

A Dual-Catalysis Approach to the Kinetic Resolution of 1,2-diaryl-1,2-diaminoethanes

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Supporting Information

General Information: Reagents and solvents were purchased from commercial sources and were used as received unless stated otherwise. Toluene was freshly distilled from sodium under nitrogen prior to use. Reactions were run under a nitrogen atmosphere. Purification of reaction products was carried out by flash chromatography using Sorbent Technologies Standard Grade silica gel (60 Å, 230–400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60 F₂₅₄ plates. Melting points were recorded on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Proton nuclear magnetic resonance spectra (¹H-NMR) were recorded on a Varian VNMRS–500 or 400 MHz instrument and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm and (CD₃)₂SO at 2.50 ppm. Data are reported as app = apparent, s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet, comp = complex, br s = broad singlet; integration; coupling constant(s) in Hz. Proton-decoupled carbon nuclear magnetic resonance spectra (¹³C-NMR) spectra were recorded on a Varian VNMRS–500 MHz instrument and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm and (CD₃)₂SO at 39.5 ppm). Mass spectra were recorded on a Finnigan LCQ-DUO mass spectrometer or on a Finnigan 2001 Fourier Transform Ion Cyclotron Resonance Mass Spectrometer. HPLC analysis was carried out on an Agilent 1100 series instrument with auto sampler and multiple wavelength detectors. Optical rotations were measured using a 1 mL cell with a 1 dm path length on a Jasco P–2000 polarimeter at 589 nm and at 20 °C. Racemic 1,2-diaryl-1,2-diaminoethanes **7a**,¹ **7b**,¹ **7c**,¹ **7d**,³ **7e**,³ **7f**,² **7g**,³ **7h**,³ and **7i**¹ were prepared based on literature methods. 1,2-Diaryl-1,2-diaminoethanes, catalyst **1**, DMAP and benzoic anhydride were purified by recrystallization prior to use.

The absolute configuration of **9f** ($[\alpha]_{20}^D +24.9$, c 0.5, CHCl₃, 65% ee) was assigned by comparison with the bis(2,2,2-trichloroethyl) ((1*R*,2*R*)-1,2-diphenylethane-1,2-diyl)diamine ($[\alpha]_{20}^D -40.8$, c 0.5, CHCl₃) synthesized from commercially available (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine. The absolute configuration of products (**8a–8i**, **9a–9e** and **9g–9i**) was assigned by analogy.

Conversions and s-factors were calculated in accord with standard procedures.⁴

General Procedure for the Resolution and Protection of Racemic Diamines:

A flame dried round bottom flask was charged with benzoic anhydride (22.6 mg, 0.1 mmol, 0.5 equiv.) and powdered 4Å MS (100 mg). Freshly distilled toluene (10 mL) and N,N-dipropylpyridine-4-amine (3.6 mg, 0.02 mmol, 0.1 equiv.) in 1 mL of toluene was added. The resulting mixture was cooled to $-78\text{ }^{\circ}\text{C}$ over 15 min and a solution of catalyst **1** (12.5 mg, 0.02 mmol, 0.1 equiv.) in 6 mL of toluene was added. After 15 min, a solution of diamine (0.2 mmol) in 3 mL of toluene was added slowly along the inner side of the flask and the reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$. When benzoic anhydride could no longer be detected by TLC analysis, an ethanolic ammonia solution (2 M, 2 mL) was added. The reaction mixture was allowed to warm to rt, diluted with 10 mL of a 1:1 water/brine mixture and extracted with EtOAc (5 x 30 mL). After drying with anhydrous sodium sulfate, the organic layer was concentrated under reduced pressure and dissolved in 10 mL of CH_2Cl_2 . The solution was cooled to $0\text{ }^{\circ}\text{C}$ and Hünig's base and Troc-Cl were added slowly. After completion of the reaction, the resulting mixture was concentrated under reduced pressure and purified by flash chromatography.

The conversion, C_{HPLC} , for each catalytic reaction was calculated using the following equation:

$$C_{\text{HPLC}} = \frac{ee_{\text{SM}}}{ee_{\text{P}} + ee_{\text{SM}}}$$

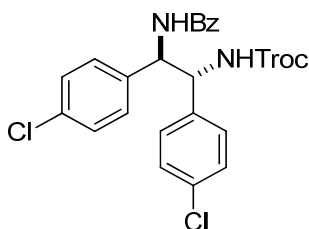
Where ee_{P} is the enantiomeric excess of the amide product and ee_{SM} is the enantiomeric excess of the recovered amine.

The s-factor was calculated using the calculated conversion and ee from either the product, ee_{P} , or recovered starting material, ee_{SM} , following the equation:

$$s = \frac{\ln((1 - C_{\text{HPLC}})(1 - ee_{\text{P}}))}{\ln((1 - C_{\text{HPLC}})(1 + ee_{\text{P}}))}$$
$$s = \frac{\ln((1 - C_{\text{HPLC}})(1 - ee_{\text{SM}}))}{\ln((1 - C_{\text{HPLC}})(1 + ee_{\text{SM}}))}$$

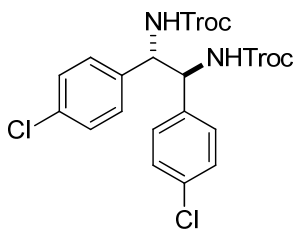
Characterization Data of Products

2,2,2-Trichloroethyl((1*R*,2*R*)-2-benzamido-1,2-bis(4-chlorophenyl)ethyl)carbamate (**8a**):



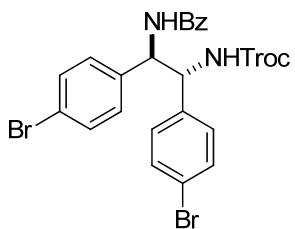
Following the general procedure, compound **8a** was obtained as a white solid in 44% yield (49 mg); mp = 222–224 °C; R_f = 0.21 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_{20}^D$ –29.2 (c 0.5, CHCl₃, 83% ee); IR (KBr) 3334, 3053, 2947, 2364, 1713, 1640, 1529, 1492, 1277, 1148, 1094, 1015, 820, 729 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.75 (d, J = 7.7 Hz, 2H), 7.65–7.32 (comp, 6H), 7.31–7.25 (m, 1H), 7.22 (d, J = 7.5 Hz, 1H), 7.06 (app t, J = 7.1 Hz, 3H), 6.20 (d, J = 8.0 Hz, 1H), 5.45 (app t, J = 9.2 Hz, 1H), 5.16–4.93 (m, 1H), 4.74 (d, J = 12.0 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 167.8, 155.5, 137.2, 136.8, 133.3, 132.1, 132.0, 129.1, 129.0, 128.7, 127.1, 122.4, 122.2, 95.1, 74.6, 60.5, 59.1; m/z (ESI-MS) 561.9 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 230 nm, t_R = 10.5 min (major) and t_R = 8.4 min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-bis(4-chlorophenyl)ethane-1,2-diyl)dicarbamate (**9a**):



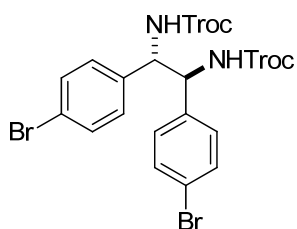
Following the general procedure, compound **9a** was obtained as a white solid in 46% yield (58.0 mg); mp = 205–207 °C; R_f = 0.48 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_{20}^D$ +36.7 (c 0.5, CHCl₃, 86% ee); IR (KBr) 3330, 2952, 1710, 1537, 1278, 1144, 1093, 820, 721 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.22 (d, J = 8.4 Hz, 4H), 7.03 (d, J = 8.4 Hz, 4H), 5.91 (br s, 2H), 4.97 (dd, J = 5.6, 2.4 Hz, 2H), 4.82 (d, J = 12.0 Hz, 2H), 4.63 (d, J = 12.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 155.0, 136.1, 134.3, 129.1, 128.6, 95.2, 74.7, 60.4; m/z (ESI-MS) 633.4[M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 98/2, Flow rate = 0.5 mL/min, UV = 230 nm, t_R = 20.6 min (major) and t_R = 27.5 min (minor). Calculated conversion = 51; **s** = 30.

2,2,2-Trichloroethyl((1*R*,2*R*)-2-benzamido-1,2-bis(4-bromophenyl)ethyl)carbamate (**8b**):



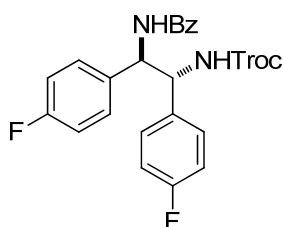
Following the general procedure, compound **8b** was obtained as a white solid in 41% yield (53 mg); mp = 218–219 °C; R_f = 0.20 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_{20}^D$ –27.8 (c 0.5, CHCl₃, 83% ee); IR (KBr) 3334, 3055, 2950, 2362, 1715, 1642, 1531, 1492, 1280, 1148, 1097, 1015, 822, 728 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 8.82 (d, J = 9.5 Hz, 1H), 8.59 (d, J = 9.5 Hz, 1H), 7.75 (d, J = 7.7 Hz, 2H), 7.60–7.50 (comp, 2H), 7.49–7.37 (comp, 5H), 7.36–7.20 (comp, 4H), 5.64–5.55 (m, 1H), 5.32–5.23 (m, 1H), 4.78 (d, J = 12.5 Hz, 1H), 4.66 (d, J = 12.5 Hz, 1H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 166.0, 154.1, 139.2, 139.1, 134.1, 131.6, 131.5, 131.4, 129.0, 128.8, 128.3, 128.0, 127.9(7), 127.2, 96.0, 73.3, 58.4, 56.3; m/z (ESI-MS) 650.4 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, t_R = 8.4 min (major) and t_R = 5.8 min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-bis(4-bromophenyl)ethane-1,2-diyl)dicarbamate



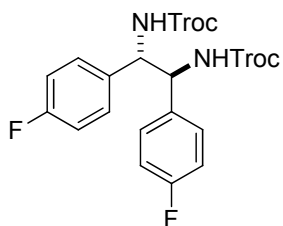
(9b): Following the general procedure, compound **9b** was obtained as a white solid in 42% yield (60 mg); mp = 208–210 °C; R_f = 0.45 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ +19.3 (c 0.5, CHCl₃, 70% ee); IR(KBr) 3330, 3058, 2954, 1716, 1529, 1489, 1248, 1148, 1075, 1011, 818, 725, 568 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.37 (d, J = 8.3 Hz, 4H), 6.97 (d, J = 8.3 Hz, 4H), 5.95 (br s, 2H), 5.06–4.91 (m, 2H), 4.81 (d, J = 12.0 Hz, 2H), 4.64 (d, J = 12.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 154.9, 136.6, 132.0, 128.9, 126.4, 95.2, 74.7, 60.3; m/z (ESI-MS) 721.9 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, t_R = 5.4 min (major) and t_R = 6.4 min (minor). Calculated conversion = 46; **s** = 22.

2,2,2-Trichloroethyl((1*R*,2*R*)-2-benzamido-1,2-bis(4-fluorophenyl)ethyl)carbamate (8c):



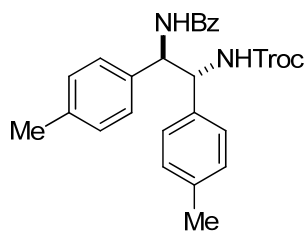
Following the general procedure, compound **8c** was obtained as a white solid in 40% yield (42 mg); mp = 211–213 °C; R_f = 0.19 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ -31.3 (c 0.5, CHCl₃, 83% ee); IR (KBr) 3332, 3056, 2366, 1715, 1640, 1532, 1490, 1148, 1097, 827 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.76 (d, J = 7.4 Hz, 2H), 7.57–7.48 (m, 1H), 7.48–7.37 (comp, 2H), 7.21–7.07 (comp, 4H), 7.01–6.84 (comp, 4H), 6.19 (d, J = 8.1 Hz, 1H), 5.47 (dd, 10.7, 8.1 Hz, 1H), 5.05 (dd, 10.7, 8.1 Hz, 1H), 4.74 (d, J = 12.0 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 167.8, 155.5, 134.3, 133.8, 133.4, 131.9, 129.1(5), 129.1(2), 129.0(9), 129.0(6), 128.6, 127.0, 115.8 (d, J_{C-F} = 21.0 Hz), 115.7 (d, J_{C-F} = 21.0 Hz), 95.1, 74.5, 60.6, 59.2; m/z (ESI-MS) 528.3 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 230 nm, t_R = 10.5 min (major) and t_R = 8.0 min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-bis(4-fluorophenyl)ethane-1,2-diyl)dicarbamate



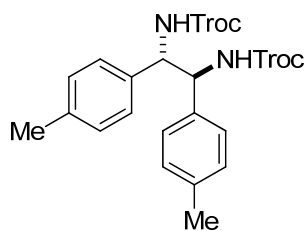
(9c): Following the general procedure, compound **9c** was obtained as a white solid in 45% yield (54 mg); mp = 202–203 °C; R_f = 0.41 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ +29.4 (c 0.5, CHCl₃, 78% ee); IR(KBr) 3331, 3055, 2952, 1714, 1530, 1490, 1248, 1148, 820, 725 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.11–7.01 (comp, 4H), 6.98–6.87 (comp, 4H), 5.89 (br s, 2H), 5.00–4.91 (m, 2H), 4.82 (d, J = 12.0 Hz, 2H), 4.63 (d, J = 12.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 163.3, 161.3, 155.0, 133.6, 129.0, 128.9, 115.13(d, J_{C-F} = 21.8 Hz), 95.2, 74.7, 60.5; m/z (ESI-MS) 600.2 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, t_R = 7.0 min (major) and t_R = 8.7 min (minor). Calculated conversion = 48; **s** = 25.

2,2,2-Trichloroethyl((1*R*,2*R*)-2-benzamido-1,2-di-*p*-tolylethyl)carbamate (8d):



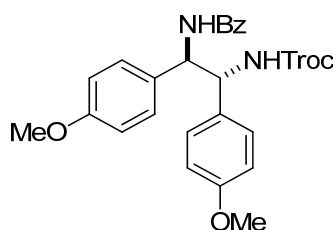
Following the general procedure, compound **8d** was obtained as a white solid in 44% yield (45 mg); mp = 229–231 °C; $[\alpha]_D^{20}$ –21.5 (c 0.5, CHCl₃, 69% ee); R_f = 0.21 (Hexanes/EtOAc 6:1 v/v); IR (KBr) 3336, 3060, 1720, 1630, 1542, 1261, 1152, 730 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.78 (d, 7.6 Hz, 2H), 7.53–7.47 (m, 1H), 7.45–7.39 (comp, 2H), 7.19–7.06 (comp, 4H), 7.05–6.97 (comp, 4H), 6.05 (d, J = 8.1 Hz, 1H), 5.54–4.47 (m, 1H), 5.10–5.03 (m, 1H), 4.71 (d, J = 12.0 Hz, 1H), 4.54 (d, J = 12.0 Hz, 1H), 2.27 (s, 3H), 2.25 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ = 167.6, 155.4, 137.8, 137.6, 135.5, 135.1, 133.8, 131.7, 129.3(5), 129.3, 128.5, 127.4, 127.3, 117.6, 95.2, 74.5, 60.8, 59.2, 21.0(8), 21.0(7); m/z (ESI-MS) 520.5 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 210 nm, t_R = 6.8 min (major) and t_R = 5.1 min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-di-*p*-tolylethane-1,2-diyl)dicarbamate (9d):



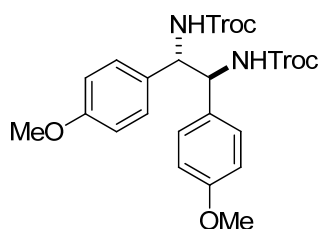
Following the general procedure, compound **9d** was obtained as a white solid in 44% yield (51 mg); mp = 165–168 °C; R_f = 0.44 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ +17.3 (c 0.5, CHCl₃, 67% ee); IR (KBr) 3318, 3061, 1706, 1636, 1541, 1257, 1152, 732 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.03 (d, J = 7.6 Hz, 4H), 6.98 (d, J = 7.6 Hz, 4H), 5.82 (br s, 2H), 5.03–4.96 (m, 2H), 4.80 (d, J = 12.0 Hz, 2H), 4.63 (d, J = 12.0 Hz, 2H), 2.27 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 154.9, 137.8, 134.9, 129.3, 127.2, 95.4, 74.6, 60.5, 21.1; m/z (ESI-MS) 592.2 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 230 nm, t_R = 7.0 min (major) and t_R = 8.9 min (minor). Calculated conversion = 49; **s** = 11.

2,2,2-Trichloroethyl((1*R*,2*R*)-2-benzamido-1,2-bis(4-methoxyphenyl)ethyl)carbamate (8e):



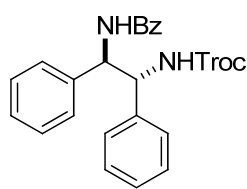
Following the general procedure, compound **8e** was obtained as a white solid in 45% yield (49 mg); mp = 210–213 °C; R_f = 0.10 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ –15.5 (c 0.5, CHCl₃, 70% ee); IR (KBr) 3330, 2950, 2831, 1718, 1637, 1515, 1250, 1176, 1028, 827, 731 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.82–7.78 (comp, 2H), 7.51–7.46 (m, 1H), 7.45–7.38 (comp, 2H), 7.17–7.07 (comp, 2H), 6.84–6.78 (comp, 4H), 6.70–6.60 (comp, 2H), 6.54 (d, J = 10.0 Hz, 1H), 5.89–5.82 (m, 1H), 5.52–5.45 (m, 1H), 4.63 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.7, 159.2, 159.0, 155.4, 133.8, 131.7, 130.9, 130.3, 128.7, 128.6, 128.5(3), 128.5(2), 127.1, 114.0, 95.2, 74.5, 60.6, 59.1, 55.2.; m/z (ESI-MS) 552.6 [M+H]⁺; HPLC: Daicel Chiralpak OJ-H, hexane/*i*-PrOH = 93/7, Flow rate = 1 mL/min, UV = 230 nm, t_R = 20.3 min (major) and t_R = 16.3 min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-bis(4-methoxyphenyl)ethane-1,2-diyl)dicarbamate



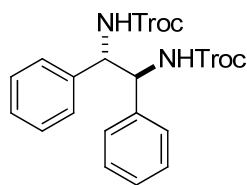
(9e): Following the general procedure, compound **9e** was obtained as a white solid in 44% yield (55mg); mp = 170–172 °C; $R_f = 0.20$ (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20} +22.4$ (c 0.5, CHCl₃, 80% ee); IR (KBr) 3331, 2953, 2836, 1701, 1614, 1516, 1250, 1180, 1031, 831, 733 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.01 v (d, $J = 8.5$ Hz, 4H), 6.75 (d, $J = 8.5$ Hz, 4H), 5.81 (br s, 2H), 5.02–4.91 (m, 2H), 4.81 (d, $J = 12.0$ Hz, 2H), 4.63 (d, $J = 12.0$ Hz, 2H), 3.75 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 159.2, 154.9, 130.0, 128.5, 114.0, 95.4, 74.6, 60.4, 55.2; m/z (ESI-MS) 623.8 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, $t_R = 11.5$ min (major) and $t_R = 9.9$ min (minor). Calculated conversion = 53; **s = 14**.

2,2,2-Trichloroethyl ((1*R*,2*R*)-2-benzamido-1,2-diphenylethyl)carbamate (8f):



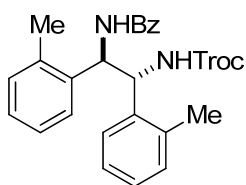
the general procedure, compound **8f** was obtained as a white solid in 40% yield (39 mg); mp = 187–190 °C; $R_f = 0.19$ (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20} -24.0$ (c 0.5, CHCl₃, 72% ee); IR (KBr) 3333, 3053, 2925, 1717, 1653, 1637, 1528, 1144, 1082, 1027, 821, 735 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.78 (d, $J = 7.8$ Hz, 2H), 7.54–7.47 (m, 1H), 7.46–7.39 (comp, 2H), 7.29–7.13 (comp, 10H), 6.15 (d, $J = 8.2$ Hz, 1H), 5.58–5.49 (m, 1H), 5.18–5.06 (m, 1H), 4.73 (d, $J = 12.0$ Hz, 1H), 4.56 (d, $J = 12.0$ Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 167.7, 155.5, 138.5, 138.0, 133.8, 131.8, 128.7(2), 128.6(8), 128.6, 128.2, 128.0, 127.5, 127.4, 127.1, 95.2, 74.5, 61.3, 59.8.; m/z (ESI-MS) 493.2 [M+H]⁺; Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, $t_R = 11.0$ min (major) and $t_R = 8.8$ min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-diphenylethane-1,2-diyl)dicarbamate(9f):



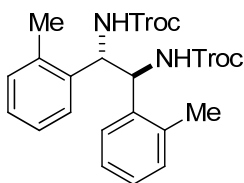
Following the general procedure, compound **9f** was obtained as a white solid in 42% yield (47 mg); mp = 147–150 °C; $R_f = 0.41$ (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20} +24.9$ (c 0.5, CHCl₃, 65% ee); IR (KBr) 3329, 3061, 2955, 1705, 1541, 1254, 1148, 1082, 1027, 820, 733 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.25–7.16 (comp, 6H), 7.15–7.01 (comp, 4H), 5.93 (br s, 2H), 5.09–4.98 (m, 2H), 4.82 (d, $J = 12.0$ Hz, 2H), 4.63 (d, $J = 12.0$, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 154.9, 137.8, 128.7, 128.2, 127.3, 95.3, 74.7, 61.1; m/z (ESI-MS) 564.1 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, $t_R = 6.1$ min (major) and $t_R = 7.4$ min (minor). Calculated conversion = 47; **s = 12**.

2,2,2-Trichloroethyl((1*R*,2*R*)-2-benzamido-1,2-di-*o*-tolylethyl)carbamate (8g):



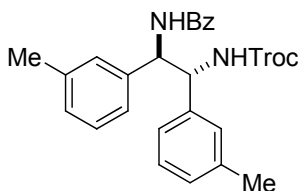
Following the general procedure, compound **8g** was obtained as a white solid in 41% yield (43 mg); mp = 220–222 °C; R_f = 0.24 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ –21.0 (c 0.5, CHCl₃, 76% ee); IR (KBr) 3328, 3061, 1713, 1636, 1541, 1257, 1152, 732 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.79 (d, J = 7.7 Hz, 2H), 7.61–7.47 (comp, 3H), 7.46–7.39 (comp, 2H), 7.27–7.17 (comp, 2H), 7.15–7.07 (comp, 3H), 7.03–6.93 (comp, 2H), 6.02–5.89 (comp, 2H), 5.52–5.45 (m, 1H), 4.67 (d, J = 12.0 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 2.08 (s, 3H), 2.03 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.7, 155.7, 136.8, 136.2, 136.6, 136.1, 133.8, 131.8, 130.7, 130.6, 128.6, 128.1, 127.9, 127.1, 126.6, 126.5, 126.4, 126.3, 95.1, 74.5, 56.8, 55.2, 19.3, 19.2(7); m/z (ESI-MS) 520.7 [M+H]⁺; Daicel Chiralpak AD-H, hexane/*i*-PrOH = 95/5, Flow rate = 1 mL/min, UV = 230 nm, t_R = 8.8 min (major) and t_R = 7.1 min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-di-*o*-tolylethane-1,2-diyl)dicarbamate (9g):



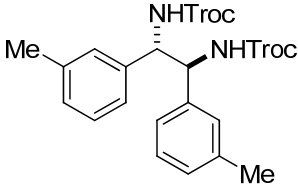
Following the general procedure, compound **9g** was obtained as a white solid in 44% yield (52 mg); mp = 177–178 °C; $[\alpha]_D^{20}$ +23.1 (c 0.5, CHCl₃, 75% ee); R_f = 0.47 (Hexanes/EtOAc 6:1 v/v); IR (KBr) 3320, 3055, 2950, 1707, 1650, 1527, 1255, 713 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.44 (d, J = 7.5 Hz, 2H), 7.20 (app t, J = 7.4 Hz, 2H), 7.11 (app t, J = 7.4 Hz, 2H), 6.96 (d, J = 7.5 Hz, 2H), 5.92 (br s, 2H), 5.40 (dd, J = 5.9, 2.3 Hz, 2H), 4.82 (d, J = 12.0 Hz, 2H), 4.64 (d, J = 12.0 Hz, 2H), 2.00 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 155.3, 136.7, 136.2, 130.7, 128.1, 126.4, 126.3(7), 95.3, 74.7, 56.5, 19.2; m/z (ESI-MS) 592.2 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 230 nm, t_R = 7.2 min (major) and t_R = 9.0 min (minor). Calculated conversion = 50; **s = 16**.

Bis(2,2,2-trichloroethyl)((1*R*,2*R*)-1,2-di-*m*-tolylethane-1,2-diyl)dicarbamate (8h):



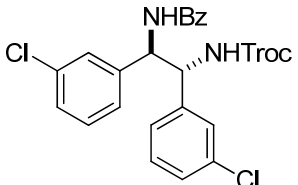
Following the general procedure, compound **8h** was obtained as a white solid in 40% yield (41 mg); mp = 199–201 °C; IR (KBr) 3337, 3056, 2947, 1718, 1653, 1527, 1254, 711, 568 cm⁻¹; R_f = 0.24 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ –14.2 (c 0.5, CHCl₃, 45% ee); ¹H NMR (500 MHz, CDCl₃) 7.79 (d, J = 7.5 Hz, 2H), 7.53–7.47 (m, 1H), 7.46–7.38 (comp, 2H), 7.20–7.07 (comp, 4H), 7.06–6.97 (comp, 4H), 6.01 (d, J = 8.4 Hz, 1H), 5.53–5.47 (m, 1H), 5.10–5.04 (m, 1H), 4.71 (d, J = 12.0 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 2.26 (s, 3H), 2.27 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.7, 155.4, 138.4, 138.3, 138.2(6), 138.0, 133.8, 131.7, 128.8, 128.7, 128.5, 128.4(7), 128.2, 128.0, 127.1, 124.6, 95.2, 74.5, 61.1, 59.5, 21.3, 21.2(8); m/z (ESI-MS) 520.8 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 230 nm, t_R = 8.6 min (major) and t_R = 5.7 min (minor).

Bis(2,2,2-trichloroethyl) ((1*S*,2*S*)-1,2-di-*m*-tolylethane-1,2-diyl)dicarbamate (9h):



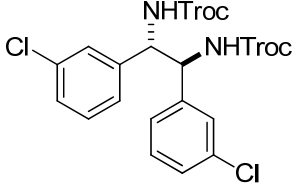
Following the general procedure, compound **9h** was obtained as a white solid in 41% yield (48 mg); mp = 190–192 °C; R_f = 0.46 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ +12.4 (c 0.5, CHCl₃, 44% ee); IR (KBr) 3318, 3055, 2950, 1707, 1650, 1527, 1255, 713 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.14–7.07 (comp, 2H), 7.06–6.98 (comp, 2H), 6.90 (s, 2H), 6.86 (d, J = 7.4 Hz, 2H), 5.88 (br s, 2H), 5.02–4.96 (m, 2H), 4.82 (d, J = 12.0 Hz, 2H), 4.63 (d, J = 12.0 Hz, 2H), 2.25 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 154.9, 138.4, 137.7, 128.9, 128.5, 128.0, 124.5, 95.4, 74.6, 60.8, 21.3; m/z (ESI-MS) 592.2 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 98/2, Flow rate = 1 mL/min, UV = 230 nm, t_R = 9.0 min (major) and t_R = 16.3 min (minor). Calculated conversion = 49; **s** = 4.0.

2,2,2-Trichloroethyl((1*R*,2*R*)-2-benzamido-1,2-bis(3-chlorophenyl)ethyl)carbamate (8i):



Following the general procedure, compound **8i** was obtained as a white solid in 39% yield (43 mg); mp = 203–205 °C; R_f = 0.21 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ -27.7 (c 0.5, CHCl₃, 82% ee); IR (KBr) 3336, 3061, 2949, 1714, 1636, 1528, 1252, 1084, 702 cm⁻¹; ¹H NMR (400 MHz, (CD₃)₂SO) δ 8.47 (s, 1H), 7.64 (d, J = 7.2, 2H), 7.58–7.34 (comp, 10H) 7.37–7.26(m, 1H), 6.82 (br s, 1H), 5.17 (d, J = 6.3 Hz, 1H), 4.68 (d, J = 6.3 Hz, 1H), 4.04 (s, 2H); ¹³C NMR (100 MHz, (CD₃)₂SO) δ 166.1, 154.1, 142.5, 142.4(8), 134.0, 132.8, 132.7(6), 131.5, 129.9, 128.3, 127.1, 127.0(9), 127.0, 126.9, 126.8, 125.8, 125.5, 96.0, 73.4, 58.4, 56.3; m/z (ESI-MS) 561.9 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 230 nm, t_R = 9.2 min (major) and t_R = 7.6 min (minor).

Bis(2,2,2-trichloroethyl)((1*S*,2*S*)-1,2-bis(3-chlorophenyl)ethane-1,2-diyl)dicarbamate

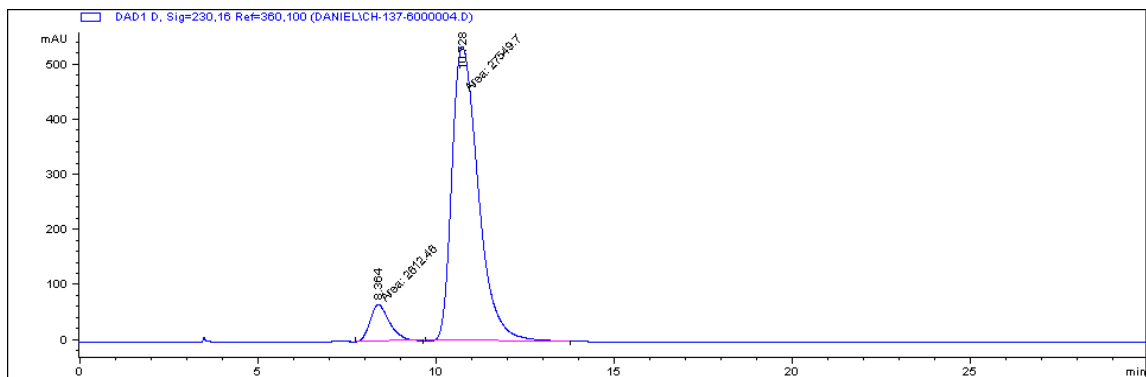
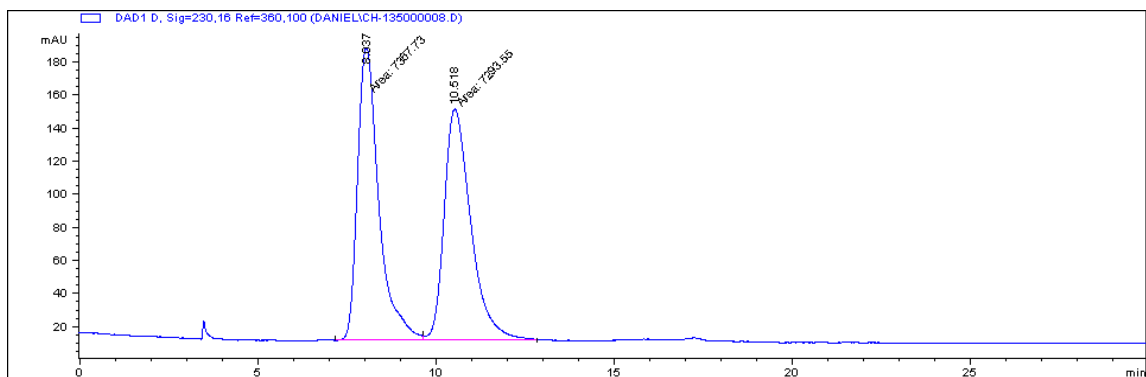
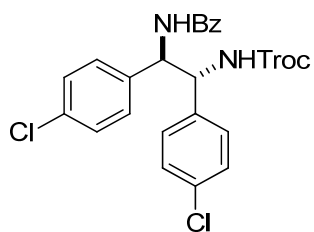


(9i): Following the general procedure, compound **9i** was obtained as a white solid in 43% yield (54 mg); mp = 199–202 °C; R_f = 0.48 (Hexanes/EtOAc 6:1 v/v); $[\alpha]_D^{20}$ +25.5 (c 0.5, CHCl₃, 70% ee); IR (KBr) 3331, 2952, 1709, 1537, 1277, 1144, 1092, 821 cm⁻¹; ¹H NMR (500 MHz, (CD₃)₂SO) δ 8.30 (d, J = 8.2 Hz, 2H), 7.50 (s, 2H), 7.36–7.26 (comp, 6H), 5.20 (d, J = 8.1 Hz, 2H), 4.72 (d, J = 12.4 Hz, 2H), 4.68 (d, J = 12.4 Hz, 2H); ¹³C NMR (125 MHz, (CD₃)₂SO) δ 154.1, 142.2, 132.9, 130.1, 127.2, 126.7, 125.5, 96.0, 73.4, 58.3; m/z (ESI-MS) 633.4 [M+H]⁺; HPLC: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 97/3, Flow rate = 1 mL/min, UV = 230 nm, t_R = 6.8 min (major) and t_R = 8.0 min (minor). Calculated conversion = 46; **s** = 21.

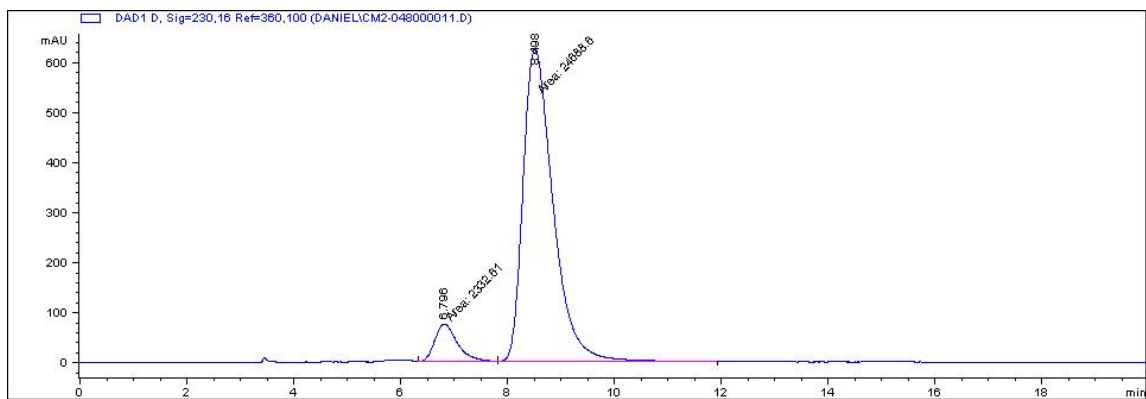
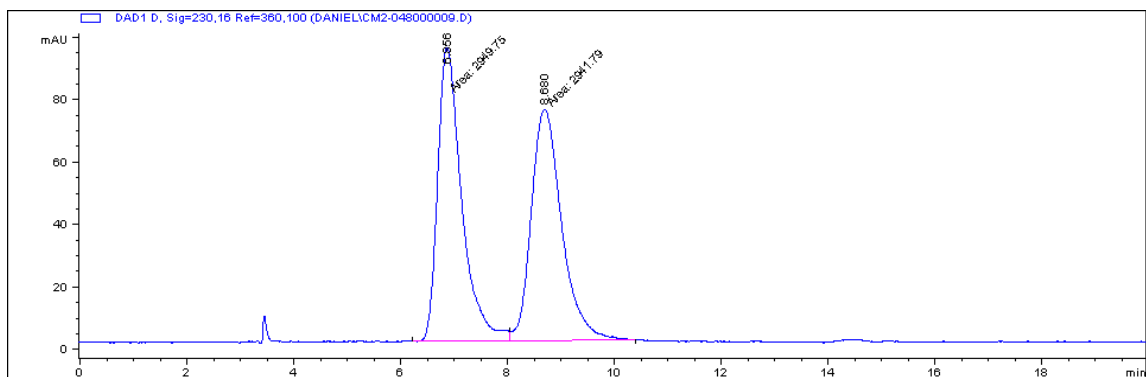
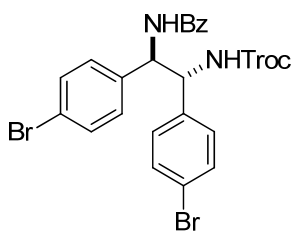
References:

- [1] D. C. Braddock, J. M. Redmond, S. A. Hermitage, A. J. White, *Adv. Synth. Catal.* 2006, **348**, 911.
- [2] E. J. Corey, F. N. M. Kuhnle, *Tetrahedron Lett.* 1997, **38**, 8631.
- [3] E. J. Corey, D. Lee, S. Sarshar, *Tetrahedron: Asymmetry* 1995, **6**, 3.
- [4] H. B. Kagan, J. C. Fiaud, *Top. Stereochem.* 1988, **18**, 249.

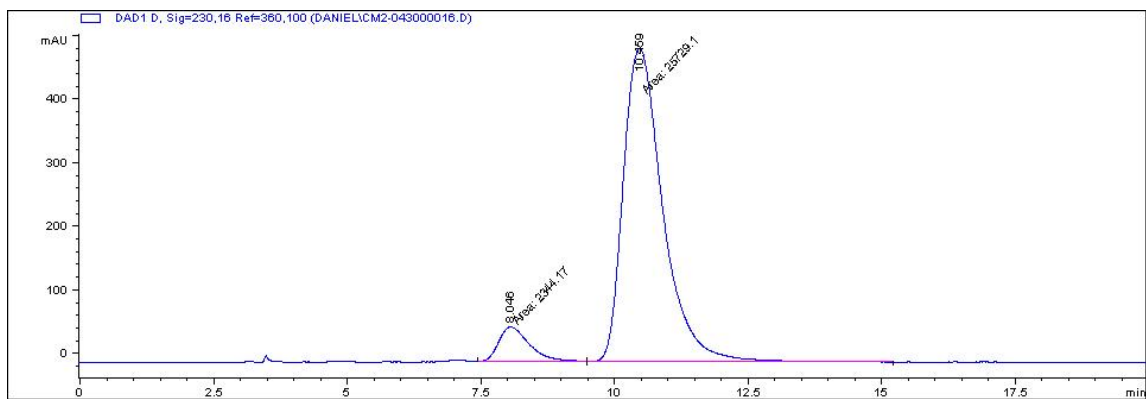
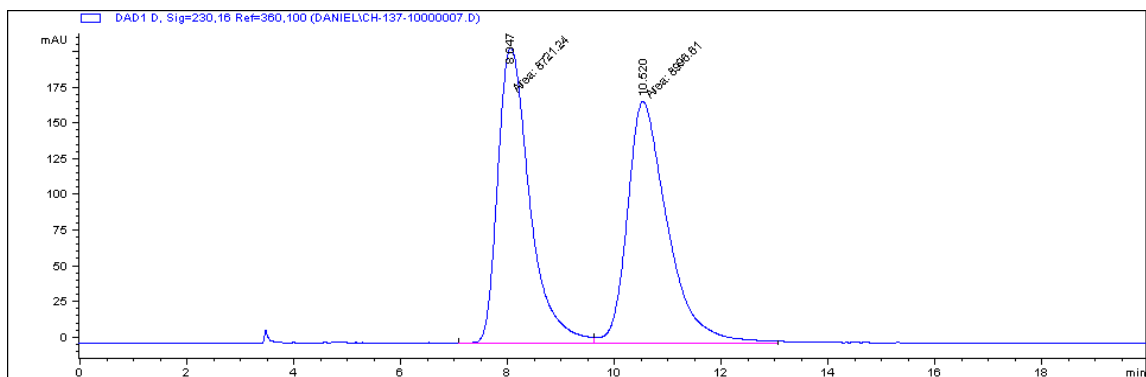
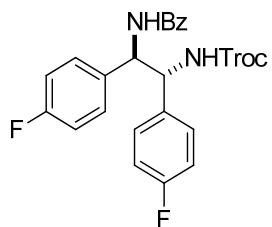
HPLC Profile of **8a**



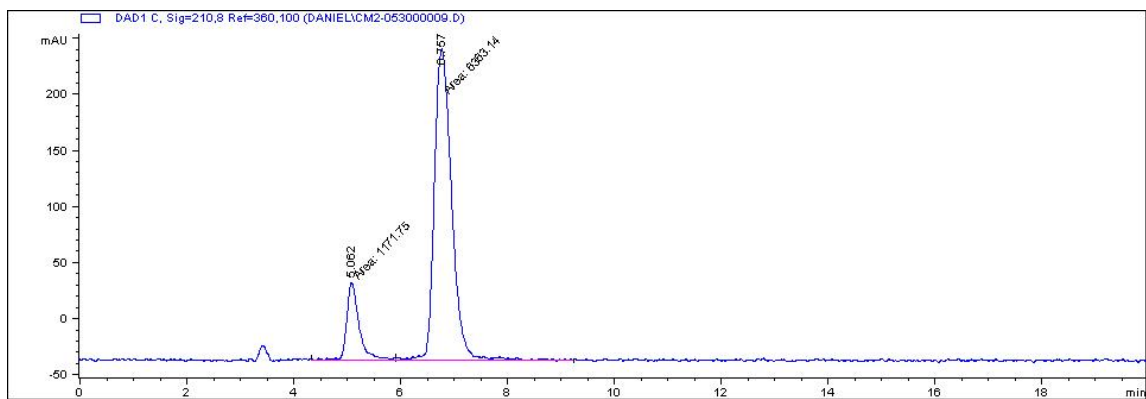
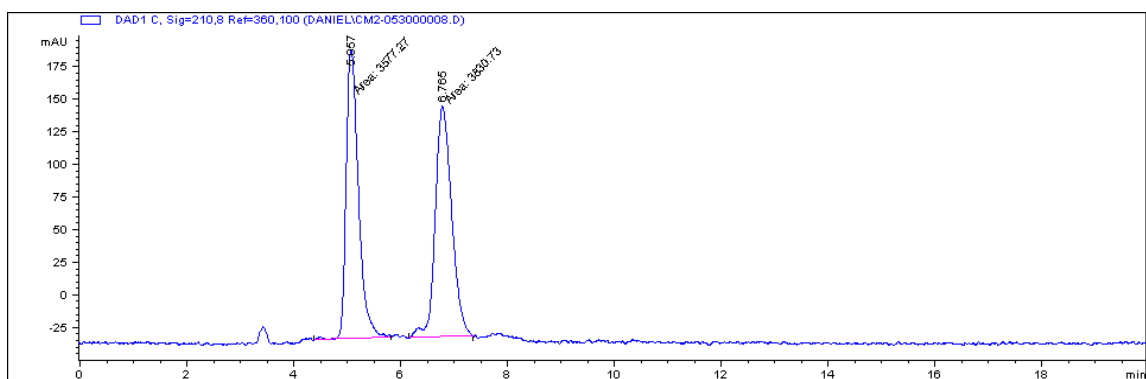
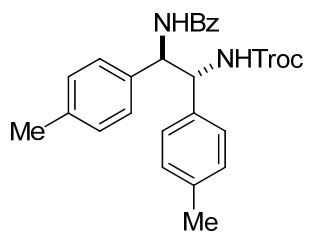
HPLC Profile of **8b**



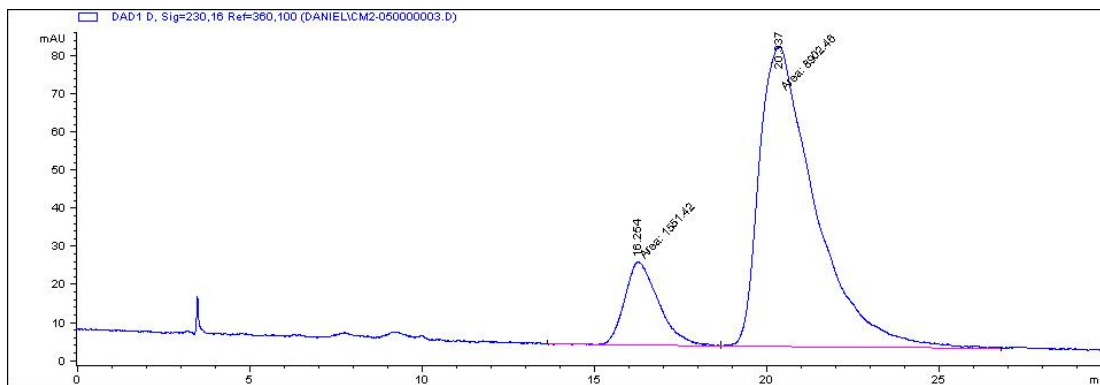
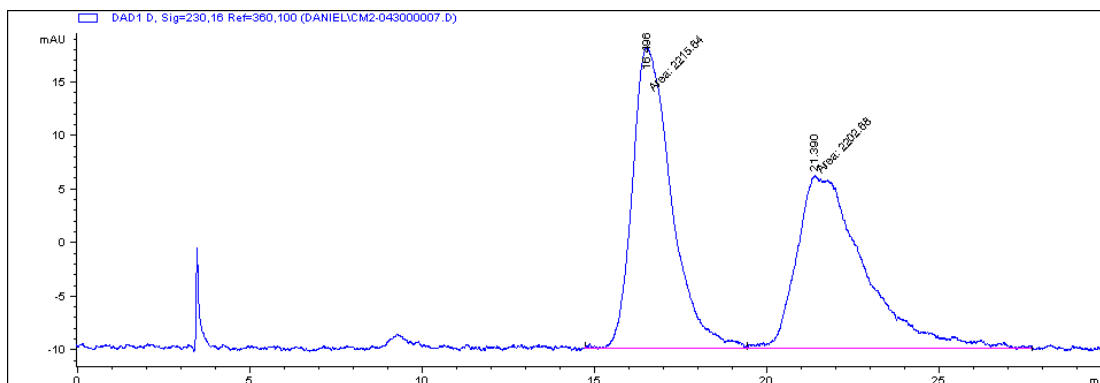
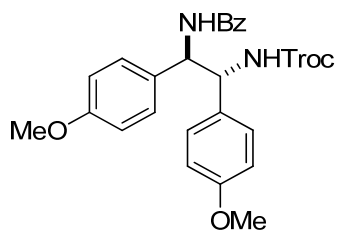
HPLC Profile of **8c**



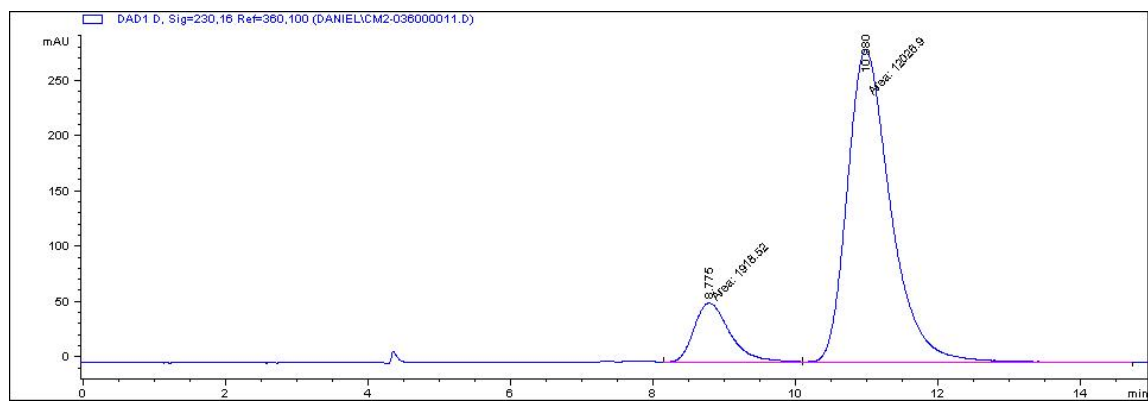
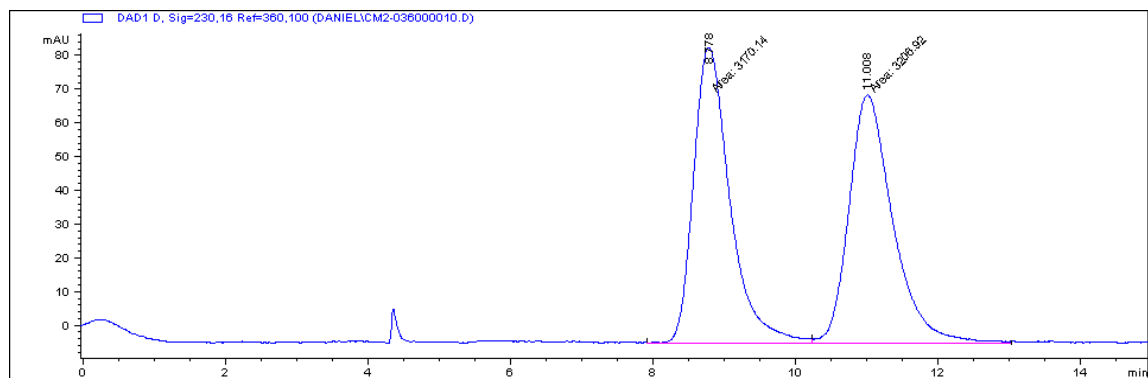
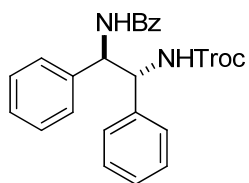
HPLC Profile of **8d**



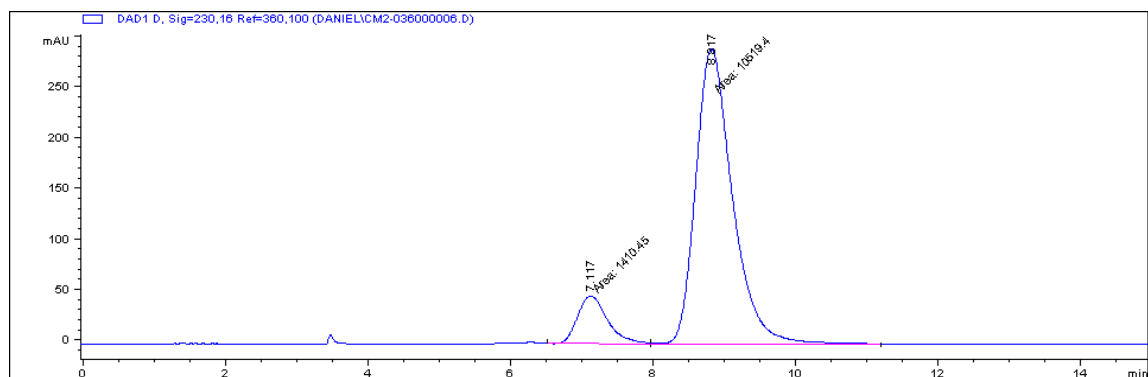
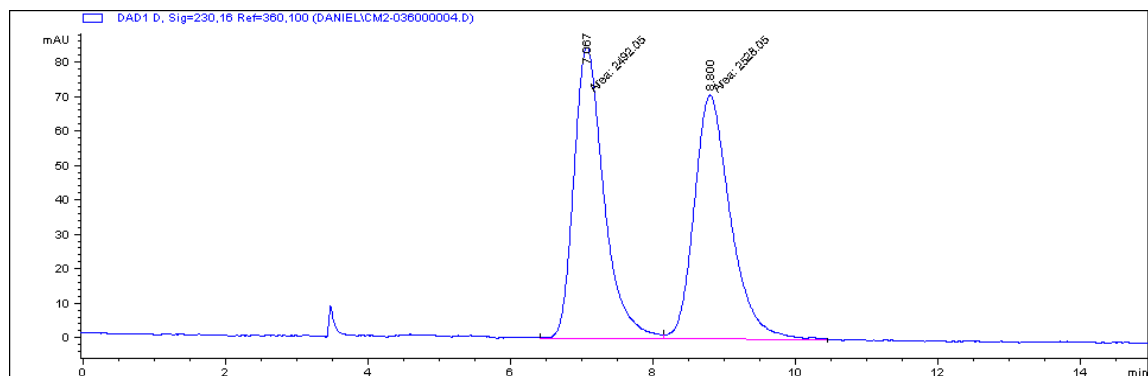
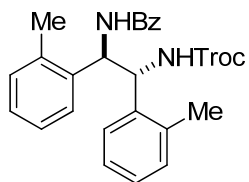
HPLC Profile of **8e**



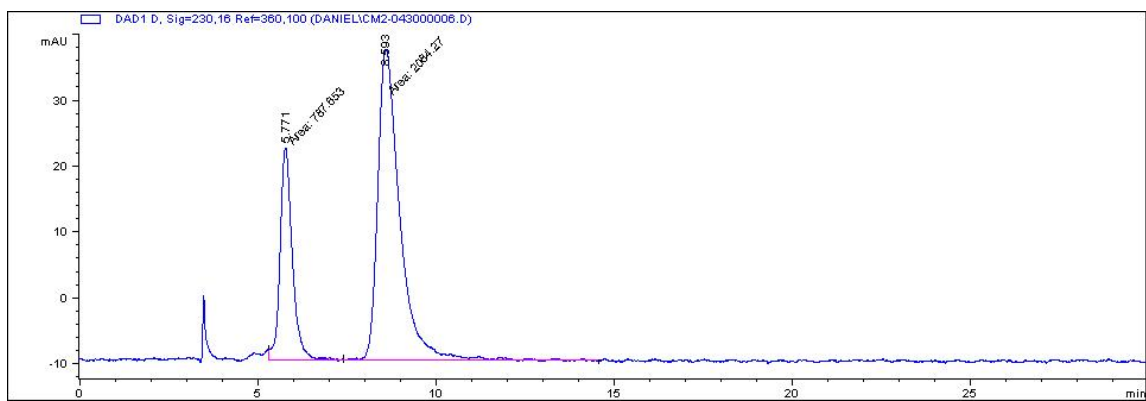
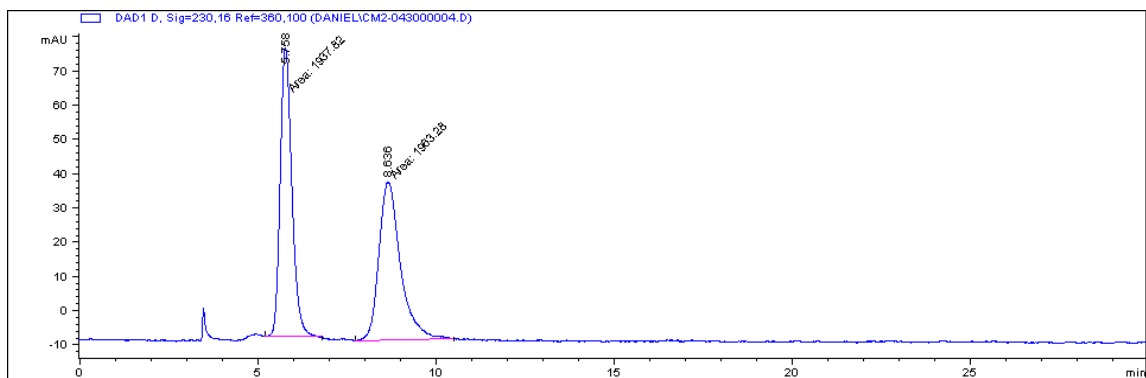
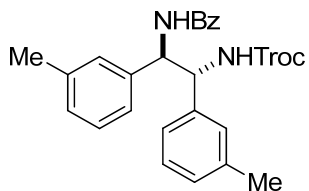
HPLC Profile of **8f**



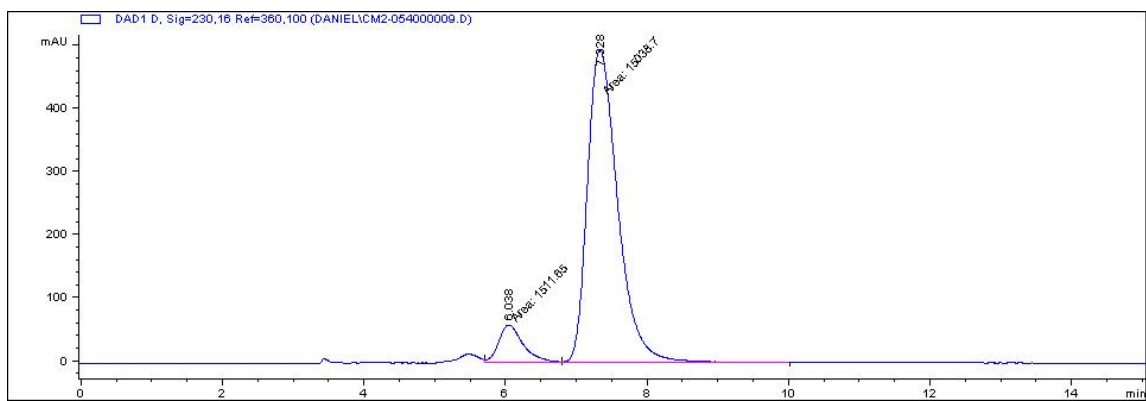
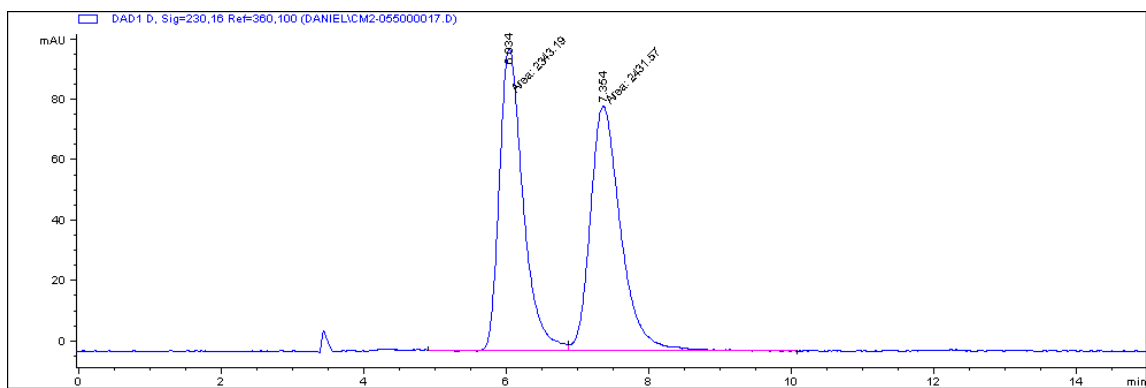
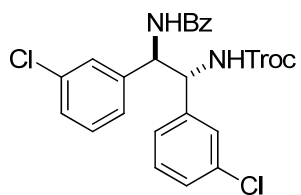
HPLC Profile of **8g**



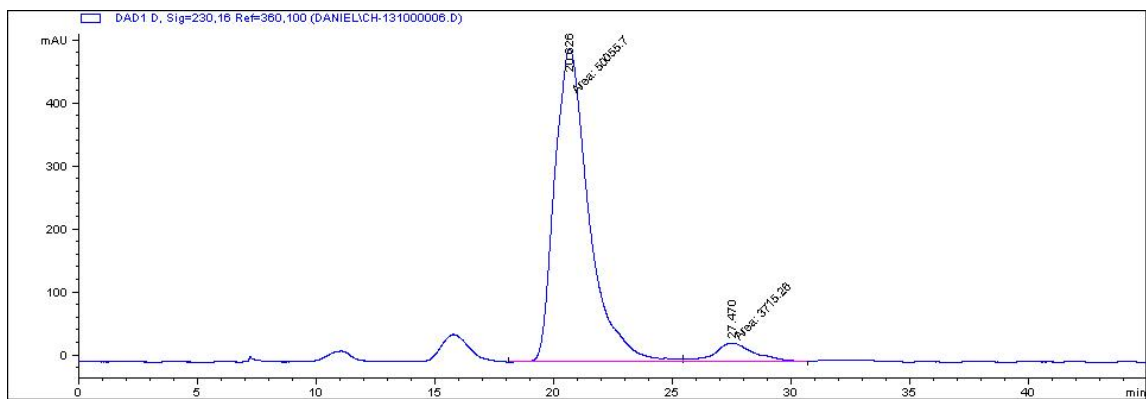
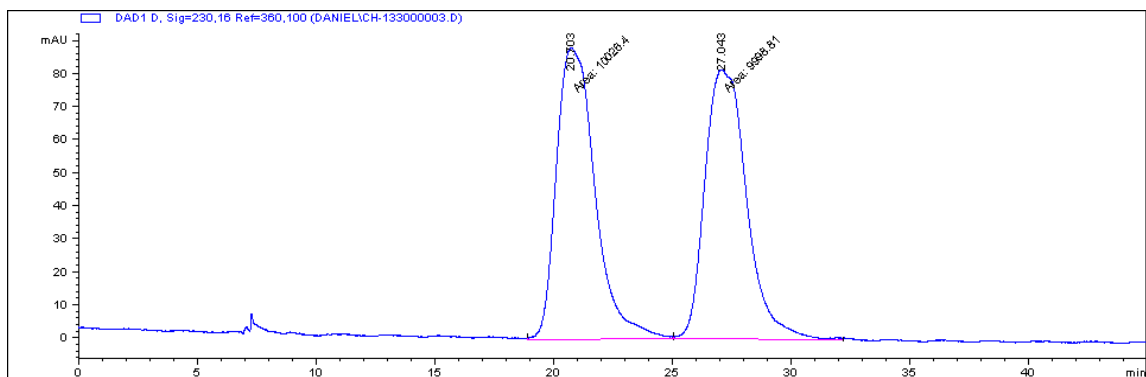
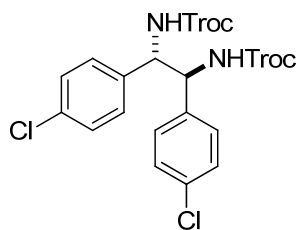
HPLC Profile of **8h**



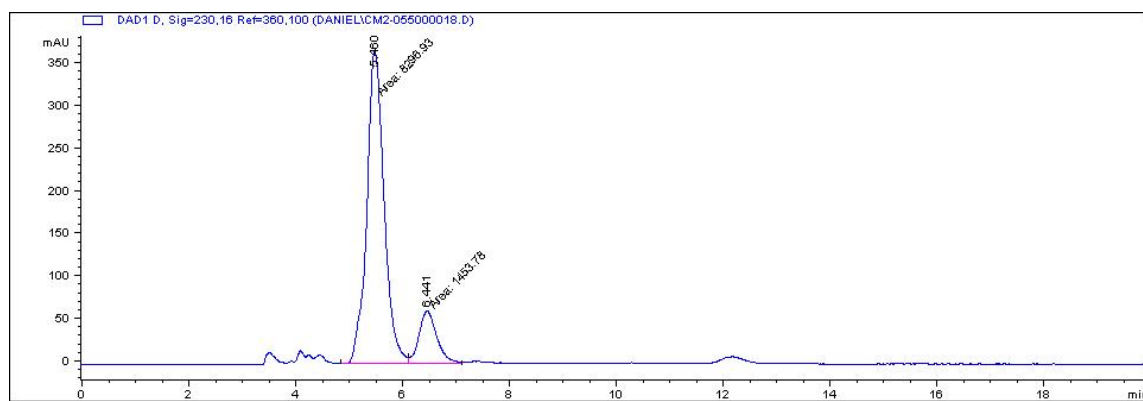
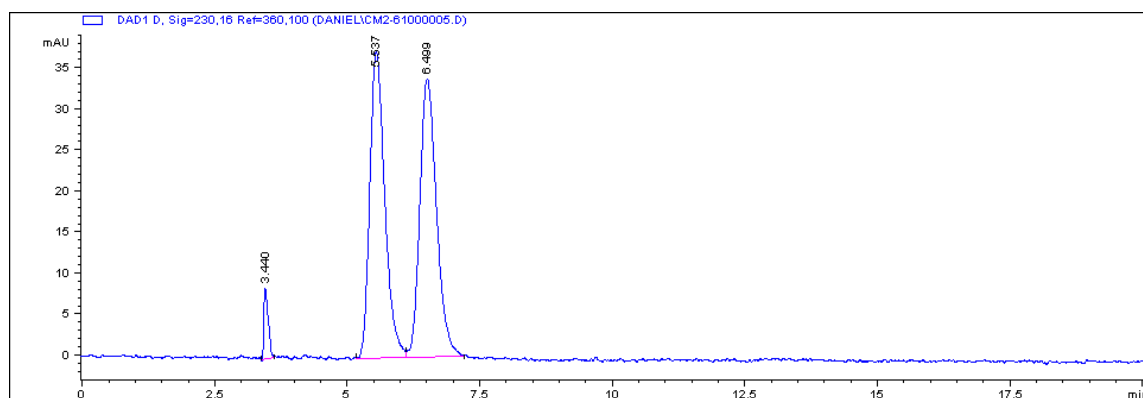
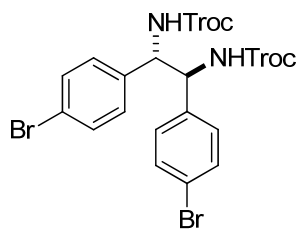
HPLC Profile of **8i**



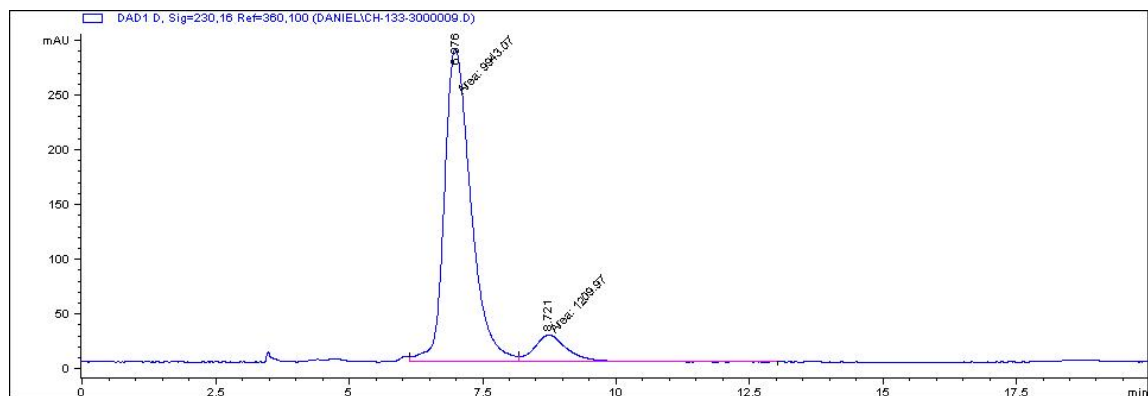
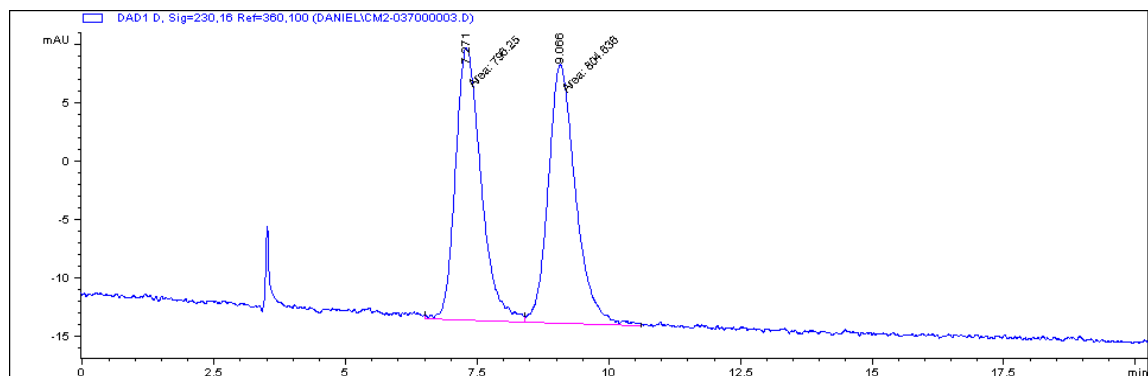
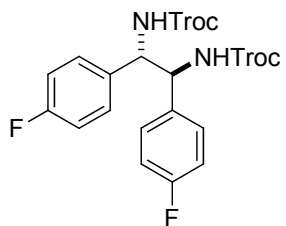
HPLC Profile of 9a



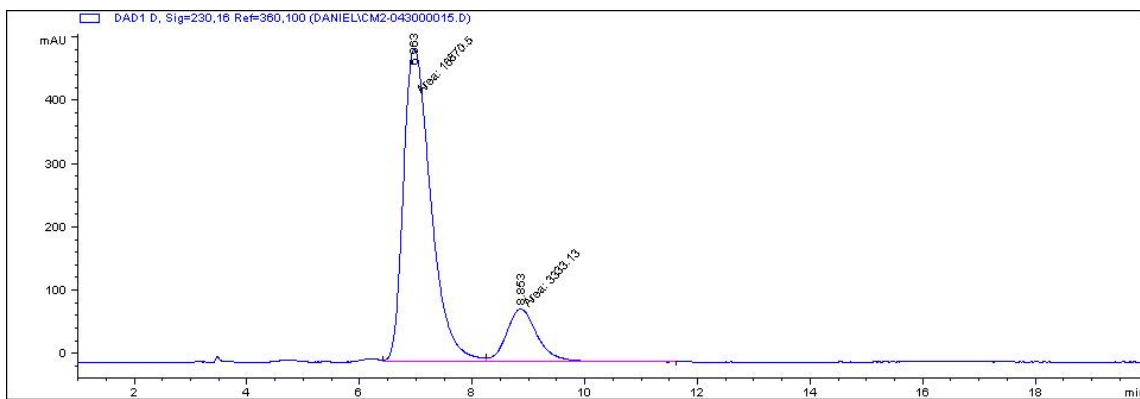
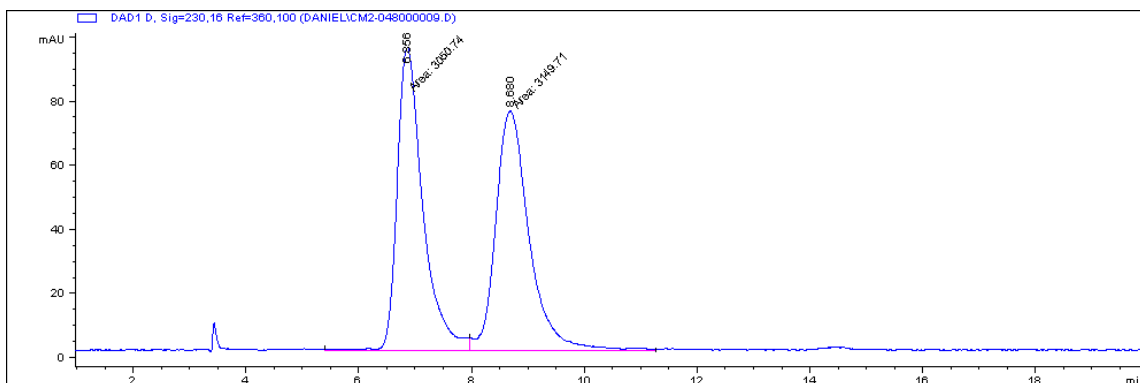
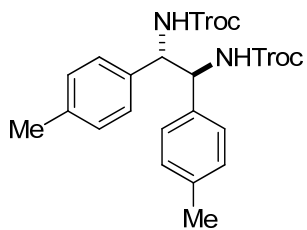
HPLC Profile of **9b**



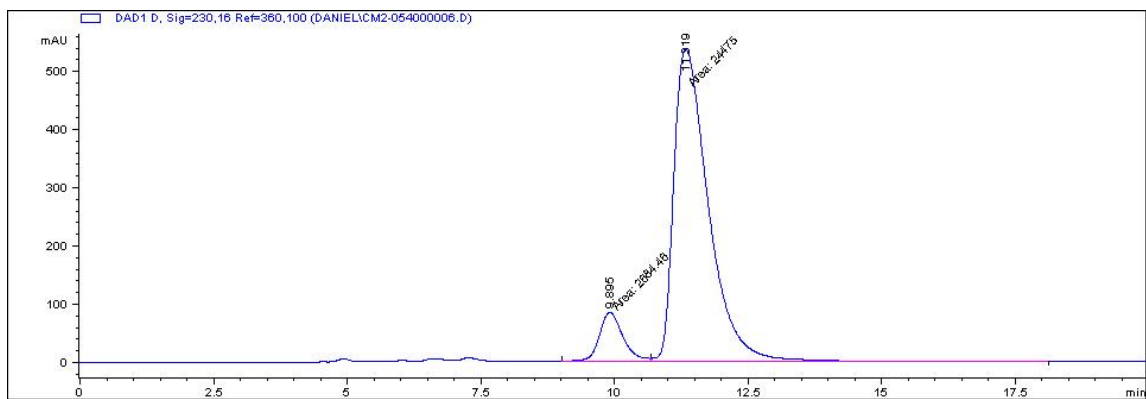
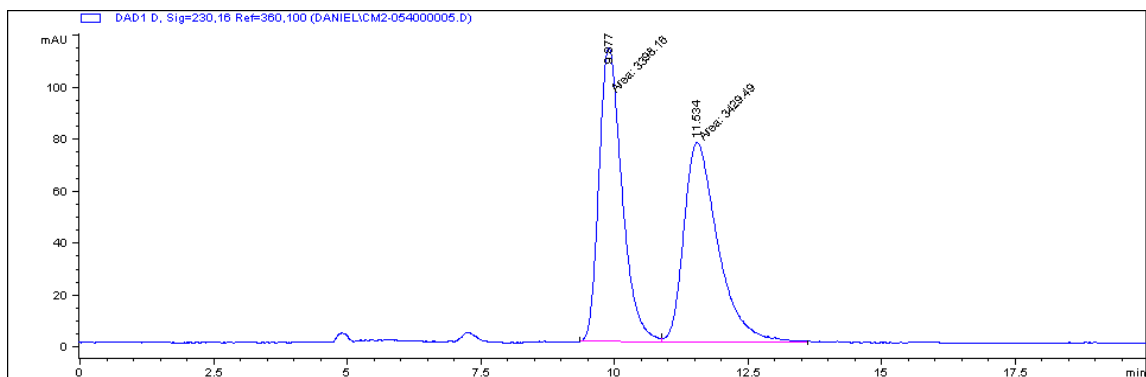
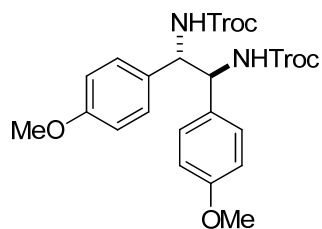
HPLC Profile of 9c



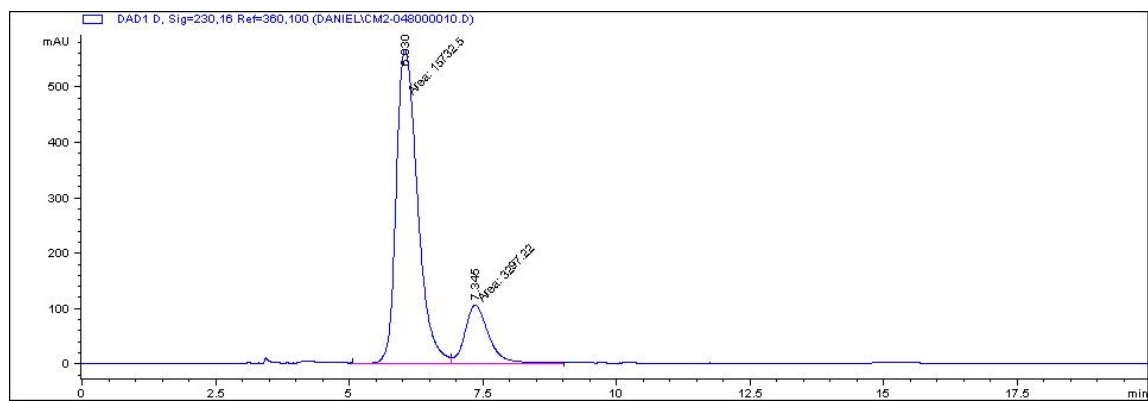
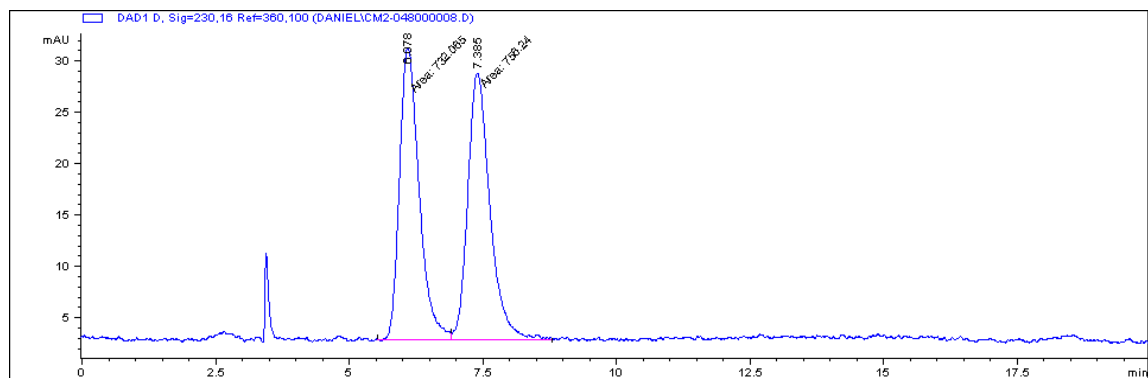
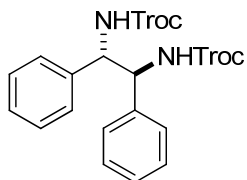
HPLC Profile of 9d



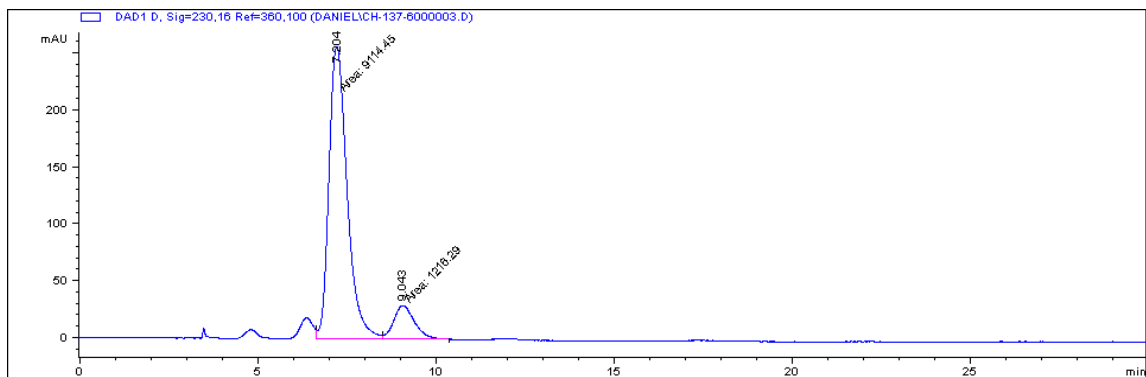
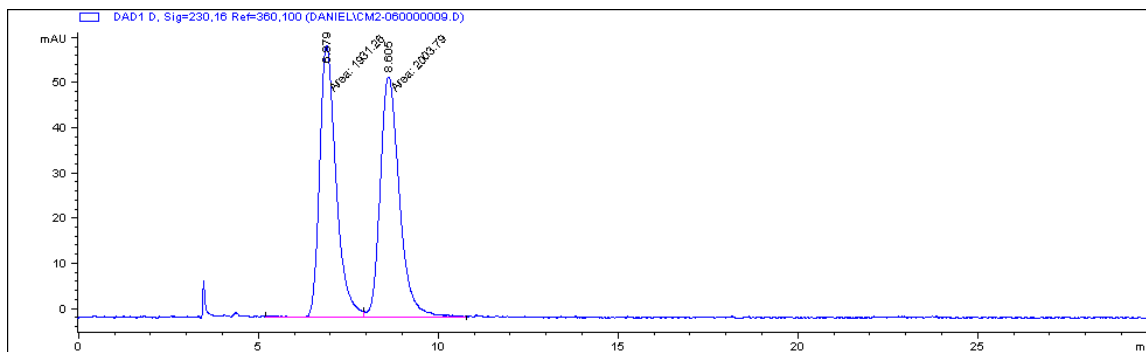
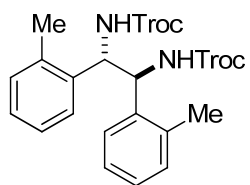
HPLC Profile of 9e



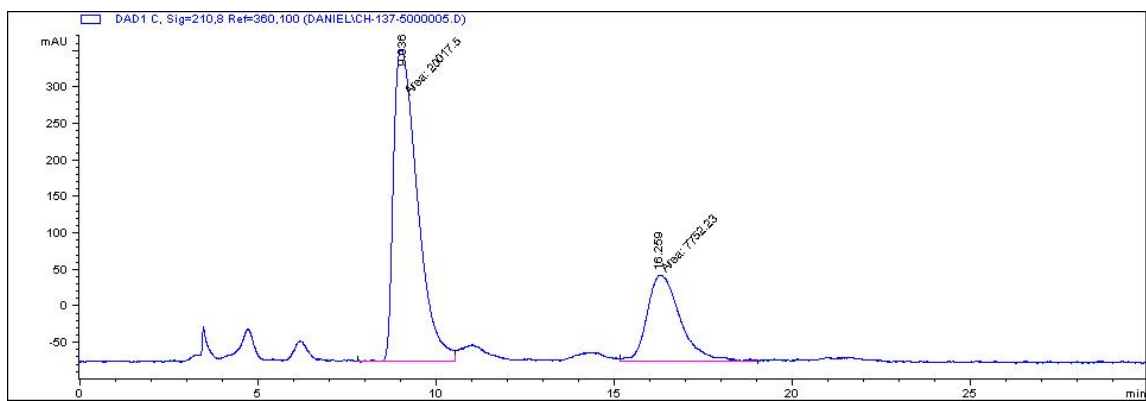
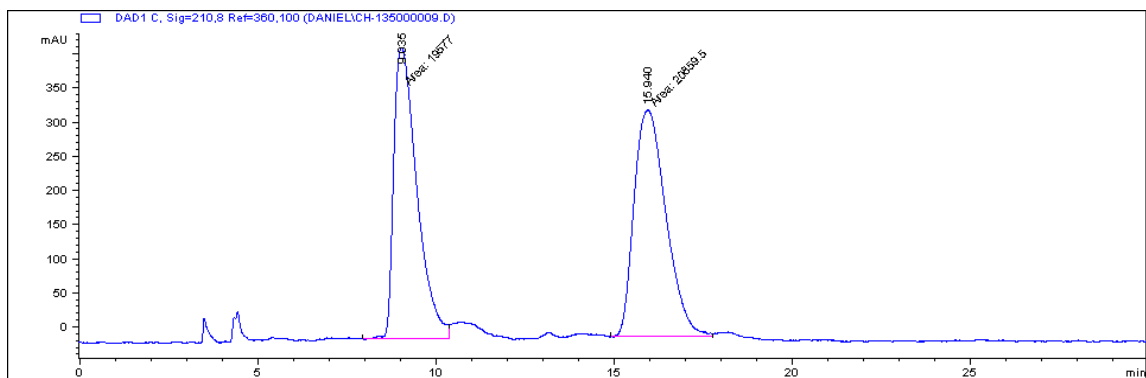
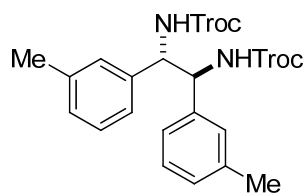
HPLC Profile of **9f**



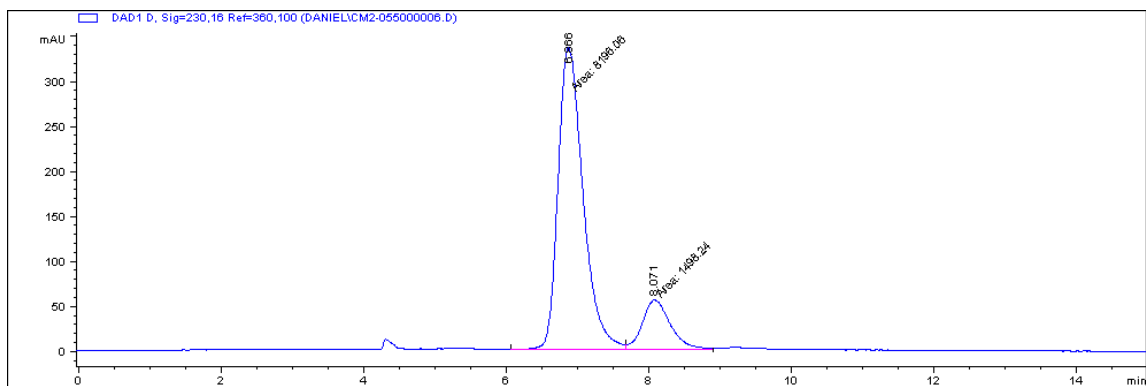
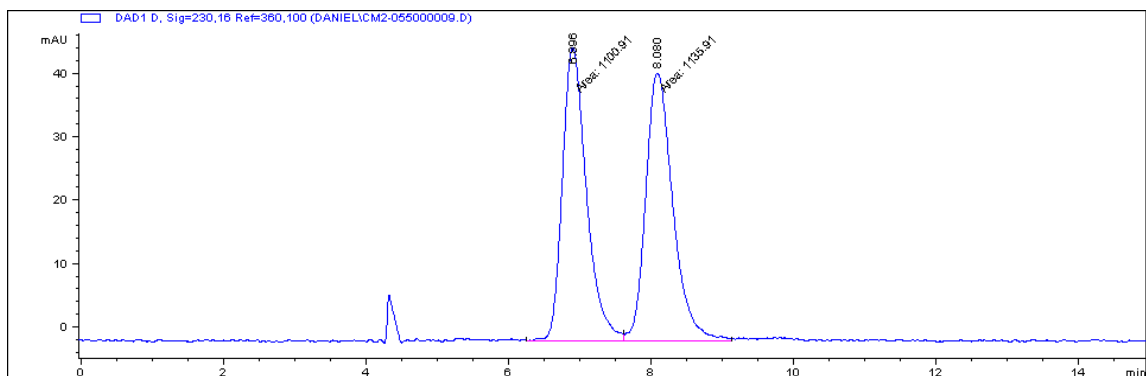
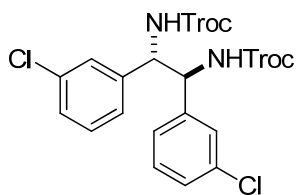
HPLC Profile of 9g



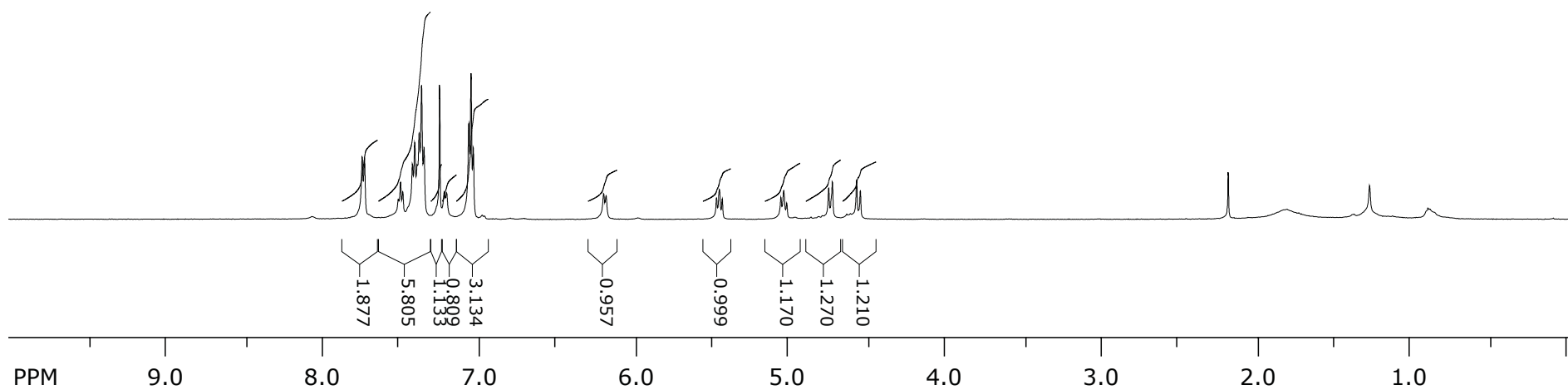
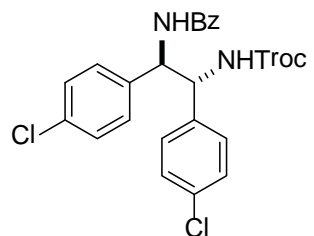
HPLC Profile of **9h**



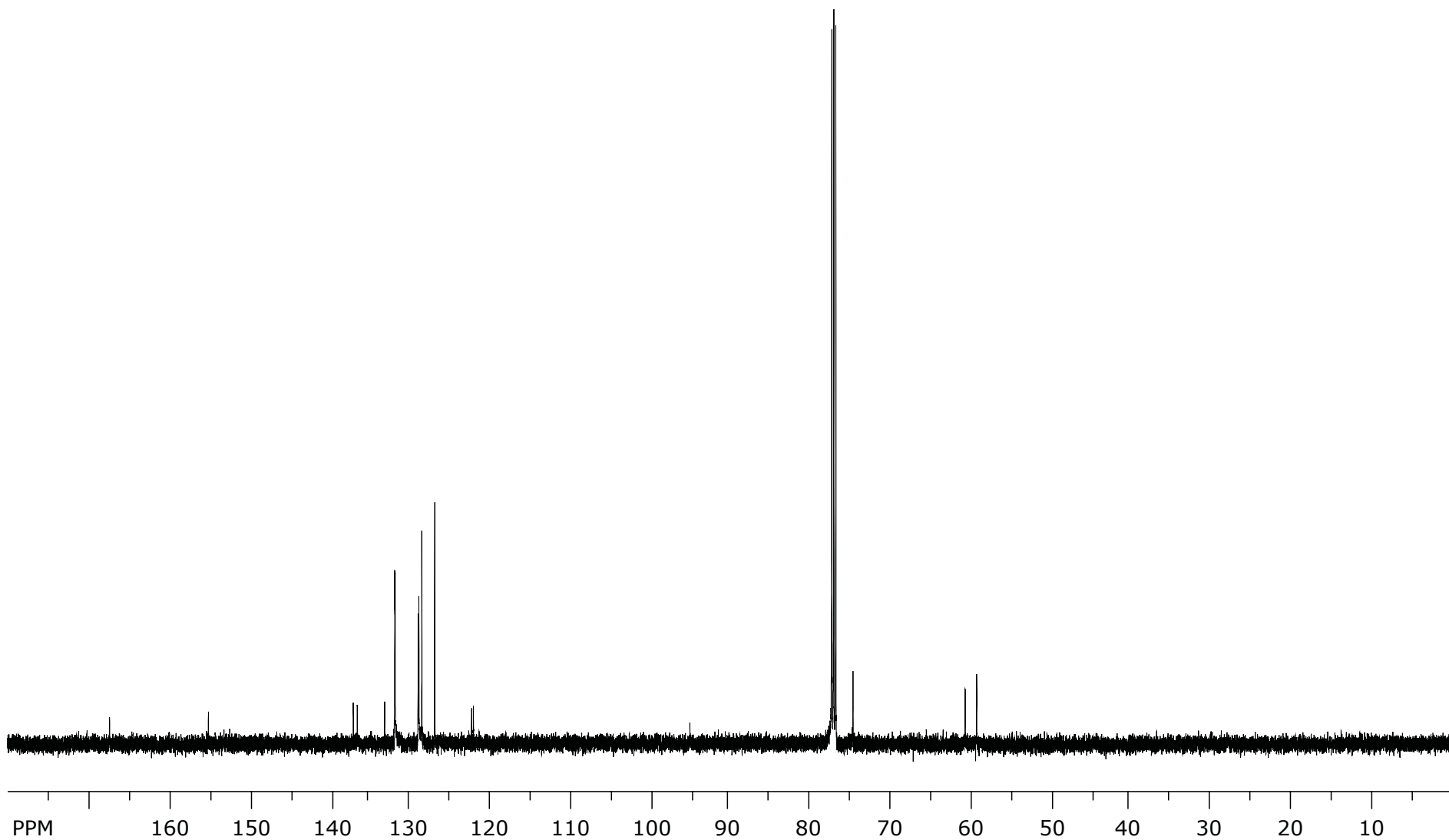
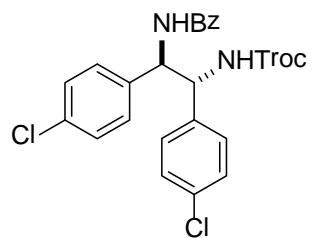
HPLC Profile of **9i**



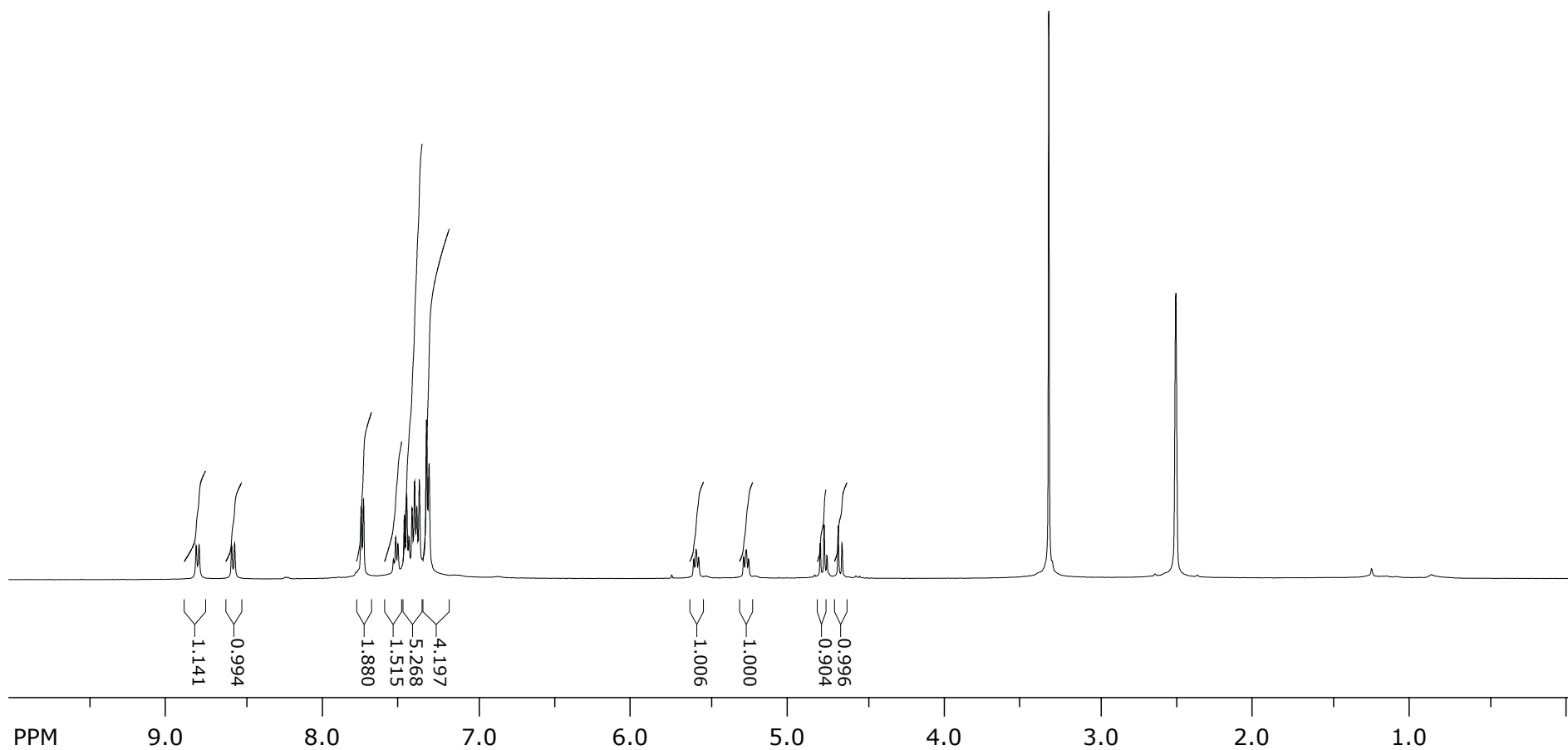
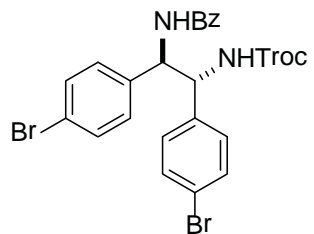
^1H NMR of **8a** in CDCl_3



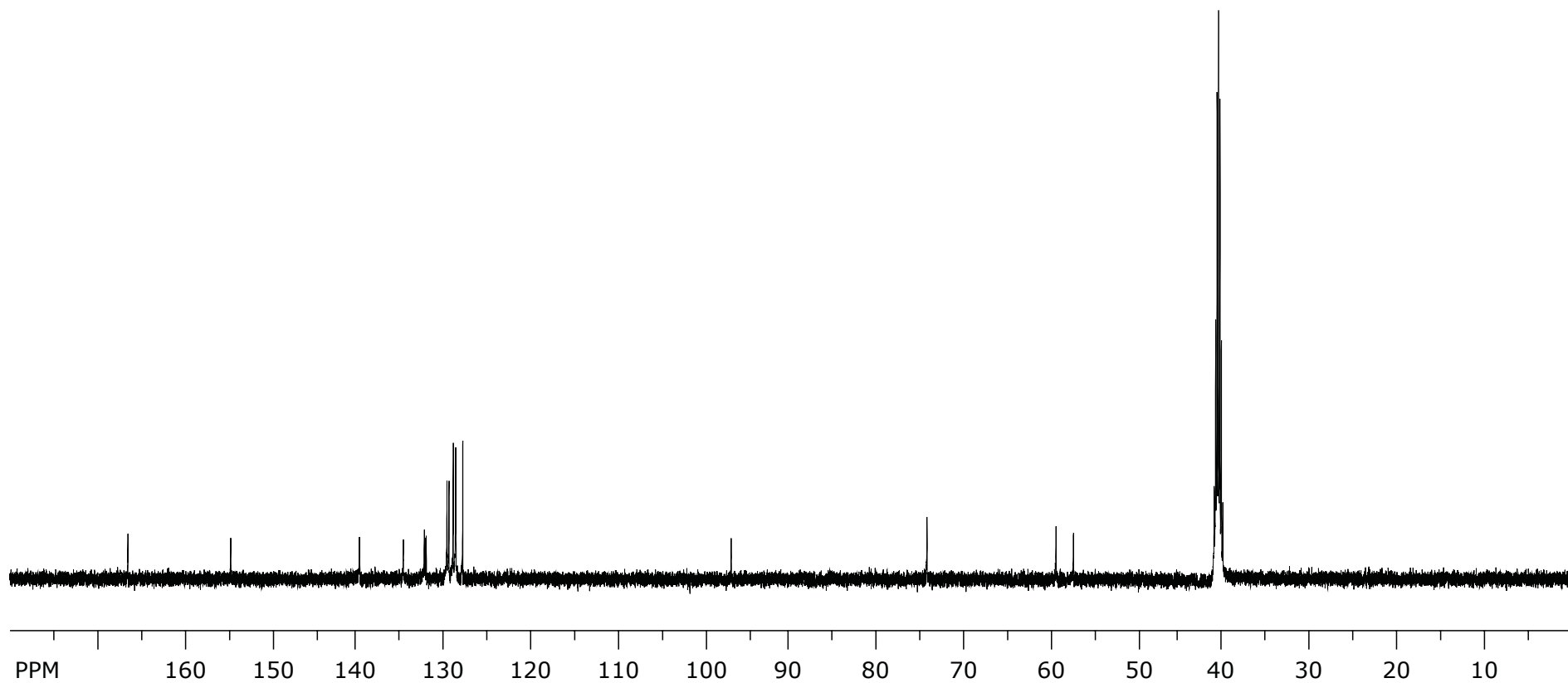
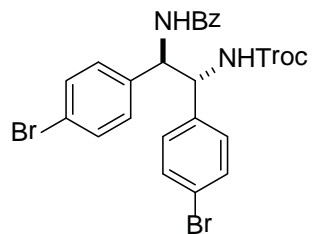
^{13}C NMR of **8a** in CDCl_3



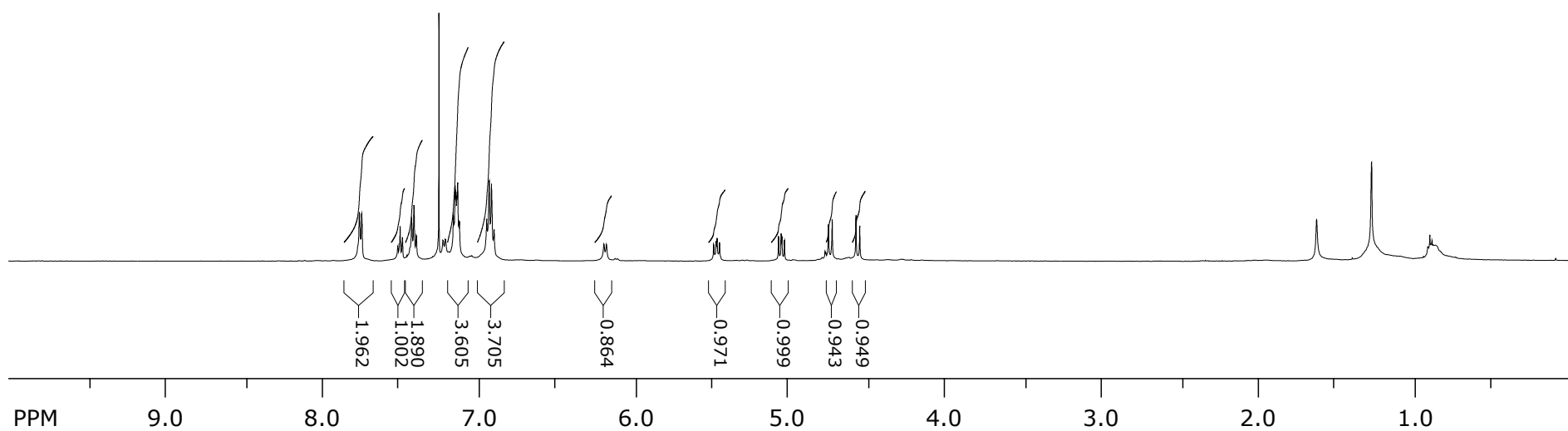
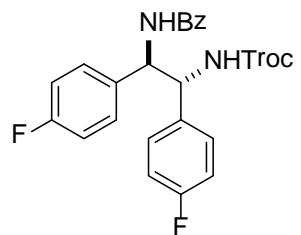
^1H NMR of **8b** in $(\text{CD}_3)_2\text{SO}$



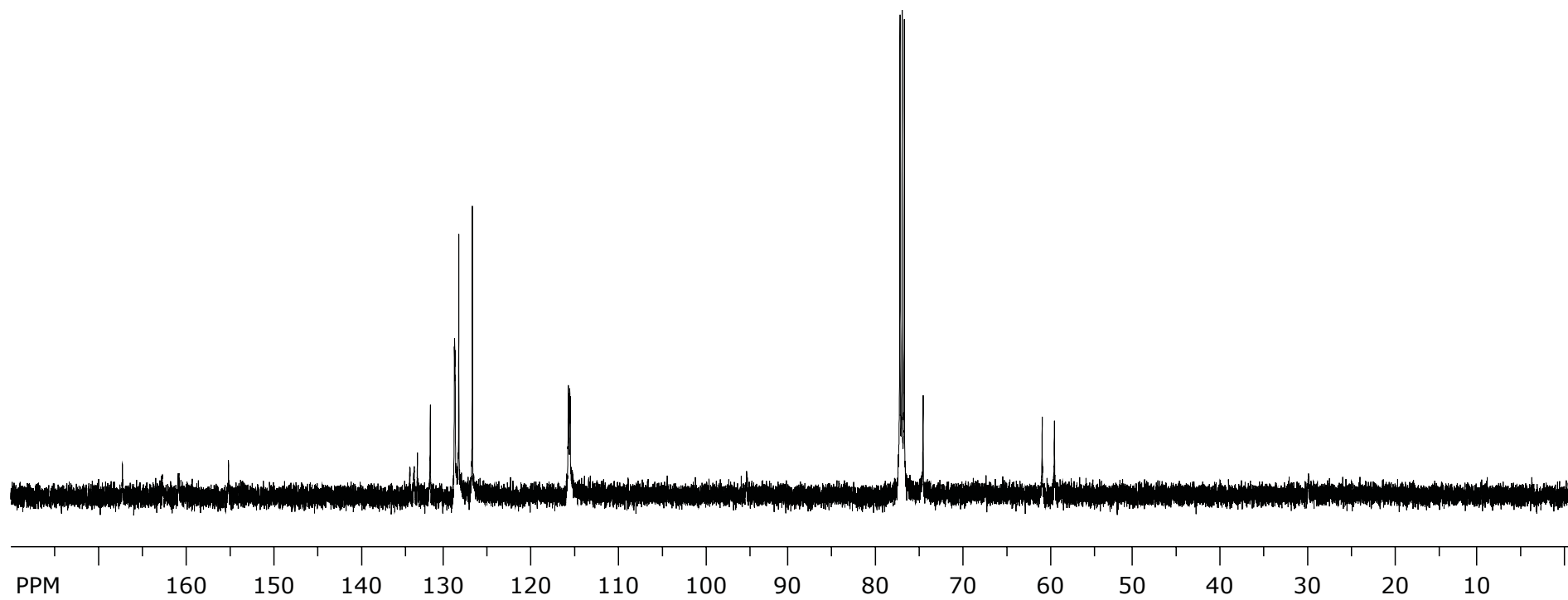
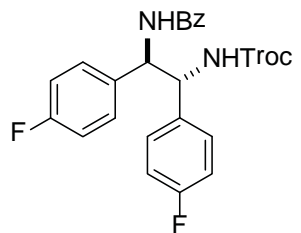
^{13}C NMR of **8b** in $(\text{CD}_3)_2\text{SO}$



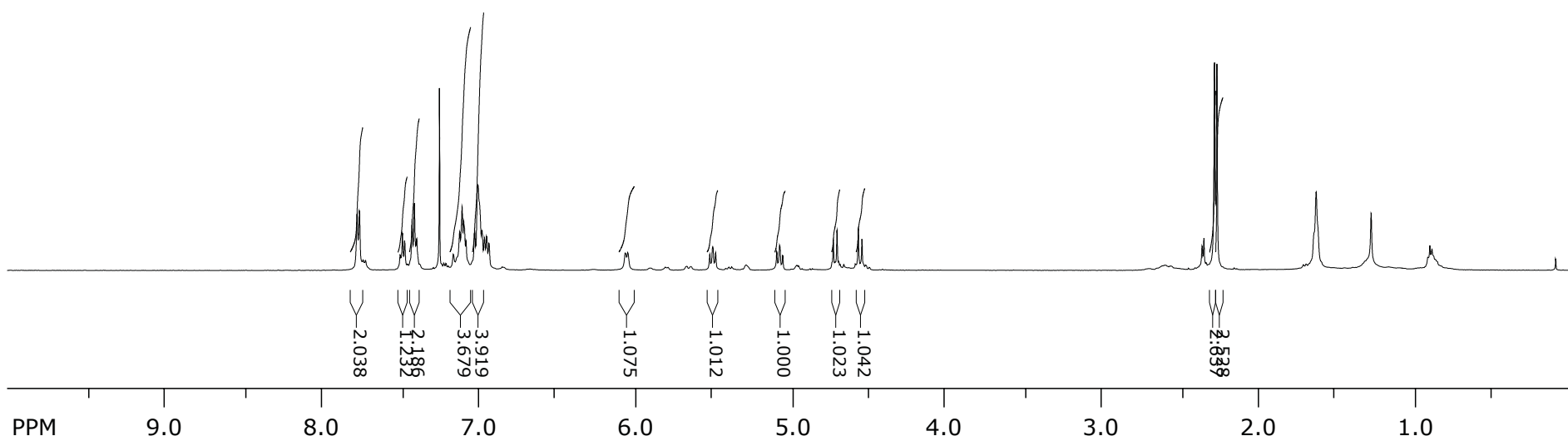
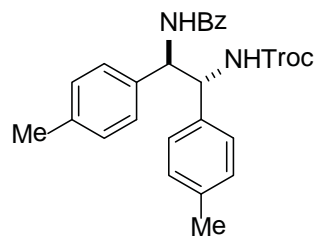
^1H NMR of **8c** in CDCl_3



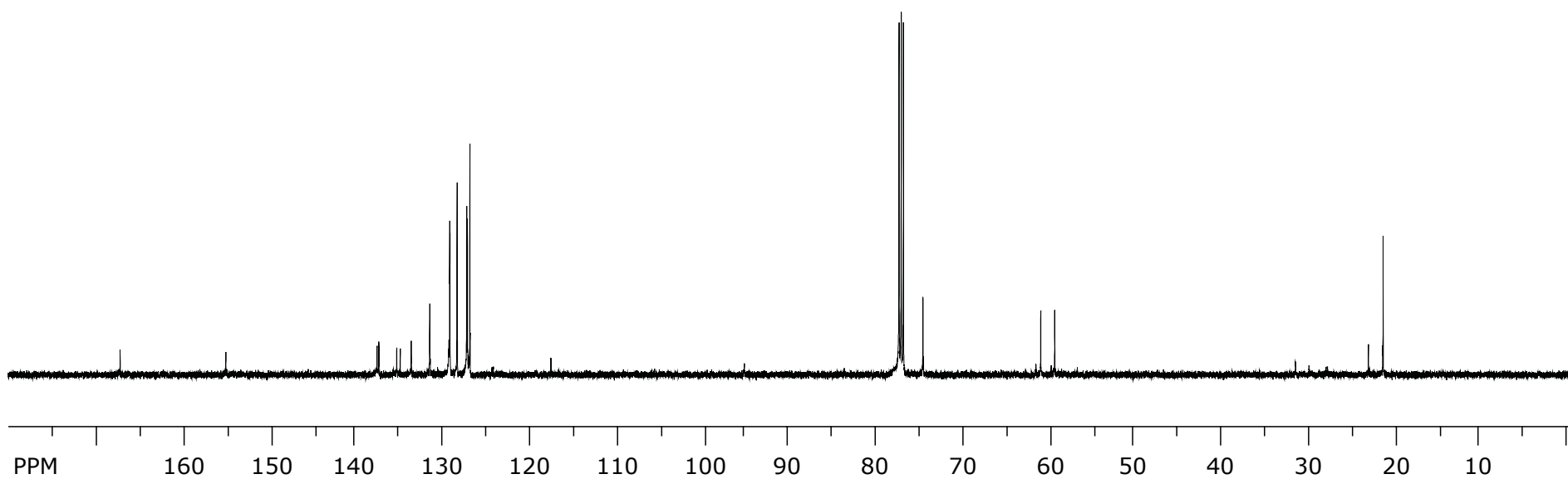
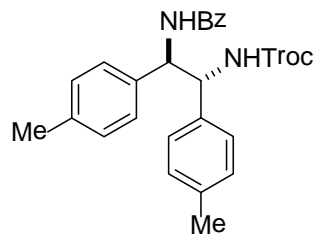
^{13}C NMR of **8c** in CDCl_3



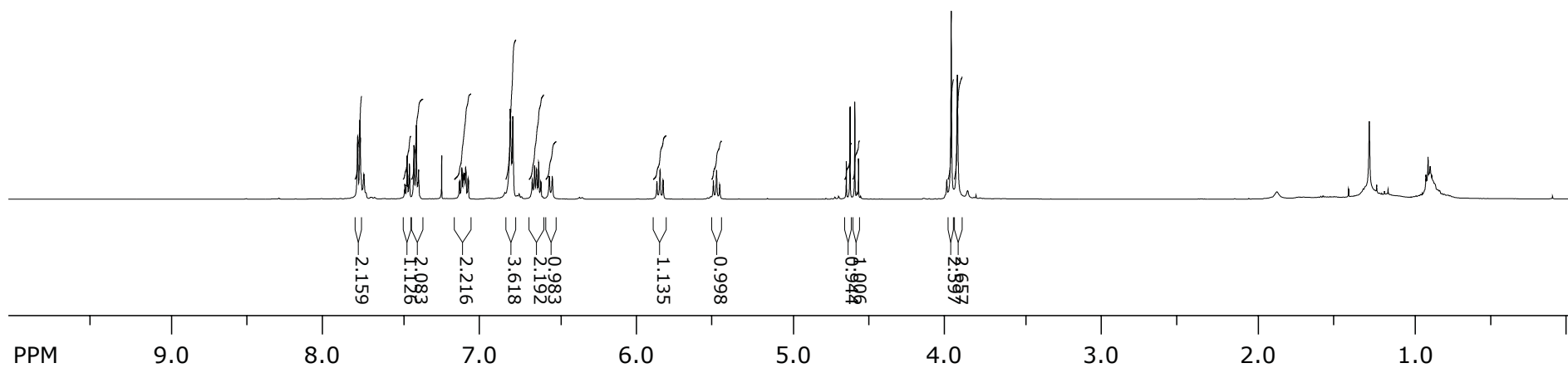
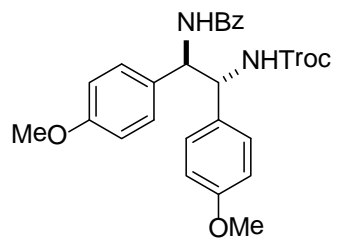
^1H NMR of **8d** in CDCl_3



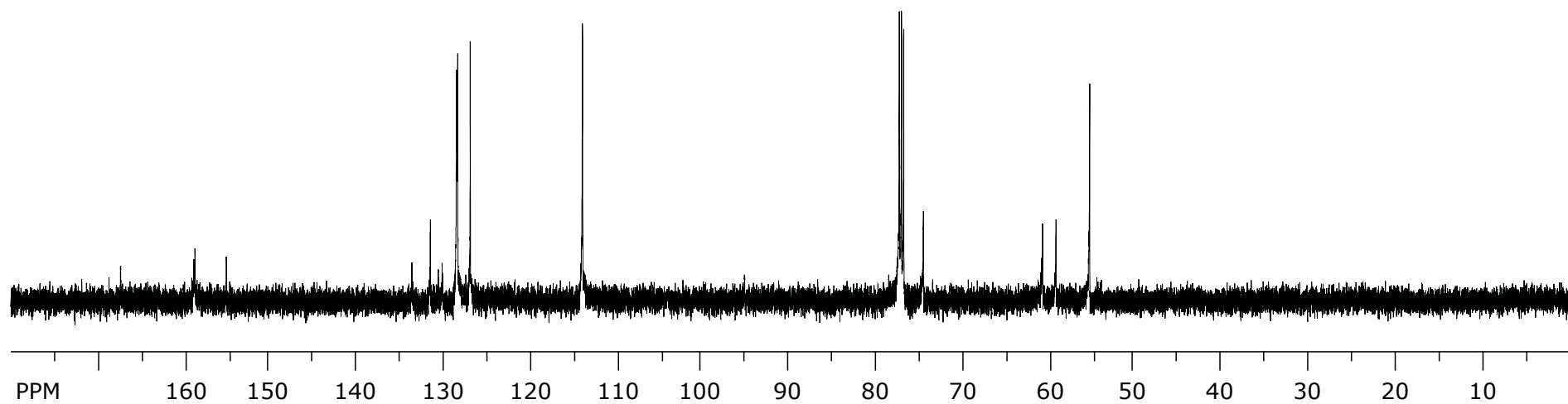
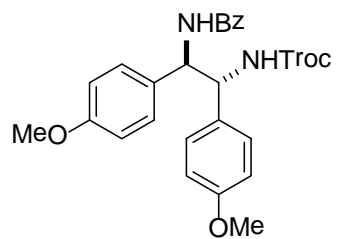
^{13}C NMR of **8d** in CDCl_3



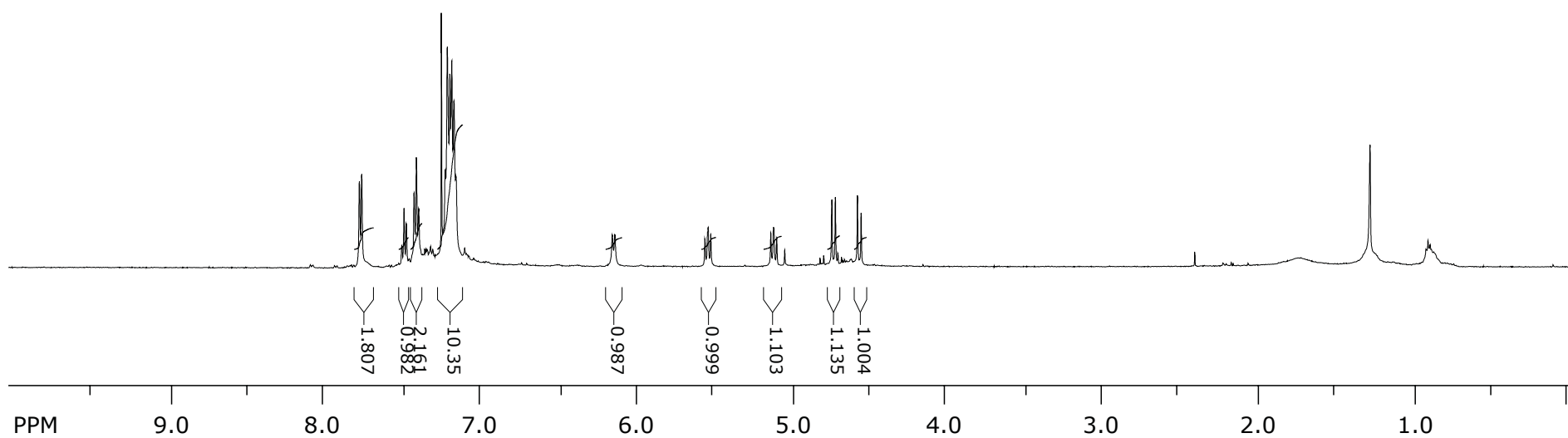
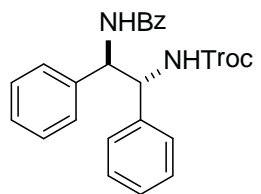
^1H NMR of **8e** in CDCl_3



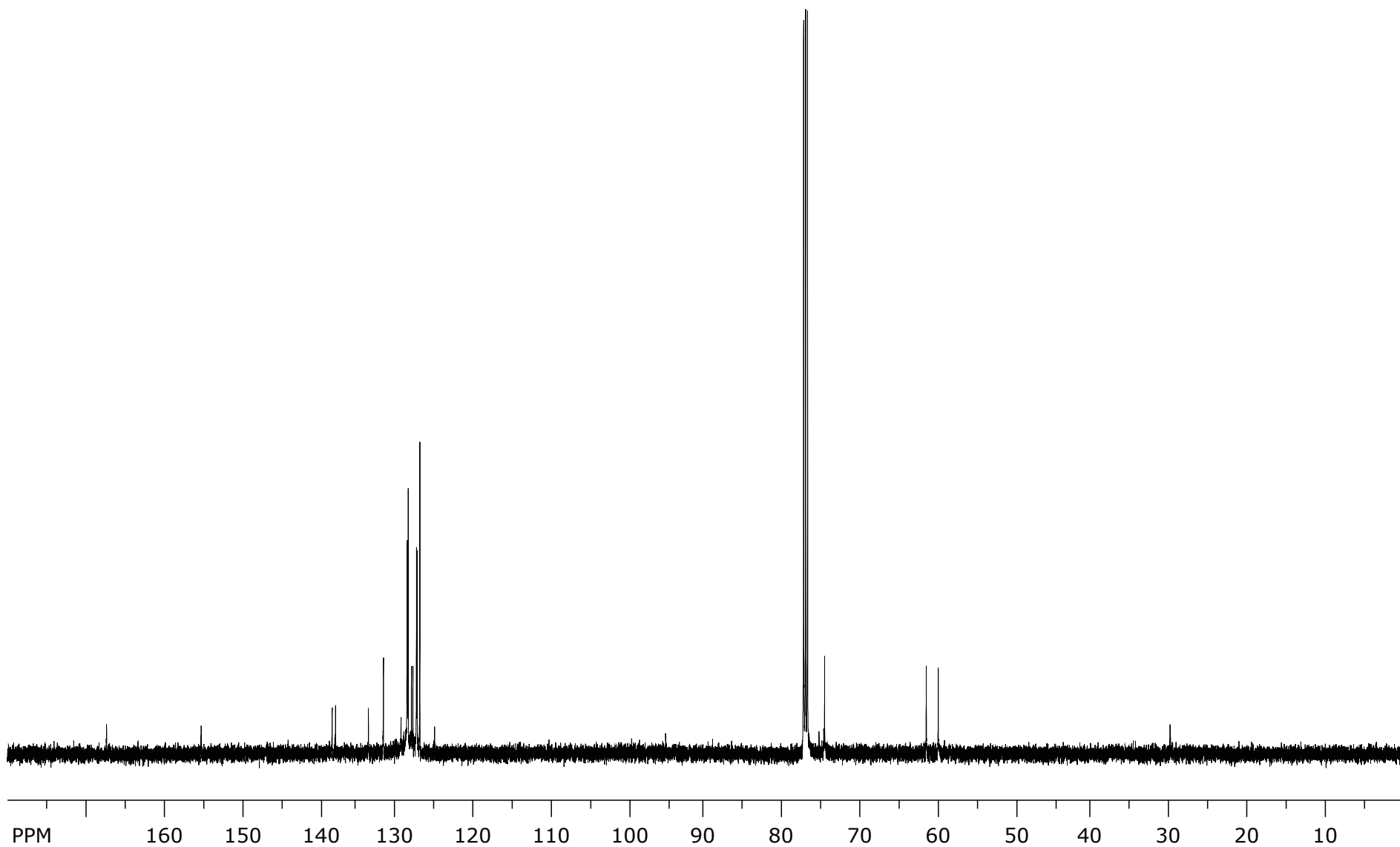
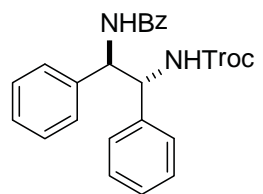
^{13}C NMR of **8e** in CDCl_3



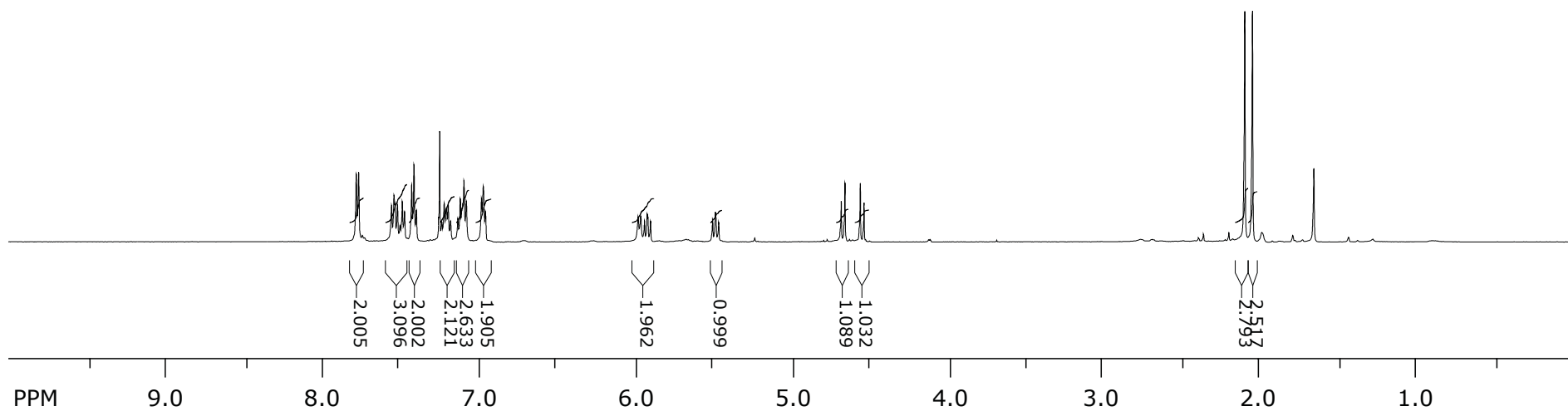
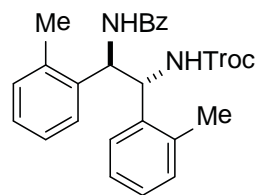
^1H NMR of **8f** in CDCl_3



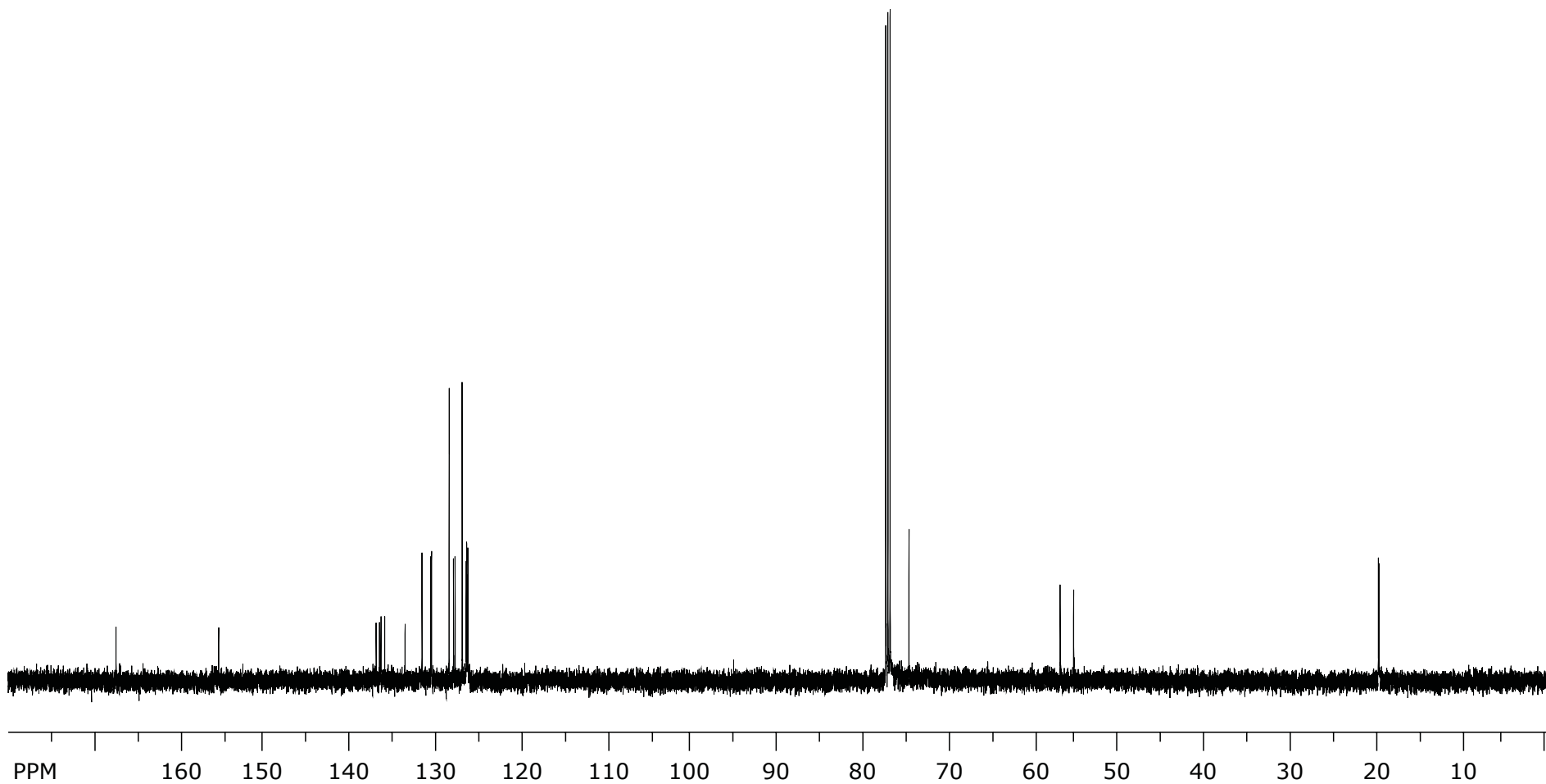
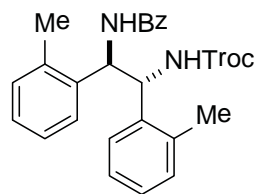
^{13}C NMR of **8f** in CDCl_3



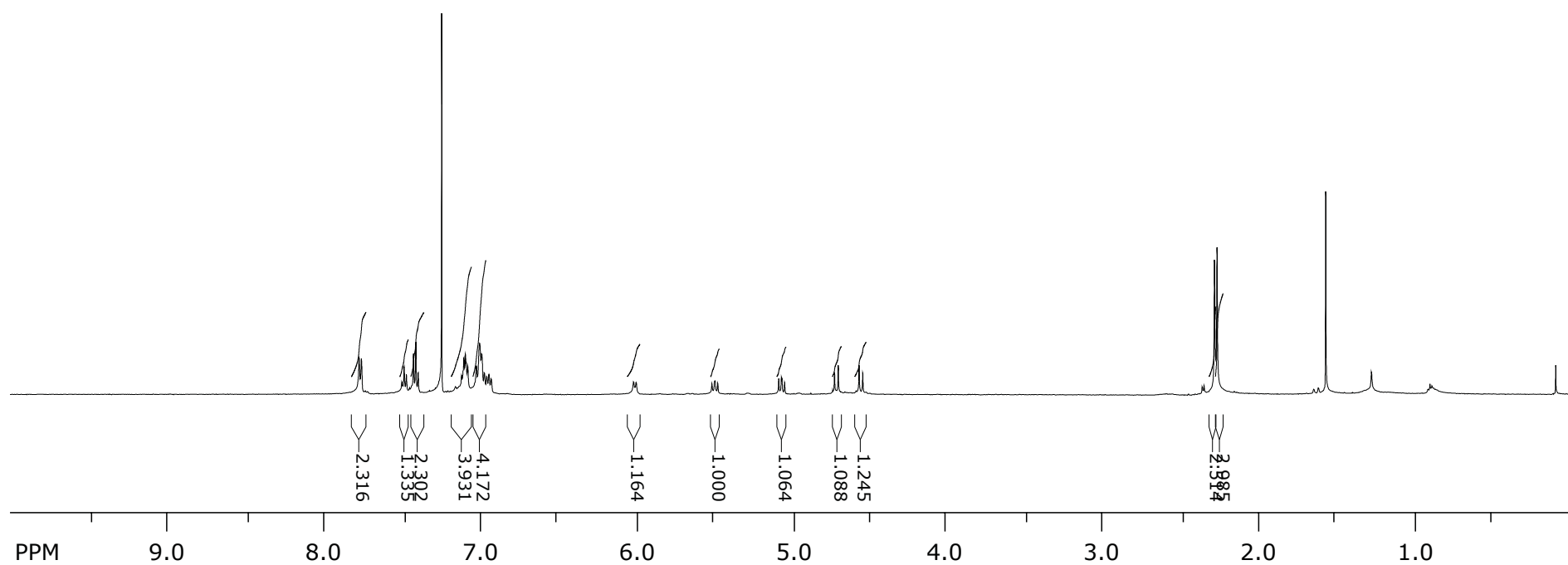
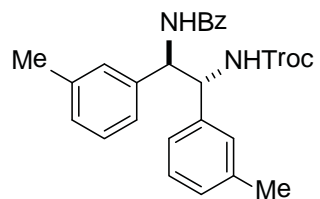
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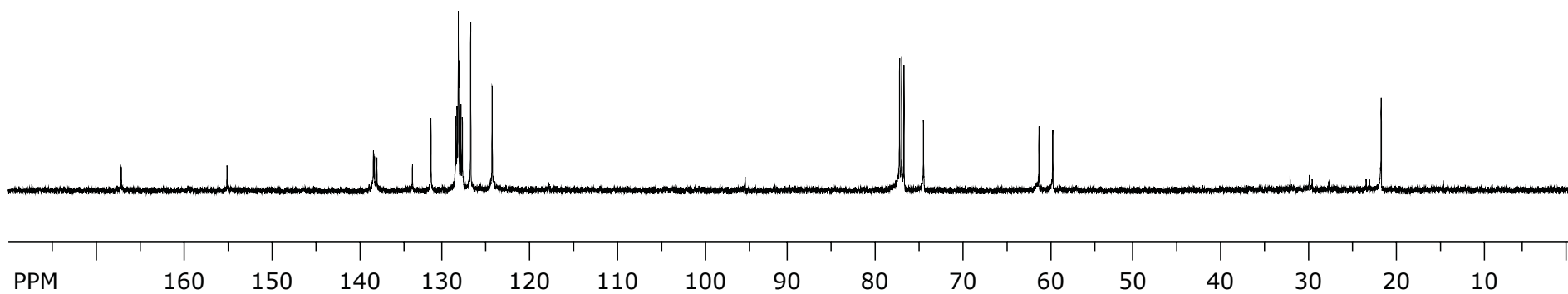
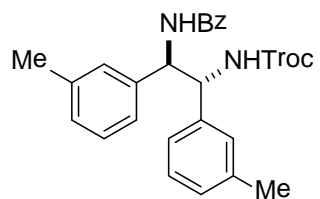
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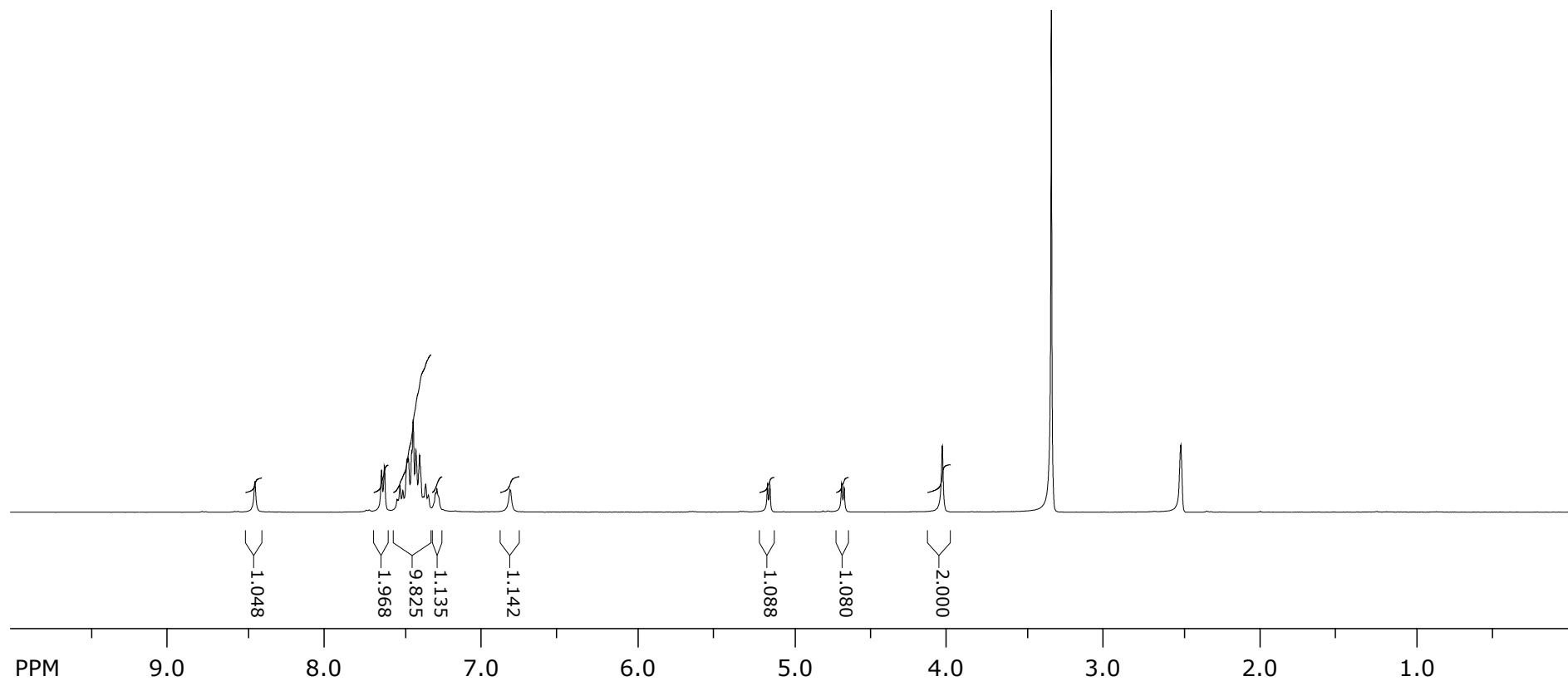
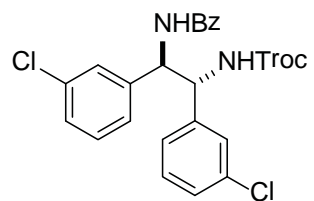
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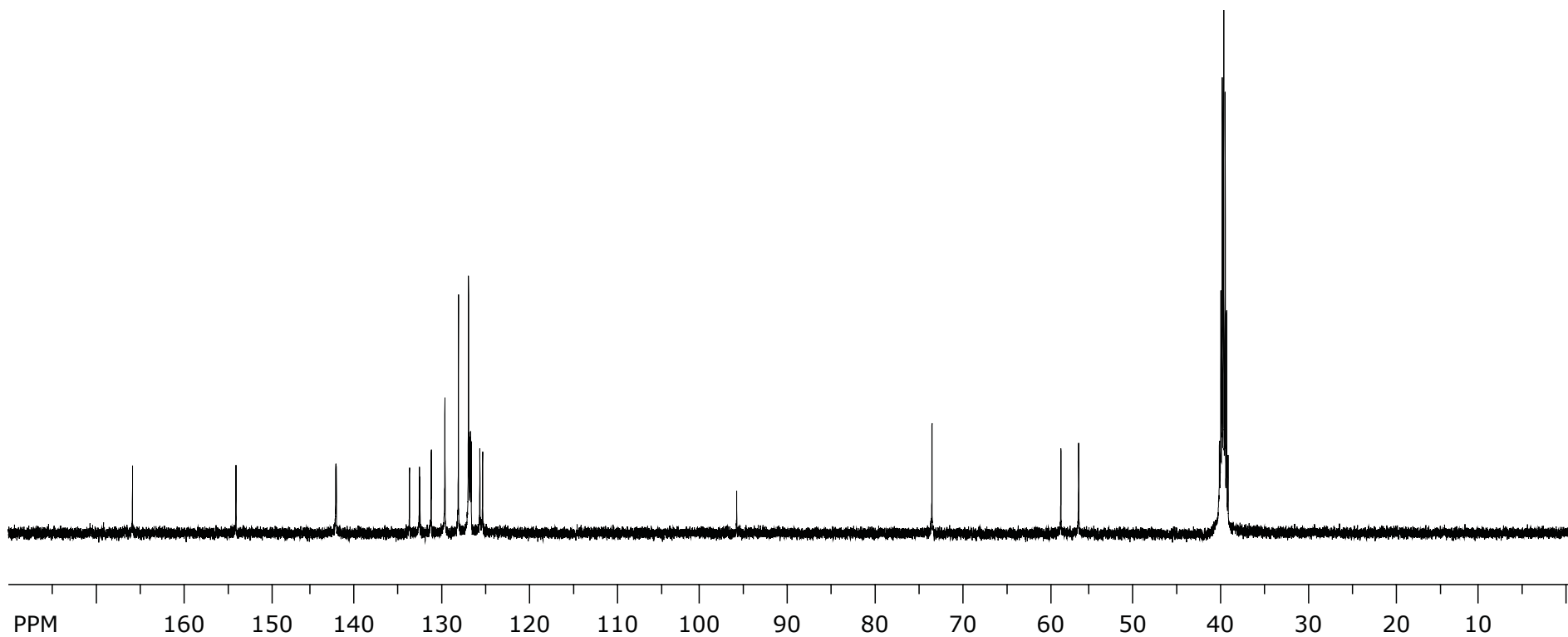
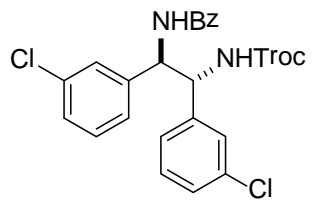
^{13}C NMR of **8h** in CDCl_3



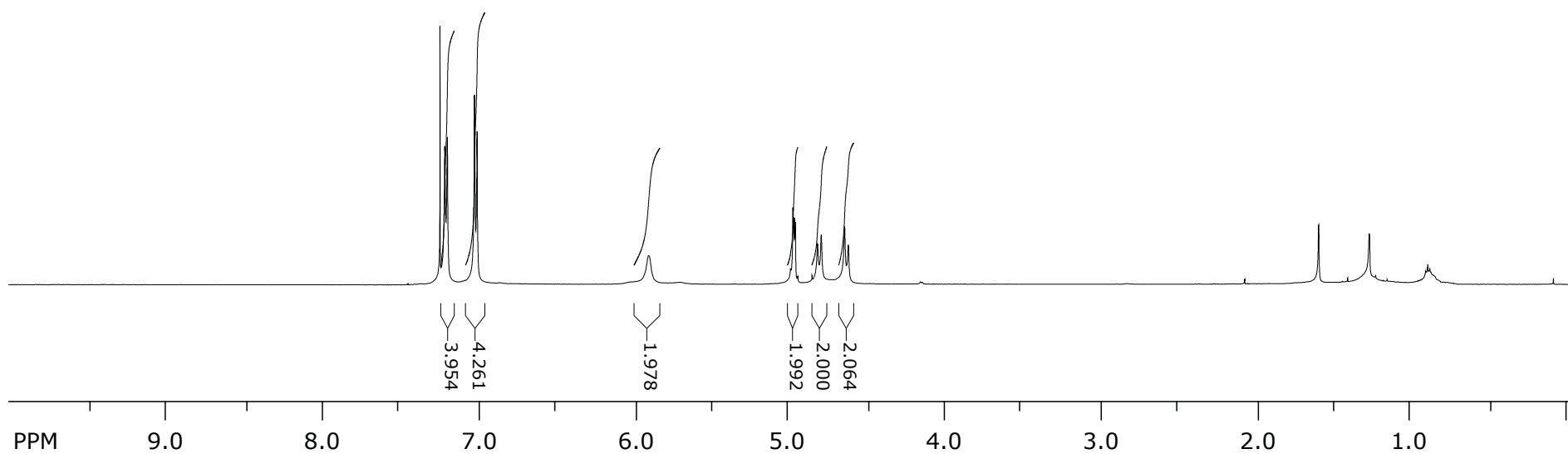
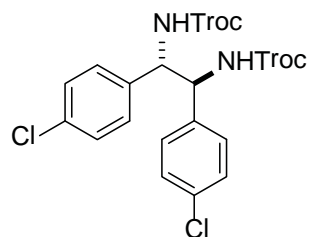
^1H NMR of **8i** in $(\text{CD}_3)_2\text{SO}$



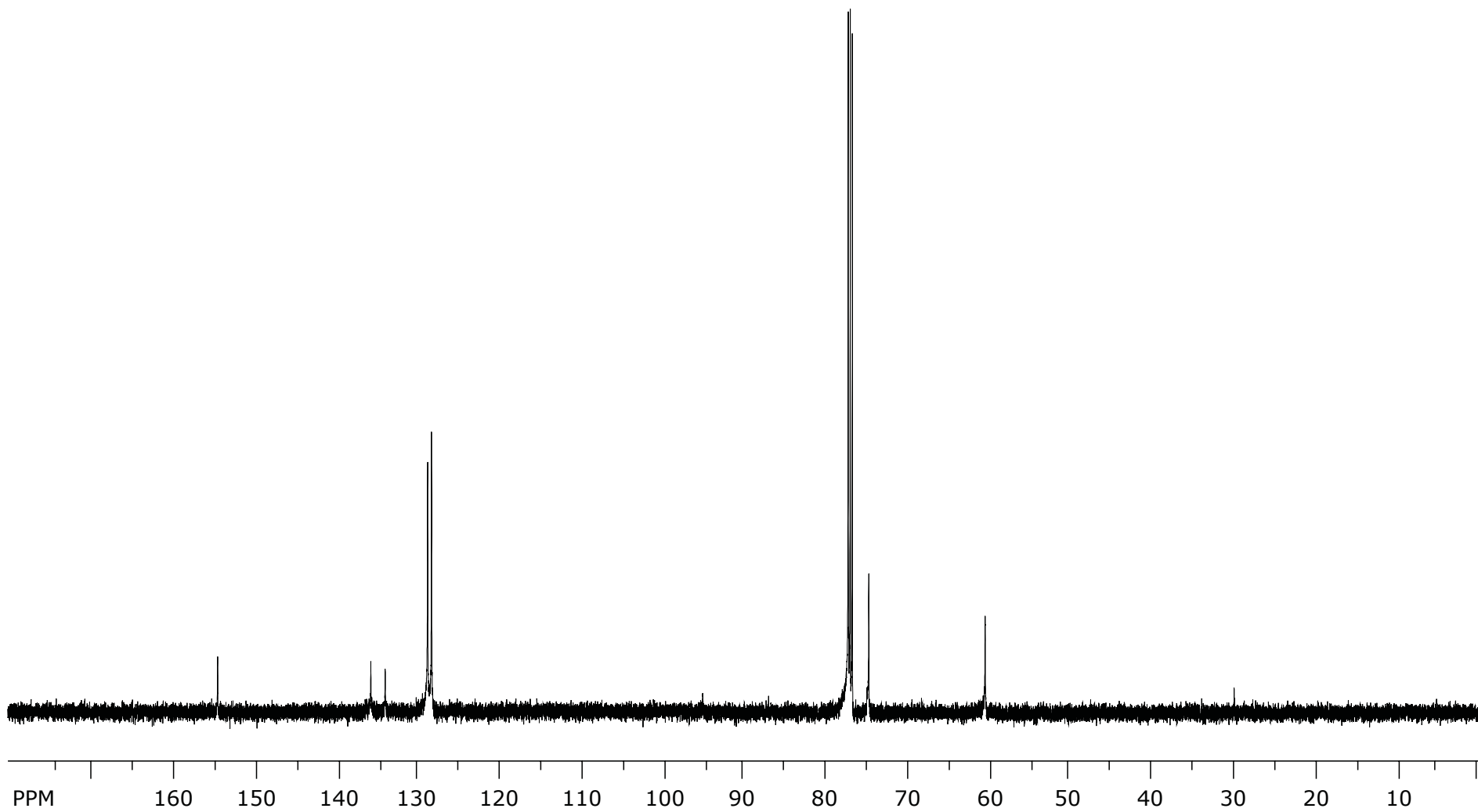
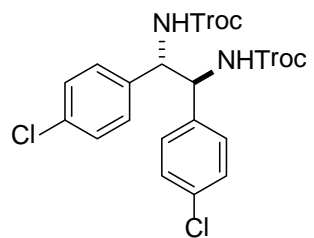
^{13}C NMR of **8i** in $(\text{CD}_3)_2\text{SO}$



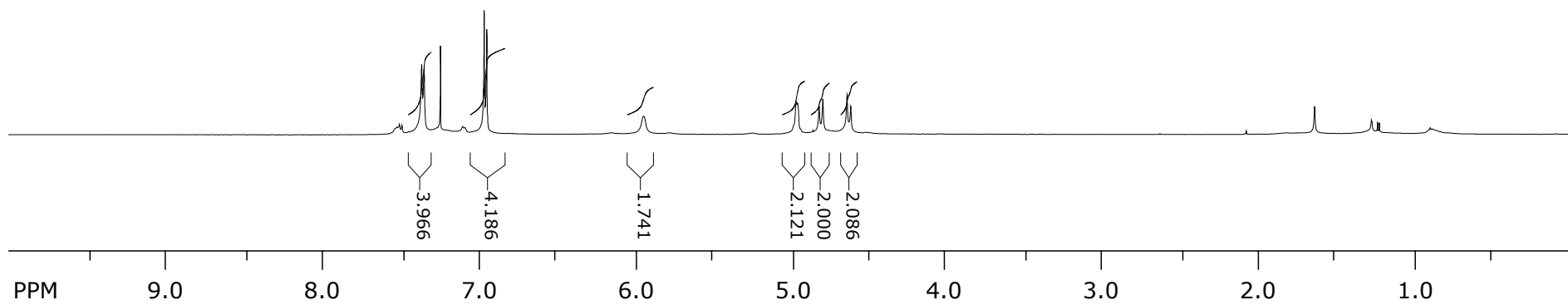
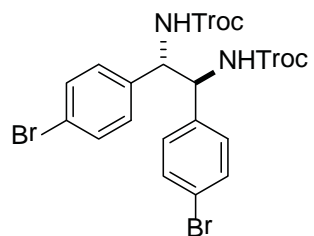
^1H NMR of **9a** in CDCl_3



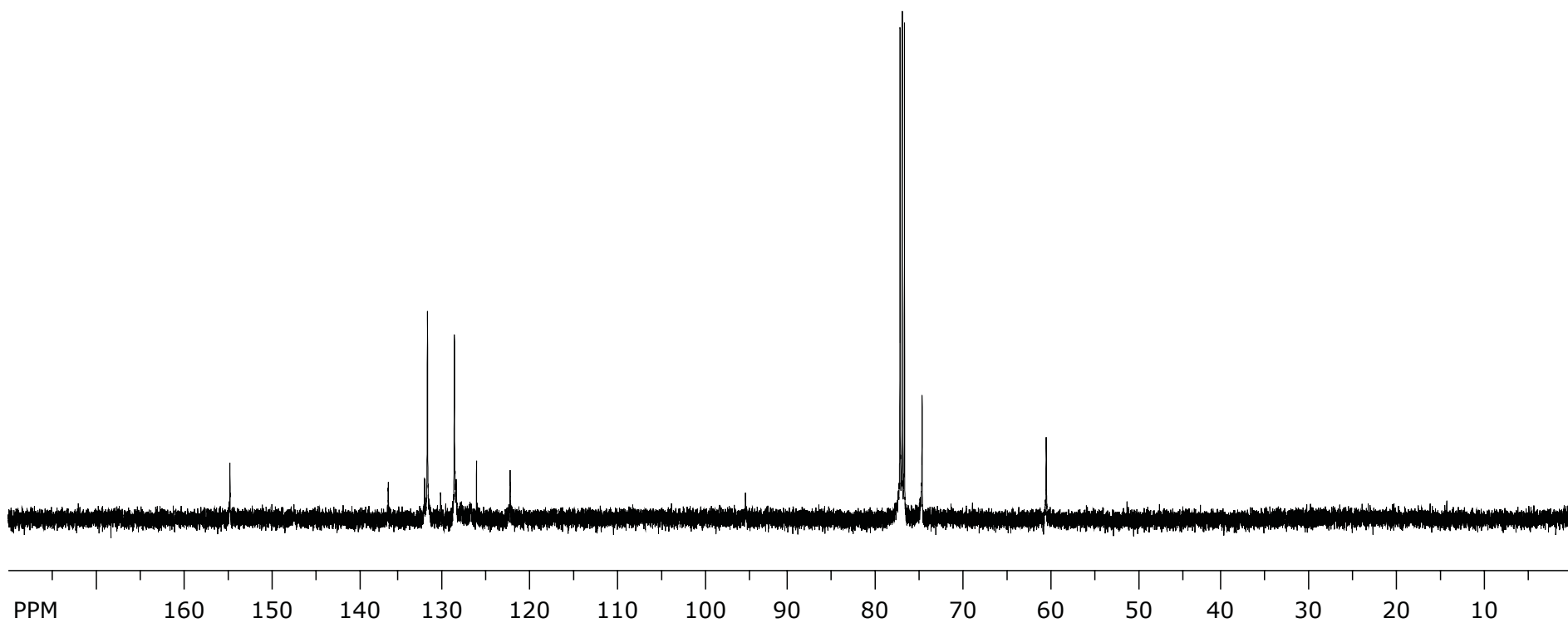
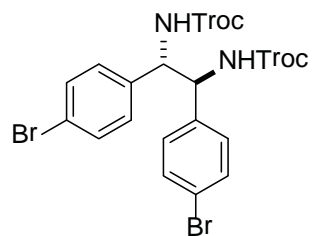
^{13}C NMR of **9a** in CDCl_3



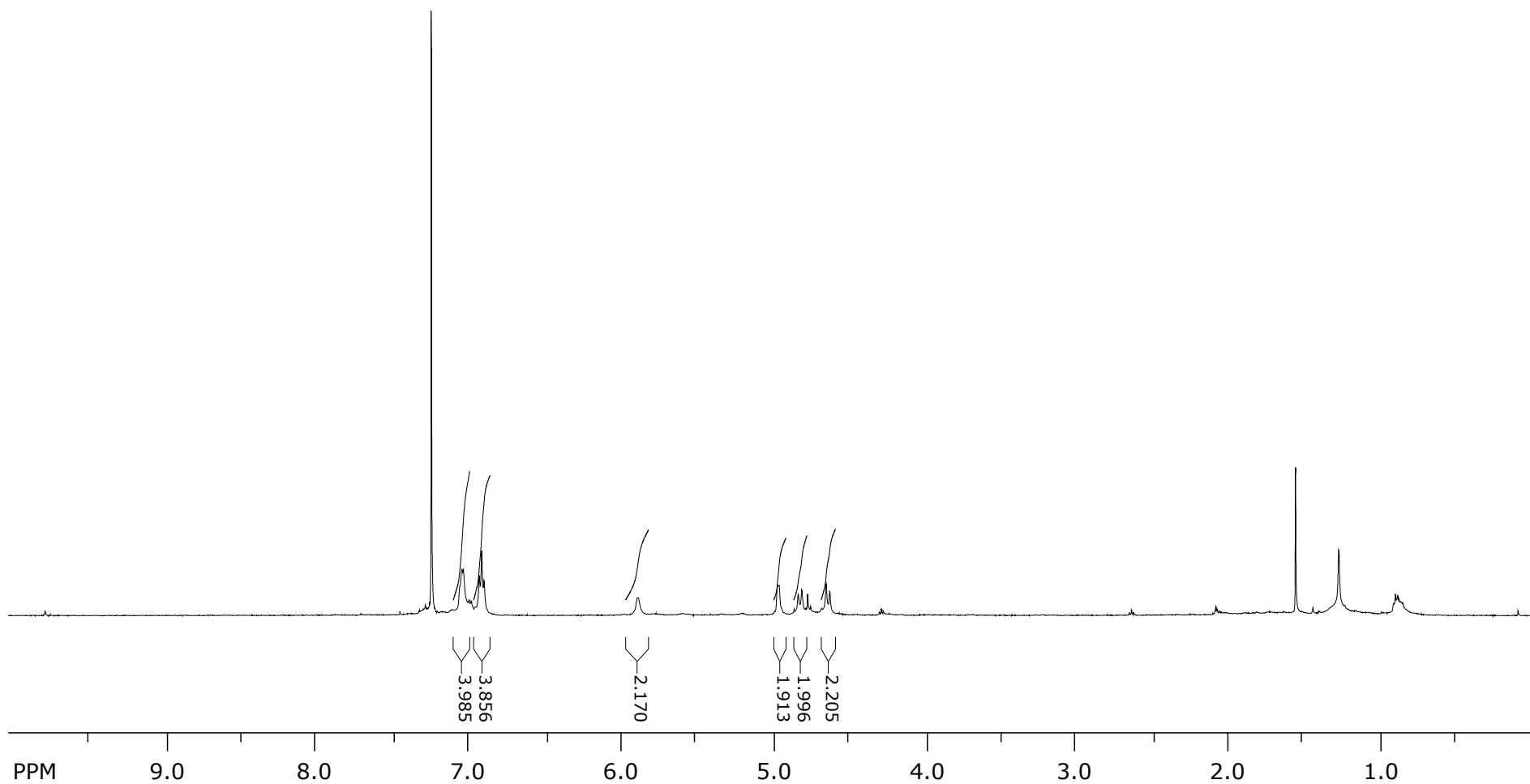
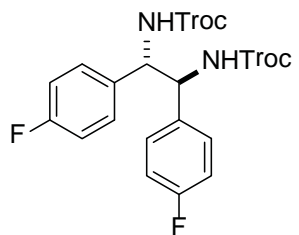
^1H NMR of **9b** in CDCl_3



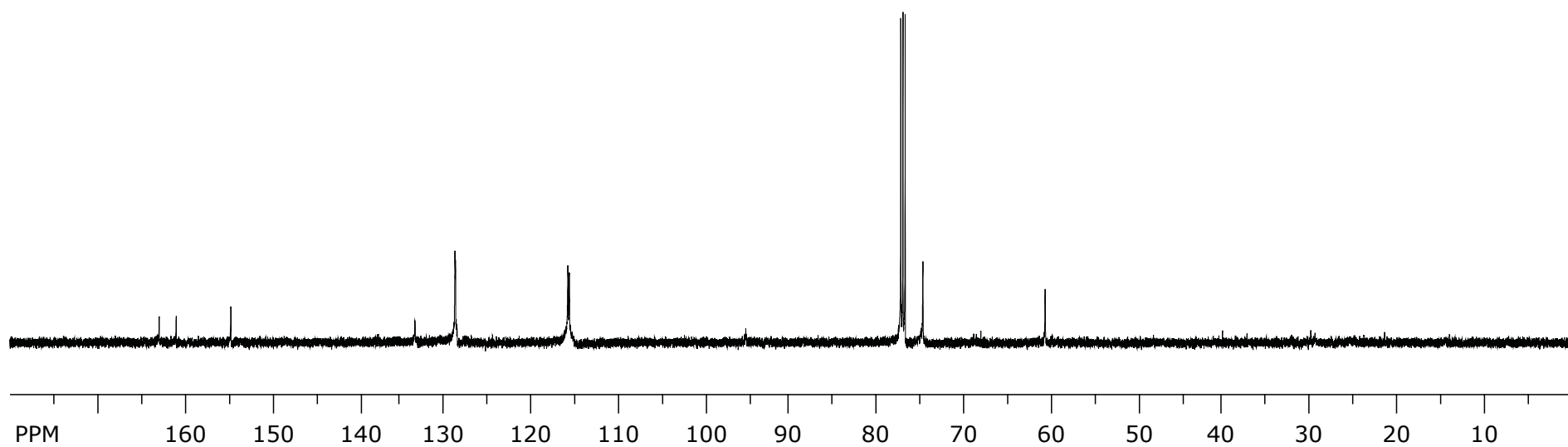
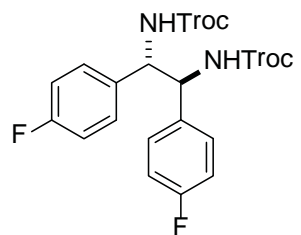
^{13}C NMR of **9b** in CDCl_3



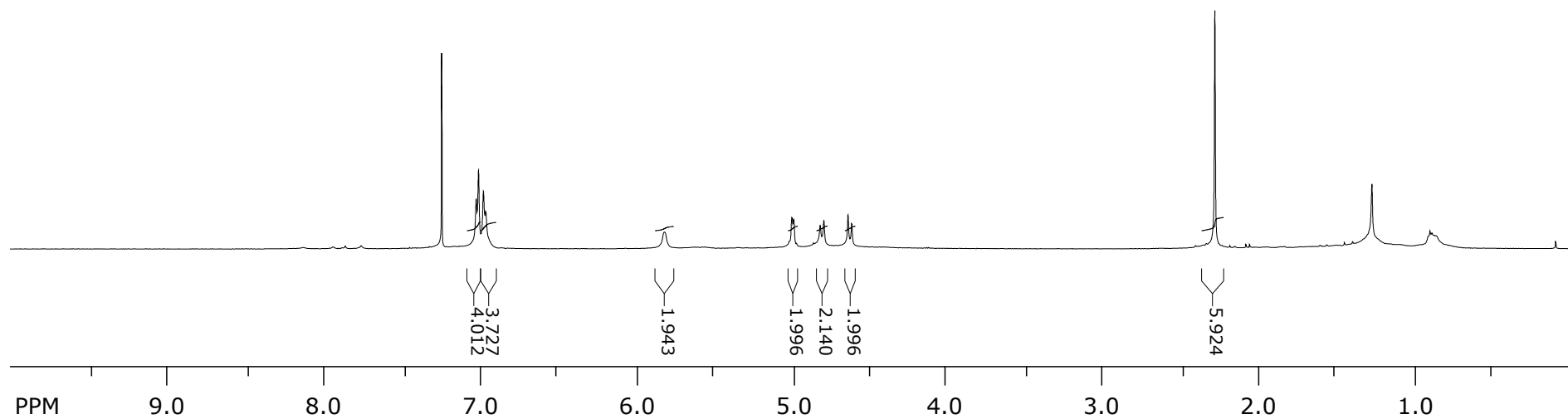
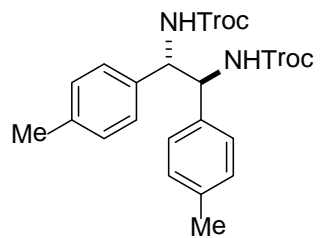
^1H NMR of **9c** in CDCl_3



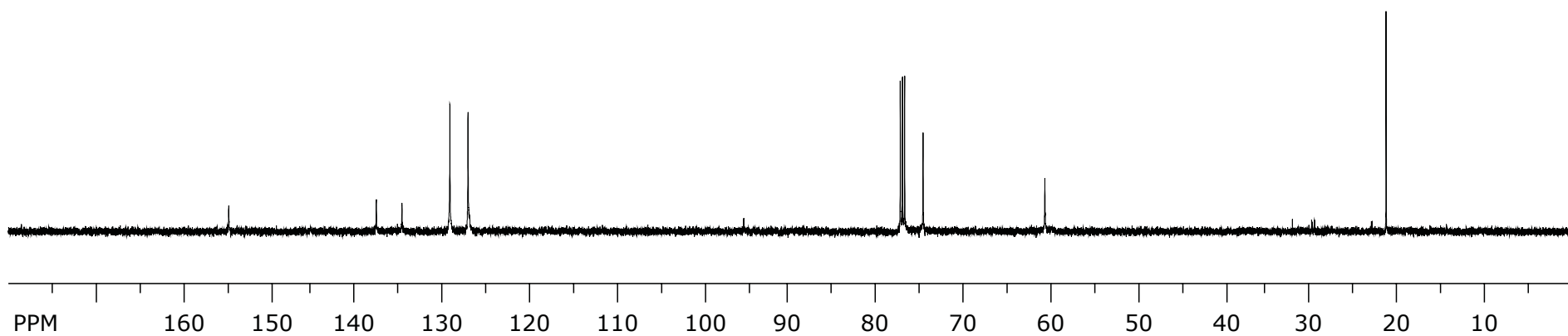
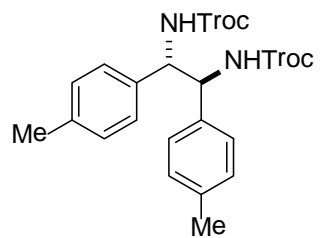
^{13}C NMR of **9c** in CDCl_3



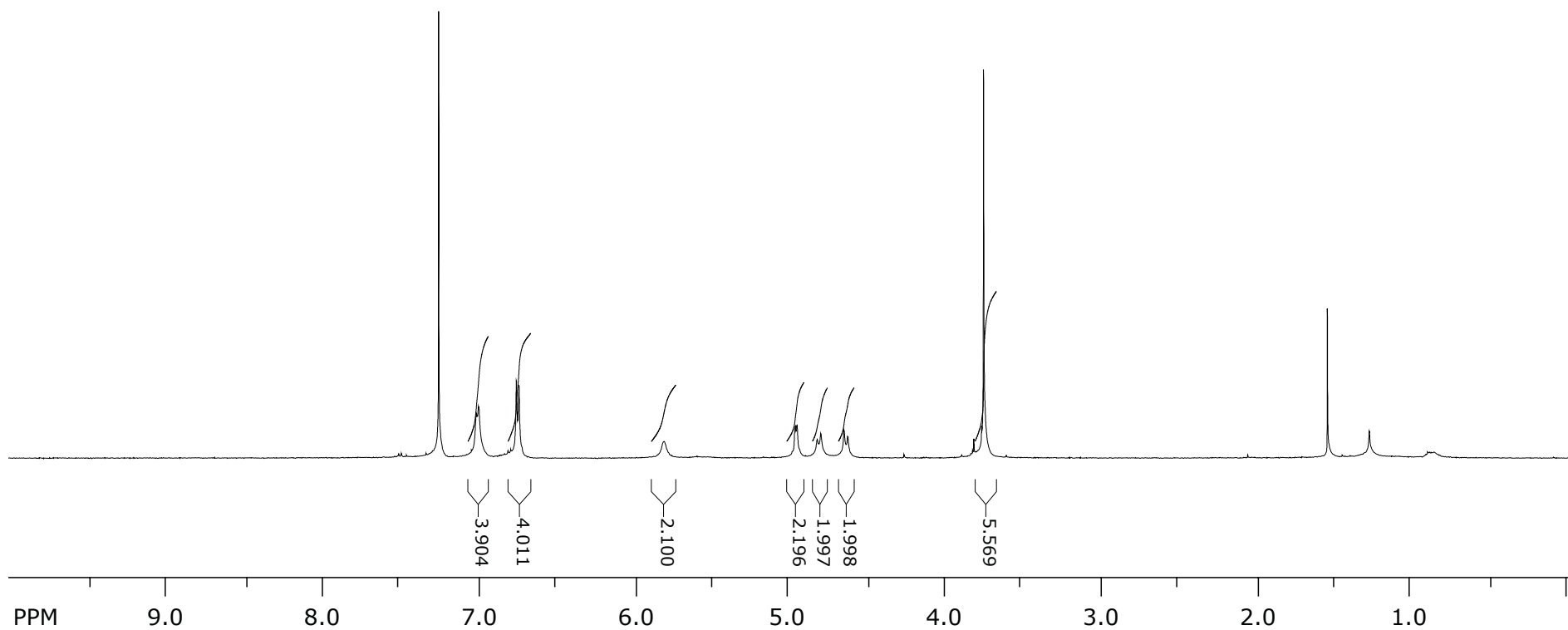
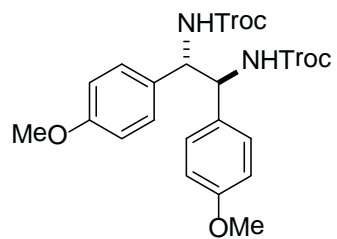
^1H NMR of **9d** in CDCl_3



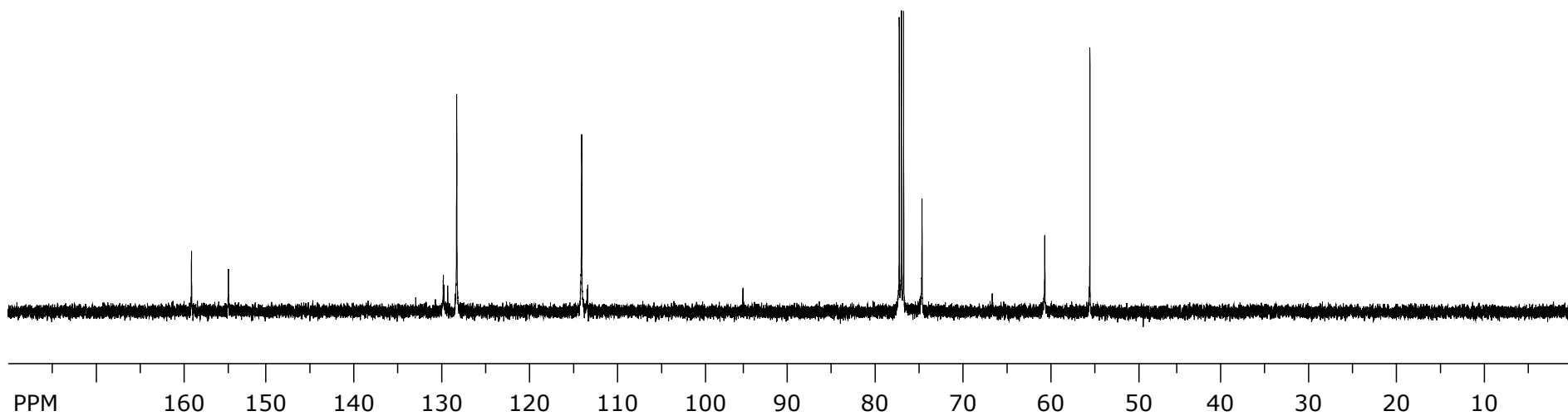
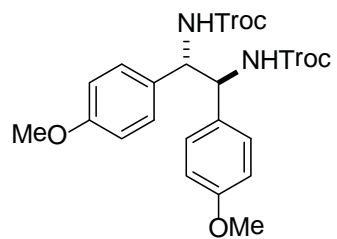
^{13}C NMR of **9d** in CDCl_3



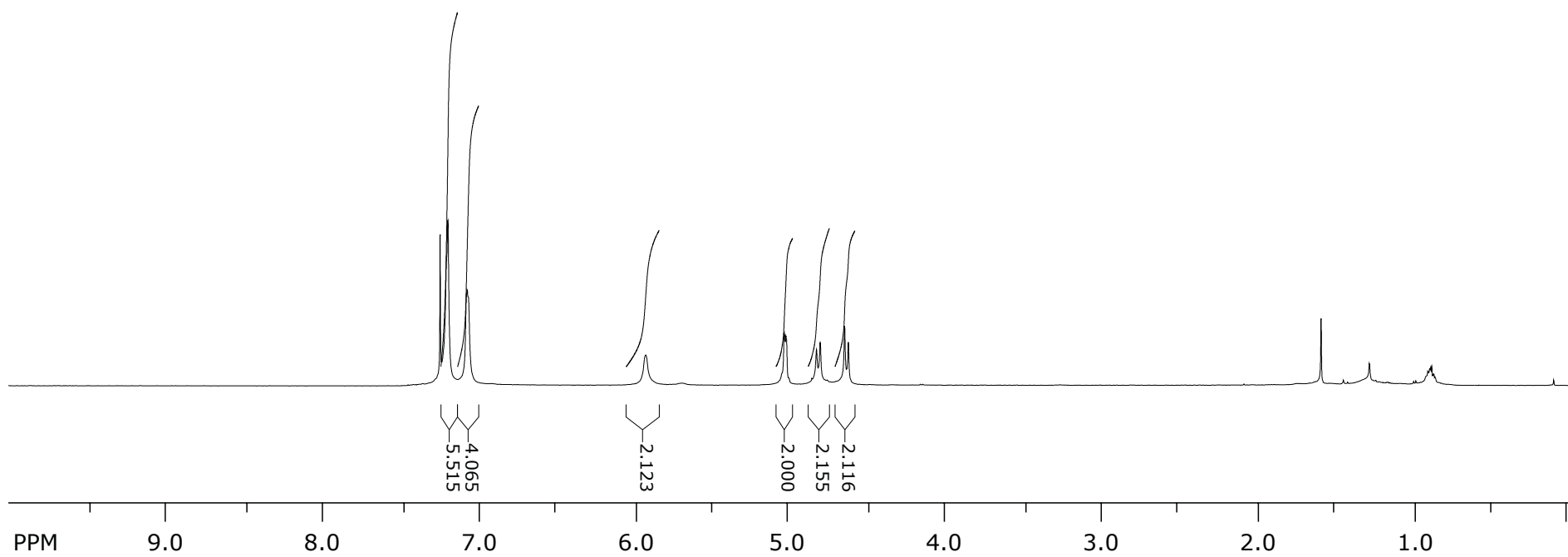
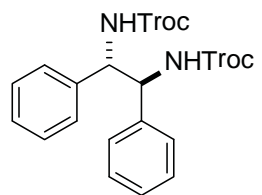
^1H NMR of **9e** in CDCl_3



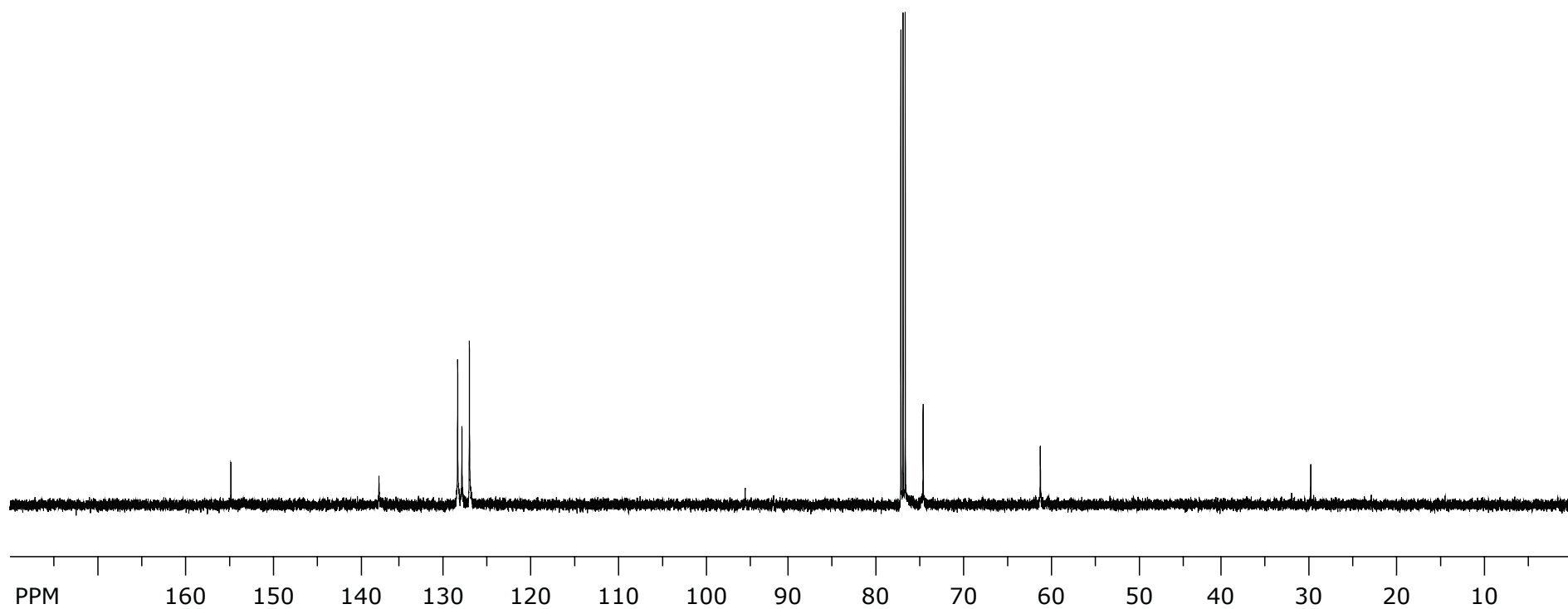
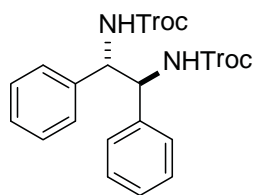
^{13}C NMR of **9e** in CDCl_3



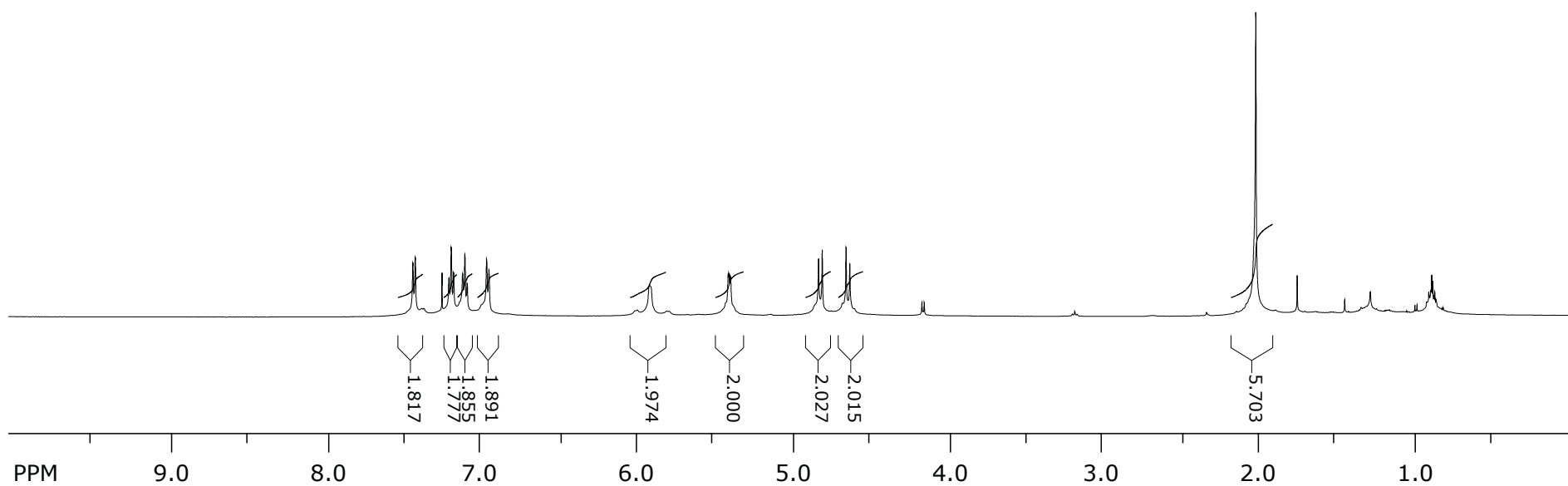
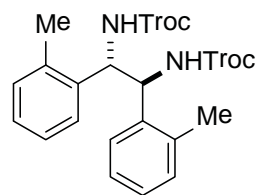
^1H NMR of **9f** in CDCl_3



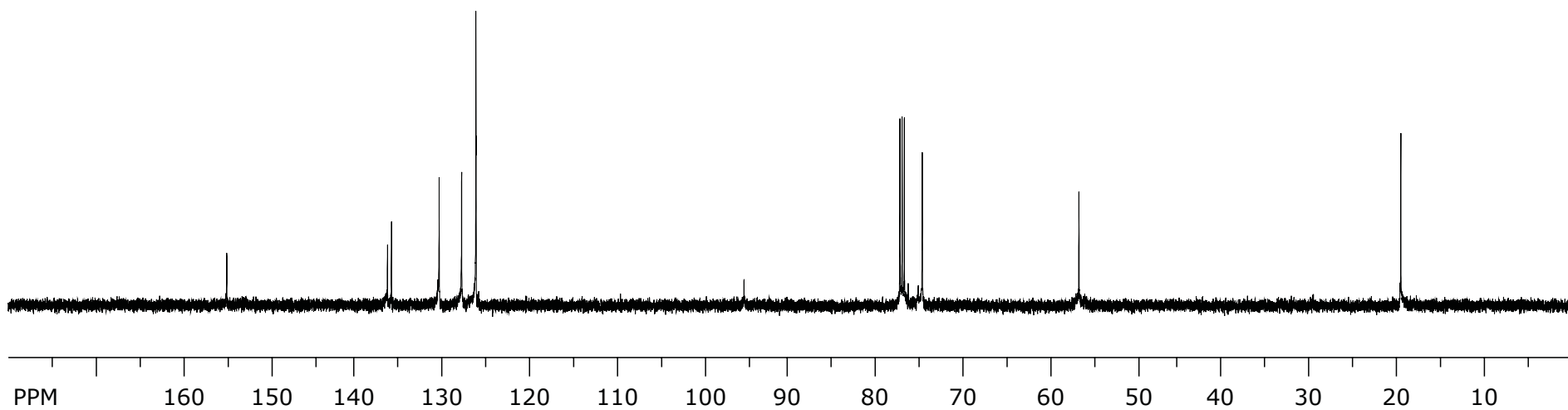
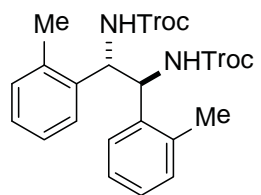
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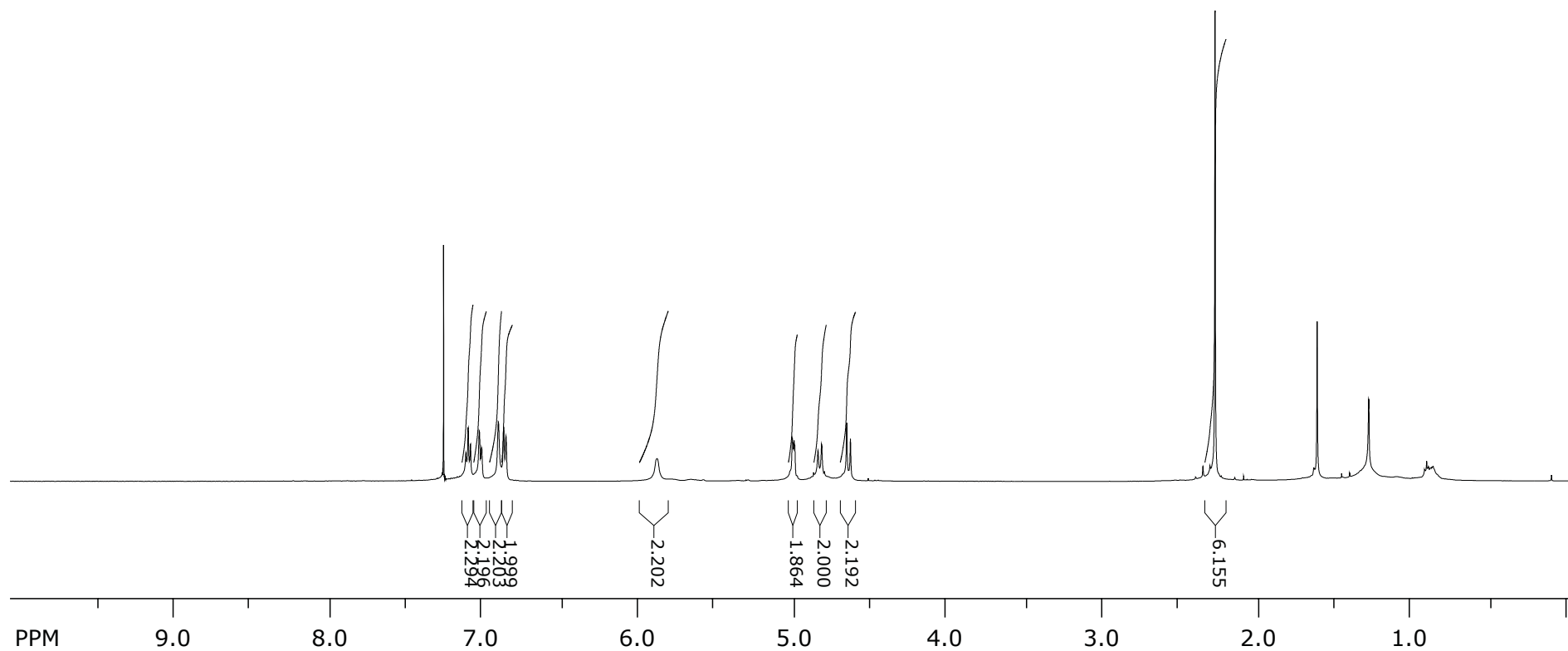
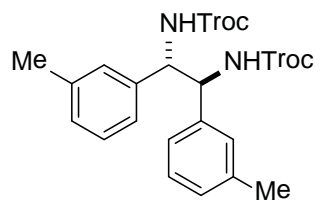
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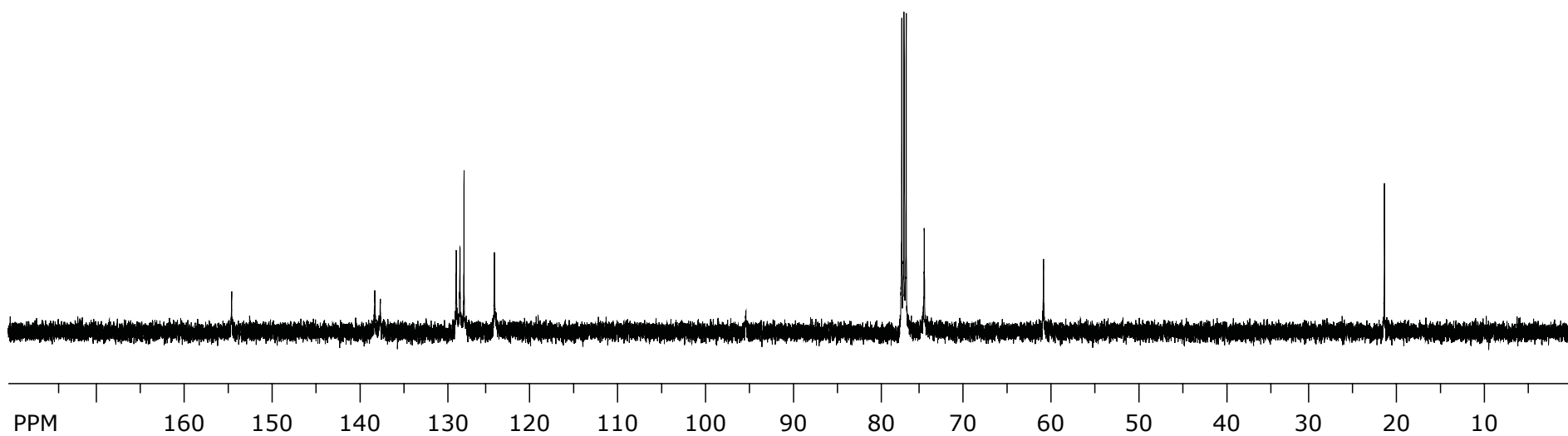
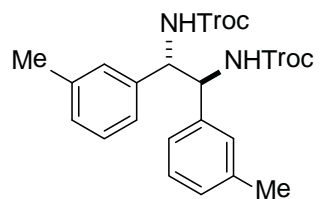
^{13}C NMR of **9g** in CDCl_3



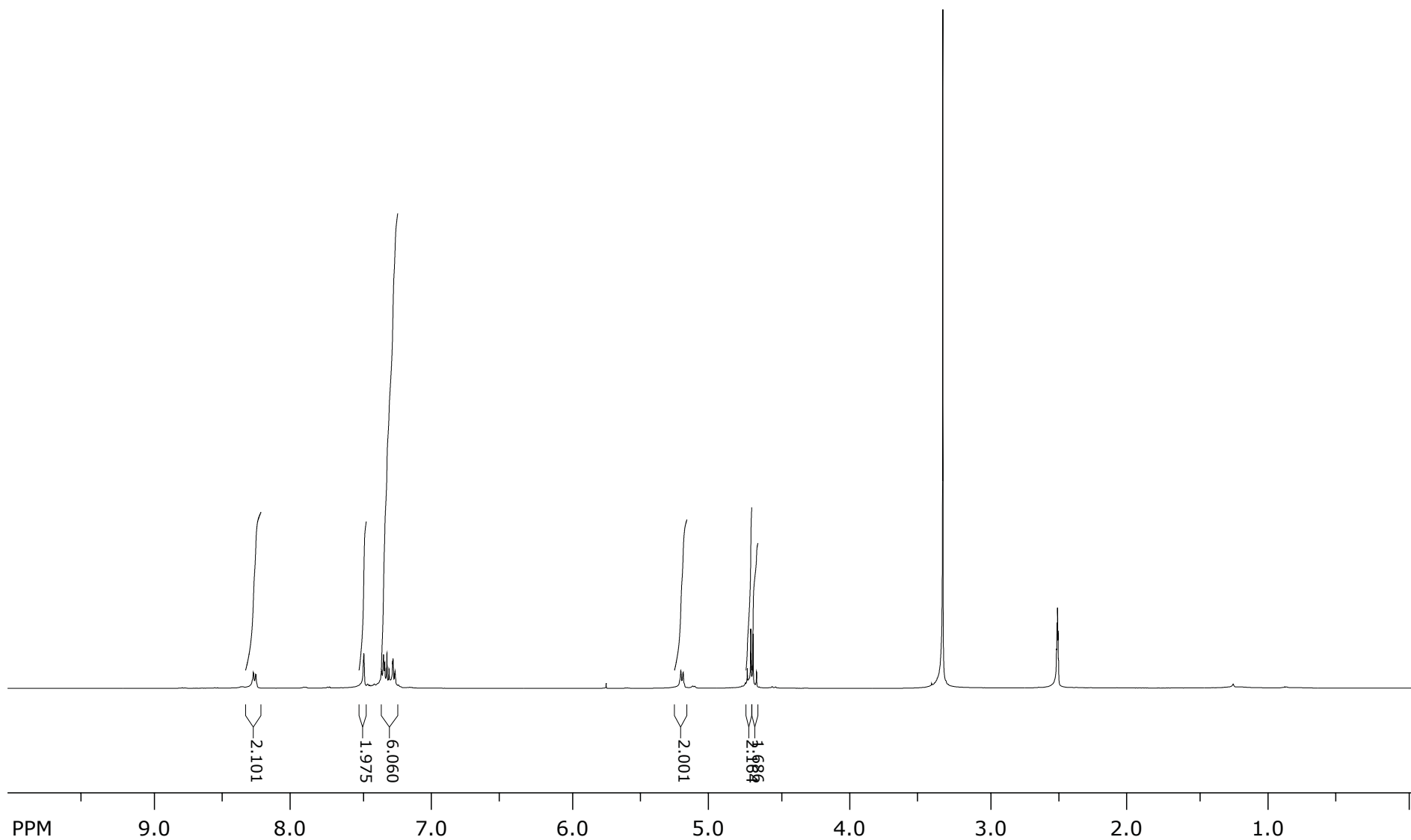
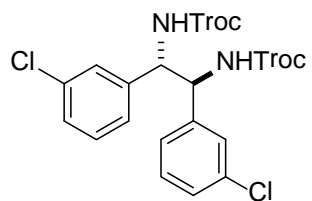
^1H NMR of **9h** in CDCl_3



^{13}C NMR of **9h** in CDCl_3



^1H NMR of **9i** in $(\text{CD}_3)_2\text{SO}$



^{13}C NMR of **9i** in $(\text{CD}_3)_2\text{SO}$

