Hz, 1 H), 4.60 (quint, *J* = 7.1 Hz, 1H), 3.36 (dd, *J* = 15.2, 5.6 Hz, 1 H), 2.94–3.05 (m, 4 H), 2.31 (s, 3 H), 1.40 (s, 9 H), 1.04 (s, 9 H), 0.98 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): -4.1, 18.3, 18.5, 25.8, 28.3, 28.6, 30.8, 31.7, 46.5, 57.7, 79.6, 90.4, 118.4, 121.1, 124.9, 128.5, 129.6, 131.0, 132.4, 137.5, 139.4, 154.1, 155.0, 167.8, 174.8.

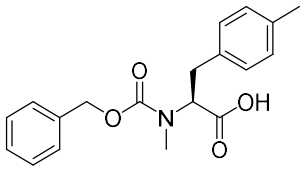
Optical rotation: $[\alpha]_D^{20}$ = -34.7 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{31}H_{47}IN_3O_5SSi$ $[M+H]^+$	728.2045	728.2051

(*S*)-2-(((Benzyloxy)carbonyl)(methyl)amino)-3-(*p*-tolyl)propanoic acid (6ab)

70.0 mg (156 µmol, 1.0 equiv) compound **3ab** were dissolved in dry CH_3CN (1.5 mL) and treated with 3.8 mg (31 µmol, 0.2 equiv) 4-DMAP and 108 µL (468 µmol, 3.0 equiv) di-*tert*-butyl dicarbonate. The reaction mixture was stirred over night at room temperature, the solvent was removed *in vacuo* and the residue was quickly passed through a short column (SiO_2, PE/EtOAc 85:15). The obtained Boc-amide was dissolved in THF (1.0 mL) and treated at 0 °C with a solution of 14.9 mg (624 µmol, 4.0 equiv) LiOH in water (0.5 mL) and 161 µL aq. H_2O_2 (1.56 mmol, 10 equiv, 33%). The reaction mixture was stirred for 6 h at room temperature, treated with sat. aq. Na_2SO_3, acidified to pH 2 and extracted with EtOAc (x3). The combined organic phases were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 7:3 + 1% AcOH) and the free acid **6ab** (45.0 mg, 137 µmol, 88%) was obtained as a colourless oil.

R_f (6ab) = 0.25 (PE/EtOAc 7:3 + 1% AcOH)



6ab

^{1}H NMR (400 MHz, $CDCl_3$): 9.71 (bs, 1 H), 6.96–7.37 (m, 9 H), 4.99–5.16 (m, 2 H), 4.94 and 4.86 (rotamers, dd, *J* = 10.9, 4.9 Hz, dd, *J* = 10.7, 4.3 Hz, 1 H), 3.33 and 3.27 (rotamers, dd, *J* = 14.6, 4.8 Hz, dd, *J* = 14.7, 4.5 Hz, 1 H), 3.05 and 2.97 (rotamers, dd, *J* = 14.4, 11.3 Hz, dd, *J* = 14.1, 11.4 Hz, 1 H), 2.85 and 2.80 (rotamers, s, s, 3 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 21.0, 32.1 and 32.2 (rotamers), 34.2 and 34.6 (rotamers), 60.4 and 60.8 (rotamers), 67.4 and 67.6 (rotamers), 127.6, 127.8, 127.9 and 128.0 (rotamers), 128.4, 128.6, 129.2 and 129.3 (rotamers), 133.7, 136.2 and 136.2 (rotamers), 136.3 and 136.4 (rotamers), 156.0 and 156.9 (rotamers), 176.1 and 176.2 (rotamers).

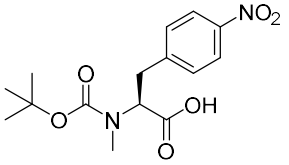
Optical rotation: $[\alpha]_D^{20}$ = -45.7 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{19}H_{22}NO_4$ $[M+H]^+$	328.1543	328.1554

(*S*)-2-((*tert*-Butoxycarbonyl)(methyl)amino)-3-(4-nitrophenyl)propanoic acid (6ad)

160 mg (359 µmol, 1.0 equiv) compound **1bd** were dissolved in dry CH_3CN (2.5 mL) and treated with 8.8 mg (72 µmol, 0.2 equiv) 4-DMAP and 334 µL (1.44 mmol, 4.0 equiv) di-*tert*-butyl dicarbonate. The reaction mixture was stirred over night at room temperature, the solvent was removed *in vacuo* and the residue was quickly passed through a short column (SiO_2, CH_2Cl_2/Et_2O 85:15). The obtained Boc-amide was dissolved in THF (1.5 mL) and treated at 0 °C with a solution of 34.4 mg (1.44 mmol, 4.0 equiv) LiOH in water (0.6 mL) and 333 µL aq. H_2O_2 (3.59 mmol, 10 equiv, 33%). The reaction mixture was stirred for 6 h at room temperature, treated with sat. aq. Na_2SO_3, acidified to pH 2 and extracted with CH_2Cl_2 (x3). The combined organic phases were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 6:4 + 1% AcOH) and the free acid **6ad** (106 mg, 327 µmol, 91%) was obtained as orange oil.

R_f (6ad) = 0.30 (PE/EtOAc 1:1 + 1% AcOH)



6ad

^{1}H NMR (400 MHz, $CDCl_3$): 9.08 (bs, 1 H), 8.13–8.21 (m, 2 H), 7.34–7.44 (m, 2 H), 4.90 and 4.61 (rotamers, dd, *J* = 10.6, 5.2 Hz, dd, *J* = 9.9, 3.6 Hz, 1 H), 3.38–3.48 (m, 1 H), 3.24 and 3.18 (rotamers, dd, *J* = 14.2, 11.0 Hz, dd, *J* = 13.6, 11.0 Hz, 1 H), 2.77 and 2.73 (rotamers, s, s, 3 H), 1.40 and 1.37 (rotamers, s, s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 28.2, 32.9, 34.6 and 35.2 (rotamers), 59.9 and 61.0 (rotamers), 81.1 and 81.3 (rotamers), 123.7 and 123.8 (rotamers), 129.8 and 129.9 (rotamers), 145.1 and 145.2 (rotamers), 146.9, 154.7 and 156.1 (rotamers), 175.4 and 175.4 (rotamers).

Optical rotation: $[\alpha]_D^{20}$ = -72.3 [$CHCl_3$, c = 1.00]

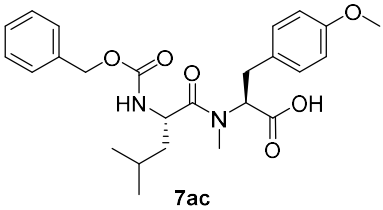
HRMS (CI):	Calculated	Found
$C_{15}H_{21}N_2O_6$ $[M+H]^+$	325.1394	325.1399

(*S*)-2-((*S*)-2-(((Benzyloxy)carbonyl)amino)-*N*,4-dimethylpentanamido)-3-(4-methoxyphenyl) propanoic acid (7ac)

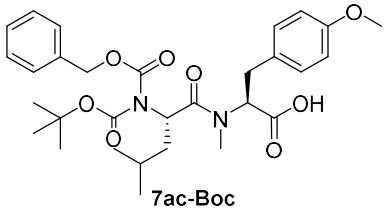
125 mg (216 µmol, 1.0 equiv) compound **5ac** were dissolved in dry CH_3CN (1.4 mL) and treated with 5.3 mg (43 µmol, 0.2 equiv) 4-DMAP and 201 µL (865 µmol, 4.0 equiv) di-*tert*-butyl dicarbonate. The reaction mixture was stirred over night at room temperature, the solvent was removed *in vacuo* and the residue was quickly passed through a short column (SiO_2, CH_2Cl_2/Et_2O 85:15). The obtained Boc-amide was dissolved in THF (1.0 mL) and treated at 0 °C with a solution of 20.7 mg (865 µmol, 4.0 equiv) LiOH in water (0.4 mL) and 201 µL aq. H_2O_2 (2.16 mmol, 10 equiv, 33%). The reaction mixture was stirred for 6 h at room temperature, treated with sat. aq. Na_2SO_3, acidified to pH 2 and extracted with CH_2Cl_2 (x3). The combined organic phases were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 6:4 + 1% AcOH) and the free acid **7ac** (65.0 mg, 142 µmol, 66%) was obtained as colourless oil as well as the Cbz/Boc-protected compound **7ac-Boc** (31 mg, 56 µmol, 27%)) as colourless oil. Compound **7ac-Boc** was redissolved in CH_2Cl_2 (0.5 mL) and 20.8 µL (269 µmol, 5 equiv) TFA were added at 0 °C. The reaction mixture was stirred over night at room temperature, the solvent was removed *in vacuo* and the residue was quickly passed through a short column (SiO_2, CH_2Cl_2/Et_2O) to obtain the title compound **7ac** (24.0 mg, 53 µmol, 24%) as a colourless oil, increasing the overall yield to 90% (89 mg, 195 µmol).

R_f (7ac) = 0.24 (PE/EtOAc 1:1 + 1% AcOH)

R_f (7ac-Boc) = 0.34 (PE/EtOAc 1:1 + 1% AcOH)



7ac



7ac-Boc

^{1}H NMR (500 MHz, $CDCl_3$): 7.28–7.38 (m, 5 H), 7.07 (d, *J* = 8.5 Hz, 2 H), 6.84 and 6.79 (rotamers, d, *J* = 8.5 Hz, d, *J* = 8.5 Hz, 2 H), 5.82 and 8.60 (rotamers, bs, bs, 1 H), 4.77–5.15 (m, 3 H), 4.61 and 4.36 (rotamers, td, *J* = 9.6, 4.1 Hz, bs, 1 H), 3.77 and 3.73 (rotamers, s, s, 3 H), 3.26–3.34 (m, 1 H), 3.00 (dd, *J* = 14.7, 10.9 Hz, 1 H), 2.96 and 2.91 (rotamers, s, s, 3 H), 1.64–1.74 (m, 1 H), 1.31–1.49 (m, 2 H), 0.94 and 0.70 (rotamers, d, *J* = 6.6 Hz, d, *J* = 6.6 Hz, 3 H), 0.90 and 0.68 (rotamers, d, *J* = 6.6 Hz, d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): 20.8 and 21.6 (rotamers), 23.1 and 23.3 (rotamers), 24.4 and 24.5 (rotamers), 33.4 and 33.9 (rotamers), 39.9, 41.9, 48.5 and 49.4 (rotamers), 55.1 and 55.2 (rotamers), 59.5 and 62.3 (rotamers), 66.8 and 67.5 (rotamers), 113.9 and 114.5 (rotamers), 127.9, 128.0, 128.2, 128.4, 128.5, 128.6, 129.8, 130.3, 135.7 and 136.4 (rotamers), 156.1 and 157.0 (rotamers), 158.5 and 158.8 (rotamers), 173.8 and 174.0 (rotamers).

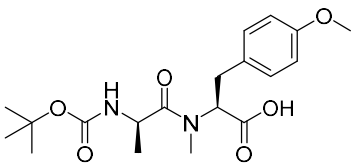
Optical rotation: $[\alpha]_D^{20}$ = -54.4 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{25}H_{33}N_2O_6$ $[M+H]^+$	457.2333	457.2340

(*S*)-2-((*R*)-2-((*tert*-Butoxycarbonyl)amino)-*N*-methylpropanamido)-3-(4-methoxyphenyl)propanoic acid (7bc)

40.0 mg (80 µmol, 1.0 equiv) compound **3ab** were dissolved in dry CH_3CN (1.0 mL) and treated with 1.9 mg (16 µmol, 0.2 equiv) 4-DMAP and 74 µL (319 µmol, 4.0 equiv) di-*tert*-butyl dicarbonate. The reaction mixture was stirred over night at room temperature, the solvent was removed *in vacuo* and the residue was quickly passed through a short column (SiO_2, PE/EtOAc 7:3). The obtained Boc-amide was dissolved in THF (1.0 mL) and treated at 0 °C with a solution of 7.6 mg (319 µmol, 4.0 equiv) LiOH in water (0.5 mL) and 74 µL aq. H_2O_2 (797 µmol, 10 equiv, 33%). The reaction mixture was stirred for 3 h at room temperature, treated with sat. aq. Na_2SO_3, acidified to pH 2 and extracted with CH_2Cl_2 (x3). The combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo* (to approximately 0.5 mL). To deprotect any possibly formed double Boc-protected side product (compare **7ac-Boc**), the solution was cooled to 0 °C and 12 µL (159 µmol, 2 equiv) TFA were added. The mixture was stirred for 5 min at room temperature and the solvent was removed *in vacuo*. The residue was purified by column chromatography (SiO_2, PE/EtOAc 1:1 + 1% AcOH) and the free acid **7bc** (28.1 mg, 74 µmol, 93%) was obtained as a white solid.

R_f (7bc) = 0.22 (PE/EtOAc 1:1 + 1% AcOH)



7bc

^{1}H NMR (400 MHz, $CDCl_3$): 7.10 (d, *J* = 8.6 Hz, 2 H), 6.81 (d, *J* = 8.6 Hz, 2 H), 5.51 (d, *J* = 7.0 Hz, 1H), 5.21 (dd, *J* = 11.2, 4.5 Hz, 1 H), 4.51 (quint, *J* = 7.1 Hz, 1 H), 3.77 (s, 3 H), 3.36 (dd, *J* = 14.7, 4.6 Hz, 1 H), 3.01 (dd, *J* = 14.4, 11.7 Hz, 1 H), 2.88 (s, 3 H), 1.43 (s, 9 H), 0.93 (d, *J* = 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): 18.1, 28.3, 33.0, 33.6, 46.5, 55.3, 59.0, 79.8, 114.0, 128.4, 129.7, 155.3, 158.5, 173.7, 174.2.

Optical rotation: $[\alpha]_D^{20}$ = -32.8 [$CHCl_3$, c = 1.00]

Melting point: 148–150 °C

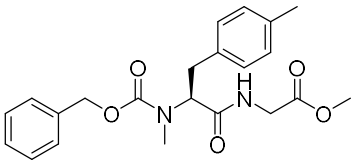
HRMS (CI):	Calculated	Found
$C_{19}H_{29}N_2O_6$ $[M+H]^+$	381.2020	381.2031

Methyl (*S*)-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-(*p*-tolyl)propanoyl)glycinate (8ab)

To a solution of 28.0 mg (86 µmol, 1.0 equiv) **6ab** in 1.0 mL anhydrous DMF were added 16.1 mg (128 µmol, 1.5 equiv) methyl glycinate hydrochloride, 19.7 mg (128 µmol, 1.5 equiv) HOBt, 24.6 mg (128 µmol, 1.5 equiv) EDC·HCl and 23.5 µL (214 µmol, 2.5 equiv) NMM at 0 °C. The reaction mixture was allowed to warm to room temperature overnight and concentrated under reduced pressure. The

residue was taken up in EtOAc and washed with 1 M $KHSO_4$ (x2), sat. aq. $NaHCO_3$ (x1) and brine (x1). After drying over Na_2SO_4 the mixture was filtrated and the solvent was removed *in vacuo*. The crude product was purified by column chromatography (SiO_2, PE/EtOAc 7:3) to obtain the dipeptide **8ab** (30.2 mg, 76 µmol, 89%, 99% ee) as colourless oil.

R_f (8ab) = 0.23 (PE/EtOAc 1:1)



8ab

^{1}H NMR (500 MHz, $CDCl_3$): 7.28–7.36 (m, 3 H), 7.18–7.27 (m, 2 H), 6.98–7.12 (m, 4 H), 6.59 and 6.28 (rotamers, bs, bs, 1 H), 4.80–5.17 (m, 3 H), 4.12 and 4.04 (rotamers, dd, *J* = 18.1, 5.8 Hz, bs, 1 H), 3.89 (dd, *J* = 18.0, 4.7 Hz, 1 H), 3.73 (s, 3 H), 3.31 (dd, *J* = 14.5, 6.0 Hz, 1 H), 2.96 (dd, *J* = 14.3, 9.6 Hz, 1 H), 2.87 (s, 3 H), 2.30 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): 21.0, 30.5 and 31.2 (rotamers), 33.4 and 33.7 (rotamers), 41.1, 52.3, 60.0 and 61.1 (rotamers), 67.5 and 67.7 (rotamers), 127.6, 128.0 and 128.2 (rotamers), 128.4, 128.8, 129.2, 133.9 and 134.2 (rotamers), 136.1 and 136.4 (rotamers), 156.0 and 157.3 (rotamers), 170.0 and 170.3 (rotamers), 170.6.

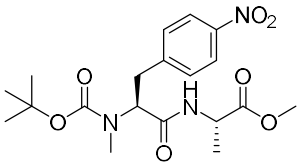
Optical rotation: $[\alpha]_D^{20}$ = -73.5 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{22}H_{27}N_2O_5$ $[M+H]^+$	399.1914	399.1921

Methyl ((*S*)-2-((*tert*-butoxycarbonyl)(methyl)amino)-3-(4-nitrophenyl)propanoyl)-*L*-alaninate (8ad)

To a solution of 55 mg (170 µmol, 1.0 equiv) **6ad** in 1.1 mL anhydrous DMF were successively added 32.6 µL (187 µmol, 1.1 equiv) diisopropylethylamine and 79.0 mg (178 µmol, 1.05 equiv) (benzotriazol-1-yloxy)-tris-(dimethylamino)phosphonium hexafluorophosphate (BOP) at 0 °C. After stirring for 30 min at 0 °C, 33.1 mg (237 µmol, 1.4 equiv) methyl *L*-alaninate hydrochloride followed by another 38.5 µL (220 µmol, 1.3 equiv) diisopropylethylamine were added. The reaction mixture was allowed to warm to room temperature overnight and quenched with 10% aq. citric acid. The aqueous phase was extracted with Et_2O (x2), the combined organic phase was washed once with sat. aq. $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was purified by column chromatography (SiO_2, CH_2Cl_2/Et_2O 9:1) to obtain the dipeptide **8ad** (65.0 mg, 159 µmol, 94%) as colourless oil.

R_f (8ad) = 0.21 (CH_2Cl_2/Et_2O 9:1)



8ad

^{1}H NMR (500 MHz, DMSO-d_6, 373 K): 8.12 (d, *J* = 8.5 Hz, 2 H), 7.96 (d, *J* = 5.3 Hz, 1 H), 7.53 (d, *J* = 8.8 Hz, 2 H), 4.85 (bs, 1 H), 4.37 (quint, *J* = 7.2 Hz, 1 H), 3.65 (s, 3 H), 3.32 (dd, *J* = 14.3, 5.2 Hz, 1 H), 3.08 (dd, *J* = 14.3, 10.2 Hz, 1 H), 2.74 (s, 3 H), 1.34 (d, *J* = 7.2 Hz, 3 H), 1.30 (s, 9 H).

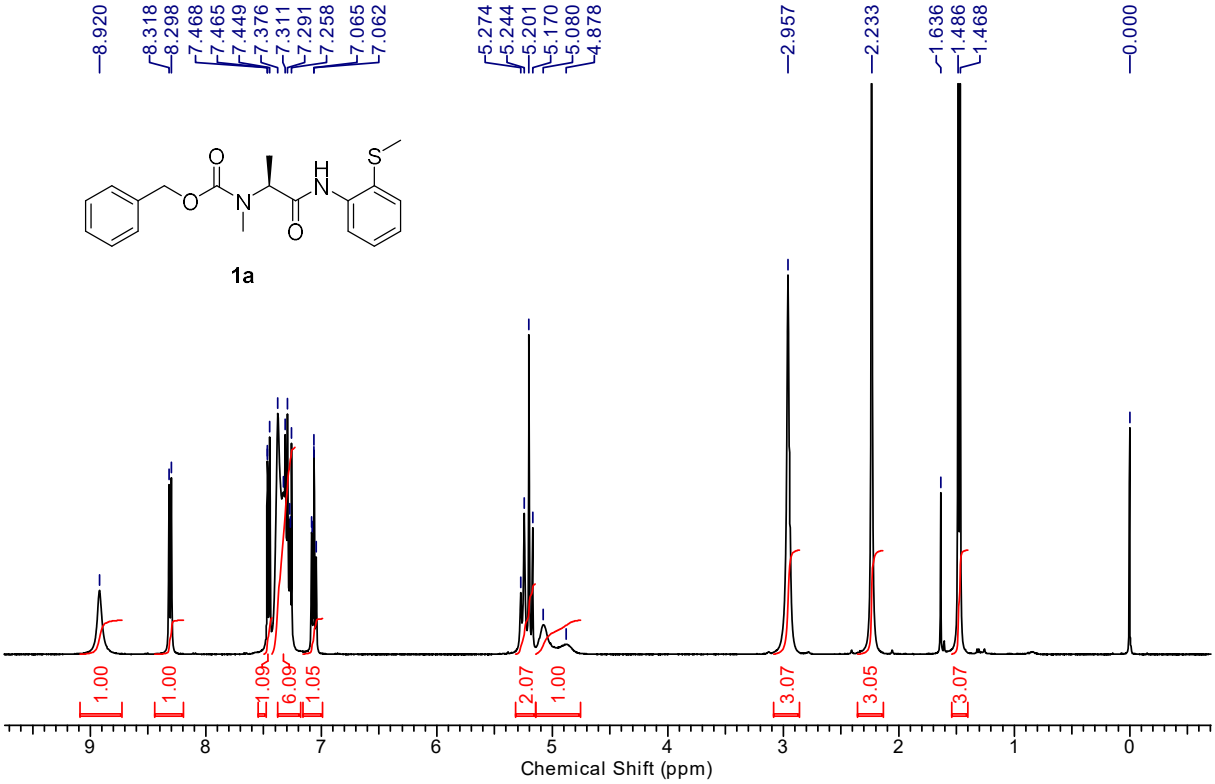
^{13}C NMR (125 MHz, DMSO-d_6, 373 K): 16.4, 27.4, 30.3, 34.0, 47.4, 51.2, 58.8, 78.8, 122.5, 129.8, 146.0, 146.1, 154.4, 169.0, 172.1.

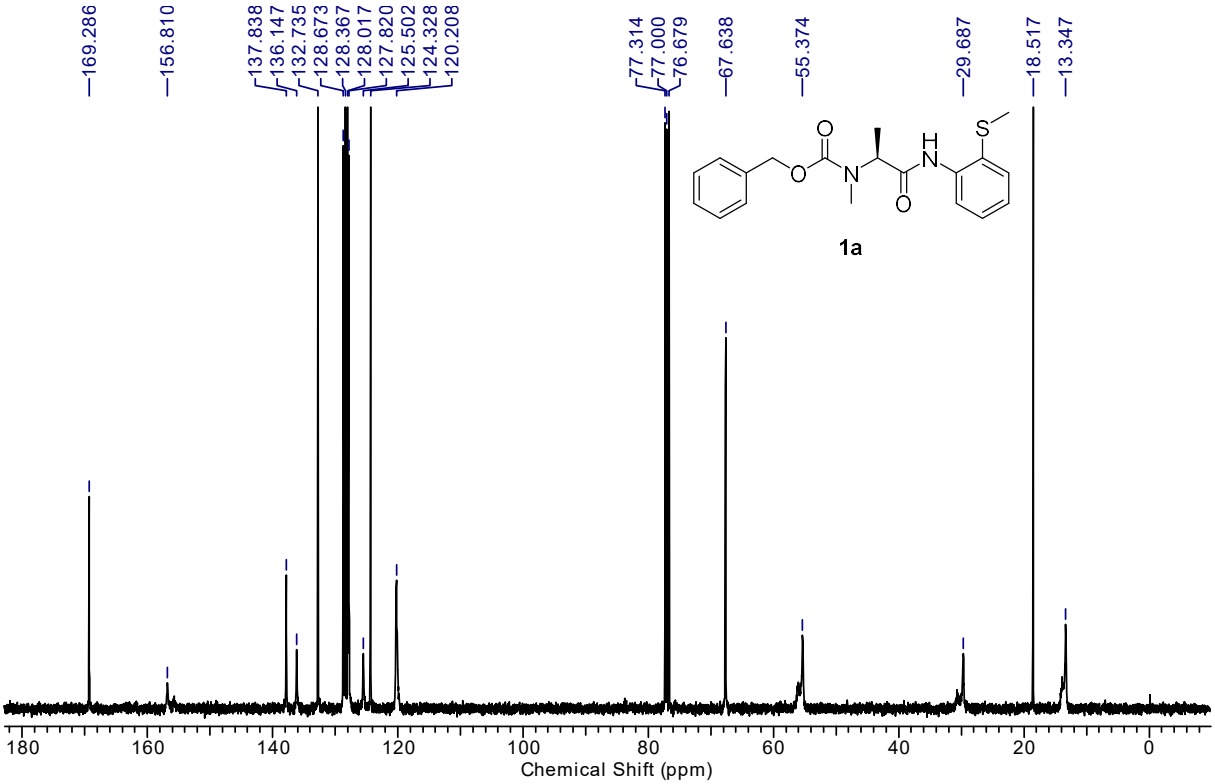
Optical rotation: $[\alpha]_D^{20}$ = -77.8 [$CHCl_3$, c = 1.00]

HRMS (CI):	Calculated	Found
$C_{19}H_{28}N_3O_7$ $[M+H]^+$	410.1922	410.1930

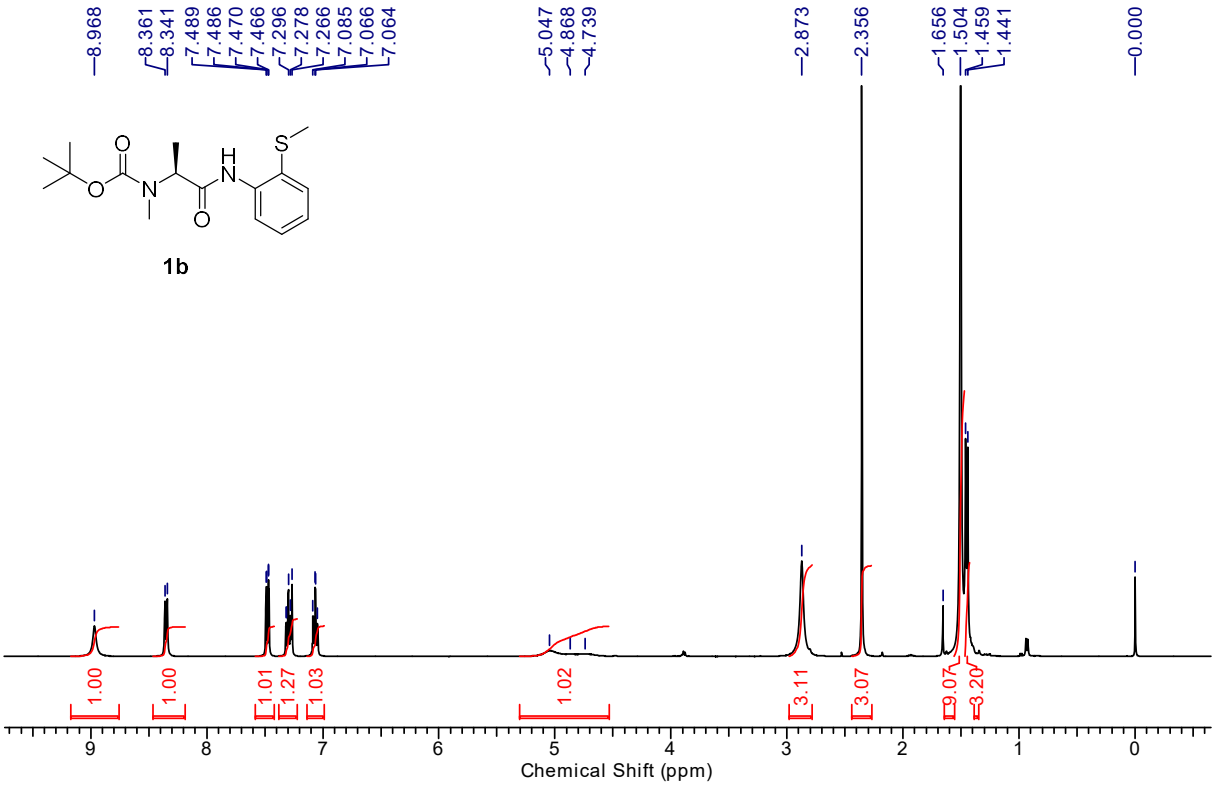
NMR spectra

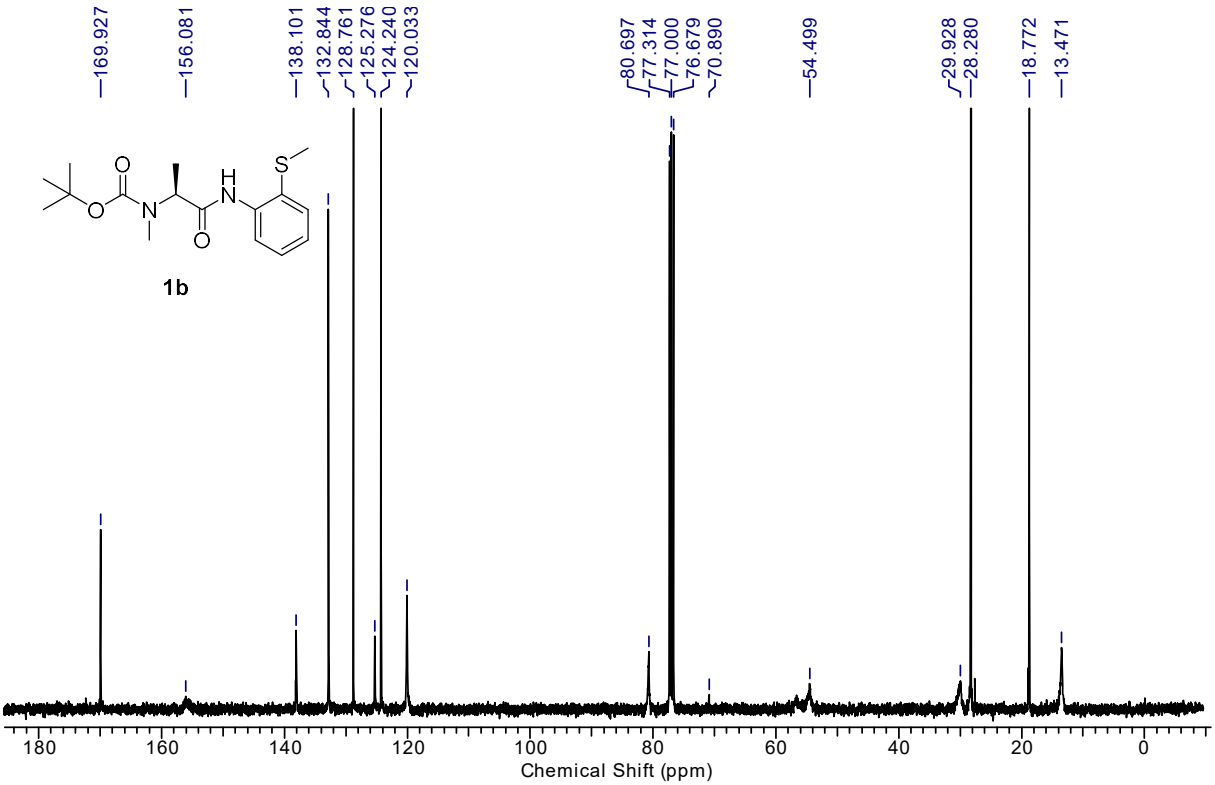
Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)carbamate (1a)



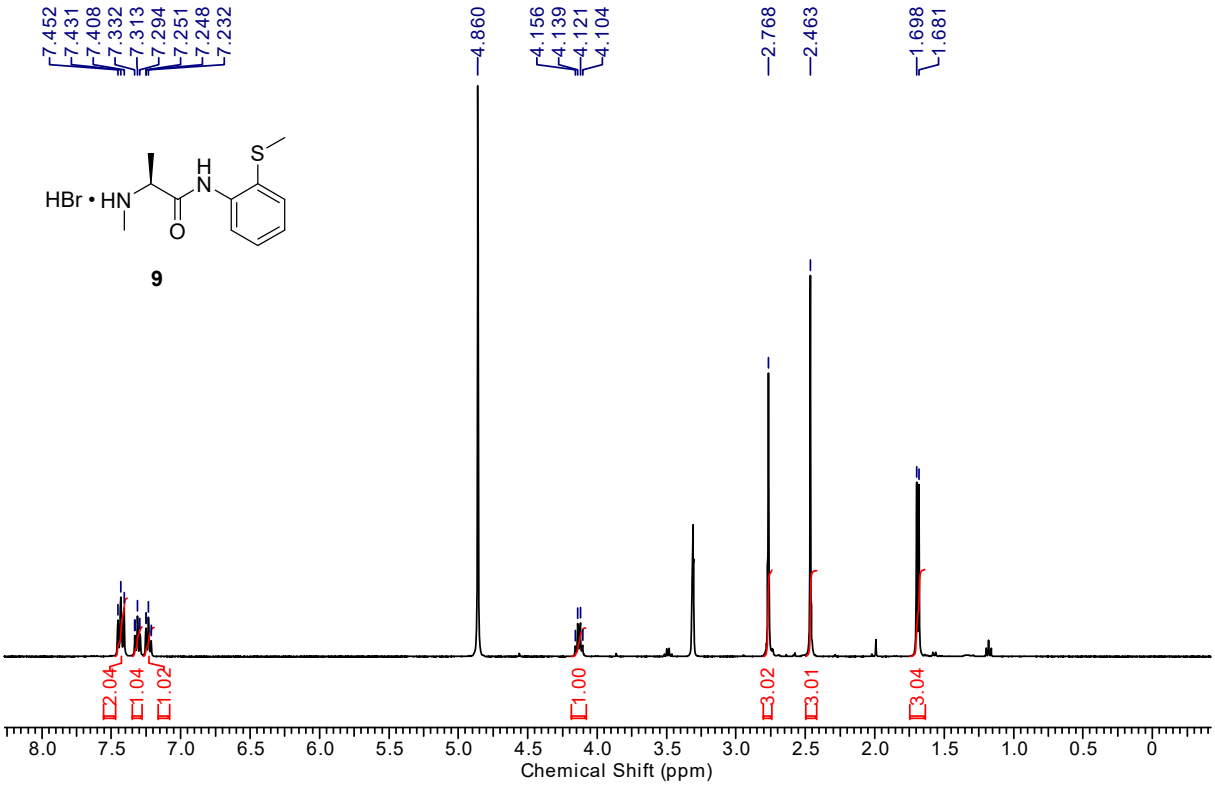


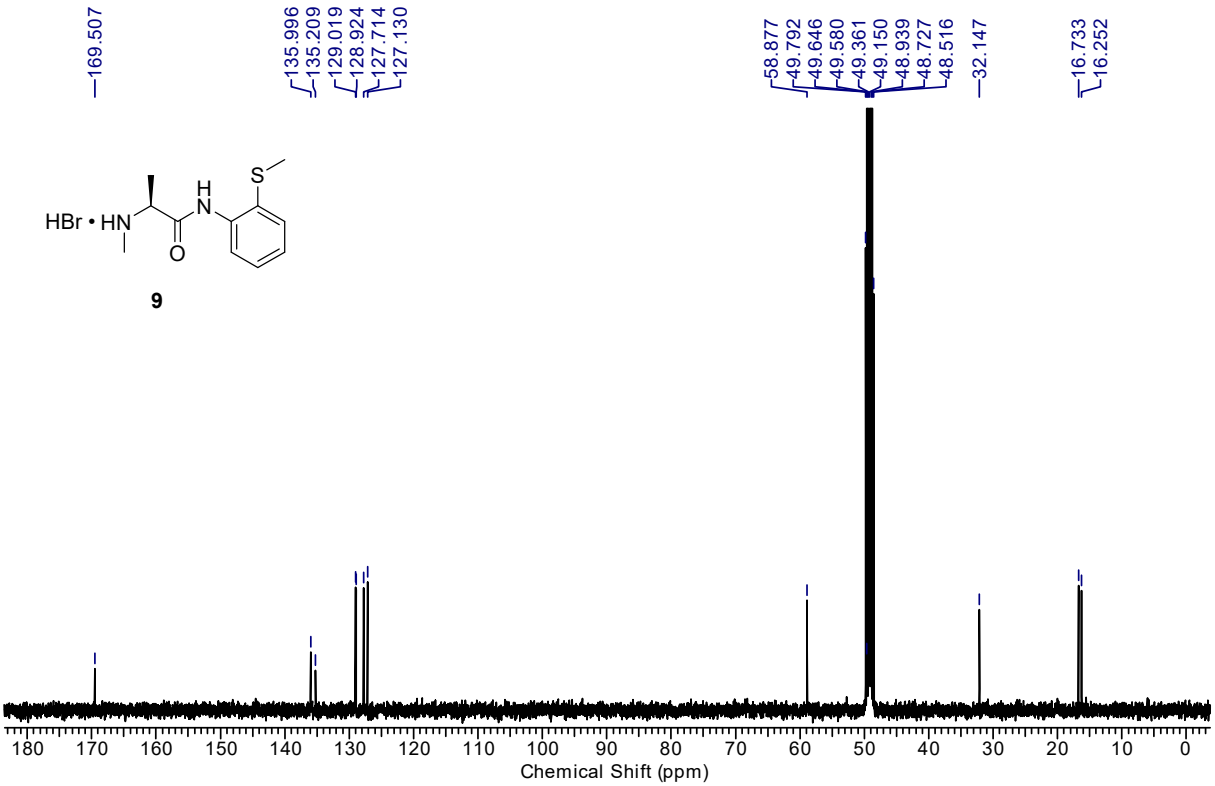
***tert*-Butyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)carbamate (1b)**



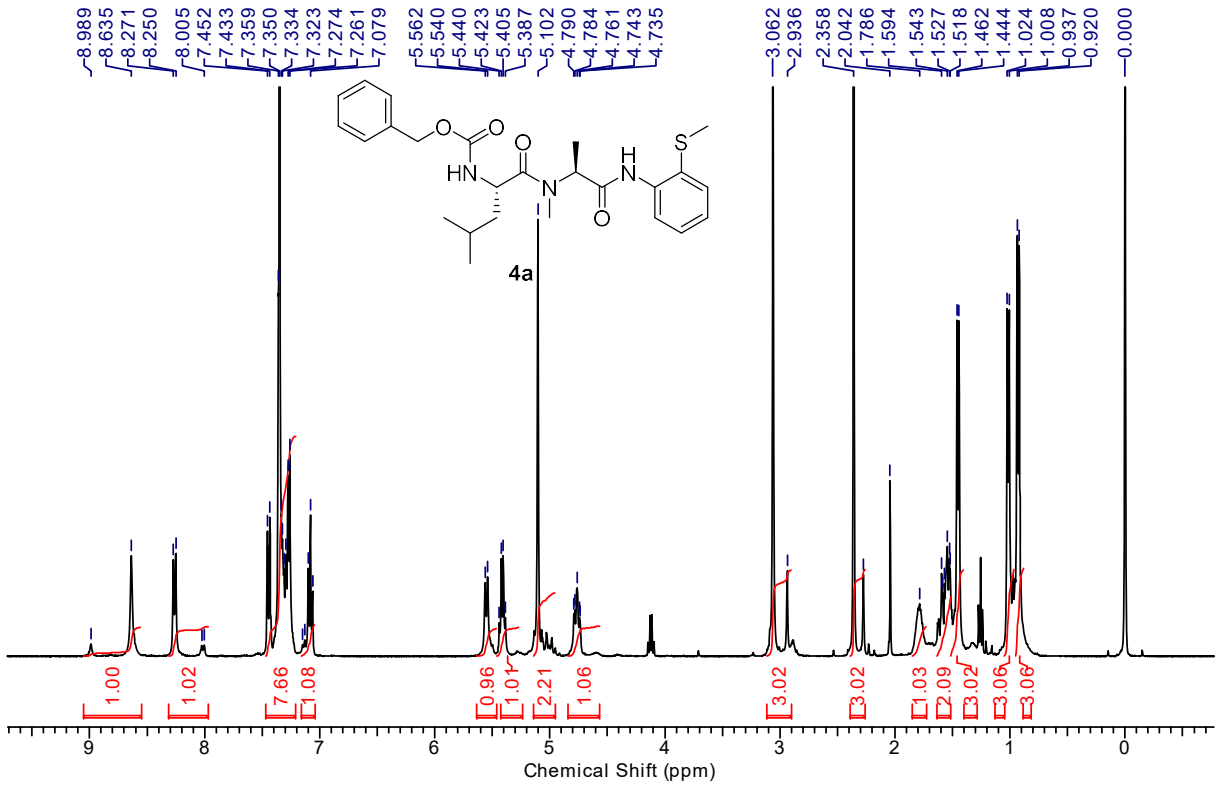


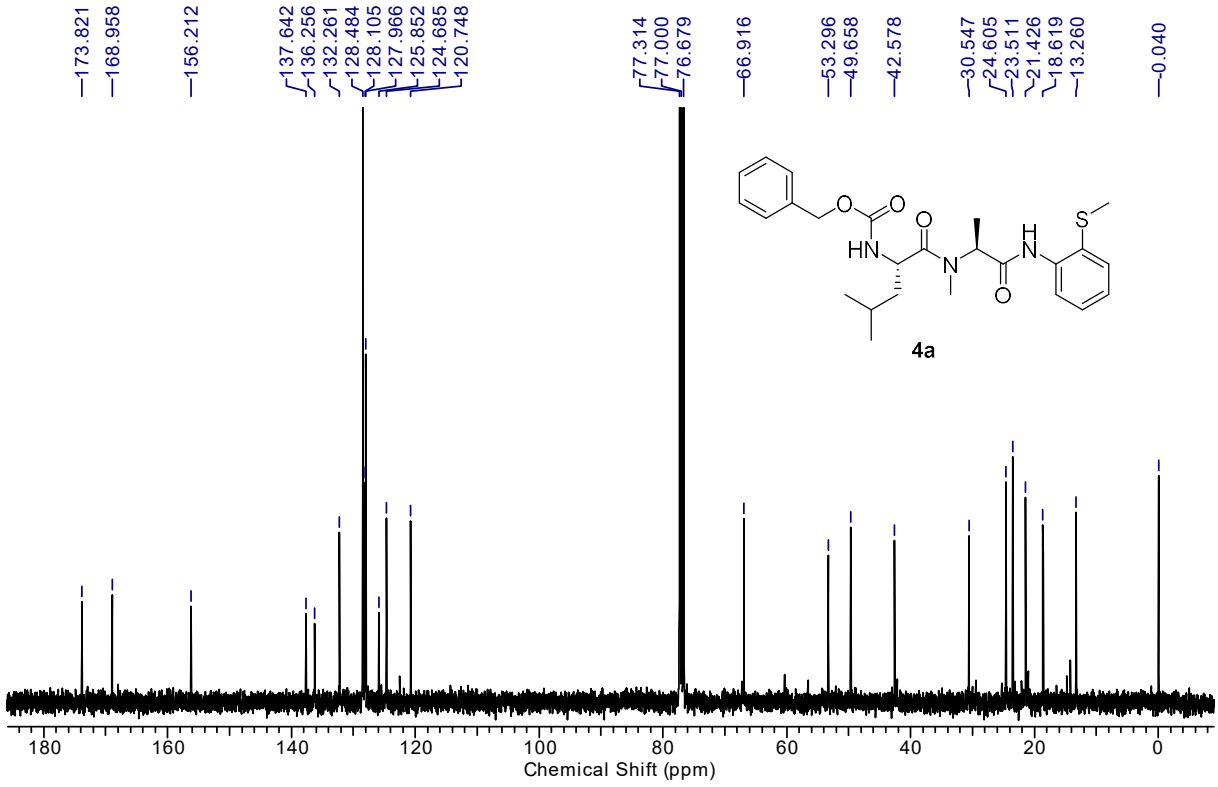
(*S*)-2-(Methylamino)-N-(2-(methylthio)phenyl)propanamide hydrobromide (9)



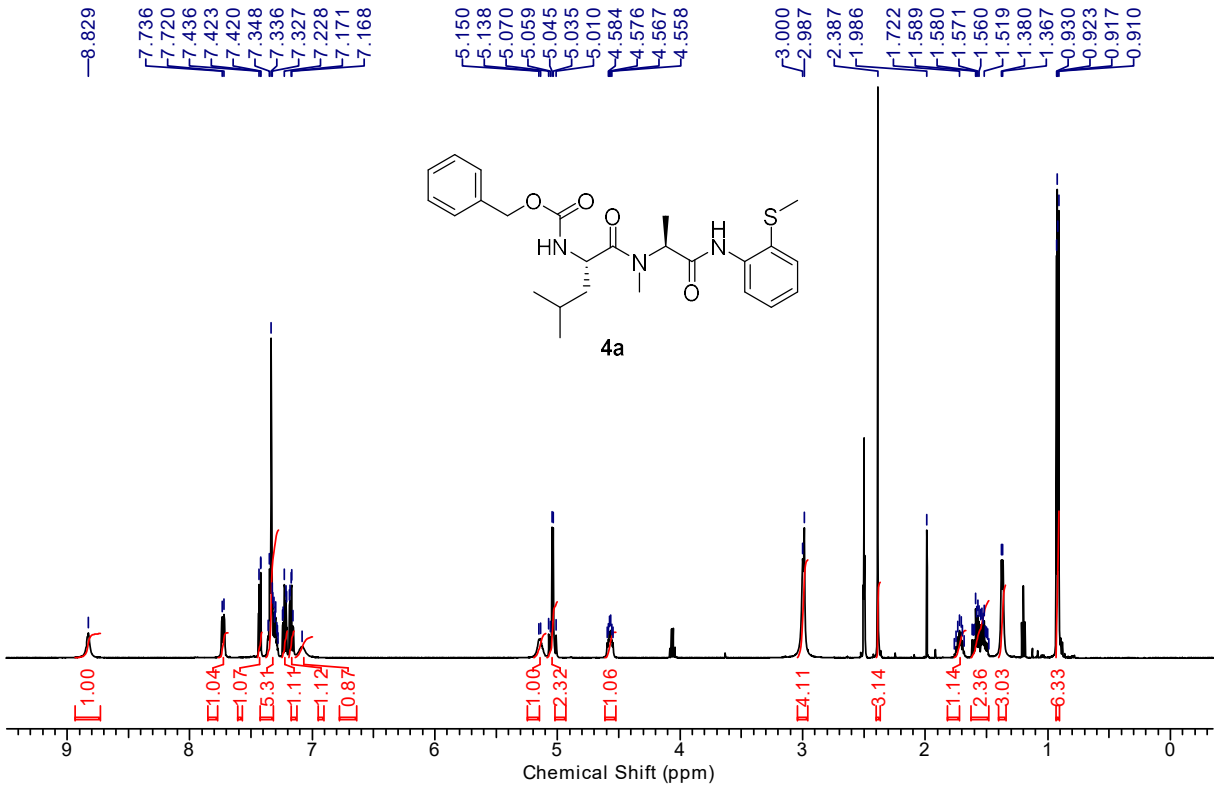


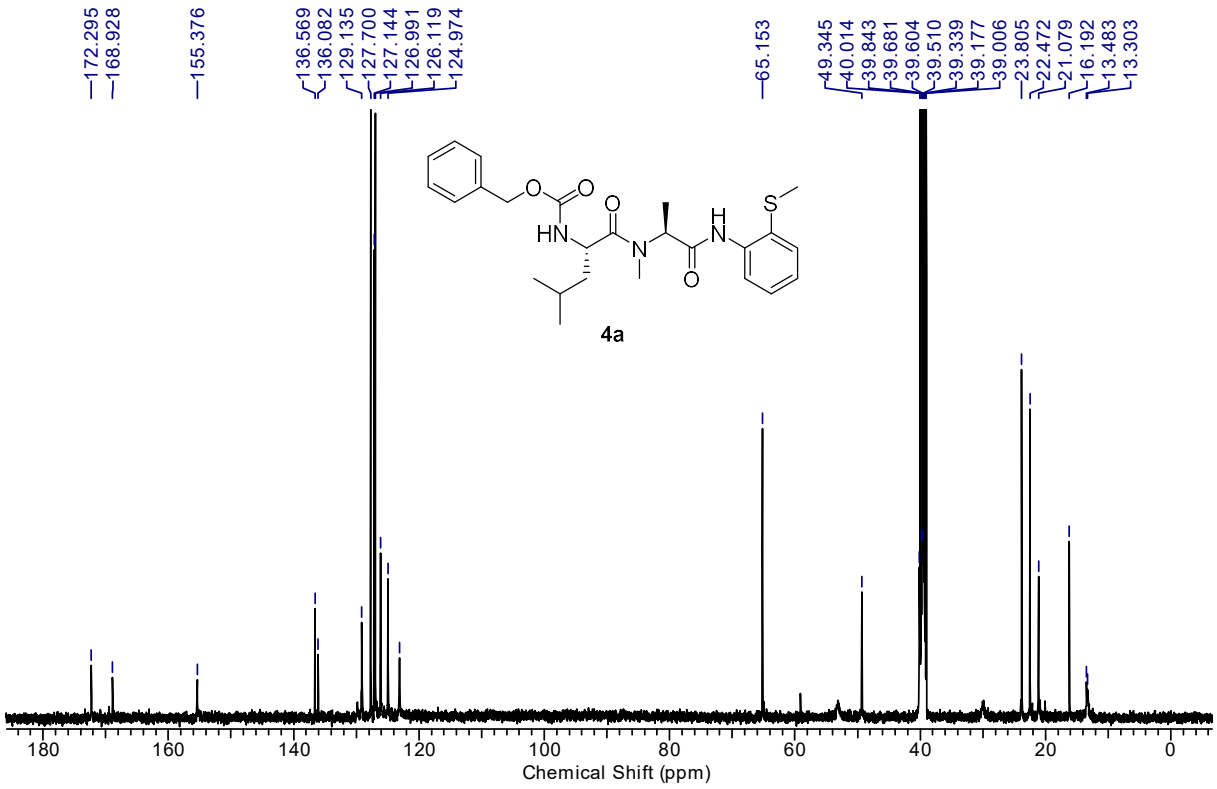
Benzyl ((*S*)-4-methyl-1-(methyl((S)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)amino)-1-oxopentan-2-yl)carbamate (4a) ($CDCl_3$)



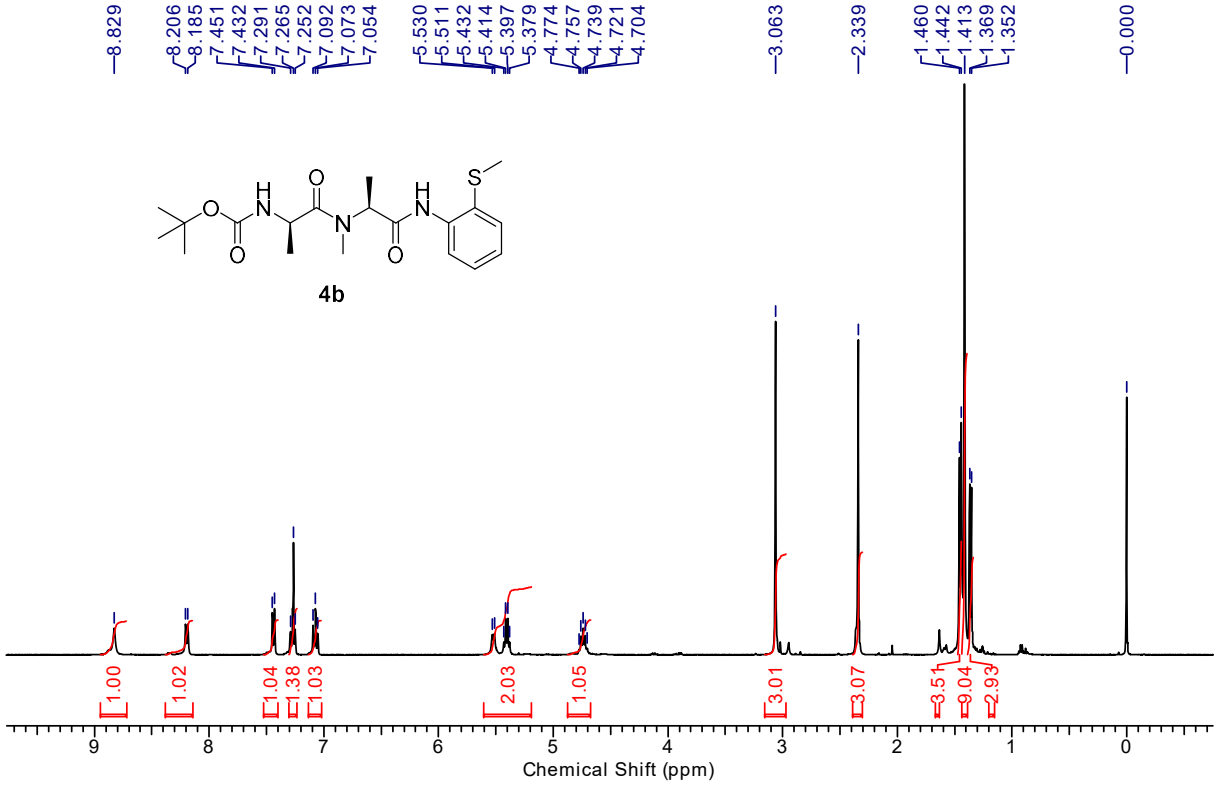


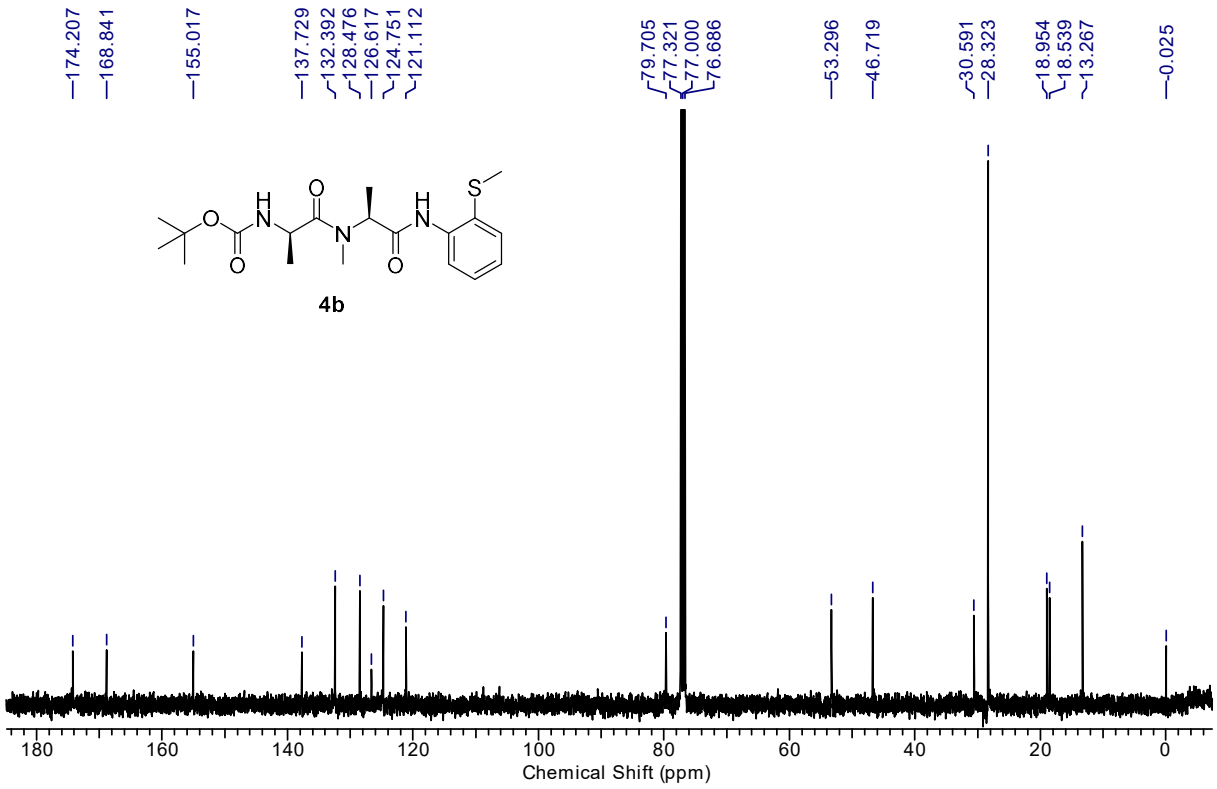
Benzyl ((*S*)-4-methyl-1-(methyl((S)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)amino)-1-oxopentan-2-yl)carbamate (4a) (DMSO-d_6 373 K)



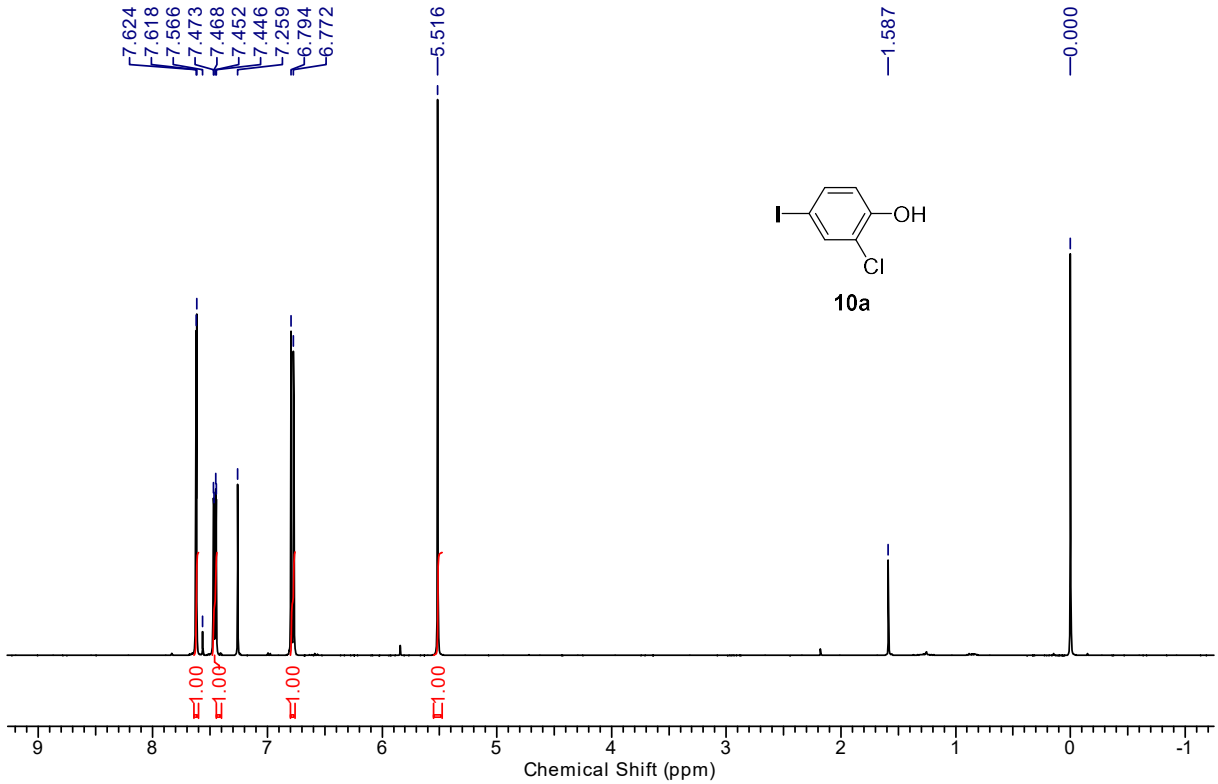


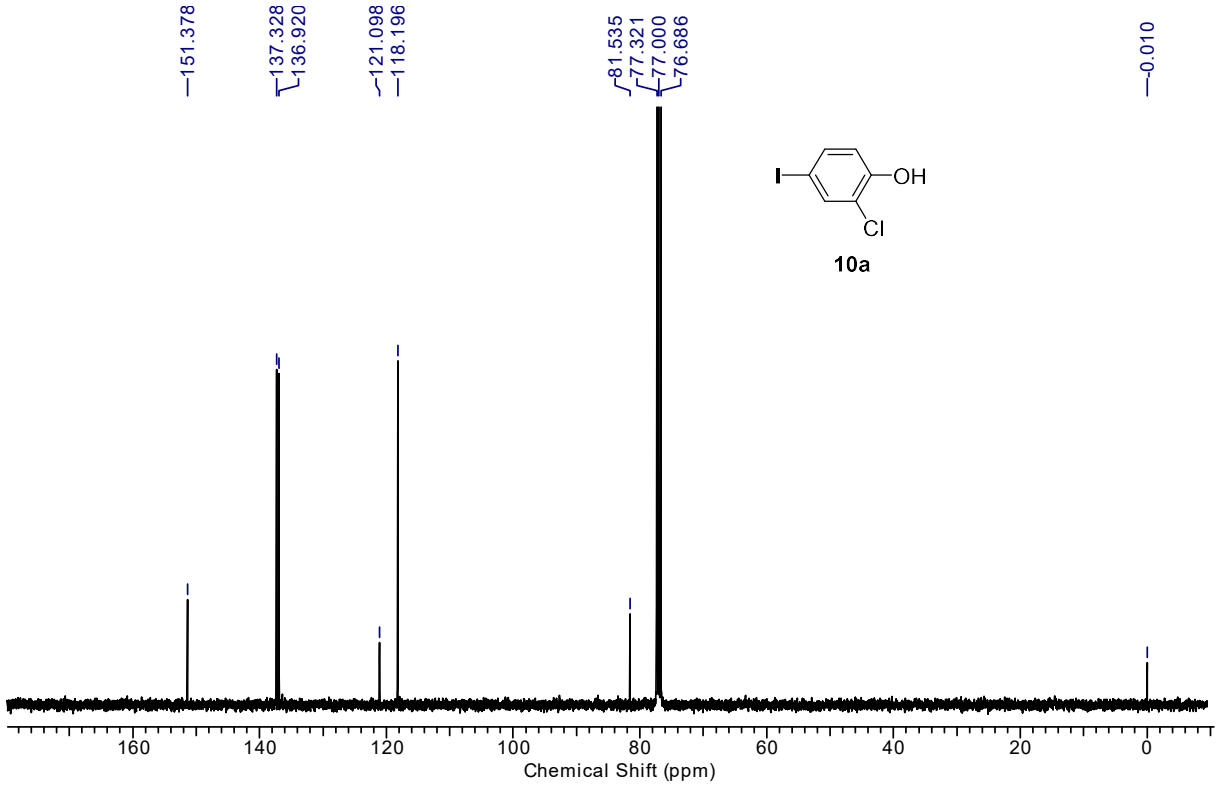
***tert*-Butyl ((*R*)-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)amino)-1-oxopropan-2-yl)carbamate (4b)**



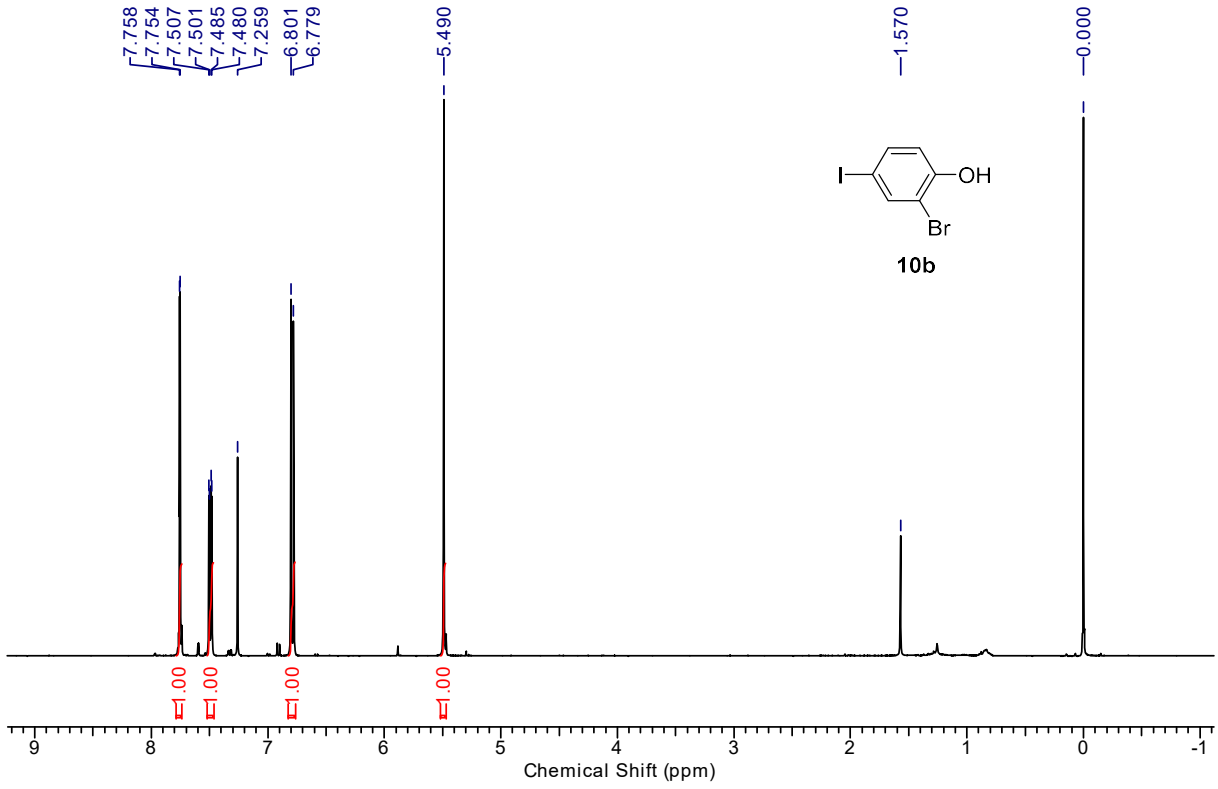


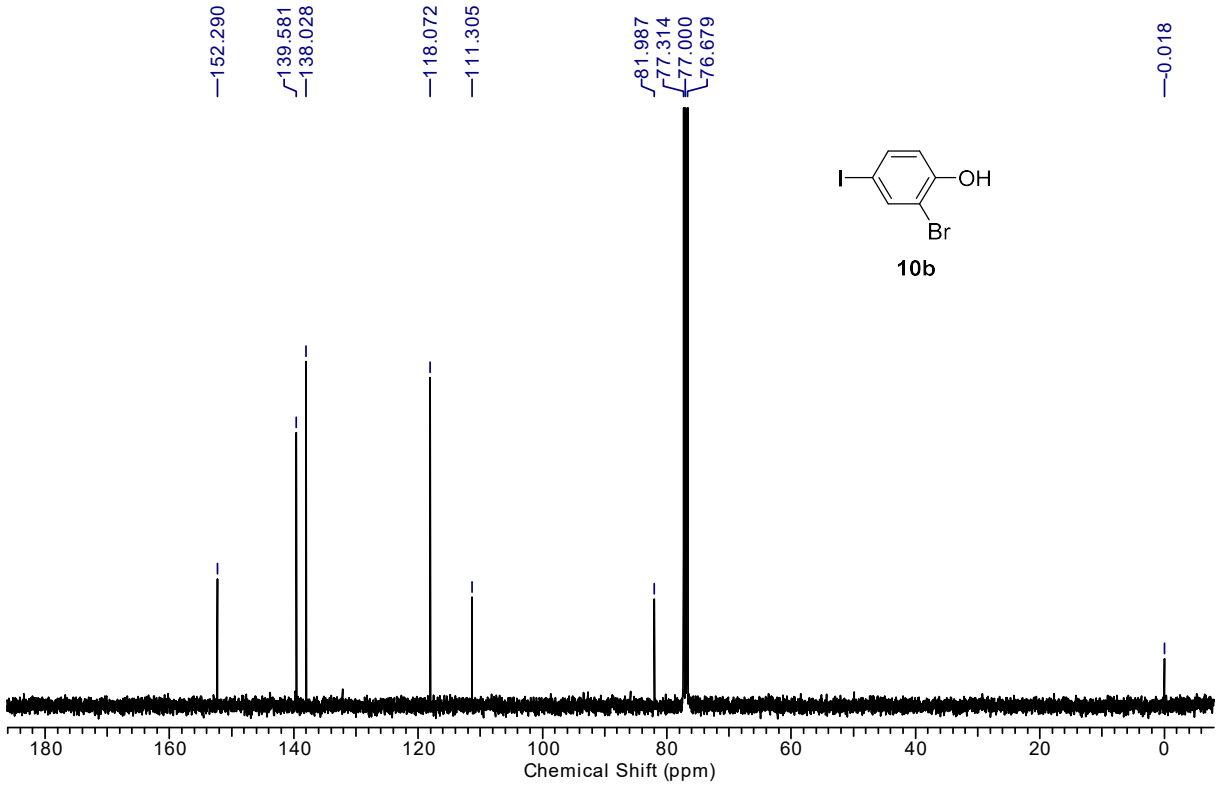
2-Chloro-4-iodophenol (10a)



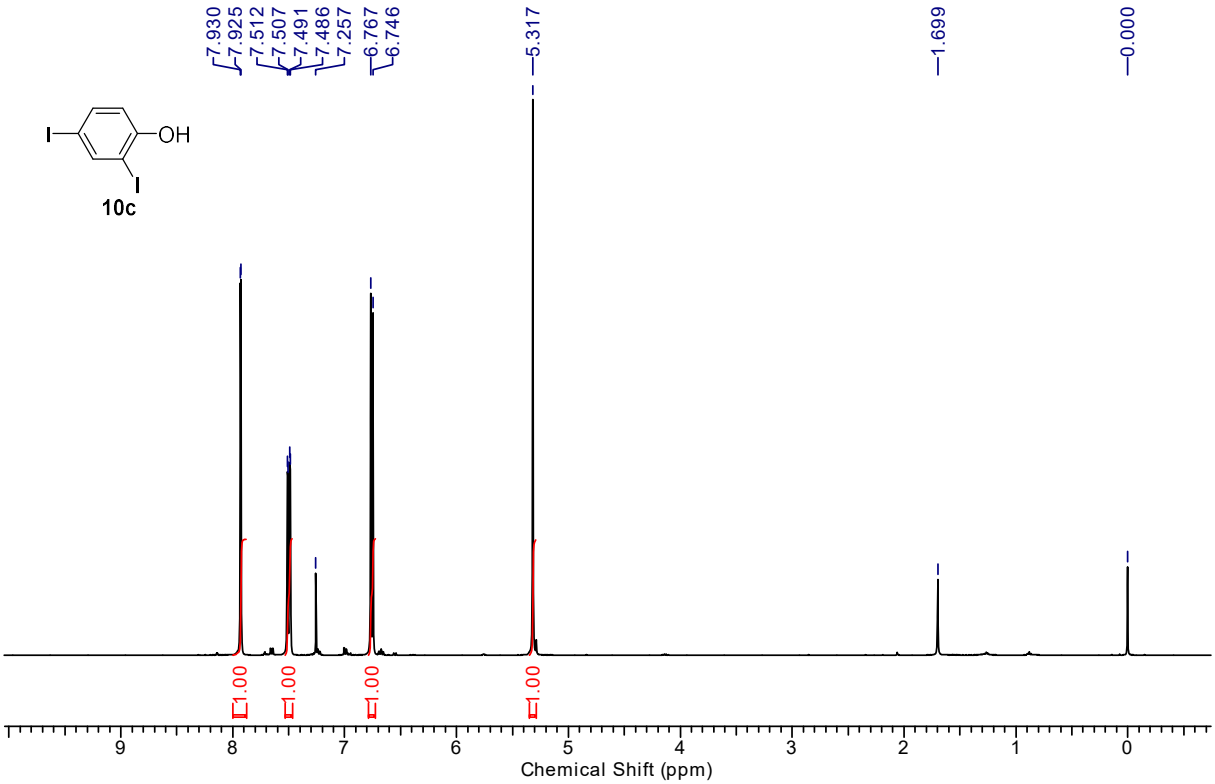


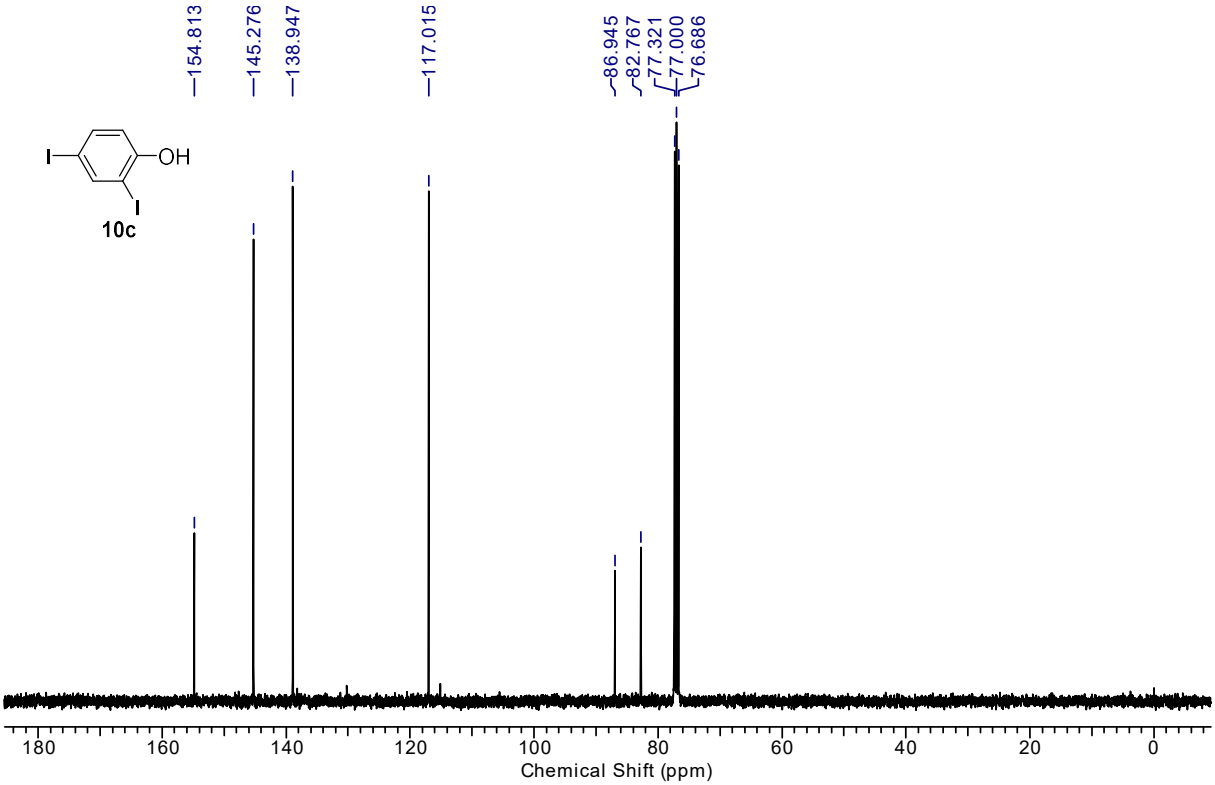
2-Bromo-4-iodophenol (10b)



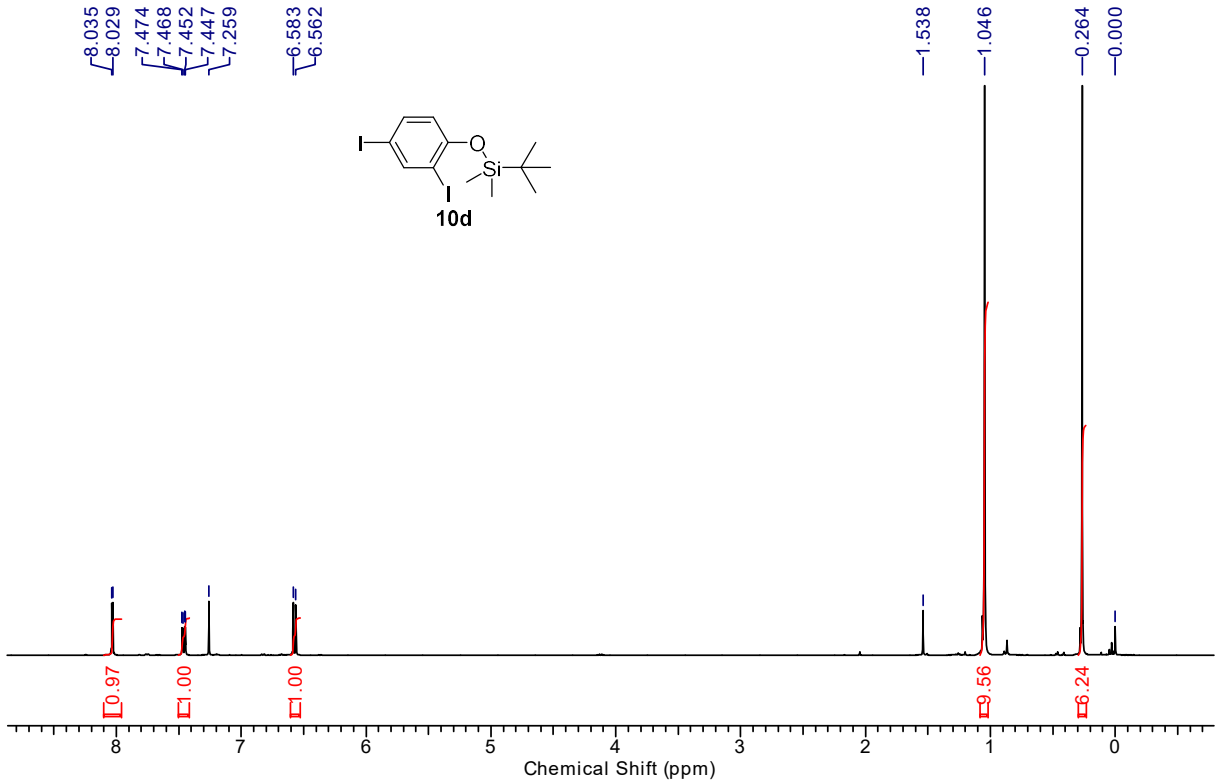


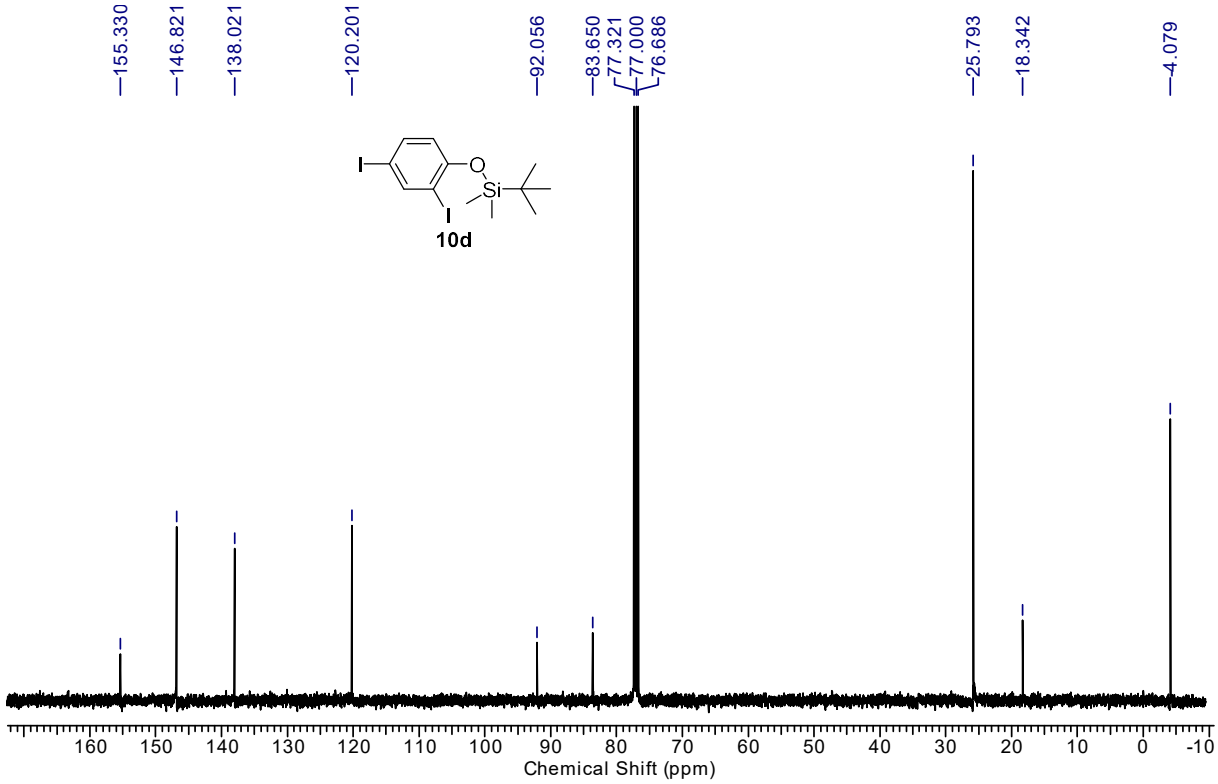
2,4-Diiodophenol (10c)



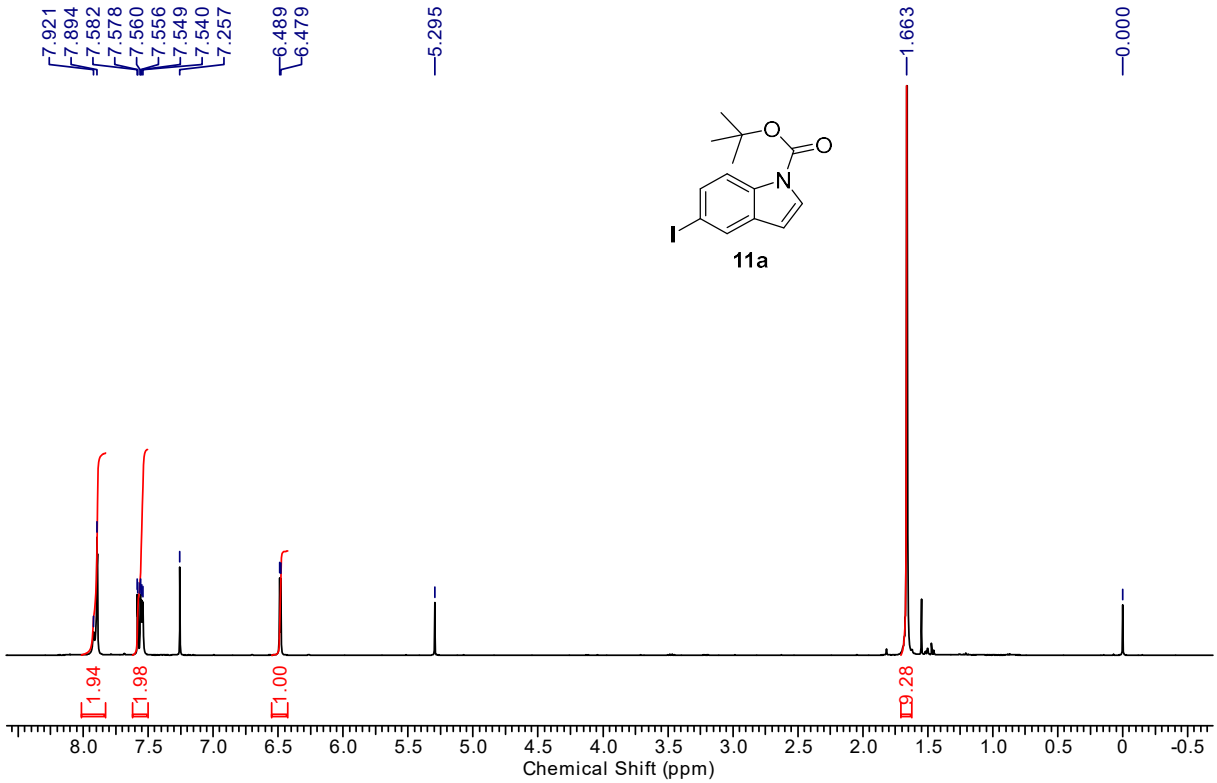


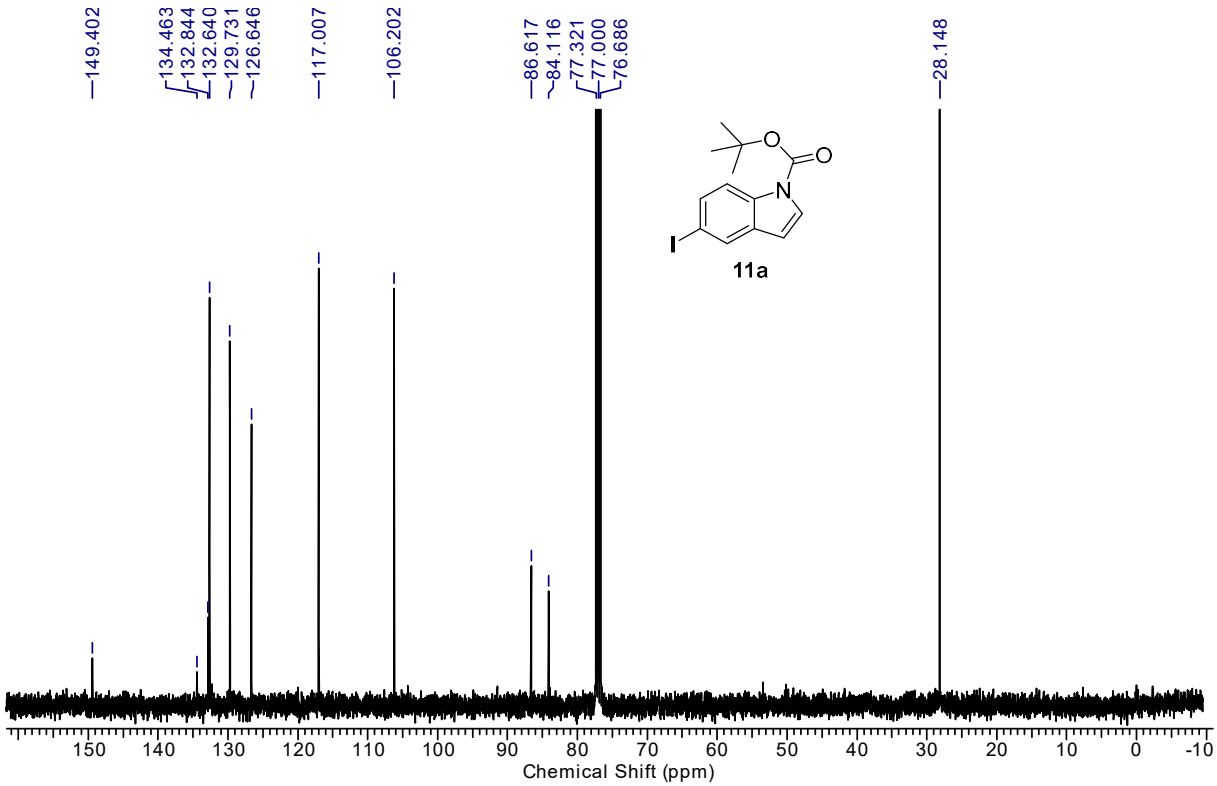
***tert*-Butyl(2,4-diiodophenoxy)dimethylsilane (10d)**



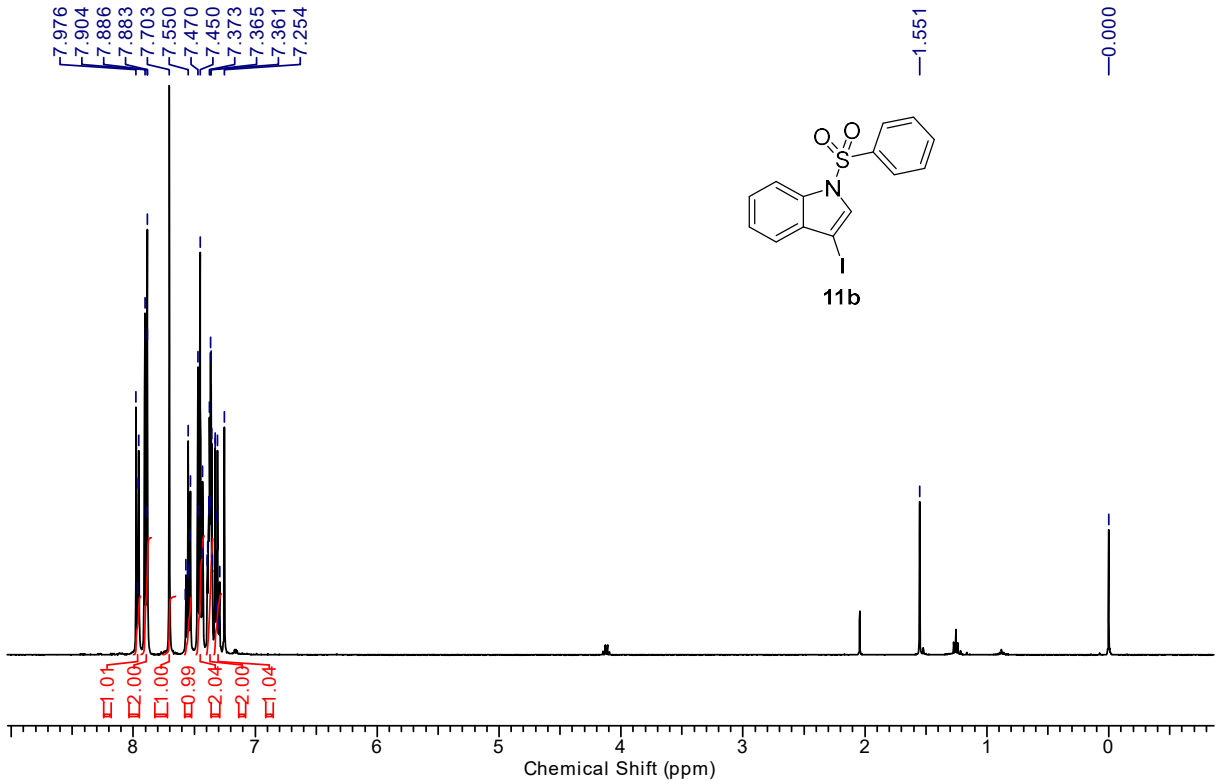


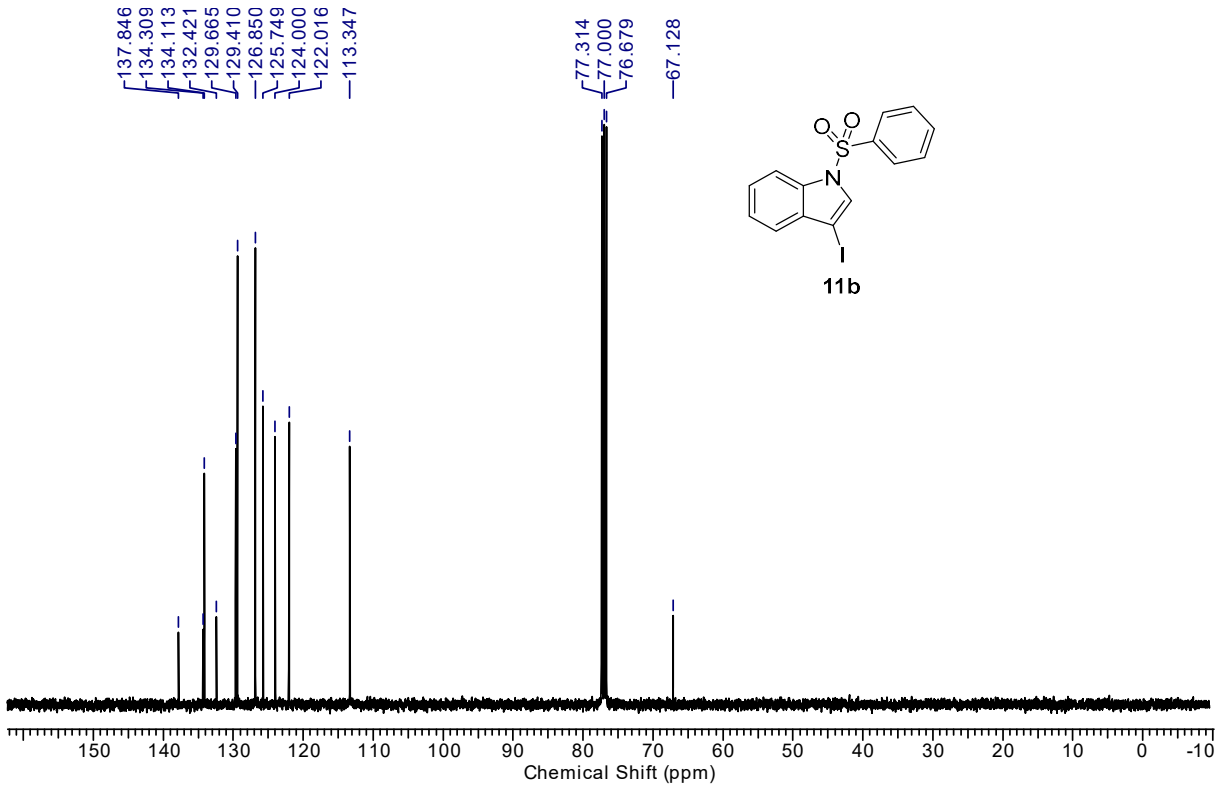
***tert*-Butyl 5-iodo-1*H*-indole-1-carboxylate (11a)**



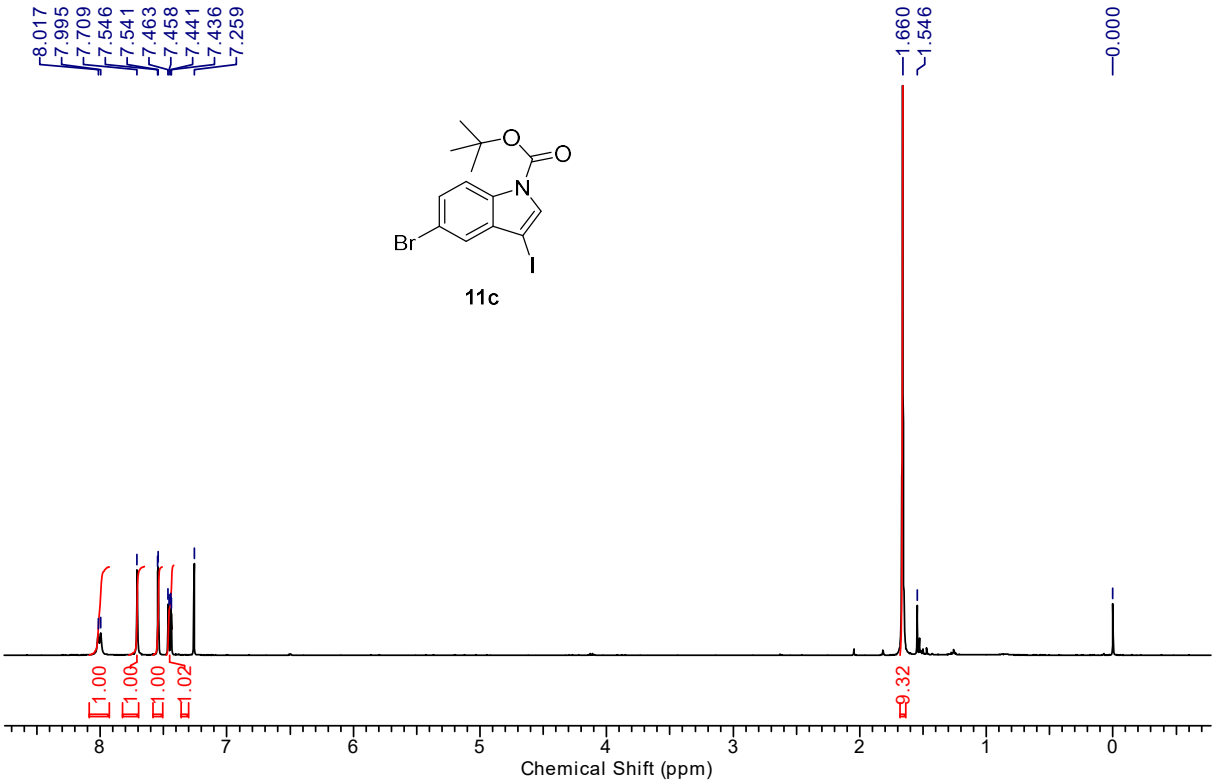


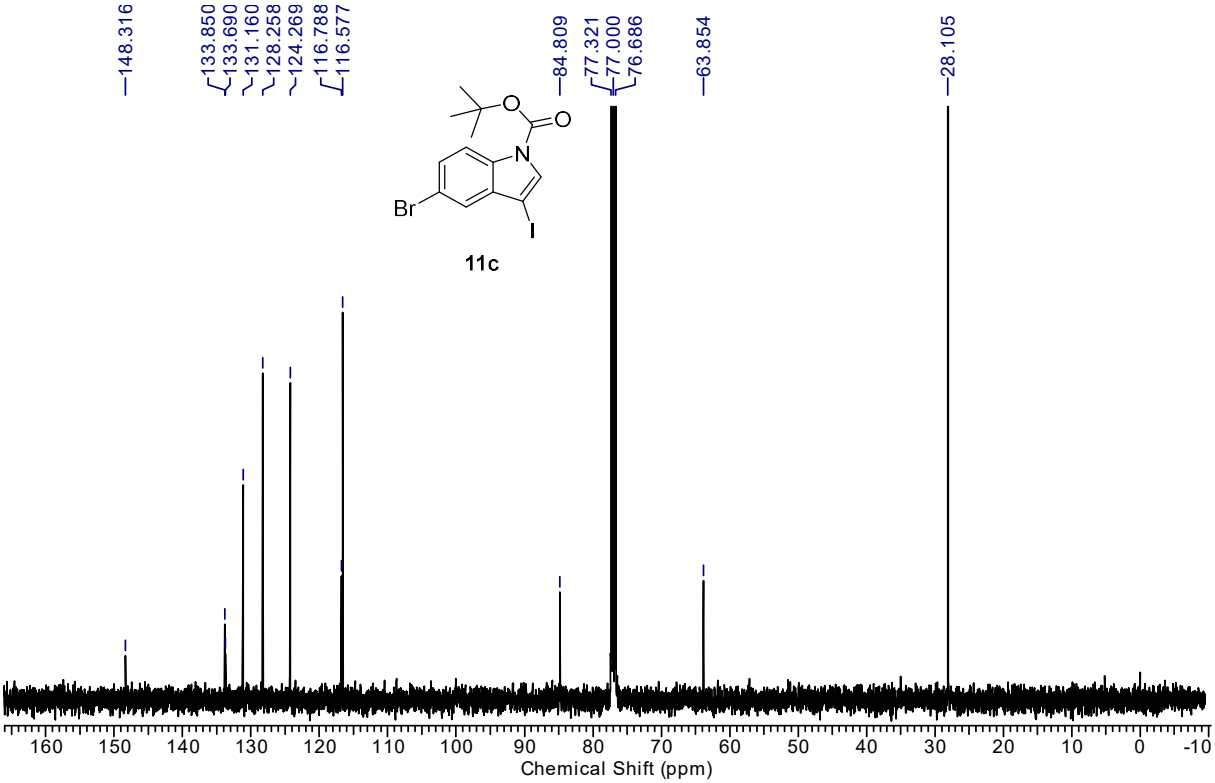
3-Iodo-1-(phenylsulfonyl)-1*H*-indole (11b)



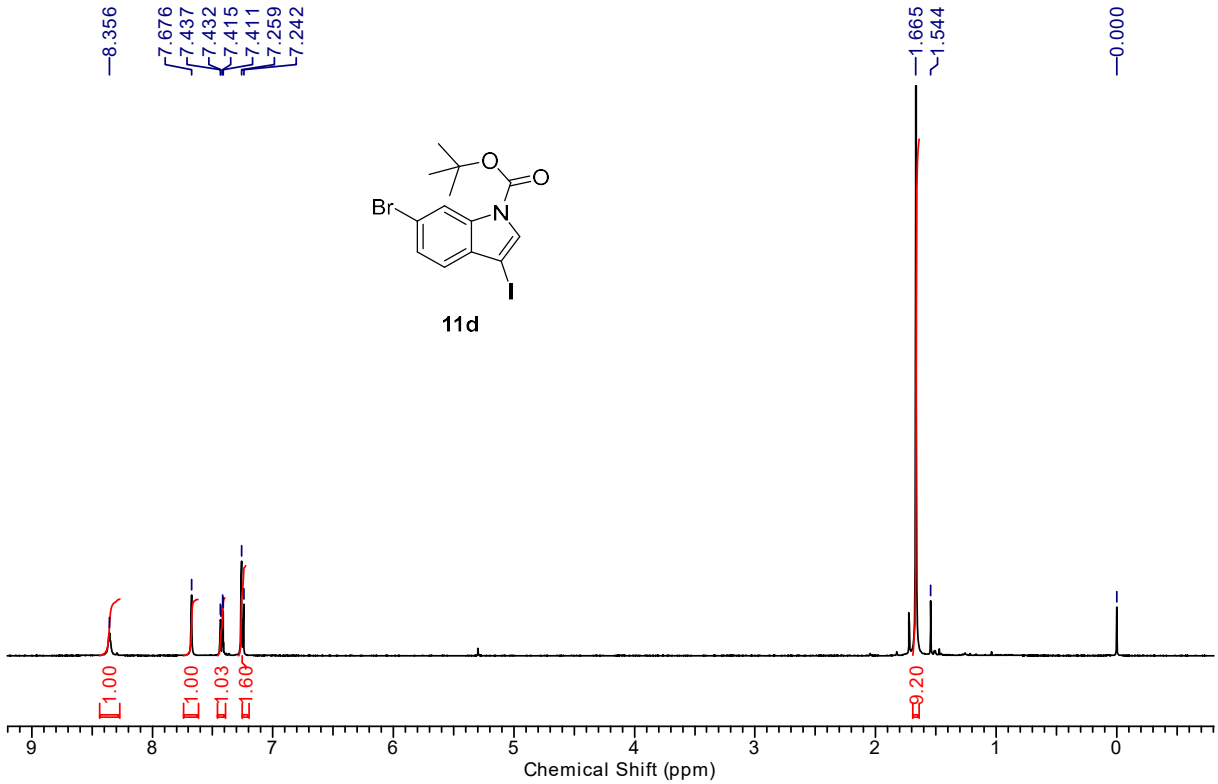


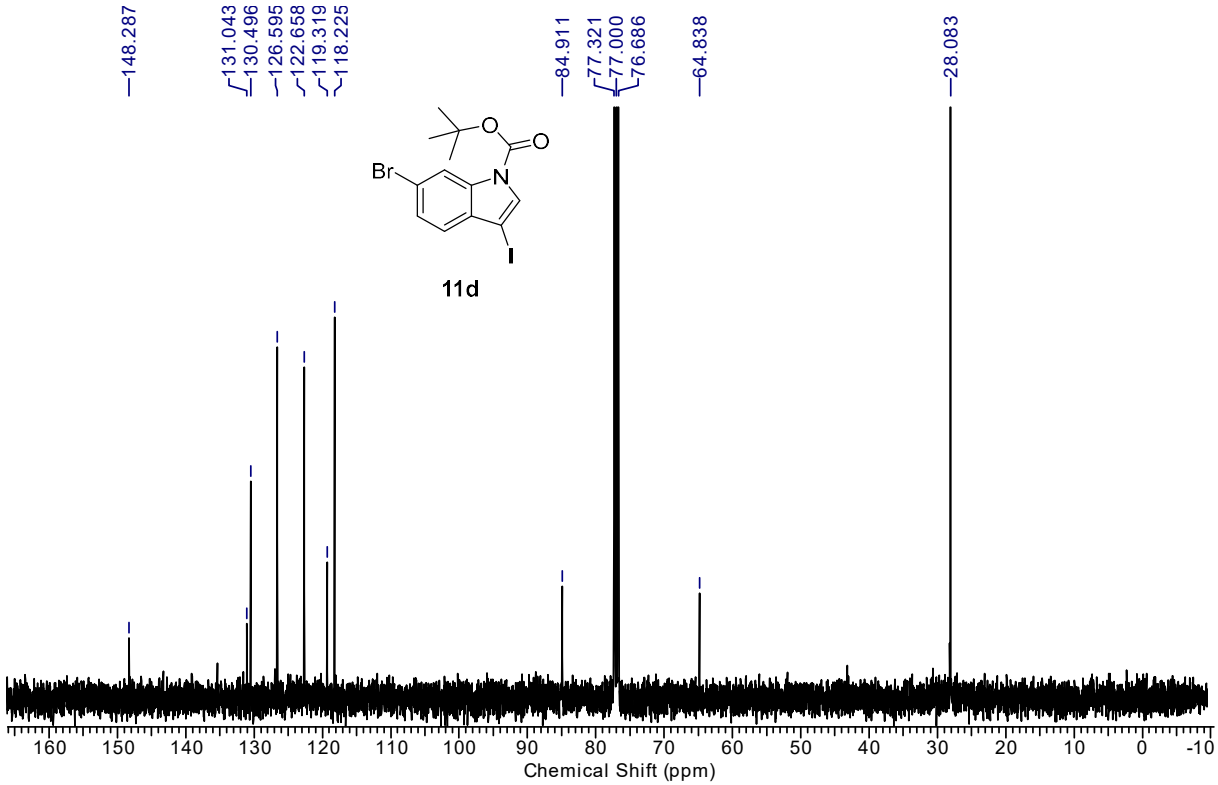
tert-Butyl 5-bromo-3-iodo-1_H_-indole-1-carboxylate (11c)



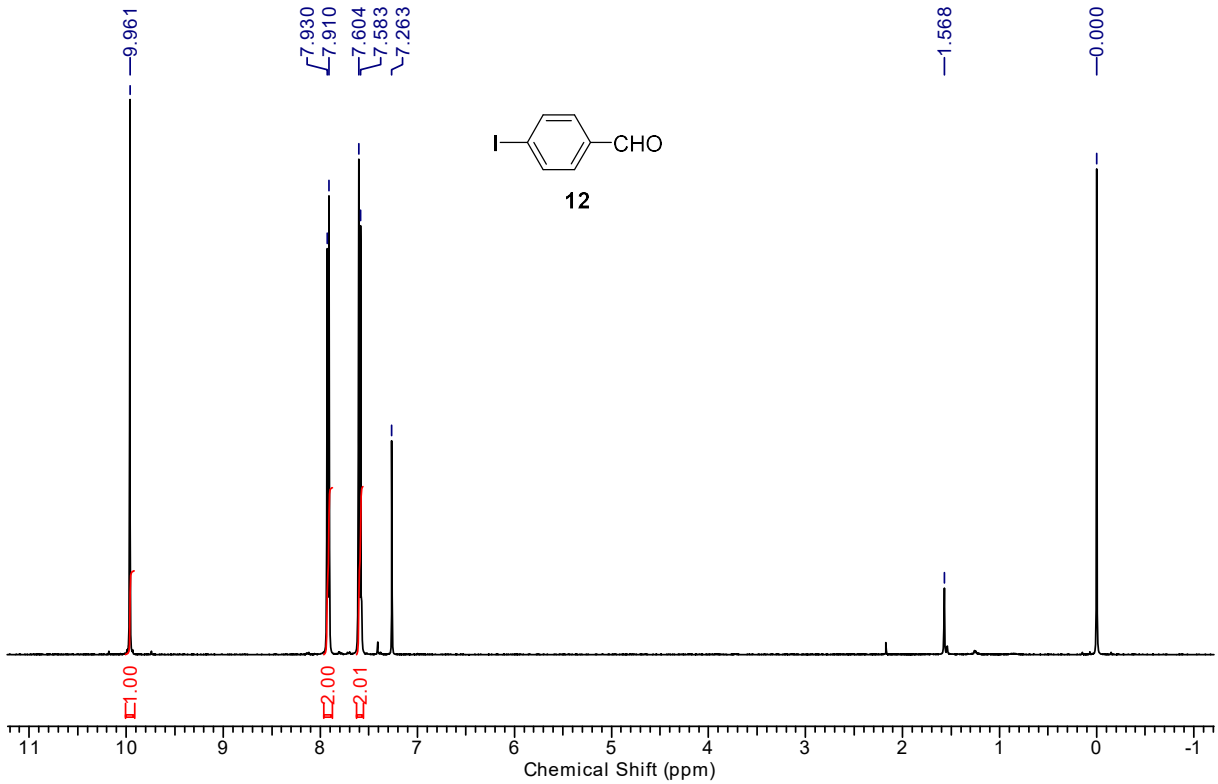


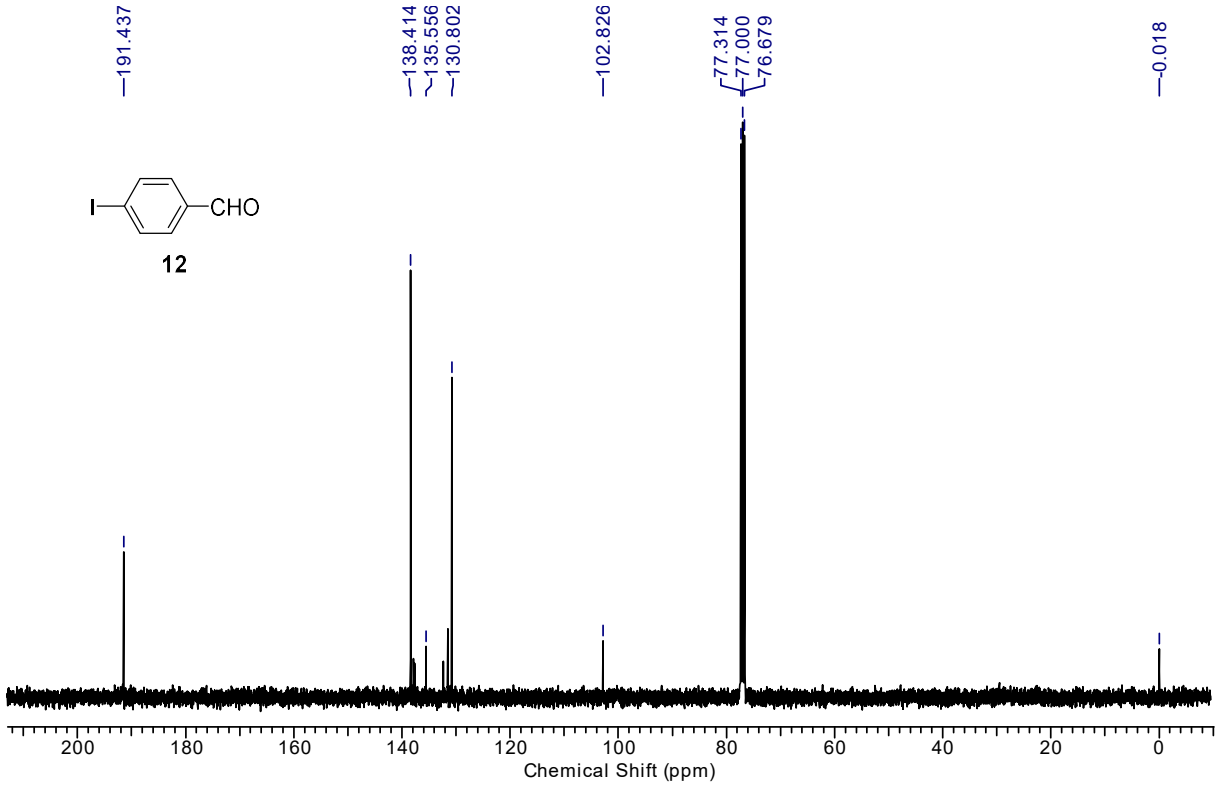
tert-Butyl 6-bromo-3-iodo-1_H_-indole-1-carboxylate (11d)



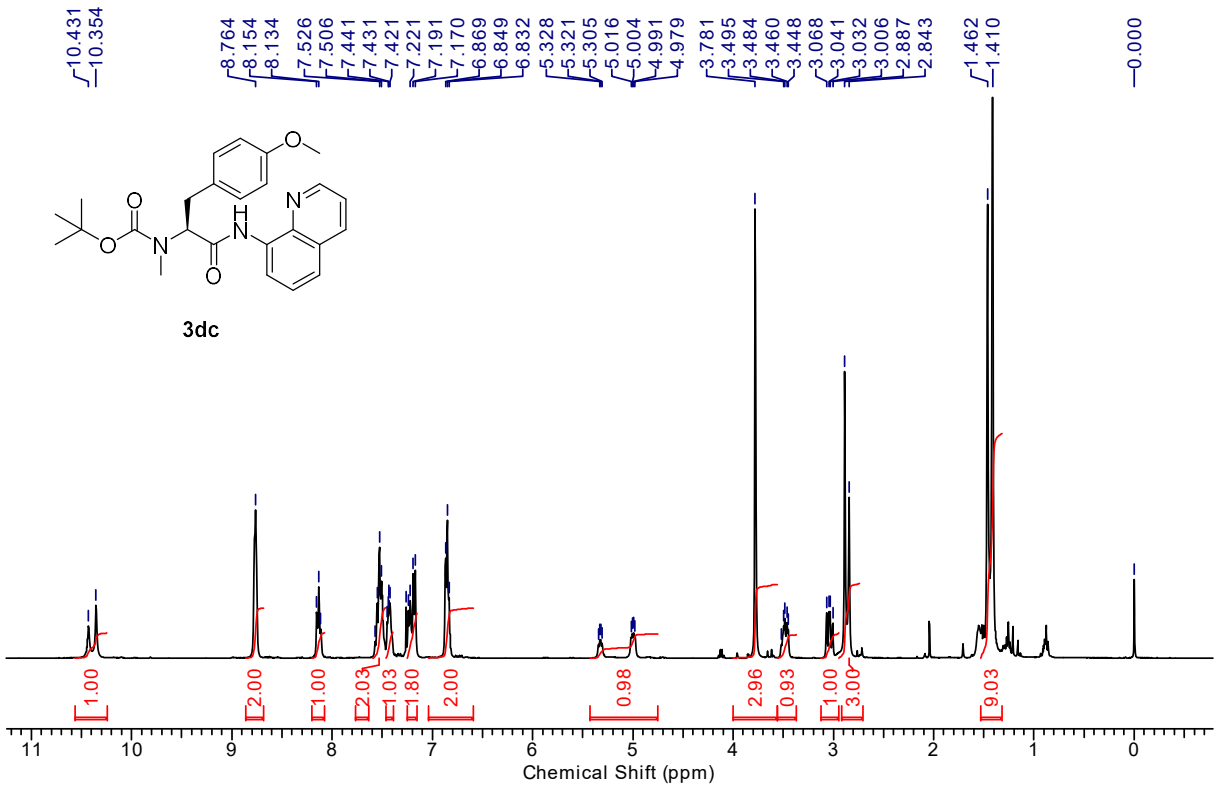


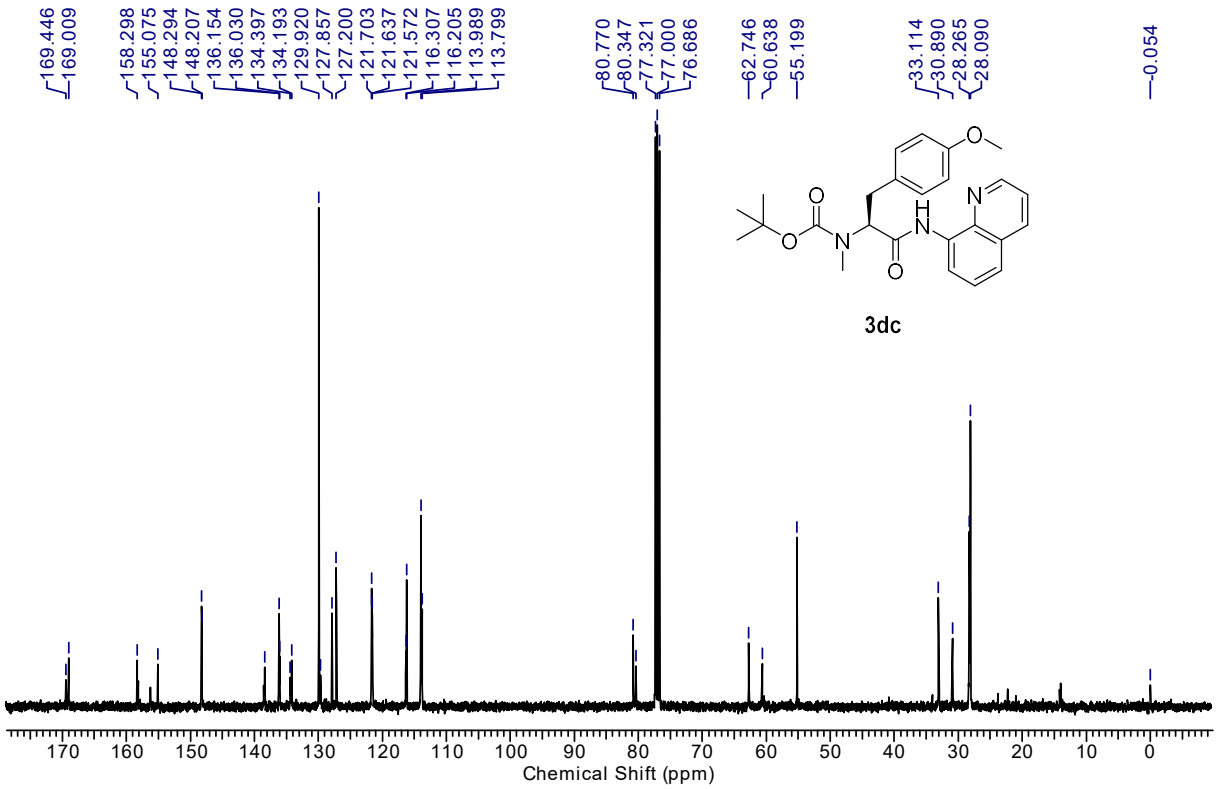
4-Iodobenzaldehyde (12)



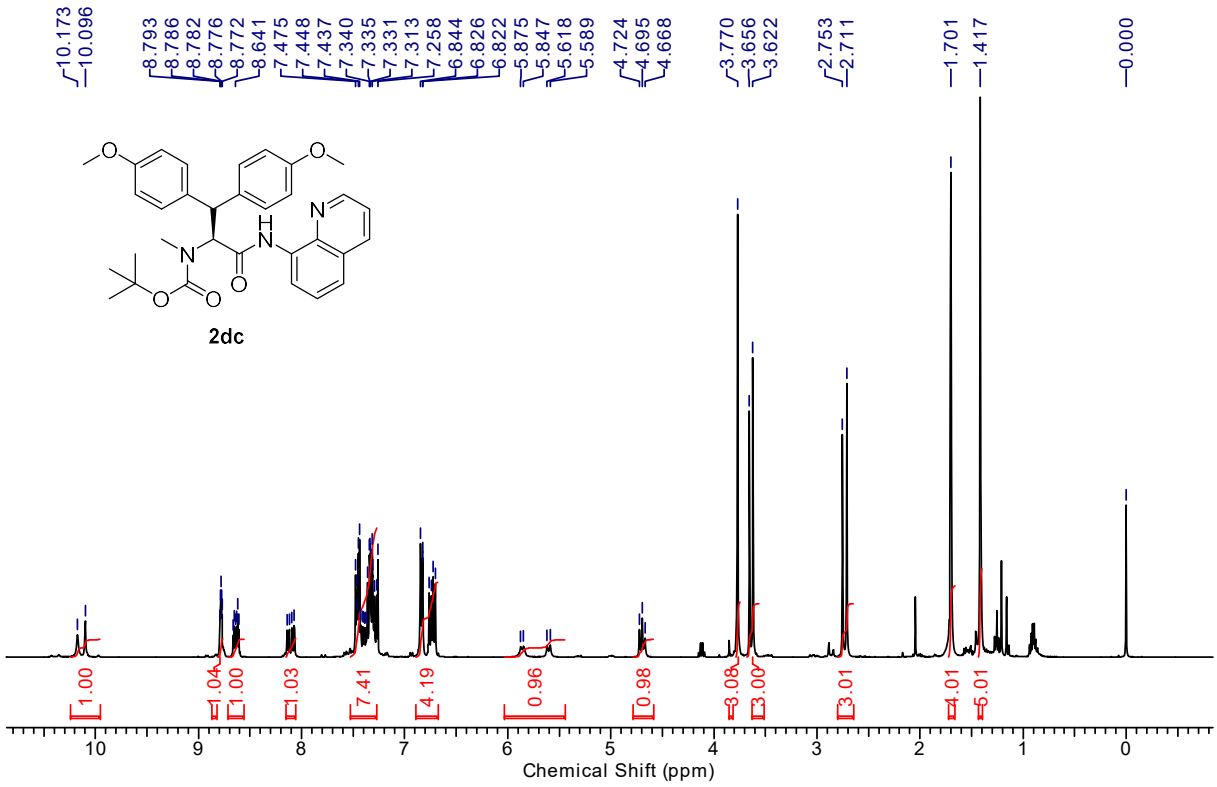


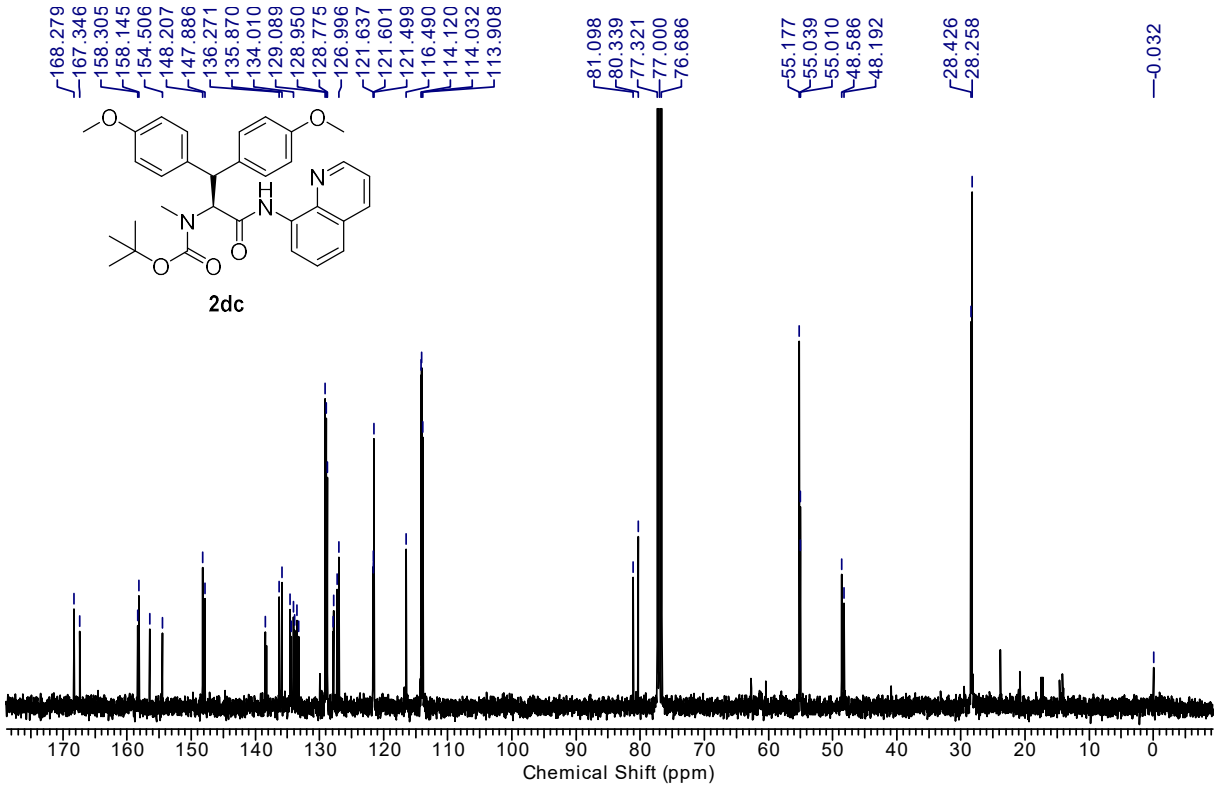
***tert*-Butyl (*S*)-(3-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)propan-2-yl)(methyl)carbamate (3dc)**



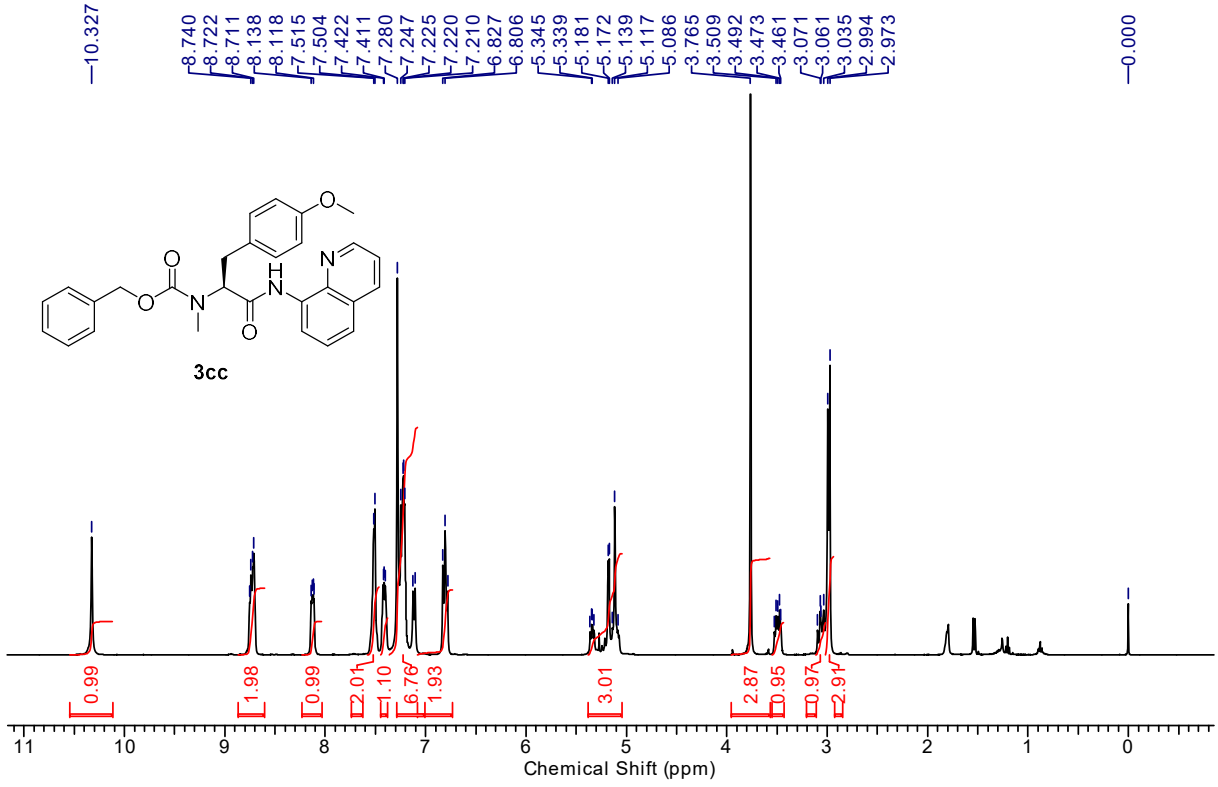


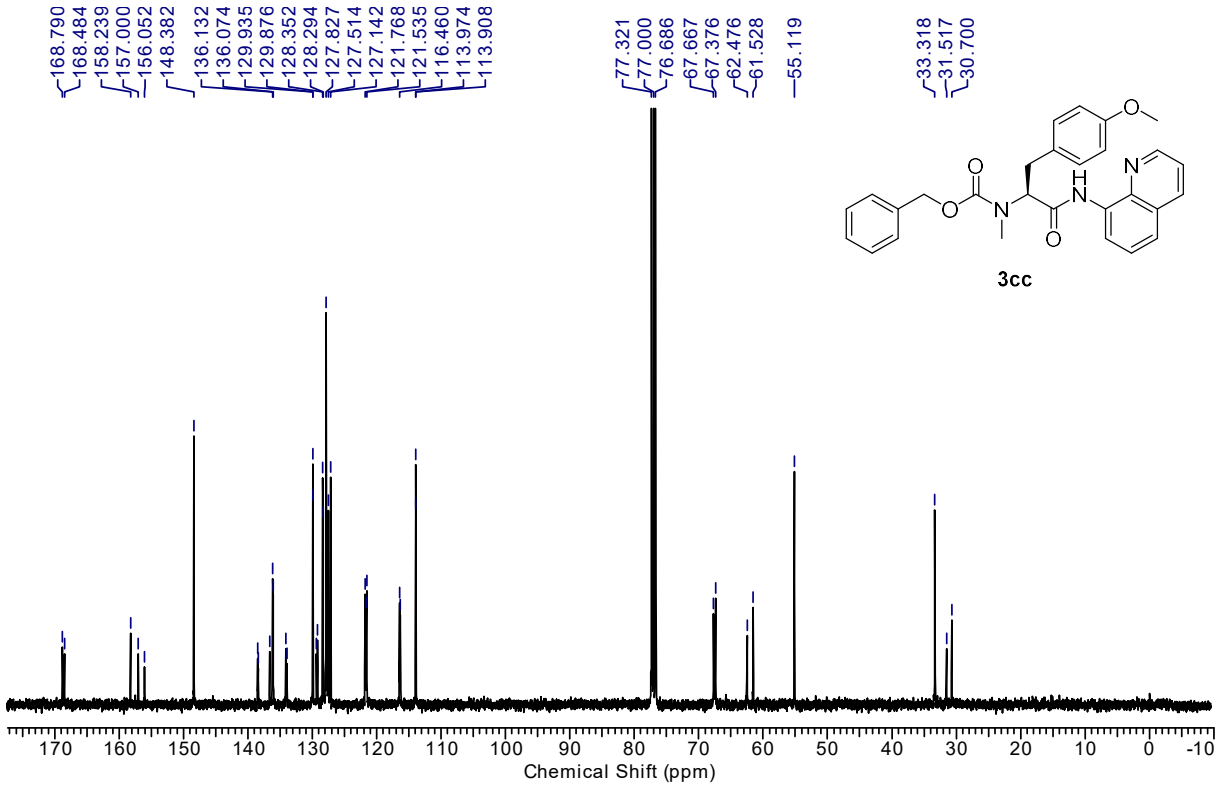
***tert*-Butyl (*S*)-(1,1-bis(4-methoxyphenyl)-3-oxo-3-(quinolin-8-ylamino)propan-2-yl)(methyl) carbamate (2dc)**



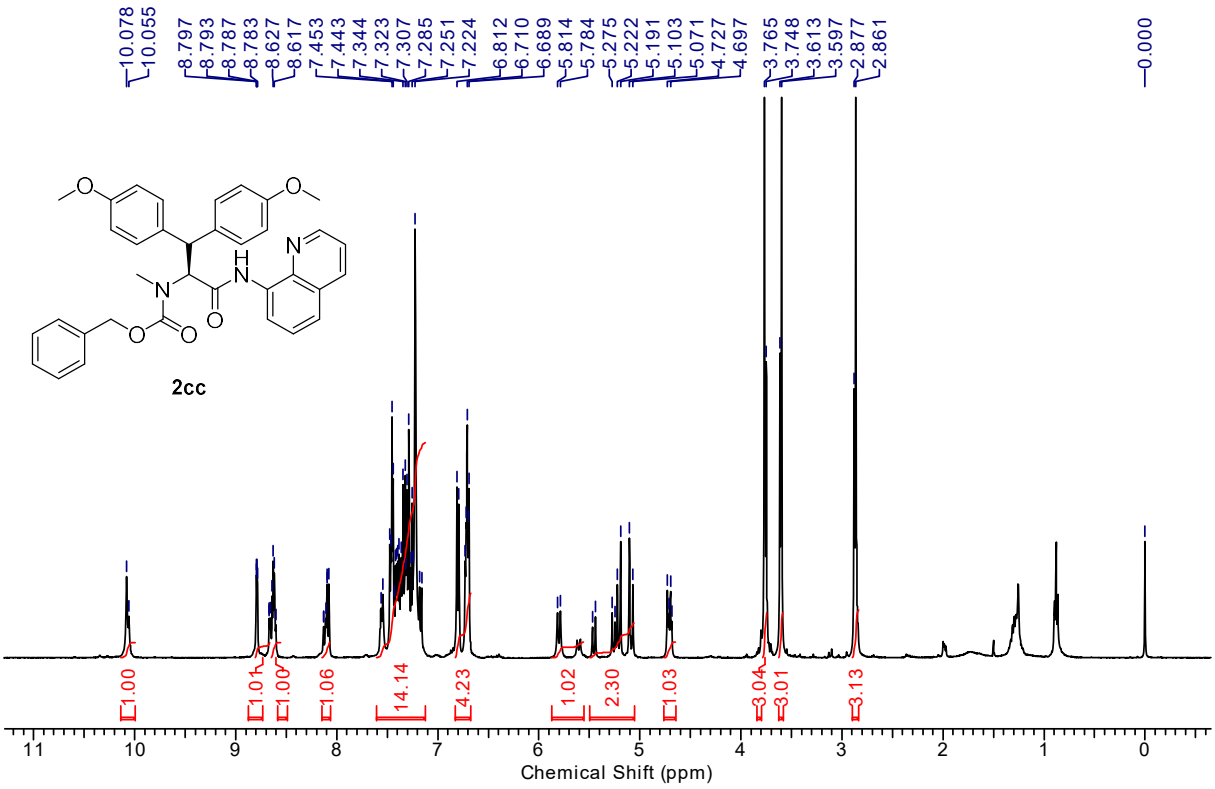


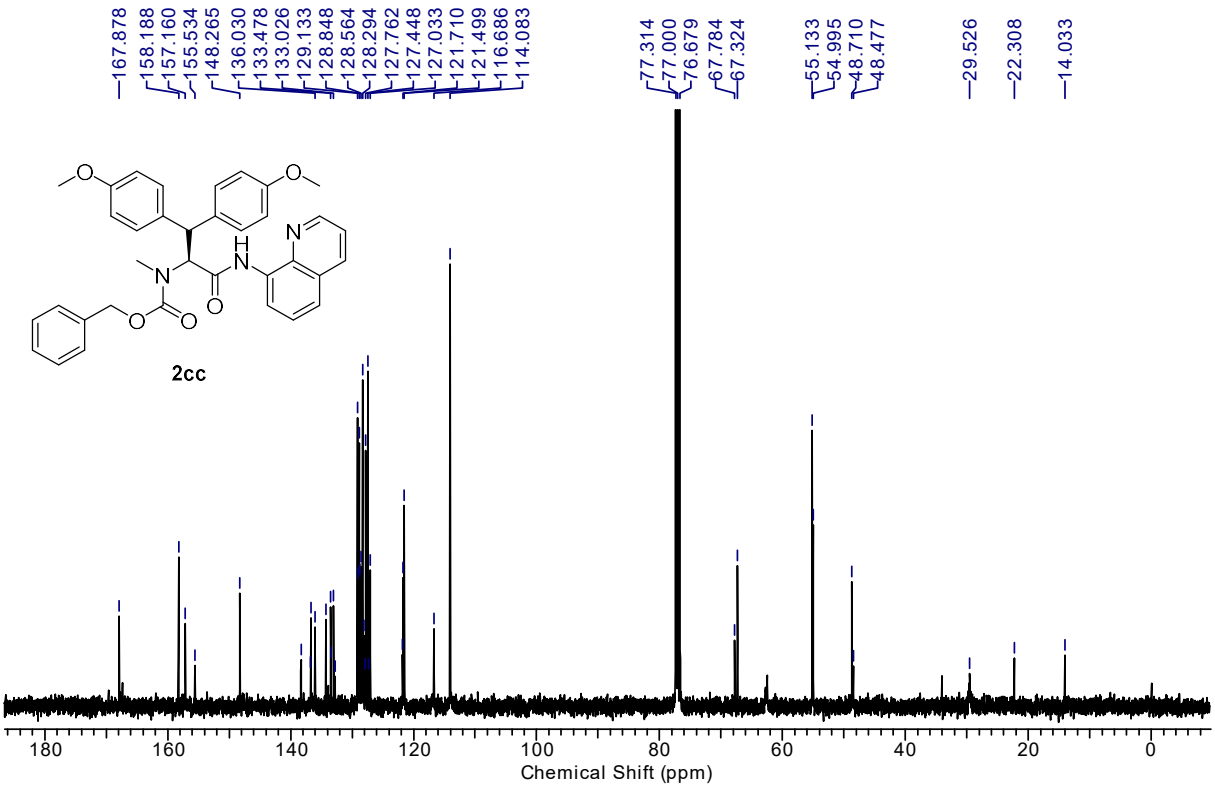
Benzyl (*S*)-(3-(4-methoxyphenyl)-1-oxo-1-(quinolin-8-ylamino)propan-2-yl)(methyl)carbamate (3cc)



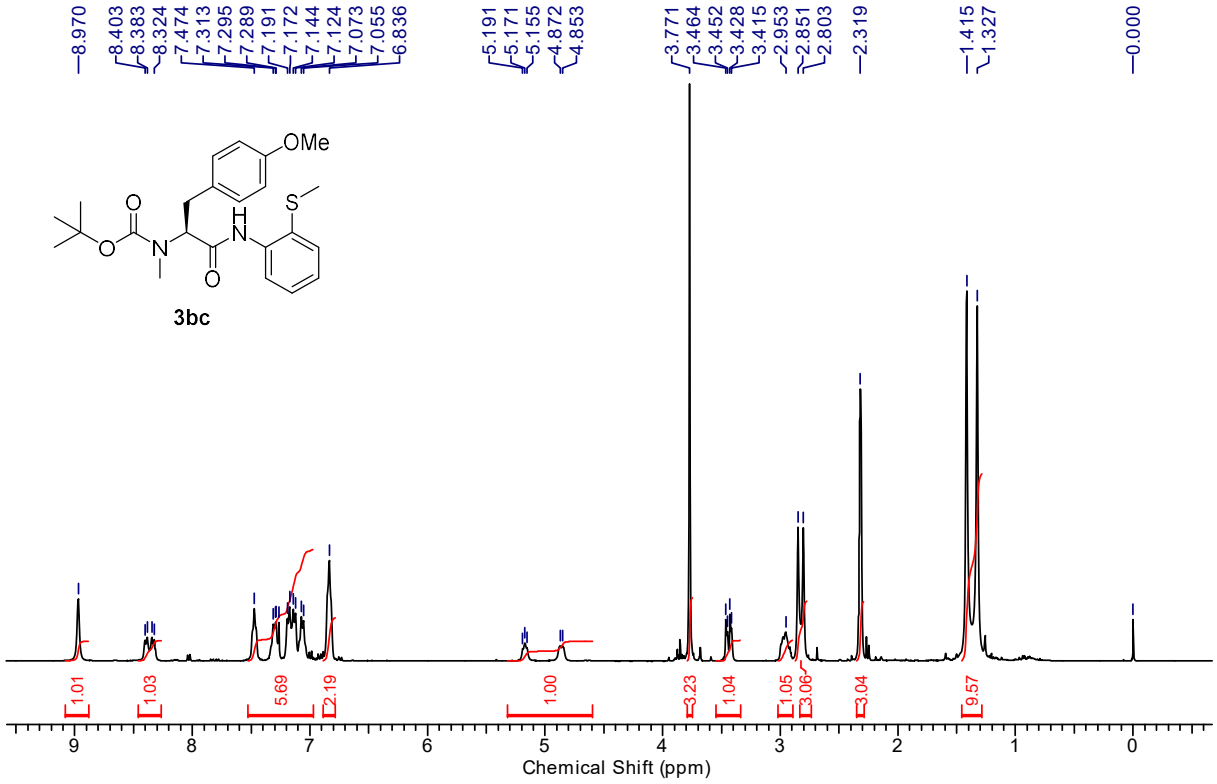


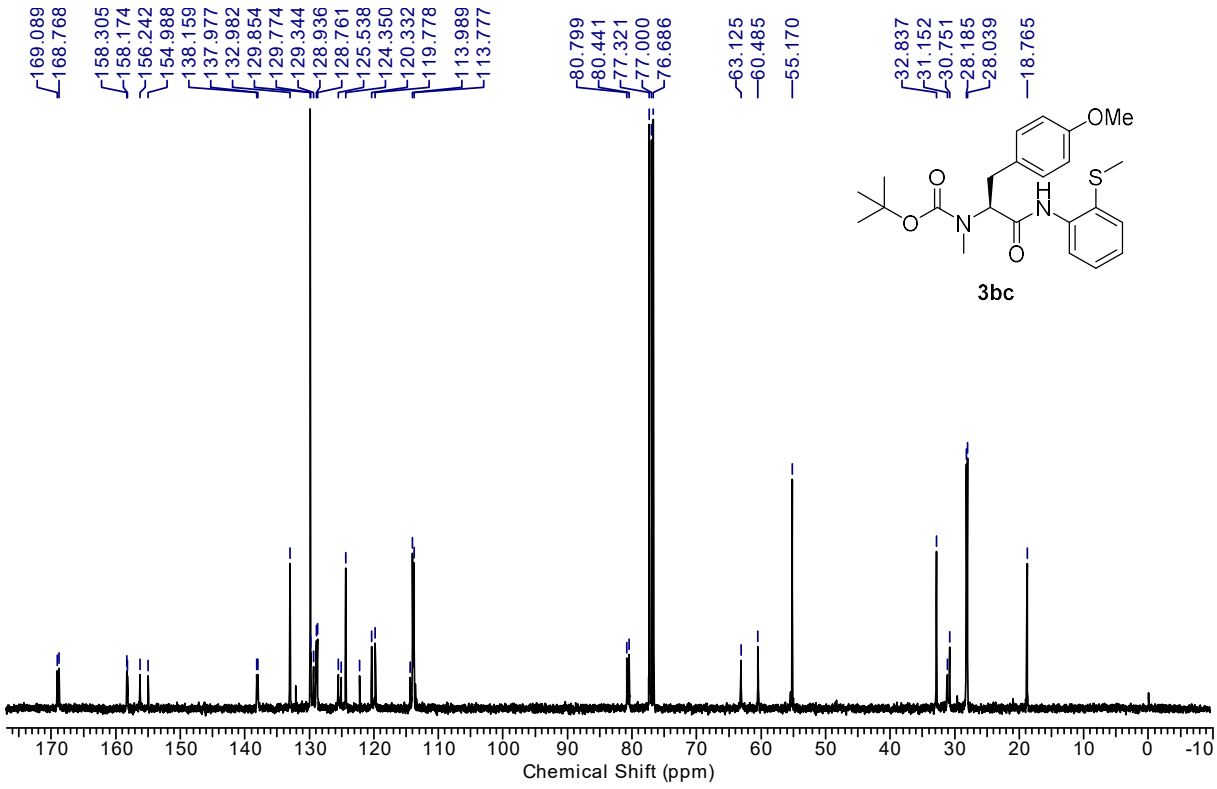
Benzyl (*S*)-(1,1-bis(4-methoxyphenyl)-3-oxo-3-(quinolin-8-ylamino)propan-2-yl)(methyl)carbamate (2cc)



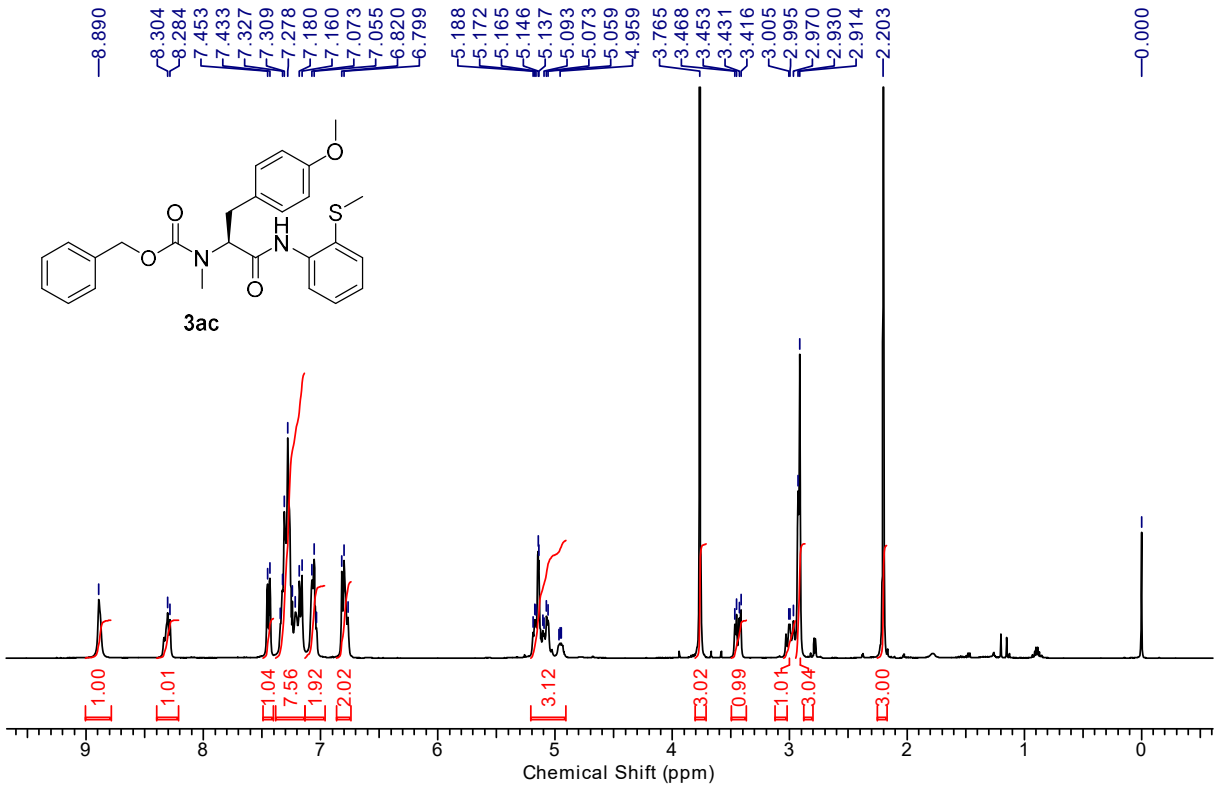


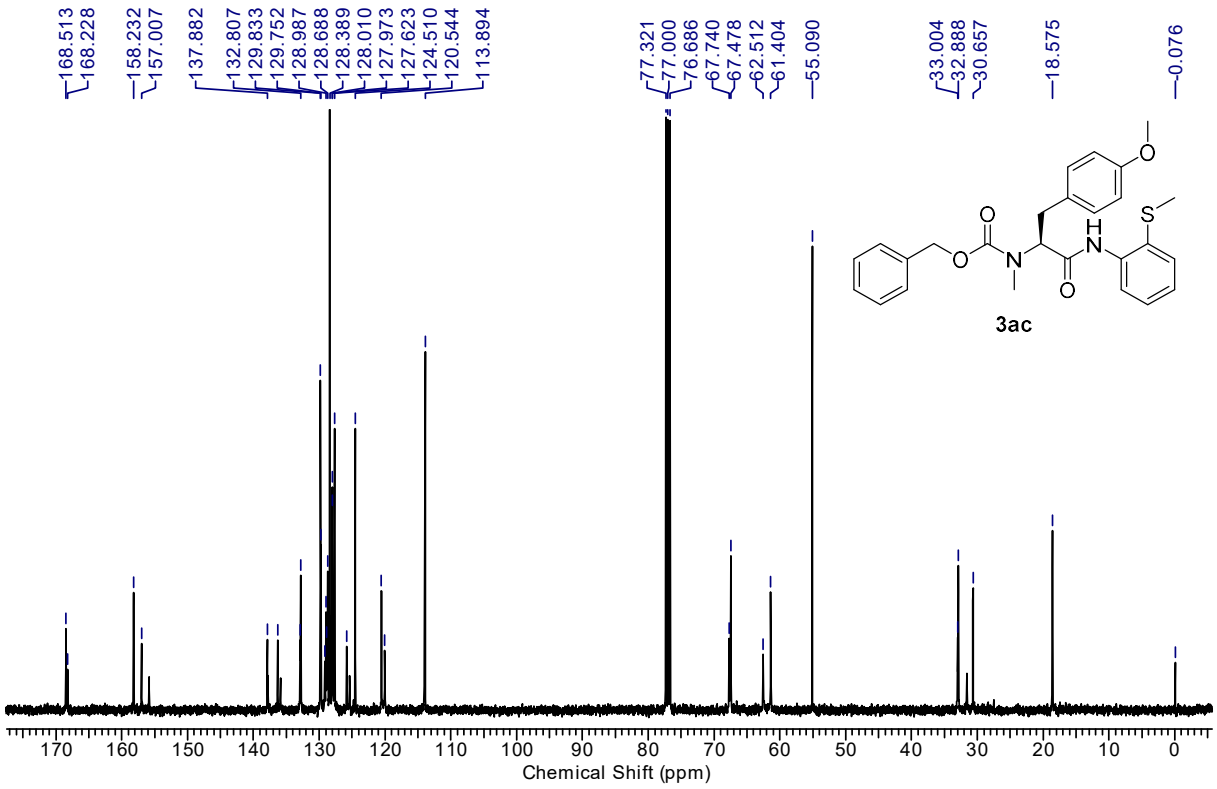
***tert*-Butyl (*S*)-(3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3bc)**



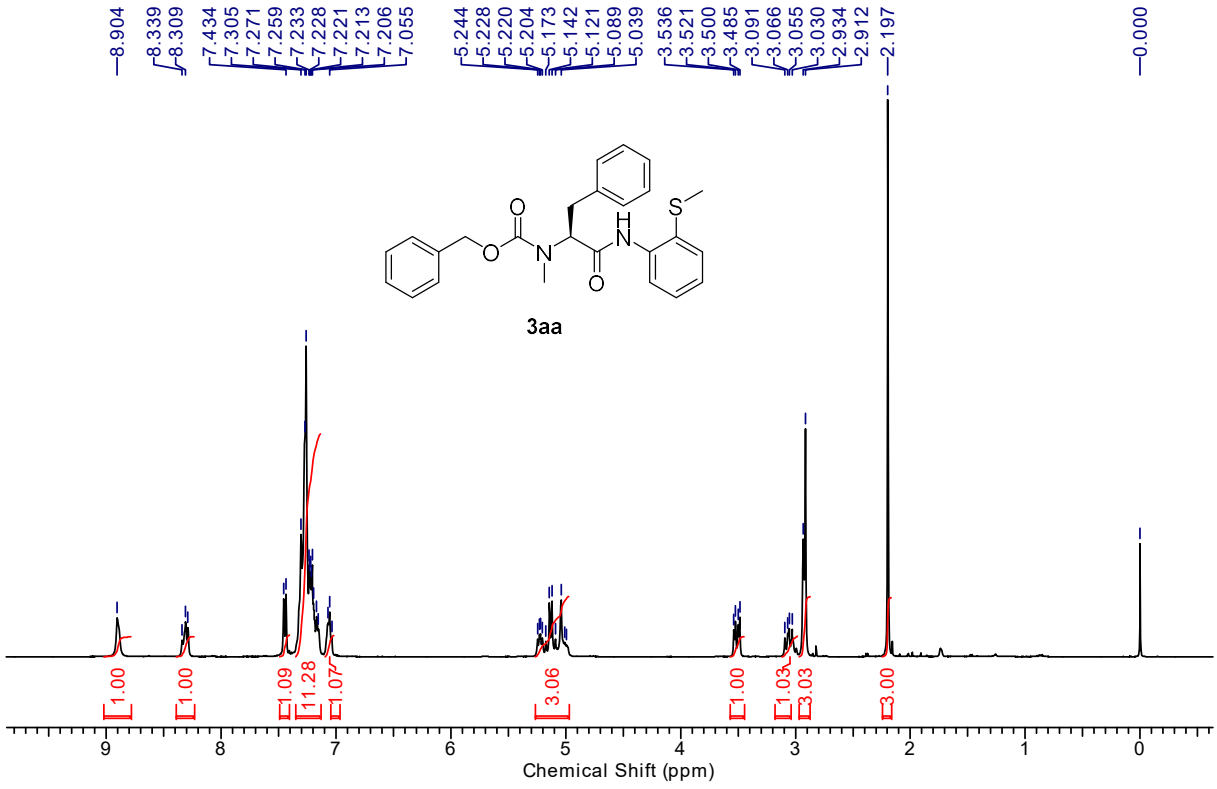


Benzyl (*S*)-(3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ac)

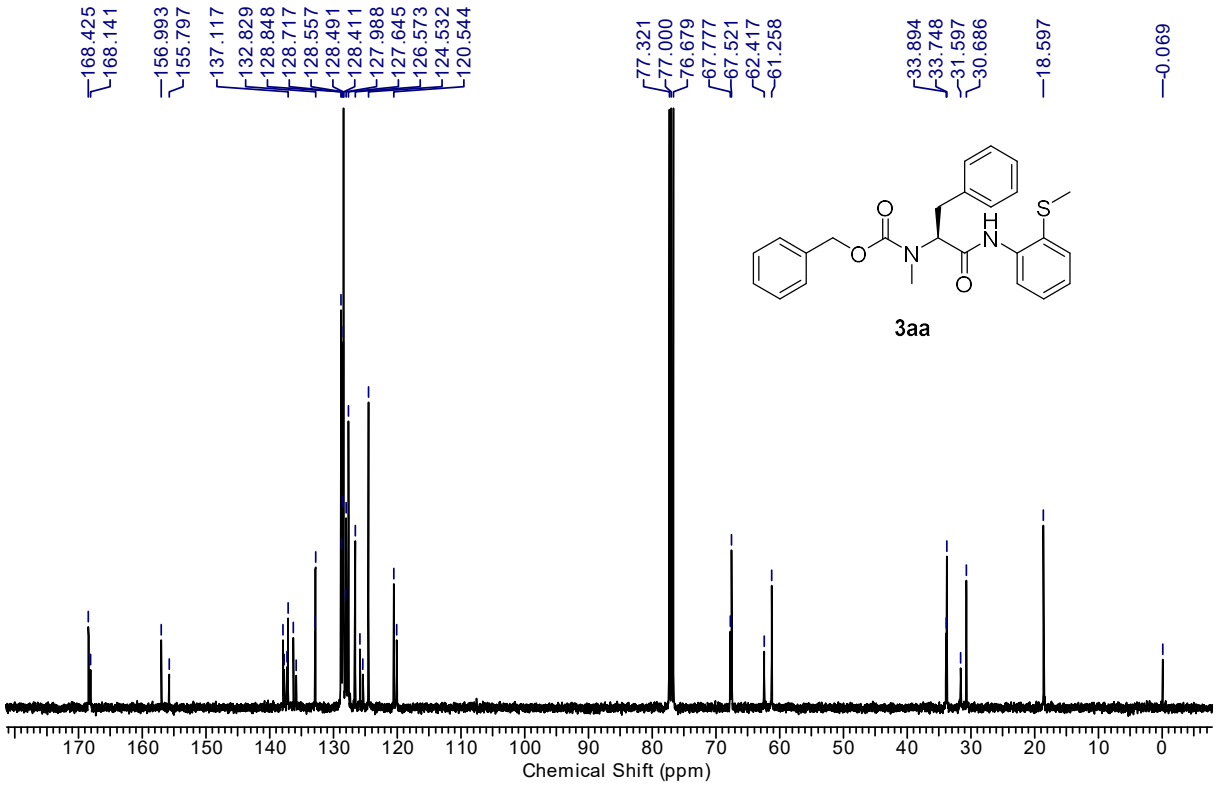




Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (3aa)

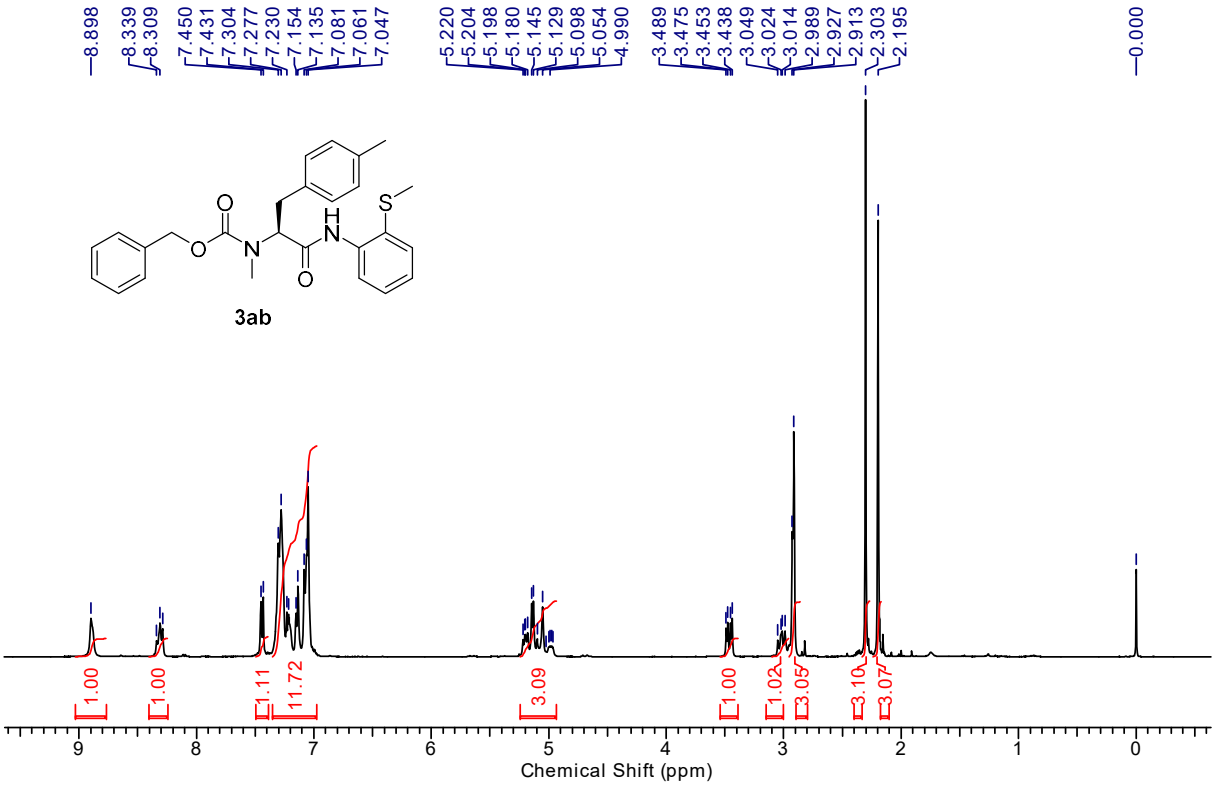


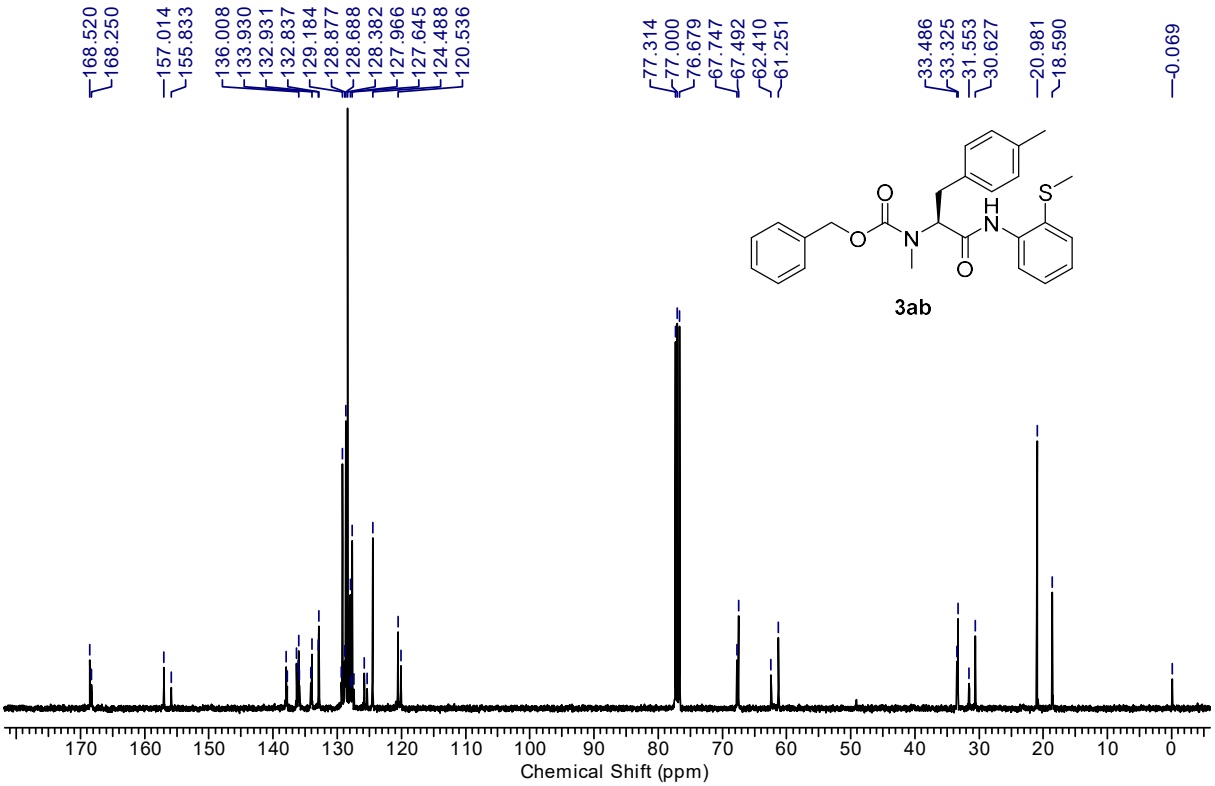
3aa



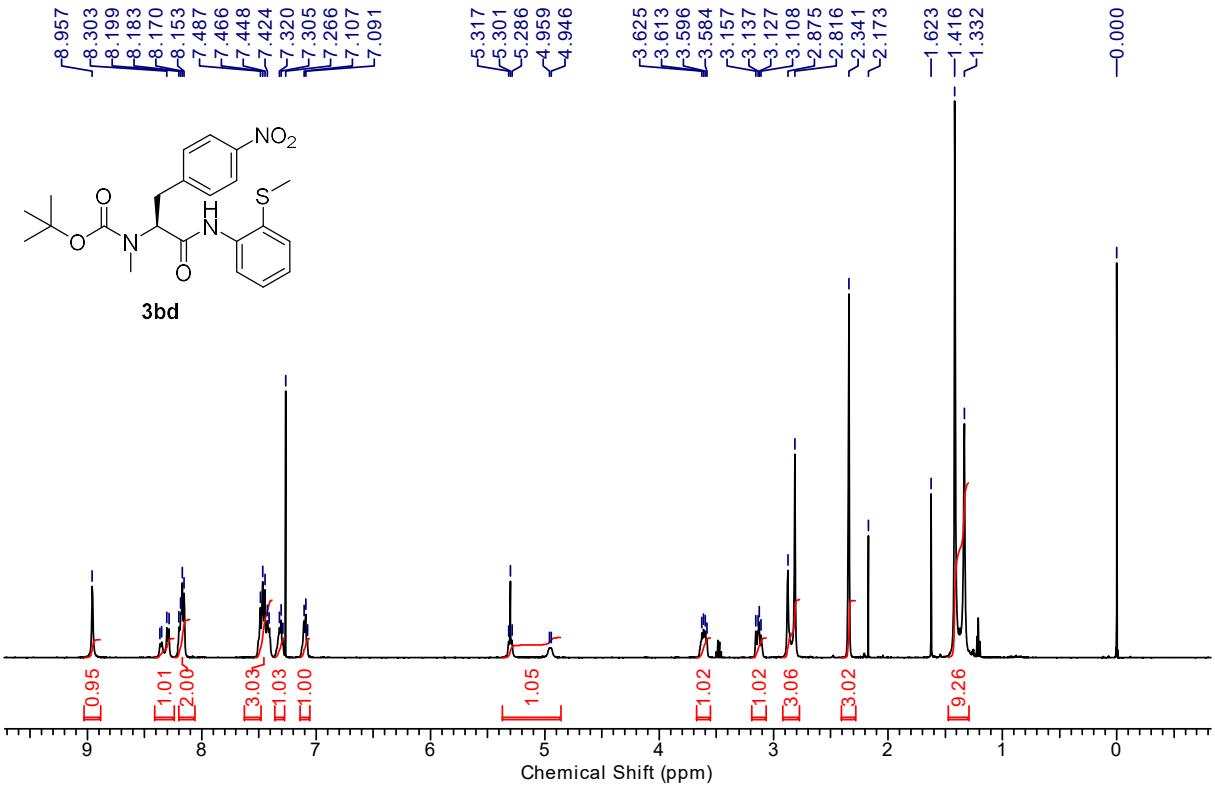
3aa

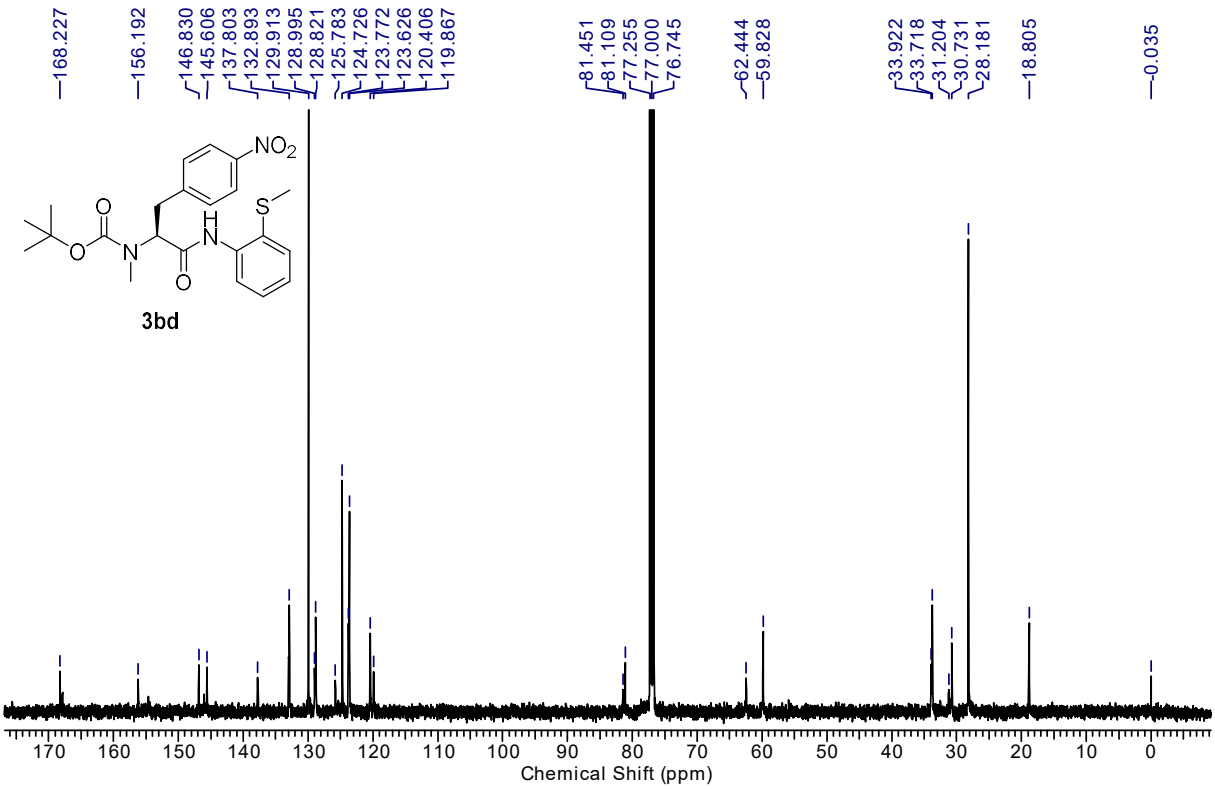
Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-(*p*-tolyl)propan-2-yl)carbamate (3ab)



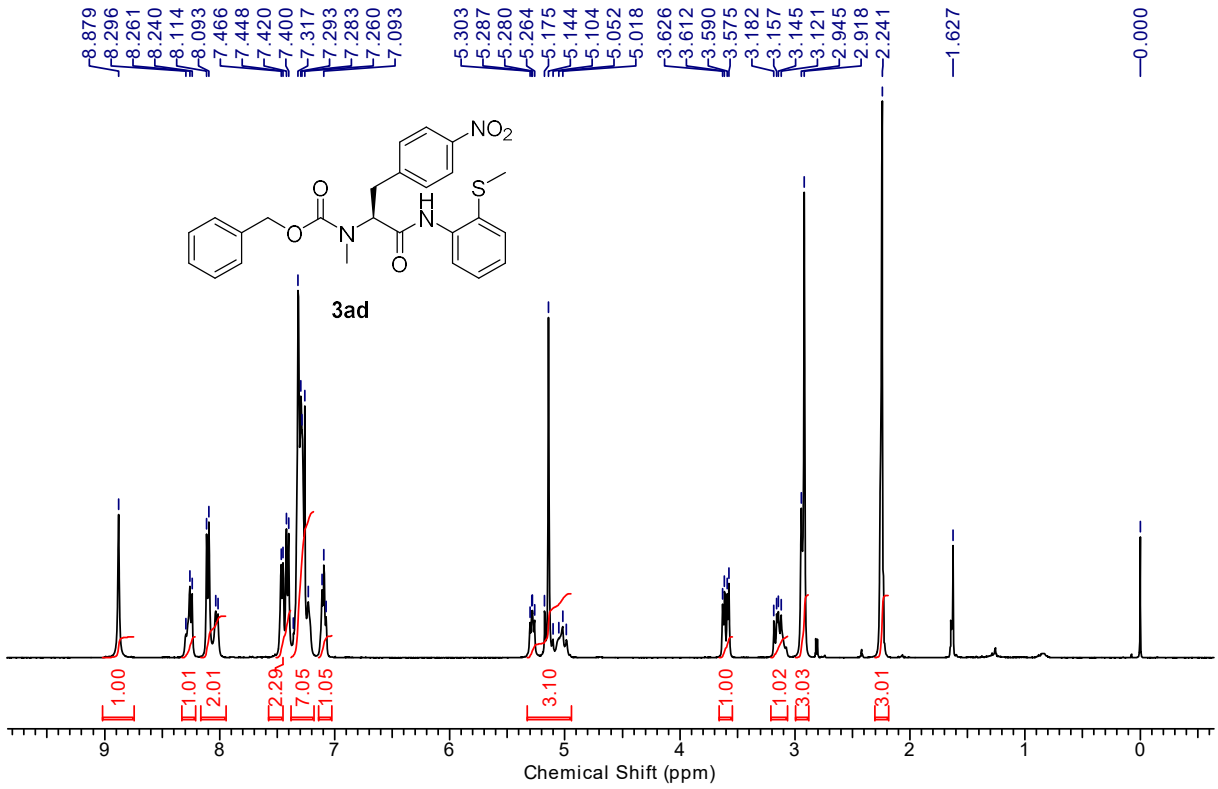


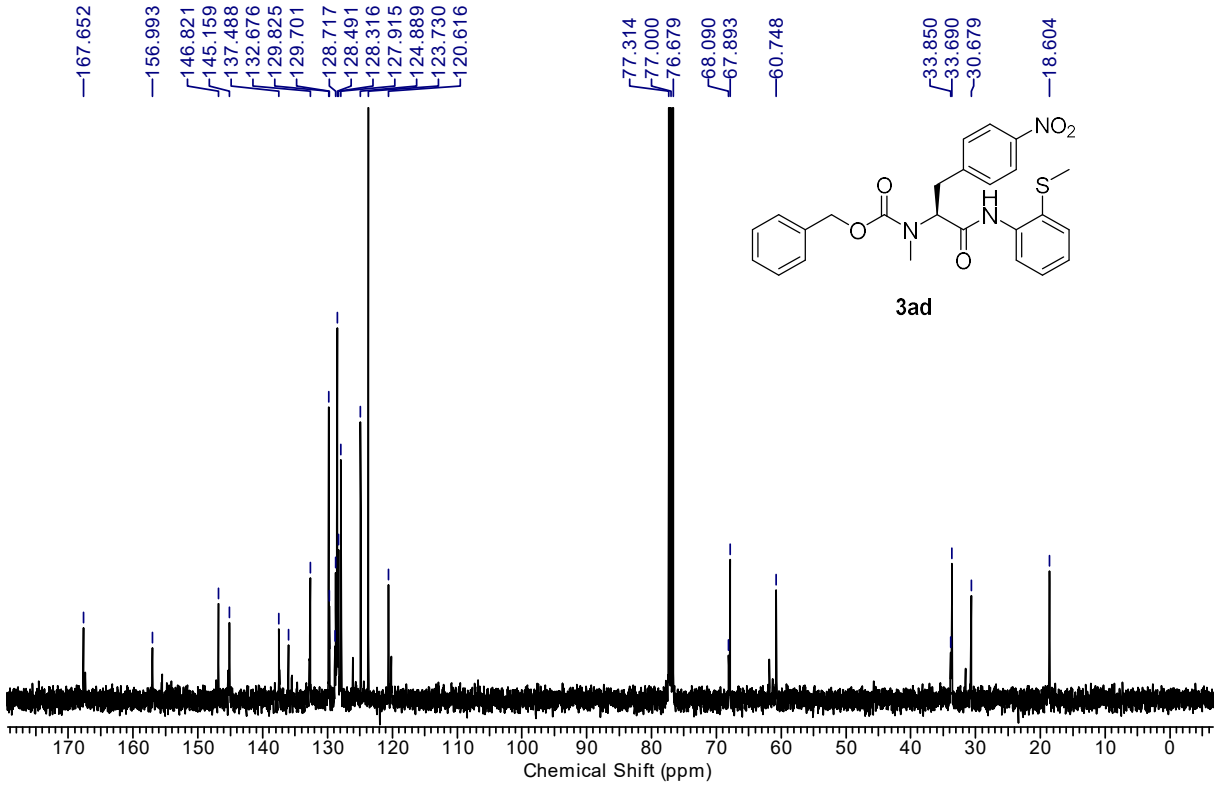
tert-Butyl (_S_)-methyl(1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl) carbamate (3bd)



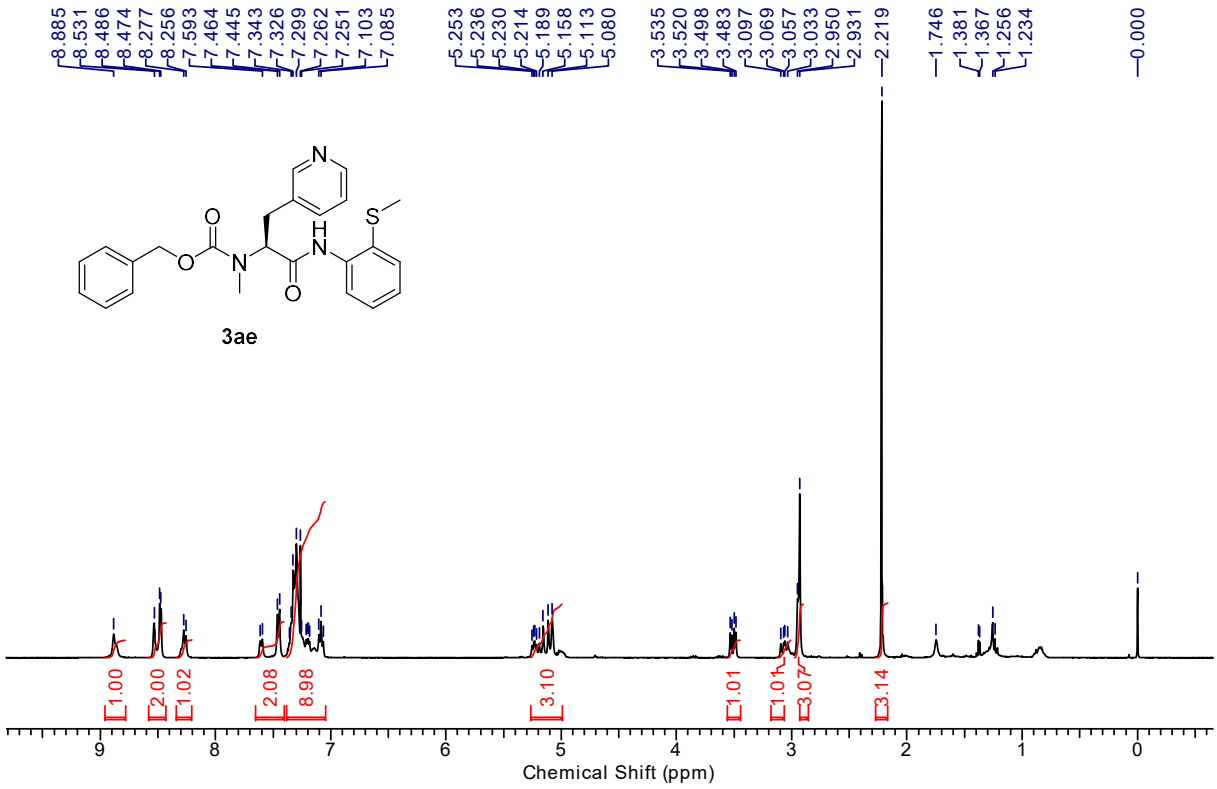


Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl)carbamate (3ad)

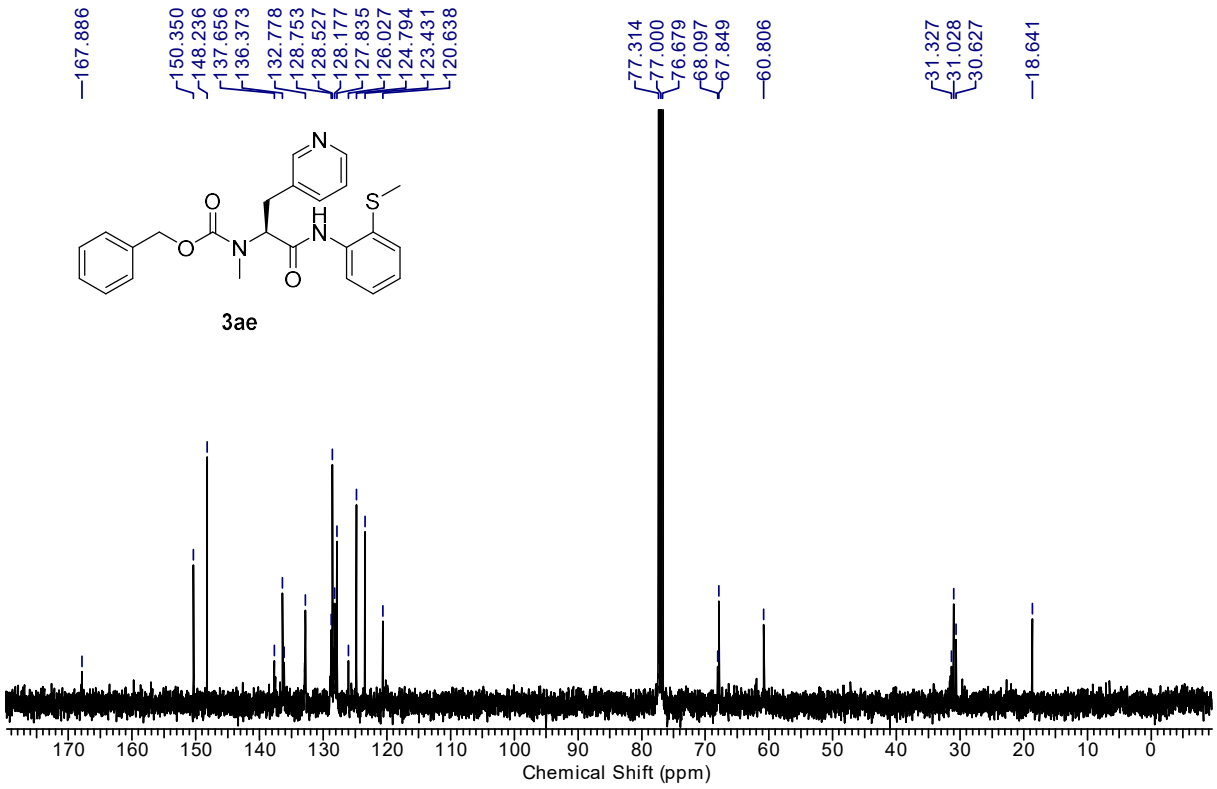




Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-(pyridin-3-yl)propan-2-yl)carbamate (3ae)

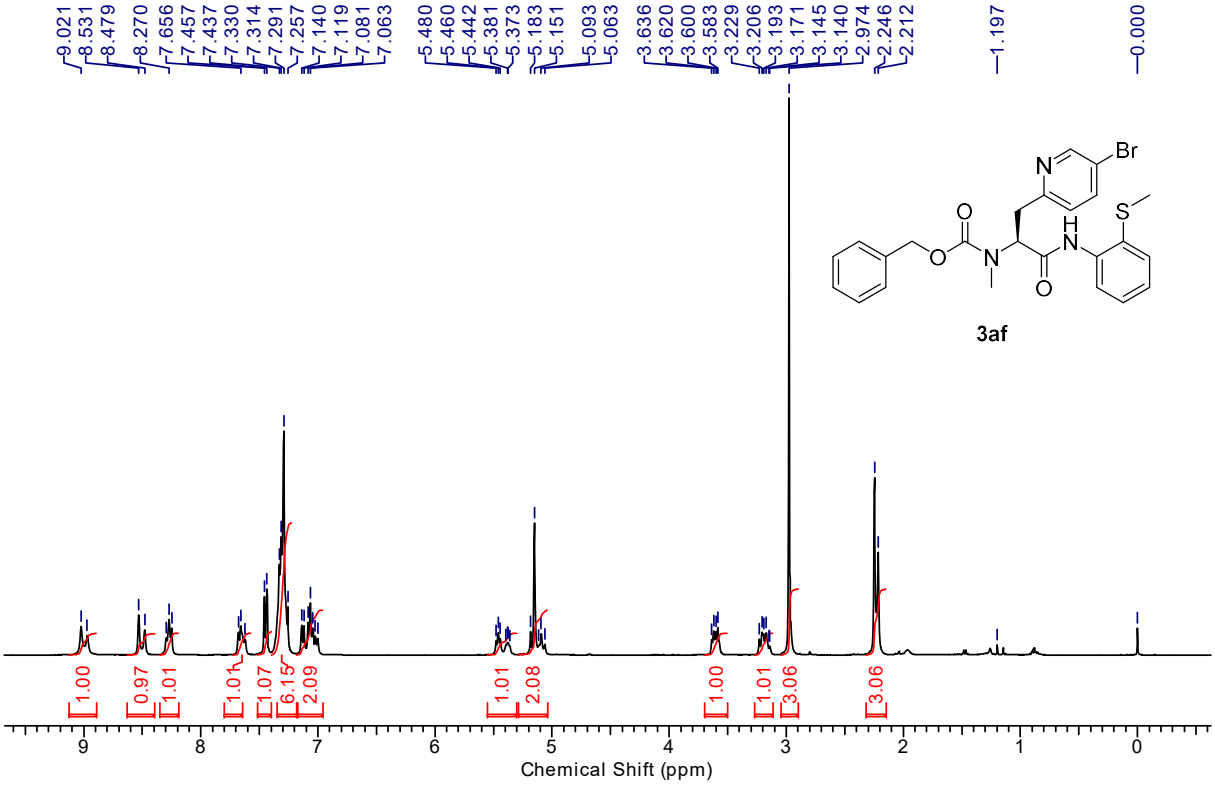


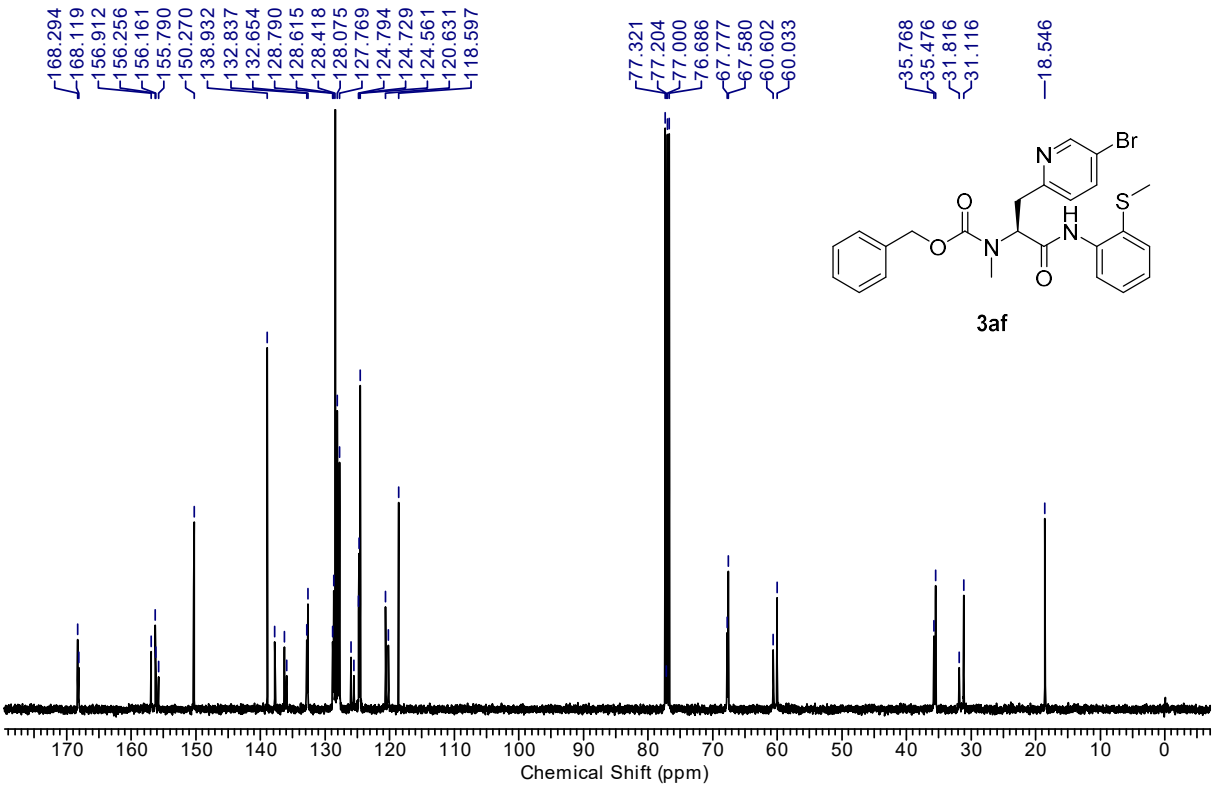
3ae



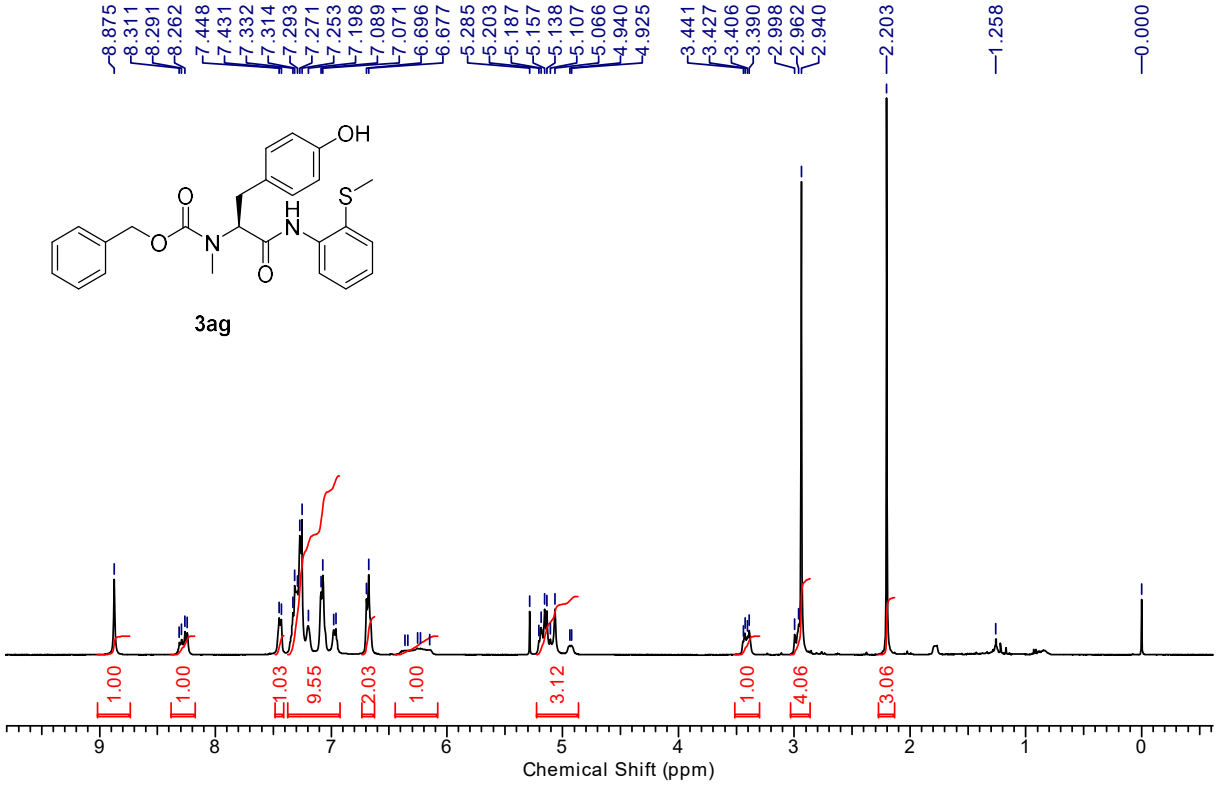
3ae

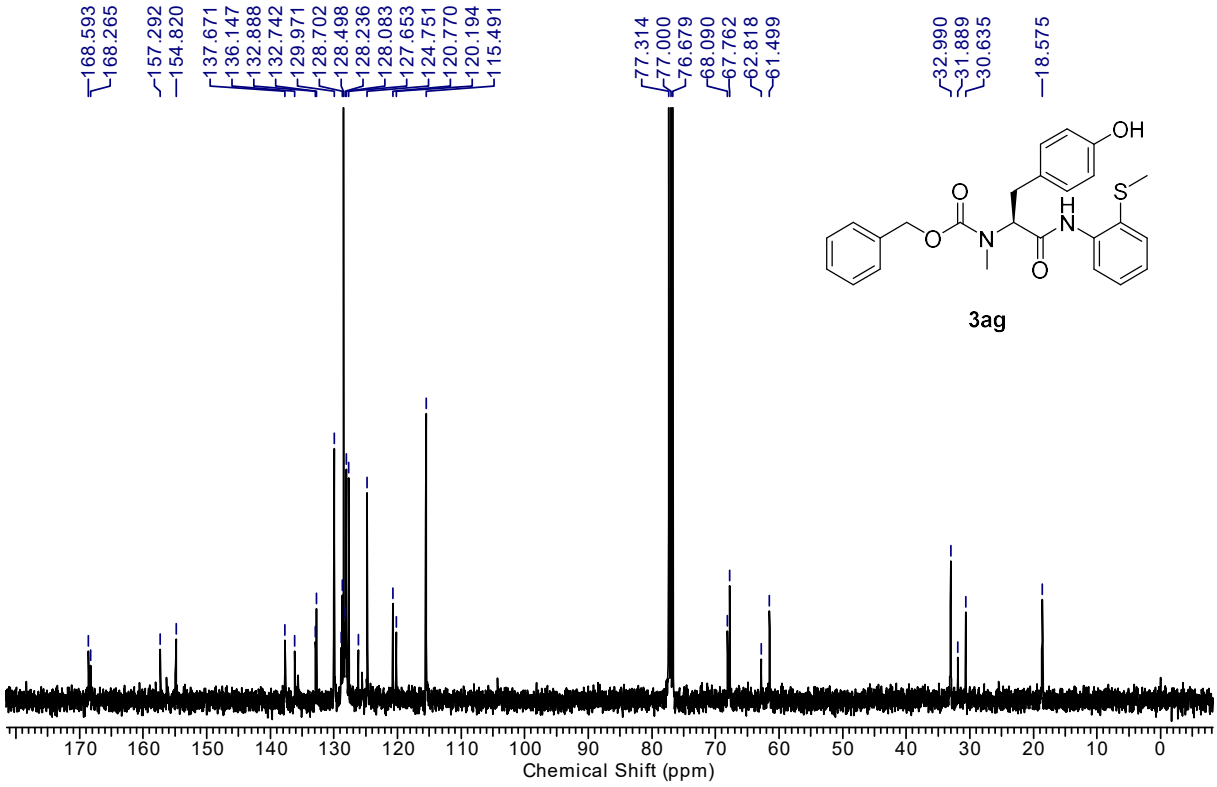
Benzyl (*S*)-(3-(5-bromopyridin-2-yl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3af)



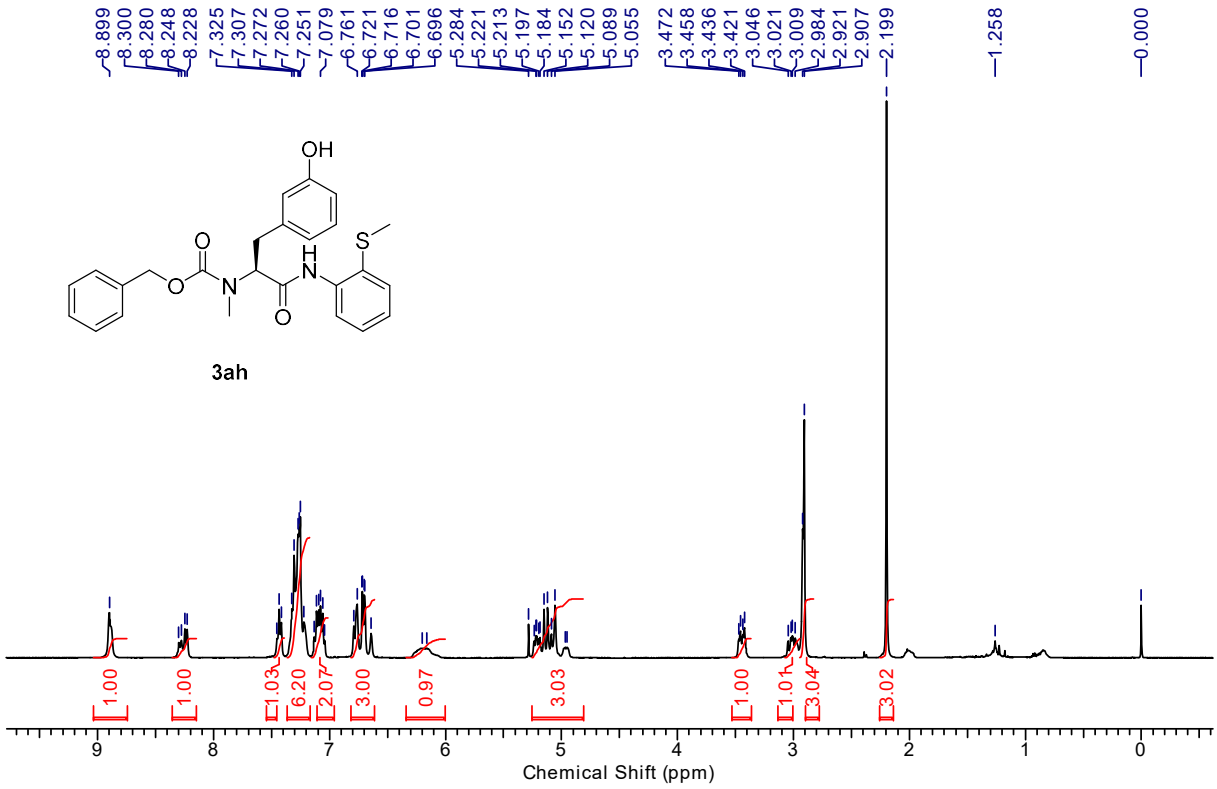


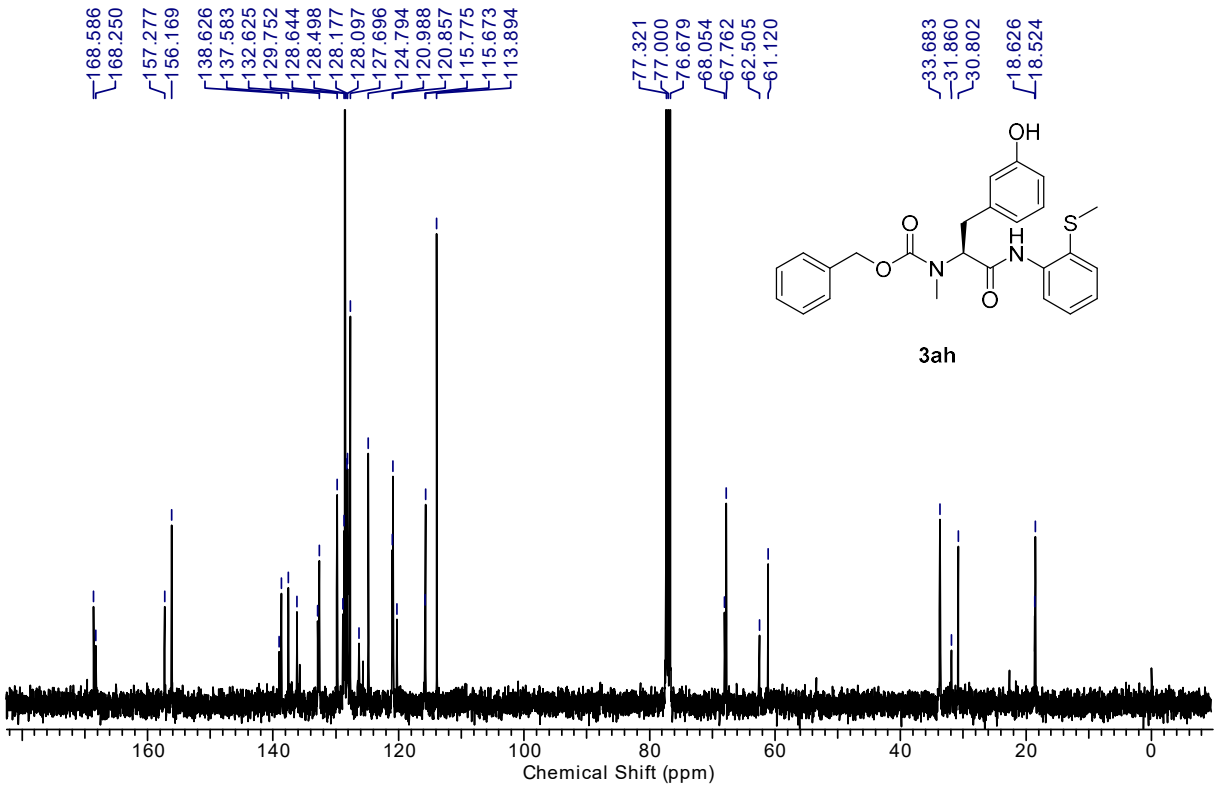
Benzyl (*S*)-(3-(4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ag)



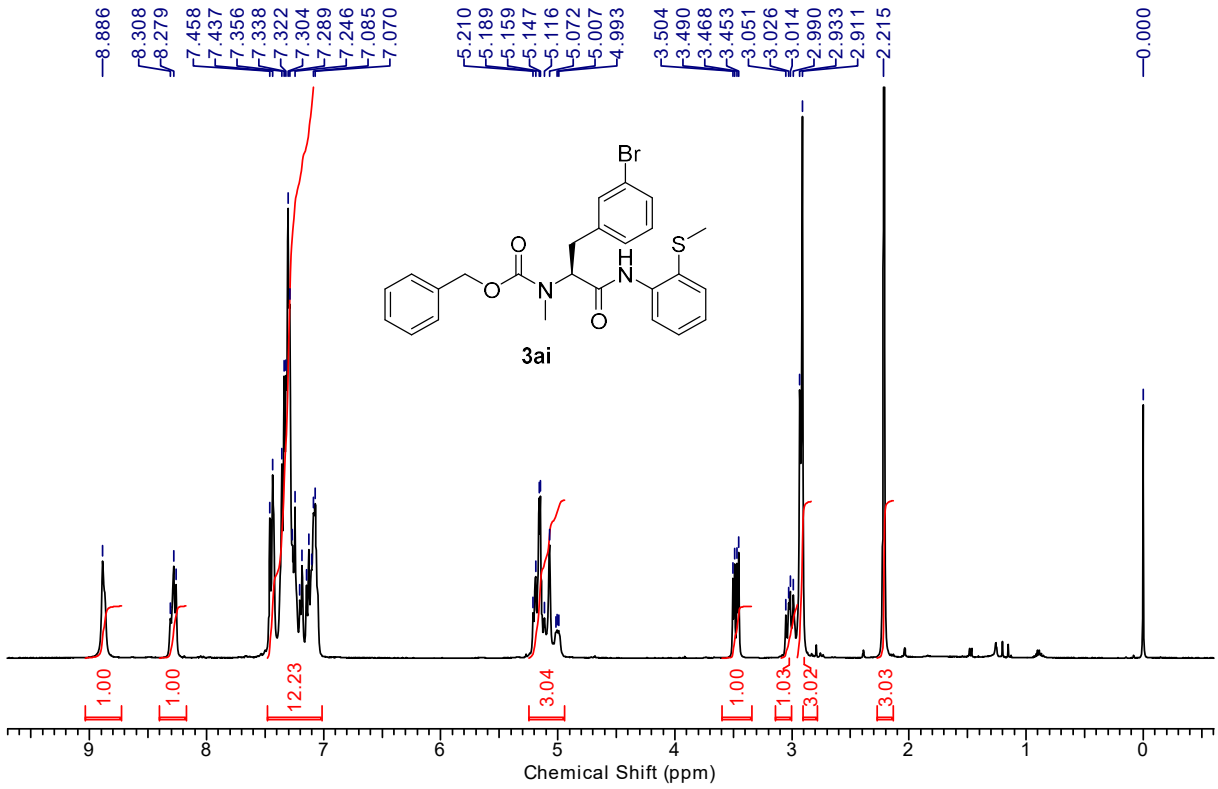


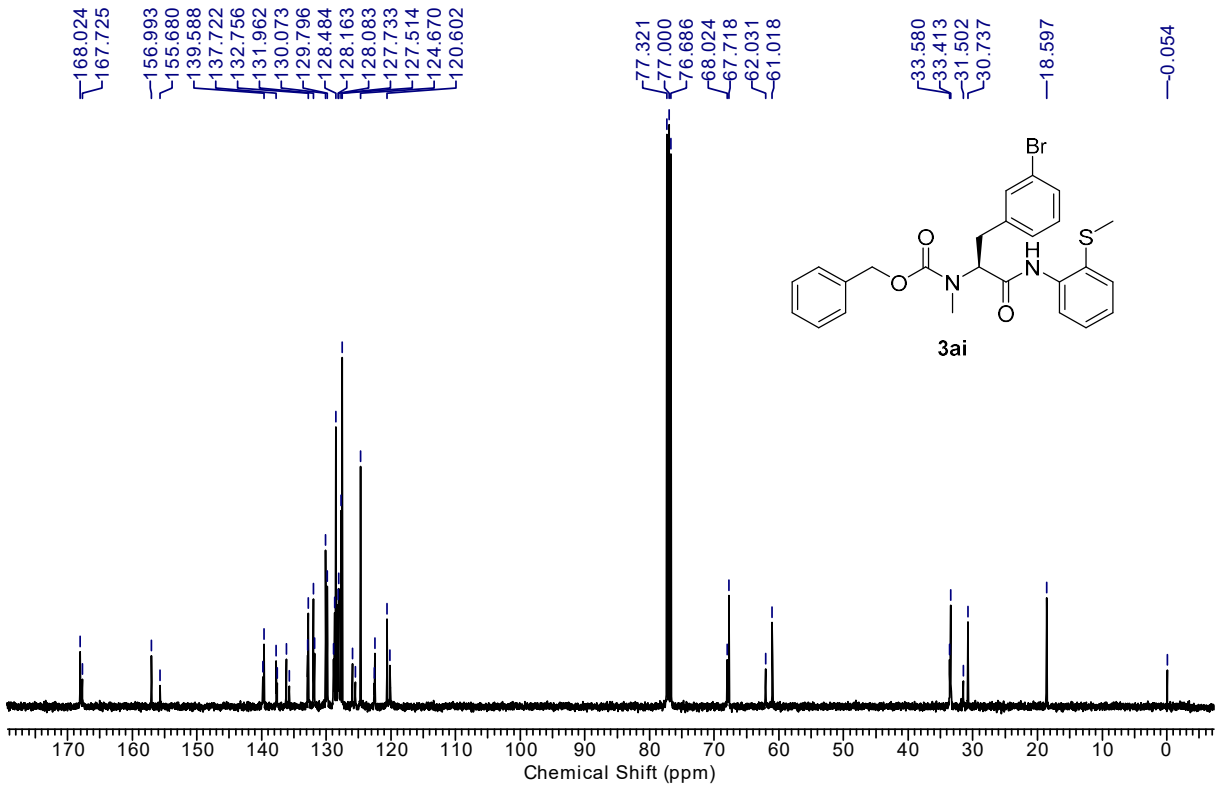
Benzyl (*S*)-(3-(3-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ah)



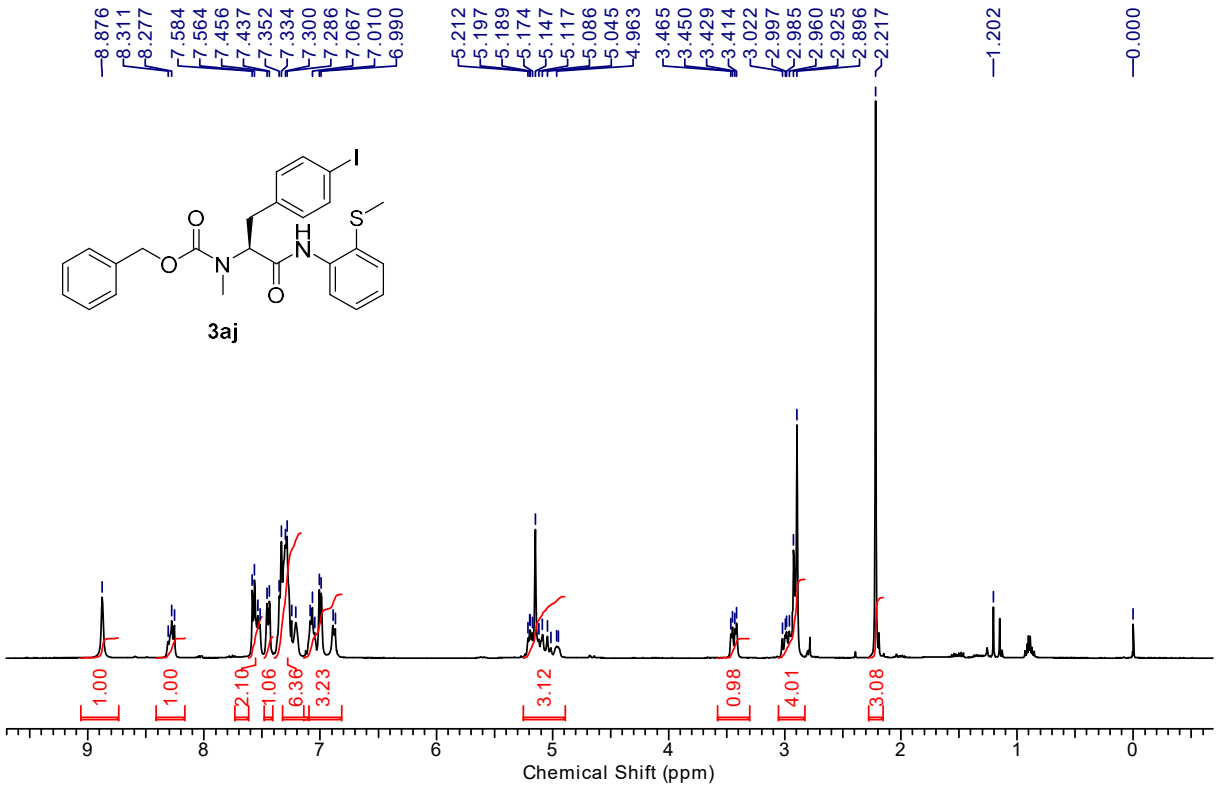


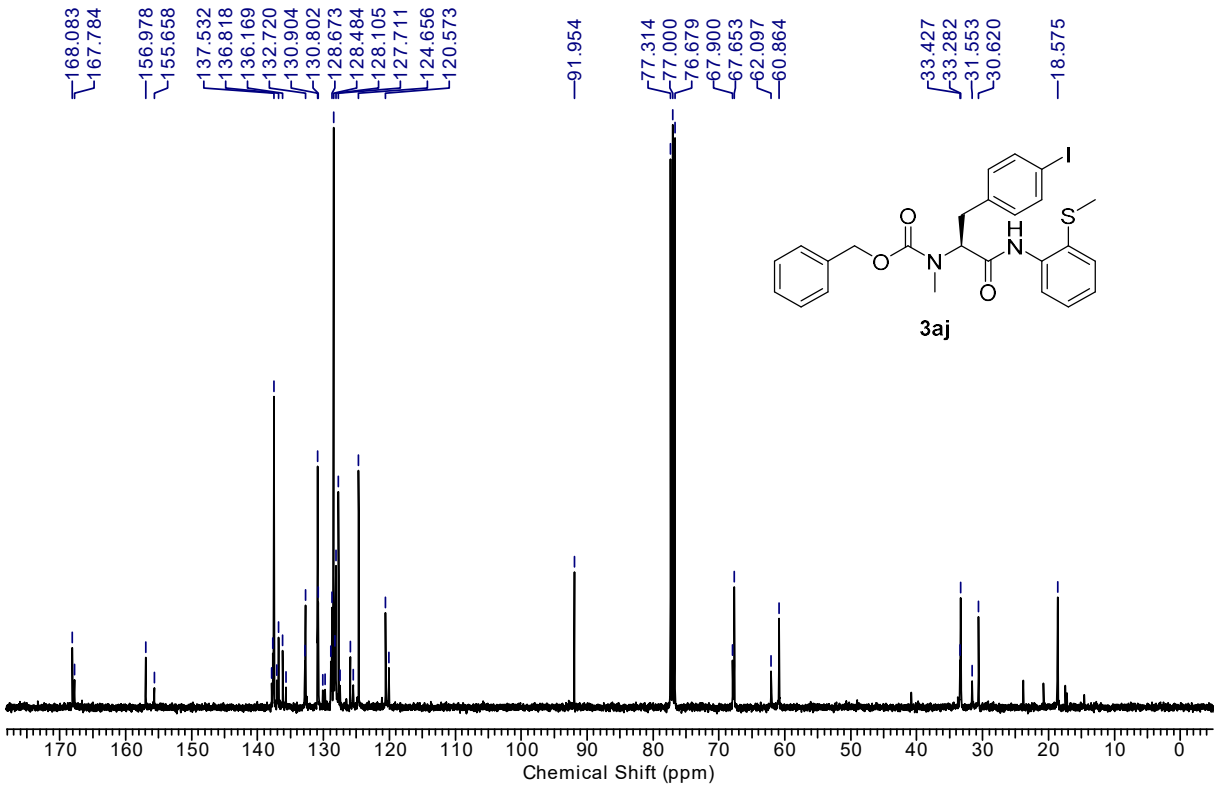
Benzyl (*S*)-(3-(3-bromophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ai)



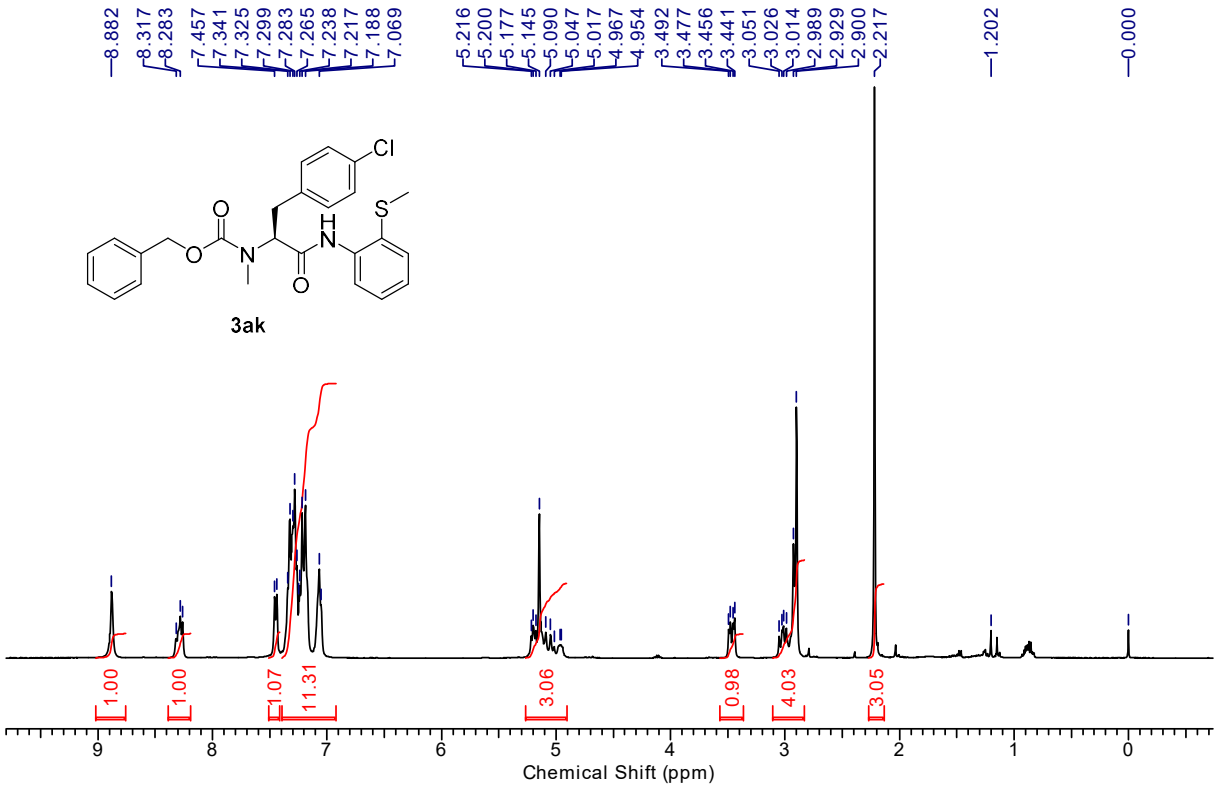


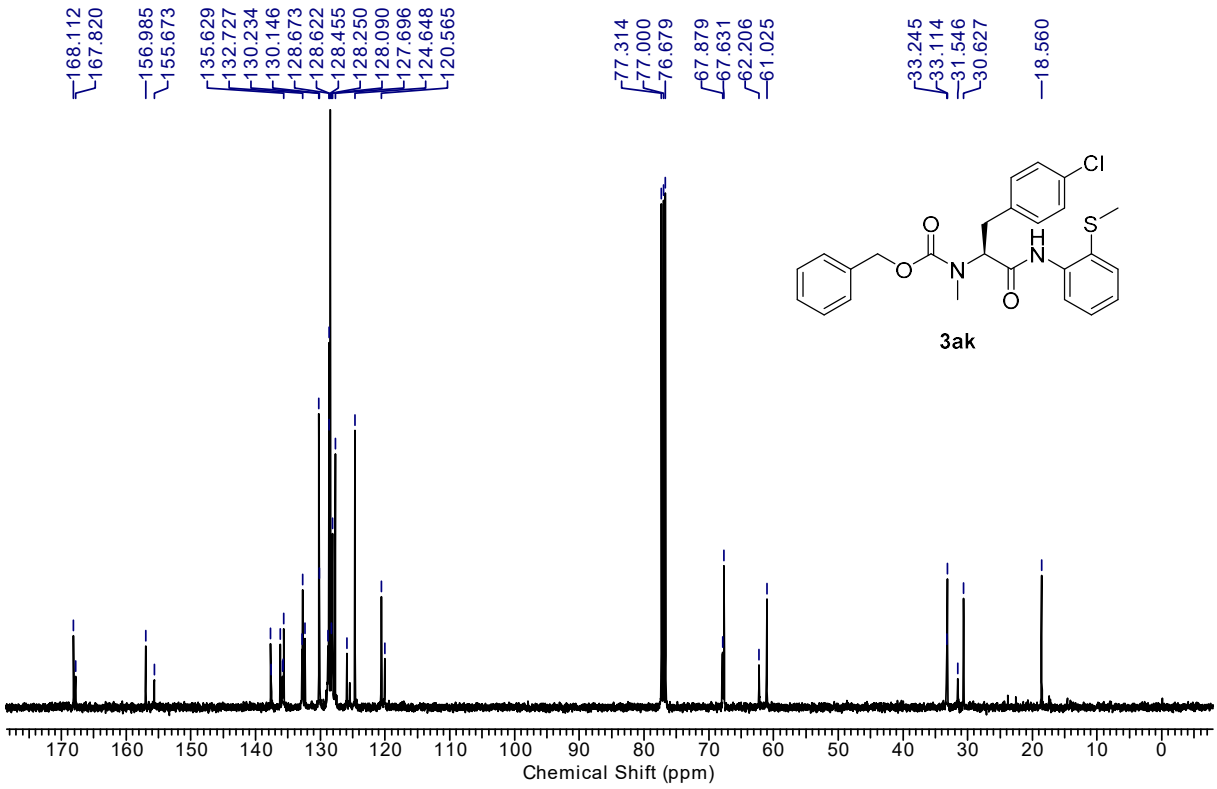
Benzyl (*S*)-(3-(4-iodophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)carbamate (3aj)



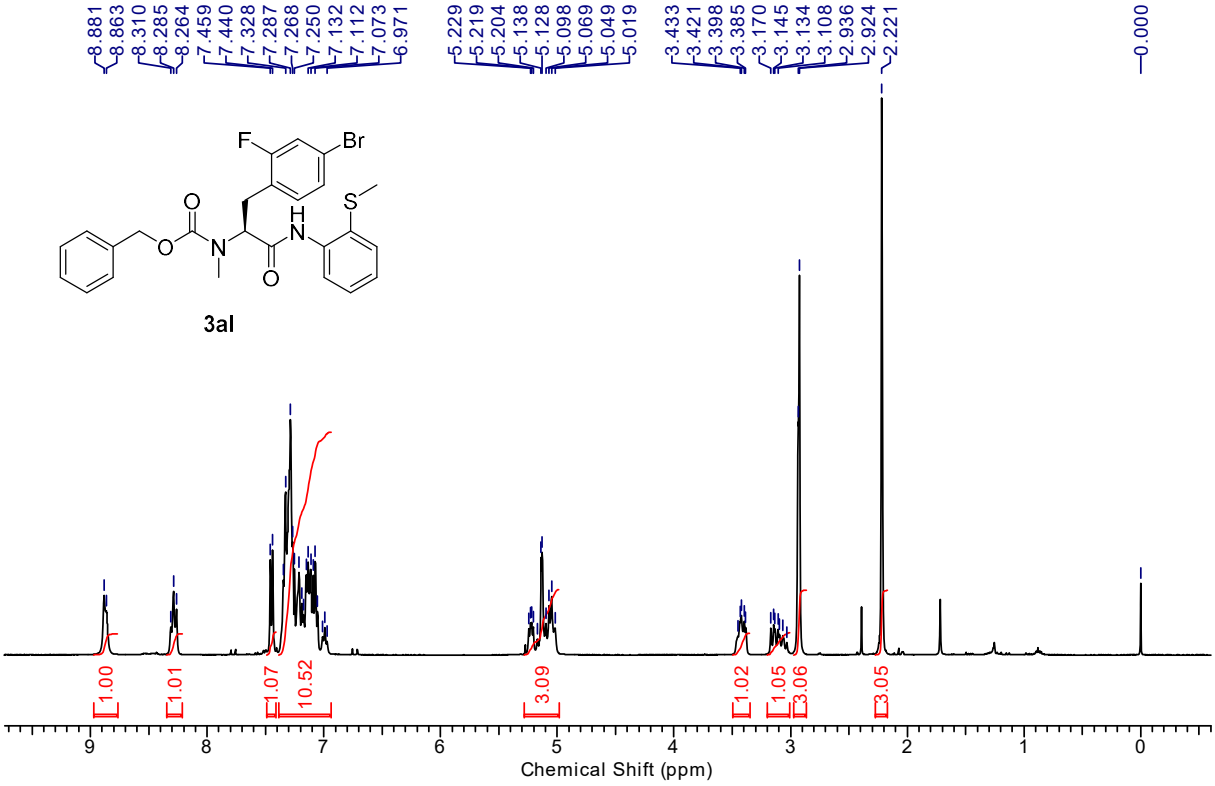


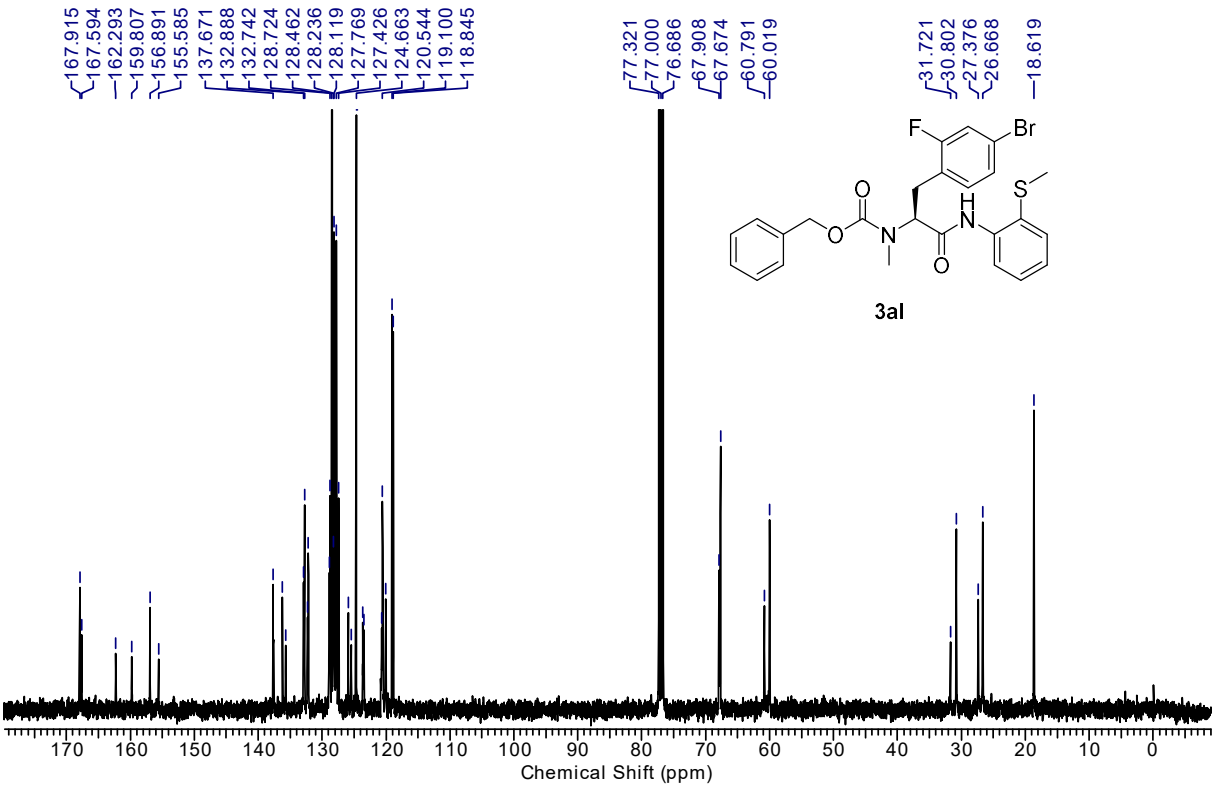
Benzyl (*S*)-(3-(4-chlorophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ak)



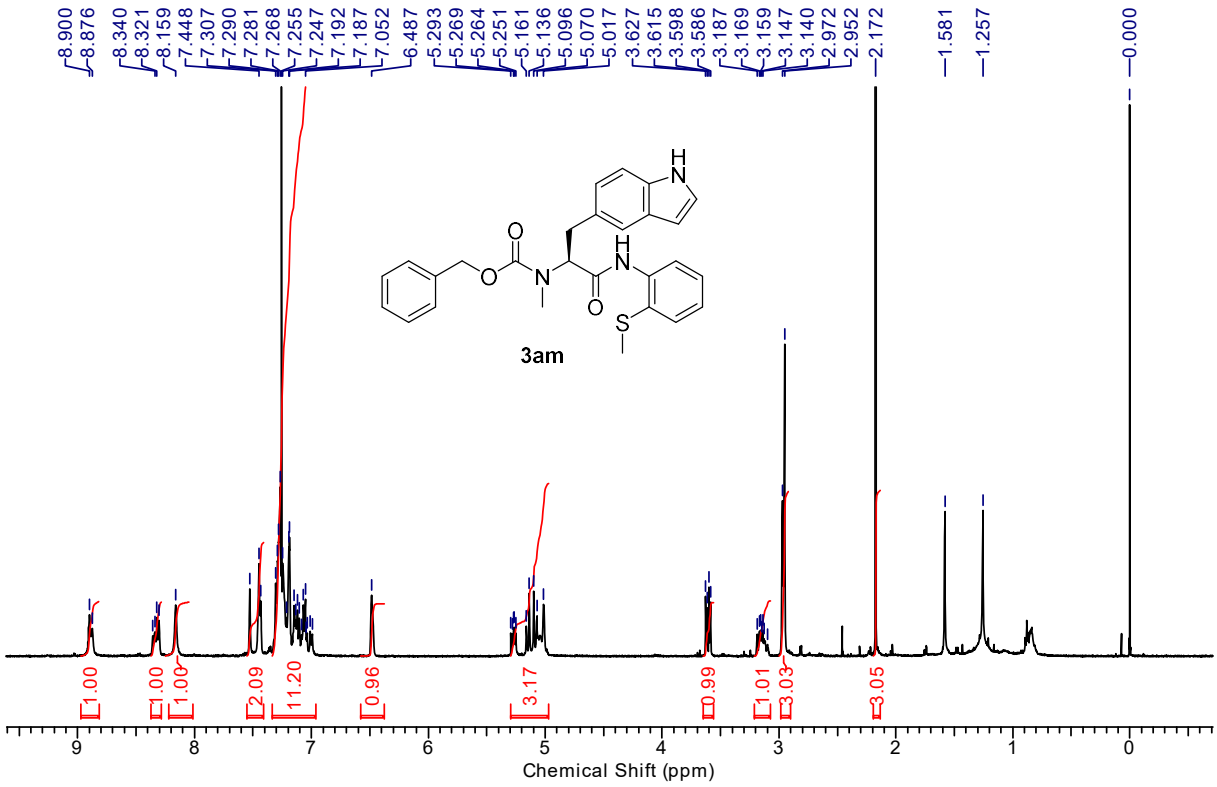


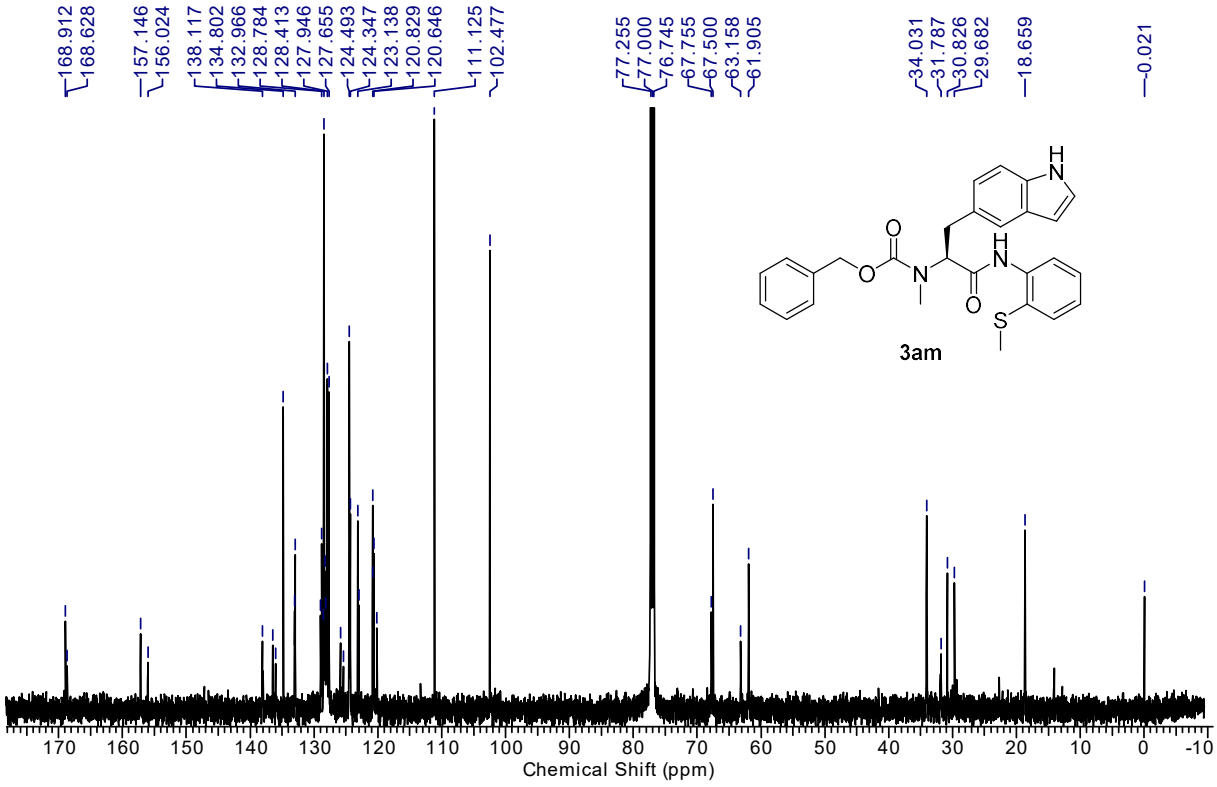
Benzyl (*S*)-(3-(4-bromo-2-fluorophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3al)



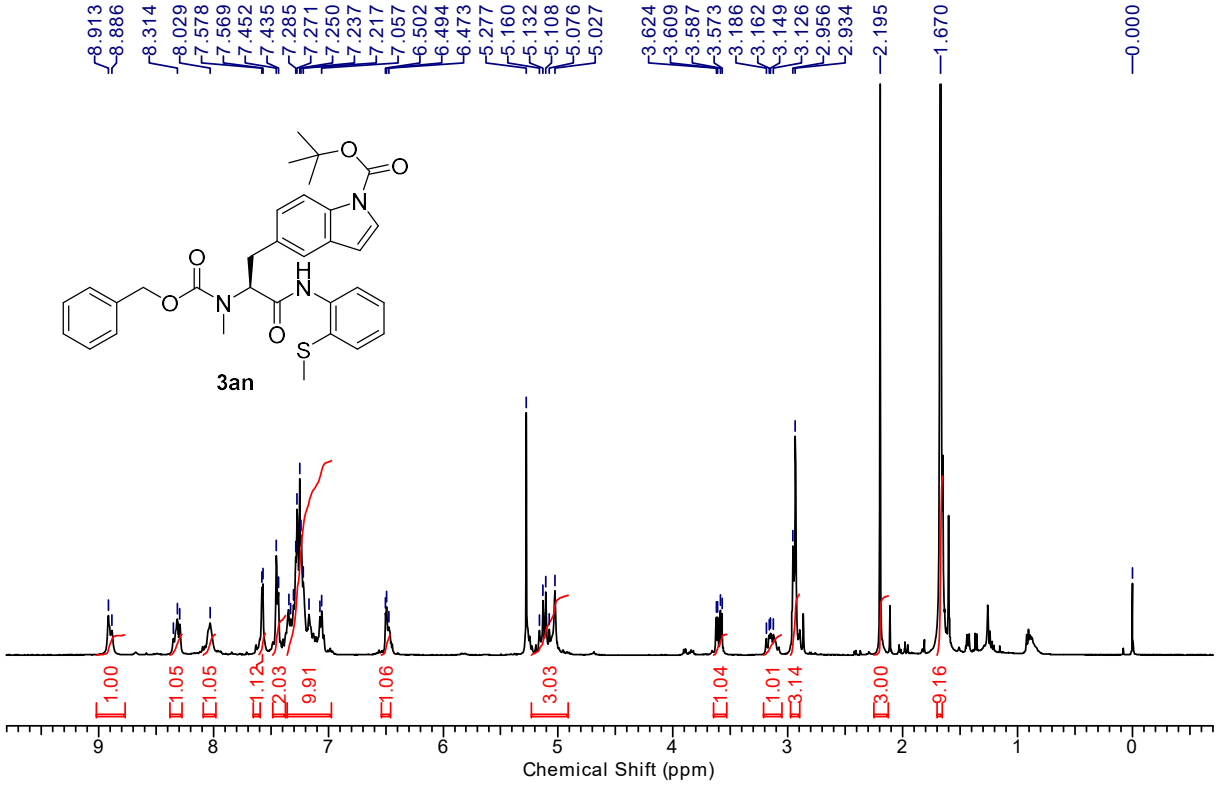


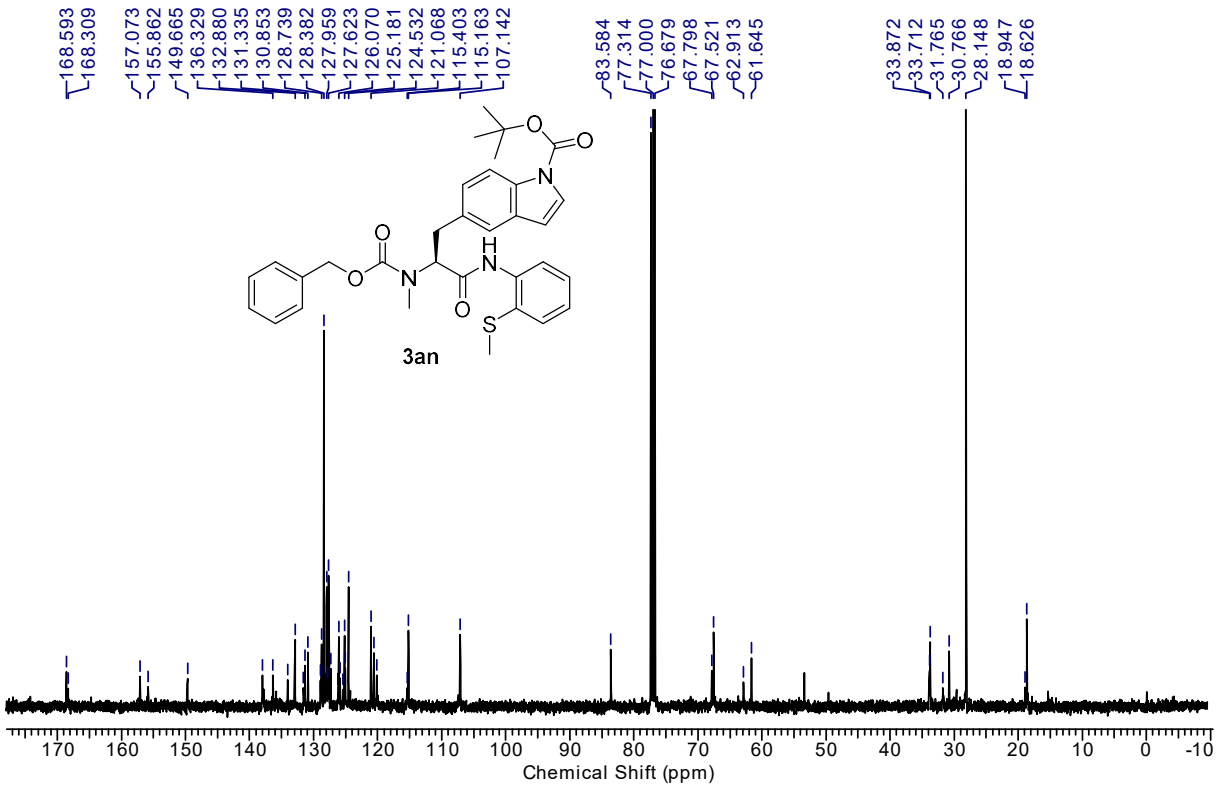
Benzyl (*S*)-(3-(1*H*-indol-5-yl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)carbamate (3am)



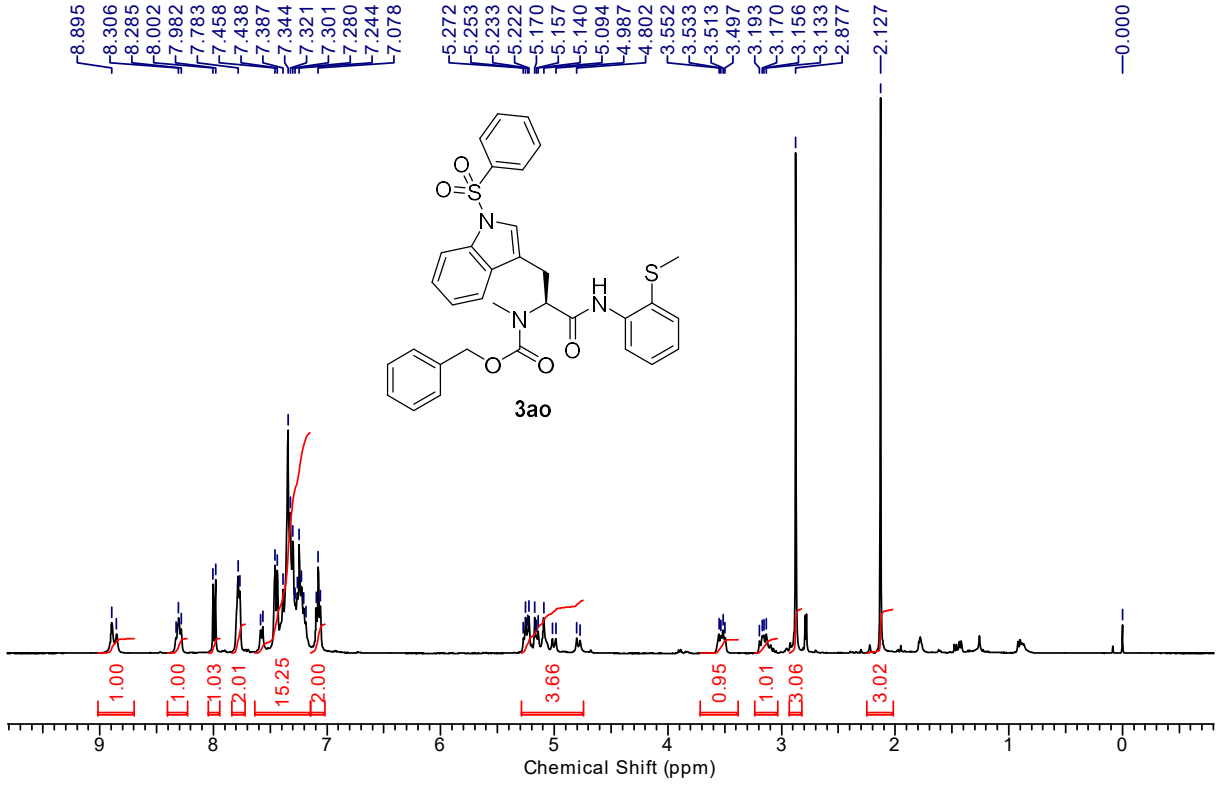


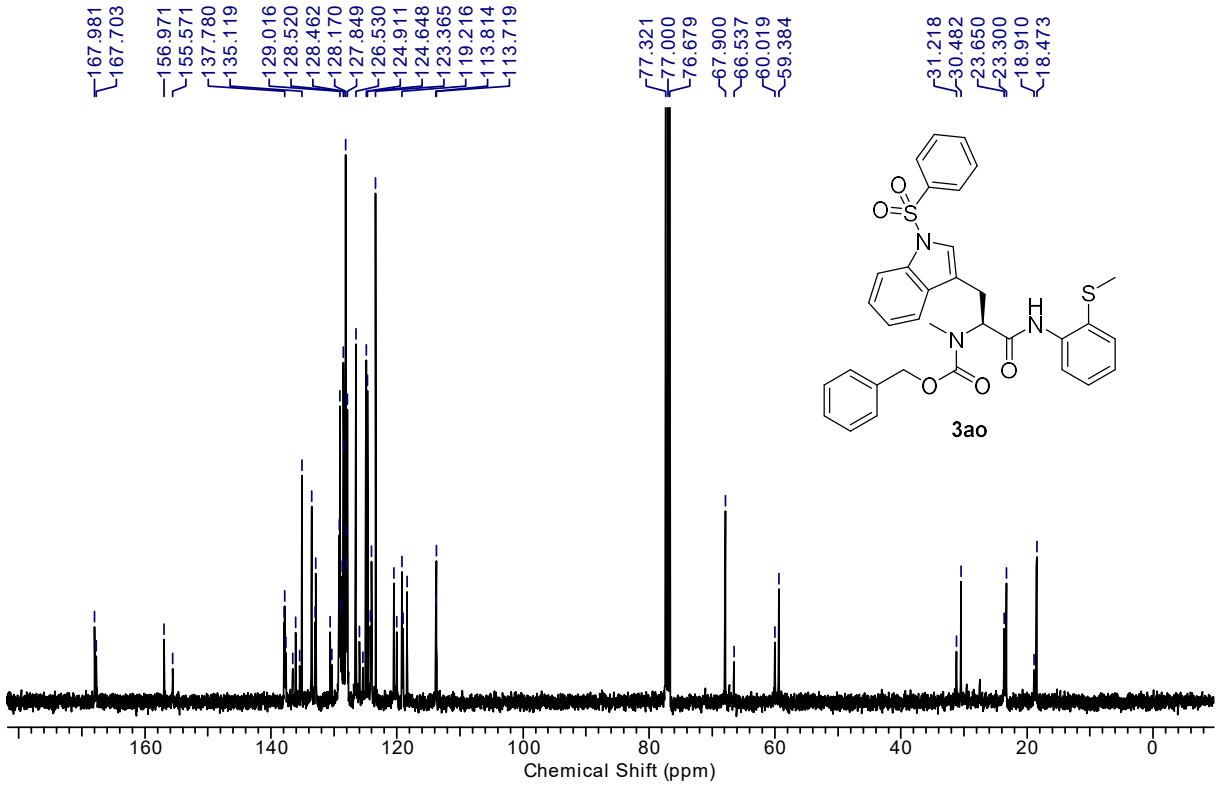
***tert*-Butyl (*S*)-5-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-1*H*-indole-1-carboxylate (3an)**



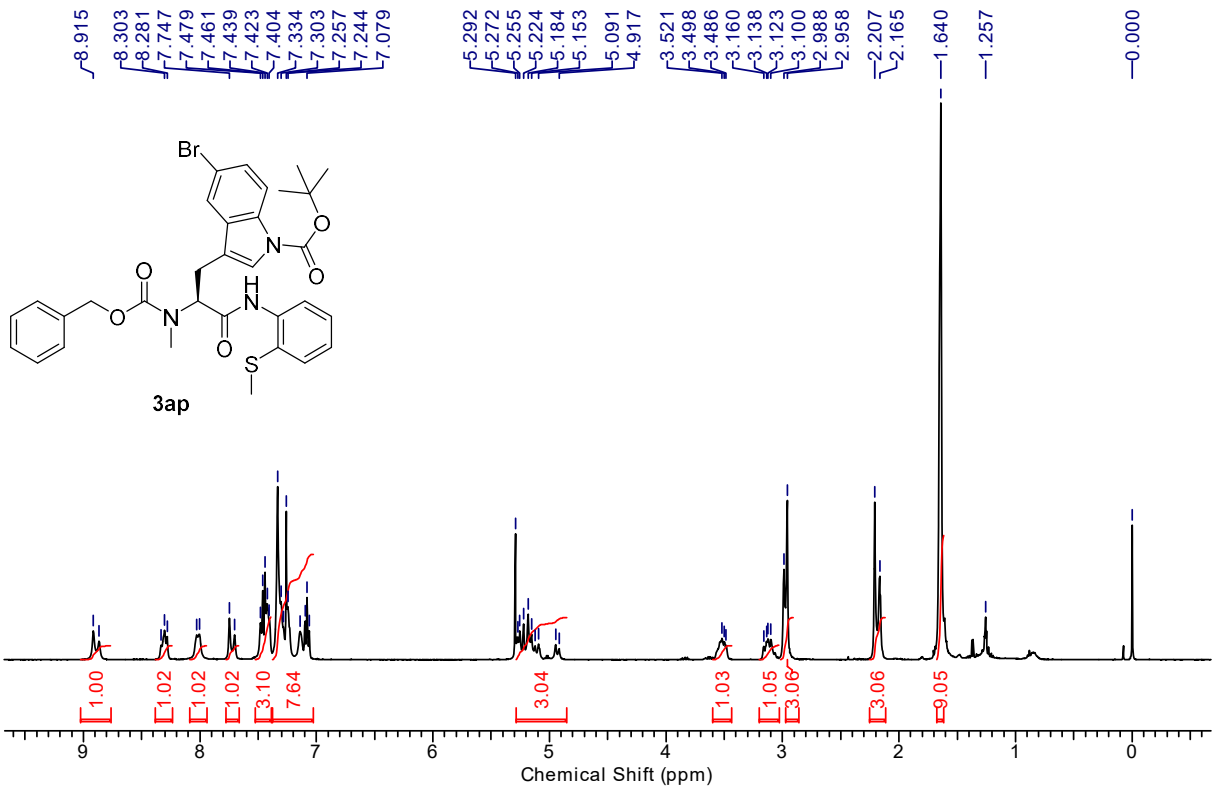


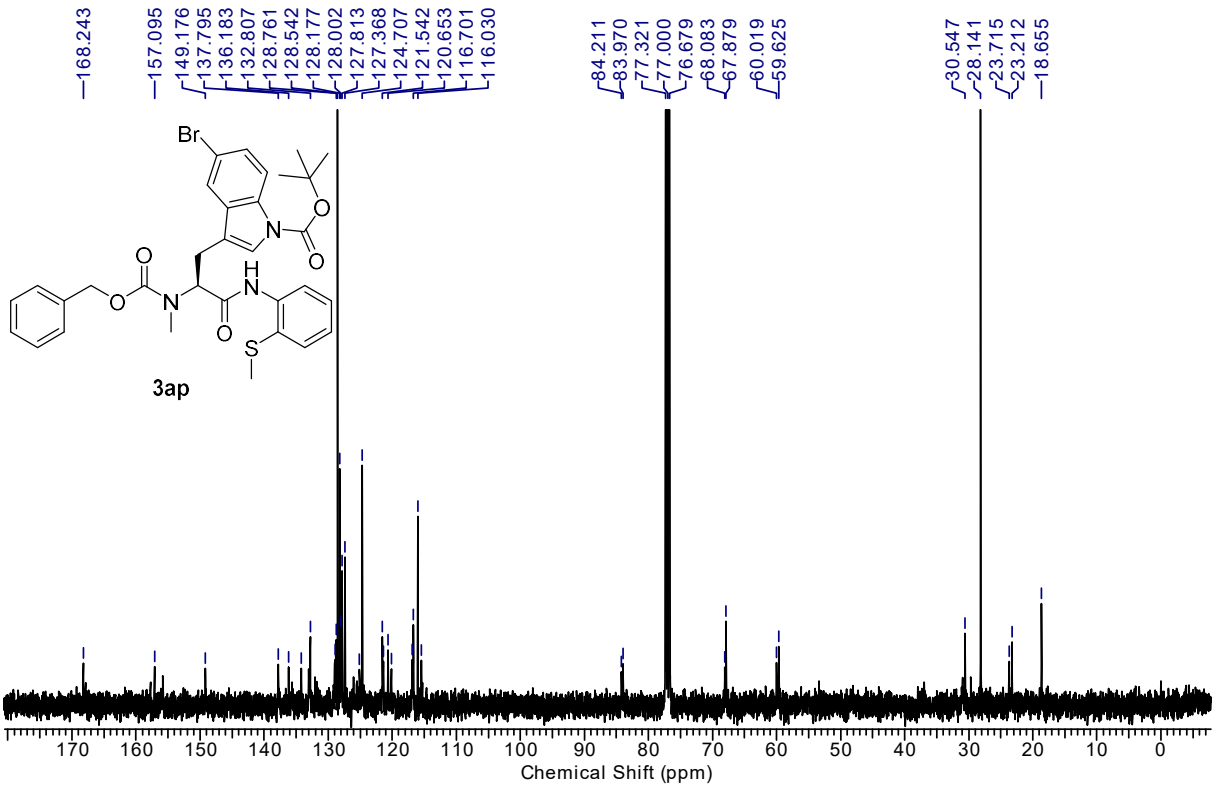
Benzyl (*S*)-methyl(1-((2-(methylthio)phenyl)amino)-1-oxo-3-(1-(phenylsulfonyl)-1*H*-indol-3-yl) propan-2-yl)carbamate (3ao)



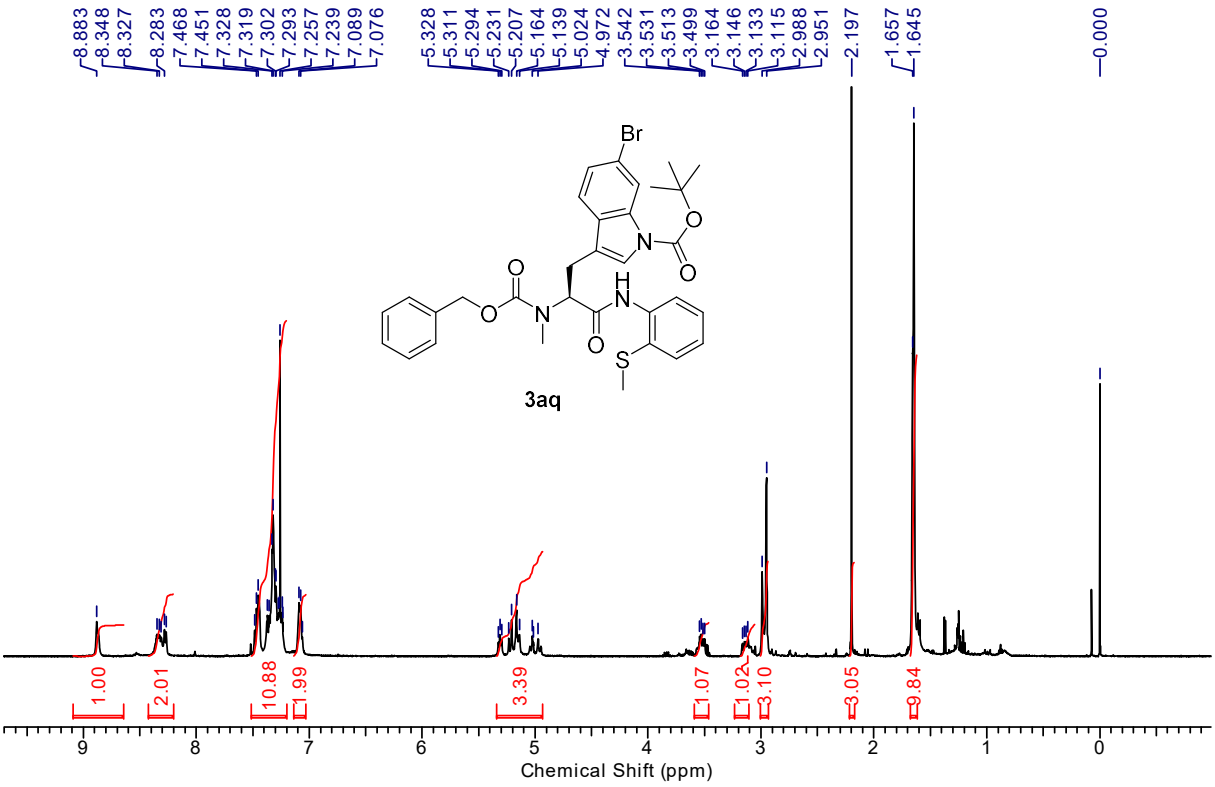


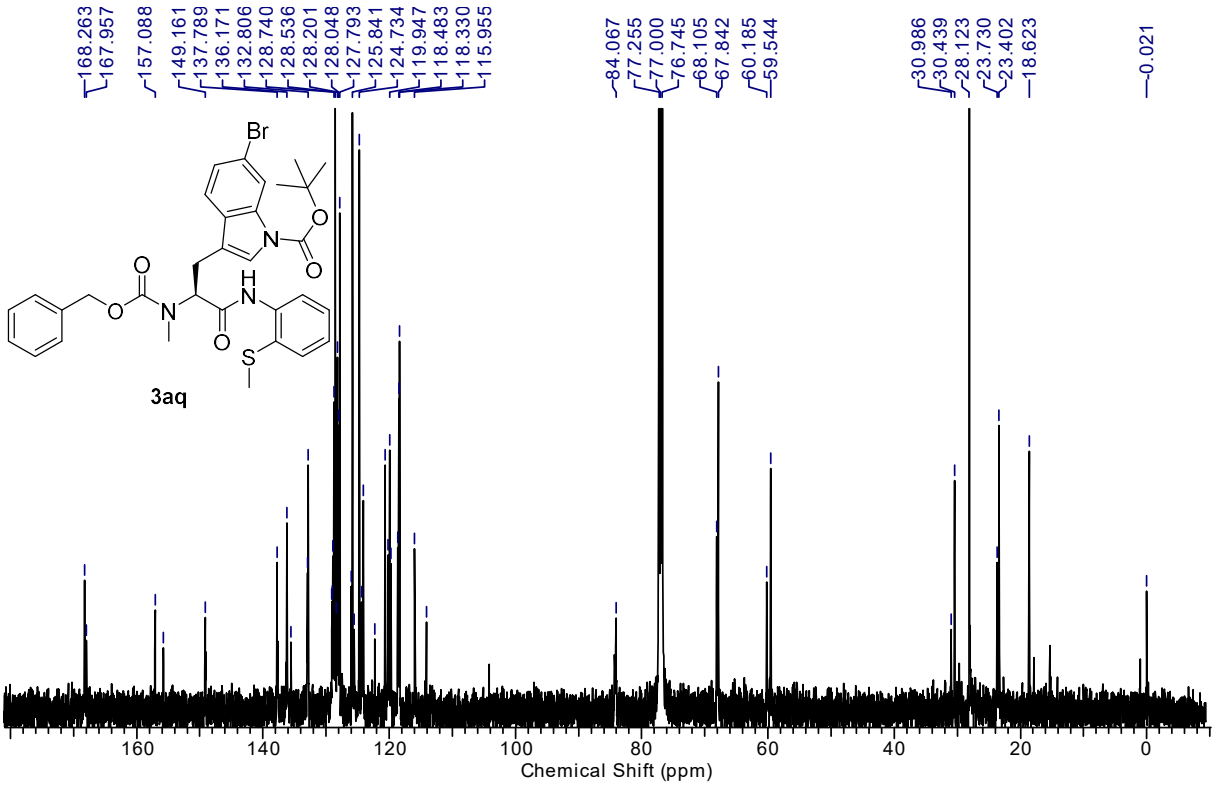
***tert*-Butyl (*S*)-3-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-5-bromo-1*H*-indole-1-carboxylate (3ap)**



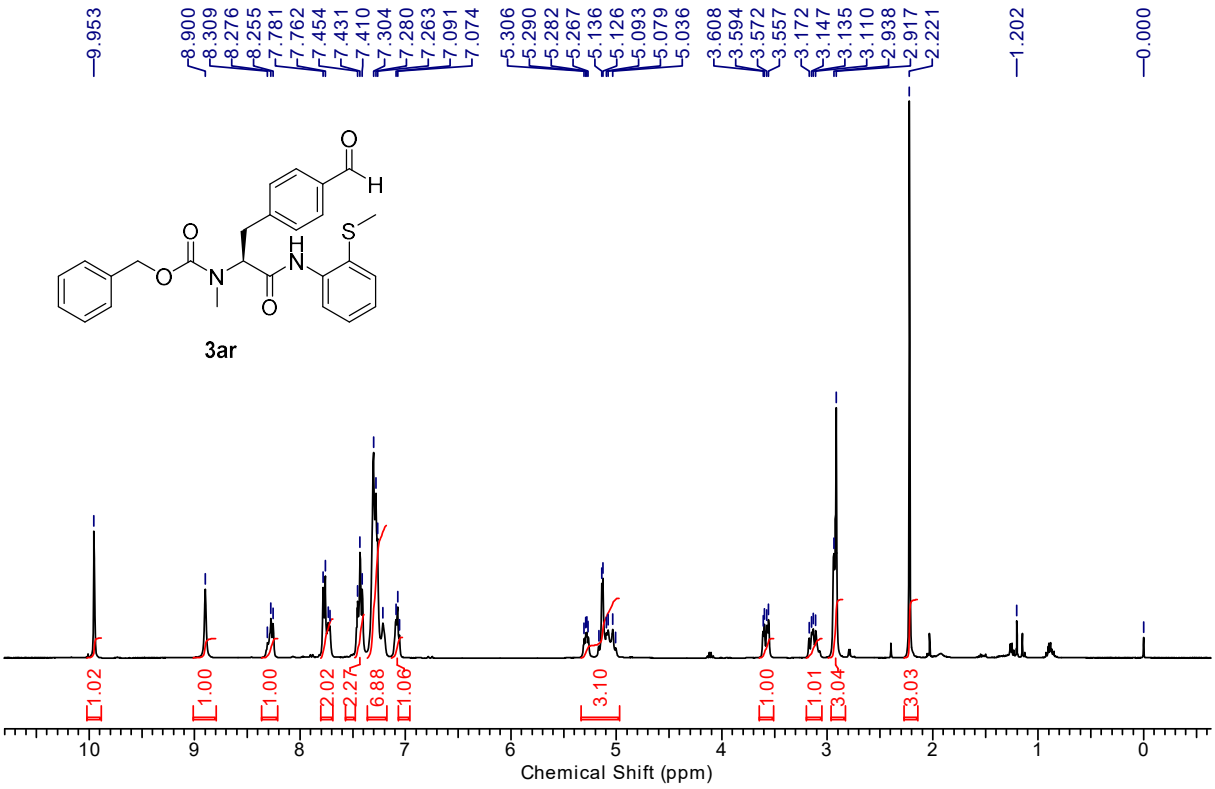


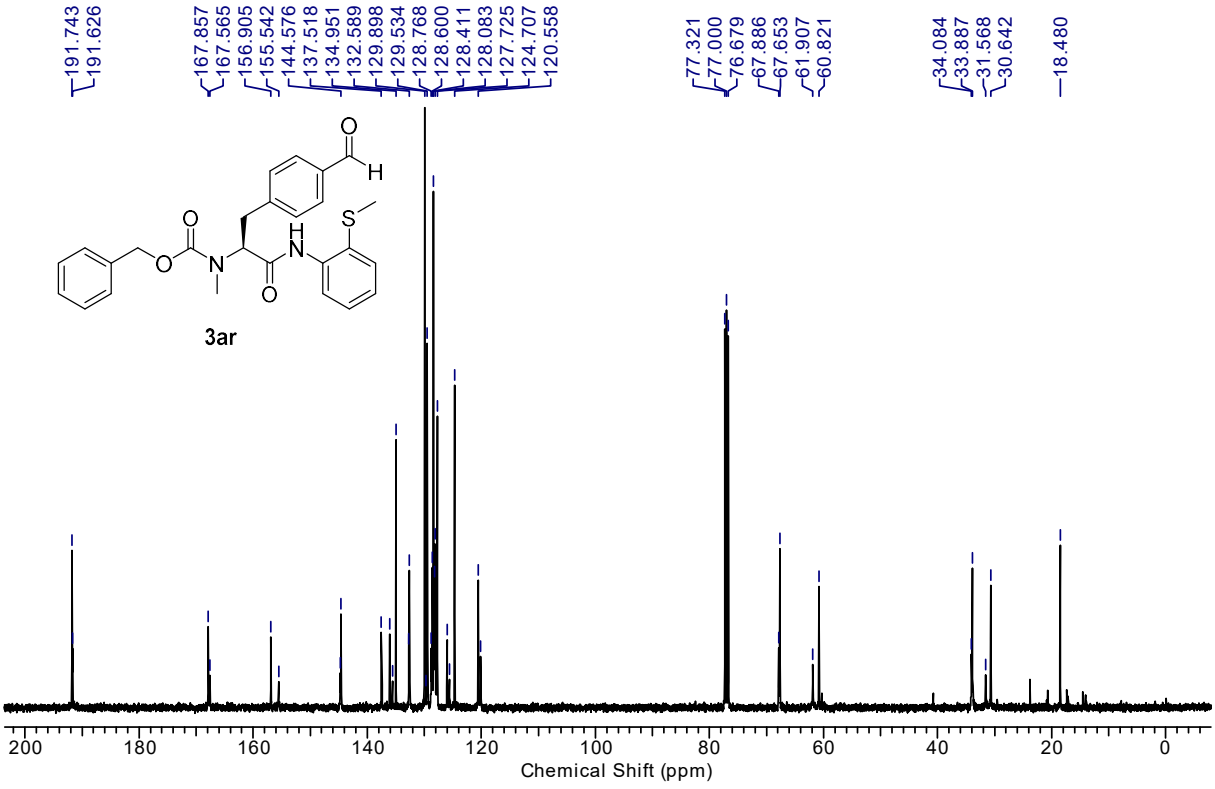
***tert*-Butyl (*S*)-3-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-6-bromo-1*H*-indole-1-carboxylate (3aq)**



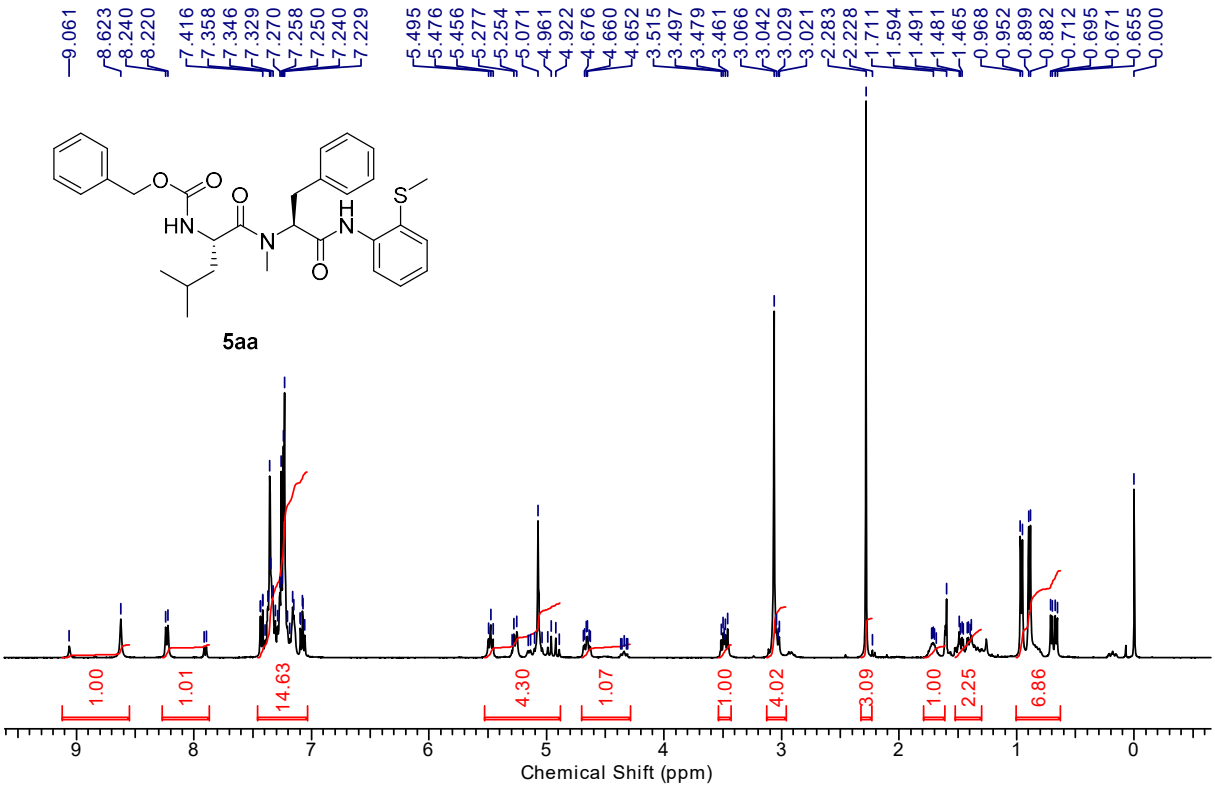


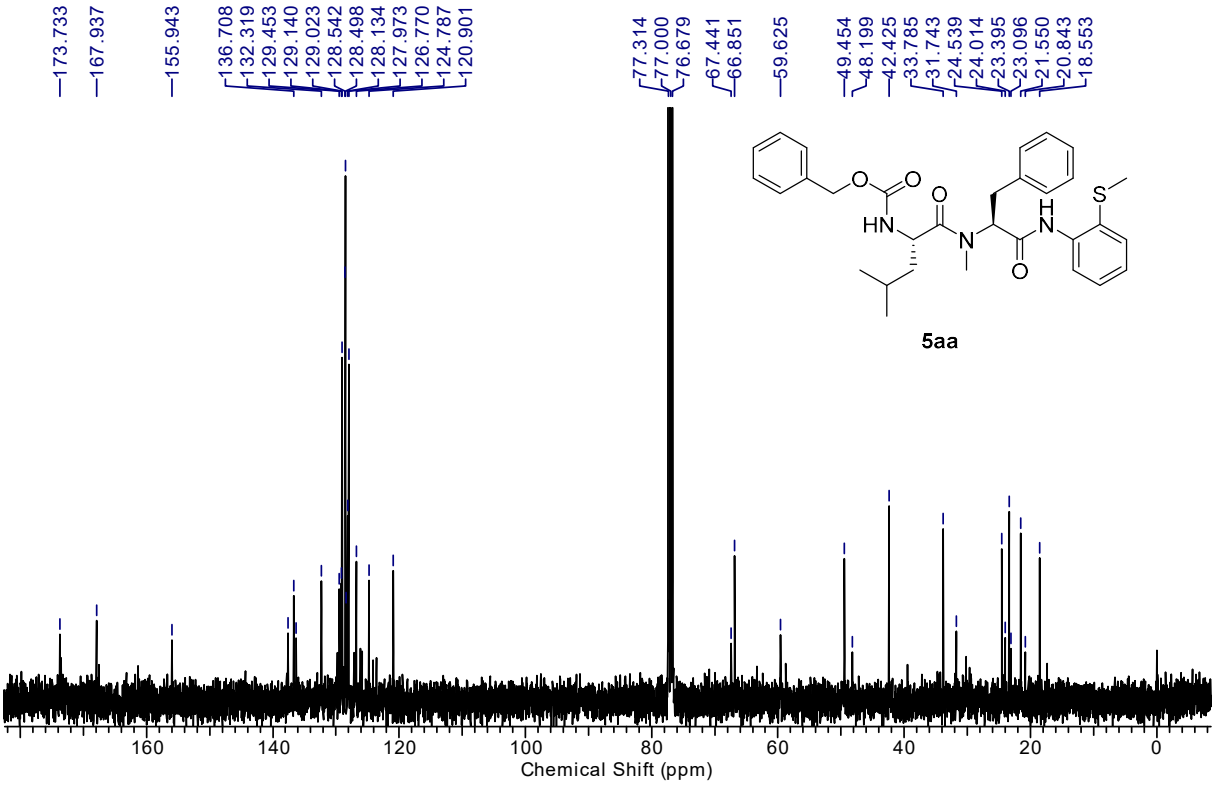
Benzyl (*S*)-(3-(4-formylphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl) carbamate (3ar)



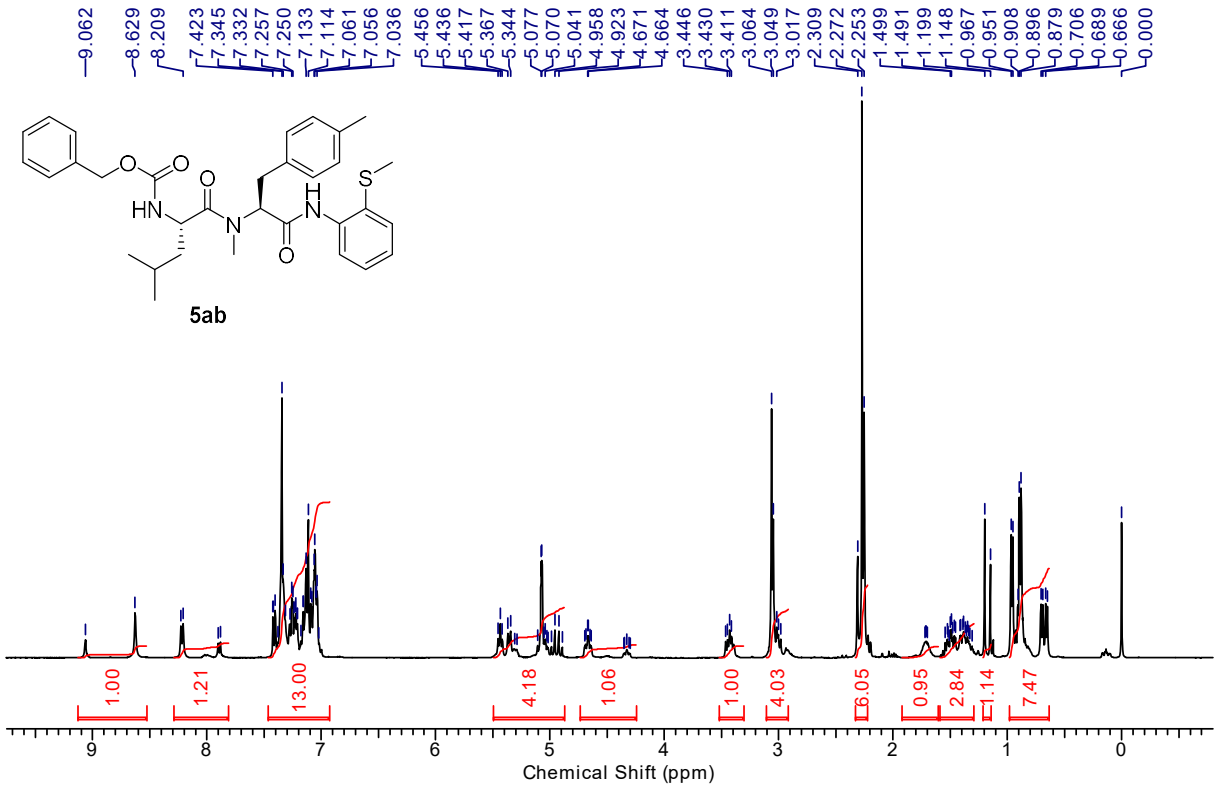


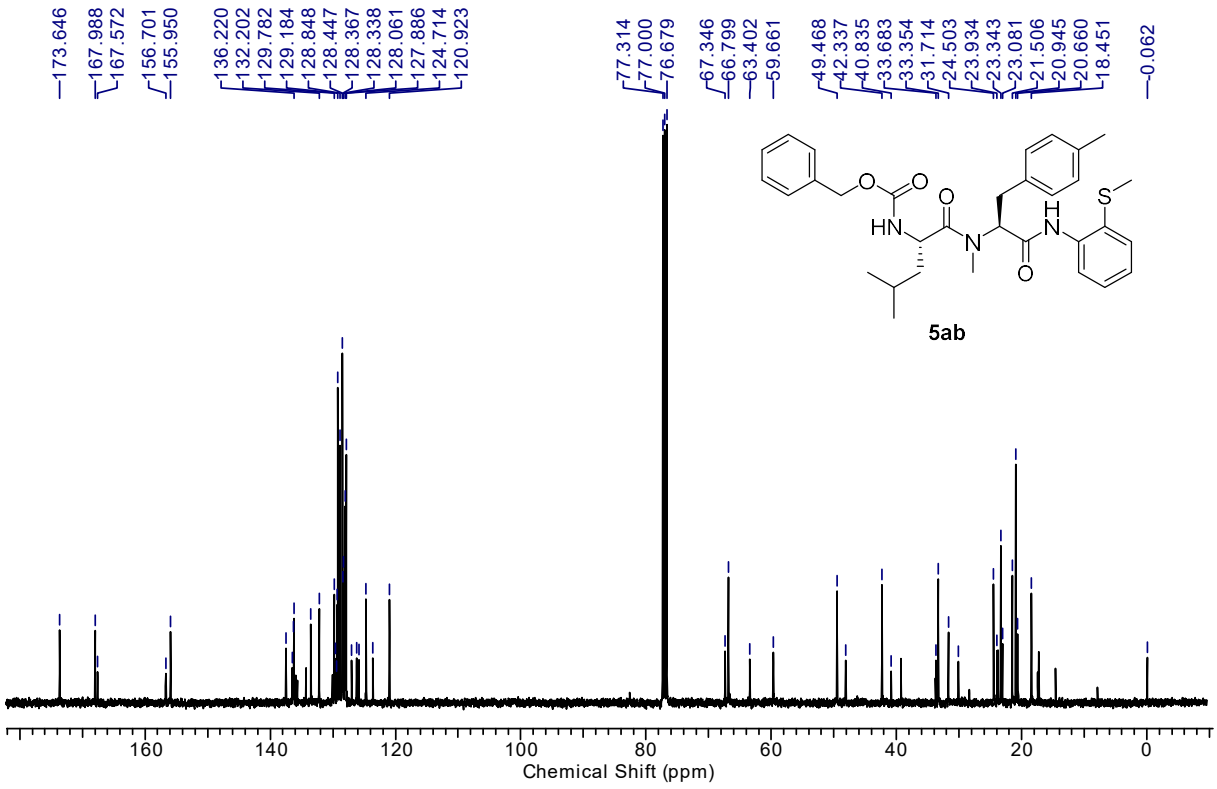
Benzyl ((*S*)-4-methyl-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-1-oxo-3-phenylpropan-2-yl) amino)-1-oxopentan-2-yl)carbamate (5aa)



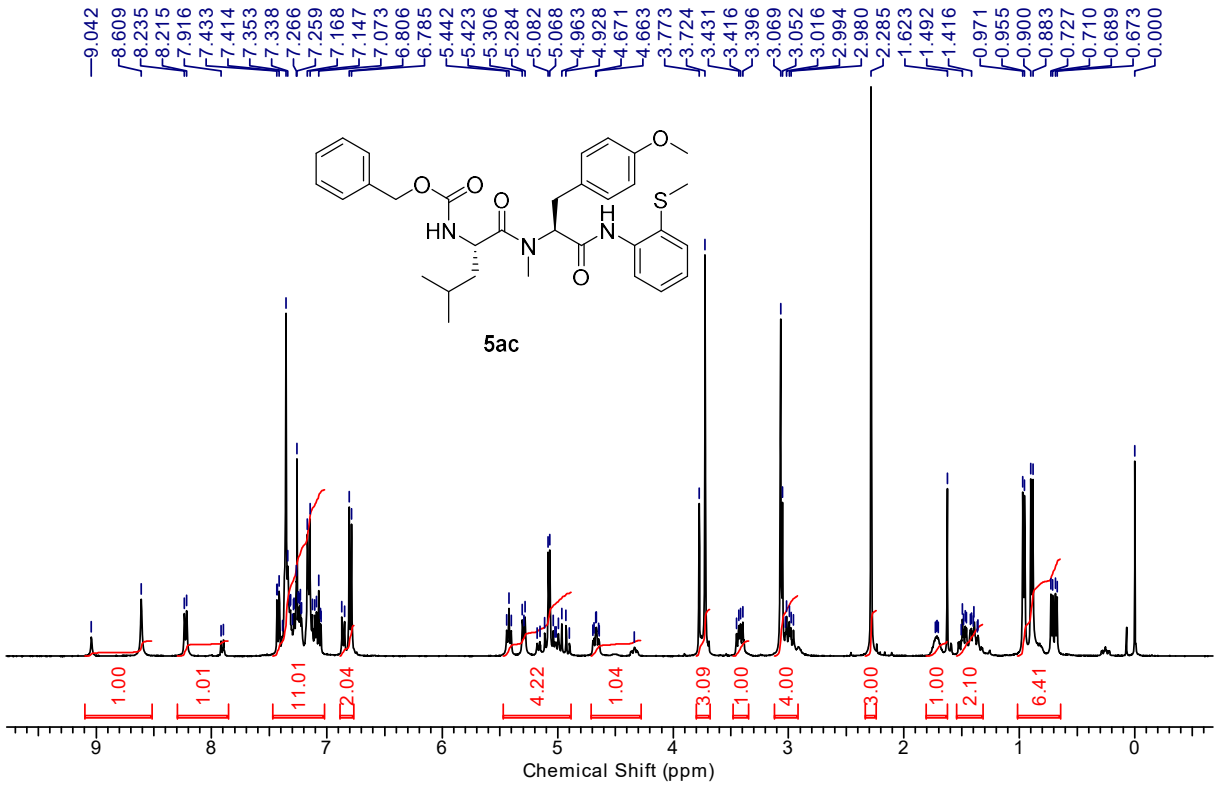


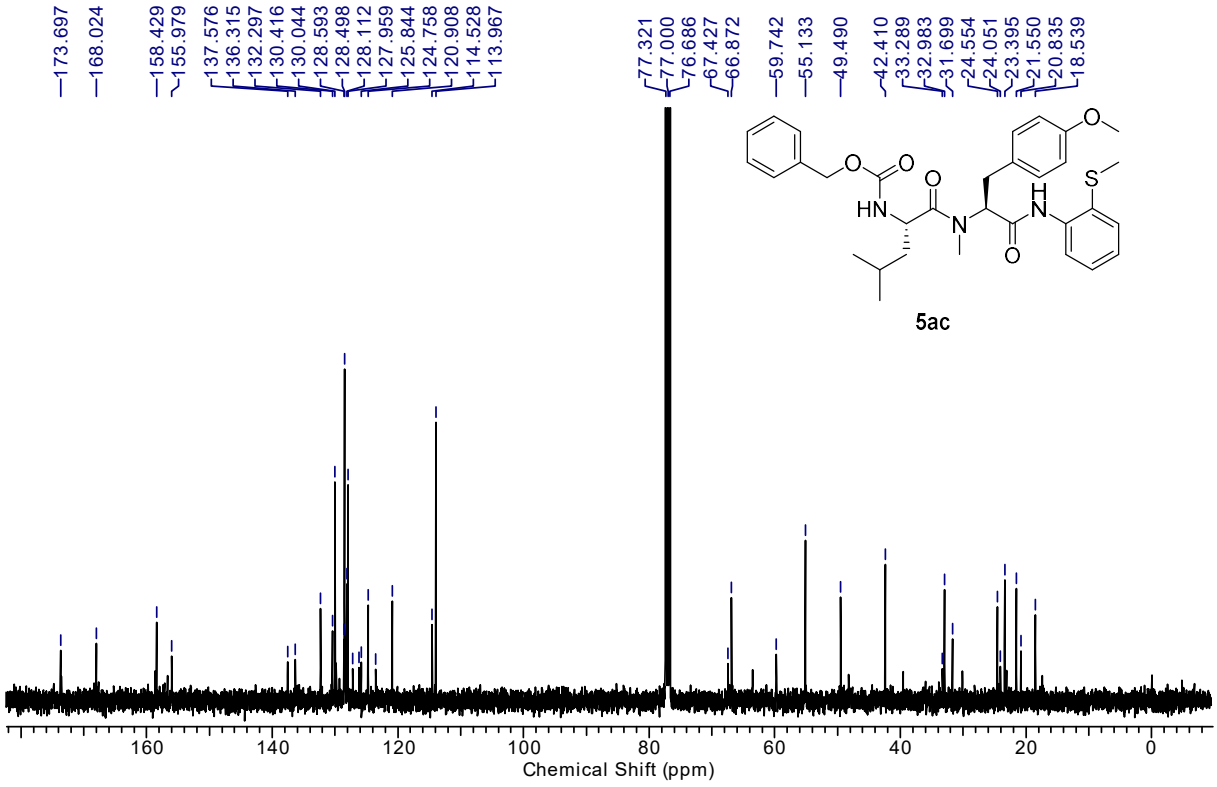
Benzyl ((*S*)-4-methyl-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-1-oxo-3-(*p*-tolyl)propan-2-yl) amino)-1-oxopentan-2-yl)carbamate (5ab)



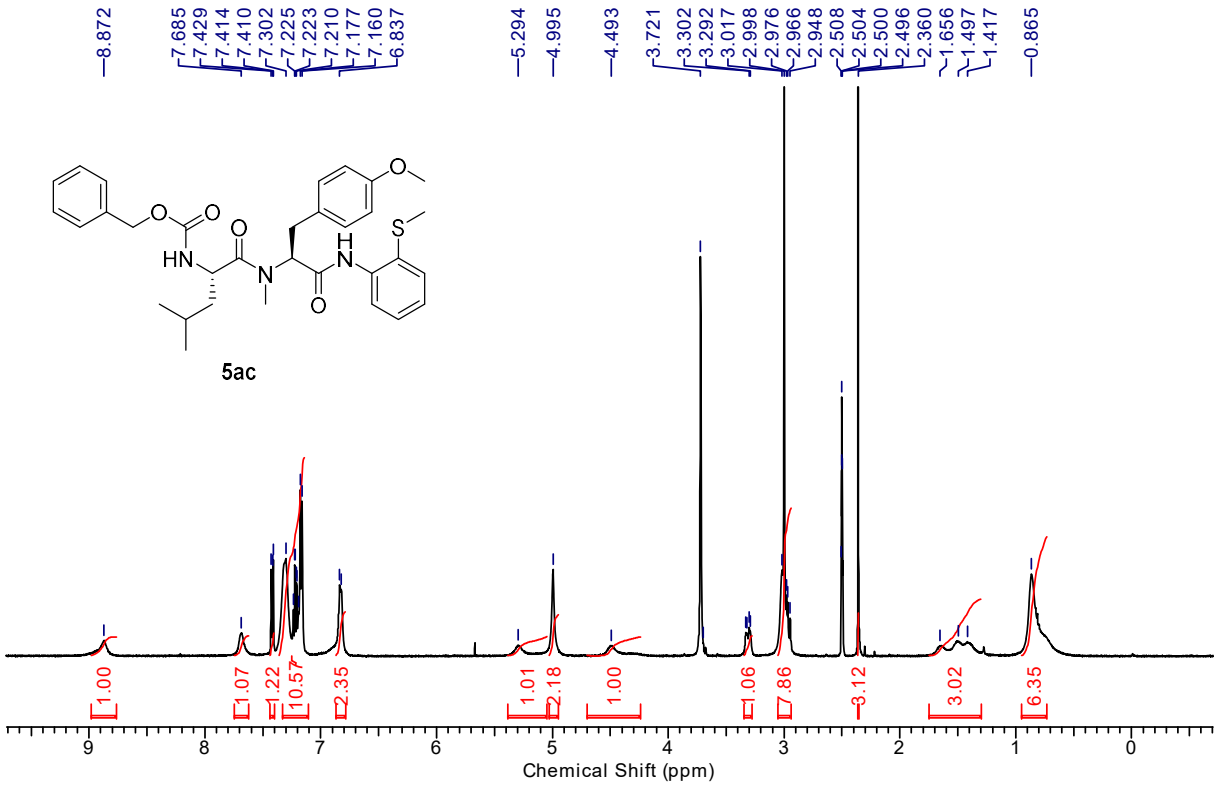


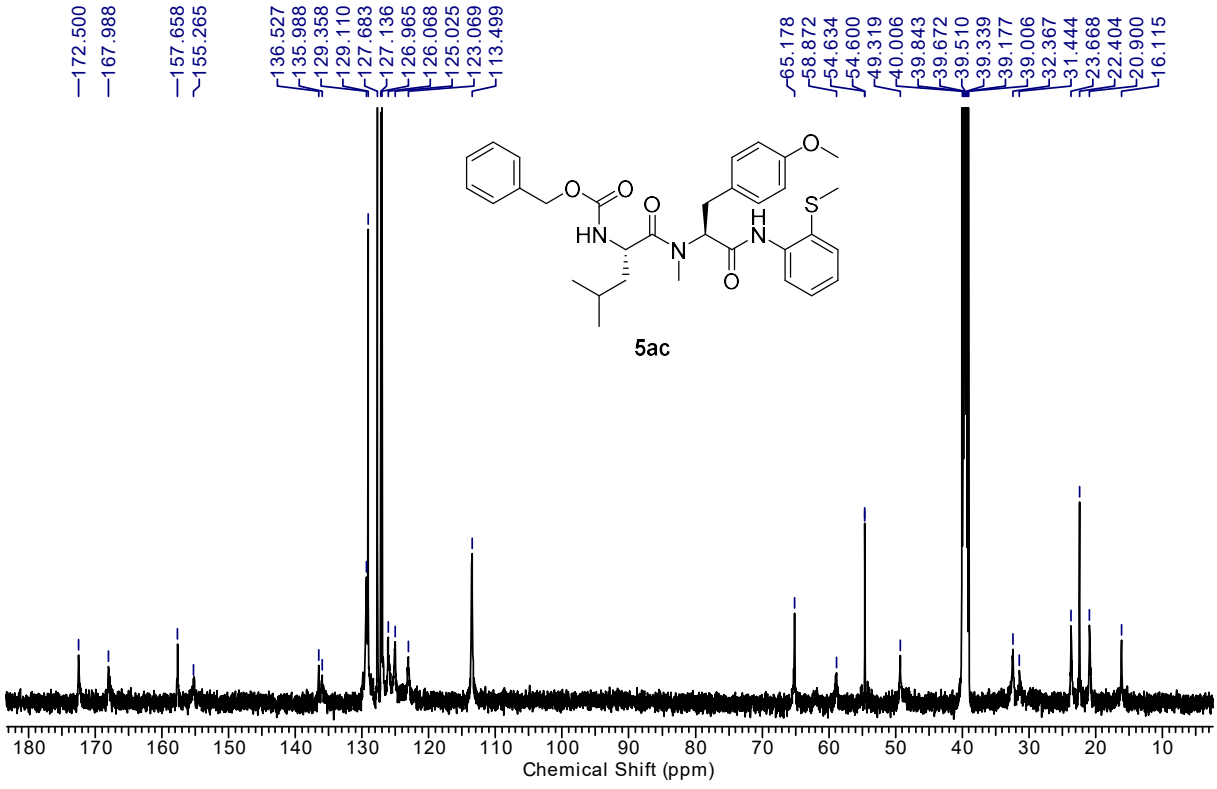
Benzyl ((*S*)-1-(((*S*)-3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate(5ac) ($CDCl_3$)



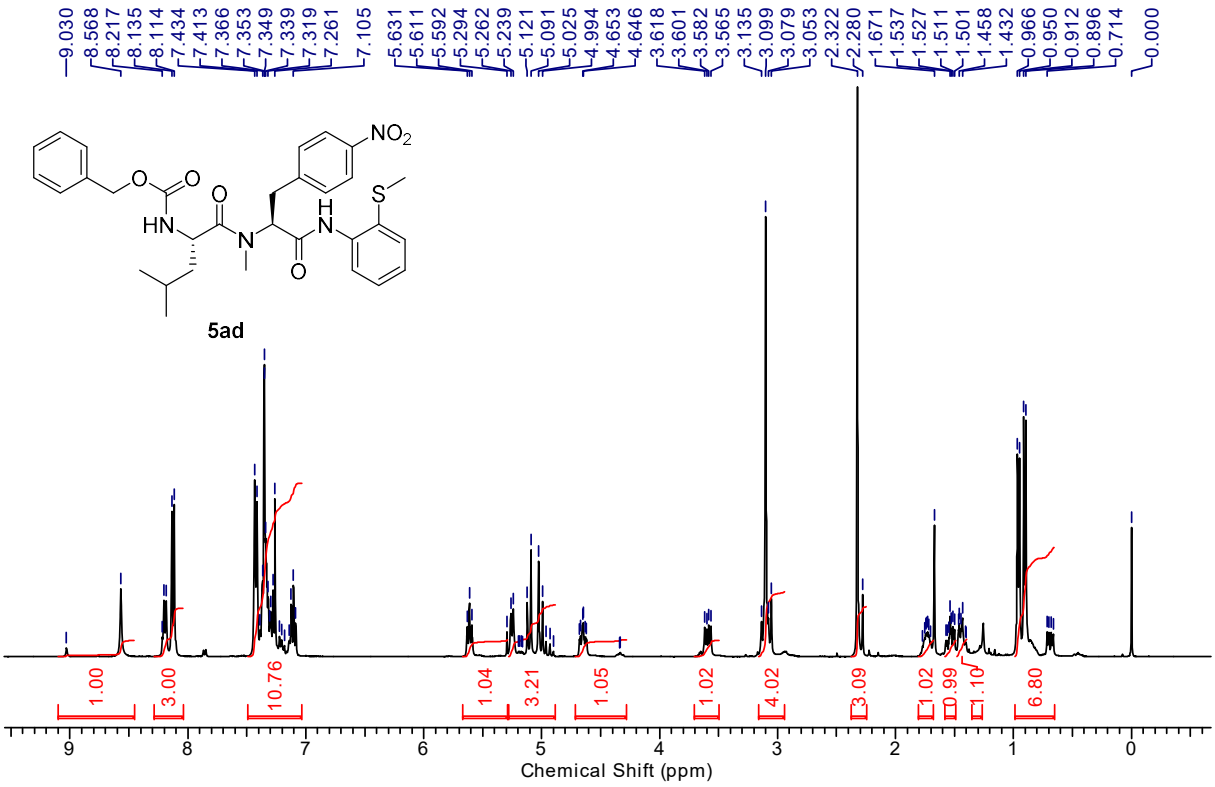


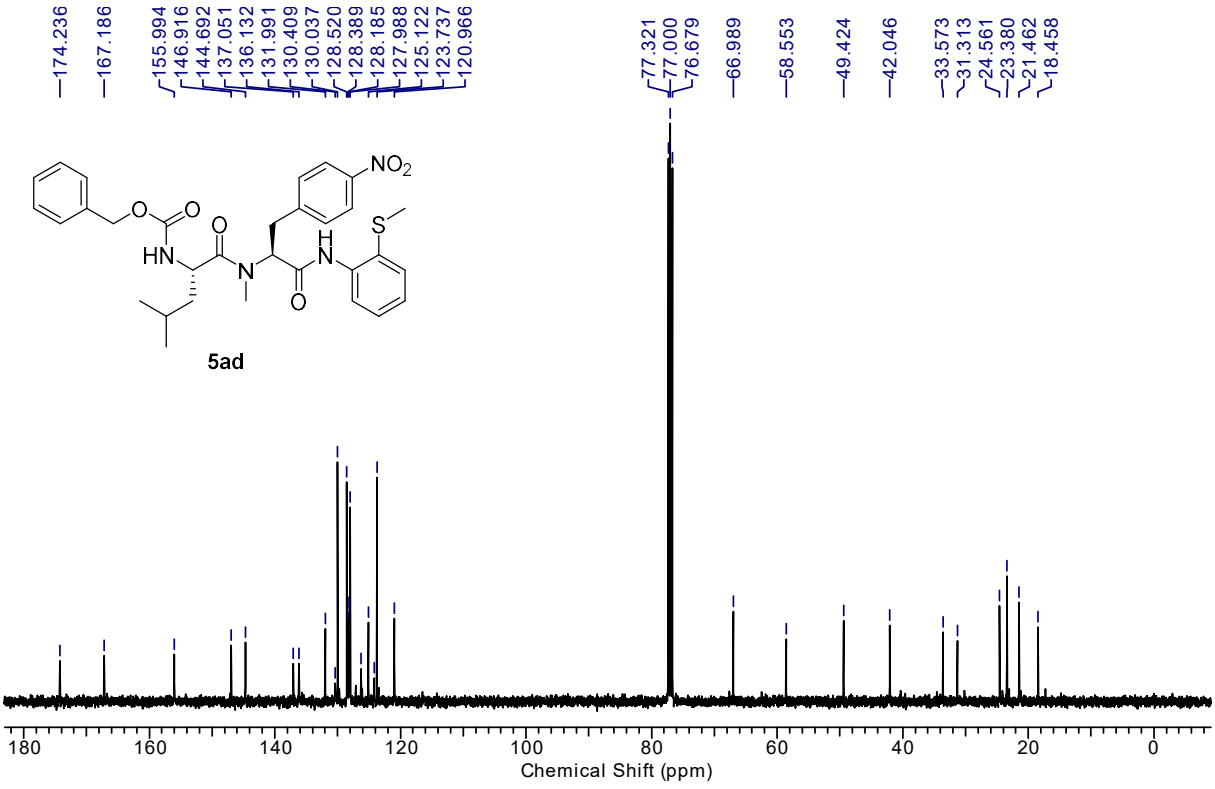
Benzyl ((*S*)-1-(((*S*)-3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate(5ac) (DMSO-d_6 373 K)



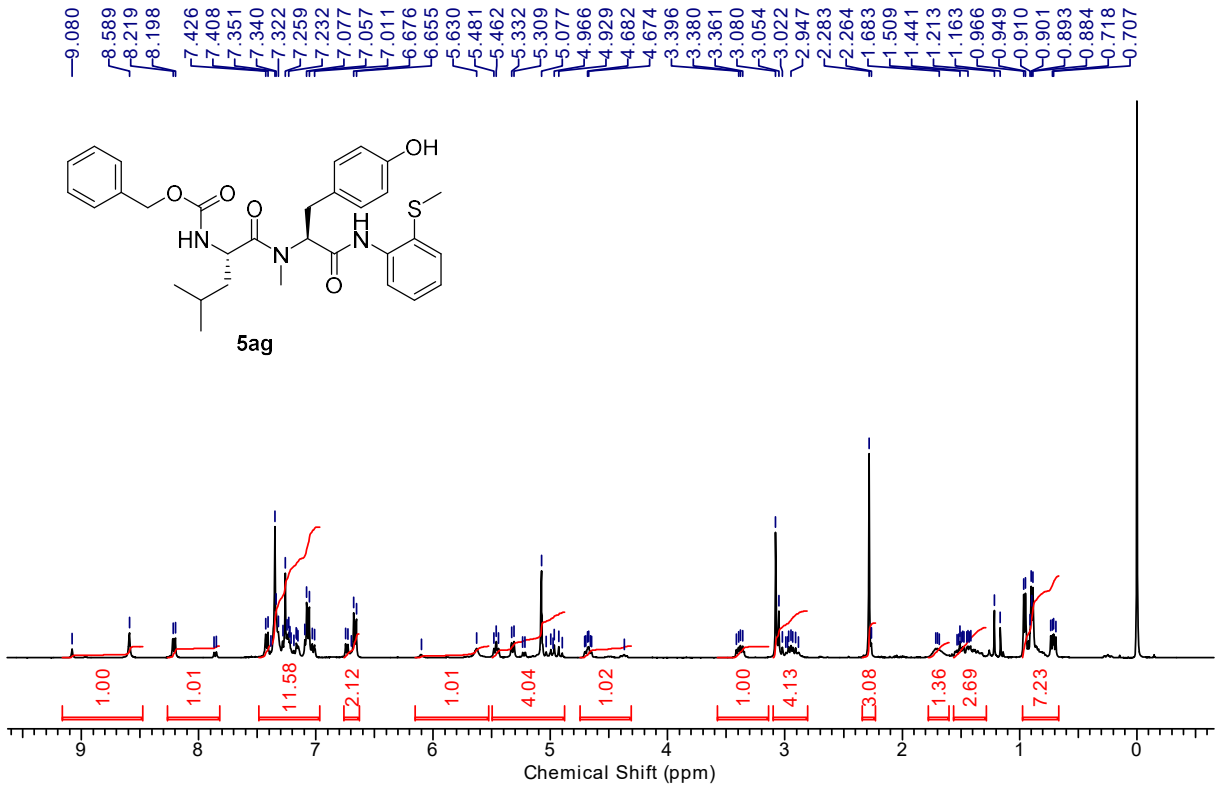


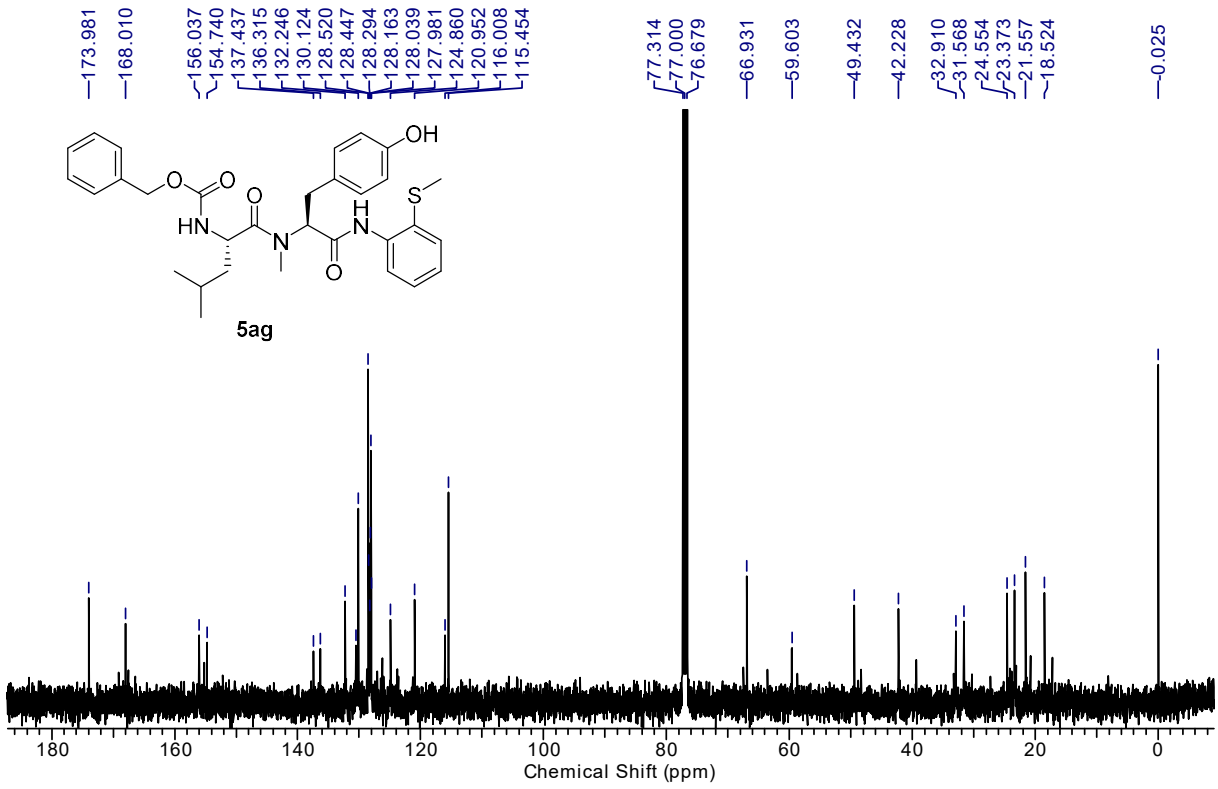
Benzyl ((*S*)-4-methyl-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl)amino)-1-oxopentan-2-yl)carbamate (5ad)



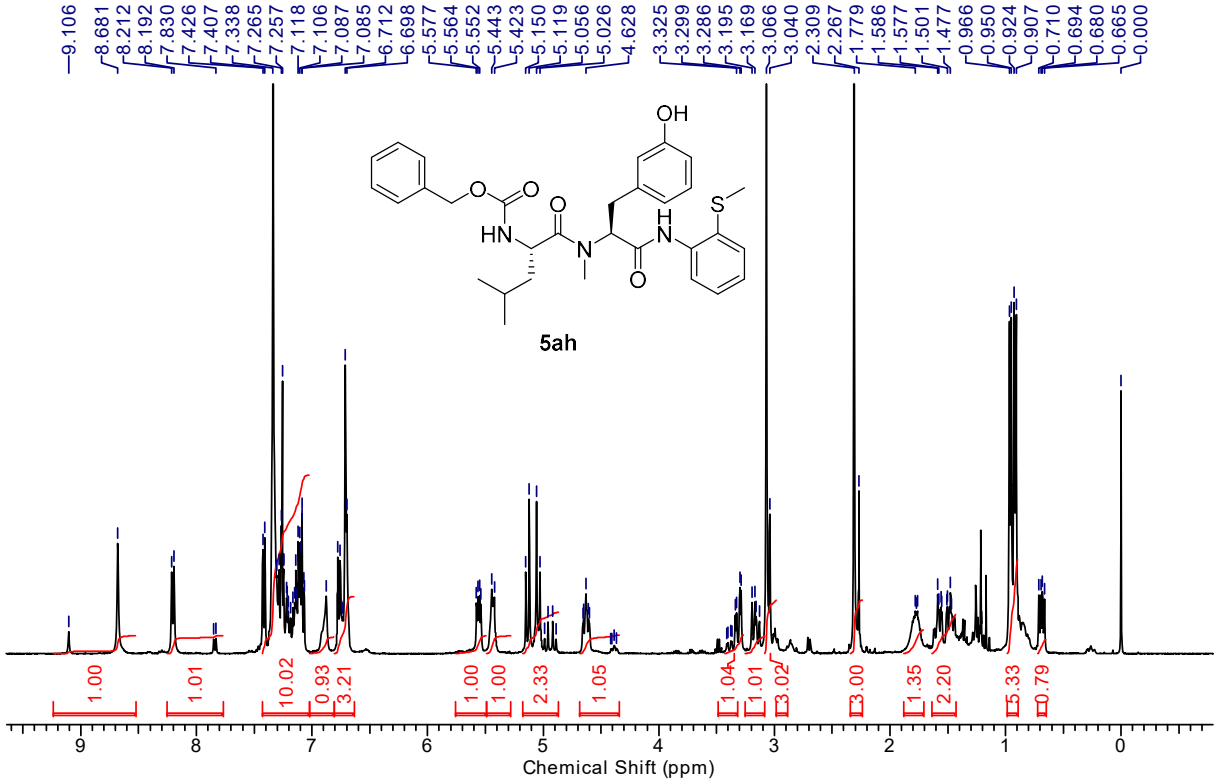


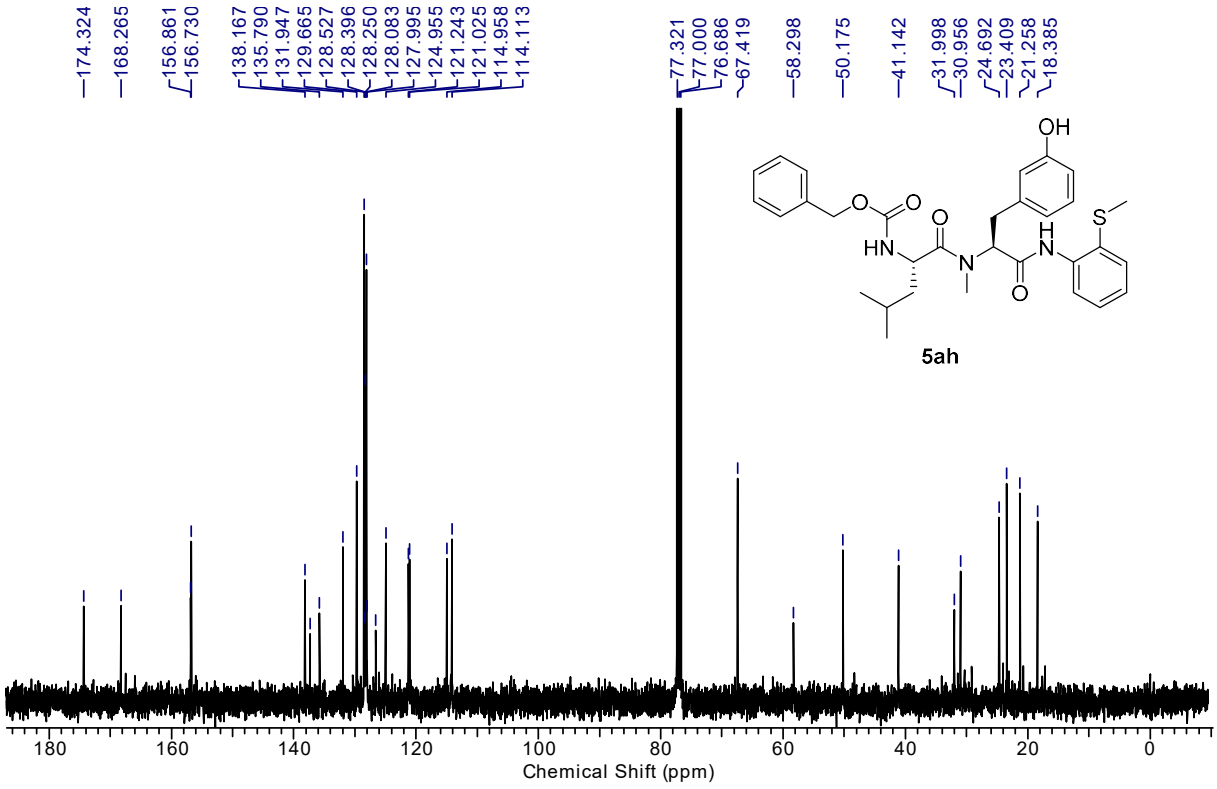
Benzyl ((*S*)-1-(((*S*)-3-(4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5ag)



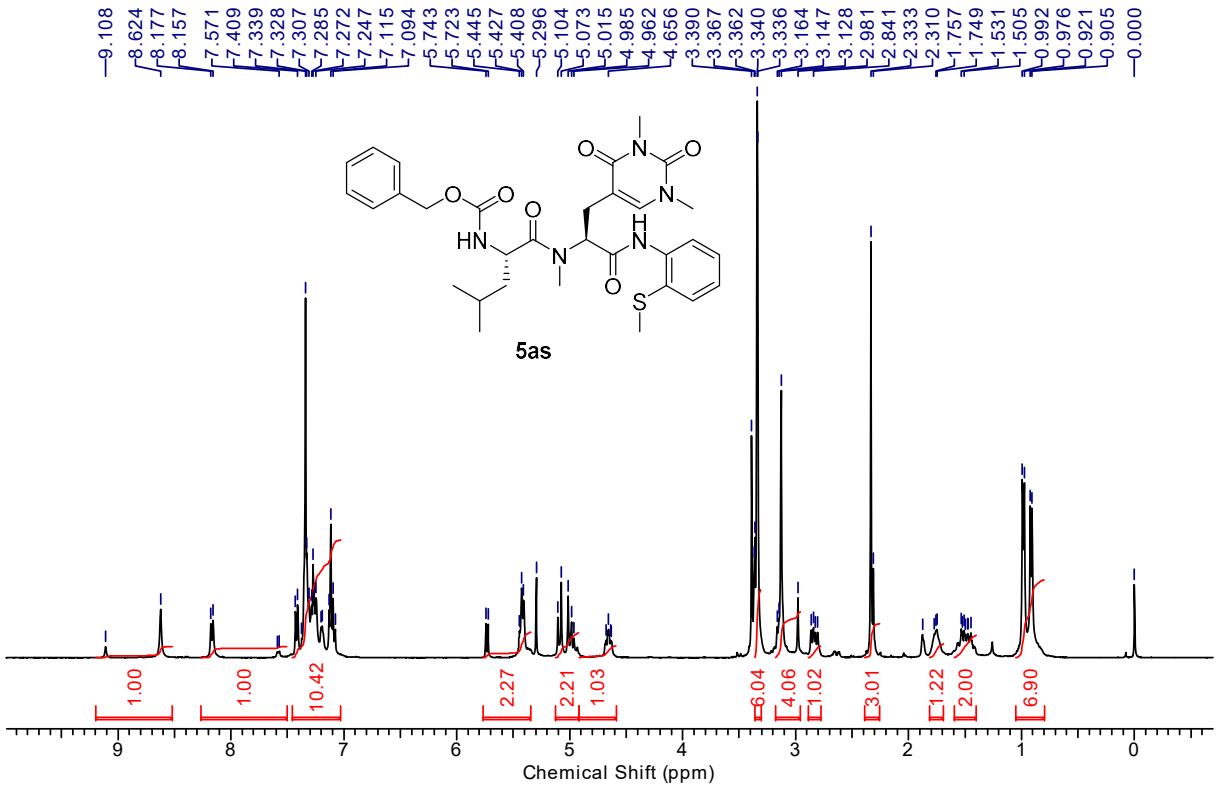


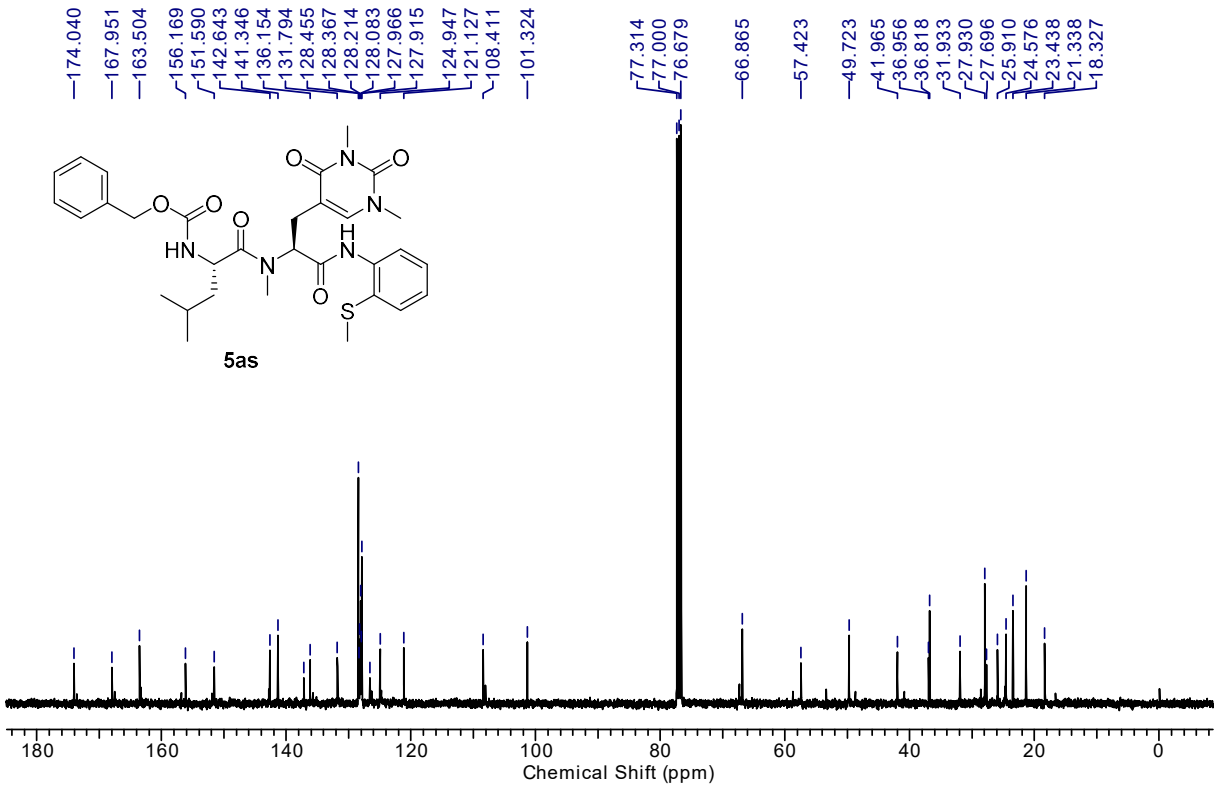
Benzyl ((*S*)-1-(((*S*)-3-(3-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5ah)



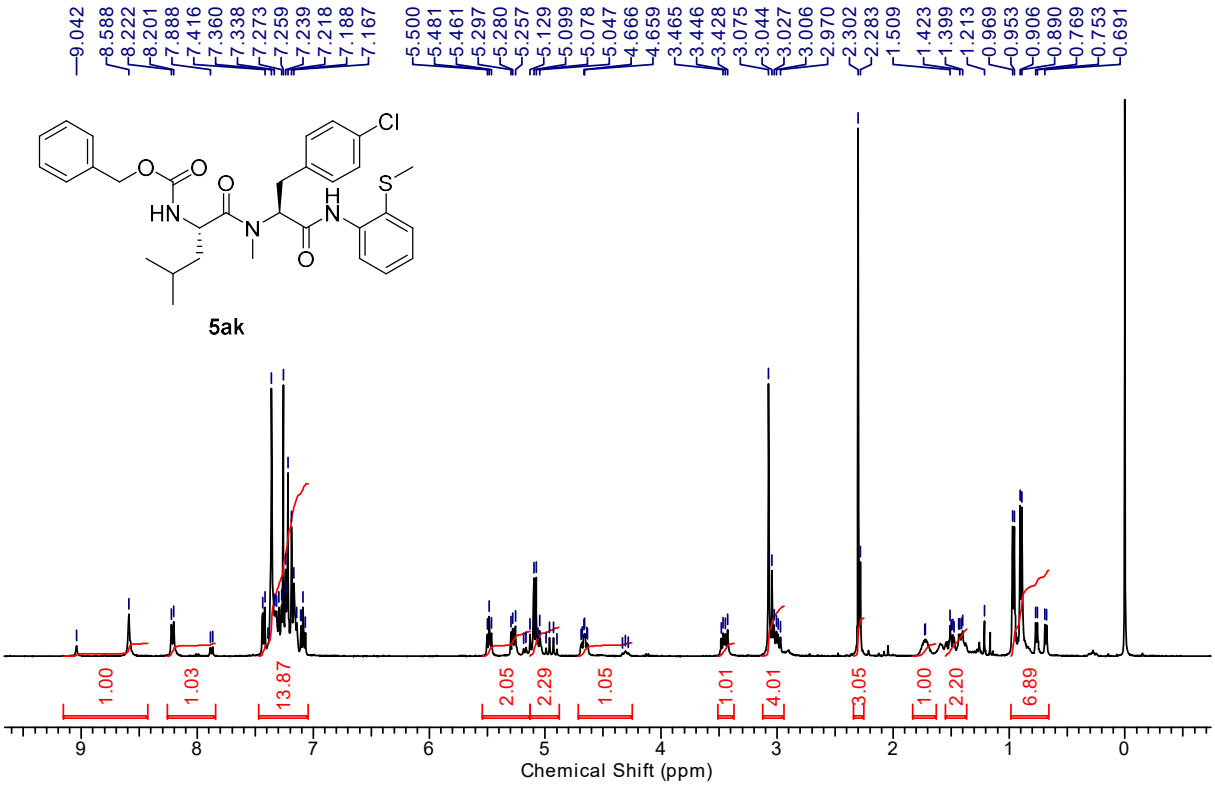


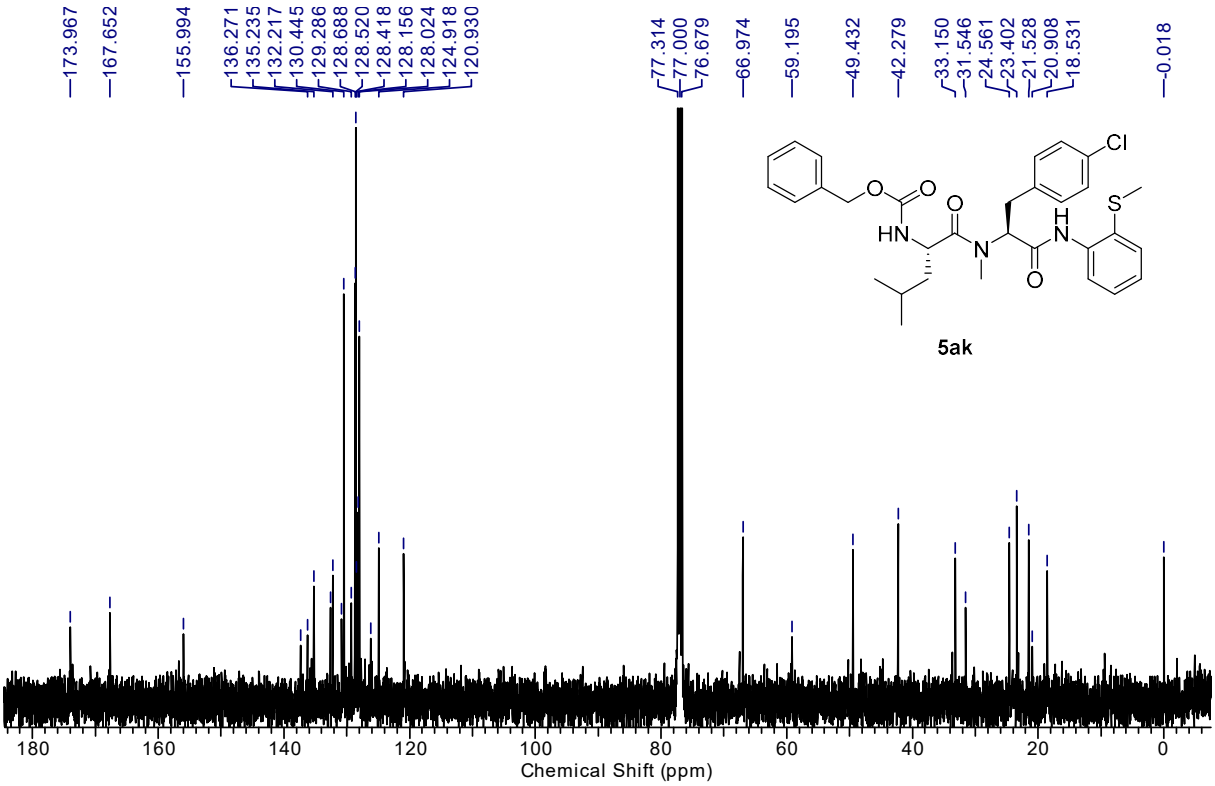
Benzyl ((*S*)-1-(((*S*)-3-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1-((2-(methylthio) phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5as)



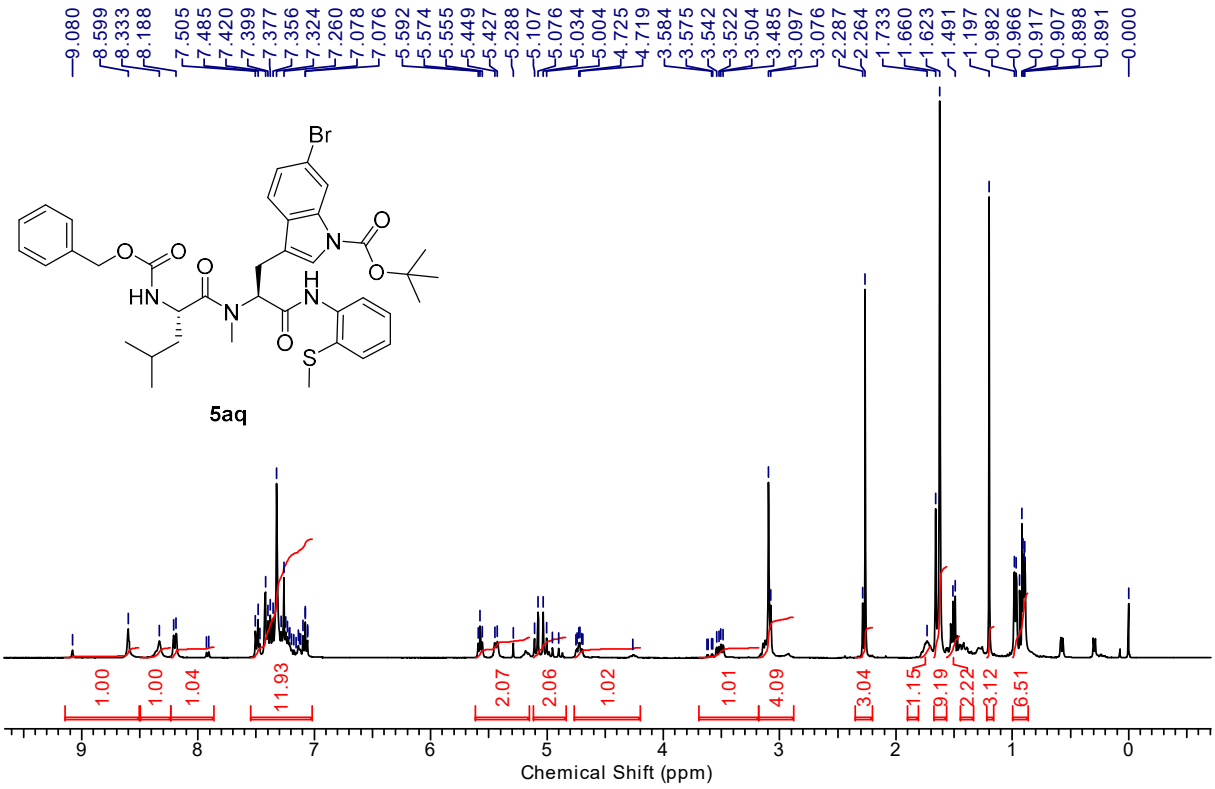


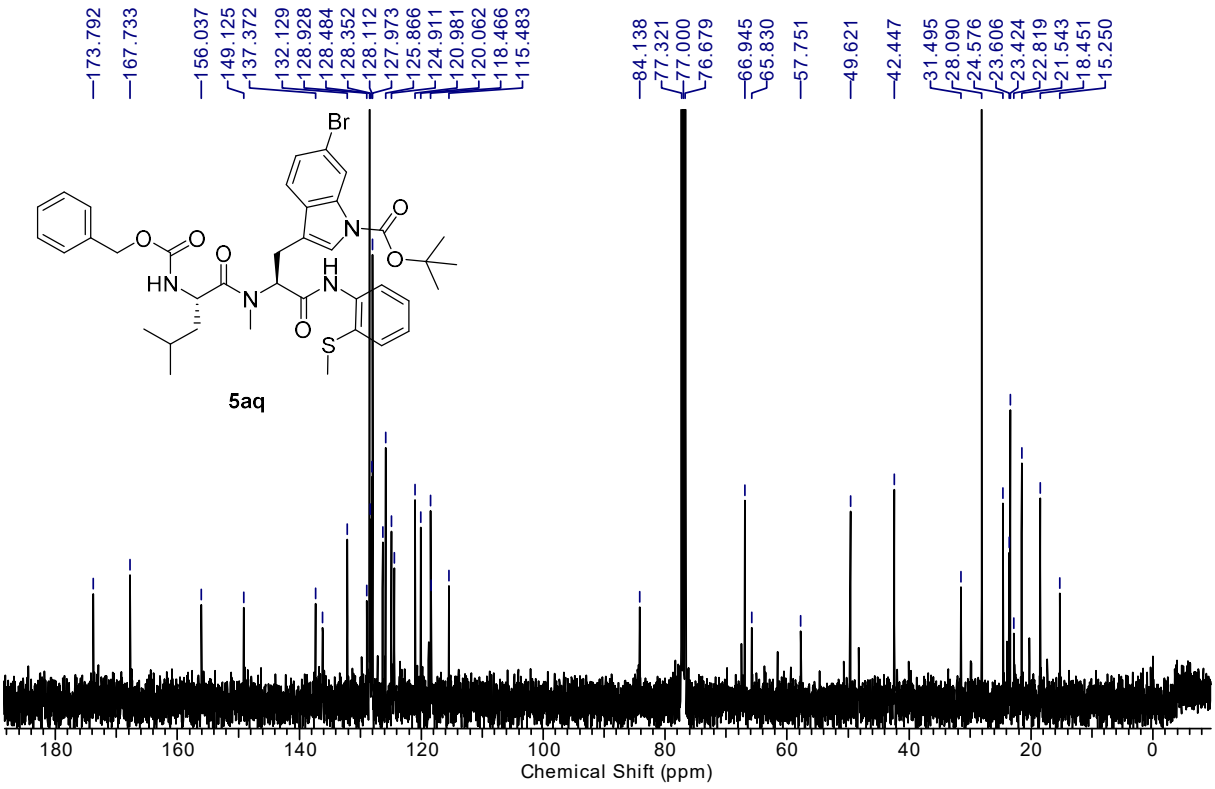
Benzyl ((*S*)-1-(((*S*)-3-(4-chlorophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5ak)



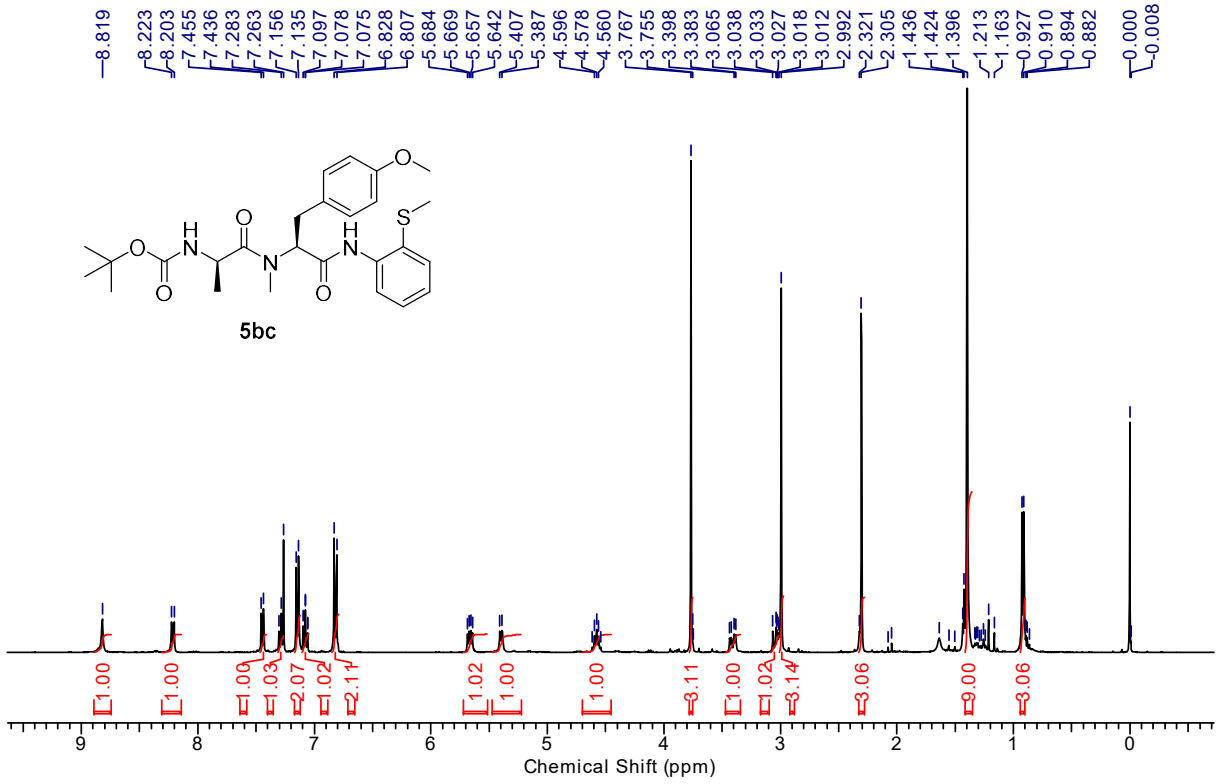


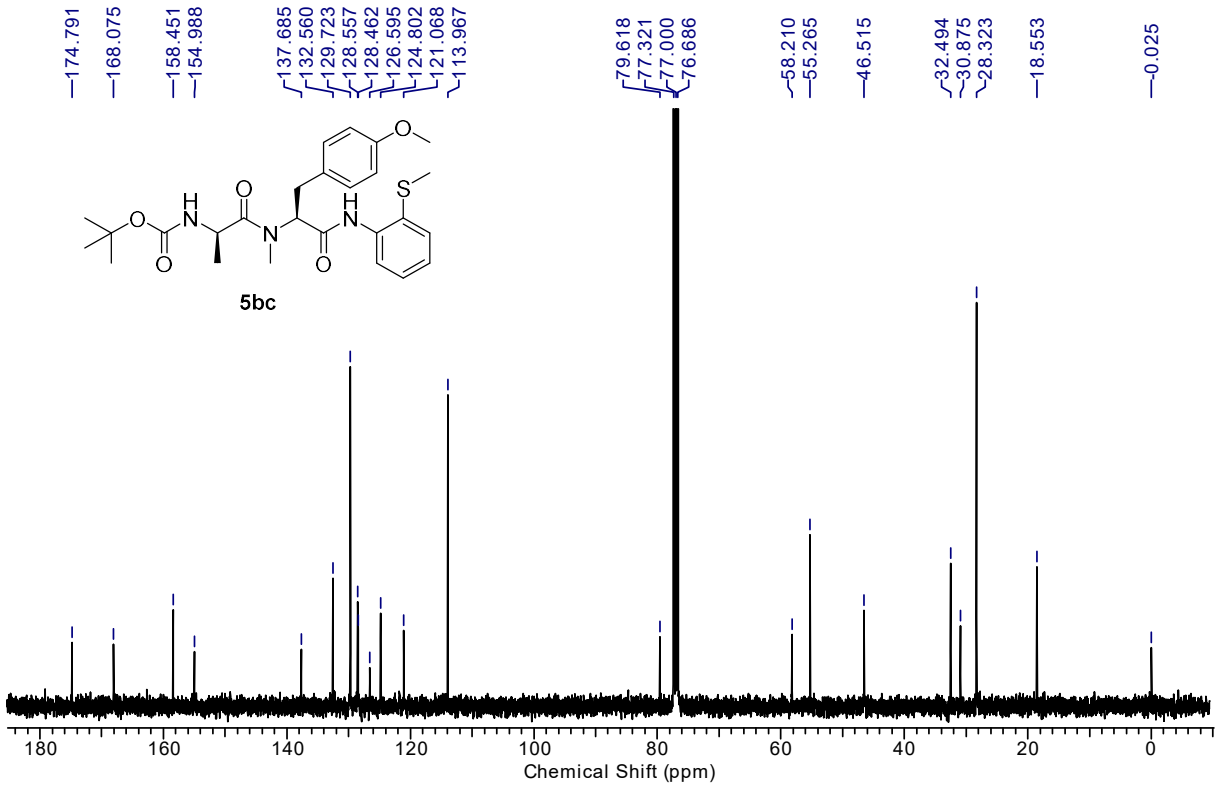
***tert*-Butyl 3-((*S*)-2-((*S*)-2-(((benzyloxy)carbonyl)amino)-*N*,4-dimethylpentanamido)-3-((2-(methylthio)phenyl)amino)-3-oxopropyl)-6-bromo-1*H*-indole-1-carboxylate (5aq)**



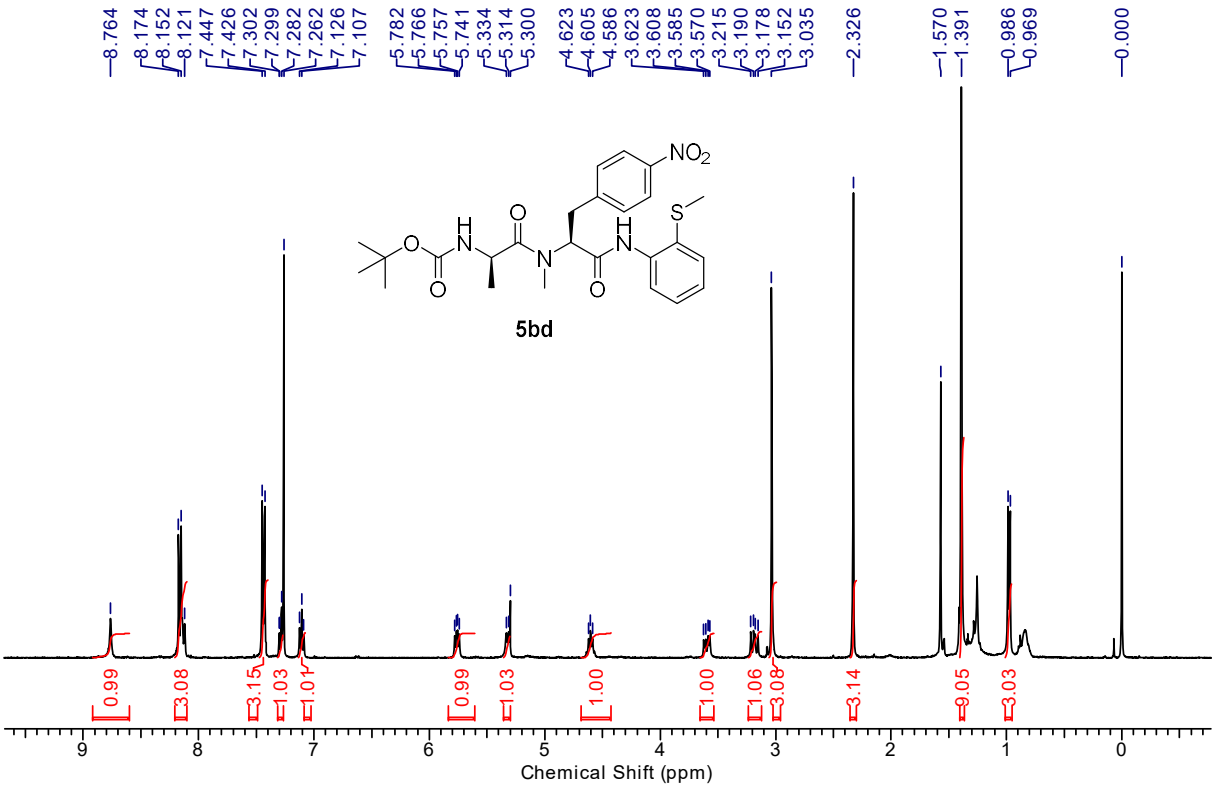


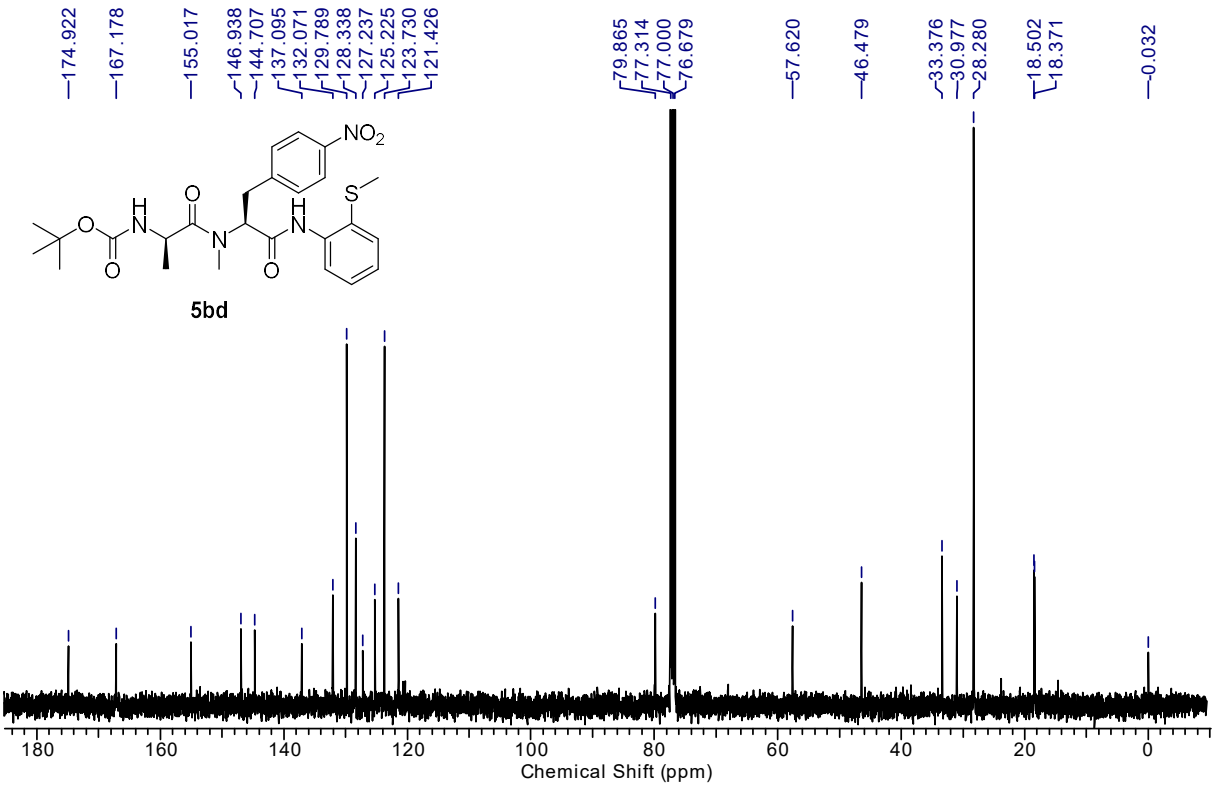
***tert*-Butyl ((*R*)-1-(((*S*)-3-(4-methoxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bc)**



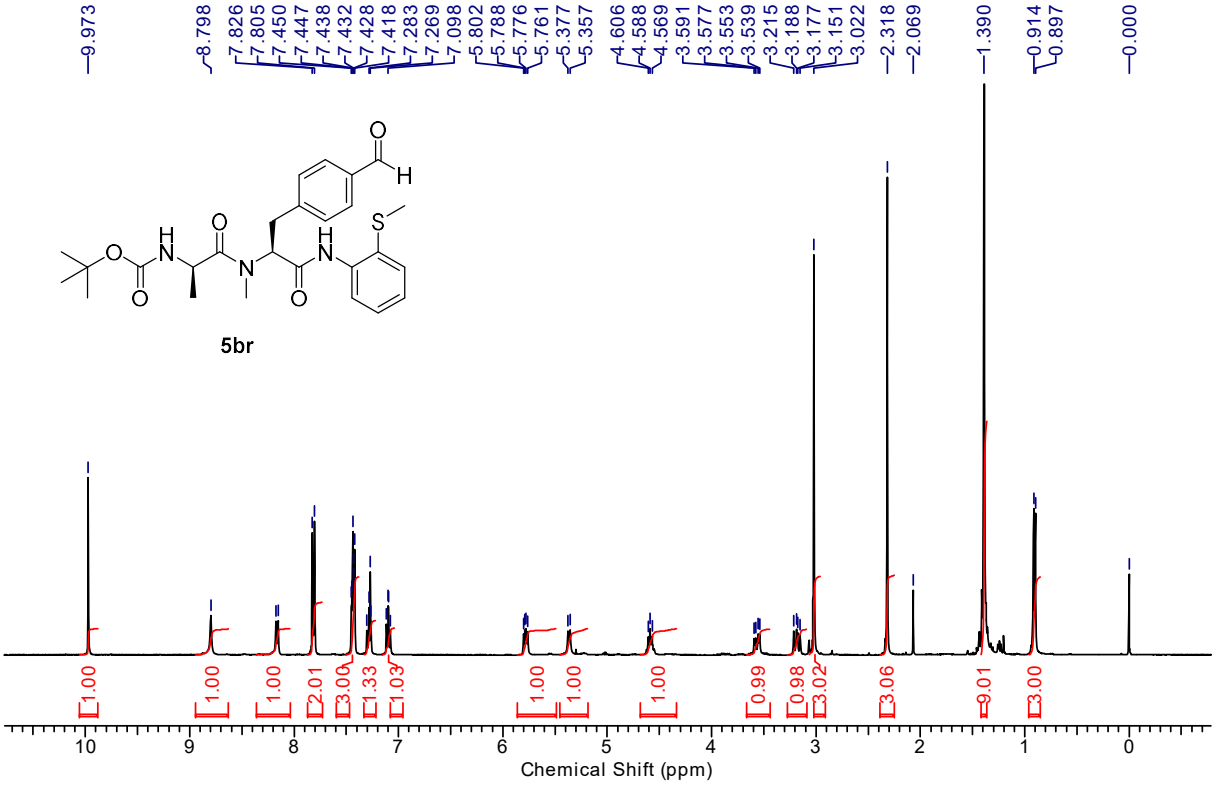


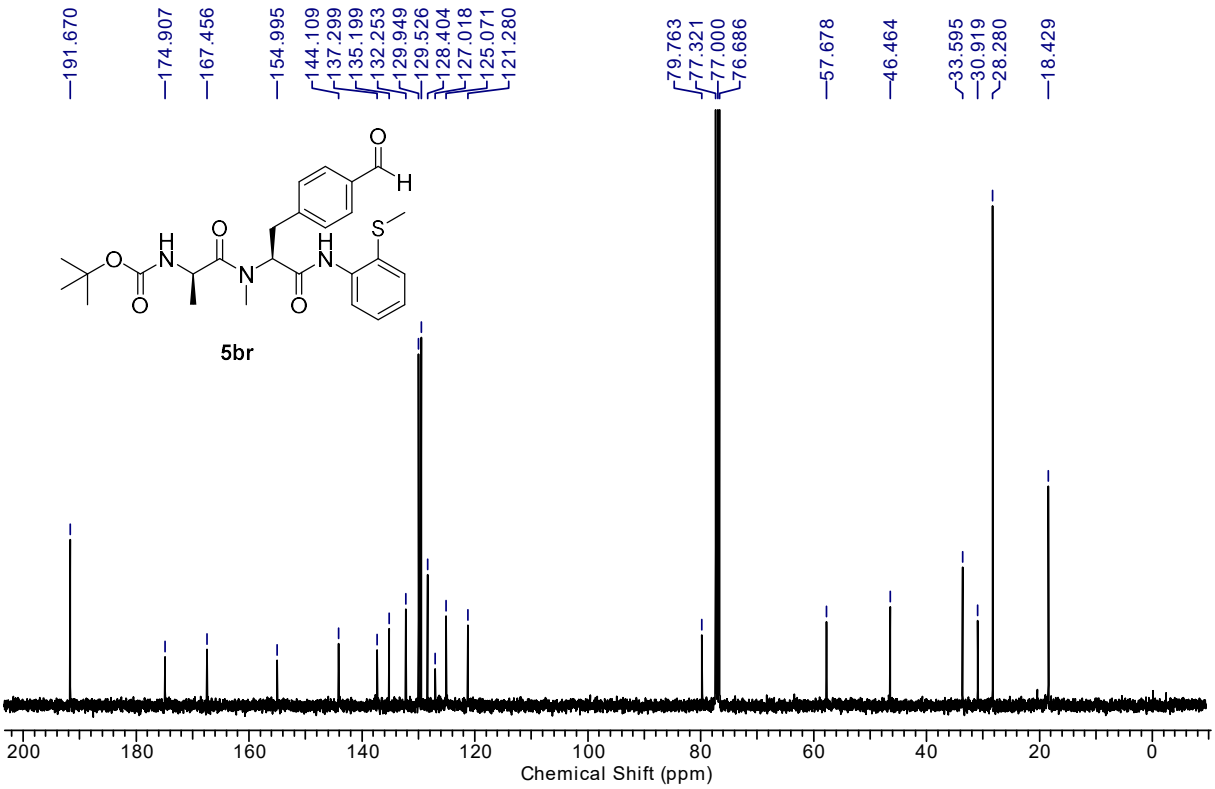
***tert*-Butyl ((*R*)-1-(methyl((*S*)-1-((2-(methylthio)phenyl)amino)-3-(4-nitrophenyl)-1-oxopropan-2-yl) amino)-1-oxopropan-2-yl)carbamate (5bd)**



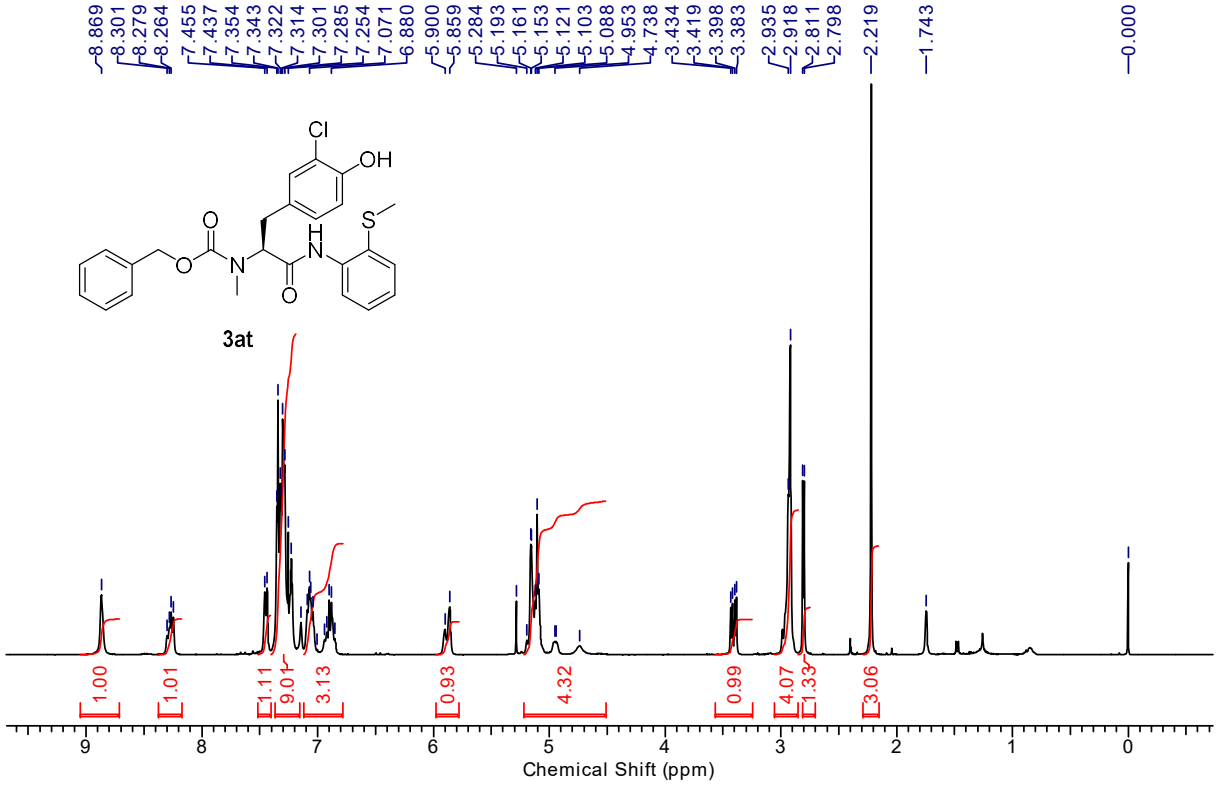


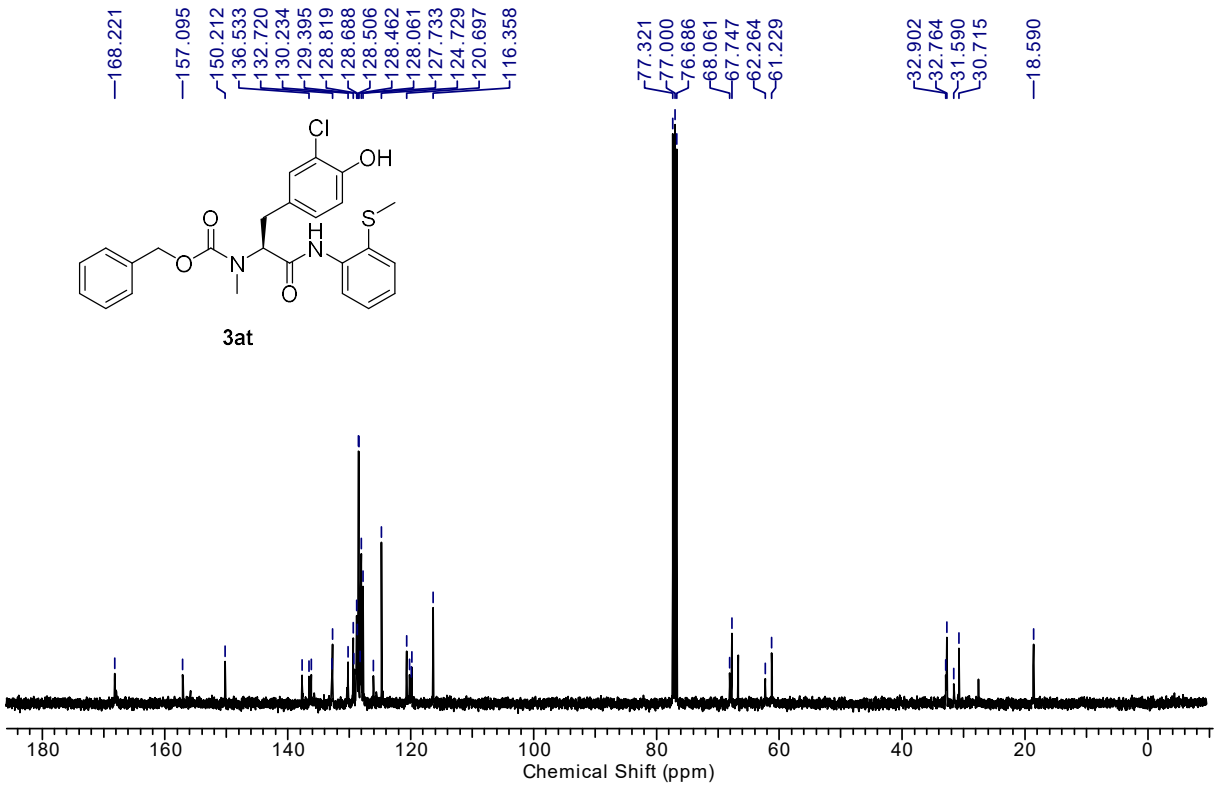
***tert*-Butyl ((*R*)-1-(((*S*)-3-(4-formylphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5br)**



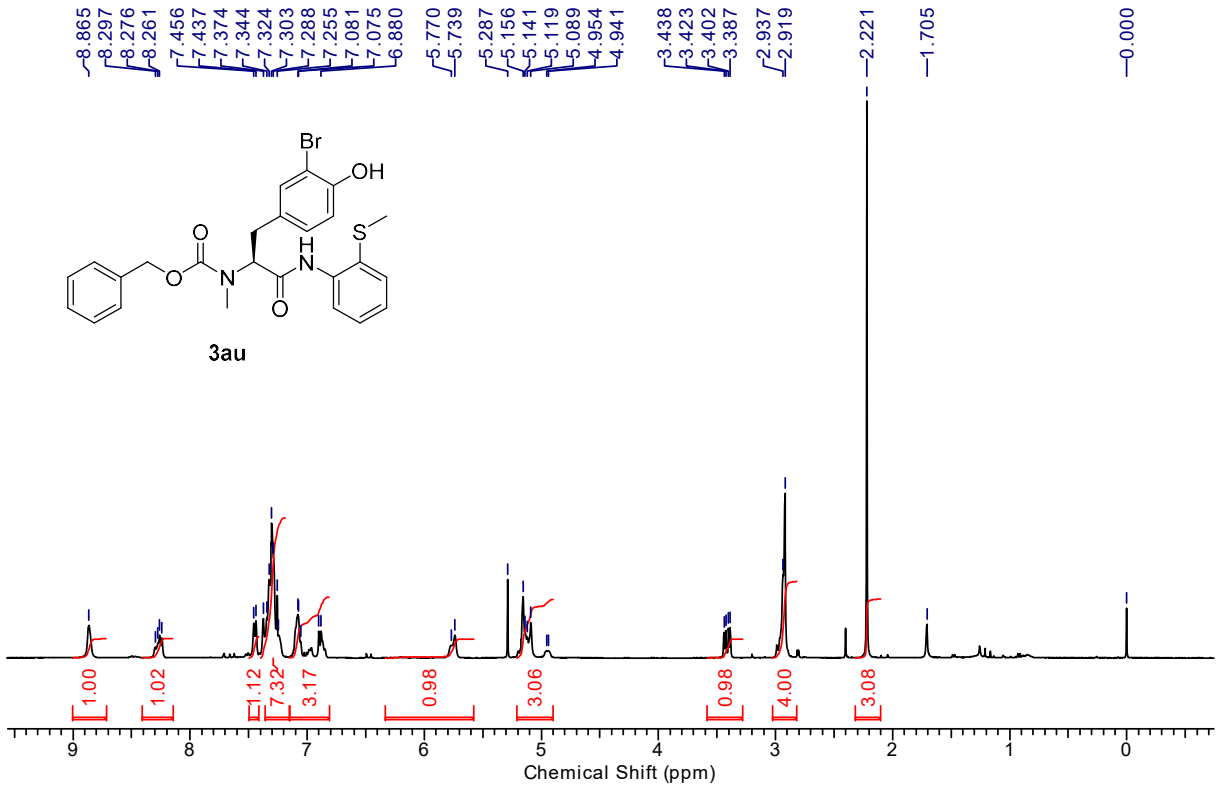


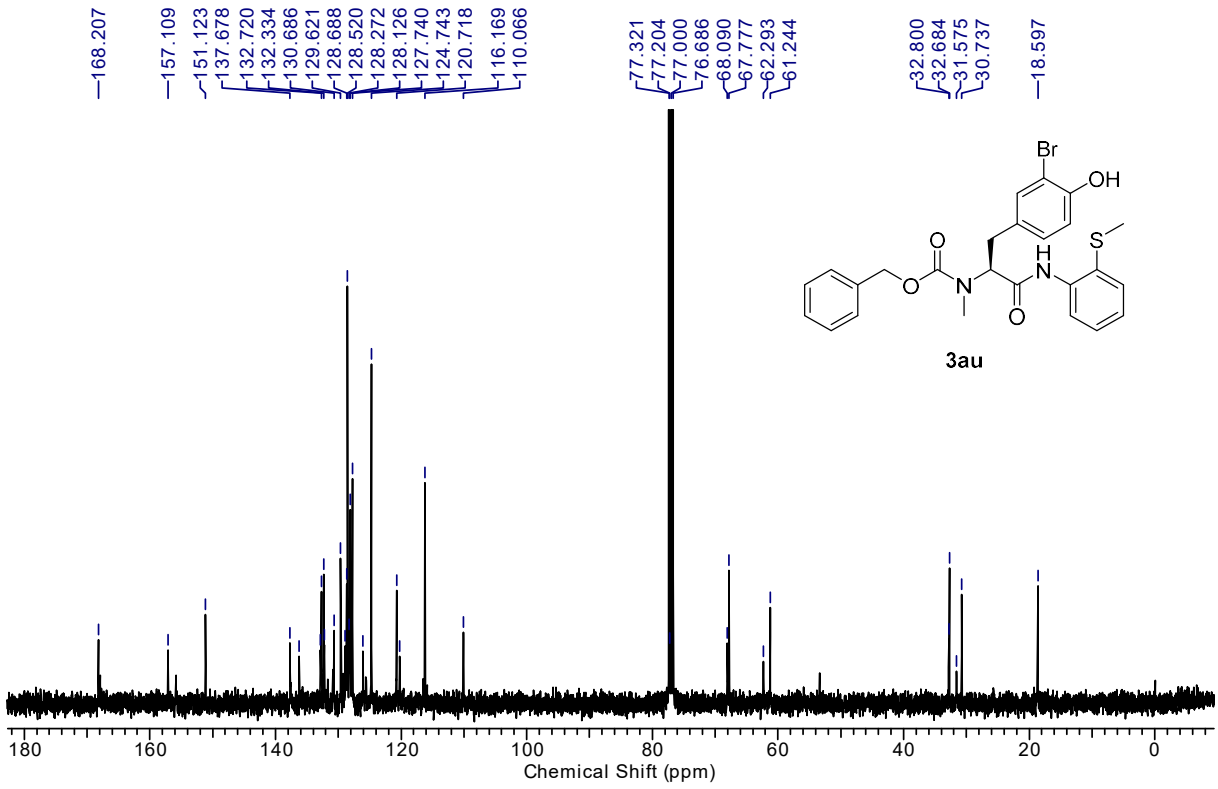
Benzyl (*S*)-(3-(3-chloro-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3at)



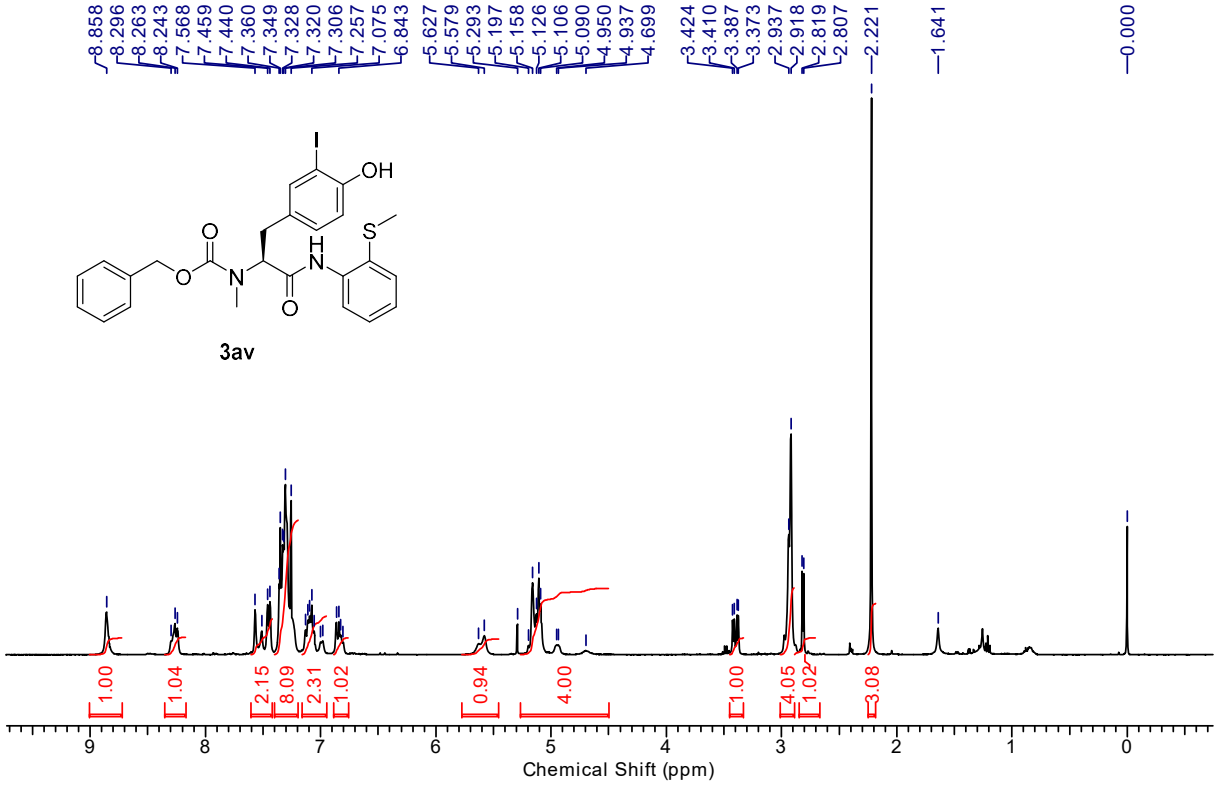


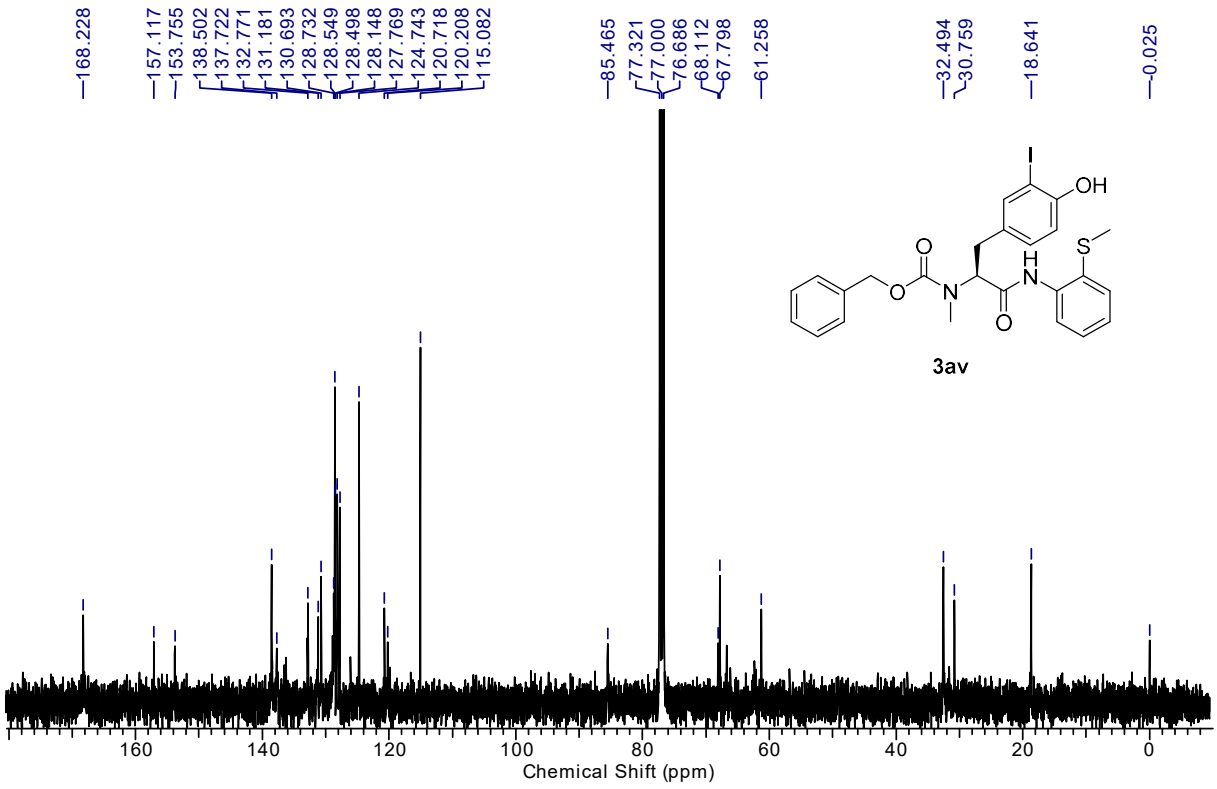
Benzyl (*S*)-(3-(3-bromo-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3au)



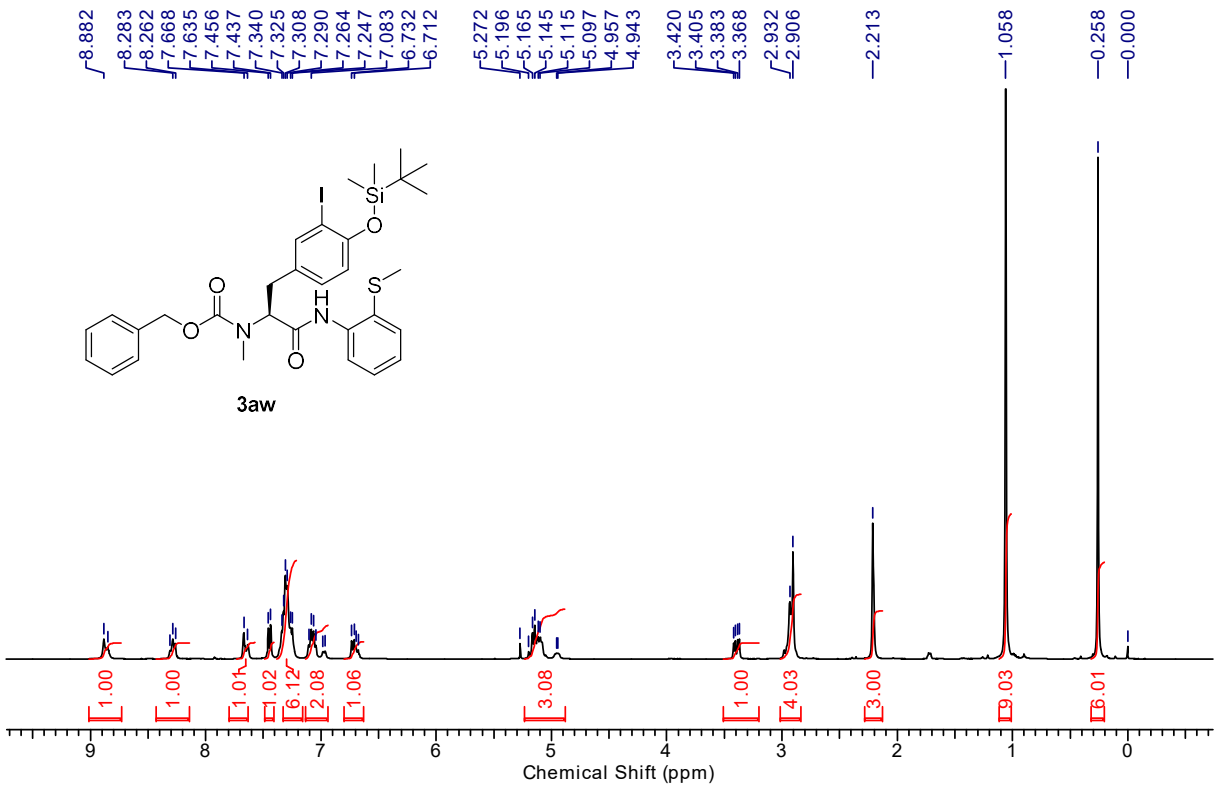


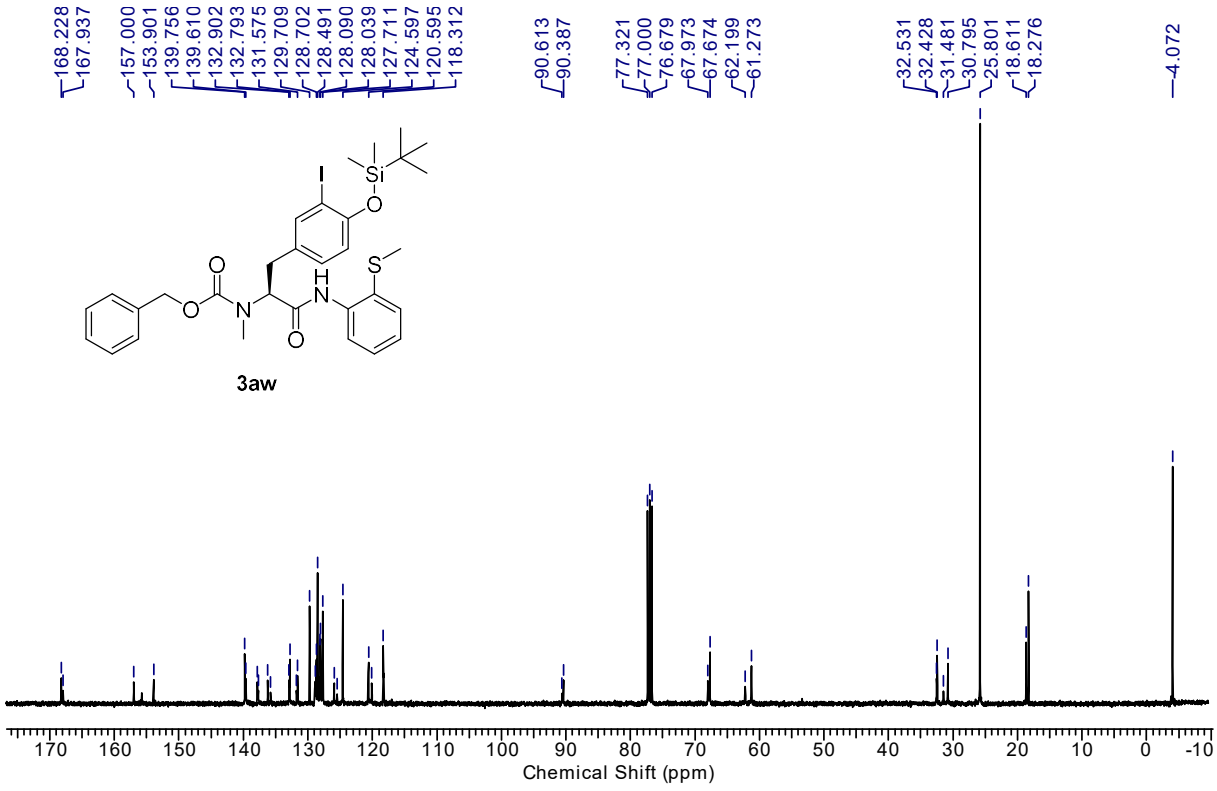
Benzyl (*S*)-(3-(4-hydroxy-3-iodophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl) (methyl)carbamate (3av)



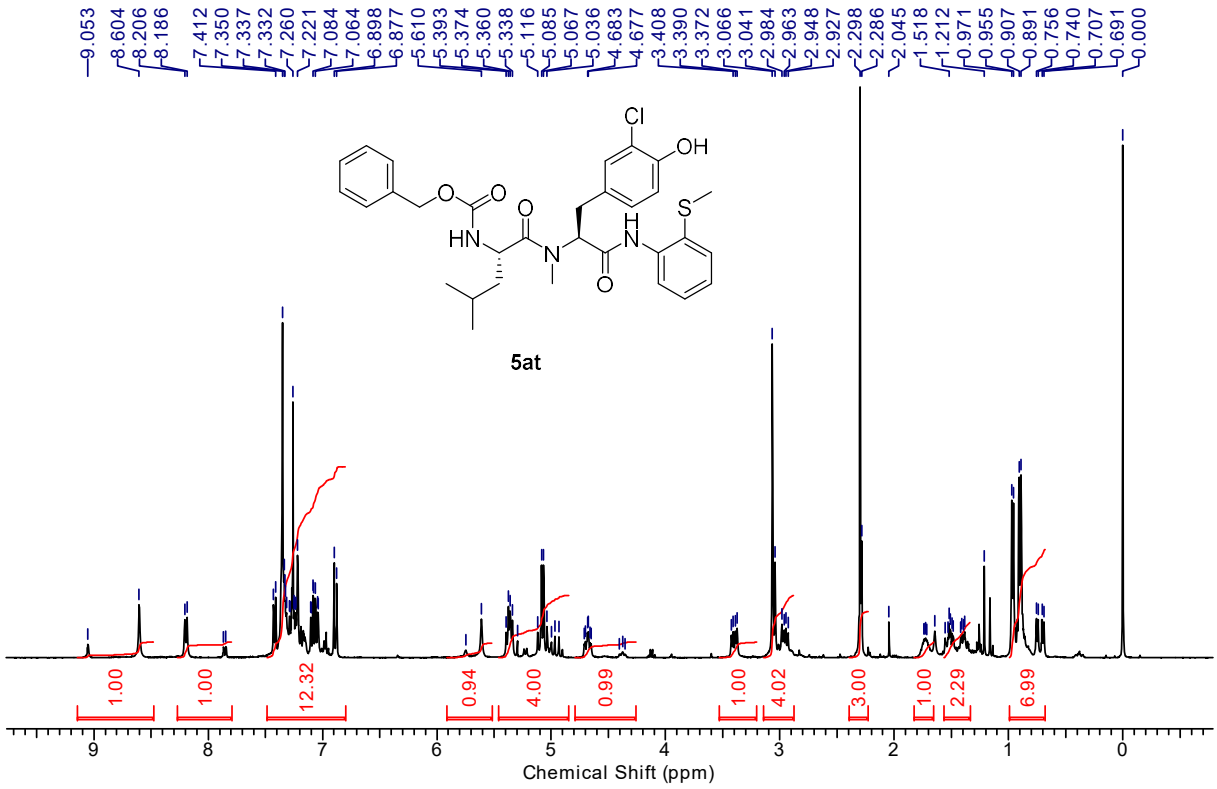


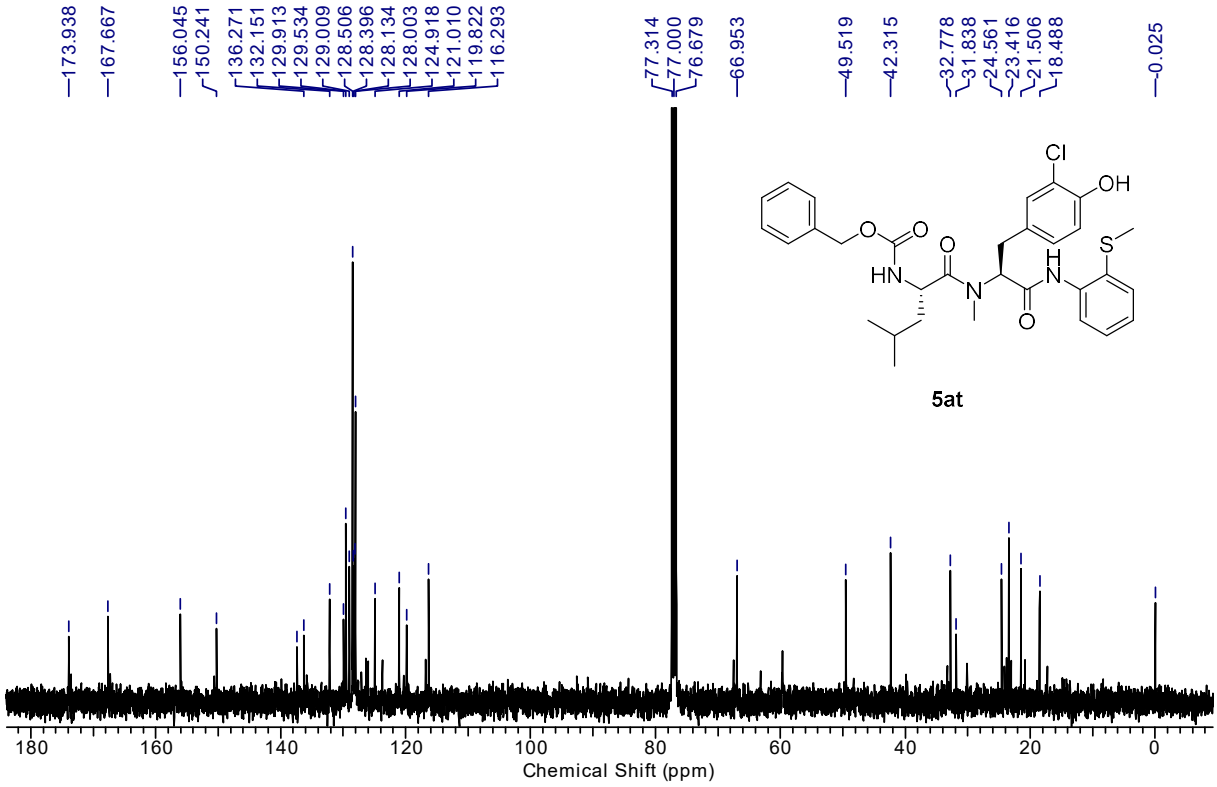
Benzyl (*S*)-(3-(4-((*tert*-butyldimethylsilyl)oxy)-3-iodophenyl)-1-((2-(methylthio) phenyl)amino)-1-oxopropan-2-yl)(methyl)carbamate (3aw)



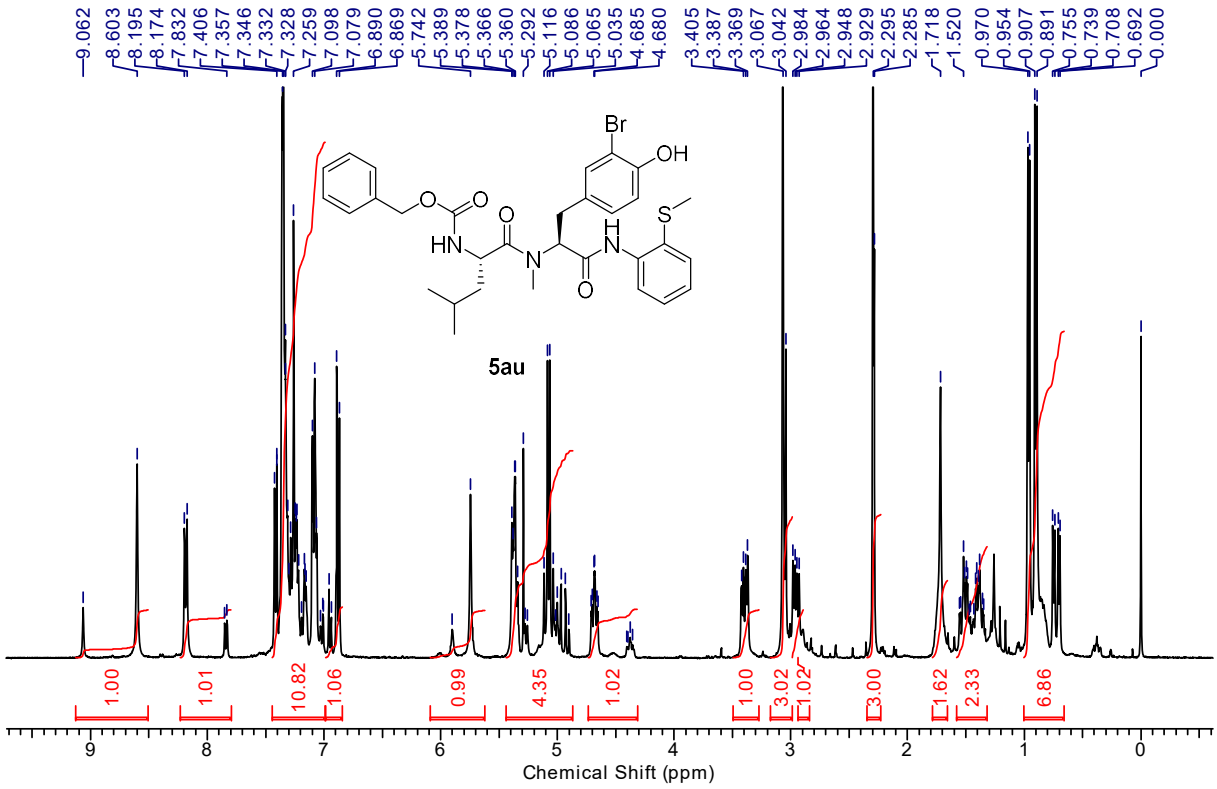


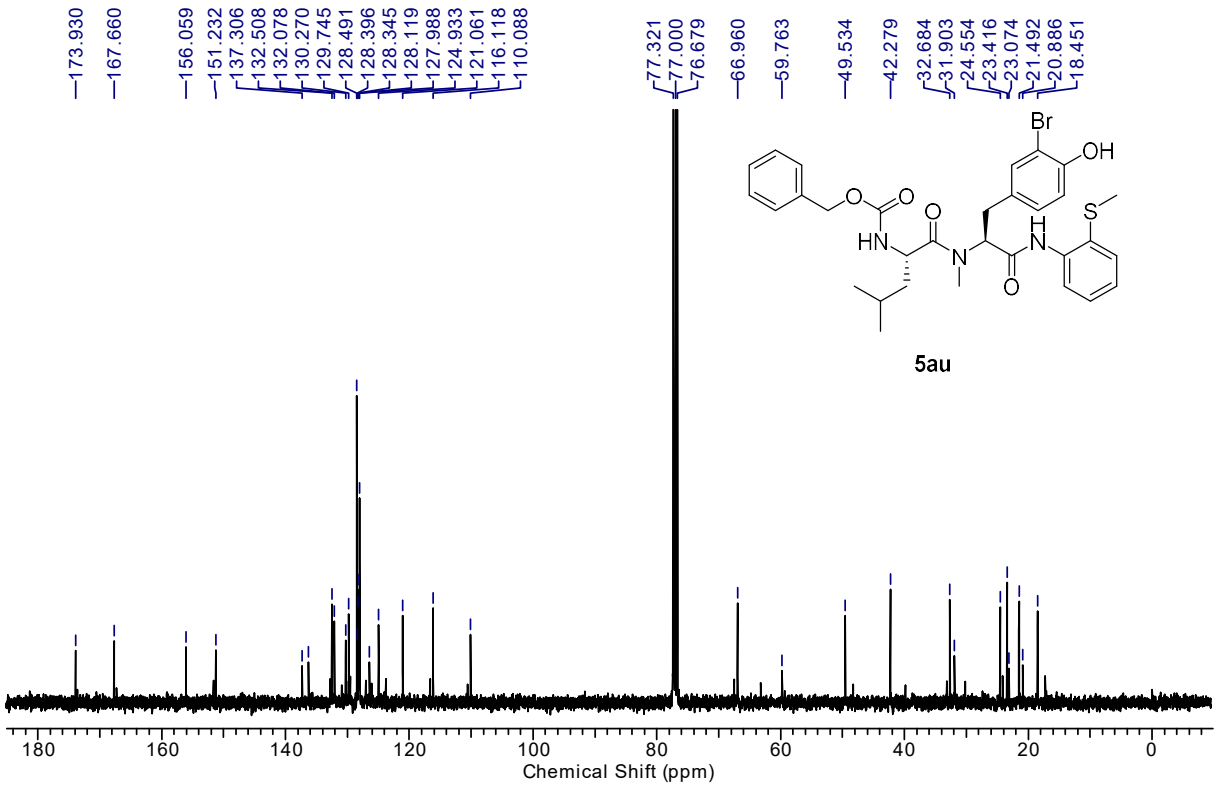
Benzyl ((*S*)-1-(((*S*)-3-(3-chloro-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5at)



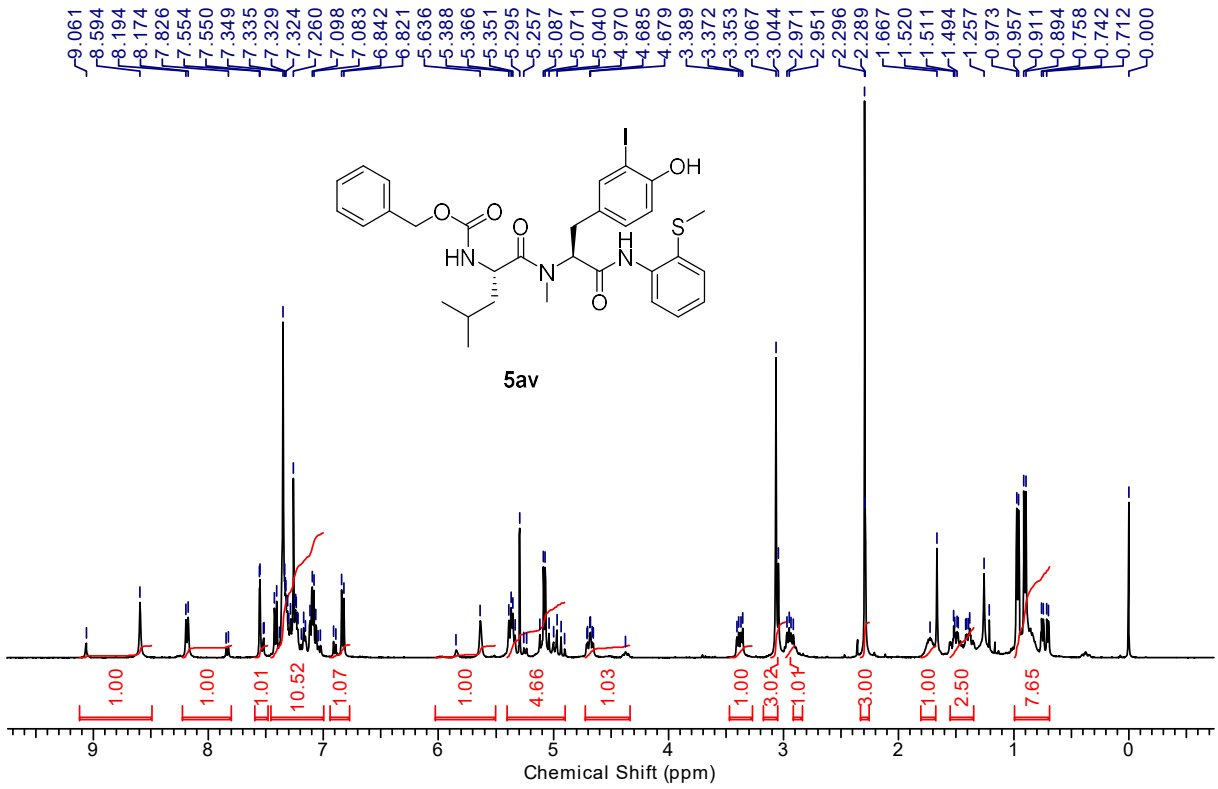


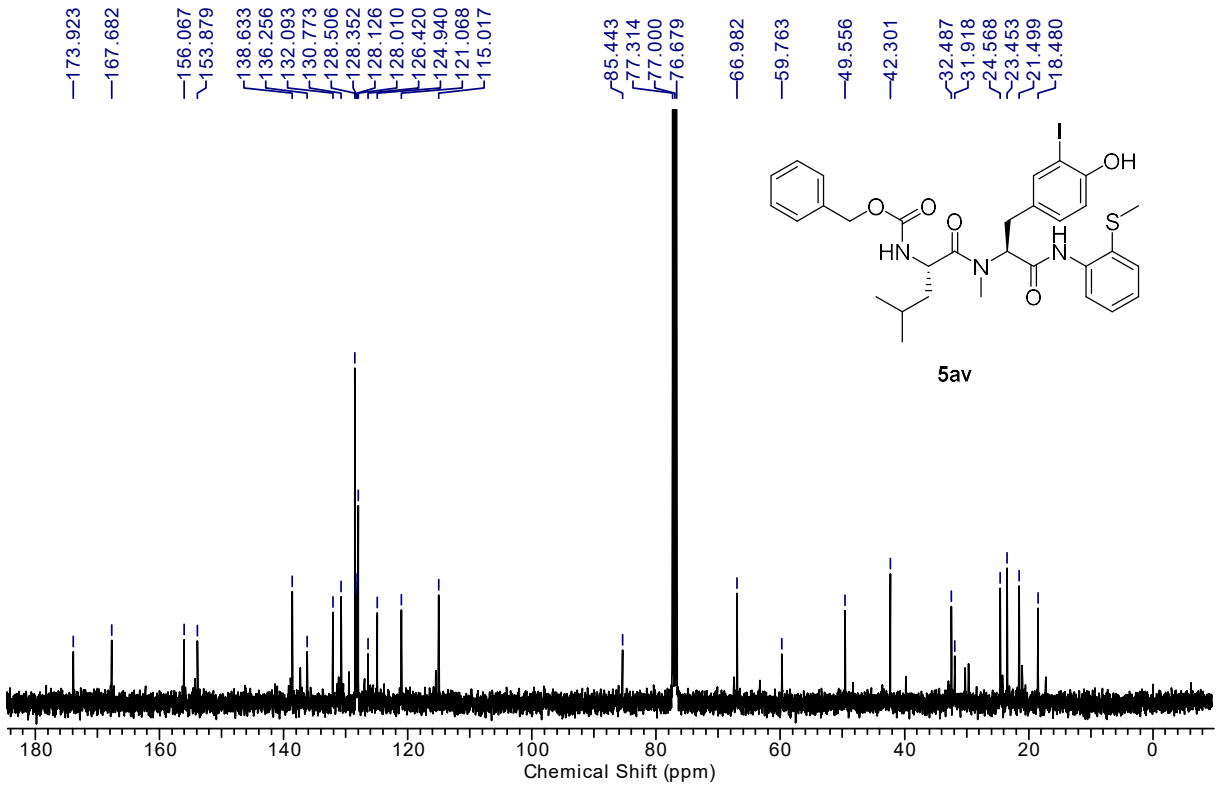
Benzyl ((*S*)-1-(((*S*)-3-(3-bromo-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5au)



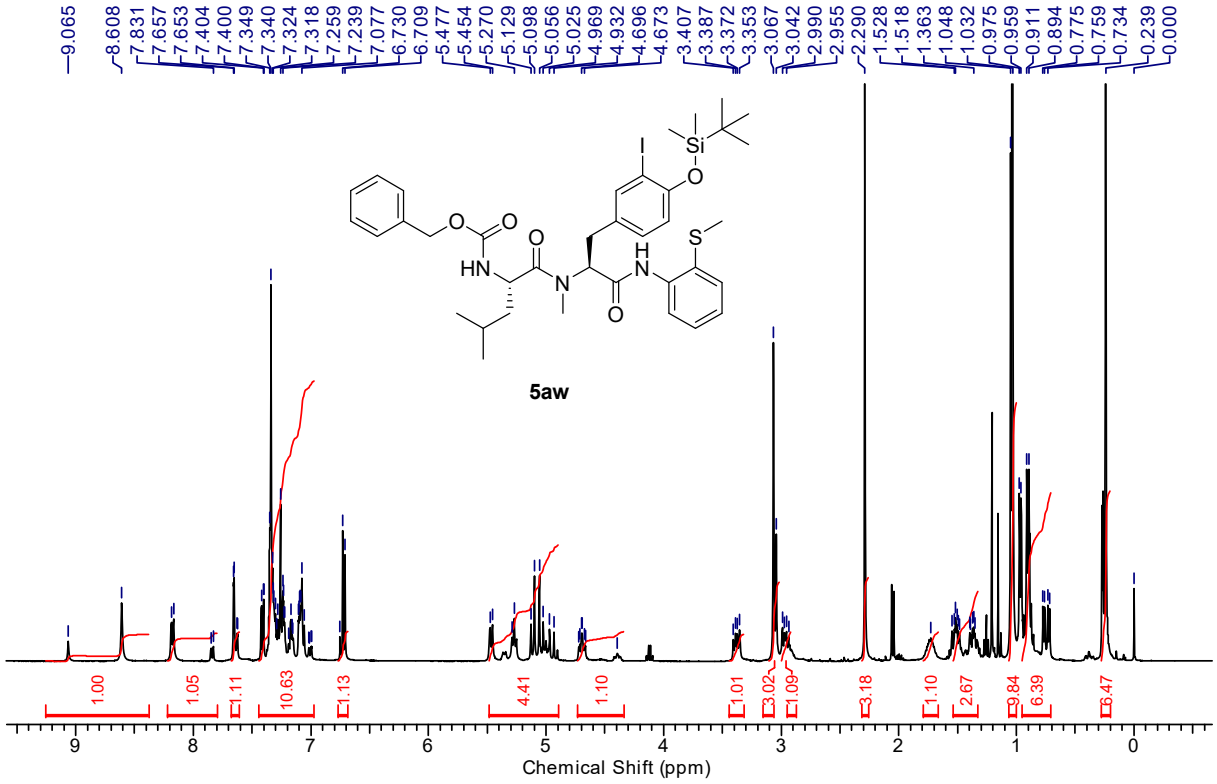


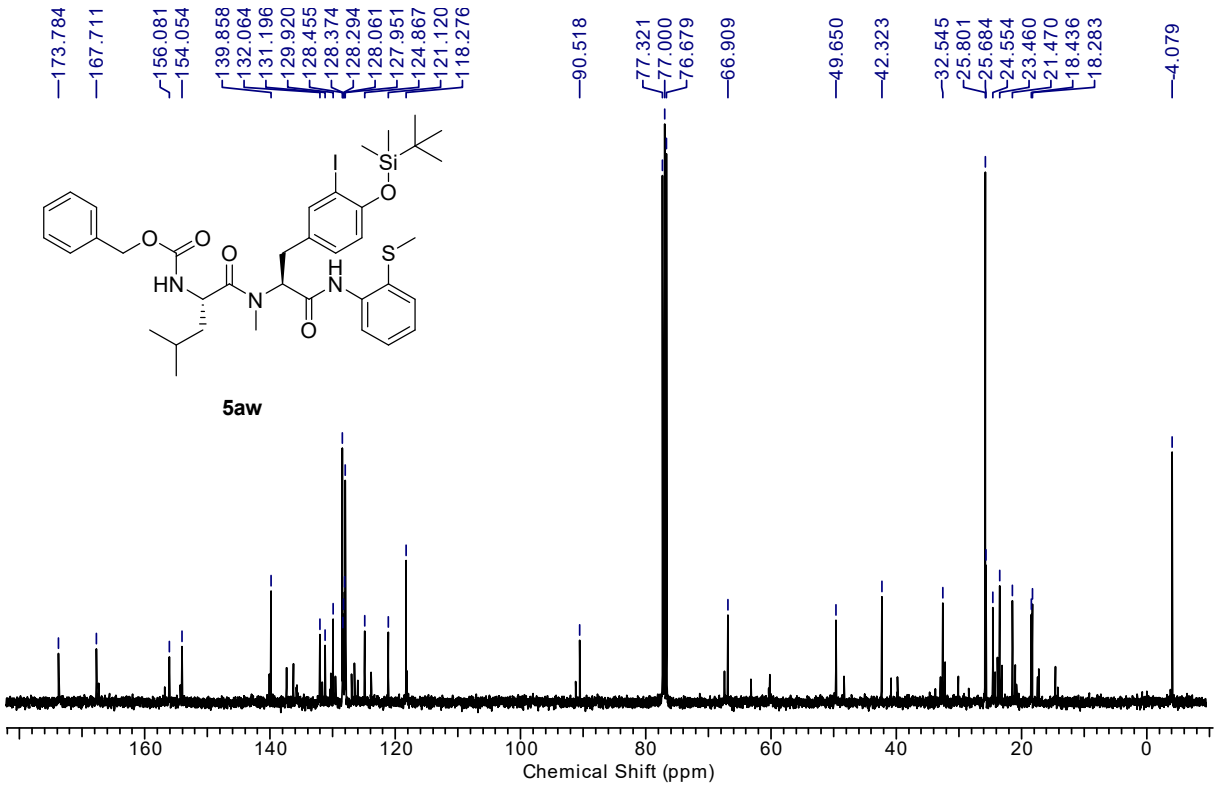
Benzyl ((*S*)-1-(((*S*)-3-(4-hydroxy-3-iodophenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5av)



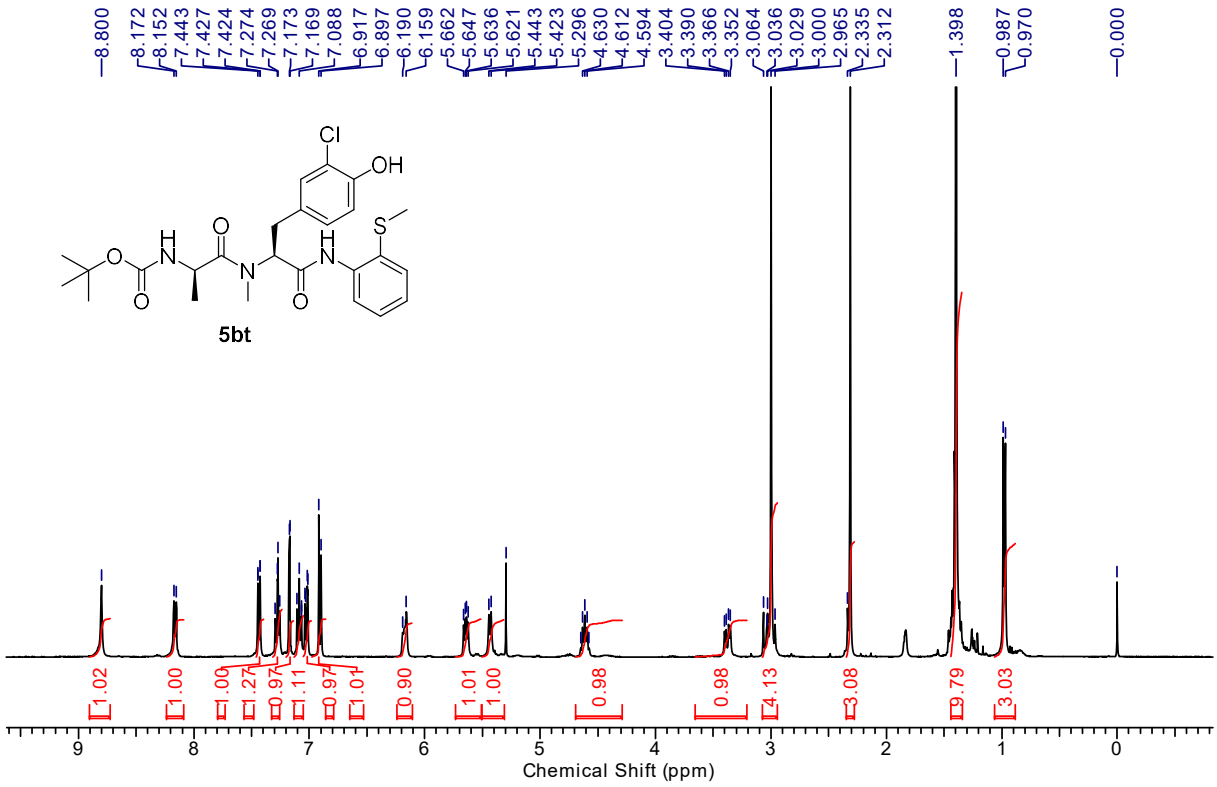


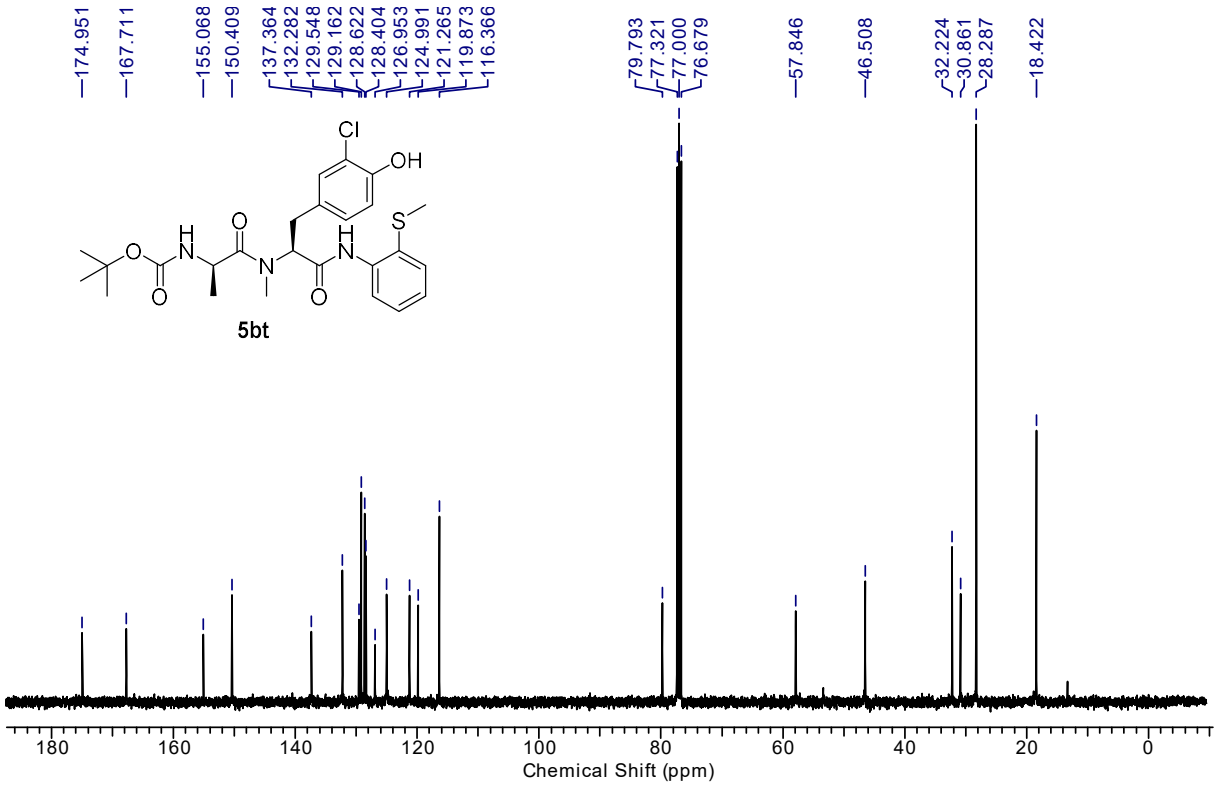
Benzyl ((*S*)-1-(((*S*)-3-(4-((*tert*-butyldimethylsilyl)oxy)-3-iodophenyl)-1-((2-(methylthio)phenyl) amino)-1-oxopropan-2-yl)(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (5aw)



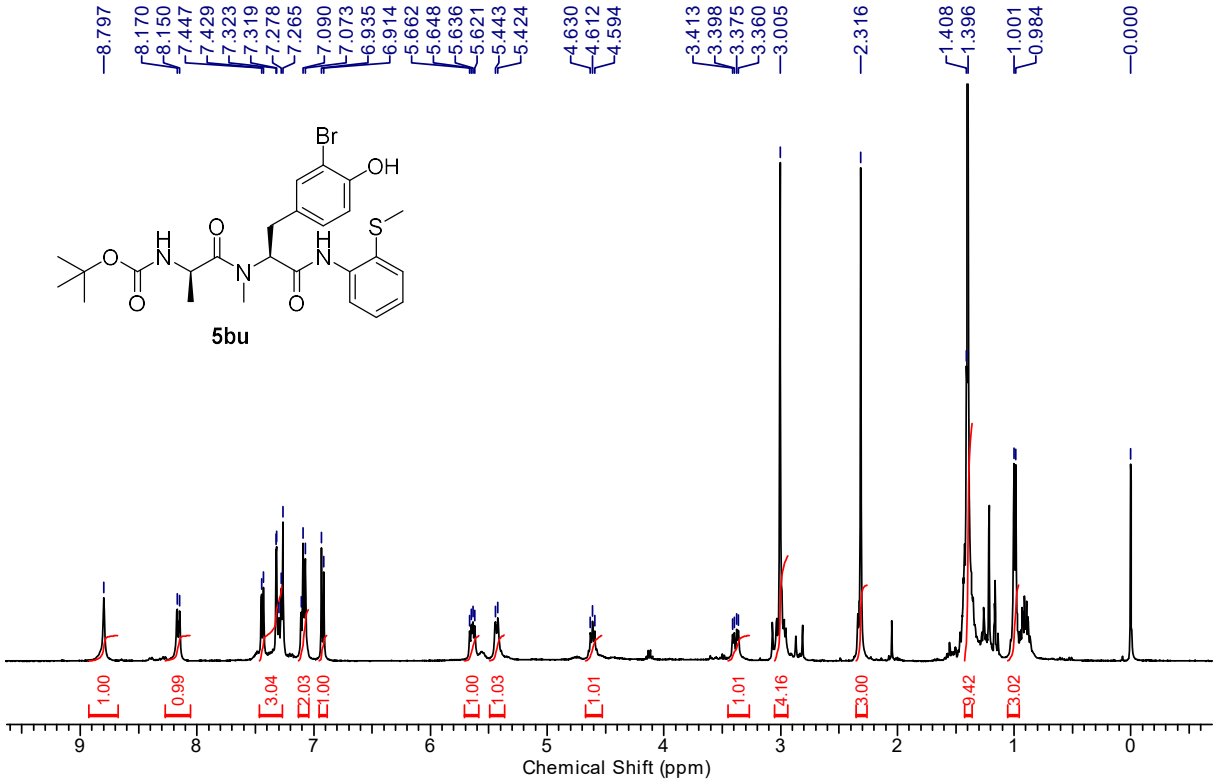


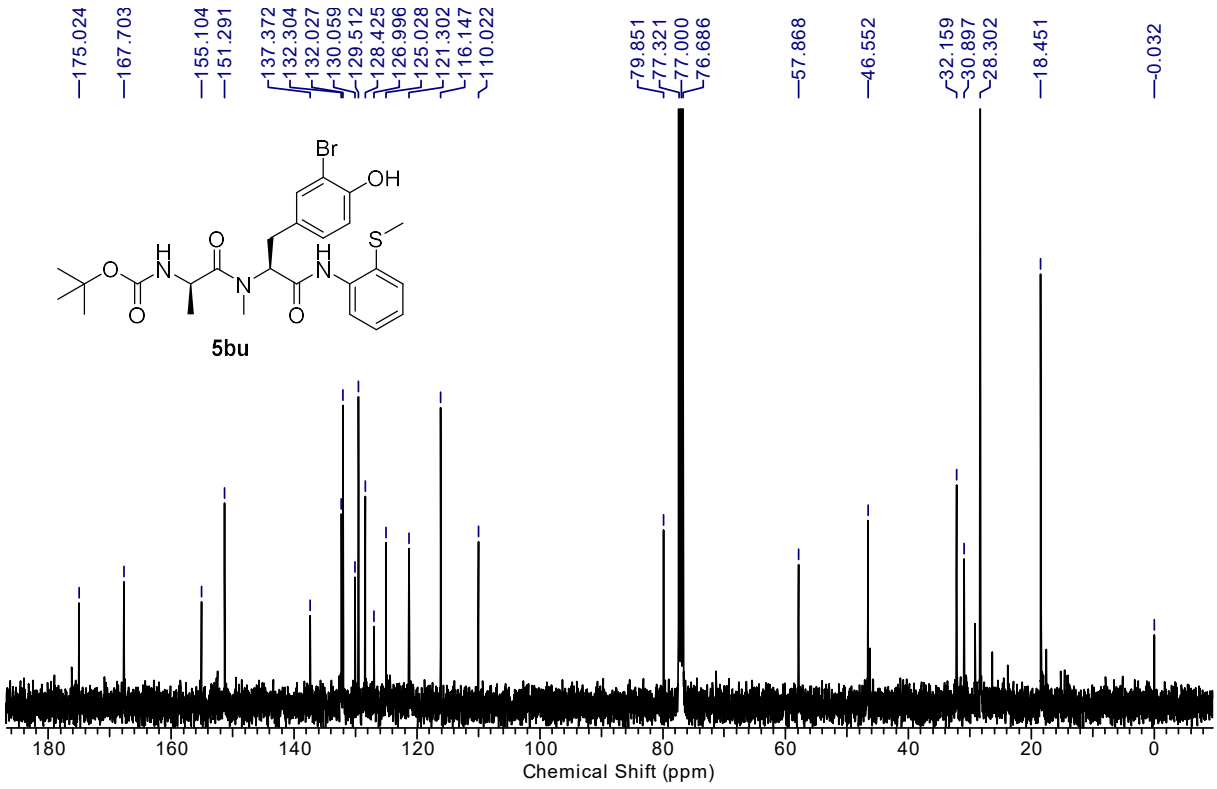
***tert*-Butyl ((*R*)-1-(((*S*)-3-(3-chloro-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bt)**



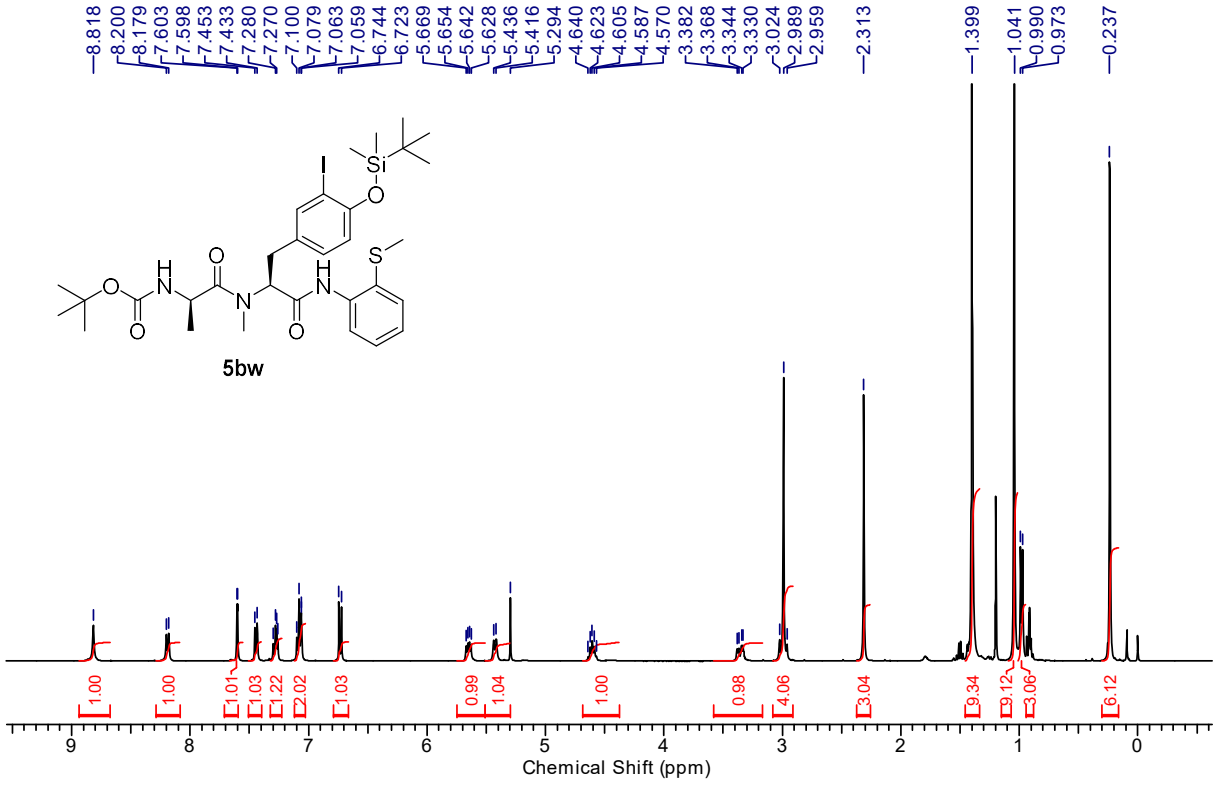


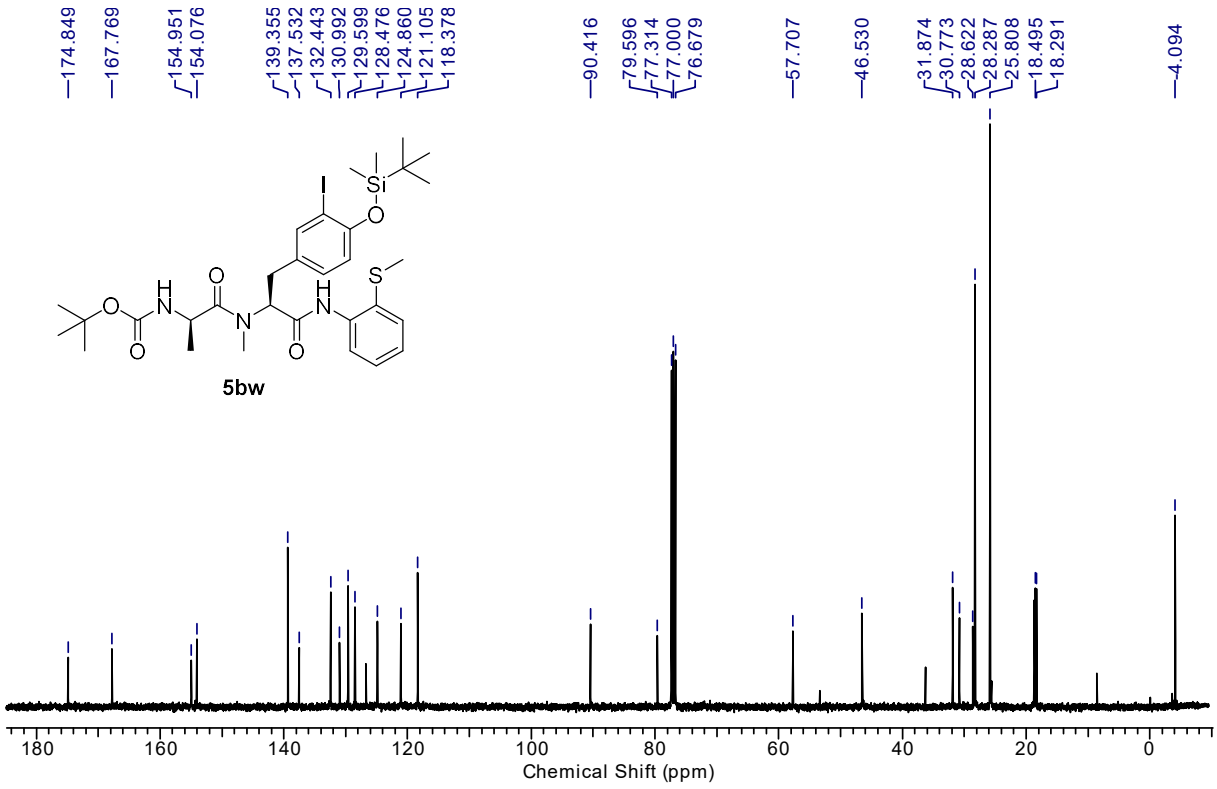
***tert*-Butyl ((*R*)-1-(((*S*)-3-(3-bromo-4-hydroxyphenyl)-1-((2-(methylthio)phenyl)amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bu)**



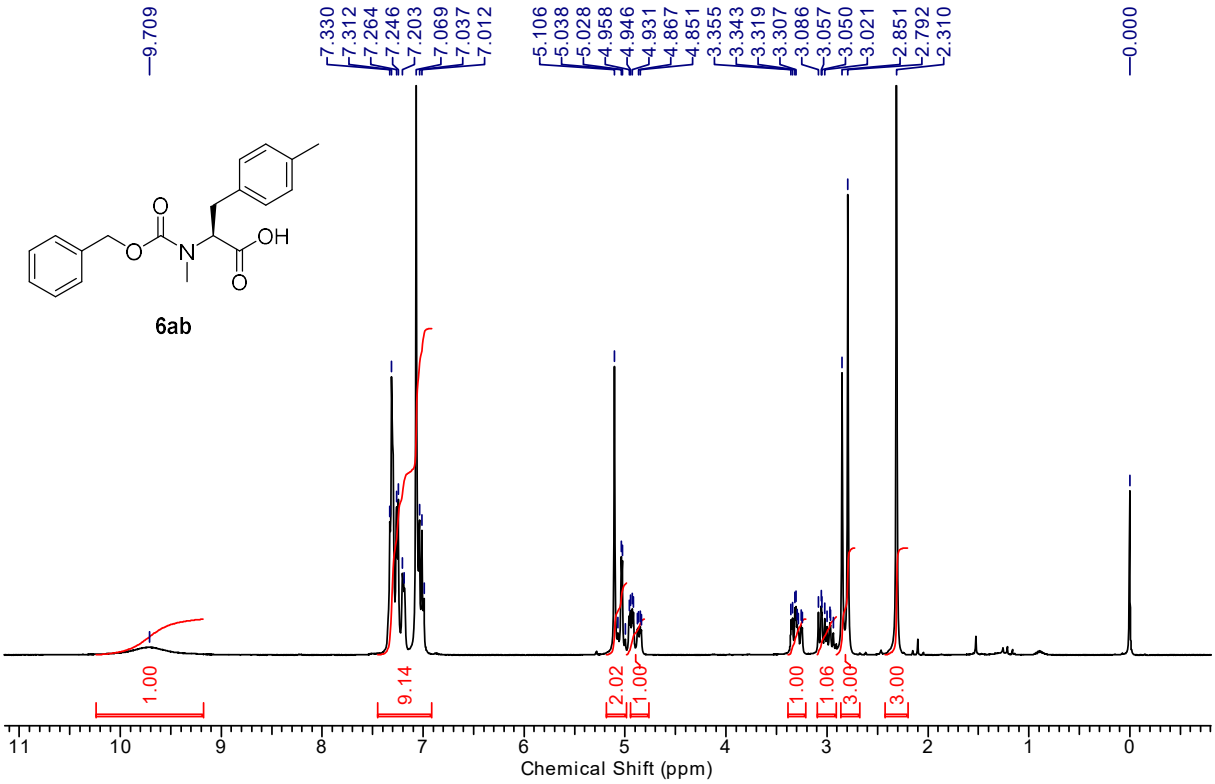


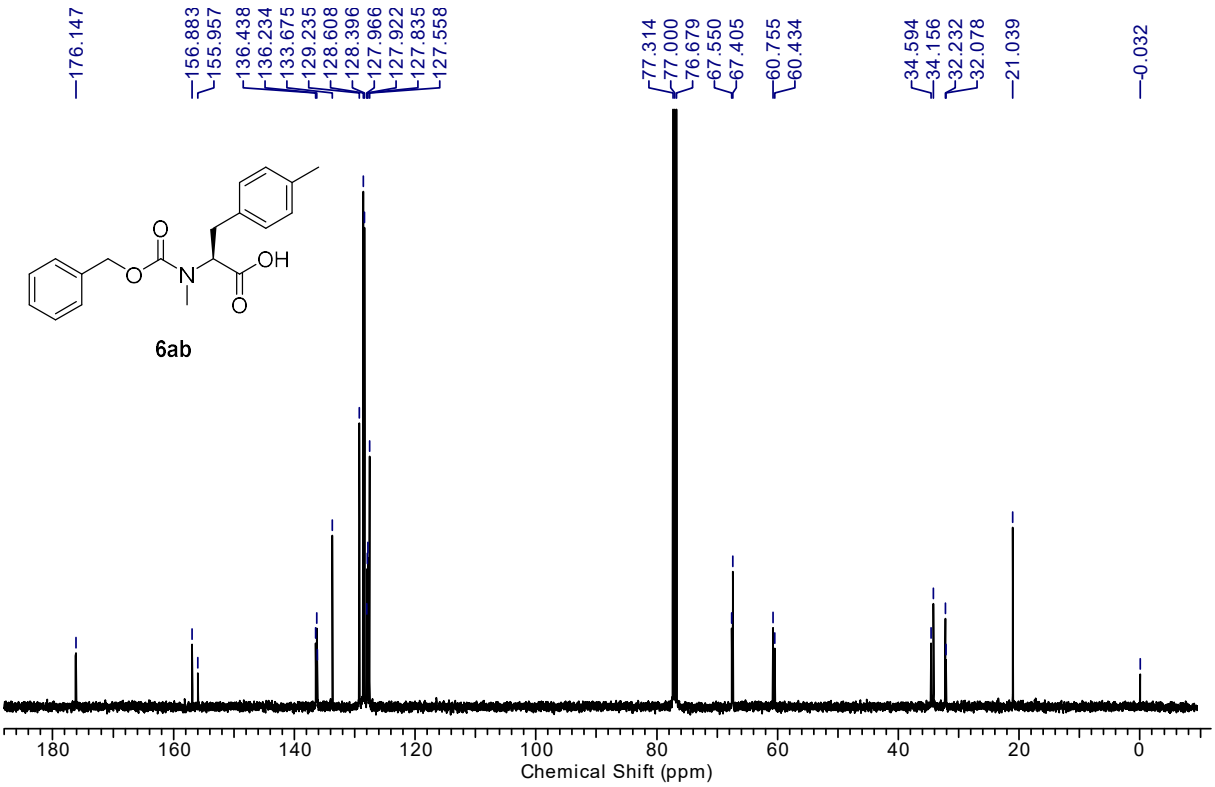
***tert*-Butyl ((*R*)-1-(((*S*)-3-(4-((*tert*-butyldimethylsilyl)oxy)-3-iodophenyl)-1-((2-(methylthio)phenyl) amino)-1-oxopropan-2-yl)(methyl)amino)-1-oxopropan-2-yl)carbamate (5bw)**



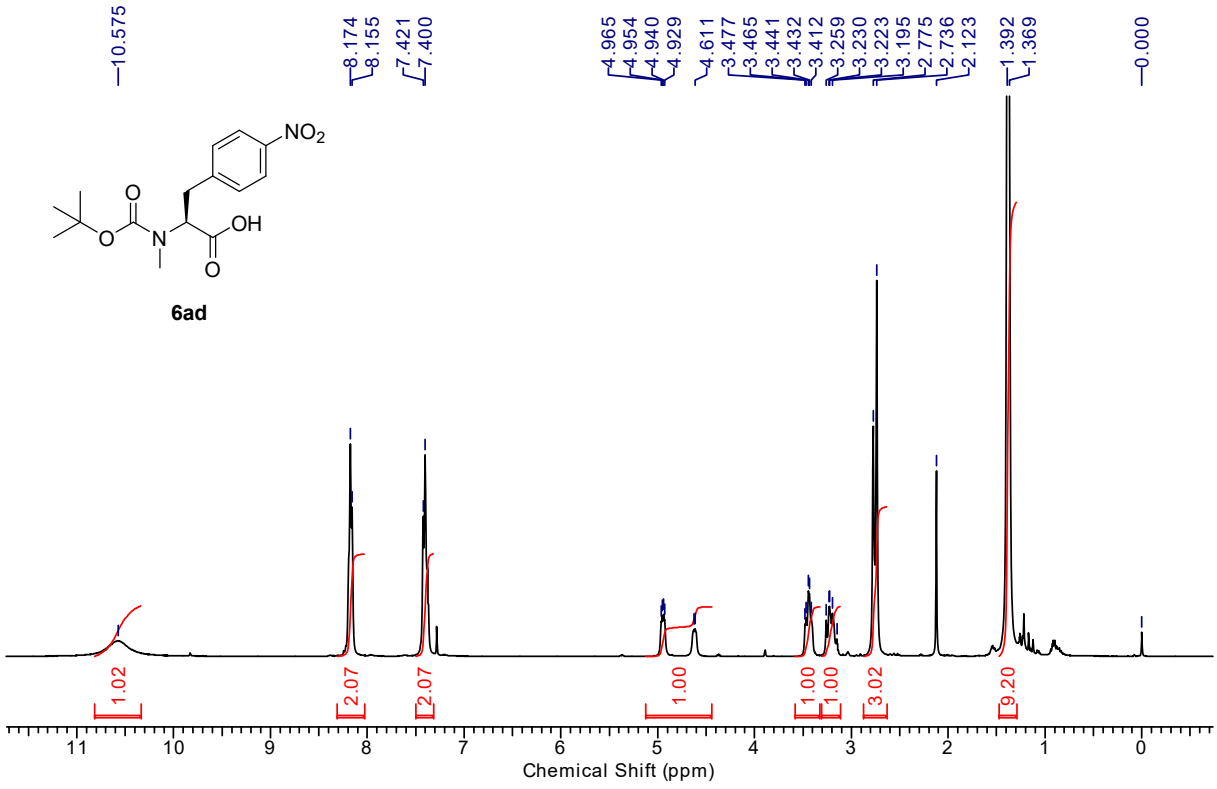


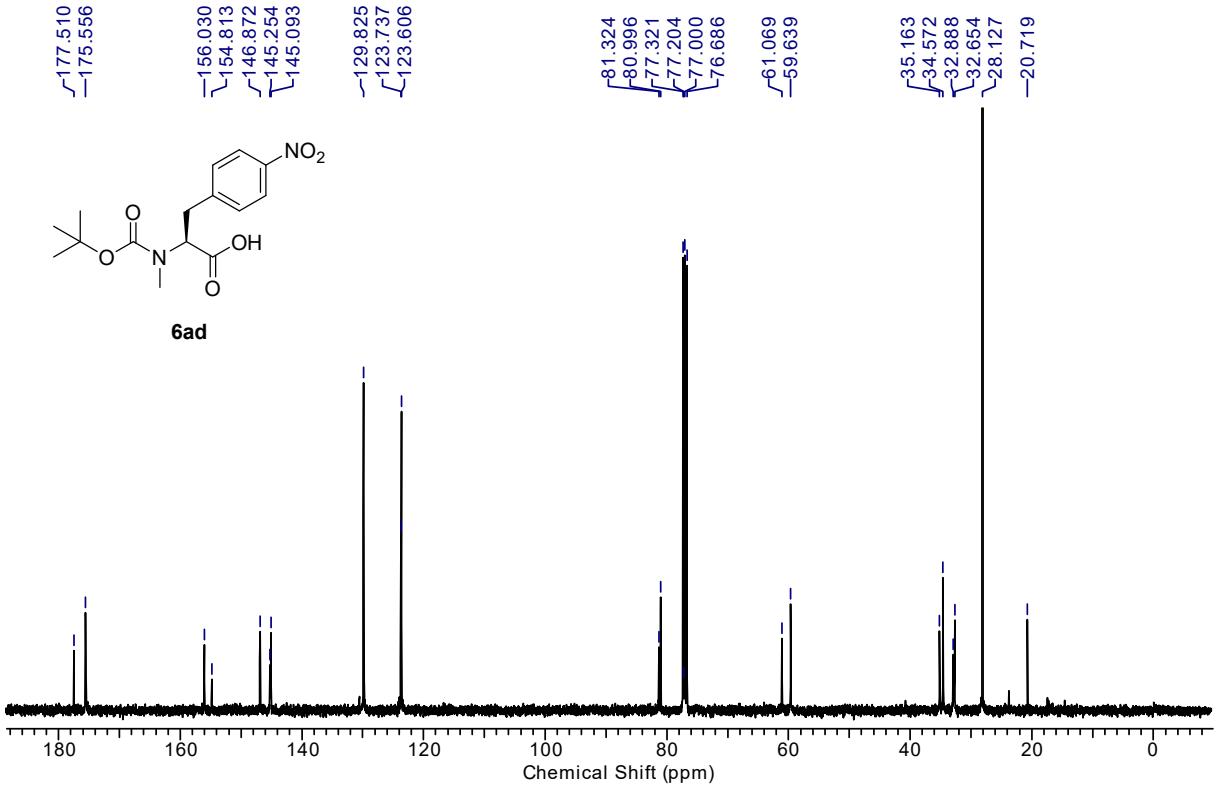
(*S*)-2-(((Benzyloxy)carbonyl)(methyl)amino)-3-(*p*-tolyl)propanoic acid (6ab)



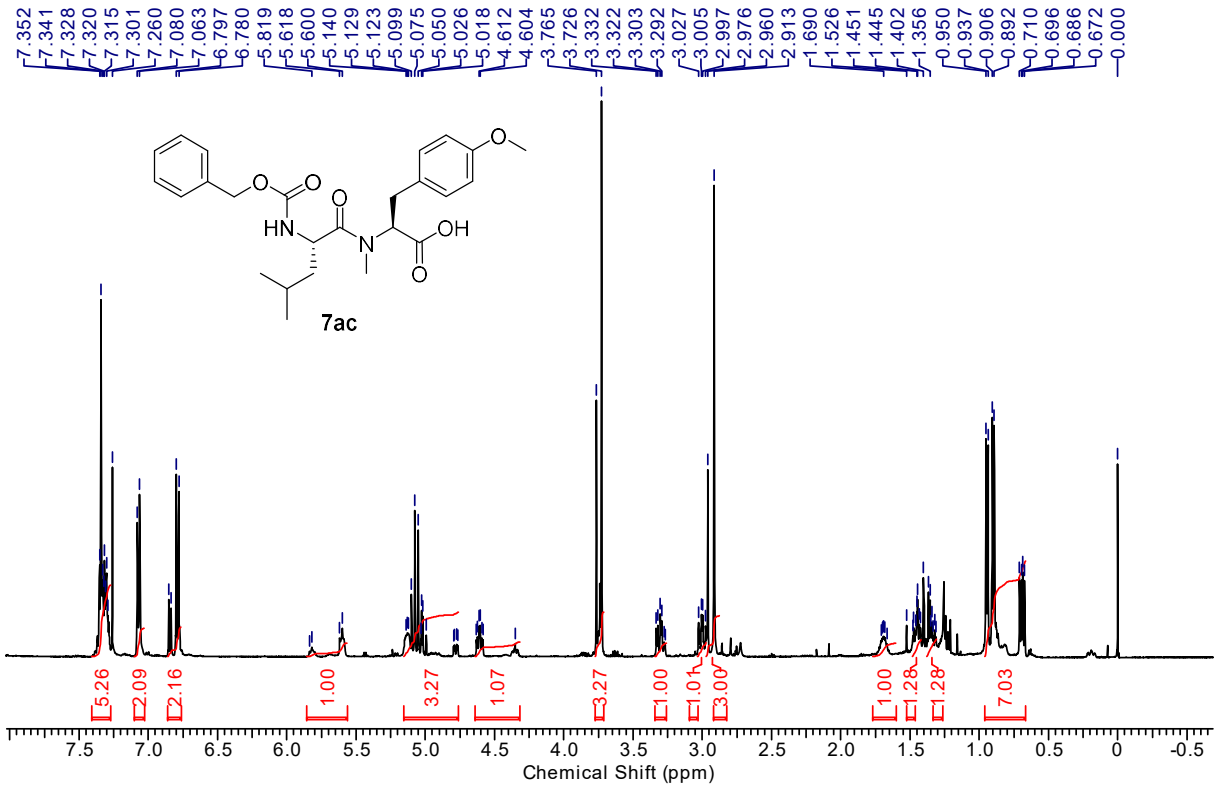


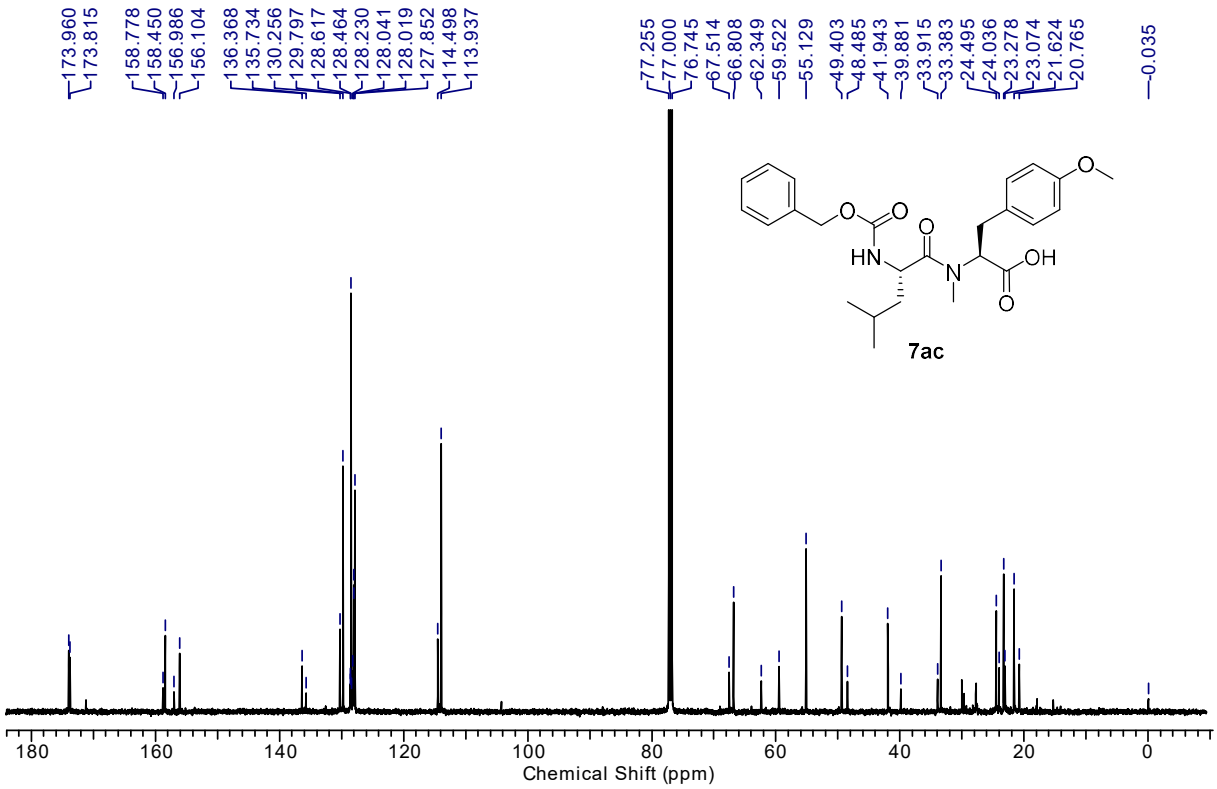
(*S*)-2-((*tert*-Butoxycarbonyl)(methyl)amino)-3-(4-nitrophenyl)propanoic acid (6ad)



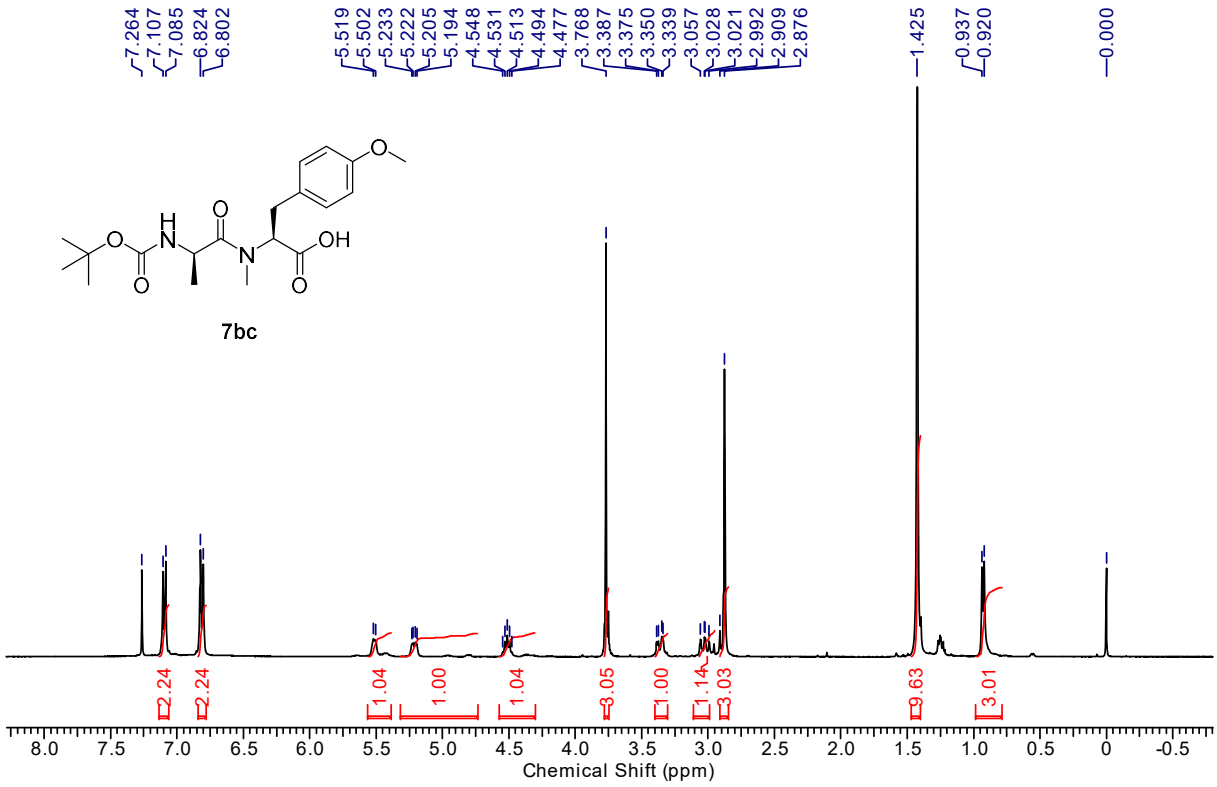


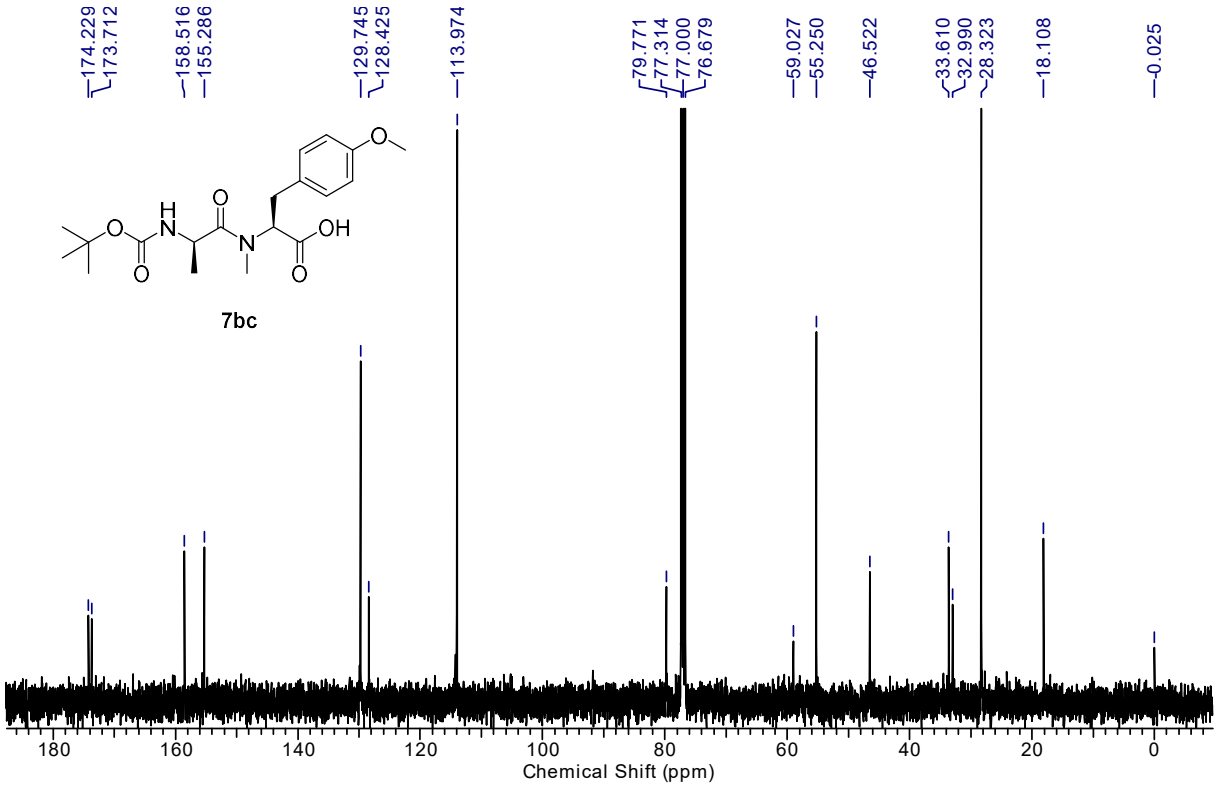
(*S*)-2-((*S*)-2-(((Benzyloxy)carbonyl)amino)-*N*,4-dimethylpentanamido)-3-(4-methoxyphenyl) propanoic acid (7ac)



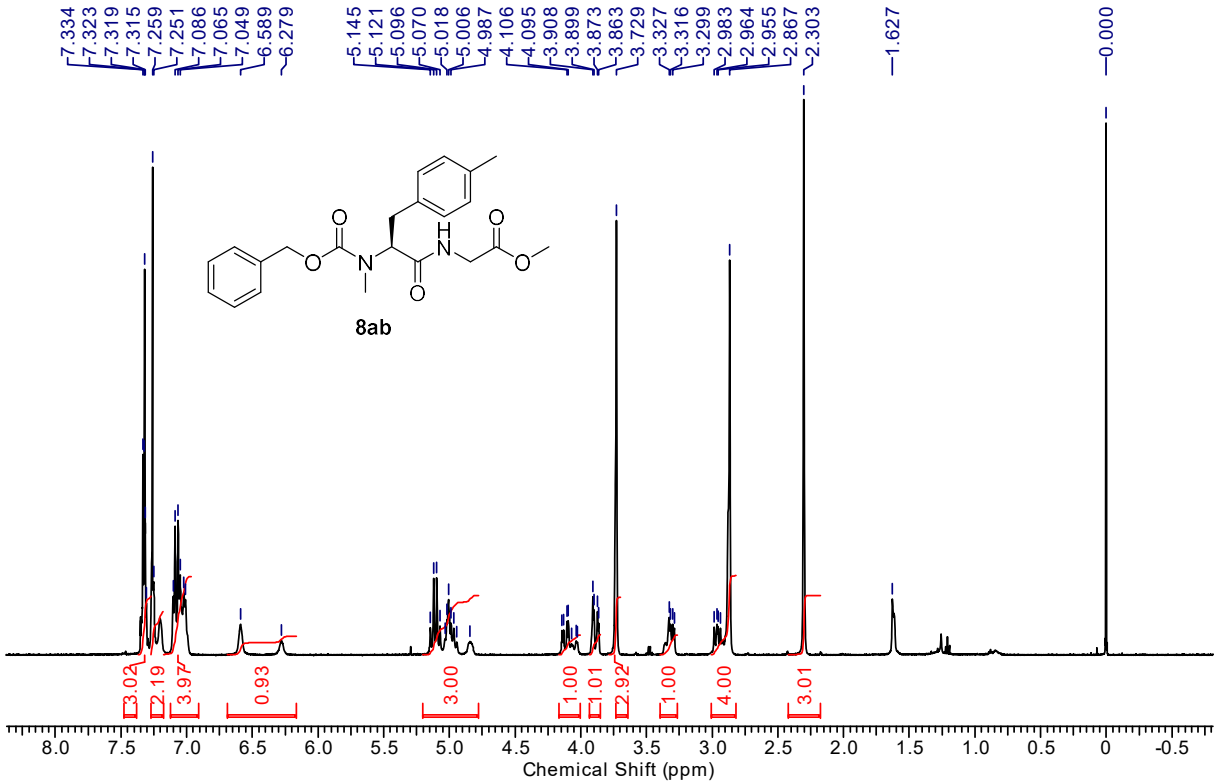


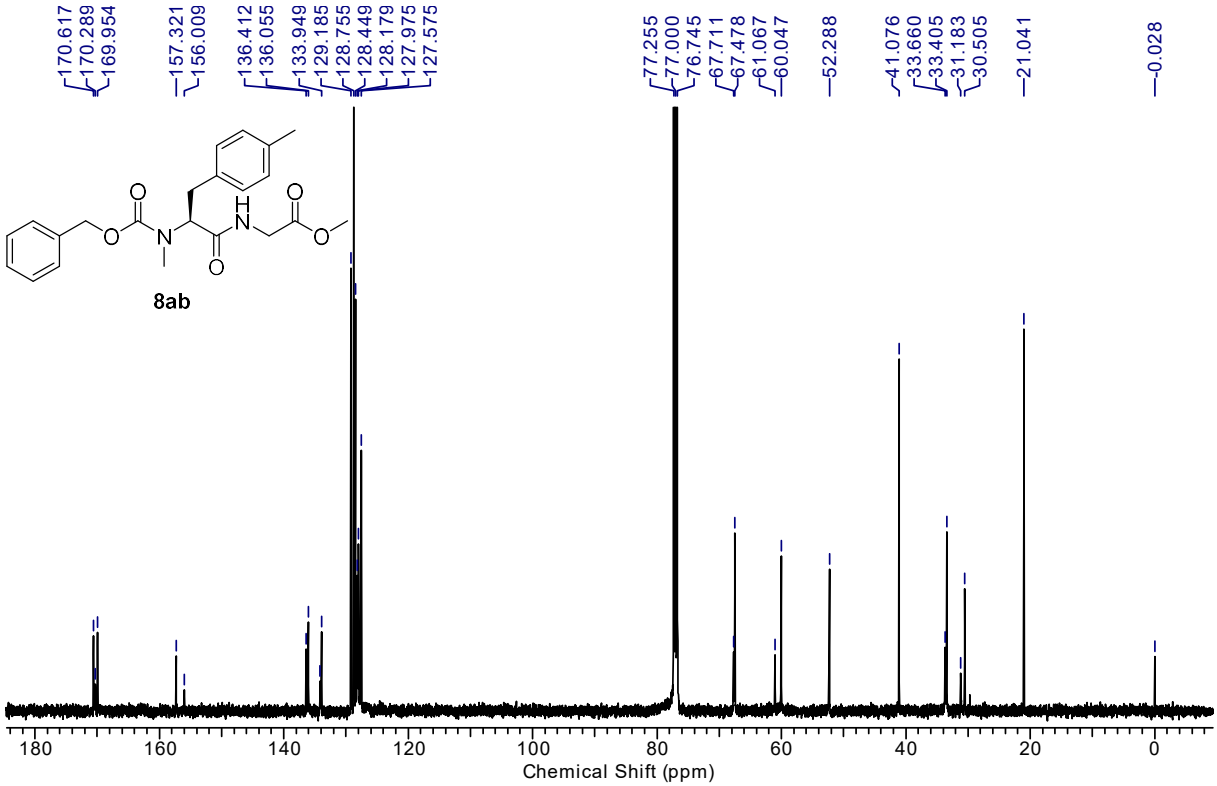
(*S*)-2-((*R*)-2-((*tert*-Butoxycarbonyl)amino)-*N*-methylpropanamido)-3-(4-methoxyphenyl)propanoic acid (7bc)



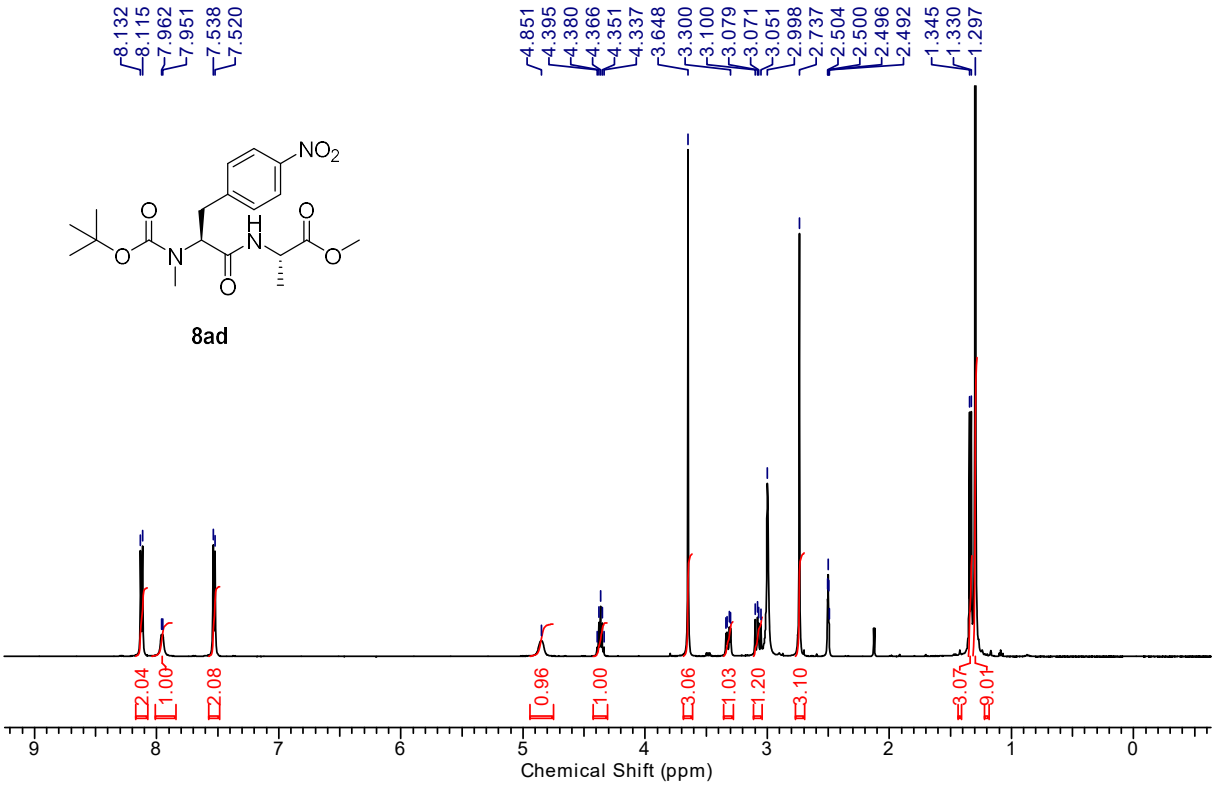


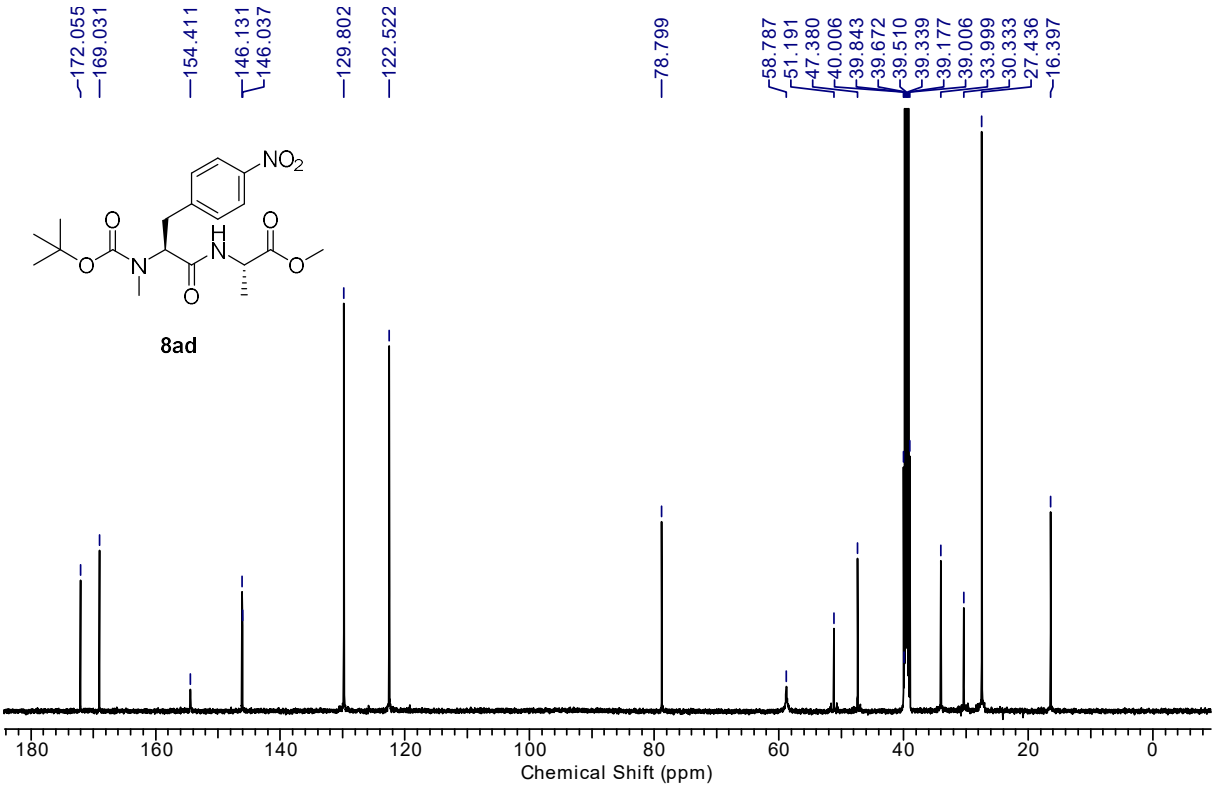
Methyl (*S*)-(2-(((benzyloxy)carbonyl)(methyl)amino)-3-(*p*-tolyl)propanoyl)glycinate (8ab)





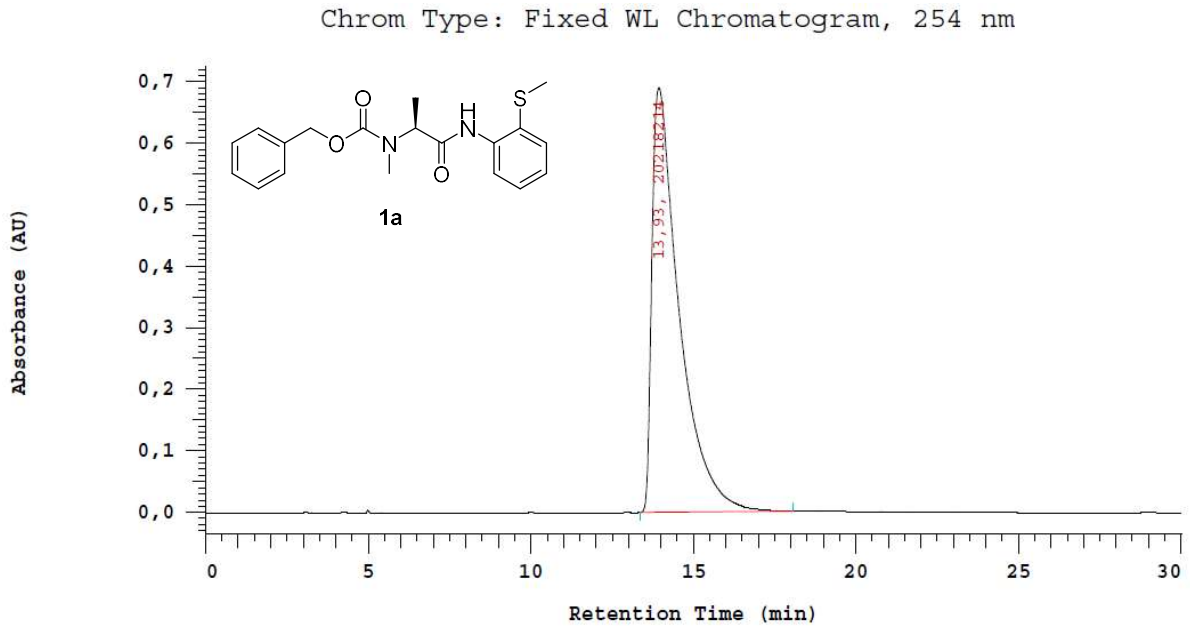
Methyl ((*S*)-2-((*tert*-butoxycarbonyl)(methyl)amino)-3-(4-nitrophenyl)propanoyl)-*L*-alaninate (8ad)

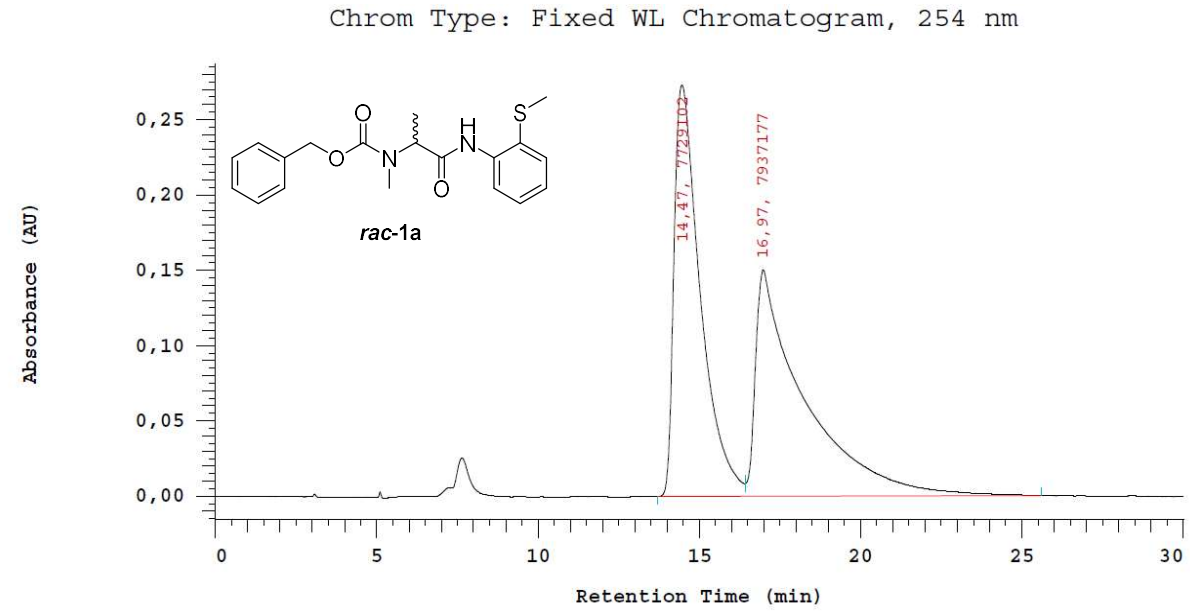




HPLC Analysis

To determine the ee value of compound **1a**, a racemic sample was prepared starting from *D*/*L*-alanine, resulting in compound ***rac*-1a**. The HPLC chromatograms of **1a** and ***rac*-1a** are shown in Fig. 1.

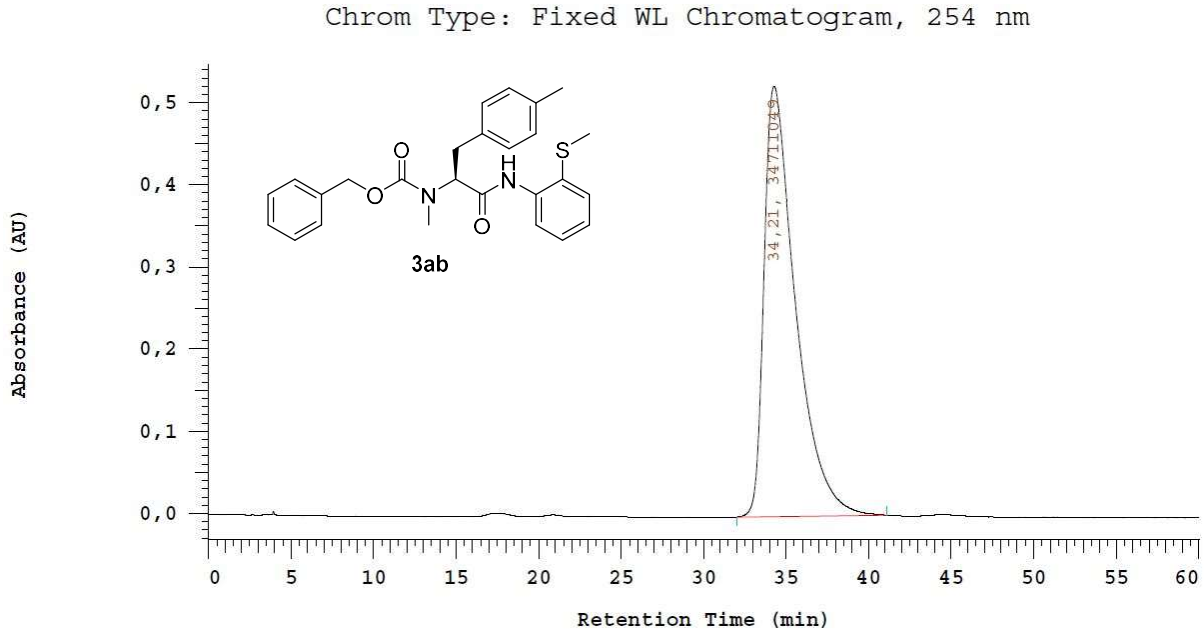


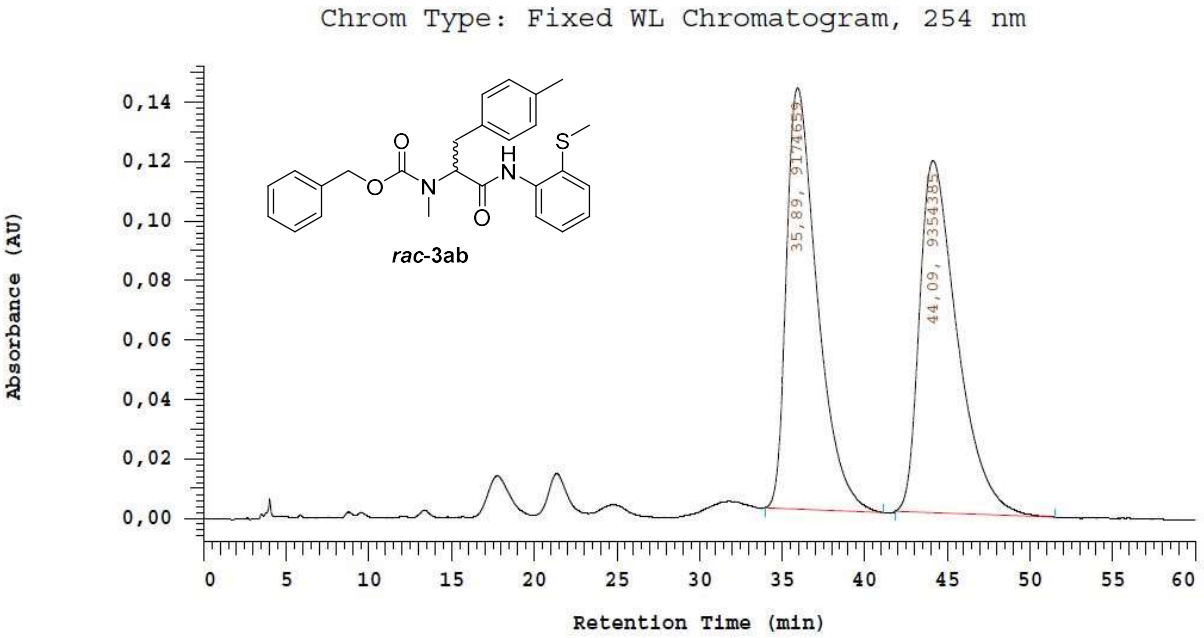


No.	RT	Area	Ar
1	14,47	7729102	4
2	16,97	7937177	5
		15666279	10

Fig. 1 HPLC analysis of compounds **1a** and ***rac*-1a**. Parameters: OD-H, *n*-hexane:*i*-PrOH 9:1, 1 mLmin^{-1}, 20 °C, t_R (**1a**) = 13.9 min.

Exemplarily for the C-H activation reactions, a racemic analogue (***rac*-3ab**) of compound **3ab** was prepared and both samples were analysed by HPLC (Fig. 2).

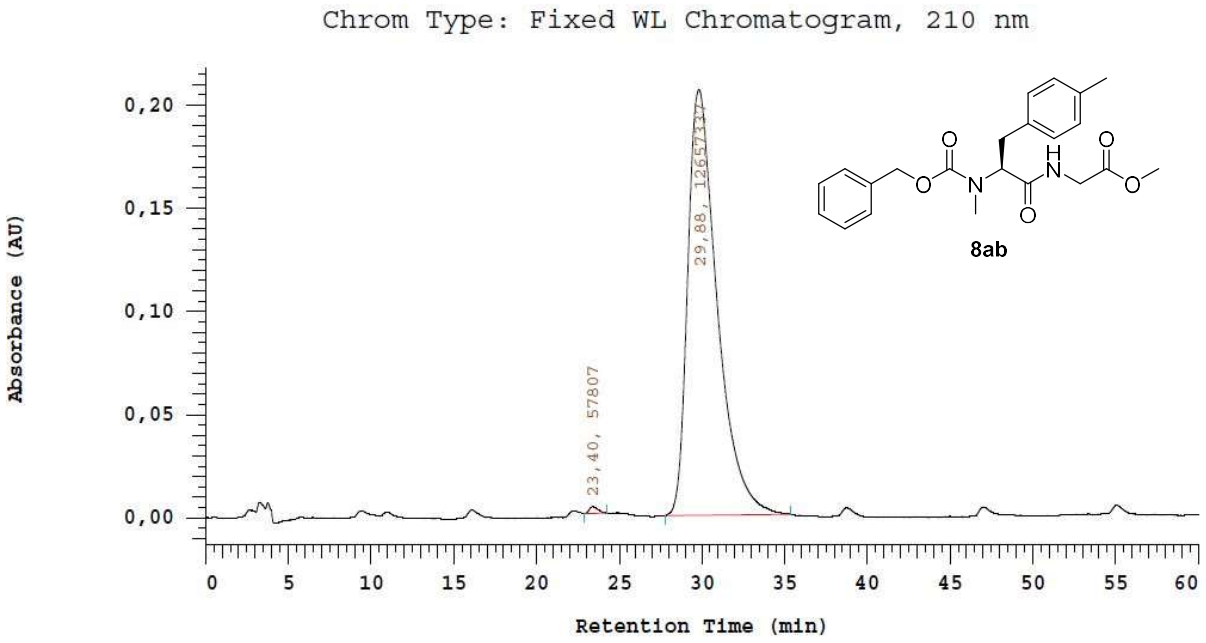




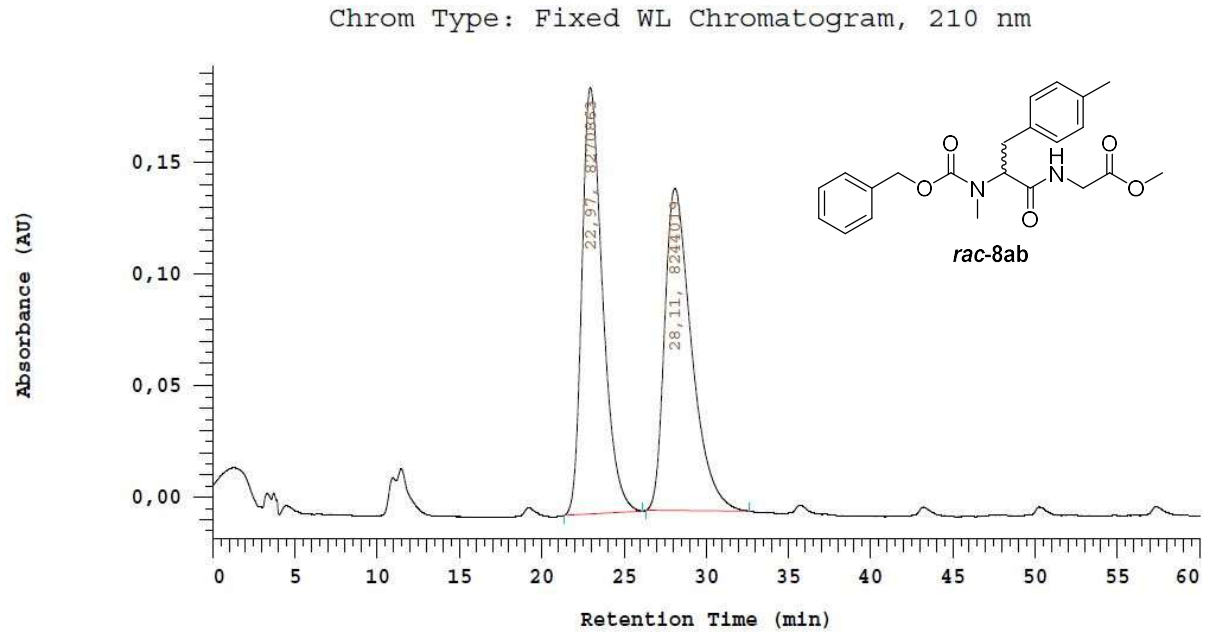
No.	RT	Area	Area %
1	35,89	9174659	49,515
2	44,09	9354385	50,485
		18529044	100,000

Fig. 2 HPLC analysis of compounds **3ab** and ***rac*-3ab**. Parameters: Reprosil, *n*-hexane:*i*-PrOH 6:4, 1 mLmin^{-1}, 20 °C, t_R (**3ab**) = 34.2 min.

Exemplarily for the peptide coupling reactions, a racemic analogue (***rac*-8ab**) of compound **8ab** was prepared and both samples were analysed by HPLC (Fig. 3). Additionally, compound **8ad** was analysed by HPLC (Fig. 4).



No.	RT	Area	Area %
1	23,40	57807	0,455
2	29,88	12657337	99,545
		12715144	100,000



No.	RT	Area	Area %
1	22,97	8270863	50,081
2	28,11	8244019	49,919
		16514882	100,000

Fig. 3 HPLC analysis of compounds **8ab** and ***rac*-8ab**. Parameters: Reprosil, *n*-hexane:*i*-PrOH 6:4, 1 mLmin^{-1}, 20 °C, t_R (**8ab**) = 29.9 min.

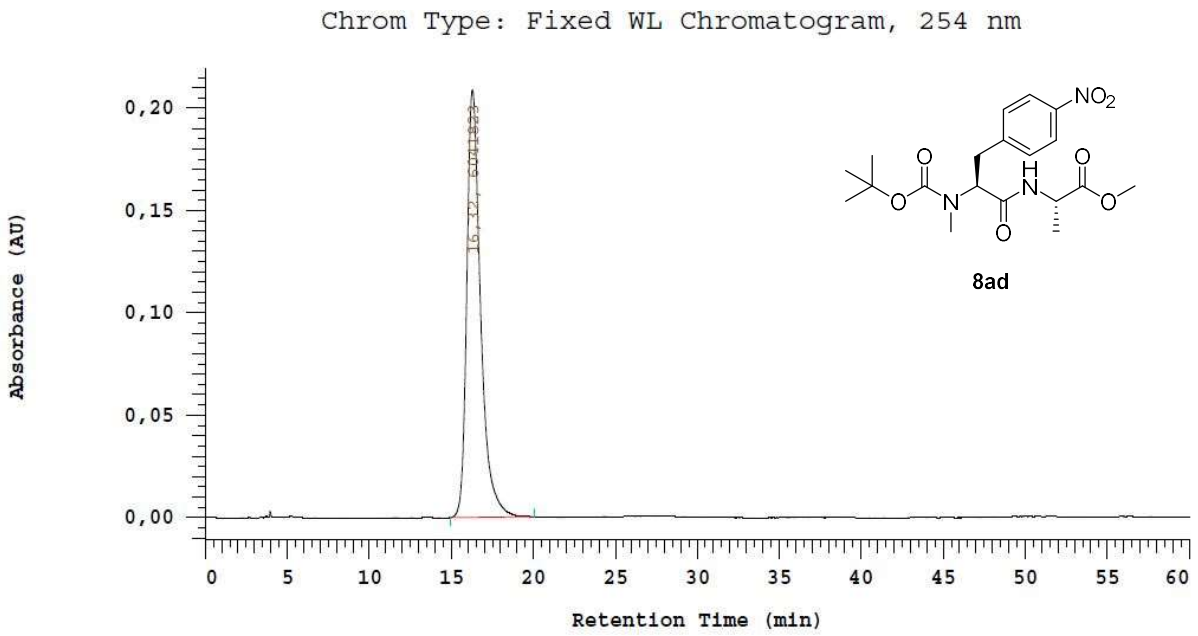


Fig. 4 HPLC analysis of compound **8ad**. Parameters: Reprosil, *n*-hexane:*i*-PrOH 6:4, 1 mLmin^{-1}, 20 °C, t_R (**8ad**) = 16.32 min.

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