Supporting Information

For

Allylic Selenosulfide Rearrangement: A Method for Chemical Ligation to Cysteine and other Thiols

David Crich,* Venkataramanan Krishnamurthy and Thomas K. Hutton

Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago Illinois 60607-7061

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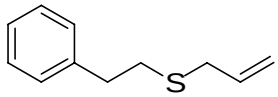
General:
All reagents were purchased from commercial sources and used as received, unless otherwise indicated. All NMR spectra were recorded with either Bruker 400 MHz or 500 MHz spectrometers with $CDCl_3$ or CD_3OD as solvent. All reactions were performed under an Argon atmosphere with degassed solvents, unless noted otherwise.

General Procedure for the Preparation of SelenoBunte Salts: A stirred suspension of 2.0 g (25.0 mmol) of finely powdered selenium in a solution of 6.0 g (40 mmol) of potassium sulfite in degassed water/ethanol (40/25 mL) was heated for 2 h at 72 °C. To this stirred solution was added dropwise 25 mmol of allyl halide in degassed ethanol. The reaction mixture was stirred for additional 1 h under an Argon atmosphere before the solution was permitted to cool to room temperature. The solvents were removed by rotary evaporation (60 mbar) taking care that the bath temperature does not exceed 50 °C. The resultant solid was washed with hexanes (200 mL) and extracted with hot methanol (2 x 200 mL). The methanol was removed under vacuum to obtain the crude Seleno Bunte salt which was used directly without further purification (crude yield 40 %).

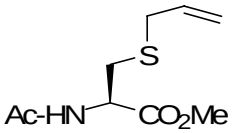
General Procedure for the Coupling Reaction: To the freshly prepared crude Bunte salt (3.0 mmol) in degassed methanol (8 mL), was added a solution of thiol (0.20 mmol) in degassed methanol (4 mL) with a syringe pump over 2 h at room temperature under an argon atmosphere. After the addition, the resulting yellow precipitate was filtered off, and to the filterate was added triphenylphosphine (0.61 mmol). The reaction mixture was stirred at room temperature for 4 h, after which the solvents were removed and the product was purified by column chromatography over silica gel.

$CH_3(CH_2)_{15}$-S-CH_2-CH=CH_2

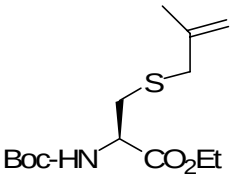
Allyl-hexadecyl-sulfide (6); Characterization data were in agreement with literature values.[1]



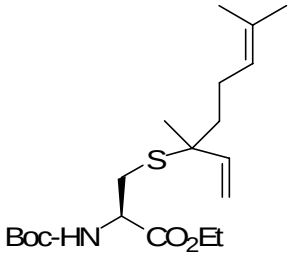
Allyl-phenethyl-sulfide (7); colorless liquid;^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.71-2.75 (m, 2H), 2.86-2.90 (m, 2H), 3.15 (d, *J* = 7.0 Hz, 2H), 5.09 (d, *J* = 16.6 Hz, 1H), 5.13 (d, *J* = 11.2 Hz, 1H), 5.72-5.82 (m, 1H), 7.20-7.33 (m, 5H);^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 32.0, 34.8, 36.0, 117.0, 126.3, 128.3, 128.4 (2C), 128.5, 134.4, 140.6;EIHRMS Calcd for $C_{11}H_{14}S$ $[M+Na]^+$: 178.0816, found: 178.0831.



***N*-Acetyl-*S*-allyl-L-cysteine methyl ester (9);** Characterization data were in agreement with literature values.[2]

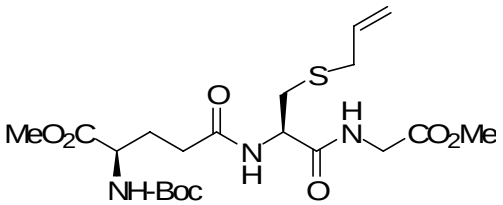


***N*-(*tert*-butoxycarbonyl)-*S*-(2-methylallyl)-L-cysteine ethyl ester (12);** colorless oil; $[\alpha]^{27}_D$ +18.4 (c = 1, $CHCl_3$);^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.29 (t, *J* = 7.2 Hz, 3H), 1.45 (s, 9H), 1.79 (s, 3H), 2.80 (dd, *J* = 5.5 Hz, *J* = 13.6 Hz, 1H), 2.89 (dd, *J* = 4.5 Hz, *J* = 13.8 Hz, 1H), 3.09 (d, *J* = 13.5 Hz, 1H), 3.11 (d, *J* = 13.5 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.47-4.49 (m, 1H), 4.84 (s, 1H), 4.87 (d, *J* = 1.5 Hz, 1H), 5.30 (d, *J* = 7.4 Hz, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 14.1, 20.5, 28.2 (3C), 33.1, 39.8, 53.1, 61.6, 80.0, 114.3, 140.6, 155.1, 171.1;ESIHRMS Calcd for $C_{14}H_{25}NO_4S$ $[M+Na]^+$: 326.1402, found: 326.1410.

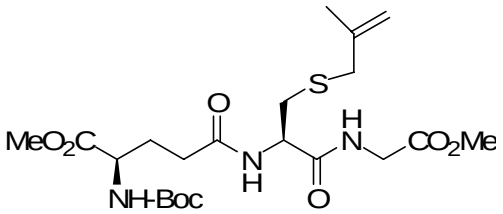


***N*-(*tert*-butoxycarbonyl)-*S*-linalyl-L-cysteine ethyl ester (14);** colorless oil;$[\alpha]^{27}_D$ +6.4 (c = 1, $CHCl_3$);^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.28 (t, *J* = 7.2 Hz, 3H), 1.33 (d, *J* = 1.1

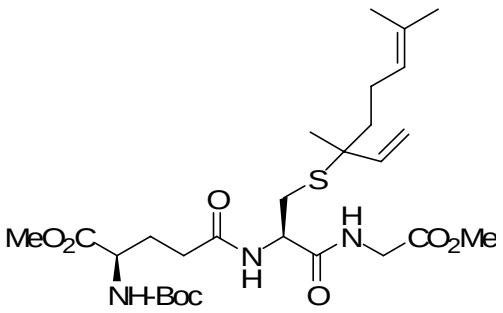
Hz, 3H), 1.45 (s, 9H), 1.57 (s, 3H), 1.55-1.60 (m, 2H), 1.66 (s, 3H), 1.92 -2.09 (m, 2H), 2.79 (d, *J* = 4.8 Hz, 2H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.47-4.49 (m, 1H), 4.95 (d, *J* = 18.3 Hz, 1H), 5.04-5.09 (m, 1H), 5.08 (d, *J* = 10.9 Hz, 1H), 5.25 (d, *J* = 7.9 Hz, 1H), 5.70-5.78 (m, 1H);^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 14.1, 17.6, 23.1, 23.3, 25.6, 28.3 (3C), 31.1, 40.2, 50.4, 53.0, 61.6, 79.9, 113.0, 123.7, 131.9, 142.9, 155.1, 170.9;ESIHRMS Calcd for $C_{20}H_{35}NO_4S$ $[M+Na]^+$: 408.2185, found: 408.2175.



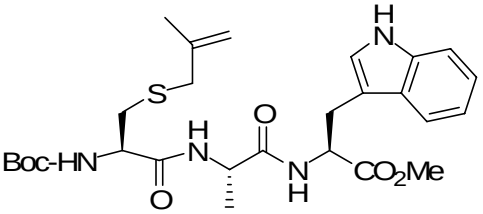
***N*-(*tert*-Butoxycarbonyl)-*S*-allyl-glutathione dimethyl ester (17);** oil;$[\alpha]^{27}_D$ -31.1 (c = 1, MeOH);^{1}H-NMR (MeOD, 400 MHz): δ = 1.44 (s, 9H), 1.86-1.95 (m, 1H), 2.11-2.17 (m, 1H), 2.37 (t, *J* = 7.6 Hz, 2H), 2.68 (dd, *J* = 8.8 Hz, *J* = 13.9 Hz,1H), 2.94 (dd, *J* = 5.5 Hz, *J* = 13.9 Hz, 1H), 3.17 (d, *J* = 6.8 Hz, 2H), 3.71 (s, 3H), 3.72 (s, 3H), 3. 95 (s, 2H), 4.13-4.17 (m, 1H), 4.53-4.56 (m, 1H), 5.09 (d, *J* = 10 Hz, 1H), 5.16 (d, *J* = 17.2 Hz, 1H), 5.75-5.82 (m, 1H);^{13}C-NMR (MeOD, 100 MHz): δ = 26.9, 27.2 (3C), 31.4, 31.8, 34.0, 40.4, 51.2, 51.3, 52.3, 53.0, 79.2, 116.4, 134.0, 156.6, 170.0, 171.9, 173.0, 173.3; ESIHRMS Calcd for $C_{20}H_{33}N_3O_8S$ $[M+Na]^+$: 498.1886, found:498.1895.



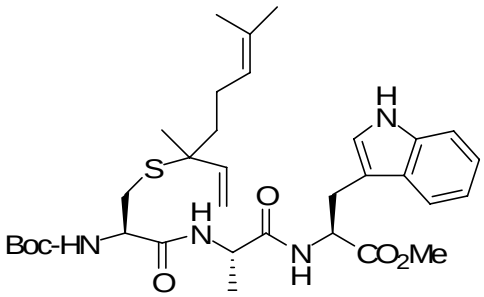
***N*-(*tert*-Butoxycarbonyl)-*S*-(2-methylallyl) glutathione dimethyl ester (18);** colorless liquid;$[\alpha]^{27}_D$ -39.1 (c = 1, MeOH);^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.42 (s, 9H), 1.79 (s, 3H), 1.93-1.97 (m, 1H), 2.17-2.18 (m, 1H), 2.37 (t, *J* = 7.5 Hz, 2H), 2.81 (d, *J* = 6.5 Hz, 2H), 3.14 (s, 2H), 3.72 (s, 3H), 3.73 (s, 3H), 3.98 (dd, *J* = 5.4 Hz, *J* = 18.0 Hz, 1H), 4.06 (dd, *J* = 5.3 Hz, *J* = 18.1 Hz, 1H), 4.36 (m, 1H), 4.59 (q, *J* = 6.8 Hz, 1H), 4.86 (d, *J* = 1.3 Hz, 1H), 4.89 (s, 1H), 5.39 (d, *J* = 7.2 Hz, 1H), 6.86 (bs, -NH, 1H), 7.05 (bs, -NH, 1H);^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 20.6, 28.2 (3C), 28.7, 32.1, 32.5, 39.5, 41.2, 52.1, 52.4, 52.5, 52.6, 80.2, 114.5, 140.7, 155.7, 169.9, 170.6, 172.1, 172.8;ESIHRMS Calcd for $C_{21}H_{35}N_3O_8S$ $[M+Na]^+$: 512.2043, found: 512.2064.



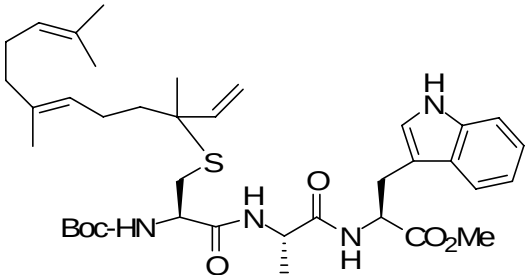
***N*-(*tert*-Butoxycarbonyl)-*S*-linalyl glutathione dimethyl ester (19);** colorless liquid; $[\alpha]^{27}_{D}$ -18.0 (c = 1, MeOH);^{1}H-NMR (MeOD, 400 MHz): δ = 1.37 (d, *J* = 3.6 Hz, 3H), 1.43 (s, 9H), 1.53-1.61 (m, 2H), 1.61 (s, 3H), 1.67 (s, 3H), 1.86-2.17 (m, 4H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.61-2.69 (m, 1H), 2.80-2.86 (m, 1H), 3.71 (s, 3H), 3.72 (s, 3H), 3.93 (s, 2H), 4.14-4.16 (m, 1H), 4.48-4.51 (m, 1H), 5.02 (d, *J* = 17.5 Hz, 1H), 5.08-5.12 (m, 1H), 5.10 (d, *J*= 10.5 Hz, 1H), 5.78-5.85 (m, 1H);^{13}C-NMR (MeOD, 100 MHz): δ = 16.3, 22.5, 22.8, 24.4, 27.0, 27.3 (3C), 30.0, 31.4, 40.2, 40.5, 50.2, 51.2, 51.3, 53.1, 53.3, 79.2, 112.1, 123.6, 131.3, 143.2, 156.7, 170.1, 171.9, 173.1, 173.2;ESIHRMS Calcd for $C_{27}H_{45}N_3O_8S$ $[M+Na]^+$: 594.2825, found: 594.2846.



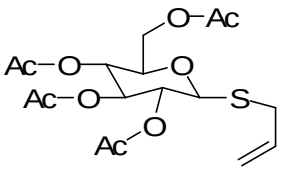
***N*-(*tert*-butoxycarbonyl)-*S*-(2-methylallyl) L-cysteinyl-L-alanyl-L-tryptophan methyl ester (20);** oil;$[\alpha]^{27}_{D}$ +15.6 (c = 1, $CHCl_3$);^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.32 (d, *J* = 7.0 Hz, 3H), 1.47 (s, 9H), 1.78 (s, 3H), 2.69 (dd, *J* = 6.2 Hz, *J* = 13.8 Hz, 1H), 2.78 (dd, *J* = 5.8 Hz, *J* = 13.9 Hz, 1H), 3.04 (d, *J* = 13.5 Hz, 1H), 3.08 (d, *J* = 13.5 Hz, 1H), 3.27 (dd, *J* = 5.8 Hz, *J* = 14.8 Hz, 1H), 3.33 (dd, *J* = 5.3 Hz, *J* = 14.8 Hz, 1H), 3.69 (s, 3H), 4.09-4.21 (m, 1H), 4.44 (t, *J* = 7.2 Hz, 1H), 4.85-4.89 (m, 3H), 5.29 (bs, 1H), 6.72 (d, *J* = 6.1 Hz, 1H), 6.78 (d, *J* = 6.9 Hz, 1H), 6.97 (s, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.1 Hz, 1H), 7.33 (d, *J* = 8 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 8.44 (bs, -NH, 1H);^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 17.8, 20.6, 27.4, 28.2 (3C), 33.3, 39.6, 48.8, 52.6, 52.8, 53.6, 80.7, 109.5, 111.3, 114.5, 118.4, 119.5, 122.1, 123.1, 127.4, 136.0, 140.7, 155.6, 170.4, 171.2, 171.9;ESIHRMS Calcd for $C_{27}H_{38}N_4O_6S$ $[M+Na]^+$: 569.2410, found: 569.2407.



***N*-(*tert*-butoxycarbonyl)-*S*-linalyl-L-cysteinyl-L-alanyl-L-tryptophan methyl ester (21);** colorless oil;$[\alpha]^{27}_{D}$ +9.0 (c = 1, $CHCl_3$);^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 1.30 (d, *J* = 7.2 Hz, 3H), 1.33 (s, 3H), 1.47 (s, 9H), 1.56 (s, 3H), 1.67 (s, 3H), 1.73-1.75 (m, 2H), 1.91-2.05 (m, 2H), 2.56-2.65 (m, 1H), 2.74-2.82 (m, 1H), 3.26 (dd, *J* = 5.8 Hz, *J* = 14.8 Hz, 1H), 3.33 (dd, *J* = 5.3 Hz, *J* = 14.8 Hz, 1H), 3.68 (s, 3H), 4.10-4.23 (m, 1H), 4.39-4.46 (m, 1H), 4.83-4.88 (m, 1H), 4.96 (d, *J* = 17.6 Hz, 1H), 5.04-5.08 (m, 1H), 5.09 (d, *J* = 11.0 Hz, 1H), 5.29 (m, 1H), 5.72-5.79 (m,1H), 6.75 (bs, -NH, 2H), 6.97 (s, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.1 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 8.50 (bs, -NH, 1H);^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 17.6, 17.7, 23.1, 23.3, 25.6, 27.4, 28.3 (3C), 30.8, 40.1, 48.8, 50.9, 52.4, 52.7, 53.8, 80.7, 109.4, 111.3, 113.3, 118.4, 119.5, 122.0, 123.2, 123.6, 127.4, 132.0, 136.0, 142.9, 155.6, 170.3, 171.2, 171.9; ESIHRMS Calcd for $C_{33}H_{48}N_4O_6S$ $[M+Na]^+$: 651.3193, found: 651.3173.



***N*-(*tert*-butoxycarbonyl)-*S*-nerolidyl L-cysteinyl-L-alanyl-L-tryptophan methyl ester (23);** colorless oil;$[\alpha]^{27}_{D}$ +9.9 (c = 1, $CHCl_3$);^{1}H-NMR ($CDCl_3$, 400 MHz):δ = 1.30 (d, *J* = 7.2 Hz, 3H), 1.34 (s, 3H), 1.47 (s, 9H), 1.58 (s, 3H), 1.61 (s, 3H), 1.67 (s, 3H), 1.71-1.73 (m, 2H), 1.93-2.07 (m, 6H), 2.56-2.65 (m, 1H), 2.74-2.82 (m, 1H), 3.26 (dd, *J* = 5.8 Hz, *J* = 14.8 Hz, 1H), 3.33 (dd, *J* = 5.3 Hz, *J* = 14.8 Hz, 1H), 3.68 (s, 3H), 4.10-4.23 (m, 1H), 4.39-4.46 (m, 1H), 4.83-4.88 (m, 1H), 4.96 (d, *J* = 17.6 Hz, 1H), 5.06-5.09 (m, 2H), 5.10 (d, *J* = 11.0 Hz, 1H), 5.24 (m 1H), 5.72-5.79 (m, 1H), 6.75 (bs, -NH, 2H), 6.97 (s, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.1 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 8.50 (bs, -NH, 1H);^{13}C-NMR ($CDCl_3$, 100 MHz): δ = 15.9, 17.6, 23.0, 23.1, 23.3, 25.7, 26.6, 27.4, 28.3 (3C), 30.8, 39.6, 40.6, 48.8, 50.9, 52.4, 52.7, 53.8, 80.7, 109.5, 111.3, 113.4, 118.4, 119.5, 122.0, 123.2, 123.5, 124.2, 127.4, 131.4, 135.6, 136.0, 143.0, 155.6, 170.3, 171.2, 171.9;ESIHRMS Calcd for $C_{38}H_{56}N_4O_6S$ $[M+Na]^+$:719.3819, found: 719.3835.



***S*-Allyl 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (25);** colorless oil;$[\alpha]^{27}_{D}$ -15.7 (c = 1, $CHCl_3$);^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 2.01 (s, 3H), 2.03 (s, 3H), 2.05 (s, 3H), 2.08 (s, 3H), 3.22 (dd, *J* = 5.9 Hz, *J* = 13.5 Hz, 1H), 3.39 (dd, *J* = 8.6 Hz, *J* = 13.5 Hz, 1H), 3.63-3.67 (m, 1H), 4.13 (dd, *J* = 2.3 Hz, *J* = 12.3 Hz, 1H), 4.22 (dd, *J* = 5.1 Hz, *J* = 12.3 Hz, 1H), 4.48 (d, *J* = 10.1 Hz, 1H), 5.06 (t, *J* = 9.9 Hz, 1H), 5.07 (t, *J* = 9.8 Hz, 1H), 5.12-5.13 (m, 1H), 5.15-5.17 (m, 1H), 5.22 (t, *J* = 9.3 Hz, 1H), 5.76-5.8(m,1H);^{13}C-

NMR ($CDCl_3$, 100 MHz): δ = 20.5, 20.6, 20.7, 20.7, 32.8, 62.2, 68.3, 69.8, 73.8, 75.7, 81.8, 118.0, 133.3, 169.4, 169.4, 170.2, 170.6;ESIHRMS Calcd for $C_{17}H_{24}O_9S$ $[M+Na]^+$: 427.1039, found: 427.1050.

Procedure for the synthesis of *N*-(*tert*-butoxycarbonyl) glutathione dimethyl ester (15)

Synthesis of *S*-trityl glutathione trifluoroacetate (15a);[3] To a mixture of glutathione (25.0 g, 81.3 mmol) and trityl alcohol (21.2 g, 81.3 mmol) was added dropwise with stirring trifluoroacetic acid (150 mL). The resultant solution was stirred for 1 h, before addition of diethyl ether (300 mL). The resulting precipitate was filtered and washed with ether (3 x 100 mL) to give **15a** as a white gum (40.2 g, 75 %).

Synthesis of *N*-(*tert*-butoxycarbonyl)-*S*-trityl glutathione (15b); To a stirred solution of **15a** (40 g, 60.3 mmol) in triethylamine (50 mL) and water (150 mL) was added a solution of di-*tert*-butyl dicarbonate (20 g, 90.4 mmol) in ether (200 mL). The resulting solution was stirred for 72 h before being concentrated *in vacuo*. EtOAc (400 mL) and aqueous $KHSO_4$ solution (1M, 100 mL) were added, and the solution was then extracted with EtOAc (3x100 mL), dried over sodium sulfate, and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (eluting with 50% MeOH in $CHCl_3$) gave **15b** as a white gum (34.8 g, 89 %);$[\alpha]^{25}_D$ +11.1 (c = 1.0, MeOH);^{1}H-NMR (500 MHz, MeOD) δ = 1.42 (s, 9H), 2.08-2.15 (m, 1H), 2.33 (t, *J* = 7.0 Hz, 2H), 2.56-2.60 (m, 1H), 2.64 (dd, *J* = 5.5 Hz, *J* = 12.5 Hz 1H), 3.34 (s, 2H), 3.77 (d, *J* = 17.5 Hz, 1H), 3.86 (d, *J* = 17.5 Hz, 1H), 4.10 (t, *J* = 7.0 Hz, 1H), 4.22 (t, *J* = 7.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 3H), 7.27 (t, *J* = 10.5 Hz, 6H), 7.38 (d, *J* = 7.5 Hz, 6H);^{13}C-NMR (125 MHz, MeOD) δ = 27.4, 27.5, 31.6, 33.2, 41.1, 48.5, 52.5, 53.3, 57.0, 66.6, 79.2, 126.6, 127.3, 127.9, 129.4, 144.6, 156.6, 171.3, 172.2, 173.4, 175.0;ESIHRMS Calcd. for $C_{34}H_{39}N_3O_8S$ $[M+Na]^+$: 672.2356, found 627.2350.

Synthesis of *N*-(*tert*-butoxycarbonyl)-*S*-trityl glutathione methyl ester (15c); To a stirred solution of **15b** (33.4 g, 51.4 mmol) in DMF (300 mL) was added $KHCO_3$ (20.6 g, 205.8 mmol) followed by iodomethane (9.6 mL, 154.4 mmol). The resulting solution was stirred for 16 h before the addition of EtOAc (300 mL). The solution was washed with water (2 x 300 mL) and the aqueous layer was back extracted with EtOAc (2 x 200 mL). The combined organic extracts were washed with 5 % aqueous sodium sulfite (500 mL) and brine (500 mL), dried over sodium sulfate and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (eluting with EtOAc) afforded **15c** as a colourless gum (30.1 g, 86 %): $[\alpha]^{25}_D$ +1.8 (c = 1.0, MeOH);^{1}H-NMR (500 MHz, MeOD) δ = 1.42 (s, 9H), 1.83-1.91 (m, 1H), 2.06-2.15 (m, 1H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.54 (dd, *J* = 8.5 Hz, *J* = 12.5 Hz, 1H), 2.62 (dd, *J* = 6.5 Hz, *J* = 12.5 Hz, 1H), 3.66 (s, 3H), 3.68 (s, 3H), 4.14 (dd, *J* = 5.0 Hz, *J* = 8.5 Hz, 1H), 4.22 (dd, *J* = 6.0 Hz, *J* = 8.5 Hz, 1H), 7.21 (t, *J* = 7.0 Hz, 3H), 7.30 (t, *J* = 7.5 Hz, 6H), 7.39 (d, *J* = 5.0 Hz, 6H);^{13}C-NMR (125 MHz, MeOD) δ = 27.1, 27.3, 31.4, 33.3, 40.5, 51.3, 51.4, 52.3, 53.1, 66.6, 79.3, 126.5, 127.7, 129.4, 144.6, 156.7, 170.0, 171.5, 173.1, 173.2;ESIHRMS Calcd. for $C_{36}H_{43}N_3O_8S$ $[M+Na]^+$: 700.2669, found 700.2670.

Synthesis of *N*-(*tert*-butoxycarbonyl)-glutathione dimethyl ester (15);[4] To a stirred solution of **15c** (30 g, 44.3 mmol) in dichloromethane (500 mL) at 0 °C was added triethylsilane (8.5 mL, 53.2 mmol) followed by trifluoroacetic acid (20 mL, approx. 4% v/v) and the resultant solution was stirred for 1 h. Saturated aqueous sodium bicarbonate (700 mL) was added and the aqueous layer was extracted with EtOAc (3 x 500 mL). The combined organic extracts were dried over sodium sulfate, and concentrated *in vacuo* to give the crude product. Purification by flash chromatography (eluting with EtOAc) afforded **15** as a white solid (12.3 g, 64 %);m.p. 92-93 °C;$[\alpha]^{25}_{D}$ -36.0 (c = 1.0, MeOH);^{1}H-NMR (500 MHz, MeOD) δ = 1.44 (s, 9H), 1.86-1.94 (m, 1H), 2.11-2.18 (m, 1H), 2.40 (t, *J* = 7.5 Hz, 2H), 2.82 (dd, *J* = 6.5 Hz, *J* = 14.0 Hz, 1H), 2.89 (dd, *J* = 6.5 Hz, *J* = 14.0 Hz, 1H), 3.72 (s, 6H), 3.93 (d, *J* = 17.5 Hz, 1H), 4.00 (d, *J* = 17.5 Hz, 1H), 4.14 (dd, *J* = 5.0 Hz, *J* = 9.0 Hz, 1H), 4.55 (t, *J* = 6.5 Hz, 1H);^{13}C-NMR (125 MHz, MeOD) δ = 25.6, 26.9, 27.4, 31.4, 40.5, 51.3, 51.4, 53.1, 55.4, 79.3, 156.7, 170.2, 171.5, 173.1, 173.4;ESIHRMS Calcd. for $C_{17}H_{29}N_3O_8S$ $[M+Na]^+$: 458.1573, found 458.1595.

Procedure for the Synthesis of *N*-(*tert*-butoxycarbonyl)-L-cysteinyl- L -alanyl- L - tryptophan methyl ester (16)
L-Alanyl-L-tryptophan methyl ester[5] was prepared from *t*BOC-alanine[6] and L-tryptophan methyl ester by HOBt/DCC coupling and deprotection of the carbamate with trifluoroacetic acid.
N-(*tert*-butoxycarbonyl)-*S*-trityl-L-cysteine was prepared from L-cysteine by protection of the thiol with trityl chloride followed by protection of the amino group with di-*tert*-butyl dicarbonate. The protected amino acid was isolated as its dicyclohexylammonium salt.[7]

Synthesis of *N*-(*tert*-butoxycarbonyl)-*S*-trityl L-cysteinyl-L-alanyl-L-tryptophan methyl ester (16a); *N*-(*tert*-butoxycarbonyl)-*S*-trityl-L-cysteine dicyclohexylammonium salt (5.3 g, 8.1 mmol) was converted to the free acid by partition between EtOAc (90 mL) and 10 % aqueous $KHSO_4$ (50 mL), followed by a second washing of the organic phase with aqueous $KHSO_4$ (50 mL) and then brine. The organic layer was dried over sodium sulfate, filtered and concentrated in *vacuo*. A solution of L-ala-L-trp-OMe (2.34 g, 8.1 mmol), triethylamine (1.3 mL, 9.3 mmol) in dichloromethane (55 mL) was added to a flask containing *N*-(*tert*-butoxycarbonyl)-*S*-trityl-L-cysteine, DCC (1.84 g, 9.3 mmol) and HOBt (219 mg, 1.6 mmol.). The mixture was stirred for 20 h at room temperature. The mixture was diluted with EtOAc (300 mL), filtered to remove the dicyclohexylurea and concentrated in *vacuo*. EtOAc (300 mL) was added to the residue and then washed with water (100 mL), 1 *N* NaOH (100 mL), 1 *N* HCl (100 mL) and brine (100 mL) were added sequentially. The organic layer was dried over sodium sulfate, and concentrated in *vacuo*. The residue was purified by flash chromatography (eluting with 3% MeOH in $CHCl_3$) to afford **16a** (5.86 g, 98 %);^{1}H-NMR (400 MHz, $CDCl_3$) δ = 1.12 (d, *J* = 7.0 Hz, 3H), 1.35 (m, 1H), 2.36 (m, 2H), 3.03 (dd, *J* = 14.6, 7.4 Hz, 1H), 3.10 (dd, *J* = 6.4, *J* = 14.6 Hz, 1H), 3.35 (s, 3H), 3.87 (m, 1H), 4.27 (m, 1H), 4.47 (q, *J* = 6.9 Hz, 1H), 6.94 (dd, *J* = 7.4, *J* = 7.5 Hz, 1H), 7.02-7.05 (m, 2H), 7.11 (d, *J* = 2.1 Hz, 1H), 7.17-7.22 (m, 3H), 7.25-7.32 (m, 10H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 8.34 (d, *J* = 7.2 Hz, 1H), 10.8 (s, 1H);^{13}C-NMR (100 MHz, $CDCl_3$) δ = 19.6, 27.9, 29.1, 48.7, 52.8, 54.1, 54.4, 66.8, 80.1, 110.0, 112.4, 118.9, 119.4, 121.9, 124.7, 127.7, 128.0, 129.0, 130.0, 136.0, 145.3, 155.9, 170.4, 172.8, 173.0.

Synthesis of *N*-(*tert*-butoxycarbonyl)-L-cysteinyl-L-alanyl-L-tryptophan methyl ester (16); To a solution of **16a** (735 mg, 1.0 mmol) in dichloromethane (10 mL) was added at 0 °C triethylsilane (192 µL, 1.2 equiv.) and trifluoroacetic acid (416 µL).[8] After 1 h, the intense yellow color had disappeared and the reaction mixture was quenched with saturated sodium bicarbonate solution, extracted with EtOAc, washed with brine, dried over sodium sulfate, filtered and concentrated under vacuum. The residue was purified by flash chromatography (eluting with 4 % MeOH in $CHCl_3$) to afford **16** (450 mg, 91 %) as a slight yellow solid. m.p. 88 °C;IR (neat): 1164, 1520, 1653, 1734, 2977, 3057, 3309, cm^{-1};$[\alpha]_D^{30}$ +14.9 (c = 1, $CHCl_3$);^{1}H-NMR (400 MHz, $CDCl_3$) δ = 1.30 (d, *J* = 7.0 Hz, 3H), 1.45 (s, 9H), 2.57 (m, 1H), 2.81 (m, 1H), 3.23-3.33 (m, 2H), 3.66 (s, 3H), 4.20 (bs, 1H), 4.50 (qt, *J* = 7.2 Hz, 1H), 4.89 (dt, *J* = 7.8, 5.5 Hz, 1H), 5.61 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 1.7 Hz, 1H), 7.02 (bs, 1H), 7.05 (bs, 1H), 7.07 (m, 1H), 7.11 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 8.74 (bs, 1H);^{13}C-NMR (100 MHz, $CDCl_3$) δ = 18.4, 27.2, 27.6, 28.5, 49.2, 52.7, 53.2, 55.9, 81.0, 109.6, 111.7, 118.6, 119.7, 122.3, 123.6, 127.7, 136.3, 155.8, 170.2, 171.9, 172.3;ESIHRMS: Calcd. for $C_{23}H_{32}N_4O_6NaS$ $[M+Na]^+$ 515.1941, found 515.1945.

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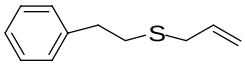

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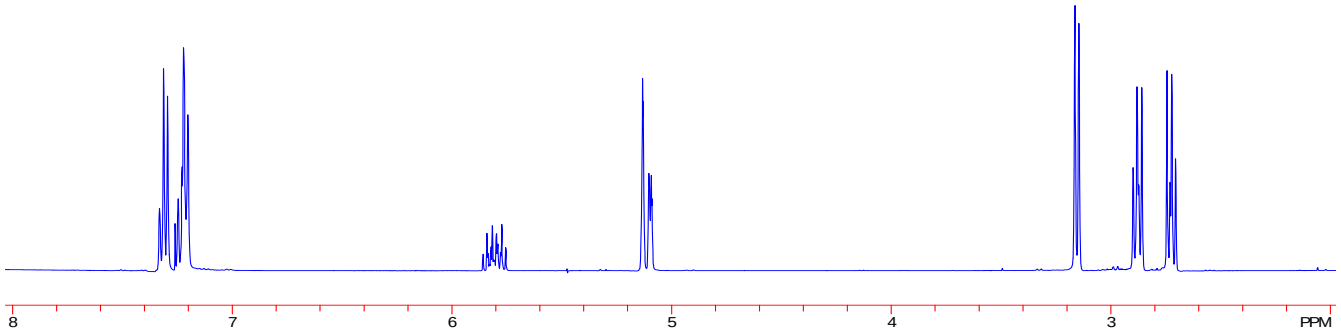

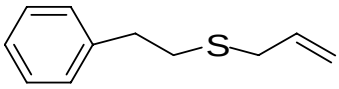

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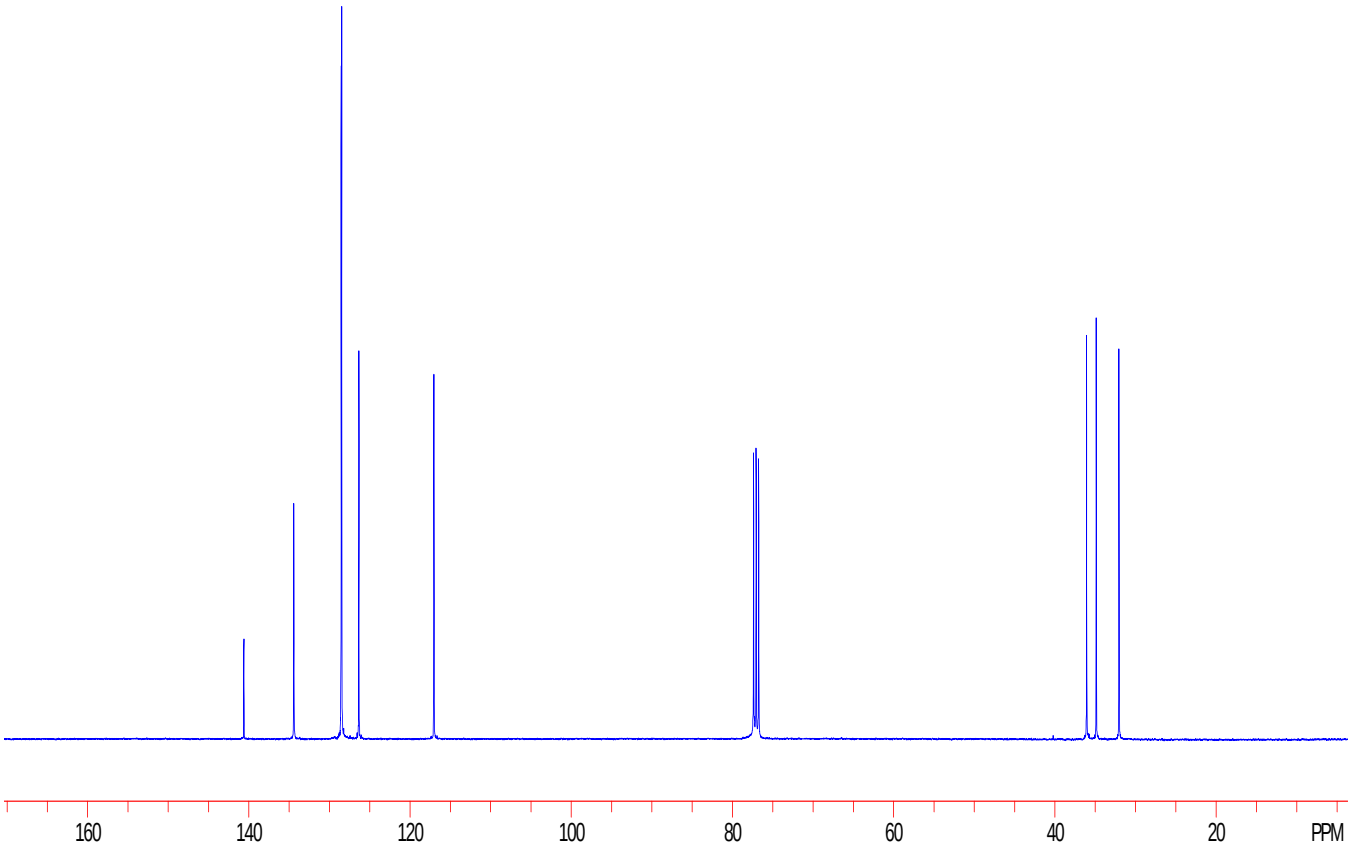

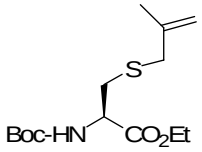

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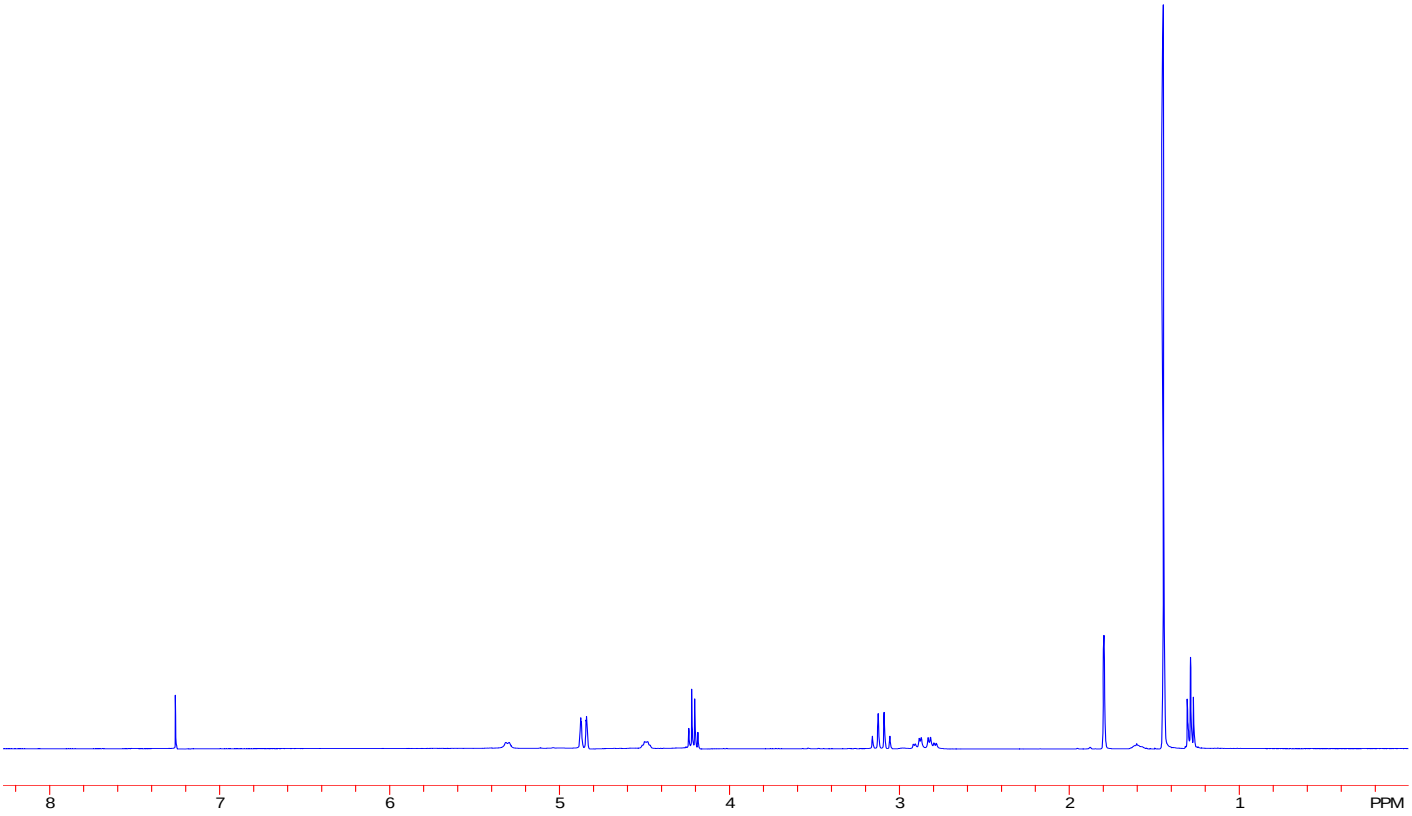

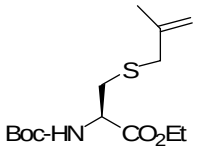

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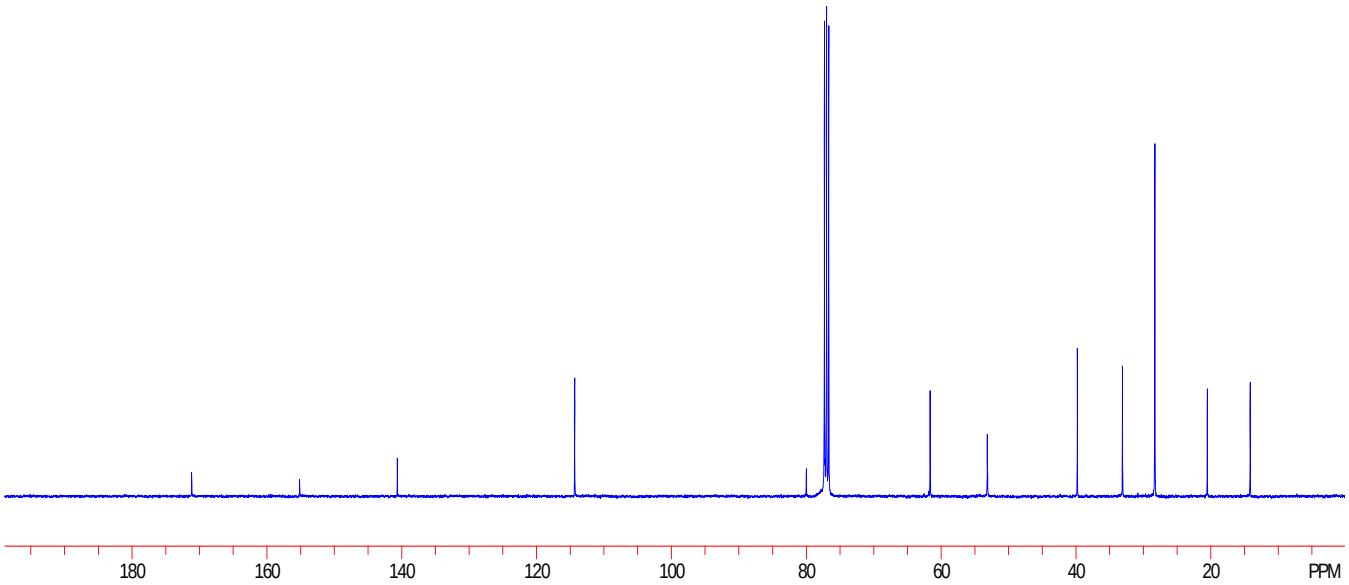

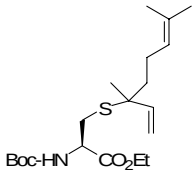

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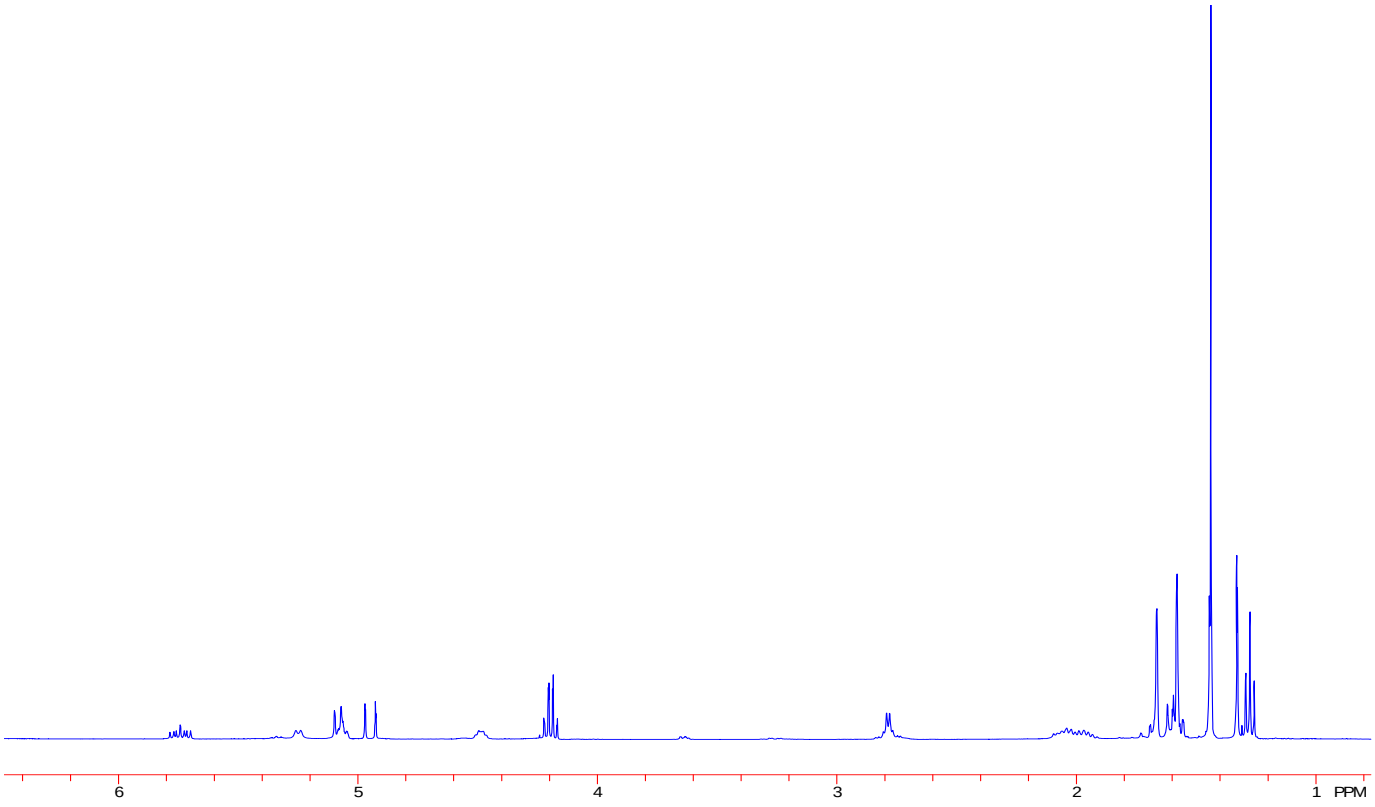

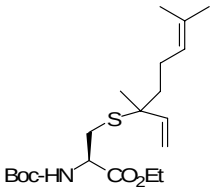

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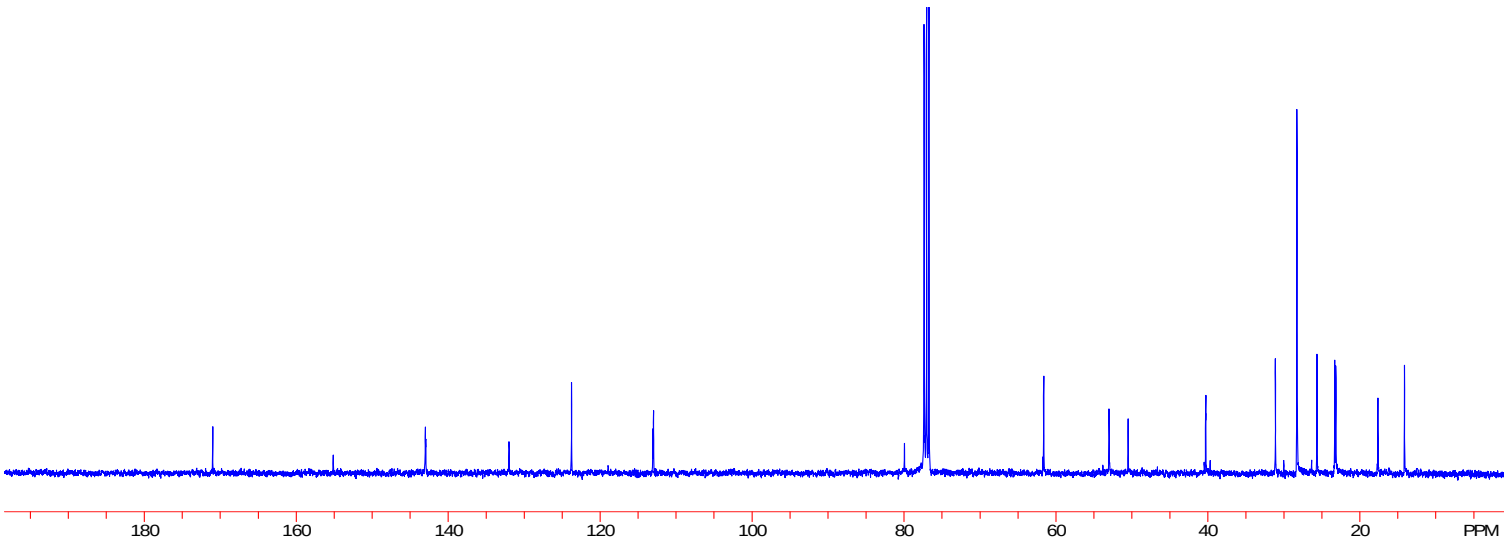

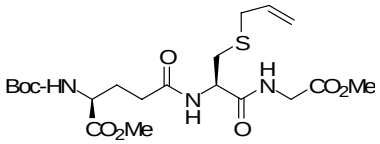

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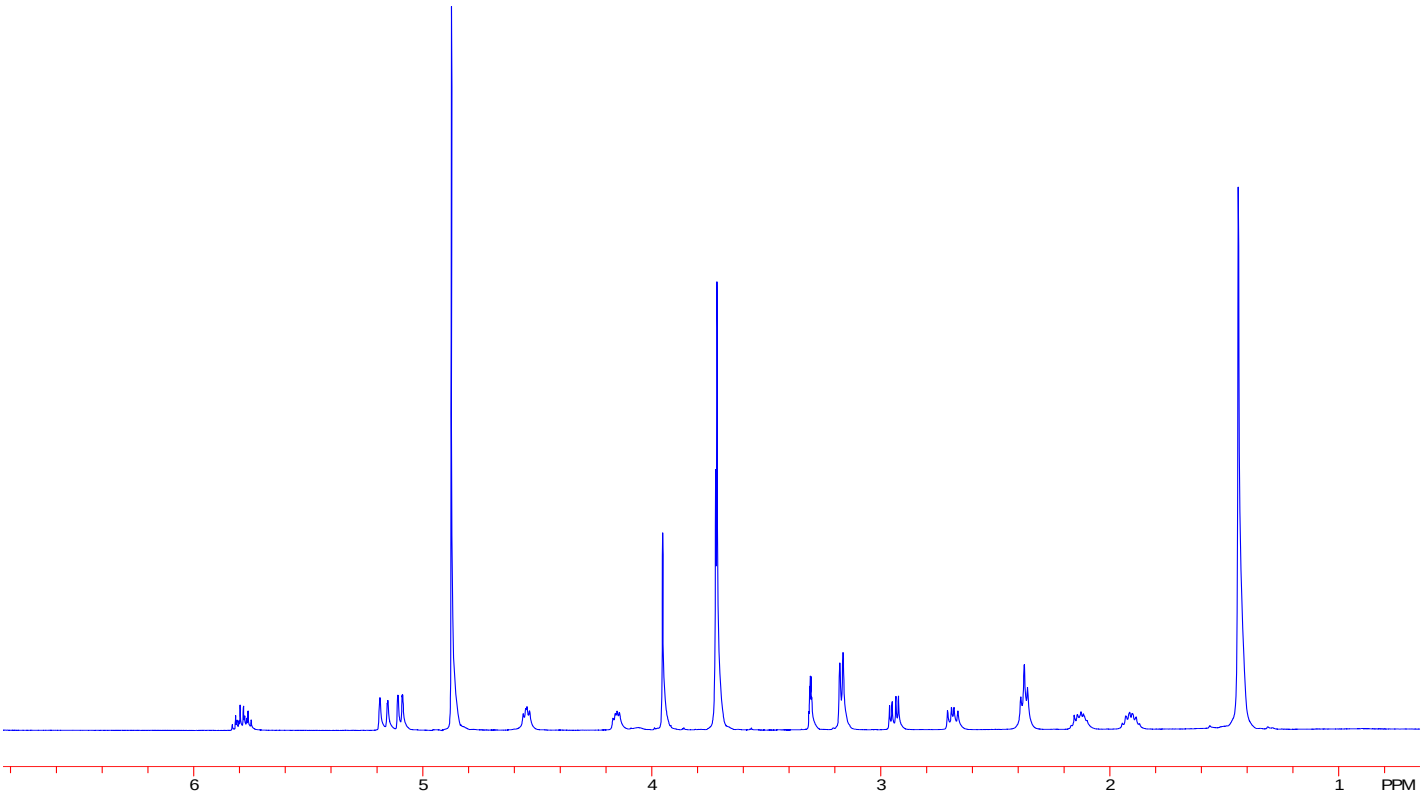

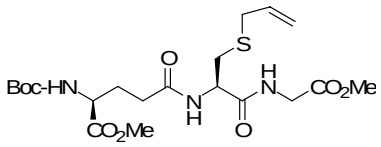

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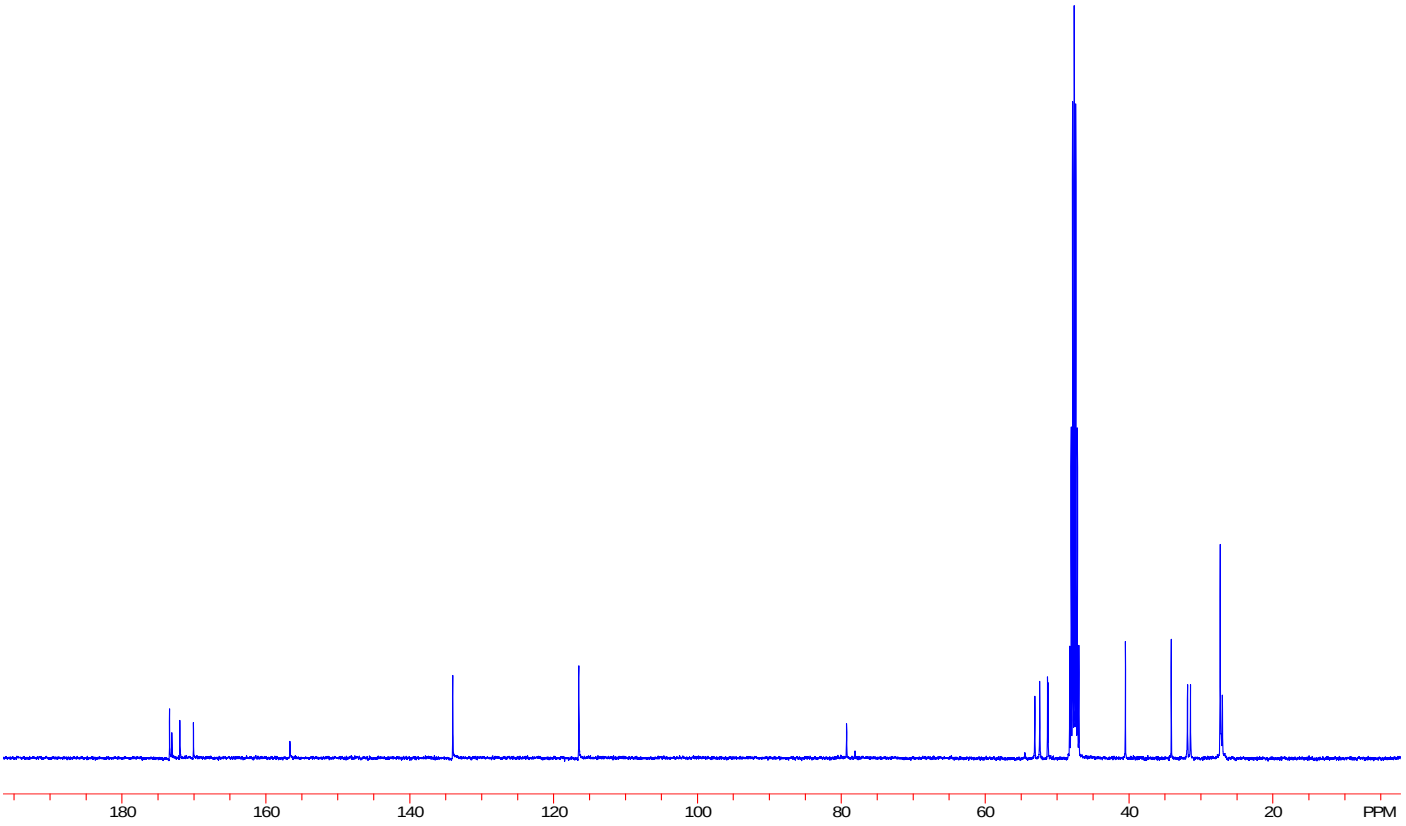

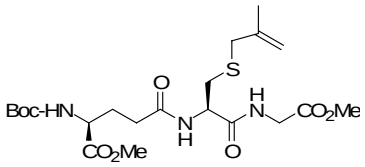

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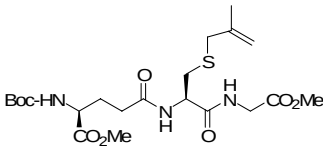

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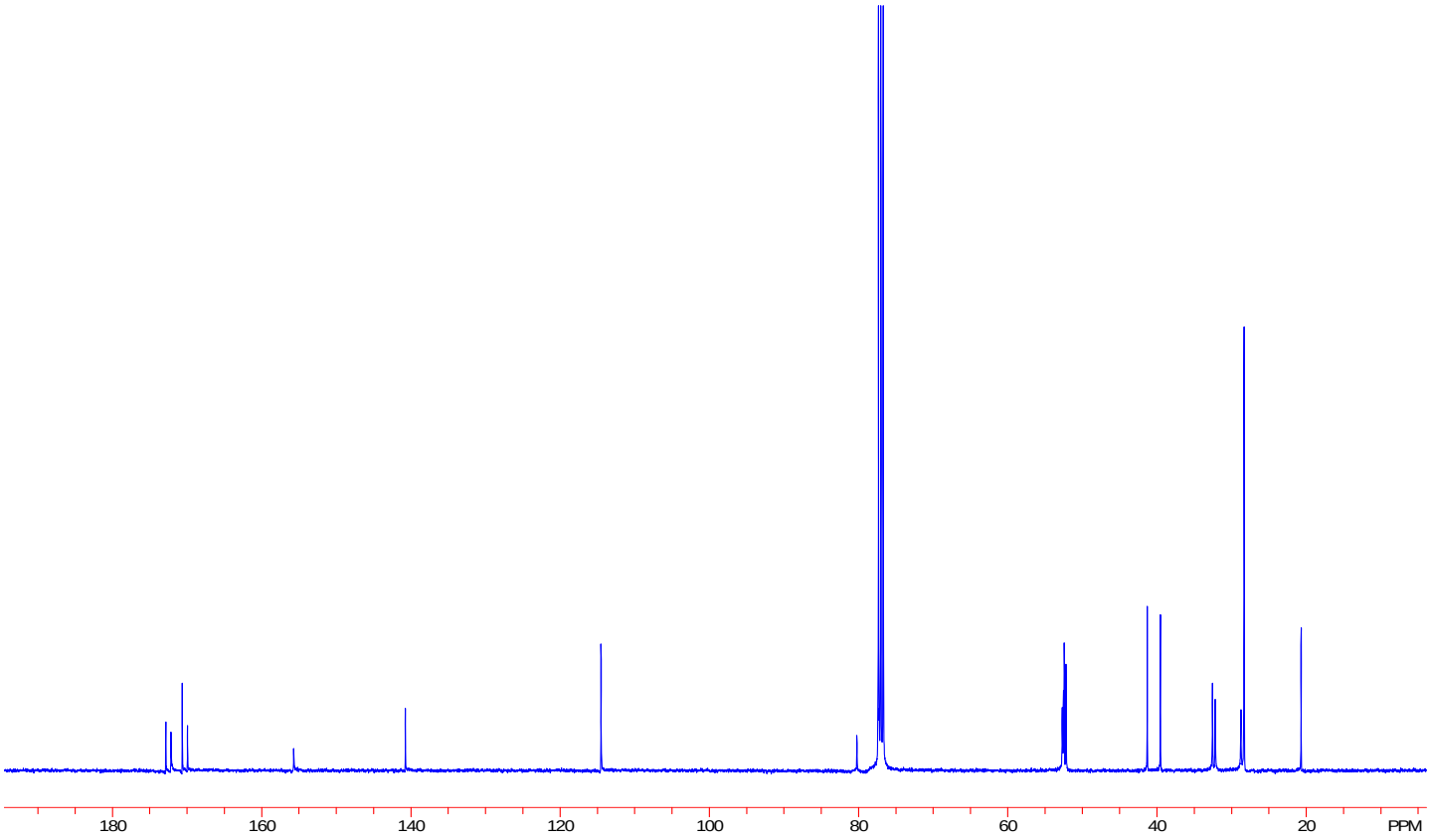

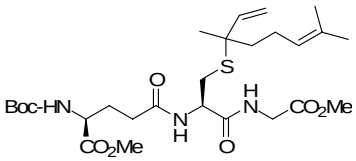

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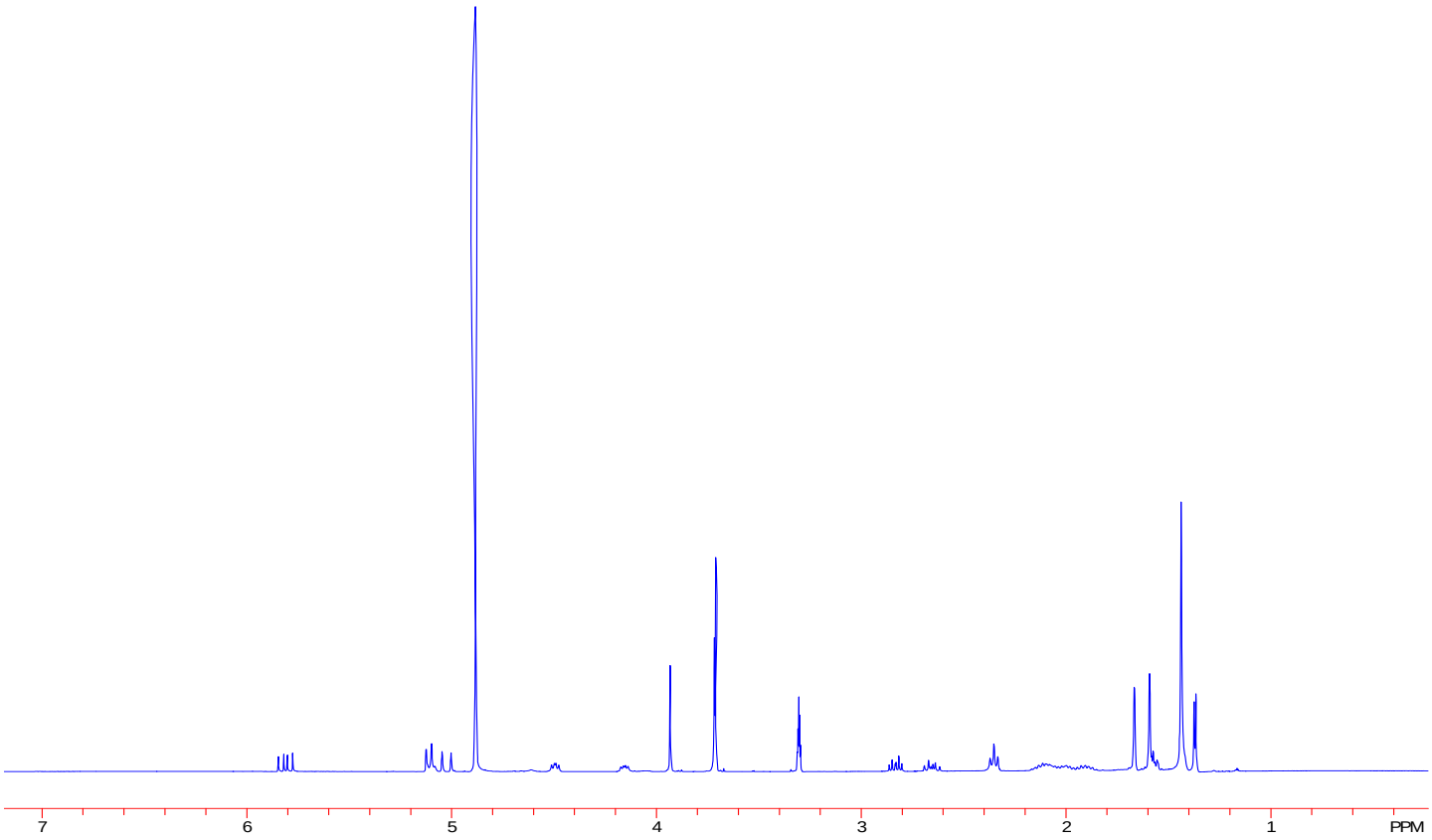

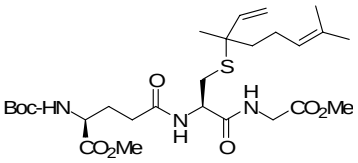

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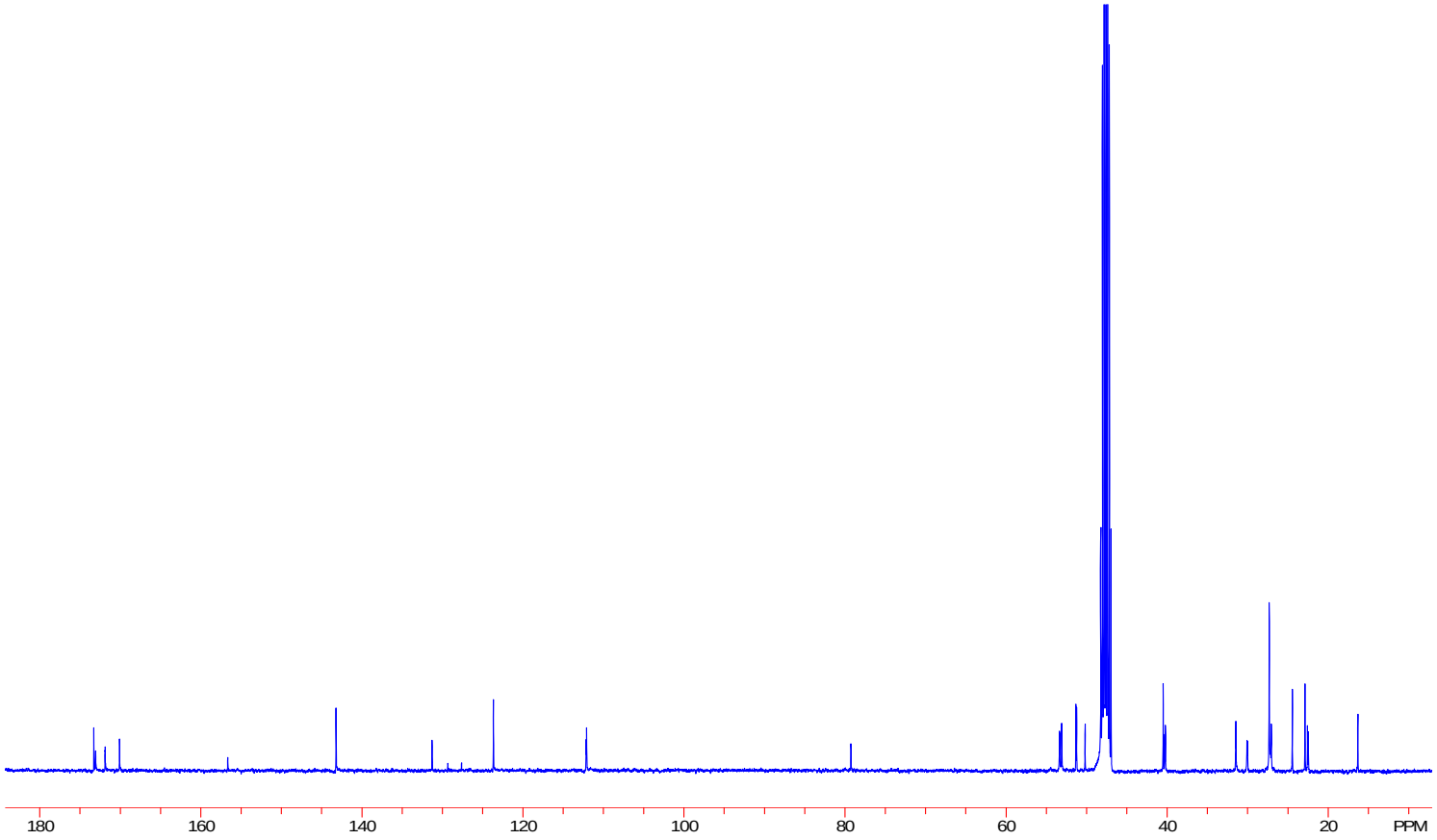

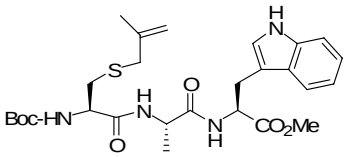

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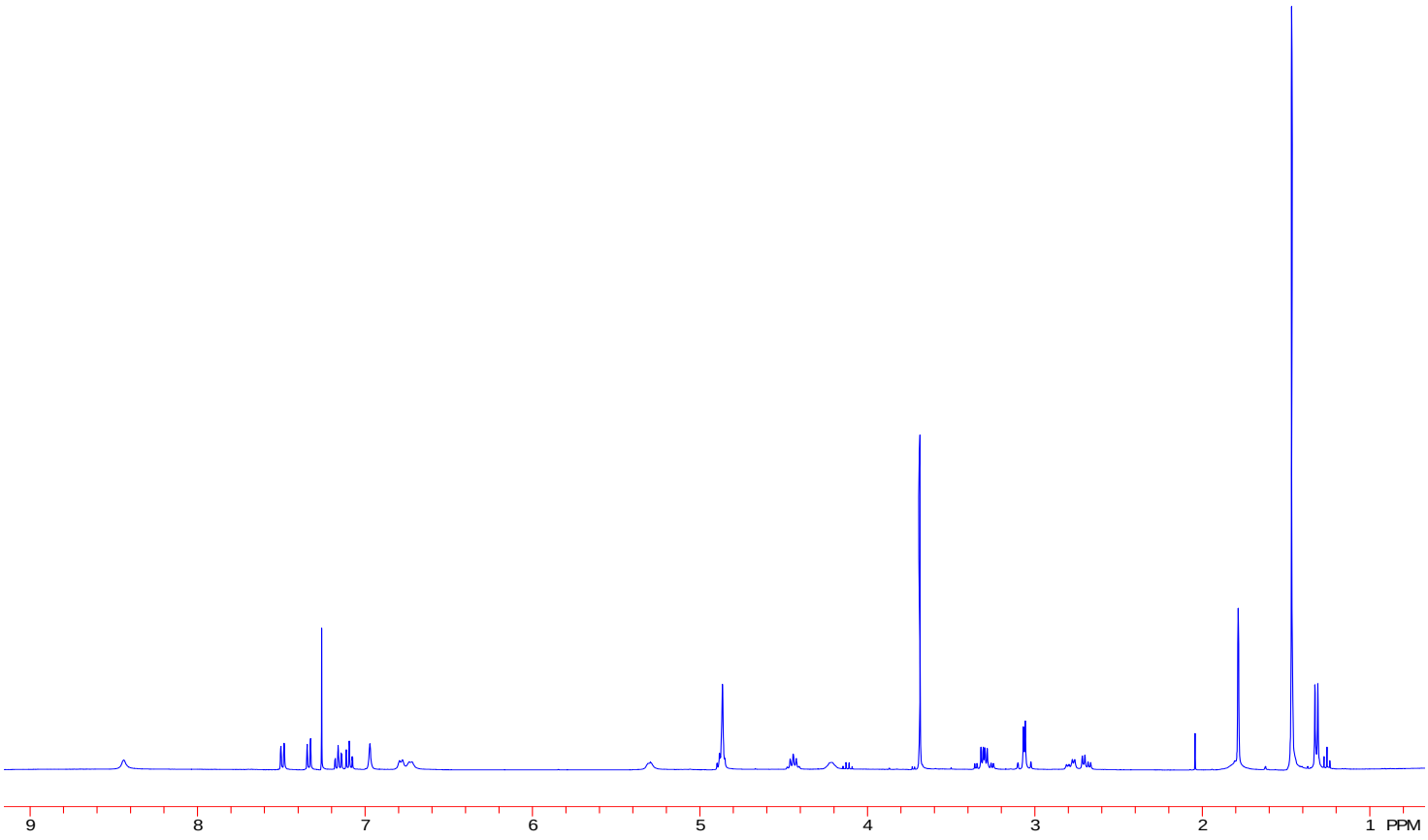

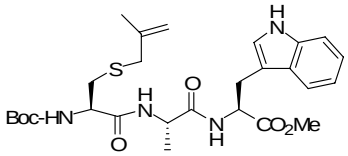

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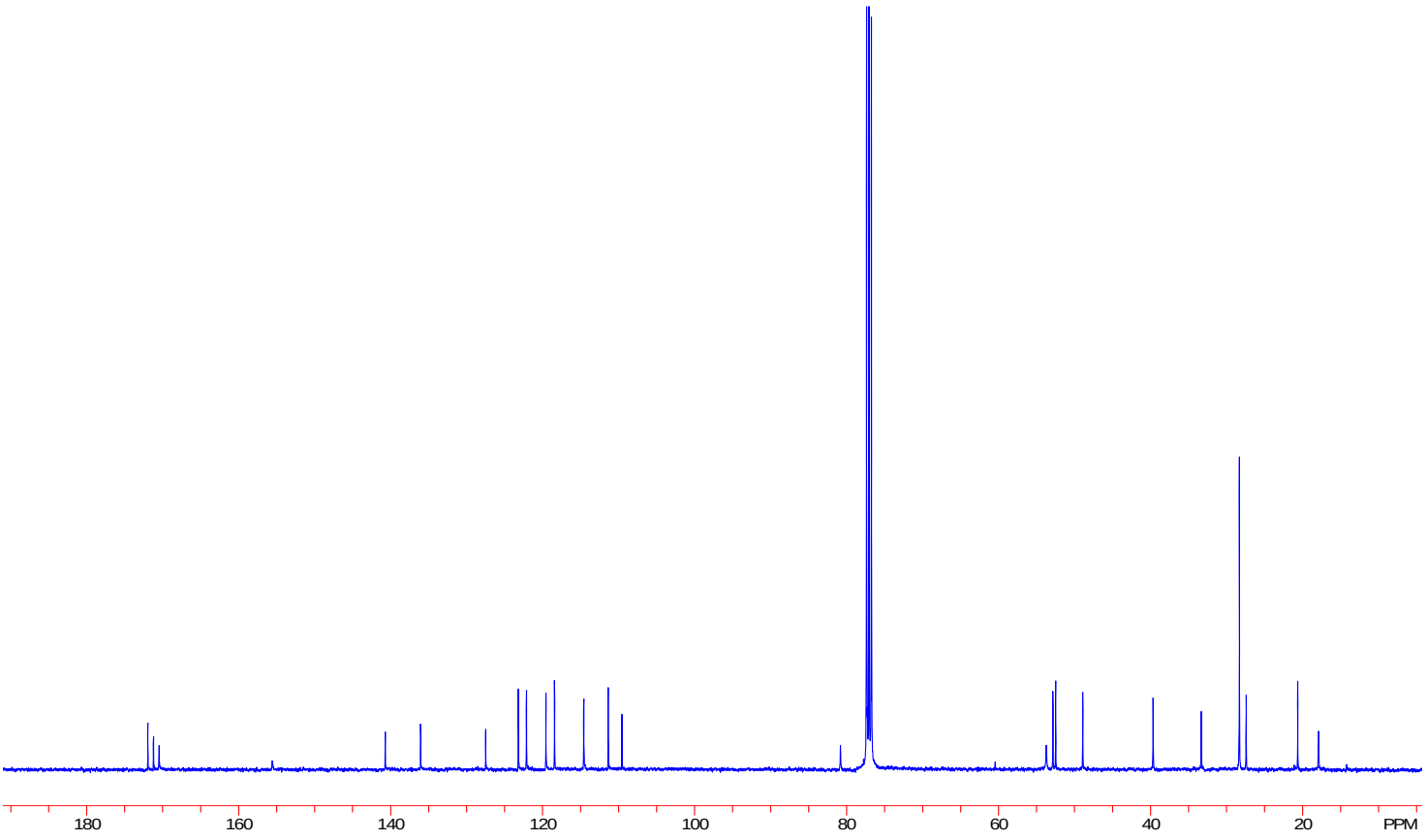

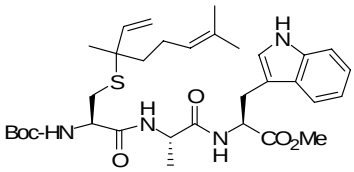

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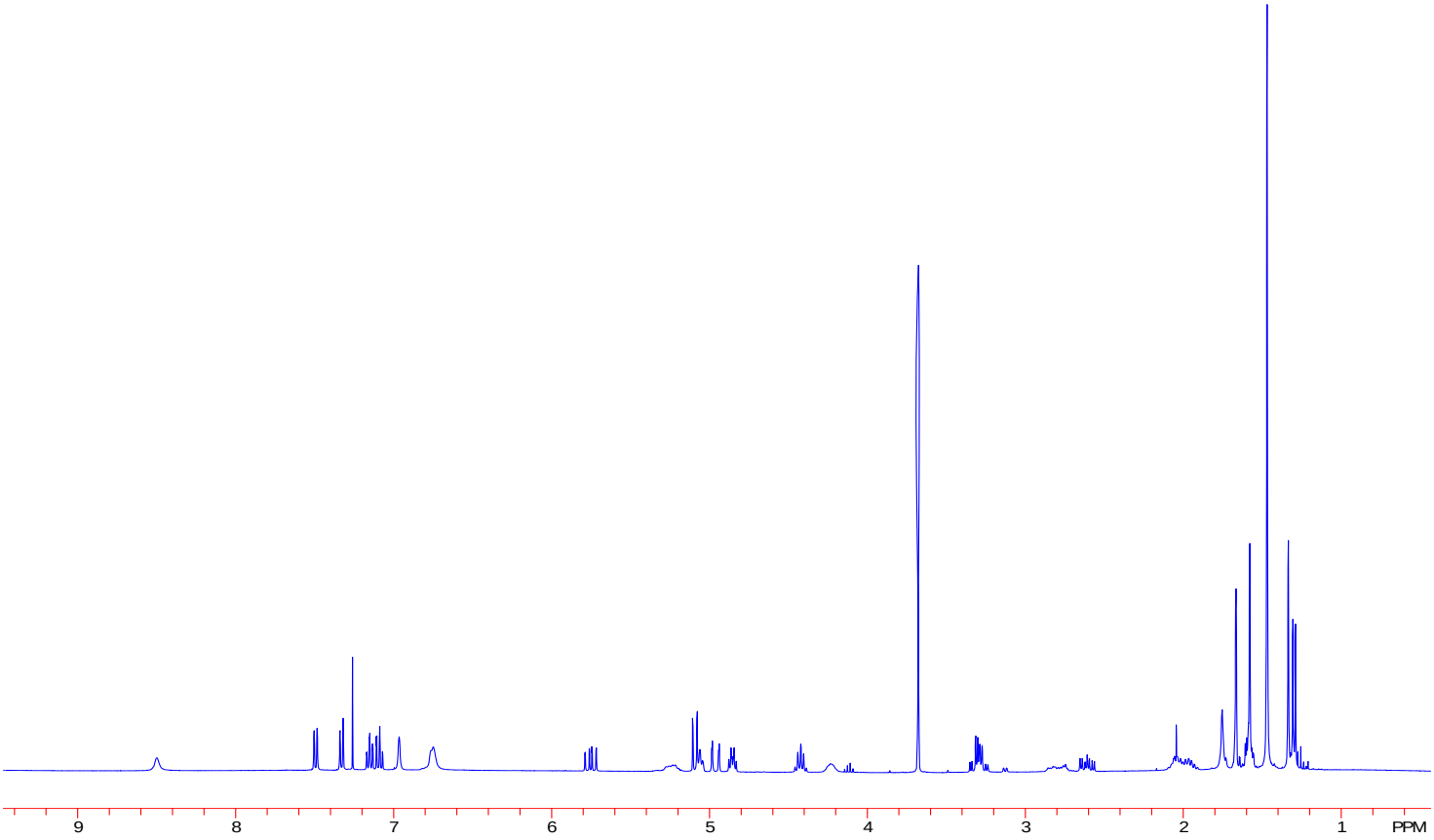

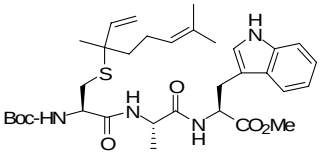

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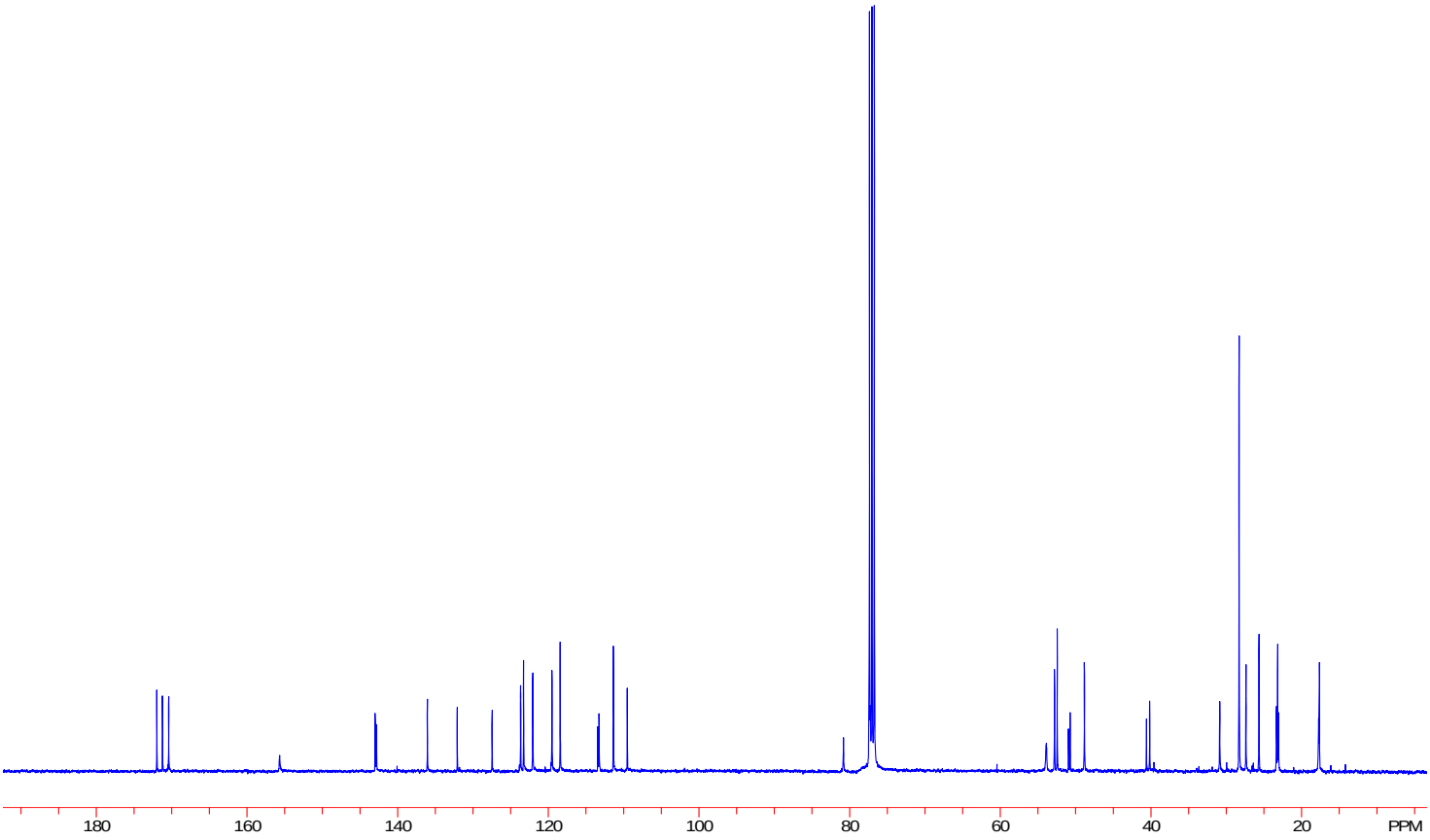

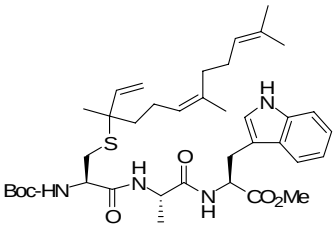

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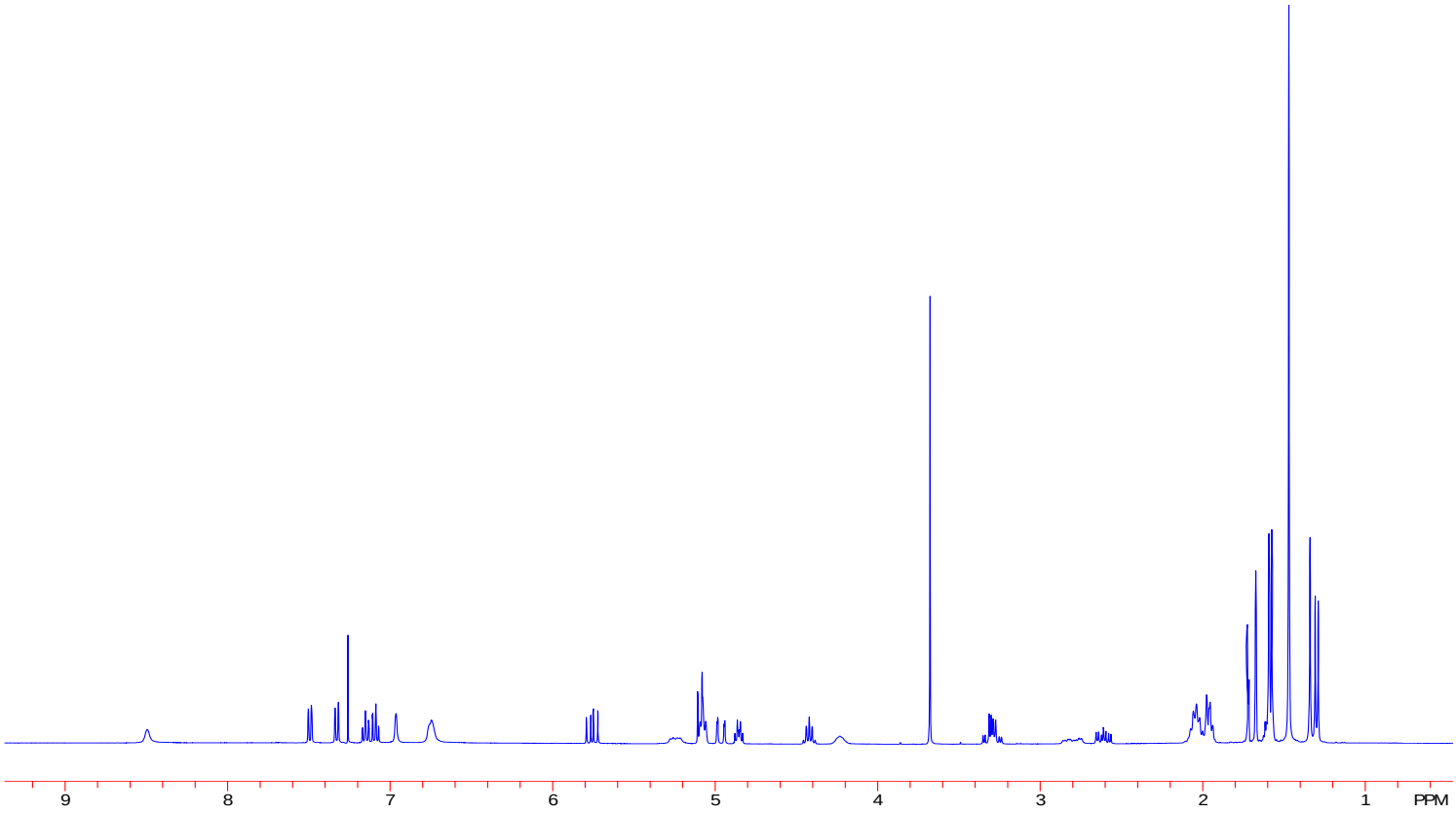

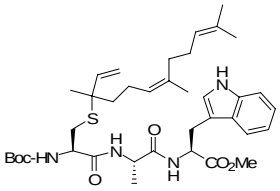

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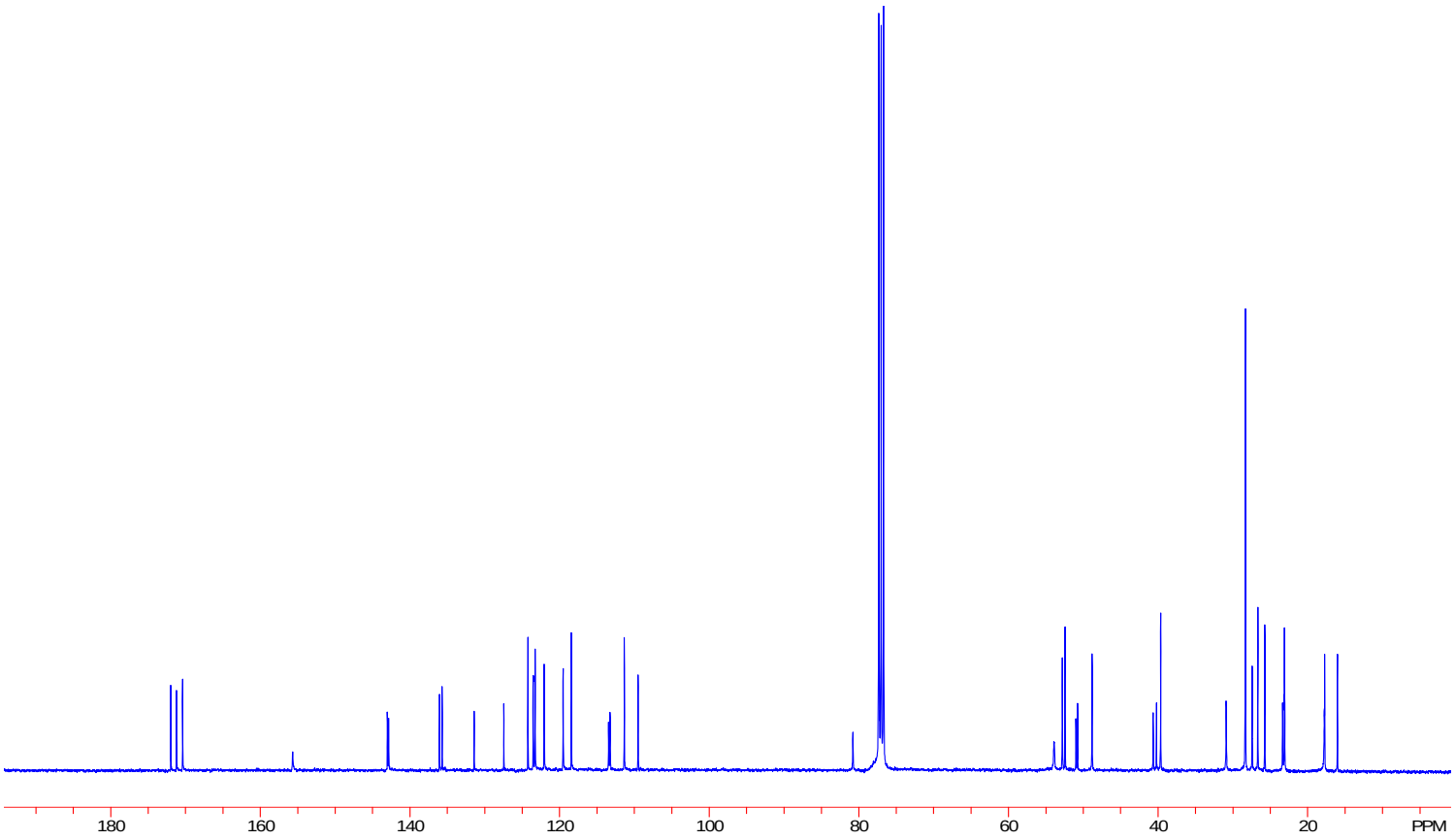

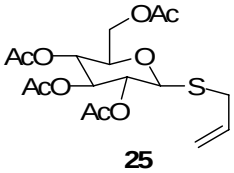

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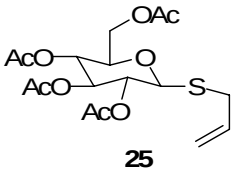

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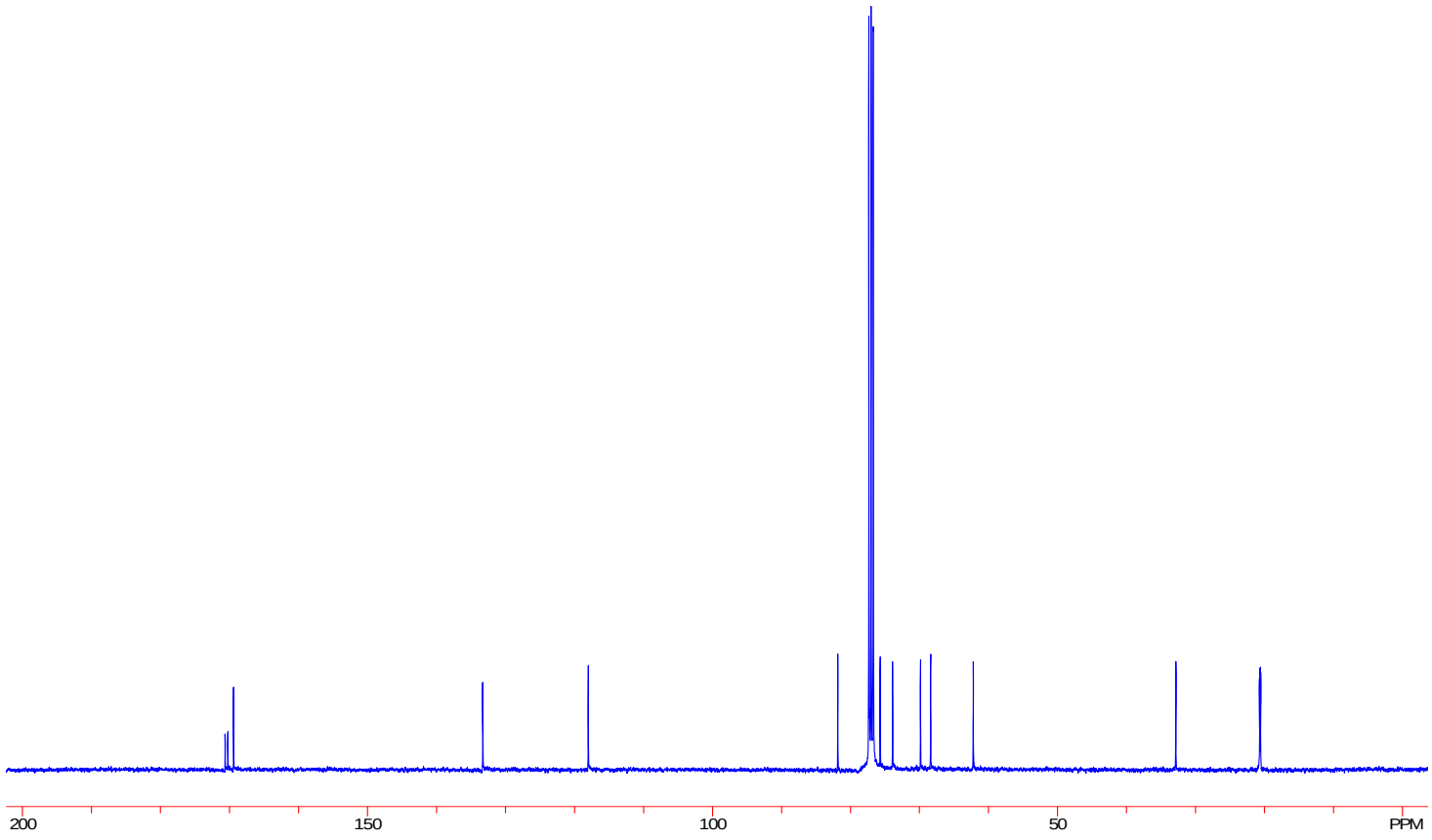

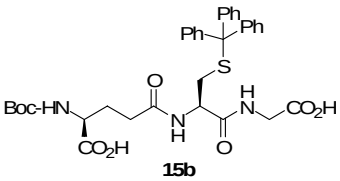

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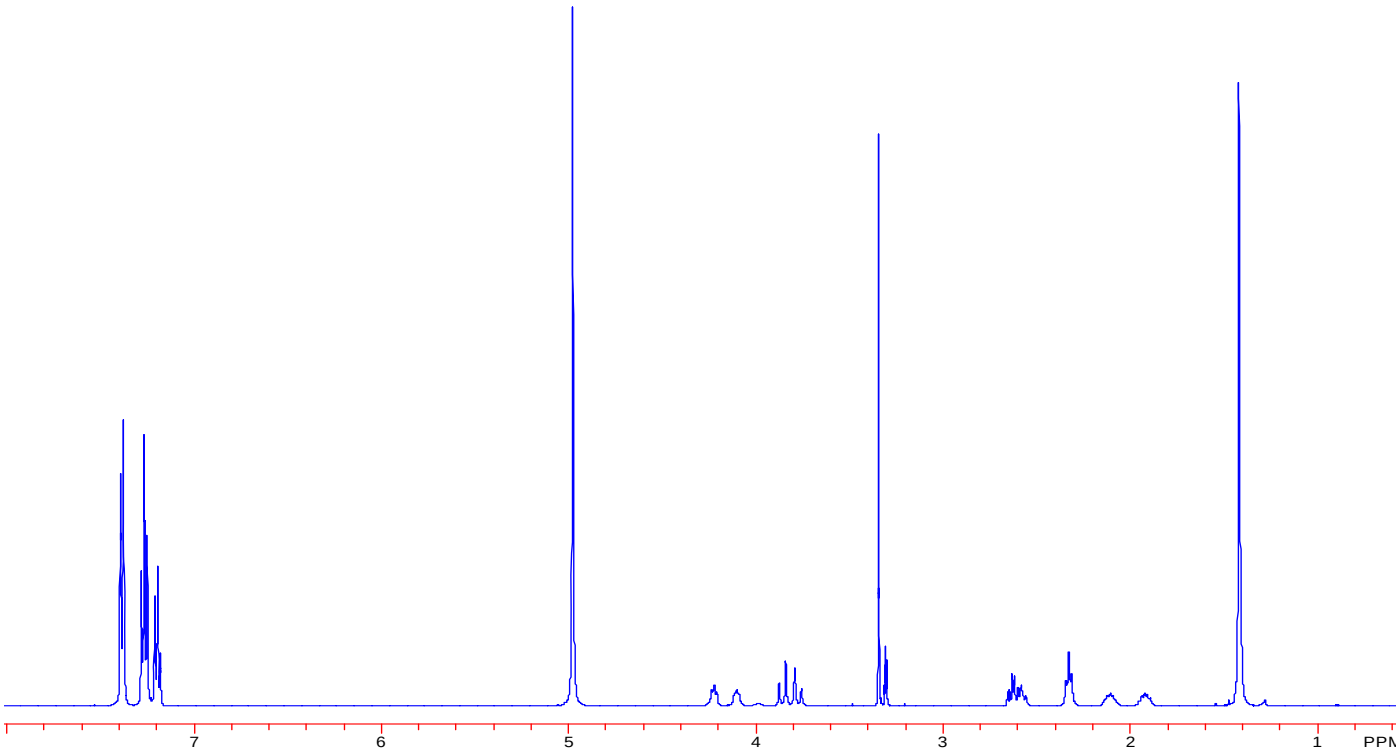

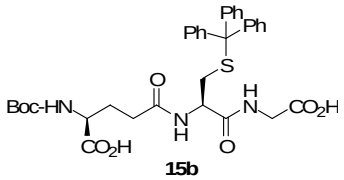

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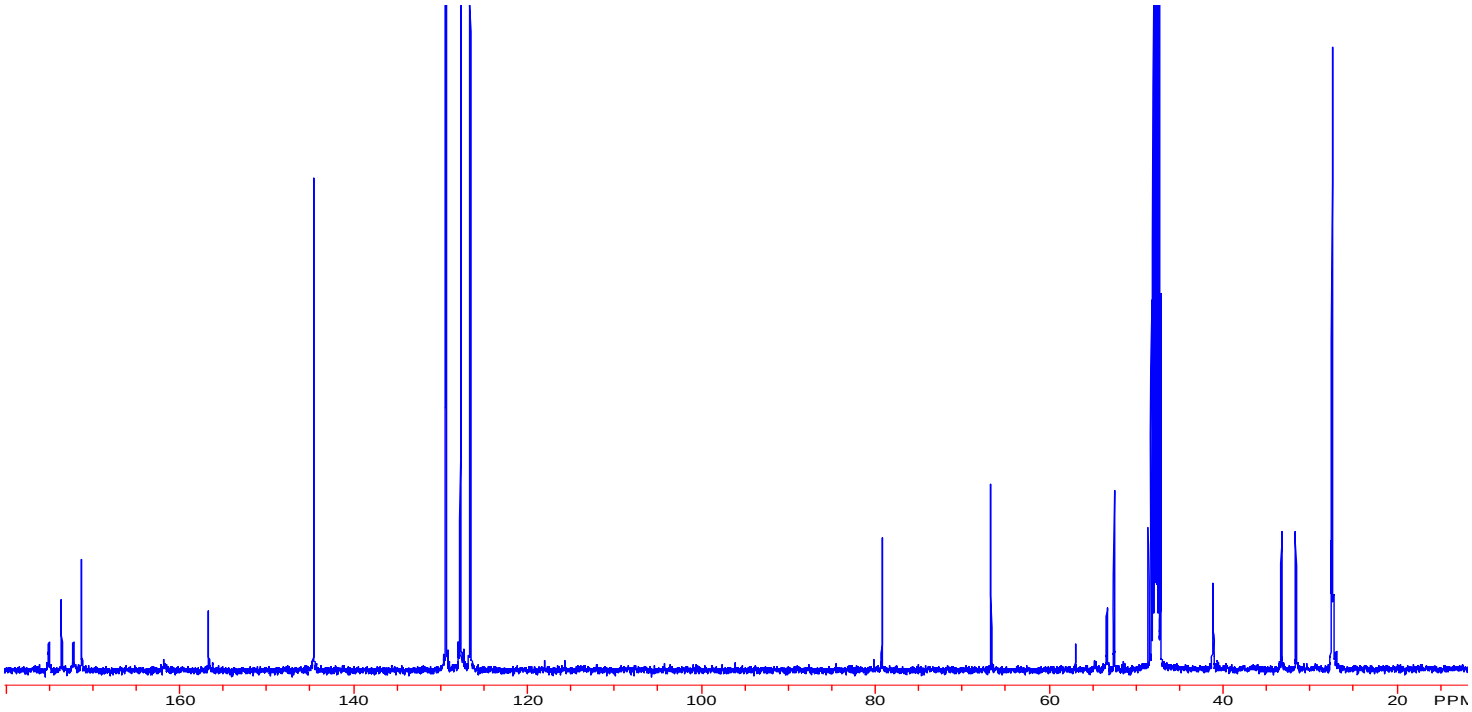

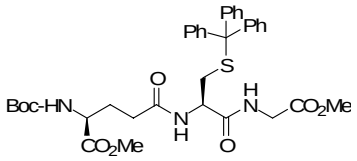

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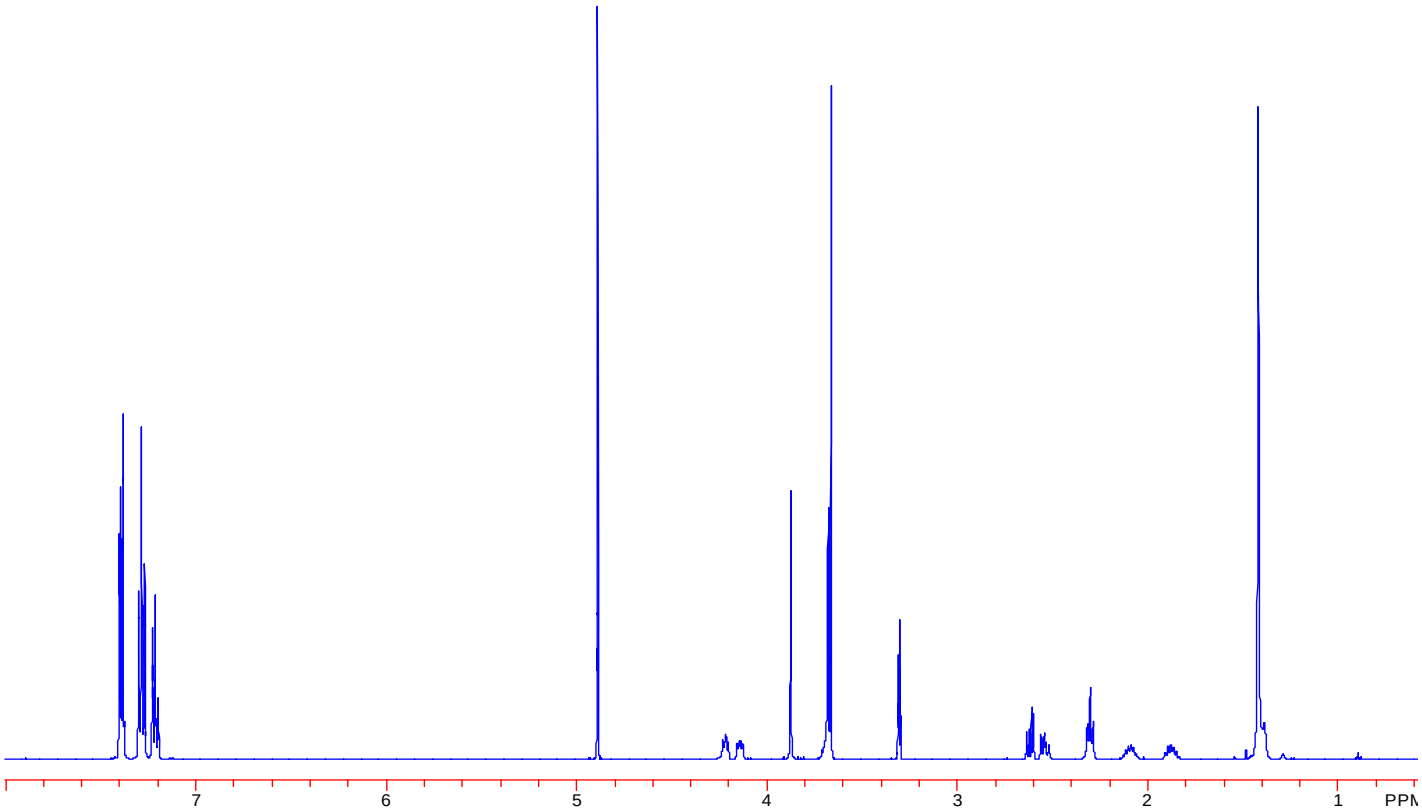

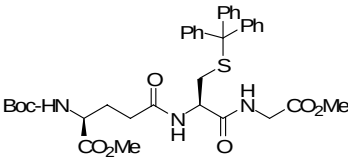
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H
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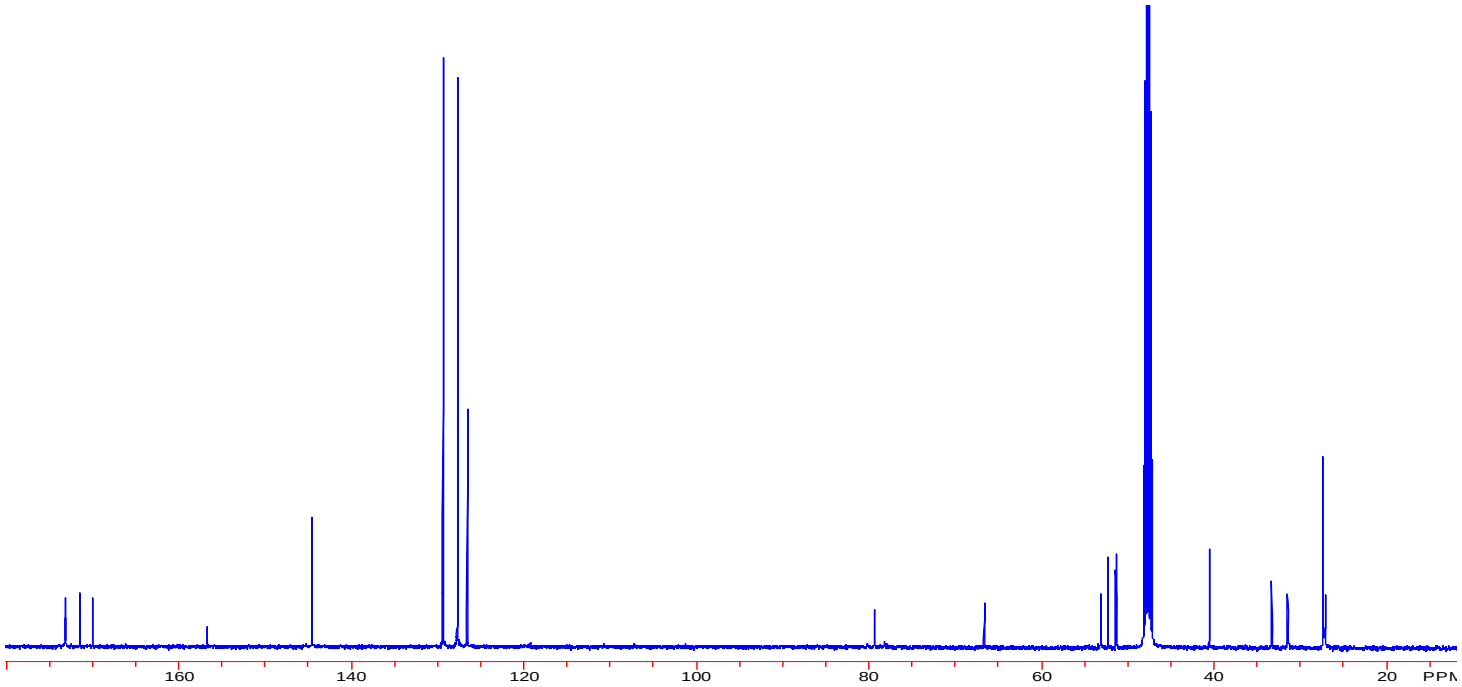
CO2Me

15c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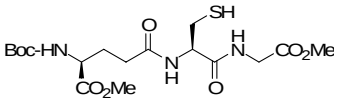

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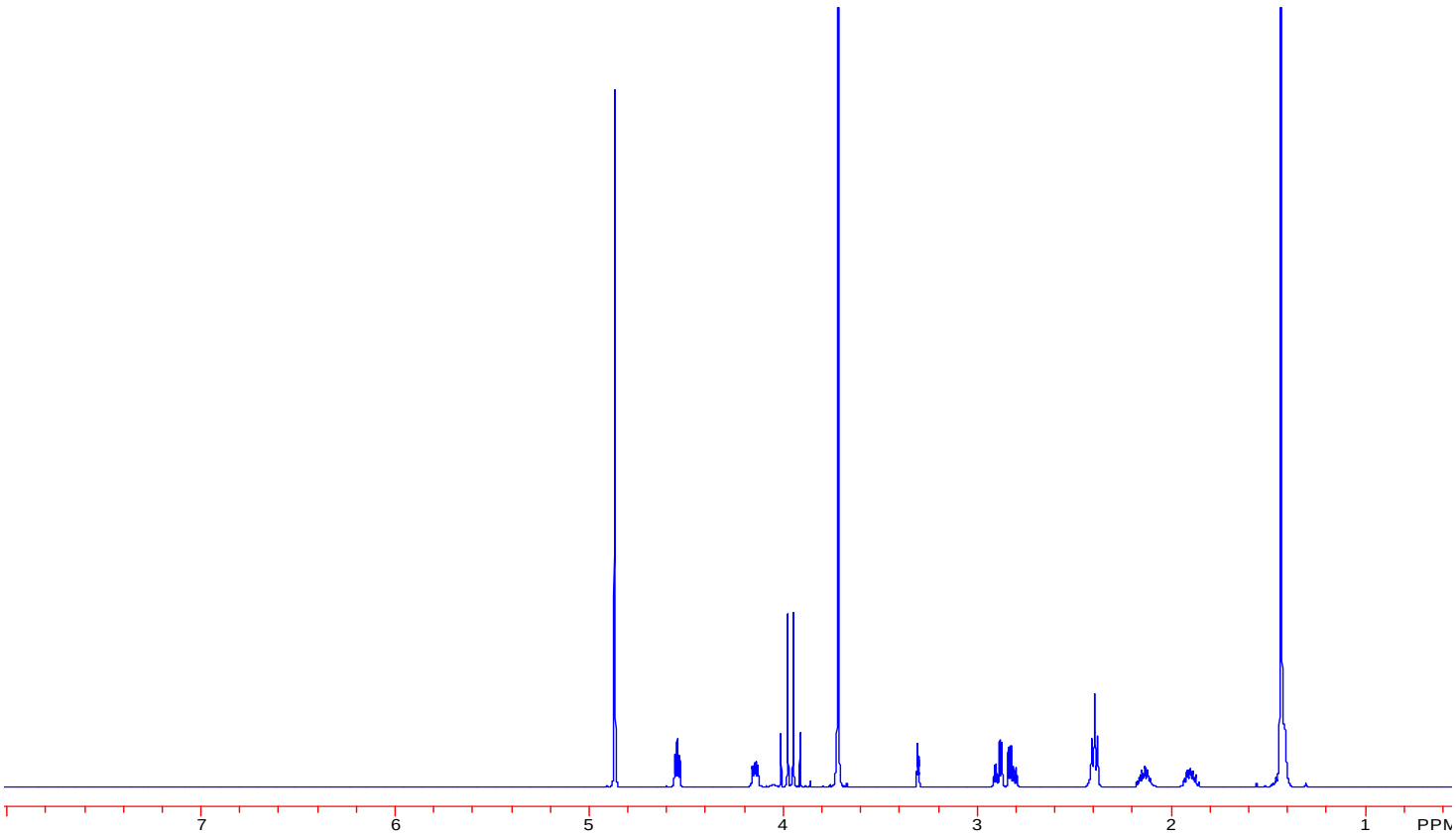

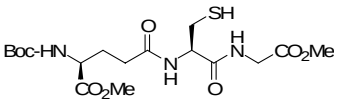

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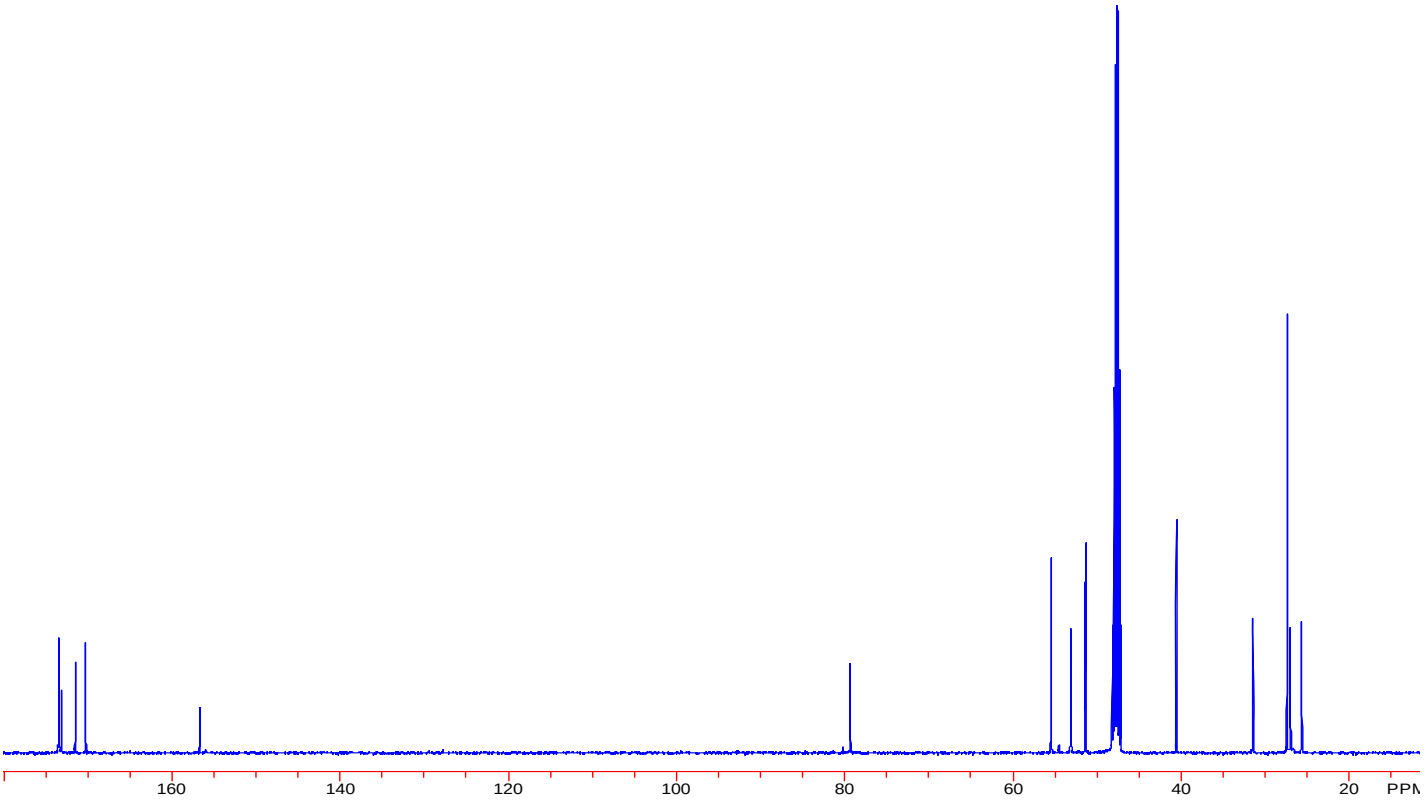

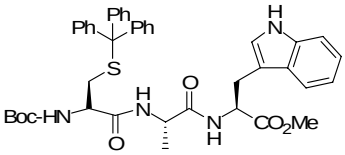

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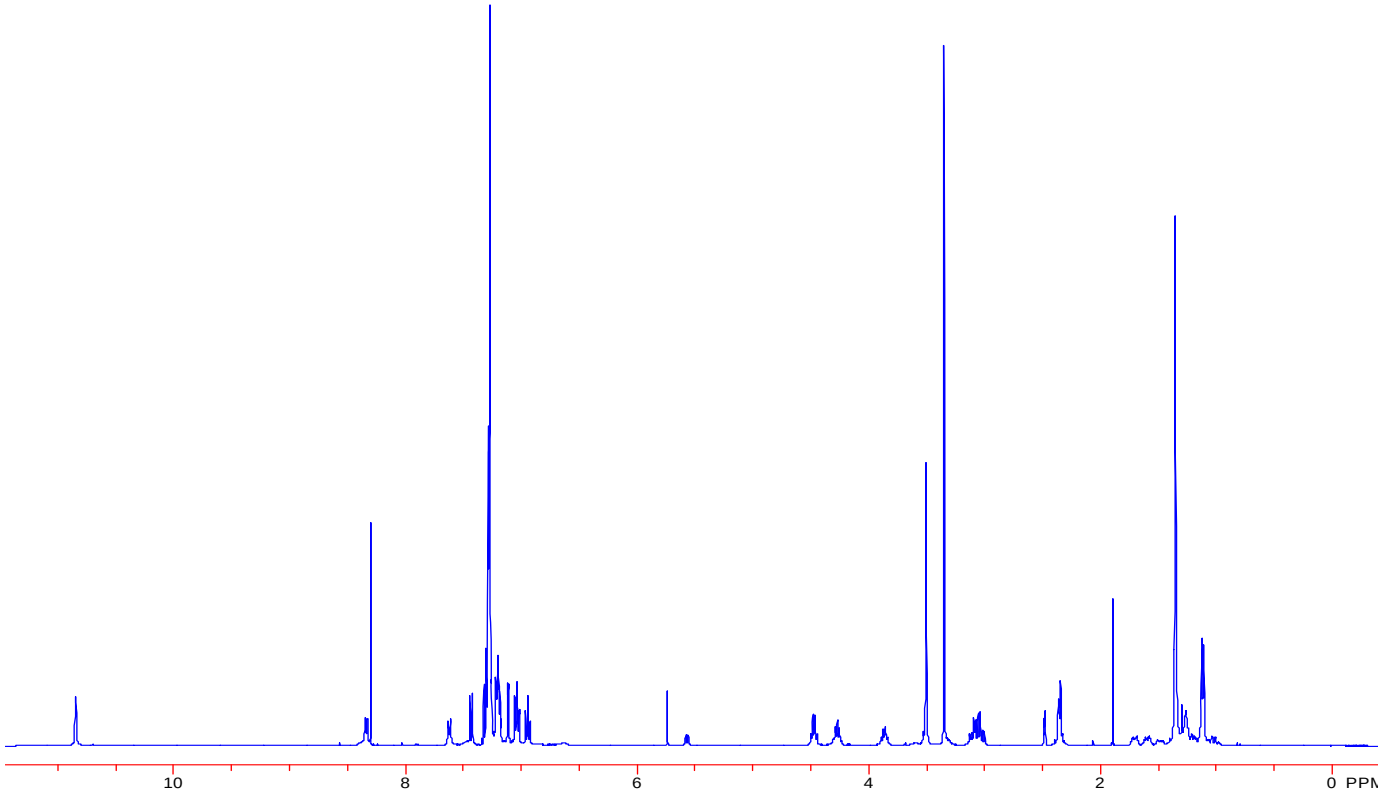

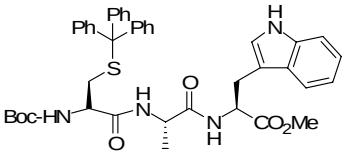
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H
CO2Me
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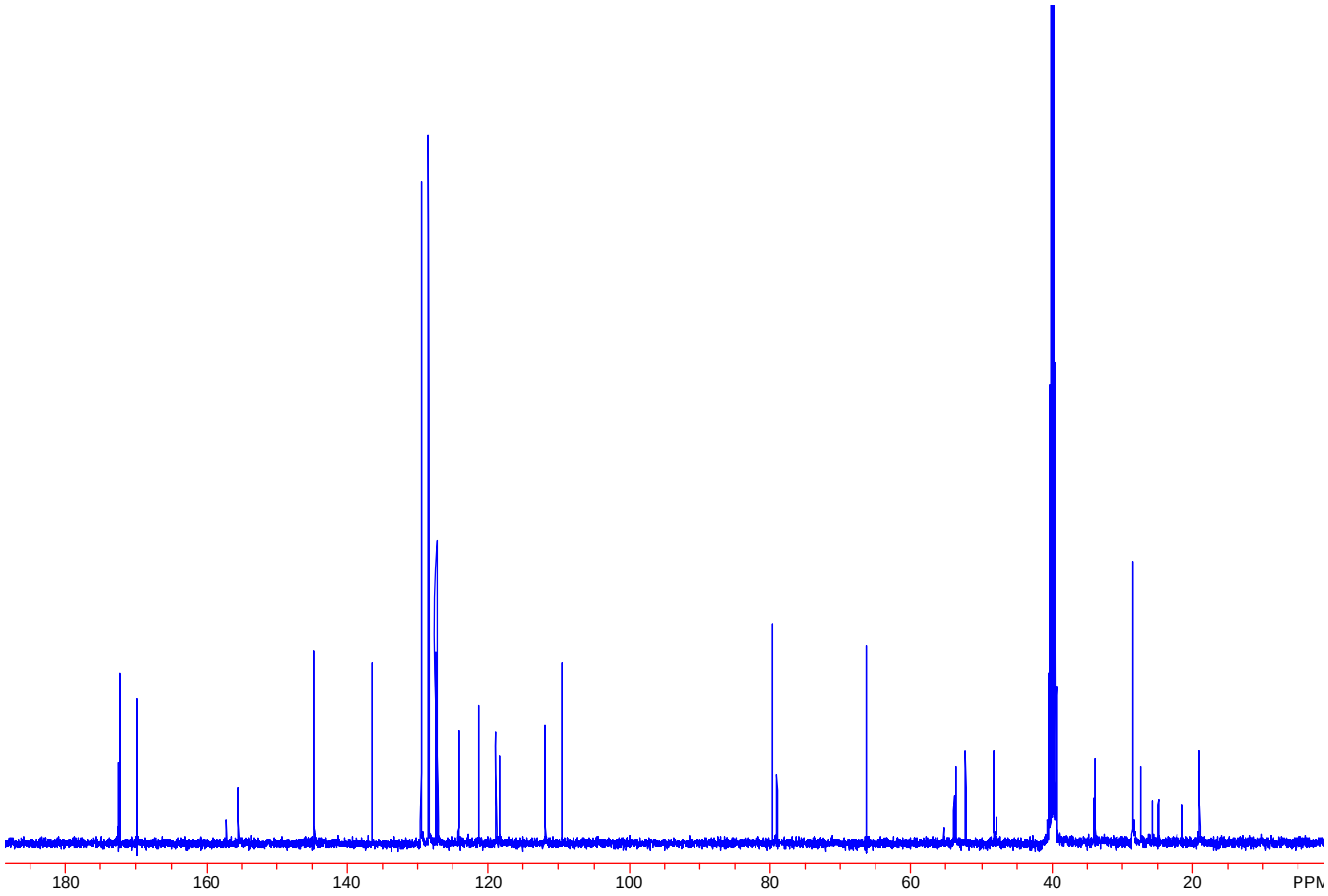
N

16a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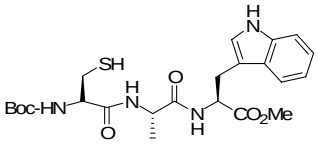

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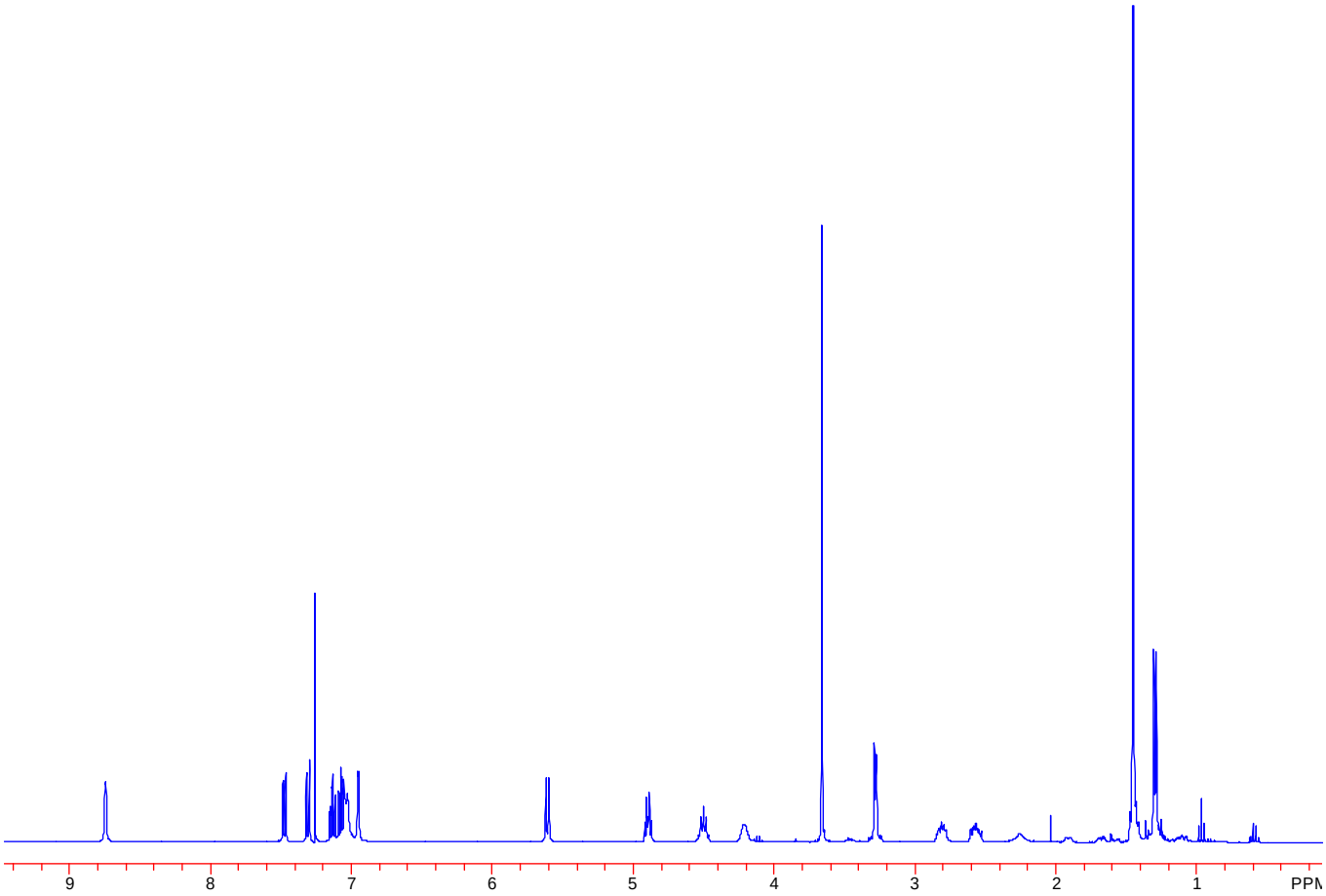

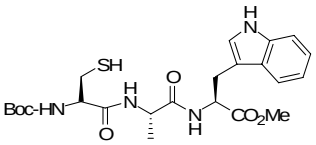

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