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Electronic Supplementary Information for

Modified McFadyen-Stevens Reaction for a Versatile Synthesis of Aliphatic/Aromatic Aldehydes: Design, Optimization, and Mechanistic Investigations

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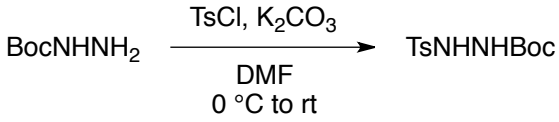
General. All non-aqueous reactions were carried out under an inert atmosphere of argon in oven-dried glassware unless otherwise noted. Dehydrated tetrahydrofuran, methylene chloride and toluene were purchased from Kanto Chemicals Co., Inc. and were purified using a Glass Contour Solvent System. Dehydrated *N*,*N*-dimethylformamide was purchased from Wako Pure Chemical Industries, Ltd. and stored over activated MS4A. Dehydrated methanol and acetonitrile were also purchased from Wako Pure Chemical Industries, Ltd. and stored over activated MS3A. All reagents were commercially available and used without further purification. Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel $60F_{254}$. Preparative thin layer chromatography (pTLC) was performed on Merck precoated analytical plates, 0.50 mm thick, silica gel $60F_{254}$. Preparative flash chromatography was performed using Silica Gel 60 (spherical, 40-100 mm) or Silica Gel 60N (spherical, neutral, 40-100 mm) purchased from Kanto Chemical Co., Inc. ^{1}H and ^{13}C NMR were recorded on a JEOL ECX-400 spectrometer. All ^{1}H NMR spectra are reported in δ units, parts per million (ppm) downfield from tetramethylsilane as the internal standard and coupling constants are indicated in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. All ^{13}C NMR spectra are reported in ppm relative to the central line of the triplet for $CDCl_3$ at 77.0 ppm. Infrared spectra (IR) were recorded on a FT/IR-4100 Fourier Transform Infrared Spectrophotometer, and are reported in wavenumbers (cm^{-1}). High resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100LP AccuTOF LC-plus in positive electrospray ionization (ESI) method using PEG as the internal standard. Melting points, determined on a Yanaco Micro Melting Point Apparatus, are uncorrected.

***tert*-Butyl 2-tosylhydrazinecarboxylate (10)**

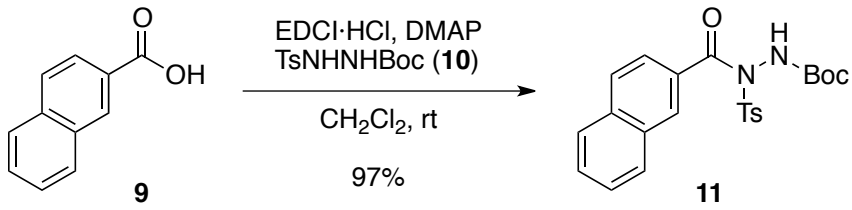


71%

To a solution of *tert*-butyl carbazate (3.96 g, 30.0 mmol) in DMF (20 mL) at 0 °C was added K_2CO_3 (4.56 g, 33.0 mmol) and *p*-toluenesulfonyl chloride (5.72 g, 30.0 mmol) in three portions, and the mixture was allowed to warm to room temperature. After 1 h, the reaction mixture was diluted with EtOAc (10 mL), quenched with saturated NH_4Cl aq. (10 mL) and partitioned between EtOAc (20 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic layer was washed with 1.0 M HCl aq. (10 mL), 10% NaCl aq. (15 mL) twice and brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (20% EtOAc in *n*-hexane). Subsequent trituration from 5% toluene in *n*-hexane gave **10** as a white powder (6.71 g, 23.4 mmol, 71%).

R*f* = 0.61 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 97.1–97.5 °C; IR (neat, cm^{-1}) 1722, 1710, 1597, 1493, 1369, 1343; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.24 (s, 9H), 2,42 (s, 3H), 6.50 (brs, 2H), 7.31 (d, J = 8.2 Hz, 2H), 7.81 (d, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.1, 144.6, 133.5, 129.5, 128.7, 82.3, 27.7, 21.6; HRMS calcd for $C_{23}H_{24}N_2NaO_5S$ ([M + Na^+]) 309.0885, found 309.0887.

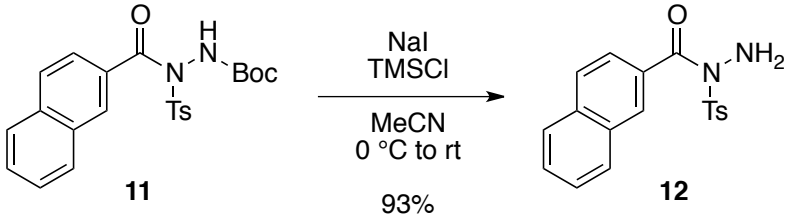
tert-Butyl 2-(2-naphthoyl)-2-tosylhydrazinecarboxylate (11)



To a solution of 2-naphthoic acid (**9**, 172 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (15% EtOAc in *n*-hexane) to afford **11** as a white powder (427.2 mg, 0.97 mmol, 97%).

R*f* = 0.53 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 157.5–157.8 °C; IR (neat, cm^{-1}) 1734, 1715, 1700, 1507, 1249; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.15 (s, 1H), 8.09 (d, J = 8.2 Hz, 2H), 7.85–7.81 (m, 3H), 7.63 (br, 1H), 7.59–7.50 (m, 2H), 7.37 (d, J = 7.8 Hz, 2H), 7.19 (brs, 1H), 2.46 (s, 3H), 1.32 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 188.4, 183.0, 182.9, 165.1, 145.6, 134.5, 132.1, 129.9, 129.4, 129.0, 127.8, 127.7, 126.9, 124.5, 83.2, 28.0, 21.7; HRMS calcd for $C_{23}H_{24}N_2NaO_5S$ ([M + Na^+]) 463.1304, found 463.1299.

***N*-(2-Naphthoyl)-4-methylbenzenesulfonohydrazide (12)**

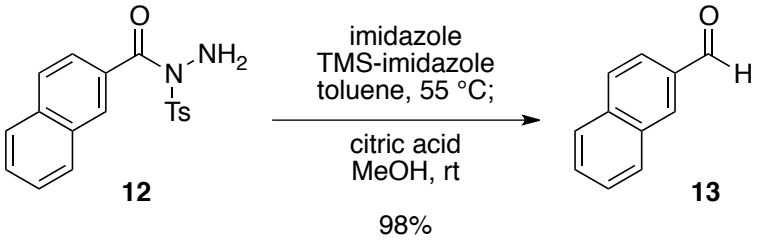


To a stirred solution of **11** (436 mg, 0.99 mmol) in MeCN (5.0 mL) at 0 °C was added NaI (445 mg, 2.97 mmol) and TMSCl (250 μL, 1.98 mmol) and the mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the

aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc in *n*-hexane, 20 to 50%) to afford **12** as a white powder (313 mg, 0.92 mmol, 93%).

R*f* = 0.68 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 160.5–160.9 °C; IR (neat, cm^{-1}) 1681, 1354, 1291, 1168; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.31 (s, 1H), 7.93–7.86 (m, 5H), 7.79 (d, J = 8.2 Hz, 1H), 7.61–7.52 (m, 2H), 7.36 (d, J = 8.3 Hz, 2H), 4.52 (s, 2H), 2.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.2, 145.2, 134.9, 133.5, 131.9, 130.9, 130.7, 129.4, 129.0, 128.9, 128.1, 127.6, 127.2, 126.5, 125.4, 21.5; HRMS calcd for $C_{18}H_{16}N_2NaO_3S$ ([M + Na^+]) 363.0779, found 363.0781.

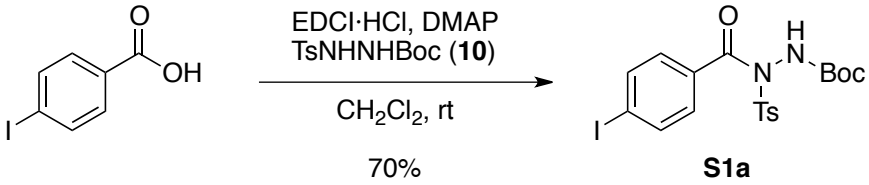
2-Naphthaldehyde (13)



To a solution of **12** (200 mg, 0.59 mmol) in toluene (2.5 mL) at room temperature was added TMS-imidazole (170 μL, 1.18 mmol). After stirring for 5 min, the reaction mixture was added imidazole (80 mg, 1.18 mmol) and the reaction was warmed to 55 °C. After 6 h, the reaction was added 1.0 M citric acid in MeOH (6.0 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (10 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutral silica gel (EtOAc in *n*-hexane, 10 to 15%) to afford **13** as a white powder (90.3 mg, 0.58 mmol, 98%).

R*f* = 0.68 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); M.p. 58.5–59.0 °C; IR (neat, cm^{-1}) 1695, 1627, 1451, 1364, 1267; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.17 (dd, J = 7.3, 1.8 Hz, 1H), 8.35 (s, 1H), 8.02–7.91 (m, 4H), 7.67–7.58 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.2, 136.5, 134.5, 134.1, 132.6, 129.5, 129.1, 128.1, 127.1, 122.8; HRMS calcd for $C_{11}H_8O$ ([M^+]) 156.0575, found 156.0571.

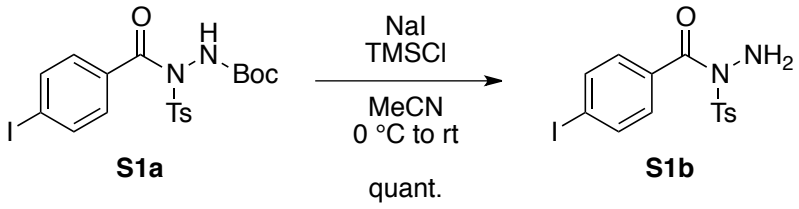
***tert*-Butyl 2-(4-iodobenzoyl)-2-tosylhydrazinecarboxylate (S1a)**



To a solution of 4-iodobenzoic acid (248 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the resulting solution was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (10% EtOAc in *n*-hexane) to afford **S1a** as a white powder (361 mg, 0.70 mmol, 70%).

R*f* = 0.45 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 147.0–149.0 °C; IR (neat, cm^{-1}) 1739, 1715, 1369, 1247, 1171; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.03 (d, J = 8.7 Hz, 2H), 7.72 (d, J = 7.4 Hz, 2H), 7.35 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 7.4 Hz, 2H), 7.10 (br, 1H), 2.45 (s, 3H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 153.6, 145.7, 137.3, 134.2, 132.3, 129.9, 129.8, 98.9, 83.4, 27.8, 21.8; HRMS calcd for $C_{19}H_{21}IN_2NaO_5S$ ([M + Na^+]) 539.0114, found 539.0120.

***N*-(4-Iodobenzoyl)-4-methylbenzenesulfonohydrazide (S1b)**

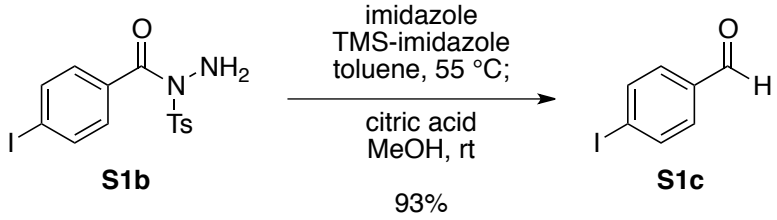


To a stirred solution of **S1a** (361 mg, 0.70 mmol) in MeCN (7.0 mL) at 0 °C was added NaI (315 mg, 2.10 mmol) and TMSCl (180 μL, 1.40 mmol). The mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene (5 mL) and *n*-hexane (20 mL) to

afford **S1b** as a white powder (293 mg, 0.70 mmol, 100%).

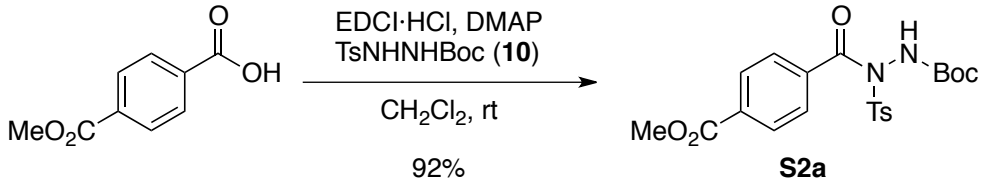
R*f* = 0.41 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 157.5-158.0 °C; IR (neat, cm^{-1}) 1683, 1653, 1541, 1507, 1338; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.88 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.7 Hz, 2H), 4.45 (s, 2H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 145.8, 137.3, 133.7, 133.2, 131.4, 129.9, 129.3, 100.0, 22.0; HRMS calcd for $C_{14}H_{13}IN_2NaO_3S$ ([M + Na^+]) 438.9589, found 438.9577.

4-Iodobenzaldehyde (S1c)



To a solution of **S1b** (200 mg, 0.48 mmol) in toluene (3.5 mL) at room temperature was added TMS-imidazole (140 μL, 0.96 mmol). After stirring for 5 min, the reaction mixture was added imidazole (65.4 mg, 0.96 mmol) and stirring was continued at 55 °C. After 6 h, the reaction was added 1.0 M citric acid in MeOH (5.0 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (20 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (3% EtOAc in *n*-hexane) to afford **S1c** as a white powder (103.3 mg, 0.45 mmol, 93%).

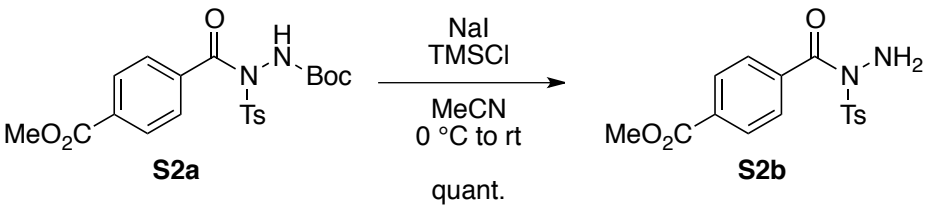
tert-Butyl 2-(4-(methoxycarbonyl)benzoyl)-2-tosylhydrazinecarboxylate (S2a)



To a solution of 4-(methoxycarbonyl)benzoic acid (180 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the resulting solution was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (5% EtOAc in *n*-hexane) to afford **S2a** as a white powder (412 mg, 0.92 mmol, 92%).

R*f* = 0.65 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 156.2−156.7 °C; IR (neat, cm^{-1}) 1732, 1716, 1370, 1281, 1172; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, J = 8.7 Hz, 2H), 8.02 (br, 2H), 7.36 (d, J = 7.8 Hz, 2H), 7.15 (br, 1H), 3.93 (s, 3H), 2.46 (s, 3H), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 153.6, 145.8, 134.2, 129.9, 129.4, 129.2, 128.0, 83.4, 52.4, 27.8, 21.8; HRMS calcd for $C_{19}H_{21}IN_2NaO_5S$ ([M + Na^+]) 471.1202, found 471.1180.

Methyl 4-(1-tosylhydrazinecarbonyl)benzoate (S2b)

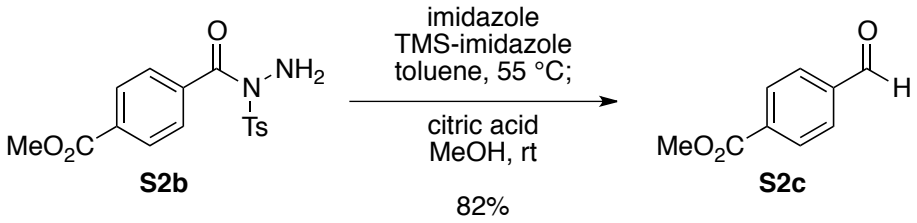


To a stirred solution of **S2a** (173 mg, 0.39 mmol) in MeCN (10 mL) at 0 °C was added NaI (174 mg, 1.16 mmol) and TMSCl (100 μL, 0.78 mmol) and the mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed

with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene (3 mL) and *n*-hexane (20 mL) to afford **S2b** as a white powder (134 mg, 0.39 mmol, 100%).

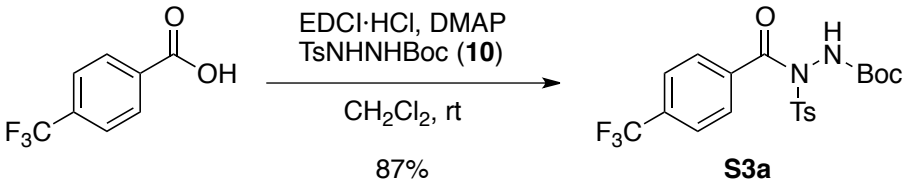
R*f* = 0.59 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 165.5–165.8 °C; IR (neat, cm^{-1}) 1721, 1672, 1342, 1278, 1168; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.07 (d, J = 8.2 Hz, 2H), 7.89 (d, J = 8.2 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.7 Hz, 2H), 4.48 (s, 2H), 3.94 (s, 3H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 166.2, 145.6, 137.8, 133.6, 133.0, 129.7, 129.3, 129.1, 129.0, 52.4, 21.7; HRMS calcd for $C_{16}H_{16}N_2NaO_5S$ ([M + Na^+]) 371.0678, found 371.0660.

Methyl 4-formylbenzoate (S2c)



To a solution of **S2b** (100 mg, 0.29 mmol) in toluene (1.4 mL) at room temperature was added TMS-imidazole (85 μL, 0.57 mmol). After stirring for 5 min, the reaction mixture was added imidazole (39 mg, 0.57 mmol) and stirring was continued at 55 °C. After 6 h, the reaction was added 1.0 M citric acid in MeOH (3.0 mL) at room temperature and stirred for 1 h. The resulting mixture was quenched with saturated $NaHCO_3$ aq. (6 mL) and partitioned between EtOAc (10 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (15 mL) twice. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (10 to 20% EtOAc in *n*-hexane) to afford **S2c** as a white powder (38.6 mg, 0.24 mmol, 82%).

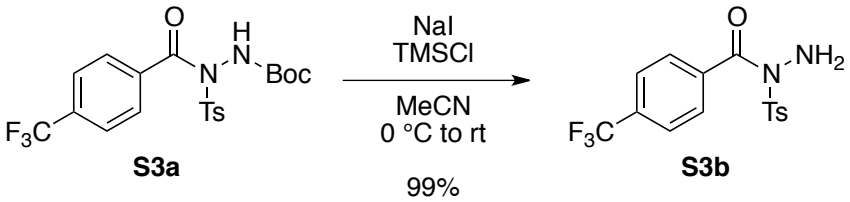
tert-Butyl 2-tosyl-2-(4-(trifluoromethyl)benzoyl)hydrazinecarboxylate (S3a)



To a solution of 4-(trifluoromethyl)benzoic acid (190 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the resulting solution was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (10% EtOAc in *n*-hexane) to afford **S3a** as a white powder (400 mg, 0.87 mmol, 87%).

R*f* = 0.58 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 145.6–146.1 °C; IR (neat, cm^{-1}) 1740, 1731, 1713, 1371, 1325, 1171; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, J = 8.2 Hz, 2H), 7.67–7.62 (m, 4H), 7.36 (d, J = 8.3 Hz, 2H), 7.15 (br, 1H), 2.46 (s, 3H), 1.34 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.7, 145.9, 136.5, 134.1, 129.9, 129.4, 128.4, 125.0, 83.4, 27.7, 21.8; HRMS calcd for $C_{21}H_{24}N_2NaO_7S$ ([M + Na^+]) 481.1021, found 481.1003.

4-Methyl-*N*-(4-(trifluoromethyl)benzoyl)benzenesulfonohydrazide (S3b)

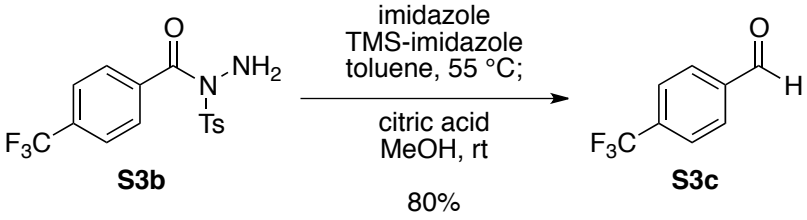


To a stirred solution of **S3a** (400 mg, 0.87 mmol) in MeCN (10 mL) at 0 °C was added NaI (392 mg, 2.62 mmol) and TMSCl (220 μL, 1.75 mmol). The mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (40 mL) and H_2O (10 mL). The combined organic layer was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene/*n*-hexane (3:20, 23 mL) to afford

S3b as a white powder (312 mg, 0.88 mmol, 99%).

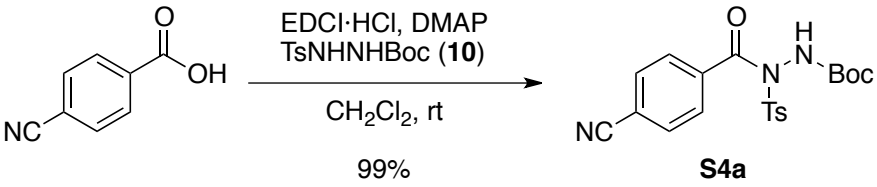
R*f* = 0.52 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 160.0–161.0 °C; IR (neat, cm^{-1}) 1683, 1507, 1408, 1338; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 4.47 (s, 2H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 145.7, 137.2, 133.5, 129.7, 129.1, 124.9, 124.8, 124.7, 122.2, 21.7; HRMS calcd for $C_{15}H_{13}F_3N_2NaO_3S$ ([M + Na^+]) 381.0497, found 381.0512.

4-(Trifluoromethyl)benzaldehyde (S3c)



To a solution of **S3b** (200 mg, 0.56 mmol) in toluene (2.5 mL) at room temperature was added TMS-imidazole (160 μL, 1.12 mmol). After stirring for 5 min, the reaction mixture was added imidazole (76 mg, 1.1 mmol) and stirring was continued at 55 °C. After 6 h, the reaction mixture was added 1.0 M citric acid in MeOH (5.0 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (20 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (2% EtOAc in *n*-hexane) to afford **S3c** as a white powder (77.9 mg, 0.45 mmol, 80%).

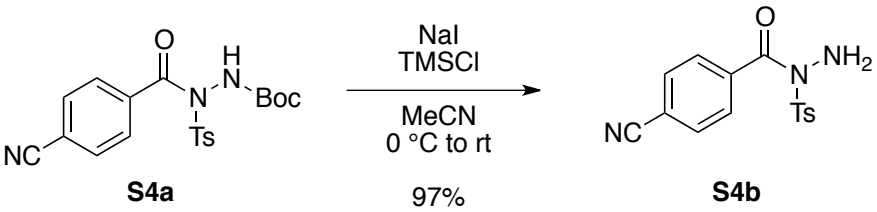
***tert*-Butyl 2-(4-cyanobenzoyl)-2-tosylhydrazinecarboxylate (S4a)**



To a solution of 4-cyanobenzoic acid (190 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the resaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (10% EtOAc in *n*-hexane) to afford **S4a** as a white powder (415 mg, 0.99 mmol, 99%).

R*f* = 0.66 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 139.1–139.5 °C; IR (neat, cm^{-1}) 2232, 1739, 1715, 1370, 1247, 1173; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.03 (d, J = 8.7 Hz, 2H), 7.66 (br, 4H), 7.36 (d, J = 8.3 Hz, 2H), 7.15 (br, 1H), 2.46 (s, 3H), 1.35 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.2, 153.6, 137.2, 133.8, 131.7, 129.9, 129.4, 128.6, 117.8, 114.9, 83.4, 27.7, 21.7; HRMS calcd for $C_{20}H_{21}N_3NaO_5S$ ([M + Na^+]) 438.1100, found 438.1079.

***N*-(4-Cyanobenzoyl)-4-methylbenzenesulfonohydrazide (S4b)**

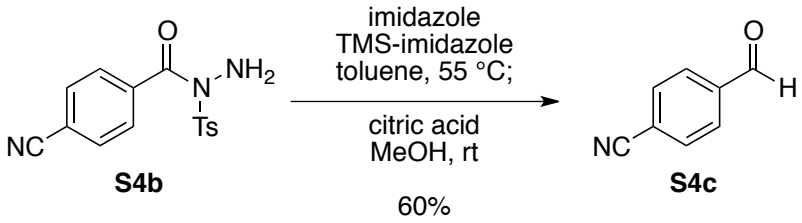


To a stirred solution of **S4a** (415 mg, 0.99 mmol) in MeCN (10 mL) at 0 °C was added NaI (450 mg, 3.00 mmol) and TMSCl (250 μL, 2.00 mmol) and the mixture was warmed to room temperature. After 30 min, the solution was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (40 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and

concentrated *in vacuo*. The residue was crystallized from toluene (10 mL) to afford **S4b** as a white powder (305 mg, 0.97 mmol, 97%).

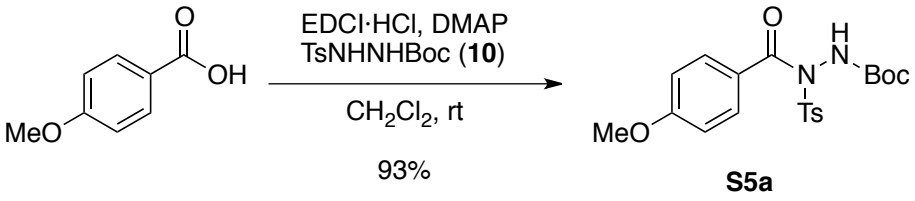
R*f* = 0.57 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 143.0–144.0 °C; IR (neat, cm^{-1}) 2234, 1681, 1344, 1173; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.89 (d, *J* = 8.3 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.37(d, *J* = 8.7 Hz, 2H), 4.47 (s, 2H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 145.9, 137.8, 133.3, 131.6, 129.9, 129.8, 129.1, 117.9, 115.4, 21.7; HRMS calcd for $C_{15}H_{13}N_3NaO_3S$ ([M + Na^+]) 338.0575, found 338.0563.

4-Formylbenzonitrile (S4c)



To a solution of **S4b** (100 mg, 0.32 mmol) in toluene (2.0 mL) at room temperature was added TMS-imidazole (95 μL, 0.63 mmol). After stirring for 5 min, the reaction mixture was added imidazole (43.2 mg, 0.63 mmol) and stirring was continued at 55 °C. After 6 h, the reaction mixture was added 1 M citric acid in MeOH (3 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between saturated $NaHCO_3$ aq. (6 mL) and EtOAc (15 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by preparative TLC (30% EtOAc in *n*-hexane) to afford **S4c** as a white powder (25.1 mg, 0.19 mmol, 60%).

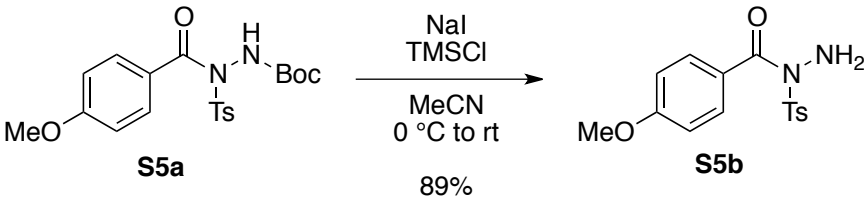
***tert*-Butyl 2-(4-methoxybenzoyl)-2-tosylhydrazinecarboxylate (S5a)**



To a solution of 4-methoxybenzoic acid (152 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 8 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (10% EtOAc in toluene) to afford **S5a** as a white amorphous solid (390 mg, 0.93 mmol, 93%).

R*f* = 0.55 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); IR (neat, cm^{-1}) 1734, 1698, 1604, 1508, 1368, 1258, 1169; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 7.07 (br, 1H), 6.86 (d, J = 8.7 Hz, 2H), 3.83 (s, 3H), 2.45 (s, 3H), 1.35 (br, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 162.6, 153.8, 145.2, 134.6, 131.0, 129.8, 129.3, 124.5, 82.7, 55.3, 27.7, 21.6; HRMS calcd for $C_{19}H_{21}IN_2NaO_5S$ ([M + Na^+]) 443.1253, found 443.1247.

***N*-(4-Methoxybenzoyl)-4-methylbenzenesulfonohydrazide (S5b)**

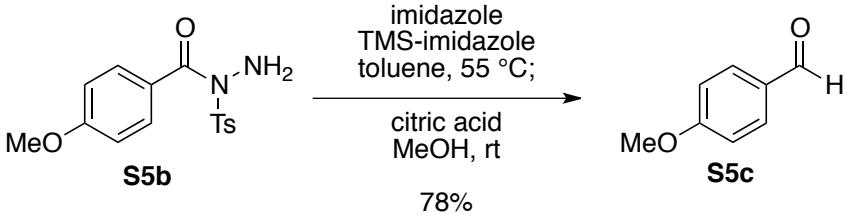


To a stirred solution of **S5a** (300 mg, 0.71 mmol) in MeCN (5.0 mL) at 0 °C was added NaI (320 mg, 2.14 mmol) and TMSCl (180 μL, 1.42 mmol) and the resulting mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and

concentrated *in vacuo*. The residue was crystallized from toluene/*n*-hexane (3:10, 13 mL) to afford **S5b** as a white powder (203 mg, 0.64 mmol, 89%).

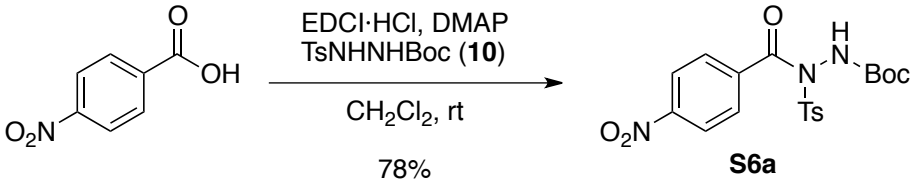
R*f* = 0.54 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 115.6–115.9 °C; IR (neat, cm^{-1}) 1683, 1603, 1507, 1352, 1257, 1165, 1025; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (d, J = 8.2 Hz, 2H), 7.82 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 4.43 (s, 2H), 3.87 (s, 3H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 163.3, 145.1, 133.5, 132.5, 129.5, 129.0, 125.4, 113.2, 55.4, 21.7; HRMS calcd for $C_{14}H_{13}IN_2NaO_3S$ ([M + Na^+]) 343.0729, found 343.0738.

4-Methoxybenzaldehyde (S5c)



To a solution of **S5b** (100 mg, 0.31 mmol) in toluene (3.0 mL) at room temperature was added TMS-imidazole (120 μL, 0.62 mmol). After stirring for 5 min, the reaction mixture was added imidazole (42.5 mg, 0.62 mmol) and stirring was continued at 55 °C. After 6 h, the reaction mixture was added 1.0 M citric acid in MeOH (5.0 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (20 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (5% EtOAc in *n*-hexane) to afford **S5c** as a white powder (33 mg, 0.24 mmol, 78%).

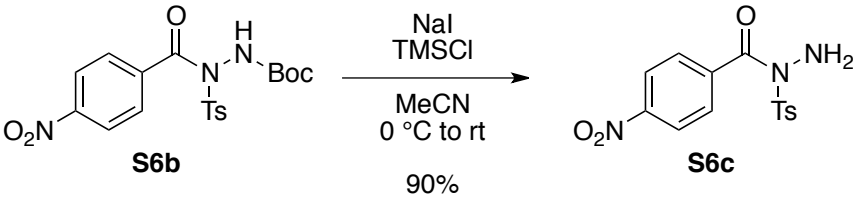
tert-Butyl 2-(4-nitrobenzoyl)-2-tosylhydrazinecarboxylate (S6a)



To a solution of 4-nitrobenzoic acid (167 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 8 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc in *n*-hexane, 10-15%) to afford **S6a** as a white amorphous solid (341 mg, 0.78 mmol, 78%).

R*f* = 0.72 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); IR (neat, cm^{-1}) 1731, 1715, 1705, 1525, 1371, 1350, 1172; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.21 (d, J = 8.2 Hz, 2H), 8.04 (d, J = 8.7 Hz, 2H), 7.73 (d, J = 7.8 Hz, 2H), 7.38 (d, J = 7.8 Hz, 2H), 7.20 (br, 1H), 2.43 (s, 3H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.8, 149.6, 149.4, 149.1, 145.9, 133.6, 129.7, 129.3, 128.8, 122.9, 83.4, 27.5, 21.6; HRMS calcd for $C_{19}H_{21}IN_2NaO_5S$ ([M + Na^+]) 458.0998, found 458.0983.

4-Methyl-*N*-(4-nitrobenzoyl)benzenesulfonohydrazide (S6b)

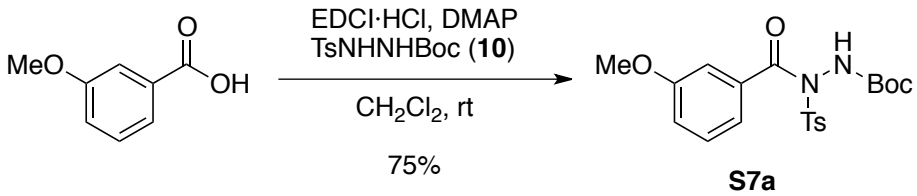


To a stirred solution of **S6a** (341 mg, 0.70 mmol) in MeCN (10 mL) at 0 °C was added NaI (350 mg, 2.35 mmol) and TMSCl (170 μL, 1.57 mmol) and the mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and

concentrated *in vacuo*. The residue was crystallized from toluene/*n*-hexane (1:4, 25 mL) to afford **S6b** as a white powder (236 mg, 0.70 mmol, 90%).

R*f* = 0.61 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 156.0–156.3 °C; IR (neat, cm^{-1}) 1678, 1604, 1528, 1343, 1173; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.28 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.2 Hz, 2H), 7.85 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 4.50 (s, 2H), 2.47 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 149.4, 145.9, 139.5, 133.3, 130.3, 129.8, 129.1, 122.9, 21.7; HRMS calcd for $C_{14}H_{13}IN_2NaO_3S$ ([M + Na^+]) 358.0474, found 358.0483.

***tert*-Butyl 2-(3-methoxybenzoyl)-2-tosylhydrazinecarboxylate (S7a)**

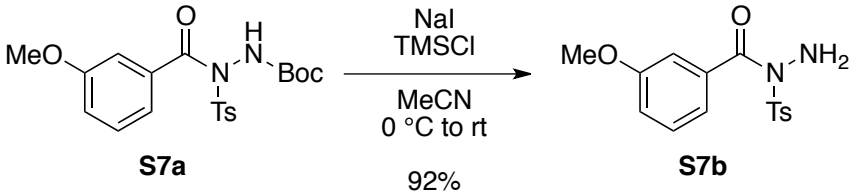


S7a

To a solution of 3-methoxybenzoic acid (154 mg, 1.01 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (10% EtOAc in *n*-hexane) to afford **S7a** as a white powder (314 mg, 0.75 mmol, 75%).

R*f* = 0.41 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 104.5–105.0 °C; IR (neat, cm^{-1}) 1740, 1708, 1597, 1489, 1368, 1170; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.06 (d, J = 8.2 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 7.11 (s, 1H), 7.11 (br, 1H), 3.78 (s, 3H), 2.45 (s, 3H), 1.07 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 184.6, 159.2, 145.5, 134.5, 129.9, 129.4, 129.1, 120.4, 118.4, 83.2, 55.4, 27.8, 21.7; HRMS calcd for $C_{20}H_{24}N_2NaO_6S$ ([M + Na^+]) 443.1253, found 443.1258.

***N*-(3-Methoxybenzoyl)-4-methylbenzenesulfonohydrazide (S7b)**



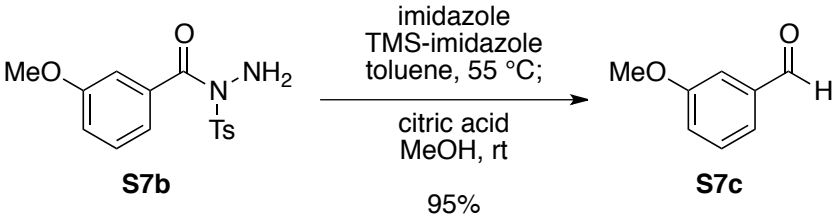
S7a **S7b**

To a stirred solution of **S7a** (314 mg, 0.75 mmol) in MeCN (7.0 mL) at 0 °C was added NaI (336 mg, 2.24 mmol) and TMSCl (190 μL, 1.49 mmol) and the reaction mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated aq. NH_4Cl (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene/*n*-hexane (1:5, 18 mL) to afford

S7b as a white powder (220 mg, 0.69 mmol, 92%).

R*f* = 0.31 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 110.0–111.0 °C; IR (neat, cm^{-1}) 1683, 1597, 1354, 1290, 1165; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.89 (d, *J* = 8.2 Hz, 2H), 7.36–7.32 (m, 5H), 7.24 (s, 1H), 4.45 (s, 2H), 3.83 (s, 3H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 159.0, 145.3, 134.9, 133.7, 129.6, 129.0, 128.8, 122.0, 118.4, 114.5, 55.4, 21.7; HRMS calcd for $C_{15}H_{16}N_2NaO_4S$ ([M + Na^+]) 343.0729, found 343.0744.

3-Methoxybenzaldehyde (S7c)

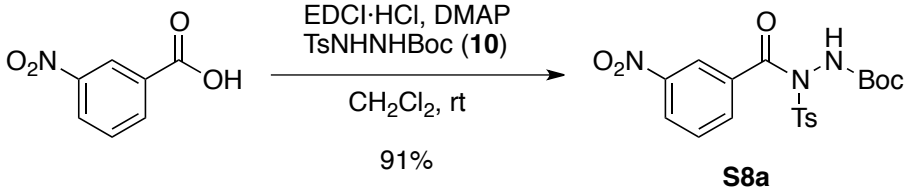


S7b **S7c**

95%

To a solution of **S7b** (160 mg, 0.50 mmol) in toluene (2.5 mL) at room temperature was added TMS-imidazole (150 μL, 1.00 mmol). After stirring for 5 min, the reaction mixture was added imidazole (68 mg, 1.00 mmol) and stirring was continued at 55 °C. After 6 h, the reaction mixture was added 1 M citric acid in MeOH (5.0 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (10 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (3% EtOAc in *n*-hexane) to afford **S7c** as a white powder (65.0 mg, 0.48 mmol, 95%).

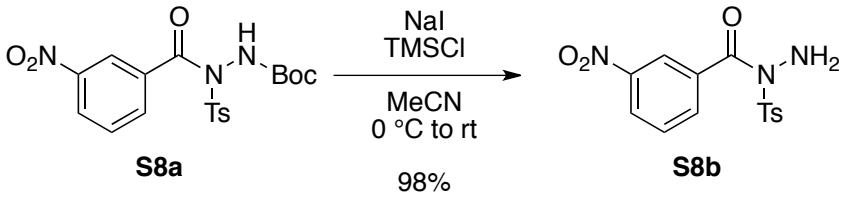
tert-Butyl 2-(3-nitrobenzoyl)-2-tosylhydrazinecarboxylate (S8a)



To a solution of 3-nitrobenzoic acid (167 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc in *n*-hexane, 10 to 15%) to afford **S8a** as a white powder (398 mg, 0.91 mmol, 91%).

R*f* = 0.73 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 150.0–151.0 °C; IR (neat, cm^{-1}) 1742, 1715, 1538, 1352, 1247, 1173; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.46 (s, 1H), 8.33 (d, J = 7.8 Hz, 1H), 8.05 (d, J = 8.2 Hz, 2H), 7.93 (d, J = 7.8 Hz, 1H), 7.58 (br, 1H), 7.38 (d, J = 7.8 Hz, 2H), 2.47 (s, 3H), 1.37 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.4, 153.7, 147.6, 146.1, 134.7, 134.1, 133.9, 130.0, 129.5, 129.3, 126.2, 123.2, 83.7, 27.8, 21.8; HRMS calcd for $C_{19}H_{21}N_3NaO_7S$ ([M + Na^+]) 458.0998, found 458.1007.

4-Methyl-*N*-(3-nitrobenzoyl)benzenesulfonohydrazide (S8b)

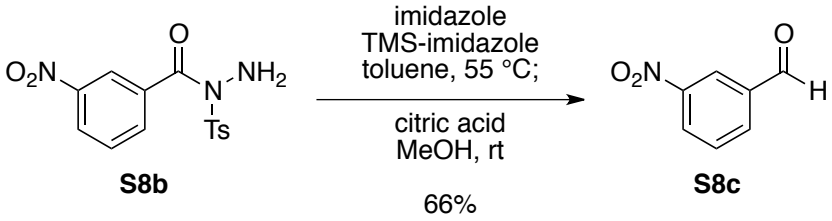


To a stirred solution of **S8a** (397 mg, 0.91 mmol) in MeCN (10 mL) at 0 °C was added NaI (410 mg, 2.74 mmol) and TMSCl (230 μL, 1.83 mmol) and the reaction mixture was warmed to room temperature. After 30 min, the resulting solution was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (40 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was

washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene/*n*-hexane (1:4, 25 mL) to afford **S8b** as a white powder (286 mg, 0.89 mmol, 98%).

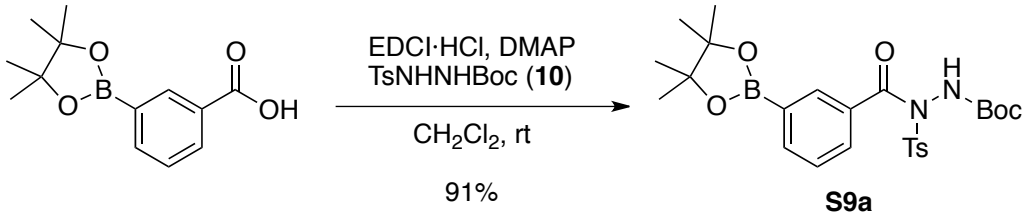
R*f* = 0.63 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 162.0–162.5 °C; IR (neat, cm^{-1}) 1682, 1530, 1351, 1169; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.58 (s, 1H), 8.36 (d, *J* = 8.3 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.62 (dd, *J* = 8.3, 7.8 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 2H), 4.53 (s, 2H), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.5, 147.6, 146.0, 135.3, 135.2, 133.3, 129.8, 129.2, 129.0, 126.4, 124.6, 21.7; HRMS calcd for $C_{14}H_{13}N_3NaO_5S$ ([M + Na^+]) 358.0474, found 358.0483.

3-Nitrobenzaldehyde (S8c)



To a solution of **S8b** (100 mg, 0.31 mmol) in toluene (1.5 mL) at room temperature was added TMS-imidazole (90 μL, 0.62 mmol). After stirring for 5 min, the reaction mixture was added imidazole (42.5 mg, 0.62 mmol) and stirring was continued at 55 °C. After 6 h, the reaction mixture was added 1.0 M citric acid in MeOH (3 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (10 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (EtOAc in *n*-hexane, 10-20%) to afford **S8c** as a white powder (31.0 mg, 0.21 mmol, 66%).

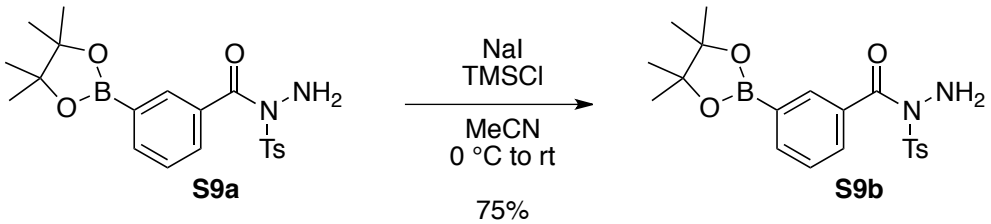
tert-Butyl-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoyl)-2-tosylhydrazinecarboxylate (S9a)



To a solution of 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (250 mg, 1.01 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the resulting solution was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene/*n*-hexane (1:2, 9 mL) to afford **S9a** as a white powder (468 mg, 0.91 mmol, 91%).

R*f* = 0.52 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 140.2–140.8 °C; IR (neat, cm^{-1}) 1741, 1716, 1600, 1361, 1243, 1171; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.06 (d, J = 8.3 Hz, 2H), 8.00 (s, 1H), 7.89 (d, J = 7.3 Hz, 1H), 7.67 (d, J = 7.3 Hz, 1H), 7.36–7.34 (m, 3H), 7.12 (br, 1H), 2.45 (s, 3H), 1.54 (s, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.5, 153.3, 145.4, 145.3, 138.0, 134.6, 132.4, 131.1, 129.9, 129.8, 129.3, 127.5, 84.1, 27.8, 24.8, 21.7; HRMS calcd for $C_{25}H_{33}BN_2NaO_7S$ ([M + Na^+]) 539.1999, found 539.1990.

4-Methyl-*N*-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoyl)benzenesulfonohydrazide (S9b)

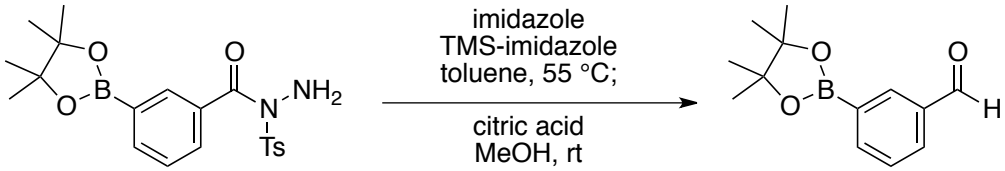


To a stirred solution of **S9a** (410 mg, 0.79 mmol) in MeCN (5.0 mL) at 0 °C was added NaI (357 mg, 2.38 mmol) and TMSCl (200 μL, 1.59 mmol) and the resulting mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and

partitioned between EtOAc (40 mL) and H_2O (20 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene/*n*-hexane (1:3, 20 mL) to afford **S9b** as a white powder (248 mg, 0.60 mmol, 75%).

R*f* = 0.45 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 147.1–148.0 °C; IR (neat, cm^{-1}) 1687, 1602, 1360, 1323, 1168, 1143; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.14 (s, 1H), 7.95 (d, *J* = 7.4 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 7.8, 7.4 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 2H), 4.46 (s, 2H), 2.46 (s, 3H), 1.35 (s, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.3, 145.3, 138.5, 135.6, 133.8, 133.2, 132.3, 129.6, 129.1, 127.2, 84.2, 24.8, 21.7; HRMS calcd for $C_{20}H_{25}BN_2NaO_5S$ ([M + Na^+]) 439.1475, found 439.1482.

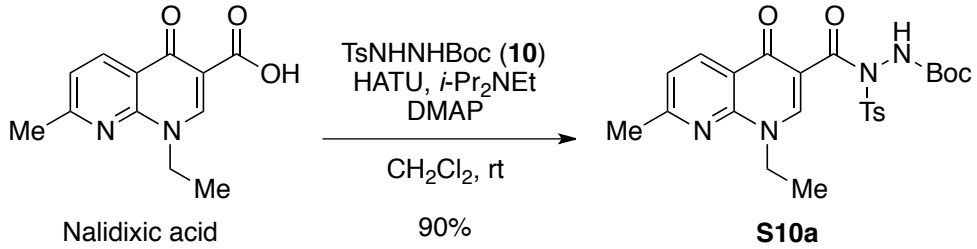
3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (S9c)



To a solution of **S9b** (150 mg, 0.36 mmol) in toluene (2.0 mL) at room temperature was added TMS-imidazole (100 μL, 0.72 mmol). After stirring for 5 min, the reaction mixture was added imidazole (49.0 mg, 0.72 mmol), and stirring was continued at 55 °C. After 12 h, the reaction mixture was added 1.0 M citric acid in H_2O (4.0 mL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between EtOAc (20 mL) and saturated $NaHCO_3$ aq. (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (10 to 20% EtOAc in *n*-hexane) to afford **S9c** as a colorless oil (66.0 mg, 0.28 mmol, 80%).

R*f* = 0.63 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA, 2,4-DNP); IR (neat, cm^{-1}) 2970, 2880, 1710, 1605, 1460, 1361, 1194, 1144; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.1 (s, 1H), 8.31 (s, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 1.37 (s, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.6, 140.7, 137.2, 135.8, 131.3, 128.4, 84.3, 24.9; HRMS calcd for $C_{13}H_{17}BNaO_3$ ([M + Na^+]) 255.1168, found 255.1158.

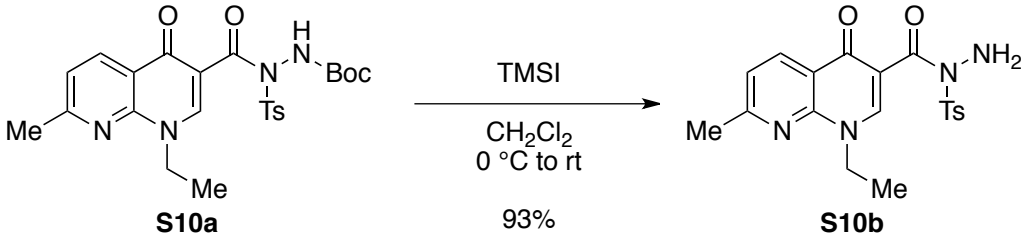
tert-Butyl-2-(1-ethyl-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carbonyl)-2-tosylhydrazinecarboxylate (S10a)



To a solution of Nalidixic acid (255 mg, 1.10 mmol) in CH_2Cl_2 (10 mL) at room temperature was added HATU (456 mg, 1.20 mmol), 4-dimethylaminopyridine (24.4 mg, 0.20 mmol), *i*-Pr_2NEt (260 μL, 1.50 mmol), and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the reaction was quenched with saturated NH_4Cl aq. (3 mL) and partitioned between EtOAc (25 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (10 to 40% EtOAc in *n*-hexane) to afford **S10a** as a white powder (547 mg, 0.99 mmol, 90%).

R*f* = 0.47 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 112.0–113.0 °C; IR (neat, cm^{-1}) 1732, 1683, 1622, 1541, 1507, 1444, 1369; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.62 (d, J = 8.3 Hz, 1H), 8.47 (s, 1H), 8.21 (s, 1H), 8.06 (d, J = 8.2 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.2 Hz, 1H), 4.49 (qd, J = 13.3, 7.3 Hz, 1H), 4.35 (qd, J = 13.3, 7.3 Hz, 1H), 2.68 (s, 3H), 2.43 (s, 3H), 1.40 (t, J = 7.3 Hz, 3H), 1.18 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.7, 167.5, 163.5, 154.4, 144.9, 136.5, 135.4, 129.7, 129.2, 121.6, 120.5, 116.3, 81.9, 46.8, 27.8, 25.2, 21.7, 15.1; HRMS calcd for $C_{24}H_{28}N_4NaO_6S$ ([M + Na^+]) 523.1627, found 523.1635.

_N_-(1-Ethyl-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carbonyl)-4-methylbenzenesulfonohydrazide (S10b)

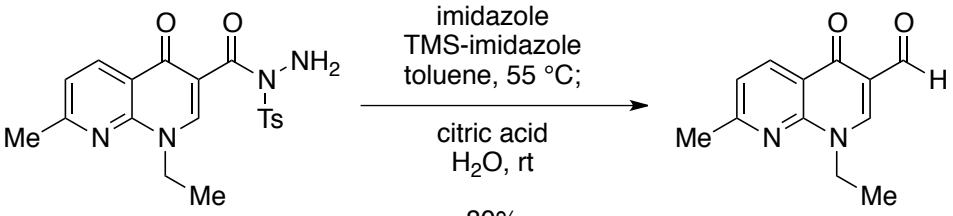


To a solution of **S10a** (200 mg, 0.40 mmol) in CH_2Cl_2 (200 μL) at 0 °C was added 1.0 M TMSI in CH_2Cl_2 (800 μL) and the resulting mixture was warmed to room temperature. After 5 min,

the reaction was quenched with saturated NH_4Cl aq. (2 mL) and partitioned between EtOAc (15 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (5 mL) and brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (50% EtOAc in *n*-hexane) to afford **S10b** as a white powder (148 mg, 0.37 mmol, 93%).

R*f* = 0.23 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 180.0–183.5 °C (decomp.); IR (neat, cm^{-1}) 1669, 1623, 1587, 1442, 1350, 1258, 1163; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.55 (d, J = 7.8 Hz, 1H), 8.12 (s, 1H), 8.00 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 1H), 4.91 (br, 2H), 4.45 (q, J = 7.3 Hz, 2H), 2.66 (s, 3H), 2.42 (s, 3H), 1.45 (t, J = 8.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.1, 168.3, 163.0, 148.6, 145.7, 145.0, 136.4, 134.5, 129.5, 129.0, 121.1, 120.3, 118.1, 46.5, 25.1, 21.7, 15.1; HRMS calcd for $C_{19}H_{20}N_4NaO_4S$ ([M + Na^+]) 423.1103, found 423.1101.

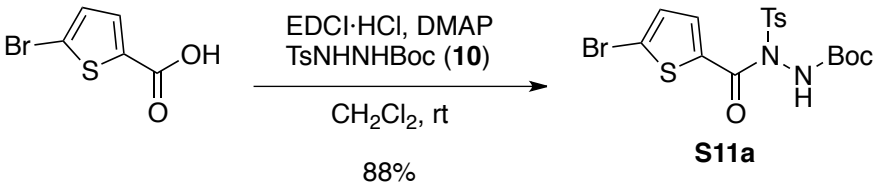
1-Ethyl-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carbaldehyde (S10c)



To a solution of **S10b** (100 mg, 0.25 mmol) in toluene (500 μL) at room temperature was added TMS-imidazole (110 μL, 0.75 mmol). After stirring for 5 min, the reaction mixture was added imidazole (34.0 mg, 0.50 mmol), and stirring was continued at 55 °C. After 20 h, the reaction mixture was added 1.0 M citric acid aq. (5.0 mL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between EtOAc (20 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (ethyl acetate in *n*-hexane, 25 to 50%) to afford **S10c** as a white powder (43.0 mg, 0.20 mmol, 80%).

R*f* = 0.33 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA, 2,4-DNP); M.p. 176.0–177.0 °C; IR (neat, cm^{-1}) 1681, 1625, 1607, 1542, 1442; ^1H NMR ($CDCl_3$, 400 MHz) δ 10.4 (s, 1H), 8.65 (d, J = 8.2 Hz, 1H), 8.45 (s, 1H), 7.29 (d, J = 8.2 Hz, 1H), 4.50 (q, J = 6.9 Hz, 2H), 2.69 (s, 3H), 1.51 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 189.0, 177.2, 163.3, 149.1, 145.8, 136.2, 121.9, 121.5, 118.0, 46.8, 25.1, 15.1; HRMS calcd for $C_{12}H_{12}N_2NaO_2$ ([M + Na^+]) 239.0796, found 239.0793.

***tert*-Butyl 2-(5-bromothiophene-2-carbonyl)-2-tosylhydrazinecarboxylate (S11a)**

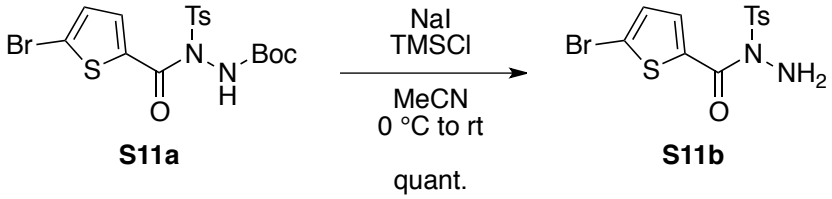


S11a

To a solution of 5-bromothiophene-2-carboxylic acid (228 mg, 1.10 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10 mmol) and TsNHNHBoc (**10**, 286 mg, 1.00 mmol). After 2 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (20 mL) and H_2O (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (15% EtOAc in *n*-hexane) to afford **S10a** as a white powder (419 mg, 0.88 mmol, 88%).

R*f* = 0.57 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 170.0–171.0 °C; IR (neat, cm^{-1}) 1749, 1674, 1408, 1368, 1346, 1246, 1171; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 4.1 Hz, 1H), 7.35 (d, J = 8.2 Hz, 2H), 7.23 (s, 1H), 7.06 (d, J = 4.1 Hz, 1H), 2.44 (s, 3H), 1.41 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.8, 154.1, 145.7, 137.3, 134.6, 131.8, 130.3, 130.1, 129.3, 123.1, 84.3, 28.1, 21.8; HRMS calcd for $C_{17}H_{19}BrN_2NaO_5S_2$ ([M + Na^+]) 496.9819, found 439.9817.

***N*-(5-Bromothiophene-2-carbonyl)-4-methylbenzenesulfonohydrazide (S11b)**



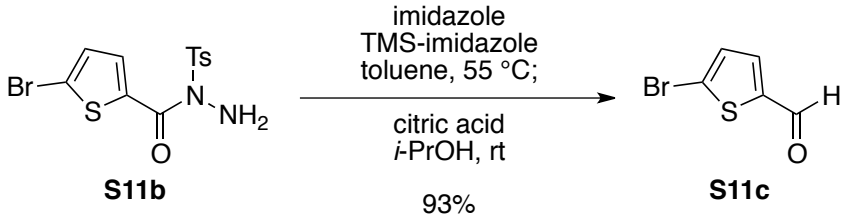
S11a **S11b**

To a stirred solution of **S10a** (404 mg, 0.85 mmol) in MeCN (10 mL) at 0 °C was added NaI (382 mg, 2.55 mmol) and TMSCl (210 μL, 1.70 mmol) and the resulting mixture was warmed to room temperature. After 30 min, the reaction was quenched with saturated NH_4Cl aq. (10 mL) and partitioned between EtOAc (40 mL) and H_2O (20 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (40 mL) twice. The combined organic extract was washed

with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized with toluene/*n*-hexane (2:1, 15 mL) to afford **S10b** as a white powder (340 mg, 0.85 mmol, quant.).

R*f* = 0.51 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 183.1–184.0 °C; IR (neat, cm^{-1}) 1646, 1541, 1507, 1405, 1339; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, J = 8.2 Hz, 2H), 7.81 (d, J = 4.1 Hz, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.06 (d, J = 4.1 Hz, 1H), 4.73 (s, 3H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.4, 145.8, 137.3, 134.6, 129.7, 129.6, 129.1, 126.2, 124.7, 21.7; HRMS calcd for $C_{12}H_{11}BrN_2NaO_3S_2$ ([M + Na^+]) 396.9292, found 396.9295.

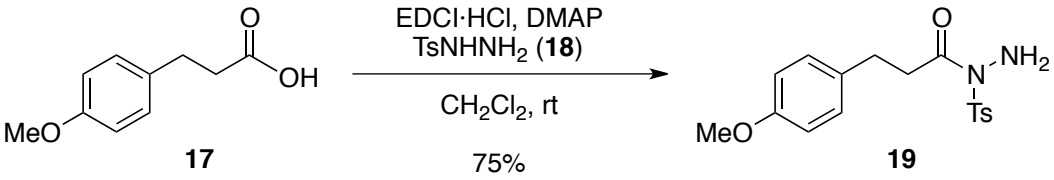
5-Bromothiophene-2-carbaldehyde (S11c)



To a solution of **S10b** (200 mg, 0.53 mmol) in toluene (2.5 mL) at room temperature was added TMS-imidazole (155 μL, 1.06 mmol). After stirring for 5 min, the reaction mixture was added imidazole (73.0 mg, 1.06 mmol), and stirring was continued at 55 °C. After 15 h, the reaction mixture was added 0.5 M citric acid in *i*-PrOH (6.0 mL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between EtOAc (20 mL) and saturated $NaHCO_3$ aq. (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (10 to 20% EtOAc in *n*-hexane) to afford **S10c** as a pale yellow oil (95.0 mg, 0.50 mmol, 93%).

R*f* = 0.64 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); IR (neat, cm^{-1}) 1518, 1410, 1202, 982, 860; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.78 (s, 1H), 7.52 (d, J = 4.1 Hz, 1H), 7.20 (d, J = 4.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 181.7, 145.2, 136.5, 131.4, 125.0; HRMS calcd for C_5H_3BrOS ([M^+]) 189.9088, found 189.9083.

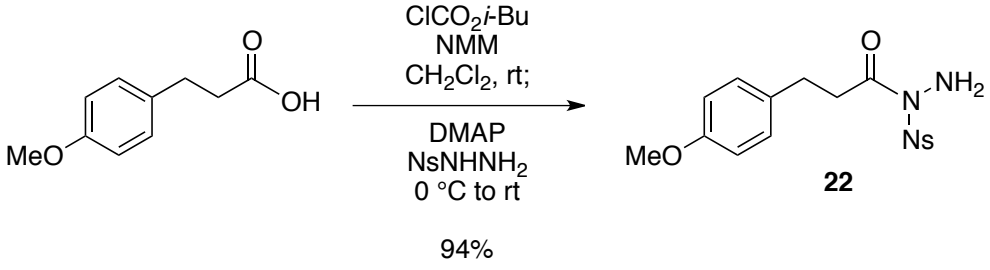
_N_-(3-(4-Methoxyphenyl)propanoyl)-4-methylbenzenesulfonohydrazide (19)



To a solution of 3-(4-methoxyphenyl)propanoic acid (**17**, 180 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (24.4 mg, 0.20 mmol) and $TsNHNH_2$ (216 mg, 1.20 mmol). After 3 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (40 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (40 mL) twice. The combined organic extract was washed with brine (20 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (20% EtOAc in *n*-hexane) to afford **19** as a white powder (260 mg, 0.75 mmol, 75%).

R*f* = 0.63 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 113.8–114.0 °C; IR (neat, cm^{-1}) 2933, 1702, 1611, 1512, 1443, 1350, 1300, 1248, 1166, 1122, 1089, 1034; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.05 (d, *J* = 8.2 Hz, 2H), 6.78 (d, *J* = 8.2 Hz, 2H), 4.27 (s, 2H), 3.78 (s, 3H), 3.02 (t, *J* = 7.8 Hz, 2H), 2.85 (t, *J* = 7.8 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.8, 158.0, 145.2, 134.7, 132.5, 129.5, 129.3, 128.7, 113.8, 55.2, 37.6, 29.7, 21.7; HRMS calcd for $C_{16}H_{17}N_3NaO_6S$ ([M + Na^+]) 371.1042, found 371.1029.

_N_-(3-(4-Methoxyphenyl)propanoyl)-2-nitrobenzenesulfonohydrazide (22)

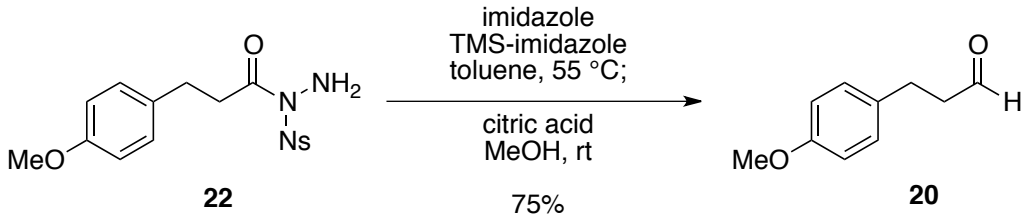


To a stirred solution of 3-(4-methoxyphenyl)propanoic acid (**17**, 180 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added *N*-methylmorpholine (120 μL, 1.10 mmol) and *i*-BuOCOCl (145 μL, 1.10 mmol). After sttirring for 1 h, the resulting solution was added 4-dimethylaminopyridine (24.4 mg, 0.20 mmol) and *o*-$NsNHNH_2$ (260 mg, 1.20 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for additional 2 h. The resulting solution was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL)

and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with brine (15 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (10 to 20% EtOAc in *n*-hexane) to afford **22** as a white powder (455 mg, 0.94 mmol, 94%).

R*f* = 0.62 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 100.1–100.5 °C; IR (neat, cm^{-1}) 1716, 1699, 1541, 1509, 1362; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.50–8.48 (m, 1H), 7.85–7.79 (m, 3H), 7.05 (d, *J* = 8.2 Hz, 2H), 6.77 (d, *J* = 8.3 Hz, 2H), 4.62 (s, 2H), 3.77 (s, 3H), 3.01 (t, *J* = 8.3 Hz, 2H), 2.82 (t, *J* = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.6, 158.0, 135.4, 134.7, 132.9, 132.5, 132.2, 129.2, 124.6, 113.9, 55.2, 36.9, 29.2; HRMS calcd for $C_{16}H_{17}N_3NaO_6S$ ([M + Na^+]) 402.0736, found 403.0725.

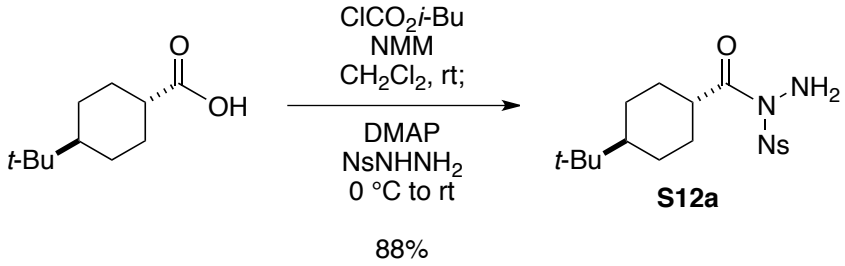
3-(4-Methoxyphenyl)propanal (20)



To a solution of **22** (200 mg, 0.53 mmol) in toluene (2.5 mL) at room temperature was added TMS-imidazole (155 μL, 1.05 mmol). After stirring for 5 min, the reaction mixture was added imidazole (72 mg, 1.05 mmol) and stirring was continued at 55 °C. After 10 h, the reaction mixture was added 1.0 M citric acid in MeOH (5.0 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (10 mL) and saturated $NaHCO_3$ aq. (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (6% EtOAc in *n*-hexane) to afford **20** as a colorless oil (65.0 mg, 0.40 mmol, 75%).

R*f* = 0.60 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); IR (neat, cm^{-1}) 1722, 1514, 1247; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.81 (s, 1H), 7.11 (d, *J* = 6.4 Hz, 2H), 6.83 (d, *J* = 6.4 Hz, 2H), 3.78 (s, 3H), 2.90 (t, *J* = 7.3 Hz, 2H), 2.75 (t, *J* = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 201.8, 158.1, 132.3, 129.2, 114.0, 55.3, 45.5, 27.3; HRMS calcd for $C_{10}H_{12}O_2$ ([M $^+$]) 164.0837, found 164.0842.

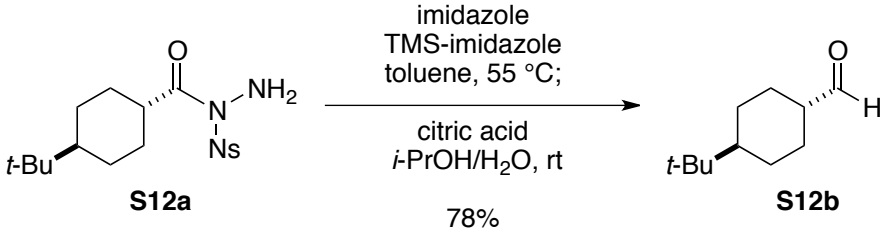
_N_-((1_r_,4_r_)-4-_tert_-butylcyclohexanecarbonyl)-2-nitrobenzenesulfonohydrazide (S12a)



To a stirred solution of 4-*tert*-butylcyclohexanecarboxylic acid (184 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added *N*-methylmorpholine (120 μL, 1.10 mmol) and *i*-BuOCOCl (145 μL, 1.10 mmol). After 1 h, the reaction mixture was added 4-dimethylaminopyridine (24.4 mg, 0.20 mmol) and *o*-$NsNHNH_2$ (260 mg, 1.20 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for additional 2 h. The reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (15% EtOAc in *n*-hexane) to afford **S12a** as a white powder (338 mg, 0.88 mmol, 88%).

R*f* = 0.56 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); M.p. 100.1–100.5 °C; IR (neat, cm^{-1}) 2946, 1698, 1541, 1362; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.49 (d, J = 5.5 Hz, 1H), 7.83–7.75 (m, 3H), 4.64 (s, 1H), 3.07 (tt, J = 11.9, 3.6 Hz, 1H), 1.93 (d, J = 11.5 Hz, 2H), 1.82 (d, J = 10.5 Hz, 2H), 1.34–1.25 (dt, J = 22.5, 10.1 Hz, 2H), 1.10–0.92 (m, 3H), 0.83 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.1, 135.3, 134.6, 133.4, 132.6, 124.6, 47.3, 42.9, 42.2, 32.4, 28.6, 27.5, 26.4; HRMS calcd for $C_{17}H_{25}N_3NaO_5S$ ([M + Na^+]) 406.1413, found 406.1400.

(1_r_,4_r_)-4-_tert_-Butylcyclohexanecarbaldehyde (S12b)

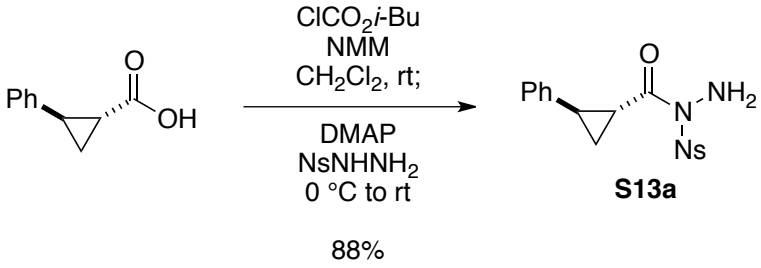


To a solution of **S12a** (200 mg, 0.52 mmol) in toluene (2.5 mL) at room temperature was

added TMS-imidazole (150 μL, 1.04 mmol). After stirring for 5 min, the reaction mixture was added imidazole (71 mg, 1.0 mmol) and stirring was continued at 55 °C. After 14 h, the reaction mixture was added 0.5 M citric acid in *i*-PrOH (10 mL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between saturated EtOAc (10 mL) and $NaHCO_3$ aq. (6 mL). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (2% EtOAc in *n*-hexane) to afford **S12b** as a colorless oil (68.0 mg, 0.40 mmol, 78%).

R*f* = 0.67 (*n*-hexane/EtOAc = 2:1, 2,4-DNP); IR (neat, cm^{-1}) 1722, 1514, 1247; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.61 (d, *J* = 1.8 Hz, 1H), 2.20–2.08 (m, 1H), 2.08–1.99 (m, 2H), 1.85–1.98 (m, 2H), 1.32–1.14 (m, 2H), 1.11–0.94 (m, 3H), 0.86 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 205.1, 50.5, 47.6, 27.5, 27.4, 26.5, 26.2; HRMS calcd for $C_{11}H_{20}O$ ($[M^+]$) 168.1514, found 168.1521.

***trans*-2-nitro-*N*-(2-Phenylcyclopropanecarbonyl)benzenesulfonohydrazide (S13a)**

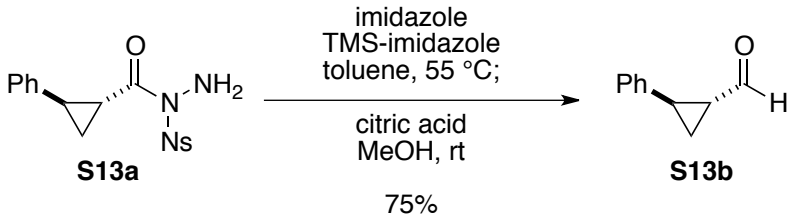


88%

To a stirred solution of 2-phenylcyclopropanecarboxylic acid (162 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added *N*-methylmorpholine (120 μL, 1.10 mmol) and *i*-BuOCOCl (145 μL, 1.10 mmol). After 1 h, the resulting solution was added 4-dimethylaminopyridine (24.4 mg, 0.20 mmol) and *o*-$NsNHNH_2$ (260 mg, 1.20 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for additional 3.5 h. The reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (15% EtOAc in *n*-hexane) to afford **S13a** as a white powder (338 mg, 0.88 mmol, 88%).

R*f* = 0.67 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 134.1–134.8 °C; IR (neat, cm^{-1}) 1697, 1683, 1541, 1362, 1173, 1129; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (d, J = 5.0 Hz, 1H), 7.85–7.79 (m, 3H), 7.30–7.19 (m, 3H), 7.12 (d, J = 3.6 Hz, 2H), 4.74 (s, 2H), 3.09–3.05 (m, 1H), 2.52–2.48 (m, 1H), 1.62–1.57 (m, 1H), 1.43–1.38 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.1, 139.6, 135.1, 134.7, 133.2, 132.5, 128.5, 126.7, 126.3, 124.6, 28.2, 23.3, 18.3; HRMS calcd for $C_{16}H_{15}N_3NaO_5S$ ([M + Na^+]) 384.0630, found 384.0642.

***trans*-2-Phenylcyclopropanecarbaldehyde (S13b)**



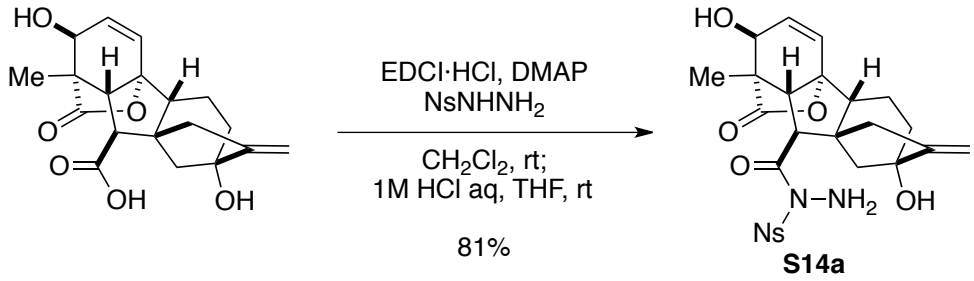
75%

To a solution of **S13a** (200 mg, 0.55 mmol) in toluene (2.5 mL) at room temperature was

added TMS-imidazole (160 μL, 1.11 mmol). After stirring for 5 min, the reaction mixture was added imidazole (75 mg, 1.1 mmol) and stirring was continued at 55 °C. After 16 h, the reaction mixture was added 1.0 M citric acid in MeOH (5.0 mL) at room temperature and stirred for additional 1 h. The resulting mixture was partitioned between saturated $NaHCO_3$ aq. (6 mL) and EtOAc (15 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (15 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (3% EtOAc in *n*-hexane) to afford **S13b** as a colorless oil (60.8 mg, 0.42 mmol, 75%).

R*f* = 0.63 (*n*-hexane/EtOAc = 2:1, UV, 2,4-DNP); IR (neat, cm^{-1}) 3023, 1708, 1128; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.33 (d, J = 4.6 Hz, 1H), 7.11–7.33 (m, 5H), 2.61–2.66 (m, 1H), 2.15–2.21 (m, 1H), 1.71–1.76 (m, 1H), 1.51–1.56 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 199.7, 138.9, 128.6, 126.8, 126.3, 33.8, 26.6, 16.4; HRMS calcd for $C_{10}H_{10}O$ ([M^+]) 146.0732, found 146.0727.

_N_-((1S,2S,4aR,4bS,7S,9aS,10S,10aR)-2,7-dihydroxy-1-methyl-8-methylene-13-oxo-1,2,4b,5,6,7,8,9,10,10a-decahydro-4a,1-(epoxymethano)-7,9a-methanobenzo[a]azulene-10-carbonyl)-2-nitrobenzenesulfonohydrazide (S14a)

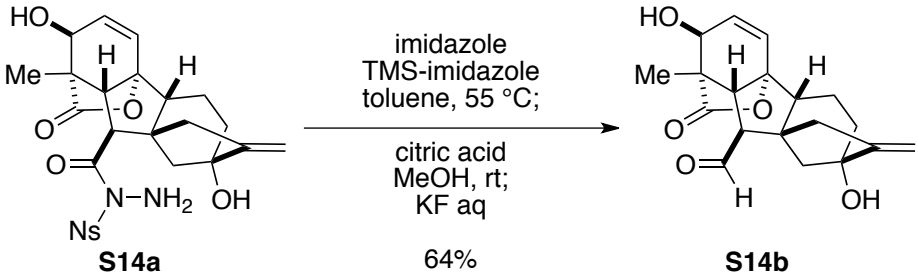


S14a

To a solution of gibberellic acid (355 mg, 1.02 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (288 mg, 1.50 mmol), 4-dimethylaminopyridine (24.4 mg, 0.20mmol) and *o*-$NsNHNH_2$ (217 mg, 1.00 mmol). After 2 h, the reaction mixture was added 1.0 M HCl aq. (5.0 mL) and THF (5.0 mL) and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (30 mL) and saturated $NaHCO_3$ aq. (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on silica gel (50 to 60% EtOAc in *n*-hexane) to afford **S14a** (449 mg, 0.82 mmol, 81%) as a white powder.

R*f* = 0.38 (*n*-hexane/EtOAc = 1:2, UV, Ce-PMA); M.p. 192.0–193.0 °C (decomp.); IR (neat, cm^{-1}) 3377, 1762, 1701, 1543, 1364, 1173; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.48 (m, 1H), 7.85 (m, 3H), 6.28 (d, J = 9.6 Hz, 1H), 5.87–5.84 (m, 1H), 5.20 (s, 1H), 4.83–4.77 (m, 3H), 4.07 (d, J = 3.2 Hz, 1H), 3.95 (d, J = 10.6 Hz, 1H), 3.15 (d, J = 10.1 Hz, 1H), 2.15 (d, J = 11.0 Hz, 1H), 2.06–1.65 (m, 8H), 1.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.3, 173.9, 156.4, 147.7, 135.5, 135.1, 132.8, 132.7, 132.6, 132.4, 124.5, 107.4, 90.4, 78.3, 69.8, 53.5, 53.2, 51.6, 51.5, 47.8, 45.1, 42.9, 37.9, 17.0, 14.3; HRMS calcd for $C_{25}H_{27}N_3NaO_9S$ ([M + Na^+]) 568.1366, found 568.1389.

(1*S*,2*S*,4a*R*,4b*S*,7*S*,9a*S*,10*S*,10a*R*)-2,7-dihydroxy-1-methyl-8-methylene-13-oxo-1,2,4b,5,6,7,8,9,10,10a-decahydro-4a,1-(epoxymethano)-7,9a-methanobenzo[*a*]azulene-10-carbaldehyde (S14b)

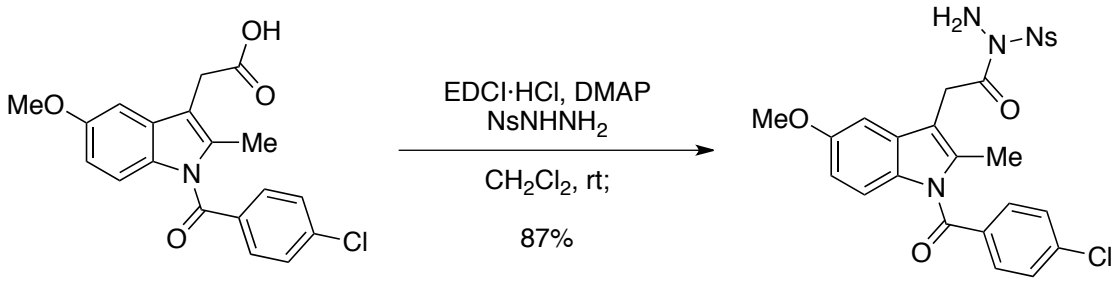


S14a **S14b**

To a solution of **S14a** (300 mg, 0.55 mmol) in toluene (3.5 mL) at room temperature was added TMS-imidazole (400 μL, 2.75 mmol). After stirring for 10 min, the reaction mixture was added imidazole (112 mg, 1.65 mmol), and stirring was continued at 55 °C. After stirring for 12 h, the reaction was added 1.0 M citric acid in MeOH (6.0 mL) at room temperature. After 2 h, the resulting solution was added 1.0 M KF aq. (1.0 mL) and stirred for additional 1 h. The resulting mixture was partitioned between EtOAc (20 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (20 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (40 to 50% EtOAc in *n*-hexane) to afford **S14b** (115 mg, 0.35 mmol, 64%) as a white powder.

R*f* = 0.42 (*n*-hexane/EtOAc = 1:2, UV, Ce-PMA, 2,4-DNP); M.p. 173.0–175.0 °C (decomp.); IR (neat, cm^{-1}) 3406, 1760, 1717, 1454, 1380; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.82 (s, 1H), 6.34 (d, *J* = 9.6 Hz, 1H), 5.92 (dd, *J* = 9.2, 3.7 Hz, 1H), 5.30 (s, 1H), 5.00 (s, 1H), 4.19 (t, *J* = 5.5 Hz, 1H), 3.74 (s, 1H), 3.21 (d, *J* = 10.1 Hz, 1H), 2.81 (d, *J* = 10.1 Hz, 1H), 2.49 (d, *J* = 13.3 Hz, 1H), 2.21 (d, *J* = 12.8 Hz, 2H), 2.12–1.68 (m, 9H), 1.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 200.7, 178.3, 156.1, 132.6, 132.5, 108.1, 90.4, 77.5, 69.7, 56.4, 53.4, 51.4, 50.9, 50.3, 45.9, 41.9, 38.2, 16.9, 14.9; HRMS calcd for $C_{19}H_{22}ONa_5$ ([M + Na^+]) 353.1365, found 353.1353.

_N_-(2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetyl)-2-nitrobenzenesulfonohydrazide (S15a)

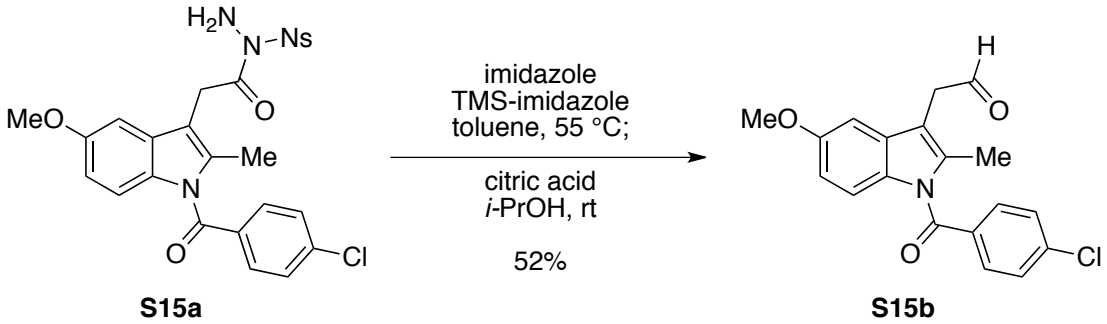


S15a

To a solution of Indomethacin (358 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (288 mg, 1.50 mmol), 4-dimethylaminopyridine (24.4 mg, 0.20 mmol) and *o*-$NsNHNH_2$ (326 mg, 1.50 mmol). After 2 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (30 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (10-20% EtOAc in *n*-hexane) to afford **S15a** (486 mg, 0.87 mmol, 87%) as a yellow powder.

R*f* = 0.66 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 93.0–95.0 °C; IR (neat, cm^{-1}) 1684, 1541, 1477, 1362, 1324; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.45 (dd, J = 7.3, 1.8 Hz, 1H), 7.81–7.69 (m, 3H), 7.65 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 8.7 Hz, 2H), 6.75 (d, J = 7.2 Hz, 1H), 6.73 (d, J = 2.3 Hz, 1H), 6.58 (dd, J = 8.7, 2.3 Hz, 1H), 4.74 (s, 2H), 4.05 (s, 2H), 3.69 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.1, 168.2, 155.7, 147.4, 139.3, 136.5, 135.5, 134.8, 133.8, 132.6, 132.4, 131.2, 130.7, 130.5, 129.1, 124.7, 114.8, 111.5, 111.3, 101.1, 55.5, 31.6, 13.4; HRMS calcd for $C_{25}H_{21}ClN_4NaO_7S$ ([M + Na^+]) 579.0717, found 579.0697.

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetaldehyde (S15b)

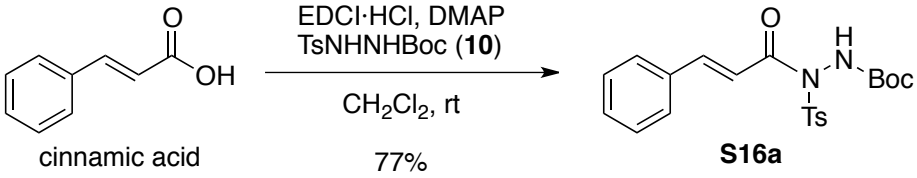


S15a **S15b**

To a solution of **S15a** (150 mg, 0.27 mmol) in toluene (1.3 mL) at room temperature was added TMS-imidazole (80 μL, 0.54 mmol). After stirring for 5 min, the reaction mixture was added imidazole (37 mg, 0.54 mmol) and stirring was continued at 55 °C. After 20 h, the reaction mixture was added 0.5 M citric acid in *i*-PrOH (5.0 mL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between EtOAc (10 mL) and saturated $NaHCO_3$ aq. (6 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (10 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (10 to 15% EtOAc in *n*-hexane) to afford **S15b** (48.3 mg, 0.14 mmol, 52%) as a yellow crystal.

R*f* = 0.44 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); M.p. 121.5–123.0 °C; IR (neat, cm^{-1}) 1723, 1683, 1590, 1477, 1357, 1317; ^1H NMR ($CDCl_3$, 400 MHz) δ 9.71 (s, 1H), 7.68 (d, J = 6.4 Hz, 2H), 7.48 (d, J = 6.8 Hz, 2H), 6.85 (d, J = 9.2 Hz, 2H), 6.68 (d, J = 9.2 Hz, 1H), 3.83 (s, 3H), 3.72 (s, 2H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 198.0, 168.2, 156.1, 139.4, 136.5, 133.7, 131.2, 130.9, 130.6, 129.2, 115.1, 111.9, 110.1, 100.8, 55.7, 39.4, 13.3; HRMS calcd for $C_{19}H_{16}ClNNaO_3$ ([M + Na^+]) 364.0716, found 364.0703.

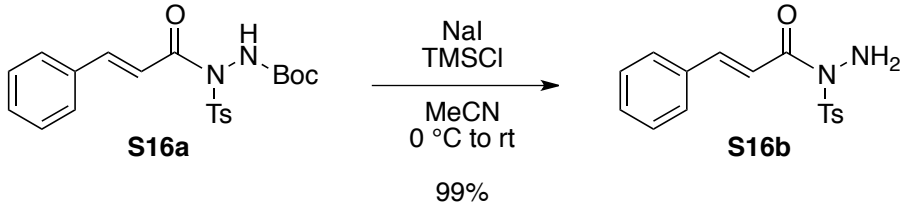
***tert*-Butyl 2-cinnamoyl-2-tosylhydrazinecarboxylate (S16a)**



To a stirred solution of cinnamic acid (**24**, 163 mg, 1.10 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (230 mg, 1.20 mmol), 4-dimethylaminopyridine (12.2 mg, 0.10mmol) and TsNHNHBoc (**10**, 286. mg, 1.00 mmol). After 2 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (40 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (40 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (10 to 15% EtOAc in *n*-hexane) to afford **S16a** (320 mg, 0.77 mmol, 77%) as a white amorphous solid.

R*f* = 0.47 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA); IR (neat, cm^{-1}) 1733, 1698, 1617, 1507, 1370, 1246, 1167, 1021; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.03 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 15.6 Hz, 1H), 7.50 (m, 2H), 7.38 (m, 3H), 7.34 (d, J = 8.2 Hz, 2H), 7.07 (br, 1H), 6.94 (d, J = 15.6 Hz, 1H), 2.43 (s, 3H), 1.52 (br, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 154.2, 147.1, 145.3, 134.9, 134.2, 130.7, 129.7, 129.2, 128.8, 128.4, 83.3, 28.0, 21.7; HRMS calcd for $C_{20}H_{21}N_3NaO_5S$ ([M + Na^+]) 439.1304, found 439.1312.

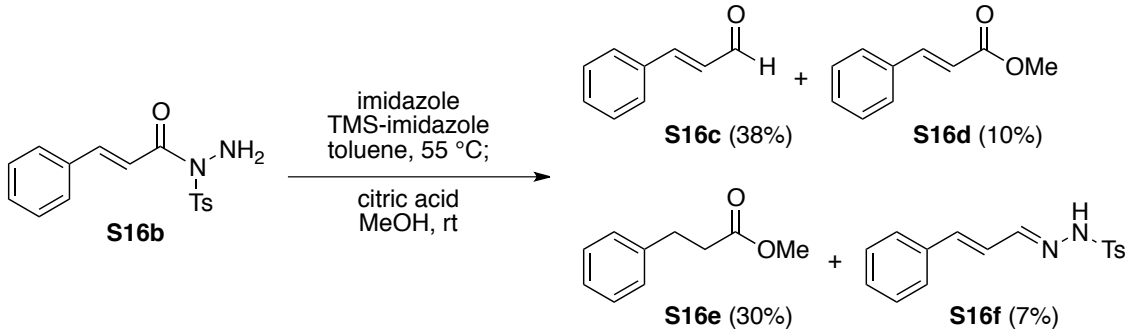
(*E*)-*N*-Cinnamoyl-4-methylbenzenesulfonohydrazide (S16b)



To a stirred solution of **S16a** (320 mg, 0.77 mmol) in MeCN (10 mL) at 0 °C was added NaI (345 mg, 2.31 mmol) and TMSCl (200 μL, 1.54 mmol). The resulting mixture was warmed to room temperature. After stirring for 30 min, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (40 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (40 mL) twice. The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was crystallized from toluene (10 mL) to afford **S16b** as a white powder (240 mg, 0.76 mmol, 99%).

R*f* = 0.67 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 146.1–146.5 °C; IR (neat, cm^{-1}) 1667, 1649, 1615, 1346, 1171, 1133, 1090; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 15.6 Hz, 1H), 7.57 (m, 2H), 7.55 (d, *J* = 15.6 Hz, 1H), 7.57 (m, 3H), 7.34(d, *J* = 8.2 Hz, 2H), 4.48 (s, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.0, 146.0, 145.2, 134.7, 134.5, 130.6, 129.6, 128.9, 128.7, 128.4, 117.3, 21.7; HRMS calcd for $C_{15}H_{13}N_3NaO_3S$ ([M + Na^+]) 339.0779, found 339.0790.

Synthesis of *trans*-cinnamicaldehyde (S16c) from S16b



To a stirred solution of **S16b** (20 mg, 0.06 mmol) in toluene (630 μL) at room temperature was added TMS-imidazole (24 μL, 0.13 mmol). After stirring for 5 min, the reaction mixture was added imidazole (8.6 mg, 0.13 mmol) and stirring was continued at 55 °C. After 12 h, the reaction mixture was added 1.0 M citric acid in MeOH (400 μL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between EtOAc (5 mL) and saturated $NaHCO_3$ aq. (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (5 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (20% EtOAc in *n*-hexane) to afford **S16f** (1.3 mg, 0.004 mmol, 6.7%) and inseparable mixture (total 7.3 mg) of **S16c** (0.024 mmol, 38%), **S16d** (0.006 mmol, 10%) and **S16e** (0.019 mmol, 30%).

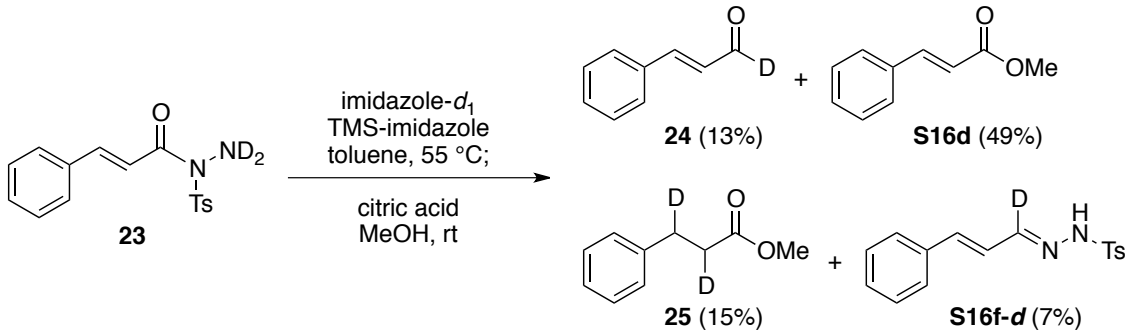
S16c: R*f* = 0.69 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.71 (d, *J* = 7.8 Hz, 1H), 7.59 (m, 2H), 7.52 (d, *J* = 16.0 Hz, 1H), 7.43 (m, 3H), 6.73 (dd, *J* = 16.0, 7.8 Hz, 1H).

S16d: R*f* = 0.68 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (d, *J* = 16.5 Hz, 1H), 7.64–7.29 (m, 5H), 6.45 (d, *J* = 16.5 Hz, 1H), 3.81 (s, 3H).

S16e: R*f* = 0.68 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29–7.13 (m, 5H), 3.67 (s, 3H), 2.96 (t, *J* = 8.2 Hz, 2H), 2.64 (t, *J* = 8.2 Hz, 2H).

S16f: R*f* = 0.21 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.67 (s, 1H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 6.4 Hz, 1H), 7.37-7.26 (m, 5H), 6.87–6.80 (m, 1H), 6.81 (d, *J* = 6.4 Hz, 1H), 2.42 (s, 3H).

Synthesis of deutetrated *trans*-cinnamaldehyde (24) via deuterated substrate 23



The stirred solution of **S16b** (11.0 mg, 0.040 mmol) in CD_3OD (650 μL) under Ar was heated at 70 °C. After stirring for 7 h, the solvent was removed under reduced pressure. The deuteriomeric content of **23** was determined by ^{1}H NMR to be >99%. To a solution of **23** (11 mg, 0.040 mmol) in toluene (350 μL) at room temperature was added TMS-imidazole (14 μL, 0.07 mmol). After stirring for 5 min, the reaction mixture was added imidazole (5.0 mg, 0.070 mmol), and stirring was continued at 55 °C. After 12 h, the reaction mixture was added 1.0 M citric acid in MeOH (400 μL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between EtOAc (5 mL) and saturated $NaHCO_3$ aq. (5 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (5 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by preparative TLC (20% EtOAc in *n*-hexane) to afford **S16f-*d*** (0.7 mg, 0.002 mmol, 7%) and inseparable mixture (total 4.3 mg) of **24** (0.005 mmol, 13%), **S16d** (0.017 mmol, 49%) and **25** (0.005 mmol, 15%).

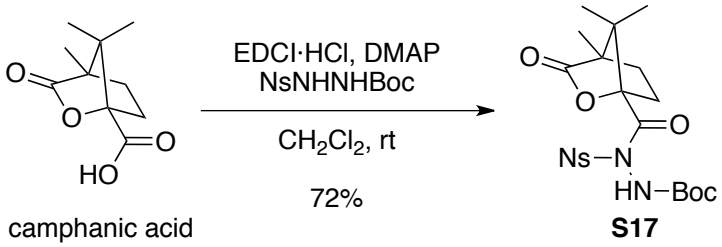
24: R*f* = 0.69 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59 (m, 2H), 7.52 (d, *J* = 16.0 Hz, 1H), 7.43 (m, 3H), 6.73 (dd, *J* = 16.0, 7.8 Hz, 1H).

25: R*f* = 0.68 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29–7.13 (m, 5H), 3.67 (s, 3H), 2.96 (t, *J* = 8.2 Hz, 2H(44%-*d*)), 2.64 (t, *J* = 8.2 Hz, 2H(63%-*d*)).*

S16f-*d*: R*f* = 0.21 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.67 (s, 1H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 6.4 Hz, 1H), 7.37–7.26 (m, 5H), 6.87–6.80 (m, 1H), 2.42 (s, 3H).

* The slight difference of the deuterated content in **25** could be explained by the H-D exchange at the α-position of the intermediate **28** under basic conditions.

***tert*-Butyl-2-((2-nitrophenyl)sulfonyl)-2-((1R)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carbonyl)hydrazinecarboxylate (S17)**

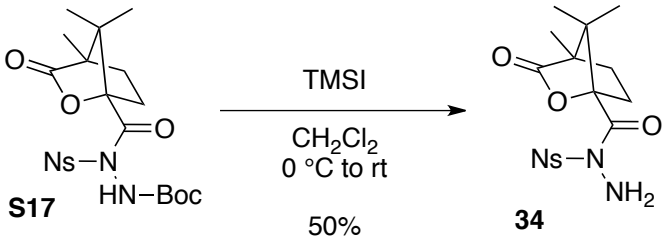


camphanic acid **S17**

To a stirred solution of (–)-camphanic acid (100 mg, 0.50 mmol) in CH_2Cl_2 (10 mL) at room temperature was added EDCI·HCl (145 mg, 0.76 mmol), 4-dimethylaminopyridine (12.0 mg, 0.05 mmol) and NsNHNHBoc (160 mg, 0.50 mmol). After 3 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and partitioned between EtOAc (40 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (40 mL) twice. The combined organic extract was washed with brine (10 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (EtOAc in *n*-hexane, 20 to 40%) to afford **S17** as a pale yellow amorphous solid (180 mg, 0.36 mmol, 72%).

R*f* = 0.42 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); IR (neat, cm^{-1}) 3387, 3101, 1793, 1744, 1592, 1545, 1468, 1371, 1249, 1180, 1092, 1039; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.55 (m, 1H), 7,82 (m, 3H), 2.42–1.23 (m, 4H), 1.53 (s, 9H), 1.06 (s, 3H), 1.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.7, 167.5, 154.3, 147.9, 135.1, 132.3, 131.5, 124.7, 91.2, 83.7, 55.1, 53.8, 30.5, 28.8, 28.0, 16.8, 16.3, 9.5; HRMS calcd for $C_{16}H_{17}N_3NaO_6S$ ([M + Na^+]) 520.1366, found 520.1344.

2-Nitro-*N*-((1R)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carbonyl)benzenesulfonohydrazide (34)



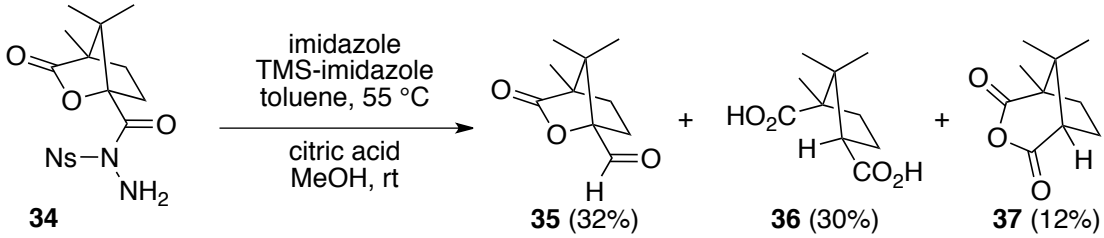
S17 50% **34**

To a stirred solution of **S17** (100 mg, 0.20 mmol) in CH_2Cl_2 (200 μL) at 0 °C was added 1.0 M TMSI in CH_2Cl_2 (1.0 mL). The resulting mixture was warmed to room temperature. After stirring for 6 h, the reaction was quenched with saturated NH_4Cl aq. (2 mL) and pertitioned between EtOAc

(15 mL) and H_2O (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (30 mL). The combined organic extract was washed with saturated $Na_2S_2O_3$ aq. (5 mL) and brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography on neutralized silica gel (40% EtOAc in *n*-hexane) to afford **34** as a white powder (40.0 mg, 0.10 mmol, 50%).

R*f* = 0.31 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA); M.p. 123.3–123.5 °C; IR (neat, cm^{-1}) 2970, 1784, 1698, 1541, 1366, 1173, 1092, 1031; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.48 (m. 1H), 7.85 (m, 3H), 4.70 (s, 2H), 2.63 (dt, *J* = 9.2, 4.6 Hz, 1H), 2.33 (dt, *J* = 12.8, 4.6 Hz, 1H), 1.86 (dt, *J* = 12.8, 4.6 Hz, 1H), 1.74 (d, *J* = 9.2, 4.6 Hz, 1H), 1.08 (s, 3H), 1.04 (s, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.2, 168.0, 147.8, 135.2, 135.0, 132.8, 132.6, 124.7, 91.5, 54.6, 53.9, 29.9, 29.1, 17.0, 16.6, 9.5; HRMS calcd for $C_{19}H_{20}N_4NaO_4S$ ([M + Na^+]) 420.0841, found 420.0833.

(1*R*)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carbaldehyde (35),
(1s,3s)-1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid (36),
1,8,8-trimethyl-3-oxabicyclo[3.2.1]octane-2,4-dione (37)



34 **35** (32%) **36** (30%) **37** (12%)

To a stirred solution of **34** (37.3 mg, 0.09 mmol) in toluene (1.0 mL) at room temperature was added TMS-imidazole (36 μL, 0.19 mmol). After stirring for 5 min, the reaction mixture was added imidazole (12.8 mg, 0.19 mmol) and stirring was continued at 55 °C. After 14 h, the reaction mixture was added 1.0 M citric acid in MeOH (2.0 mL) at room temperature and stirred for additional 2 h. The resulting mixture was partitioned between saturated NH_4Cl aq. (5 mL) and EtOAc (10 mL). The organic phase was collected and the aqueous phase was extracted with EtOAc (40 mL) twice. The combined organic extract was washed with brine, and dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo*. The residue was purified by preparative TLC (33% EtOAc in *n*-hexane) to afford **37** (2.1 mg, 0.012 mmol, 12%), and inseparable mixture (total 11.3 mg) of **35** and **36**. The mixture was partitioned between saturated $NaHCO_3$ aq. (2 mL) and EtOAc (2 mL). The organic pahase was washed with saturated $NaHCO_3$ aq. (2 mL) twice, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo* to afford **35** (5.5 mg, 0.030 mmol, 32%). The

combined aqueous phase was added 1.0 M HCl aq. until it becomes acidic (pH = 2), and extracted with CH_2Cl_2 (2 mL) twice. The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrared *in vacuo* to afford **36** (5.7 mg, 0.029 mmol, 30%).

35: R*f* = 0.30 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.92 (s, 1H), 2.37–2.30 (m, 1H), 1.95–1.88 (m, 2H), 1.74–1.70 (m, 1H), 1.12 (s, 3H), 1.02 (s, 6H).

36[*]: R*f* = 0.16 (*n*-hexane/EtOAc = 1:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.96 (t, *J* = 10.1 Hz, 1H), 2.25–2.15 (m, 2H), 2.10–2.00 (m, 1H), 1.71–1.61 (m, 1H), 1.19 (s, 3H), 1.16 (s, 3H), 0.93 (s, 3H); ^{1}H NMR (DMSO-d_6, 400 MHz) δ 12.11 (brs, 2H), 2.83 (t, *J* = 9.1 Hz, 1H), 2.07–1.93 (m, 2H), 1.84–1.79 (m, 1H), 1.56–1.50 (m, 1H), 1.04 (s, 3H), 1.01 (s, 3H), 0.81 (s, 3H).

37: R*f* = 0.48 (*n*-hexane/EtOAc = 2:1, UV, Ce-PMA, 2,4-DNP); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.83 (d, *J* = 6.4 Hz, 1H), 2.26–2.23 (m, 1H), 2.17–2.09 (m, 1H), 2.04–1.93 (m, 2H), 1.27 (s, 3H), 1.10 (s, 3H), 1.00 (s, 3H).

[*] Lesac, A.; Moslavac-Forjan, D.; Bruce, D. W.; Šunjić, V. *Helv. Chim. Acta*, **1999**, 82, 1707.

Computational Section

Details of Computational Methods

All calculations were carried with the Gaussian 09 program package.[*] The global reaction route mapping method (GRRM) based on Gaussian 09 was utilized for locating all local equilibrium structures and TS structures and for geometry optimization. The molecular structures and harmonic vibrational frequencies were obtained using the hybrid density functional method based on M062X.[†] We used 6–31+G* for the other atoms. Geometry optimization and vibrational analysis were performed at the same level. All stationary points were optimized without any symmetry assumptions, and characterized by normal coordinate analysis at the same level of theory (number of imaginary frequencies, NIMAG, 0 for minima and 1 for TSs). The intrinsic reaction coordinate (IRC) method was used to track minimum energy paths from transition structures to the corresponding local minima.

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[*] Gaussian 09, Revision C.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

[†] (a) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215-241; (b) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157-167.

3-1. Cartesian Coordinates and Free Energies

CP1

Δ*G*298K = -1304.273940 A.U.

C	-0.69655724	2.01872742	0.33174632
N	-1.48391599	1.71046765	-0.81953432
C	0.02103935	0.87759562	1.01897083
O	-0.54988406	3.16202469	0.67202293
N	-2.04426982	2.80109494	-1.48647941
H	-0.61864255	0.01830487	1.21923548
H	0.86920712	0.56867363	0.39934052
H	0.40940285	1.27148740	1.95713605
H	-2.02077123	2.62558222	-2.48417794
H	-3.00552723	2.94468397	-1.15508578
S	-2.23660895	0.18909954	-1.04968335
O	-2.66553053	-0.38843004	0.22972877
O	-3.21725573	0.37993707	-2.10462045
C	-0.94058188	-0.84923894	-1.69898240
H	-1.41352705	-1.80538576	-1.93032135
H	-0.16191697	-0.97885773	-0.94956081
H	-0.55538900	-0.37779369	-2.60286461
C	-5.84374577	2.91062541	-1.17154190
C	-6.97352293	2.31421333	-0.67909807
N	-6.58758911	1.72387691	0.49769259
C	-5.26041801	1.95569254	0.65613745
N	-4.77986202	2.68099147	-0.32917258
H	-5.73428764	3.48484303	-2.07969977
H	-7.97893226	2.23077295	-1.05880990
H	-7.14296739	1.07445635	1.04087479
H	-4.69491859	1.57386037	1.49462179
C	-7.63908563	-1.46984503	0.46147700
C	-6.41268992	-1.56147949	1.07836146
N	-5.50266830	-1.18514096	0.12353457
C	-6.19890580	-0.87265108	-1.00020379
N	-7.49419369	-1.03783853	-0.83382481
H	-8.60943282	-1.70857820	0.87324270
H	-6.11728865	-1.87660602	2.06693734
H	-4.50240890	-1.05953188	0.24894133
H	-5.70694599	-0.49777921	-1.88774525

TS1

Δ*G*298K = -1304.259383 A.U.

C	-0.40847102	1.95386458	-0.45710886
N	-1.74863737	2.39660332	-0.02850191
C	0.47979914	1.57008533	0.686646801
O	-0.07405457	2.05492092	-1.61525505
N	-2.45484794	2.78439106	-0.97762040
H	-0.10638200	1.21061065	1.53290621
H	1.19351996	0.81555156	0.353739827
H	1.04152449	2.45834335	0.994892271
H	-2.05030984	2.68718507	-1.92282493
H	-3.57801052	2.96406741	-0.73697852
S	-2.13973257	-0.09014624	-0.445707940
O	-2.87531058	-0.78021893	0.67927924
O	-3.02068943	0.34255882	-1.58335671
C	-1.07233987	-1.36181723	-1.163891566
H	-1.72806119	-2.14666914	-1.546959719
H	-0.42130091	-1.74866418	-0.379029016
H	-0.49885760	-0.90477986	-1.971813429
C	-6.12500363	3.37168358	-0.74349234
C	-7.15328290	2.58686269	-0.30205107
N	-6.56673859	1.57721340	0.42092949
C	-5.23393417	1.75160137	0.38404038
N	-4.93396990	2.83799686	-0.30616070
H	-6.16270673	4.26815195	-1.34239218
H	-8.21933640	2.64449584	-0.44805620
H	-7.03164123	0.74325703	0.77131309
H	-4.52156449	1.06668561	0.82743182
C	-7.72544315	-1.46438191	-0.08697489
C	-6.61304833	-1.69525117	0.69278891
N	-5.54344402	-1.35158745	-0.09354977
C	-6.03840008	-0.92742472	-1.28466275
N	-7.35523486	-0.98285939	-1.31841415
H	-8.76195756	-1.64086189	0.16405367
H	-6.49245868	-2.09166989	1.68915514
H	-4.55509136	-1.32746899	0.18426293
H	-5.38608397	-0.56078044	-2.06598362

CP2

Δ*G*298K = -1304.269348 A.U.

C	-0.08850677	2.24810310	-0.48391968
N	-1.36893284	2.89722979	-0.03902276
C	0.82822658	1.96764912	0.65856483
O	0.12261262	2.05134717	-1.64988885
N	-2.21045929	2.98094283	-0.93491664
H	0.28905219	1.38992920	1.41402062
H	1.70980521	1.43097930	0.31187999
H	1.11653100	2.91823724	1.11896345
H	-1.88222850	2.55787223	-1.82876403
H	-3.94985044	2.92316883	-0.53544314
S	-2.19268322	-0.17627020	-0.29042696
O	-3.12205546	-0.760223708	0.79386321
O	-3.03317743	0.58477266	-1.31828957
C	-1.72792352	-1.66134916	-1.21791789
H	-2.65531074	-2.11366032	-1.58021320
H	-1.19840807	-2.34446508	-0.55148866
H	-1.09603858	-1.36199956	-2.05625385
C	-6.09248508	3.26191609	-0.71506613
C	-7.12321135	2.48442368	-0.28302018
N	-6.55461860	1.43910188	0.40996223
C	-5.22604608	1.55263258	0.37962121
N	-4.93051801	2.66098927	-0.28628488
H	-6.09028691	4.17158910	-1.29194251
H	-8.18780439	2.57074903	-0.42185923
H	-7.03927600	0.59966849	0.73118673
H	-4.51004493	0.83881356	0.77785171
C	-7.75541144	-1.51713896	-0.20716826
C	-6.67602240	-1.779801797	0.61192606
N	-5.56927901	-1.44368861	-0.12264259
C	-6.01080152	-0.98929026	-1.32205814
N	-7.32807478	-1.01963728	-1.41342771
H	-8.80356091	-1.68634165	-0.00292836
H	-6.60223585	-2.197647791	1.60446182

H	-4.58099655	-1.372873252	0.21750761
H	-5.32180422	-0.60893856	-2.06581001

CP3

Δ*G*298K = -715.694614 A.U.

C	-0.15697434	0.71856442	1.25051390
C	-1.10496386	1.41910235	2.16440201
O	0.36402697	-0.36769492	1.46369590
N	0.41812747	1.49609448	0.18910299
N	0.07116992	1.39450444	-0.99085098
H	-0.52377876	2.07460535	2.82198379
H	-1.62798917	0.67811807	2.76848984
H	-1.81262356	2.02701432	1.59906631
H	1.86393392	-0.52353507	0.58317129
C	3.78790180	-1.42878826	0.20597619
C	4.80481465	-1.02023902	-0.60073821
N	4.37952585	0.15139996	-1.19106946
C	3.15114199	0.45257759	-0.76456431
N	2.77882639	-0.49974434	0.08352776
H	3.70219763	-2.28867323	0.85034496
H	5.77279511	1.45112118	-0.79869497
H	4.90973843	0.70821749	-1.84956502
H	2.55890338	1.30871920	-1.05671696
C	-4.39307959	-0.82198456	-0.39875431
C	-3.49503381	0.17856952	-0.65132432
N	-2.24979272	-0.18009519	-0.18351275
C	-2.39166703	-1.37962739	0.34369320
N	-3.67162546	-1.80492447	0.23486532
H	-5.44635543	-0.92003140	-0.60694603
H	-3.67001970	1.12548027	-1.14021508
H	-0.75608483	0.75695478	-1.06265451
H	-1.60943738	-1.95541959	0.81877575
H	-4.03248925	-2.68860581	0.56424620

TS2

Δ*G*298K = -715.678519 A.U.

C	0.04999462	1.15958623	0.141650459
C	0.60526193	1.44451238	1.505123323
O	0.55430944	0.25326831	-0.651693412
N	-0.90686628	1.89572048	-0.305746513
N	-1.96556292	2.31557649	-0.665287129
H	1.65212503	1.74888007	1.417214936
H	0.55994552	0.52746454	2.098725164
H	0.04344602	2.23188619	2.007209465
H	1.59600910	0.00372117	-0.422202471
C	3.51124559	-1.02440205	0.840974647
C	4.86068482	-1.11630326	0.652446855
N	5.11670472	-0.43396500	-0.513277135
C	3.95154316	0.04294356	-0.992738052
N	2.95985282	-0.29850459	-0.191034765
H	2.91020487	-1.43516513	1.637444531
H	5.63797881	-1.59603014	1.224856038
H	6.02313316	-0.31106370	-0.943013777
H	3.86282350	0.61501950	-1.904445831
C	-4.80525321	-1.43164340	0.334571023
C	-4.58831140	-0.08413835	0.383857517
N	-3.33703691	0.18479513	-0.121413052
C	-2.80174272	-0.97019028	-0.473836866
N	-3.66300592	-1.97171820	-0.209714915
H	-5.64919016	-2.03573391	0.625788121
H	-5.24165681	0.69756026	0.738675568
H	-2.73150725	1.44995584	-0.391697006
H	-1.82160650	-1.10816931	-0.912019364
H	-3.49947104	-2.95146780	-0.394387338

CP4

Δ*G*298K = -715.680966 A.U.

C	0.02271145	0.99748750	0.52145883
C	0.55424012	1.46337754	1.83891337
O	0.29900032	0.23808661	0.03103654
N	-0.73937807	1.73731114	-0.20114125
N	-1.50410055	2.31220354	-0.86628870
H	1.64896241	1.47616609	1.81510766
H	0.23838188	0.77667204	2.63030912
H	0.20014222	2.46826284	2.07408721
H	1.32715636	0.35332816	-0.06718782
C	3.72142719	0.89664487	0.81188354
C	5.01381107	0.79777892	0.37806123
N	4.93579812	0.24613200	-0.87860325
C	3.63338386	0.03142114	-1.16425929
N	2.87253484	0.41538412	-0.15891541
H	3.35234264	1.28353149	1.74948496
H	5.95269305	1.06406508	0.83592443
H	5.71533218	0.03781036	-1.48593486
H	3.28889626	0.39436725	-2.09506295
C	-4.84255795	-1.35161225	0.01069833
C	-4.72965243	-0.02129146	-0.25224590
N	-3.38438458	0.24971779	-0.36497859
C	-2.68194458	-0.86339674	-0.18054807
N	-3.55551800	-1.84663607	0.04955999
H	-5.70812607	-1.97410400	0.16935469
H	-5.48288392	0.74082849	-0.37005042
H	-2.94805447	1.17415449	-0.56817175
H	-1.59644043	-0.95150025	-0.20704455
H	-3.29766126	-2.80941611	0.22602145

CP5

Δ*G*298K = -263.122057 A.U.

C	0.33104469	0.03516788	0.07354113
C	1.17244582	-1.19685422	0.00546320
O	0.91582069	1.27722230	0.20948293
H	1.69370390	-1.37130765	0.95311743
H	1.92797902	-1.09795943	-0.78176710
H	0.55581262	-2.07196076	-0.20962631
H	0.99177784	1.50286999	1.14553728
N	-0.92553497	0.01548945	-0.22200779
N	-2.04646843	-0.00480437	-0.46677544

TS3

Δ*G*298K = -263.103863 A.U.

C	0.37918525	0.02760445	0.47252188
C	1.20152857	-1.12056598	-0.05799520
O	1.01439302	1.19488836	0.17565171
H	2.00986568	-1.27051399	0.66304713
H	1.65516723	-0.92402416	-1.03762693
H	0.61177347	-2.03914734	-0.09727552
H	0.66132767	1.89360167	0.73907957
N	-1.00742523	-0.01308962	-0.40307919
N	-2.12110367	0.00602860	-0.46845343

CP6

ΔG298K = -263.151063 A.U.

C	0.91804856	0.08556793	0.79327605
C	1.49990596	-1.05108294	0.01441135
O	1.34053464	1.19896461	0.23531702
H	2.18289175	-1.57370434	0.69689407
H	2.03237732	-0.76248583	-0.89976563
H	0.70311370	-1.76808540	-0.20648664
H	0.99065947	1.95066367	0.73321630
N	-1.74880344	-0.16385992	-0.85060506
N	-2.73773524	-0.02883713	-0.39191275

CP7

ΔG298K = -379.732311 A.U.

C	-2.700252	0.307634	-0.444338
O	-2.267944	-0.930486	-0.580845
H	-2.394340	-1.198314	-1.501106
N	0.567262	0.479625	-0.429354
C	1.819155	1.039180	-0.514222
C	0.738457	-0.673242	0.172826
C	2.756054	0.210045	0.046041
H	1.974707	2.004911	-0.971931
H	-0.045337	-1.382594	0.401273
H	3.823941	0.294821	0.169423
H	2.426175	-1.696121	0.946193
N	2.047860	-0.885146	0.482522
C	-2.431537	0.722534	0.964187
H	-3.296300	1.263691	1.357667
H	-2.130886	-0.090124	1.639094
H	-1.611533	1.449363	0.887006

TS4

Δ*G*298K = -379.718766 A.U.

ImagF = -200.9603 cm^{-1}

C	-1.55639674	0.03093230	0.62318828
O	-0.52821316	0.88384914	0.33578899
H	-0.08803771	1.08880727	1.16782989
N	-0.57398855	-1.71483425	0.20328627
C	-0.85328693	-2.98610882	0.62442912
C	0.56854109	-1.75894918	-0.43585703
C	0.15081202	-3.82607477	0.22189133
H	-1.74561401	-3.20430495	1.19181107
H	1.06183123	-0.90728107	-0.88371769
H	0.30739324	-4.88453597	0.35463721
H	1.91480864	-3.33049278	-0.87193304
N	1.04928547	-3.02863545	-0.45156682
C	-2.40252142	-0.01399527	-0.63127150
H	-3.07431099	0.85138463	-0.56797823
H	-1.82951260	0.06650457	-1.56781843
H	-3.02120098	-0.91384559	-0.64889277

CP8

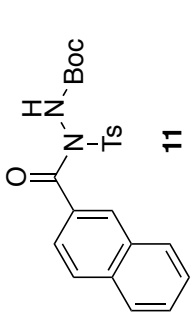
ΔG298K = -379.733023 A.U.

C	-1.379127	0.043628	-0.440293
O	-1.836753	-1.238015	-0.016569
H	-2.297156	-1.629439	-0.762856
N	0.025163	0.030855	-0.174976
C	0.878025	1.124984	-0.256768
C	0.765336	-1.038144	0.135397
C	2.149774	0.692041	-0.026816
H	0.509518	2.102651	-0.515105
H	0.376823	-2.030276	0.271797
H	3.082165	1.232196	-0.018224
H	2.846021	-1.272358	0.385693
N	2.073384	-0.653697	0.202548
C	-2.047197	1.121086	0.386926
H	-3.122800	1.095473	0.199621
H	-1.887730	0.980747	1.474171
H	-1.703508	2.123451	0.113777

CP9

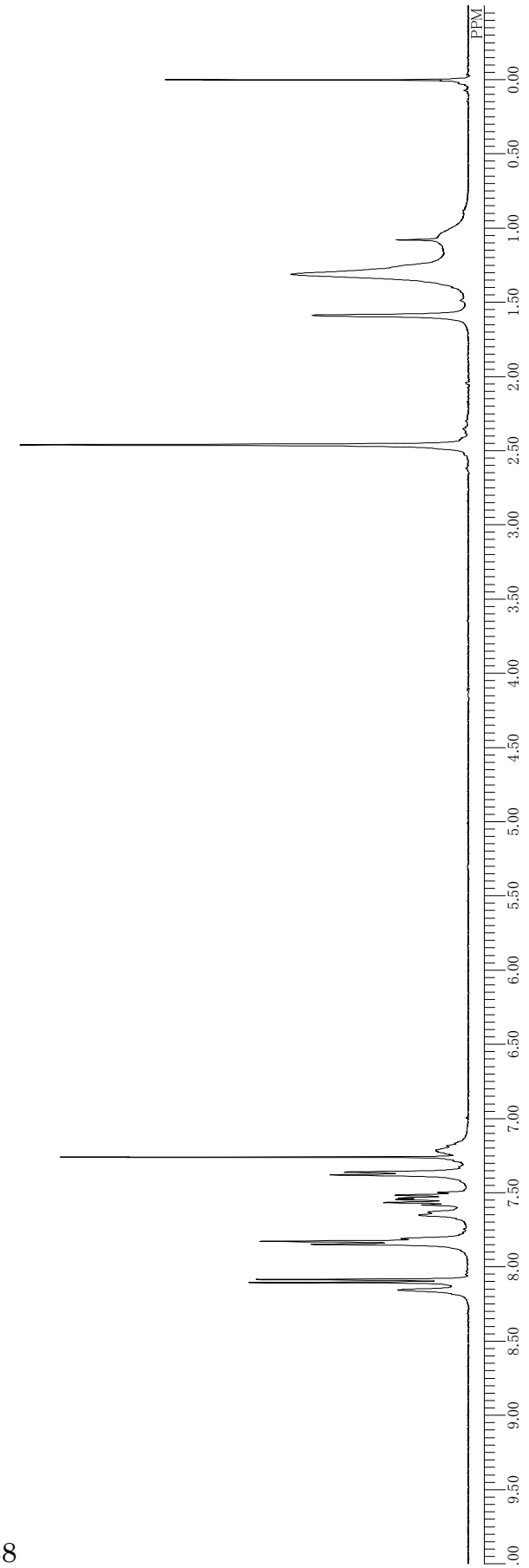
Δ*G*298K = -379.822156 A.U.

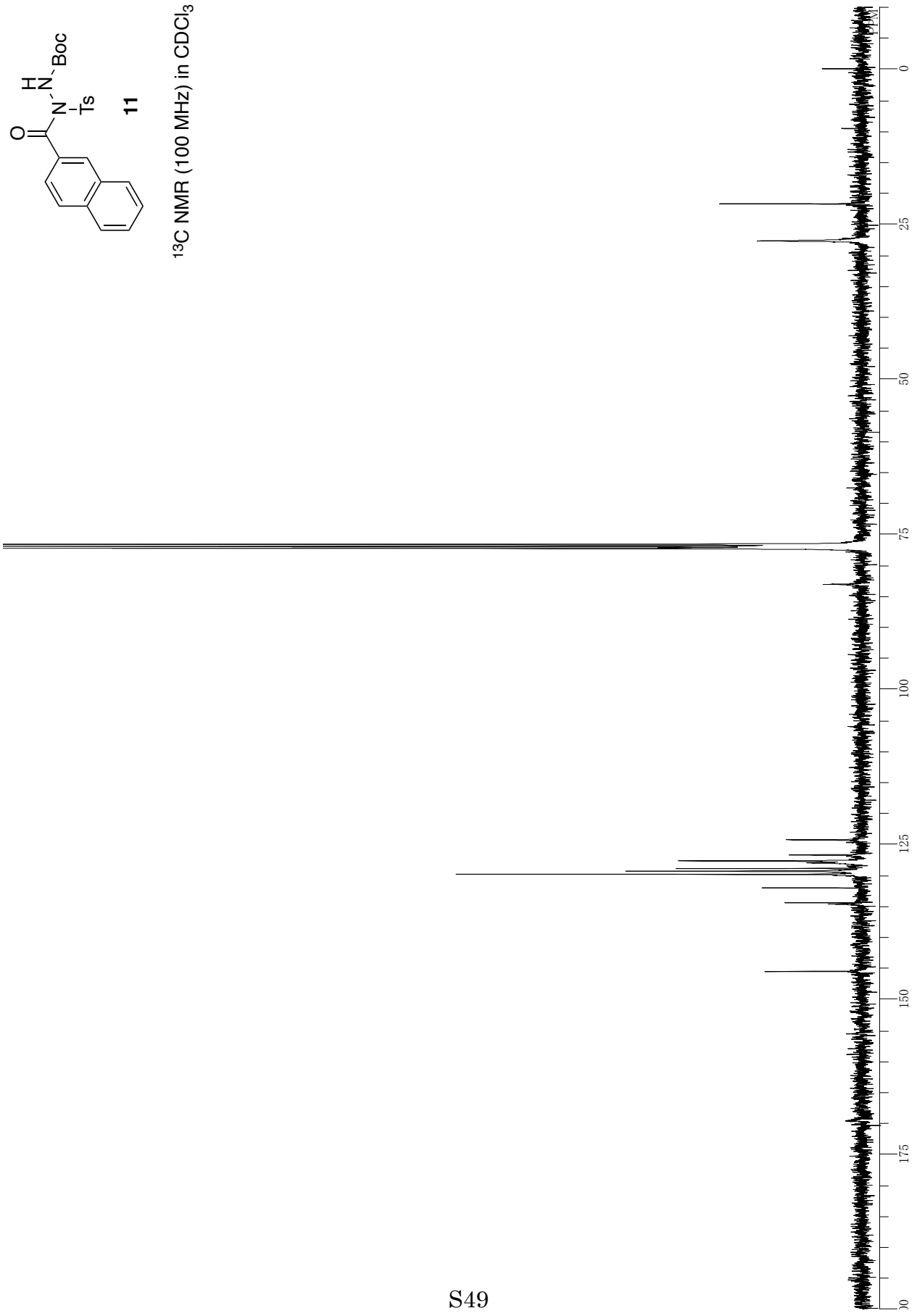
C	-1.316962	0.353200	-0.244048
H	-1.431768	1.300509	-0.787701
C	-1.989737	0.436127	1.112377
H	-1.869108	-0.513025	1.640603
H	-1.540893	1.235613	1.705537
H	-3.055690	0.632553	0.981046
O	-1.909581	-0.709393	-0.941160
H	-1.497103	-0.791214	-1.810064
N	0.124169	0.142720	-0.124594
C	1.117236	1.055450	-0.400457
C	0.743285	-0.979758	0.344804
C	2.293101	0.424812	-0.084307
H	0.897164	2.039811	-0.785509
H	0.185864	-1.862350	0.626577
H	3.297896	0.812067	-0.167389
N	2.048509	-0.845263	0.375446

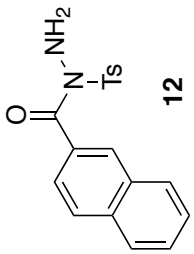


11

^{1}H NMR (400 MHz) in $CDCl_3$

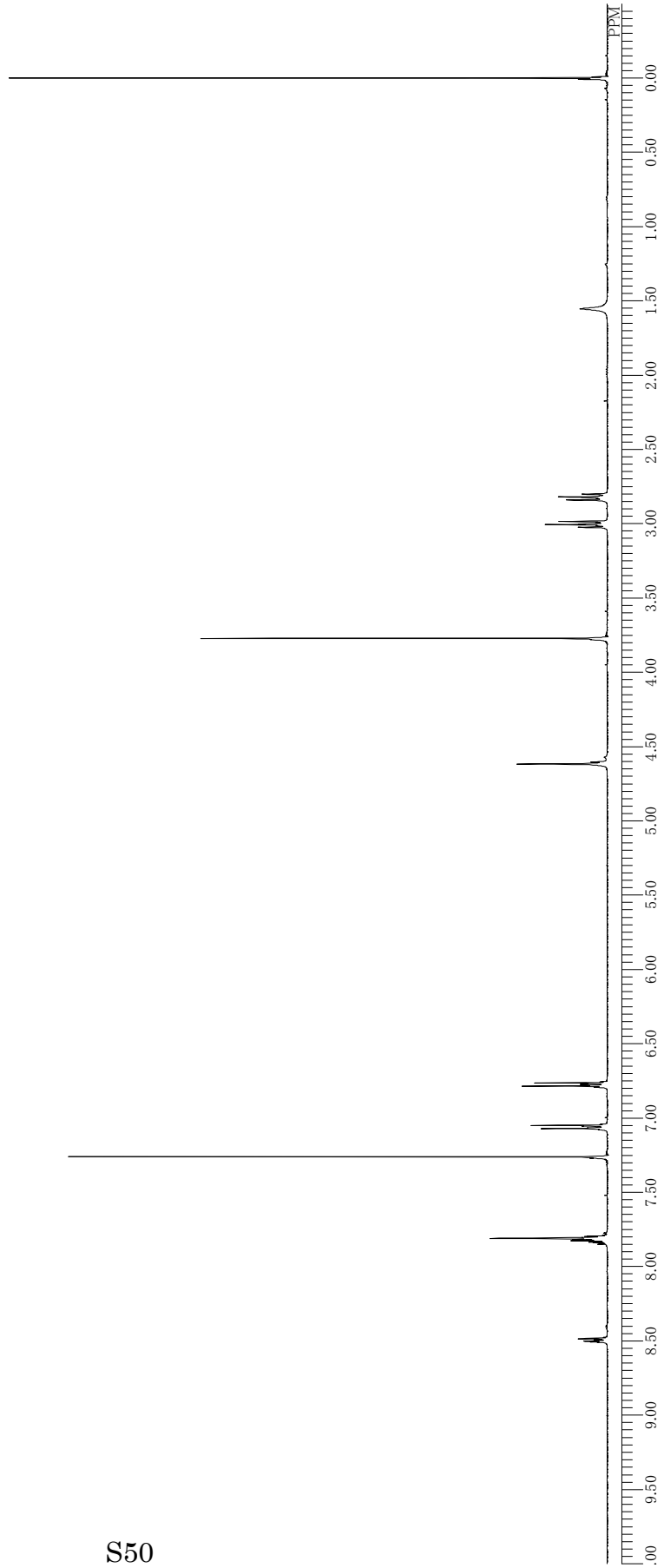


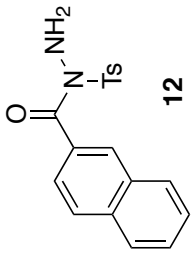

11
^{13}C NMR (100 MHz) in $CDCl_3$
Boc
Ts
0
25
50
75
100
125
150
175



12

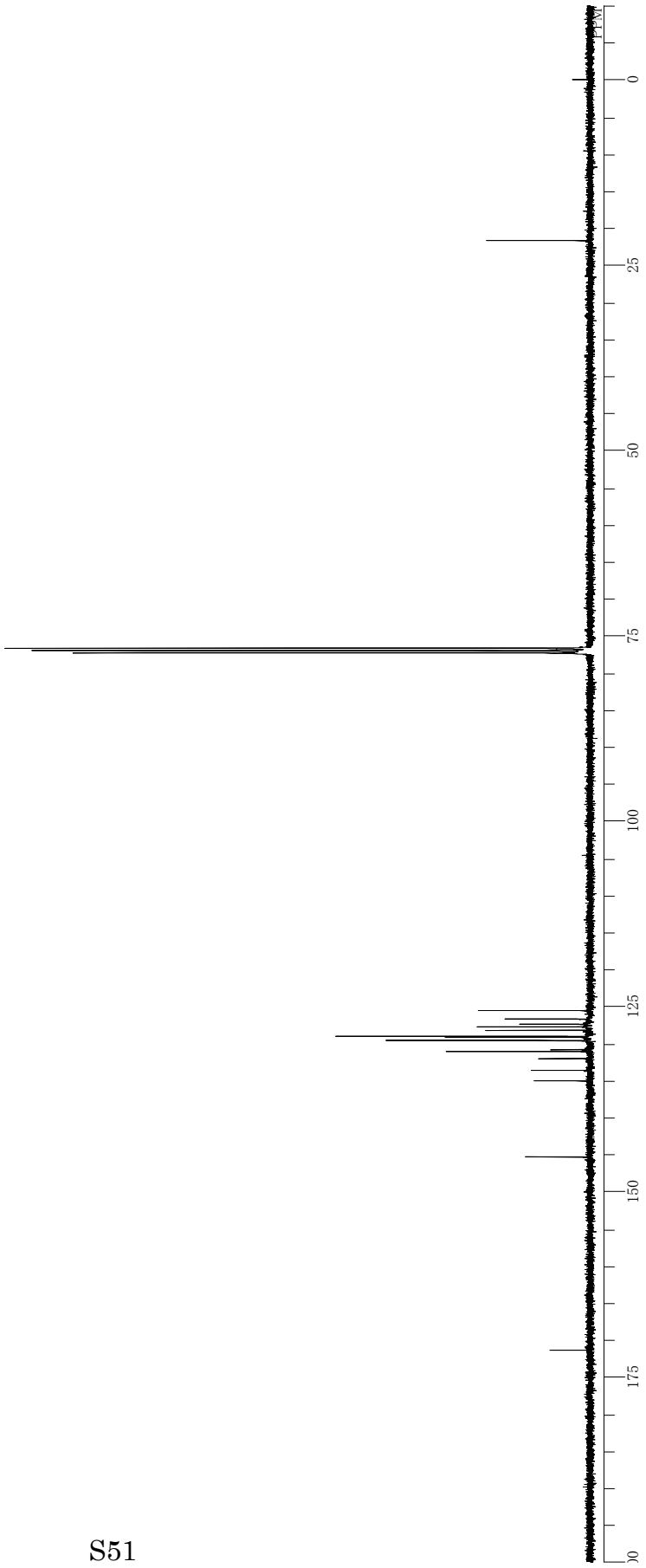
^{1}H NMR (400 MHz) in $CDCl_3$

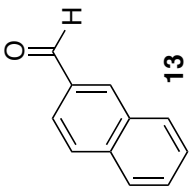




12

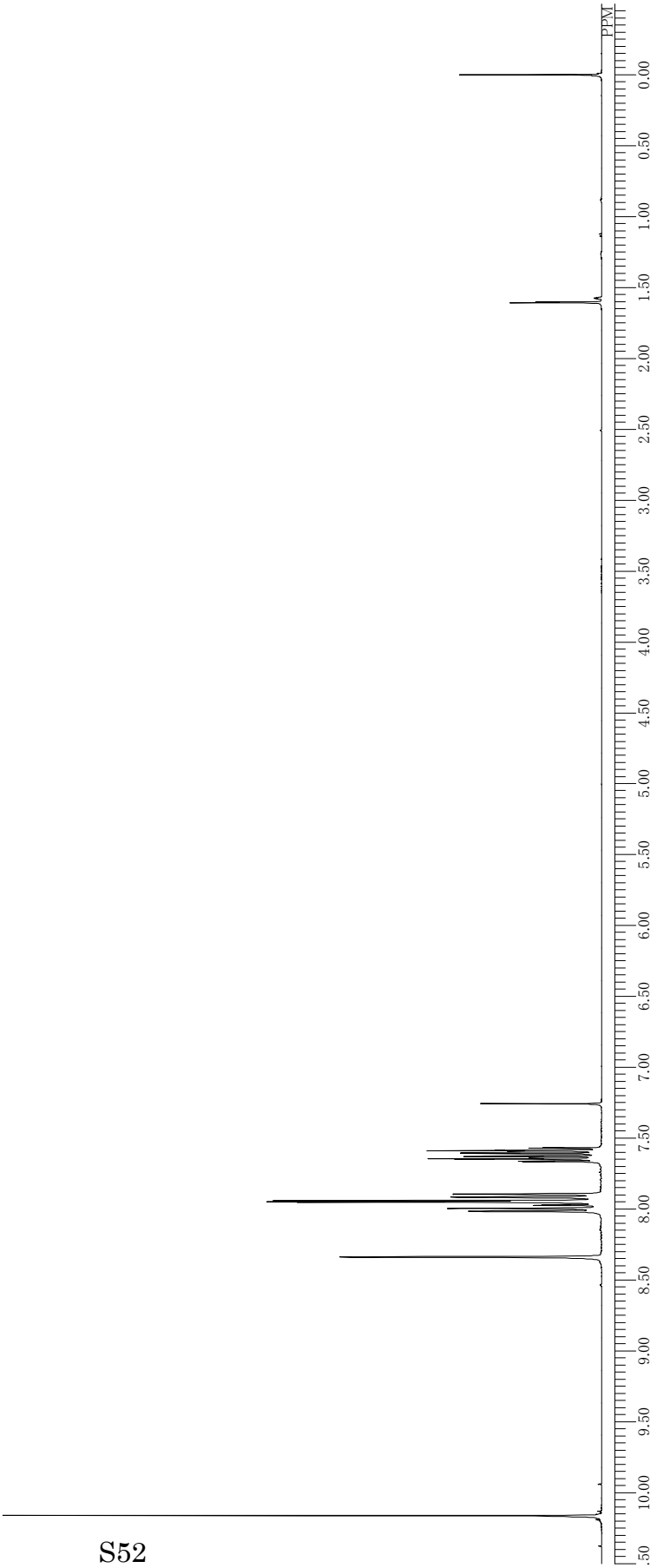
^{13}C NMR (100 MHz) in $CDCl_3$

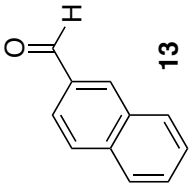




13

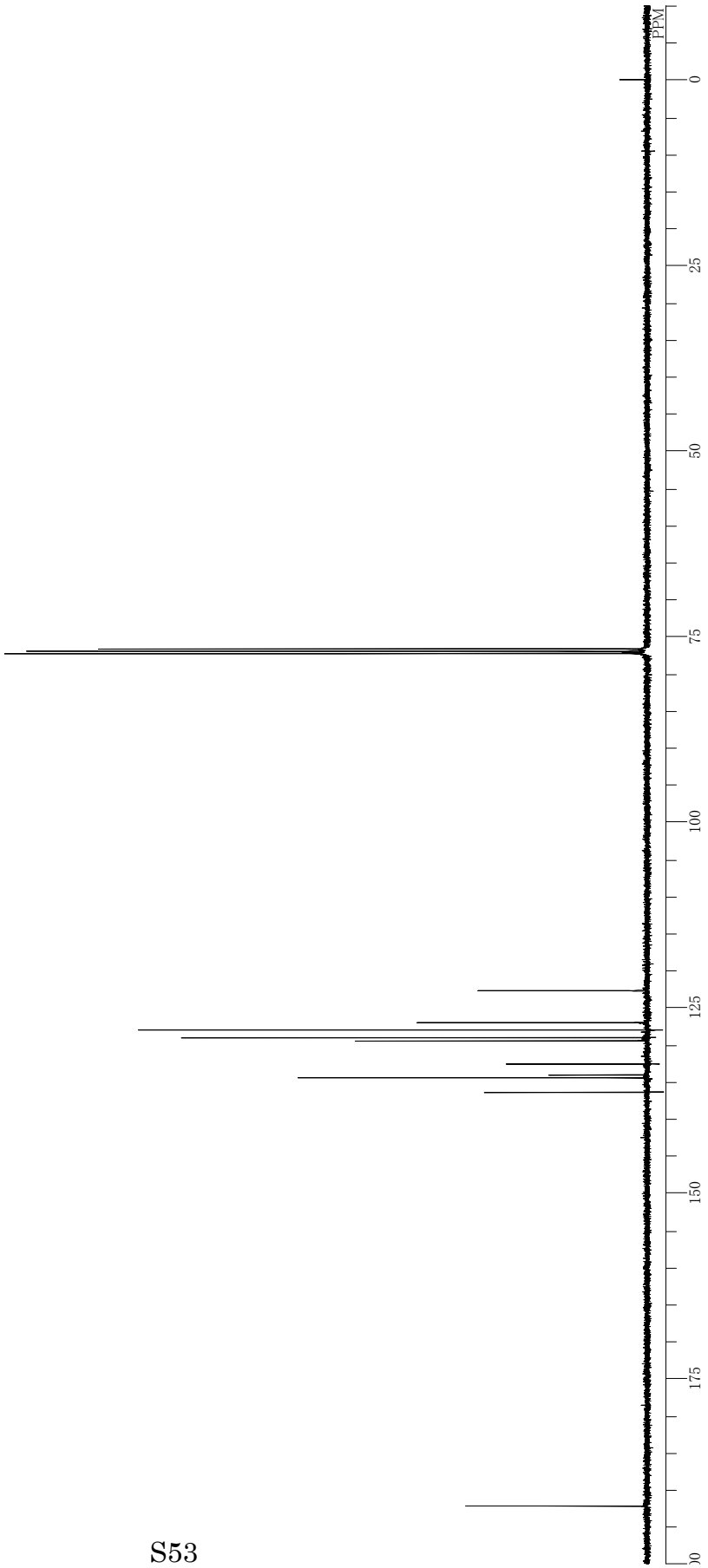
^{1}H NMR (400 MHz) in $CDCl_3$

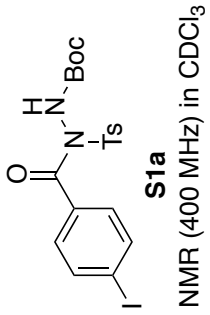




13

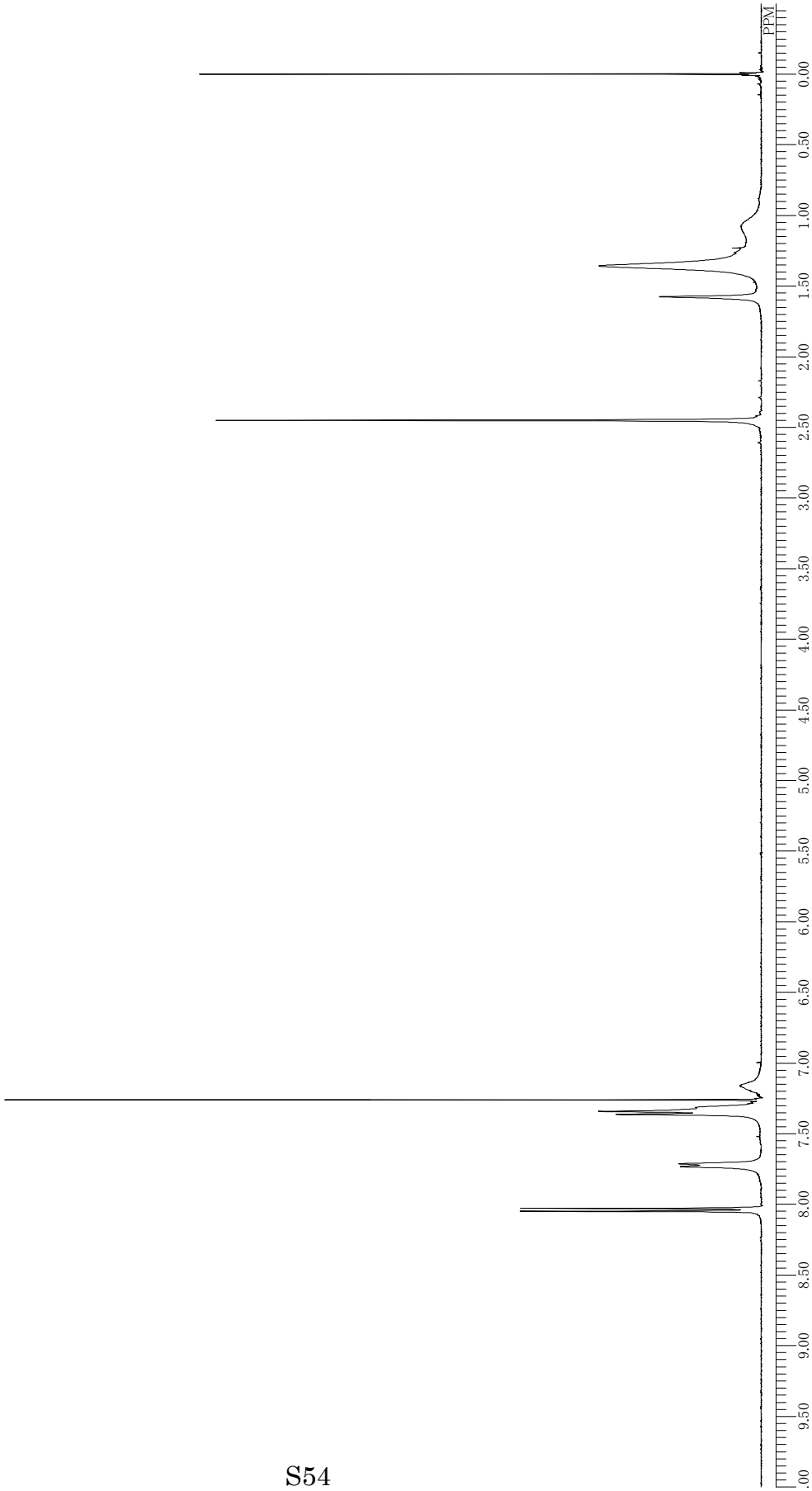
^{13}C NMR (100 MHz) in $CDCl_3$

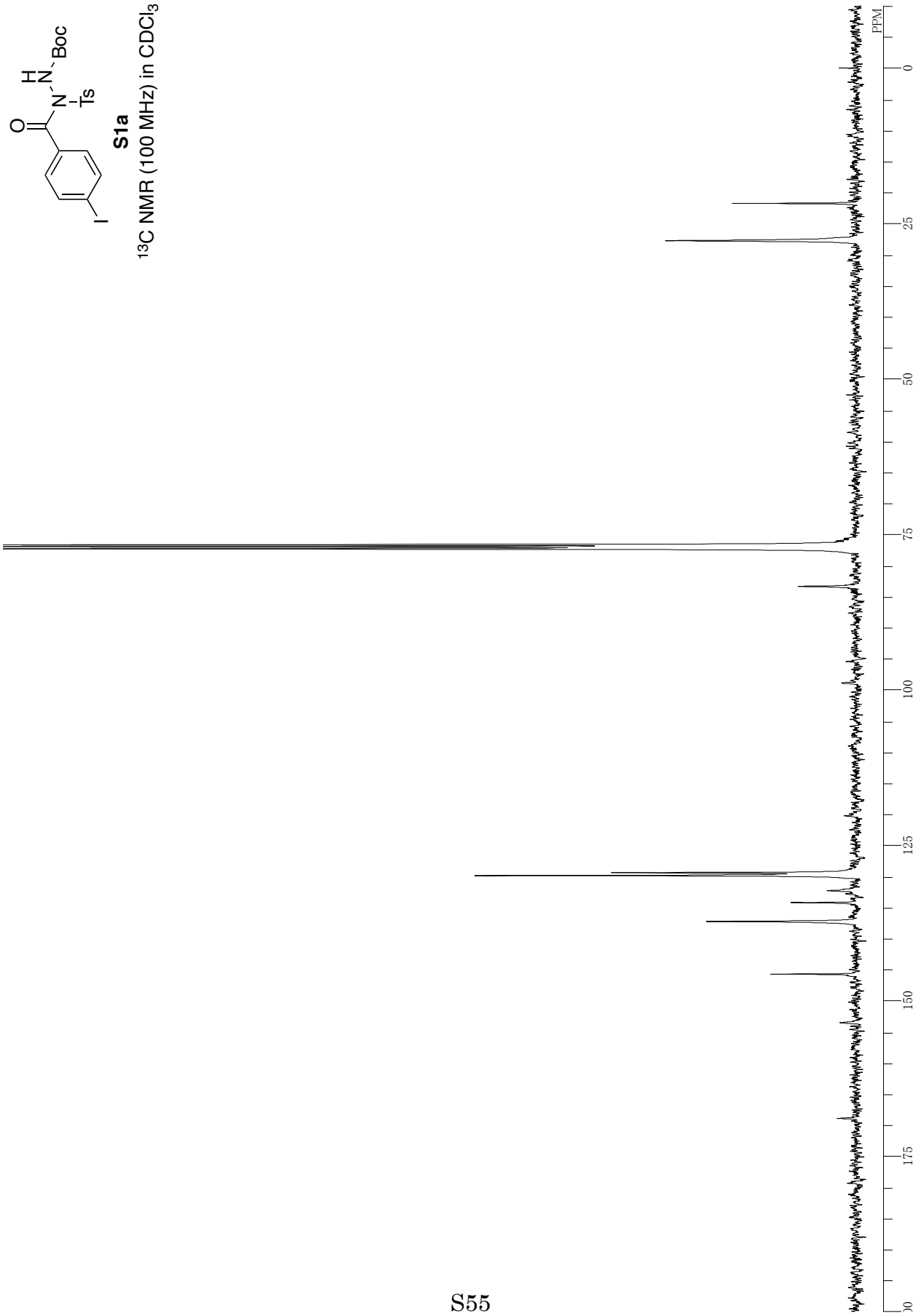


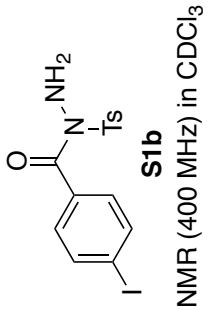


S1a

^{1}H NMR (400 MHz) in $CDCl_3$

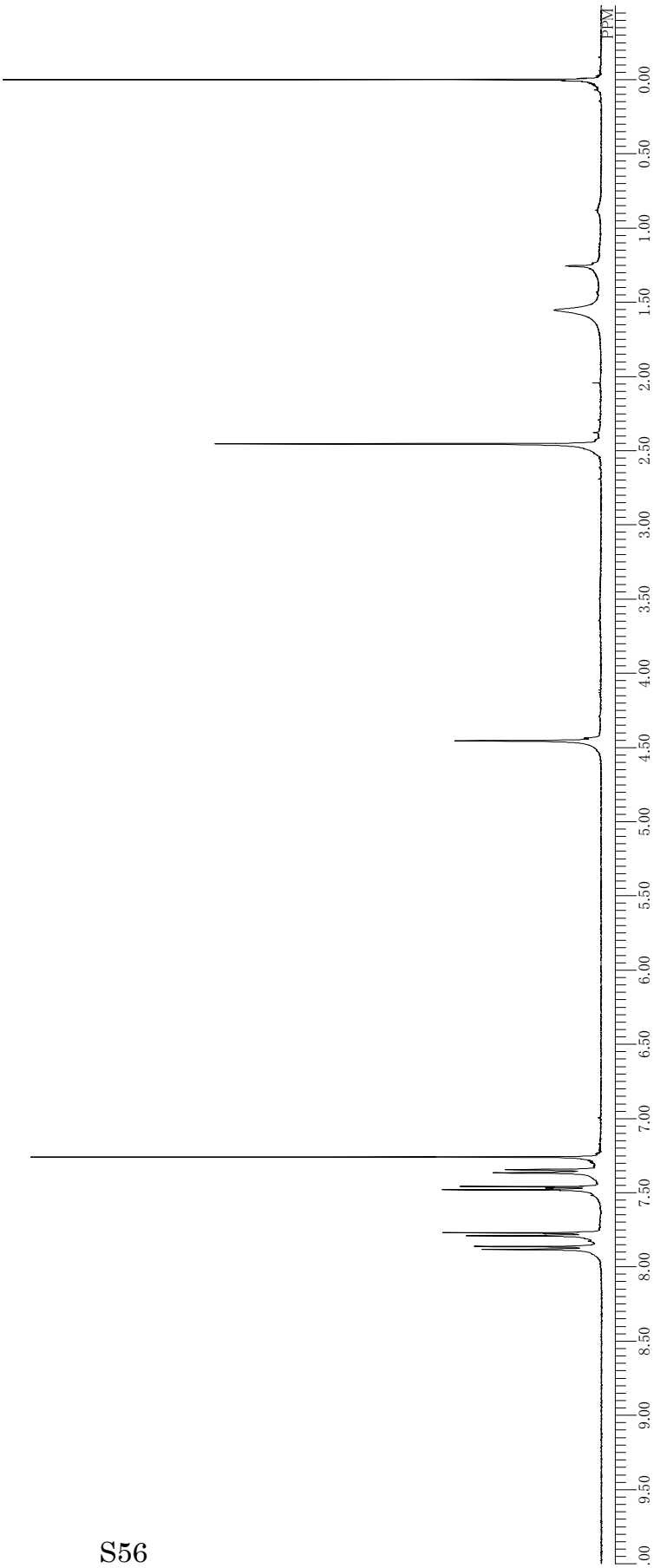


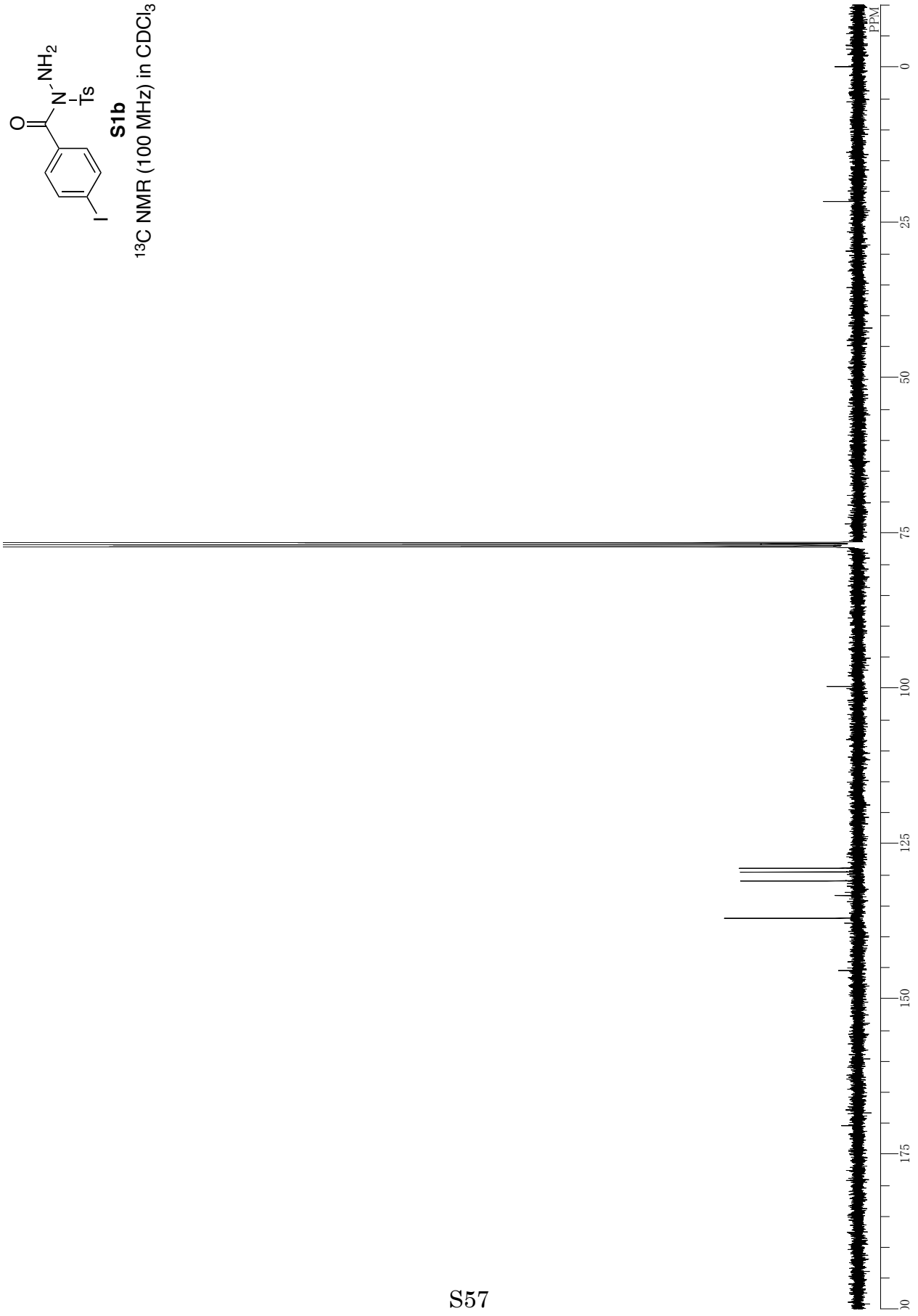

Boc
H
N
N
Ts
O
I
S1a
^{13}C NMR (100 MHz) in $CDCl_3$
PPM
0
25
50
75
100
125
150
175

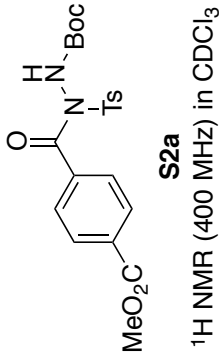


S1b

^{1}H NMR (400 MHz) in $CDCl_3$

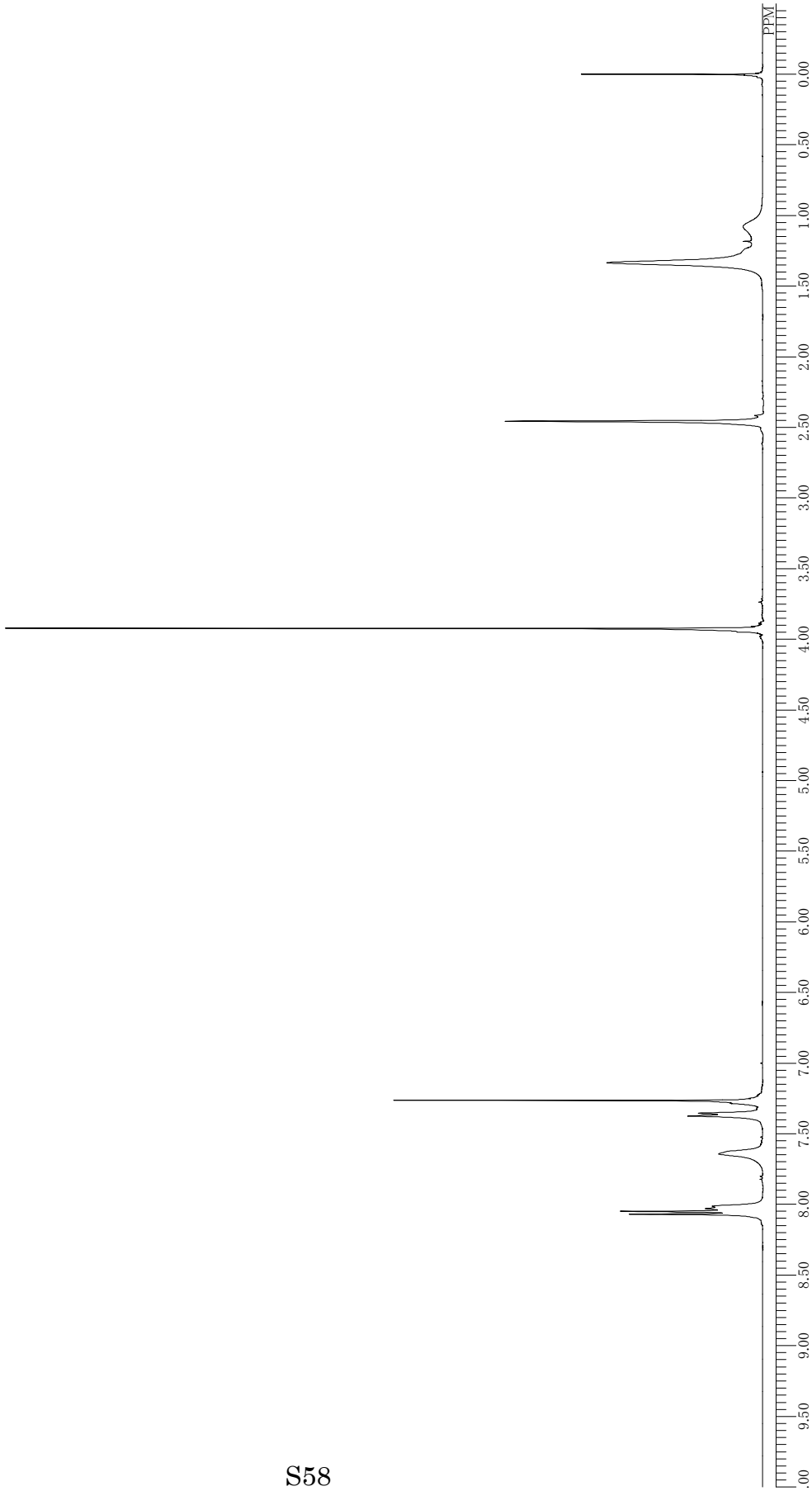


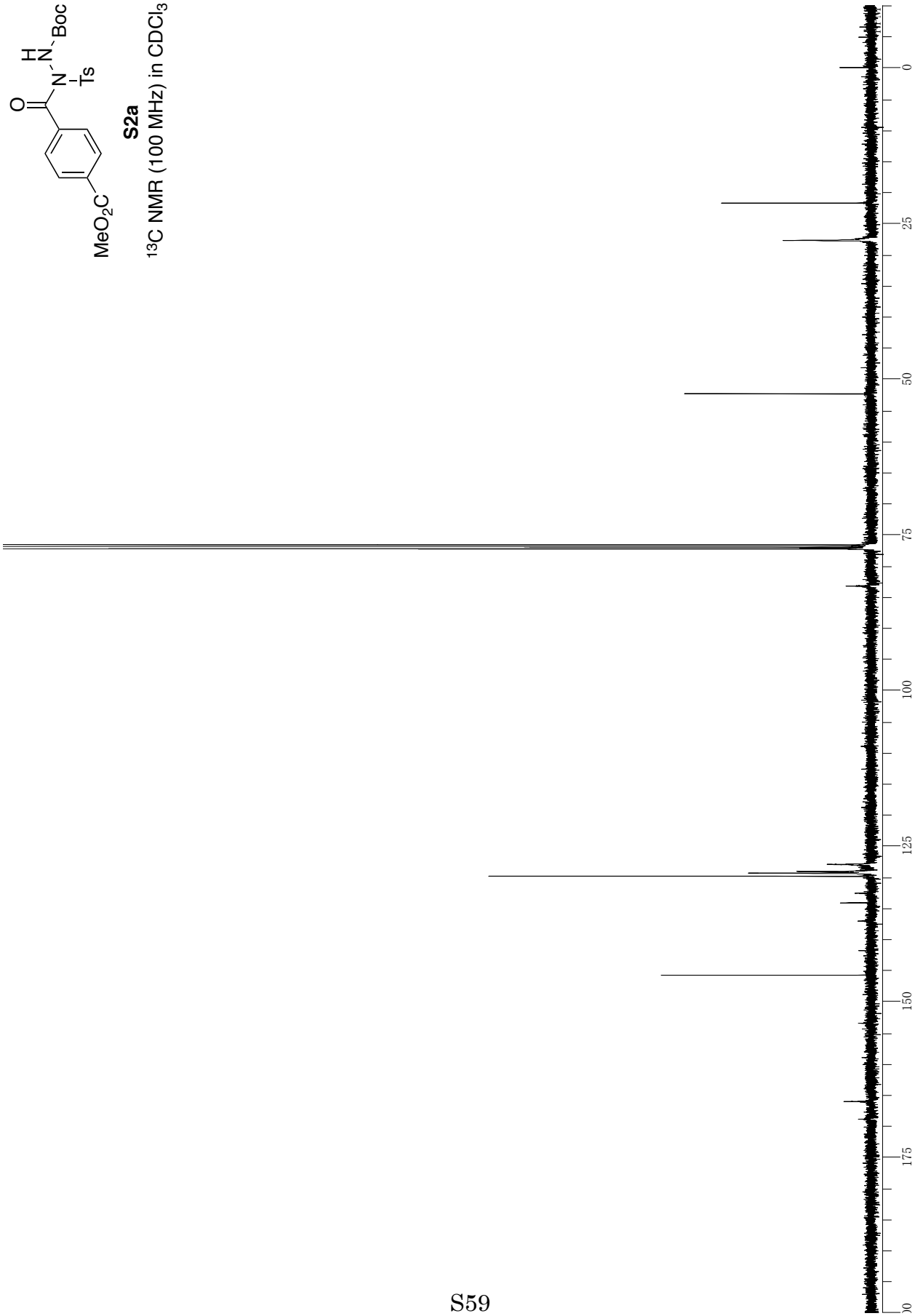

NH2
N
Ts
O
I
S1b
13C NMR (100 MHz) in CDCl3
PPM
0
25
50
75
100
125
150
175

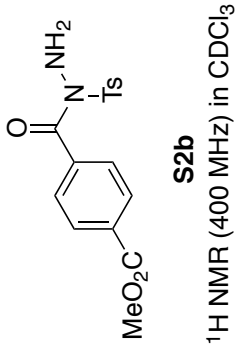


S2a

^{1}H NMR (400 MHz) in $CDCl_3$

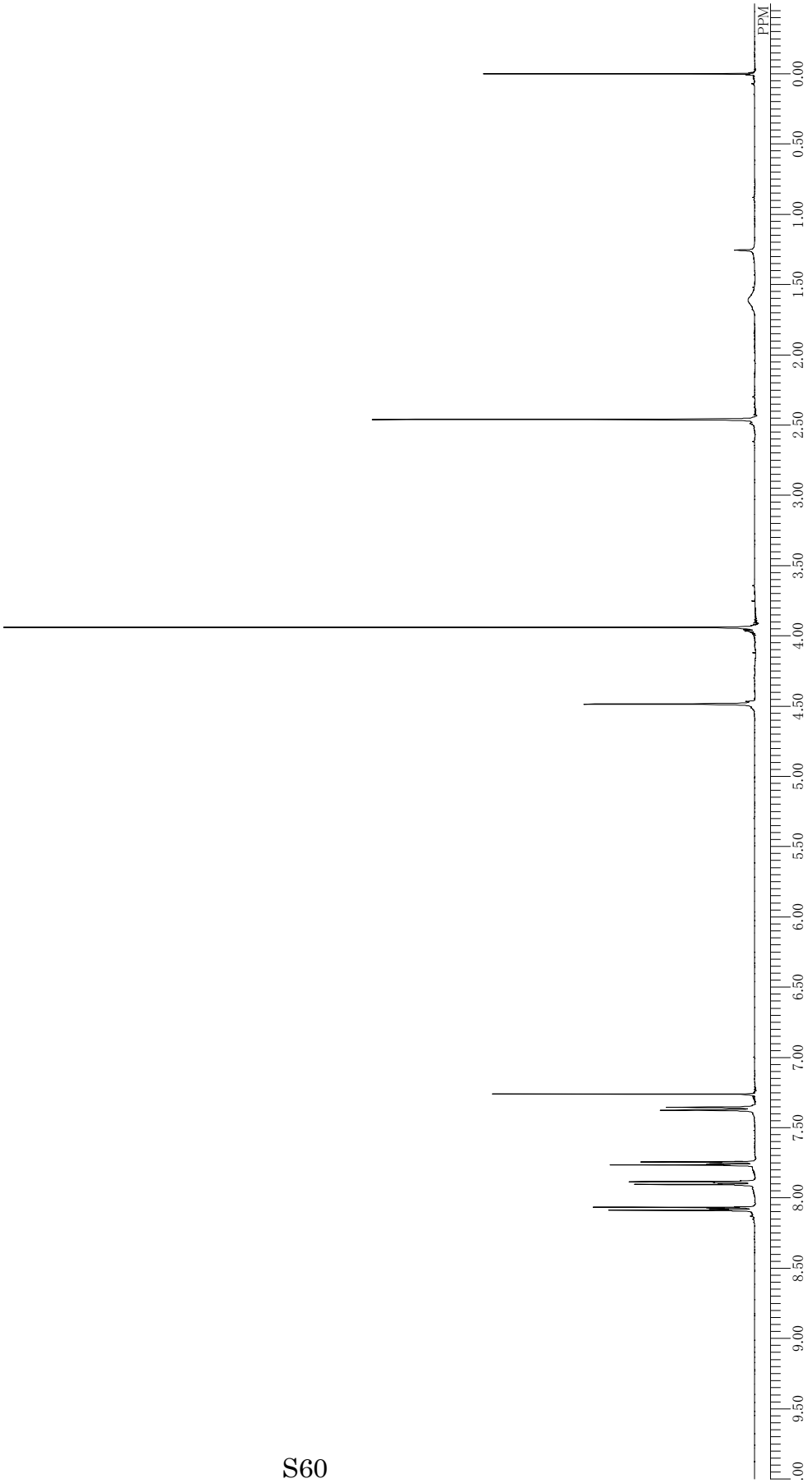


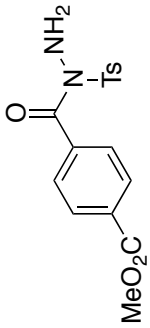




S2b

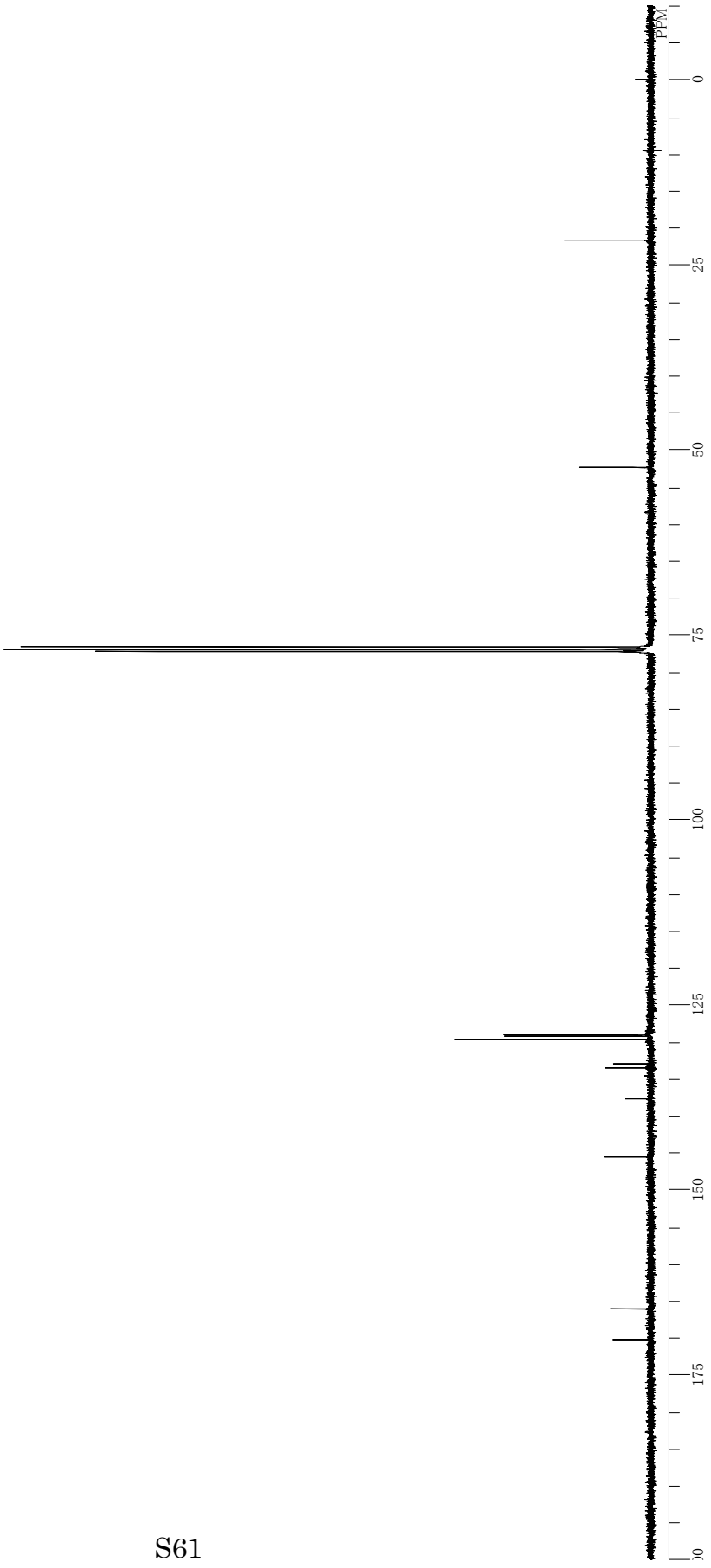
^{1}H NMR (400 MHz) in $CDCl_3$

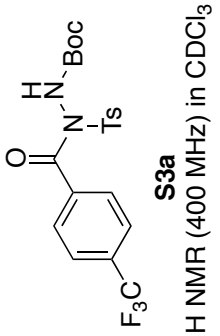




S2b

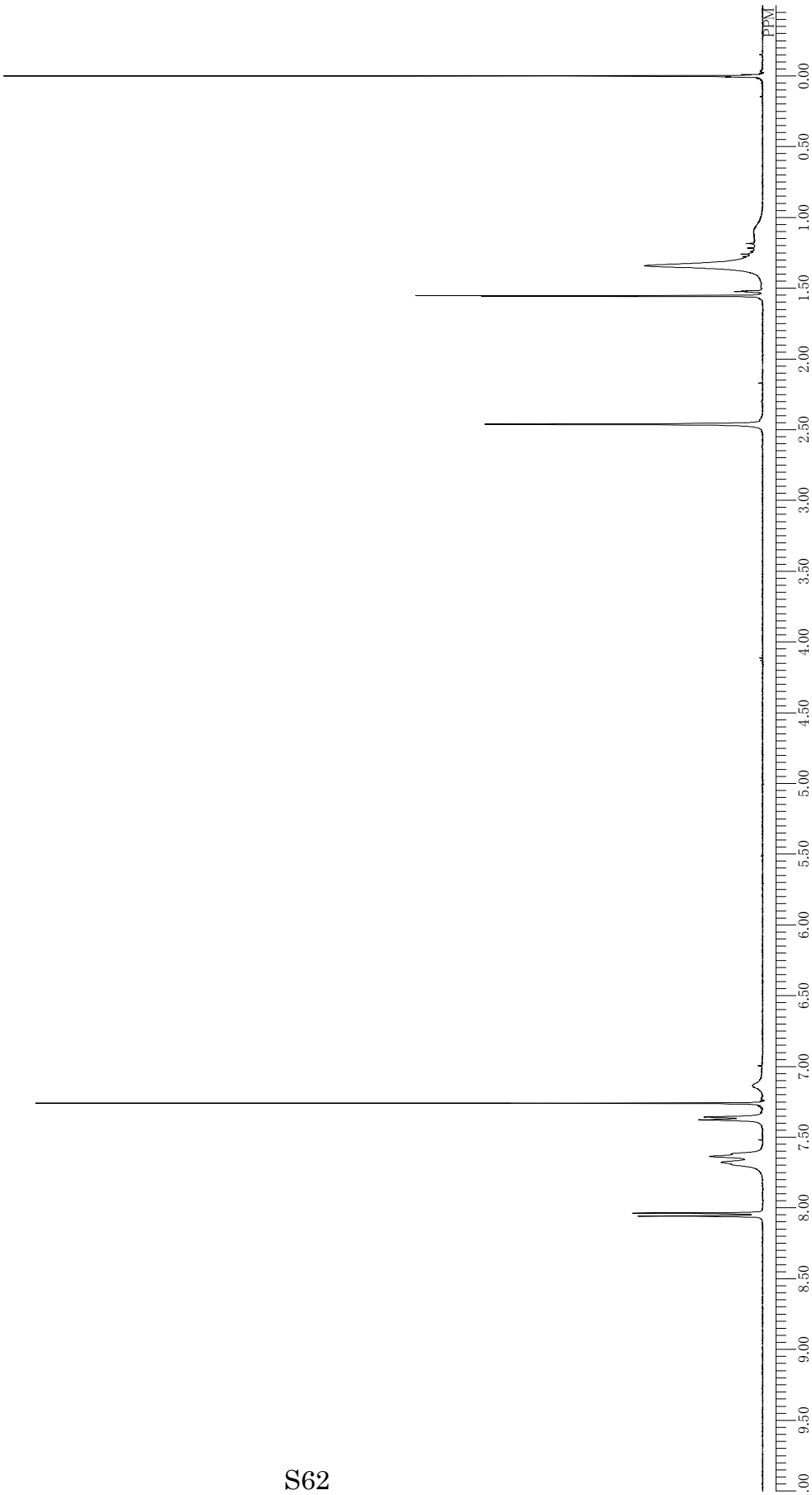
^{13}C NMR (100 MHz) in $CDCl_3$

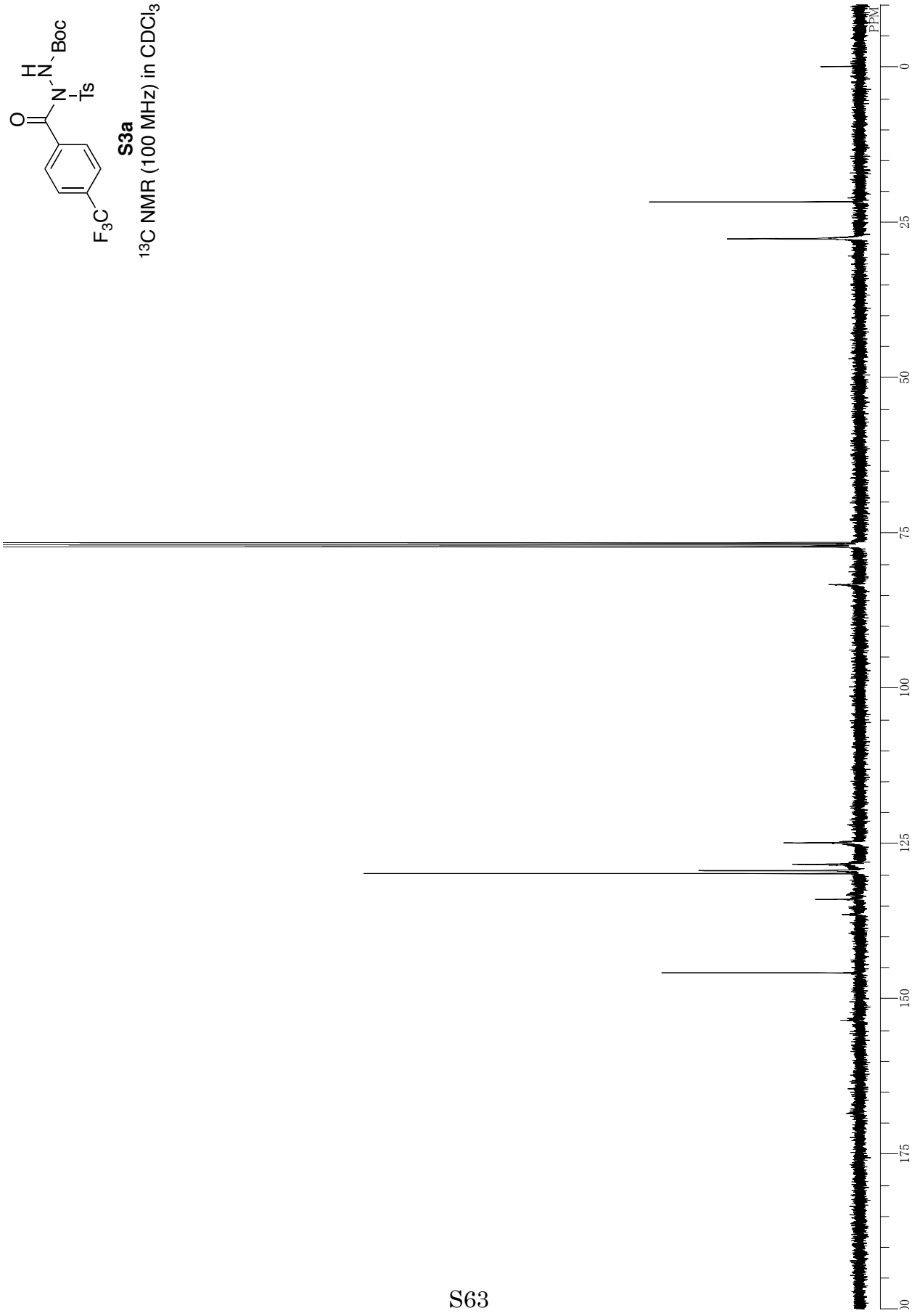


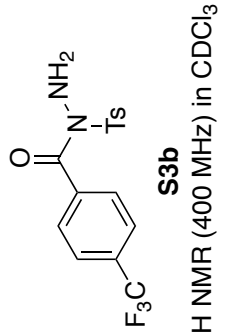


S3a

^{1}H NMR (400 MHz) in $CDCl_3$

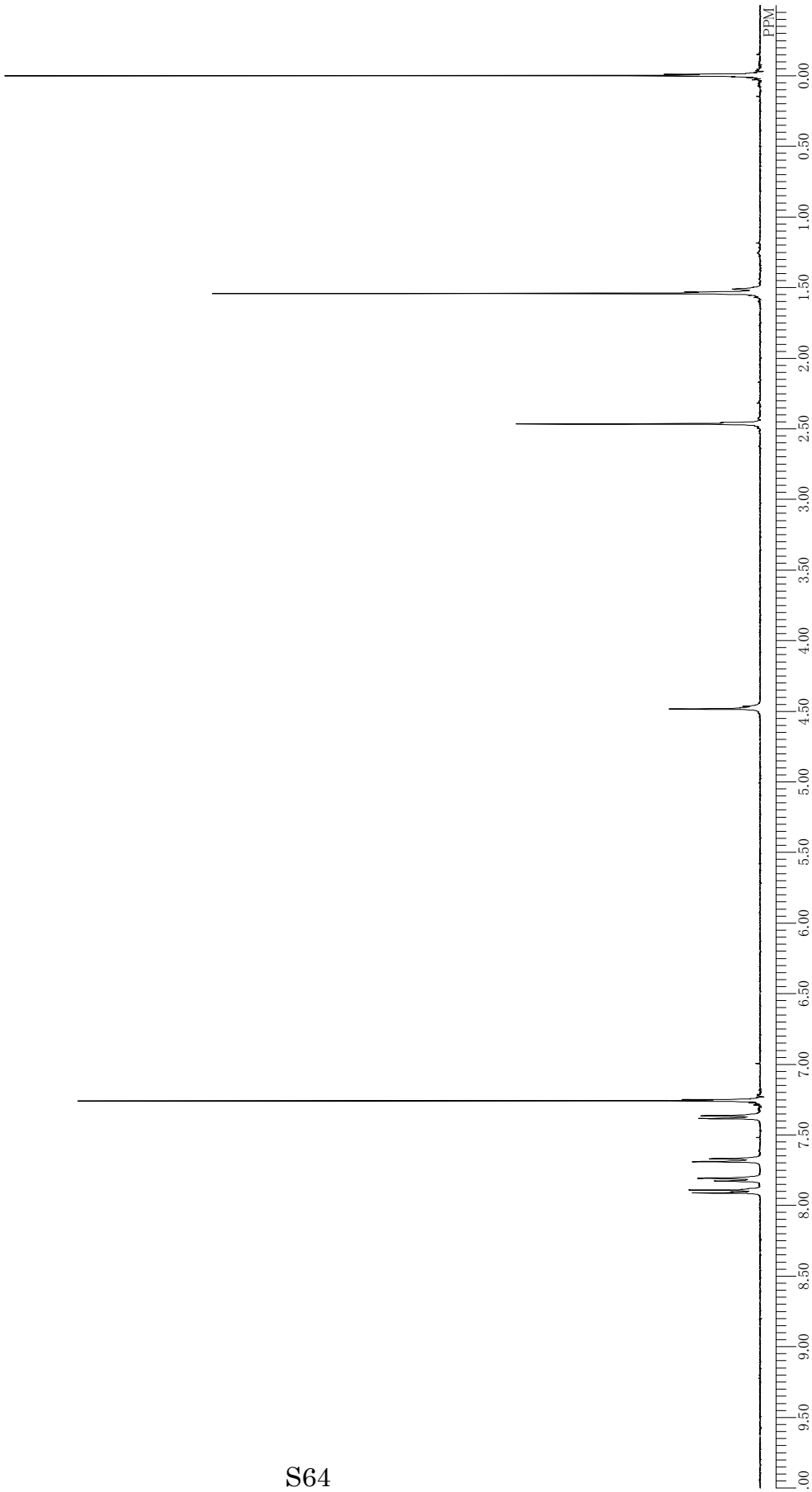


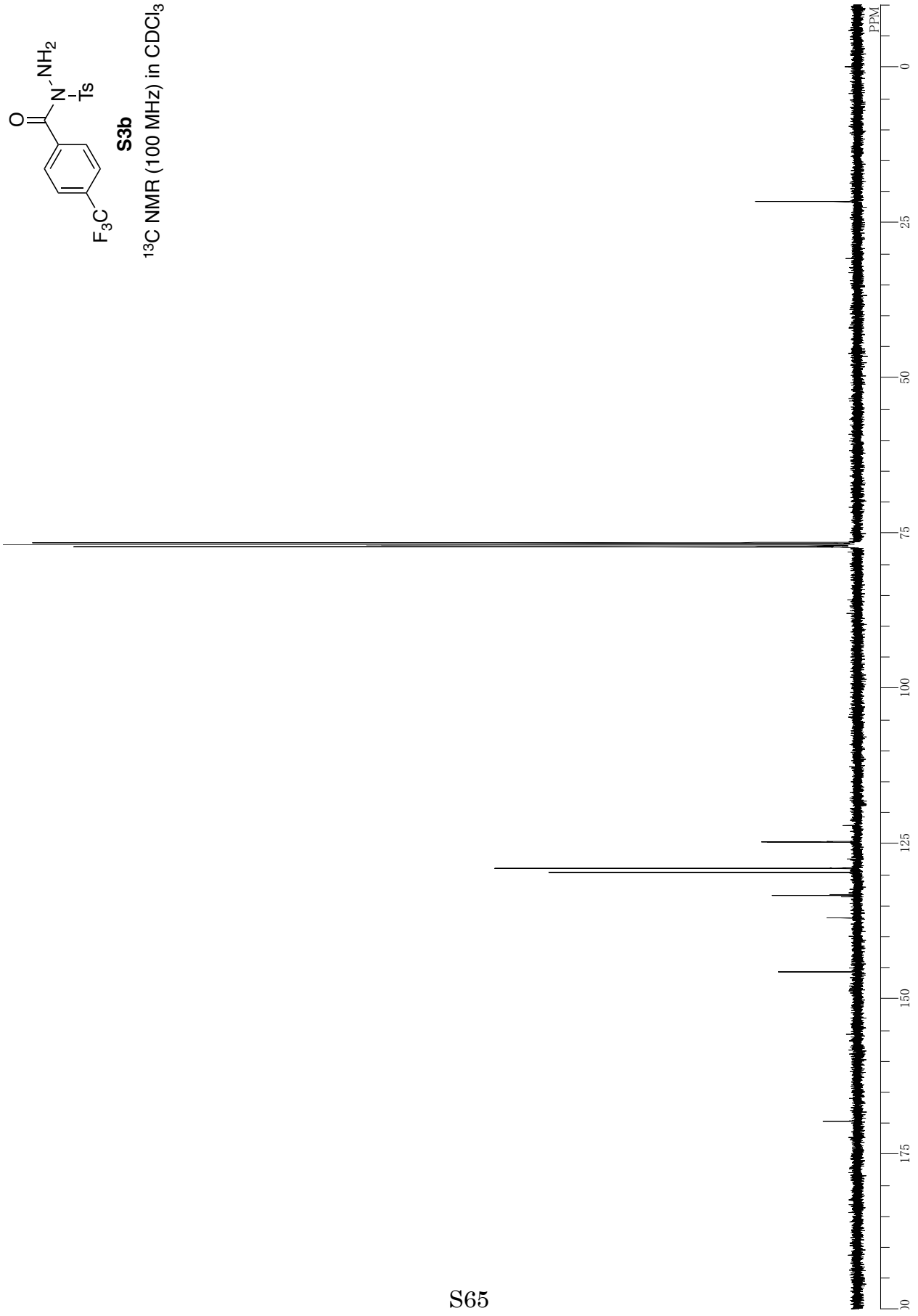

Boc
H
N
N
Ts
O
F3C
S3a
13C NMR (100 MHz) in CDCl3
PPM
0
25
50
75
100
125
150
175

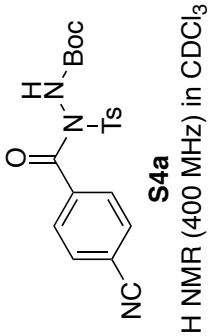


S3b

^{1}H NMR (400 MHz) in $CDCl_3$

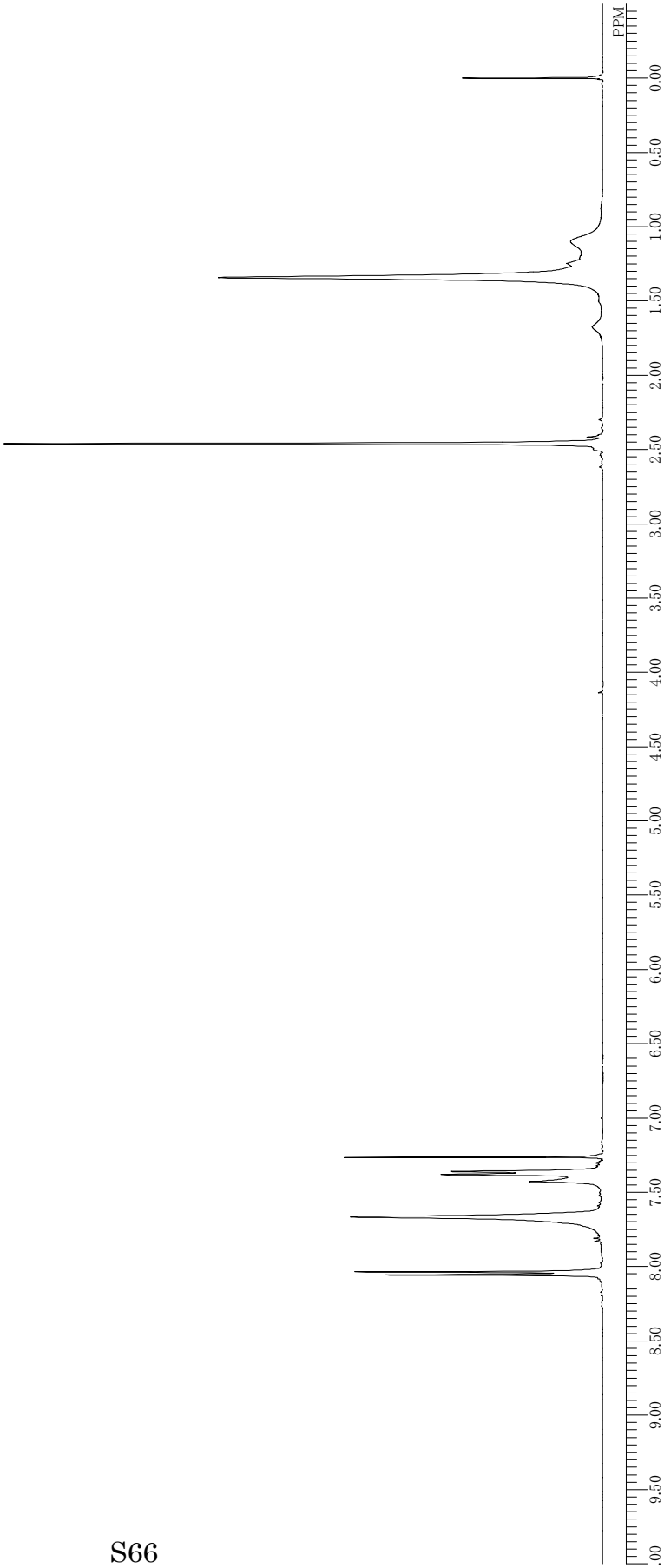


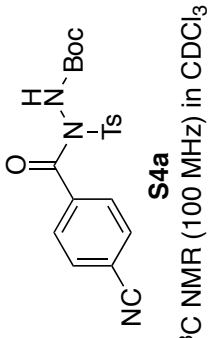

O
NH2
N
Ts
F3C
S3b
13C NMR (100 MHz) in CDCl3
PPM
0
25
50
75
100
125
150
175



S4a

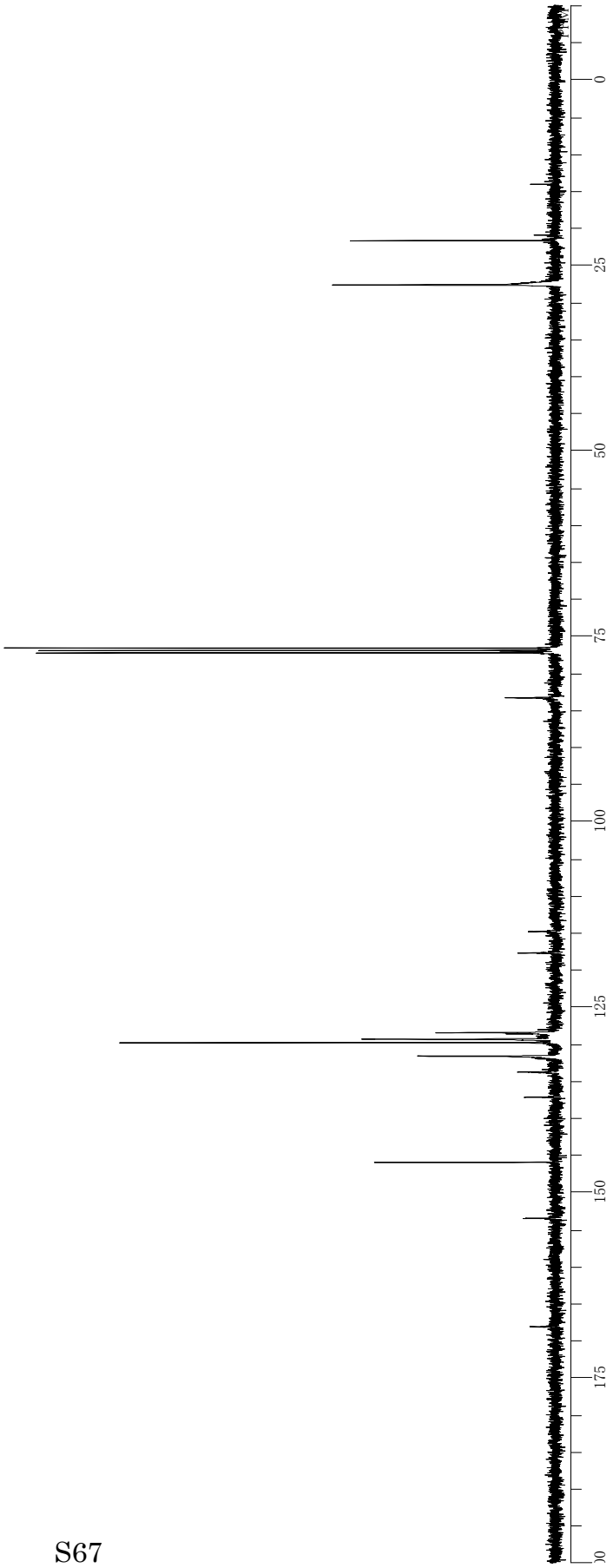
^{1}H NMR (400 MHz) in $CDCl_3$

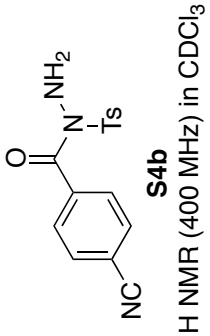




S4a

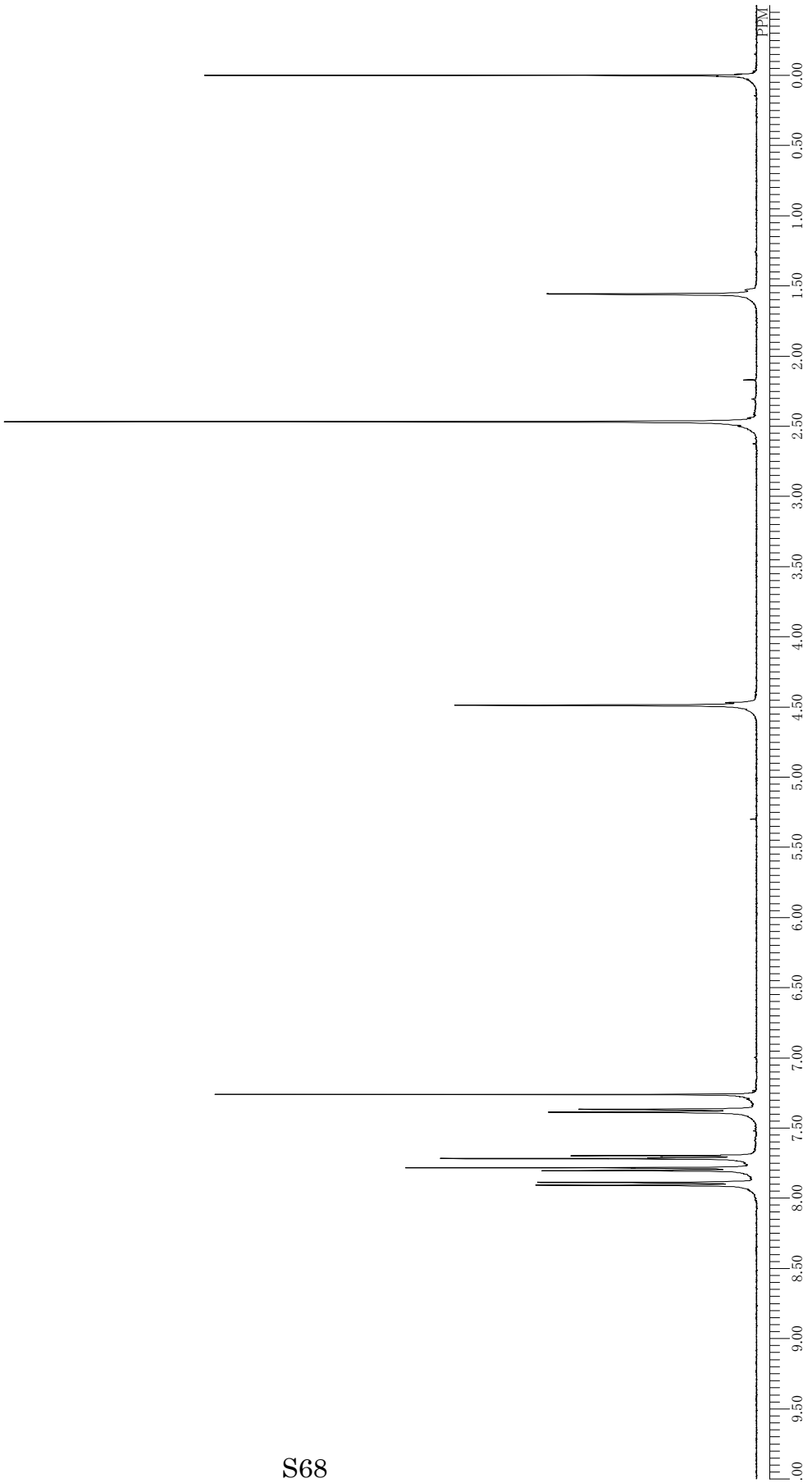
^{13}C NMR (100 MHz) in $CDCl_3$

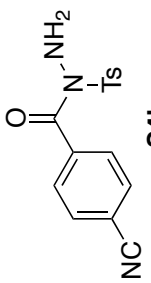




S4b

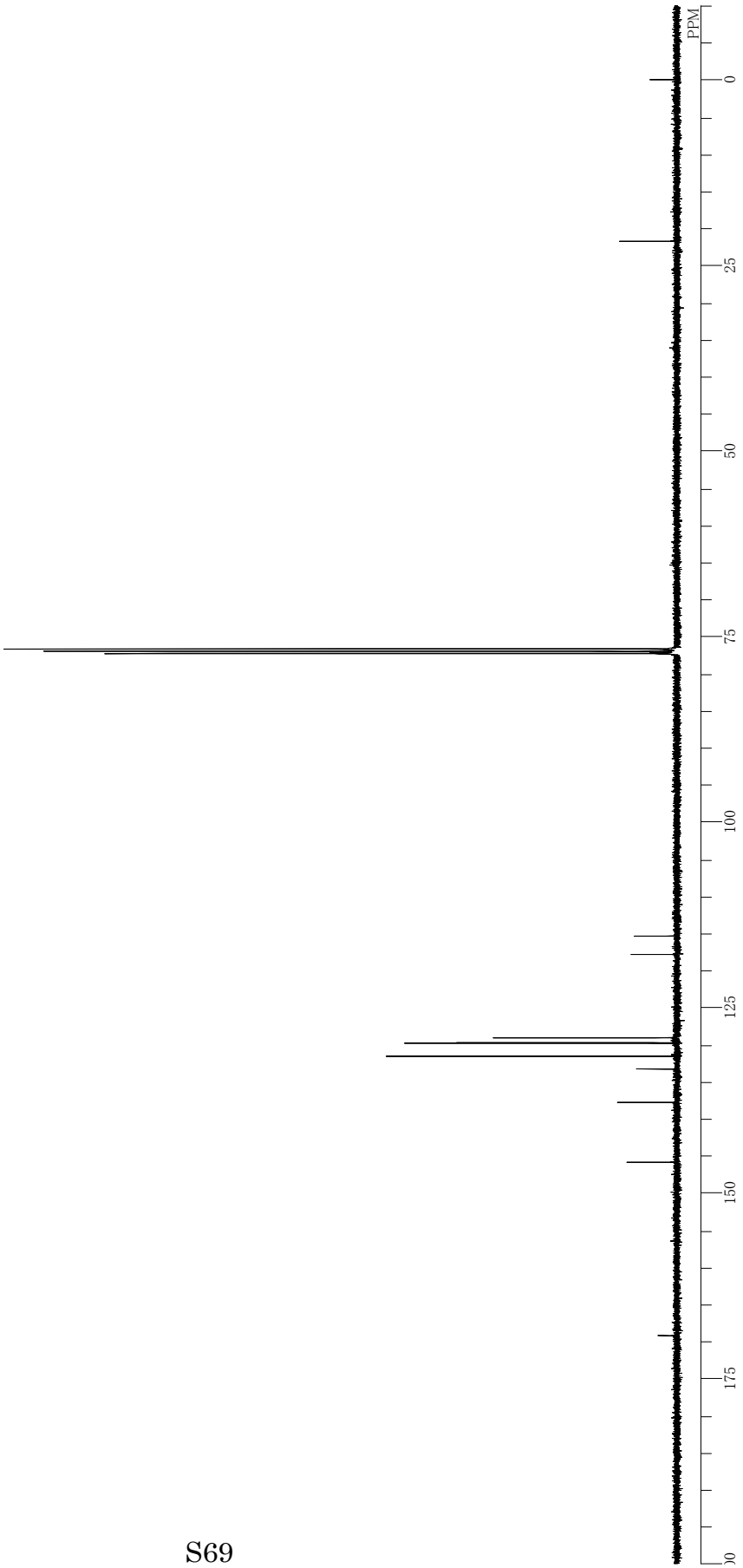
^{1}H NMR (400 MHz) in $CDCl_3$

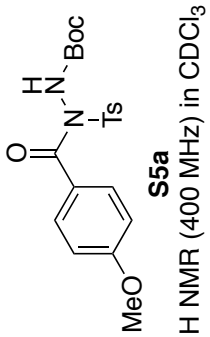




S4b

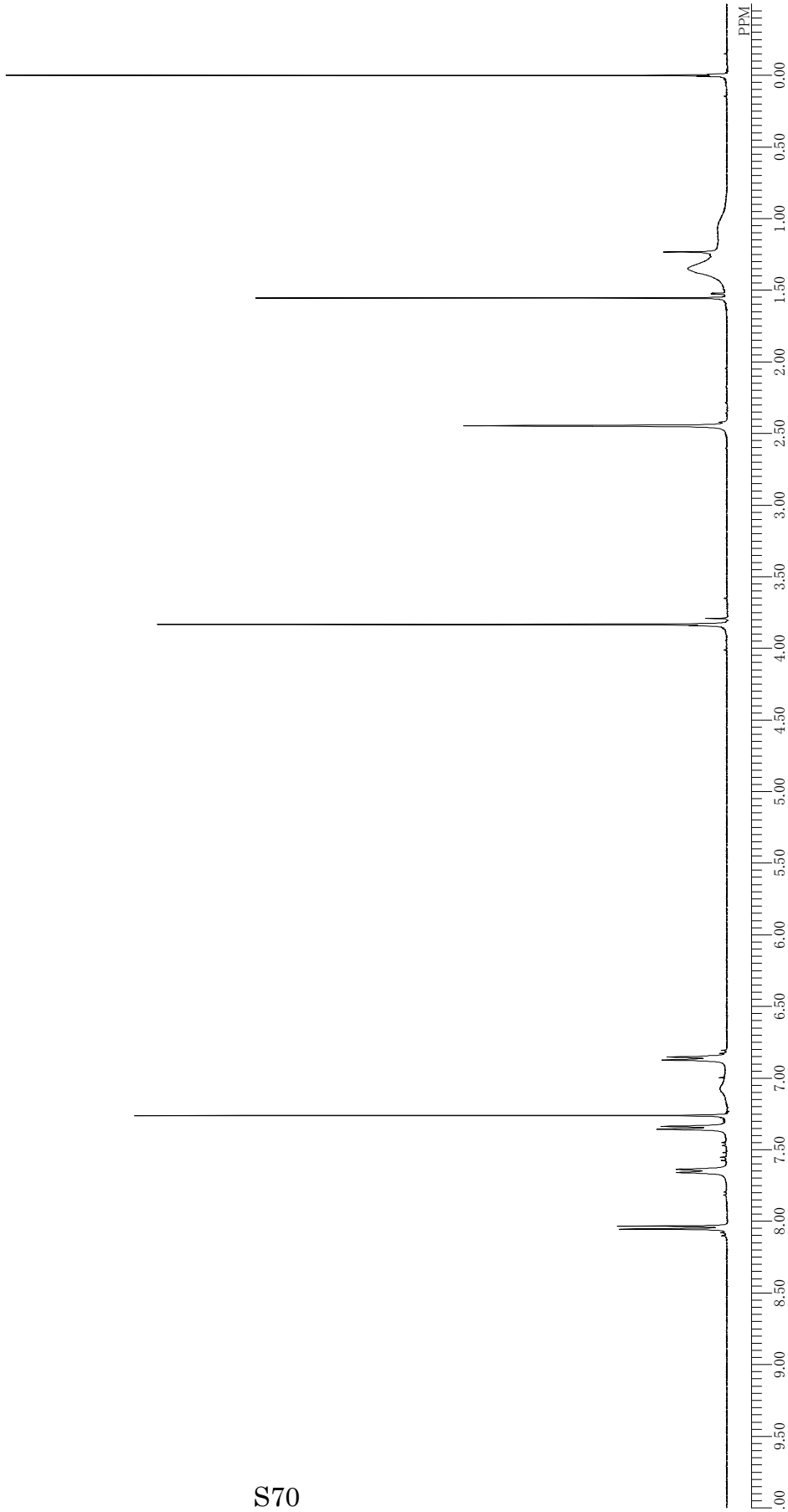
^{13}C NMR (100 MHz) in $CDCl_3$

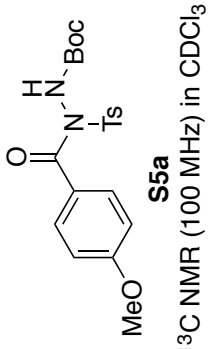




S5a

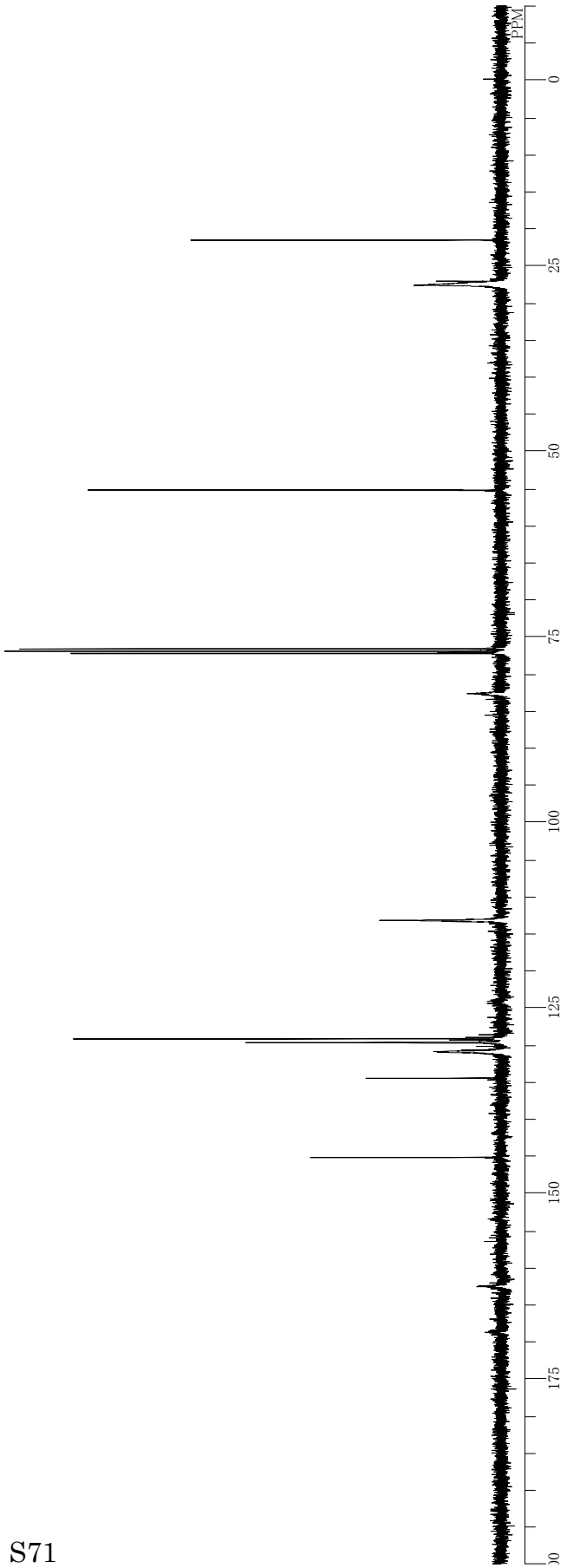
^{1}H NMR (400 MHz) in $CDCl_3$

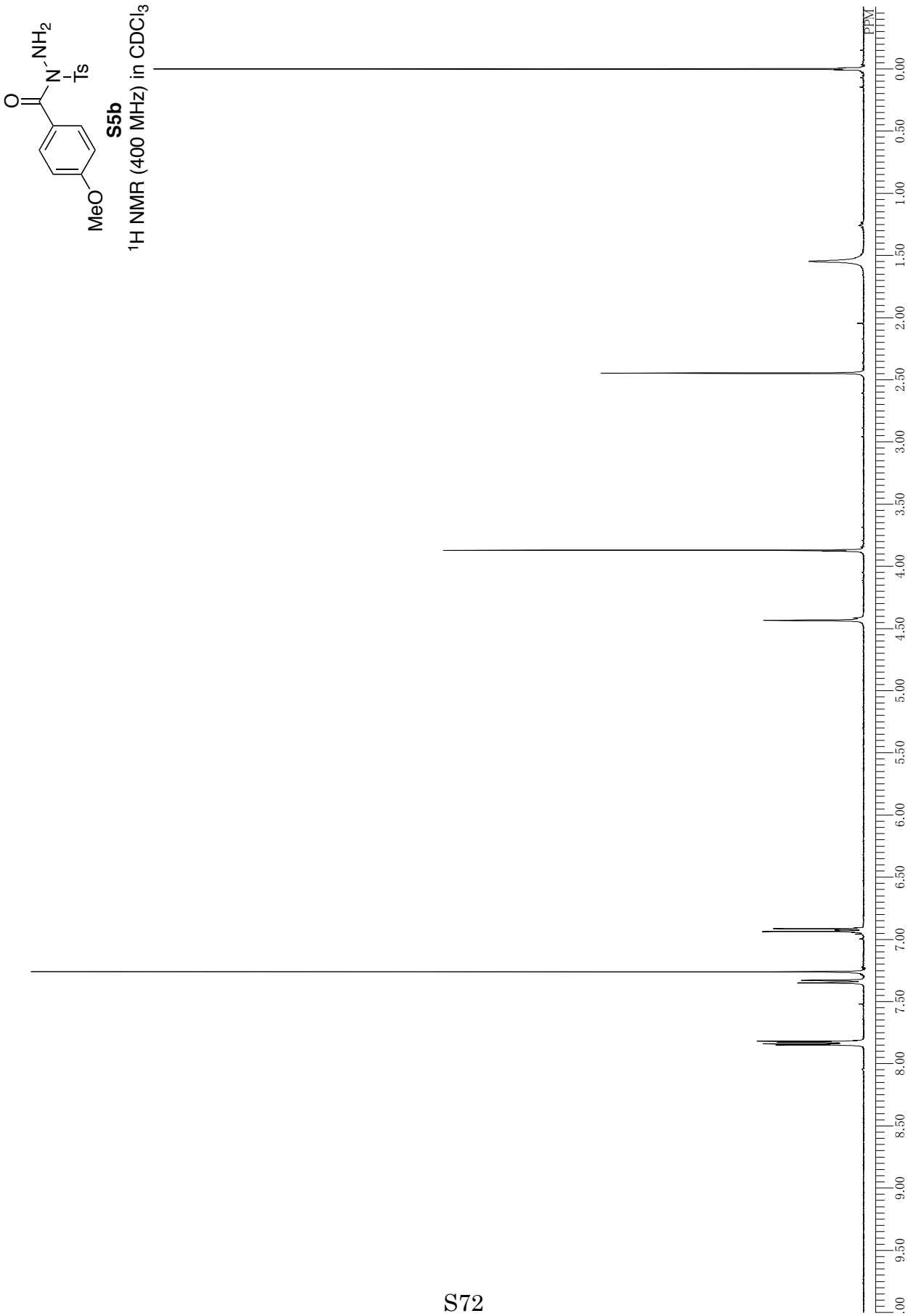


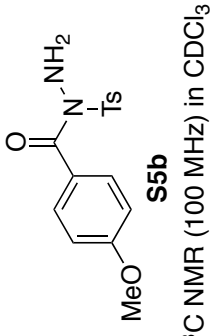


S5a

^{13}C NMR (100 MHz) in $CDCl_3$

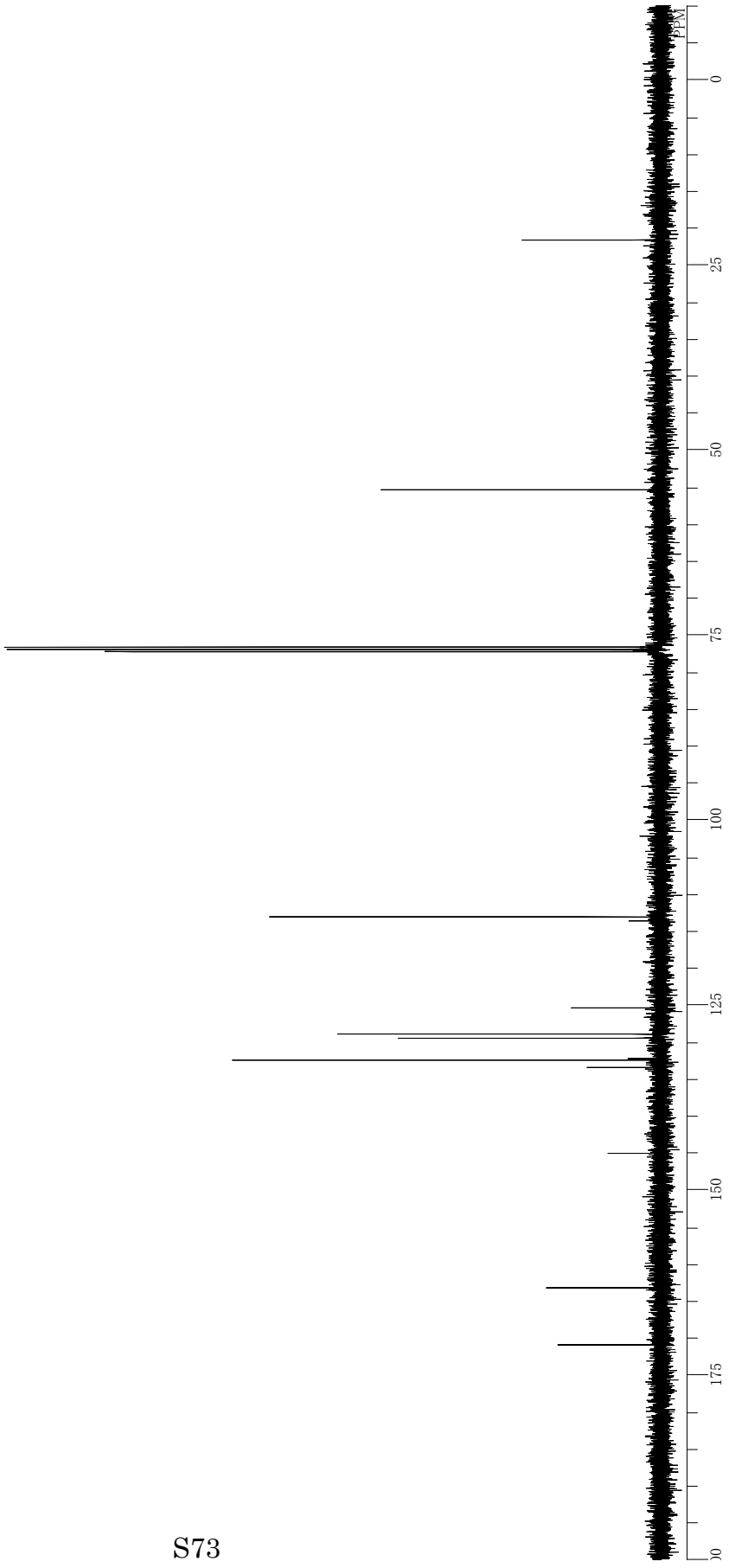


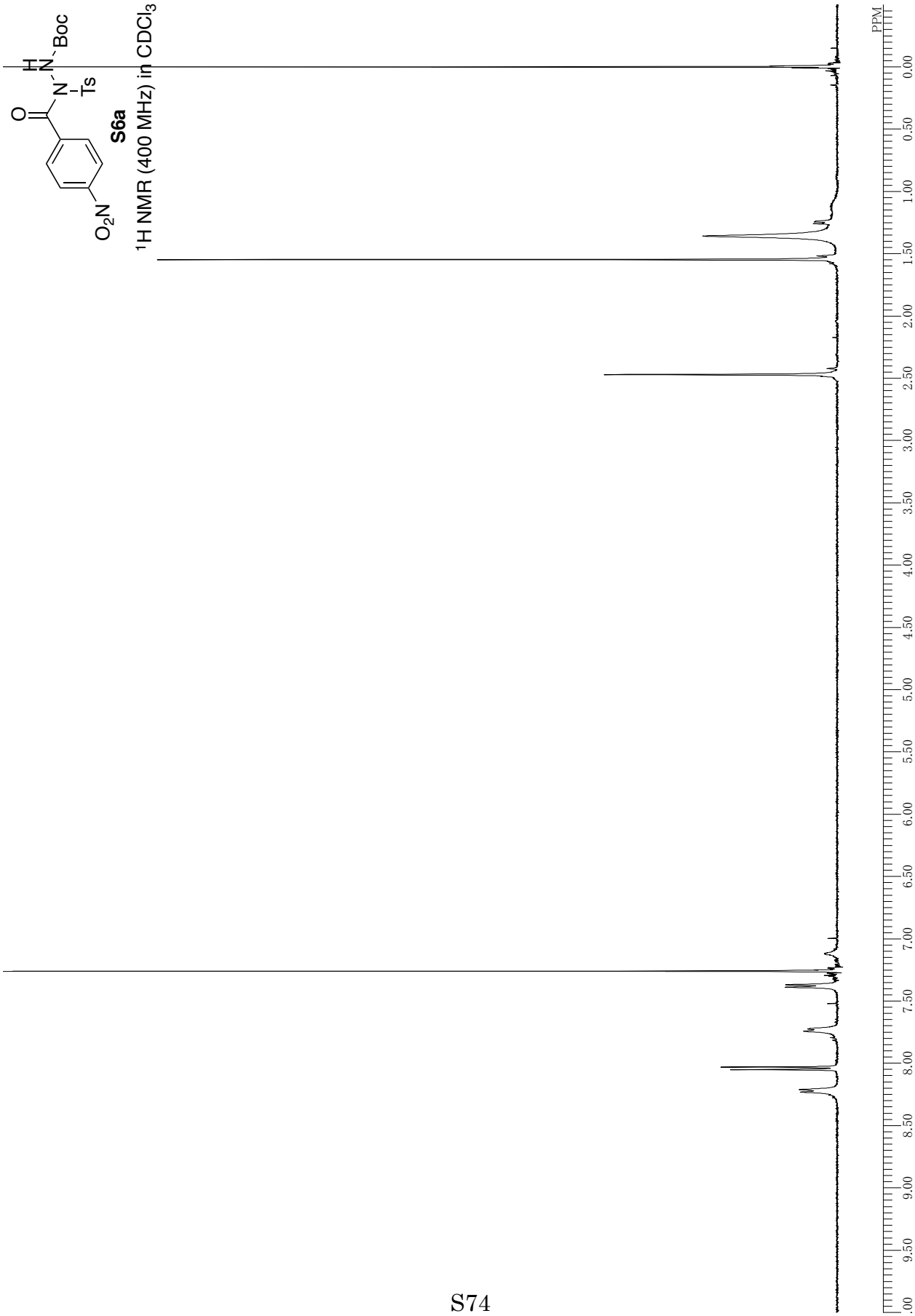

NH2
N
Ts
O
MeO
S5b
1H NMR (400 MHz) in CDCl3
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
.00

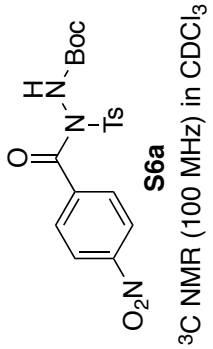


S5b

^{13}C NMR (100 MHz) in $CDCl_3$

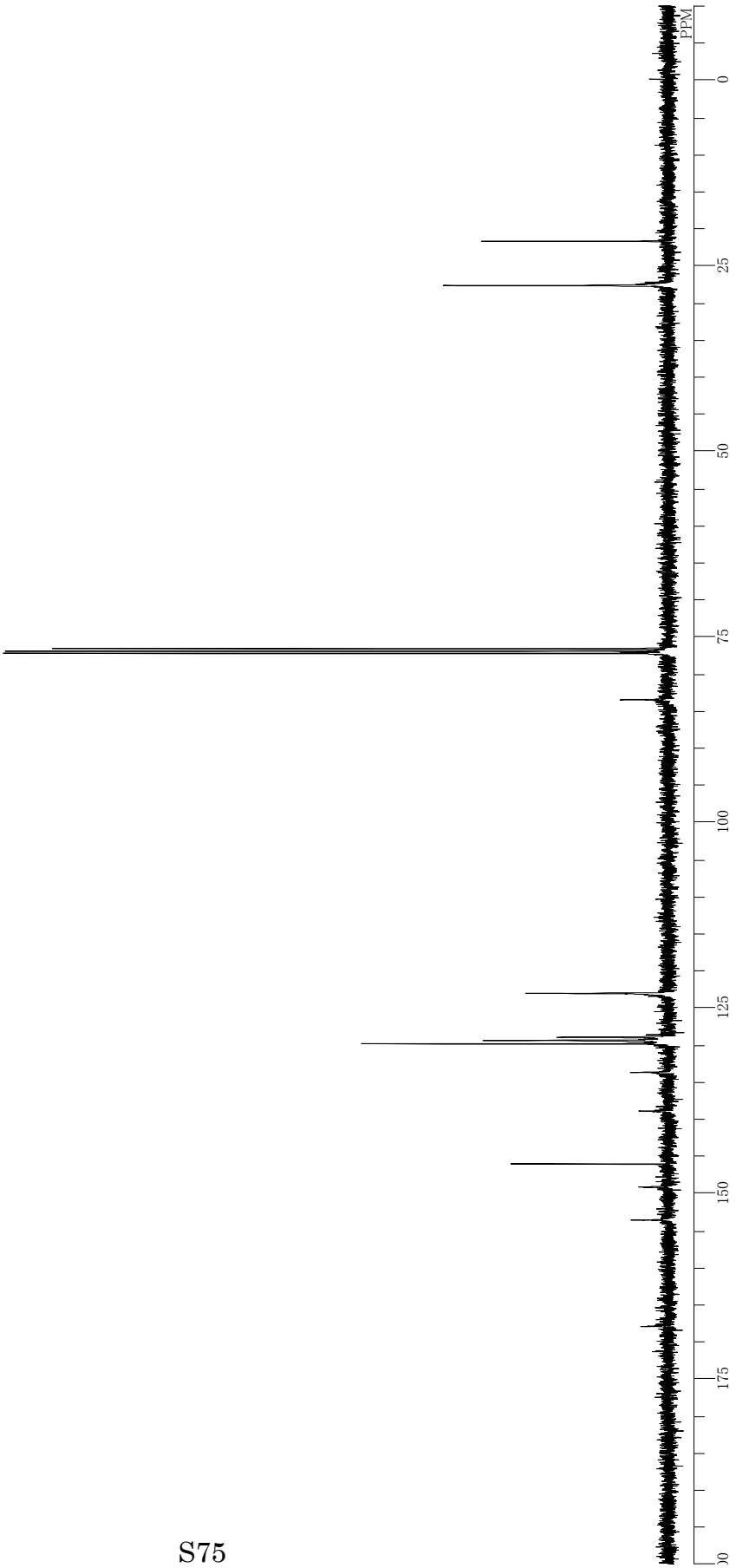


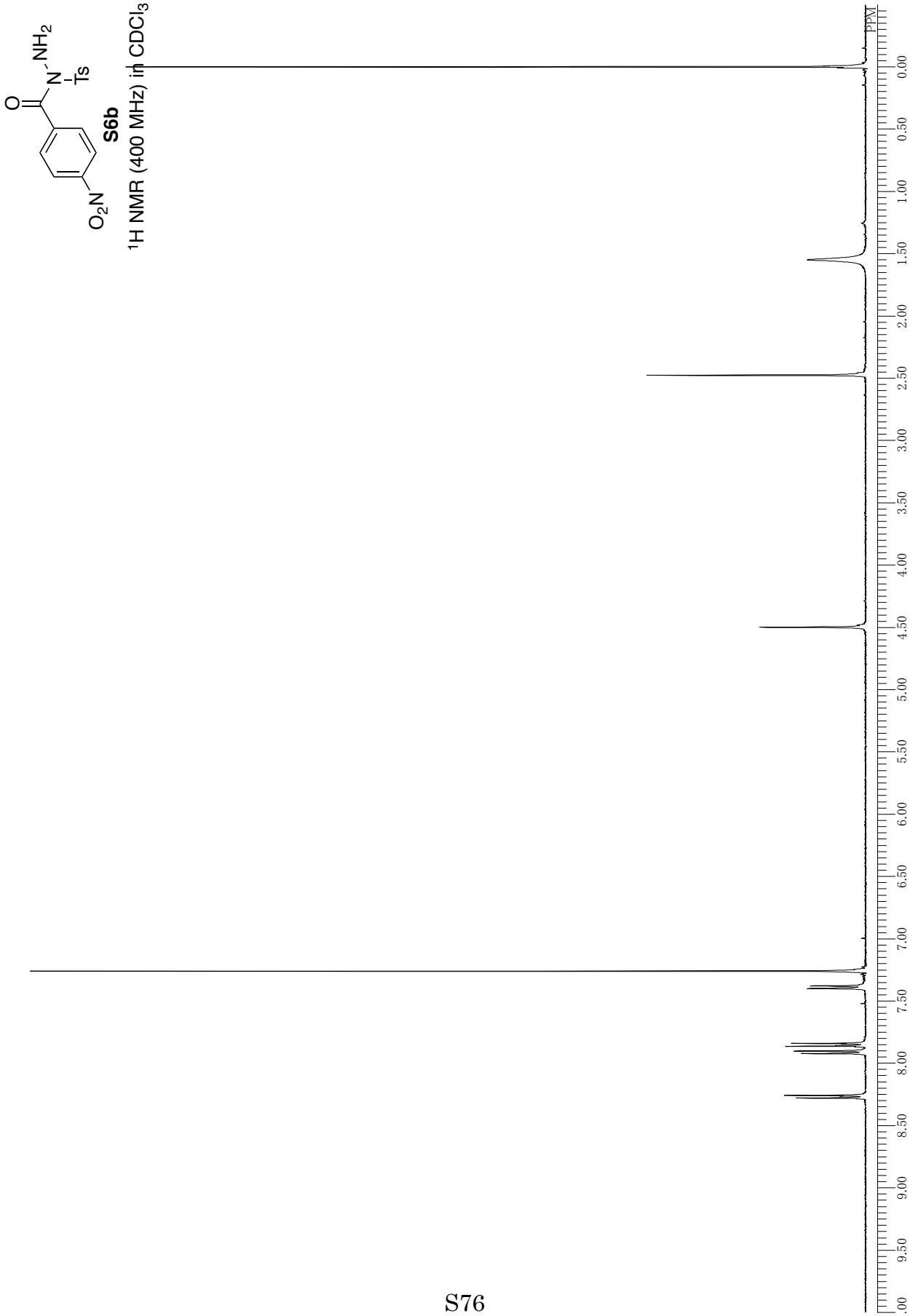

S6a
^{1}H NMR (400 MHz) in $CDCl_3$
PPM

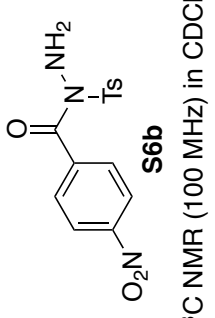


S6a

^{13}C NMR (100 MHz) in $CDCl_3$

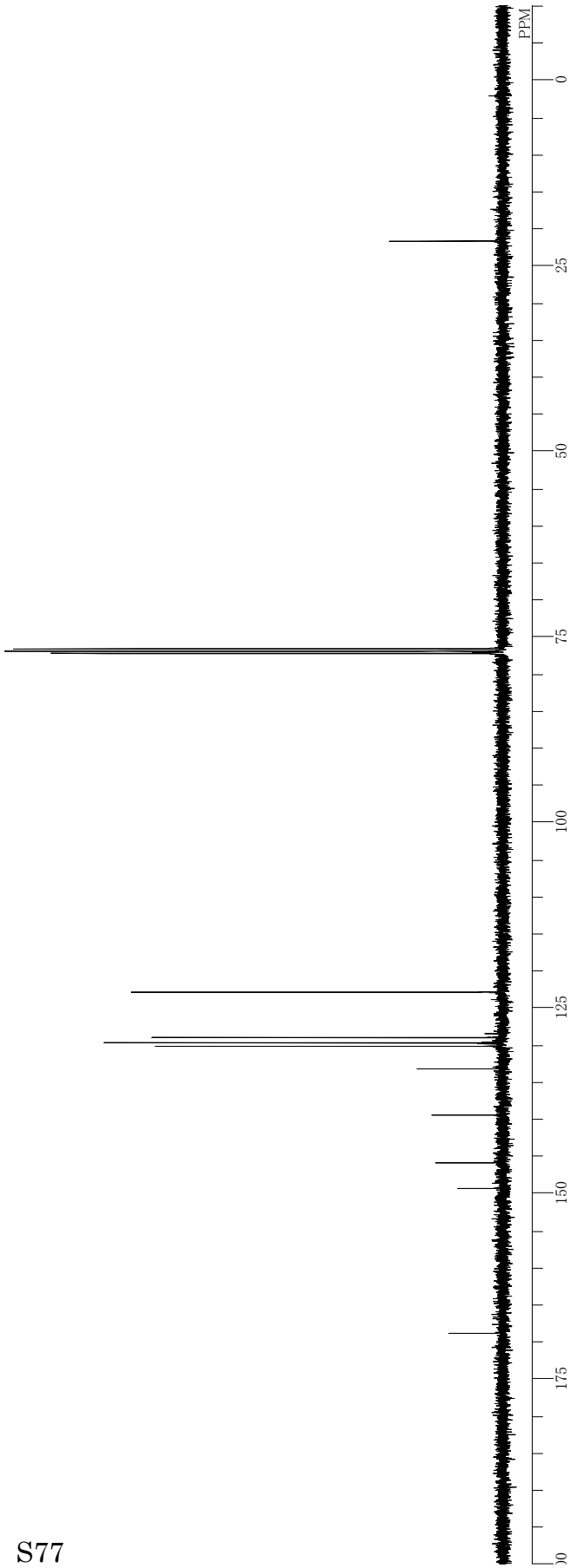


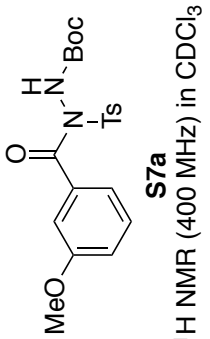

NH2
N
Ts
O
O2N
S6b
1H NMR (400 MHz) in CDCl3
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50



S6b

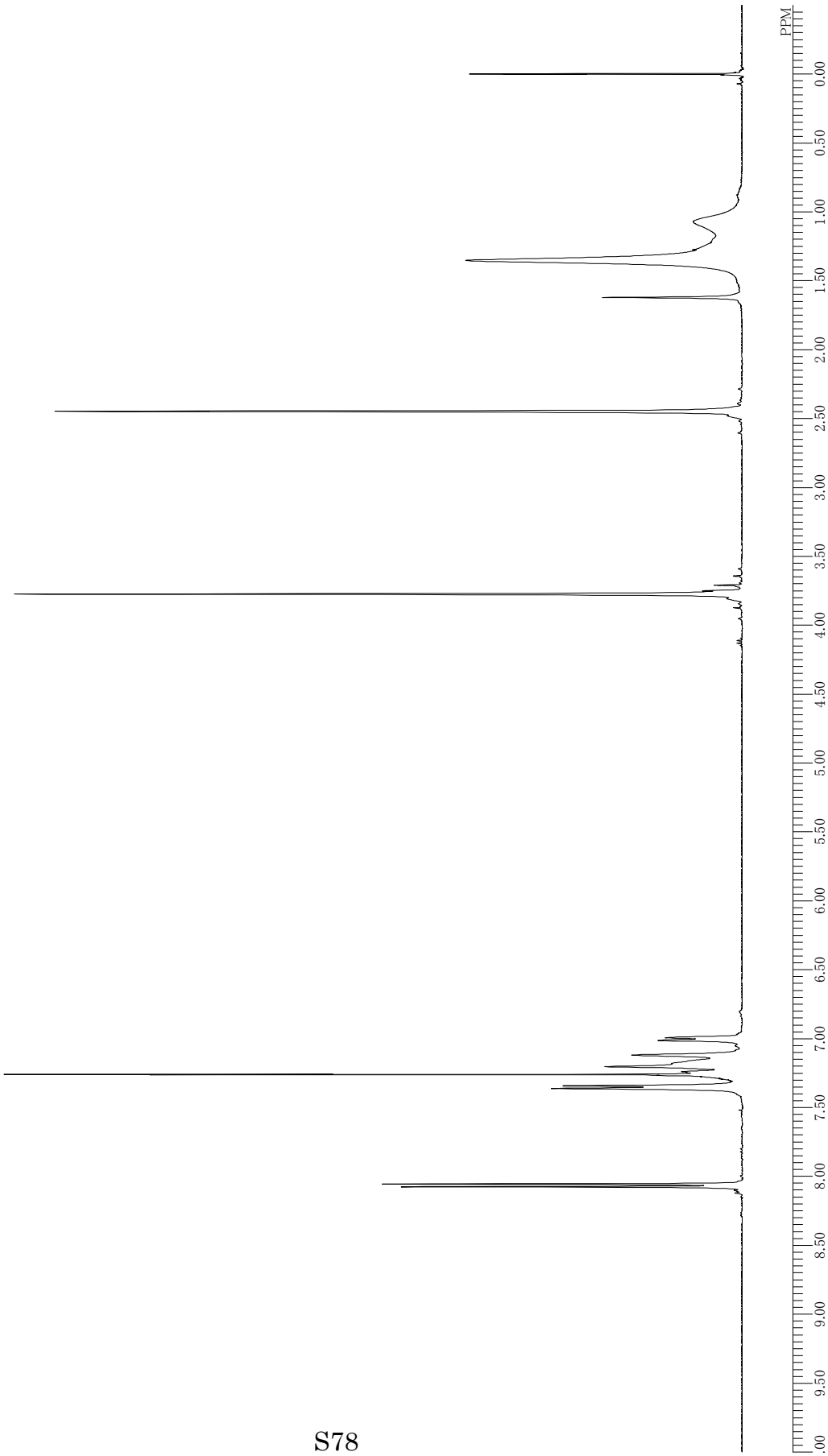
^{13}C NMR (100 MHz) in $CDCl_3$

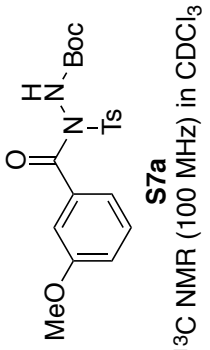




S7a

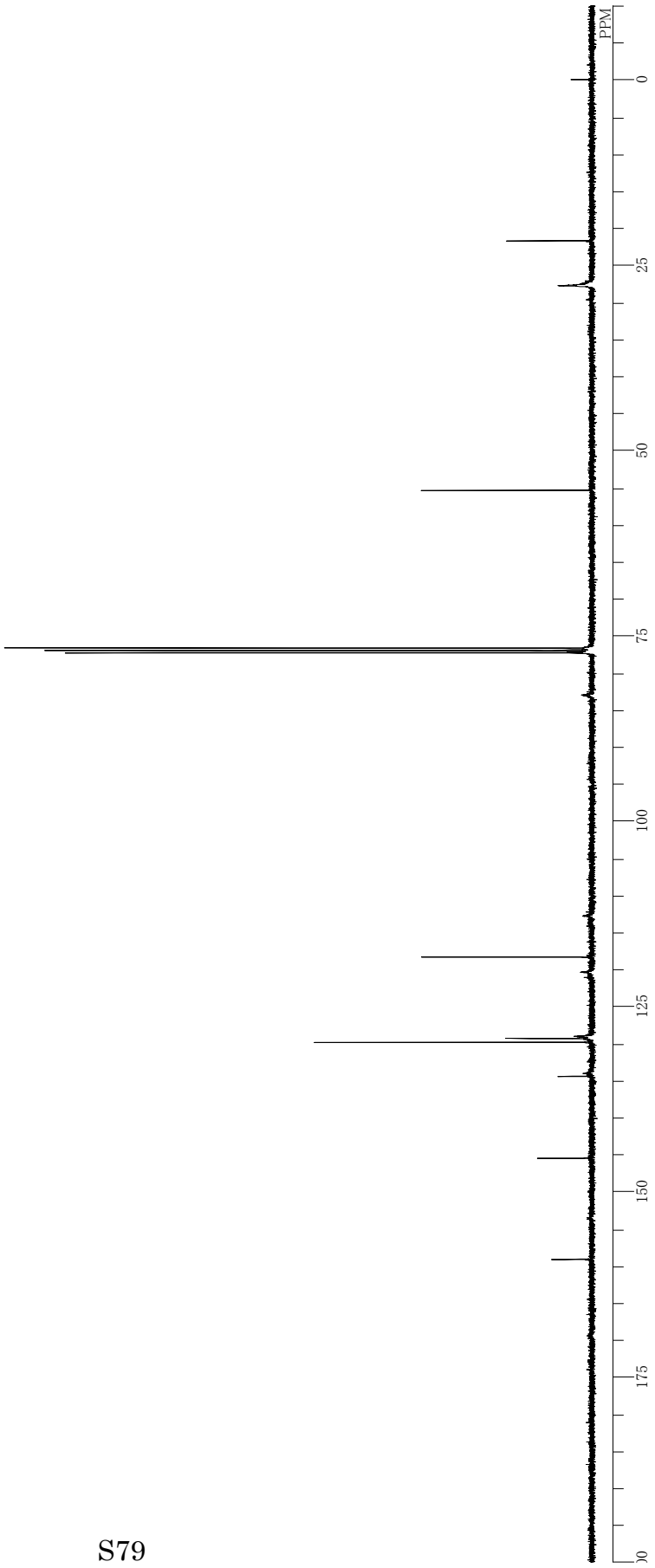
^{1}H NMR (400 MHz) in $CDCl_3$

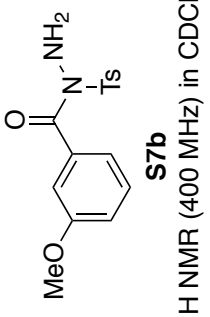




S7a

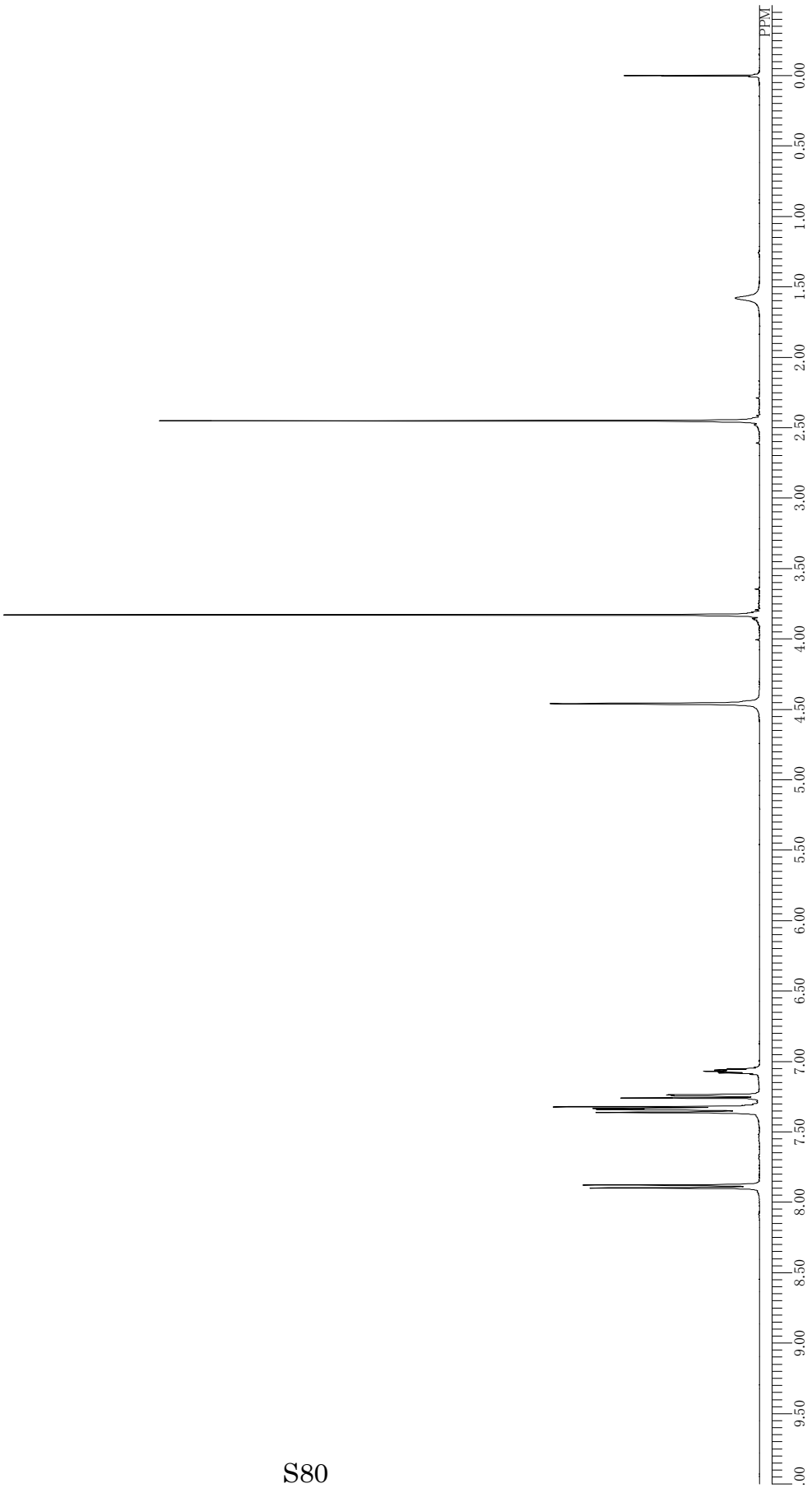
^{13}C NMR (100 MHz) in $CDCl_3$

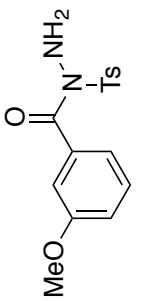




S7b

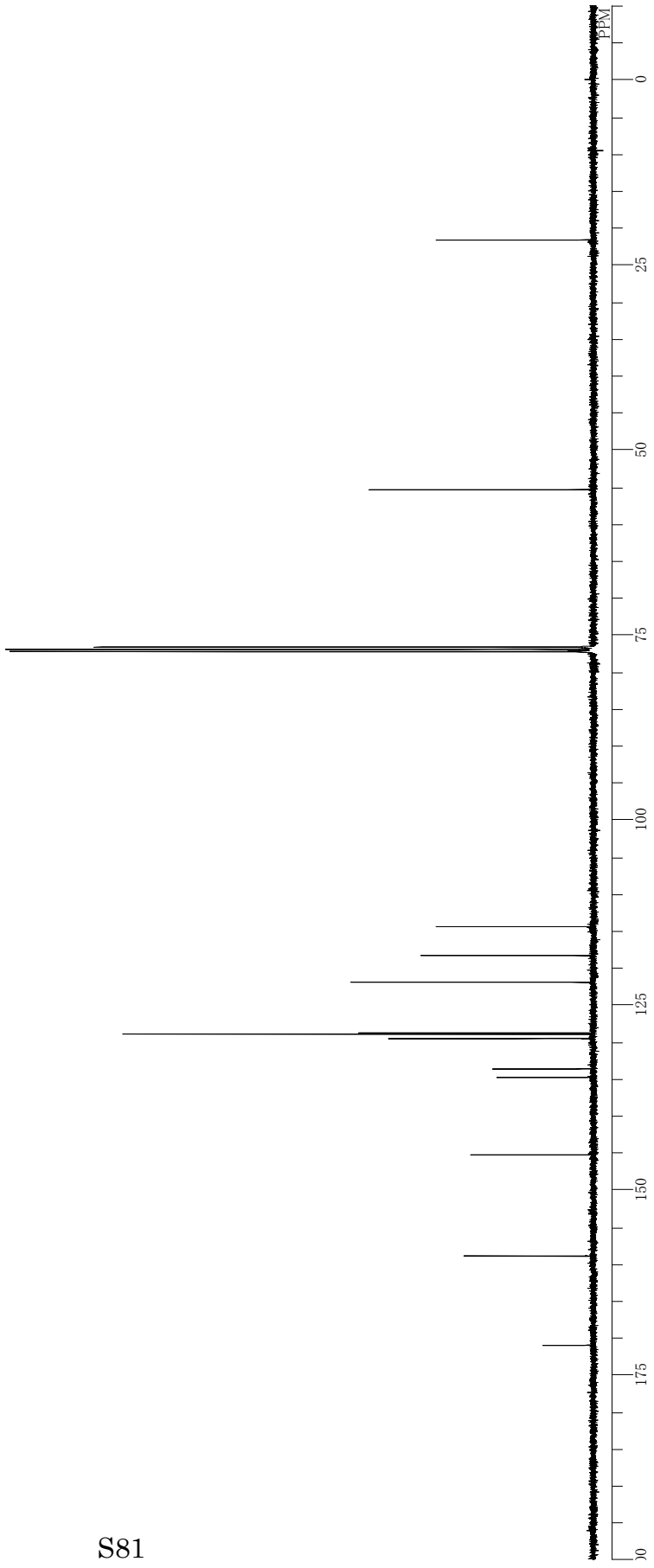
^{1}H NMR (400 MHz) in $CDCl_3$

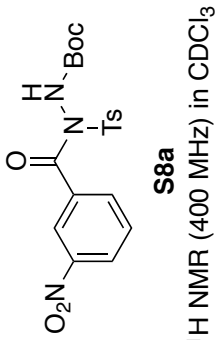




S7b

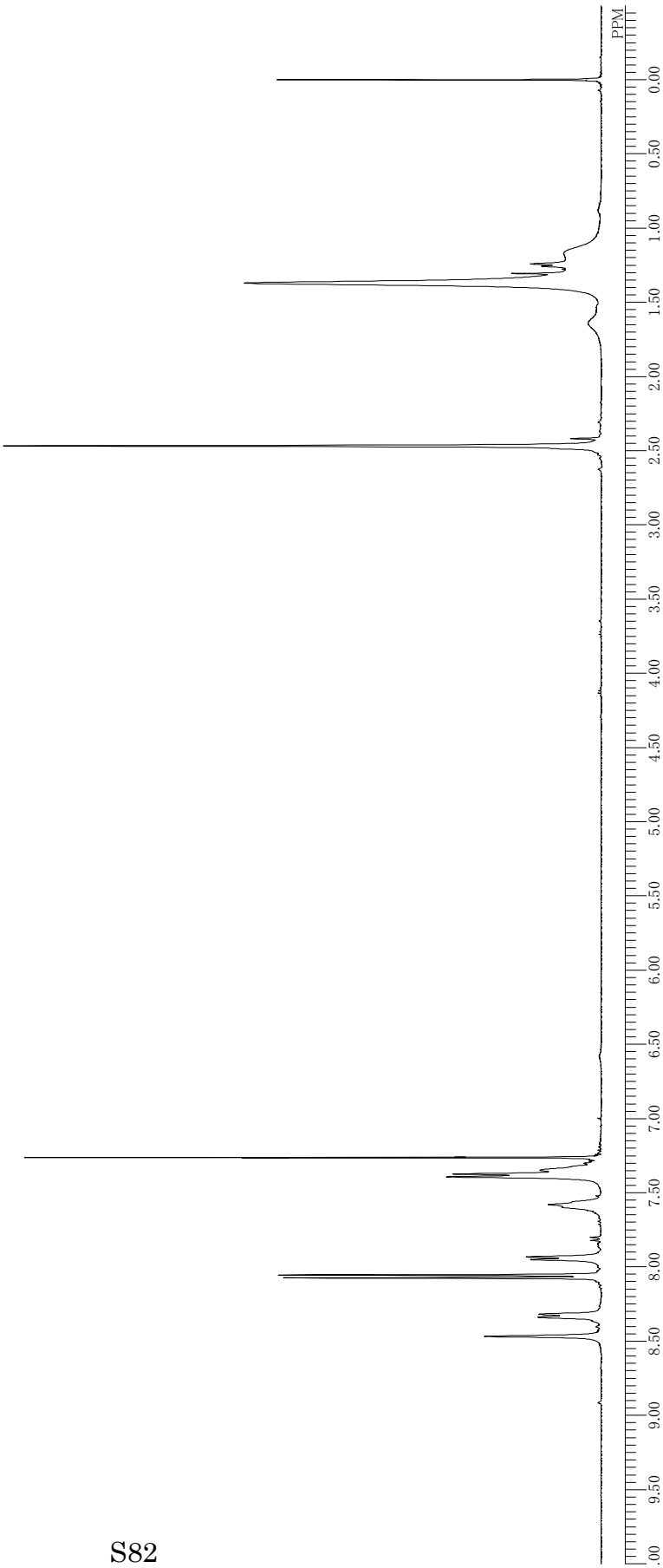
^{13}C NMR (100 MHz) in $CDCl_3$

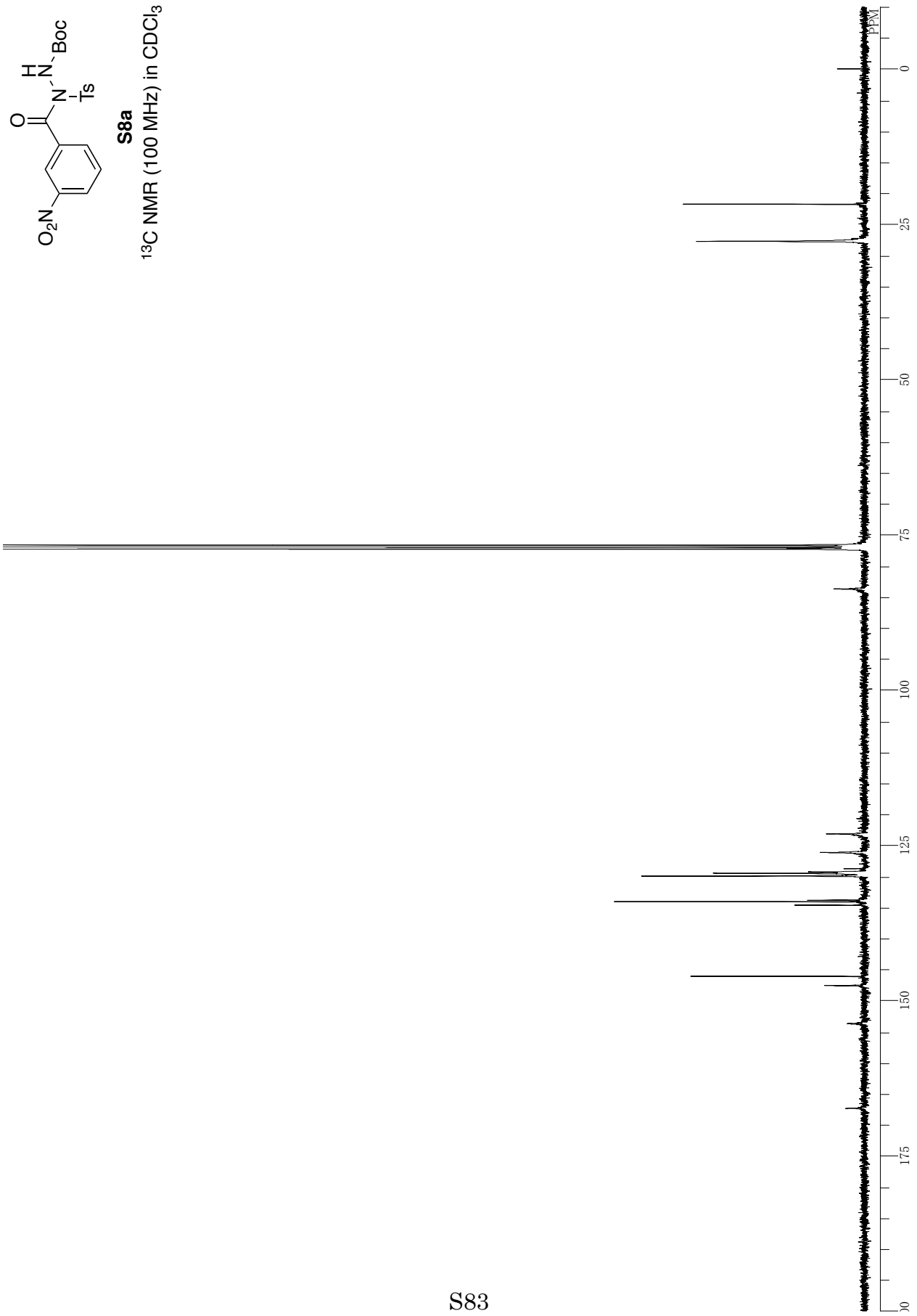


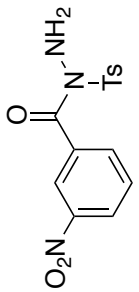


S8a

^{1}H NMR (400 MHz) in $CDCl_3$

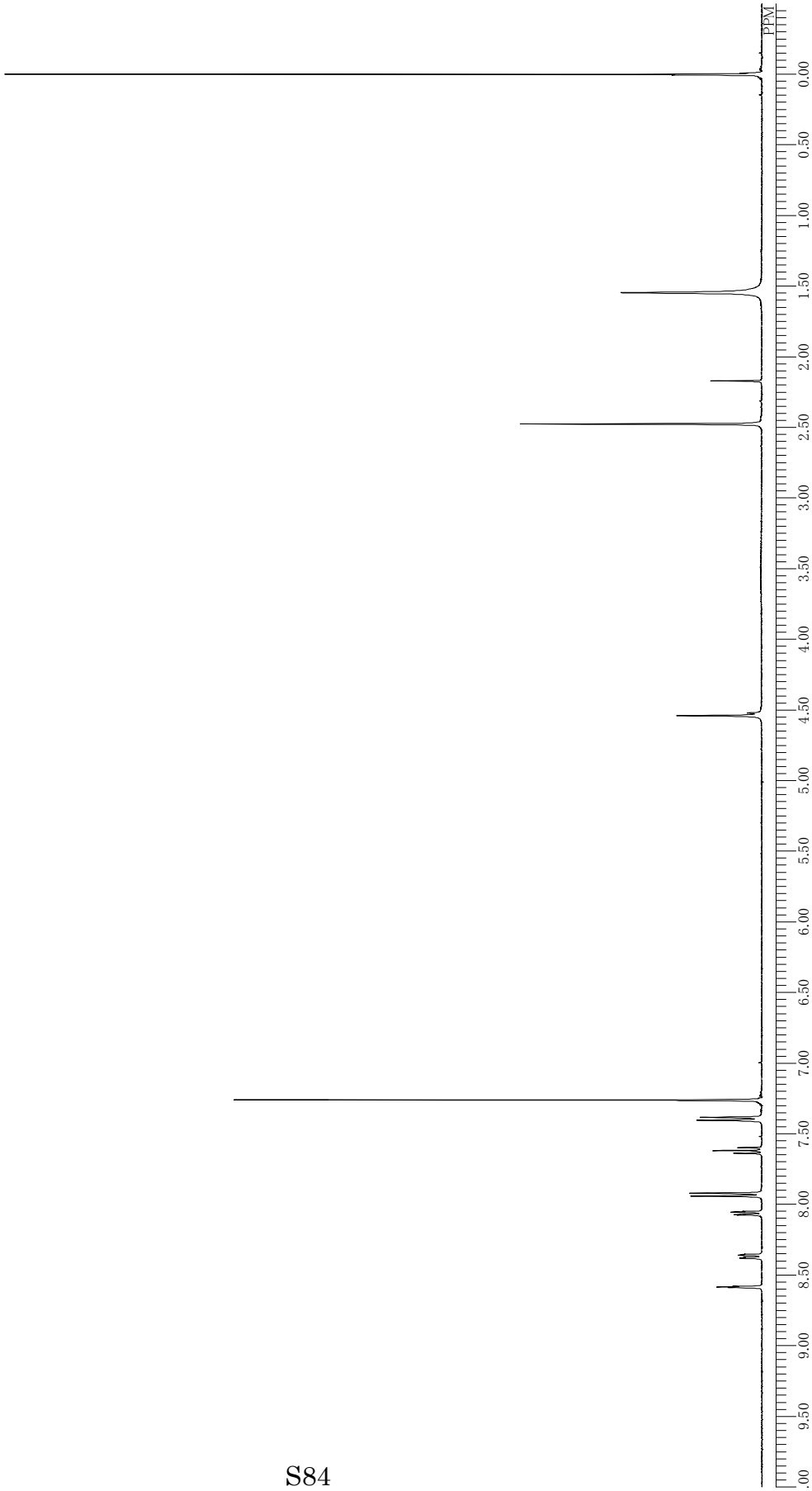


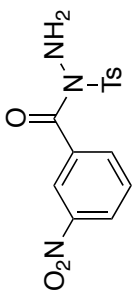

O
H
N
Boc
N
Ts
O2N
S8a
13C NMR (100 MHz) in CDCl3
PPM
0
25
50
75
100
125
150
175



S8b

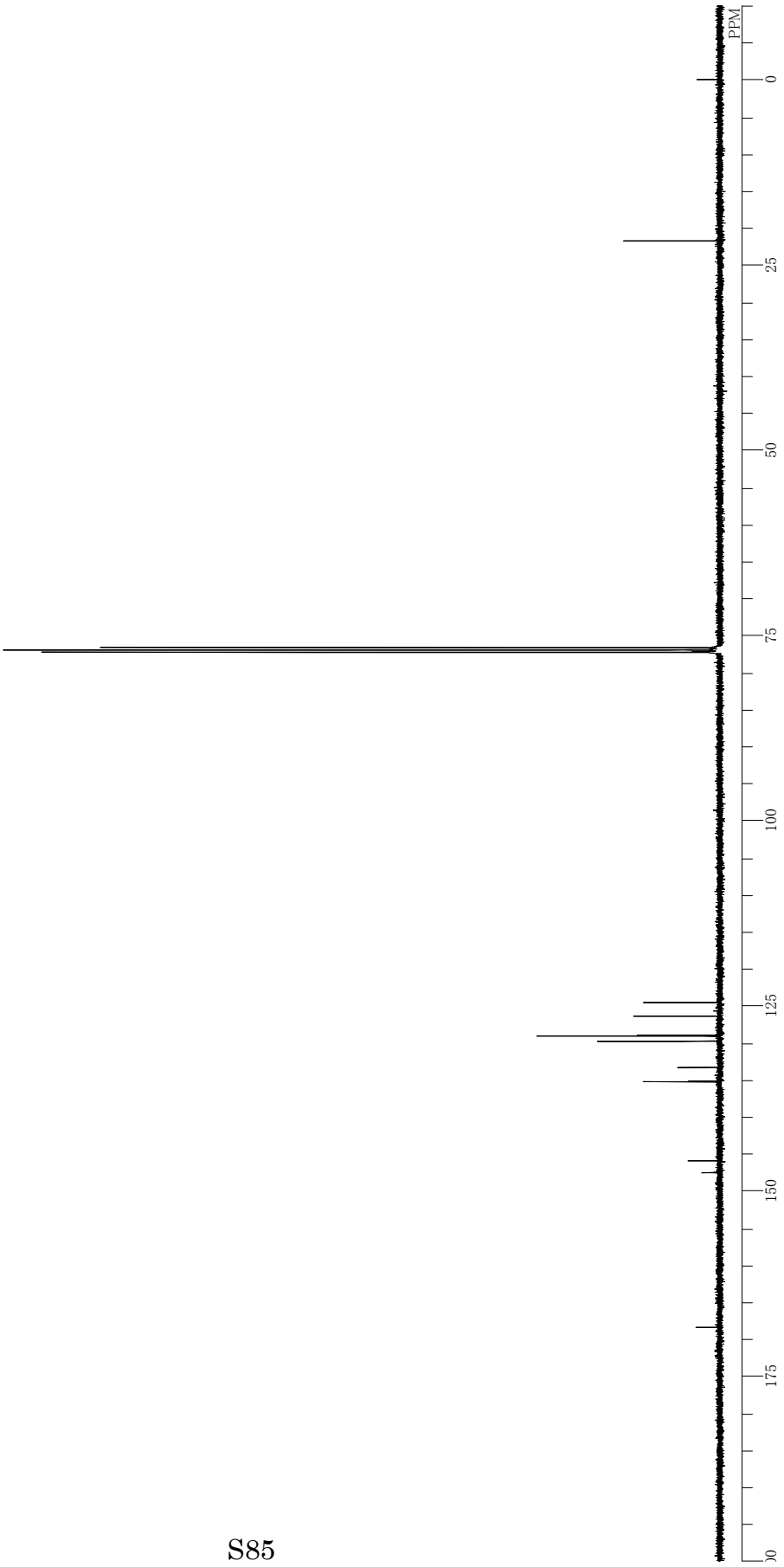
^{1}H NMR (400 MHz) in $CDCl_3$

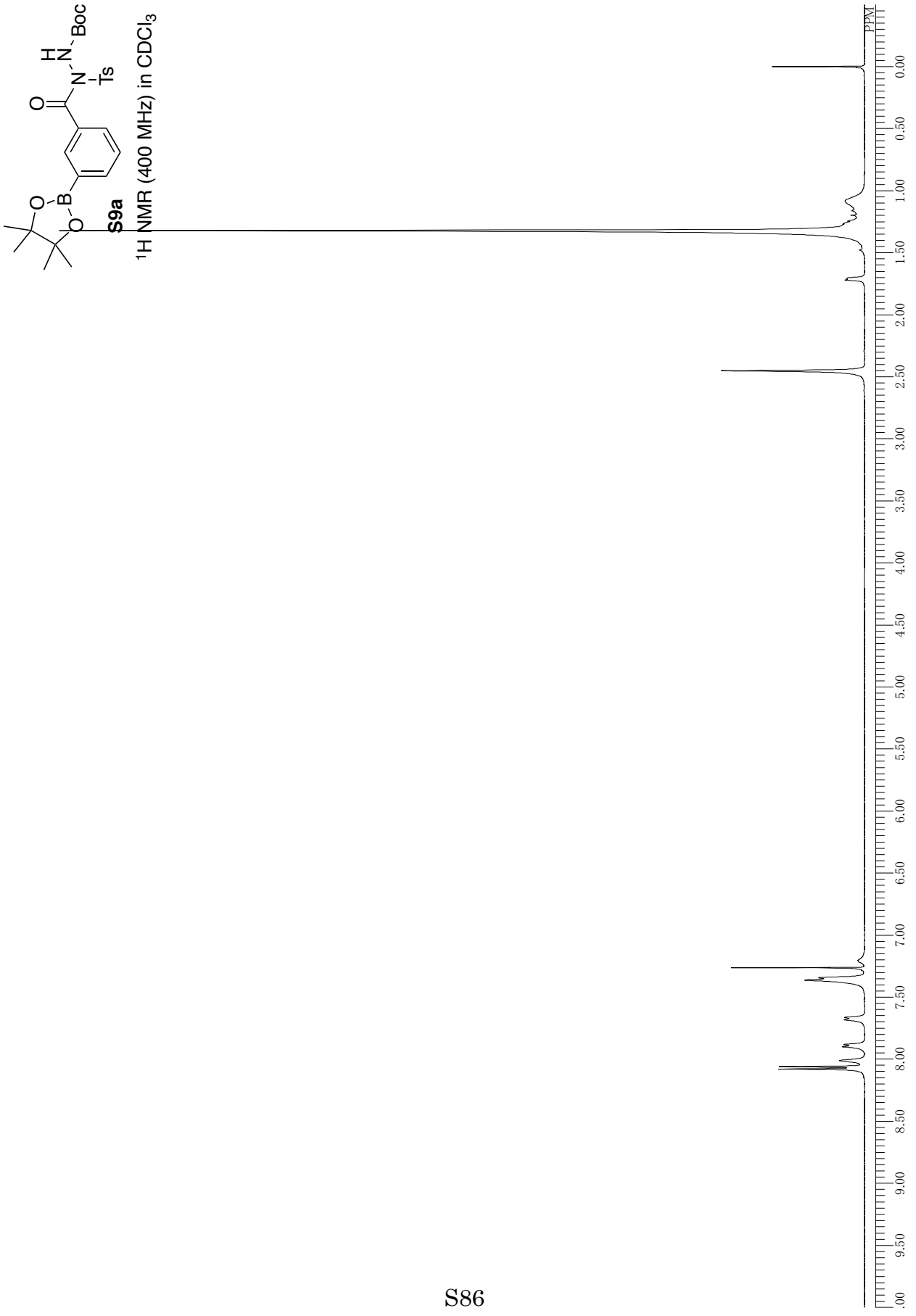


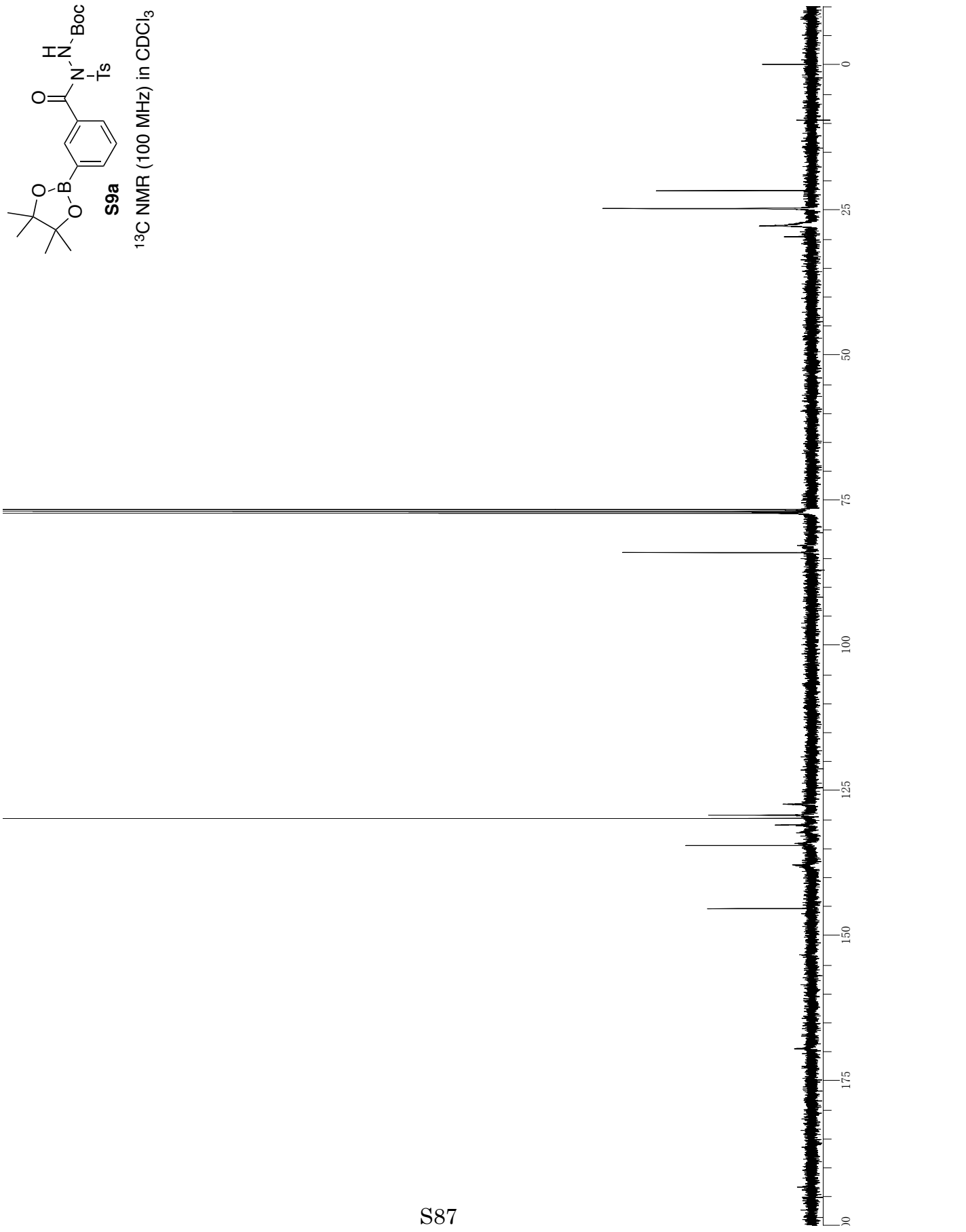


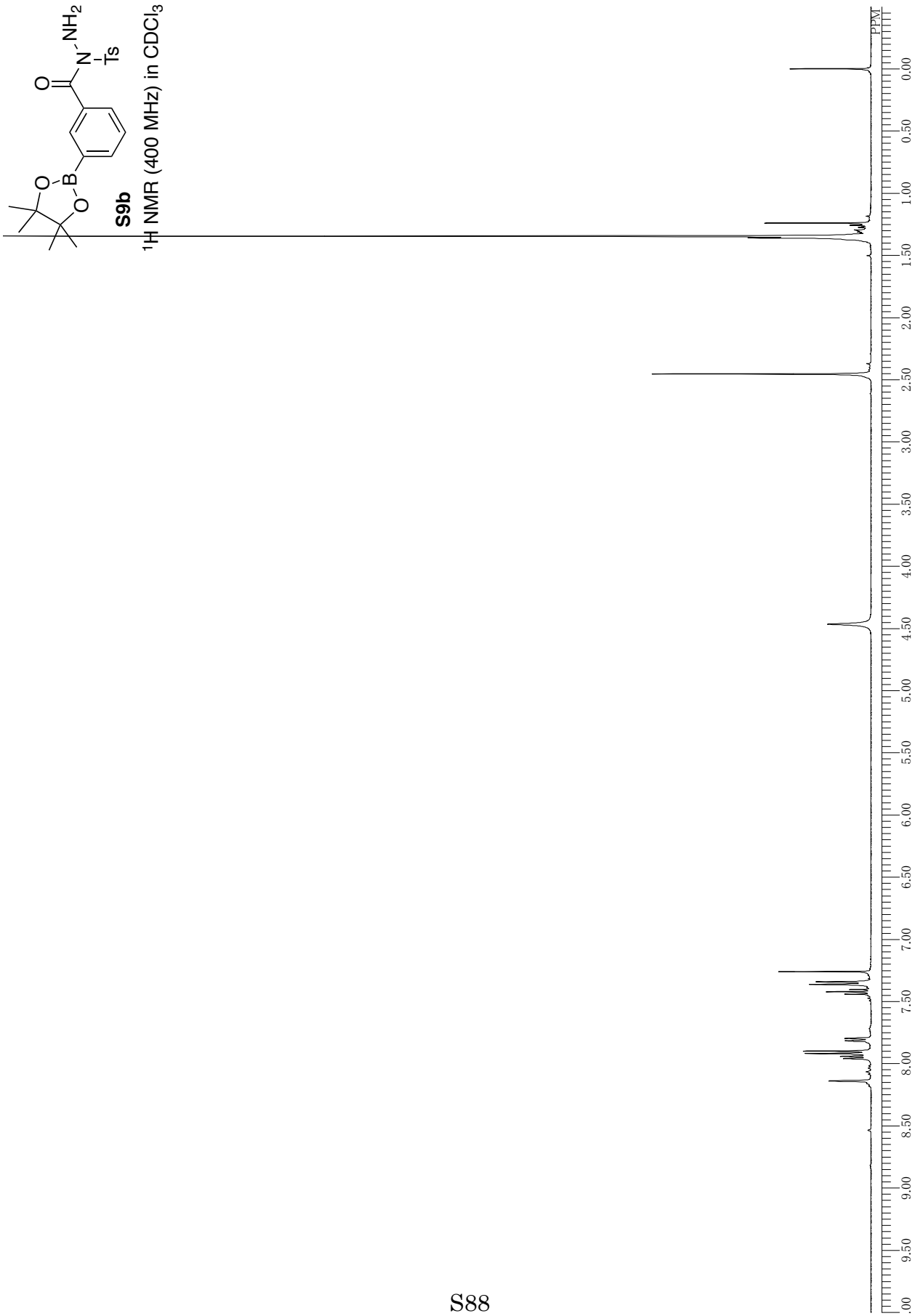
S8b

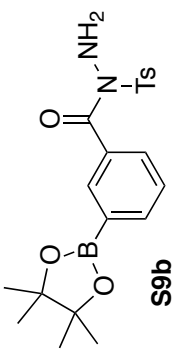
^{13}C NMR (100 MHz) in $CDCl_3$




S9a
^{1}H NMR (400 MHz) in $CDCl_3$
PPM

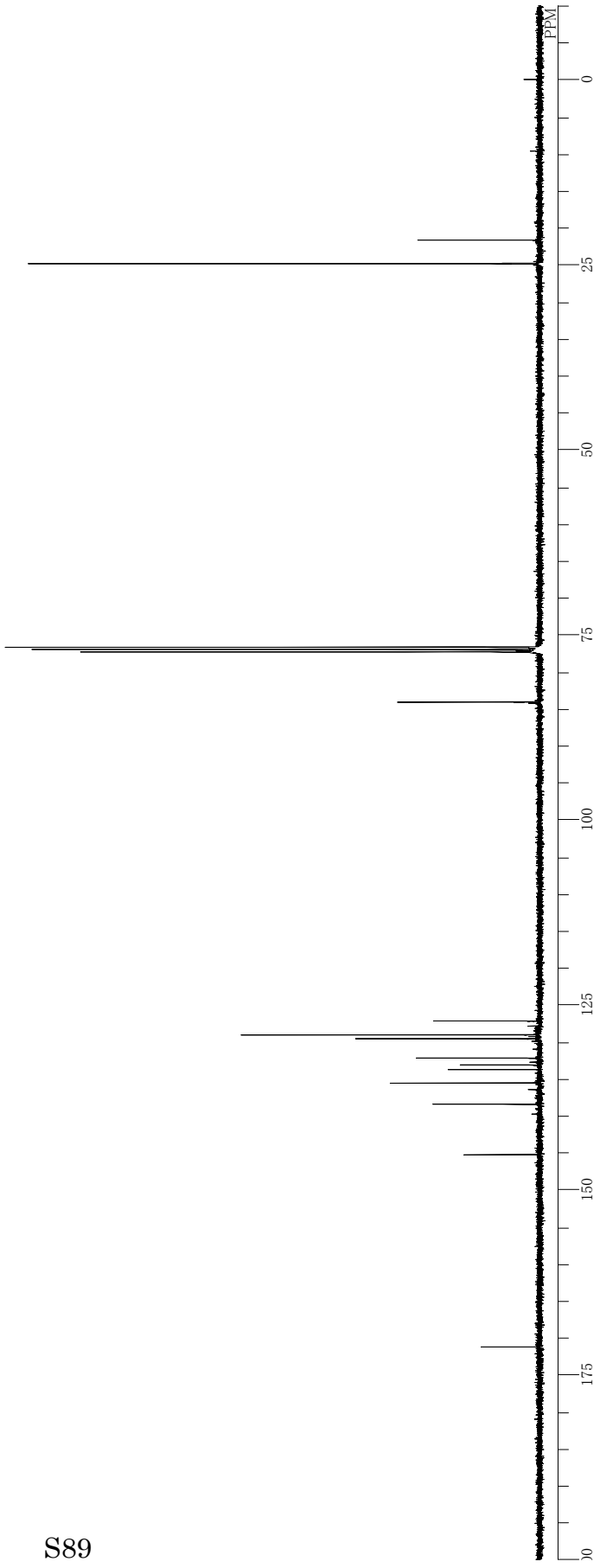

S9a
^{13}C NMR (100 MHz) in $CDCl_3$
Boc
Ts
0
25
50
75
100
125
150
175

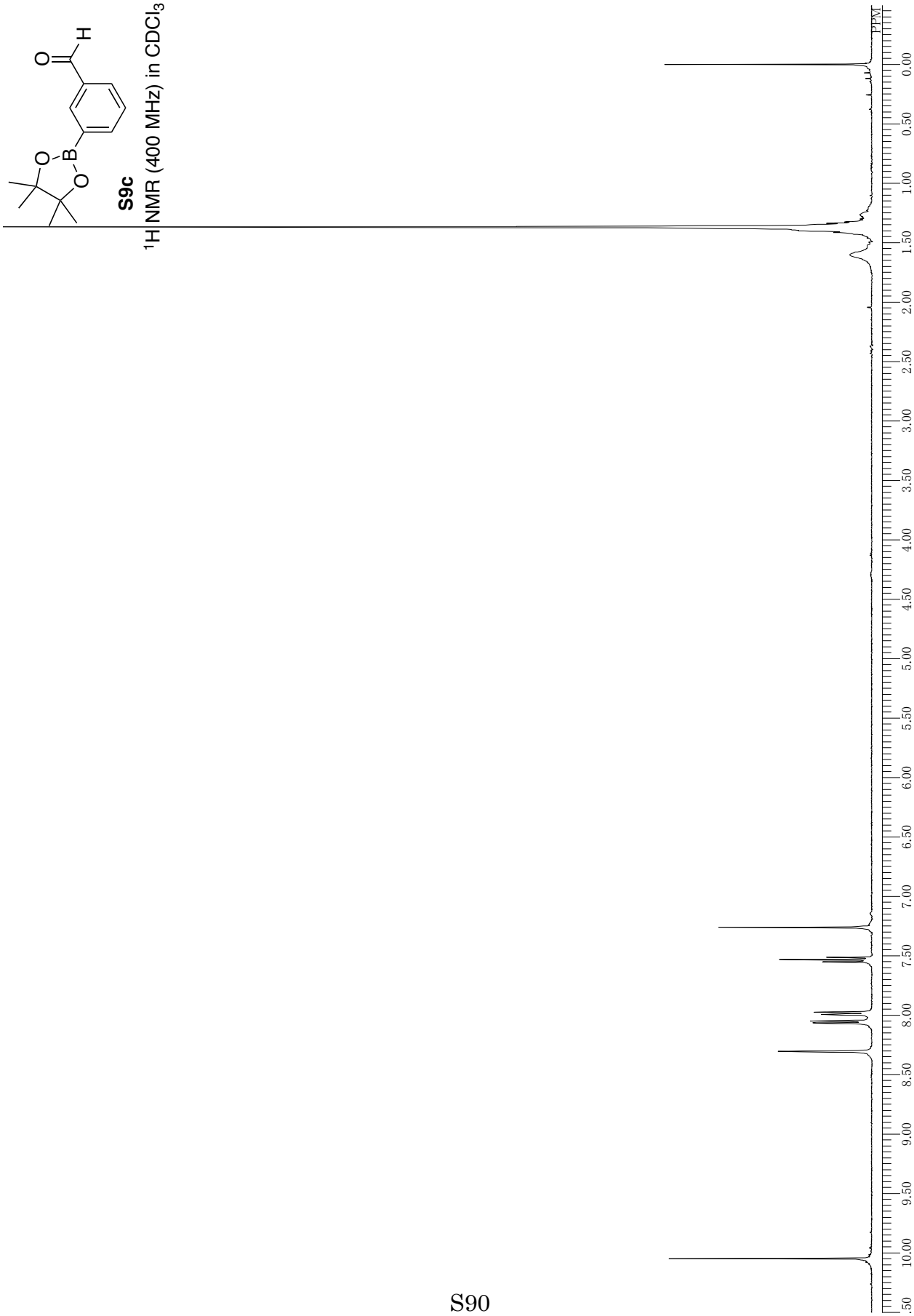

S9b
^{1}H NMR (400 MHz) in $CDCl_3$
PPM

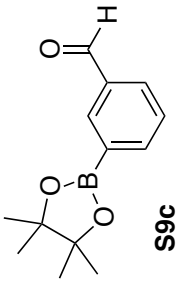


S9b

^{13}C NMR (100 MHz) in $CDCl_3$

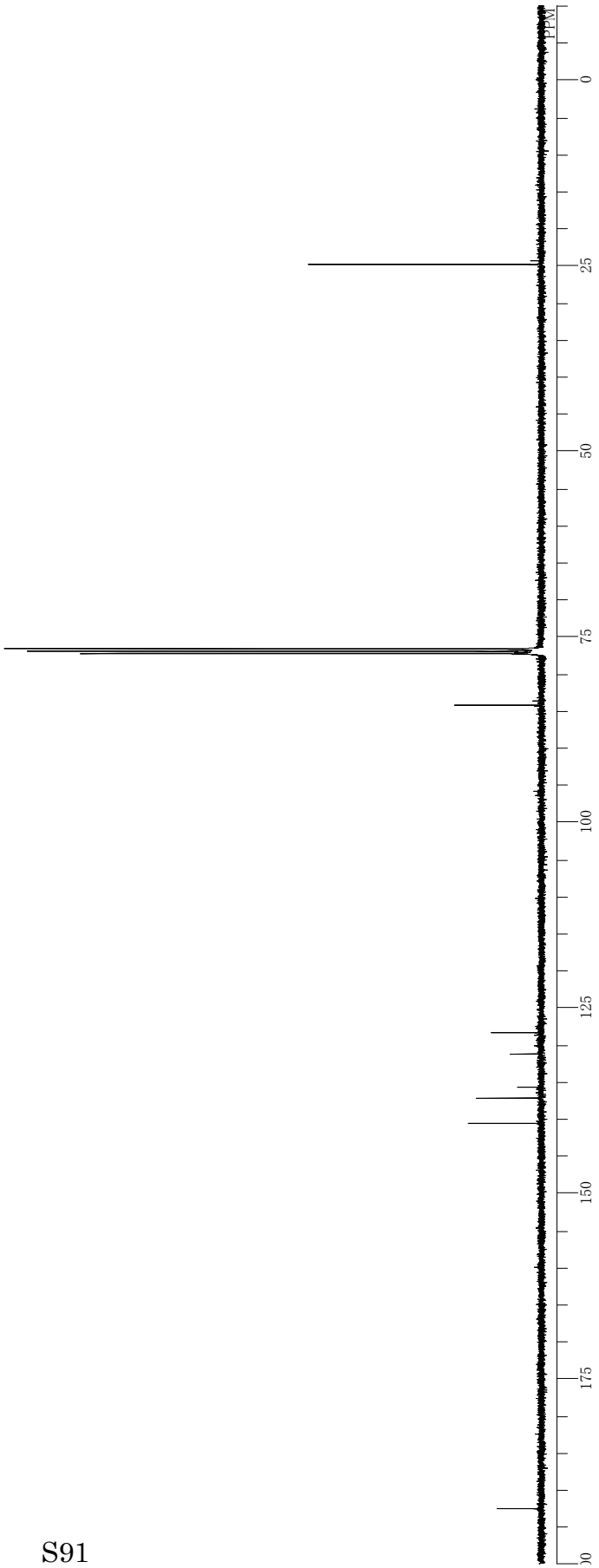


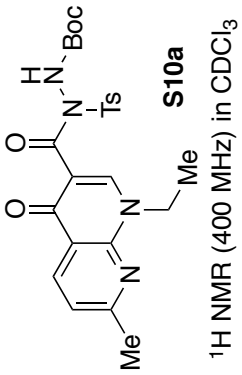

S9c
^{1}H NMR (400 MHz) in $CDCl_3$
PPM



S9c

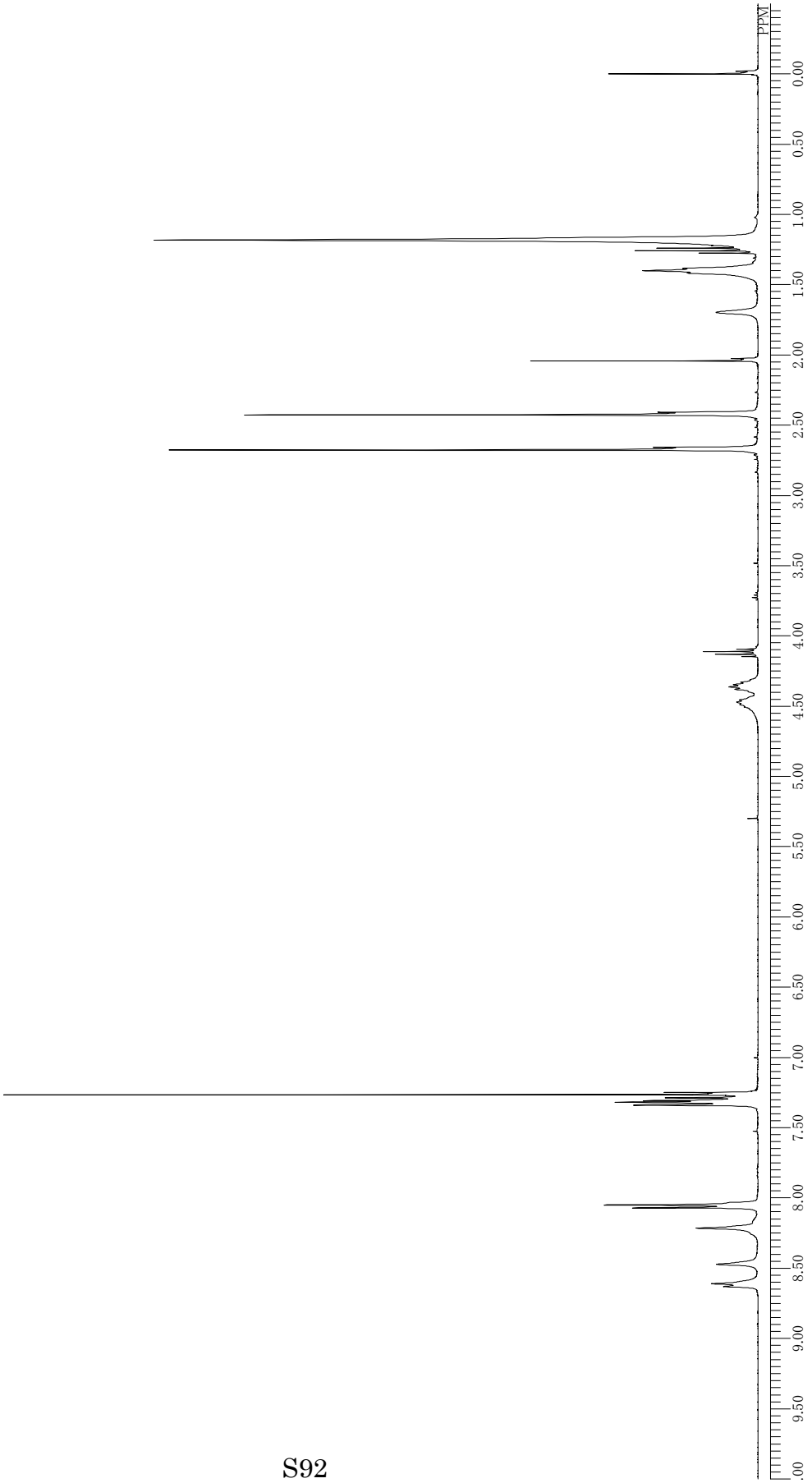
^{13}C NMR (100 MHz) in $CDCl_3$

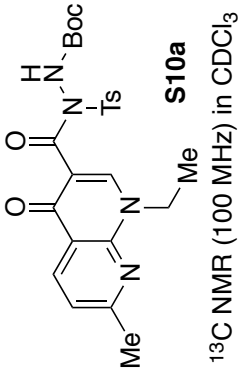




S10a

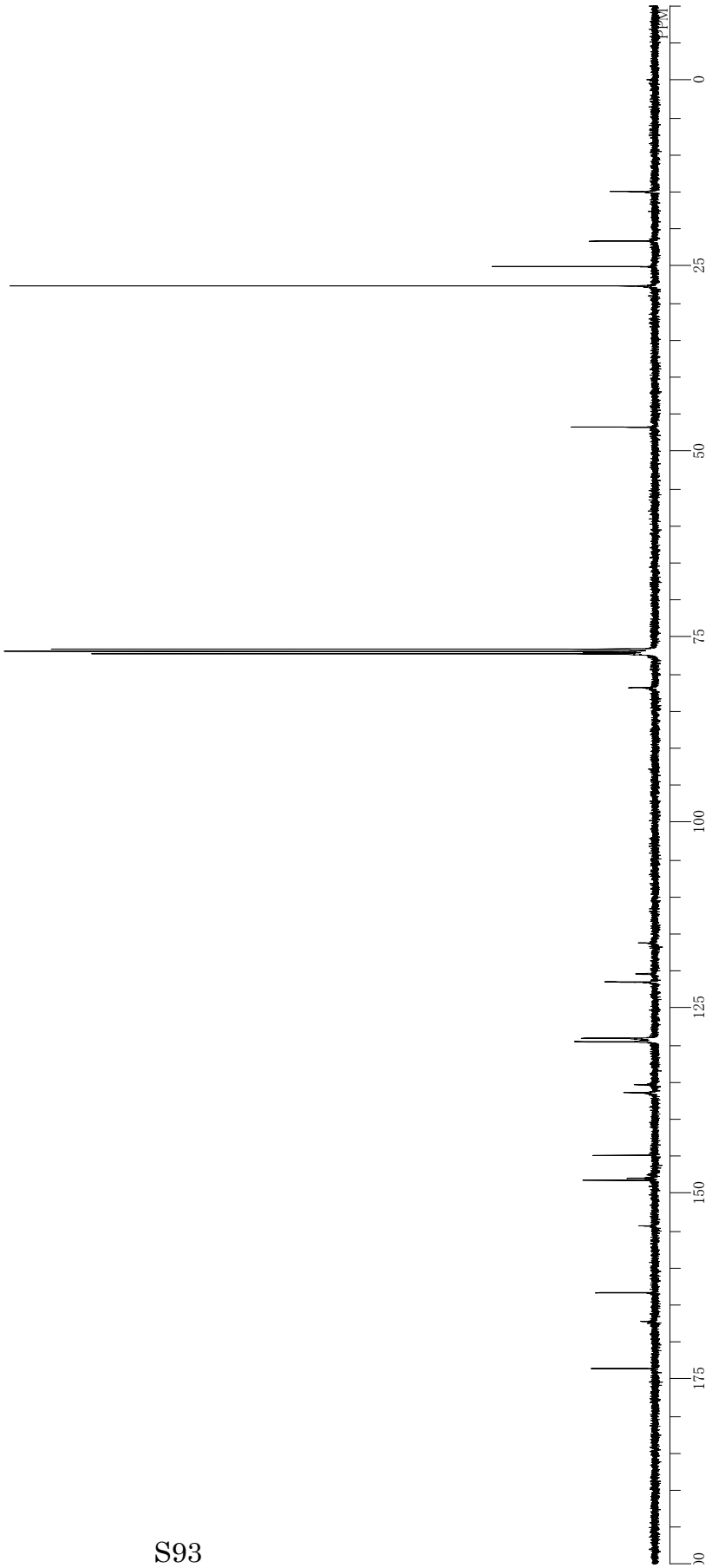
^{1}H NMR (400 MHz) in $CDCl_3$

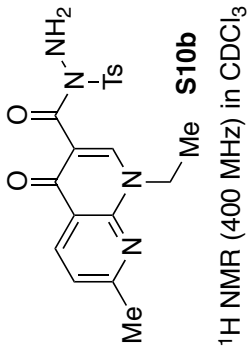




S10a

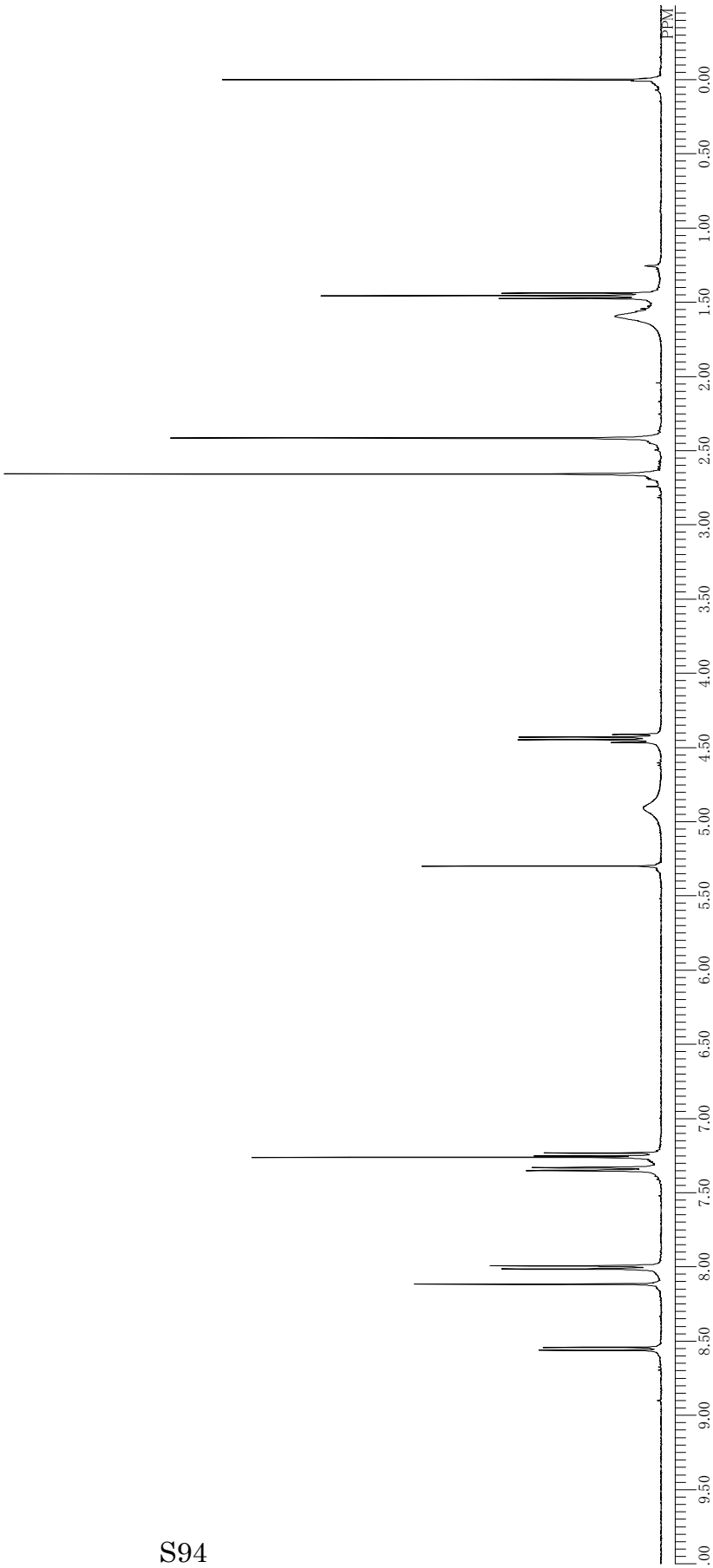
^{13}C NMR (100 MHz) in $CDCl_3$

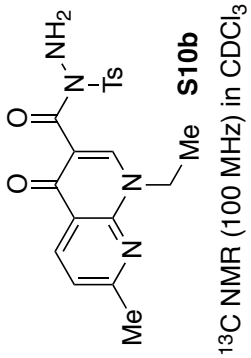




S10b

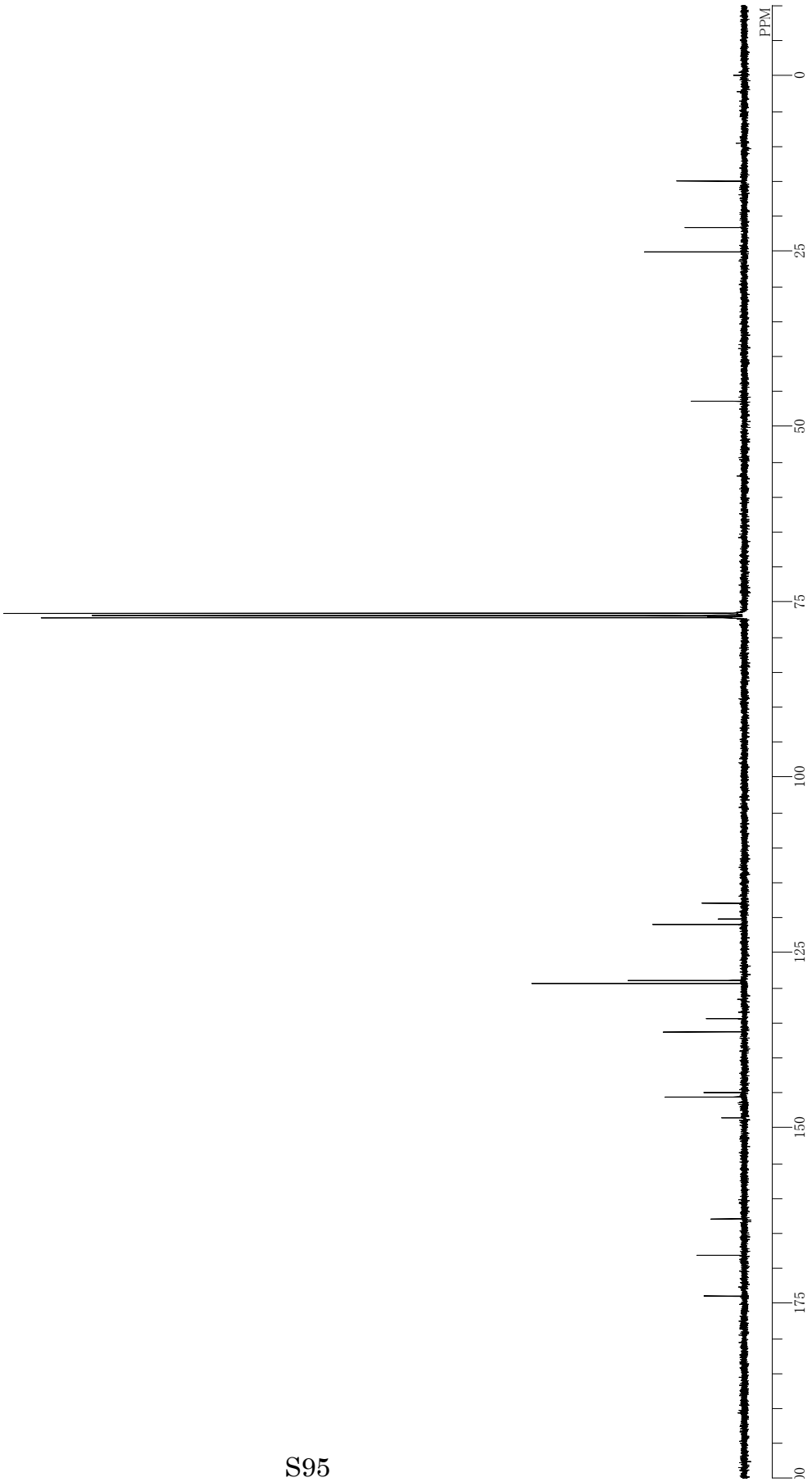
^{1}H NMR (400 MHz) in $CDCl_3$

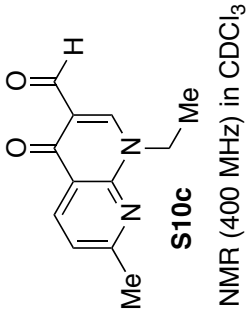




S10b

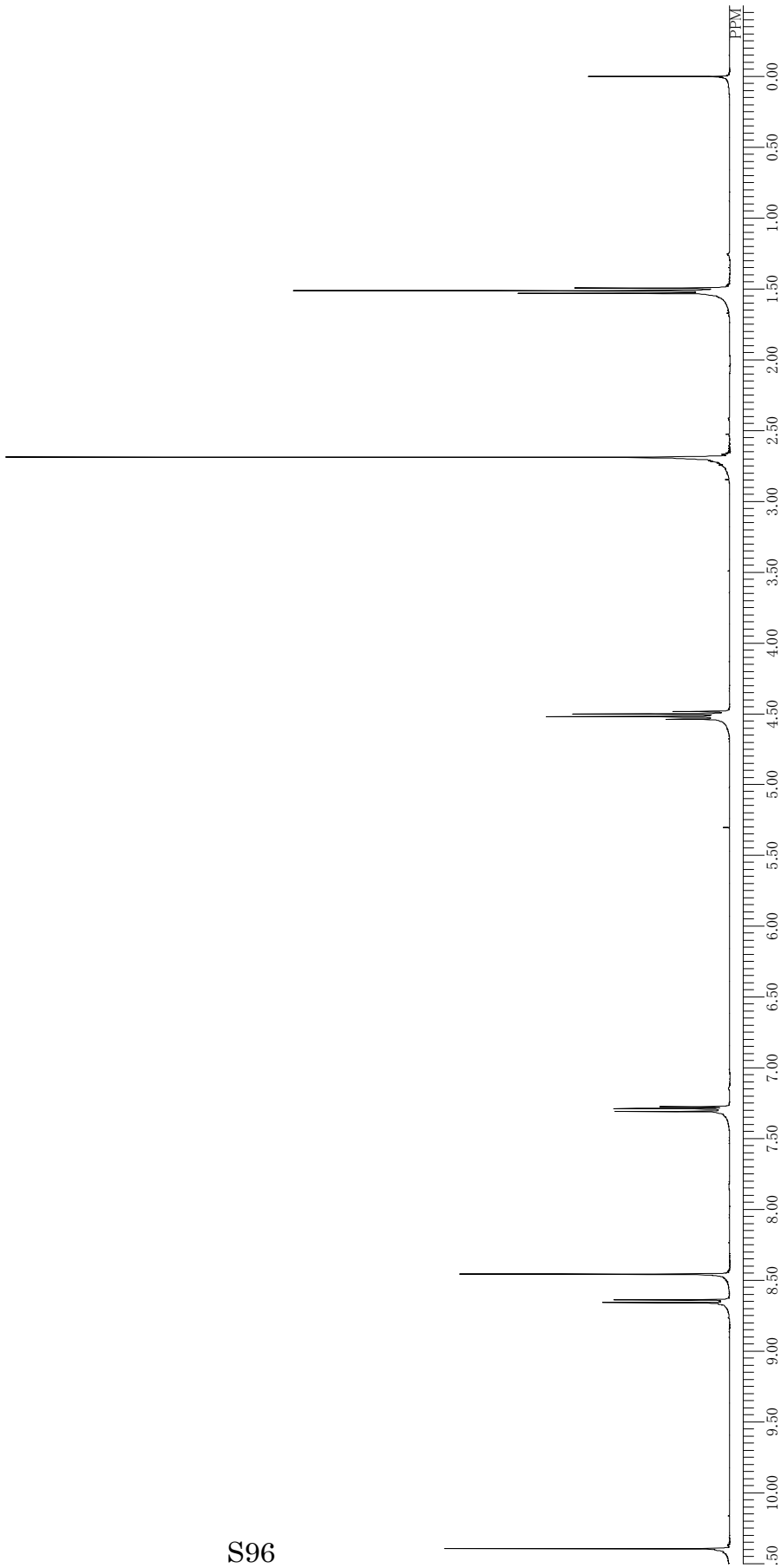
^{13}C NMR (100 MHz) in $CDCl_3$

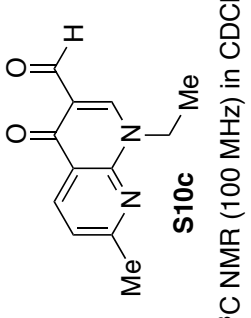




S10c

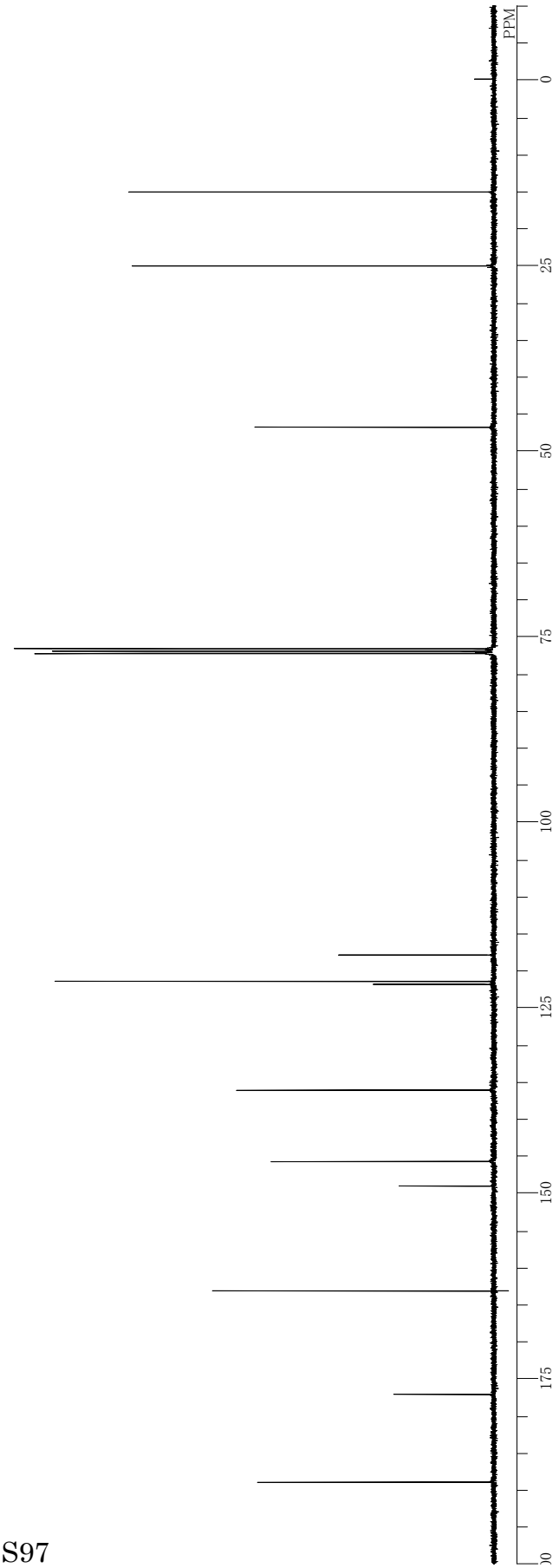
^{1}H NMR (400 MHz) in $CDCl_3$

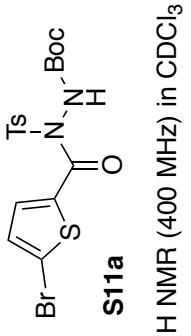




S10c

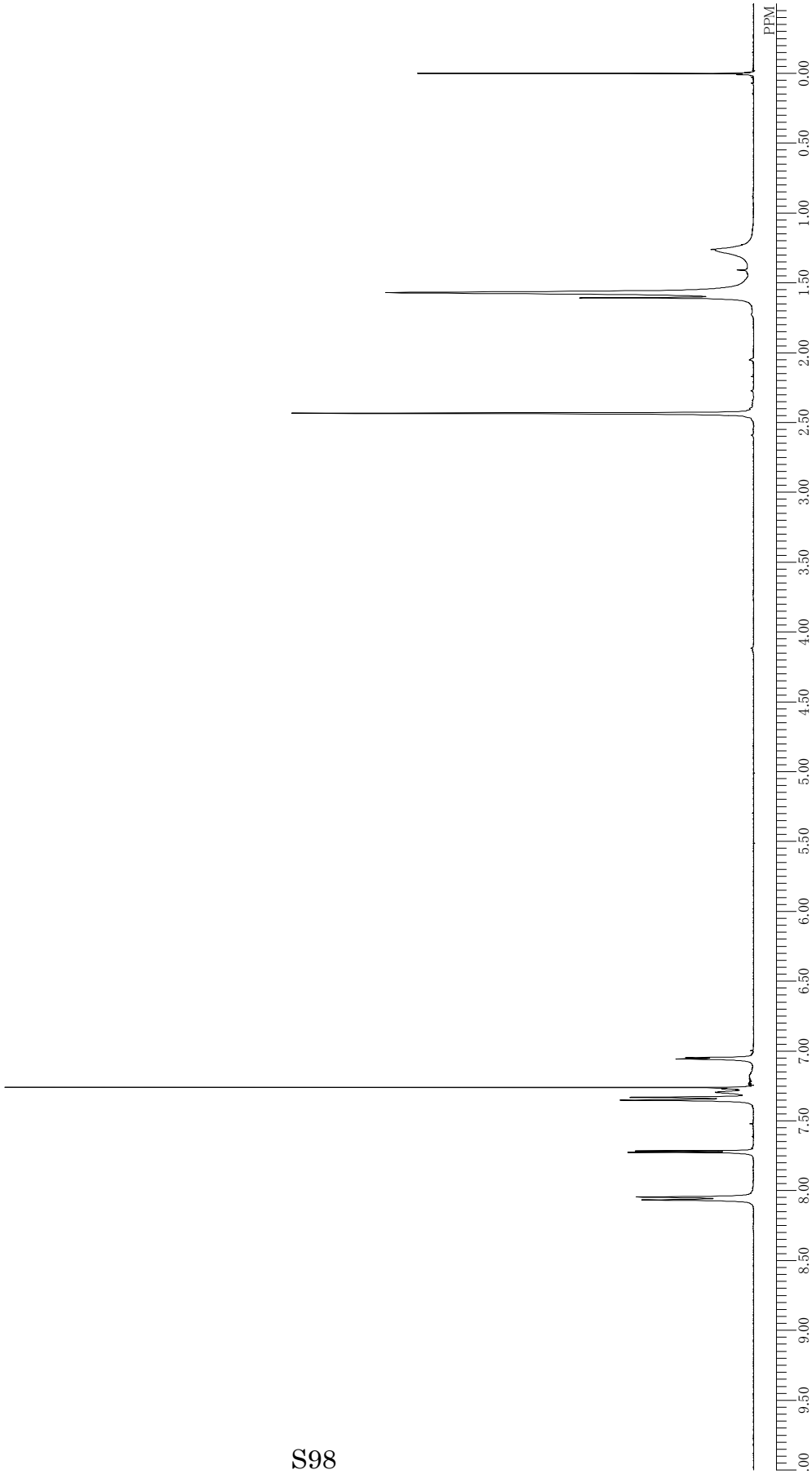
^{13}C NMR (100 MHz) in $CDCl_3$

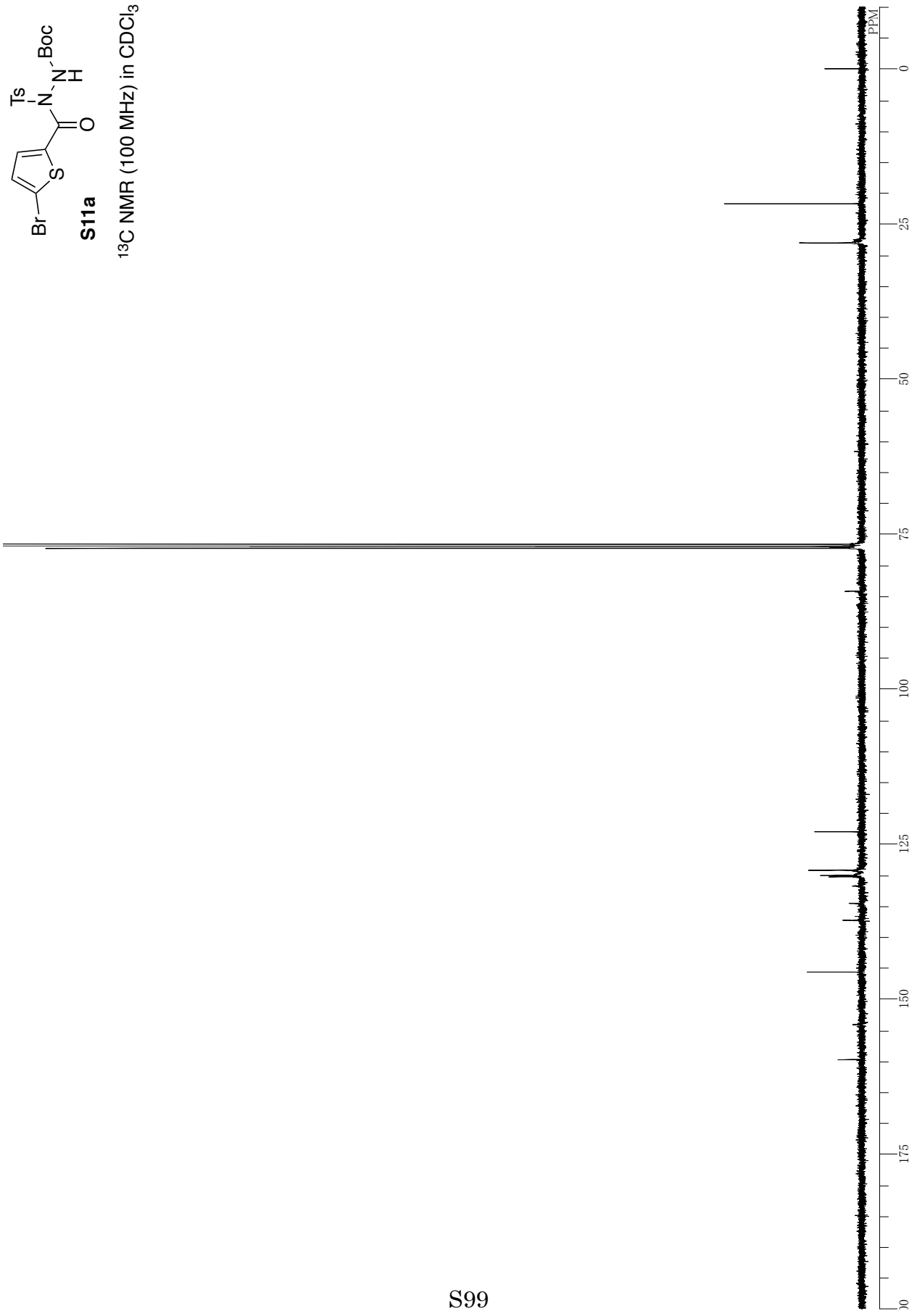


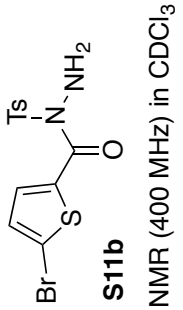


S11a

^{1}H NMR (400 MHz) in $CDCl_3$

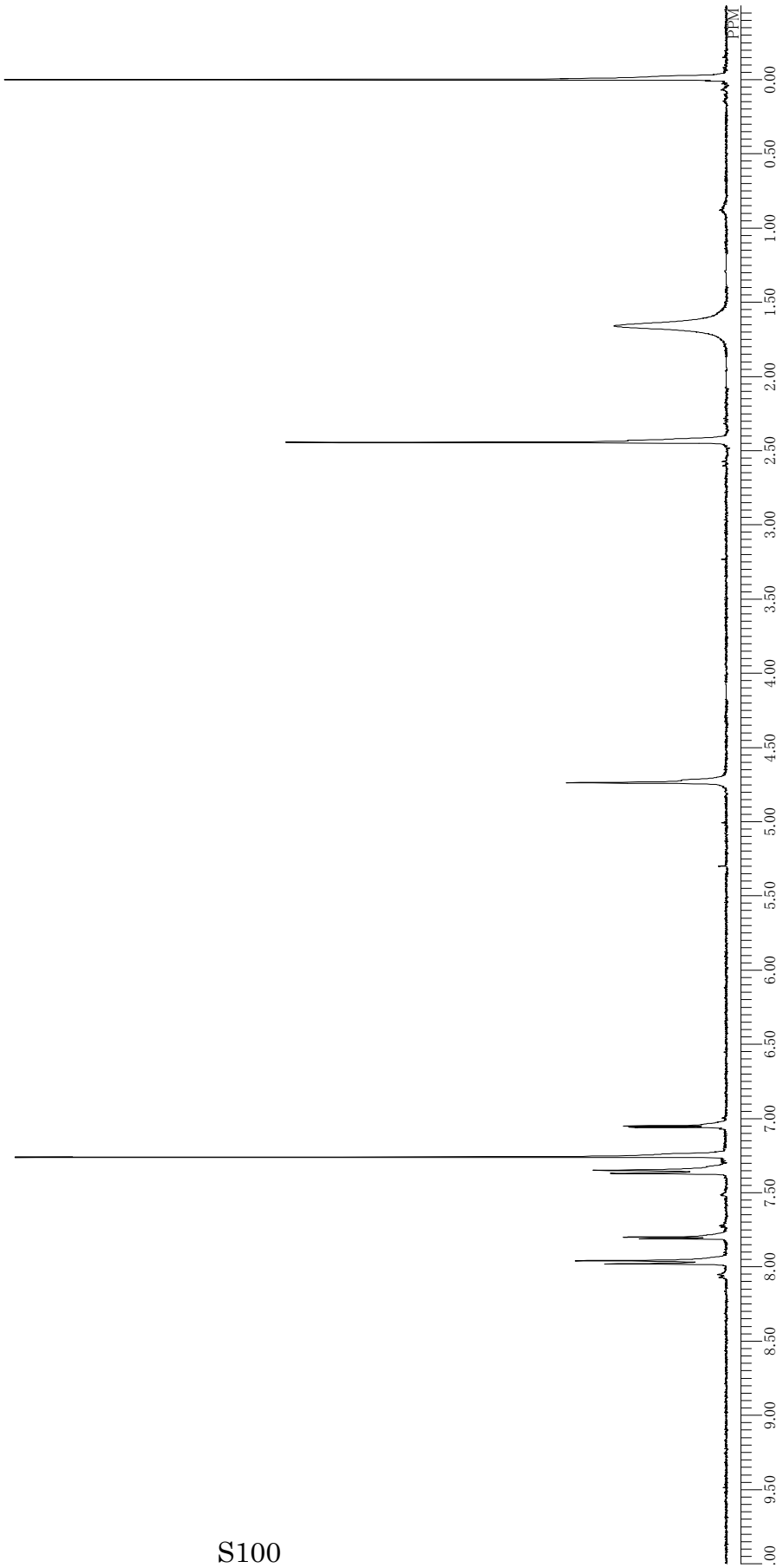


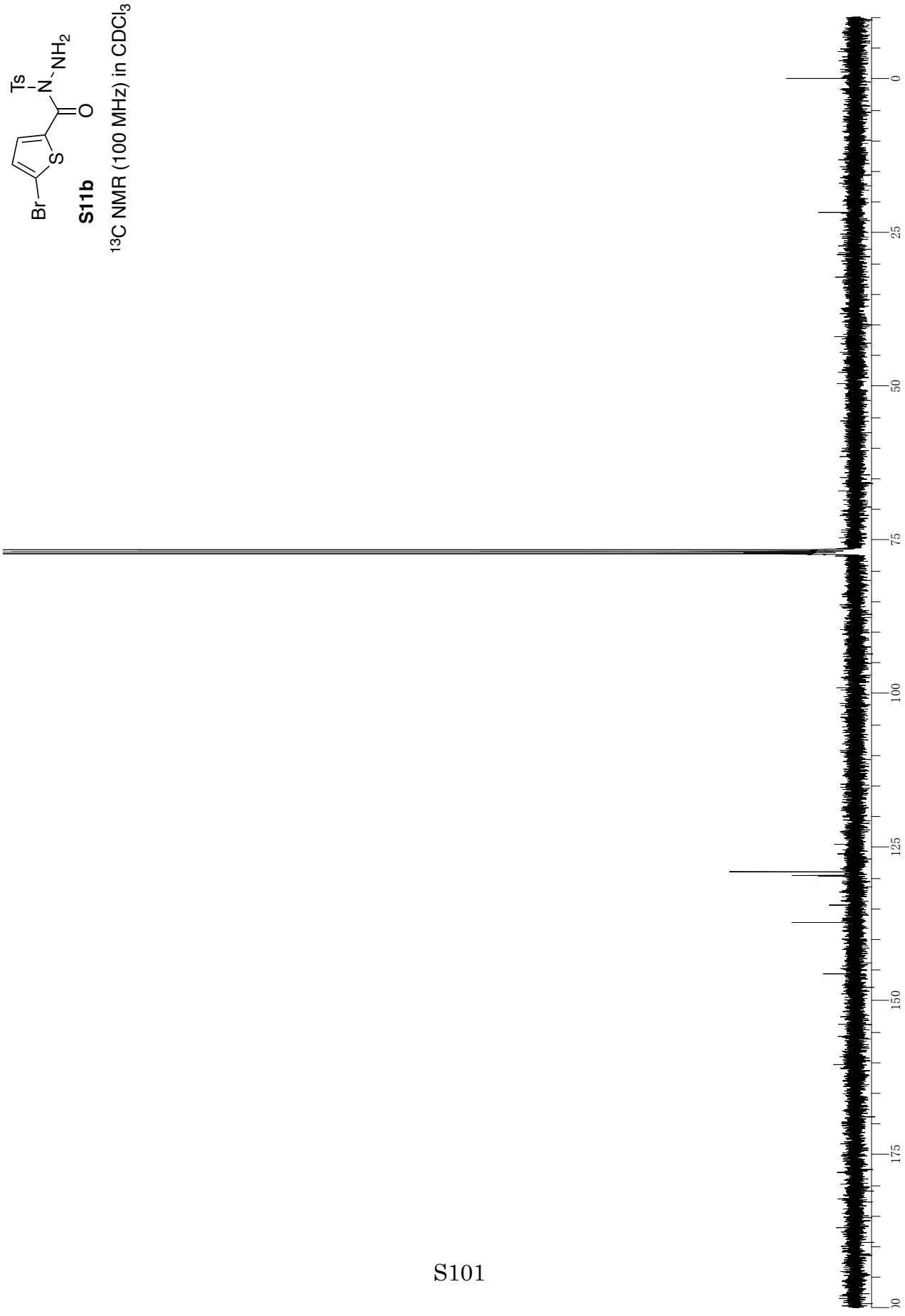

Ts
N
N
Boc
H
O
S
Br
S11a
^{13}C NMR (100 MHz) in $CDCl_3$
PPM
0
25
50
75
100
125
150
175

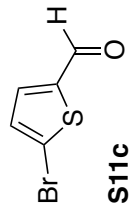


S11b

^{1}H NMR (400 MHz) in $CDCl_3$

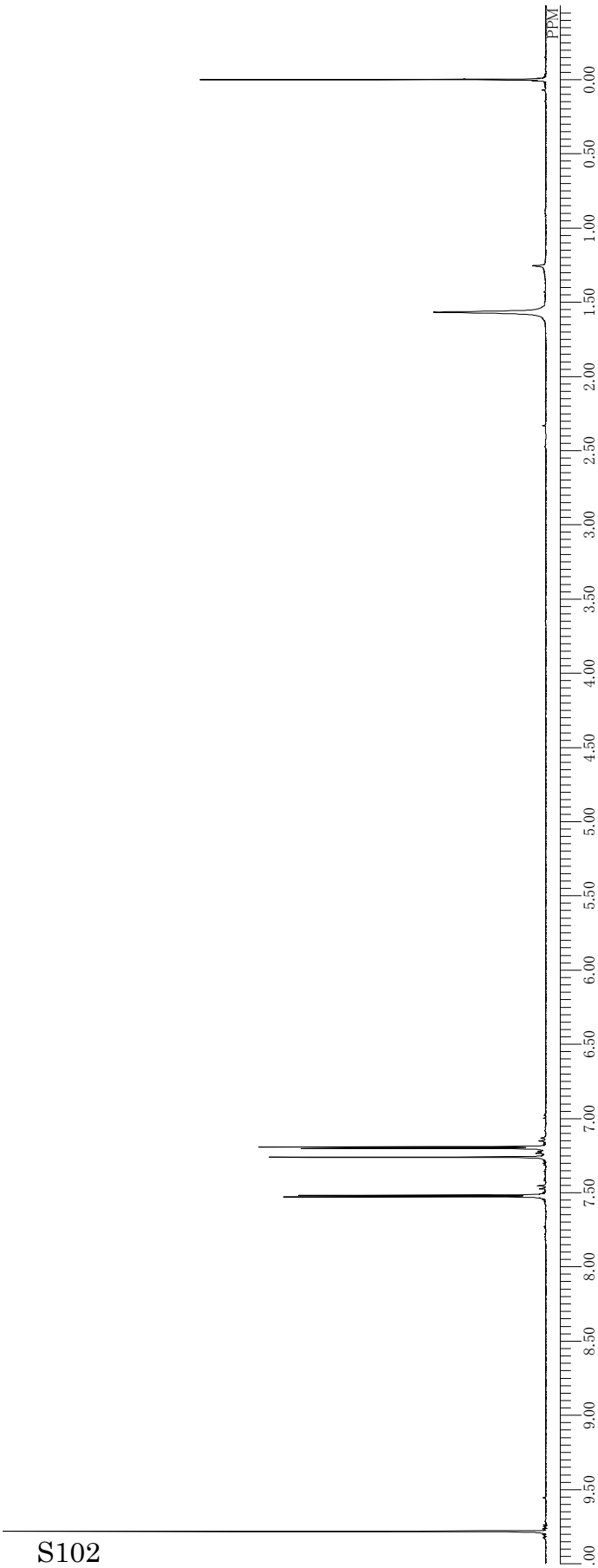


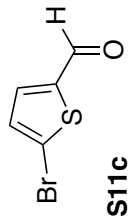

Ts
N
NH2
O
S
Br
S11b
13C NMR (100 MHz) in CDCl3
0
25
50
75
100
125
150
175
200



S11c

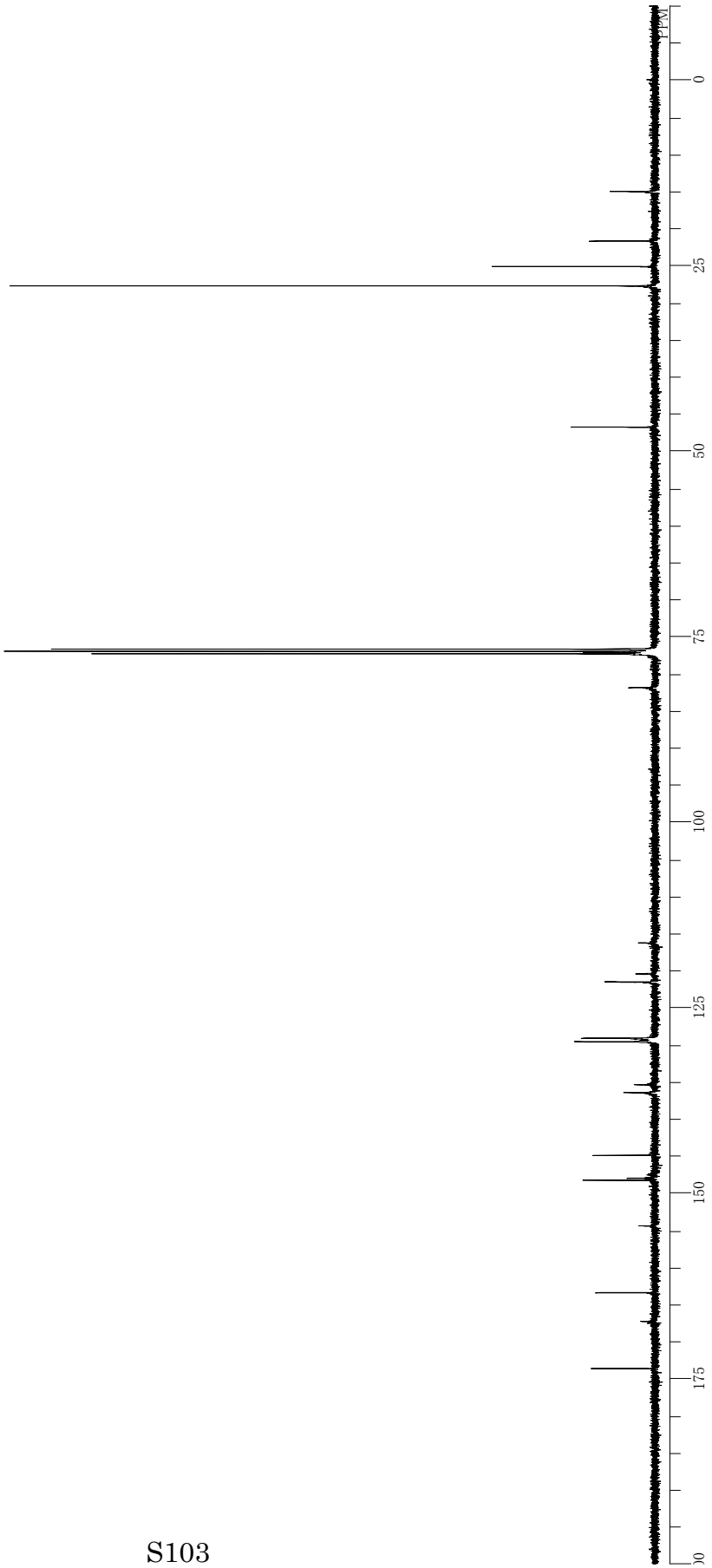
^{1}H NMR (400 MHz) in $CDCl_3$

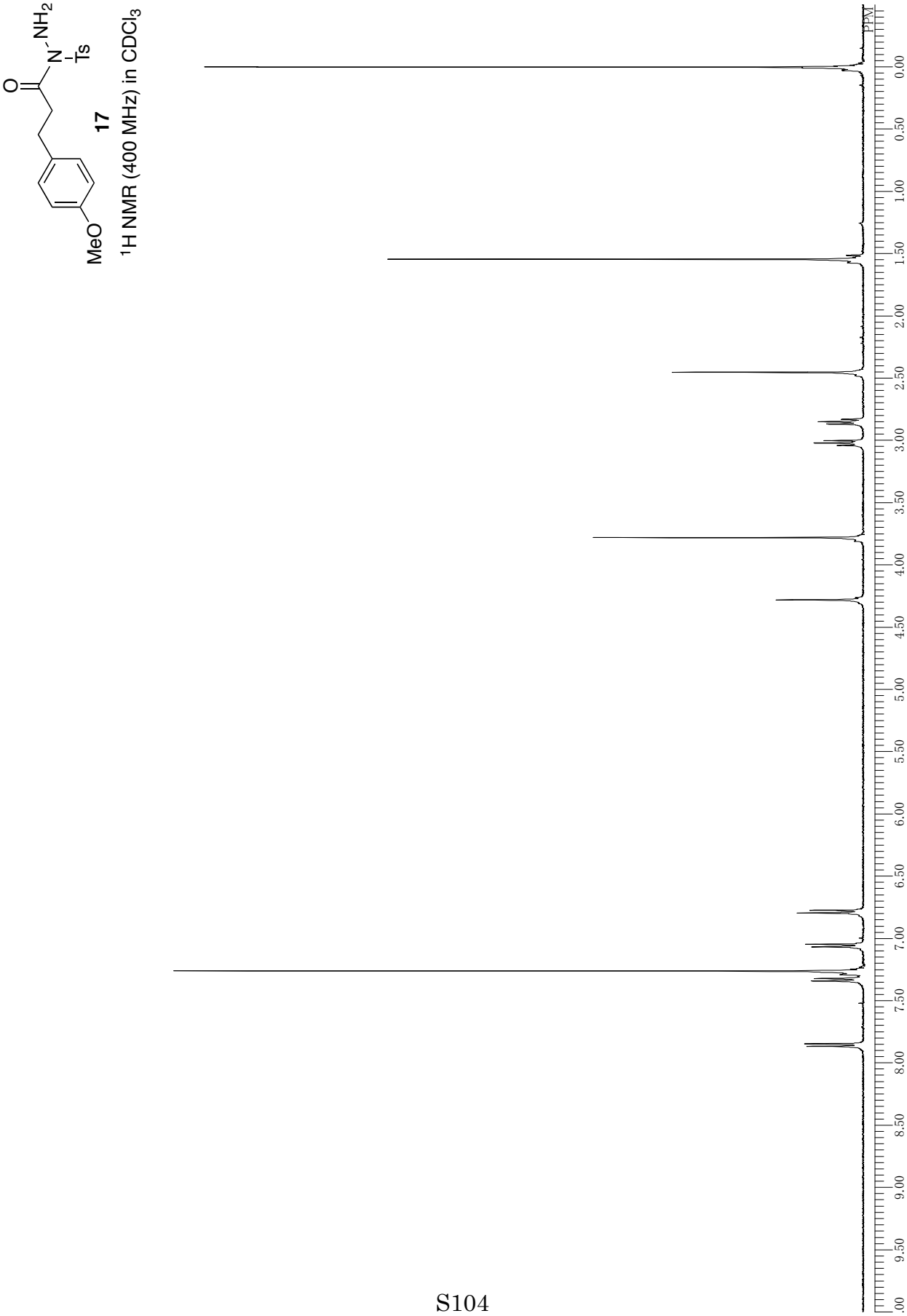


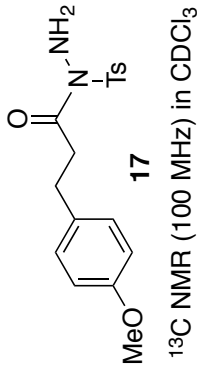


S11c

^{13}C NMR (100 MHz) in $CDCl_3$

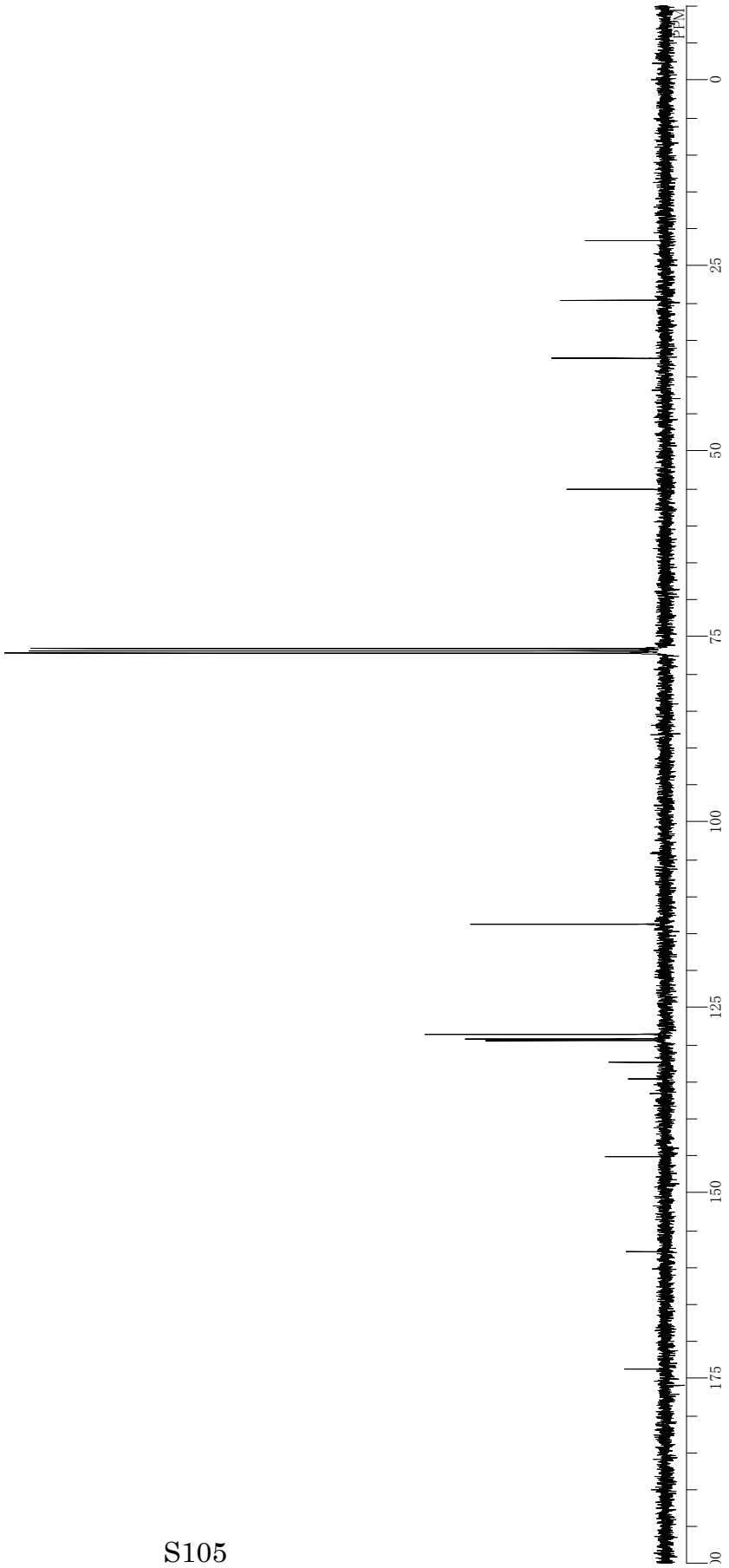


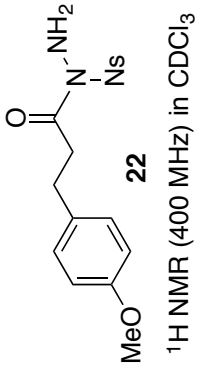

NH2
N
Ts
O
MeO
17
1H NMR (400 MHz) in CDCl3
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
.00



17

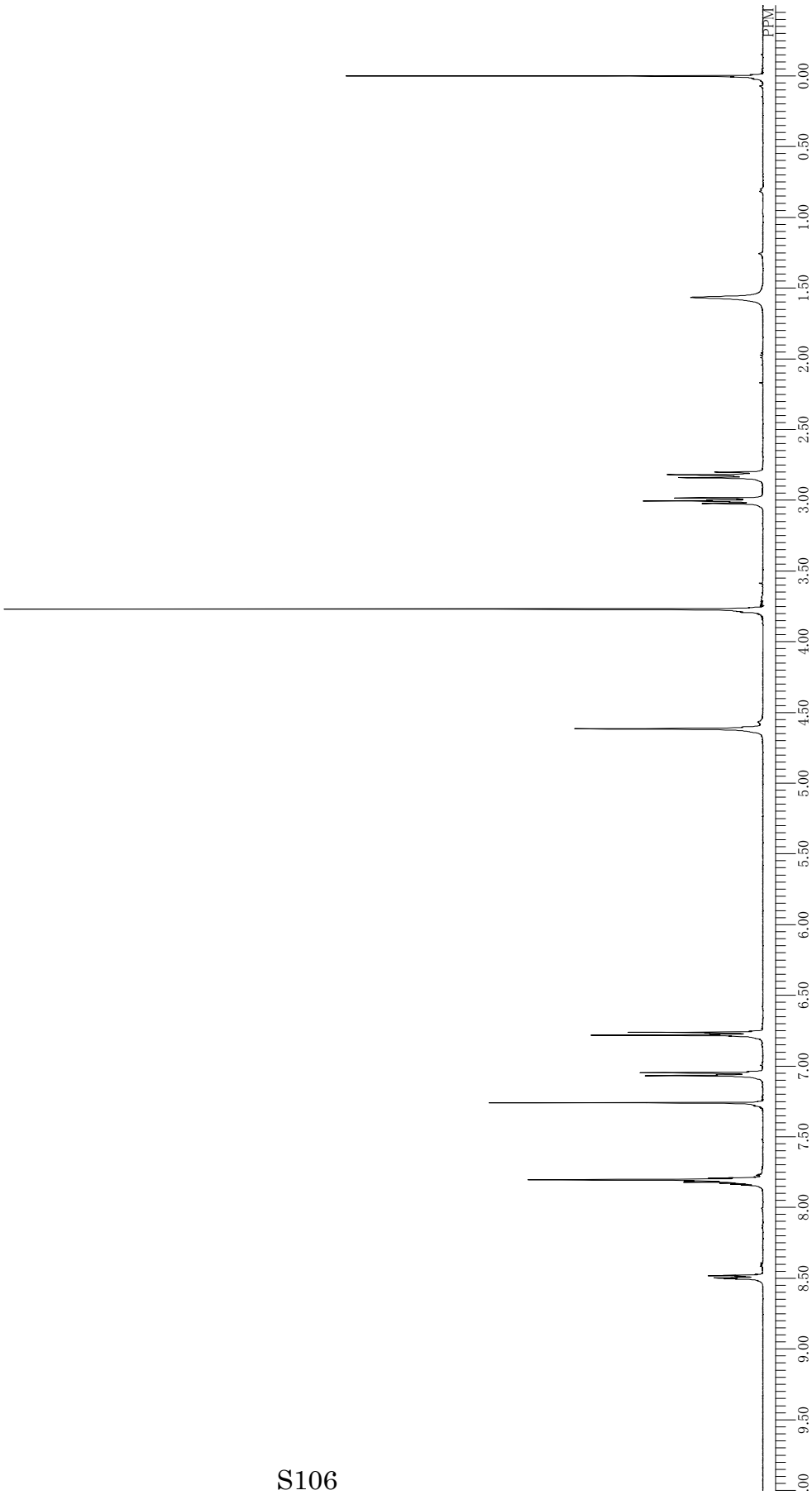
^{13}C NMR (100 MHz) in $CDCl_3$

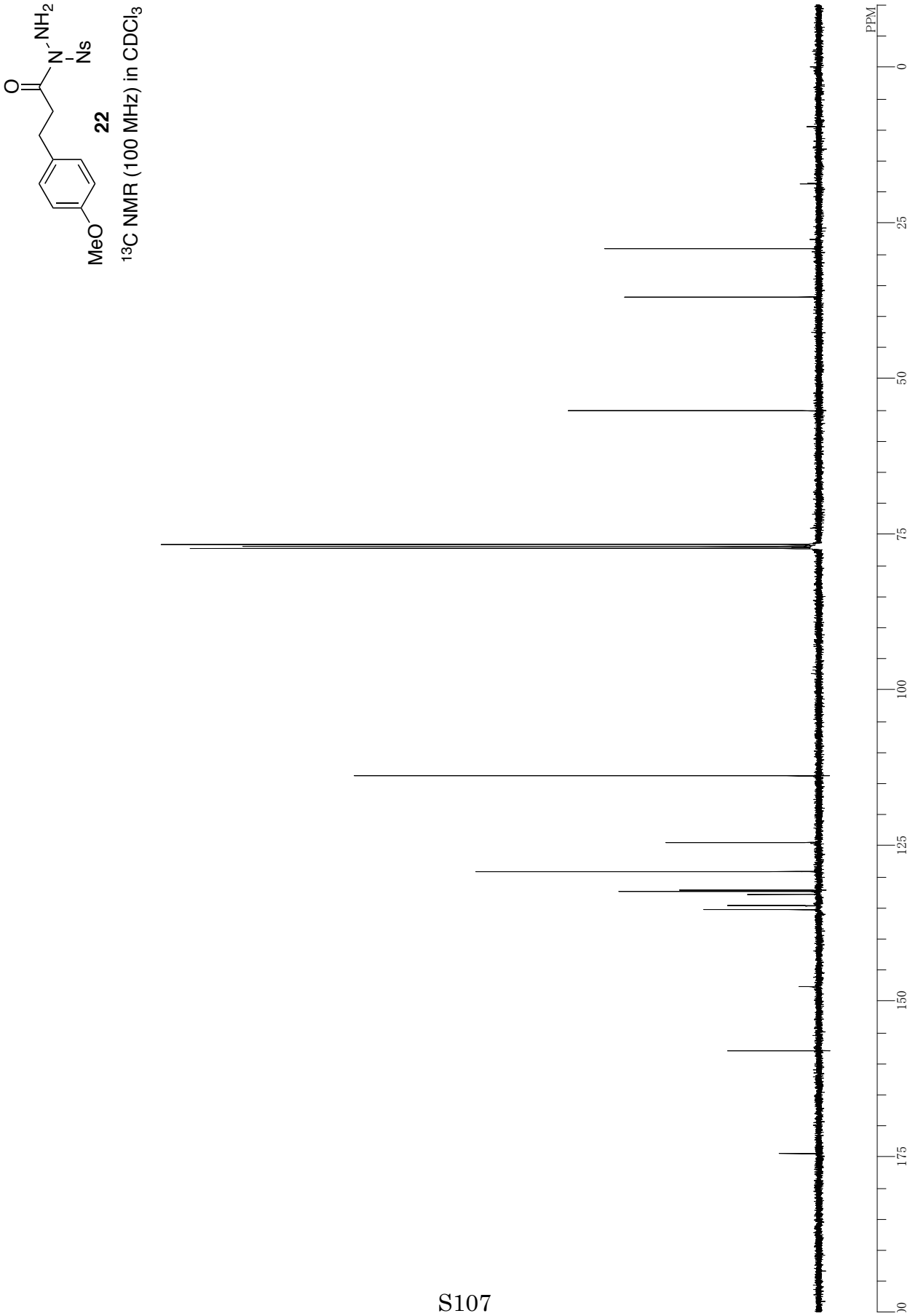


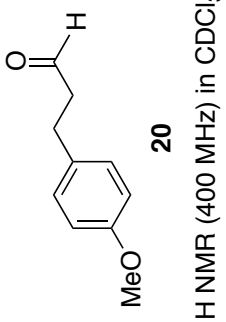


22

^{1}H NMR (400 MHz) in $CDCl_3$

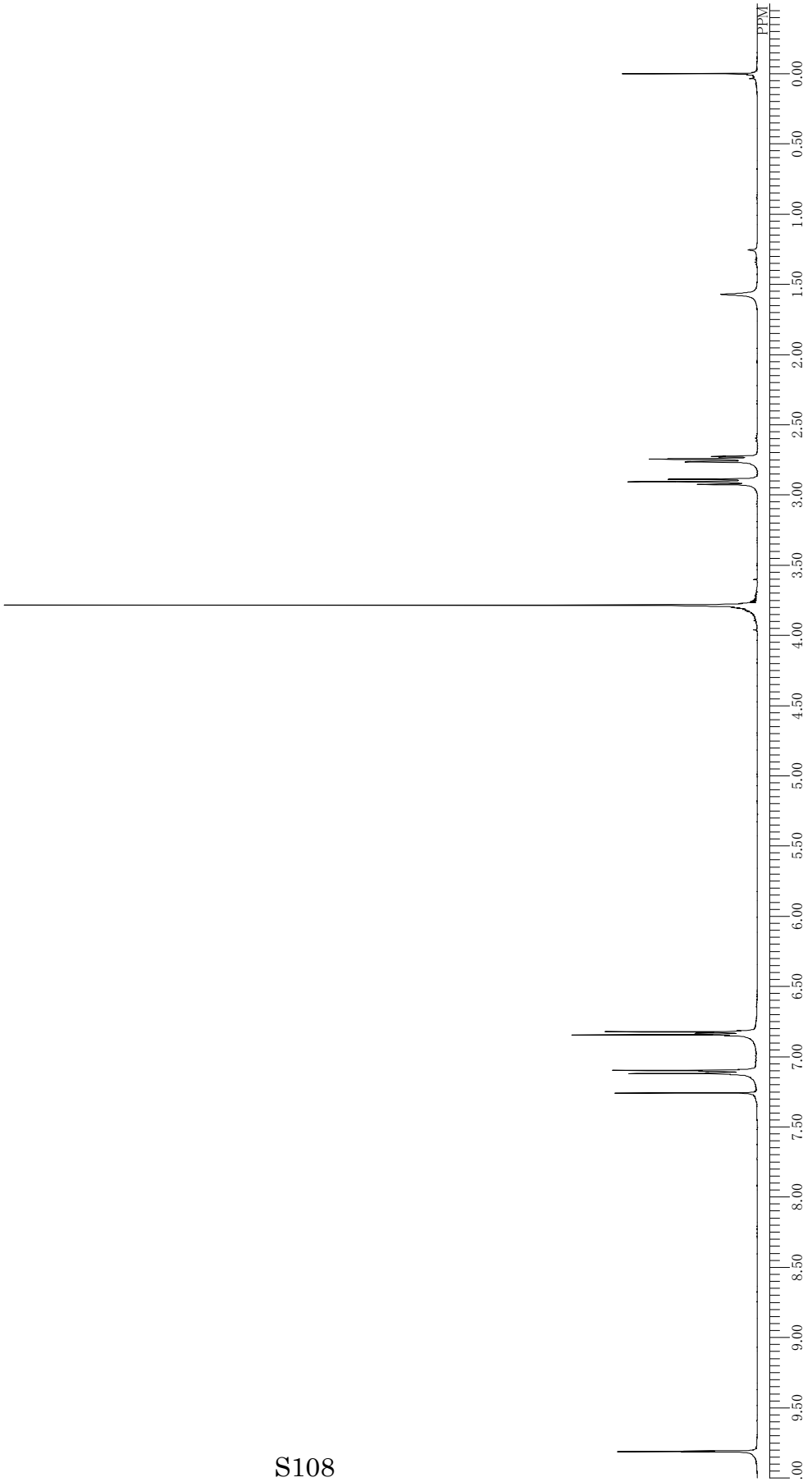


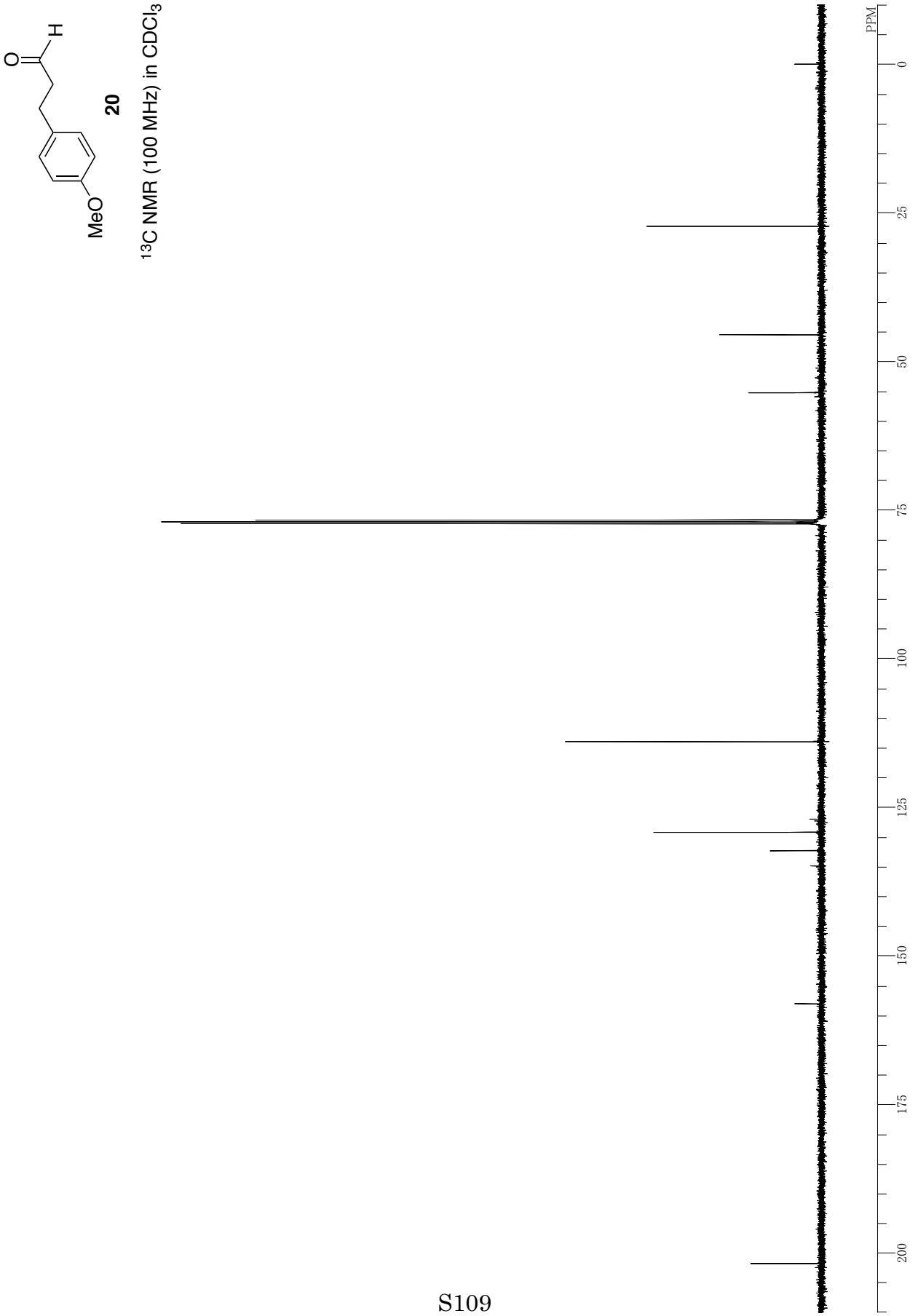

NH2
N
Ns
O
MeO
22
13C NMR (100 MHz) in CDCl3
PPM
0
25
50
75
100
125
150
175

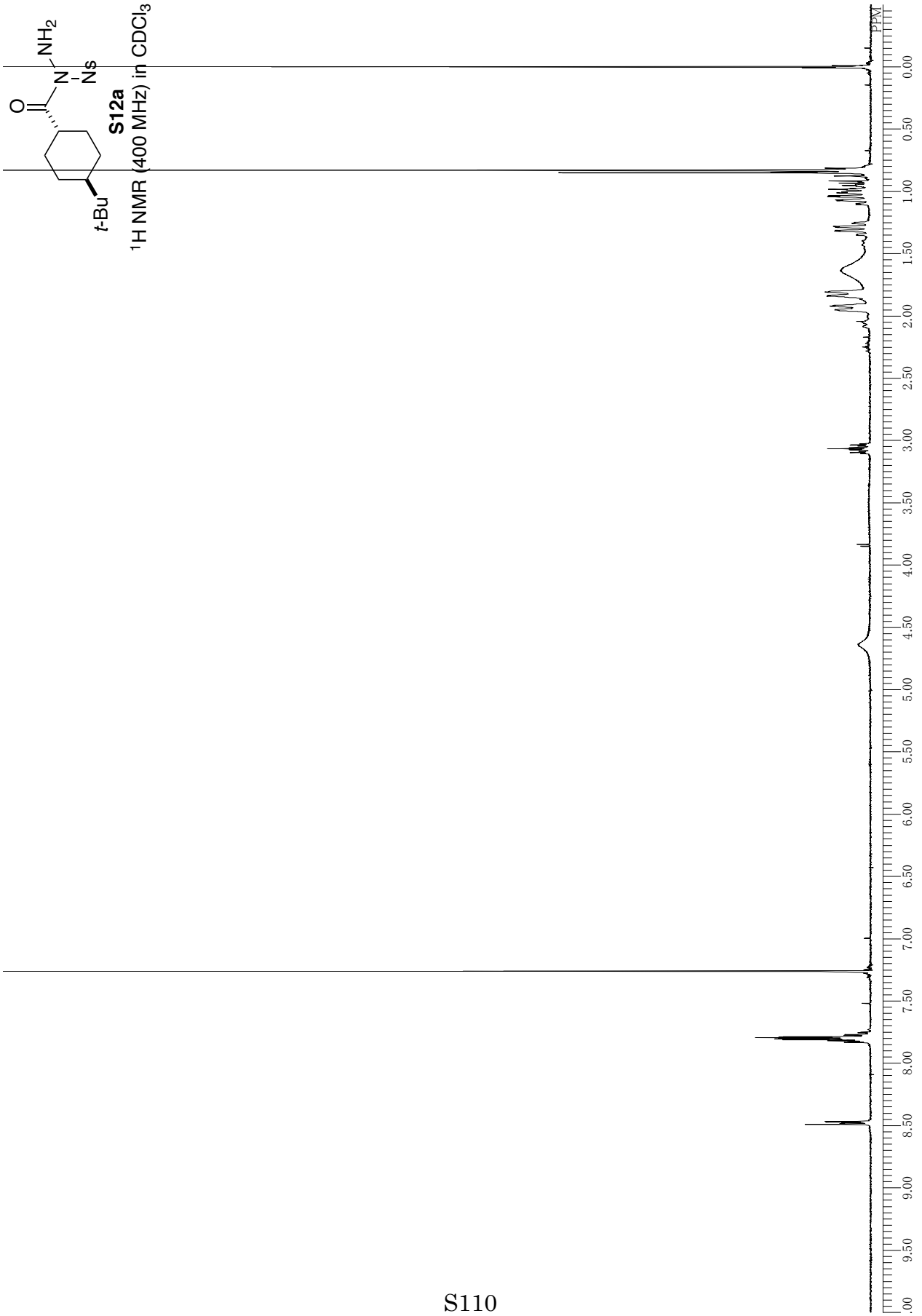


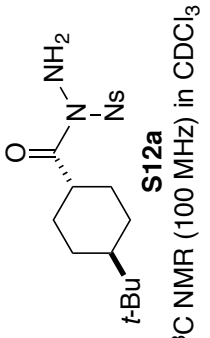
20

^{1}H NMR (400 MHz) in $CDCl_3$



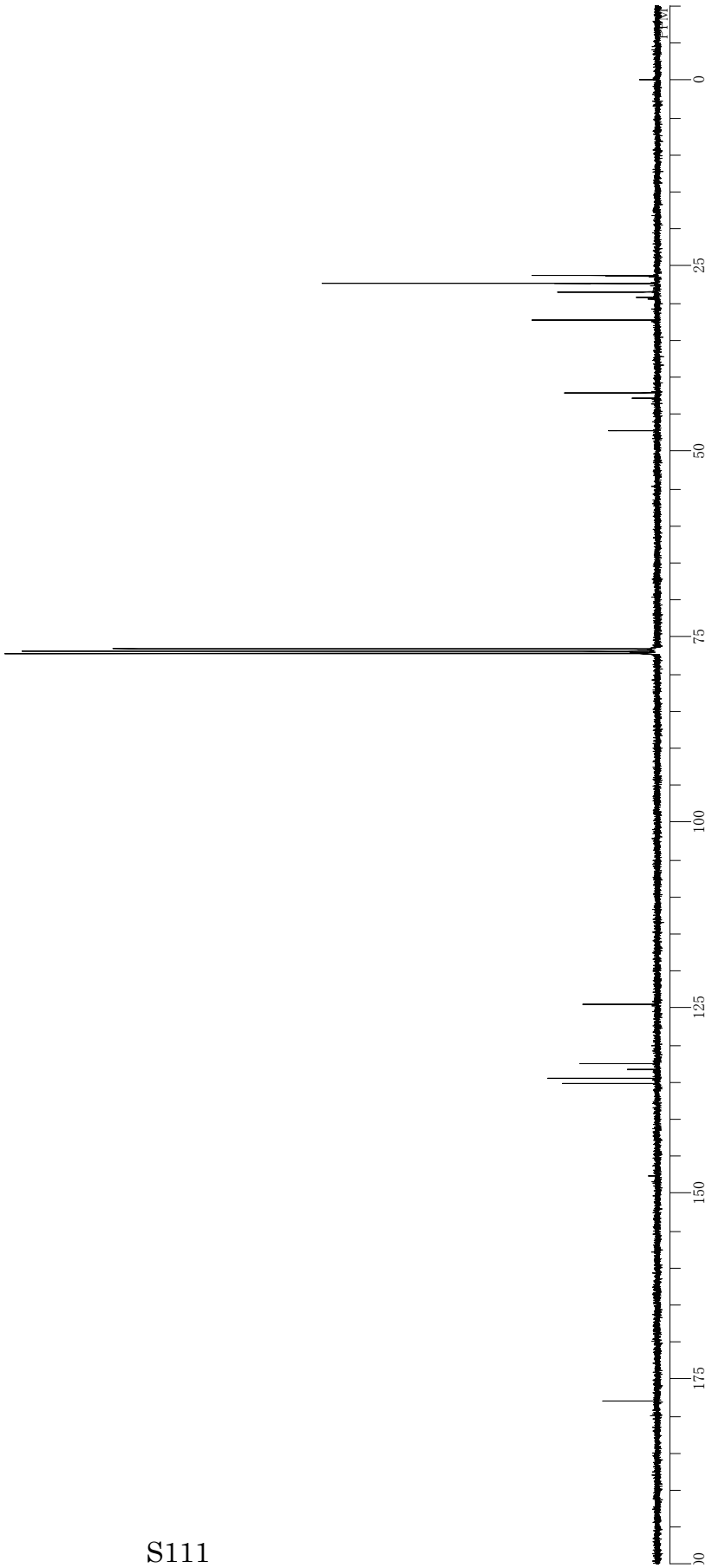

O
H
MeO
20
^{13}C NMR (100 MHz) in $CDCl_3$
PPM
0
25
50
75
100
125
150
175
200

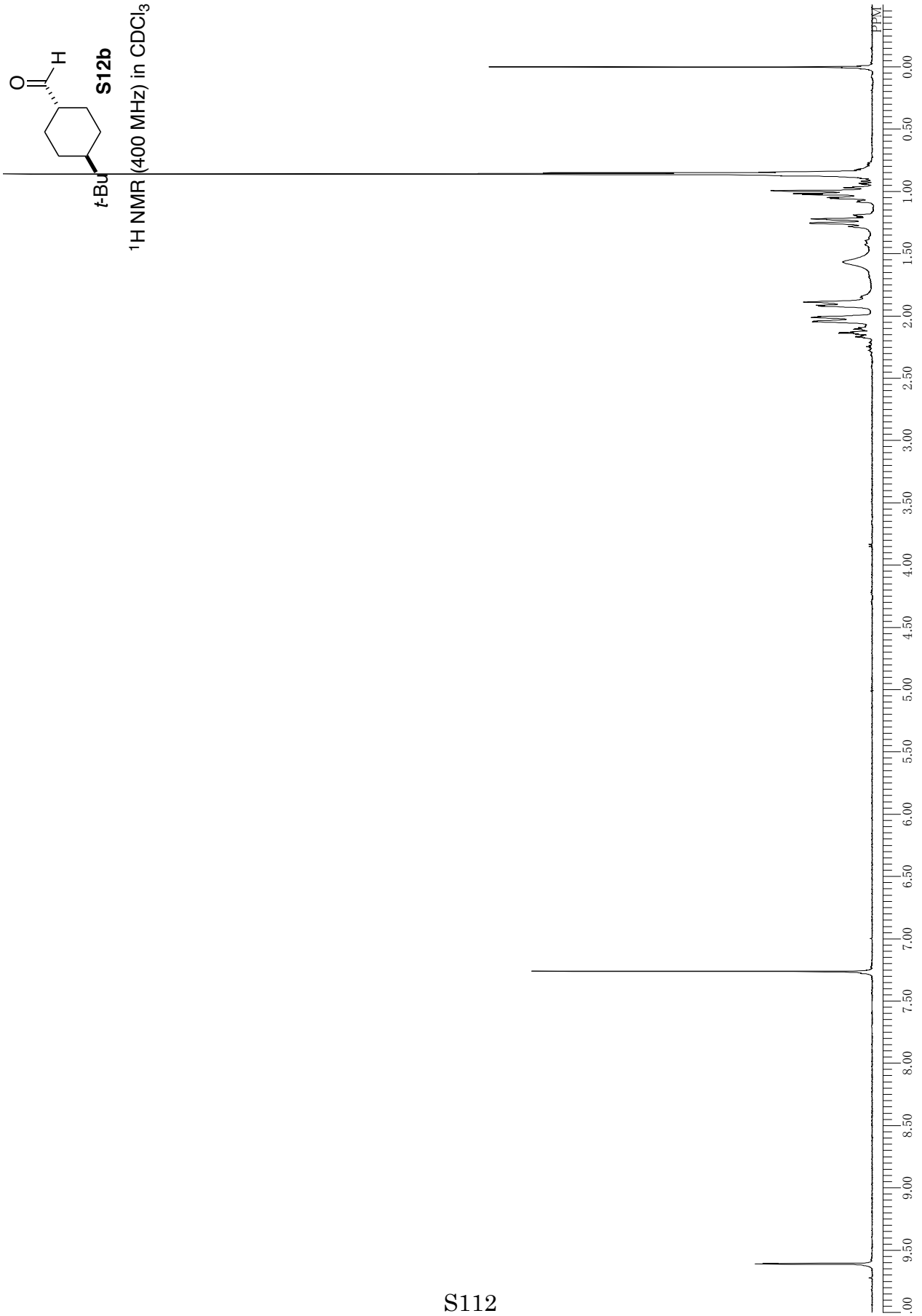

NH2
N
Ns
O
t-Bu
S12a
1H NMR (400 MHz) in CDCl3
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50

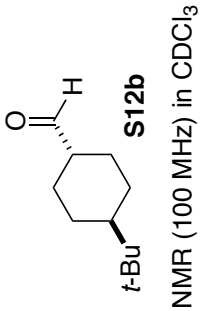


S12a

^{13}C NMR (100 MHz) in $CDCl_3$

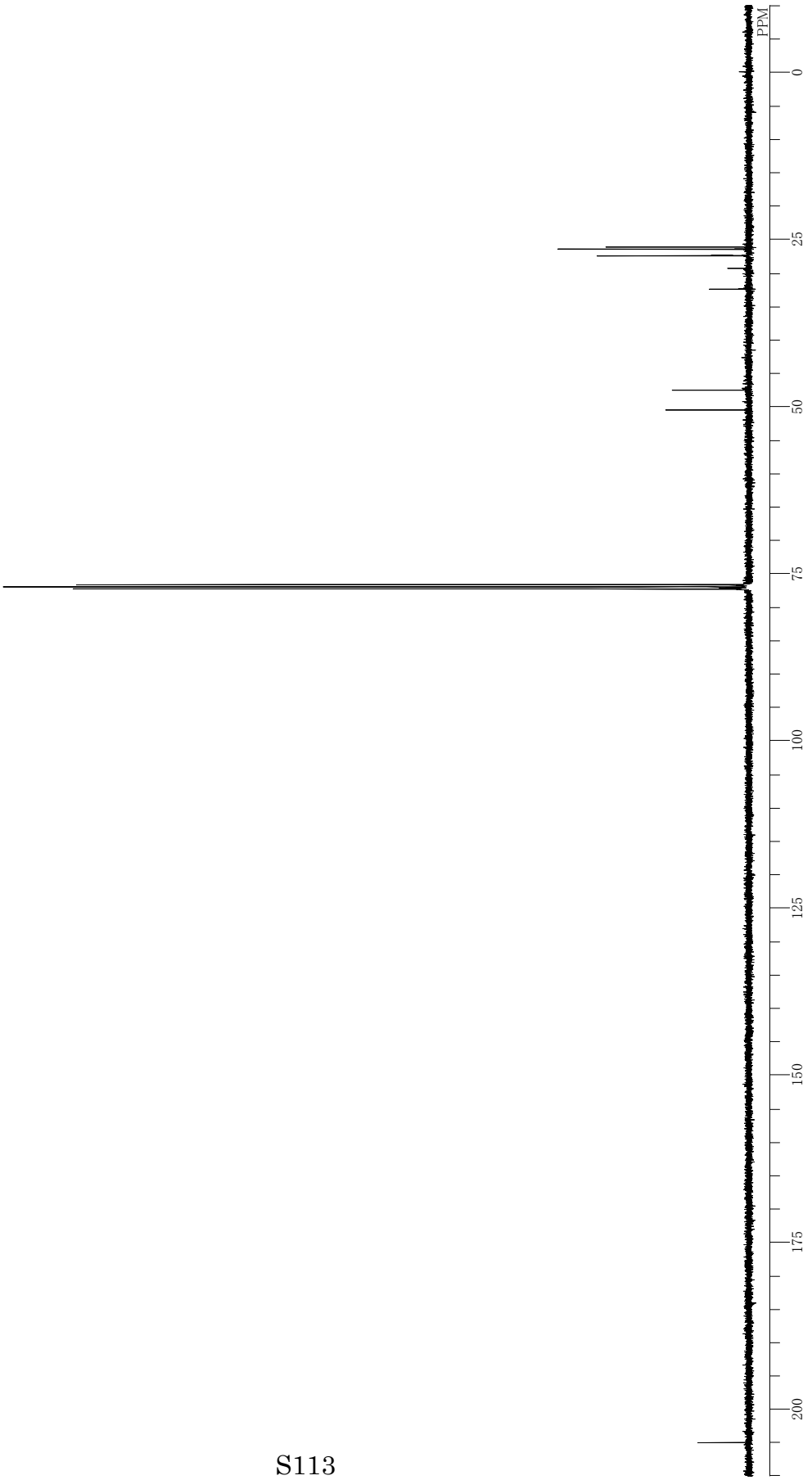


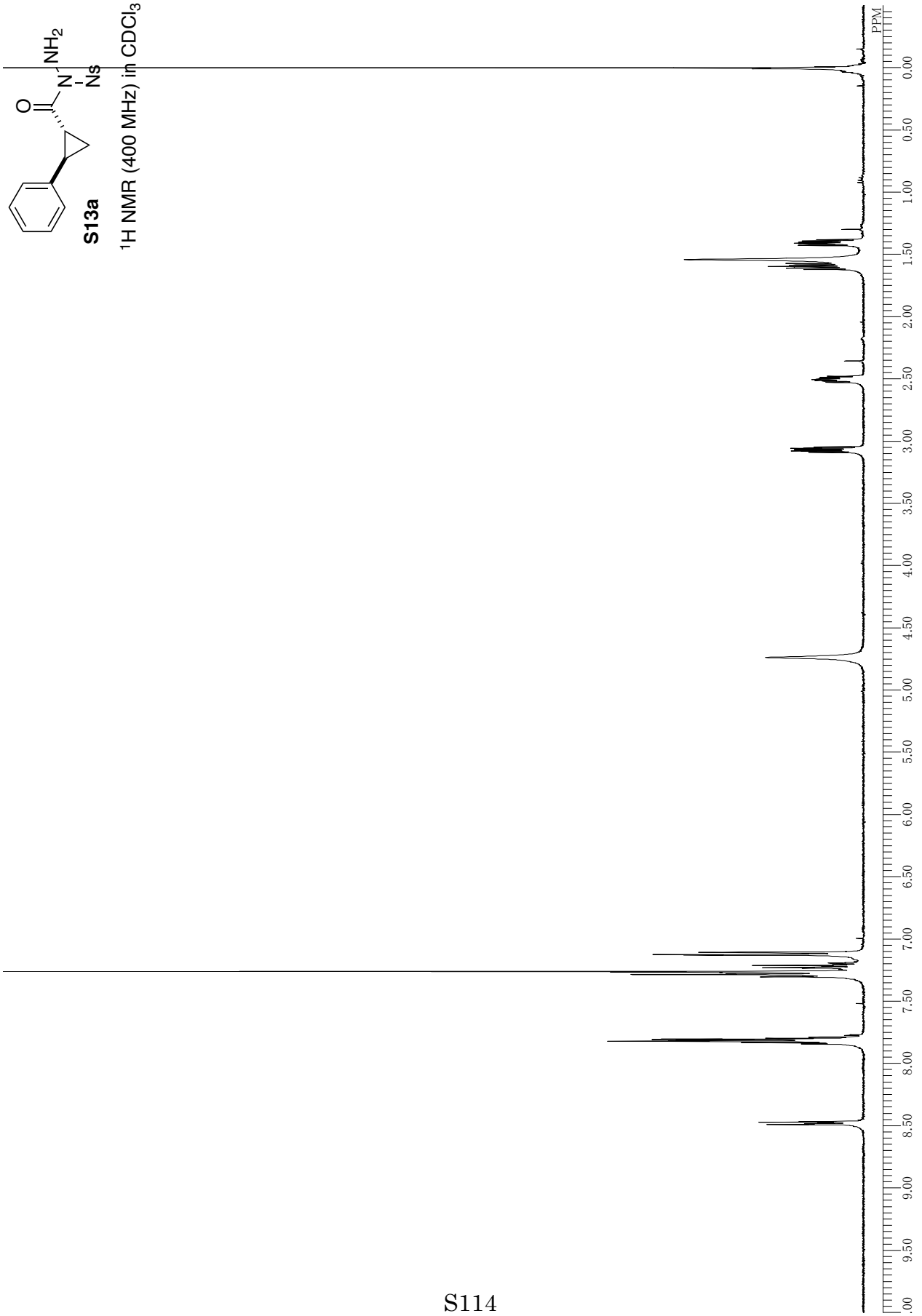

O
H
S12b
t-Bu
^{1}H NMR (400 MHz) in $CDCl_3$
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
.00

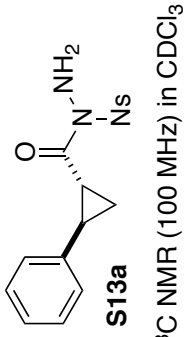


S12b

^{13}C NMR (100 MHz) in $CDCl_3$

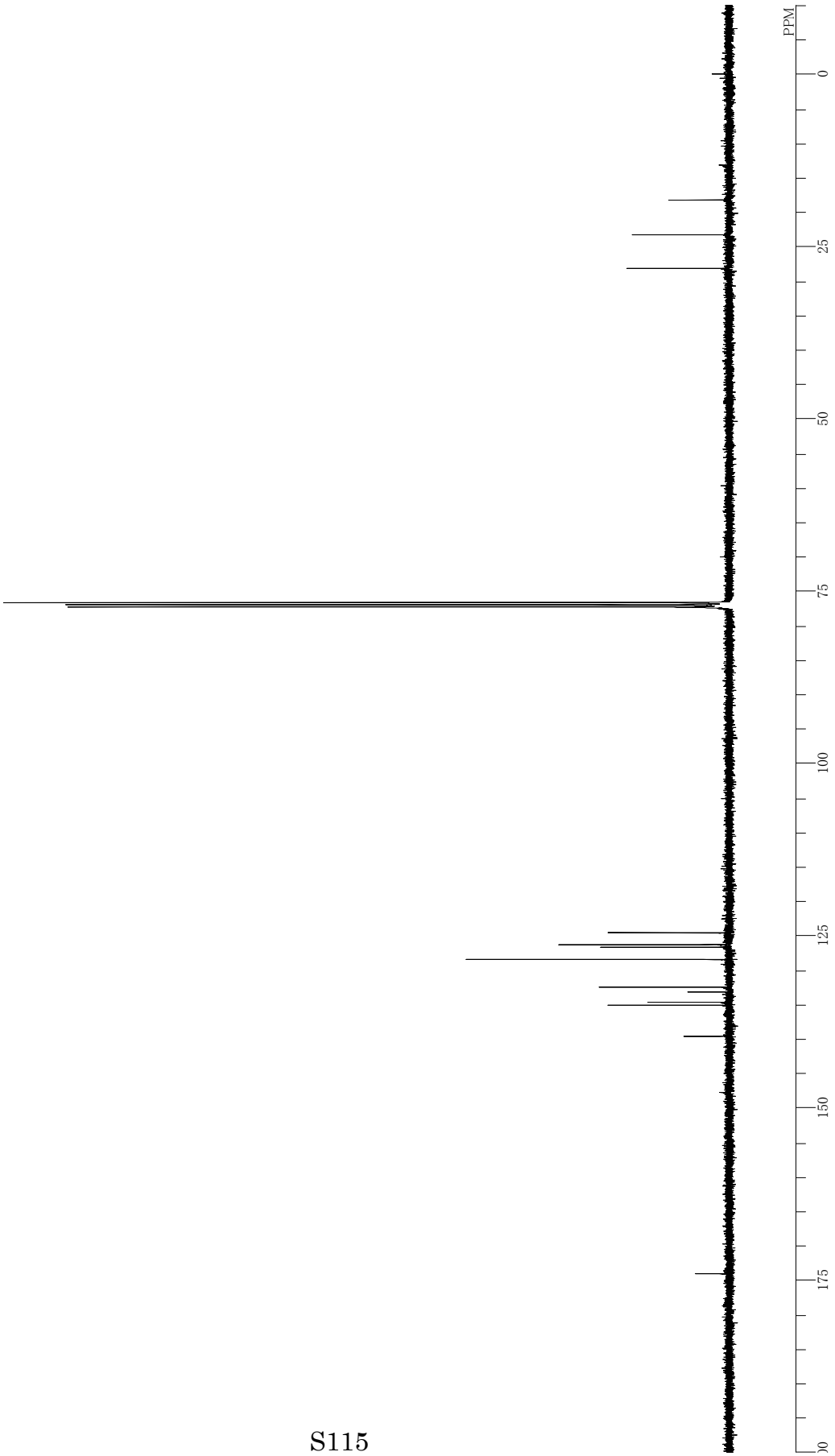


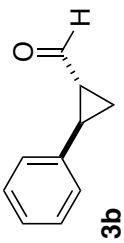

NH2
N
Ns
O
S13a
1H NMR (400 MHz) in CDCl3
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50



S13a

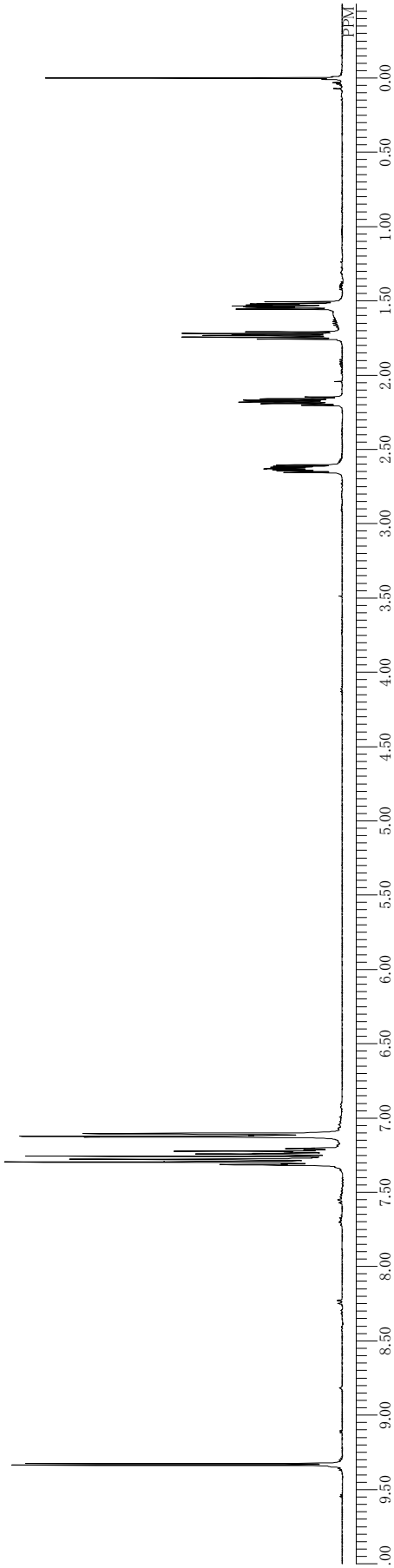
^{13}C NMR (100 MHz) in $CDCl_3$

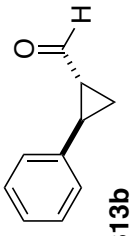




S13b

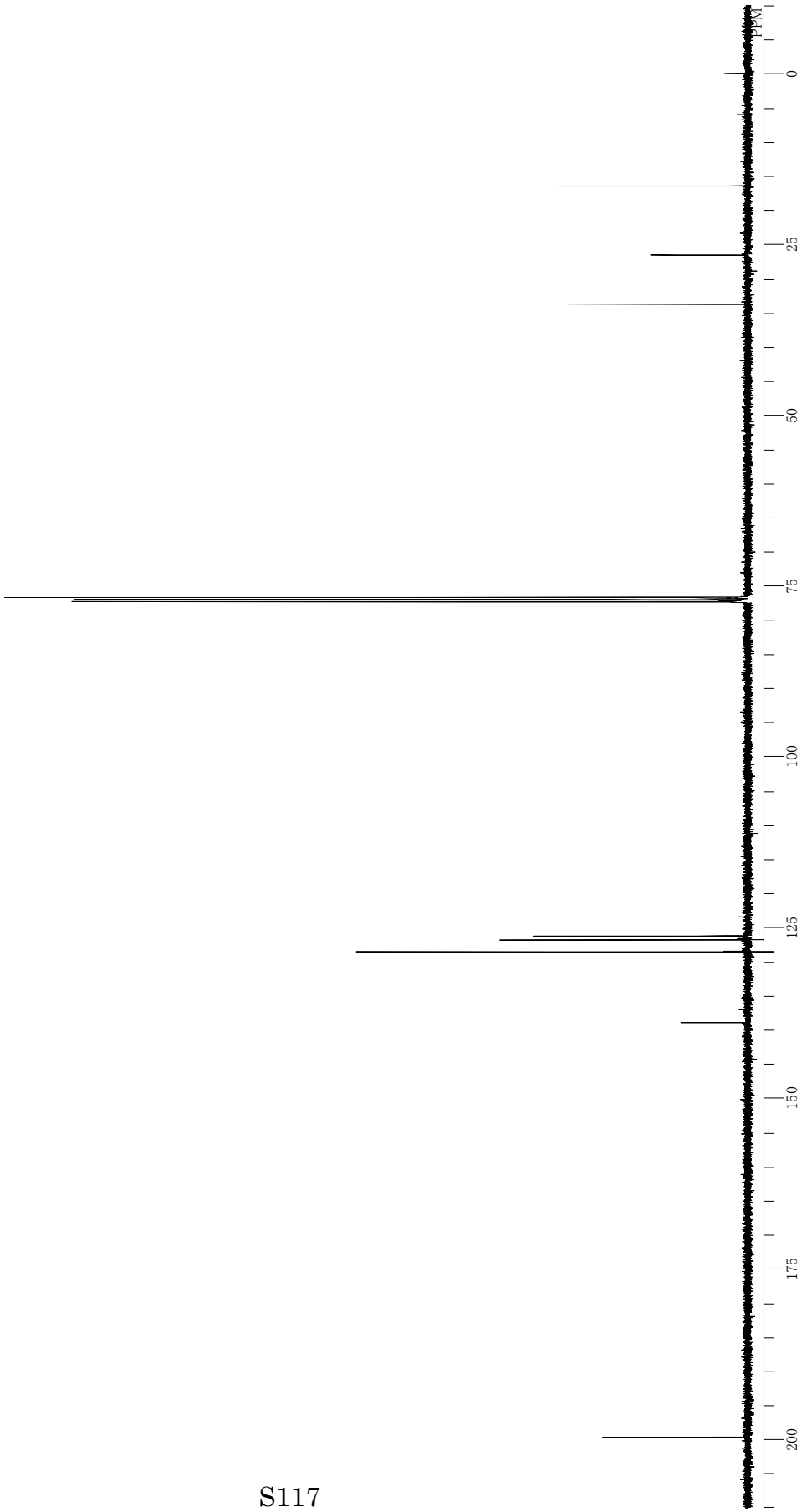
^{1}H NMR (400 MHz) in $CDCl_3$

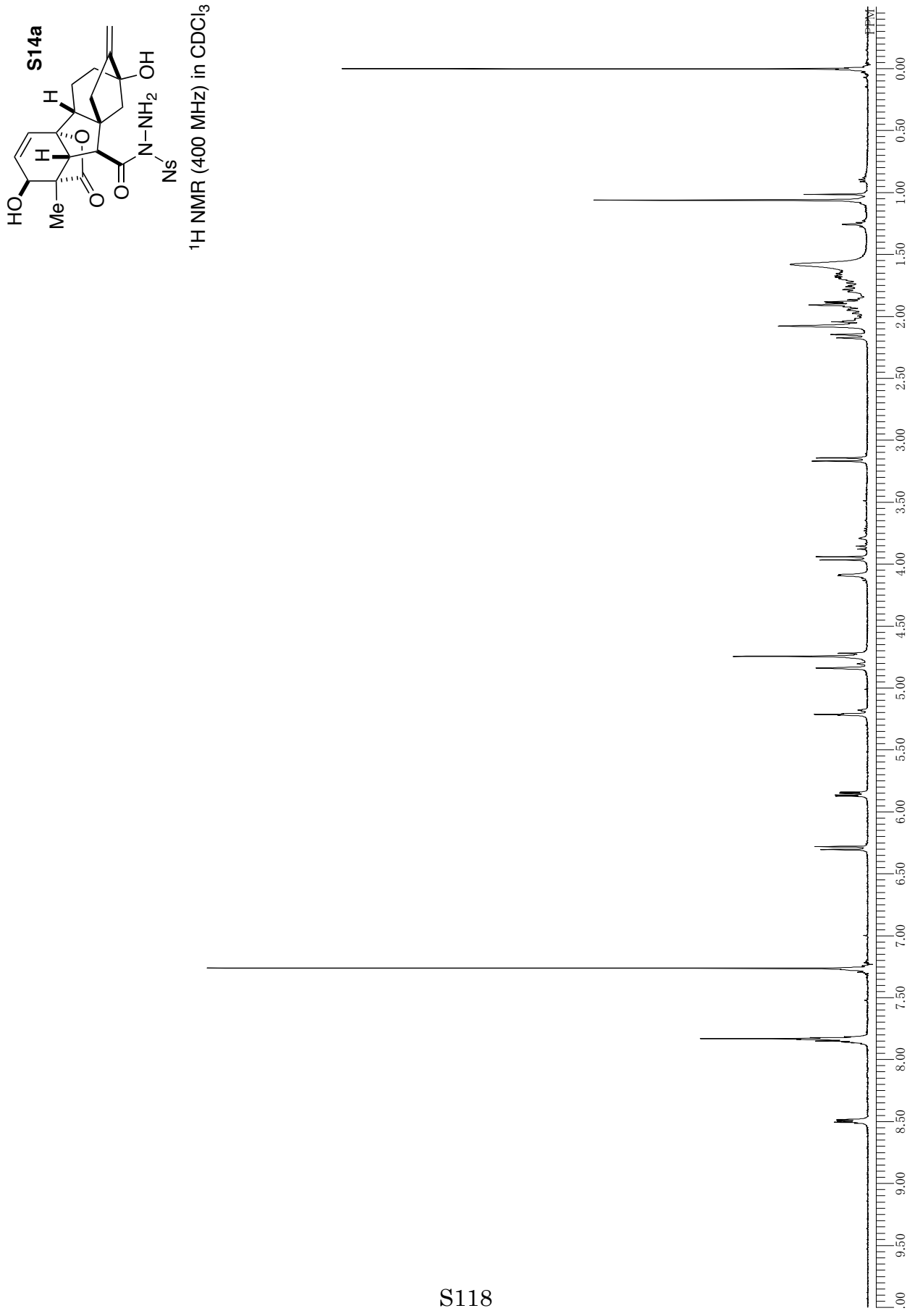


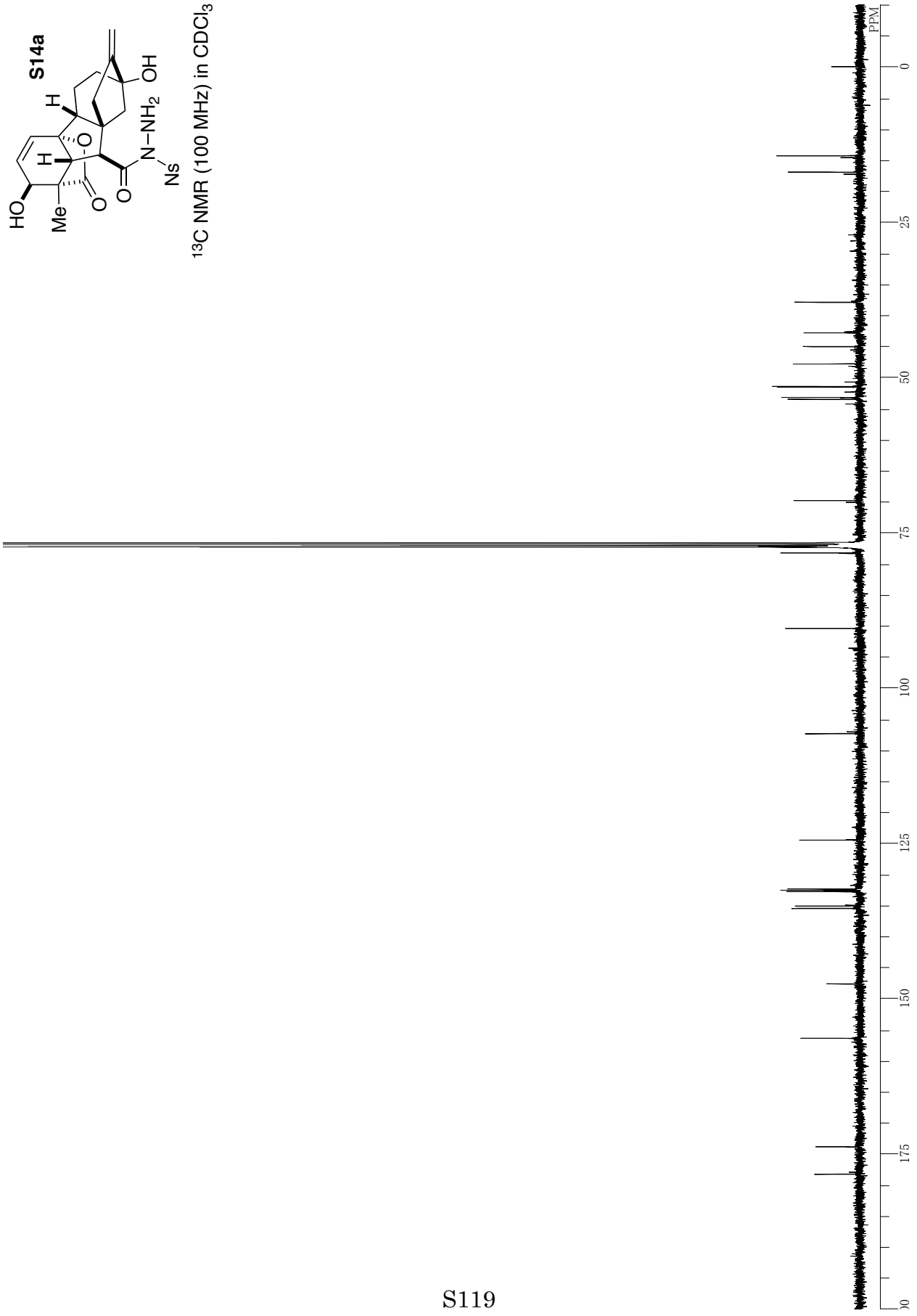


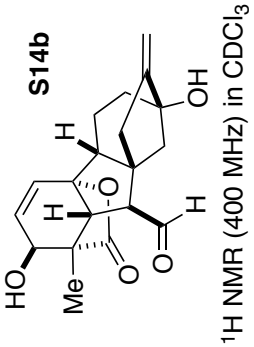
S13b

^{13}C NMR (100 MHz) in $CDCl_3$

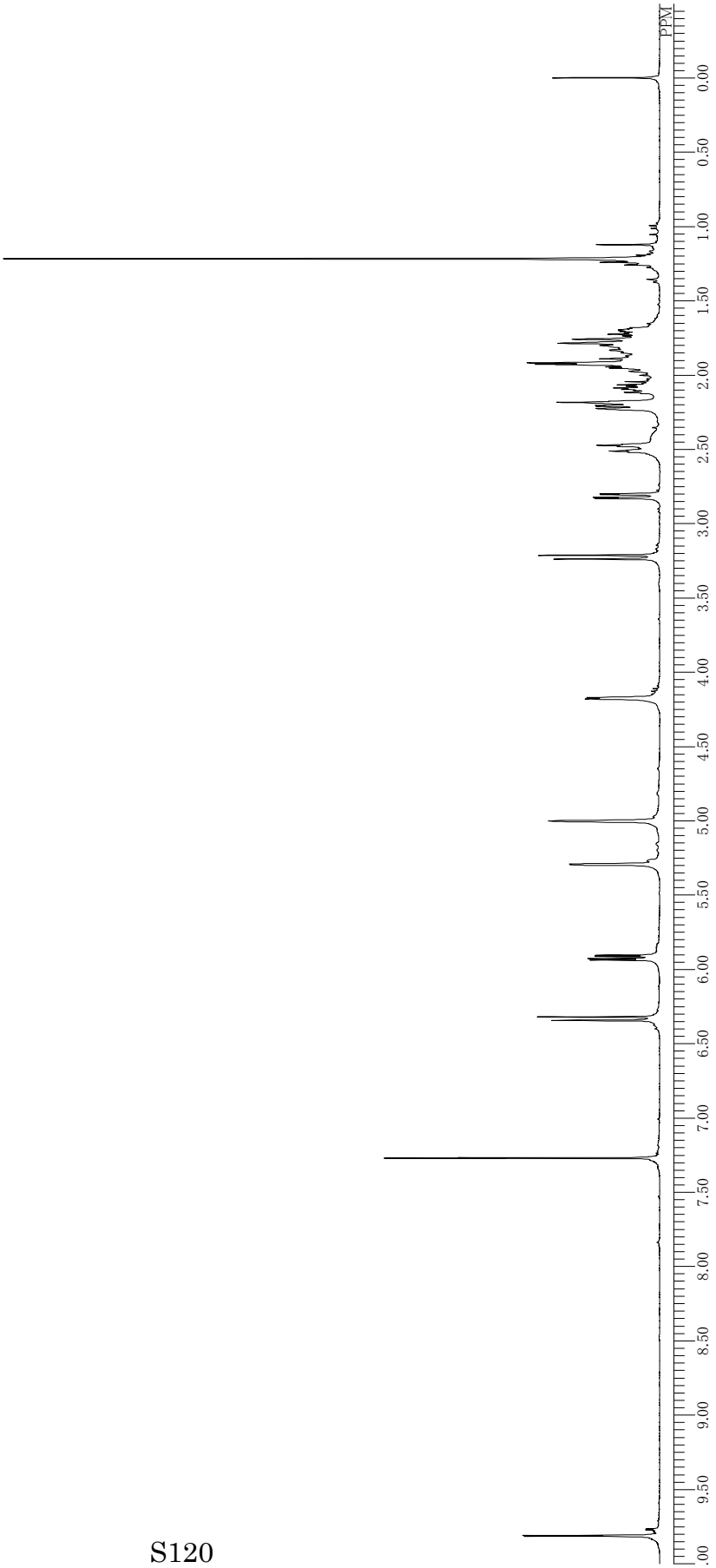


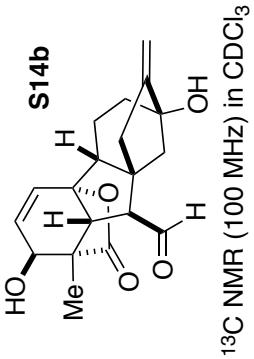



S14a
HO
Me
O
O
H
H
O
O
N–NH2
OH
Ns
13C NMR (100 MHz) in CDCl3
PPM
0
25
50
75
100
125
150
175

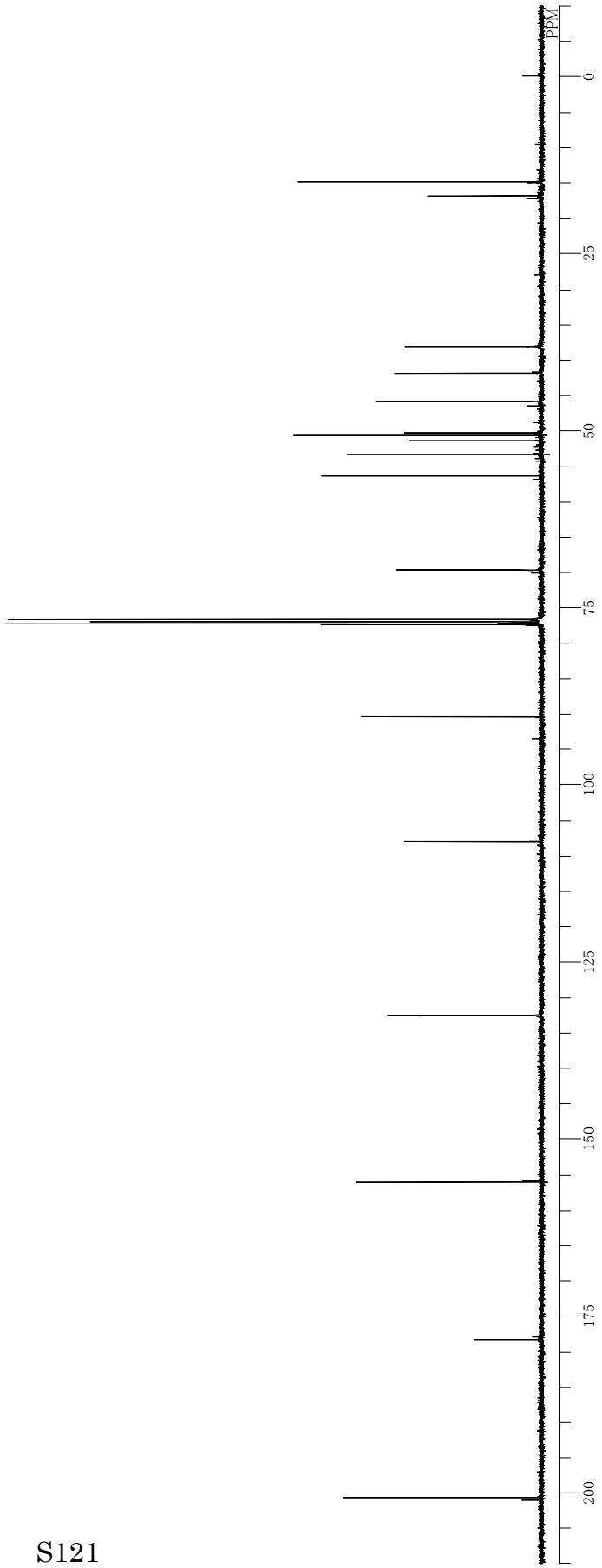


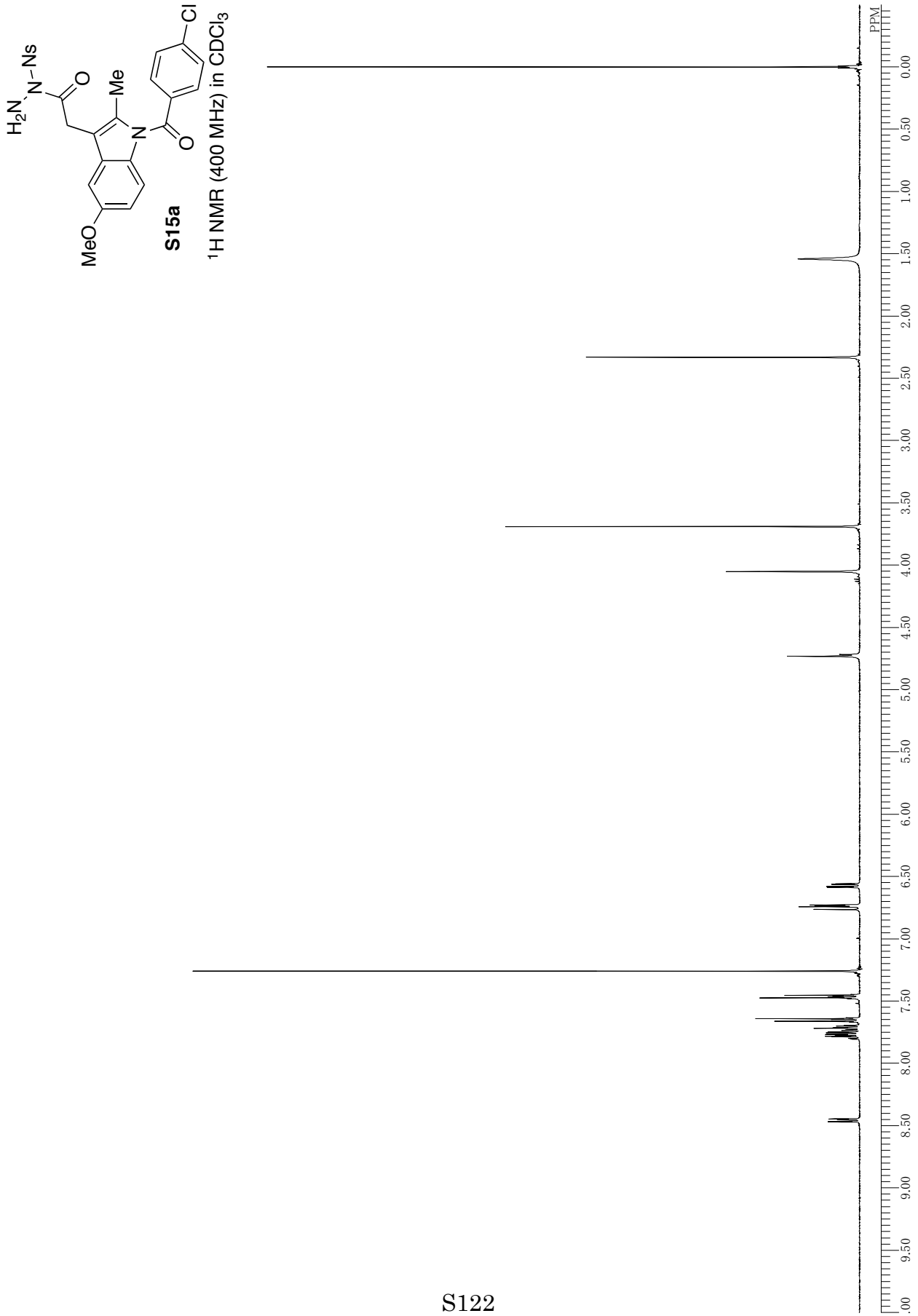
^{1}H NMR (400 MHz) in $CDCl_3$

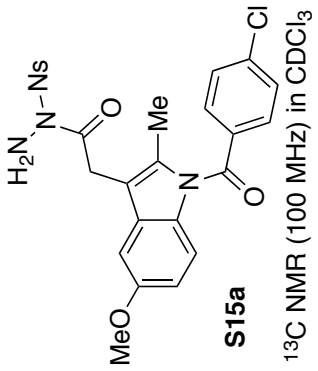




^{13}C NMR (100 MHz) in $CDCl_3$

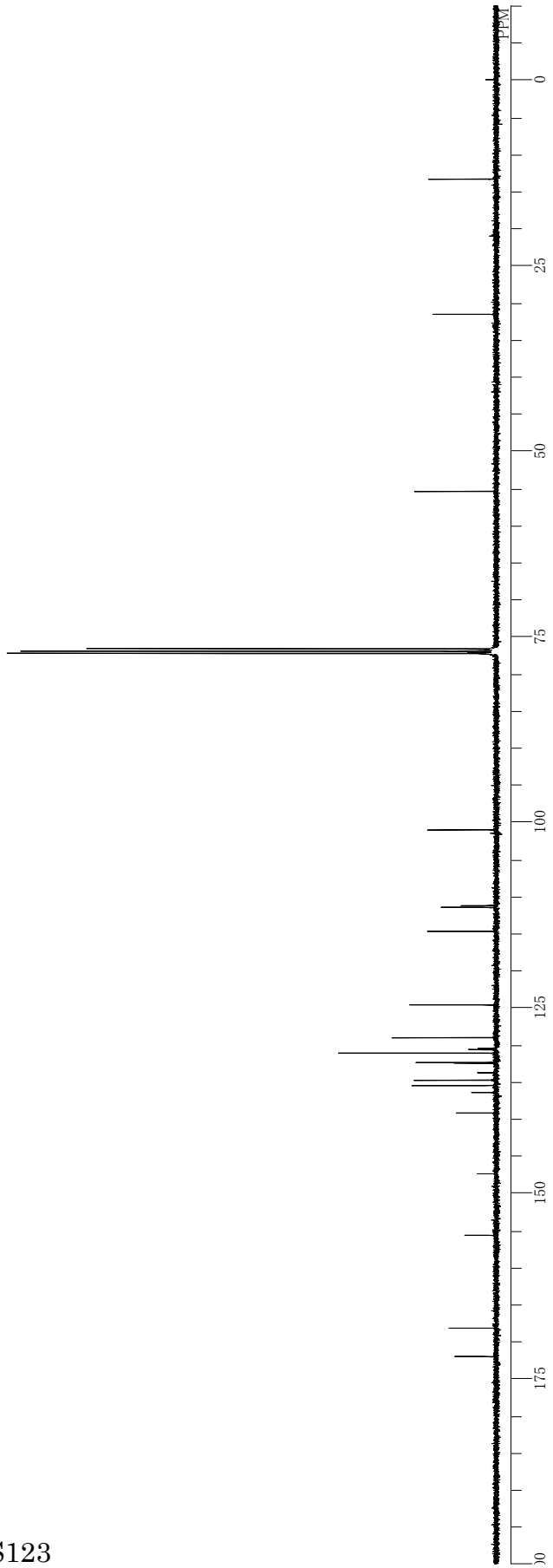


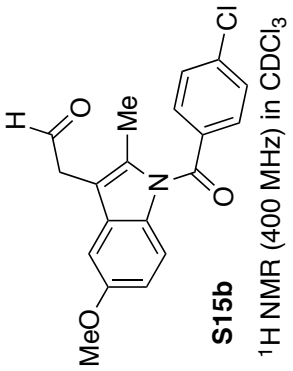

H2N
N
Ns
O
Me
N
O
Cl
MeO
S15a
1H NMR (400 MHz) in CDCl3
PPM
.00
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00



S15a

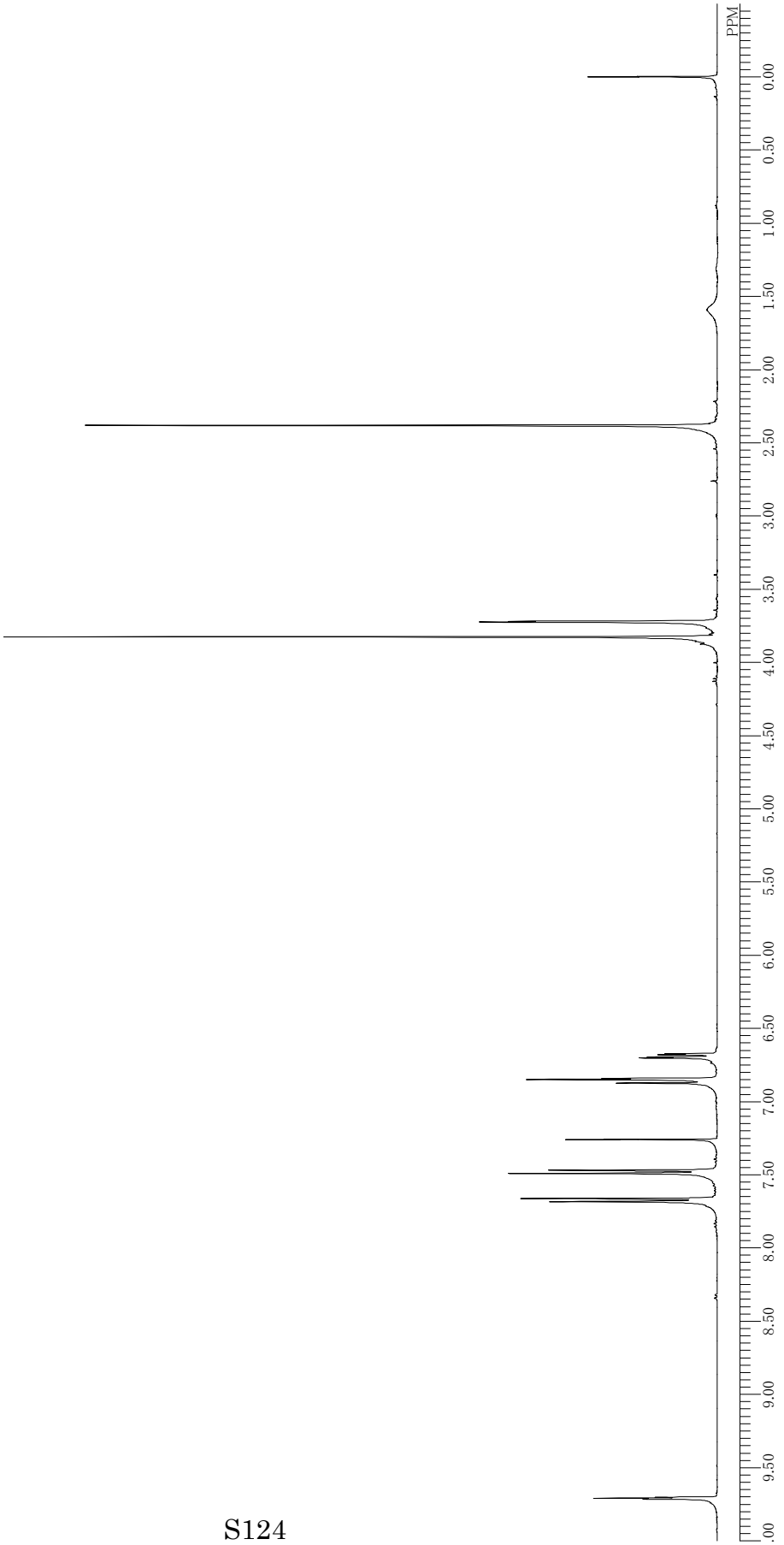
^{13}C NMR (100 MHz) in $CDCl_3$

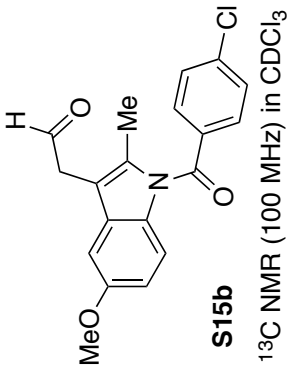




S15b

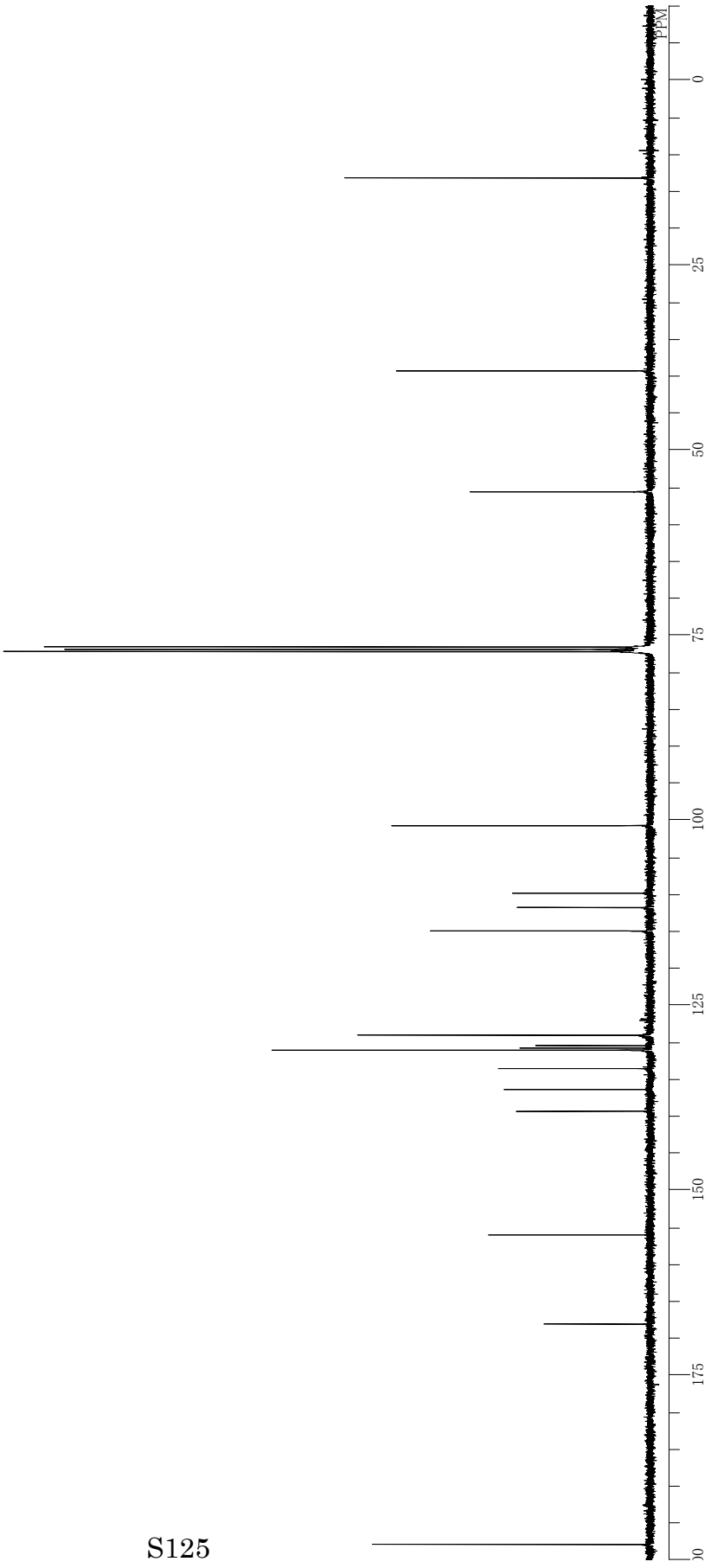
^{1}H NMR (400 MHz) in $CDCl_3$

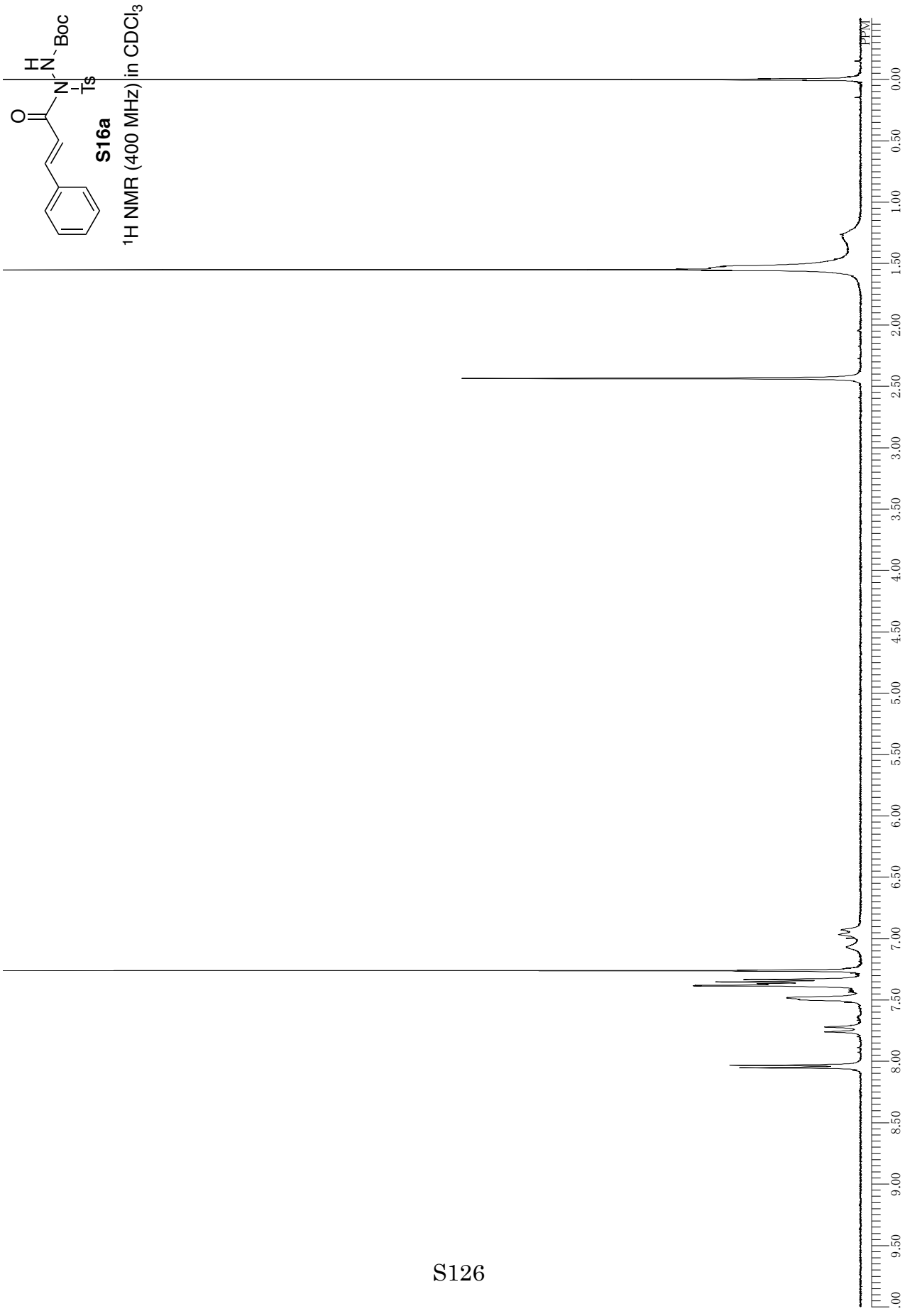


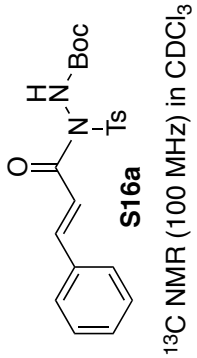


S15b

^{13}C NMR (100 MHz) in $CDCl_3$

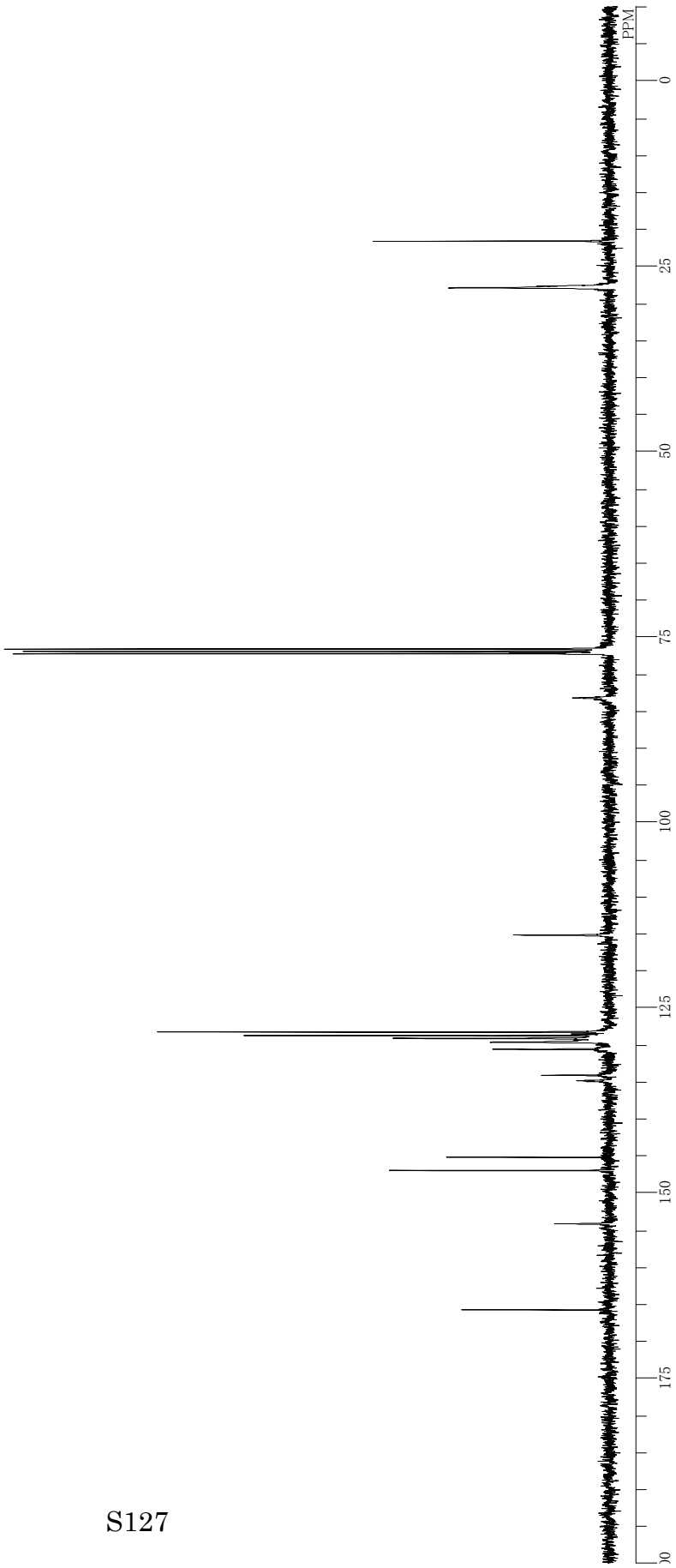


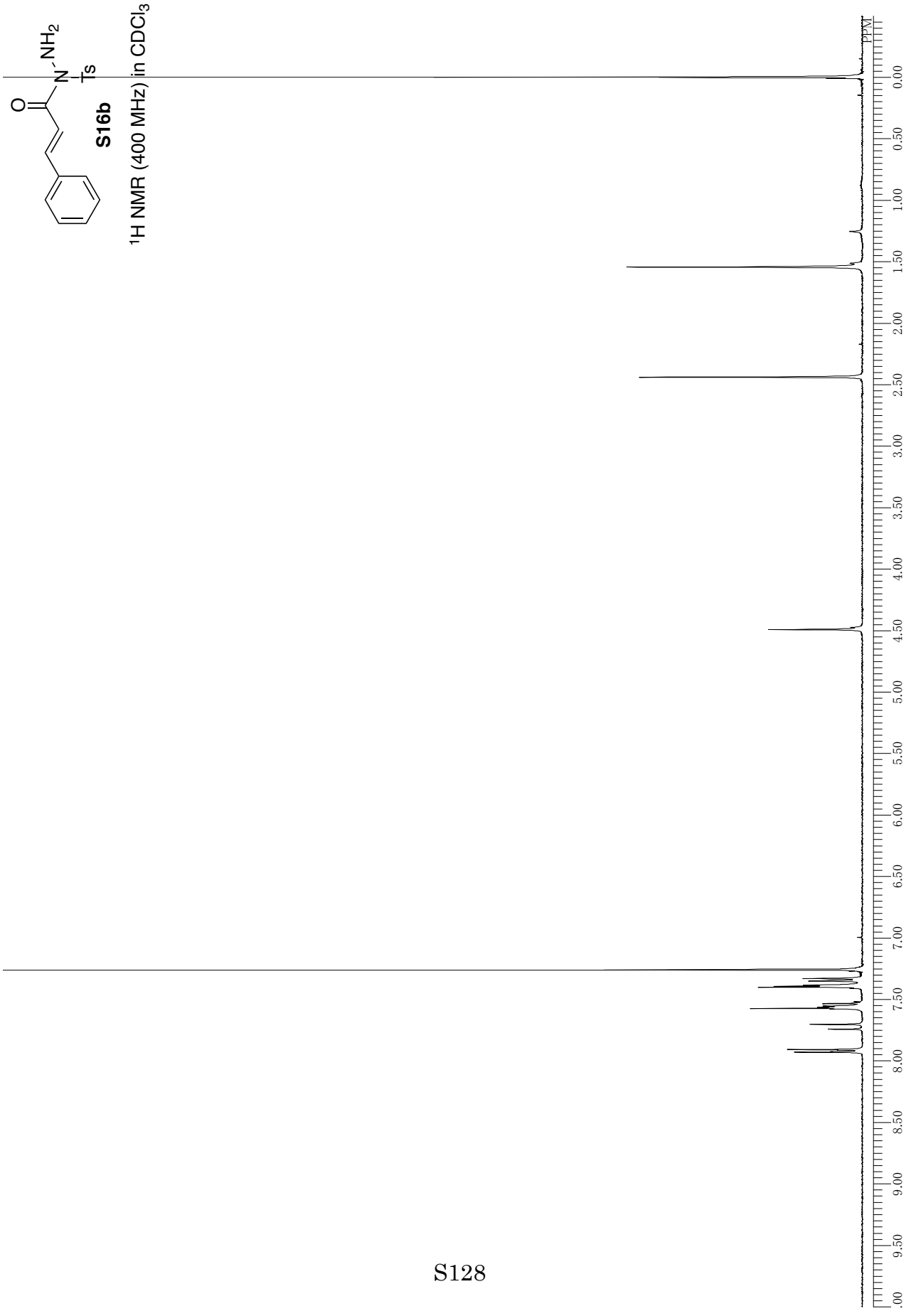

S16a
^{1}H NMR (400 MHz) in $CDCl_3$
PPM

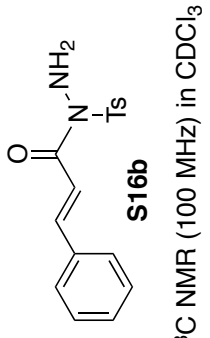


S16a

^{13}C NMR (100 MHz) in $CDCl_3$

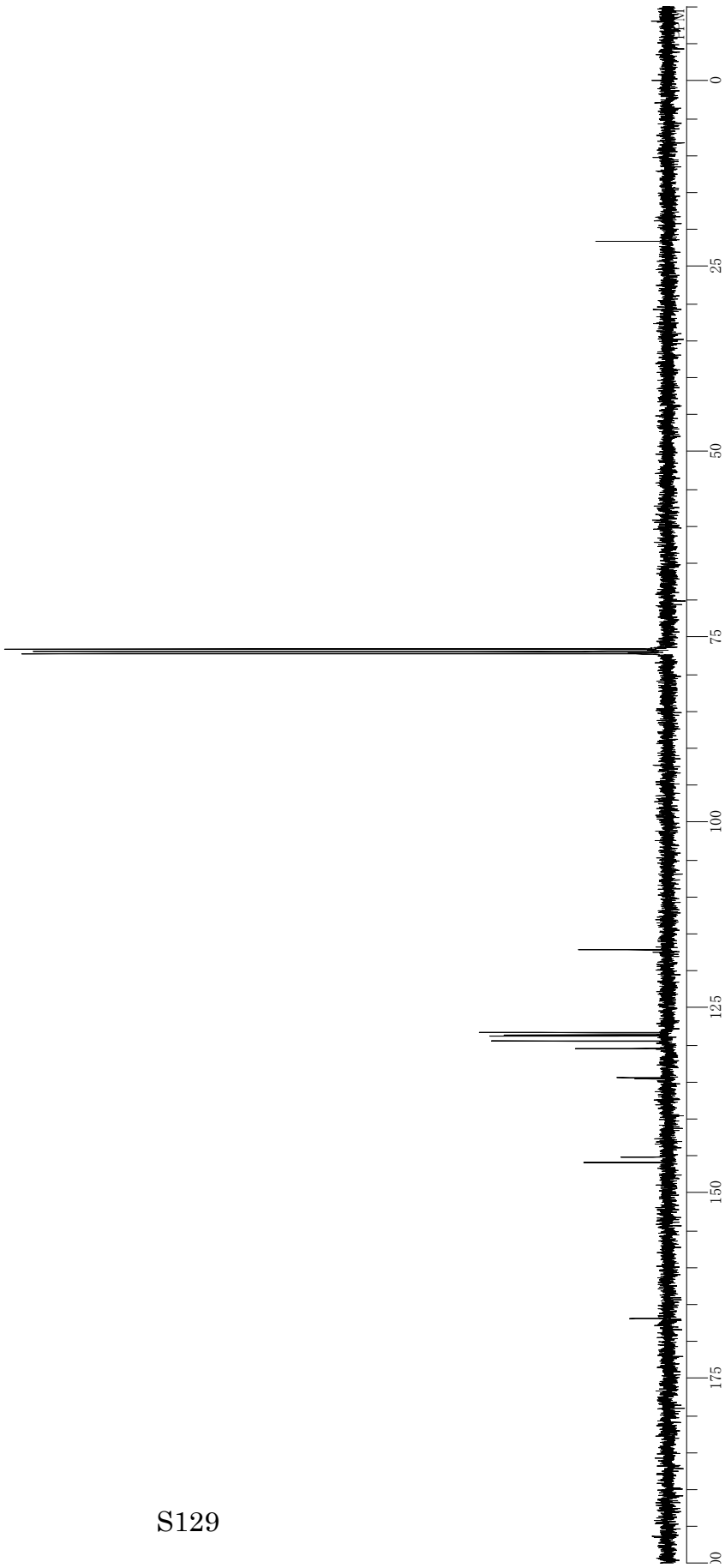


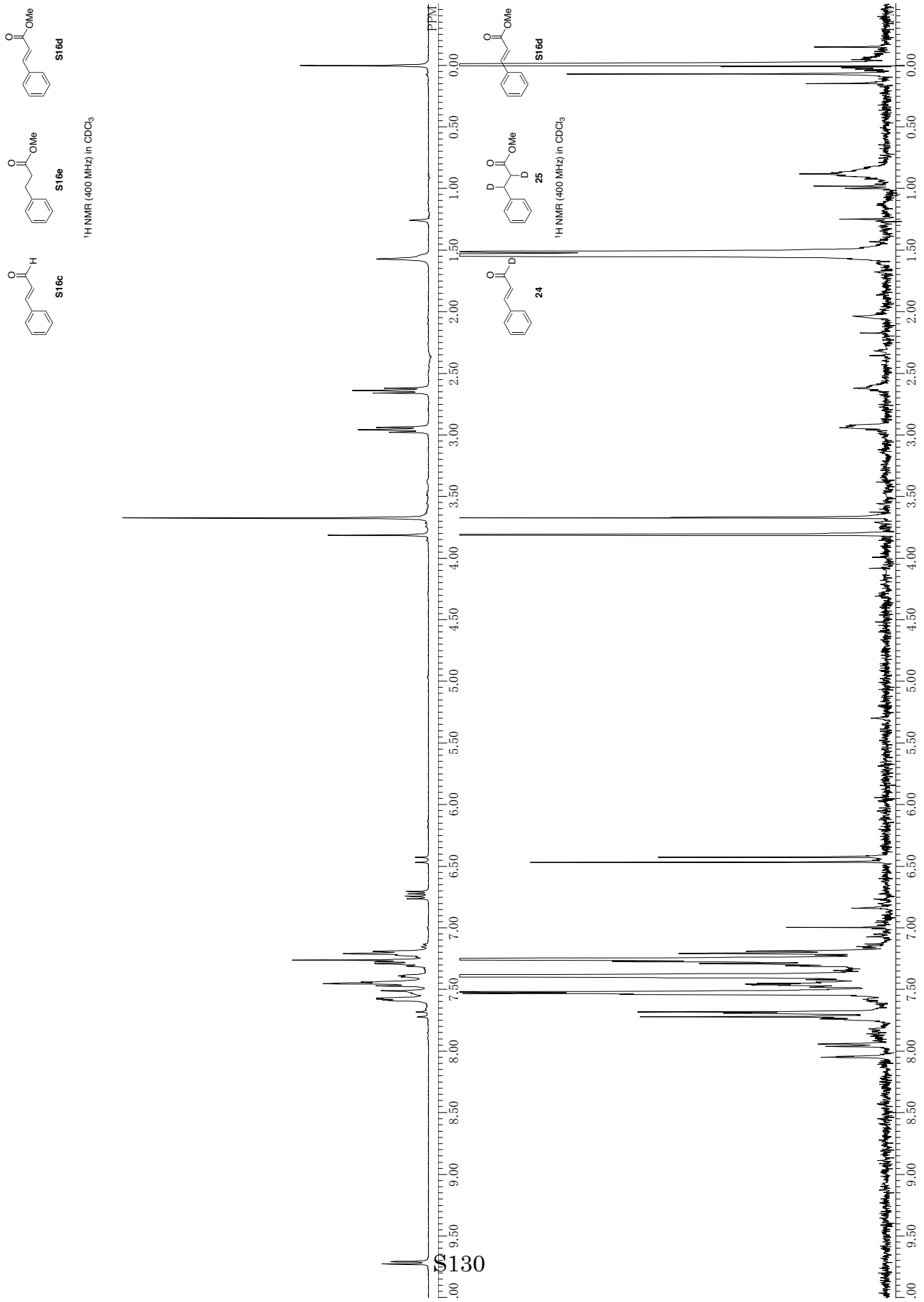

NH2
N
Ts
O
S16b
1H NMR (400 MHz) in CDCl3
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50

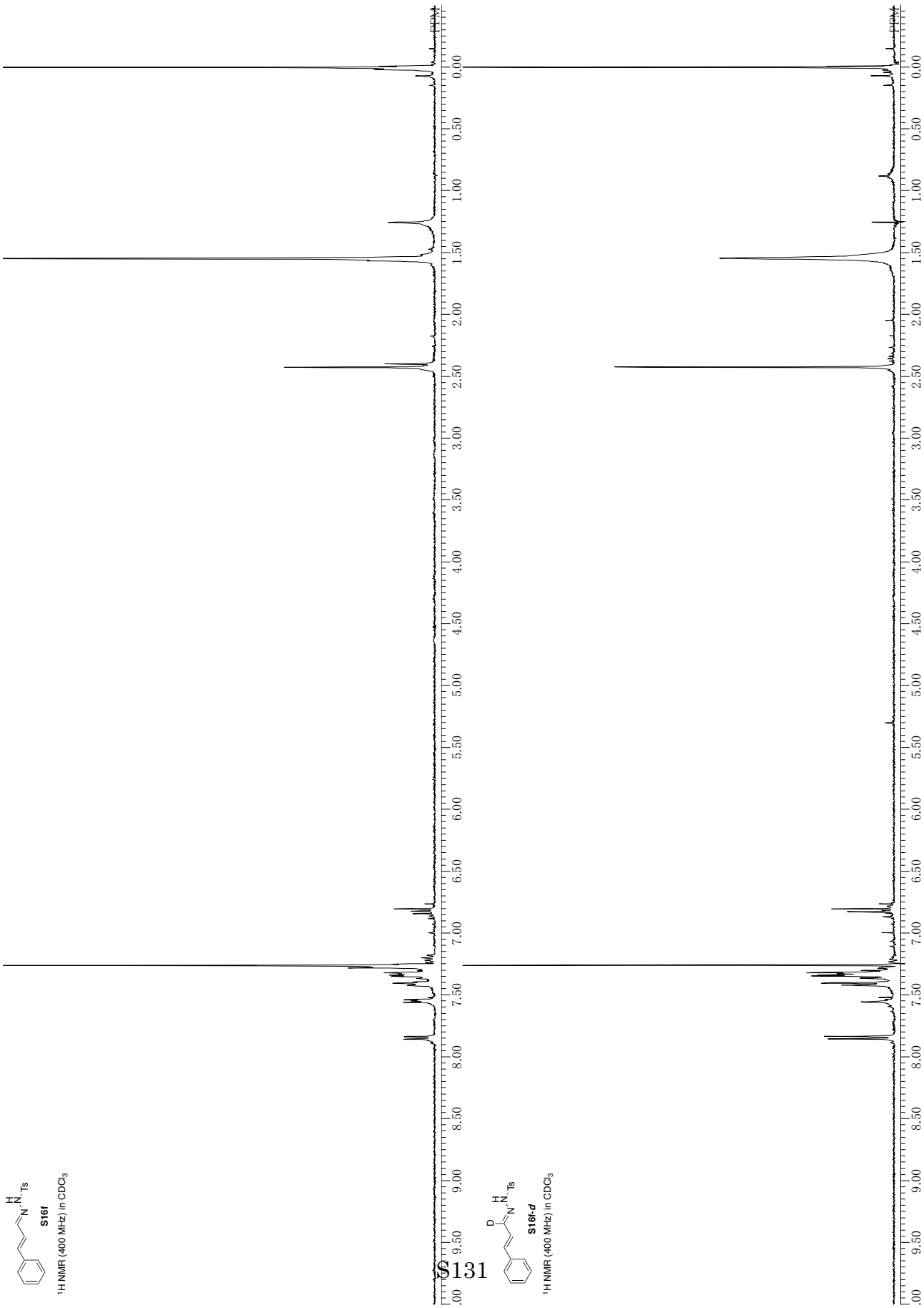


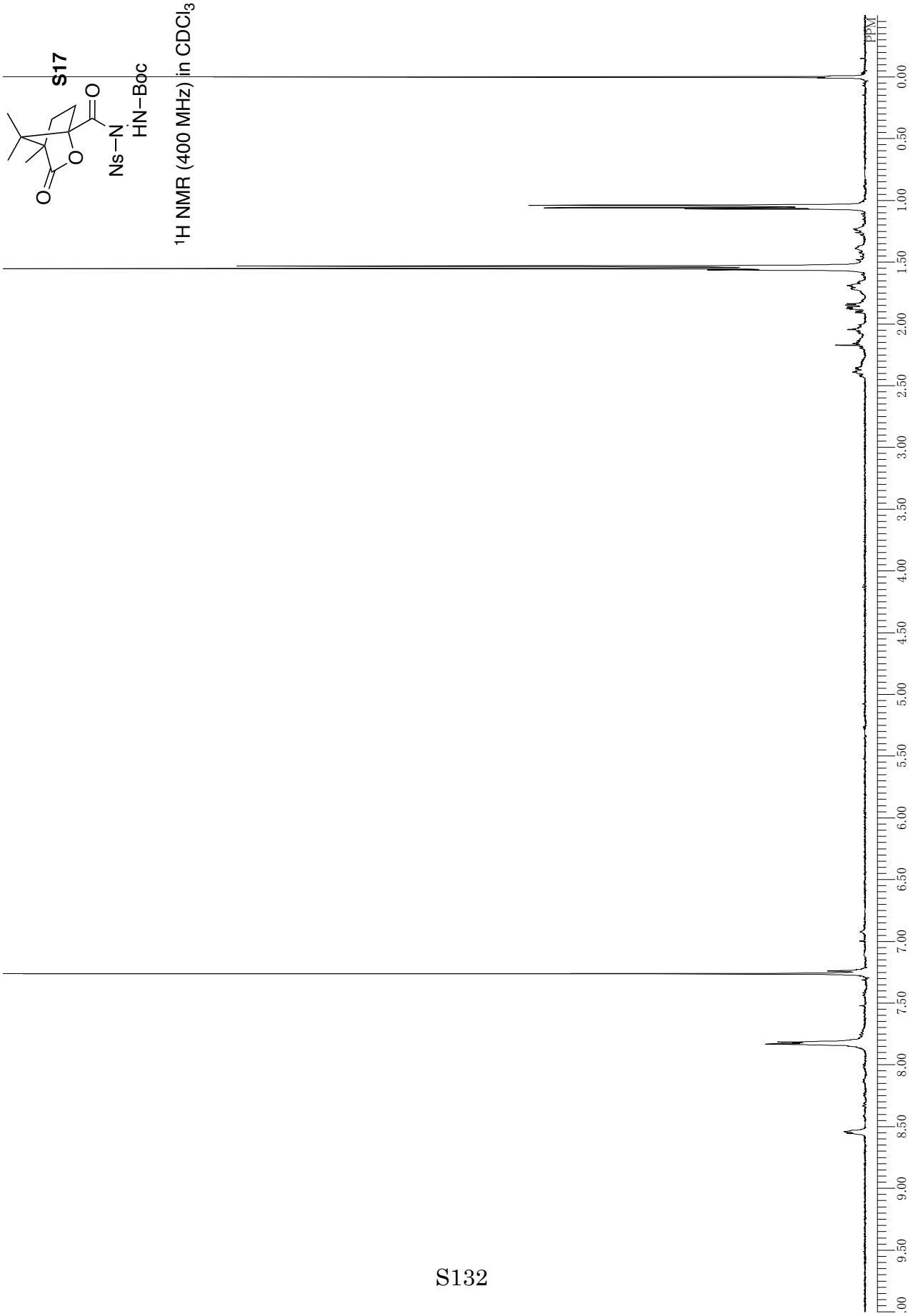
S16b

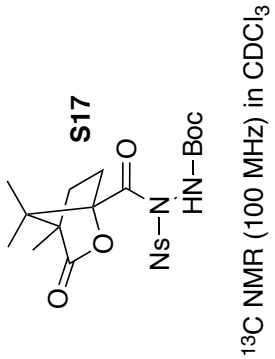
^{13}C NMR (100 MHz) in $CDCl_3$



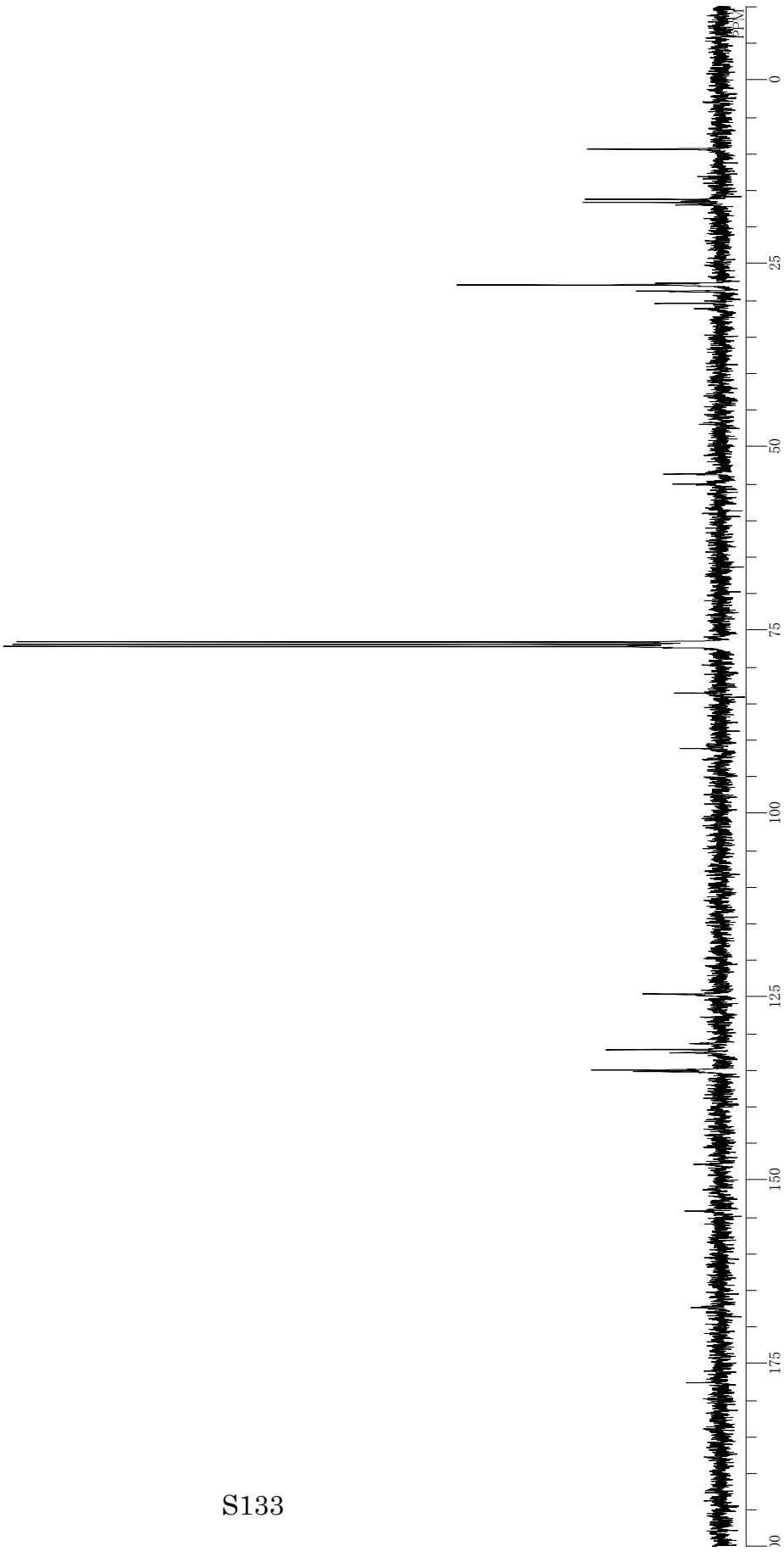


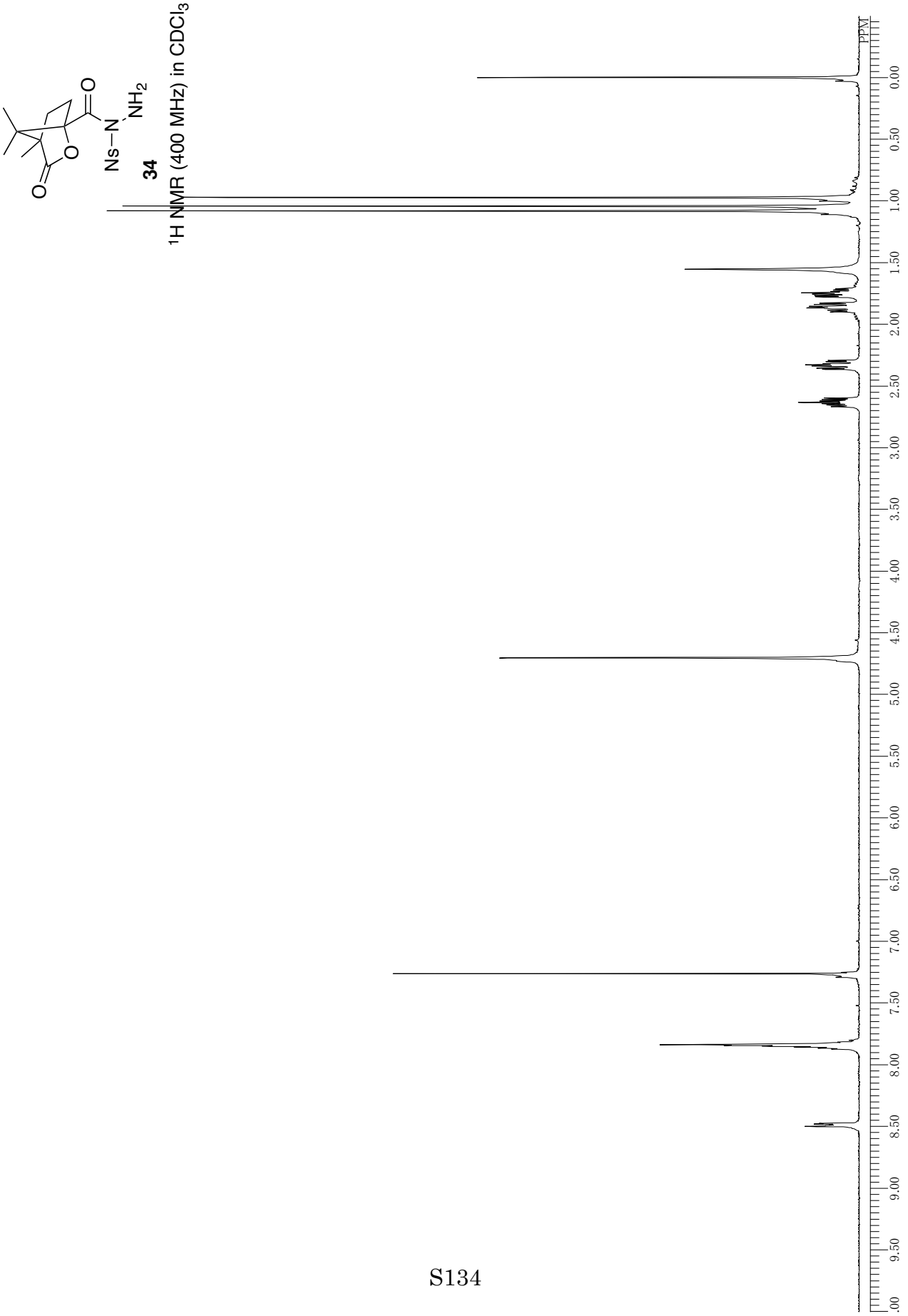

S16f
^{1}H NMR (400 MHz) in $CDCl_3$
S16f-*d*
^{1}H NMR (400 MHz) in $CDCl_3$
PPM
PPM

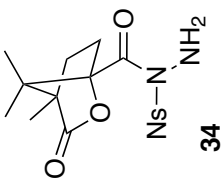

S17
Ns–N
HN–Boc
O
O
O
^{1}H NMR (400 MHz) in $CDCl_3$
PPM
.00
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00



^{13}C NMR (100 MHz) in $CDCl_3$

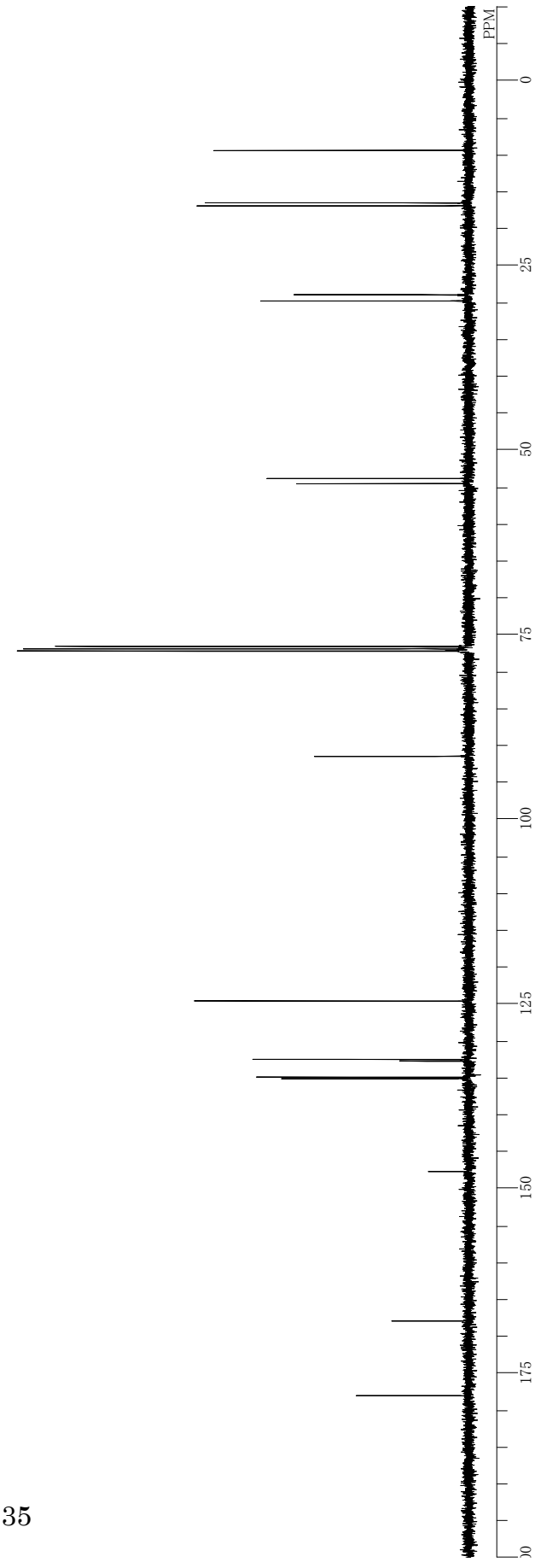


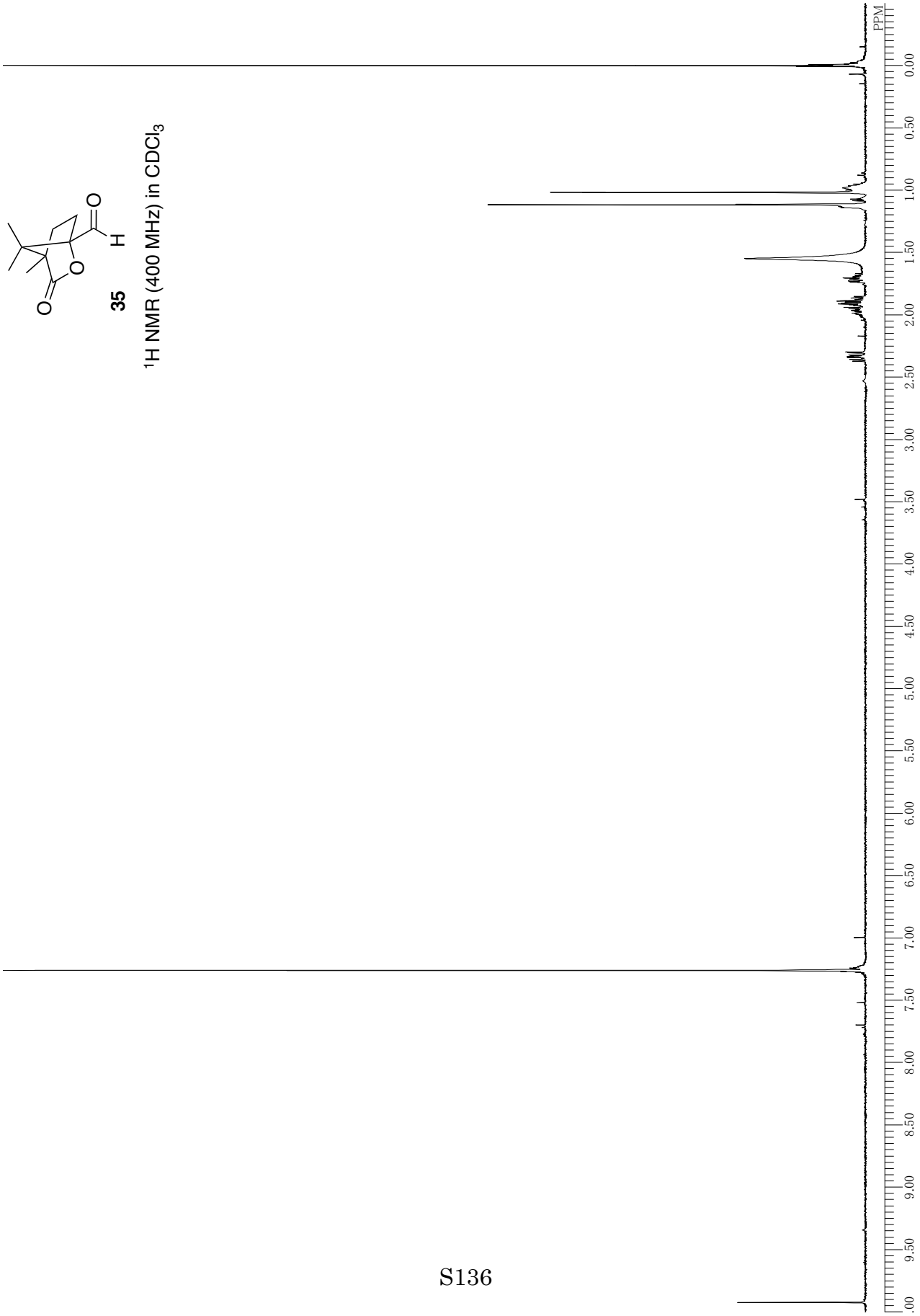

Ns–N
NH2
34
1H NMR (400 MHz) in CDCl3
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50

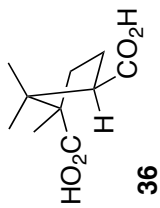


34

^{13}C NMR (100 MHz) in $CDCl_3$

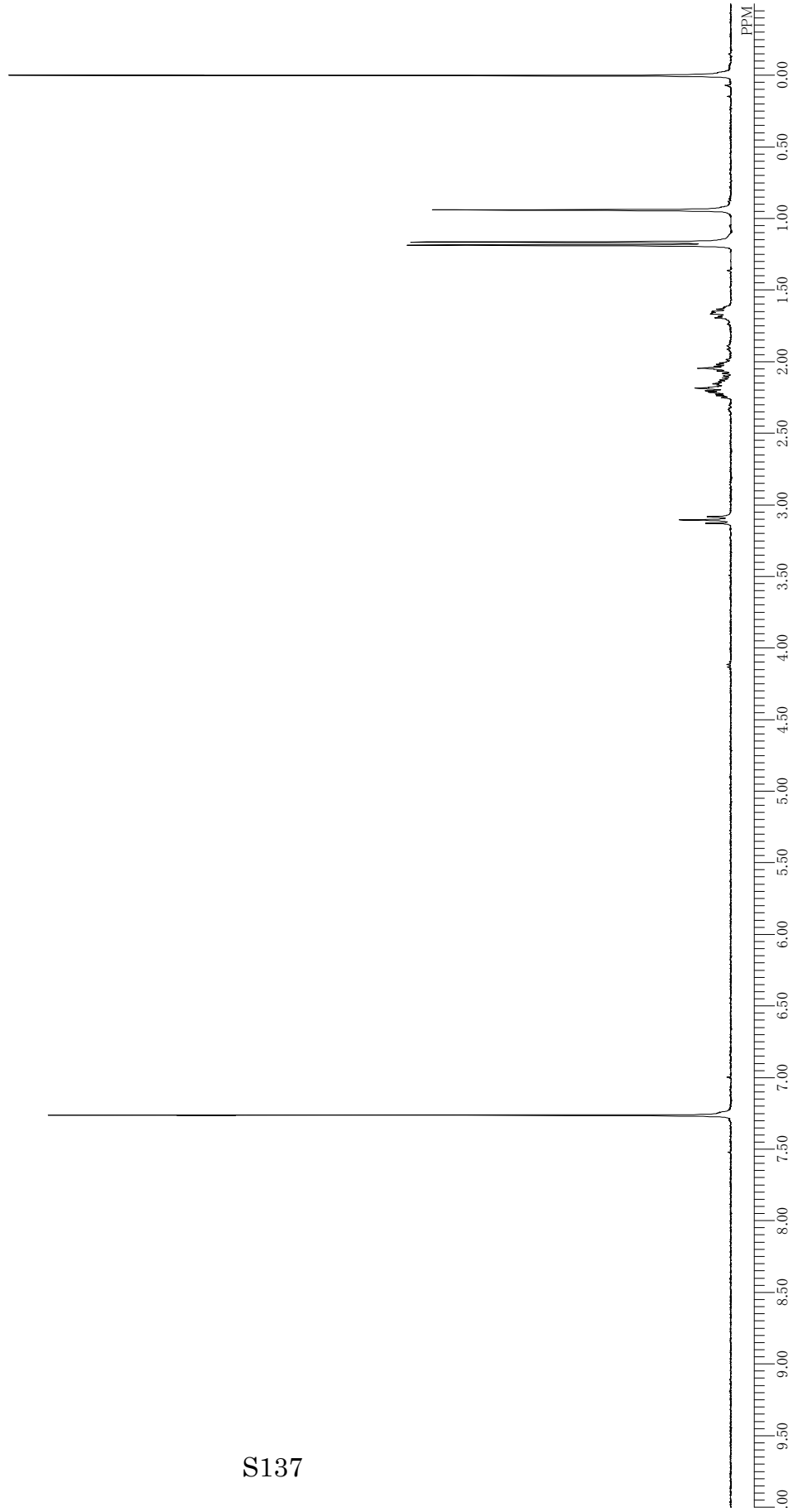


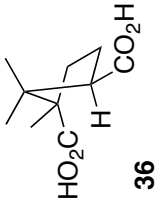

35
^{1}H NMR (400 MHz) in $CDCl_3$
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50



36

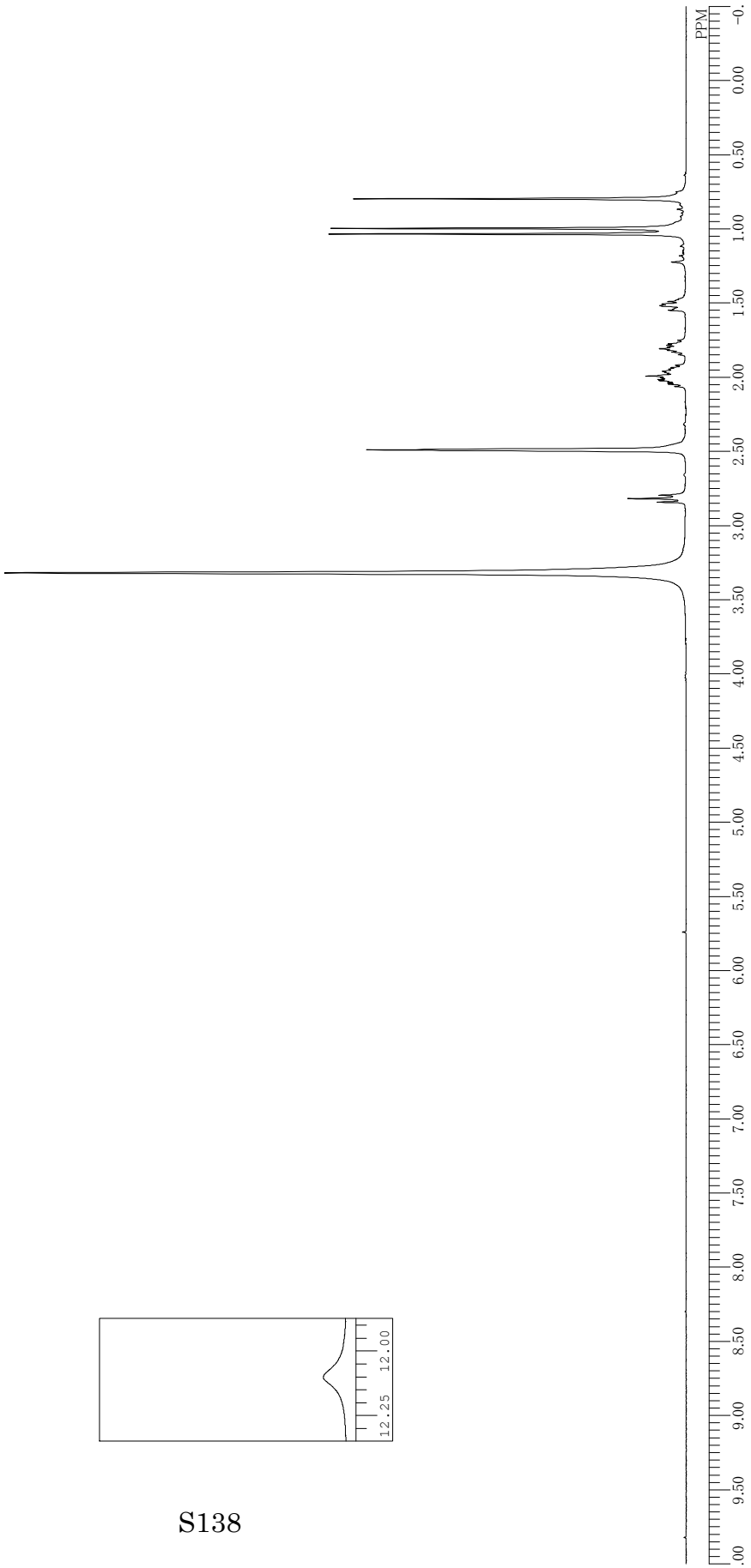
^{1}H NMR (400 MHz) in $CDCl_3$

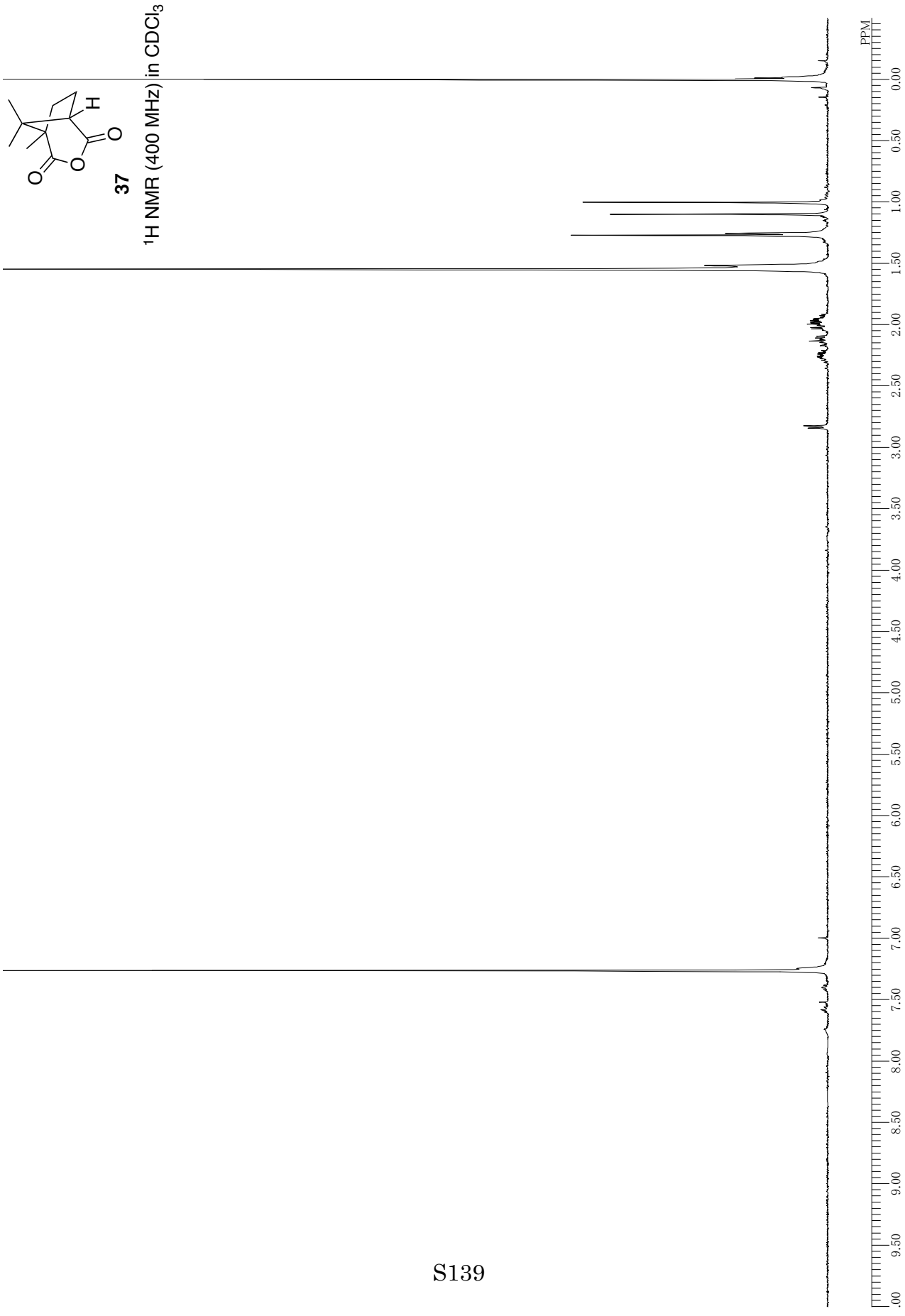




36

^{1}H NMR (400 MHz) in DMSO-d_6




37
^{1}H NMR (400 MHz) in $CDCl_3$
PPM
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50