An EDCI-Mediated Oxazole Rearrangement: Gaining Access to a Unique Marine Alkaloid Scaffold

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Supporting Information

Table of Contents **Page #**

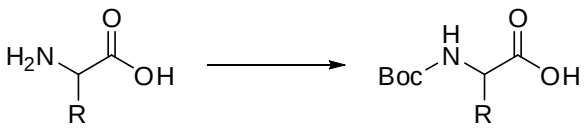
General Information

Reactions were carried out in flame-dried glassware under nitrogen atmosphere. All reactions were magnetically stirred and monitored by TLC with 0.25 μm pre-coated silica gel plates using either UV light, iodine, or potassium permanganate stain to visualize the compounds. Column chromatography was carried out on Silica Gel 60 (230-400 mesh) supplied by EM Science. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. Chemical shifts are reported relative to the residue peaks of the solvent ($CDCl_3$: 7.24 ppm for ^1H and 77.0 ppm for ^{13}C) (Acetone-d_6: 2.04 ppm for ^1H and 29.8 ppm for ^{13}C) (DMSO-d_6: 2.49 ppm for ^1H and 39.5 ppm for ^{13}C). The following abbreviations are used to denote the multiplicities: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, and m = multiplet. The melting points recorded are uncorrected.

Materials

Reagents and solvents were purchased from commercial suppliers and used without further purification. Anhydrous methylene chloride and toluene were dispensed from a delivery system which passes the solvents through a column packed with dry neutral alumina.

General procedure for t-Boc protection of amino acids. The preparation of all N-boc protected amino acids followed a literature procedure.[1]



2-(tert-butoxycarbonylamino)propanoic acid (2a)
Yield (1.73 g, 82%). ^{1}H NMR (500MHz), DMSO: δ 1.20 (d, J = 8 Hz, 3H), 1.36 (s, 9H), 3.90 (p, J = 8 Hz, 1H), 7.05 (d, J = 8 Hz, 1H), 12.4 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 17.0, 28.2, 48.8, 77.9, 155.2, 174.6. IR: (KBr) 3350 (broad) cm^{-1}, 1720 cm^{-1} (with shoulder). HRMS: [M + H]$^{+}$ = 190.1089, calculated for $C_8H_{16}NO_4$, 190.1079. Melting Point = 104-106˚C.

2-(tert-butoxycarbonylamino)-3-phenylpropanoic acid (2b)
Yield (1.46 g, 91%). ^{1}H NMR (500MHz), DMSO: δ 1.30 (s, 9H), 2.78-2.85 (m, 1H), 2.98-3.04 (m, 1H), 4.05-4.12 (m, 1H), 7.07 (d, J = 8 Hz, 1H), 7.16-7.28 (m, 5H), 12.58 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 28.1, 36.4, 55.1, 78, 126.2, 128.1, 129.0, 138.0, 155.4, 173.5. IR: (KBr) 3325 (broad) cm^{-1}, 1720 cm^{-1}(with shoulder). HRMS: [M + H]$^{+}$ = 266.1420, calculated for $C_{14}H_{20}NO_4$, 266.1392. Melting Point = 106-108˚C.

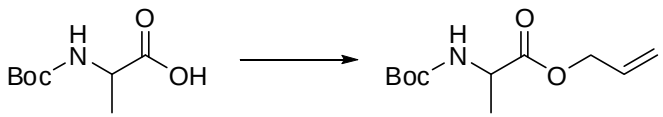
2-(tert-butoxycarbonylamino)-2-phenylacetic acid (2c)
Yield (4.9 g, 98%). ^{1}H NMR (500MHz), DMSO: δ 1.38 (s, 9H), 5.10 (d, J = 8 Hz, 1H), 7.3-7.39 (m, 5H), 7.55 (d, J = 8 Hz, 1H), 12.75 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 28.2, 57.5, 78.3, 127.7, 128.3, 137.4, 155.1, 172.2. IR: (KBr) 3300 (broad) cm^{-1}, 1720 cm^{-1}, 1660 cm^{-1}. HRMS: [M + H]$^{+}$ = 252.1237, calculated for $C_{13}H_{18}NO_4$, 252.1236. Melting Point = 108-109˚C.

2-(tert-butoxycarbonylamino)-2-(4-methoxyphenyl)acetic acid (2d)
Yield (1.07 g, 69%). ^{1}H NMR (500MHz), DMSO: δ 1.37 (s, 9H), 3.72 (s, 3H), 5.01 (d, J = 8 Hz, 1H), 6.88 (d, J = 9 Hz, 2H), 7.29 (d, J = 9 Hz, 2H), 7.49 (d, J = 8 Hz, 1H), 12.6 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 28.5, 55.4, 57.2, 78.6, 114.0, 129.2, 129.6, 155.4, 159.1, 172.9. IR: (KBr) 3395 (broad) cm^{-1}, 1724 cm^{-1}, 1686 cm^{-1}. HRMS: [M + H]$^{+}$ = 282.1343, calculated for $C_{14}H_{20}NO_5$, 282.1341. Melting Point = 104-106˚C.

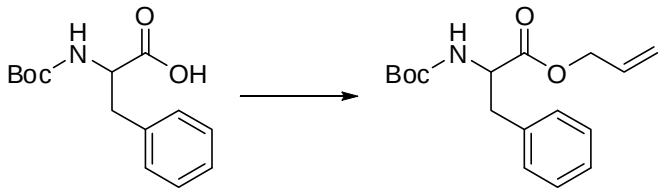
2-(tert-butoxycarbonylamino)-2-(4-fluorophenyl)acetic acid (2e)
Yield (660 mg, 98%). ^{1}H NMR (500MHz), DMSO: δ 1.37 (s, 3H), 5.11 (d, J = 8 Hz, 1H), 7.15 (m, 2H), 7.42 (m, 2H), 7.59 (d, J = 8 Hz, 1H), 12.79 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 28.1, 56.8, 78.4, 114.9, 115.1, 129.7, 129.8, 133.7, 155.1, 160.7, 162.6, 172.1. IR: (KBr) 3370 (broad) cm^{-1}, 1730 cm^{-1}, 1657 cm^{-1}. Melting Point = 41-43˚C.

2-(tert-butoxycarbonylamino)-2-(naphthalen-1-yl)acetic acid (2f)
Yield (1.38 g, 93%). ^{1}H NMR (500MHz), DMSO: δ 1.38 (s, 9H), 5.91 (d, J = 8 Hz, 1H), 7.48-7.62 (m, 4H), 7.71 (d, J = 8 Hz, 1H), 7.90 (m, 1H), 7.95 (d, J = 9 Hz, 1H), 8.11 (d, J = 8 Hz, 1H), 12.88 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 28.1, 53.9, 78.3, 123.3, 125.3, 125.5, 125.8, 126.5, 128.3, 128.6, 130.8, 133.3, 133.7, 155.2, 172.5. IR: (KBr) 3395 (broad) cm^{-1}, 1720 cm^{-1},

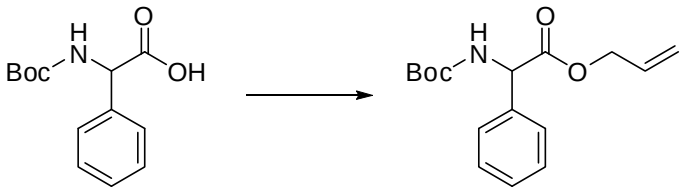
1690 cm^{-1}. HRMS: $[M + H]^+$ = 302.1392, calculated for $C_{17}H_{20}NO_4$, 302.1392. Melting Point = 116-118˚C.



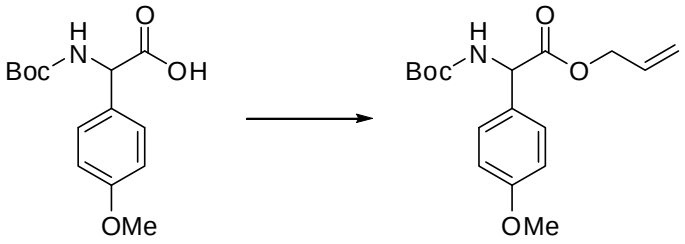
allyl 2-(tert-butoxycarbonylamino)propanoate (3a). To a flame dried 100 mL round bottom flask was added (**2a**) (1 g, 5.29 mmol) and anhydrous DCM (50 mL). Then allyl alcohol (0.72 mL, 10.58 mmol) and DMAP (65 mg, 0.529 mmol) were added and the mixture was brought down to 0ºC. DCC (1.63 g, 7.94 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as an oil. Yield (1.09 g, 90%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.33 (d, J = 7 Hz, 3H), 1.37 (s, 9H), 4.26 (bs, 1H), 4.56 (m, 2H), 5.08 (bs, 1H), 5.17-5.27 (m, 2H), 5.81-5.87 (m, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 18.4, 28.2, 49.1, 65.6, 79.6, 118.4, 131.6, 155.0, 172.9. IR: (NaCl) 3380 cm^{-1} , 1750 cm^{-1}, 1710 cm^{-1}. HRMS: $[M + H]^+$ = 230.1401, calculated for $C_{11}H_{20}NO_4$, 230.1392. Anal. Calcd. For $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 58.89; H, 8.22; N, 5.90.



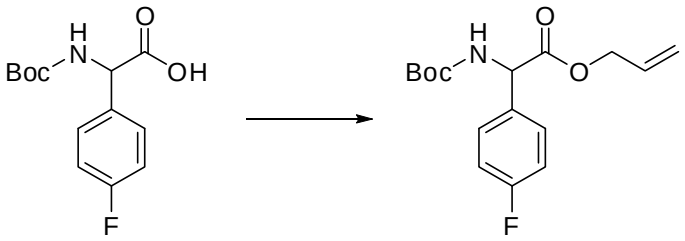
allyl 2-(tert-butoxycarbonylamino)-3-phenylpropanoate (3b). To a flame dried 100 mL round bottom flask was added (**2b**) (1.38 g, 5.23 mmol) and anhydrous DCM (50 mL). Then allyl alcohol (0.71 mL, 10.46 mmol) and DMAP (64 mg, 0.523 mmol) were added and the mixture was brought down to 0ºC. DCC (1.62 g, 7.85 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as a whitish solid. Yield (1.34 g, 84%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.39 (s, 9H), 3.02-3.14 (m, 2H), 4.58 (d, J = 6 Hz, 2H), 4.96 (bs, 1H), 5.2-5.3 (m, 2H), 5.8-5.88 (m, 1H), 7.12 (m, 2H), 7.2-7.29 (m, 3H); ^{13}C NMR (125MHz), $CDCl_3$: δ 28.2, 38.3, 54.4, 65.8, 79.8, 118.8, 126.9, 128.4, 129.3, 131.5, 135.9, 155.0, 171.5. IR: (NaCl) 3380 cm^{-1} , 1750 cm^{-1}, 1710 cm^{-1}. HRMS: $[M + H]^+$ = 306.1703, calculated for $C_{17}H_{24}NO_4$, 306.1705. Anal. Calcd. For $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 68.29; H, 7.41; N, 4.62. Melting Point = 62-64˚C.



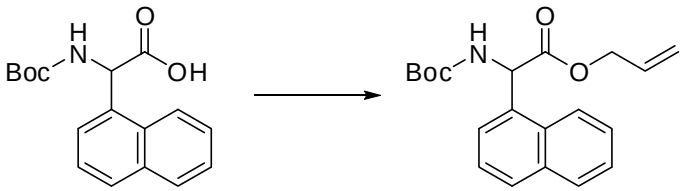
allyl 2-(tert-butoxycarbonylamino)-2-phenylacetate (3c). To a flame dried 100 mL round bottom flask was added (**2c**) (1.5 g, 5.97 mmol) and anhydrous DCM (50 mL). Then allyl alcohol (0.82 mL, 11.95 mmol) and DMAP (73 mg, 0.597 mmol) were added and the mixture was brought down to 0ºC. DCC (1.85 g, 8.96 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as a whitish solid. Yield (1.49 g, 86%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.41 (s, 9H), 4.58-4.6 (m, 2H), 5.12-5.17 (m, 2H), 5.32 (d, J = 8 Hz, 1H), 5.56 (bs, 1H), 5.75-5.83 (m, 1H), 7.26-7.36 (m, 5H); ^{13}C NMR (125MHz), $CDCl_3$: δ 28.2, 57.6, 65.9, 80.0, 118.3, 127, 128.3, 128.7, 131.3, 136.8, 154.7, 170.7. IR: (NaCl) 3390 cm^{-1} , 1750 cm^{-1}, 1710 cm^{-1}. HRMS: $[M + H]^+$ = 292.1559, calculated for $C_{16}H_{22}NO_4$, 292.1549. Anal. Calcd. For $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 66.78; H, 7.14; N, 4.78. Melting Point = 40-42˚C.



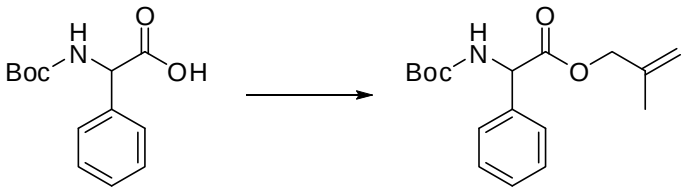
allyl 2-(tert-butoxycarbonylamino)-2-(4-methoxyphenyl)acetate (3d). To a flame dried 100 mL round bottom flask was added (**2d**) (992 mg, 3.53 mmol) and anhydrous DCM (50 mL). Then allyl alcohol (0.48 mL, 7.06 mmol) and DMAP (43 mg, 0.353 mmol) were added and the mixture was brought down to 0ºC. DCC (1.09 g, 5.3 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane) affording the product as a whitish solid. Yield (1.07 g, 94%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.32 (s, 9H), 3.63 (s, 3H), 4.48 (d, J = 6 Hz, 2H), 5.14 (m, 2H), 5.19 (d, J = 8 Hz, 1H), 5.69 (m, 2H), 6.74 (d, J = 8 Hz, 2H), 7.18 (d, J = 8 Hz, 2H); ^{13}C NMR (125MHz), $CDCl_3$: δ 27.9, 54.7, 56.7, 65.4, 79.4, 113.8, 117.8, 128.0, 128.5, 131.1, 154.5, 159.2, 170.6. IR: (NaCl) 3395 cm^{-1} , 1743 cm^{-1}, 1711 cm^{-1}. HRMS: $[M + H]^+$ = 322.1653, calculated for $C_{17}H_{24}NO_5$, 322.1654. Anal. Calcd. For $C_{17}H_{23}NO_5$: C, 63.54; H, 7.21; N, 4.36. Found: C, 63.69; H, 7.14; N, 4.61. Melting Point = 60-62˚C.



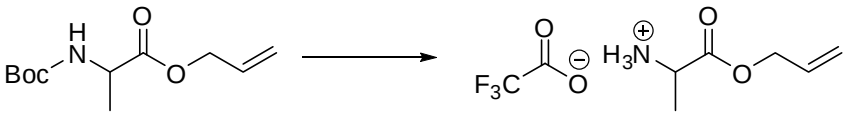
allyl 2-(tert-butoxycarbonylamino)-2-(4-fluorophenyl)acetate (3e). To a flame dried 100 mL round bottom flask was added (**2e**) (625 mg, 2.32 mmol) and anhydrous DCM (50 mL). Then allyl alcohol (0.32 mL, 4.65 mmol) and DMAP (28 mg, 0.232 mmol) were added and the mixture was brought down to 0ºC. DCC (717 mg, 3.48 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as an oil. Yield (626 mg, 87%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.40 (s, 9H), 4.59 (d, J = 6 Hz, 2H), 5.15 (m, 2H), 5.29 (d, J = 7 Hz, 1H), 5.57 (s, 1H), 5.79 (m, 1H), 6.09-7.02 (m, 2H), 7.31-7.33 (m, 2H); ^{13}C NMR (125MHz), $CDCl_3$: δ 28.2, 56.9, 66.1, 80.2, 115.6, 115.8, 118.6, 128.80, 128.86, 131.1, 132.8, 154.7, 161.6, 163.6, 170.5. IR: (NaCl) 3383 cm^{-1} , 1749 cm^{-1}, 1711 cm^{-1}. HRMS: $[M + H]^+$ = 310.1463, calculated for $C_{16}H_{21}FNO_4$, 310.1455. Anal. Calcd. For $C_{16}H_{20}FNO_4$: C, 62.12; H, 6.52; N, 4.53. Found: C, 61.93; H, 6.29; N, 4.49.



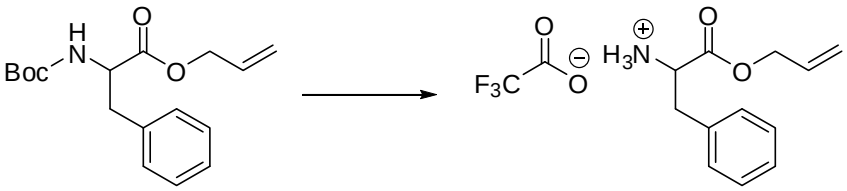
allyl 2-(tert-butoxycarbonylamino)-2-(naphthalen-1-yl)acetate (3f). To a flame dried 100 mL round bottom flask was added (**2f**) (1.3 g, 4.32 mmol) and anhydrous DCM (50 mL). Then allyl alcohol (0.59 mL, 8.64 mmol) and DMAP (53 mg, 0.432 mmol) were added and the mixture was brought down to 0ºC. DCC (1.33 g, 6.48 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as an oil. Yield (1.13 mg, 77%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.42 (s, 9H), 4.61-4.64 (m, 2H), 5.08-5.15 (m, 2H), 5.49 (d, J = 7 Hz, 1H), 5.77 (m, 1H), 6.09 (d, J = 7 Hz, 1H), 7.4-7.58 (m, 4H), 7.82 (m, 1H), 7.86 (d, J = 9 Hz, 1H), 8.17 (d, J = 8 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 28.2, 54.7, 66.1, 80.2, 118.4, 123.3, 125.2, 125.4, 126.0, 126.9, 128.8, 129.3, 131.0, 131.3, 132.8, 134.0, 155.0, 171.5. IR: (NaCl) 3389 cm^{-1} , 1749 cm^{-1}, 1711 cm^{-1}. HRMS: $[M + H]^+$ = 342.1706, calculated for $C_{20}H_{24}NO_4$, 342.1705. Anal. Calcd. For $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 67.48; H, 6.43; N, 3.85.



2-methylallyl 2-(tert-butoxycarbonylamino)-2-phenylacetate (3g). To a flame dried 100 mL round bottom flask was added (**2g**) (1.5 g, 5.97 mmol) and anhydrous DCM (50 mL). Then 2-methyl-2-propen-1-ol (1.0 mL, 11.95 mmol) and DMAP (73 mg, 0.597 mmol) were added and the mixture was brought down to 0ºC. DCC (1.85 g, 8.96 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as a whitish solid. Yield (1.39 g, 76%). %). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.41 (s, 9H), 1.58 (s, 3H), 4.46-4.58 (m, 2H), 4.78 (s, 1H), 4.81 (s, 1H), 5.33 (d, J = 7 Hz, 1H), 5.56 (s, 1H), 7.27-7.37 (m, 5H); ^{13}C NMR (125MHz), $CDCl_3$: δ 19.1, 28.2, 57.7, 68.6, 80.0, 113.2, 127.1, 128.3, 128.8, 136.9, 139.1, 154.7, 170.8. IR: (NaCl) 3389 cm^{-1} , 1743 cm^{-1}, 1711 cm^{-1}. HRMS: $[M + H]^+$ = 306.1705, calculated for $C_{17}H_{24}NO_4$, 306.1705. Anal. Calcd. For $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.95; H, 7.66; N, 4.64. Melting Point = 38-40˚C.

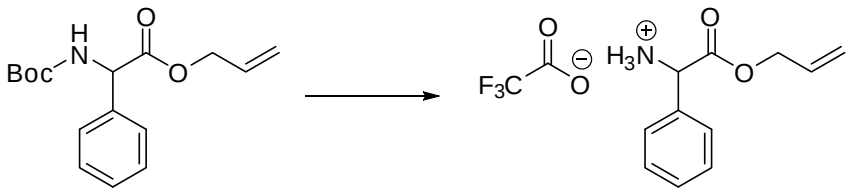


1-(allyloxy)-1-oxopropan-2-aminium 2,2,2-trifluoroacetate (4a). To a 100 mL round bottom flask was added (**3a**) (1.32 g, 4.32 mmol), DCM (2.5 mL) and TFA (2.5 mL). The resulting solution stirred for 30 min. The excess TFA and DCM were removed and $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The crude material was taken on without further purification. Yield (1.0 g, 88%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.56 (d, J = 7 Hz, 3H), 4.10 (q, J = 7 Hz, 1H), 4.63 (m, 2H), 5.25-5.32 (m, 2H), 5.8-5.9 (m, 1H), 8.24 (s, 3H); ^{13}C NMR (125MHz), $CDCl_3$: δ 15.6, 49.2, 67.1, 112.3, 114.6, 116.9, 119.2, 119.7, 130.5, 161.3, 161.6, 161.9, 162.2, 169.9. IR: (KBr) 3100 (br) cm^{-1}, 1748cm^{-1}, 1675 cm^{-1}. HRMS: $[M + H]^+$ = 130.0872, calculated for $C_6H_{11}NO_2$, 130.0868.

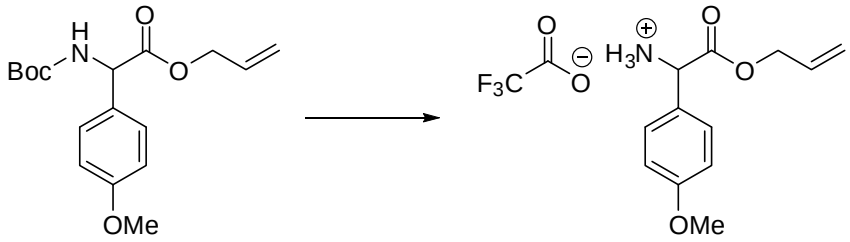


1-(allyloxy)-1-oxo-3-phenylpropan-2-aminium 2,2,2-trifluoroacetate (4b). To a 100 mL round bottom flask was added (**3b**) (1.32 g, 4.32 mmol), DCM (2.5 mL) and TFA (2.5 mL). The resulting solution stirred for 30 min. The excess TFA and DCM were removed and $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The product was precipitated out of the crude residue using ether/petroleum ether to afford the product as a white solid. Yield (1.27 g, 92%). ^{1}H NMR (500MHz), DMSO: δ 3.04-3.19 (m, 2H), 4.32 (t, J = 6 Hz, 1H), 4.58 (m, 2H), 5.18-5.26 (m, 2H), 5.73-5.81 (m, 1H), 7.2-7.36 (m, 5H), 8.64 (bs, 3H); ^{13}C NMR (125MHz), DMSO: δ 36.1, 53.2, 65.8, 113.6, 115.9, 118.3, 118.6, 120.7, 127.2, 128.5,

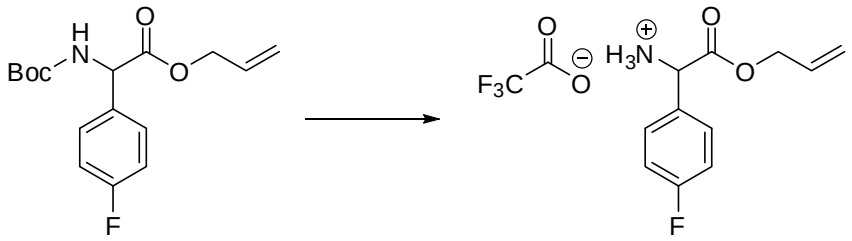
129.3, 131.4, 134.6, 158.0, 158.2, 158.5, 158.7, 168.7. IR: (KBr) 3100 (br) cm^{-1}, 1745 cm^{-1}, 1660 cm^{-1}. HRMS: $[M + H]^+$ = 206.1188, calculated for $C_{12}H_{16}NO_2$, 206.1181. Anal. Calcd. For $C_{14}H_{16}F_3NO_4$: C, 52.67; H, 5.05; N, 4.39. Found: C, 52.69; H, 4.91; N, 4.31. Melting Point = 88-90˚C.



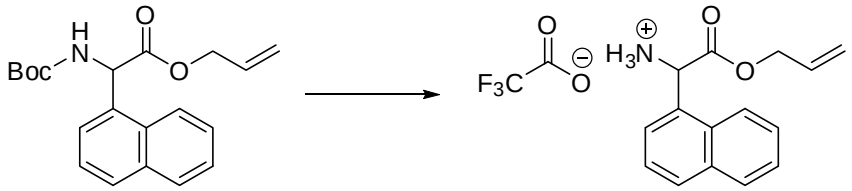
2-(allyloxy)-2-oxo-1-phenylethanaminium 2,2,2-trifluoroacetate (4c). To a 100 mL round bottom flask was added (**3c**) (1.44 g, 4.95 mmol), DCM (2.5 mL) and TFA (2.5 mL). The resulting solution stirred for 30 min. The excess TFA and DCM were removed and $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The product was precipitated out of the crude residue using ether/petroleum ether to afford the product as a white solid. Yield (1.48 g, 98%).^{1}H NMR (500MHz), DMSO: δ 4.66 (m, 2H), 5.12-5.16 (m, 2H), 5.33 (s, 1H), 5.8 (m, 1H), 7.44-7.5 (m, 5H), 9.07 (bs, 3H); ^{13}C NMR (125MHz), DMSO: δ 55.4, 66.0, 113.6, 115.9, 118.1, 118.3, 120.7, 128.1, 129.0, 129.5, 131.5, 132.6, 157.9, 158.2, 158.4, 158.7, 168.1. IR: (KBr) 3150 (br) cm^{-1}, 1745 cm^{-1}, 1675 cm^{-1}. HRMS: $[M + H]^+$ = 192.1027, calculated for $C_{11}H_{14}NO_2$, 192.1025. Anal. Calcd. For $C_{13}H_{14}F_3NO_4$: C, 51.15; H, 4.62; N, 4.59. Found: C, 50.95; H, 4.51; N, 4.45. Melting Point = 96-98˚C.



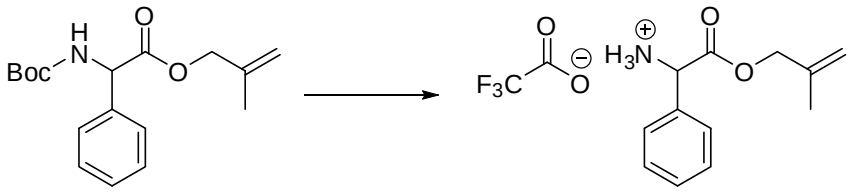
2-(allyloxy)-1-(4-methoxyphenyl)-2-oxoethanaminium 2,2,2-trifluoroacetate (4d). To a 100 mL round bottom flask was added (**3d**) (1.02 g, 3.17 mmol), DCM (2 mL) and TFA (2 mL). The resulting solution stirred for 30 min. The excess TFA and DCM were removed and $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The product was precipitated out of the crude residue using ether/petroleum ether to afford the product as a white solid. Yield (953 mg, 90%). ^{1}H NMR (500MHz), DMSO: δ 3.76 (s, 3H), 4.66 (m, 2H), 5.14-5.18 (m, 2H), 5.26 (s, 1H), 5.82 (m, 1H), 7.01 (d, J = 8 Hz, 2H), 7.41 (d, J = 8 Hz, 2H), 8.91 (s, 3H); ^{13}C NMR (125MHz), DMSO: δ 54.8, 55.2, 65.9, 114.3, 116.0, 118.2, 118.4, 124.4, 129.6, 131.5, 157.9, 158.2, 160.0, 168.4. IR: (KBr) 3088 (br) cm^{-1} , 1749 cm^{-1}, 1680 cm^{-1}. HRMS: $[M + H]^+$ = 222.1140, calculated for $C_{14}H_{16}NO_3$, 222.1130. Anal. Calcd. For $C_{14}H_{16}F_3NO_5$: C, 50.15; H, 4.81; N, 4.18. Found: C, 50.29; H, 4.64; N, 4.19. Melting Point = 88-90˚C.



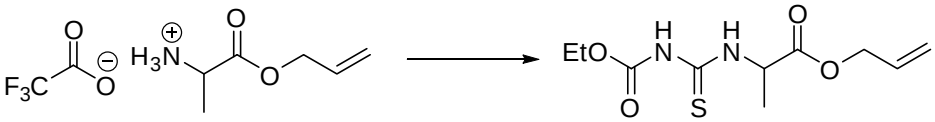
2-(allyloxy)-1-(4-fluorophenyl)-2-oxoethanaminium 2,2,2-trifluoroacetate (4e). To a 100 mL round bottom flask was added (**3e**) (600 mg, 1.94 mmol), DCM (2 mL) and TFA (2 mL). The resulting solution stirred for 30 min. The excess TFA and DCM were removed and $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The product was precipitated out of the crude residue using ether/petroleum ether to afford the product as a white solid. Yield (424 mg, 68%). ^{1}H NMR (500MHz), DMSO: δ 4.67 (m, 2H), 5.13-5.19 (m, 2H), 5.4 (s, 1H), 5.82 (m, 1H), 7.33 (m, 2H), 7.56 (m, 2H), 8.98 (s, 3H); ^{13}C NMR (125MHz), DMSO: δ 54.6, 66.1, 115.9, 116.02, 116.07, 118.2, 118.4, 128.9, 128.9, 130.5, 130.6, 131.4, 157.9, 158.1, 161.6, 163.5, 168.0. IR: (KBr) 3100 (br) cm^{-1} , 1749 cm^{-1}, 1680 cm^{-1}. HRMS: $[M + H]^+$ = 210.0933, calculated for $C_{11}H_{13}FNO_2$, 210.0930. Anal. Calcd. For $C_{13}H_{13}F_4NO_4$: C, 48.30; H, 4.05; N, 4.33. Found: C, 48.33; H, 3.77; N, 4.23. Melting Point = 68-70˚C.



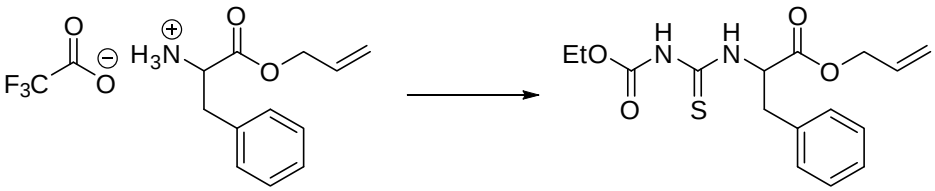
2-(allyloxy)-1-(naphthalen-1-yl)-2-oxoethanaminium 2,2,2-trifluoroacetate (4f). To a 100 mL round bottom flask was added (**3f**) (1.11 g, 3.26 mmol), DCM (2 mL) and TFA (2 mL). The resulting solution stirred for 30 min. The excess TFA and DCM were removed and $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The product was precipitated out of the crude residue using ether/petroleum ether to afford the product as a white solid. Yield (962 mg, 83%). ^{1}H NMR (500MHz), DMSO: δ 4.65 (m, 2H), 5.02-5.09 (m, 2H), 5.75 (m, 1H), 6.19 (s, 1H), 7.58-7.72 (m, 4H), 8.04 (t, J = 9 Hz, 2H), 8.31 (d, J = 9 Hz, 1H), 9.15 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 51.3, 66.1, 113.6, 116.0, 118.0, 118.4, 120.8, 123.3, 125.3, 125.9, 126.5, 127.2, 128.8, 129.1, 130.2, 130.5, 131.4, 133.5, 157.8, 158.0, 158.3, 158.5, 168.5. IR: (KBr) 3090 (br) cm^{-1} , 1730 cm^{-1}, 1667 cm^{-1}. HRMS: $[M + H]^+$ = 242.1192, calculated for $C_{15}H_{16}NO_2$, 242.1181. Anal. Calcd. For $C_{17}H_{16}F_3NO_4$: C, 57.47; H, 4.54; N, 3.94. Found: C, 57.33; H, 4.47; N, 3.87. Melting Point = 112-114˚C.



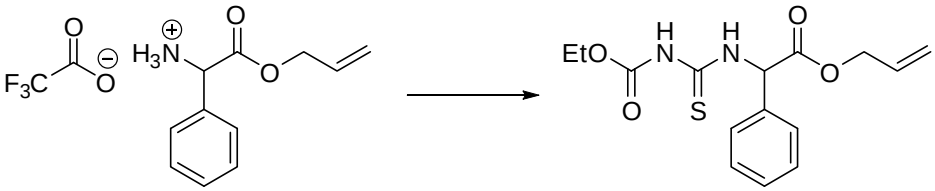
2-(2-methylallyloxy)-2-oxo-1-phenylethanaminium 2,2,2-trifluoroacetate (4g). To a 100 mL round bottom flask was added (**3g**) (1.39g, 4.56 mmol), DCM (3 mL) and TFA (3 mL). The resulting solution stirred for 30 min. The excess TFA and DCM were removed and $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The product was precipitated out of the crude residue using ether to afford the product as a white solid. Yield (1.32 g, 91%). ^{1}H NMR (500MHz), DMSO: δ 1.53 (s, 3H), 4.58 (dd, J = 14, 34 Hz, 2H), 4.76 (s, 1H), 4.82 (s, 1H), 5.35 (s, 1H), 7.42-7.53 (m, 5H), 9.00 (s, 3H); ^{13}C NMR (125MHz), DMSO: δ 18.7, 55.3, 68.4, 112.9, 116.0, 118.4, 128.0, 129.0, 129.5, 132.6, 139.0, 157.7, 157.9, 158.1, 158.4, 168.1. IR: (KBr) 3150 (br) cm^{-1} , 1743 cm^{-1}, 1680 cm^{-1}. HRMS: $[M + H]^+$ = 206.1182, calculated for $C_{12}H_{16}NO_2$, 206.1181. Anal. Calcd. For $C_{14}H_{16}F_3NO_4$: C, 52.67; H, 5.05; N, 4.39. Found: C, 52.63; H, 4.99; N, 4.34. Melting Point = 142-144˚C.



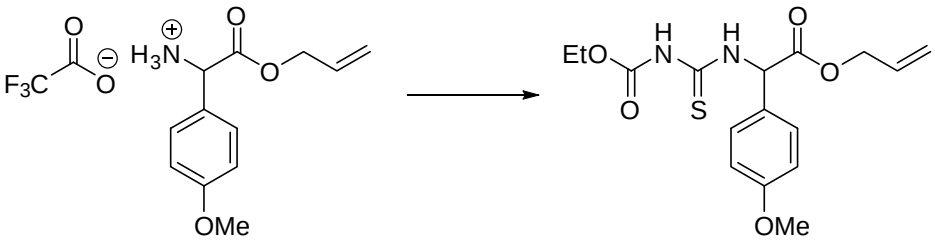
allyl 2-(3-(ethoxycarbonyl)thioureido)propanoate (5a). To a flame dried 100 mL round bottom flask was added (**4a**) (1 g, 4.11 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.63 mL, 4.52 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.56 mL, 4.93 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane) affording the product as a whitish solid. Yield (1.04 g, 97%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.28 (t, J = 7 Hz, 3H), 1.54 (d, J = 7 Hz, 3H), 4.21 (q, J = 7 Hz, 2H), 4.65 (m, 2H), 5.0 (p, J = 7 Hz, 1H), 5.22-5.26 (m, 1H), 5.3-5.35 (m, 1H), 5.89 (m, 1H), 8.15 (s, 1H), 10.14 (d, J = 6 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.0, 17.5, 53.6, 62.7, 66.0, 118.7, 131.3, 152.5, 171.4, 178.8. IR: (KBr) 3295 cm^{-1} , 3240 cm^{-1}, 1750 cm^{-1}, 1725 cm^{-1}. HRMS: $[M + H]^+$ =261.0920, calculated for $C_{10}H_{17}N_2O_4S$, 261.0909. Anal. Calcd. For $C_{10}H_{16}N_2O_4S$: C, 46.14; H, 6.20; N, 10.76. Found: C, 46.88; H, 6.06; N, 10.80. Melting Point = 43-45˚C.



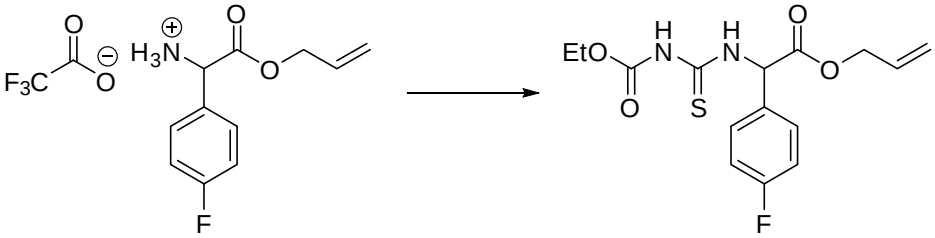
allyl 2-(3-(ethoxycarbonyl)thioureido)-3-phenylpropanoate (5b). To a flame dried 100 mL round bottom flask was added (**4b**) (1.27 g, 3.98 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.61 mL, 4.38 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.54 mL, 4.78 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The product was recrystallized from the crude residue with EtOAc/hexanes affording the product as a whitish solid. Yield (1.08 g, 81%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.27 (t, J = 7 Hz, 3H), 3.2-3.34 (m, 2H), 4.19 (q, J = 7 Hz, 2H), 4.6 (m, 2H), 5.24 (m, 3H), 5.82 (m, 1H), 7.15-7.3 (m, 5H), 8.1 (s, 1H), 10.08 (d, J = 6 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.0, 37.2, 59.2, 62.8, 66.1, 118.9, 127.1, 128.5, 129.2, 131.2, 135.3, 152.3, 170.0, 179.1. IR: (KBr) 3290 cm^{-1} , 3225 cm^{-1}, 1730 cm^{-1}(with shoulder). HRMS: $[M + H]^+$ =337.1227, calculated for $C_{16}H_{21}N_2O_4S$, 337.1222. Anal. Calcd. For $C_{16}H_{20}N_2O_4S$: C, 57.12; H, 5.99; N, 8.33. Found: C, 55.80; H, 5.80; N, 8.30. Melting Point = 79-81˚C.



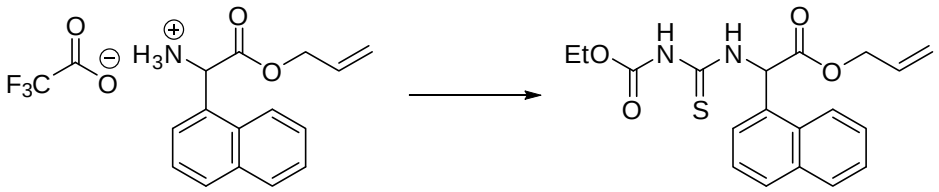
allyl 2-(3-(ethoxycarbonyl)thioureido)-2-phenylacetate (5c). To a flame dried 100 mL round bottom flask was added (**4c**) (1.48 g, 4.85 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.74 mL, 5.33 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.66 mL, 5.82 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane) affording the product as a whitish solid. Yield (1.39 g, 89%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.29 (t, J = 7 Hz, 3H), 4.23 (m, 2H), 4.64 (m, 2H), 5.14-5.22 (m, 2H), 5.81 (m, 1H), 5.98 (d, J = 7 Hz, 1H), 7.3-7.45 (m, 5H), 8.06 (s, 1H), 10.59 (d, J = 6 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.0, 61.8, 62.8, 66.2, 118.5, 127.5, 128.7, 128.9, 131.1, 135.0, 152.5, 169.3, 178.9. IR: (KBr) 3290 cm^{-1} , 3225 cm^{-1}, 1750 cm^{-1}, 1720 cm^{-1}. HRMS: $[M + H]^+$ =323.1070, calculated for $C_{15}H_{19}N_2O_4S$, 323.1066. Anal. Calcd. For $C_{15}H_{18}N_2O_4S$: C, 55.88; H, 5.63; N, 8.69. Found: C, 55.46; H, 5.51; N, 8.68. Melting Point = 44-46˚C.



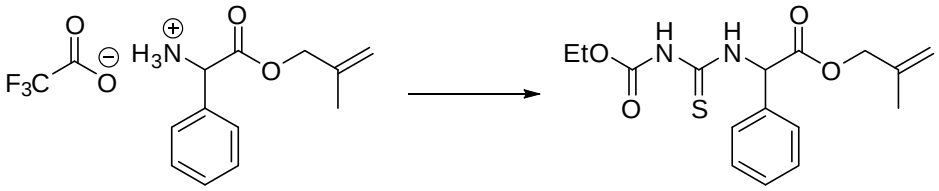
allyl 2-(3-(ethoxycarbonyl)thioureido)-2-(4-methoxyphenyl)acetate (5d). To a flame dried 100 mL round bottom flask was added (**4d**) (900 mg, 2.69 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.41 mL, 2.96 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.36 mL, 3.22 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane) affording the product as a whitish solid. Yield (917 mg, 97%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.31 (t, J = 7 Hz, 3H), 3.8 (s, 3H), 4.22-4.26 (m, 2H), 4.6-4.72 (m, 2H), 5.19-5.25 (m, 2H), 5.85 (m, 1H), 5.93 (d, J = 7 Hz, 1H), 6.90 (d, J = 9 Hz, 2H), 7.36 (d, J = 9 Hz, 2H), 8.20 (s, 1H), 10.55 (d, J = 7 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.0, 55.2, 61.2, 62.8, 66.2, 114.3, 118.5, 127.1, 128.8, 131.2, 152.5, 159.8, 169.5, 178.7. IR: (KBr) 3289 cm^{-1} , 3226 cm^{-1}, 1751 cm^{-1}, 1724 cm^{-1}. HRMS: $[M + H]^+$ = 353.1180, calculated for $C_{16}H_{21}N_2O_5S$, 353.1171. Anal. Calcd. For $C_{16}H_{20}N_2O_5S$: C, 54.53; H, 5.72; N, 7.95. Found: C, 52.68; H, 5.45; N, 7.55.



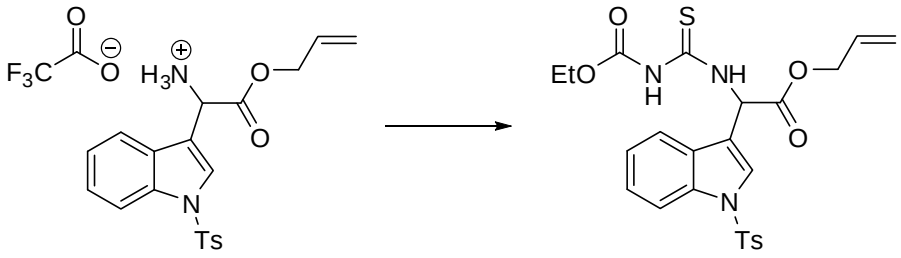
allyl 2-(3-(ethoxycarbonyl)thioureido)-2-(4-fluorophenyl)acetate (5e). To a flame dried 50 mL round bottom flask was added (**4e**) (394 mg, 1.22 mmol) and anhydrous DCM (20 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.19 mL, 1.34 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.16 mL, 1.46 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane) affording the product as a whitish solid. Yield (383 mg, 92%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.29 (t, J = 7 Hz, 3H), 4.2-4.26 (m, 2H), 4.59-4.69 (m, 2H), 5.15-5.25 (m, 2H), 5.8 (m, 1H), 5.96 (d, J = 7 Hz, 1H), 7.02-7.07 (m, 2H), 7.38-7.42 (m, 2H), 8.10 (s, 1H), 10.61 (d, J = 7 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.1, 61.0, 62.9, 66.4, 115.8, 116.0, 118.8, 129.3, 129.4, 131.06, 131.08, 131.1, 152.6, 161.8, 163.8, 169.2, 178.9. IR: (KBr) 3282 cm^{-1} , 3232 cm^{-1}, 1751 cm^{-1}, 1724 cm^{-1}. HRMS: $[M + H]^+$ = 341.0974, calculated for $C_{15}H_{18}FN_2O_4S$, 341.0971. Anal. Calcd. For $C_{15}H_{17}FN_2O_4S$: C, 52.93; H, 5.03; N, 8.23. Found: C, 51.76; H, 4.89; N, 8.07.



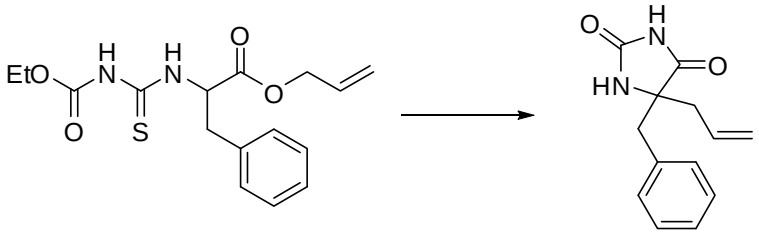
allyl 2-(3-(ethoxycarbonyl)thioureido)-2-(naphthalen-1-yl)acetate (5f). To a flame dried 100 mL round bottom flask was added (**4f**) (902 mg, 2.54 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.39 mL, 2.79 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.34 mL, 3.05 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane) affording the product as a whitish solid. Yield (897 mg, 95%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.24 (t, J = 7 Hz, 3H), 4.12-4.22 (m, 2H), 4.58-4.72 (m, 2H), 5.1-5.18 (m, 2H), 5.78 (m, 1H), 6.80 (d, J = 8 Hz, 1H), 7.42-7.6 (m, 4H), 7.85 (t, J = 9 Hz, 2H), 8.20 (m, 2H), 10.57 (d, J = 7 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.0, 58.9, 62.8, 66.3, 118.5, 123.2, 125.2, 126.0, 126.1, 127.0, 128.8, 129.7, 131.0, 131.1, 131.2, 134.0, 152.5, 169.7, 179.2. IR: (KBr) 3289 cm^{-1} , 3226 cm^{-1}, 1749 cm^{-1}, 1718 cm^{-1}. HRMS: $[M + H]^+$ = 373.1222, calculated for $C_{19}H_{21}N_2O_4S$, 373.1222. Anal. Calcd. For $C_{19}H_{20}N_2O_4S$: C, 61.27; H, 5.41; N, 7.52. Found: C, 58.71; H, 4.85; N, 7.15.



2-methylallyl 2-(3-(ethoxycarbonyl)thioureido)-2-phenylacetate (5g). To a flame dried 100 mL round bottom flask was added (**4g**) (1 g, 3.13 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.48 mL, 3.45 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.42 mL, 3.76 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The product was recrystallized from the crude residue with EtOAc/hexanes affording the product as a whitish solid. Yield (960 mg, 91%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.28 (t, J = 7 Hz, 3H), 1.59 (s, 3H), 4.23 (m, 2H), 4.55 (m, 2H), 4.83 (d, J = 5 Hz, 2H), 5.98 (d, J = 7 Hz, 1H), 7.3-7.44 (m, 5H), 8.08 (s, 1H), 10.62 (d, J = 6 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.1, 19.1, 61.9, 62.9, 68.9, 113.5, 127.5, 128.8, 128.9, 135.1, 139.0, 152.5, 169.4, 178.9. IR: (KBr) 3289 cm^{-1} , 3232 cm^{-1}, 1749 cm^{-1}, 1724 cm^{-1}. HRMS: $[M + H]^+$ = 337.1230, calculated for $C_{16}H_{21}N_2O_4S$, 337.1222. Anal. Calcd. For $C_{16}H_{20}N_2O_4S$: C, 57.12; H, 5.99; N, 8.33. Found: C, 55.96; H, 5.84; N, 8.03. Melting Point = 62-64˚C.

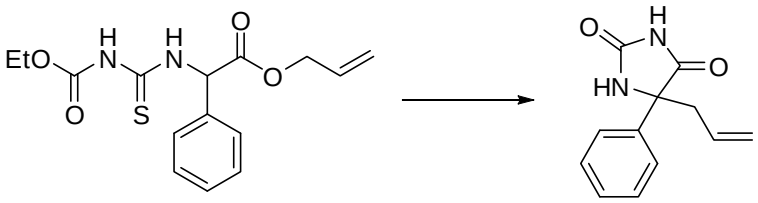


allyl 2-(3-(ethoxycarbonyl)thioureido)-2-(1-tosyl-1H-indol-3-yl)acetate (5h). To a flame dried 100 mL round bottom flask was added (**40, see SI-3 for scheme**) (1.3 g, 2.61 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and anhydrous TEA (0.4 mL, 2.87 mmol) was added followed by dropwise addition of ethoxycarbonyl isothiocyanate (0.35 mL, 3.13 mmol). The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The product was recrystallized from the crude residue with EtOAc/Hexanes affording a whitish solid. Yield (1.19 g, 89%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.26 (t, J = 7 Hz, 3H), 2.31 (s, 3H), 4.2 (m, 2H), 4.64 (m, 2H), 5.13-5.22 (m, 2H), 5.78 (m, 1H), 6.26 (d, J = 7 Hz, 1H), 7.19-7.25 (m, 3H), 7.30 (t, J = 8 Hz, 1H), 7.63 (d, J = 8 Hz, 1H), 7.72 (s, 1H), 7.74 (d, J = 8 Hz, 2H), 7.93 (d, J = 8 Hz, 1H), 8.04 (s, 1H), 10.59 (d, J = 7 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.1, 21.5, 54.7, 62.9, 66.6, 113.7, 115.9, 119.0, 119.9, 123.6, 125.1, 126.2, 126.9, 128.2, 129.9, 131.0, 134.8, 135.0, 145.1, 152.4, 168.7, 179.0. IR: (KBr) 3282 cm^{-1} , 3232 cm^{-1}, 1749 cm^{-1}, 1724 cm^{-1}. HRMS: $[M + H]^+$ = 516.1273, calculated for $C_{24}H_{26}N_3O_6S_2$, 516.1263. Anal. Calcd. For $C_{24}H_{25}N_3O_6S_2$: C, 55.91; H, 4.89; N, 8.15. Found: C, 55.91; H, 4.79; N, 8.09. Melting Point = 117-119˚C.

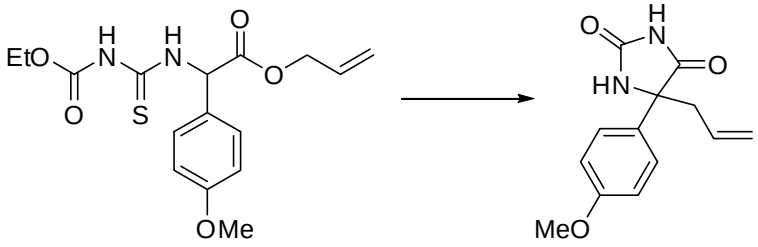


5-allyl-5-benzylimidazolidine-2,4-dione (6b). To a flame dried 50 mL round bottom flask was added (**5b**) (150 mg, 0.446 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.2 mL, 1.34 mmol) was added and the mixture was cooled to 0ºC. EDCI (189 mg, 0.982 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (89 mg, 2.33 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% DCM) affording the product as a whitish solid. Yield (20 mg, 19%). ^{1}H NMR (500MHz), Acetone: δ 2.5 (dd, J = 7, 14 Hz, 1H), 2.61 (dd, J = 7, 14 Hz, 1H), 2.90 (d, J = 14 Hz, 1H), 3.06 (d, J = 14 Hz, 1H), 5.15 (m, 2H), 5.79 (m, 1H), 7.07 (s, 1H), 7.2-7.28 (m, 5H), 9.28 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 42.1, 42.9, 67.9, 120.2, 127.6, 128.8, 131.1, 132.3, 136.0, 156.5, 176.7.

IR: (KBr) 3220 cm^{-1} (broad), 1761cm^{-1}, 1711 cm^{-1}. HRMS: $[M + H]^+$ = 231.1141, calculated for $C_{13}H_{15}N_2O_2$, 231.1134. Anal. Calcd. For $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 66.59; H, 6.14; N, 12.09. Melting Point = 203-205˚C.

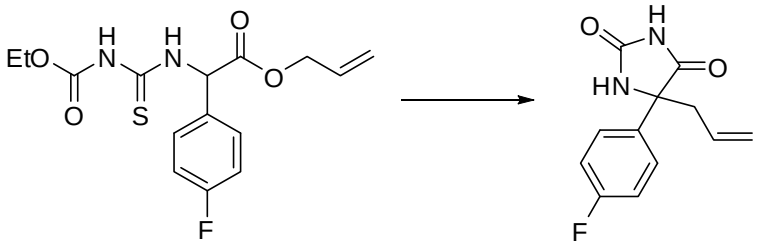


5-allyl-5-phenylimidazolidine-2,4-dione (6c). To a flame dried 50 mL round bottom flask was added (**5c**) (150 mg, 0.466 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.2 mL, 1.4 mmol) was added and the mixture was cooled to 0ºC. EDCI (197 mg, 1.02 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (93 mg, 2.33 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% DCM) affording the product as a whitish solid. Yield (70 mg, 70%). ^{1}H NMR (500MHz), Acetone: δ 2.78 (dd, J = 7, 14 Hz, 1H), 2.95 (dd, J = 7, 14 Hz, 1H), 5.13 (d, J = 10 Hz, 1H), 5.21 (d, J = 17 Hz, 1H), 5.73 (m, 1H), 7.33 (t, J = 8 Hz, 1H), 7.4 (t, J = 8 Hz, 2H), 7.64 (d, J = 8 Hz, 2H), 7.68 (s, 1H), 9.65 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 43.5, 68.6, 120.8, 126.3, 128.7, 129.3, 132.0, 139.7, 157.0, 175.9. IR: (KBr) 3245 cm^{-1} (broad), 1774cm^{-1}, 1724 cm^{-1}. HRMS: $[M + H]^+$ = 217.0979, calculated for $C_{12}H_{13}N_2O_2$, 217.0977. Anal. Calcd. For $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.43; H, 5.49; N, 12.90. Melting Point = 172-174˚C.

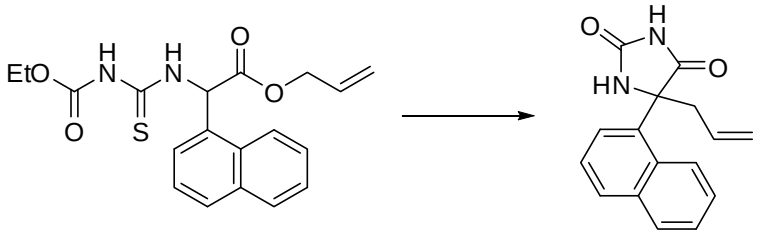


5-allyl-5-(4-methoxyphenyl)imidazolidine-2,4-dione (6d). To a flame dried 50 mL round bottom flask was added (**5d**) (155 mg, 0.440 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.18 mL, 1.32 mmol) was added and the mixture was cooled to 0ºC. EDCI (186 mg, 0.968 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (88 mg, 2.2 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% DCM) affording the product as a whitish solid. Yield (72 mg, 67%). ^{1}H NMR

(500MHz), Acetone: δ 2.74 (dd, J = 8, 14 Hz, 1H), 2.92 (dd, J = 8, 14 Hz, 1H), 3.78 (s, 3H), 5.12 (m, 1H), 5.2 (m, 1H), 5.72 (m, 1H), 6.94 (d, J = 9 Hz, 2H), 7.52 (d, J = 9 Hz, 2H), 7.64 (s, 1H), 9.63 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 43.4, 55.5, 68.2, 114.6, 120.6, 127.6, 131.7, 132.2, 156.9, 160.3, 176.1. IR: (KBr) 3251 cm^{-1} (broad), 1774cm^{-1}, 1724cm^{-1}. HRMS: $[M + H]^+$ = 247.1086, calculated for $C_{13}H_{15}N_2O_3$, 247.1083. Anal. Calcd. For $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 62.74; H, 5.53; N, 11.35. Melting Point = 166-168˚C.

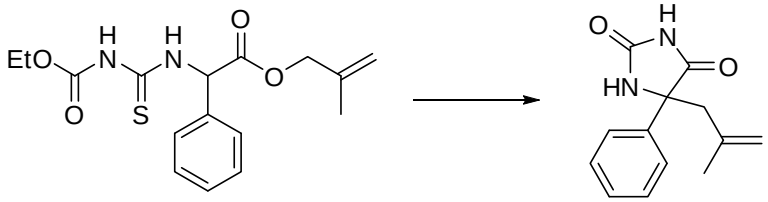


5-allyl-5-(4-fluorophenyl)imidazolidine-2,4-dione (6e). To a flame dried 50 mL round bottom flask was added (**5e**) (151 mg, 0.444 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.18 mL, 1.33 mmol) was added and the mixture was cooled to 0ºC. EDCI (188 mg, 0.977 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (88 mg, 2.2 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% DCM) affording the product as a whitish solid. Yield (60 mg, 57%). ^{1}H NMR (500MHz), Acetone: δ 2.76 (dd, J = 7, 14 Hz, 1H), 2.95 (dd, J = 7, 14 Hz, 1H), 5.14 (dd, J = 2, 10 Hz, 1H), 5.21 (dd, J = 2, 10 Hz, 1H), 5.72 (m, 1H), 7.16 (m, 2H), 7.67 (m, 2H), 7.75 (s, 1H), 9.74 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 43.6, 68.2, 115.8, 116.0, 121.0, 128.5, 128.6, 131.8, 135.91, 135.93, 156.8, 162.2, 164.2, 175.8. IR: (KBr) 3220 cm^{-1} (broad), 1780cm^{-1}, 1730cm^{-1}. HRMS: $[M + H]^+$ = 235.0876, calculated for $C_{12}H_{12}FN_2O_2$, 235.0883. Anal. Calcd. For $C_{12}H_{11}FN_2O_2$: C, 61.53; H, 4.73; N, 11.96. Found: C, 61.48; H, 4.61; N, 11.81. Melting Point = 178-180˚C.

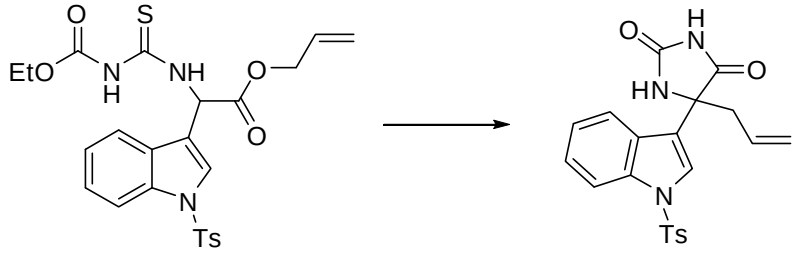


5-allyl-5-(naphthalen-1-yl)imidazolidine-2,4-dione (6f). To a flame dried 50 mL round bottom flask was added (**5f**) (156 mg, 0.419 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.17 mL, 1.26 mmol) was added and the mixture was cooled to 0ºC. EDCI (177 mg, 0.922 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0 ºC and a solution of NaH (84 mg, 2.09 mmol) in MeOH (5 mL) was added dropwise. The cloudy

mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% DCM) affording the product as a whitish solid. Yield (34 mg, 31%). ^{1}H NMR (500MHz), $CDCl_3$: δ 3.07 (dd, J = 7, 14 Hz, 1H), 3.26 (dd, J = 7, 14 Hz, 1H), 5.12 (d, J = 11 Hz, 1H), 5.2 (d, J = 18 Hz, 1H), 5.71 (m, 1H), 7.33 (t, J = 8 Hz, 1H), 7.42-7.53 (m, 3H), 7.67 (d, J = 7 Hz, 1H), 7.78 (d, J = 8 Hz, 1H), 7.84 (d, J = 8 Hz, 1H), 8.22 (d, J = 8 Hz, 1H), 9.68 (s, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 42.1, 69.7, 121.4, 124.4, 124.8, 125.6, 126.5, 129.6, 130.05, 130.08, 130.14, 132.3, 134.8, 157.6, 175.3. IR: (KBr) 3245 cm^{-1} (broad), 1774cm^{-1}, 1724cm^{-1}. HRMS: $[M + H]^+$ = 267.1134, calculated for $C_{16}H_{15}N_2O_2$, 267.1134.

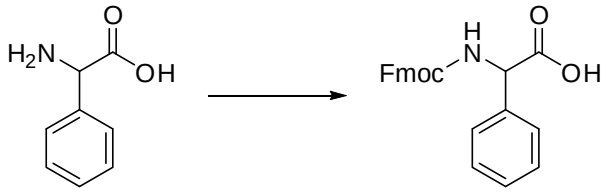


5-(2-methylallyl)-5-phenylimidazolidine-2,4-dione (6g). To a flame dried 50 mL round bottom flask was added (**5g**) (150 mg, 0.446 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.19 mL, 1.34 mmol) was added and the mixture was cooled to 0ºC. EDCI (188 mg, 0.981 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (89 mg, 2.23 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 10% Acetone; 90% DCM) affording the product as a whitish solid. Yield (68 mg, 66%). ^{1}H NMR (500MHz), Acetone: δ 1.70 (s, 3H), 2.70 (d, J = 13 Hz, 1H), 2.99 (d, J = 13 Hz, 1H), 4.85 (m, 1H), 4.91 (m, 1H), 7.3-7.42 (m, 3H), 7.66 (m, 2H), 7.69 (s, 1H), 9.64 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 24.1, 46.8, 68.7, 116.7, 126.3, 128.7, 129.2, 140.4, 140.7, 156.8, 176.1. IR: (KBr) 3243 cm^{-1}, 1772 cm^{-1}, 1724 cm^{-1}. HRMS: $[M + H]^+$ = 231.1139, calculated for $C_{13}H_{15}N_2O_2$, 231.1134. Anal. Calcd. For $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 66.99; H, 5.86; N, 11.81. Melting Point = 169-171˚C.

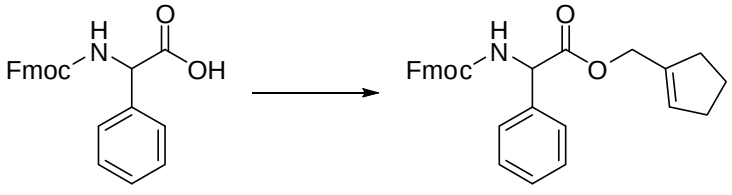


5-allyl-5-(1-tosyl-1H-indol-3-yl)imidazolidine-2,4-dione (6h). To a flame dried 50 mL round bottom flask was added (**5h**) (150 mg, 0.291 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.12 mL, 0.874 mmol) was added and the mixture was cooled to 0ºC. EDCI (123 mg, 0.640 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and

then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (58 mg, 1.46 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% DCM) affording the product as a whitish solid. Yield (83 mg, 69%). ^{1}H NMR (500MHz), Acetone: δ 2.33 (s, 3H), 2.99 (dd, J = 7, 14 Hz, 1H), 3.05 (dd, J = 7, 14 Hz, 1H), 5.15 (d, J = 10 Hz, 1H), 5.22 (d, J = 17 Hz, 1H), 5.75 (m, 1H), 7.27 (t, J = 8 Hz, 1H), 7.36 (m, 3H), 7.65 (s, 1H), 7.83 (s, 1H), 7.88 (d, J = 8 Hz, 3H), 8.01 (d, J = 8 Hz, 1H), 9.83 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 21.3, 41.5, 65.7, 114.4, 121.1, 121.8, 122.4, 124.2, 125.4, 125.7, 127.8, 128.7, 130.9, 131.4, 135.6, 136.3, 146.5, 156.7, 175.0. IR: (KBr) 3232 cm^{-1}, 1780cm^{-1}, 1730 cm^{-1}. HRMS: $[M + H]^+$ = 410.1178, calculated for $C_{21}H_{20}N_3O_4S$, 410.1175. Anal. Calcd. For $C_{21}H_{19}N_3O_4S$: C, 61.60; H, 4.68; N, 10.26. Found: C, 61.59; H, 4.60; N, 9.80. Melting Point = 226-228˚C.

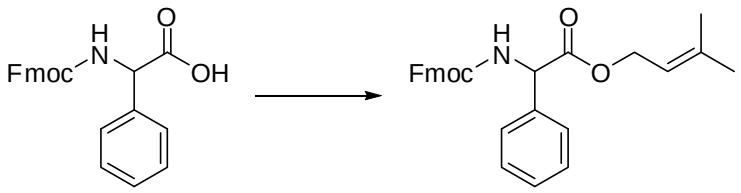


2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-2-phenylacetic acid (7). To a 250 mL round bottom flask was added phenylglycine (2 g, 13.25 mmol), dioxane (25 mL), H_2O (25 mL), and Na_2CO_3 (2.81 g, 26.5 mmol). The resulting solution was brought down to 0ºC and then 9-Fluorenylmethyl-N-succinimidylcarbonate (5 g, 14.57 mmol) was added to the solution and the mixture slowly warmed to room temperature overnight under nitrogen. The solvent was then removed and the crude residue was taken then acidified using 1M HCl and extracted with EtOAc (3 x 50 mL). The organics were then washed with brine (1 x 30 mL), combined, dried using anhydrous sodium sulfate and concentrated. The crude product was taken on without further purification. Yield (3.5 g, 70 %).^{1}H NMR (500MHz), DMSO: δ 4.25 (m, 3H), 5.18 (d, J = 8 Hz, 1H), 7.27-7.46 (m, 9H), 7.75 (d, J = 8 Hz, 2H), 7.87 (d, J = 8 Hz, 2H), 8.21 (d, J = 8 Hz, 1H), 12.89 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 46.5, 58.0, 65.9, 120.0, 125.3, 125.3, 127.0, 127.6, 127.7, 127.8, 128.4, 137.1, 140.6, 143.7, 143.8, 155.8, 172.0. IR: (KBr) 3407 cm^{-1}, 1730 cm^{-1}, 1700 cm^{-1}. Melting Point = 191-194˚C.

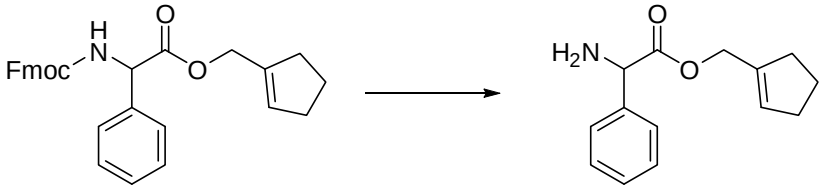


cyclopentenylmethyl 2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-2-phenylacetate (8a). To a flame dried 100 mL round bottom flask was added (**7**) (1.21 g, 3.24 mmol) and anhydrous DCM (50 mL). Then cyclopent-1-enylmethanol[2] (477 mg, 4.87 mmol) and DMAP (40 mg, 0.324 mmol) were added and the mixture was brought down to 0ºC. DCC (1 g, 4.87 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed

with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as a whitish solid. Yield (997 mg, 68%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.82 (p, J = 8 Hz, 2H), 2.13 (s, 2H), 2.27 (s, 2H), 4.2 (t, J = 7 Hz, 1H), 4.38 (m, 2H), 4.70 (m, 2H), 5.40 (d, J = 7 Hz, 1H), 5.52 (s, 1H), 5.89 (d, J = 7 Hz, 1H), 7.28-7.4 (m, 9H), 7.57 (d, J = 7 Hz, 2H), 7.74 (d, J = 8 Hz, 2H); ^{13}C NMR (125MHz), $CDCl_3$: δ 23.1, 32.3, 32.5, 47.1, 58.0, 64.4, 67.1, 119.9, 125.0, 127.0, 127.1, 127.6, 128.5, 128.8, 129.1, 136.6, 138.1, 141.2, 143.7, 143.8, 155.3, 170.6. IR: (NaCl) 3350 cm^{-1} , 1725 cm^{-1} (broad). HRMS: $[M + H]^+$ = 454.2020, calculated for $C_{29}H_{28}NO_4$, 454.2018. Anal. Calcd. For $C_{29}H_{27}NO_4$: C, 76.80; H, 6.00; N, 3.09. Found: C, 76.97; H, 5.84; N, 3.12. Melting Point = 96-98˚C.

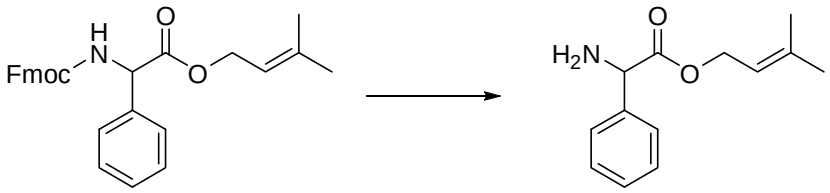


3-methylbut-2-enyl 2-(((9H-fluoren-9-yl)methoxy)carbonylamino)-2-phenylacetate (8b). To a flame dried 100 mL round bottom flask was added (**7**) (1.25 g, 3.35 mmol) and anhydrous DCM (50 mL). Then 3-methyl-2-buten-1-ol (0.69 mL, 6.7 mmol) and DMAP (41 mg, 0.335 mmol) were added and the mixture was brought down to 0ºC. DCC (1.04 g, 5.03 mmol) was then added and the mixture was allowed to warm to room temperature overnight while stirring under nitrogen. The white precipitate that formed was filtered off and the DCM filtrate was washed with brine (1 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as a whitish solid. Yield (1.15 g, 77%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.62 (s, 3H), 1.71 (s, 3H), 4.21 (t, J = 7 Hz, 1H), 4.35-4.44 (m, 2H), 4.54-4.72 (m, 2H), 5.27 (m, 1H), 5.40 (d, J = 8 Hz, 1H), 5.91 (d, J = 7 Hz, 1H), 7.27-7.41 (m, 9H), 7.58 (d, J = 7 Hz, 2H), 7.75 (d, J = 7 Hz, 2H); ^{13}C NMR (125MHz), $CDCl_3$: δ 17.9, 25.6, 47.1, 57.9, 62.7, 67.0, 117.7, 119.9, 125.0, 127.0, 127.1, 127.6, 128.4, 128.8, 136.7, 140.0, 141.2, 143.7, 143.8, 155.3, 170.7. IR: (NaCl) 3351 cm^{-1} , 1724 cm^{-1} (broad). HRMS: $[M + H]^+$ = 442.2019, calculated for $C_{28}H_{28}NO_4$, 442.2018. Anal. Calcd. For $C_{28}H_{27}NO_4$: C, 76.17; H, 6.16; N, 3.17. Found: C, 75.87; H, 6.10; N, 3.19. Melting Point = 108-110˚C.

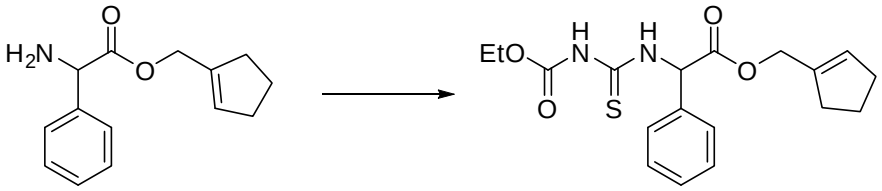


cyclopentenylmethyl 2-amino-2-phenylacetate (9a). To a 100 mL round bottom flask was added (**8a**) (947 mg, 2.09 mmol) and DCM (8 mL). The solution was brought down to 0ºC and then piperidine (2 mL, 20.9 mmol) was added and the mixture stirred under nitrogen for 1 h and then 1 h at room temperature. The solvent was then removed and the crude residue was taken up in EtOAc (40 mL) and washed with sat. NH_4Cl (1 x 10 mL) and brine (1 x 10 mL). The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane, then 90% DCM 10% MeOH) affording the product as an oil. Yield (434 mg, 90%).^{1}H NMR (500MHz), $CDCl_3$: δ 1.77-1.83

(m, 2H), 1.91 (s, 2H), 2.1-2.15 (m, 2H), 2.22-2.28 (m, 2H), 4.59 (s, 1H), 4.63 (m, 2H), 5.49 (m, 1H), 7.24-7.37 (m, 5H); ^{13}C NMR (125MHz), $CDCl_3$: δ 23.4, 32.5, 32.9, 59.0, 64.1, 127.0, 128.1, 128.9, 138.8, 140.6, 174.0. IR: (KBr) 3385 (br) cm^{-1} , 3321 cm^{-1}, 1733 cm^{-1}. HRMS: $[M + H]^+$ = 232.1341, calculated for $C_{14}H_{18}NO_2$, 232.1338. Anal. Calcd. For $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.05; H, 7.30; N, 6.09.

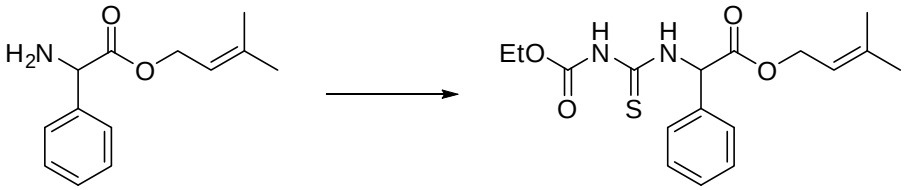


3-methylbut-2-enyl 2-amino-2-phenylacetate (9b). To a 100 mL round bottom flask was added (**8b**) (1.15 g, 2.61 mmol) and DCM (10 mL). The solution was brought down to 0ºC and then piperidine (2.6 mL, 26.1 mmol) was added and the mixture stirred under nitrogen for 1 h and then 1 h at room temperature. The solvent was then removed and the crude residue was taken up in EtOAc (50 mL) and washed with sat. NH_4Cl (1 x 20 mL) and brine (1 x 20 mL). The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexane, then 90% DCM 10% MeOH) affording the product as an oil. Yield (488 mg, 85%). Characterization is for the TFA salt. ^{1}H NMR (500MHz), DMSO: δ 1.58 (s, 3H), 1.66 (s, 3H), 4.60 (dd, J = 7, 12 Hz, 1H), 4.67 (dd, J = 7, 12 Hz, 1H), 5.22 (m, 1H), 5.26 (s, 1H), 7.45 (m, 5H), 8.89 (s, 3H); ^{13}C NMR (125MHz), DMSO: δ 17.7, 25.2, 55.3, 62.6, 116.0, 117.5, 118.4, 128.1, 128.9, 129.5, 132.5, 139.8, 157.8, 158.0, 168.3. IR: (KBr) 3164 (br) cm^{-1} , 1736 cm^{-1}, 1675 cm^{-1}. HRMS: $[M + H]^+$ = 220.1341, calculated for $C_{13}H_{18}NO_2$, 220.1338. Anal. Calcd. For $C_{15}H_{18}F_3NO_4$: C, 54.05; H, 5.44; N, 4.20. Found: C, 53.92; H, 5.26; N, 4.18. Melting Point = 118-120˚C.

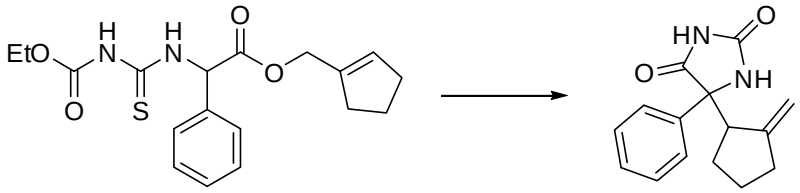


cyclopentenylmethyl 2-(3-(ethoxycarbonyl)thioureido)-2-phenylacetate (10a). To a flame dried 100 mL round bottom flask was added (**9a**) (406 mg, 1.76 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and ethoxycarbonyl isothiocyanate (0.24 mL, 2.11 mmol) was added dropwise. The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) and the product was recrystallized with EtOAc/Hexanes affording the product as a white solid. Yield (518 mg, 81%). ^{1}H NMR (500MHz), $CDCl_3$: δ 1.29 (t, J = 7 Hz, 3H), 1.81 (m, 2H), 2.13 (m, 2H), 2.26 (m, 2H), 4.23 (m, 2H), 4.69 (s, 2H), 5.53 (s, 1H), 5.97 (d, J = 7 Hz, 1H), 7.3-7.42 (m, 5H), 8.08 (s, 1H), 10.62 (d, J = 6 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.1, 23.1, 32.3, 32.5, 61.8, 62.8, 64.5, 127.5, 128.7, 128.9, 129.1, 135.2, 138.1, 152.5, 169.4, 178.8. IR: (KBr) 3289 cm^{-1} , 3226 cm^{-1}, 1743cm^{-1}, 1724 cm^{-1}. HRMS: $[M + H]^+$ = 363.1387, calculated for $C_{18}H_{23}N_2O_4S$, 363.1379.

Anal. Calcd. For $C_{18}H_{22}N_2O_4S$: C, 59.65; H, 6.12; N, 7.73. Found: C, 59.36; H, 5.78; N, 7.69. Melting Point = 58-60˚C.

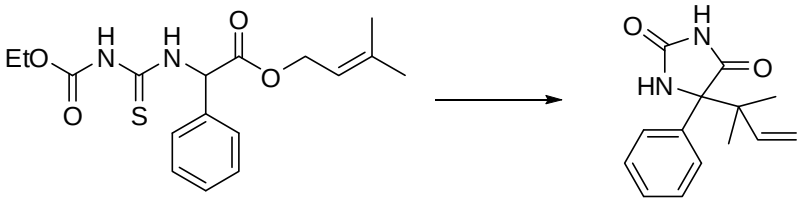


3-methylbut-2-enyl 2-(3-(ethoxycarbonyl)thioureido)-2-phenylacetate (10b). To a flame dried 100 mL round bottom flask was added (**9b**) (428 mg, 1.95 mmol) and anhydrous DCM (50 mL). Then the solution was brought down to 0ºC and ethoxycarbonyl isothiocyanate (0.26 mL, 2.35 mmol) was added dropwise. The solution was allowed to warm to room temperature overnight while stirring under a nitrogen atmosphere. The solvent was removed and ether (30 mL) was added to the crude residue and was washed with sat. sodium bicarbonate. The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% EtOAc; 80% Hexane) affording the product as an oil. Yield (678 mg, 99%).^{1}H NMR (500MHz), $CDCl_3$: δ 1.29 (t, J = 7 Hz, 3H), 1.60 (s, 3H), 1.69 (s, 3H), 4.23 (m, 2H), 4.55 (dd, J = 7, 12 Hz, 1H), 4.68 (dd, J = 7, 12 Hz, 1H), 5.26 (m, 1H), 5.95 (d, J = 7Hz, 1H), 7.3-7.44 (m, 5H), 7.96 (s, 1H), 10.59 (d, J = 6 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 14.1, 18.0, 25.6, 61.9, 62.88, 62.89, 117.7, 127.5, 128.6, 128.9, 135.3, 140.0, 152.5, 169.6, 178.8. IR: (KBr) 3282 cm^{-1} , 3232 cm^{-1}, 1724 cm^{-1}(with shoulder). HRMS: $[M + H]^+$ = 351.1380, calculated for $C_{17}H_{23}N_2O_4S$, 351.1379. Anal. Calcd. For $C_{17}H_{22}N_2O_4S$: C, 58.27; H, 6.33; N, 7.99. Found: C, 54.58; H, 5.86; N, 7.46.

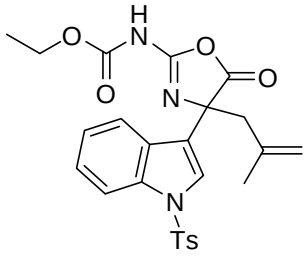


5-(2-methylenecyclopentyl)-5-phenylimidazolidine-2,4-dione (11a). To a flame dried 50 mL round bottom flask was added (**10a**) (150 mg, 0.414 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.17 mL, 1.24 mmol) was added and the mixture was cooled to 0ºC. EDCI (175 mg, 0.911 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (83 mg, 2.07 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 10% Acetone; 90% DCM) affording the two unseparatable diastereomers as a whitish solid. Yield (70 mg, 66%). ^{1}H NMR (500MHz), Acetone: δ 1.28-1.96 (m, 8H), 2.26-2.38 (m, 4H), 3.45 (t, J = 8 Hz, 1H), 3.56 (t, J = 8 Hz, 1H), 4.03 (s, 1H), 4.73 (s, 1H), 4.94 (s, 1H), 5.03 (s, 1H), 7.3-7.43 (m, 6H), 7.55 (s, 1H), 7.64-7.71 (m, 4H), 7.87 (s, 1H), 9.66 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 24.9, 25.2, 35.9, 36.6, 49.9, 50.0, 71.2, 72.3, 108.4, 109.2, 126.7, 127.0, 128.63, 128.69, 129.21, 129.22, 139.7, 139.8, 150.7, 151.7, 157.2, 157.4, 175.7, 176.3. IR: (KBr) 3289

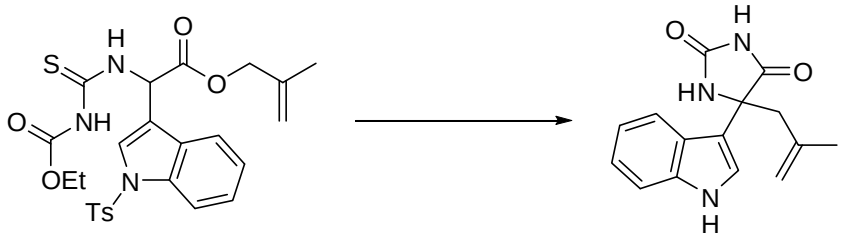
cm^{-1}, 1774 cm^{-1}, 1718 cm^{-1}. HRMS: $[M + H]^+$ = 257.1295, calculated for $C_{15}H_{17}N_2O_2$, 257.1290. Anal. Calcd. For $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 68.27; H, 6.37; N, 10.48. Melting Point = 234-236˚C.



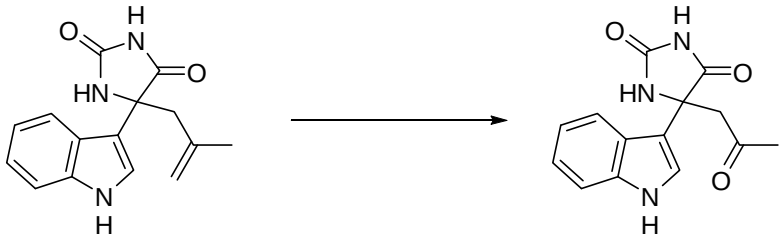
5-(2-methylbut-3-en-2-yl)-5-phenylimidazolidine-2,4-dione (11b). To a flame dried 50 mL round bottom flask was added (**11a**) (150 mg, 0.429 mmol) and anhydrous DCM (15 mL). Then anhydrous TEA (0.18 mL, 1.29 mmol) was added and the mixture was cooled to 0ºC. EDCI (181 mg, 0.944 mmol) was then added and the mixture stirred at 0ºC under nitrogen for 1 h and then refluxed for 15 h. After the first step was completed (as indicated by TLC), the solution was cooled to 0ºC and a solution of NaH (86 mg, 2.15 mmol) in MeOH (5 mL) was added dropwise. The cloudy mixture stirred at 0ºC for 1 h and then at room temperature for 2 h. The mixture was acidified with 5% HCl and then the solvents were removed. The aqueous mixture was extracted with EtOAc (3 x 30 mL) and then the organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 10% Acetone; 90% DCM) affording the product as a whitish solid. Yield (49 mg, 47%). ^{1}H NMR (500MHz), Acetone: δ 1.09 (s, 3H), 1.14 (s, 3H), 4.99 (dd, J = 1, 17 Hz, 1H), 5.07 (dd, J = 1, 11 Hz, 1H), 6.02 (dd, J = 10, 17 Hz, 1H), 7.35 (m, 3H), 7.75 (m, 2H), 7.95 (s, 1H), 9.7 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 22.1, 22.8, 44.6, 72.7, 115.3, 128.1, 128.3, 128.6, 136.8, 142.9, 156.6, 175.2. IR: (KBr) 3243 cm^{-1}, 1772 cm^{-1}, 1718 cm^{-1}. HRMS: $[M + H]^+$ = 245.1292, calculated for $C_{14}H_{17}N_2O_2$, 245.1290. Anal. Calcd. For $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.67; H, 6.39; N, 11.26. Melting Point = 229-231˚C.



ethyl 4-(2-methylallyl)-5-oxo-4-(1-tosyl-1H-indol-3-yl)-4,5-dihydrooxazol-2-ylcarbamate (14). The procedure to make (**14**) follows that described for the preparation of (**6a-h**) and (**11a-b**) except that the last step with NaOMe was negated. The yield was not calculated and only enough sample to confirm identity was isolated. ^{1}H NMR (500MHz), $CDCl_3$: δ 1.38 (t, J = 8 Hz, 3H), 1.52 (s, 3H), 2.36 (s, 3H), 3.00 (d, J = 14 Hz, 1H), 3.04 (d, J = 14 Hz, 1H), 4.42 (dq, J = 7, 3 Hz, 2H), 4.85 (s, 1H), 4.98 (m, 1H), 6.46 (s, 1H), 7.24-7.38 (m, 4H), 7.64 (s, 1H), 7.79 (d, J = 8 Hz, 2H), 7.91 (d, J = 8 Hz, 1H), 8.0 (d, J = 8 Hz, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 13.9, 21.5, 23.8, 44.4, 63.2, 64.5, 113.7, 118.0, 119.3, 121.6, 123.7, 124.1, 125.3, 127.0, 127.1, 130.0, 134.7, 135.7, 138.2, 145.4, 147.5, 151.4, 169.4. IR: (KBr) 3340 cm^{-1}, 1812 cm^{-1}, 1770 cm^{-1}, 1726 cm^{-1}. HRMS: $[M + H]^+$ = 496.1548, calculated for $C_{25}H_{26}N_3O_6S$, 496.1542.

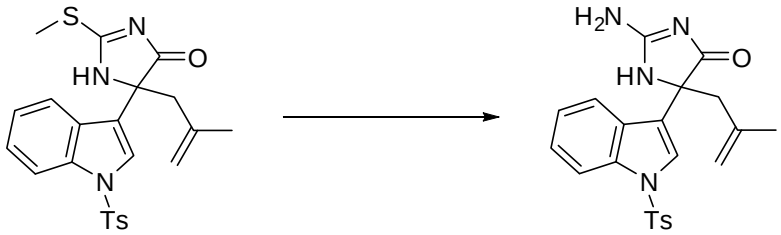


5-(1H-indol-3-yl)-5-(2-methylallyl)imidazolidine-2,4-dione (24). To a flame dried 250 mL round bottom flask was added (**22**) (1 g, 1.89 mmol), anhydrous DCM (75 mL), and anhydrous TEA (0.78 mL, 5.67 mmol). The solution was cooled to 0ºC and then EDCI (798 mg, 4.16 mmol) was added and the mixture stirred at 0ºC for 1 h and then refluxed until disappearance of the starting material, as indicated on TLC. A solution of NaH (750 mg, 18.9 mmol) in MeOH (70 mL) was then added to the mixture and refluxed for 8 h. Since the de-tosylation was sluggish with NaOMe the solvent was removed and ethanol (120 ml) was added followed by KOEt (793 mg, 9.45 mmol) and the mixture refluxed overnight. The solvent was removed and residue was acidified using 1% HCl and extracted using EtOAc (3 x 50 mL). The organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% Acetone; 80% DCM) affording the product as a white solid. Yield (426 mg, 83%). ^{1}H NMR (500MHz), DMSO: δ 1.75 (s, 3H), 2.72 (d, J = 13 Hz, 1H), 3.01 (d, J = 13 Hz, 1H), 4.82 (s, 1H), 4.91 (s, 1H), 6.99 (t, J = 7 Hz, 1H), 7.09 (t, J = 7 Hz, 1H), 7.37 (m, 2H), 7.57 (d, J = 9 Hz, 1H), 8.38 (s, 1H), 10.7 (s, 1H), 11.1 (s, 1H); ^{13}C NMR (125MHz), Acetone-d6: δ 23.9, 44.1, 65.9, 111.9, 114.7, 115.9, 119.5, 120.4, 121.9, 123.1, 125.2, 137.6, 140.3, 156.6, 175.8. IR: (NaCl) 3300 cm^{-1}, 1790 cm^{-1}, 1720 cm^{-1}. HRMS: $[M + H]^{+}$ = 270.1255, calculated for $C_{15}H_{16}N_3O_2$, 270.1243. Anal. Calcd. For $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.38; H, 5.69; N, 15.11. Melting Point = 238-240˚C.

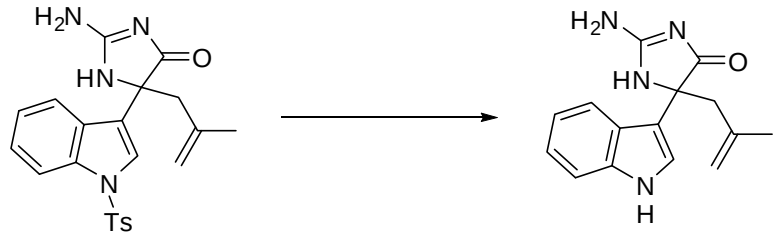


5-(1H-indol-3-yl)-5-(2-oxopropyl)imidazolidine-2,4-dione (25). To a 25 mL round bottom flask was added (**24**) (172 mg, 0.639 mmol), THF (8 mL) and water (1 mL). Then NMO (112 mg, 0.959 mmol) and OsO_4 (0.65 mL of a 0.098 M solution in THF, 0.0639 mmol) were added. The solution stirred at room temperature for 2 h and then was cooled to 0ºC before a solution of $NaIO_4$ (410 mg, 1.917 mmol) in water (3 mL) was added and stirred at room temperature overnight. The solvents were removed and EtOAc (10 mL) was added along with a sat. solution of K_2SO_3 (10 mL). This biphasic mixture stirred for 10 min and then the organic layer was separated and the aqueous layer was extracted with n-BuOH (3 x 10 mL). The EtOAc layer and nBuOH layers were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 10% MeOH; 90% DCM) affording the product as an off white solid. Yield (107 mg, 61%). Product was recrystallized over 1 week with EtOAc. ^{1}H NMR (500MHz), CD_3OD: δ 2.15 (s, 3H), 3.49 (d, J = 8 Hz, 1H), 3.59 (d, J = 8 Hz, 1H), 7.02 (t, J = 8 Hz, 1H), 7.11 (t, J = 8 Hz, 1H), 7.27 (s, 1H), 7.35 (d, J = 8 Hz, 1H), 7.69 (d, J = 8 Hz, 1H); ^{13}C NMR (125MHz), CD_3OD: δ 30.5, 49.2, 64.1, 112.7, 113.9,

120.5, 120.6, 122.9, 123.9, 125.6, 138.8, 160.0, 179.0. IR: (KBr) 3364 (br) cm^{-1}, 1774 cm^{-1}, 1711 cm^{-1}. HRMS: $[M + H]^+$ = 272.1055, calculated for $C_{14}H_{14}N_3O_3$, 272.1035. Anal. Calcd. For $C_{14}H_{13}N_3O_3$: C, 61.99; H, 4.83; N, 15.49. Found: C, 61.10; H, 4.82; N, 15.38. Melting Point = 234-236˚C.

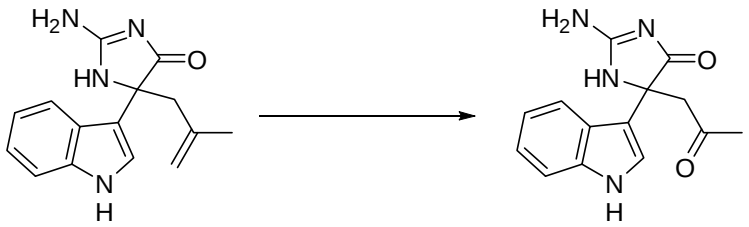


2-amino-5-(2-methylallyl)-5-(1-tosyl-1H-indol-3-yl)-1H-imidazol-4(5H)-one (27). To a sealed tube was added (**26**) (850 mg, 1.876 mmol) in THF (5 mL) and NH_4OH (15 mL). The mixture was heated at 90ºC until the disappearance of the starting material, as indicated by TLC. The precipitate that formed was filtered, acidified with 5% HCl and extracted with nBuOH (3 x 20 mL), dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 10% MeOH; 90% DCM) affording the product as an off white solid. Yield (575 mg, 72%). ^{1}H NMR (500MHz), DMSO: δ 1.62 (s, 3H), 2.3 (s, 3H), 2.72 (d, J = 13 Hz, 1H), 2.81 (d, J = 13 Hz, 1H), 4.72 (s, 1H), 4.77 (s, 1H), 7.22 (t, J = 8 Hz, 1H), 7.32 (t, J = 8 Hz, 1H), 7.37 (d, J = 9 Hz, 2H), 7.64 (d, J = 8 Hz, 1H), 7.69 (s, 1H), 7.85 (d, J = 9 Hz, 2H), 7.90 (d, J = 8 Hz, 1H), 8.25 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 20.9, 23.7, 43.1, 66.0, 113.0, 115.2, 121.5, 123.0, 123.3, 124.7, 126.7, 128.0, 130.2, 134.0, 134.5, 139.9, 145.5, 170.9, 187.5. IR: (KBr) 3470 cm^{-1}, 3351 cm^{-1}, 3307 cm^{-1}, 3088 cm^{-1}, 1707 cm^{-1}, 1657 cm^{-1}. HRMS: $[M + H]^+$ = 423.1494, calculated for $C_{22}H_{23}N_4O_3S$, 423.1491. Anal. Calcd. For $C_{22}H_{22}N_4O_3S$: C, 62.54; H, 5.25; N, 13.25. Found: C, 61.21; H, 5.17; N, 13.05. Melting Point = 273-275˚C.

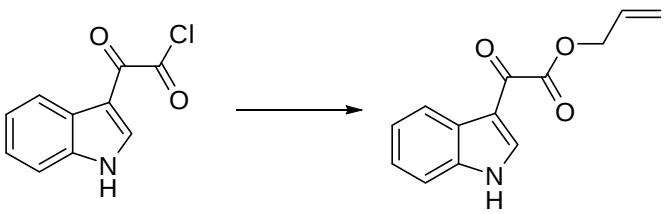


2-amino-5-(1H-indol-3-yl)-5-(2-methylallyl)-1H-imidazol-4(5H)-one (28). To a 100 mL round bottom flask was added (**27**) (500 mg, 1.18 mmol) and EtOH (60 mL). Then KOEt (991 mg, 11.8 mmol) was added and the mixture refluxed for 24 h. The EtOH was taken off and the pH of an aqueous mixture of the crude residue was adjusted to 8. The aqueous mixture was then extracted with nBuOH (3 x 40 mL). The organics were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% MeOH; 90% DCM) affording the product as an off white solid. The product was recrystallized from EtOH. Yield (150 mg, 47%). ^{1}H NMR (500MHz), DMSO: δ 1.67 (s, 3H), 2.75 (d, J = 14 Hz, 1H), 2.81 (d, J = 14 Hz, 1H), 4.75 (s, 1H), 4.78 (s, 1H), 6.92 (t, J = 7 Hz, 1H), 7.04 (t, J = 7 Hz, 1H), 7.26 (d, J = 2 Hz, 1H), 7.33 (d, J = 8 Hz, 1H), 7.48 (d, J = 8 Hz, 1H), 8.03 (s, 1H), 10.9 (s, 1H); ^{13}C NMR (125MHz), DMSO: δ 23.9, 43.4, 66.3, 111.4, 114.7, 115.3, 118.3, 119.7, 120.9, 122.6, 124.8, 136.5, 140.7, 170.8, 189.1. IR: (KBr) 3470 cm^{-1}, 3390 (br) cm^{-1}, 3200 (br) cm^{-1}, 1692 cm^{-1}, 1650 cm^{-1}. HRMS: $[M + H]^+$ = 269.1405, calculated for $C_{15}H_{17}N_4O$, 269.1402.

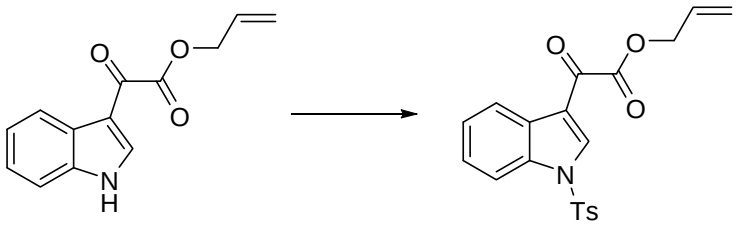
Anal. Calcd. For $C_{15}H_{16}N_4O$: C, 67.15; H, 6.01; N, 20.88. Found: C, 63.98; H, 5.89; N, 19.84. Melting Point = 264-266˚C.



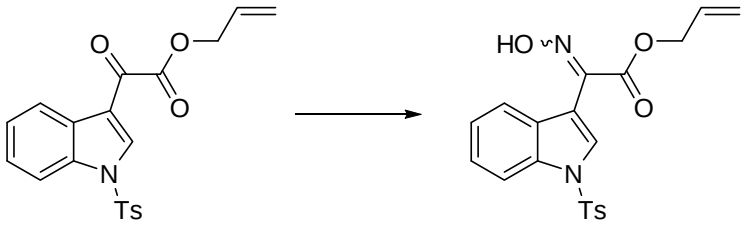
2-amino-5-(1H-indol-3-yl)-5-(2-oxopropyl)-1H-imidazol-4(5H)-one (29). To a 25 mL round bottom flask was added (**28**) (99 mg, 0.366 mmol), DMF (7 mL), THF (1 mL) and water (1 mL). Then NMO (64 mg, 0.549 mmol) and OsO_4 (0.37 mL of a 0.098 M solution in THF, 0.0366 mmol) were added. The solution stirred at room temperature for 3 h and then was cooled to 0ºC before a solution of $NaIO_4$ (235 mg, 1.098 mmol) in water (2 mL) was added and stirred at room temperature overnight. The solvents were removed and EtOAc (10 mL) was added along with a sat. solution of K_2SO_3 (10 mL). This biphasic mixture stirred for 10 min and then the organic layer was separated and the aqueous layer was extracted with n-BuOH (6 x 10 mL). The EtOAc layer and nBuOH layers were combined, dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 20% MeOH; 90% DCM) affording the product as an off white solid. The product was recrystallized from EtOH. Yield (19 mg, 19%). ^{1}H NMR (500MHz), CD_3OD: δ 2.18 (s, 3H), 3.19 (d, J = 7 Hz, 1H), 3.64 (d, J = 7 Hz, 1H), 6.97 (t, J = 8 Hz, 1H), 7.08 (t, J = 8 Hz, 1H), 7.20 (s, 1H), 7.33 (d, J = 8 Hz, 1H), 7.51 (d, J = 8 Hz, 1H); ^{13}C NMR (125MHz), CD_3OD: δ 30.9, 66.5, 112.5, 114.1, 120.28, 120.29, 122.7, 124.0, 125.9, 138.5, 171.7, 192.5, 207.7. IR: (KBr) 3470 cm^{-1}, 3420 cm^{-1}, 3270 (br) cm^{-1}, 3176 (br) cm^{-1}, 1720 cm^{-1}, 1690 cm^{-1}, 1650 cm^{-1}. HRMS: $[M + H]^+$ = 271.1191, calculated for $C_{14}H_{15}N_4O_2$, 271.1195. Melting Point = 283-285˚C.



allyl 2-(1H-indol-3-yl)-2-oxoacetate (30, see scheme after experimental). To a flame dried 50 mL round bottom flask was added 2-(1H-indol-3-yl)-2-oxoacetyl chloride[3,4] (1.55 g, 7.49 mmol) and anhydrous CH_3CN. Then allyl alcohol (2.56 mL, 37.45 mmol) was added and the mixture stirred at room temperature under nitrogen overnight. The solvent was removed and the residue was put into solution with EtOAc (200 mL) and washed with sat. sodium bicarbonate (1 x 100 mL). The organics were dried using anhydrous sodium sulfate and concentrated to give pure product. Yield (1.7 g, 99%). ^{1}H NMR (500MHz), Acetone: δ 4.85 (m, 2H), 5.27-5.31 (m, 1H), 5.42-5.48 (m, 1H), 6.07 (m, 1H), 7.27-7.32 (m, 2H), 7.56-7.6 (m, 1H), 8.32 (m, 1H), 8.46 (s, 1H), 11.35 (s, 1H); ^{13}C NMR (125MHz), Acetone: δ 66.5, 113.2, 114.2, 119.0, 122.5, 123.6, 124.7, 126.8, 132.8, 137.7, 138.2, 164.0, 179.5. IR: (KBr) 3200cm^{-1} , 1743cm^{-1}, 1620 cm^{-1}. HRMS: $[M + H]^+$ =230.0819, calculated for $C_{13}H_{12}NO_3$, 230.0817. Anal. Calcd. For $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11. Found: C, 66.14; H, 4.80; N, 5.93. Melting Point = 159-161˚C.

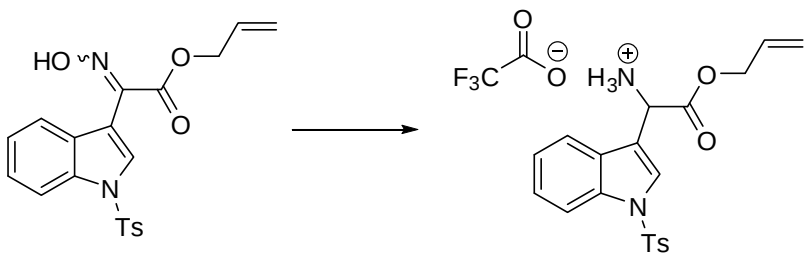


allyl 2-oxo-2-(1-tosyl-1H-indol-3-yl)acetate (31, see scheme after experimental). To a flame dried 250 mL round bottom flask was added (**30**) (1.7 g, 7.42 mmol) and anhydrous DCM (100 mL). Then TsCl (2.82 g, 14.84 mmol), DMAP (2.26 g, 18.55 mmol), and DIPEA (3.2 mL, 18.55 mmol) were added and the mixture stirred at room temperature overnight under a nitrogen atmosphere. The resulting brown solution was washed with 5% HCl (1 x 30 mL) and brine (1 x 30 mL) and the organics were dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexanes) and recrystallized with EtOAc/Hexanes to afford the product. Yield (2.46 g, 86%). ^{1}H NMR (500MHz), $CDCl_3$: δ 2.35 (s, 3H), 4.86 (m, 2H), 5.35 (m, 1H), 5.46 (m, 1H), 6.03 (m, 1H), 7.27 (d, J = 8 Hz, 2H), 7.37 (m, 2H), 7.85 (d, J = 8 Hz, 2H), 7.94 (m, 1H), 8.34 (m, 1H), 8.82 (s, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 21.6, 66.9, 113.1, 116.9, 120.0, 122.9, 125.2, 126.1, 127.3, 127.6, 130.3, 130.7, 134.2, 134.4, 136.8, 146.2, 161.2, 178.3. IR: (KBr) 1730cm^{-1}, 1674 cm^{-1}. HRMS: $[M + H]^+$ = 384.0914, calculated for $C_{20}H_{18}NO_5S$, 383.0906. Anal. Calcd. For $C_{20}H_{17}NO_5S$: C, 62.65; H, 4.47; N, 3.65. Found: C, 62.47; H, 4.48; N, 3.64. Melting Point = 104-106˚C.



allyl 2-(hydroxyimino)-2-(1-tosyl-1H-indol-3-yl)acetate (32, see scheme after experimental). To a 250 mL round bottom flask was added (**31**) (2.3 g, 6.01 mmol) and dioxane (100 mL). Then hydroxylamine hydrochloride (1.24 g, 18.02 mmol) and pyridine (1.55 mL, 19.23 mmol) were added and the mixture refluxed under nitrogen overnight (enough water to dissolve the hydroxylamine salt was added). The solvent was taken off and the residue was put into solution with EtOAc (100 mL). The organics were washed with 1% HCl (1 x 30 mL) and brine (1 x 30 mL), then dried using anhydrous sodium sulfate and concentrated. The crude residue was purified by column chromatography (silica gel, 30% EtOAc; 70% Hexanes) affording the product as a mixture of isomers. Yield (2.22 g, 93%). Isomer A: ^{1}H NMR (500MHz), $CDCl_3$: δ 2.32 (s, 3H), 4.83 (d, J = 6 Hz, 2H), 5.28 (d, J = 11 Hz, 1H), 5.38 (d, J = 18 Hz, 1H), 5.96 (m, 1H), 7.21 (d, J = 8 Hz, 2H), 7.25 (t, J = 8 Hz, 1H), 7.35 (t, J = 8 Hz, 1H), 7.52 (d, J = 8 Hz, 1H), 7.83 (d, J = 8 Hz, 2H), 8.01 (d, J = 8 Hz, 1H), 8.25 (s, 1H), 10.59 (s, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 21.4, 66.8, 109.5, 113.2, 119.6, 122.4, 123.3, 124.8, 126.9, 128.0, 129.9, 130.1, 130.9, 133.9, 134.7, 143.1, 145.3, 162.7. Isomer B: ^{1}H NMR (500MHz), $CDCl_3$: δ 2.25 (s, 3H), 4.91 (d, J = 6 Hz, 2H), 5.33 (d, J = 10 Hz, 1H), 5.45 (d, J = 17 Hz, 1H), 6.02 (m, 1H), 7.14-7.21 (m, 3H), 7.32 (t, J = 8 Hz, 1H), 7.74 (d, J = 8 Hz, 2H), 7.76 (s, 1H), 7.94 (d, J = 8 Hz, 1H), 8.00 (d, J = 8 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR (125MHz), $CDCl_3$: δ 21.3, 66.5, 113.2, 113.6, 119.7, 122.9, 124.1, 125.6, 126.8, 126.9, 127.3, 129.9, 130.7, 134.4, 135.0, 145.4, 146.5, 162.4. IR: (NaCl)

3276 cm^{-1}, 1730cm^{-1}. HRMS: $[M + H]^+$ = 399.1017, calculated for $C_{20}H_{19}N_2O_5S$, 399.1015. Anal. Calcd. For $C_{20}H_{18}N_2O_5S$: C, 60.29; H, 4.55; N, 7.03. Found: C, 58.91; H, 4.30; N, 6.82.



2-(allyloxy)-2-oxo-1-(1-tosyl-1H-indol-3-yl)ethanaminium 2,2,2-trifluoroacetate (33, see scheme after experimental). To a 250 mL round bottom flask was added water (55 mL) and AcOH (55 mL). Then (**32**) (2.12 g, 5.33 mmol) was dissolved in THF (25 mL) and was added to the aqueous acid. The mixture was brought down to 0ºC and zinc (3.46 g, 53.3 mmol) was then slowly added in small portions over 20 min. The suspension stirred at 0˚C for 2 h. The solid was filtered off and the filtrate was reduced and then brought to a pH of 8 using concentrated ammonium hydroxide. The amine was extracted into ethyl acetate (4 x 50 ml), dried using anhydrous sodium sulfate and concentrated. The crude residue was then put into solution with DCM (5 mL) and TFA (3 mL) was added. The mixture stirred for 10 min and then the solvent and excess TFA was removed. $CHCl_3$ (3 x 15 mL) was added and subsequently taken off to remove any residual TFA. The product was precipitated out of the crude residue using ether/petroleum ether to afford the product as a white solid. Yield (2.25 g, 85%). ^{1}H NMR (500MHz), DMSO: δ 2.31 (s, 3H), 4.66 (m, 2H), 5.06 (m, 1H), 5.09 (m, 1H), 5.71 (s, 1H), 5.75 (m, 1H), 7.33 (t, J = 8 Hz, 1H), 7.4 (m, 3H), 7.75 (d, J = 8 Hz, 1H), 7.85 (d, J = 8 Hz, 2H), 7.94 (d, J = 8 Hz, 1H), 8.09 (s, 1H), 9.12 (s, 3H); ^{13}C NMR (125MHz), DMSO: δ 20.9, 47.8, 66.2, 113.1, 114.1, 115.9, 118.1, 118.3, 120.3, 123.6, 125.5, 126.7, 126.8, 127.8, 130.3, 131.3, 133.7, 133.8, 145.9, 158.1, 158.4, 158.6, 163.9, 167.5. IR: (KBr) 3100 (br) cm^{-1} , 1736 cm^{-1}, 1674 cm^{-1}. HRMS: $[M + H]^+$ = 385.1235, calculated for $C_{20}H_{21}N_2O_4S$, 385.1222. Anal. Calcd. For $C_{22}H_{21}F_3N_2O_6S$: C, 53.01; H, 4.25; N, 5.62. Found: C, 52.95; H, 4.05; N, 5.50. Melting Point = 170-172˚C.

References

(1) Caplar, V.; Zinic, M.; Pozzo, J.-L.; Fages, F.; Mieden-Gundert, G.; Voegtle, F. *Eur. J. Org. Chem.* **2004**, 4048-4059.

(2) Kim, D. D.; Lee, S. J.; Beak, P. *J. Org. Chem.* **2005**, *70*, 5376-5386.

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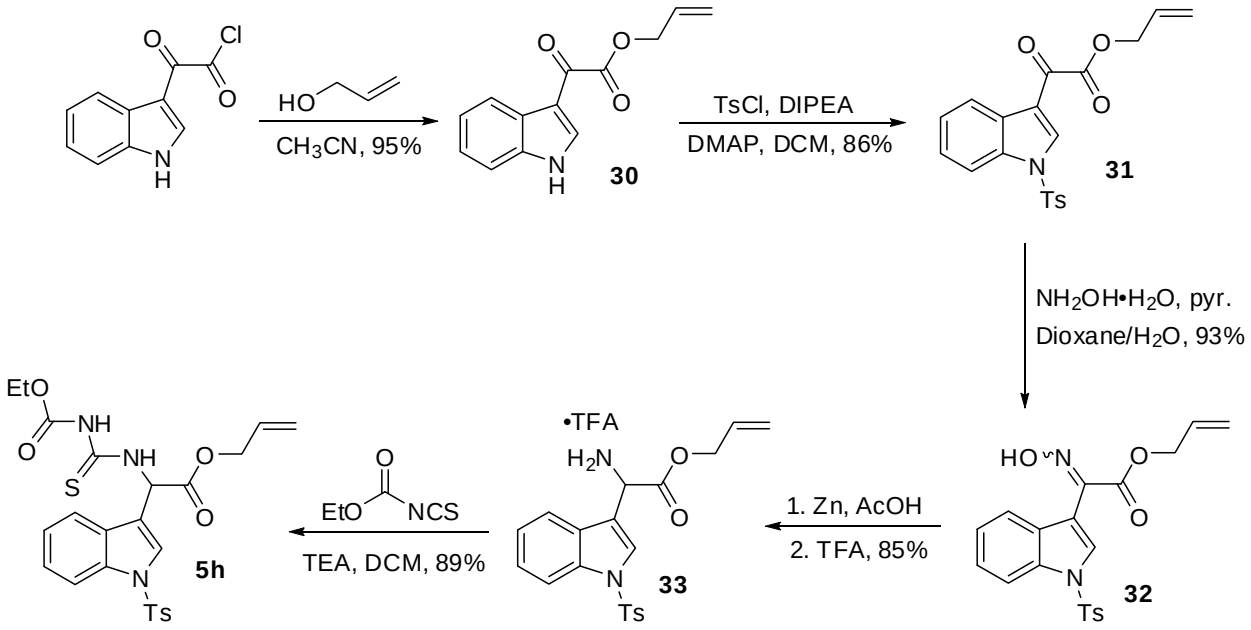
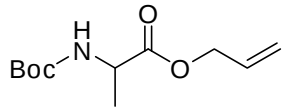
Reaction scheme of the synthesis of thiourea 5h

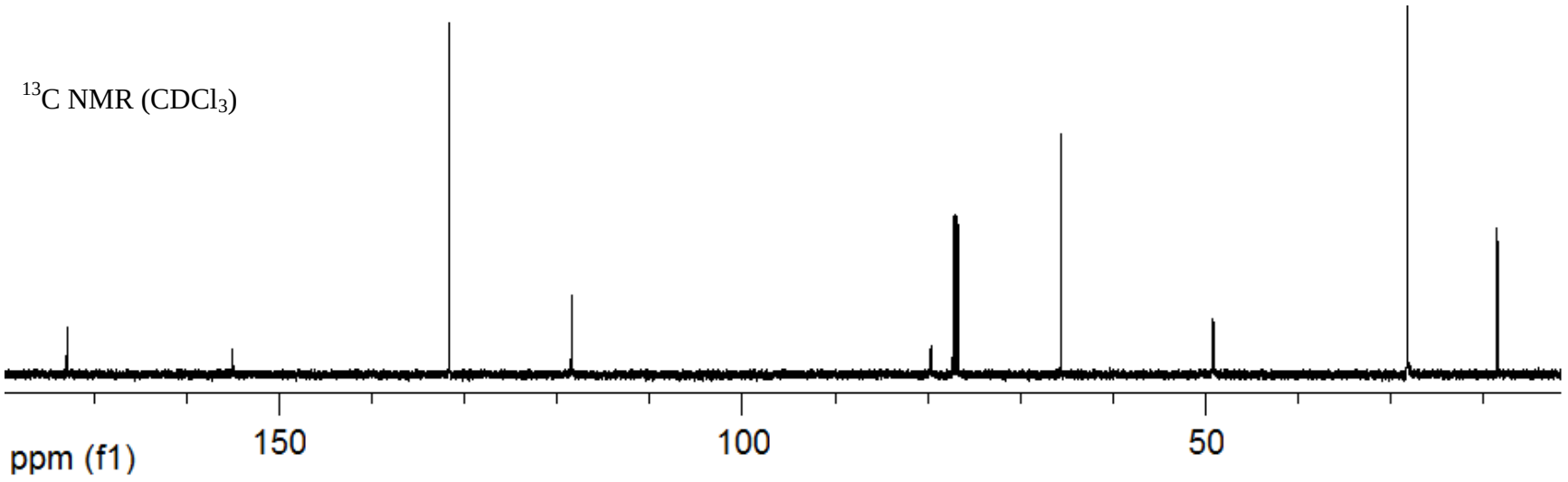


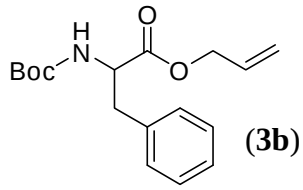


(3a)

^{1}H NMR ($CDCl_3$)

^{13}C NMR ($CDCl_3$)

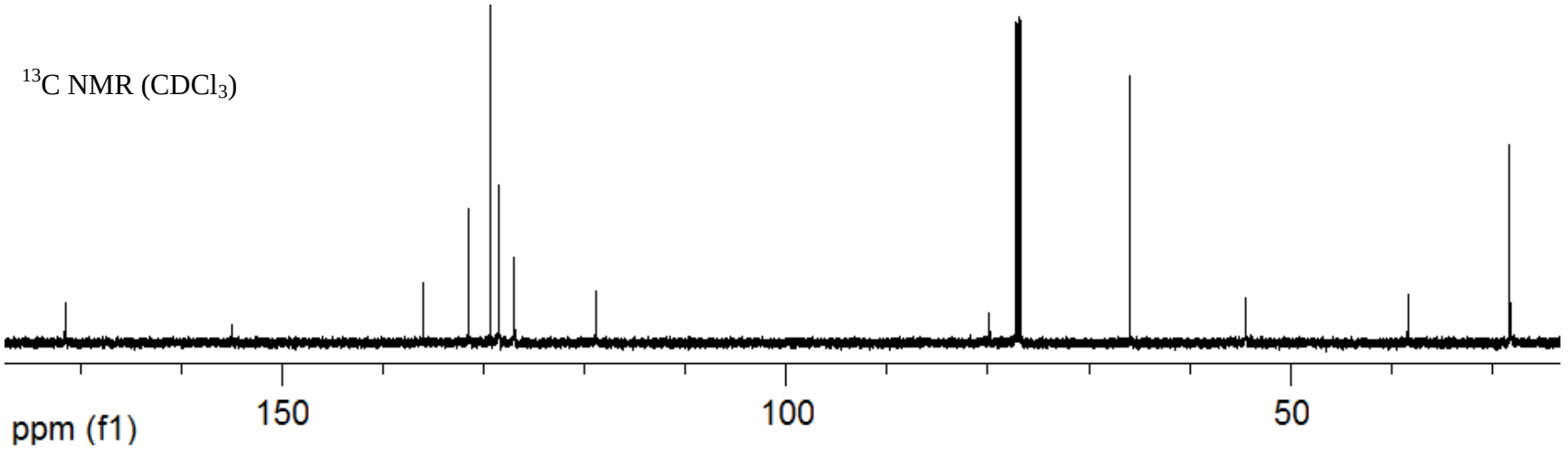


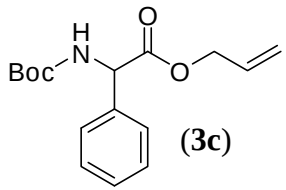


(3b)

^{1}H NMR ($CDCl_3$)

^{13}C NMR ($CDCl_3$)

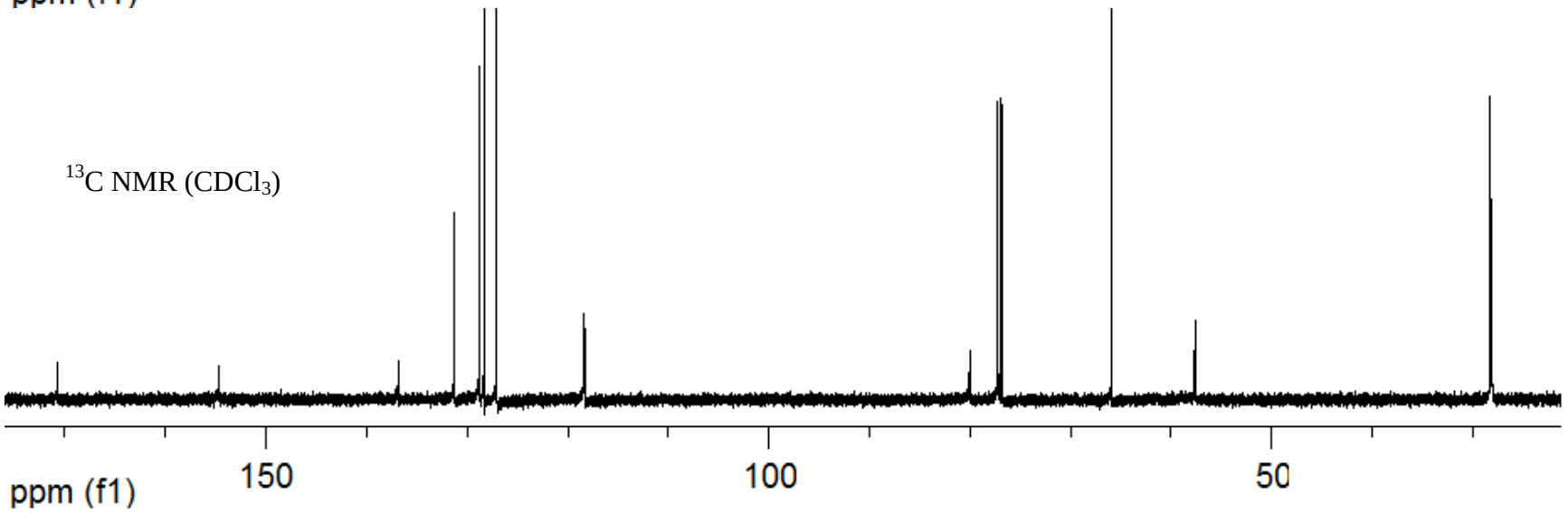


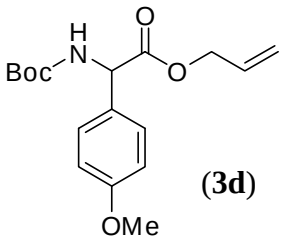


(3c)

^{1}H NMR ($CDCl_3$)

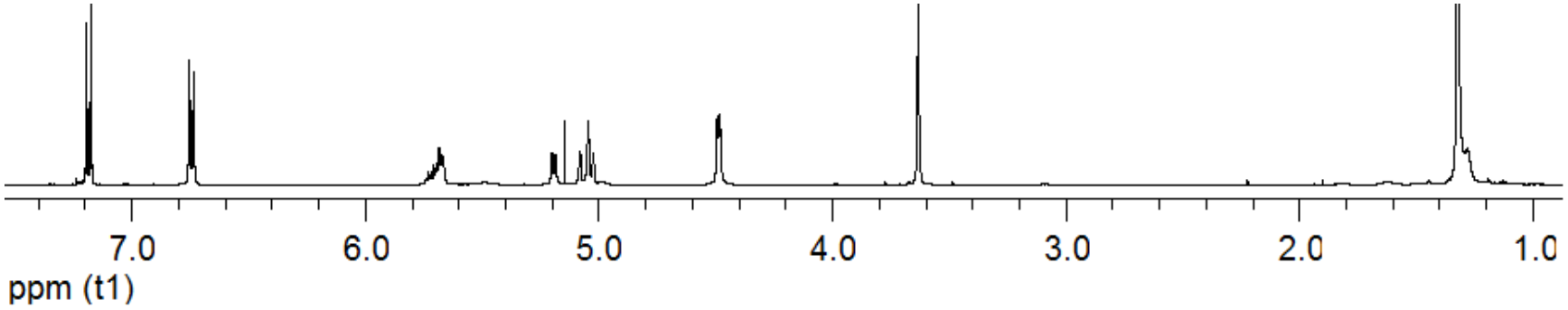
^{13}C NMR ($CDCl_3$)



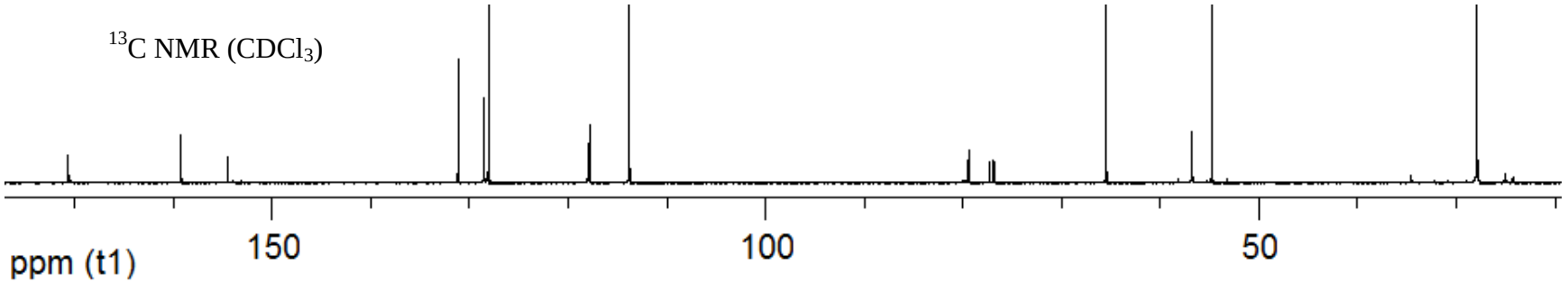


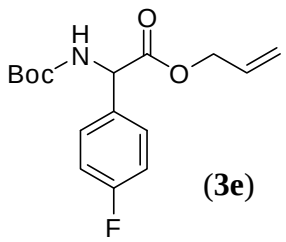
(**3d**)

^{1}H NMR ($CDCl_3$)



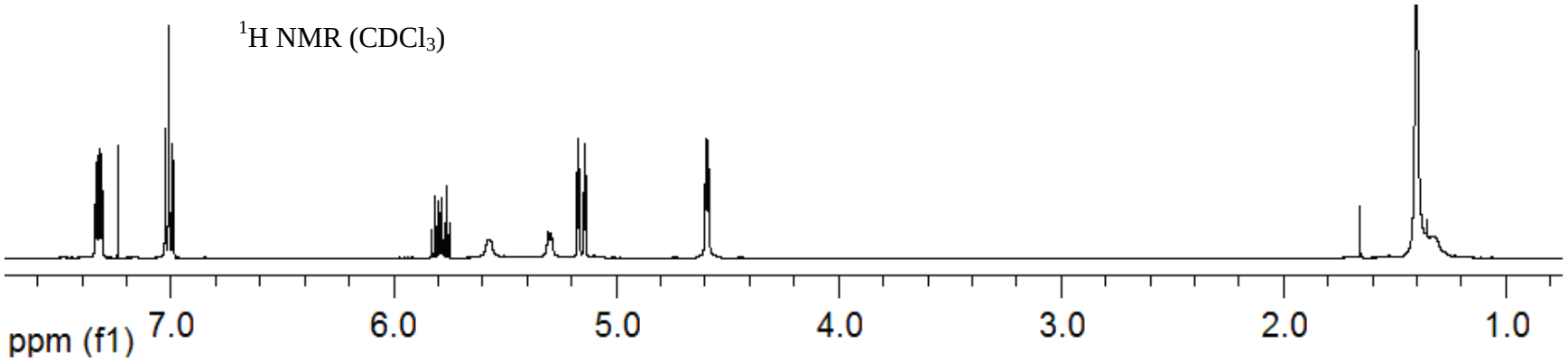
^{13}C NMR ($CDCl_3$)



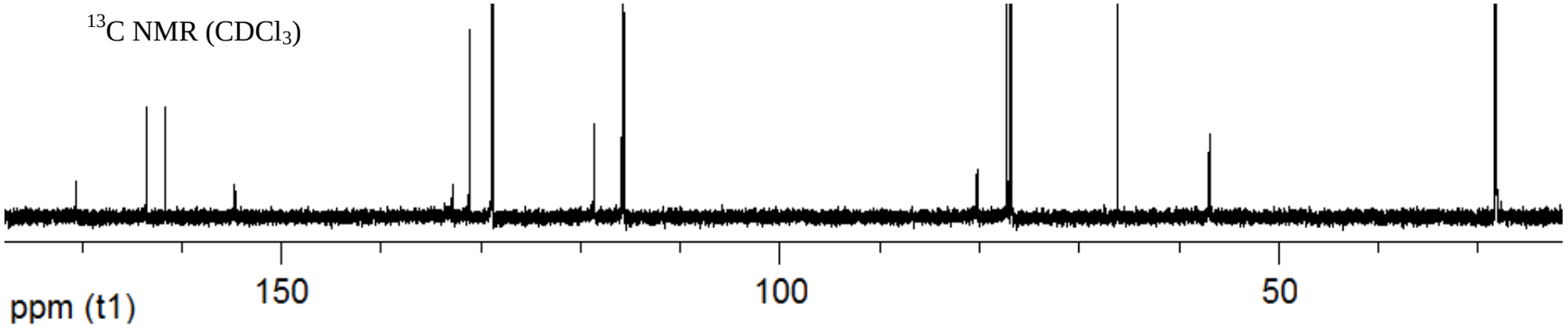


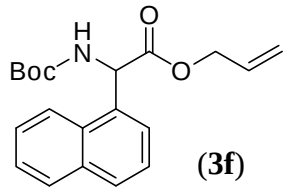
(**3e**)

^{1}H NMR ($CDCl_3$)



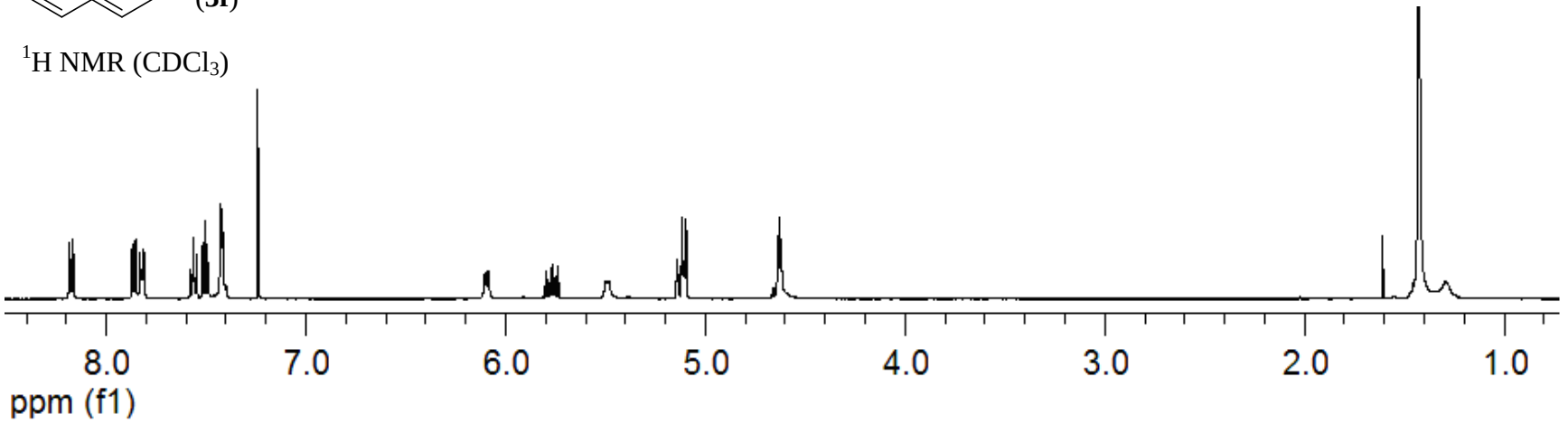
^{13}C NMR ($CDCl_3$)



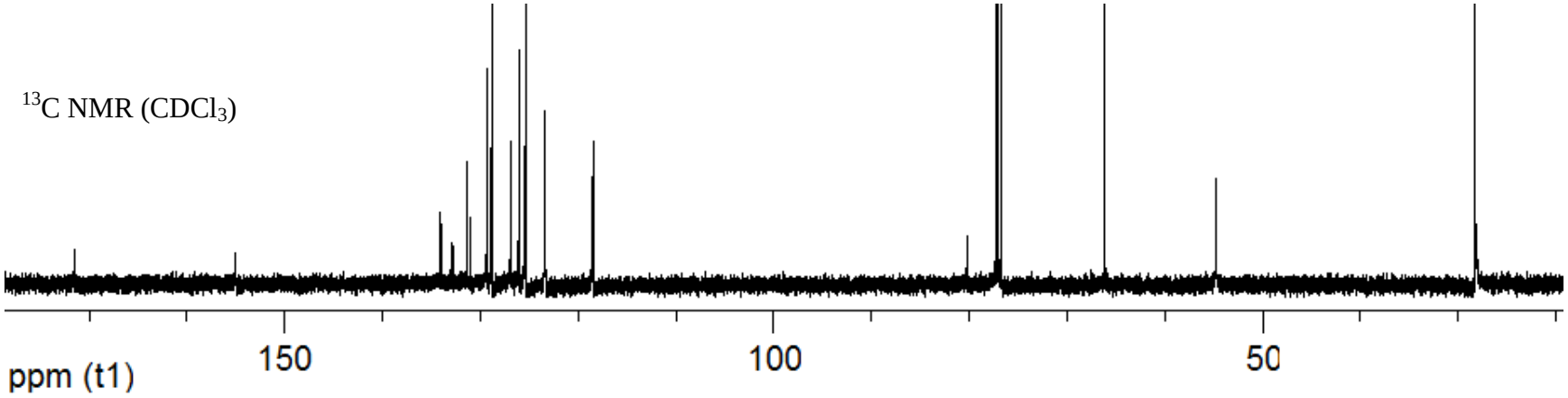


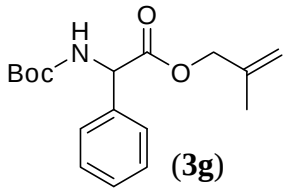
(**3f**)

^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

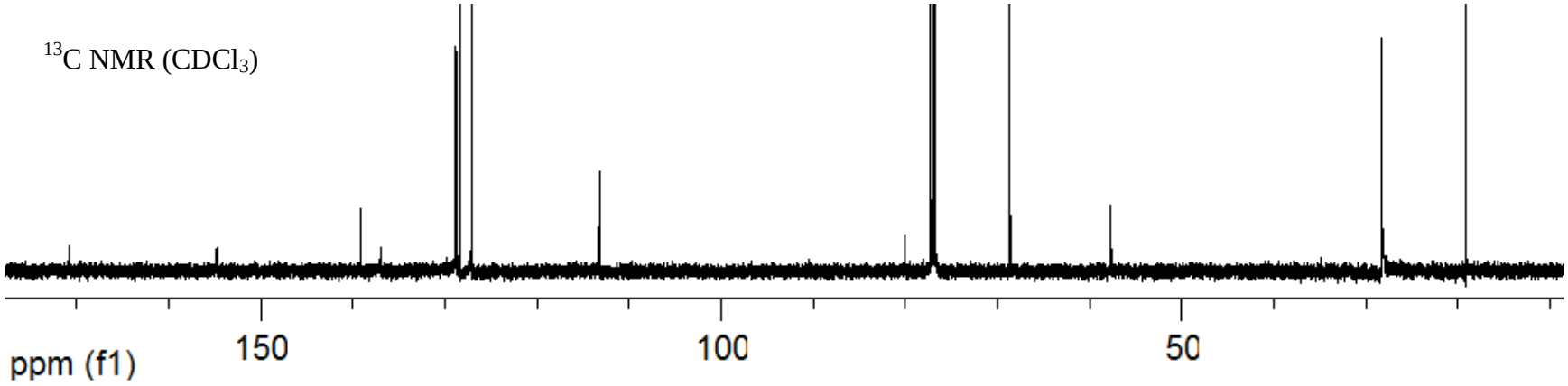


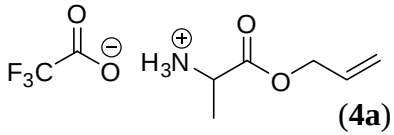


(3g)

^{1}H NMR ($CDCl_3$)

^{13}C NMR ($CDCl_3$)

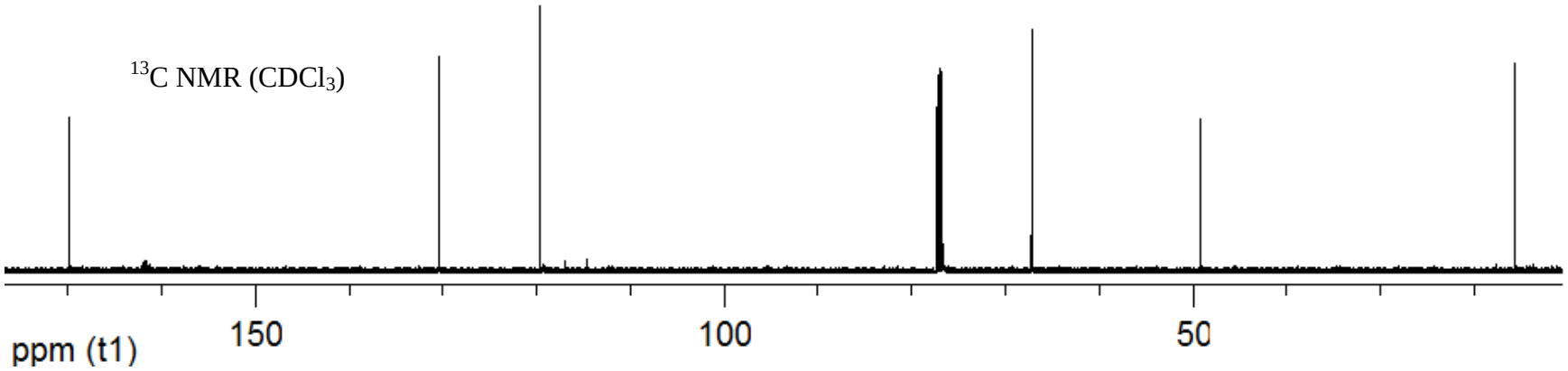


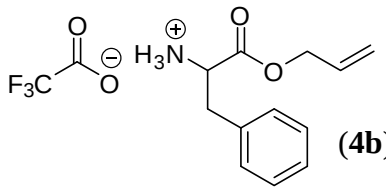


(**4a**)

^{1}H NMR ($CDCl_3$)

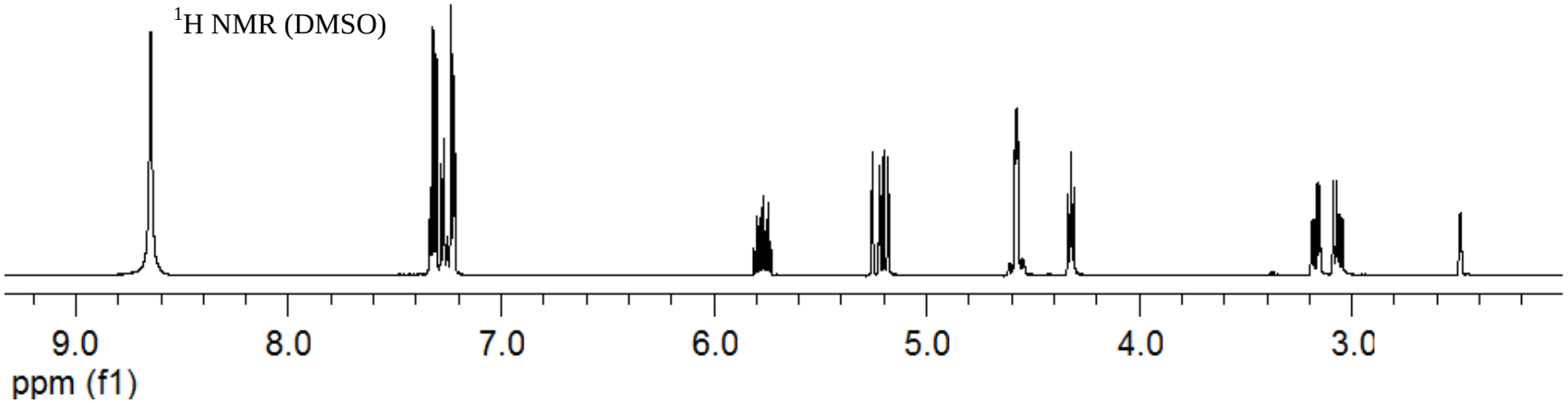
^{13}C NMR ($CDCl_3$)



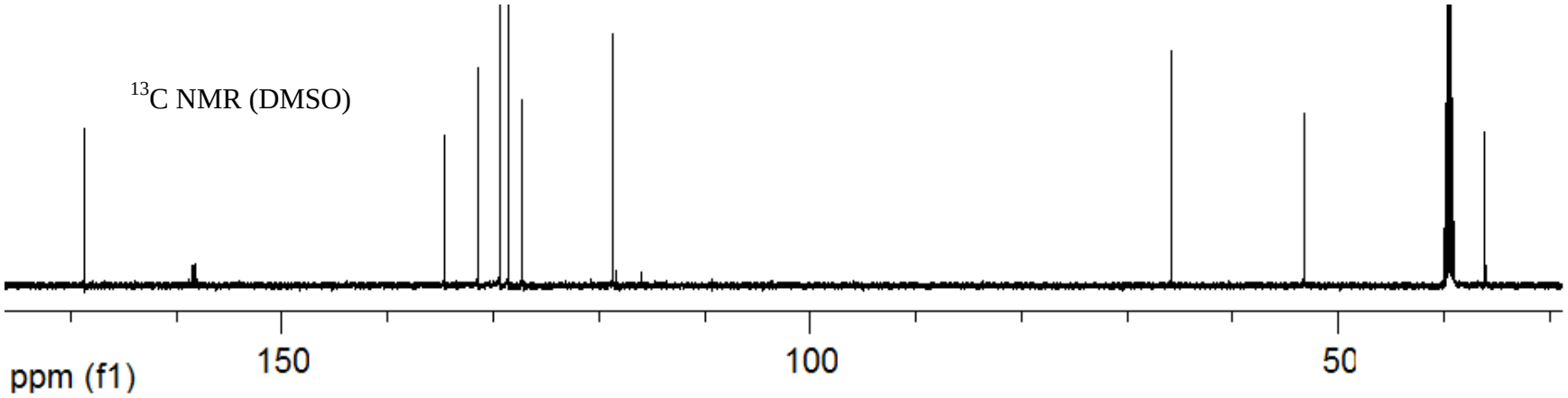


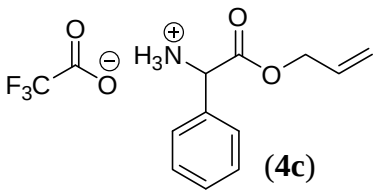
(4b)

^{1}H NMR (DMSO)



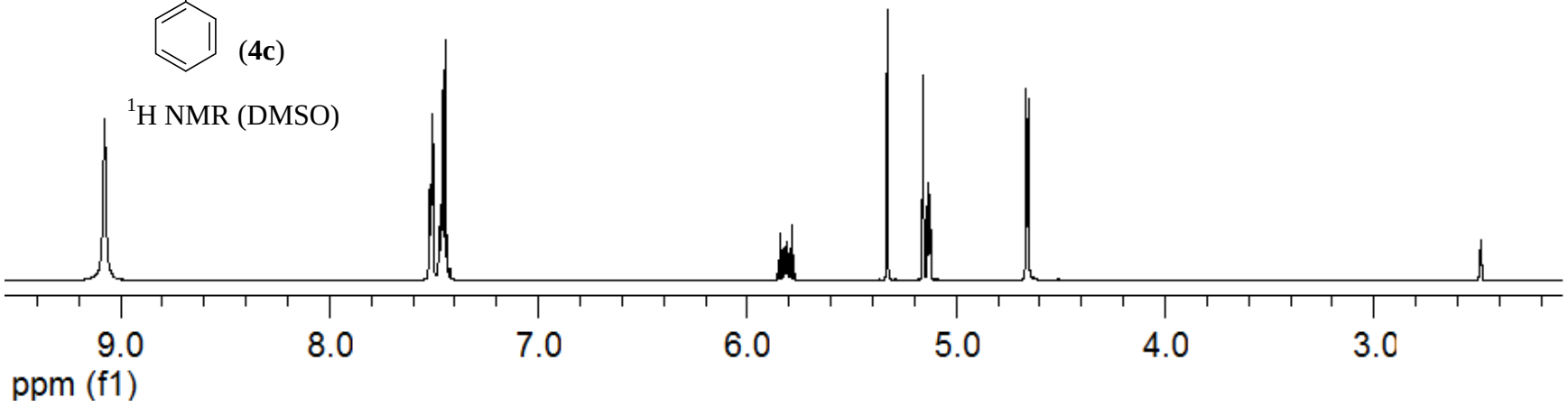
^{13}C NMR (DMSO)



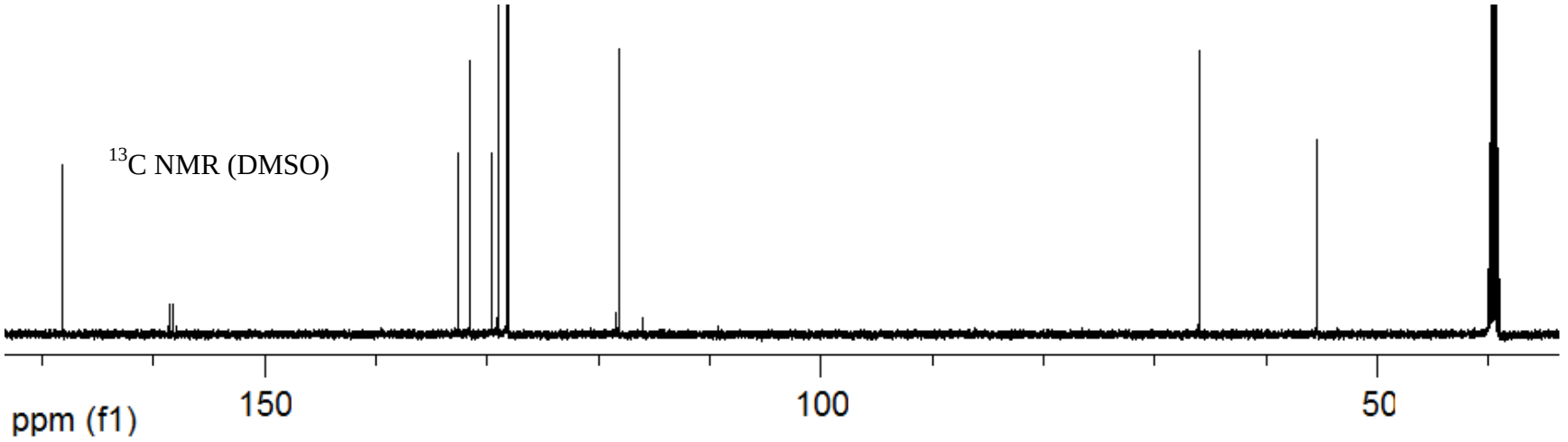


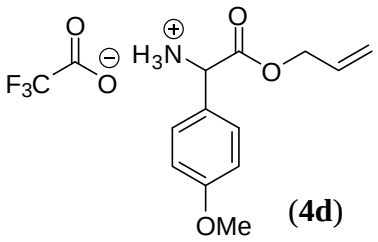
(**4c**)

^{1}H NMR (DMSO)



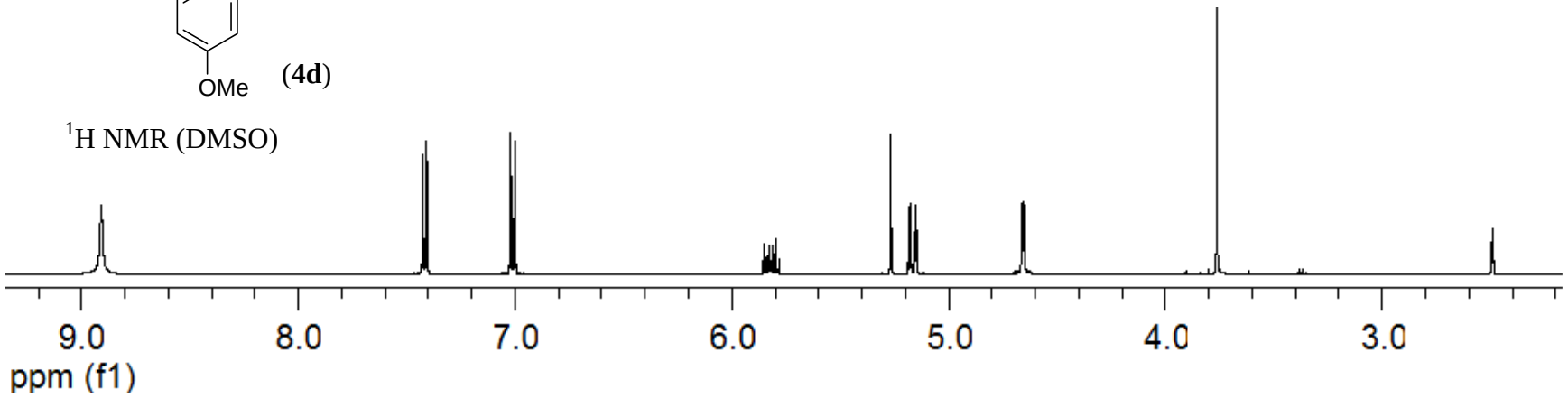
^{13}C NMR (DMSO)



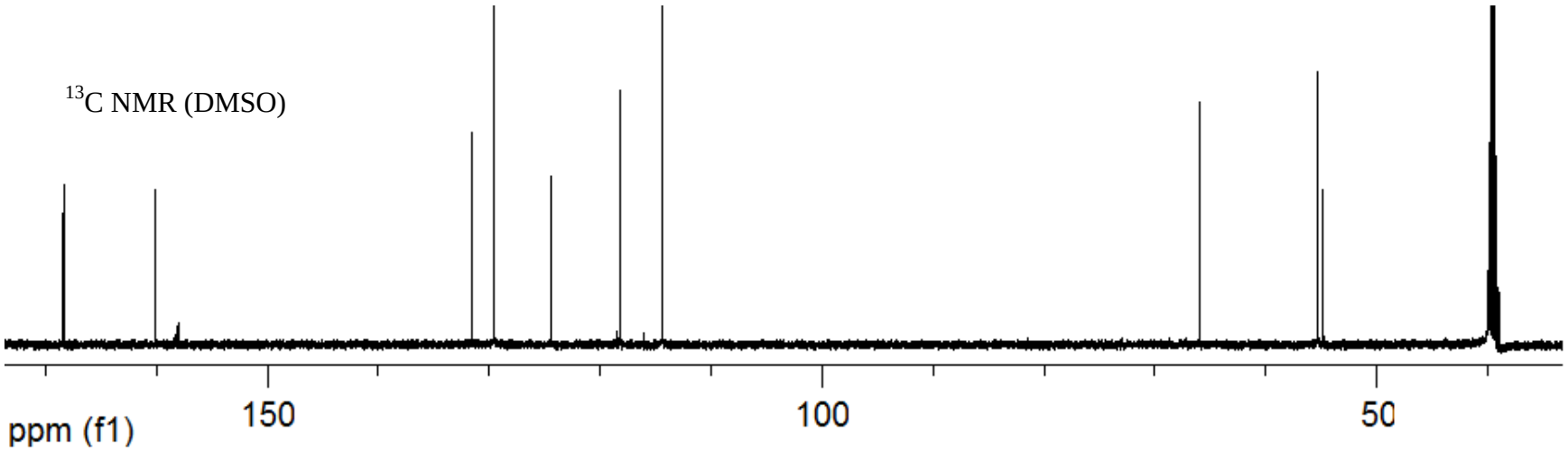


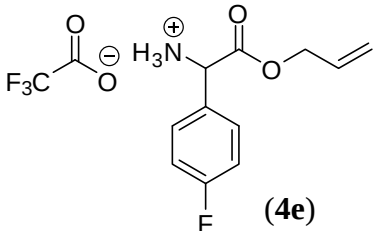
(4d)

^{1}H NMR (DMSO)



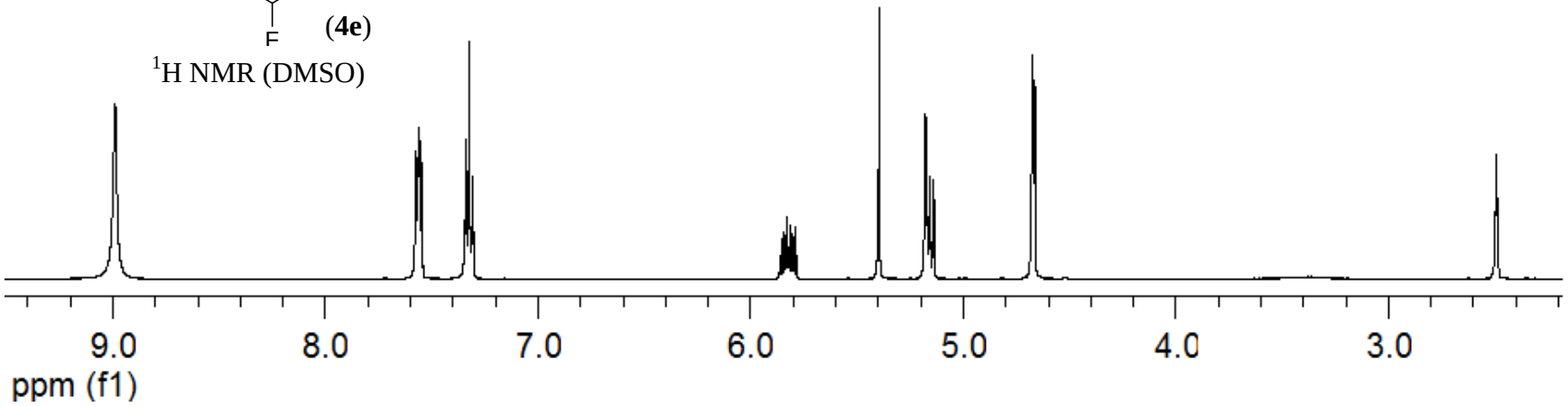
^{13}C NMR (DMSO)



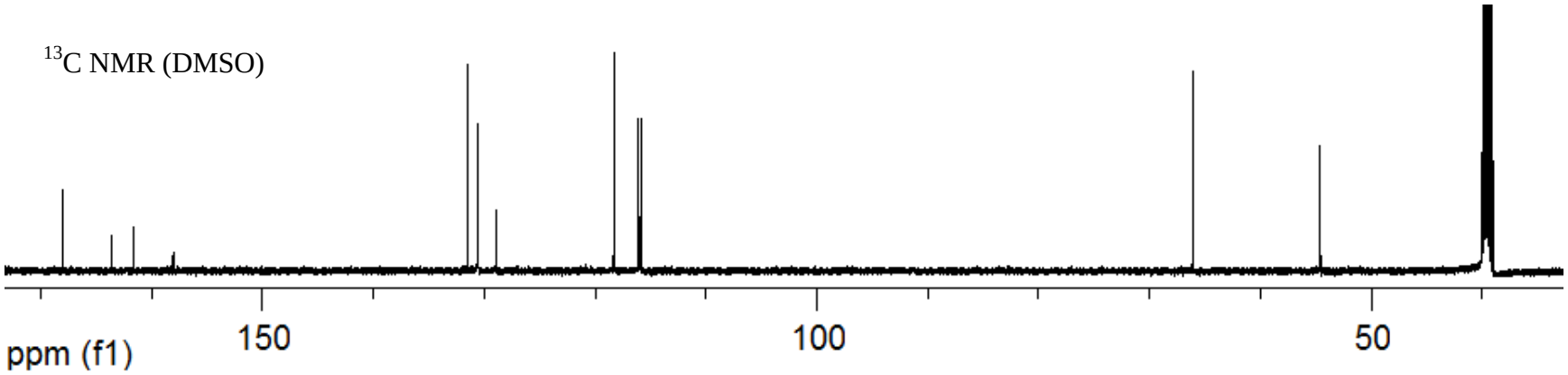


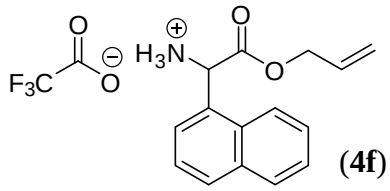
(**4e**)

^{1}H NMR (DMSO)



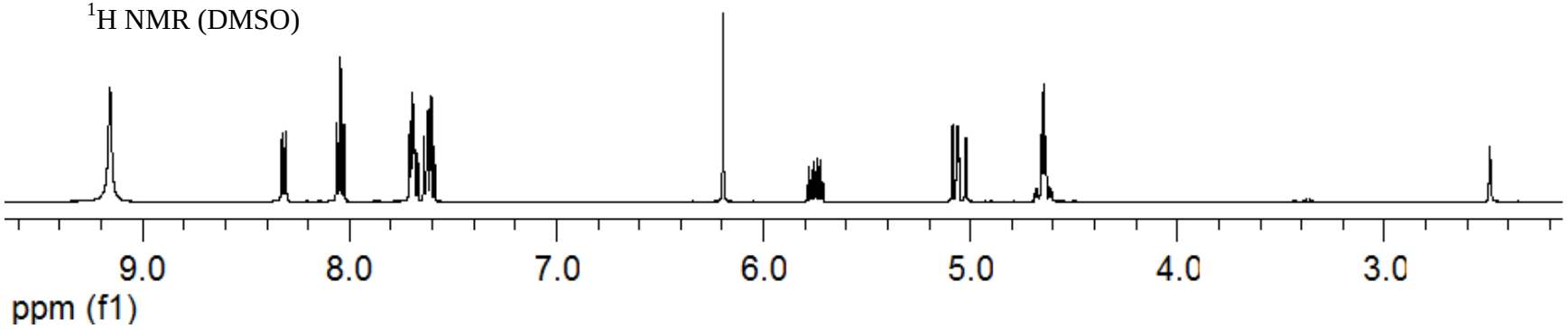
^{13}C NMR (DMSO)



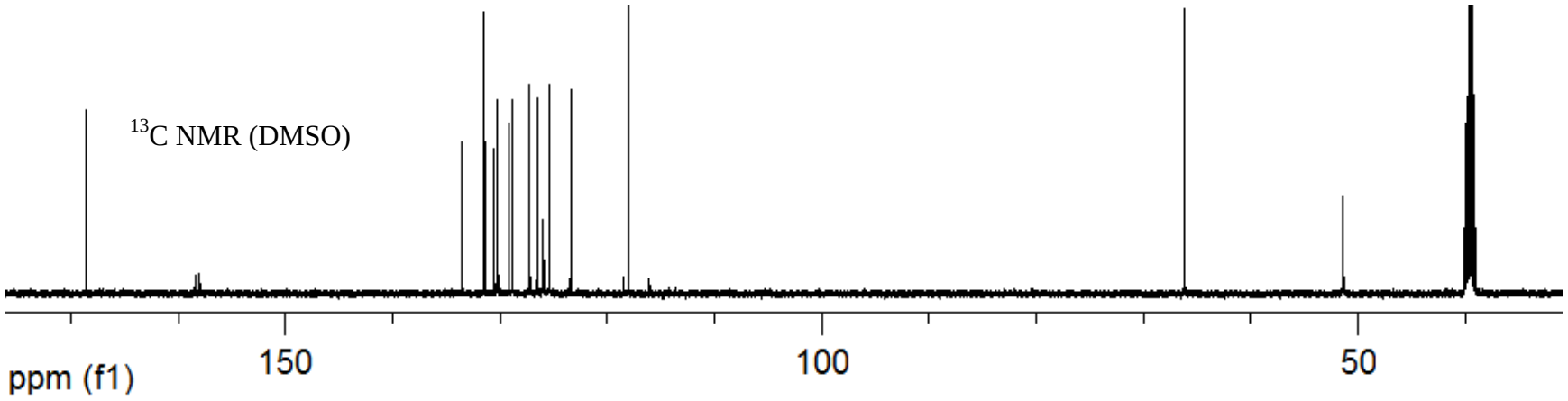


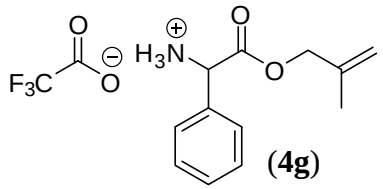
(**4f**)

^{1}H NMR (DMSO)



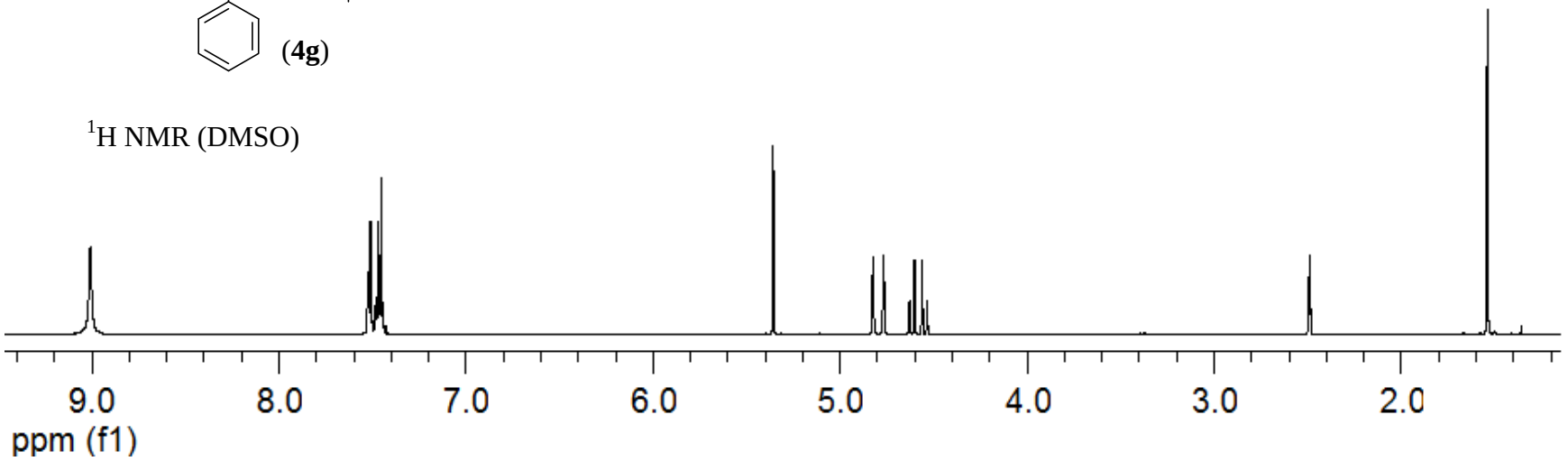
^{13}C NMR (DMSO)



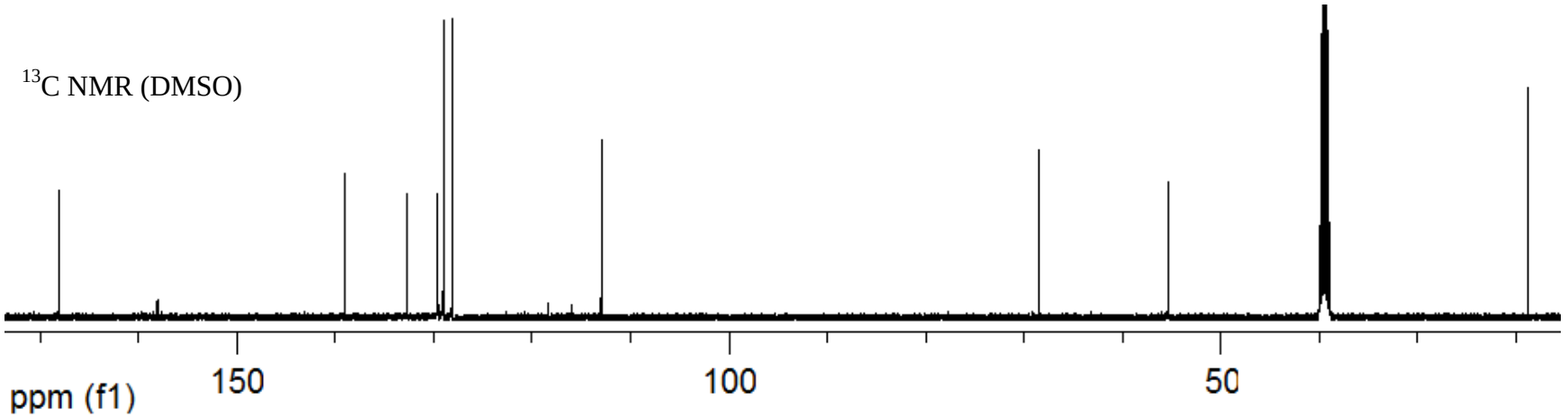


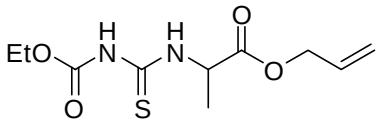
(**4g**)

^{1}H NMR (DMSO)



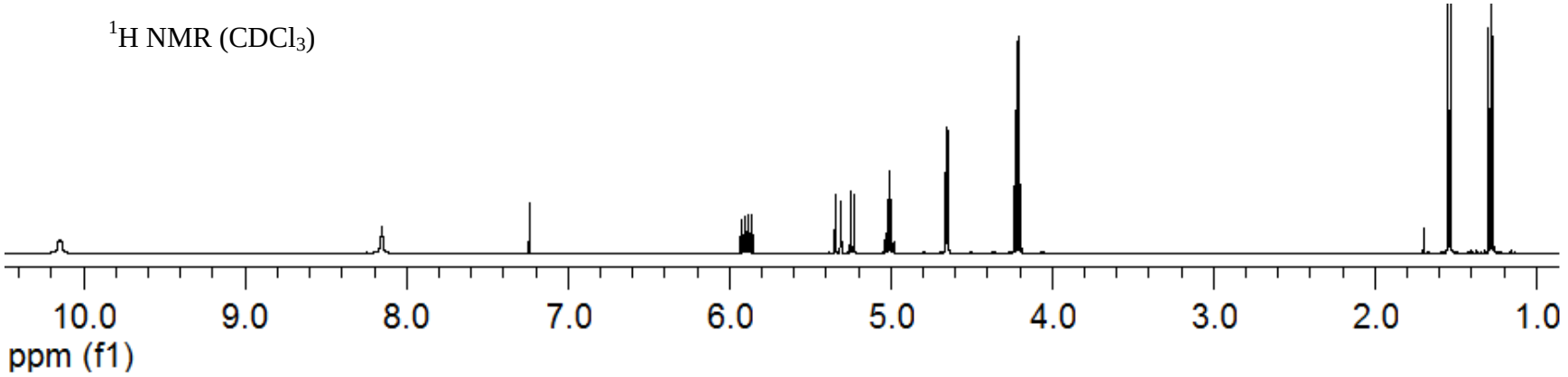
^{13}C NMR (DMSO)



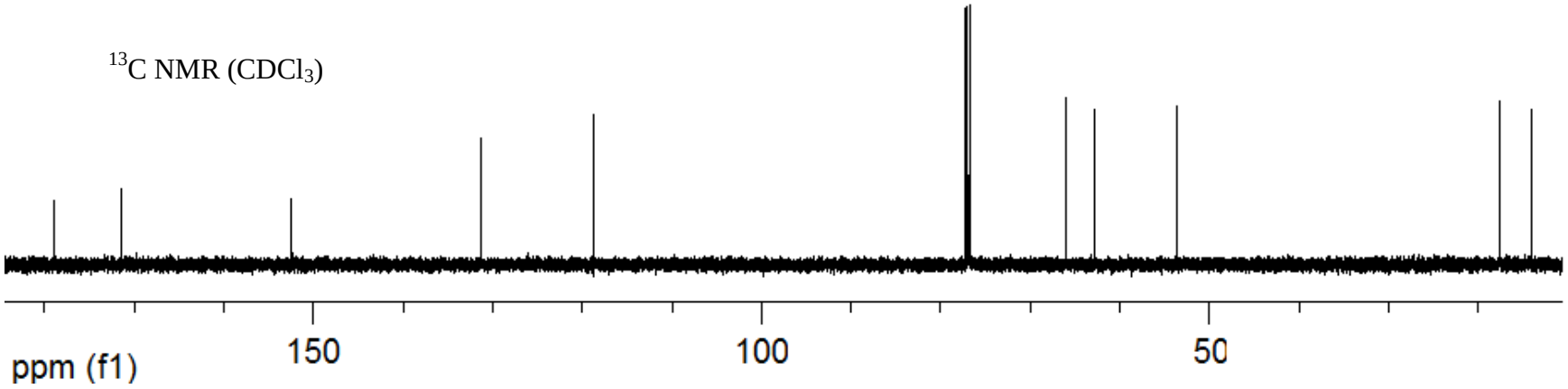


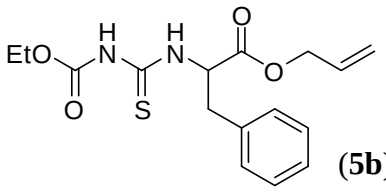
(**5a**)

^{1}H NMR ($CDCl_3$)



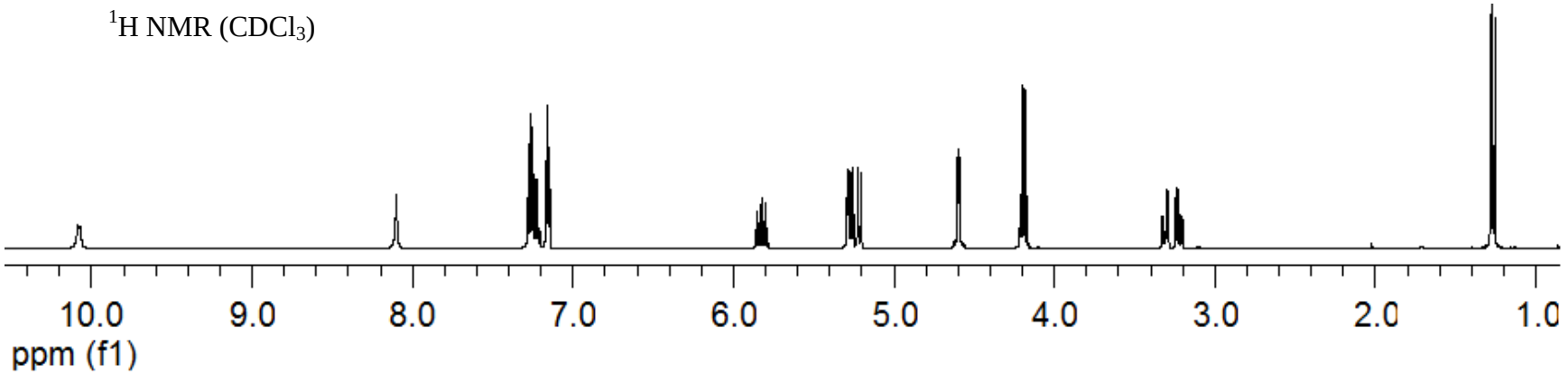
^{13}C NMR ($CDCl_3$)



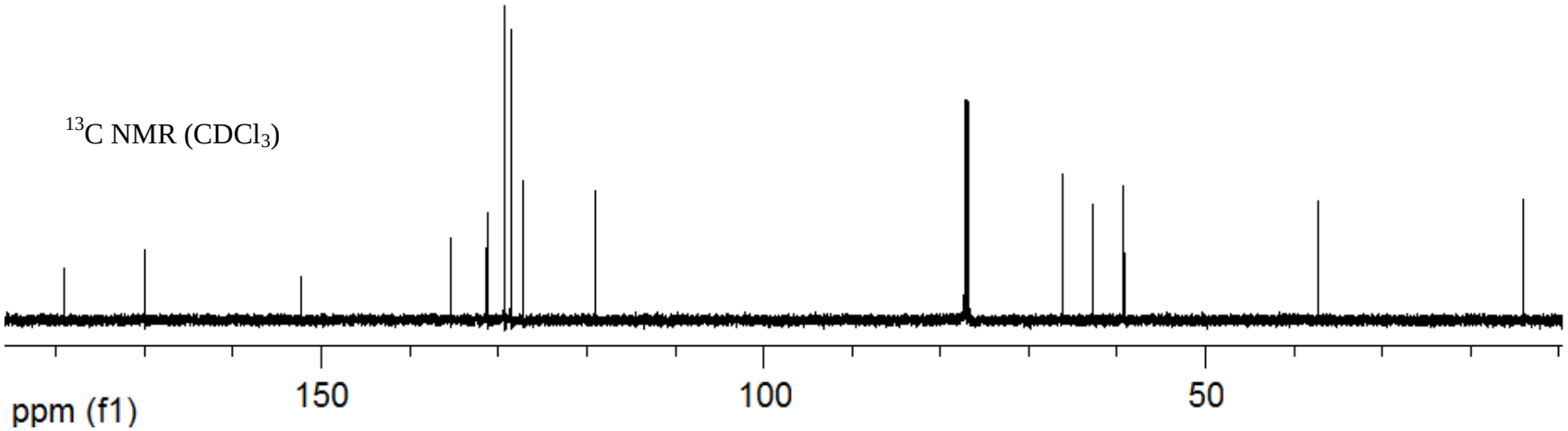


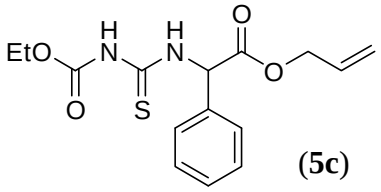
(**5b**)

^{1}H NMR ($CDCl_3$)



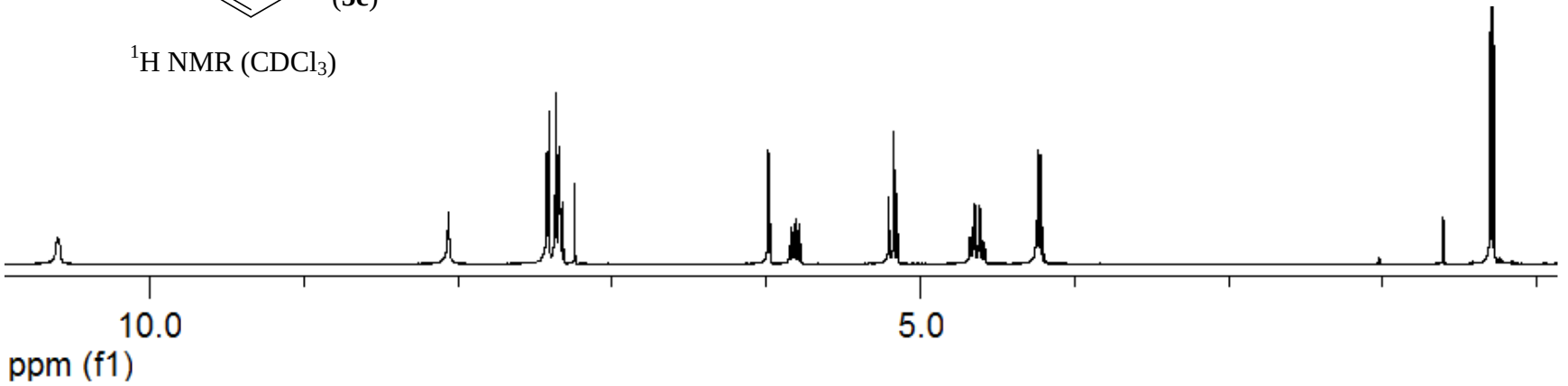
^{13}C NMR ($CDCl_3$)



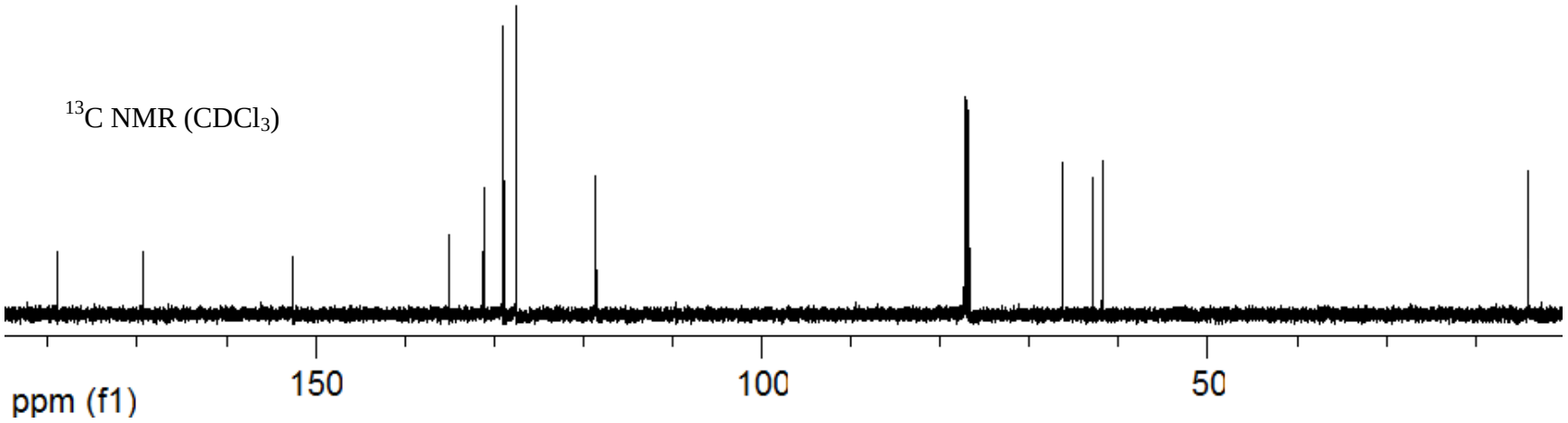


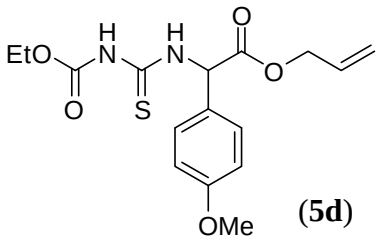
(**5c**)

^{1}H NMR ($CDCl_3$)



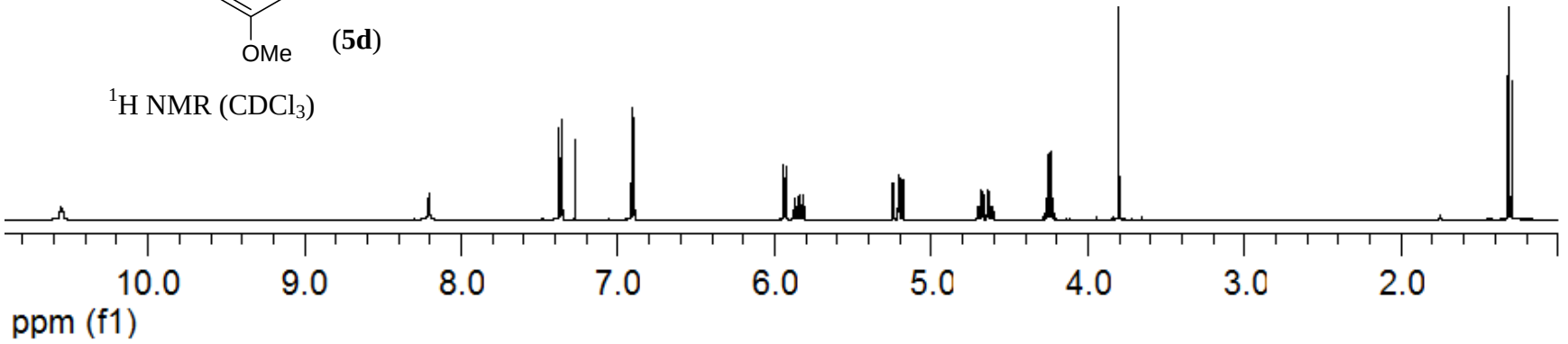
^{13}C NMR ($CDCl_3$)



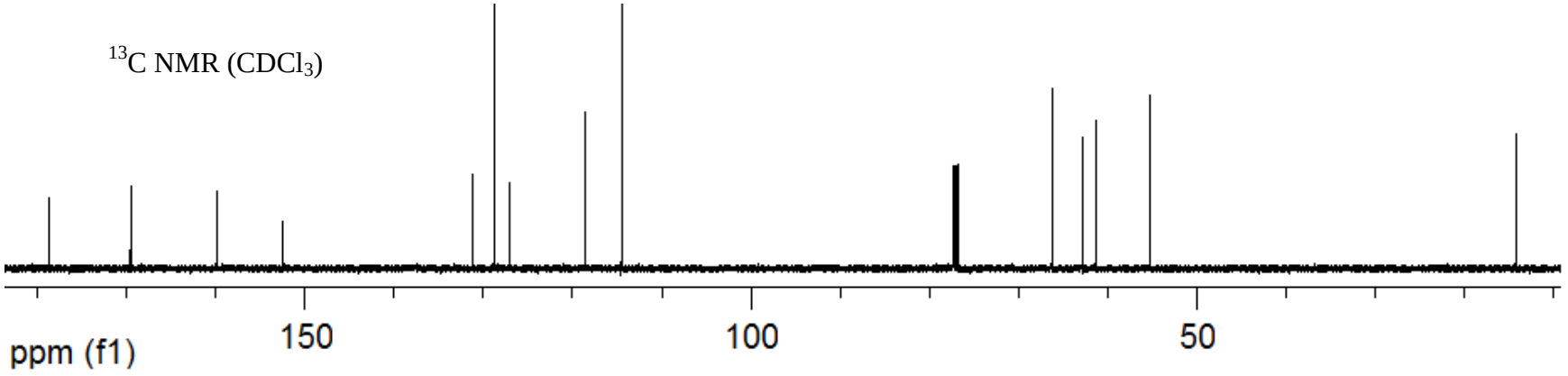


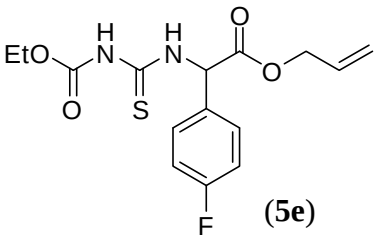
(5d)

^{1}H NMR ($CDCl_3$)



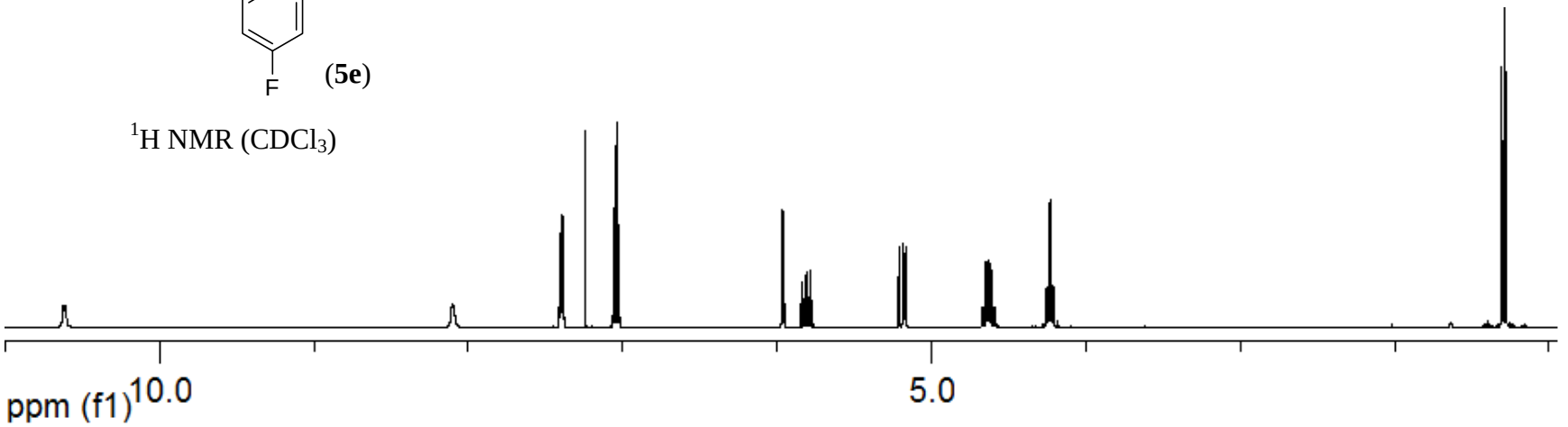
^{13}C NMR ($CDCl_3$)



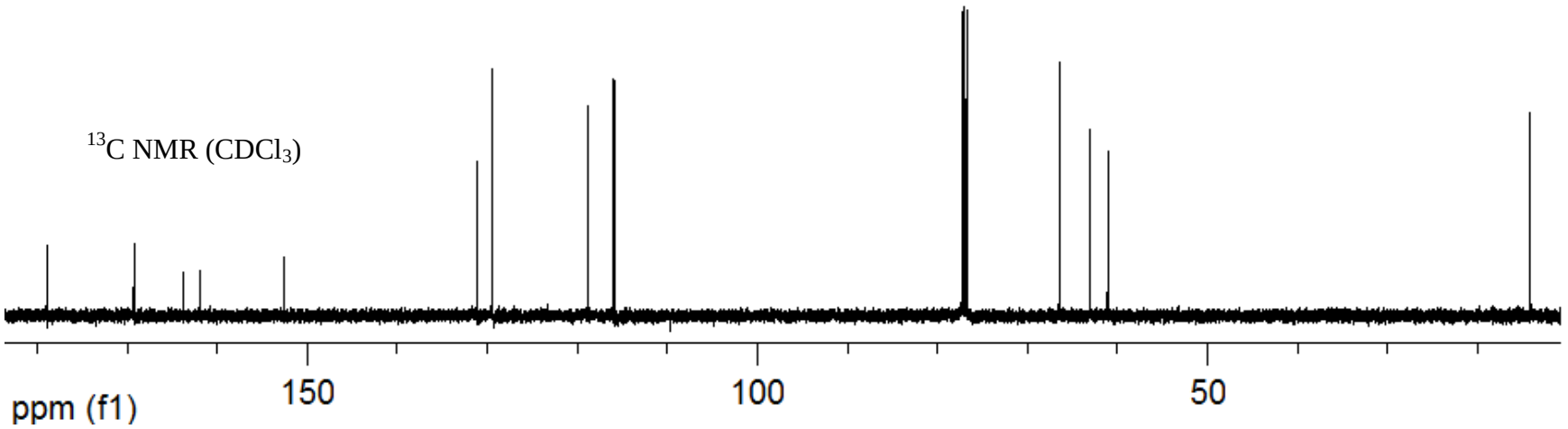


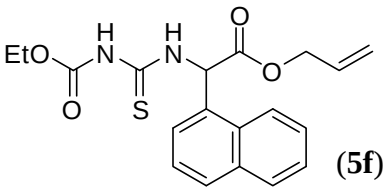
(5e)

^{1}H NMR ($CDCl_3$)



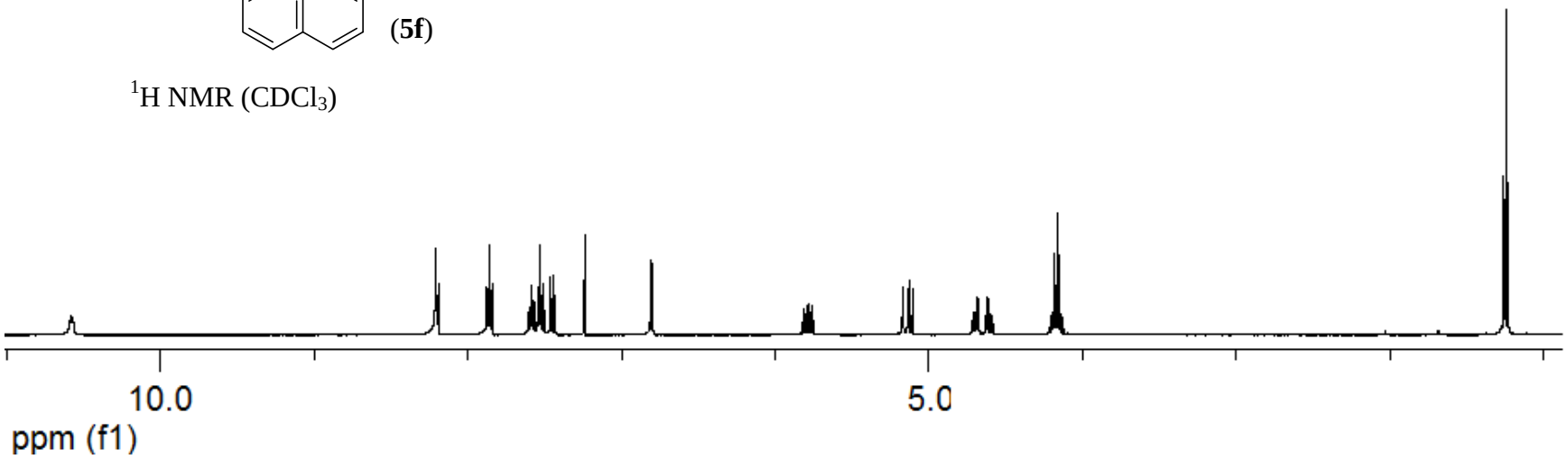
^{13}C NMR ($CDCl_3$)



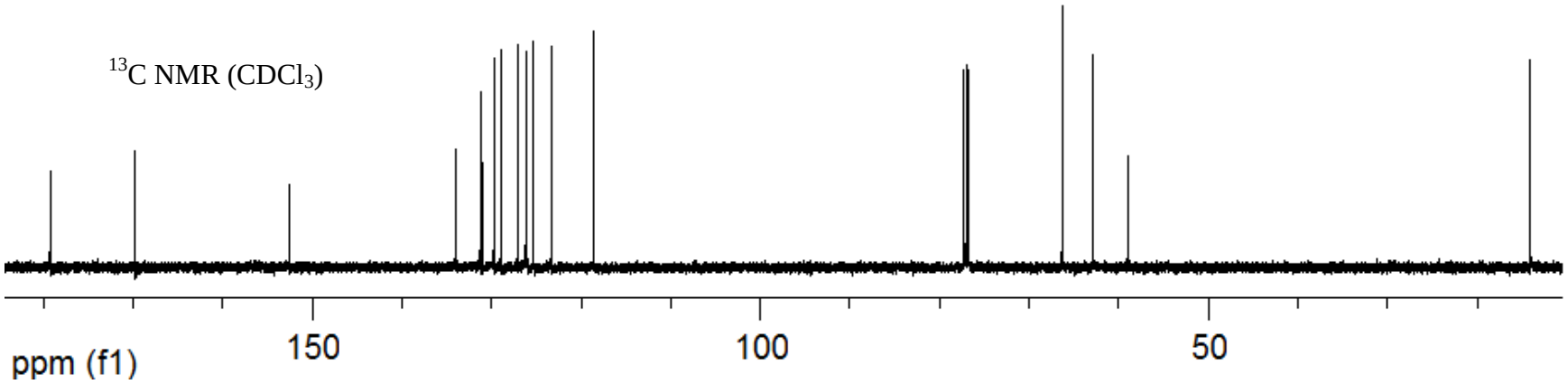


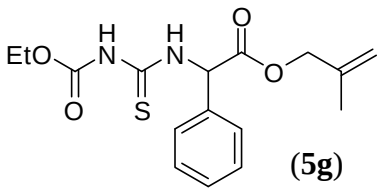
(**5f**)

^{1}H NMR ($CDCl_3$)



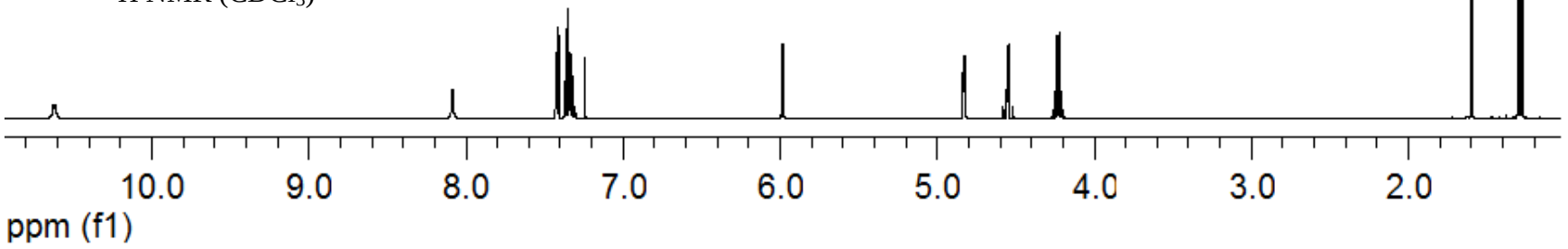
^{13}C NMR ($CDCl_3$)



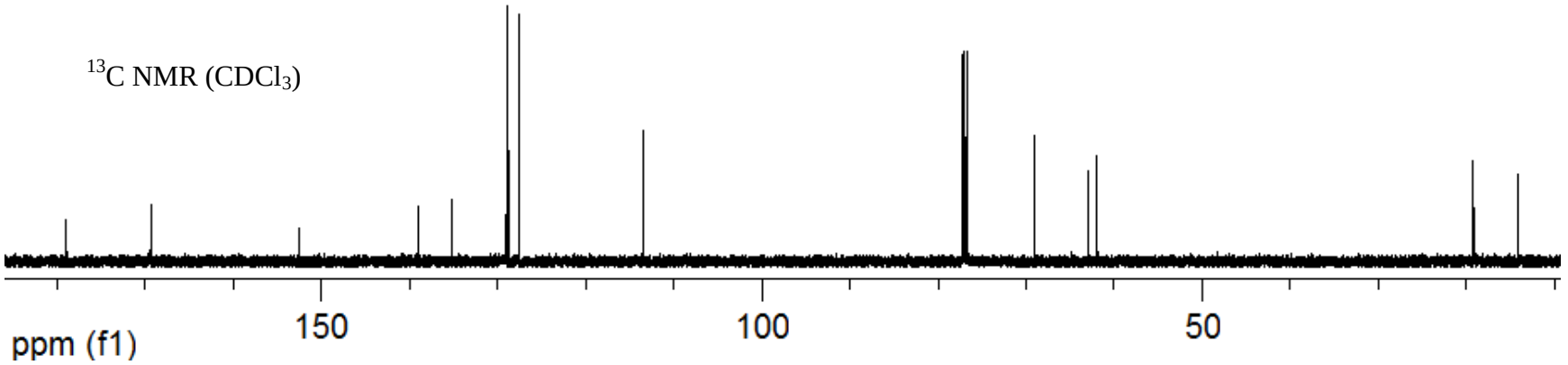


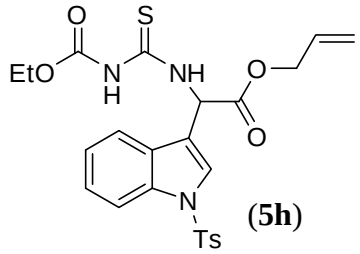
(5g)

^{1}H NMR ($CDCl_3$)



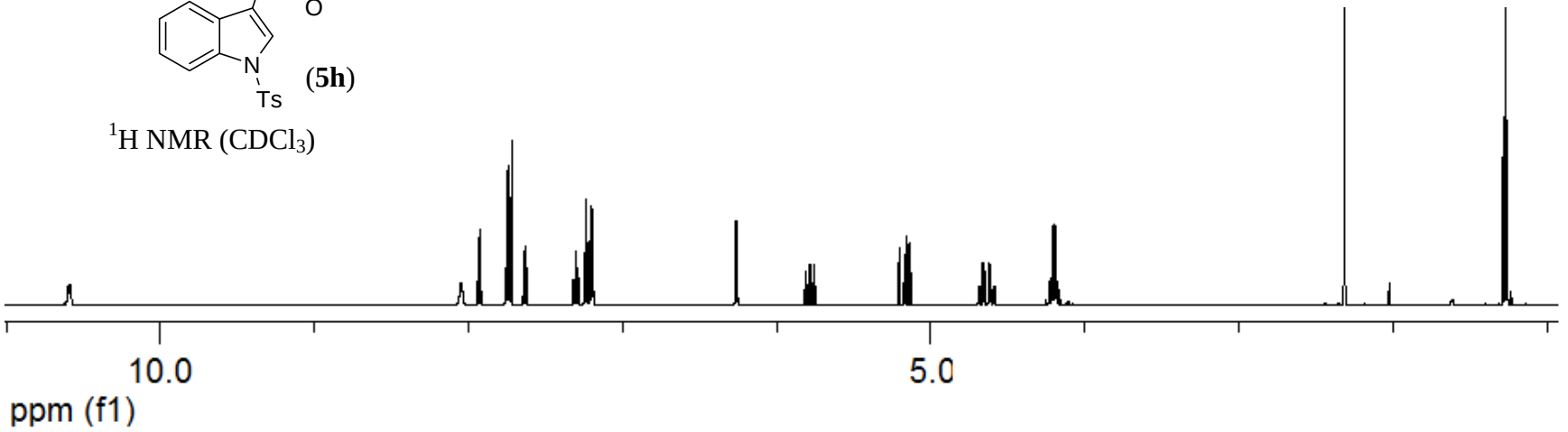
^{13}C NMR ($CDCl_3$)



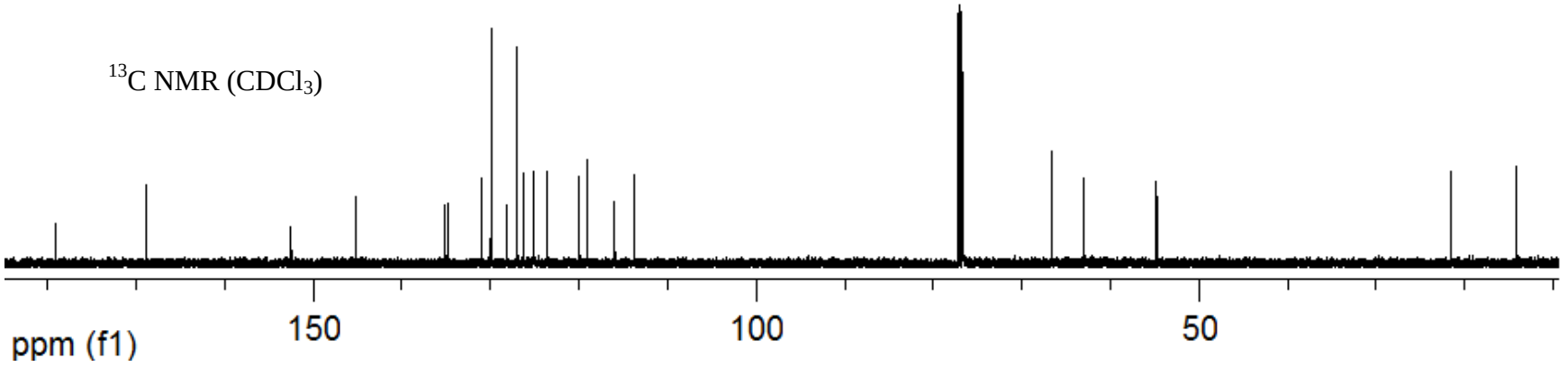


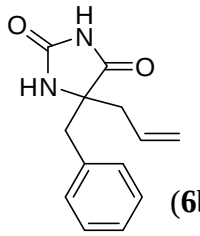
(**5h**)

^{1}H NMR ($CDCl_3$)



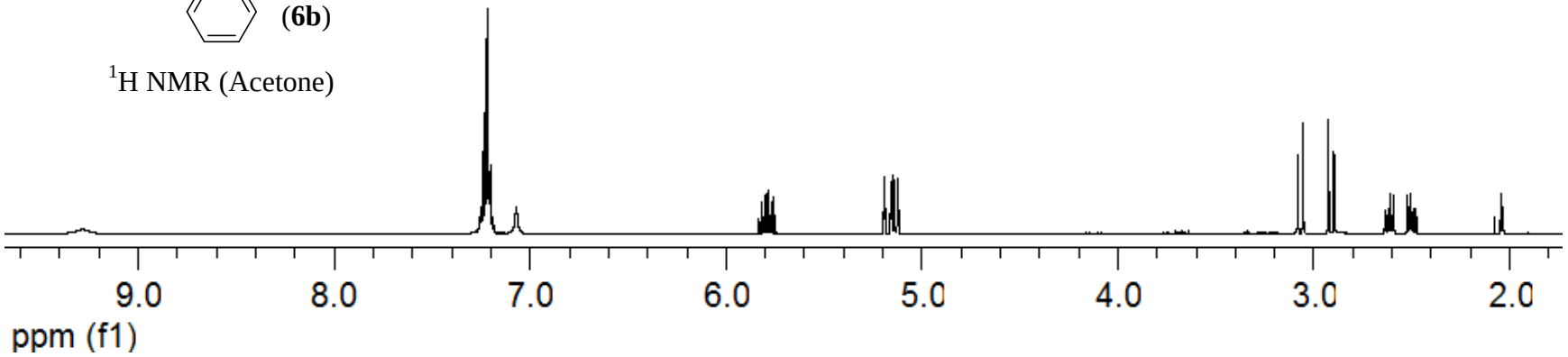
^{13}C NMR ($CDCl_3$)



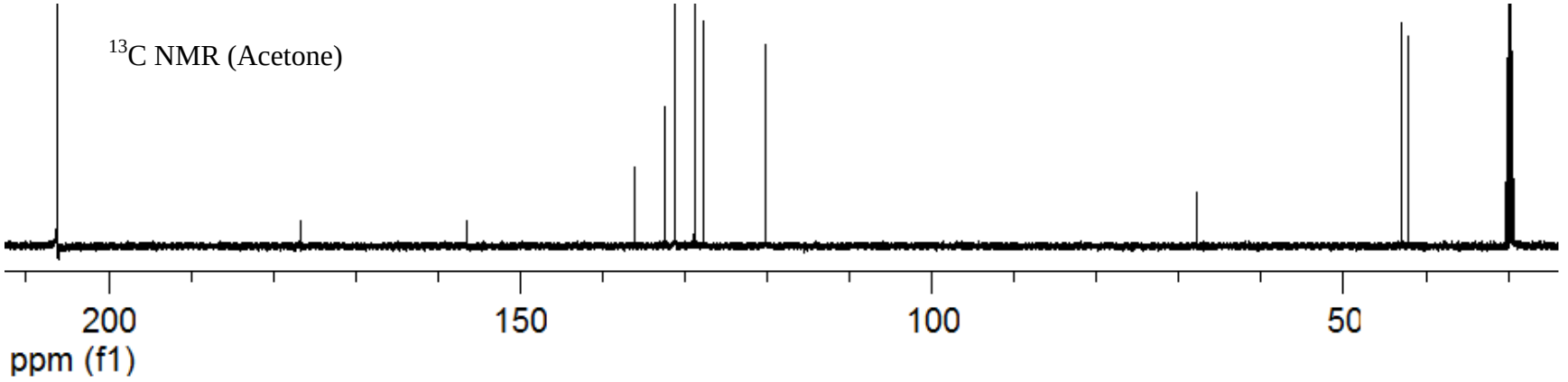


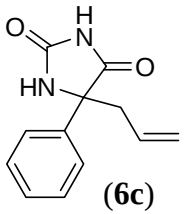
(**6b**)

^{1}H NMR (Acetone)



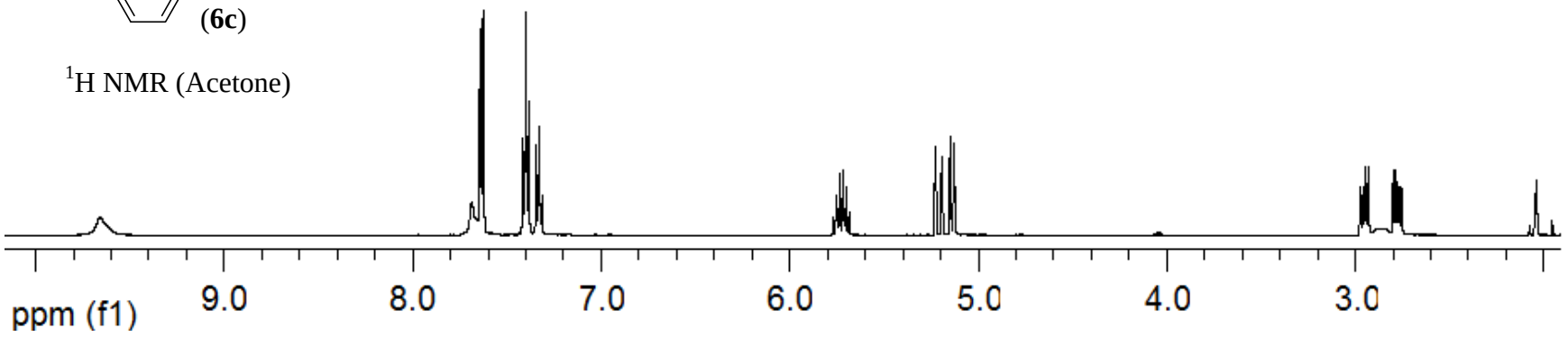
^{13}C NMR (Acetone)



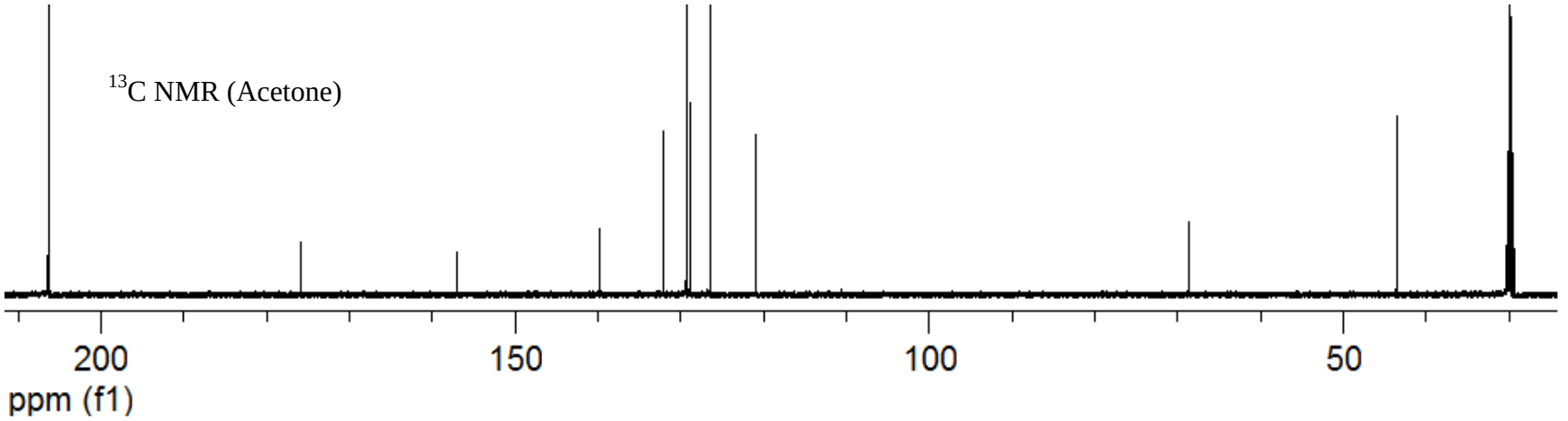


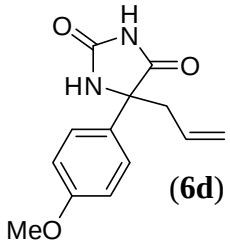
(**6c**)

^{1}H NMR (Acetone)



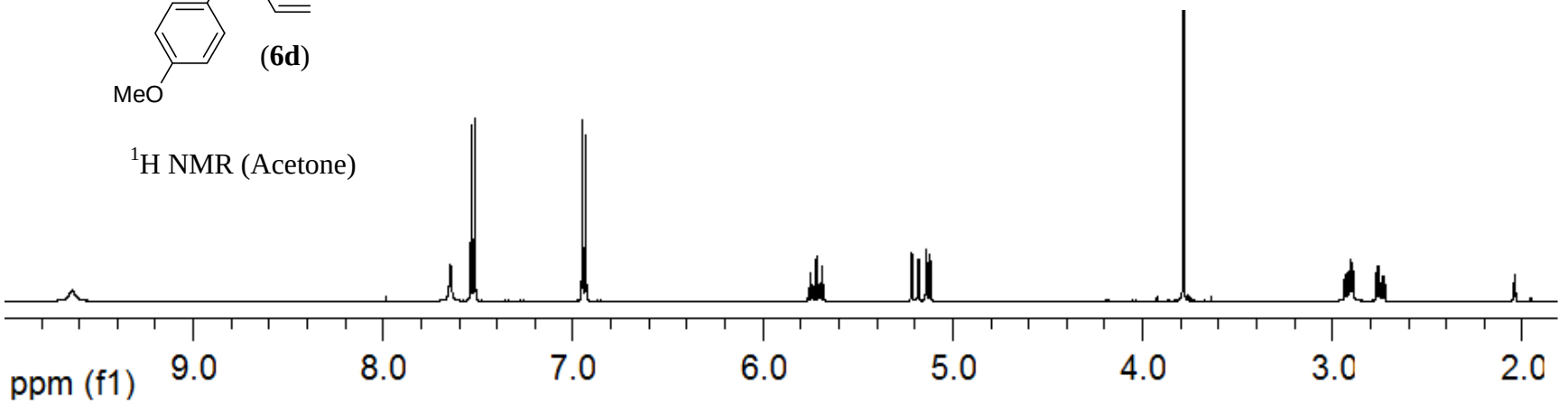
^{13}C NMR (Acetone)



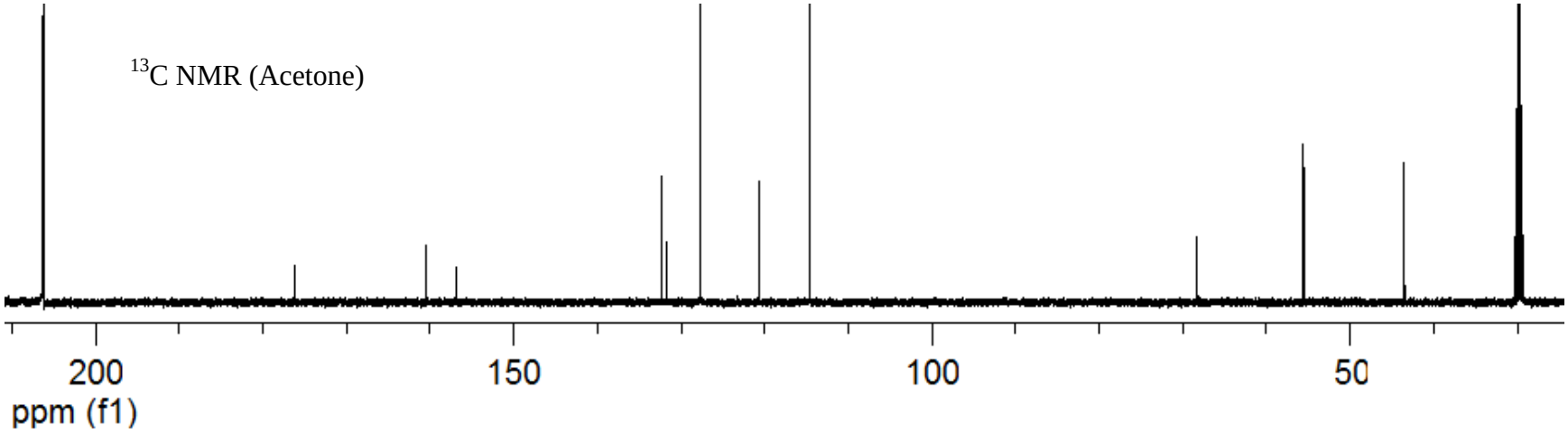


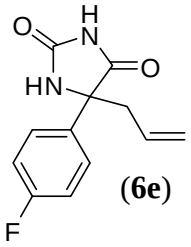
(**6d**)

^{1}H NMR (Acetone)



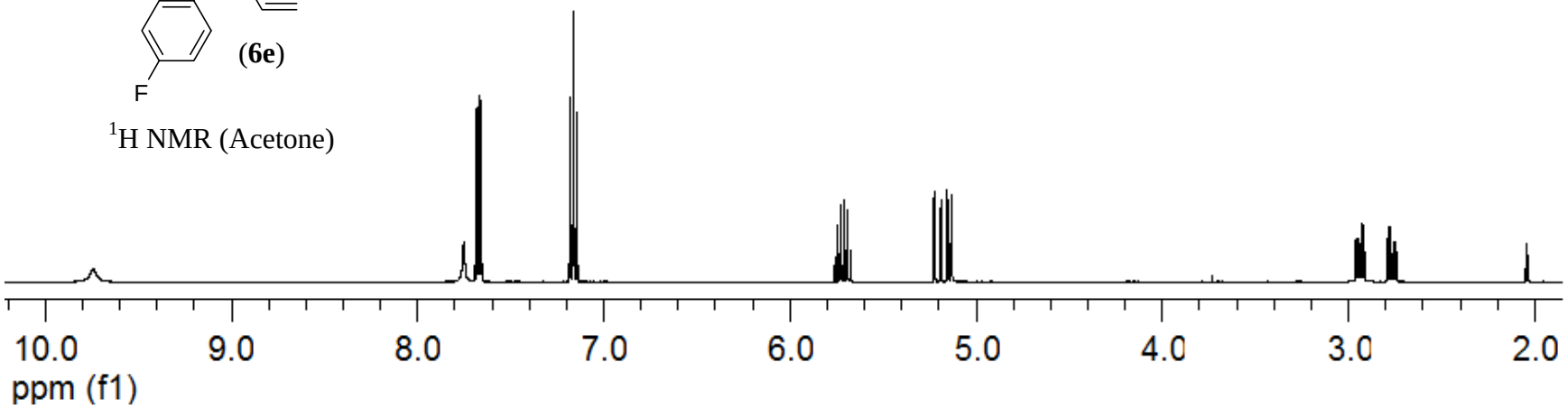
^{13}C NMR (Acetone)



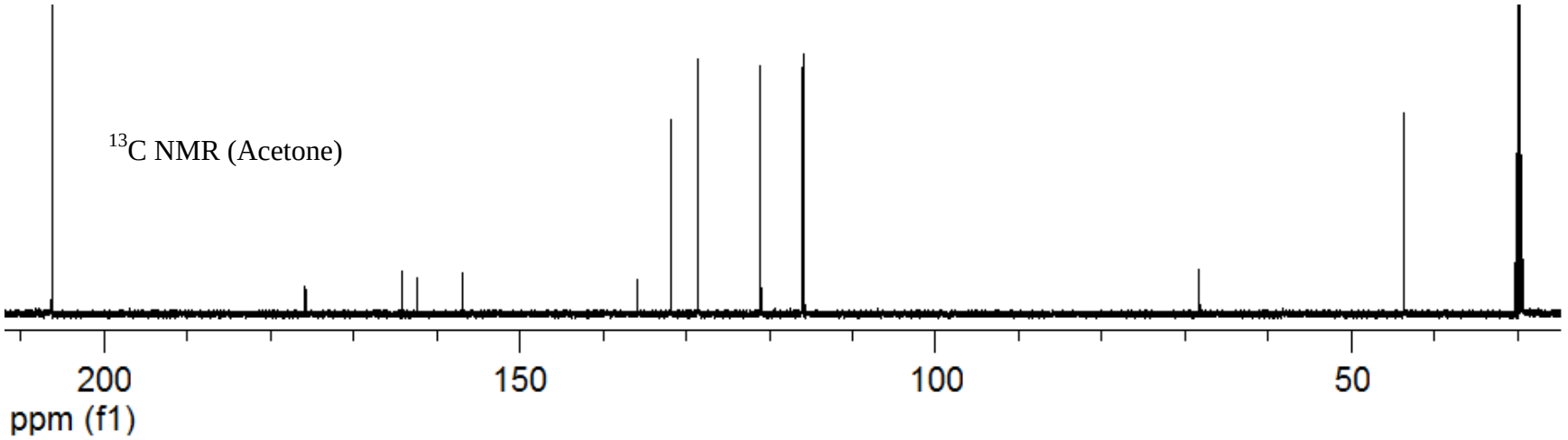


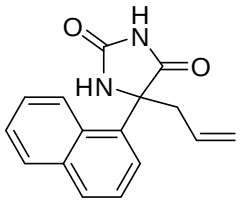
(**6e**)

^{1}H NMR (Acetone)



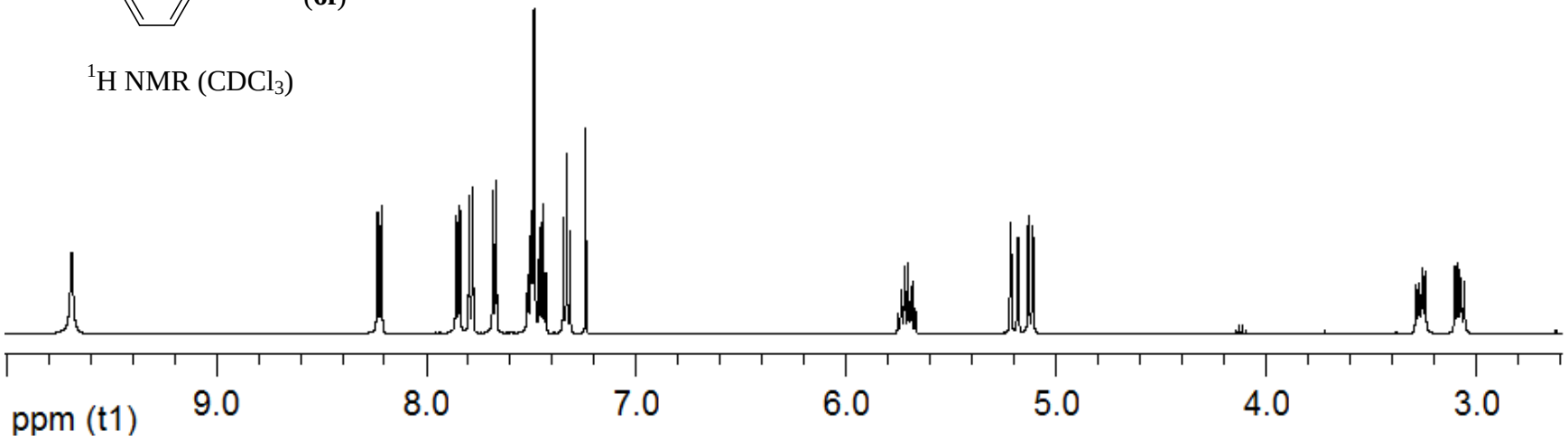
^{13}C NMR (Acetone)



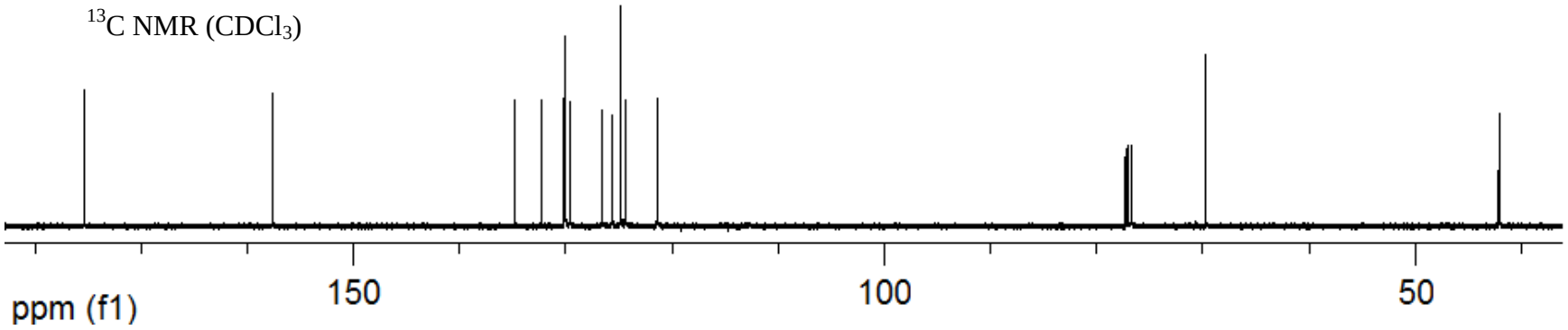


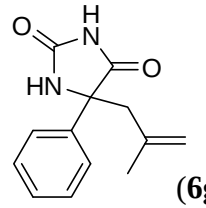
(**6f**)

^{1}H NMR ($CDCl_3$)



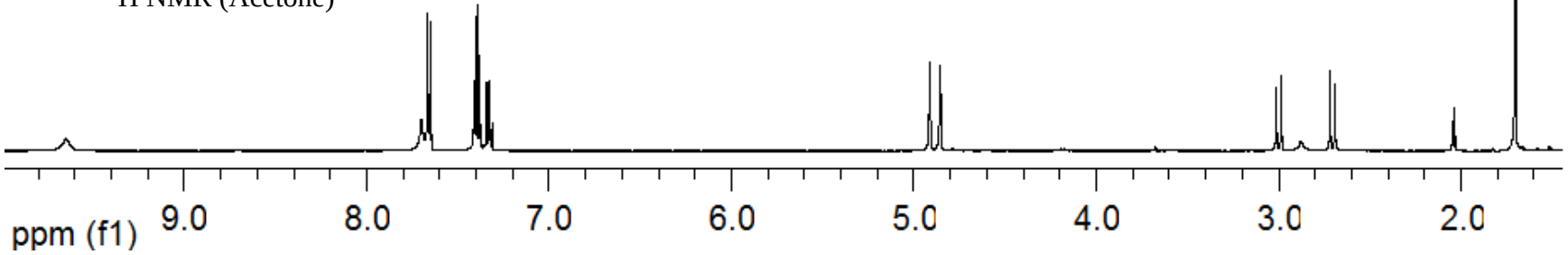
^{13}C NMR ($CDCl_3$)



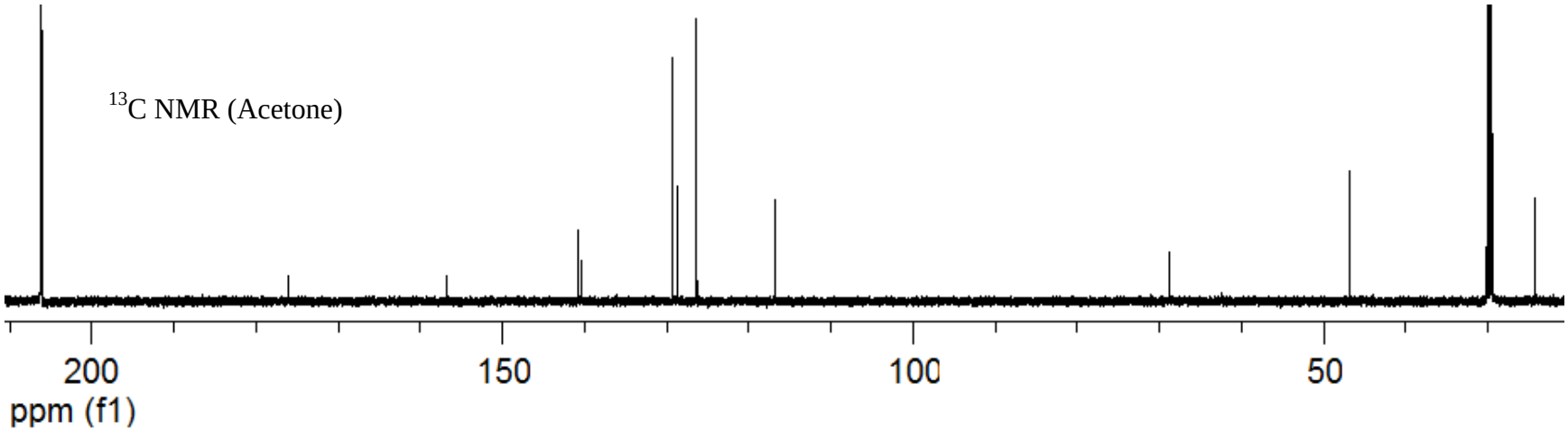


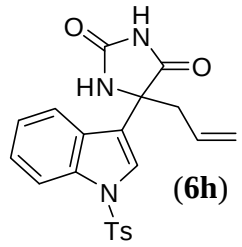
(**6g**)

^{1}H NMR (Acetone)



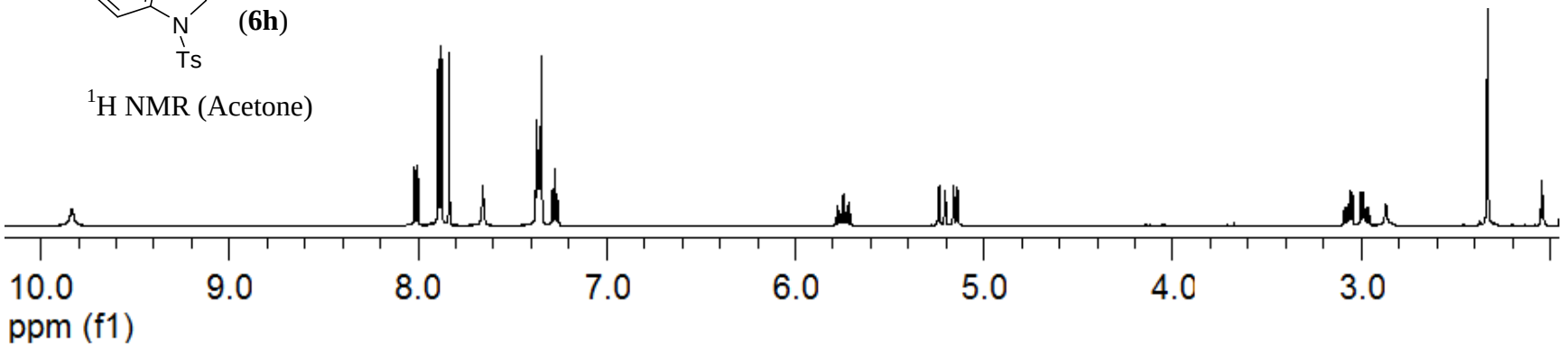
^{13}C NMR (Acetone)



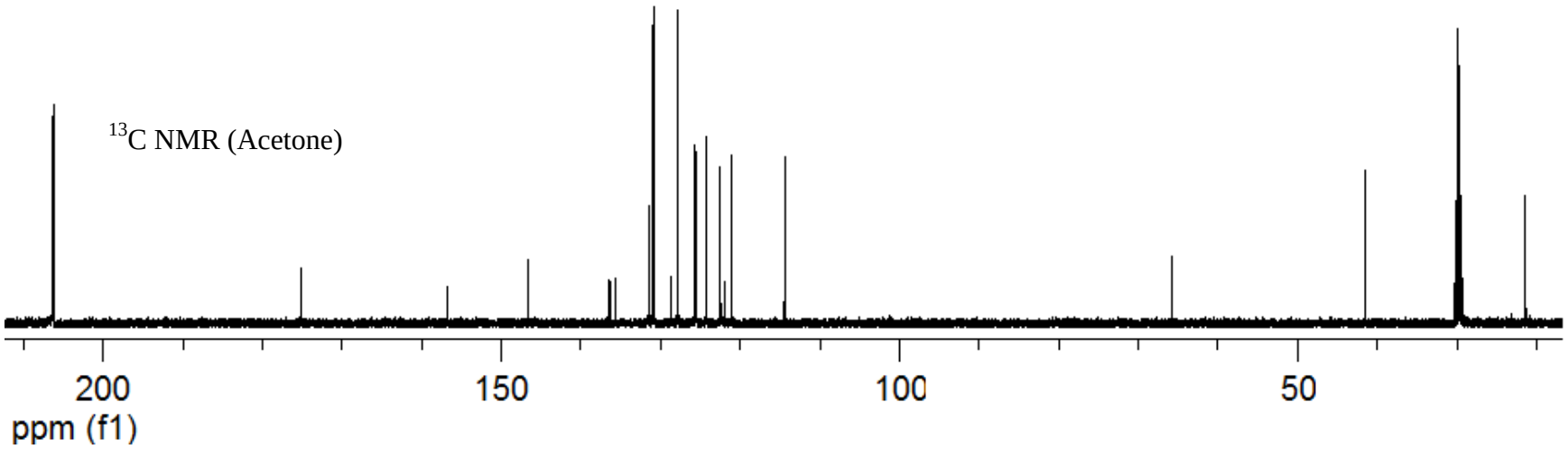


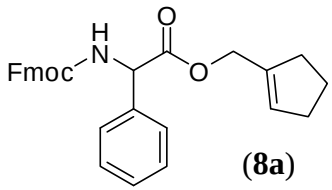
(**6h**)

^{1}H NMR (Acetone)



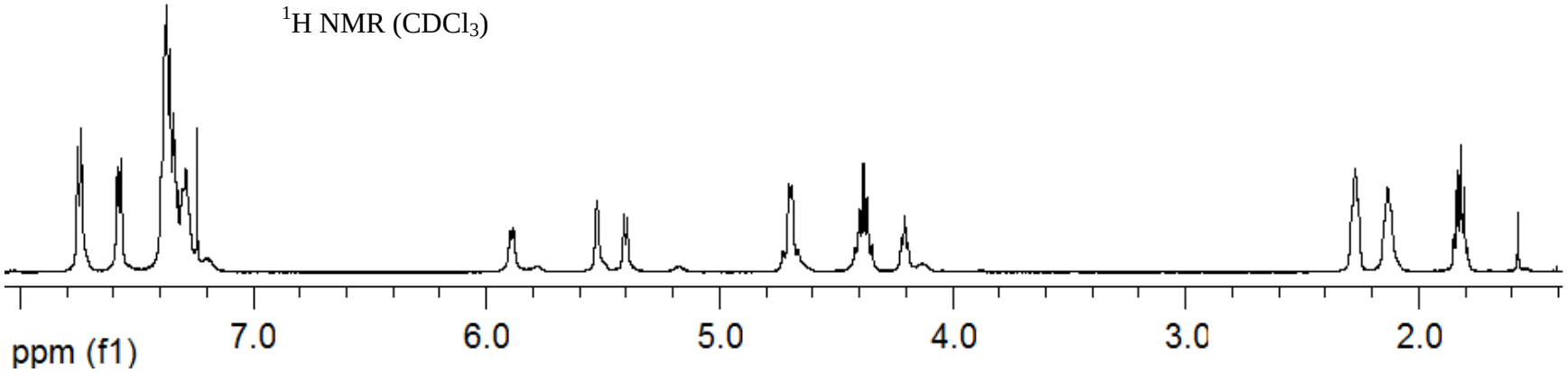
^{13}C NMR (Acetone)



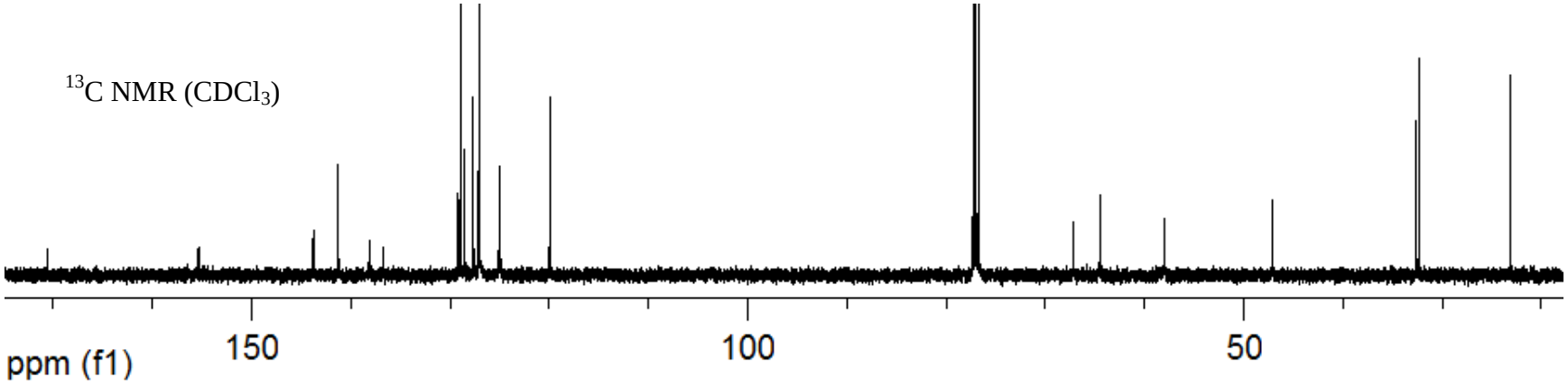


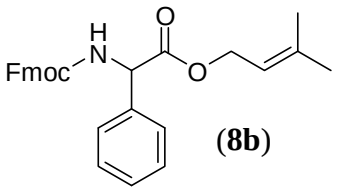
(**8a**)

^{1}H NMR ($CDCl_3$)



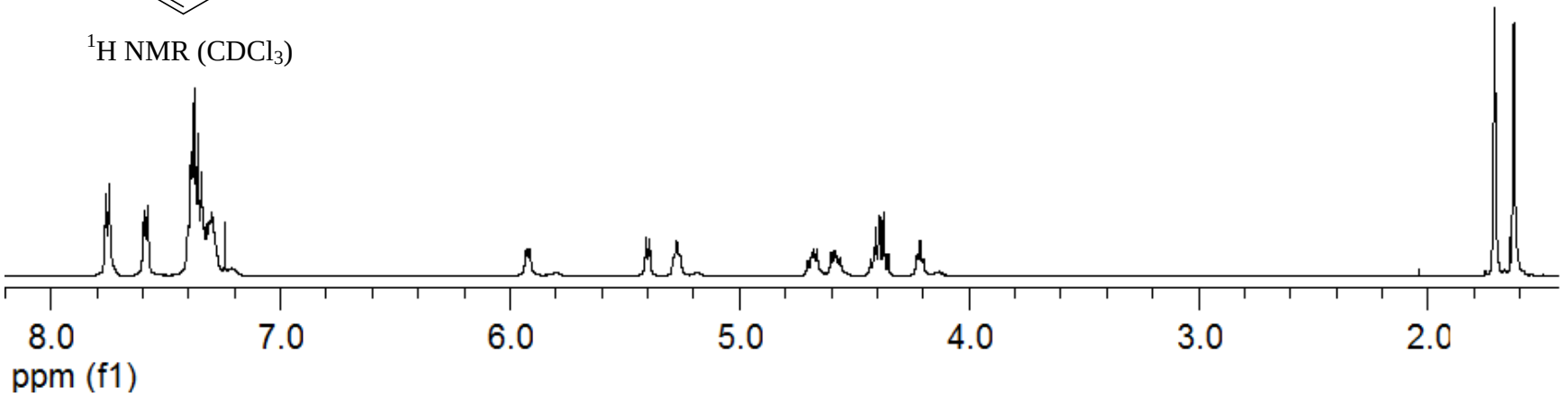
^{13}C NMR ($CDCl_3$)



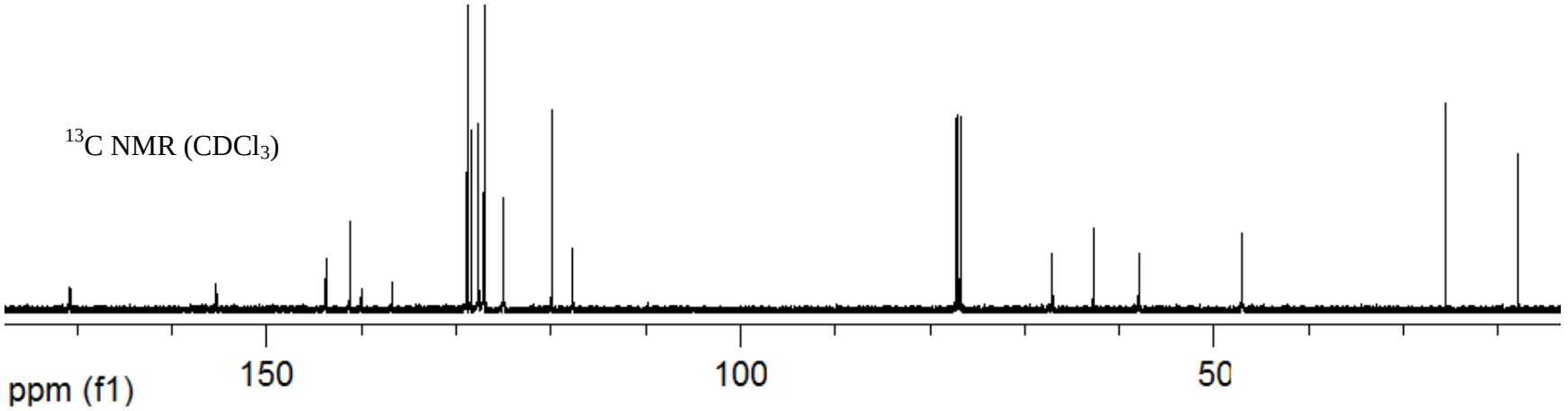


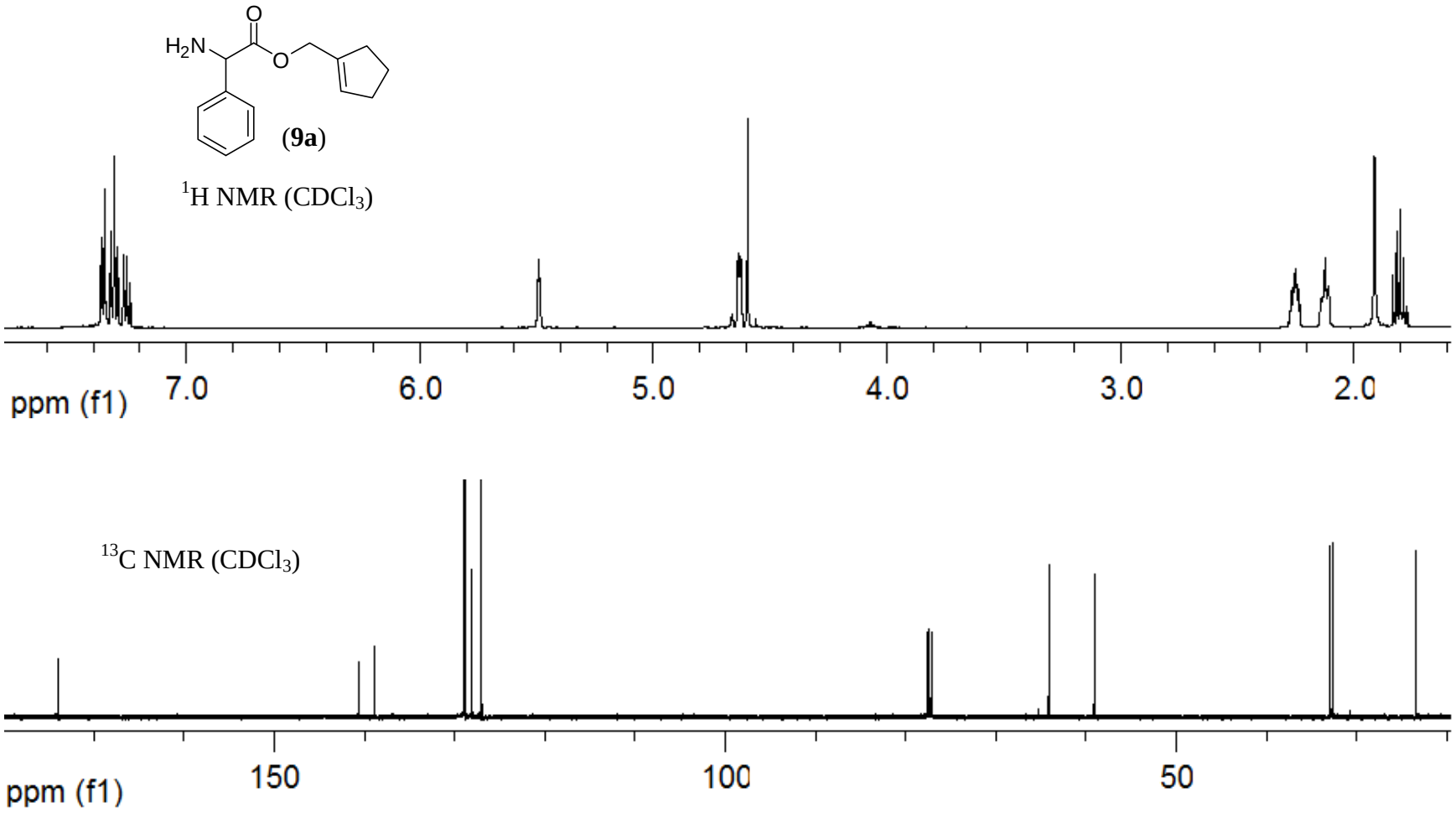
(**8b**)

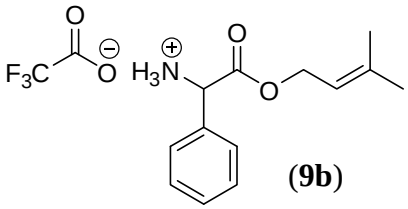
^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

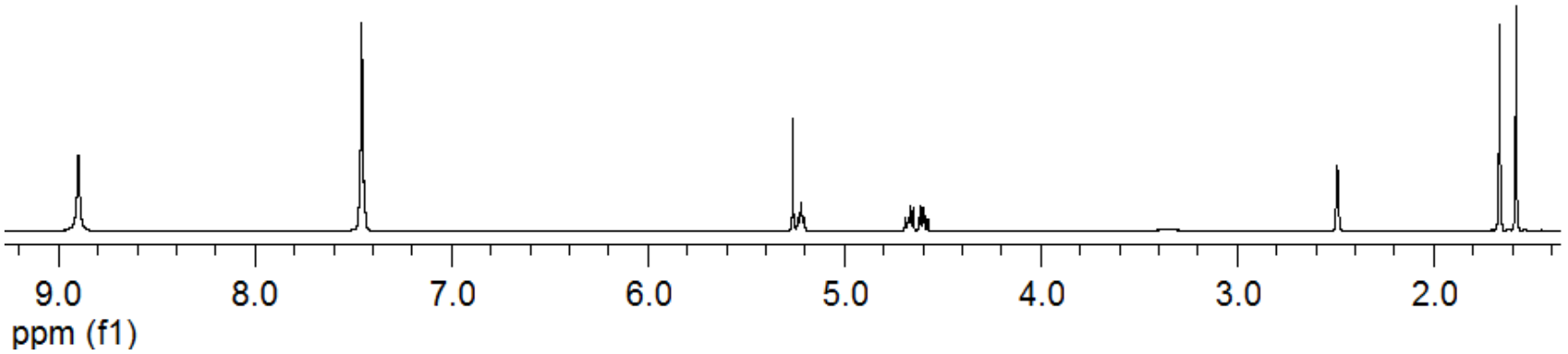



O
H2N
O
(9a)
1H NMR (CDCl3)
ppm (f1)
7.0
6.0
5.0
4.0
3.0
2.0
13C NMR (CDCl3)
ppm (f1)
150
100
50

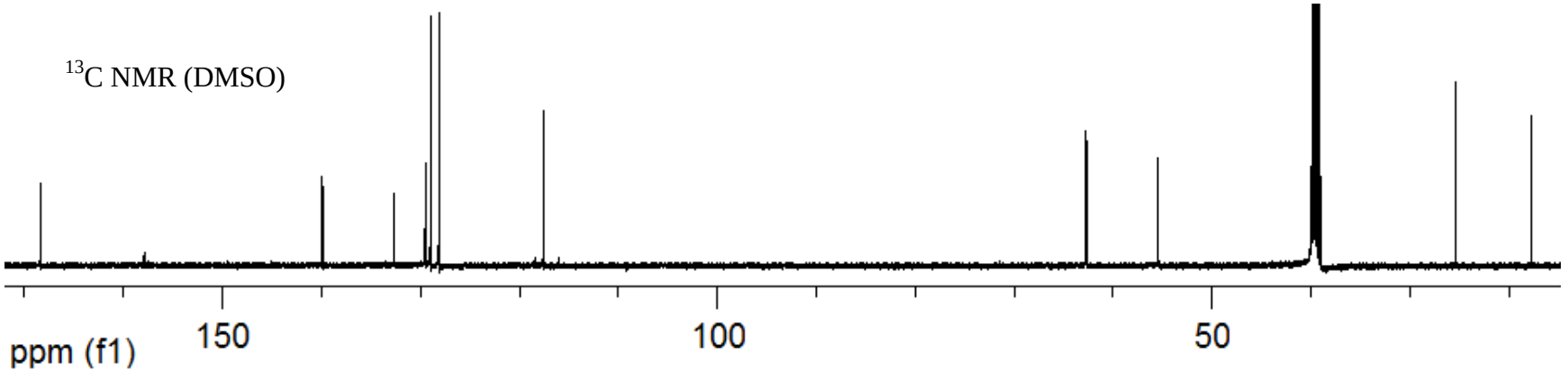


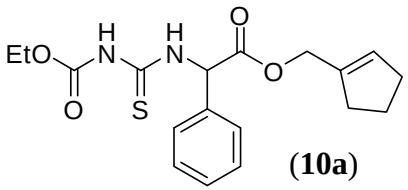
(**9b**)

^{1}H NMR (DMSO)



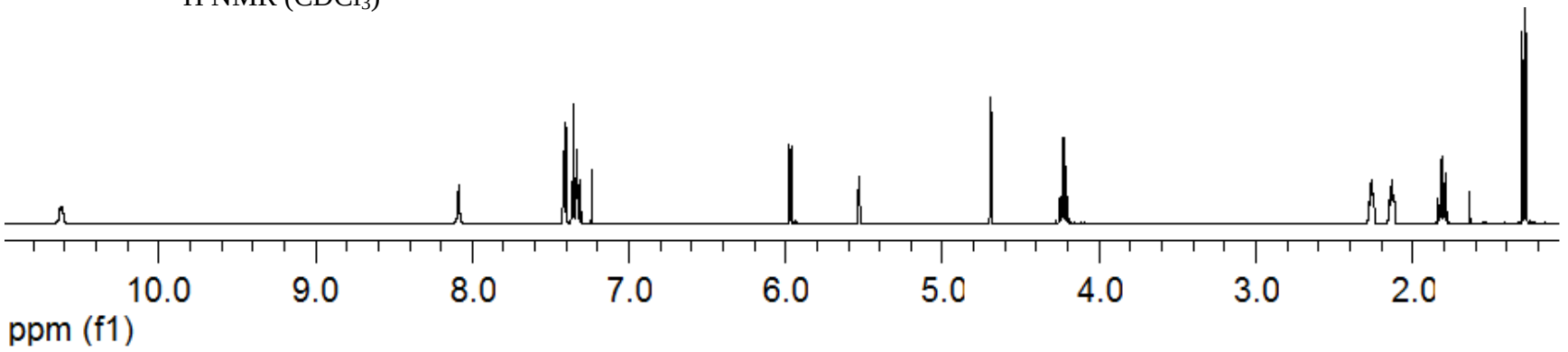
^{13}C NMR (DMSO)



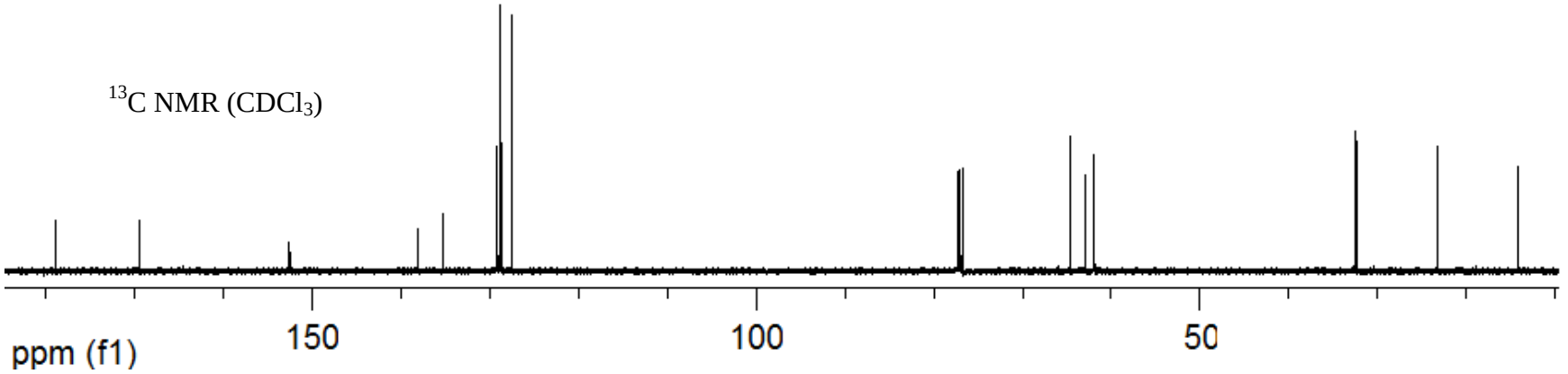


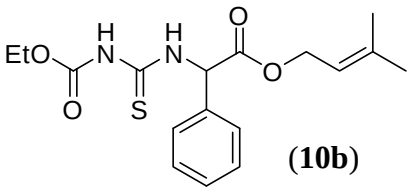
(**10a**)

^{1}H NMR ($CDCl_3$)



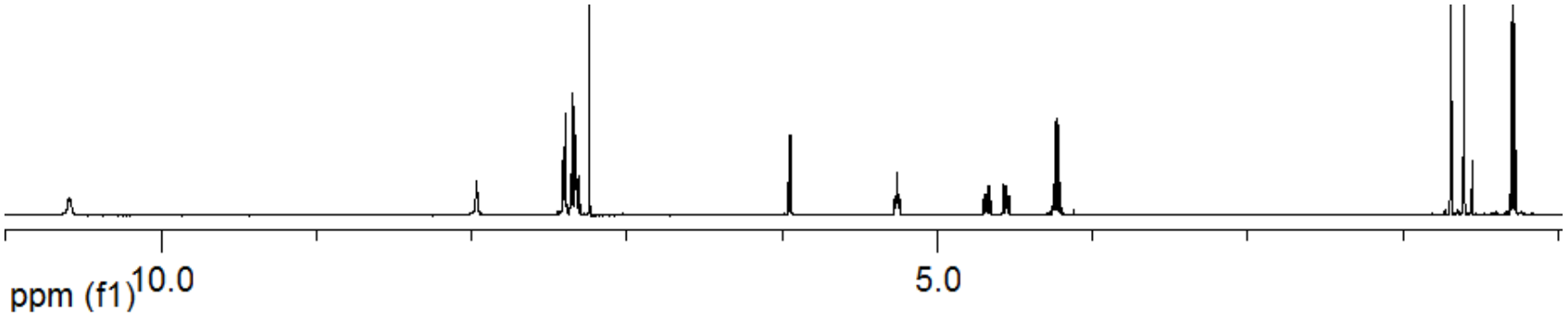
^{13}C NMR ($CDCl_3$)



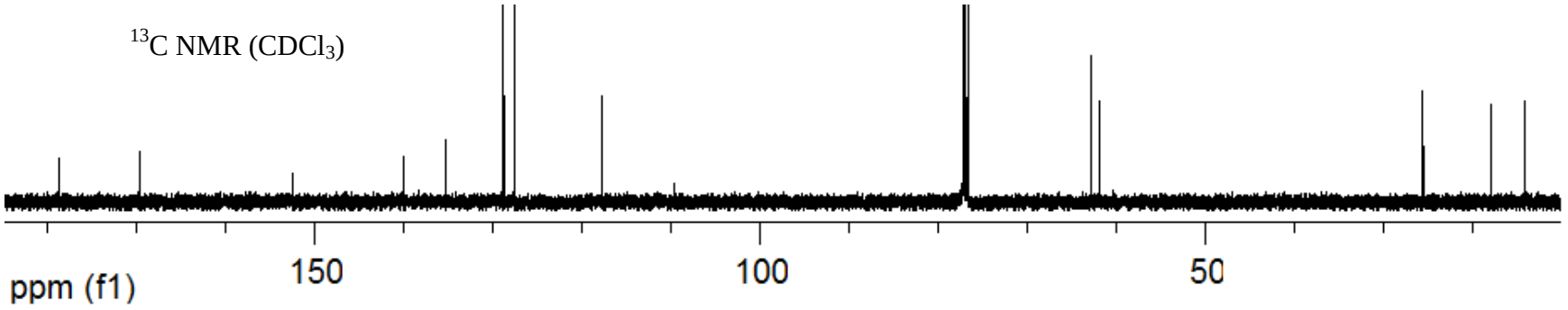


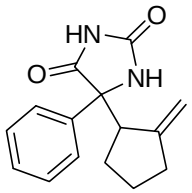
(**10b**)

^{1}H NMR ($CDCl_3$)



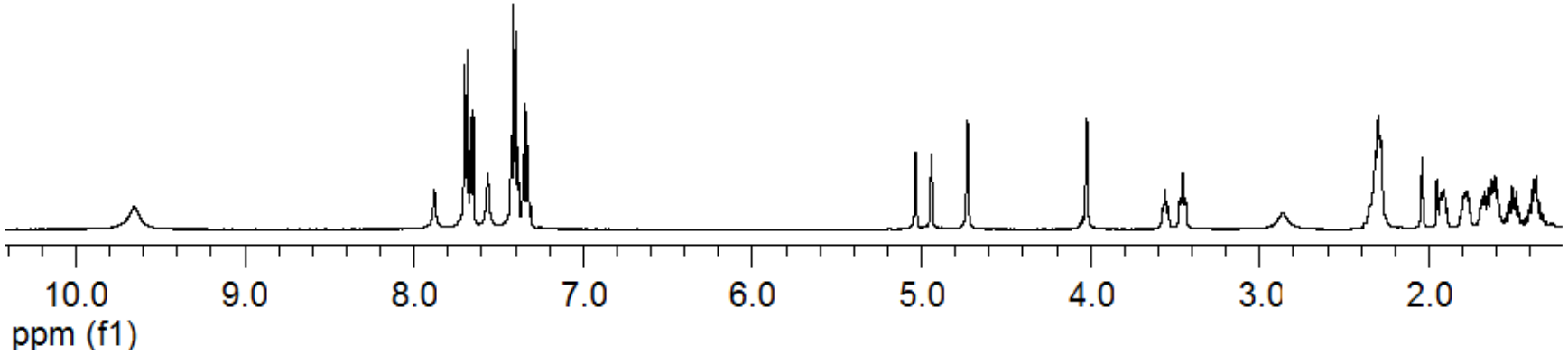
^{13}C NMR ($CDCl_3$)



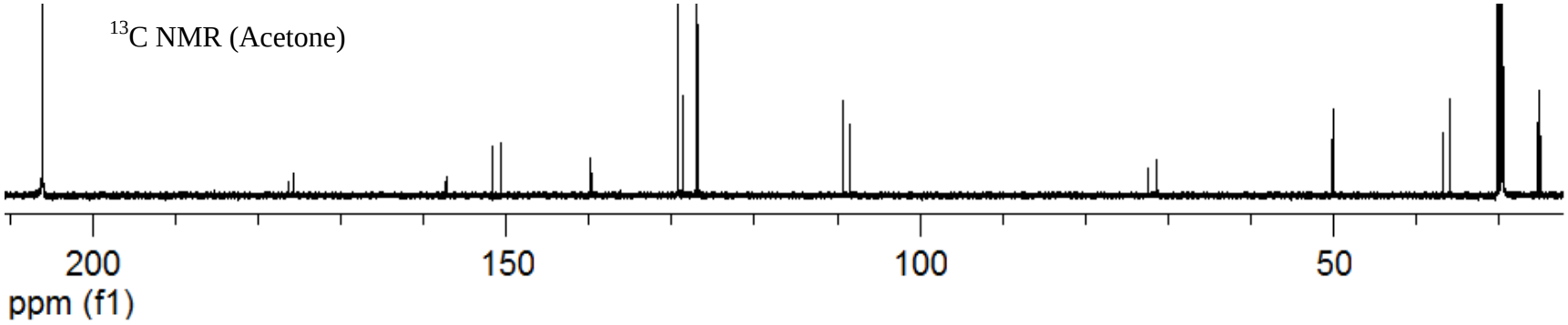


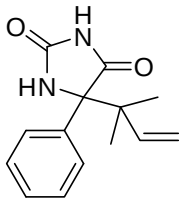
(**11a**)

^{1}H NMR (Acetone)



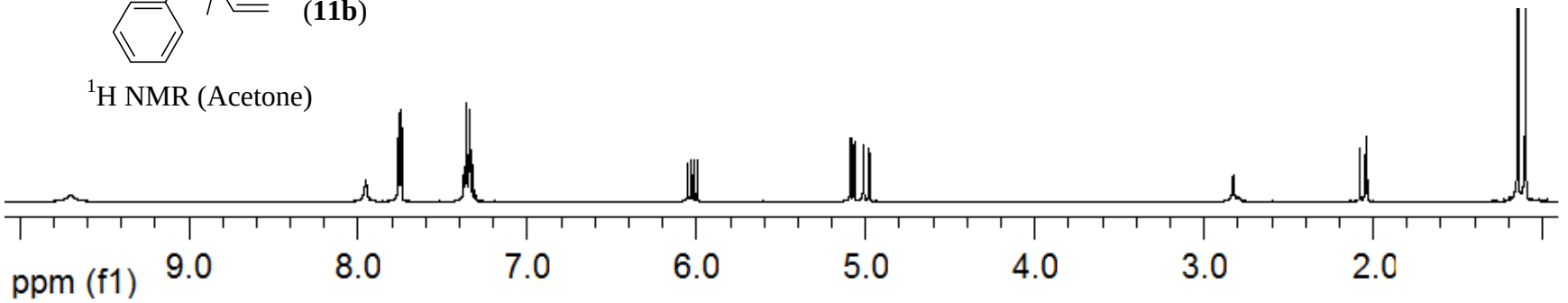
^{13}C NMR (Acetone)



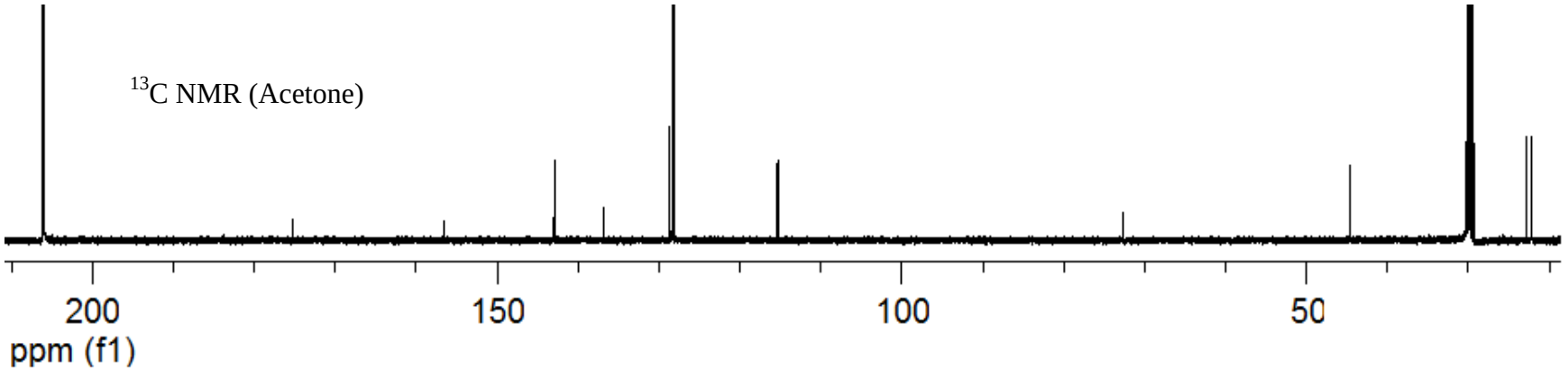


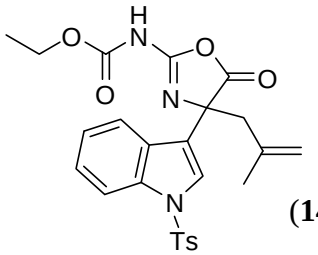
(**11b**)

^{1}H NMR (Acetone)



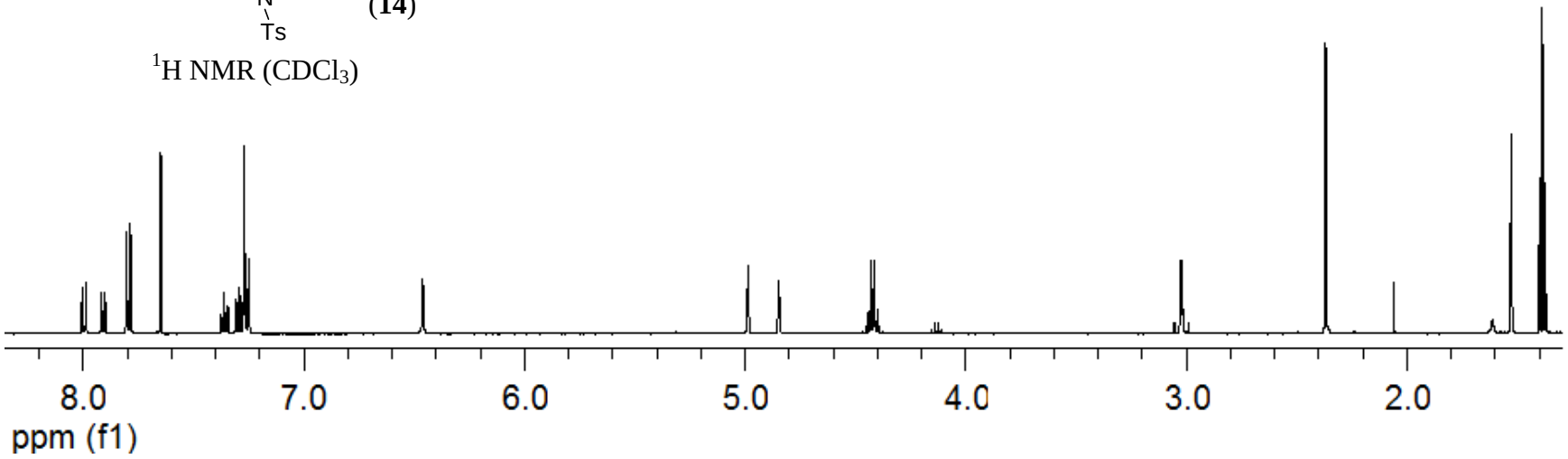
^{13}C NMR (Acetone)



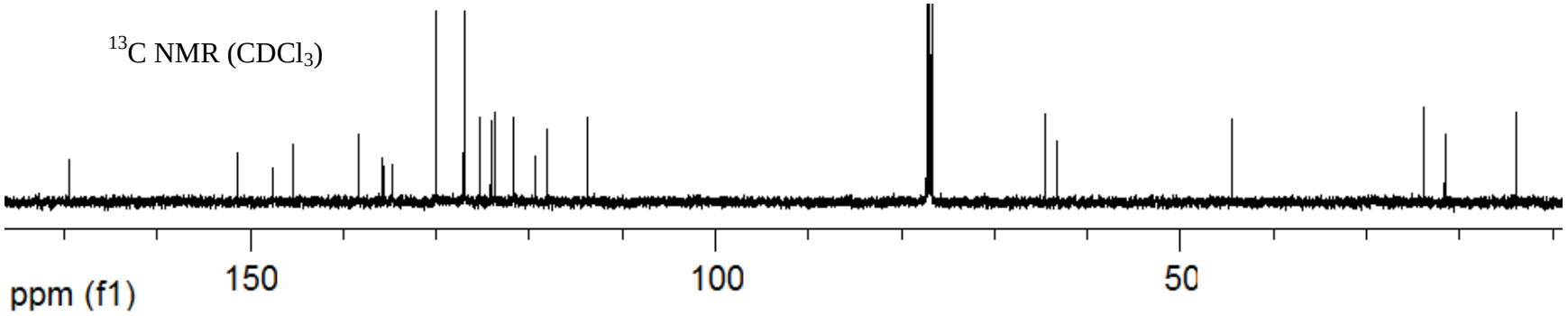


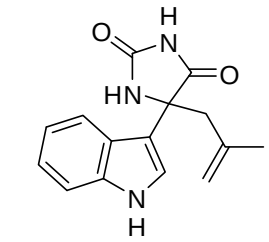
(**14**)

^{1}H NMR ($CDCl_3$)



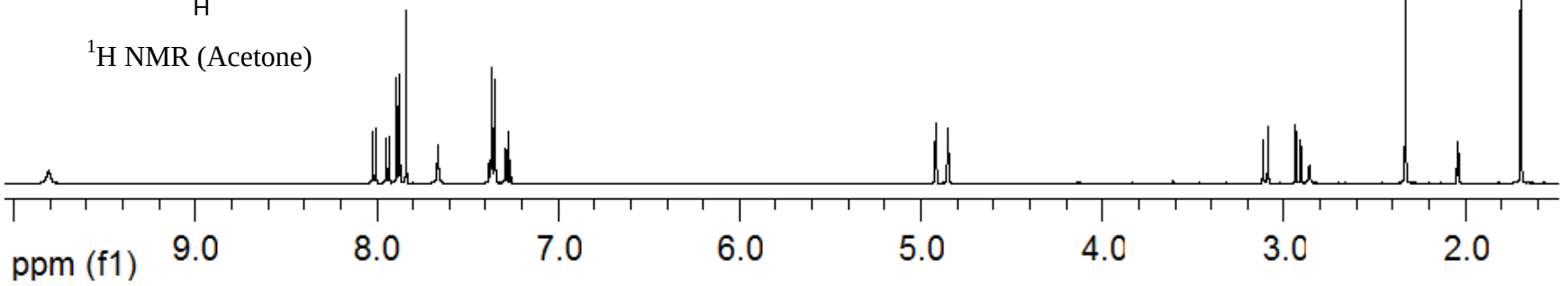
^{13}C NMR ($CDCl_3$)



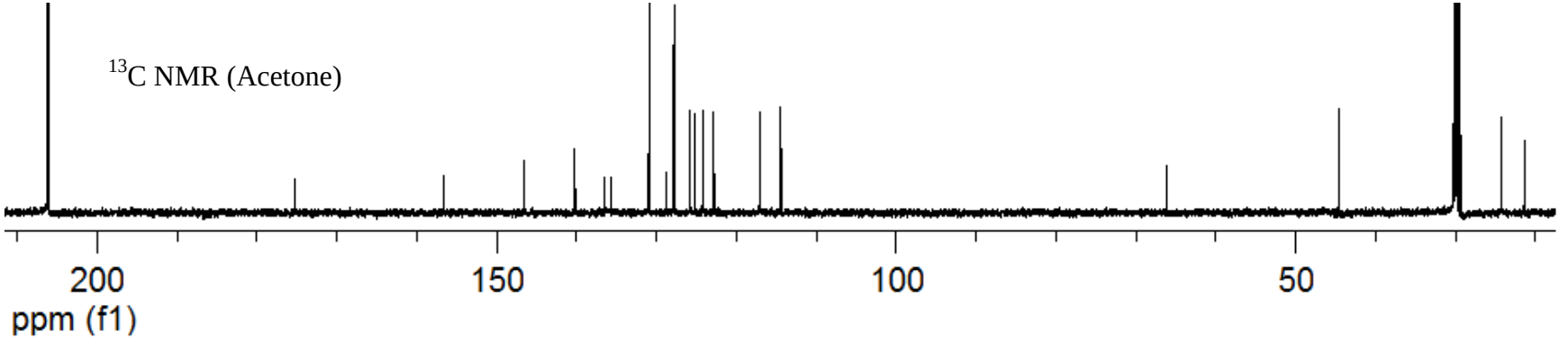


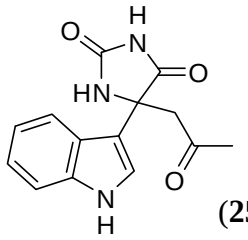
(**24**)

^{1}H NMR (Acetone)



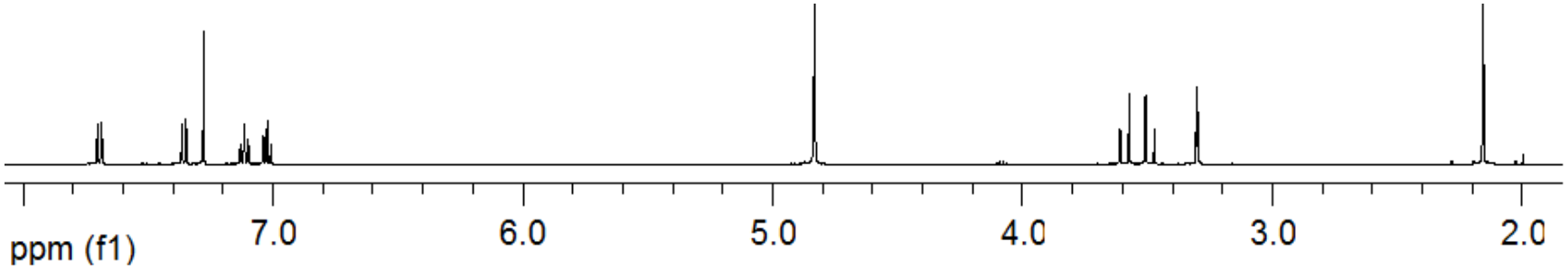
^{13}C NMR (Acetone)



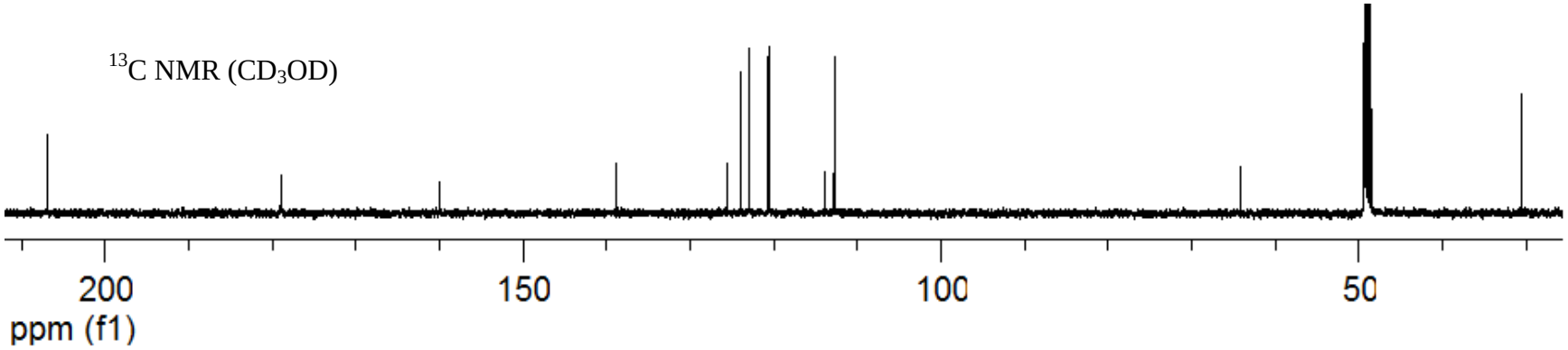


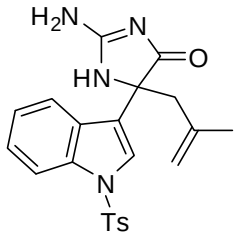
(**25**)

^{1}H NMR (CD_3OD)



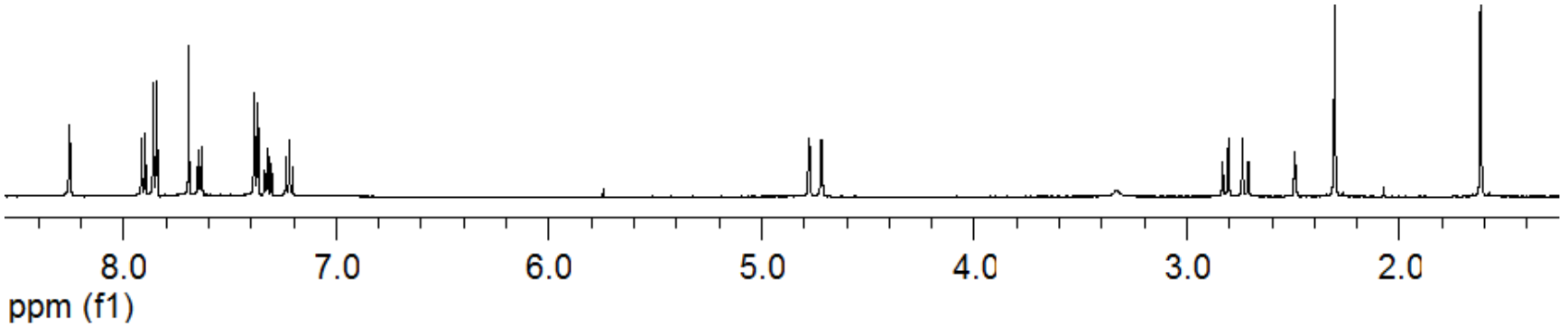
^{13}C NMR (CD_3OD)



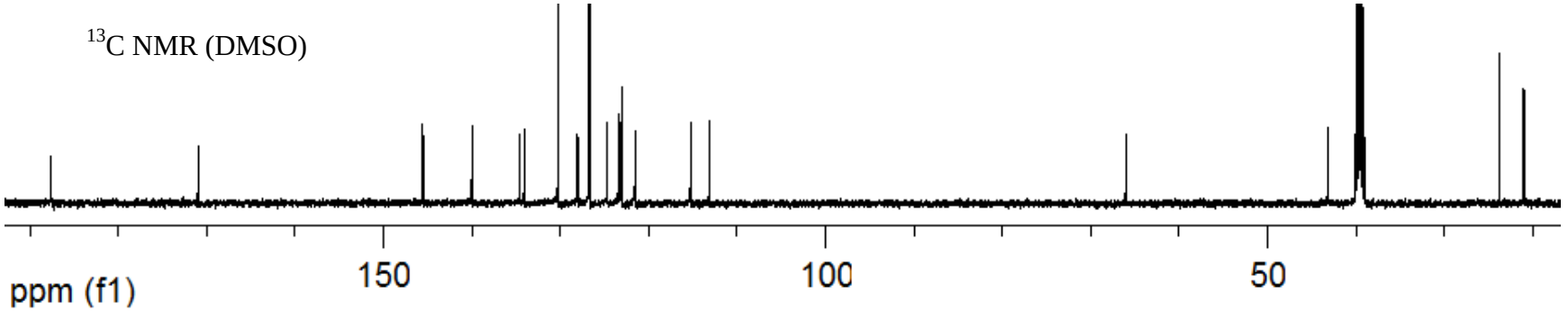


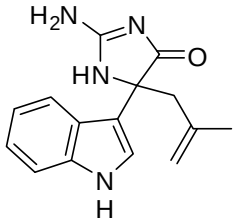
(**27**)

^{1}H NMR (DMSO)



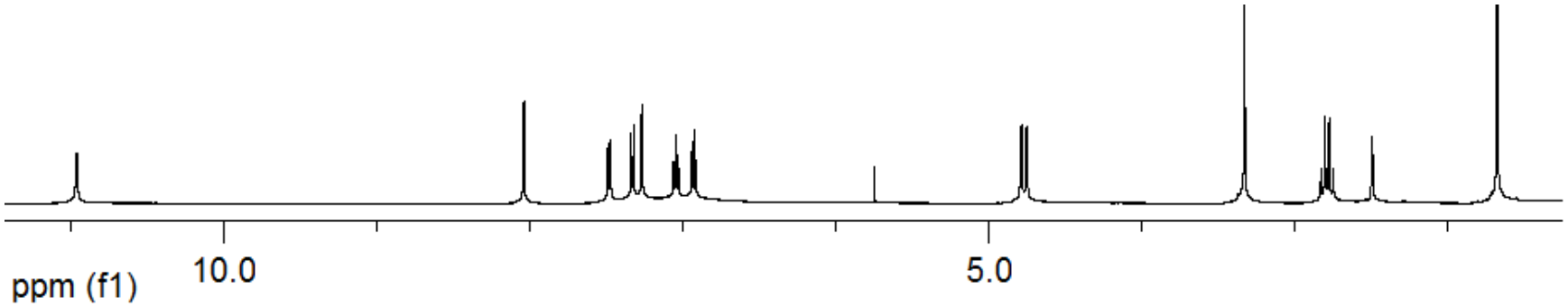
^{13}C NMR (DMSO)



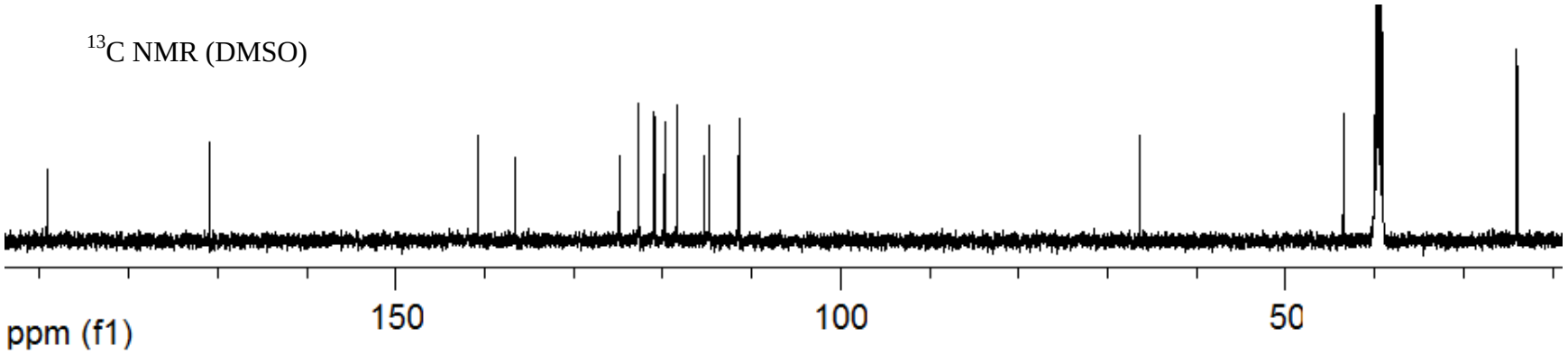


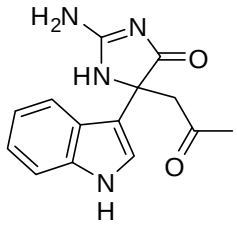
(**28**)

^{1}H NMR (DMSO)



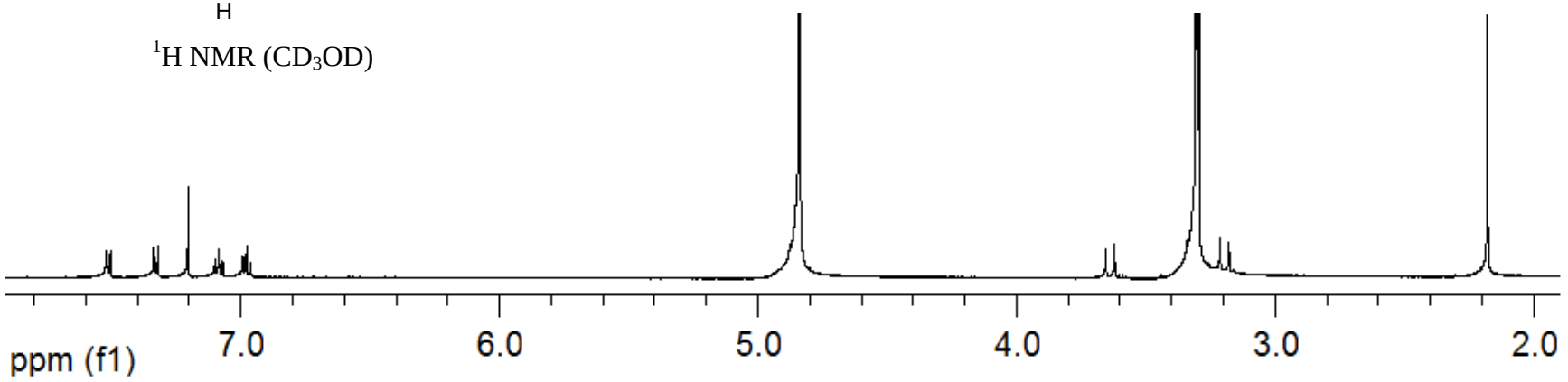
^{13}C NMR (DMSO)



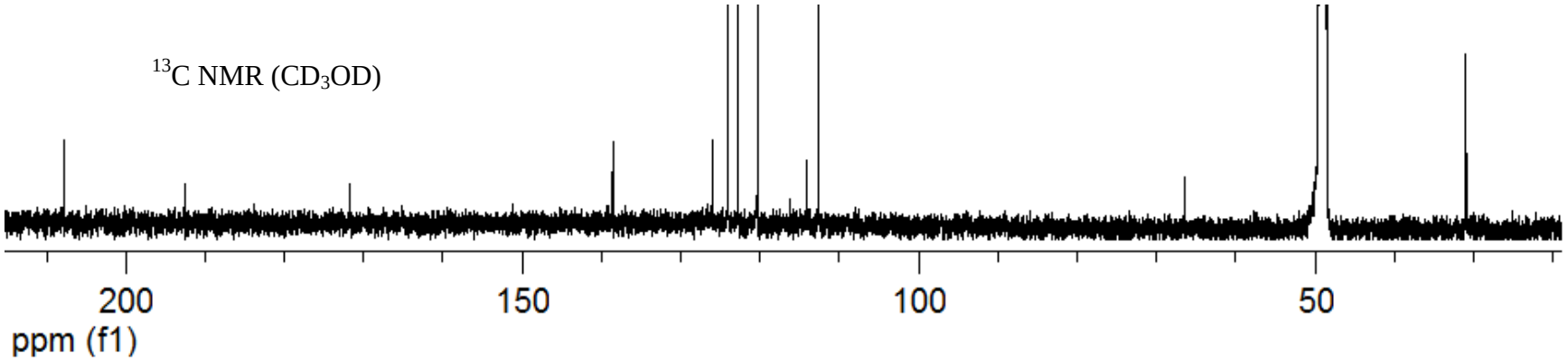


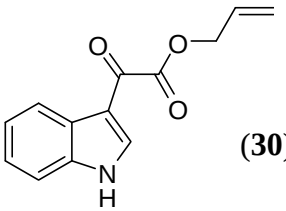
(**29**)

^{1}H NMR (CD_3OD)



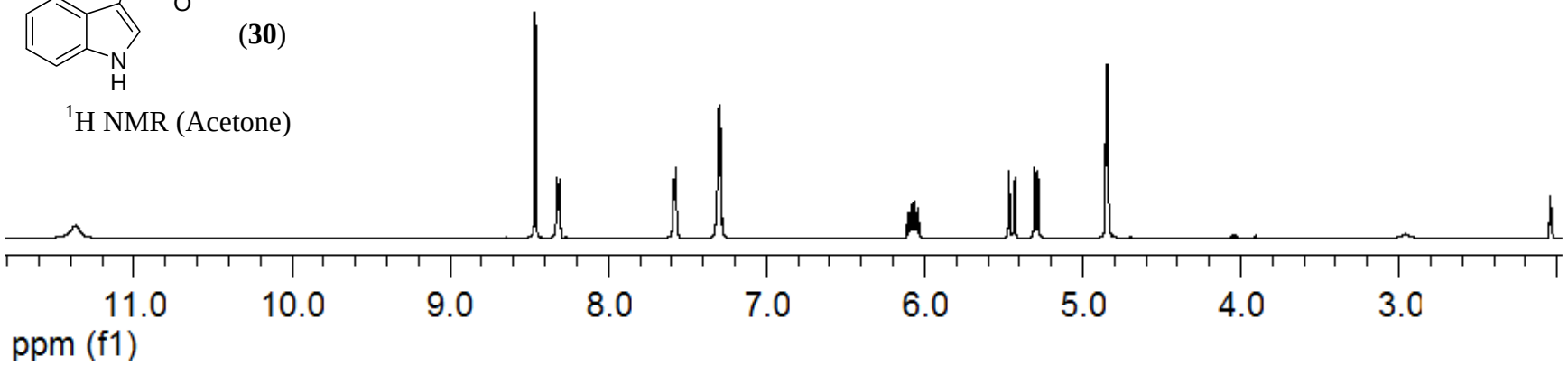
^{13}C NMR (CD_3OD)



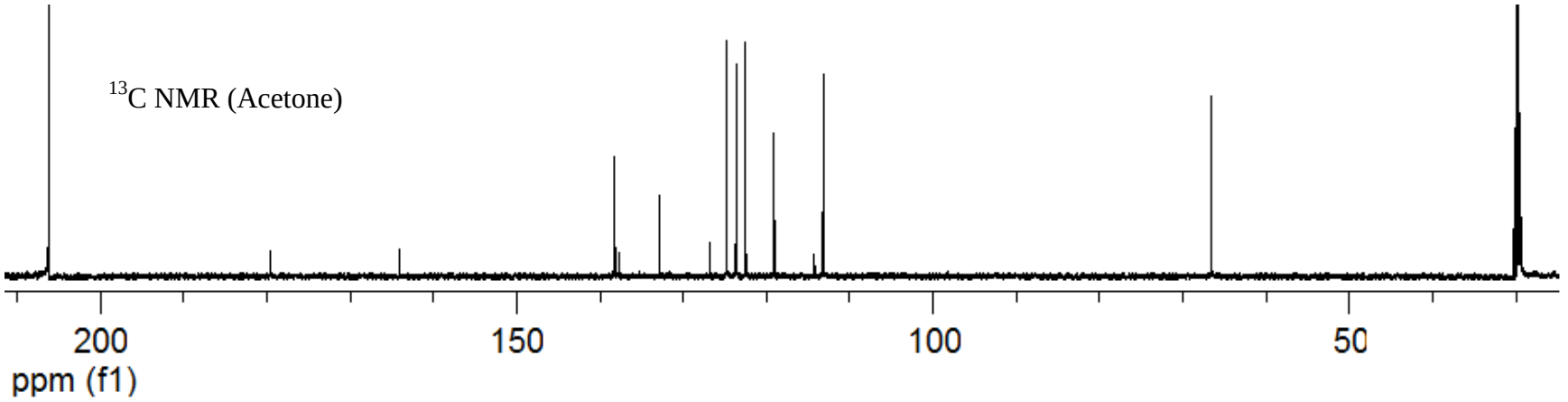


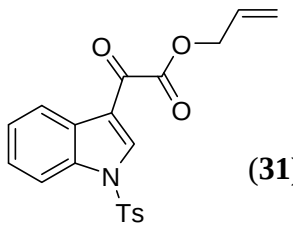
(**30**)

^{1}H NMR (Acetone)



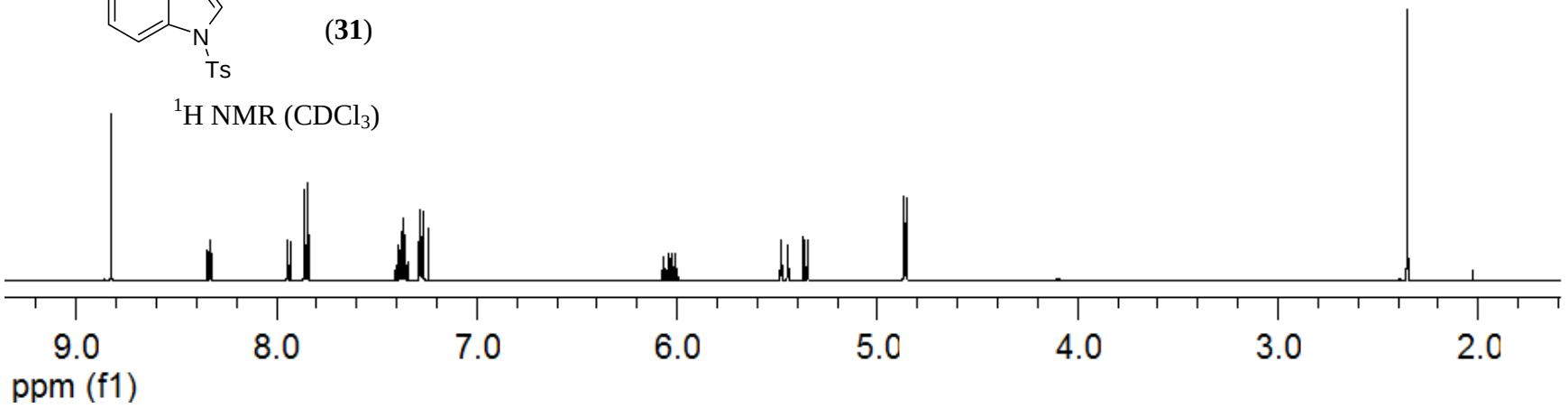
^{13}C NMR (Acetone)



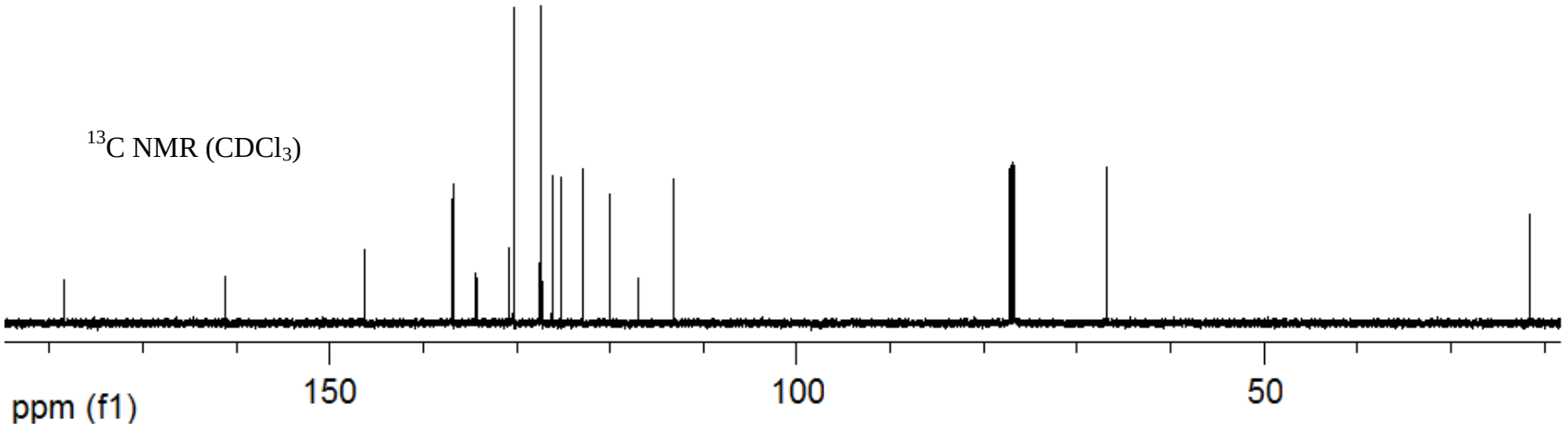


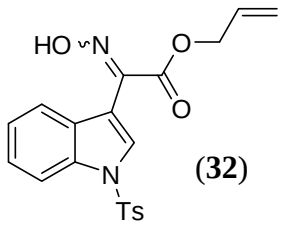
(**31**)

^{1}H NMR ($CDCl_3$)



^{13}C NMR ($CDCl_3$)

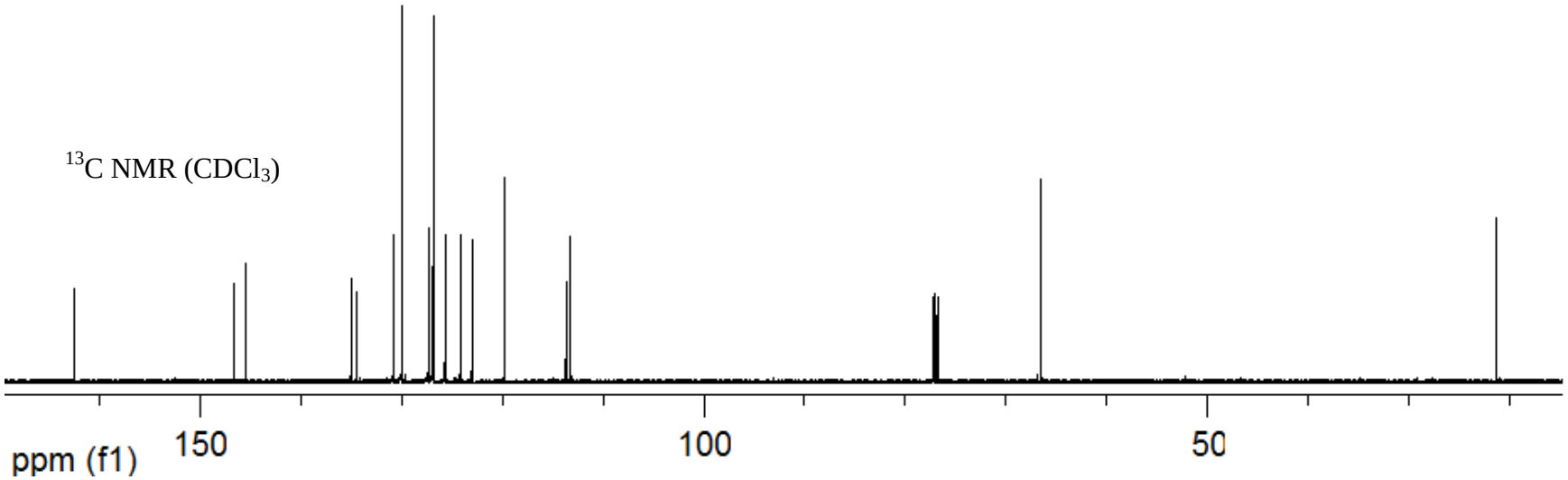


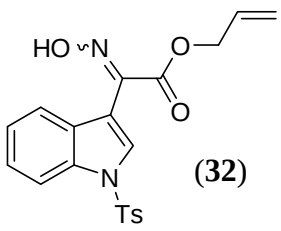


(32)

^{1}H NMR ($CDCl_3$)

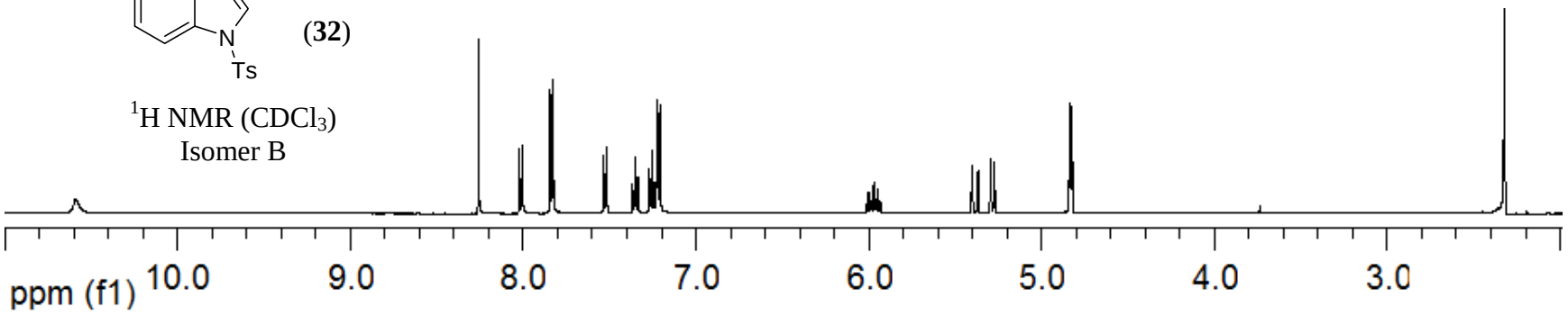
^{13}C NMR ($CDCl_3$)



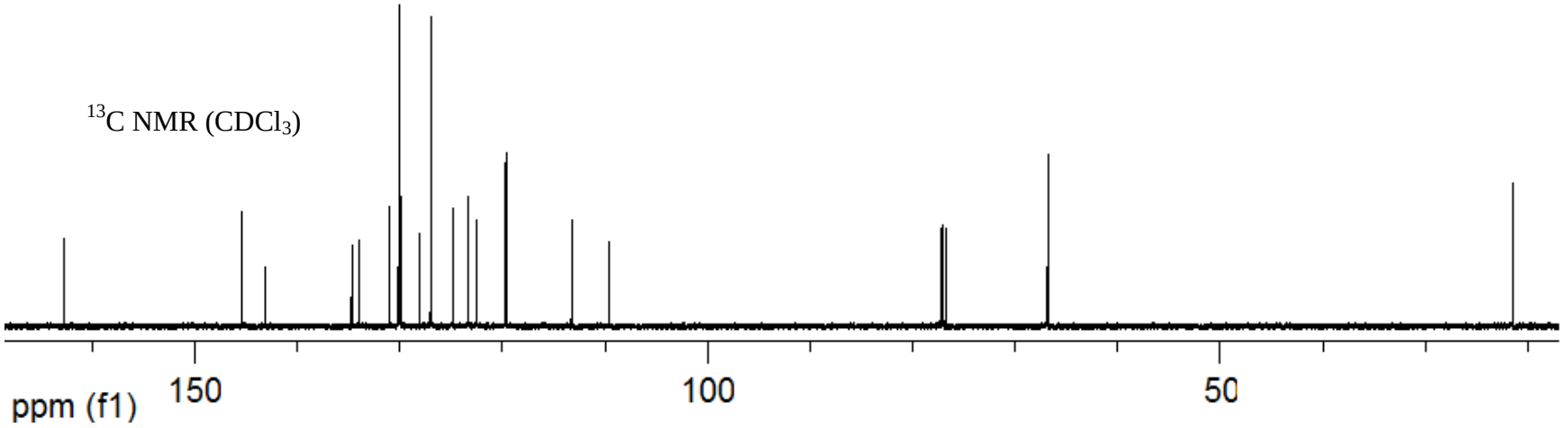


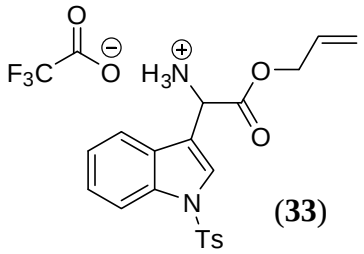
(**32**)

^{1}H NMR ($CDCl_3$)
Isomer B



^{13}C NMR ($CDCl_3$)





(**33**)

^{1}H NMR (DMSO)

^{13}C NMR (DMSO)