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SUPPORTING INFORMATION

Title: Straightforward Synthesis of Non-Natural Selenium Containing Amino Acid Derivatives and Peptides
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Ref. No.: O200500530

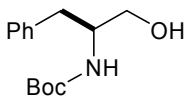
MATERIALS AND METHODS

^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz respectively with tetramethylsilane as internal standard. High resolution mass spectra were recorded on a Bruker BioApex 70e FT-ICR (Bruker Daltonics, Billerica, USA) instrument in ESI-mode. Column chromatography was performed using Merck Silica Gel (230-400 mesh) following the methods described by Still.[1] Thin layer chromatography (TLC) was performed using Merck Silica Gel GF_{254}, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor, or acidic vanillin. THF was dried over sodium benzophenone ketyl and distilled prior to use. Dichloromethane and chloroform were distilled from phosphorus pentoxide. All other solvents were used as purchased unless otherwise noted.

General Procedure for the preparation of N-Boc aminoalcohols.

To a solution of the appropriate aminoalcohol (10 mmol) in acetonitrile (50 mL), Boc_2O (10 mmol, 2,182 g) was added dropwise, at 0 ^{o}C. The mixture was stirred at rt for 4 h and the solvent was removed under vacuum and the crude product was purified by flash chromatography eluting with a mixture of hexanes/ethyl acetate (70:30).

N-Boc phenylalaninol (5a).

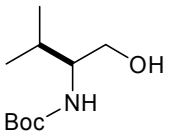


Yield: 87%; α_D^{20} = -27(*c*=1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.32-7.20 (m, 5H), 4.79-4.77 (m, 1H), 3.81-3.78 (m, 1H), 3.65 (dd,

[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem*. **1978**, *43*, 2923-2925

1H, *J*=3.7, *J*=11.0), 3.54 (dd, 1H, *J*=5.2, *J*= 11.0), 2.83 (d, 2H, *J*= 7.1), 2.45 (m, 1H), 1.41 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 156.1, 137.8, 129.3, 128.5, 126.5, 79.7, 64.3, 53.7, 37.5, 28.3.

N-Boc valinol (5b).

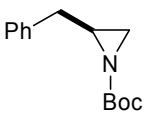


Yield: 89%; α_D^{20} = -23 (*c*=1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 4.99-4.96 (m, 1H), 3.63-3.60 (m, 2 H), 3.39-3.36 (m, 2 H), 1.86-1.82 (m, 1 H), 1.44 (s, 9H), 0.94 (d, *J*= 8.5 Hz, 3H), 0.92 (d, *J*= 8.5 Hz, 3H); ^{13}C NMR ($CDCl_3$,100 MHz) δ = 156.6, 79.1, 63.4, 60.2, 57.8, 28.2, 19.36, 18.3.

Preparation of N-Boc aziridines (4).

Under an argon atmosphere, KOH (40 mmol, 2,25 g) was added to a solution of N-Boc aminoalcohol (10 mmol) **5** in THF (50 mL). After that, TsCl (12 mmol, 2,29 g) was added. The reaction mixture was stirred for 2 h under reflux and a second portion of KOH (40 mmol, 2,25 g) was added and the system was refluxed for additional 2 h. After this time, the reacton was cooled to rt and washed with brine (20 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic layers were dried with $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography first eluting with hexanes and then with a mixture of hexanes/ethyl acetate (95:5).

(*S*)-*tert*-butyl 2-benzylaziridine-1-carboxylate (4a).[2]

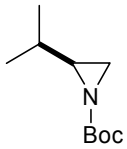


Yield: 75%; α_D^{20} = +51 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.30-7.20 (m, 5H), 2.95 (dd, J^1= 5.6 Hz, J^2= 13.9 Hz, 1H), 2.68-2.60 (m, 2H), 2.30 (d, *J*= 5.6 Hz, 1H), 2.01 (d, *J*= 3.4 Hz, 1H), 1.43 (s, 9H);

[2] Braga, A. L.; Paixão, M. W.; Lüdtke, D. S.; Silveira, C. C.; Rodrigues, O. E. D. *Org. Lett.* **2003**, *5*, 2635-2638.

^{13}C NMR ($CDCl_3$, 100 MHz) δ = 162.3, 137.9, 128.7, 128.3, 126.4, 81.0, 38.3, 38.2, 31.2, 27.8.

(*S*)-*tert*-butyl 2-isopropylaziridine-1-carboxylate (4b).[2]

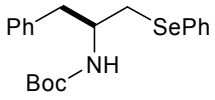


Yield: 72%; α_D^{20} = +60 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 2.22 (d, *J*=6.2 Hz, 1H), 2.15-2.12 (m, 1H), 1.93 (d, *J*= 3.8 Hz, 1H), 1.49-1.47 (m, 1H), 1.45 (s, 9H), 1.06 (d, *J*=6.6 Hz, 3H), 0.96 (d, *J*=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 162.7, 80.5, 44.2, 30.8, 30.4, 27.7, 19.5, 19.0.

General Procedure for the synthesis of N-Boc seleno-amines (3).

Under an argon atmosphere, sodium borohydride was added to a solution of diphenyl diselenide (0.172g, 0.55 mmol) in THF (4 mL). Ethanol (2 mL) was then dropwise added and the clear solution formed was stirred at room temperature for 10 minutes. After this time a THF (1mL) solution of the appropriate aziridine (1 mmol) was added dropwise. After stirring for 24 h at room temperature, the reaction mixture was quenched with aqueous saturated NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography first eluting with hexanes and then with a mixture of hexanes/ethyl acetate (80:20).

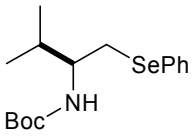
(*S*)-*tert*-butyl 1-phenyl-3-(phenylselanyl)propan-2-ylcarbamate (3a).



Yield: 72%; α_D^{20} = +14 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.50-7.12 (m, 10H), 4.69-4.67 (m, 1H), 4.09-4.07 (m, 1H), 3.02-2.98 (m, 2H), 2.87-2.82 (m, 2H), 1.38 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 154.8, 137.4, 132.4, 129.9, 129.1, 128.9, 128.2, 126.1, 126.2, 78.9, 51.4,

40.1, 32.5, 28.1; HRMS *m/z* calcd for $C_{20}H_{25}NO_2Se$ + Na^+ 414.0942, found 414.0939.

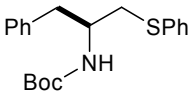
(*S*)-*tert*-butyl 3-methyl-1-(phenylselanyl)butan-2-ylcarbamate (3b).



Yield: 78%; α_D^{20} = +35 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 200 MHz) δ = 7.52 (s, 2H), 7.25-7.23 (m, 3H), 4.60-4.58 (m, 1H), 3.66-3.69 (m, 1H), 3.07-3.04 (m, 1H), 1.88-1.81 (m, 2H), 1.42 (s, 9H), 0.90-0,89 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 155.6, 132.9, 130.3, 129.0, 127.0, 79.1, 55.6, 31.7, 32.4, 28.3, 19.4, 18.0; HRMS *m/z* calcd for $C_{16}H_{25}NO_2Se$ M + Na^+ 366,0942, found 366,0947.

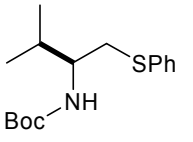
The sulfur derivatives were prepared with the same procedure, just using diphenyl disulfide.

(*S*)-*tert*-butyl 1-phenyl-3-(phenylthio)propan-2-ylcarbamate (6a). [3]



Yield: 77%; α_D^{20} = +22 (*c*=1.05, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.17–7.37 (m, 10H), 4.67 (br, 1H), 4.06-4.02 (m, 1H), 3.04-3.05 (m, 2H), 2.92-2.90 (m, 2H), 1.40 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 155.3, 137.7, 136.3, 129.8, 129.6, 129.2, 128.7, 126.8, 126.5, 79.6, 51.6, 39.7, 38.0, 28.8; HRMS *m/z* calcd for $C_{20}H_{25}NO_2S$ + Na^+ 366.1496, found 366.1498.

(*S*)-*tert*-butyl 3-methyl-1-(phenylthio)butan-2-ylcarbamate (6b).[3]



Yield: 74%; α_D^{20} = +31 (*c*=1.0, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.37-7.16 (m, 5H), 4.69-4.66 (m, 1H), 3.67-3.66 (m, 1H), 3.07-

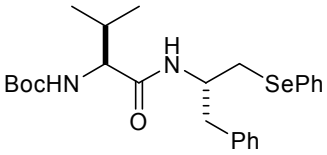
[3] Granader, J.; Sott, R.; Hilmersson, G. *Tetrahedron: Asymmetry* **2003**, *14*, 439-447.

3.05 (m, 2H), 1.92-1.89 (m, 1H), 1.42 (m, 9H), 0.92-0.90 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 155.5, 136.3, 129.5, 128.8, 126.0, 78.9, 55.0, 37.3, 30.7, 28.2, 19.3, 17.7.

General procedure for the synthesis of selenium-containing amino acids (1).

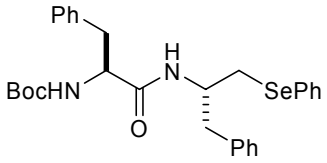
Under an argon atmosphere, N-methylmorpholine (50 mg, 0.5 mmol) was added to a solution of the N-Boc protected amino acid **2** (0.5 mmol) in chloroform (5 mL) at 0 ^{o}C. After stirring for 15 minutes at this temperature, ethyl chloroformate (54 mg, 0.5 mmol) was added and stirring was prolonged for additional 30 minutes before addition of **3** (0.5 mmol). The resulting reaction mixture was stirred at 0 ^{o}C for 1 h and then at room temperature for 16 h. After this time it was diluted with chloroform and washed with 1M NaOH (2 x 10 mL), 1M HCl (2 x 10 mL), and brine (10 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated. The crude product was purified by flash chromatography, when required, eluting with a mixture of hexanes/ethyl acetate (80:20).

tert-butyl (S)-3-methyl-1-oxo-1-((S)-1-phenyl-3-(phenylselanyl)propan-2-ylamino)butan-2-ylcarbamate (1a).



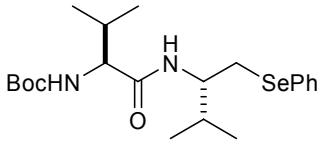
Yield 98 %; α_D^{20}= +22 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.49-7.48 (m, 2H), 7.25-7.11 (m, 8H), 6.10 (br, 1H), 4.96 (br, 1H), 4.39-4.38 (m, 1H), 3.80-3.76 (m, 1H), 3.02-3.01 (m, 2H), 2.92-2.90 (m, 2H), 2.01-2.11 (m, 1H), 1.43 (s, 9H), 0.97-0.80 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.0, 155.8, 137.2, 135.3, 132.8, 129.8, 129.3, 128.7, 126.7, 126.4, 79.8, 60.1, 50.3, 40.0, 32.2, 30.6, 28.3, 19.3, 17.5; HRMS *m/z* calcd for $C_{25}H_{34}O_3N_2Se + Na^+$ 513.1619, found 513.1626.

tert-butyl (S)-1-oxo-3-phenyl-1-((S)-1-phenyl-3-(phenylselanyl)propan-2-ylamino)propan-2-ylcarbamate (1b).



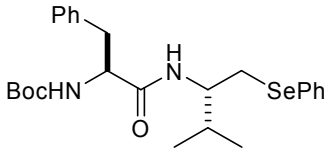
Yield 97 %; α_D^{20}= +10 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.44-7.43 (m, 2H), 7.21-7.15 (m, 11H), 7.03-7.02 (m, 2H), 6.19 (br, 1H), 5.09 (br, 1H), 4.28-4.24 (m, 2H), 2.94-2.80 (m, 6H), 1.38 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.6, 155.2, 137.0, 136.7, 133.0, 132.6, 129.3, 129.2, 128.6, 128.5, 128.4, 127.0, 126.7, 126.5, 79.9, 55.8, 50.3, 39.6, 38.3, 31.6, 28.2; HRMS *m/z* calcd for $C_{29}H_{34}O_3N_2Se$ + Na^+ 561.1617, found 561.1626.

tert-butyl (S)-3-methyl-1-((S)-3-methyl-1-(phenylselanyl)butan-2-ylamino)-1-oxobutan-2-ylcarbamate (1c).



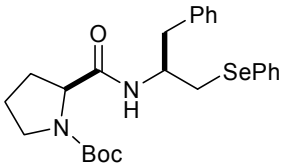
Yield 85 %; α_D^{20}= +23 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.53-7.51 (m, 2H), 7.26-7.24 (m, 3H), 6.06 (br, 1H), 5.03 (br, 1H), 4.02-3.98 (m, 1H), 3.80-3.76 (m, 1H), 3.13-3.00 (m, 2H), 2.11-2.03 (m, 1H), 1.93-1.88 (m, 1H), 1.43 (s, 9H), 0.94-0.83 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.4, 155.9, 132.9, 130.1, 129.1, 127.1, 79.7, 60.5, 54.1, 31.8, 31. 5, 30.2, 28.3, 19.5, 19.4, 19.3, 17.9; HRMS *m/z* calcd for $C_{21}H_{34}O_3N_2Se$ + Na^+ 465.1628, found 465.1626.

tert-butyl (S)-1-((S)-3-methyl-1-(phenylselanyl)butan-2-ylamino)-1-oxo-3-phenylpropan-2-ylcarbamate (1d).



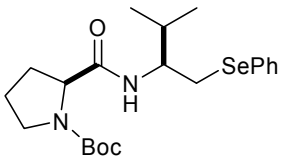
Yield 83 %; α_D^{20}= +44 (*c*=0.9, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.48-7.46 (m, 2H), 7.23-7.21 (m, 8H), 6.25 (br, 1H), 5.32 (br, 1H), 4.37-4.34 (m, 1H), 3.99-3.88 (m, 1H), 3.08-2.87 (m, 4H), 1.90-1.81 (m, 1H), 1.38 (s, 9H), 0.82-0.77 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.9, 155.4, 136,9; 132.7, 130.1, 129.2, 128.9, 128.5, 126.9, 126.6, 79.8, 55.8, 54.0, 37.9, 31.2, 31.0, 28.1, 19.2, 17.5; HRMS *m/z* calcd for $C_{25}H_{34}O_3N_2Se$ + Na^+ 513.1636, found 513.1626.

(S)-tert-butyl 2-((S)-1-phenyl-3-(phenylselanyl)propan-2-ylcarbamoyl)-pyrrolidine-1-carboxylate (1e).



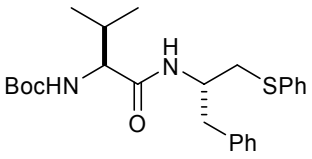
Yield 82 %; α_D^{20}= -36 (*c*=1.4, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.54-7.51 (m, 2H), 7.25-7.09 (m, 9H), 4.38-4.36 (m, 1H), 4.14-4.12 (m, 1H), 3.26-3.22 (m, 1H), 3.13-3.00 (m, 4H), 2.98-2.76 (m, 1H), 2.04-1.69 (m, 4H), 1.44 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.5, 154.6, 137.5, 132.5, 129.9, 129.1, 128.4, 126.9, 126.5, 126.4, 80.4, 59.9, 50.1, 46.9, 39.9, 32.1, 30.8, 28.3, 24.3; HRMS *m/z* calcd for $C_{25}H_{32}O_3N_2Se$ + Na^+ 511.1461, found 511.1470.

(S)-tert-butyl 2-((S)-3-methyl-1-(phenylselanyl)butan-2-ylcarbamoyl)-pyrrolidine-1-carboxylate (1f).



Yield 84 %; α_D^{20}= +32 (*c*=1.3, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.54-7.52 (m, 2H), 7.26-7.23 (m, 4H), 4.21-4.20 (m, 1H), 3.98-3.94 (m, 1H), 3.52-3.29 (m, 2H), 3.12-3.04 (m, 2H), 1.97-1.87 (m, 5H), 1.46 (s, 9H), 0.86-0.85 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.5, 155.8, 132.8, 130.1, 128.9, 126.8, 80.2, 59.6, 54.2, 46.9, 31.3, 30.9, 28.3, 27.2, 24.5, 19.4, 17.2; HRMS *m/z* calcd for $C_{21}H_{32}O_3N_2Se$ + Na^+ 463.1463, found 463.1470.

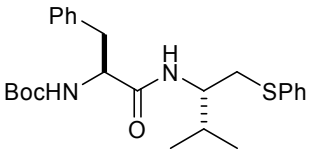
tert-butyl (S)-3-methyl-1-oxo-1-((S)-1-phenyl-3-(phenylthio)propan-2-yl-amino)butan-2-ylcarbamate (1g).



Yield 90 %; α_D^{20}= +23 (*c*=1.2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.34-7.14 (m, 10H), 6.15 (br, 1H), 5.01 (br, 1H), 4.37-4.35 (m, 1H), 3.83-3.79 (m, 1H), 3.02-2.93 (m, 4H), 2.05-2.04 (m, 1H), 1.43 (s, 9H), 0.90-0.82 (m, 6H); ^{13}C NMR ($CDCl_3$, 100

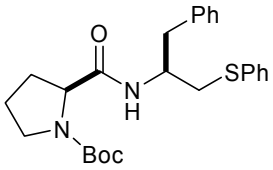
MHz): δ = 171.2, 155.8, 137.1, 135.7, 129.6, 129.2, 129.0, 128.6, 126.7, 126.4, 79.8, 60.1, 49.9, 39.1, 37.4, 30.6, 28.3, 19.2, 17.6; HRMS *m/z* calcd for $C_{25}H_{34}O_3N_2S + Na^+$ 465.2177, found 465.2182.

tert-butyl (S)-1-((S)-3-methyl-1-(phenylthio)butan-2-ylamino)-1-oxo-3-phenylpropan-2-ylcarbamate (1h).



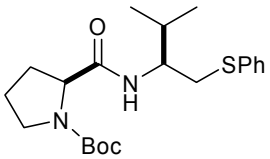
Yield 71 %; α_D^{20}= +24 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.34-7.18 (m, 10H), 5.88 (br, 1H), 5.04 (br, 1H), 4.27-4.22 (m, 1H), 3.94-3.91 (m, 1H), 3.09-2.95 (m, 4H), 1.95-1.90 (m, 1H), 1.40 (s, 9H), 0.85 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.9, 155.5, 136.9, 136.2, 129.5, 129.3, 128.9, 128.60, 126.8, 126.2, 80.1, 56.0, 53.6, 38.0, 36.6, 30.0, 28.2, 19.3, 17.4; HRMS *m/z* calcd for $C_{25}H_{34}O_3N_2S + Na^+$ 465.2189, found 465.2182.

(S)-tert-butyl 2-((S)-1-phenyl-3-(phenylthio)propan-2-ylcarbamoyl)pyrrolidine-1-carboxylate (1i).



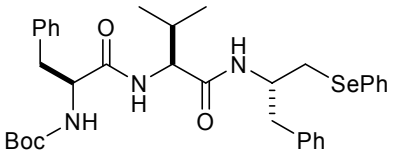
Yield 67 %; α_D^{20}= -60 (*c*=1.2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.40-7.12 (m, 11H), 4.35-4.34 (m, 1H), 4.18-4.17 (m, 1H), 3.26-3.14 (m, 2H), 3.03-2.99 (m, 1H), 2.97-2.94 (m, 2H), 2.83-2.78 (m, 1H), 1.75-1.43 (m, 4H), 1.25 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.9, 155.7, 137.4, 135.2, 129.1, 129.0, 128.9, 128.4, 126.5, 126.1, 80.4, 59.9, 49.6, 46.9, 38.9, 37.3, 30.7, 28.3, 24.3; HRMS *m/z* calcd for $C_{25}H_{32}O_3N_2S + Na^+$ 463.2021, found 463.2025.

(S)-tert-butyl 2-((S)-3-methyl-1-(phenylthio)butan-2-ylcarbamoyl)pyrrolidine-1-carboxylate (1j).



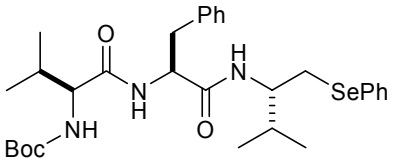
Yield 68 %; α_D^{20}= -68 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.39-7.16 (m, 6H), 4.25-4.24 (m, 1H), 3.97-3.96 (m, 1H), 3.52-3.29 (m, 2H), 3.10-3.08 (m, 2H), 2.01-1.87 (m, 5H), 1.46 (s, 9H), 0.88-0.87 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.9, 155.7, 129.4, 129.4, 128.8, 126.0, 80.2, 59.6, 53.4, 46.9, 36.6, 30.0, 28.3, 27.2, 24.5, 19.4, 16.9; HRMS *m/z* calcd for $C_{21}H_{32}O_3N_2S$ + Na^+ 415.2024, found 415.2025.

tert-butyl (S)-1-((S)-3-methyl-1-oxo-1-((S)-1-phenyl-3-(phenylselanyl)-propan-2-ylamino)butan-2-ylamino)-1-oxo-3-phenylpropan-2-ylcarbamate (7a).



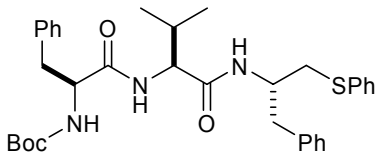
Yield 92 %; α_D^{20}= +10 (*c*=0.8, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.25-7.24 (m, 2H), 7.23-7.17 (m, 13H), 6.75 (br, 1H), 6.54 (br, 1H), 5.21 (br, 1H), 4.38-4.33 (m, 2H), 4.19-4.15 (m, 1H), 3.11-2.99 (m, 4H), 2.87-2.85 (m, 2H), 2.05-2.02 (m, 1H), 1.38 (s, 9H), 0.86-0.76 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.4, 170.2, 155.5, 137.3, 136.5, 132.6, 129.9, 129.21, 129.19, 129.12, 128.6, 128.4, 127.0, 126.8, 126.5, 80.2, 58.7, 55.8, 50.6, 40.1, 37.7, 31.8, 30.5, 28.2, 19.3, 17.7; HRMS *m/z* calcd for $C_{34}H_{43}N_3O_4Se$ + Na^+ 660.2311, found 660.2304.

tert-butyl (S)-3-methyl-1-((S)-1-((S)-3-methyl-1-(phenylselanyl)butan-2-ylamino)-1-oxo-3-phenylpropan-2-ylamino)-1-oxobutan-2-ylcarbamate (7b).



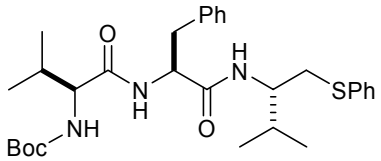
Yield 87 %; α_D^{20}= +18 (*c*=1.0, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.50-7.49 (m, 2H), 7.24-7.17 (m, 8H), 6.85 (br, 1H), 6.23 (br, 1H), 5.07 (br, 1H), 4.64-4.62 (m, 1H), 3.95-3.93 (m, 2H), 3.04-2.89 (m, 4H), 2.11-2.03 (m, 1H), 1.86-1.83 (m, 1H), 1.42 (s, 9H), 0.89-0.74 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.6, 170.3, 155.7, 136.6, 132.8, 130.2, 129.3, 128.6, 127.1, 127.0, 126.9, 79.9, 60.1, 54.5, 54.4, 38.3, 31.3, 31.0, 30.6, 28.3, 19.3, 19.2, 17.6, 17.5; HRMS *m/z* calcd for $C_{30}H_{43}N_3O_4Se$ + Na^+ 612.2302, found 612.2310.

tert-butyl (S)-1-((S)-3-methyl-1-oxo-1-((S)-1-phenyl-3-(phenylthio)propan-2-ylamino)butan-2-ylamino)-1-oxo-3-phenylpropan-2-ylcarbamate (7c).



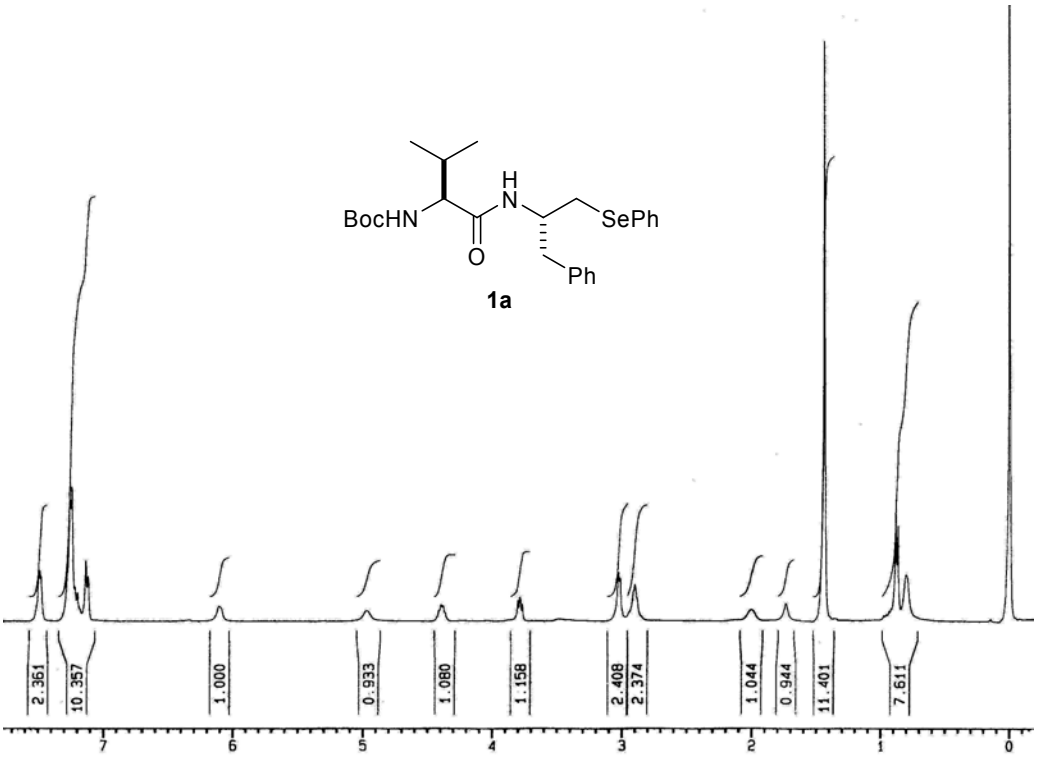
Yield 83 %; α_D^{20}= +7 (*c*=1.4, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.32-7.13 (m, 15H), 6.88 (br, 1H), 6.38 (br, 1H), 5.09 (br, 1H), 4.63-4.27 (m, 1H), 4.08-3.93 (m, 2H), 3.10-2.91 (m, 6H), 1.95-1.85 (m, 1H), 1.38 (s, 9H), 0.87-0.77 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.1, 170.5, 155.3, 136.7, 136.6, 129.6, 129.46, 129.3, 129.2, 128.9, 128.6, 128.5, 128.5, 126.7, 126.2, 80.1, 58.5, 54.5, 53.7, 38.5, 36.4, 30.4, 30.3, 28.2, 19.1, 17.6; HRMS *m/z* calcd for $C_{34}H_{43}N_3O_4S$ + Na^+ 612.2866, found 612.2872.

tert-butyl (S)-3-methyl-1-((S)-1-((S)-3-methyl-1-(phenylthio)butan-2-ylamino)-1-oxo-3-phenylpropan-2-ylamino)-1-oxobutan-2-ylcarbamate (7d).

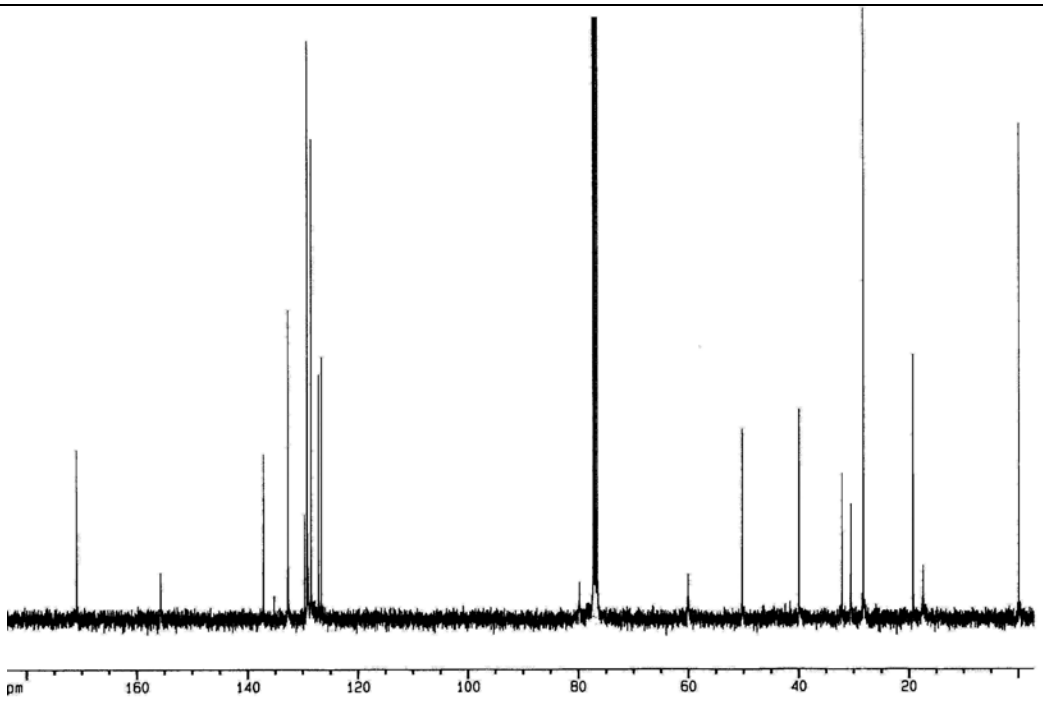


Yield 89 %; α_D^{20}= +12 (*c*=0.9, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.33-7.16 (m, 10H), 6.90 (br, 1H), 6.03 (br, 1H), 5.14 (br, 1H), 4.61-4.59 (m, 1H), 4.08-3.87 (m, 2H), 3.07-2.90 (m, 4H), 1.93-1.89 (m, 2H), 1.42 (s, 9H), 0.89-0.75 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.6, 170.4, 155.8, 136.6, 136.2, 129.6, 129.3, 128.9, 128.6, 127.0, 126.2, 79.9, 60.1, 54.7, 53.9, 38.1, 36.6, 36.5, 30.2, 28.3, 19.4, 19.3, 17.7, 17.4; HRMS *m/z* calcd for $C_{30}H_{43}N_3O_4S$ + Na^+ 564.2861, found 564.2866.

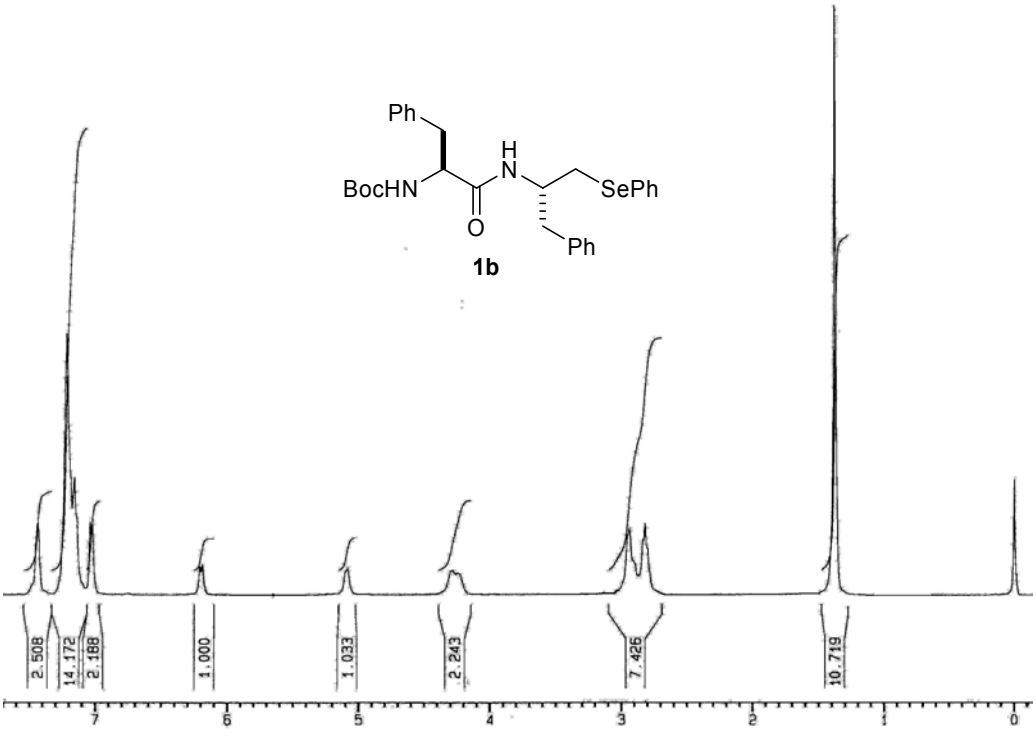
SELECTED SPECTRA



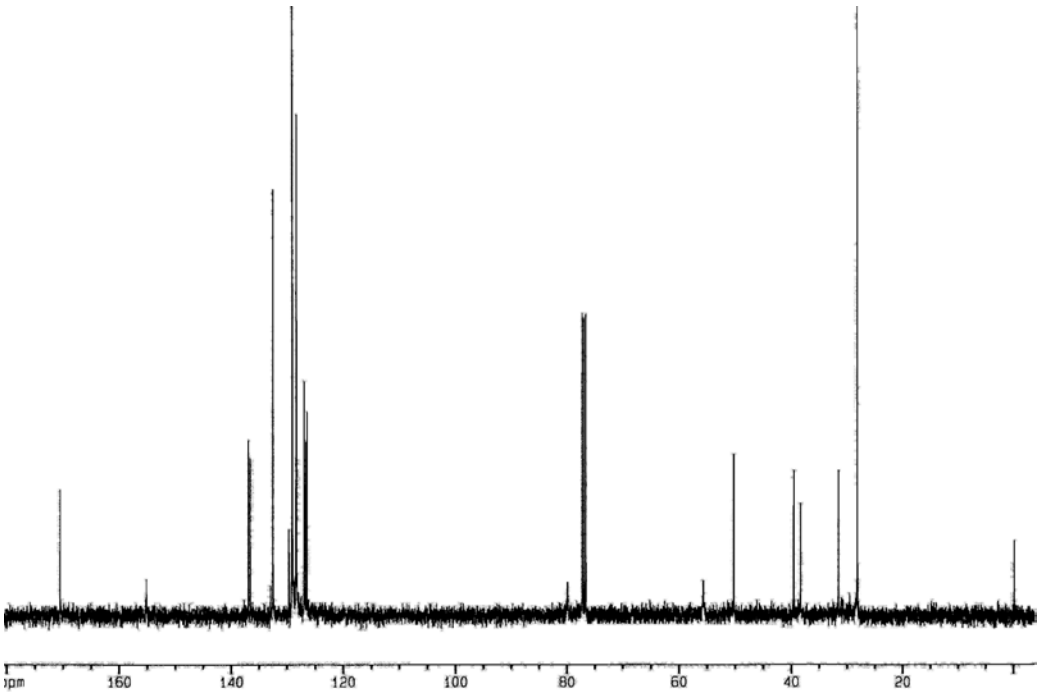
^{1}H NMR of **1a** in $CDCl_3$ at 400 MHz



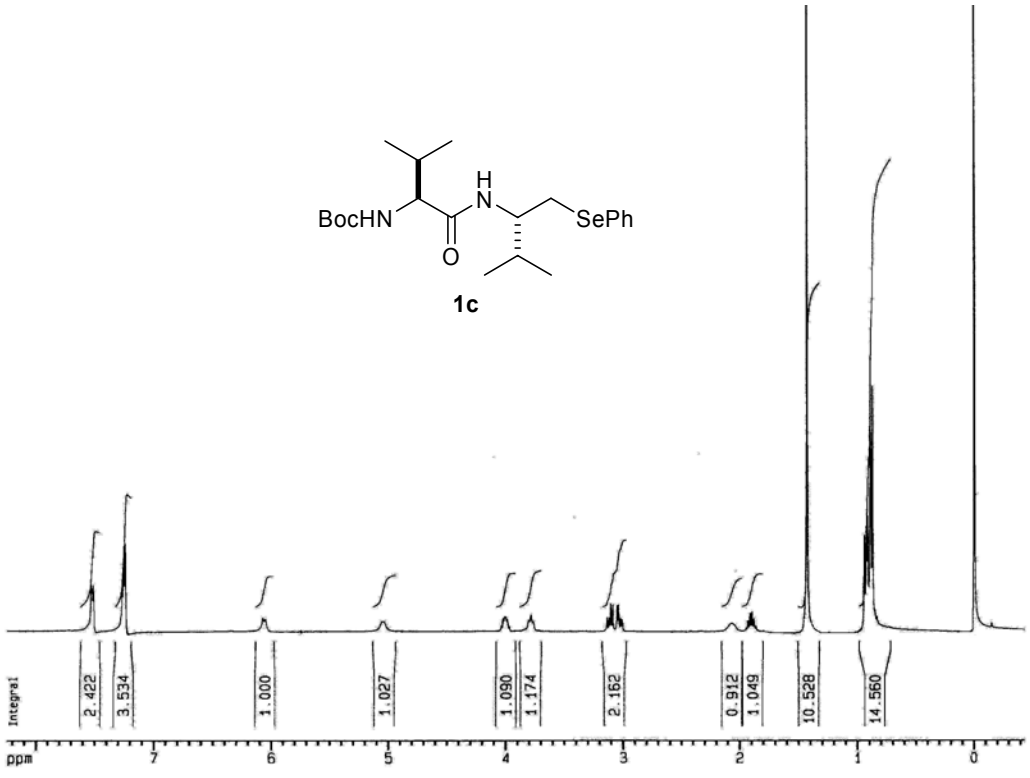
^{13}C NMR of **1a** in $CDCl_3$ at 100 MHz



^{1}H NMR of **1b** in $CDCl_3$ at 400 MHz

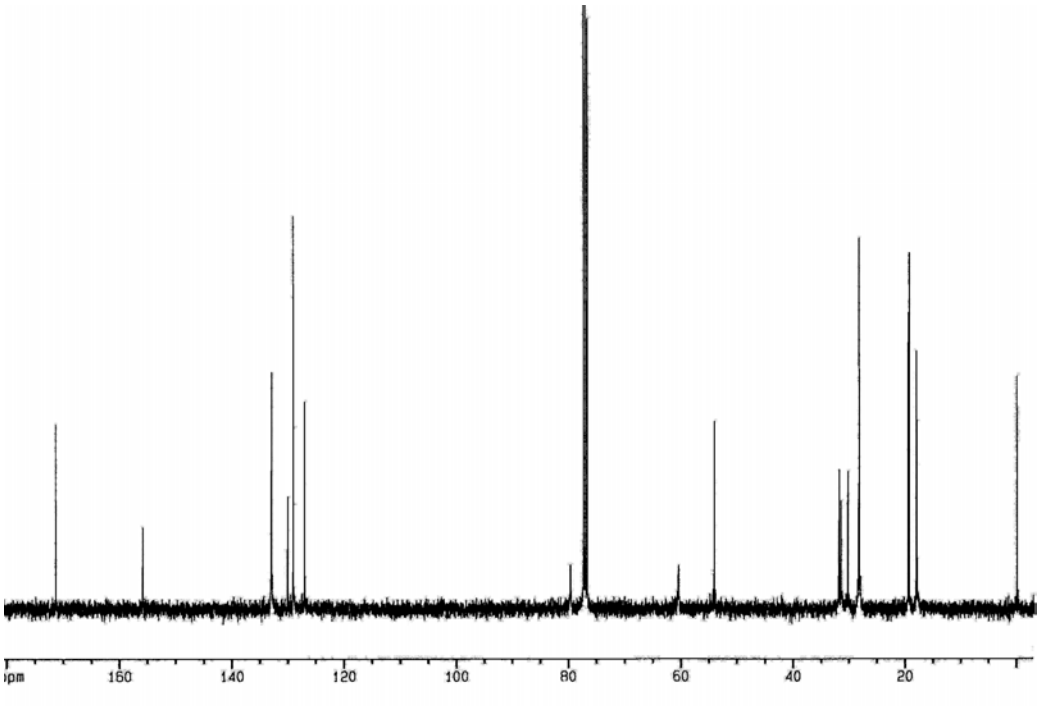


^{13}C NMR of **1b** in $CDCl_3$ at 100 MHz

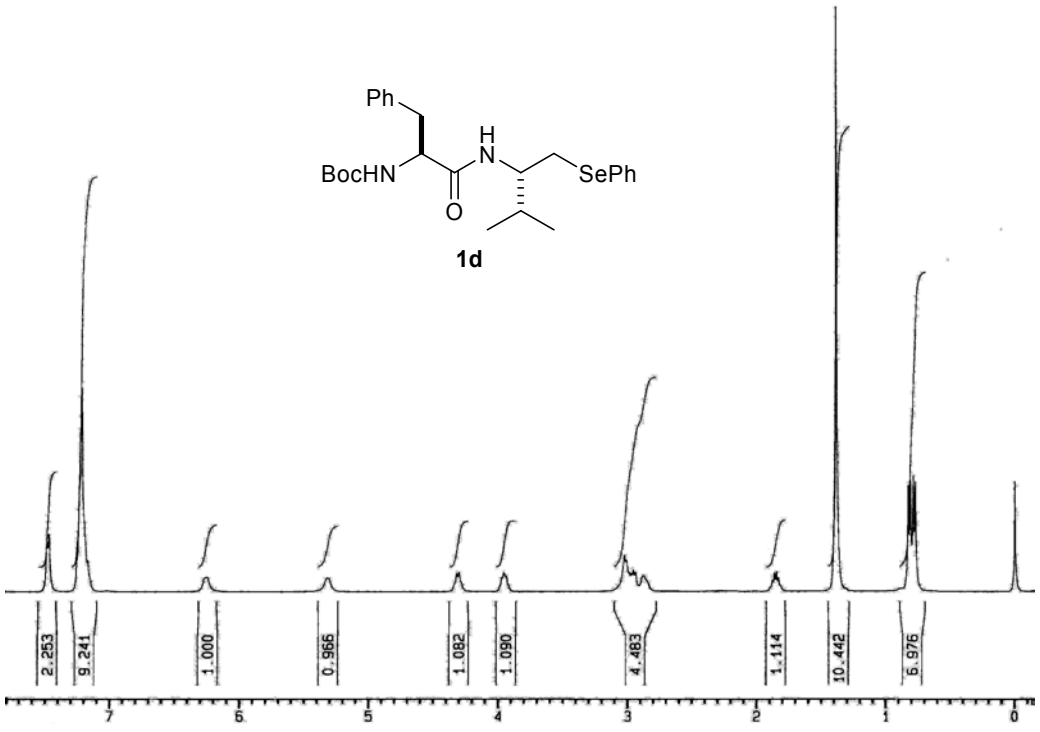


1c

^{1}H NMR of **1c** in $CDCl_3$ at 400 MHz

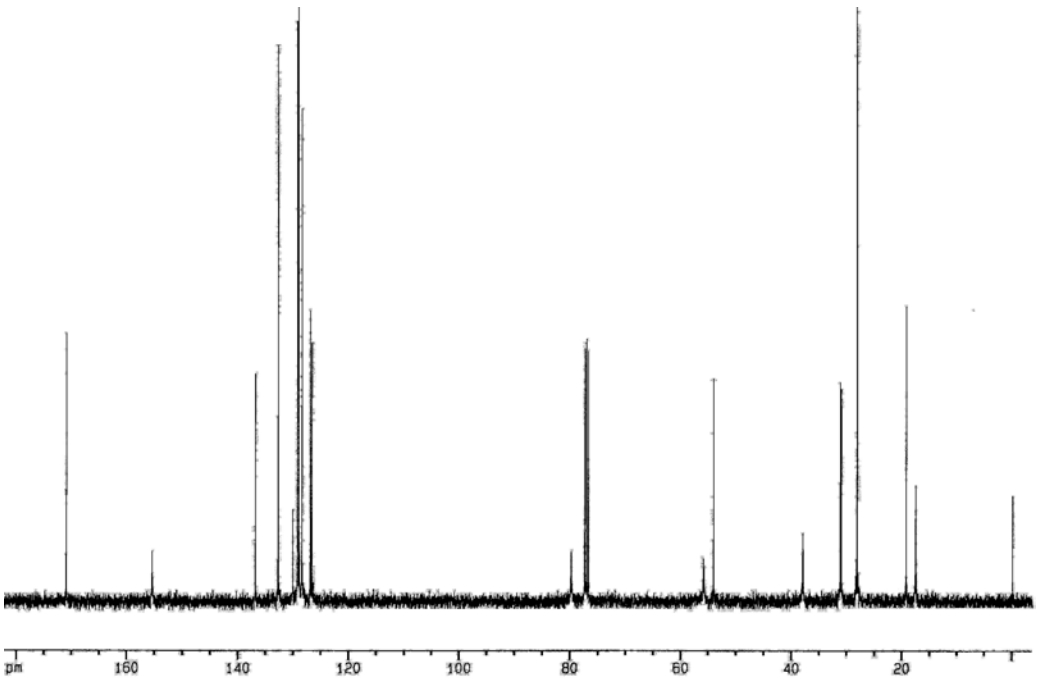


^{13}C NMR of **1c** in $CDCl_3$ at 100 MHz

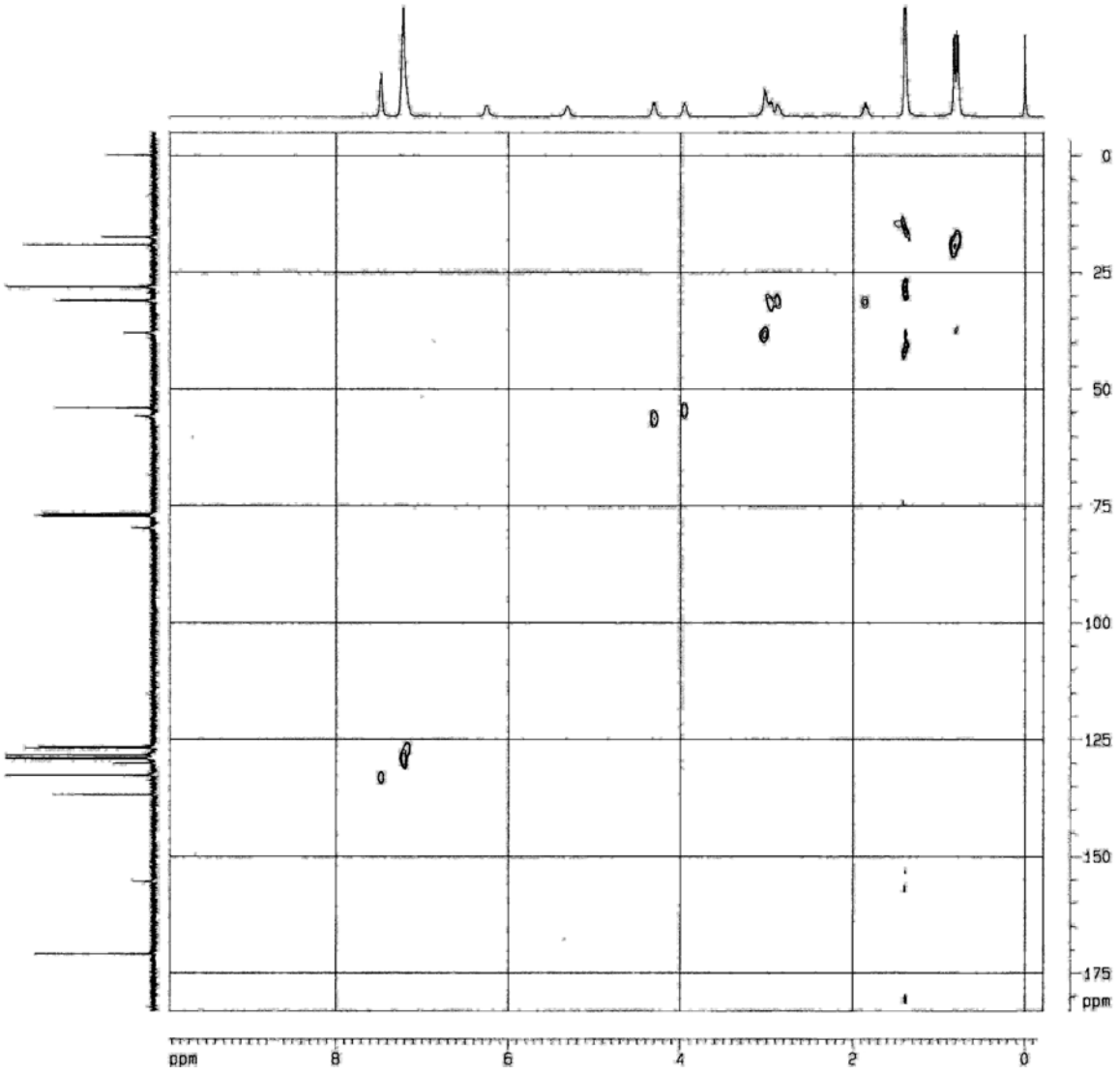


1d

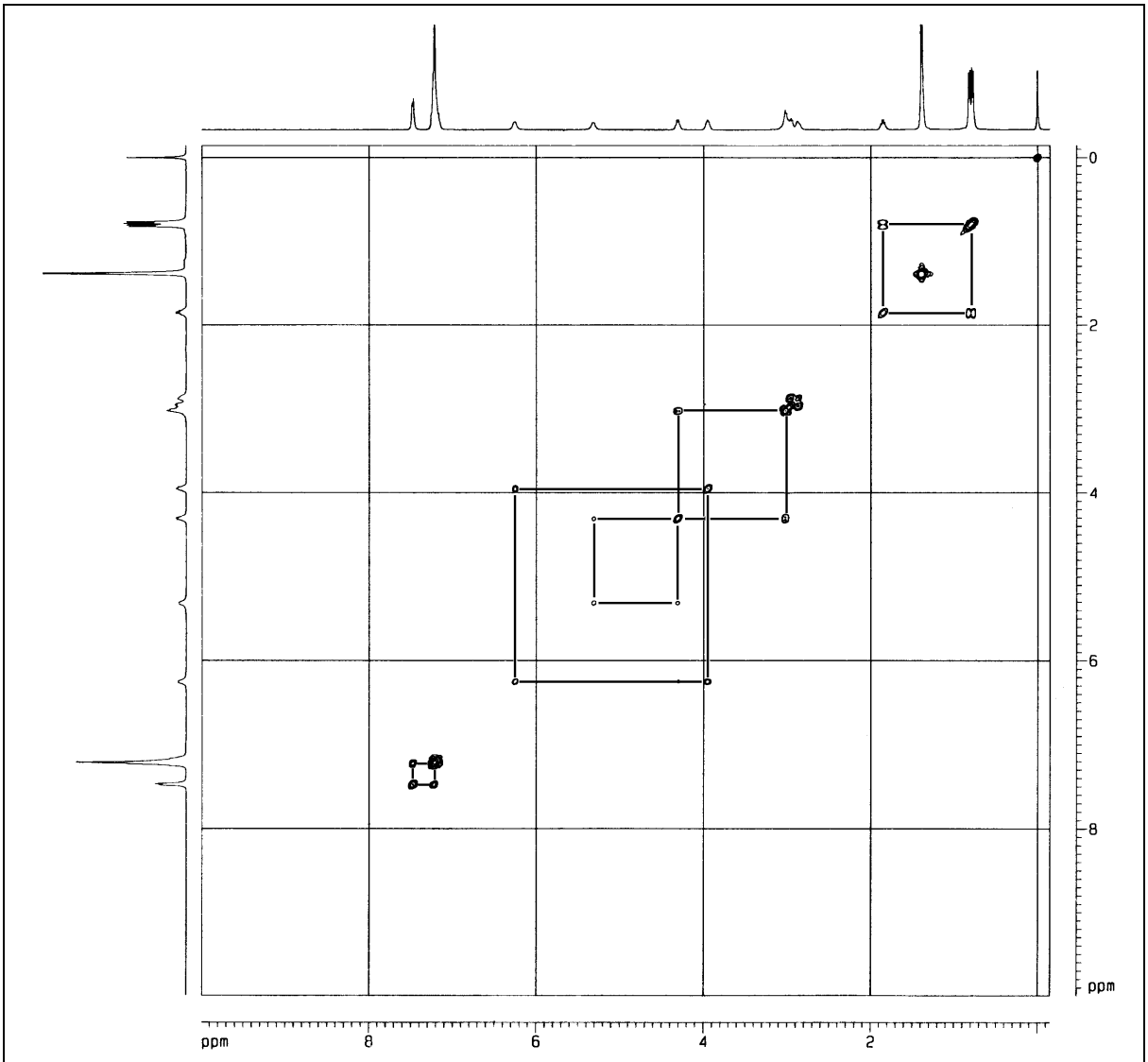
^{1}H NMR of **1d** in $CDCl_3$ at 400 MHz



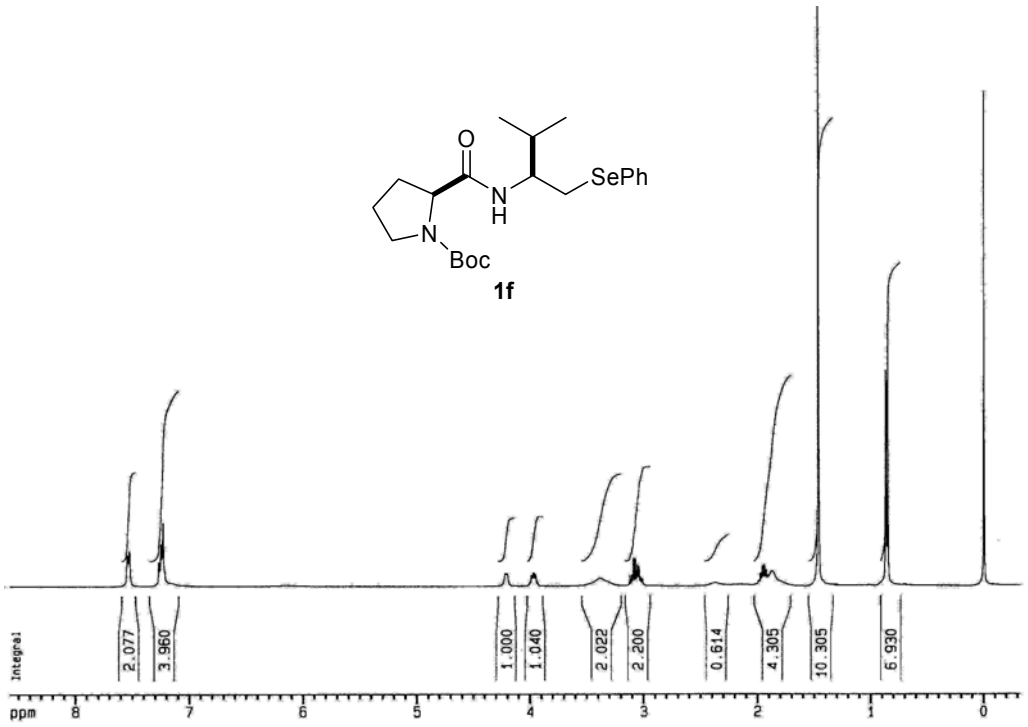
^{13}C NMR of **1d** in $CDCl_3$ at 100 MHz



2D-NMR HMQC of **1d** in $CDCl_3$ at 400 MHz

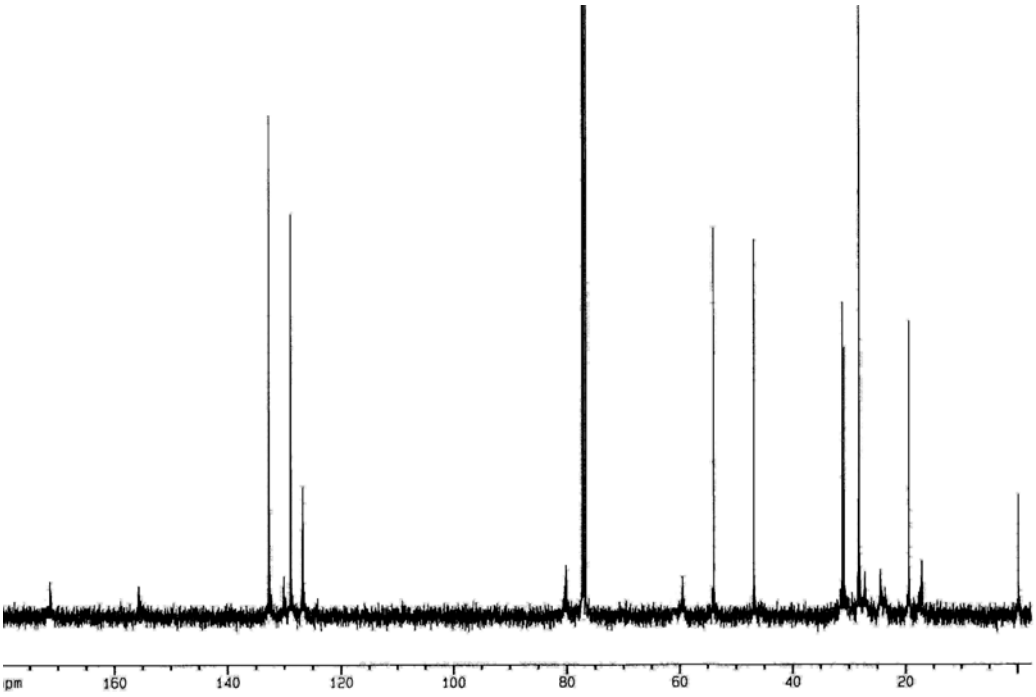


2D-NMR COSY ^{1}H-^{1}H of **1d** in $CDCl_3$ at 400 MHz

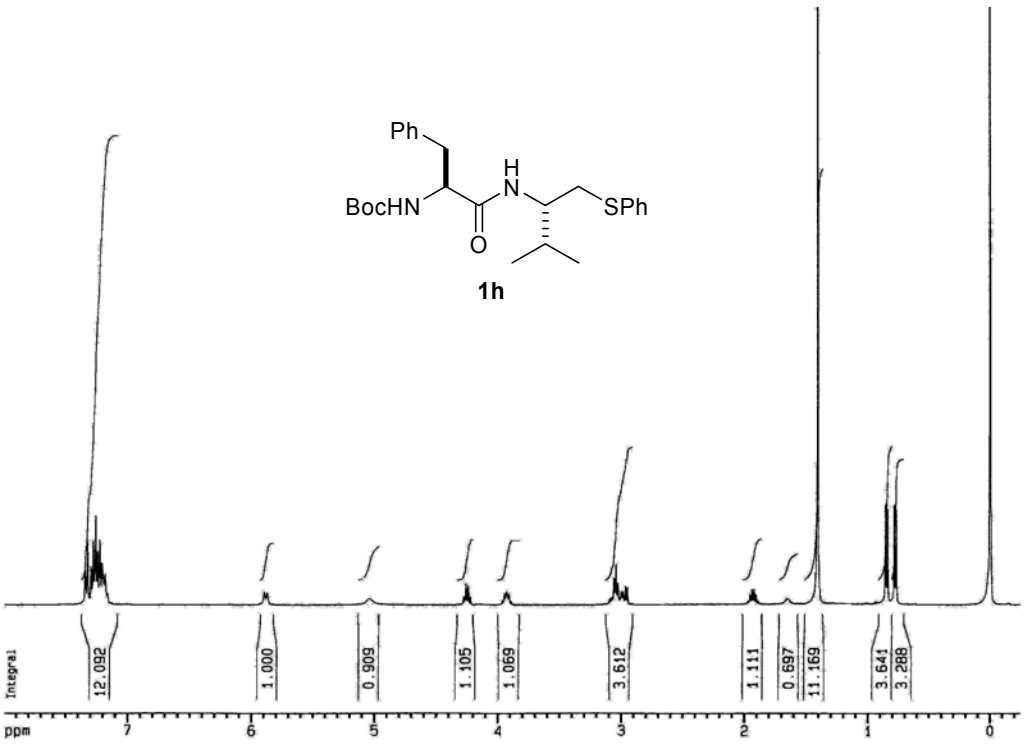


1f

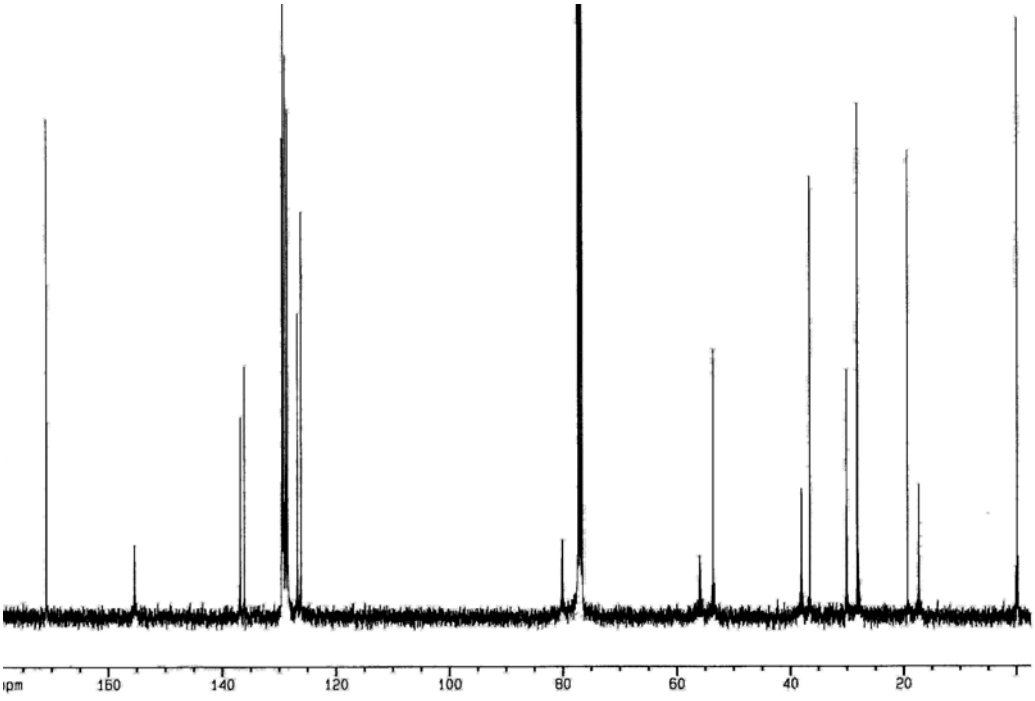
^{1}H NMR of **1f** in $CDCl_3$ at 400 MHz



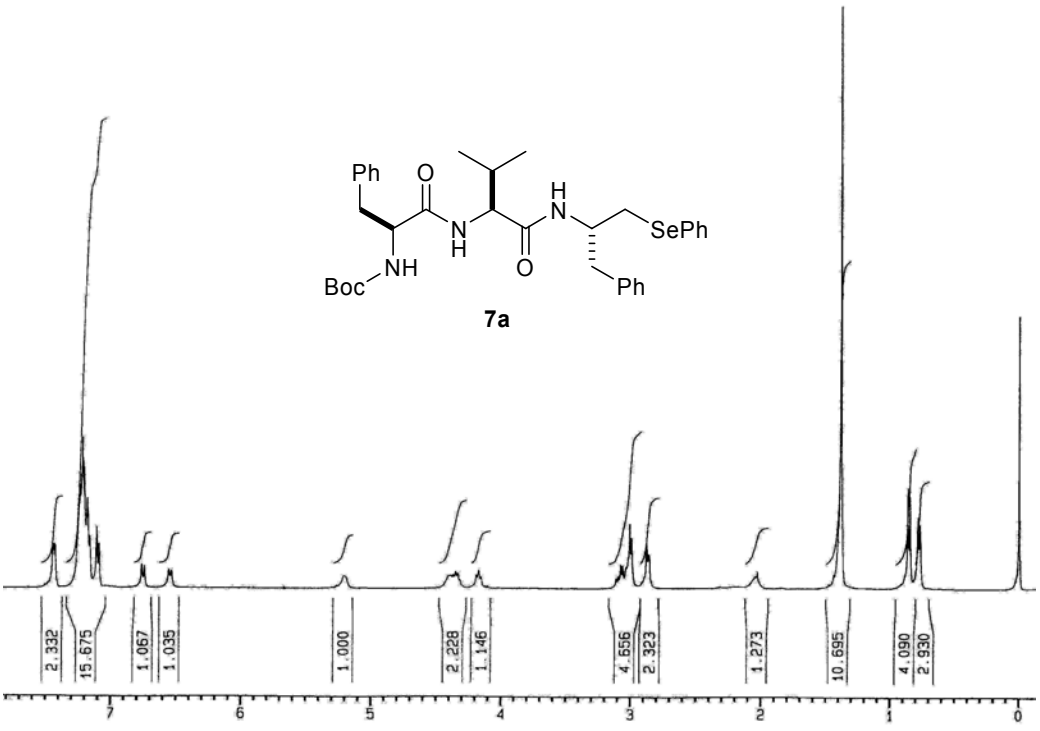
^{13}C NMR of **1f** in $CDCl_3$ at 100 MHz



^{1}H NMR of **1h** in $CDCl_3$ at 400 MHz

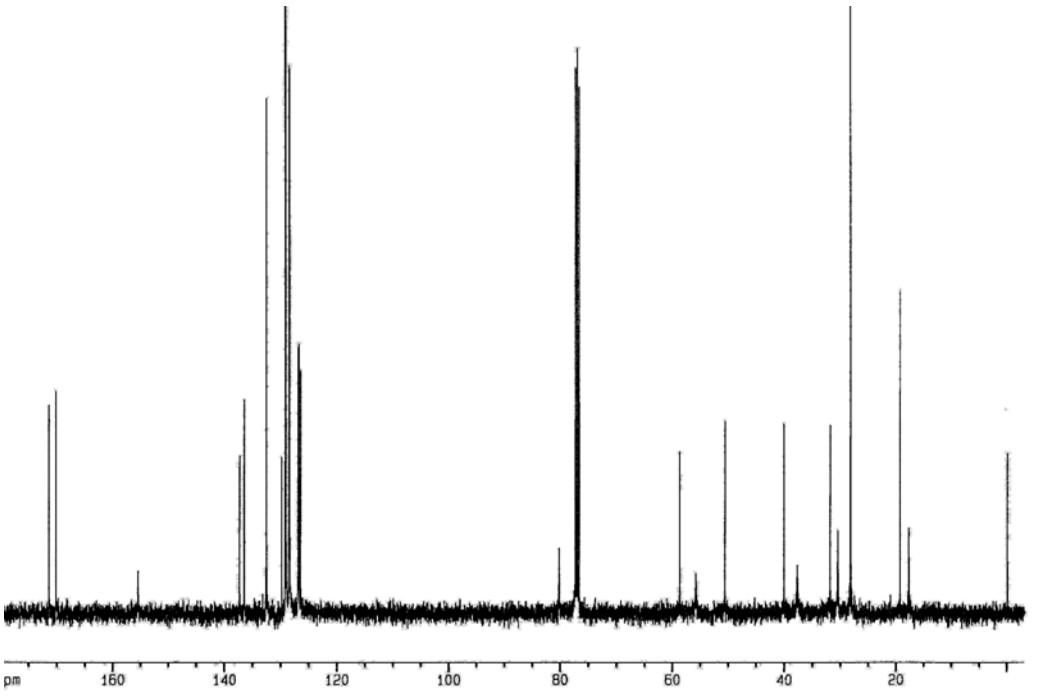


^{13}C NMR of **1h** in $CDCl_3$ at 100 MHz

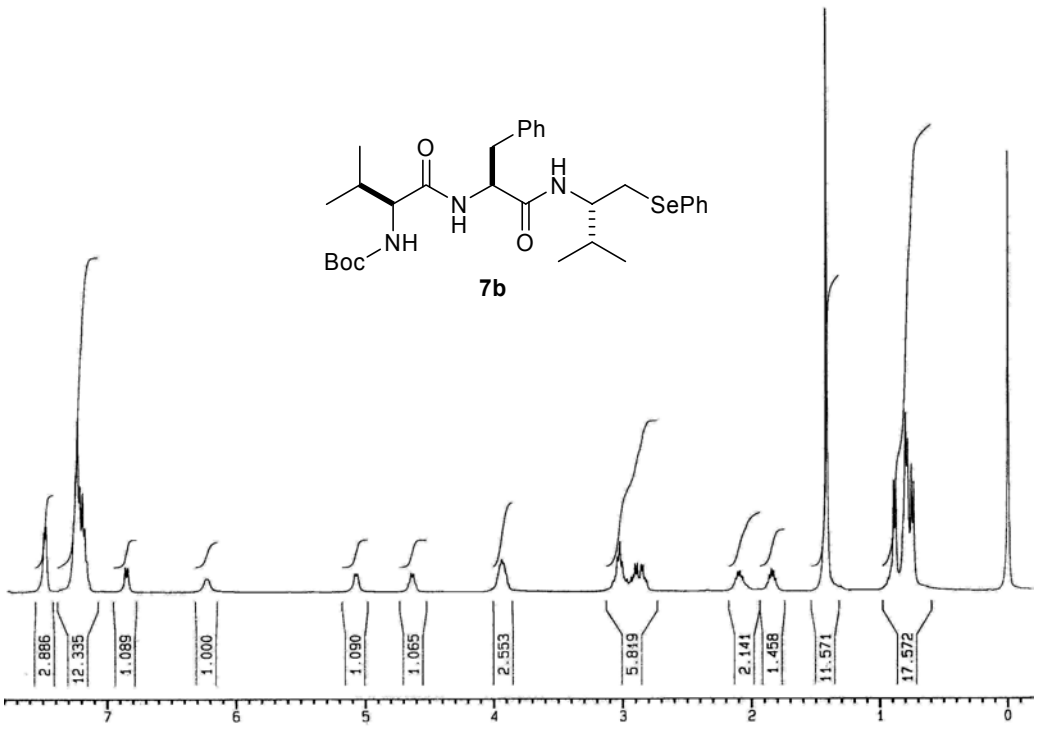


7a

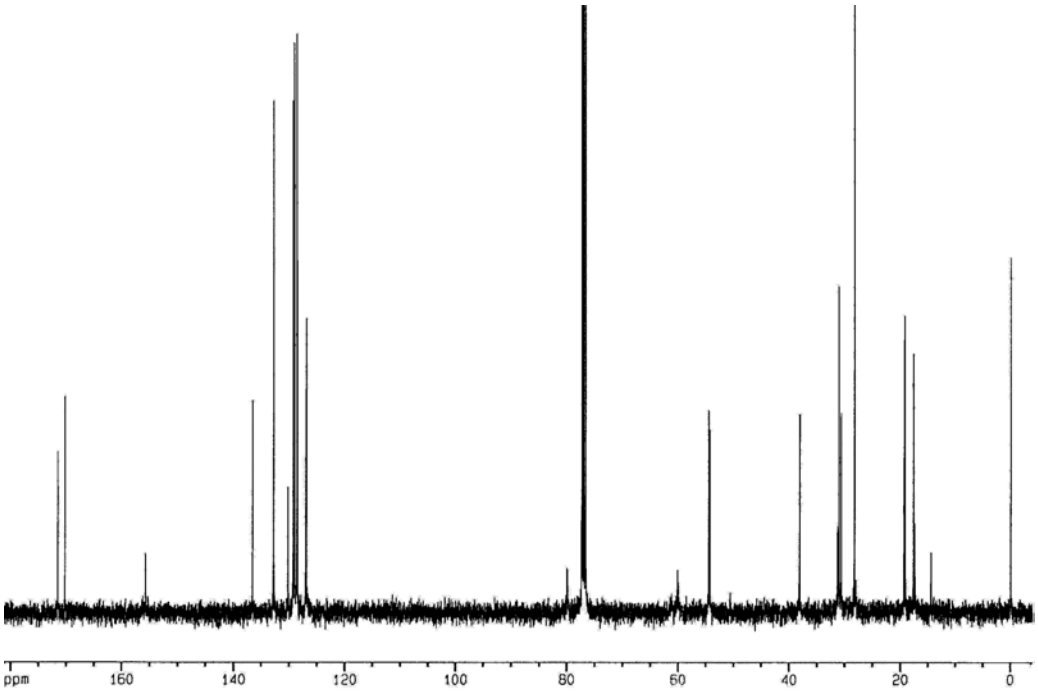
^{1}H NMR of **7a** in $CDCl_3$ at 400 MHz



^{13}C NMR of **7a** in $CDCl_3$ at 100 MHz



^{1}H NMR of **7b** in $CDCl_3$ at 400 MHz



^{13}C NMR of **7b** in $CDCl_3$ at 100 MHz