Stereoselective Synthesis of 2-Oxyenamides

Sara-Cathrin Krieg,[‡[a]] Jennifer Grimmer,[‡[a]], Annika Maria Pick[[a]], Harlad Kelm[[a]], Martin Breugst,[[b,c]] Georg Manolikakes[[a]]*

[a] Department of Organic Chemistry,
Technical University Kaiserslautern
Erwin-Schrödinger-Str. Geb. 54,
67663 Kaiserslautern, Germany
E-mail: manolikakes@chemie.uni-kl.de
https://www.chemie.uni-kl.de/manolikakes

[b] Prof. Dr. M. Breugst
Department of Chemistry, University of Cologne
Greinstraße 4, 50939 Köln, Germany
Email: mbreugst@uni-koeln.de

[c] Prof. Dr. M. Breugst
Institut für Chemie, TU Chemnitz
Straße der Nationen 62, 09111 Chemnitz, Germany
Email: martin.breugst@chemie.tu-chemnitz.de

SUPPORTING INFORMATION

1 GENERAL INFORMATION

EXPERIMENTAL METHODS. Unless otherwise mentioned, all reactions were carried out without any precautions to exclude ambient air or moisture. All yields refer to isolated yields of compounds estimated to be > 95% pure as determined by ^{1}H-NMR.

CHROMATOGRAPHY. *Flash column chromatography* was performed using a puriflash XS 420+ Flash purifier machine from Interchim with prepacked flash columns (Puriflash_SilicaHP_15µm_F0012, Puriflash_SilicaHP_15µm_F0025 or Puriflash_SilicaHP_15µm_F0040) and the respectively specified solvent mixture. *Column chromatography* was performed with Silica 60 (0.04-0.063 mm, 230-400 mesh) and the specified solvent mixture. *Thin layer chromatography* was performed on aluminum sheets coated with SiO_2 (TLC silica gel 60 F254). The spots were visualized by ultraviolet light, iodine, cerium ammonium molybdate (CAM) or $KMnO_4$.

SOLVENTS. Solvents for reactions and column chromatography were obtained from different commercial suppliers in >97% purity and used as received. Solvents for column chromatography were technical standard.

MATERIALS. All starting materials obtained from commercial sources were used without further purification.

ANALYTICAL DATA AND INSTRUMENTATION.

NMR SPECTROSCOPY. Proton nuclear magnetic resonance spectra (^{1}H NMR), carbon spectra (^{13}C NMR) and fluorine (^{19}F NMR) were recorded at 400 or 600 MHz (^{1}H), 101 or 151 MHz (^{13}C) and 376 MHz (^{19}F), respectively. Chemical shifts are reported as δ - values relative to the residual $CDCl_3$ (δ = 7.26 ppm for ^{1}H and δ = 77.16 ppm for ^{13}C), DMSO-d^{6} (δ = 2.50 ppm for 1H and δ = 39.51 ppm for ^{13}C). Coupling constants (J) are given in Hz and multiplicities of the signals are abbreviated as follows: s = singlet; d = doublet; t = triplet; q = quartet; sp = septet; m = multiplet; dd = doublet of doublets and dt = doublet of triplets dqd = doublet of quartets of doublets.

MELTING POINTS. Melting points are reported uncorrected.

MASS SPECTROMETRY. Mass spectra (MS) were measured on an Advion Mass Express (expression-LCMS) using electrospray ionization (ESI) techniques. High resolution mass spectra were acquired on a Waters GCT Premium using electron ionization mass spectroscopy (EI-MS-TOF).

INFRARED SPECTROSCOPY. Infrared spectra (IR) of neat substances were recorded on a Shimadzu IRSpirit (QATR-S). The absorption bands are reported in wave numbers (cm^{-1}).

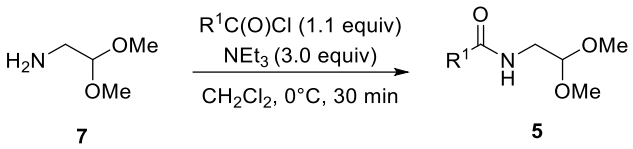
***E:Z* RATIO.** The *E:Z* ratios were determined via ^{1}H-NMR analysis of the unpurified product after aqueous workup and after isolation via column chromatography. An *E:Z* ratio of <2:98 indicates that no minor isomer was observed by ^{1}H NMR. Yields refer to isolated yields of the analytically pure oxyenamides. If the second isomer could be isolated, a combined yield is given in addition.

.

2 PREPARATION AND ANALYTICAL DATA

2.1 Amides

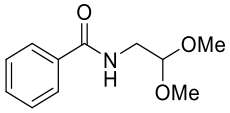
GENERAL PROCEDURE 1 (GP1)



7 **5**

To a solution of 2,2-dimethoxyethanamine (2.12 mL, 20.0 mmol, 1.0 equiv) and Et_3N (12.6 mL, 60.0 mmol, 3.0 equiv) in CH_2Cl_2 (30 mL) was added dropwise the corresponding acyl chloride (22.0 mmol, 1.1 equiv) at 0 °C. After stirring for 30 min at 0°C, the reaction was quenched with saturated aqueous NH_4Cl (20 mL) and the mixture was extracted with CH_2Cl_2 (3x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the crude residue by flash column chromatography afforded the analytically pure product.[1]

2.1.1 *N*-(2,2-Dimethoxyethyl)benzamide **5a**



5a

Prepared according to **GP1** from 2,2-dimethoxyethanamine (5.50 mL, 50.0 mmol, 1.0 equiv), Et_3N (21.0 mL, 150 mmol, 3.0 equiv) and benzoylchloride (6.406 mL, 55.0 mmol, 1.1 equiv) in CH_2Cl_2 (85 mL). Purification by column chromatography (*n*-hexane:EtOAc = 7:3 → 1:1) afforded *N*-(2,2-dimethoxyethyl)benzamide **5a** as a colorless solid (10.4 g, 99%). Analytical data is in accordance with the literature.[1]

R_f (*n*-hexane:EtOAc = 1:1) 0.33.

m.p. 54-56 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.58 (m, 2H), 7.49 (d, J = 7.4 Hz, 1H), 7.47 – 7.40 (m, 2H), 6.36 (s, 1H), 4.48 (d, J = 5.2 Hz, 1H), 3.61 (t, J = 5.5 Hz, 2H), 3.43 (s, 6H).

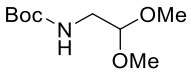
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 134.5, 131.7, 128.0, 127.1, 102.9, 54.8, 41.6.

MS (ESI) m/z calcd for $C_{11}H_{15}NO_3Na^+$ 232.1 $[M+Na]^+$, found 232.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{11}H_{15}NO_3$ 209.1052 $[M]^+$, found 209.1052 $[M]^+$.

IR (ν in cm^{-1}): 3345 (w), 3308 (w), 2937 (w), 1632 (m), 1542 (s), 1428 (w), 1327 (m), 1340 (m), 1128 (s), 1110 (s), 1068 (s), 1018 (m), 960 (m), 885 (w), 796 (m), 693 (m), 658 (s).

2.1.2 *Tert-butyl (2,2-dimethoxyethyl)carbamate* 5b



5b

Prepared according to **GP1** from 2,2-dimethoxyethanamine (1.6 mL, 15.0 mmol, 1.0 equiv), Et_3N (6.24 mL, 45.0 mmol, 3.0 equiv) and di-*tert*-butyldicarbonat (3.53 mL, 16.5 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Aqueous work up afforded *tert*-butyl (2,2-dimethoxyethyl)carbamate **5b** as a colorless liquid (2.96 g, 96%). %). Analytical data is in accordance with the literature.[2]

R_f (*n*-hexane:EtOAc = 4:1) 0.42.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.72 (s, 1H), 4.36 (t, J = 5.4 Hz, 1H), 3.38 (s, 6H), 3.25 (t, J = 5.7 Hz, 2H), 1.44 (s, 9H).

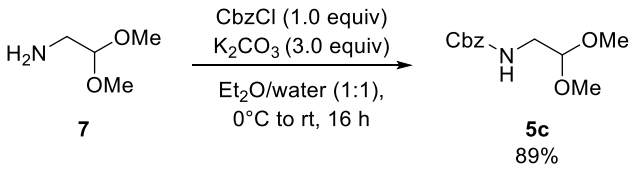
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 103.1, 79.6, 54.4, 42.2, 28.5.

MS (ESI) m/z calcd for $C_9H_{19}NO_4Na^+$ 228.1 $[M+Na]^+$, found 228.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_9H_{19}NO_4$ 205.1314 $[M]^+$, found 2005.1313 $[M]^+$.

IR (ν in cm^{-1}): 3358 (w), 2977 (w), 2936 (w), 1712 (s), 1515 (m), 1455 (w), 1391 (w), 1365 (m), 1249 (m), 1171 (s), 1126 (s), 1061 (s), 949 (m),, 873 (w), 780 (w), 765 (w). 545 (w).

2.1.3 *Benzyl (2,2-dimethoxyethyl)carbamate* 5c



7 **5c** 89%

Prepared according to literature.[3]

To a solution of 2,2-dimethoxyethylamine (1.6 mL, 15.0 mmol) in Et_2O (75 mL) was added K_2CO_3 (6.20 g, 44.9 mmol) and water (75 mL). The reaction mixture was cooled to 0 °C and benzyl chloroformate (2.1 mL, 15.0 mmol) was added dropwise. The reaction mixture was allowed to warm to rt and stirred for 16 h. The two layers were separated and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic layers were washed with 5% aqueous citric acid (3 × 80 mL) and brine (2 × 80 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Benzyl (2,2-dimethoxyethyl)carbamate **5c** was obtained without further purification as a colorless liquid (3.19 g, 89%). Analytical data is in accordance with the literature.[3]

R_f (*n*-hexane:EtOAc = 7:3) 0.27.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.42 – 7.27 (m, 5H), 5.10 (s, 2H), 4.96 (s, 1H), 4.38 (t, J=5.4 Hz, 1H), 3.39 (s, 6H), 3.34 (t, J=5.7 Hz, 2H).

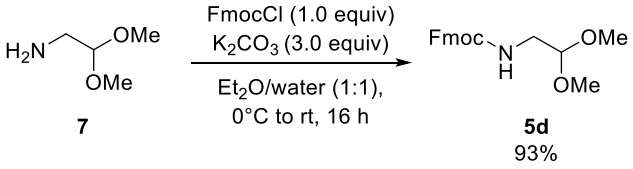
^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.5, 136.5, 128.7, 128.3, 128.3, 102.9, 67.0, 54.5, 42.6.

MS (ESI) m/z calcd for $C_{12}H_{17}NO_4Na^+$ 262.1 $[M+Na]^+$, found 261.9 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{17}NO_4$ 239.1158 $[M]^+$, found 239.1149 $[M]^+$.

IR (ν in cm^{-1}): 3342 (w), 2940 (w), 2834 (w), 1705 (s), 1522 (s), 1455 (m), 1366 (w), 1244 (s), 1128 (s), 1061 (s), 966 (m), 736 (m), 696 (s), 547 (w).

2.1.4 *(9H-fluoren-9-yl)methyl (2,2-dimethoxyethyl)carbamate* 5d



Prepared according to literature.[3]

To a solution of 2,2-dimethoxyethylamine (1.6 mL, 15.0 mmol) in Et_2O (75 mL) was added K_2CO_3 (6.20 g, 44.9 mmol) and water (75 mL). The reaction mixture was cooled to 0 °C and 9-fluorenylmethyl chloroformate (3.88 g, 15.0 mmol) was added in one portion. The reaction mixture was allowed to warm to rt and stirred for 16 h. The two layers were separated and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic layers were washed with 5% aqueous citric acid (3 × 80 mL) and brine (2 × 80 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. (9*H*-fluoren-9-yl)methyl (2,2-dimethoxyethyl)carbamate **5d** was obtained without further purification as a colorless solid (4.59 g, 93%). Analytical data is in accordance with the literature.[4]

R_f (*n*-hexane:EtOAc = 4:1) 0.14.

m.p. 100-102 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.80 – 7.74 (m, 2H), 7.63 – 7.57 (m, 2H), 7.45 – 7.37 (m, 2H), 7.32 (td, J=7.4, 1.2, 2H), 5.00 (t, J=6.1, 1H), 4.59 – 4.35 (m, 3H), 4.23 (t, J=7.0, 1H), 3.41 (s, 5H), 3.35 (t, J=5.7, 3H).

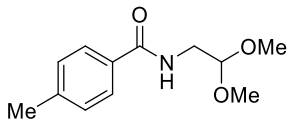
^{13}C NMR (101 MHz, $CDCl_3$) δ = 156.6, 144.0, 141.4, 127.8, 127.2, 125.2, 120.1, 103.0, 66.9, 54.6, 47.4, 42.7.

MS (ESI) m/z calcd for $C_{19}H_{21}NO_4Na^+$ 350.1 $[M+Na]^+$, found 350.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{19}H_{21}NO_4$ 327.1471 $[M]^+$, found 327.1455 $[M]^+$.

IR (ν in cm^{-1}): 3333 (w), 2945 (w), 2836 (w), 1697 (s), 1534 (s), 1447 (w), 1332 (w), 1271 (s), 1199 (w), 1149 (w), 1132 (m), 1108 (s), 1049 (s), 998 (s), 966 (m), 918 (w), 758 (s), 732 (s), 620 (m). 536 (m).

2.1.5 *N*-(2,2-Dimethoxyethyl)-4-methylbenzamide **5e**



5e

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 4-methylbenzoyl chloride (2.93 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5→40:60) afforded *N*-(2,2-dimethoxyethyl)-3-methylbenzamide **5e** as a colorless solid (4.20 g, 94%).

R_f (*n*-hexane:EtOAc = 1:1) 0.47.

m.p. 62-63 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.54 (m, 2H), 7.25 – 7.20 (m, 2H), 6.31 (s, 1H), 4.48 (t, J = 5.3 Hz, 1H), 3.60 (t, J = 5.6 Hz, 2H), 3.43 (s, 6H), 2.39 (s, 3H).

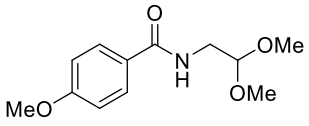
^{13}C NMR *(*101 MHz*,* $CDCl_3$*)* δ 167.6, 142.1, 131.6, 129.4, 127.1, 103.0, 54.8, 54.7, 41.6, 21.6.

MS (ESI) m/z calcd for $C_{12}H_{17}NO_3Na^+$ 246.1 $[M+Na]^+$, found 246.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{17}NO_3$ 223.1208 $[M]^+$, found 223.1212 $[M]^+$.

IR (ν in cm^{-1}): 3270 (w), 2945 (w), 2831 (w), 1630 (m), 1550 (s), 1507 (s), 1371 (w), 1336 (m), 1304 (m), 1195 (m), 1111 (s), 1062 (s), 1040 (m), 979 (w), 844 (m), 714 (w), 664 (s).

2.1.6 *N*-(2,2-Dimethoxyethyl)-4-methoxybenzamide **5f**



5f

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 4-methoxybenzoyl chloride (2.98 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)-4-methoxybenzamide **5f** as a colorless solid (4.15 g, 87%).

R_f (*n*-hexane:EtOAc = 1:1) 0.20.

m.p. 106-107 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 6.25 (s, 1H), 4.48 (t, J = 5.3 Hz, 1H), 3.85 (s, 3H), 3.59 (t, J = 5.6 Hz, 2H), 3.43 (s, 6H).

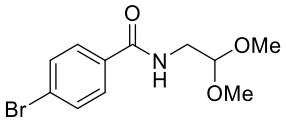
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 162.3, 128.9, 126.6, 113.8, 113.8, 103.0, 55.4, 54.7, 54.6, 41.5.

MS (ESI) m/z calcd for $C_{12}H_{17}NO_4Na^+$ 262.1 $[M+Na]^+$, found 262.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{17}NO_4$ 239.1158 $[M]^+$, found 239.1161 $[M]^+$.

IR (ν in cm^{-1}): 3300 (w), 2983 (w), 2836 (w), 1632 (m), 1607 (w), 1540 (m), 1503 (m), 1457 (w), 1302 (m), 1251 (s), 1204 (w), 1184 (m), 1097 (w), 1068 (s), 970 (m), 845 (m) 685 (w).

2.1.7 4-Bromo-*N*-(2,2-dimethoxyethyl)benzamide **5g**



5g

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 4-bromobenzoyl chloride (4.83 g, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded 4-bromo-*N*-(2,2-dimethoxyethyl)benzamide **5g** as a colorless solid (4.66 g, 81%).

R_f (*n*-hexane:EtOAc = 1:1) 0.43.

m.p. 72-73 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.67 – 7.62 (m, 2H), 7.60 – 7.55 (m, 2H), 6.29 (s, 1H), 4.48 (t, J=5.2 Hz, 1H), 3.65 – 3.56 (m, 2H), 3.44 (s, 6H).

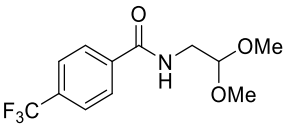
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 133.2, 131.9, 131.9, 128.7, 126.4, 54.8, 54.7, 41.7.

MS (ESI) m/z calcd for $C_{11}H_{14}BrNO_3Na^+$ 310.0 $[M+Na]^+$, found 310.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{11}H_{14}BrNO_3$ 239.1158 $[M]^+$, found 239.1161 $[M]^+$.

IR (ν in cm^{-1}): 3253 (w), 2942 (w), 1630 (m), 1589 (m), 1551 (s), 1485 (m), 13887 (w), 1304 (w), 1191 (w), 1096 (m), 1058 (s), 1039 (s), 1008 (m), 917 (m), 852 (s), 752 (w), 669 (s).

2.1.8 *N*-(2,2-Dimethoxyethyl)-4-(trifluoromethyl)benzamide **5h**



5h

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 4-(trifluoromethyl)benzoyl chloride (3.28 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)-4-(trifluoromethyl)-benzamide **5h** as a colorless solid (4.75 g, 86%).

R_f (*n*-hexane:EtOAc = 1:1) 0.40.

m.p. 62-64 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.84 (m, 2H), 7.74 – 7.64 (m, 2H), 6.40 (s, 1H), 4.50 (t, J = 5.1 Hz, 1H), 3.62 (t, J = 5.4 Hz, 2H), 3.44 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 137.7, 133.4 (q, J = 32.7 Hz), 127.6, 125.7(q, J = 3.8 Hz), 125.1, 122.4, 119.7, 102.6, 54.8, 54.8, 41.7.

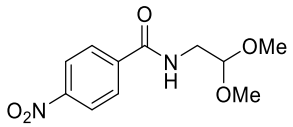
^{19}F {1H} NMR (376 MHz, $CDCl_3$) δ -63.0.

MS (ESI) m/z calcd for $C_{12}H_{14}F_3NO_3Na^+$ 300.1 $[M+Na]^+$, found 300.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{13}F_3NO_3$ 276.0853 $[M-H]^-$, found 276.0852 $[M-H]^-$.

IR (ν in cm^{-1}): 3288 (w), 2942 (w), 1637 (m), 1553 (m), 1429 (w), 1326 (s), 1309 (m), 1205 (w), 1159 (m), 1109 (s), 1064 (s), 1012 (m), 973 (w), 856 (m), 685 (m).

2.1.9 *N*-(2,2-Dimethoxyethyl)-4-nitrobenzamide **5i**



5i

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 4-nitrobenzoyl chloride (4.83 g, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)-4-nitrobenzamide **5i** as a yellow solid (4.52 g, 89%).

R_f (*n*-hexane:EtOAc = 1:1) 0.27.

m.p. 81-82 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 8.8 Hz, 2H), 7.93 (d, J = 8.8 Hz, 2H), 6.52 (s, 1H), 4.49 (t, J = 5.0 Hz, 1H), 3.62 (dd, J = 5.7, 5.1 Hz, 2H), 3.43 (s, 6H).

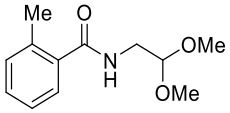
^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 149.7, 140.0, 123.9, 123.9, 102.6, 102.5, 54.9, 54.8, 41.8.

MS (ESI) m/z calcd for $C_{11}H_{14}N_2O_5Na^+$ 253.1 $[M+Na]^+$, found 253.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{11}H_{14}N_2O_5$ 254.0903 $[M]^+$, found 254.0891 $[M]^+$.

IR (ν in cm^{-1}): 3335 (w), 2944 (w), 1637 (m), 1599 (m), 1543 (m), 1523 (m), 1419 (w), 1340 (s), 1290 (s), 1203 (m), 1122 (m), 1058 (s), 947 (m), 851 (m). 717 (m).

2.1.10 *N*-(2,2-Dimethoxyethyl)-2-methylbenzamide **5j**



5j

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 2-methylbenzoyl chloride (3.33 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)-2-methylbenzamide **5j** as a colorless solid (4.07 g, 91%).

R_f (*n*-hexane:EtOAc = 1:1) 0.40.

m.p. 58-59 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 2H), 7.25 – 7.16 (m, 2H), 5.96 (s, 1H), 4.50 (t, J = 5.3 Hz, 1H), 3.59 (t, J = 5.6 Hz, 2H), 3.43 (s, 6H), 2.45 (s, 3H).

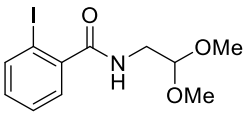
^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 136.4, 136.1 131.1, 130.0, 126.9, 125.8, 102.8, 54.6, 54.5, 41.3, 19.9.

MS (ESI) m/z calcd for $C_{12}H_{17}NO_3Na^+$ 246.1 $[M+Na]^+$, found 246.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{17}NO_3$ 223.1208 $[M]^+$, found 223.1214 $[M]^+$.

IR (ν in cm^{-1}): 3288 (w), 2941 (w), 1636 (s), 1600 (w), 1536 (s), 1369 (w), 1288 (w), 1205 (w), 1096 (w), 1066 (s), 1037 (m), 970 (m), 853 (w), 720 (s), 688 (s).

2.1.11 *N*-(2,2-Dimethoxyethyl)-2-iodobenzamide **5k**



5k

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 2-iodobenzoyl chloride (4.65 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)-2-iodobenzamide **5k** as a colorless solid (5.33 g, 79%).

R_f (*n*-hexane:EtOAc = 1:1) 0.30.

m.p. 63-65 °C

^{1}H NMR (400 MHz, $CDCl_3$) 7.93 – 7.78 (m, 1H), 7.46 – 7.32 (m, 2H), 7.10 (ddd, J = 7.9 Hz, 6.1 Hz, 3.1 Hz, 1H), 5.99 (s, 1H), 4.54 (t, J = 5.4 Hz, 1H), 3.60 (t, J = 5.6 Hz, 2H), 3.44 (s, 6H).

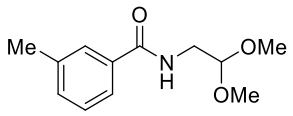
^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 142.2, 140.0, 131.3, 128.4, 128.3, 102.5, 92.5, 54.6, 41.5.

MS (ESI) m/z calcd for $C_{11}H_{14}INO_3Na^+$ 358.0 $[M+Na]^+$, found 358.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{11}H_{14}INO_3$ 335.0018 $[M]^+$, found 335.0026 $[M]^+$.

IR (ν in cm^{-1}): 3267 (w), 2935 (w), 1641 (s), 1534 (s), 1458 (w), 1420 (w), 1309 (m), 1191 (w), 1134 (m), 1095 (w), 1066 (s), 1034 (m), 967 (s), 808 (w), 680 (s).

2.1.12 *N*-(2,2-Dimethoxyethyl)-3-methylbenzamide 5l



5l

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and 3-methylbenzoyl chloride (2.91 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)-3-methylbenzamide **5l** as a colorless solid (4.15 g, 93%).

R_f (*n*-hexane:EtOAc = 1:1) 0.33.

m.p. 48-49 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.57 – 7.48 (m, 1H), 7.36 – 7.29 (m, 2H), 6.33 (bs, 1H), 4.49 (t, J = 5.3 Hz, 1H), 3.60 (t, J = 5.5 Hz, 2H), 3.43 (s, 3H), 2.39 (s, 3H).

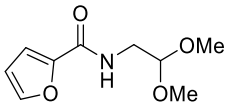
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 138.6, 134.4, 132.4, 128.6, 127.9, 127.8, 124.0, 102.9, 54.8, 41.6, 21.5.

MS (ESI) m/z calcd for $C_{12}H_{17}NO_3Na^+$ 246.1 $[M+Na]^+$, found 246.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{17}NO_3$ 223.1208 $[M]^+$, found 223.1218 $[M]^+$.

IR (ν in cm^{-1}):3297 (w), 2938 (w), 1639 (s), 1587 (w), 1536 (s), 1458 (w). 1313 (m), 1208 (m), 1131 (m), 1100 (m), 1067 (s), 1036 (m), 974 (m), 815 (w), 698 (s).

2.1.13 *N*-(2,2-Dimethoxyethyl)furan-2-carboxamide 5m



5m

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and furan-2-carbonyl chloride (2.18 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)furan-2-carboxamide **5m** as a colorless solid (3.80 g, 95%).

R_f (*n*-hexane:EtOAc = 7:3) 0.30.

m.p. 89-90 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.38 (m, 1H), 7.18 – 7.08 (m, 1H), 6.53 (s, 1H), 6.49 (dd, J = 3.5, 1.7 Hz, 1H), 4.46 (t, J = 5.3 Hz, 1H), 3.62 – 3.53 (m, 2H), 3.43 (s, 5H).

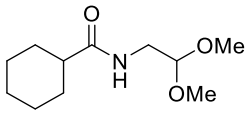
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 147.9, 144.1, 114.5, 112.2, 102.8, 54.6, 54.6, 40.6.

MS (ESI) m/z calcd for $C_9H_{13}NO_4Na^+$ 222.1 $[M+Na]^+$, found 222.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_9H_{13}NO_4$ 199.0845 $[M]^+$, found 199.0842 $[M]^+$.

IR (ν in cm^{-1}): 3253 (w), 2950 (w), 1637 (m), 1591 (s), 1527 (s), 1472 (m), 1368 (w), 1309 (m), 1189 (s), 1133 (s), 1065 (s), 1010 (m), 968 (m), 863 (w), 768 (m), 695 (m).

2.1.14 *N*-(2,2-Dimethoxyethyl)cyclohexanecarboxamide 5n



5n

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and cyclohexanecarbonyl chloride (3.02 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)cyclohexane-carboxamide **5n** as a colorless solid (3.96 g, 92%).

R_f (*n*-hexane:EtOAc = 1:1) 0.33.

m.p. 70-71 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.63 (s, 1H), 4.36 (t, J = 5.3 Hz, 1H), 3.39 (s, 6H), 3.43 – 3.34 (m, 2H), 2.08 (tt, J = 11.7, 3.5 Hz, 1H), 1.89 – 1.74 (m, 4H), 1.72 – 1.61 (m, 1H), 1.54 – 1.36 (m, 2H), 1.33 – 1.17 (m, 3H).

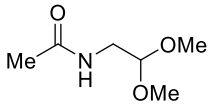
^{13}C NMR (101 MHz, $CDCl_3$) δ 176.4, 102.9, 54.6, 54.6, 45.6, 40.9, 29.7, 25.8.

MS (ESI) m/z calcd for $C_{11}H_{21}NO_3Na^+$ 238.1 $[M+Na]^+$, found 338.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{11}H_{21}NO_3$ 215.1521 $[M]^+$, found 215.1531 $[M]^+$.

IR (ν in cm^{-1}): 3281 (m), 2928 (m), 2852 (w), 1645 (s), 1558 (s), 1144 (w), 1321 (w), 1257 (w), 1189 (s), 1133 (s), 1099 (s), 1060 (s), 971 (s), 858 (w), 705 (m).

2.1.15 *N*-(2,2-Dimethoxyethyl)acetamide 5o



5o

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and acetyl chloride (1.56 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)acetamide **5o** as a yellow oil (1.61 g, 55%).

R_f (*n*-hexane:EtOAc = 1:1) 0.15.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.70 (s, 1H), 4.37 (t, J=5.2, 1H), 3.46 – 3.36 (m, 8H), 1.99 (s, 3H).

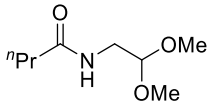
^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.5, 102.7, 54.5, 41.1, 23.3.

MS (ESI) m/z calcd for $C_6H_{14}NO_3$ 148.1 $[M+H]^+$, found 148.0 $[M+H]^+$.

HRMS (EI) m/z calcd for $C_6H_{13}NO_3$ 147.0895 $[M]^+$, found 147.0887 $[M]^+$.

IR (ν in cm^{-1}): 3299 (w), 2939 (w), 2834 (w), 1738 (w), 1652 (s), 1545 (s), 1435 (m), 1372 (m), 1285 (w), 1194 (m), 1128 (s), 1096 (s), 1058 (s), 971 (w), 923 (w), 818 (w), 600 (m).

2.1.16 *N*-(2,2-Dimethoxyethyl)butyramide 5p



5p

Prepared according to **GP1** from 2,2-dimethoxyethanamine (2.20 mL, 20.0 mmol, 1.0 equiv), Et_3N (8.34 mL, 60.0 mmol, 3.0 equiv) and butanoyl chloride (2.30 mL, 22.0 mmol, 1.1 equiv) in CH_2Cl_2 (30 mL). Purification by flash chromatography via puriflash XS 420+ purifier machine, HP_30µm_F0040 flash column (*n*-hexane:EtOAc = 95:5 → 40:60) afforded *N*-(2,2-dimethoxyethyl)butyramide **5p** as a colorless oil (2.72 g, 78%).

R_f (*n*-hexane:EtOAc = 1:1) 0.30.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.71 (s, 1H), 4.35 (t, J=5.3 Hz, 1H), 3.51 – 3.28 (m, 8H), 2.19 – 2.08 (m, 2H), 1.71 – 1.56 (m, 2H), 0.92 (t, J=7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 173.3, 102.8, 54.5, 40.9, 38.7, 19.2, 13.8.

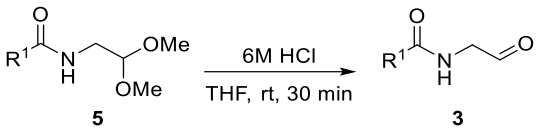
MS (ESI) m/z calcd for $C_8H_{17}NO_3Na^+$ 198.1 $[M+Na]^+$, found 198.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{11}H_{21}NO_3$ 175.1208 $[M]^+$, found 175.1201 $[M]^+$.

IR (ν in cm^{-1}): 3300 (w), 2962 (w), 2834 (w), 1646 (s), 1542 (s), 1459 (m), 1369 (w), 1276 (w), 1196 (m), 1128 (s), 1099 (s), 1056 (s), 973 (m), 929 (w), 823 (w), 709 (w).

2.2 Aldehydes

GENEREAL PROCEDURE 2 (TP2)

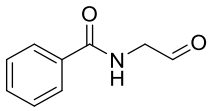


5 **3**

Aldehydes were prepared according to modified procedure.[5]

Acetale **5** (1.0 equiv) was dissolved in THF (4 mL/mmol) and cooled to 0 °C. HCl (4 mL/mmol, 6 M in water) was slowly added. The ice bath was removed and the reaction was stirred for 30 min at room temperature. After TLC analysis showed complete consumption of the acetale, sat. aq. NaCl solution (15 mL) was added and diluted with CH_2Cl_2 (30 mL). The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (2x 30 mL). The combined organic extracts were dried over Na_2SO_4. (Note! The crude aldehydes of type **3** are unstable towards prolonged contact with water. Therefore, a rapid workup is recommended). After evaporation of the solvents the crude product is dried at room temperature over 2-3 h under oil pump vacuum (10^{-2} mbar). Crude aldehydes **3** were only characterized briefly via ^{1}H-NMR and used without further purification for the synthesis of the 2-oxyenamides.

2.2.1 *N*-(2-Oxoethyl)benzamide 3a



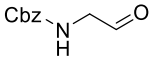
3a

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)benzamide **5a** (1.01g, 6.1 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3a** as a colorless solid (990 mg, 99%). Analytical data are in accordance with the literature.[5]

R_f (*n*-hexane:EtOAc = 3:7) 0.32.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.81 (d, J = 7.4 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 4.36 (d, J = 4.8 Hz, 1H).

2.2.2 *Benzyl (2-oxoethyl)carbamate* 3c



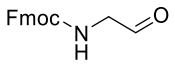
3c

Prepared according to GP2 from benzyl (2,2-dimethoxyethyl)carbamate **5c** (1.20 g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3c** as a colorless oil (561 mg, 58%).

R_f (*n*-hexane:EtOAc = 1:1) 0.38.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 7.39 – 7.32 (m, 5H), 5.43 (s, 1H), 5.13 (s, 2H), 4.16 (d, J = 5.1 Hz, 2H).

2.2.3 *(9H-fluoren-9-yl)methyl (2-oxoethyl)carbamate* 3d



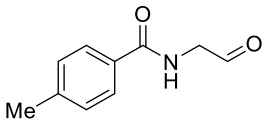
3d

Prepared according to GP2 from (9*H*-fluoren-9-yl)methyl (2,2-dimethoxyethyl)carbamate **5d** (1.64 g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3d** as a colorless solid (1.39 mg, 99%).

R_f (*n*-hexane:EtOAc = 1:1) 0.35.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.83 – 7.74 (m, 2H), 7.60 (d, J = 7.5 Hz, 2H), 7.46 – 7.37 (m, 2H), 7.31 (dd, J = 7.5, 1.2 Hz, 2H), 5.44 (s, 1H), 4.43 (d, J = 7.0 Hz, 2H), 4.24 (t, J = 6.9 Hz, 1H), 4.17 (d, J = 5.1 Hz, 2H).

2.2.4 4-Methyl-*N*-(2-oxoethyl)benzamide 3e



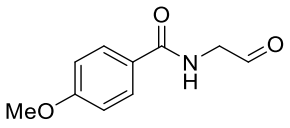
3e

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)-3-methylbenzamide **5e** (1.12 g, 5.0 mmol, 1.0 equiv) and 6 M HCl (17 mL) in THF (17 mL). Removal of the solvents afforded the crude aldehyde **3e** as a colorless solid (813 mg, 92%).

R_f (*n*-hexane:EtOAc = 3:7) 0.41.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 4.40 (d, *J* = 4.7 Hz, 2H), 2.40 (s, 3H).

2.2.5 4-Methoxy-*N*-(2-oxoethyl)benzamide **3f**



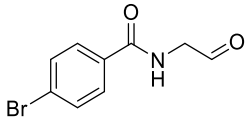
3f

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)-4-methoxybenzamide **5f** (1.20g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3f** as a colorless solid (460 mg, 48%).

R_f (*n*-hexane:EtOAc = 3:7) 0.27.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.79 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 6.83 (s, 1H), 4.40 (d, J = 4.7 Hz, 2H), 3.85 (s, 3H).

2.2.6 4-Bromo-*N*-(2-oxoethyl)benzamide **3g**



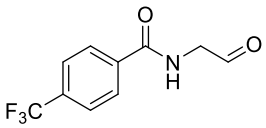
3g

Prepared according to GP2 from 4-bromo-*N*-(2,2-dimethoxyethyl)benzamide **5g** (1.44 g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3g** as a colorless solid (1.19 g, 98%).

R_f (*n*-hexane:EtOAc = 3:7) 0.34.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.73 – 7.67 (m, 2H), 7.63 – 7.56 (m, 2H), 6.89 (s, 1H), 4.42 (d, J = 4.7 Hz, 2H).

2.2.7 *N*-(2-Oxoethyl)-4-(trifluoromethyl)benzamide **3h**



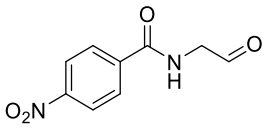
3h

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)-4-(trifluoromethyl)benzamide **5h** (1.39 g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3h** as a colorless solid (1.07 mg, 93%).

R_f (*n*-hexane:EtOAc = 3:7) 0.33.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.93 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 6.94 (s, 1H), 4.46 (d, *J* = 4.6 Hz, 2H).

2.2.8 4-Nitro-*N*-(2-oxoethyl)benzamide **3i**



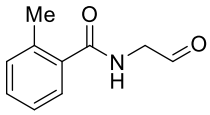
3i

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)-4-nitrobenzamide **5i** (1.27 g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3i** as a colorless solid (770 mg, 74%).

R_f (*n*-hexane:EtOAc = 3:7) 0.20.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.36 – 8.21 (m, 2H), 8.08 – 7.94 (m, 2H), 6.99 (s, 1H), 4.48 (d, J = 4.6 Hz, 2H).

2.2.9 2-Methyl-*N*-(2-oxoethyl)benzamide **3j**



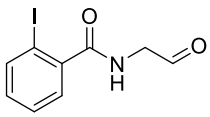
3j

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)-2-methylbenzamide **5j** (1.12g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3j** as a colorless solid (720 mg, 81%).

R_f (*n*-hexane:EtOAc = 3:7) 0.40.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.44 – 7.39 (m, 1H), 7.36 – 7.30 (m, 1H), 7.25 – 7.18 (m, 2H), 6.60 (s, 1H), 4.36 (d, *J* = 5.0 Hz, 2H), 2.44 (s, 3H).

2.2.10 2-Iodo-*N*-(2-oxoethyl)benzamide **3k**



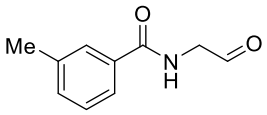
3k

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)-2-iodobenzamide **5k** (838 mg, 2.5 mmol, 1.0 equiv) and 6 M HCl (9 mL) in THF (9 mL). Removal of the solvents afforded the crude aldehyde **3k** as a yellow solid (700 mg, 97%).

R_f (*n*-hexane:EtOAc = 3:7) 0.33.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 7.94 – 7.84 (m, 1H), 7.48 – 7.36 (m, 2H), 7.18 – 7.10 (m, 1H), 6.55 (s, 1H), 4.44 (d, *J* = 4.8 Hz, 2H).

2.2.11 3-Methyl-*N*-(2-oxoethyl)benzamide 3l



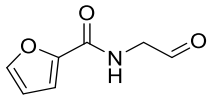
3l

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)-3-methylbenzamide **5l** (1.12g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3l** as a colorless oil (720 mg, 81%).

R_f (*n*-hexane:EtOAc = 3:7) 0.40.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.71 – 7.54 (m, 2H), 7.43 – 7.28 (m, 2H), 6.94 (s, 1H), 4.41 (d, *J* = 4.7 Hz, 2H), 2.40 (s, 3H).

2.2.12 *N*-(2-Oxoethyl)furan-2-carboxamide 3m



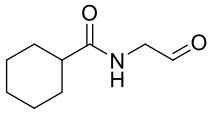
3m

Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)furan-2-carboxamide **5m** (996 mg, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3m** as a colorless solid (393 mg, 51%).

R_f (*n*-hexane:EtOAc = 3:7) 0.28.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 7.55 – 7.41 (m, 1H), 7.22 – 7.09 (m, 1H), 7.02 (s, 1H), 6.52 (dd, *J* = 3.5, 1.8 Hz, 1H), 4.39 (d, *J* = 5.0 Hz, 2H).

2.2.13 *N*-(2-Oxoethyl)cyclohexanecarboxamide 3n



3n

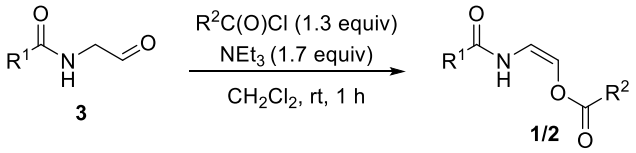
Prepared according to GP2 from *N*-(2,2-dimethoxyethyl)cyclohexanecarboxamide **5n** (1.08 g, 5.0 mmol, 1.0 equiv) and 6 M HCl (18 mL) in THF (18 mL). Removal of the solvents afforded the crude aldehyde **3n** as a colorless solid (747 mg, 88%).

R_f (*n*-hexane:EtOAc = 3:7) 0.25.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 6.18 (s, 1H), 4.22 (d, *J* = 4.8 Hz, 2H), 2.18 (tt, *J* = 11.7, 3.5 Hz, 1H), 1.93 – 1.85 (m, 2H), 1.84 – 1.77 (m, 2H), 1.72 – 1.64 (m, 1H), 1.51 – 1.38 (m, 2H), 1.36 – 1.14 (m, 3H).

2.3 (*Z*)-Oxyenamides/(Z)-oxyencarbamates

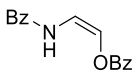
GENERAL PROCEDURE 3 (GP3)



Prepared according to our previously reported procedure.[6]

To a stirred solution of triethylamine (1.7 equiv) and the corresponding acyl chloride (1.3 equiv) in dichlormethane (2 mL/mmol) was added dropwise a solution of the aldehyde **3** (1.0 equiv) in dichlormethane (2 mL/mmol) over 5 min. The reaction mixture was stirred for 1 h at room temperature. After TLC analysis showed complete consumption of the aldehyde, saturated $NaHCO_3$ solution was added (20 mL). The organic layers were separated and the aqueous phase was extracted with dichlormethane (2x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by flash chromatography afforded the desired (*Z*)-oxyenamide/(Z)-oxyencarbamate **1/2** as analytically pure product. All oxyenamides of type **1/2** tend to decompose upon contact to any type of acid. Therefore, column chromotography was performed with 0.2 vol% NEt_3 as additive. $CDCl_3$ for NMR spectroscopy was passed through a short plug of basic alumina before use.

2.3.1 (*Z*)-2-Benzamidovinyl benzoate 1a



1a

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (774 mg, 4.74 mmol, 1.0 equiv), triethylamine (1.1 mL, 8.06 mmol, 1.7 equiv) and benzoyl chloride (0.72 mL, 6.16 mmol, 1.3 equiv) in a total of 20 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl benzoate **1a** (927 mg, 73%) as colorless solid. Analytical data are in accordance with those previously reported.[6]

R_f (*n*-hexane:EtOAc = 4:1) 0.38.

m.p. 172-175 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.17 – 8.06 (m, 2H), 7.97 (d, J=10.2 Hz, 1H), 7.91 – 7.81 (m, 2H), 7.68 – 7.62 (m, 1H), 7.61 – 7.56 (m, 1H), 7.55 – 7.48 (m, 4H), 7.11 (d, J=5.1 Hz, 1H), 6.86 (dd, J=10.7 Hz, 5.1 Hz, 1H).

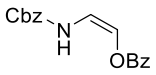
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 162.7, 134.0, 133.4, 132.4, 130.0, 129.0, 128.9, 128.8, 127.3, 121.9, 109.5.

IR (ATR, ν in cm^{-1}): 3275 (w), 3110 (w), 3032 (w), 1723 (m), 1686 (w), 1643 (m), 1601 (w), 1580 (w), 1519 (s), 1484 (s), 1451 (w), 1249 (s), 1146 (m), 1113 (s), 1093 (s), 1068 (s), 798 (w), 687 (s).

MS (ESI) m/z calcd for $C_{16}H_{13}NO_3Na$ 290.1 $[M+Na]^+$, found 290.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{16}H_{13}NO_3$ 267.0895 $[M]^+$, found 267.0901 $[M]^+$.

2.3.2 (*Z*)-2-(((Benzyloxy)carbonyl)amino)vinyl benzoate **1c**



1c

Prepared according to **GP3** from benzyl (2-oxoethyl)carbamate **3c** (561 mg, 4.59 mmol, 1.0 equiv), triethylamine (0.69 mL, 4.93 mmol, 1.7 equiv) and benzoyl chloride (0.43 mL, 3.77 mmol, 1.3 equiv) in a total of 12 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(((benzyloxy)carbonyl)amino)vinyl benzoate **1c** (505 mg, 59%) as colorless solid. Analytical data are in accordance with those previously reported.[6]

R_f (*n*-hexane:EtOAc = 4:1) 0.47.

m.p. 69-71 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.7 Hz, 2H), 7.62 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.42 – 7.33 (m, 5H), 6.95 (d, J = 5.1 Hz, 1H), 6.67 (d, J = 11.3 Hz, 1H), 6.38 (dd, J = 11.0, 5.1 Hz, 1H), 5.20 (s, 2H).

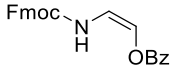
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 153.1, 135.7, 133.8, 130.0, 128.8, 128.7, 128.7, 128.6, 119.9, 110.5, 67.8.

IR (ATR, ν in cm^{-1}): 3270 (w), 3128 (w), 3030 (w), 1729 (s), 1689 (s), 1601 (w), 1518 (s), 1450 (m), 1360 (w), 1228 (s), 1159 (m), 1100 (s), 1074 (s), 1026 (m), 906 (w), 741 (m), 696 (s).

MS (ESI) m/z calcd for $C_{17}H_{15}NO_4Na$ 320.1 $[M+Na]^+$, found 320.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{25}NO_3$ 297.1001 $[M]^+$, found 297.0997 $[M]^+$.

2.3.3 (*Z*)-2-((((9*H*-fluoren-9-yl)methoxy)carbonyl)amino)vinyl benzoate **1d**



1d

Prepared according to **GP3** from (9*H*-fluoren-9-yl)methyl (2-oxoethyl)carbamate **3d** (1.39 mg, 4.95 mmol, 1.0 equiv), triethylamine (1.2 mL, 8.50 mmol, 1.7 equiv) and benzoyl chloride (0.75 mL, 6.5 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-((((9*H*-fluoren-9-yl)methoxy)-carbonyl)amino)vinyl benzoate **1d** (1.30 g, 67%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.41.

m.p. 140-142 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.07 (m, 2H), 7.80 (s, 2H), 7.62 (t, *J* = 7.4 Hz, 3H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.45 – 7.41 (m, 2H), 7.34 (td, *J* = 7.4, 1.2 Hz, 2H), 6.95 (d, *J* = 5.1 Hz, 1H), 6.67 (d, *J* = 11.2 Hz, 1H), 6.38 (dd, *J* = 10.9, 5.1 Hz, 1H), 4.54 (d, *J* = 6.8 Hz, 2H), 4.29 (d, *J* = 6.9 Hz, 1H).

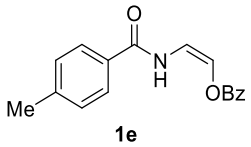
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 153.2, 143.7, 141.5, 133.9, 130.1, 128.8, 128.0, 127.3, 125.1, 120.2, 120.1, 110.5, 67.7, 47.2.

IR (ATR, ν in cm^{-1}): 327 (w), 3063 (w), 1738 (m), 1717 (s), 1472 (w), 1448 (m), 1398 (m), 1314 (s), 1264 (s), 1161 (m), 1103 (s), 1031 (m), 941 (w), 763 (m), 739 (s), 705 (s), 699 (s), 593 (m), 5542 (m).

MS (ESI) m/z calcd for $C_{24}H_{19}NO_4Na$ 408.1 $[M+Na]^+$, found 408.0 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{24}H_{19}NO_4$ 385.1314 $[M]^+$, found 385.1299 $[M]^+$.

2.3.4 (*Z*)-2-(4-Methylbenzamido)vinyl benzoate **1e**



1e

Prepared according to **GP3** from 4-methyl-*N*-(2-oxoethyl)benzamide **3e** (813 mg, 4.59 mmol, 1.0 equiv), triethylamine (1.08 mL, 7.80 mmol, 1.7 equiv) and benzoyl chloride (0.69 mL, 5.97 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(4-methylbenzamido)vinyl benzoate **1e** (890 mg, 69%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.39.

m.p. 161-162 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.16 – 8.01 (m, 2H), 7.79 (d, J=7.6 Hz, 2H), 7.63 (dd, J=15.6 Hz, 7.6 Hz, 3H), 7.52 (t, J=7.7 Hz, 2H), 7.43 (t, J=7.4 Hz, 2H), 7.34 (td, J=7.4 Hz, 1.2, 2H), 6.94 (d, J=5.2 Hz, 1H), 6.64 (d, J=11.0 Hz, 1H), 6.44 – 6.18 (m, 1H), 4.54 (d, J=6.7 Hz, 2H), 4.29 (t, J=6.8 Hz, 1H).

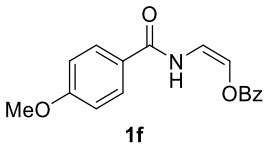
^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.9, 153.2, 143.6, 141.5, 133.9, 130.1, 128.8, 128.0, 127.3, 125.0, 120.2, 120.0, 110.5, 67.6, 47.1.

IR (ATR, ν in cm^{-1}): 3248 (w), 3120 (w), 2359 (w), 1725 (s). 1695 (w), 1632 (s), 1524 (s), 1495 (s), 1450 (m), 1251 (s), 1183 (m), 1150 (s), 1090 (s), 1068 (s), 646 (w), 835 (m), 706 (s).

MS (ESI) m/z calcd for $C_{17}H_{15}NO_3Na$ 304.1 $[M+Na]^+$, found 304.3 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{15}NO_3$ 281.1052 $[M]^+$, found 281.1049 $[M]^+$.

2.3.5 (*Z*)-2-(4-Methoxybenzamido)vinyl benzoate **1f**



1f

Prepared according to GP3 from 4-methoxy-N-(2-oxoethyl)benzamide 3f (460 mg, 2.38 mmol, 1.0 equiv), triethylamine (0.56 mL, 4.05 mmol, 1.7 equiv) and benzoyl chloride (0.36 mL, 3.09 mmol, 1.3 equiv) in a total of 5 mL dichlormethane. Purification by column chromatography (n-hexane:EtOAc + 0.2 vol% NEt3 = 19:1 → 9:1) afforded (Z)-2-(4-methoxybenzamido)vinyl benzoate 1f (550 mg, 78%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.33.

m.p. 144-146 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.13 – 8.06 (m, 2H), 7.94 (d, J=10.7 Hz, 1H), 7.85 – 7.78 (m, 2H), 7.68 – 7.59 (m, 1H), 7.51 (t, J=7.7 Hz, 2H), 7.06 (d, J=5.1 Hz, 1H), 7.00 – 6.93 (m, 2H), 6.83 (dd, J=10.6, 5.1 Hz, 1H), 3.86 (s, 3H).

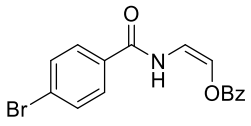
^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.4, 162.9, 162.7, 133.9, 130.0, 129.2, 128.9, 125.5, 121.4, 114.2, 109.7, 55.6.

IR (ATR, ν in cm^{-1}): 3272 (w), 2935 (w), 2361 (w), 1722 s), 1695 (w), 1630 (s), 1602 (s), 1527 (m), 1494 (s), 1310 (m), 1248 (s), 1172 (s), 1150 (m), 1113 (s), 1092 (s), 1026 (s), 842 (s), 755 (m), 707 (s).

MS (ESI) m/z calcd for $C_{17}H_{15}NO_4Na$ 320.1 $[M+Na]^+$, found 320.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{15}NO_4$ 297.0001 $[M]^+$, found 296.0988 $[M]^+$.

2.3.6 (*Z*)-2-(4-Bromobenzamido)vinyl benzoate **1g**



1g

Prepared according to **GP3** from 4-bromo-*N*-(2-oxoethyl)benzamide **3g** (1.12 g, 4.63 mmol, 1.0 equiv), triethylamine (1.06 mL, 7.87 mmol, 1.7 equiv) and benzoyl chloride (0.70 mL, 6.02 mmol, 1.3 equiv) in

a total of 20 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl benzoate **1g** (1.21 g, 76%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.33.

m.p. 145-147 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.15 – 8.04 (m, 2H), 7.92 (d, J = 10.6 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.69 – 7.60 (m, 3H), 7.57 – 7.47 (m, 2H), 7.10 (d, J = 5.1 Hz, 1H), 6.82 (dd, J = 10.6, 5.1 Hz, 1H).

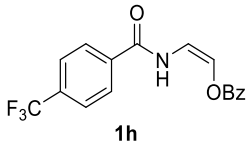
^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.1, 162.7, 134.1, 132.3, 130.0, 128.9, 128.9, 128.7, 127.2, 122.2, 109.3.

IR (ATR, ν in cm^{-1}): 3262 (w), 2922 (w), 2361 (w), 1722 (m), 1692 (m), 1634 (s), 1586 (m), 1519 (m), 1449 (w), 1301 (w), 1249 (s), 1151 (m), 1090 (s), 1067 (s), 1006 (m), 844 (m), 703 (s).

MS (ESI) m/z calcd for $C_{16}H_{11}BrNO_3$ 344.0 $[M-H]^-$, found 344.1 $[M-H]^-$.

HRMS (EI) m/z calcd for $C_{16}H_{12}BrNO_3$ 345.0001 $[M]^+$, found 345.0001 $[M]^+$.

2.3.7 (*Z*)-2-(4-(Trifluoromethyl)benzamido)vinyl benzoate 1h



1h

Prepared according to **GP3** from *N*-(2-oxoethyl)-4-(trifluoromethyl)benzamide **3h** (1.07 mg, 4.63 mmol, 1.0 equiv), triethylamine (1.09 mL, 7.87 mmol, 1.7 equiv) and benzoyl chloride (0.70 mL, 6.02 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(4-(trifluoromethyl)benzamido)vinyl benzoate **1h** (1.21 g, 78%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.36.

m.p. 136-138 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.15 – 8.07 (m, 2H), 8.00 – 7.92 (m, 3H), 7.77 (d, J=8.1 Hz, 2H), 7.70 – 7.62 (m, 1H), 7.53 (t, J=7.8 Hz, 2H), 7.14 (d, J=5.1 Hz, 1H), 6.85 (dd, J=10.6, 5.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.0, 162.8, 162.7, 136.7, 134.2, 133.9, 133.8, 130.3, 130.0, 129.0, 128.7, 128.6, 127.8, 126.1 (q, J=3.8), 122.3 (q, J=274), 109.2.

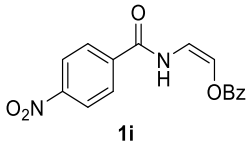
^{19}F {H} NMR (376 MHz, $CDCl_3$) δ = -63.03.

IR (ATR, ν in cm^{-1}): 3288 (w), 3012 (w), 2361 (w), 1730 (m), 1679 /w), 1647 (s), 1581 (w), 1522 (m), 1497 (m), 1407 (w), 1322 (s), 1261 (s), 1174 (m), 1119 (s), 1064 (s), 1012 (w), 859 (m), 702 (s).

MS (ESI) m/z calcd for $C_{17}H_{12}F_3NO_3Na$ 358.1 $[M+Na]^+$, found 358.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{12}F_3NO_3$ 335.0769 $[M]^+$, found 335.0758 $[M]^+$.

2.3.8 (*Z*)-2-(4-Nitrobenzamido)vinyl benzoate **1i**



1i

Prepared according to **GP3** from 4-nitro-*N*-(2-oxoethyl)benzamide **3i** (770 mg, 3.70 mmol, 1.0 equiv), triethylamine (0.87 mL, 6.25 mmol, 1.7 equiv) and benzoyl chloride (0.56 mL, 4.81 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(4-nitrobenzamido)vinyl benzoate **1i** (860 mg, 87%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.17.

m.p. 182-185 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.44 – 8.28 (m, 2H), 8.13 – 8.07 (m, 2H), 8.05 – 8.00 (m, 2H), 7.99 (s, 1H), 7.74 – 7.61 (m, 1H), 7.53 (t, J=7.8 Hz, 2H), 7.15 (d, J=5.1 Hz, 1H), 6.84 (dd, J=10.5, 5.1 Hz, 1H).

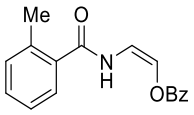
^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.6, 162.0, 150.1, 138.9, 134.3, 130.0, 128.6, 128.5, 124.3, 123.0, 109.0.

IR (ATR, ν in cm^{-1}): 3269 (w), 3115 (w), 2360 (w), 1722 (m), 1688 (w), 1645 (m), 1601 (m), 1517 (s), 1452 (w), 1341 (m), 1245 (s), 1149 (m), 1116 (s), 1093 (s), 1068 (m), 843 (m), 702 (s).

MS (ESI) m/z calcd for $C_{16}H_{11}N_2O_5$ 311.1 $[M-H]^-$, found 311.1 $[M-H]^-$.

HRMS (EI) m/z calcd for $C_{16}H_{12}N_2O_5$ 312.0746 $[M]^+$, found 312.0732 $[M]^+$.

2.3.9 (*Z*)-2-(2-Methylbenzamido)vinyl benzoate **1j**



1j

Prepared according to **GP3** from 2-methyl-*N*-(2-oxoethyl)benzamide **3j** (719 mg, 4.06 mmol, 1.0 equiv), triethylamine (0.96 mL, 6.70 mmol, 1.7 equiv) and benzoyl chloride (0.61 mL, 5.27 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(2-methylbenzamido)vinyl benzoate **1j** (720 mg, 63%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.23.

m.p. 118-121 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09 – 8.02 (m, 2H), 7.66 – 7.55 (m, 2H), 7.54 – 7.44 (m, 3H), 7.44 – 7.36 (m, 1H), 7.33 – 7.27 (m, 2H), 7.09 (d, J=5.1 Hz, 1H), 6.84 (dd, J=10.8, 5.1 Hz, 1H), 2.53 (s, 3H).

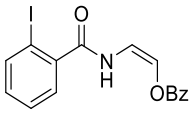
^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.3, 162.7, 137.1, 134.9, 131.5, 130.8, 130.0, 128.8, 128.6, 127.0, 126.1, 121.6, 109.2, 20.1.

IR (ATR, ν in cm^{-1}): 3229 (w), 3105 (w), 2361 (w), 1727 (s), 1683 (w) 1640 (s), 1507 (s) 1486 (m), 1451 (m), 1298 (w), 1242 (s), 1156 (m), 1129 (s), 1107 (s), 1086 (s),1026 (w), 860 (m), 700 (s).

MS (ESI) m/z calcd for $C_{17}H_{15}NO_3Na$ 304.1 $[M+Na]^+$, found 304.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{15}NO_3$ 281.1052 $[M]^+$, found 281.1045 $[M]^+$.

2.3.10 (*Z*)-2-(2-Iodobenzamido)vinyl benzoate **1k**



1k

Prepared according to **GP3** from 2-iodo-*N*-(2-oxoethyl)benzamide **3k** (700 mg, 2.42 mmol, 1.0 equiv), triethylamine (0.57 mL, 4.11 mmol, 1.7 equiv) and benzoyl chloride (0.37 mL, 3.14 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(2-iodobenzamido)vinyl benzoate **1k** (1.40 g, 58%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.33.

m.p. 154-157 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.13 – 8.07 (m, 2H), 7.98 – 7.92 (m, 1H), 7.73 (d, J=10.9 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.52 – 7.41 (m, 3H), 7.20 (dd, J=7.9, 1.7 Hz, 1H), 7.16 (d, J=5.1 Hz, 1H), 6.82 (dd, J=10.7 Hz, 5.1, 1H).

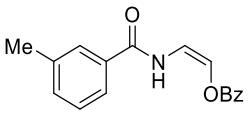
^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.3, 162.7, 140.6, 140.5, 134.0, 132.1, 130.1, 129.5, 128.8, 128.6, 128.6, 122.4, 108.8, 92.4.

IR (ATR, ν in cm^{-1}): 3277 (w), 3112 (w), 2360 (w), 1723 (s), 1687 (w), 1647 (s), 1582 (w), 1502 (s), 1448 (m), 1297 (w), 1249 (s), 1159 (m), 1127 (s), 1093 (s), 1086 (s), 1018 (s), 864 (m), 705 (s).

MS (ESI) m/z calcd for $C_{16}H_{12}INO_3Na$ 416.0 $[M+Na]^+$, found 416.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{16}H_{12}INO_3$ 392.9862 $[M]^+$, found 392.9851 $[M]^+$.

2.3.11 (*Z*)-2-(3-Methylbenzamido)vinyl benzoate **1l**



1l

Prepared according to **GP3** from 3-methyl-*N*-(2-oxoethyl)benzamide **3l** (719 mg, 4.06 mmol, 1.0 equiv), triethylamine (0.96 mL, 6.90 mmol, 1.7 equiv) and benzoyl chloride (0.61 mL, 5.28 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(3-methylbenzamido)vinyl benzoate **1l** (590 mg, 62%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.33.

m.p. 126-127 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 – 8.03 (m, 2H), 7.94 (d, J=10.8 Hz, 1H), 7.75 – 7.59 (m, 3H), 7.52 (dd, J=8.4, 7.1 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.10 (d, J=5.1 Hz, 1H), 6.86 (dd, J=10.7, 5.1 Hz, 1H), 2.44 (s, 3H).

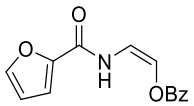
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.2, 162.7, 139.0, 134.0, 133.4, 133.2, 130.0, 128.9, 128.8, 128.2, 124.0, 121.8, 109.6, 21.5.

IR (ATR, ν in cm^{-1}): 3290 (w), 3067 (w), 2360 (w), 1724 (s), 1695 (w), 1635 (m), 1585 (w), 1507 (s), 1477 (m), 1364 (w), 1261 (s), 1247 (s), 1186 (m), 1143 (s), 1116 (s), 1091 (s), 810 (m), 736 (m), 700 (s).

MS (ESI) m/z calcd for $C_{17}H_{15}NO_3Na$ 304.1 $[M+Na]^+$, found 304.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{15}NO_3$ 281.1052 $[M]^+$, found 281.1048 $[M]^+$.

2.3.12 (*Z*)-2-(Furan-2-carboxamido)vinyl benzoate 1m



1m

Prepared according to **GP3** from *N*-(2,2-dimethoxyethyl)furan-2-carboxamide **3m** (394 mg, 2.57 mmol, 1.0 equiv), triethylamine (607 µL, 7.80 mmol, 1.7 equiv) and benzoyl chloride (388 µL, 3.34 mmol, 1.3 equiv) in a total of 10 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(furan-2-carboxamido)vinyl benzoate **1m** (474 mg, 72 %) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.29.

m.p. 133-135 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.19 (s, 1H), 8.17 – 8.12 (m, 2H), 7.71 – 7.61 (m, 1H), 7.58 – 7.50 (m, 3H), 7.28 – 7.23 (m, 1H), 7.11 (d, J=5.0 Hz, 1H), 6.79 (dd, J=10.9, 5.1 Hz, 1H), 6.58 (dd, J=3.5, 1.8 Hz, 1H).

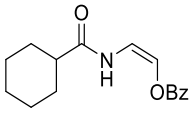
^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.7, 154.7, 147.1, 144.8, 134.0, 130.1, 128.9, 128.8, 121.9, 116.2, 112.8, 108.4.

IR (ATR, ν in cm^{-1}): 3243 (w), 3118 (w), 2361 (w), 1718 (m), 1692 (w), 1645 (s), 1564 (m), 1515 (s), 1453 (w), 1304 (m), 1252 (s), 1184 (s), 1146 (s), 1116 ()s), 1096 (s), 1022 (m), 947 (m), 833 (w), 706 (s).

MS (ESI) m/z calcd for $C_{14}H_{14}NO_4Na$ 286.1 $[M+Na]^+$, found 279.9 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{14}H_{11}NO_4$ 257.0688 $[M]^+$, found 257.0688 $[M]^+$.

2.3.13 (*Z*)-2-(Cyclohexanecarboxamido)vinyl benzoate 1n



1n

Prepared according to **GP3** from *N*-(2-oxoethyl)cyclohexanecarboxamide **3n** (747 mg, 4.41 mmol, 1.0 equiv), triethylamine (1.04 mL, 7.50 mmol, 1.7 equiv) and benzoyl chloride (0.67 mL, 5.73 mmol, 1.3 equiv) in a total of 18 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-(cyclohexanecarboxamido)vinyl benzoate **1n** (1.03 g, 85%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.37.

m.p. 170-173 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.16 – 8.04 (m, 2H), 7.70 – 7.61 (m, 1H), 7.58 – 7.47 (m, 2H), 7.23 (s, 1H), 6.97 (d, J=5.1 Hz, 1H), 6.66 (dd, J=10.8, 5.1 Hz, 1H), 2.22 (tt, J=11.7, 3.6 Hz, 1H), 2.02 – 1.89 (m, 2H), 1.88 – 1.78 (m, 2H), 1.74 – 1.66 (m, 1H), 1.61 – 1.45 (m, 2H), 1.40 – 1.17 (m, 3H).

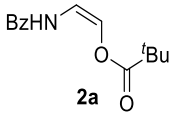
^{13}C NMR (101 MHz, $CDCl_3$) δ = 172.9, 162.8, 133.9, 130.0, 128.9, 128.8, 120.9, 109.3, 45.5, 29.6, 25.7, 25.7.

IR (ATR, ν in cm^{-1}): 3261 (w), 2934 (m), 2852 (w), 2360 (w), 1727 (s), 1695 (w), 1645 (s), 1602 (w), 1513 (s), 1450 (m), 1316 (w), 1251 (s), 1244 (s), 1201 (s), 1119 (s), 1090 (s), 1026 (m), 888 (m), 701 (s).

MS (ESI) m/z calcd for $C_{16}H_{19}NO_3Na$ 296.1 $[M+Na]^+$, found 296.2 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{16}H_{19}NO_3$ 273.1365 $[M]^+$, found 273.1351 $[M]^+$.

2.3.14 (*Z*)-2-Benzamidovinyl pivalate 2a



2a

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (721 mg, 4.42 mmol, 1.0 equiv), triethylamine (1.04 mL, 7.51 mmol, 1.7 equiv) and pivaloyl chloride (0.71 mL, 5.75 mmol, 1.3 equiv) in a total of 20 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl pivalate **2a** (609 mg, 56%) as colorless solid. Analytical data are in accordance with those previously reported.[6]

R_f (*n*-hexane:EtOAc = 4:1) 0.45.

m.p. 93 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 – 7.70 (m, 3H), 7.61 – 7.54 (m, 1H), 7.53 – 7.42 (m, 2H), 6.90 (d, *J*=5.0 Hz, 1H), 6.75 (dd, *J*=10.6 Hz, 5.0 Hz, 1H), 1.32 (s, 9H).

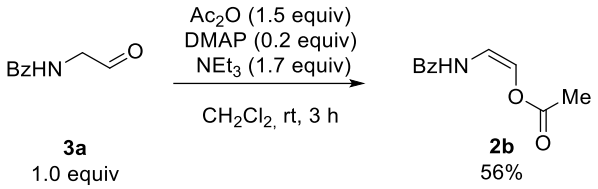
^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.1, 163.6, 133.4, 132.4, 129.1, 127.1, 122.0, 108.9, 39.2, 27.3.

IR (ATR, ν in cm^{-1}): 3345 (w), 2984 (w), 1741 (s), 1687 (w), 1645 (s), 1503 (s), 1478 (s), 1395 (w), 1364 (w), 1272 (s), 1124 (s), 1026 (w), 929 (w), 885 (m), 751 (m), 717 (m), 694 (m).

MS (ESI) m/z calcd for $C_{14}H_{17}NO_3Na$ 270.1 $[M+Na]^+$, found 270.1 $[M+Na]^+$

HRMS (EI) m/z calcd for $C_{14}H_{17}NO_3$ 247.1208 $[M]^+$, found 247.1206 $[M]^+$.

2.3.15 (*Z*)-2-Benzamidovinyl acetate **2b**



To a stirred solution of triethylamine (1.17 mL, 8.43 mmol, 1.7 equiv), 4-dimethylaminopyridine (122 mg, 0.992 mmol, 0.2 equiv) and acetic anhydride (0.58 mL, 7.44 mmol, 1.3 equiv) in dichlormethane (10 mL) was added dropwise a solution of the aldehyde **3a** (810 mg, 4.96 mmol, 1.0 equiv) in dichlormethane (10 mL). The reaction mixture was stirred for 3 h at room temperature. After TLC analysis showed complete consumption of the aldehyde, saturated $NaHCO_3$ solution was added (20 mL). The organic layers were separated and the aqueous phase was extracted with dichlormethane (2x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 9:1 → 4:1) afforded (*Z*)-2-benzamidovinyl acetate **2b** (572 mg, 56%) as colorless solid. Analytical data are in accordance with those previously reported.[6]

R_f (*n*-hexane:EtOAc = 4:1) 0.22.

m.p. 81 °C.

^{1}H NMR (400 MHz $CDCl_3$) δ = 7.97 – 7.78 (m, 3H), 7.60 – 7.51 (m, 1H), 7.52 – 7.43 (m, 2H), 6.90 (d, *J*=5.2 Hz, 1H), 6.71 (dd, *J*=10.7, 5.1 Hz, 1H), 2.22 (s, 3H).

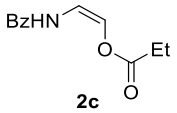
^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.7, 164.0, 133.4, 132.4, 128.9, 127.3, 121.5, 108.6, 20.8.

IR (ATR, ν in cm^{-1}): 3255 (w), 3206 (w), 3221 (w), 1750 (m), 1702 (w), 1640 (s), 1603 (w), 1579 (w), 1514 (s), 1484 (s), 1362 (m) 1294 (m), 1207 (s), 1147 (s), 1116 (s), 1040 (m), 1028 (m), 878 (m), 756 (m), 682 (m).

MS (ESI) m/z calcd for $C_{11}H_{11}NO_3Na$ 228.1 $[M+Na]^+$, found 228.1 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{11}H_{11}NO_3$ 205.0739 $[M]^+$, found 205.0740 $[M]^+$.

2.3.16 (*Z*)-2-Benzamidovinyl propionate 2c



2c

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and propionyl chloride (90 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl propionate **2c** (21 mg, 19%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.23.

m.p. 85.3 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 – 7.81 (m, 1H), 7.60 – 7.54 (m, 1H), 7.49 (t, J = 7.5 Hz, 1H), 6.93 (d, J = 5.1 Hz, 1H), 6.73 (dd, J = 10.7, 5.1 Hz, 1H), 2.52 (q, J = 7.5 Hz, 1H), 1.24 (t, J = 7.5 Hz, 1H).

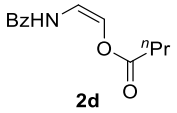
^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.3, 163.9, 133.5, 132.4, 129.0, 127.3, 121.6, 108.6, 27.4, 9.0.

IR (ATR, ν in cm^{-1}): 3356 (w), 2979 (w), 2919 (w), 1751 (s), 1690 (w), 1642 (s), 1582 (w), 1505 (m), 1482 (s), 1448 (w), 1345 (m), 1291 (m), 1134 (s), 1113 (s),1023 (s), 901 (m), 873 (m), 705 (s), 600 (s).

MS (ESI) m/z calcd $C_{12}H_{12}NO_3$ 218.1 $[M-H]^-$, found 218.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{12}H_{13}NO_3$ 219.0895 $[M]^+$, found 219.0890 $[M]^+$.

2.3.17 (*Z*)-2-Benzamidovinyl butyrate 2d



2d

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and butyryl chloride (100 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (Z)-2-benzamidovinyl butyrate **2d** (23 mg, 19%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.29.

m.p. 62 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83 (d, *J* = 7.2 Hz, 3H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 2H), 6.93 (d, *J* = 5.1 Hz, 1H), 6.72 (dd, *J* = 10.7, 5.1 Hz, 1H), 2.47 (t, *J* = 7.4 Hz, 2H), 1.79 – 1.68 (m, 2H), 1.01 (t, *J* = 7.4 Hz, 3H).

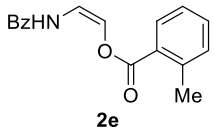
^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.4, 163.9, 133.5, 132.4, 129.0, 127.3, 121.5, 108.6, 35.9, 18.4, 13.8.

IR (ATR, ν in cm^{-1}): 3351 (m), 3116 (w), 2965 (w), 1752 (s), 1689 (m), 1642 (s), 1603 (m), 1582 (w), 1507 (m), 1481 (s), 1415 (m), 1352 (m), 1289 (m), 1117 (s), 1075 (s), 1001 (m), 941 (m), 904 (m), 879 (m), 796 (m), 756 (m), 713 (s), 698 (m).

MS (ESI) m/z calcd $C_{13}H_{14}NO_3$ 232.1 $[M-H]^-$, found 232.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{13}H_{15}NO_3$ 233.1052 $[M]^+$, found 233.1044 $[M]^+$.

2.3.18 (*Z*)-2-Benzamidovinyl 2-methylbenzoate **2e**



2e

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 2-methylbenzoyl chloride (130 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (Z)-2-benzamidovinyl 2-methylbenzoate **2e** (44 mg, 32%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.40.

m.p. 101 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (d, *J* = 7.7 Hz, 1H), 7.94 (s, 1H), 7.83 (d, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.48 (dd, *J* = 10.2, 4.5 Hz, 3H), 7.33 (dd, *J* = 7.3, 4.2 Hz, 2H), 7.11 (d, *J* = 5.1 Hz, 1H), 6.85 (dd, *J* = 10.7, 5.1 Hz, 1H), 2.67 (s, 3H).

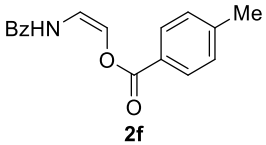
^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.9, 163.2, 141.1, 133.4, 133.1, 132.4, 132.2, 130.8, 129.0, 128.2, 127.3, 126.2, 121.8, 109.3, 22.0.

IR (ATR, ν in cm^{-1}): 3239 (w), 1726 (s), 1640 (m), 1602 (w), 1579 (w), 1517 (s), 1486 (m), 1379 (w), 1298 (m), 1233 (s), 1153 (m), 1137 (m), 1117 (s), 1066 (s), 913 (w), 861 (m), 800 (w), 733 (m), 693 (m).

MS (ESI) m/z calcd $C_{17}H_{14}NO_3$ 280.1 $[M-H]^-$, found 280.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{17}H_{15}NO_3$ 281.1052 $[M]^+$, found 281.1043 $[M]^+$.

2.3.19 (*Z*)-2-Benzamidovinyl 4-methylbenzoate **2f**



2f

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 4-methylbenzoyl chloride (130 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (Z)-2-benzamidovinyl 4-methylbenzoate **2f** (71 mg, 51%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.40.

m.p. 160 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 (d, *J* = 8.1 Hz, 2H), 7.95 (d, *J* = 10.4 Hz, 1H), 7.86 (d, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 5.1 Hz, 1H), 6.85 (dd, *J* = 10.7, 5.1 Hz, 1H), 2.45 (s, 3H).

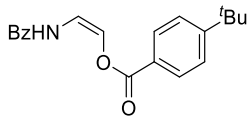
^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.9, 162.8, 145.0, 133.6, 132.4, 130.1, 129.7, 129.1, 127.3, 126.07, 122.0, 109.4, 21.9.

IR (ATR, ν in cm^{-1}): 3386 (w), 3112 (w), 1708 (m), 691 (m), 1664 (s), 1609 (m), 1501 (m), 1478 (s), 1281 (w), 1261 (s), 1249 (s), 1178 (m), 1112 (s), 1093 (s), 1016 (m), 839 (w), 748 (m), 709 (s), 603 (s).

MS (ESI) m/z calcd $C_{17}H_{14}NO_3$ 280.1 $[M-H]^-$, found 280.1 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{17}H_{15}NO_3$ 281.1052 $[M]^+$, found 281.1033 $[M]^+$.

2.3.20 (*Z*)-2-Benzamidovinyl 4-(*tert*-butyl)benzoate **2g**



2g

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 4-(*tert*-butyl)benzoyl chloride (200 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (Z)-2-benzamidovinyl 4-(*tert*-butyl)benzoate **2g** (62 mg, 38%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.45.

m.p. 89 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.03 (d, J = 8.4 Hz, 3H), 7.85 (d, J = 7.3 Hz, 2H), 7.59 – 7.47 (m, 5H), 7.09 (d, J = 5.1 Hz, 1H), 6.83 (dd, J = 10.6, 5.1 Hz, 1H), 1.36 (s, 9H).

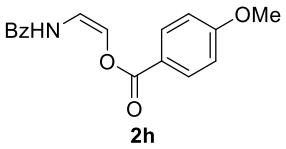
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 162.7, 157.9, 133.5, 132.4, 129.9, 129.0, 127.3, 125.9, 125.9, 122.0, 109.3, 35.4, 31.2.

IR (ATR, ν in cm^{-1}): 3398 (m), 2965 (m), 1707 (m), 1689 (m), 1664 (m), 1606 (m), 1515 (m), 1479 (m), 1409 (w), 1364 (w), 1263 (s), 1186 (m), 1145 (m), 1115 (s), 1015 (m), 923 (m), 853 (m), 768 (m), 747 (w), 701 (s).

MS (ESI) m/z calcd $C_{20}H_{20}NO_3$ 322.1 $[M-H]^-$, found 322.1 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{20}H_{21}NO_3$ 323.1521 $[M]^+$, found 323.1521 $[M]^+$.

2.3.21 (*Z*)-2-Benzamidovinyl 4-methoxybenzoate **2h**



2h

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 4-methoxybenzoyl chloride (140 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (Z)-2-benzamidovinyl 4-methoxybenzoate **2h** (89 mg, 60%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.43.

m.p. 130 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 – 8.03 (m, 2H), 7.98 (d, *J* = 10.4 Hz, 1H), 7.85 (d, *J* = 7.3 Hz, 2H), 7.57 (dd, *J* = 8.5, 6.2 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.07 (d, *J* = 5.1 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 2H), 6.82 (dd, *J* = 10.6, 5.1 Hz, 1H), 3.88 (s, 3H).

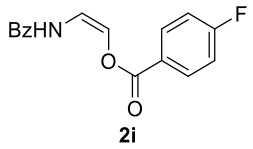
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.2, 163.9, 162.4, 133.5, 132.4, 132.2, 129.0, 127.3, 122.0, 121.0, 114.2, 109.1, 55.7.

IR (ATR, ν in cm^{-1}): 3276 (w), 3029 (w), 1713 (m), 1690 (m), 1650 (m), 1605 (m), 1580 (m), 1511 (s), 1487 (m), 1461 (m), 1370 (w), 1321 (w), 1255 (s), 1184 (m), 1168 (m), 1152 (s), 1118 (s), 1098 (s), 1019 (s), 862 (w), 848 (m), 794 (m), 758 (m), 721 (w), 687(s).

MS (ESI) m/z calcd $C_{17}H_{14}NO_4$ 296.1 $[M-H]^-$, found 296.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{17}H_{15}NO_4$ 297.1001 $[M]^+$, found 297.0999 $[M]^+$.

2.3.22 (*Z*)-2-Benzamidovinyl 4-fluorobenzoate **2i**



2i

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 4-fluorobenzoyl chloride (159 mg, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl 4-fluorobenzoate **2i** (100 mg, 70%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.38.

m.p. 177 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.09– 8.02 (m, 2H), 7.87 (d, *J* = 10.1 Hz, 1H), 7.78 (d, *J* = 7.3 Hz, 2H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.12 (t, *J* = 8.6 Hz, 2H), 7.00 (d, *J* = 5.1 Hz, 1H), 6.78 (dd, *J* = 10.7, 5.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.7, 165.1, 164.0, 161.8, 133.4, 132.7, 132.6, 132.5, 129.1, 127.3, 125.1, 121.8, 116.3, 116.1, 109.6.

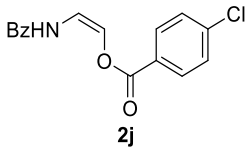
^{19}F {H} NMR (376 MHz, $CDCl_3$) δ = 103.5.

IR (ATR, ν in cm^{-1}): 3262 (w), 3115 (w), 1722 (s), 1691 (m), 1641 (m), 1578 (w), 1519 (m), 1478 (s), 1298 (w), 1258 (s), 1229 (s), 1146 (s), 1116 (s), 1089 (s), 853 (m), 799 (w), 759 (s), 680 (s), 606 (s).

MS (ESI) m/z calcd $C_{16}H_{11}FNO_3$ 284.1 $[M-H]^-$, found 284.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{16}H_{12}FNO_3$ 285.0801 $[M]^+$, found 285.0817 $[M]^+$.

2.3.23 (*Z*)-2-Benzamidovinyl 4-chlorobenzoate **2j**



2j

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 4-chlorobenzoyl chloride (130 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl 4-chlorobenzoate **2j** (109 mg, 72%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.37.

m.p. 143 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 – 8.02 (m, 2H), 7.94 (d, *J* = 10.3 Hz, 1H), 7.85 (d, *J* = 7.3 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.51 (t, *J* = 8.2 Hz, 4H), 7.07 (d, *J* = 5.1 Hz, 1H), 6.86 (dd, *J* = 10.7, 5.1 Hz, 1H).

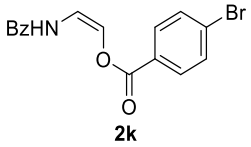
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 161.9, 140.7, 133.4, 132.5, 131.4, 129.3, 129.1, 127.3, 127.3, 121.8, 109.8.

IR (ATR, ν in cm^{-1}): 3268 (w), 3115 (w), 1732 (s), 1694 (m), 1641 (s), 1594 (m), 1578 (w), 1517 (s), 1484 (s), 1401 (m), 1256 (s), 1149 (s), 1116 (s), 1089 (s), 1013 (s), 913 (w), 8423 (m), 752 (s), 692 (s), 678 (s).

MS (ESI) m/z calcd $C_{16}H_{11}ClNO_3$ 300.1 $[M-H]^-$, found 300.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{16}H_{12}ClNO_3$ 301.0506 $[M]^+$, found 301.0521 $[M]^+$.

2.3.24 (*Z*)-2-Benzamidovinyl 4-bromobenzoate **2k**



2k

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 4-bromorobenzoyl chloride (130 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl 4-bromobenzoate **2k** (119 mg, 69%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.45.

m.p. 139 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 10.3 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 7.5 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.05 (d, *J* = 5.0 Hz, 1H), 6.84 (dd, *J* = 10.6, 5.1 Hz, 1H).

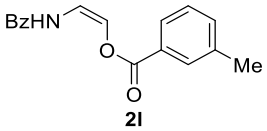
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 162.1, 133.4, 132.45, 132.3, 131.4, 129.3, 129.0, 127.7, 127.3, 121.7, 109.7.

IR (ATR, ν in cm^{-1}): 3266 (w), 3115 (w), 1732 (s), 1695 (m), 1641 (s), 1589 (m), 1515 (s), 1487 (s), 1398 (m), 1258 (s), 1149 (s), 1116 (s), 1092 (s), 1066 (s), 1011 (s), 913 (w), 839 (m), 749 (s), 692 (s), 675 (s).

MS (ESI) m/z calcd C16H11BrNO3 344.0 $[M-H]^-$, found 344.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{16}H_{12}BrNO_3$ 345.0001 $[M]^+$, found 344.9990 $[M]^+$.

2.3.25 (*Z*)-2-Benzamidovinyl 3-methylbenzoate **2l**



2l

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 3-methylbenzoyl chloride (130 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl 3-methylbenzoate **2l** (116 mg, 82%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.36.

m.p. 128 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 10.0 Hz, 1H), 7.88 (dd, *J* = 15.3, 9.5 Hz, 4H), 7.61 – 7.55 (m, 1H), 7.53 – 7.44 (m, 3H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.09 (d, *J* = 5.1 Hz, 1H), 6.86 (dd, *J* = 10.7, 5.1 Hz, 1H), 2.44 (s, 3H).

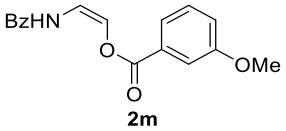
^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.9, 162.9, 138.8, 134.8, 133.5, 132.4, 130.7, 129.1, 128.8, 128.8, 127.3, 127.1, 122.0, 109.5, 21.5.

IR (ATR, ν in cm^{-1}): 3247 (w), 1731 (s), 1686 (m), 1641 (s), 1602 (w), 1580 (w), 1516 (s), 1486 (m), 1380 (w), 1325 (w), 1265 (s), 1195 (s), 1151 (m), 1118 (s), 1099 (m), 1076 (s), 1039 (m), 927 (w), 894 (m), 848 (w), 799 (w), 757 (w), 738 (s), 689 (s).

MS (ESI) m/z calcd $C_{17}H_{14}NO_3$ 280.1 $[M-H]^-$, found 280.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{17}H_{15}NO_3$ 281.1052 $[M]^+$, found 281.1054 $[M]^+$.

2.3.26 (*Z*)-2-Benzamidovinyl 3-methoxybenzoate **2m**



2m

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and 3-methoxybenzoyl chloride (140 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (*Z*)-2-benzamidovinyl 3-methoxybenzoate **2m** (90 mg, 60%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.33.

m.p. 118 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.04 (d, *J* = 10.5 Hz, 1H), 7.84 (d, *J* = 7.3 Hz, 2H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.60 – 7.53 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.16 (dd, *J* = 8.2, 2.6 Hz, 1H), 7.06 (d, *J* = 5.1 Hz, 1H), 6.83 (dd, *J* = 10.6, 5.1 Hz, 1H), 3.86 (s, *J* = 11.4 Hz, 3H).

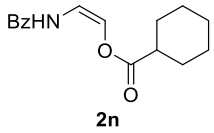
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 162.6, 159.9, 133.4, 132.4, 130.0, 129.9, 129.0, 127.3, 122.2, 121.9, 120.2, 114.8, 109.5, 55.6.

IR (ATR, ν in cm^{-1}): 3307 (m), 3125 (w), 1729 (s), 1694 (m), 1640 (s), 1609 (m), 1584 (m), 1509 (s), 1483 (s), 1432 (m), 1365 (w), 1271 (s), 1247 (m), 1214 (s), 1178 (m), 1146 (s), 1115 (s), 1095 (m), 1054 (s), 909 (m), 883 (m), 811 (w), 798 (m), 745 (s), 713 (m), 680 (m).

MS (ESI) m/z calcd $C_{17}H_{14}NO_4$ 296.1 $[M-H]^-$, found 295.9 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{17}H_{15}NO_4$ 297.1001 $[M]^+$, found 297.1017 $[M]^+$.

2.3.27 (*Z*)-2-Benzamidovinyl cyclohexanecarboxylate **2n**



2n

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and cyclohexanecarbonyl chloride (140 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (Z)-2-benzamidovinyl cyclohexanecarboxylate **2n** (94 mg, 69%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.47.

m.p. 106 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 8.4, 7.0 Hz, 3H), 7.60 – 7.54 (m, 1H), 7.53 – 7.47 (m, 2H), 6.92 (d, *J* = 5.1 Hz, 1H), 6.73 (dd, *J* = 10.7, 5.1 Hz, 1H), 2.48 (tt, *J* = 11.3, 3.6 Hz, 1H), 1.99 (dd, *J* = 13.2, 2.9 Hz, 2H), 1.85 – 1.78 (m, 2H), 1.73 – 1.61 (m, 2H), 1.59 – 1.47 (m, 2H), 1.39 – 1.24 (m, 2H).

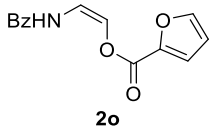
^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.8, 163.9, 133.5, 132.4, 129.0, 127.3, 121.7, 108.6, 43.0, 29.1, 25.7, 25.4.

IR (ATR, ν in cm^{-1}): 3272 (w), 2931 (m), 2856 (w), 1743 (s), 1701 (m), 1647 (m), 1602 (w), 1582 (w), 1514 (s), 1485 (m), 1449 (m), 1377 (m), 1286 (m), 1244 (m), 1125 (s), 1040 (m), 1026 (m), 1001 (m), 933 (w), 892 (m), 845 (w), 801 (m), 742 (w), 694 (s).

MS (ESI) m/z calcd $C_{16}H_{18}NO_3$ 272.1 $[M-H]^-$, found 272.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{16}H_{19}NO_3$ 273.1365 $[M]^+$, found 273.1366 $[M]^+$.

2.3.28 (*Z*)-2-Benzamidovinyl furan-2-carboxylate **2o**



2o

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and furan-2-carbonyl chloride (100 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 4:1) afforded (Z)-2-benzamidovinyl furan-2-carboxylate **2o** (83 mg, 65%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.19.

m.p. 156 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (d, *J* = 10.1 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.66 – 7.65 (m, 1H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.35 (d, *J* = 3.5 Hz, 1H), 7.03 (d, *J* = 5.0 Hz, 1H), 6.83 (dd, *J* = 10.7, 5.0 Hz, 1H), 6.58 (dd, *J* = 3.3, 1.4 Hz, 1H).

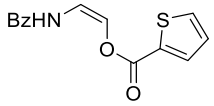
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 154.5, 147.4, 143.3, 133.3, 132.4, 128.9, 127.3, 121.0, 119.9, 112.5, 109.7.

IR (ATR, ν in cm^{-1}): 2971 (w), 1737 (s), 1640 (m), 1519 (m), 1467 (w), 1366 (m), 1284 (m), 1227 (m), 1176 (m), 1149 (m), 1117 (s), 1017 (m), 930 (w), 905 (m), 847 (w), 799 (w), 758 (m), 697 (m).

MS (ESI) m/z calcd $C_{14}H_{10}NO_4$ 256.1 $[M-H]^-$, found 255.9 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{14}H_{11}NO_4$ 257.0688 $[M]^+$, found 257.0684 $[M]^+$.

2.3.29 (*Z*)-2-Benzamidovinyl thiophene-2-carboxylate **2p**



2p

Prepared according to **GP3** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and thiophene-2-carbonyl chloride (130 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by column chromatography (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 19:1 → 9:1) afforded (Z)-2-benzamidovinyl thiophene-2-carboxylate **2p** (100 mg, 73%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.23.

m.p. 144 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (d, *J* = 10.2 Hz, 1H), 7.94 (d, *J* = 3.5 Hz, 1H), 7.86 (d, *J* = 7.4 Hz, 2H), 7.67 (d, *J* = 4.9 Hz, 1H), 7.58 (dd, *J* = 8.4, 6.2 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 2H), 7.21 – 7.17 (m, 1H), 7.05 (d, *J* = 5.0 Hz, 1H), 6.84 (dd, *J* = 10.7, 5.0 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 163.8, 158.0, 135.0, 133.8, 133.4, 132.5, 131.8, 129.0, 128.5, 127.2, 121.6, 109.5.

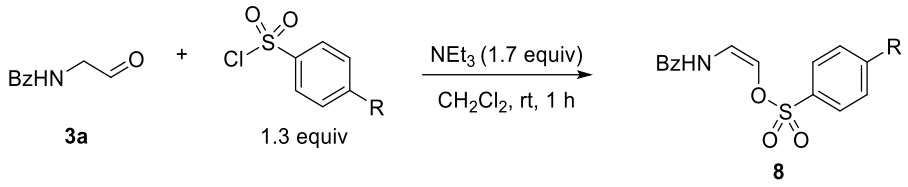
IR (ATR, ν in cm^{-1}): 3262 (w), 1716 (m), 1689 (m), 1645 (m), 1579 (w), 1515 (m), 1486 (m), 1416 (m), 1354 (m), 1245 (s), 1218 (s), 1149 (m), 1113 (m), 1084 (s), 905 (w), 862 (m), 800 (w), 737 (m), 689 (m).

MS (ESI) m/z calcd $C_{14}H_{11}NNaO_3S$ 296.0 $[M+Na]^+$, found 296.0 $[M+Na]^+$.

HRMS (EI) m/z calcd $C_{14}H_{11}NO_3S$ 273.0460 $[M]^+$, found 273.0461 $[M]^+$.

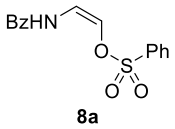
2.4 (*Z*)-Enol sulfonates

GENERAL PROCEDURE 4 (GP4)



To a stirred solution of triethylamine (1.7 equiv) and the corresponding sulfonyl chloride (1.3 equiv) in dichlormethane (2 mL/mmol) was added dropwise a solution of the aldehyde **3a** (1.0 equiv) in dichlormethane (2 mL/mmol) over 5 min. The reaction mixture was stirred for 1 h at room temperature. After TLC analysis showed complete consumption of the aldehyde, saturated $NaHCO_3$ solution was added (20 mL). The organic layers were separated and the aqueous phase was extracted with dichlormethane (2x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by flash chromatography afforded the desired (*Z*)-enol sulfonates **7a-c** as analytically pure product. All enol sulfonates of type **7** tend to decompose upon contact to any type of acid. Therefore, column chromotography was performed with 0.2 vol% NEt_3 as additive. $CDCl_3$ for NMR spectroscopy was passed through short plug of basic alumina before use.

2.4.1 (*Z*)-2-Benzamidovinyl benzenesulfonate 8a



Prepared according to **GP4** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and benzenesulfonyl chloride (85 µL, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by flash chromatography via puriflash XS 420+ machine, HP_15µm_F0012 flash column (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 98:2 → 80:20) afforded (*Z*)-2-benzamidovinyl benzenesulfonate **7a** (92 mg, 61%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.20.

m.p. 91 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 – 7.95 (m, 3H), 7.74 – 7.70 (m, 2H), 7.69 – 7.64 (m, 1H), 7.59 – 7.52 (m, 3H), 7.45 (t, *J* = 7.6 Hz, 2H), 6.85 (dd, *J* = 10.8, 4.7 Hz, 1H), 6.04 (d, *J* = 4.7 Hz, 1H).

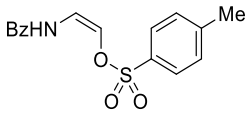
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 135.0, 134.8, 132.7, 132.6, 129.6, 128.9, 128.2, 127.4, 121.4, 114.8.

IR (ATR, ν in cm^{-1}): 3300 (m), 3102 (w), 3063 (w), 1692 (m), 1651 (s), 1582 (m), 1508 (m), (1481 (s), 1378 (s), 1282 (s), 1189 (s), 1146 (s), 1111 (m), 988 (s), 913 (w), 810 (s), 728 (m), 676 (s), 633 (s).

MS (ESI) m/z calcd $C_{15}H_{12}NO_4S$ 302.0 $[M-H]^-$, found 301.9 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{15}H_{13}NO_4S$ 303.0565 $[M]^+$, found 303.0557 $[M]^+$.

2.4.2 (*Z*)-2-Benzamidovinyl 4-methylbenzenesulfonate **8b**



8b

Prepared according to **GP4** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and *p*-toluenesulfonyl chloride (124 mg, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by flash chromatography via puriflash XS 420+ machine, HP_15µm_F0012 flash column (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 98:2 → 80:20) afforded (Z)-2- benzamidovinyl 4-methylbenzenesulfonate **7b** (90 mg, 57%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.28.

m.p. 80 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, *J* = 10.5 Hz, 1H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.74 – 7.70 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 6.84 (dd, *J* = 10.8, 4.7 Hz, 1H), 6.02 (d, *J* = 4.7 Hz, 1H), 2.40 (s, 3H).

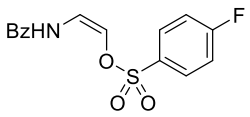
^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.0, 146.2, 132.7, 132.6, 132.0, 130.3, 128.9, 128.3, 127.4, 121.5, 114.7, 21.8.

IR (ATR, ν in cm^{-1}): 3314 (m), 1740 (m), 1691 (m), 1651 (s), 1597 (m), 1582 (m), 1507 (m), 1482 (s), 1375 (s), 1305 (w), 1280 (m), 1190 (m), 1178 (m), 1147 (s), 1111 (m), 1091 (s), 990 (s), 910 (w), 810 (m), 789 (m), 747 (m), 715 (w), 683 (m), 665 (m).

MS (ESI) m/z calcd $C_{16}H_{15}NNaO_4S$ 340.1 $[M + Na]^+$, found 340.1 $[M + Na]^+$.

HRMS (EI) m/z calcd $C_{15}H_{15}NO_4S$ 317.0724 $[M]^+$, found 317.0724 $[M]^+$.

2.4.3 (*Z*)-2-Benzamidovinyl 4-fluorobenzenesulfonate **8c**



8c

Prepared according to **GP4** from *N*-(2-oxoethyl)benzamide **3a** (82 mg, 0.5 mmol, 1.0 equiv), triethylamine (120 µL, 0.85 mmol, 1.7 equiv) and *p*-fluorobenzenesulfonyl chloride (127 mg, 0.65 mmol, 1.3 equiv) in a total of 2 mL dichlormethane. Purification by flash chromatography via puriflash

XS 420+ machine, HP_15µm_F0012 flash column (*n*-hexane:EtOAc + 0.2 vol% NEt_3 = 98:2 → 80:20) afforded (*Z*)-2-benzamidovinyl 4-fluorobenzenesulfonate **7c** (79 mg, 49%) as colorless solid.

R_f (*n*-hexane:EtOAc = 4:1) 0.23.

m.p. 100 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (dd, *J* = 8.9, 4.9 Hz, 3H), 7.79 – 7.72 (m, 2H), 7.58 (t, *J* =7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.31 – 7.21 (m, 2H), 6.89 (dd, *J* = 10.8, 4.7 Hz, 1H), 6.04 (d, *J* = 4.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.7, 165.1, 164.1, 132.7, 132.6, 131.3, 131.2, 131.0, 130.9, 129.0, 127.4, 121.2, 117.2, 117.0, 114.9.

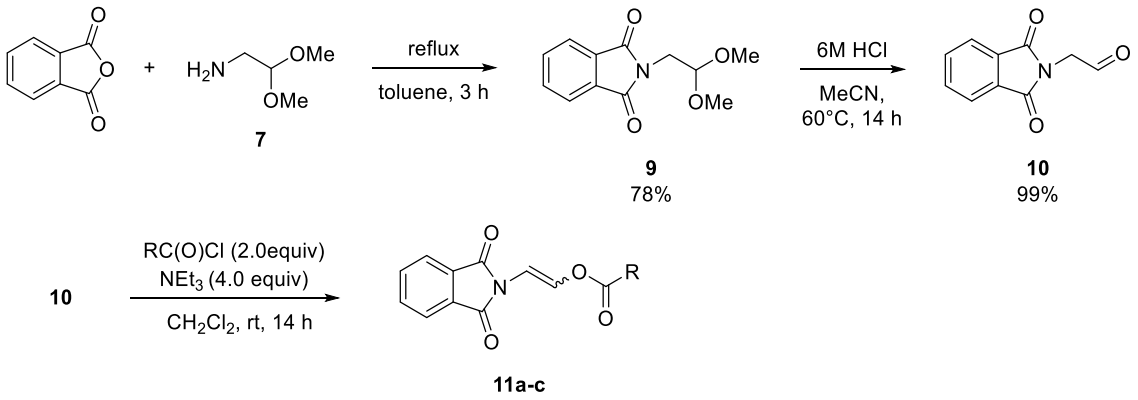
^{19}F {H} NMR (376 MHz, $CDCl_3$) δ = -100.9

IR (ATR, ν in cm^{-1}): 3261 (m), 3107 (w), 1739 (m), 1688 (m), 1652 (m), 1591 (m), 1510 (m), 1484 (m), 1411 (w), 1374 (s), 1286 (m), 1232 (m), 1188 (s), 1161 (m), 1148 (s), 1109 (m), 1090 (m), 982 (s), 926 (w), 908 (w), 838 (m), 822 (m), 806 (m), 761 (m), 694 (s), 670 (m).

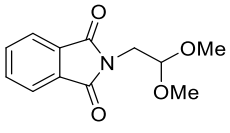
MS (ESI) m/z calcd $C_{15}H_{13}FNO_4S$ 320.0 $[M-H]^-$, found 320.0 $[M-H]^-$.

HRMS (EI) m/z calcd $C_{15}H_{12}NO_4S$ 321.0471 $[M]^+$, found 321.0461 $[M]^+$.

2.5 2-Oxyenimides



2.5.1 2-(2,2-Dimethoxyethyl)isoindoline-1,3-dione 9



9

Prepared according to the literature.[7]

A solution of amino acetaldehyde dimethylacetal **7** (2.18 mL, 20.0 mmol, 1.0 equiv) and phthalic anhydride (2.96 g, 20.0 mmol, 1.0 equiv) in a total of 70 mL toluene was refluxed for 3 h. Afterwards the solvent was removed under reduced pressure. Purification of the crude residue by flash

chromatography (*n*-hexane:EtOAc = 9:1 → 4:1) afforded 2-(2,2-dimethoxyethyl)isoindoline-1,3-dione **9** (3.56 mg, 76%) as colorless solid. Analytical data are in accordance with the literature.[7]

R_f (*n*-hexane:EtOAc = 4:1) 0.47.

m.p. 108-110°C

^{1}H NMR (400 MHz, $CDCl_3$) δ = δ 7.92 – 7.78 (m, 2H), 7.76 – 7.64 (m, 2H), 4.76 (t, J = 5.8 Hz, 1H), 3.82 (d, J = 5.8 Hz, 2H), 3.37 (s, 6H).

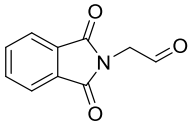
^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.2, 134.1, 132.1, 123.5, 100.1, 53.3, 38.8.

IR (ATR, ν in cm^{-1}): 3066 (w), 2947 (w), 1771 (m), 1708 (s), 1469 (m), 1432 (m), 1395 (s), 1372 (m), 1321 (s), 1216 (w), 1191 (m), 1125 (s), 1055 (s), 1039 (s), 1013 (s), 909 (m), 799 (m), 713 (s), 609 (m).

MS (ESI) m/z calcd $C_{12}H_{13}NNaO_4$ 258.1 $[M+Na]^+$, found 258.1 $[M+Na]^+$.

HRMS (EI) m/z calcd $C_{12}H_{12}NO_4$ 234.0761 [M-H], found 317.0765 [M-H].

2.5.2 2-(1,3-Dioxoisoindolin-2-yl)acetaldehyde 10



10

Prepared according to a modified procedure.[7]

To a solution of 2-(2,2-dimethoxyethyl)isoindoline-1,3-dione **9** (1.18 g, 5.0 mmol, 1.0 equiv) in acetonitrile (50 mL) was added HCl (50 mL, 6 M in water). The reaction mixture was stirred at 60 °C for 14 h. Afterwards brine (50 mL) was added and the aqueous solution was extracted with ethylacetate (3x 50 mL). The combined organic layers were dried over Na_2SO_4 and the solvents were removed under reduced pressure. The analytically pure 2-(1,3-dioxoisoindolin-2-yl)acetaldehyde **10** was obatained without further purification as colorless solid (934 mg, 98%). Analytical data are in accordance with the literature.[7] Aldehyde **10** seems to be more stable than all other aminoaldehyde derivatives. Therefore compound **10** could be fully characterized.

R_f (*n*-hexane:EtOAc = 4:1) 0.15.

m.p. 109-111°C

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.66 (s, 1H), 7.94 – 7.85 (m, 2H), 7.80 – 7.71 (m, 2H), 4.56 (s, 2H).

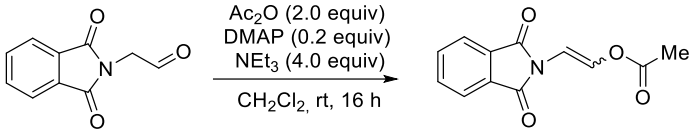
^{13}C NMR (101 MHz, $CDCl_3$) δ = 193.6, 167.6, 134.5, 132.0, 123.8, 47.5.

IR (ATR, ν in cm^{-1}): 2937 (w), 2890 (w), 1778 (m), 1705 (s), 1615 (w), 1467 (m), 1405 (s), 1388 (s), 1301 (s), 1191 (m), 1141 (s), 1088 (w), 1016 (s), 871 (s), 773 (s), 713 (s), 597 (w). 530 (m).

MS (ESI) m/z calcd $C_{11}H_{11}NNaO_4$ 244.1 $[M + Na + MeOH]^+$, found 243.9 $[M + Na + MeOH]^+$.

HRMS (EI) m/z calcd $C_{10}H_7NO_3$ 189.0426 $[M]^+$, found 189.0439 $[M]^+$.

2.5.3 (*E/Z*)-2-(1,3-Dioxoisoindolin-2-yl)vinyl acetate **11a**



9 → **11a** *E:Z = 48:52* 49%

To a stirred solution of triethylamine (0.55 mL, 4.0 mmol, 4.0 equiv), 4-dimethylaminopyridine (25 mg, 0.2 mmol, 0.2 equiv) and acetic anhydride (0.19 mL, 2.0 mmol, 2.0 equiv) in dichlormethane (6 mL) was added 2-(1,3-dioxoisoindolin-2-yl)acetaldehyde **10** (189 mg, 1.0 mmol, 1.0 equiv) in one portion. The reaction mixture was stirred for 16 h at room temperature. After TLC analysis showed complete consumption of the aldehyde, saturated $NaHCO_3$ solution was added (6 mL). The organic layers were separated and the aqueous phase was extracted with dichlormethane (2x 6 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by flash chromatography via puriflash XS 420+ machine, HP_15µm_F0012 flash column (*n*-hexane:CH_2Cl_2 = 90:10 → 20:80) afforded (*E/Z*)-2-(1,3-dioxoisoindolin-2-yl)vinyl acetate **11a** (114 mg, 49%, *E:Z* = 48:52) as yellow solid (*E*-isomer) and colorless solid (*Z*-isomer). Separation of both isomers could be achieved by flash column chromatography with the above given conditions.

(E)-Isomer:

R_f (*n*-hexane:EtOAc = 4:1) 0.30

m.p. 149-150°C.

^{1}H NMR (400 MHz $CDCl_3$) δ = 8.40 (d, J=12.0 Hz, 1H), 7.94 – 7.81 (m, 2H), 7.79 – 7.66 (m, 2H), 6.88 (d, J=11.9 Hz, 1H), 2.19 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.8, 165.8, 134.6, 132.7, 131.8, 123.8, 108.7, 20.7.

IR (ATR, ν in cm^{-1}): 3136 (w), 1780 (w), 1752 (m), 1725 (s), 1609 (w), 1469 (w), 1392 (s), 1374 (s), 1306 (m), 1199 (s), 1144 (s), 1089 (s), 991 (s), 898 (s), 789 (m), 710 (s), 626 (m), 566 (w), 529 (s).

MS (ESI) m/z calcd for $C_{12}H_9NO_4Na$ 254.2 $[M+Na]^+$, found 253.9 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_9NO_4$ 231.0532 $[M]^+$, found 231.0527 $[M]^+$.

(Z)-Isomer:

R_f (*n*-hexane:EtOAc = 4:1) 0.21

m.p. 105-106°C.

^{1}H NMR (400 MHz $CDCl_3$) δ = 7.92 – 7.85 (m, 2H), 7.79 – 7.72 (m, 2H), 7.31 (d, J=5.0, 1H), 5.83 (d, J=5.0, 1H), 2.14 (s, 3H).

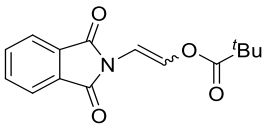
^{13}C NMR (101 MHz, $CDCl_3$) δ = 167.0, 165.9, 134.4, 133.1, 132.2, 123.8, 102.6, 20.7.

IR (ATR, ν in cm^{-1}): 3110 (w), 3015 (w), 1782 (w), 1755 (m). 1712 (s), 1687 (s), 1469 (w), 1392 (s9, 1366 (s), 1259 (w9, 1201 (s9, 1186 (s), 1128 (m), 1065 (s), 966 (w), 883 (s), 730 (m), 710 (s), 672 (s), 590 (m).

MS (ESI) m/z calcd for $C_{12}H_9NO_4Na$ 254.2 $[M+Na]^+$, found 253.9 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_9NO_4$ 231.0532 $[M]^+$, found 231.0542 $[M]^+$.

2.5.4 (*E/Z*)- 2-(1,3-Dioxoisoindolin-2-yl)vinyl pivalate **11b**



11b

To a stirred solution of triethylamine (0.55 mL, 4.0 mmol, 4.0 equiv) and pivaloyl chloride (0.25 mL, 2.0 mmol 2.0 equiv) in dichlormethane (6 mL) was added 2-(1,3-dioxoisoindolin-2-yl)acetaldehyde **10** (189 mg, 1.0 mmol, 1.0 equiv) in one portion. The reaction mixture was stirred for 16 h at room temperature. After TLC analysis showed complete consumption of the aldehyde, saturated $NaHCO_3$ solution was added (6 mL). The organic layers were separated and the aqueous phase was extracted with dichlormethane (2x 6 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by flash chromatography via puriflash XS 420+ machine, HP_15µm_F0012 flash column (*n*-hexane:CH_2Cl_2 = 90:10 → 40:60) afforded (*E/Z*)- 2-(1,3-dioxoisoindolin-2-yl)vinyl pivalate **11b** (222 mg, 81%, *E:Z* = 71:29) as pale yellow solid (*E*-isomer) and colorless solid (*Z*-isomer). Separation of both isomers could be achieved by flash column chromatography with the above given conditions.

(E)-Isomer:

R_f (*n*Hex:EtOAc = 4:1) 0.61.

m.p. 98-99 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.40 (d, J=11.9 Hz, 1H), 7.93 – 7.84 (m, 2H), 7.80 – 7.70 (m, 2H), 6.91 (d, J=11.9 Hz, 1H), 1.28 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.3, 165.9, 134.6, 133.2, 131.8, 123.8, 108.4, 38.9, 27.1.

IR (ATR, ν in cm^{-1}): 3130 (w), 2973 (w), 1778 (w), 1745 (s), 1724 (s), 1711 (s), 1469 (w), 1385 (s), 1279 (m), 1205 (w), 1146 (s), 1118 (s), 1066 (m), 1015 (m), 996 (m), 923 (s), 881 (m), 756 (w), 713 (s).

MS (ESI) m/z calcd $C_{15}H_{15}NNaO_4$ 296.1 $[M+Na]^+$; found 296.0 $[M+Na]^+$.

HRMS (EI) m/z calcd $C_{15}H_{15}NO_4$ 273.1001 $[M]^+$; found 273.0987 $[M]^+$.

(Z)-Isomer:

R_f (*n*-hexane:EtOAc = 4:1) 0.55.

m.p. 103-106°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 – 7.86 (m, 2H), 7.79 – 7.72 (m, 2H), 7.35 (d, J=5.1 Hz, 1H), 5.84 (d, J=5.1 Hz, 1H), 1.21 (s, 9H).

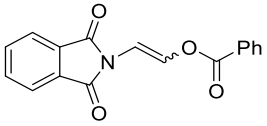
^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.5, 165.9, 134.5, 133.3, 132.2, 123.8, 102.2, 39.0, 27.0.

IR (ATR, ν in cm^{-1}): 3113 (w), 2976 (w), 1780 (w), 1744 (m), 1717 (s), 1464 (m), 1382 (s), 1272 (m), 1244 (m), 1116 (s), 1048 (m), 955 (w), 885 (m), 736 (m), 716 (s), 672 (m), 530 (m).

MS (ESI) m/z calcd $C_{15}H_{15}NNaO_4$ 296.1 $[M+Na]^+$; found 296.0 $[M+Na]^+$.

HRMS (EI) m/z calcd $C_{15}H_{15}NO_4$ 273.1001 $[M]^+$; found 273.0992 $[M]^+$.

2.5.5 (*E/Z*)- 2-(1,3-Dioxoisoindolin-2-yl)vinyl benzoate **11c**



11c

To a stirred solution of triethylamine (0.55 mL, 4.0 mmol, 4.0 equiv) and benzoyl chloride (0.23 mL, 2.0 mmol 2.0 equiv) in dichlormethane (6 mL) was added 2-(1,3-dioxoisoindolin-2-yl)acetaldehyde **10** (189 mg, 1.0 mmol, 1.0 equiv) in one portion. The reaction mixture was stirred for 16 h at room temperature. After TLC analysis showed complete consumption of the aldehyde, saturated $NaHCO_3$ solution was added (6 mL). The organic layers were separated and the aqueous phase was extracted with dichlormethane (2x 6 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by flash chromatography via puriflash XS 420+ machine, HP_15µm_F0012 flash column (*n*-hexane:CH_2Cl_2 = 90:10 → 20:80) afforded (*E/Z*)- 2-(1,3-dioxoisoindolin-2-yl)vinyl benzoate **11c** (257 mg, 88%, *E:Z* = 73:27) as pale yellow solid (*E*-isomer) and colorless solid (*Z*-isomer). Separation of both isomers could be achieved by flash column chromatography with the above given conditions.

Configuration of the double bond could be assigned via the ^{3}J coupling constants of the oelfinic protons (11.9 Hz for the *E*- and 5.2 Hz for the *Z*-isomer). Assignment using vincinal coupling constants was verified by single crystal X-ray structures of ***E*-11c** (CCDC 2180324) and ***Z*-11c** (CCDC 2180325).

(E)-Isomer:

R_f (*n*-hexane:EtOAc = 4:1) 0.40

m.p. >200°C.

^{1}H NMR (400 MHz $CDCl_3$) δ = 8.69 (d, J=11.9 Hz, 1H), 8.17 – 8.11 (m, 2H), 7.95 – 7.84 (m, 2H), 7.81 – 7.71 (m, 2H), 7.66 – 7.58 (m, 1H), 7.54 – 7.46 (m, 2H), 7.11 (d, J=11.9 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.9, 163.5, 134.7, 133.8, 132.9, 131.9, 128.8, 128.7, 123.9, 109.1.

IR (ATR, ν in cm^{-1}): 3132 (w), 3073 (w), 1778 (w9, 1728 (s), 1712 (s), 1601 (m), 1449 (m), 1384 (s), 1276 (s), 1145 (s), 1036 (m), 1016 (s), 919 (s), 852 (w), 786 (w), 703 (s), 630 (m), 530 (m).

MS (ESI) m/z calcd for $C_{17}H_{11}NO_4Na$ 316.1 $[M+Na]^+$, found 316.0 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{11}NO_4$ 293.0688 $[M]^+$, found 293.0671 $[M]^+$.

(Z)-Isomer:

R_f (*n*-hexane:EtOAc = 4:1) 0.31

m.p. 169-171°C.

^{1}H NMR (400 MHz $CDCl_3$) δ = 8.12 – 8.00 (m, 2H), 7.98 – 7.88 (m, 2H), 7.85 – 7.71 (m, 2H), 7.65 – 7.51 (m, 2H), 7.49 – 7.37 (m, 2H), 5.99 (d, J=5.2 Hz, 1H).

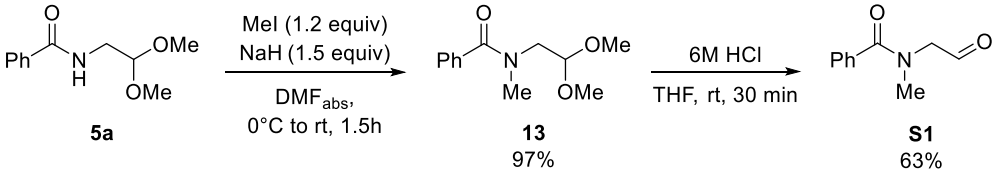
^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.9, 162.8, 134.5, 134.0, 132.5, 132.2, 130.4, 128.7, 128.4, 123.9, 102.8.

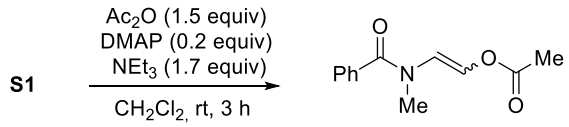
IR (ATR, ν in cm^{-1}): 3093 (w), 3030 (w), 1738 (m), 1705 (s), 1682 (m), 1454 8w), 1397 (m), 1266 (m), 1226 (m), 1176 (m), 1106 (s), 1099 (s), 1078 (m), 893 (w), 879 (s), 738 (m), 705 (s), 529 (m).

MS (ESI) m/z calcd for $C_{17}H_{11}NO_4Na$ 316.1 $[M+Na]^+$, found 316.0 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{17}H_{11}NO_4$ 293.0688 $[M]^+$, found 293.0682 $[M]^+$.

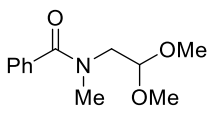
2.6 *N*-Methylated 2-oxyenamide





12
E:Z = 27:73
50%

2.6.1 *N*-(2,2-Dimethoxyethyl)-*N*-methylbenzamide 13



13

Prepared according to a modified procedure.[1]

Under nitrogen atmosphere *N*-(2,2-dimethoxyethyl)benzamide **5a** (1.05 g, 5.0 mmol, 1.0 equiv) was added in one portion at 0°C to a suspension of sodium hydride (300 mg, 7.5 mmol, 1.5 equiv, 60% in mineral oil) in DMF_{abs} (10 mL). After stirring for 5 min at 0°C, iodomethane (0.35 mL, 5.5 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at room temperature for 1.5 h. After TLC analysis showed complete consumption of the acetale, saturated $NaHCO_3$ solution was added (10 mL). The aqueous layer was extracted with ethylacetate (3x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by column chromatography (*n*-hexane:EtOAc = 4:1 → 7:3) afforded *N*-(2,2-dimethoxyethyl)-*N*-methylbenzamide **12** (1.09 g, 97%) as colorless liquid. Compound **13** exists as a mixture of different rotamers. NMR signals could not be assigend to individual romatmers.

R_f (*n*-hexane:EtOAc = 4:1) 0.17.

^{1}H NMR (600 MHz, $CDCl_3$, a mixture of rotamers) δ 7.50 – 7.31 (m, 5H), 4.70 (t, J=5.5 Hz, 0.65H), 4.36 (s, 0.35H), 3.63 (d, J=5.4 Hz, 1.25H), 3.46 (s, 4H), 3.41 – 3.35 (m, 0.75H), 3.26 (s, 2H), 3.13 (s, 1H), 3.03 (s, 2H).

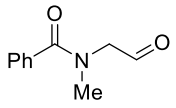
^{13}C NMR (111 MHz, $CDCl_3$, a mixture of rotamers) δ 172.6, 171.8, 136.5, 129.7, 129.5, 128.5, 127.1, 103.5, 103.1, 54.9, 53.2, 50.0, 39.6, 34.5.

IR (ATR, ν in cm^{-1}): 2936 (w), 2833 (w), 1630 (s), 1578 (w), 1445 (m), 1398 (s), 1296 (w), 1192 (w), 1125 (s), 1069 (s9, 1025 (s), 978 (m), 932 (w), 789 (m), 719 (m), 699 (s), 553 (w).

MS (ESI) m/z calcd $C_{12}H_{17}NNaO_3$ 246.1 $[M+Na]^+$, found 246.0 $[M+Na]^+$.

HRMS (EI) m/z calcd $C_{12}H_{17}NO_3$ 223.1208 $[M]^+$, found 223.1197 $[M]^+$.

2.6.2 *N*-Methyl-*N*-(2-oxoethyl)benzamide S1



S1

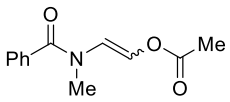
Prepared according to **GP2** from *N*-(2,2-dimethoxyethyl)-*N*-methylbenzamide **13** (1.09g, 4.88 mmol, 1.0 equiv) and 6 M HCl (17 mL) in THF (17 mL). Removal of the solvents afforded the crude aldehyde **S1** (543 mg, 63%) as colorless liquid. (Note! Aldehyde **S1** proved to be very unstable. Therefore, the crude aldehyde was subjected directly to the next step). Compound **12** exists as a mixture of different rotamers. NMR signals could not be assigend to individual romatmers.

R_f (n-hexane:EtOAc = 1:1) 0.15.

^{1}H NMR (400 MHz, $CDCl_3$, a mixture of rotamers) δ 9.91 – 9.47 (m, 1H), 7.53 – 7.32 (m, 5H), 4.44 – 4.04 (m, 2H), 3.39 – 2.85 (m, 3H).

MS (ESI) m/z calcd for $C_{17}H_{11}NO_4Na$ 200.1 $[M+Na]^+$, found 200.0 $[M+Na]^+$.

2.6.3 (*E/Z*)-2-(*N*-Methylbenzamido)vinyl acetate 12



12

To a stirred solution of triethylamine (0.72 mL, 5.20 mmol, 1.7 equiv), 4-dimethylaminopyridine (75 mg, 0.61 mmol, 0.2 equiv) and acetic anhydride (0.33 mL, 4.59 mmol, 1.5 equiv) in dichlormethane (12 mL) was added *N*-methyl-*N*-(2-oxoethyl)benzamide **S1** (543 mg, 3.06 mmol, 1.0 equiv) in one portion. The reaction mixture was stirred for 16 h at room temperature. After TLC analysis showed complete consumption of the aldehyde, saturated $NaHCO_3$ solution was added (10 mL). The organic layers were separated and the aqueous phase was extracted with dichlormethane (2x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. Purification by flash chromatography via puriflash XS 420+ machine, HP_15µm_F0012 flash column (*n*-hexane: EtOAc = 99:1 → 80:20) afforded (*E/Z*)-2-(*N*-methylbenzamido)vinyl acetate **12** (334 mg, 50%, *E:Z* = 27:73) as colorless liquid (*E*-isomer) and a colorless solid (*Z*-isomer). Separation of both isomers could be achieved by flash column chromatography with the above given conditions.

For the *E*-isomer different rotamers exist in solution at ambient temperature. At higher temperature (363 K) a clearly resolved spectrums showing only on single species could be obtained. For the *Z*-isomer, no rotamers were detected at ambient temperature.

Configuration of the double bond could be assigned via the ^3J coupling constants of the oelfinic protons (11.5 Hz for the *E*- and 5.4 Hz for the *Z*-isomer). Assignment using vincinal coupling constants was verified by single crystal X-ray structures of ***Z*-12** (CCDC 2180326).

(E)-Isomer:

R_f (*n*-hexane:EtOAc = 4:1) 0.25

^{1}H NMR (600 Hz, 363 K, DMSO-d^6) δ = 7.61 – 7.35 (m, 5H), 7.11 (d, J=11.5 Hz, 1H), 7.03 (m, 1H), 3.13 (s, 3H), 2.10 (s, 3H).

^{13}C NMR (151 MHz, 363 K, DMSO-d^6) δ = 168.5, 167.5, 134.6, 129.6, 128.0, 126.9, 124.7, 120.4, 32.3, 19.7.

IR (ATR, ν in cm^{-1}): 3113 (w), 2949 (w), 1752 (s), 1644 (s), 1489 (w), 1415 (m), 1364 (s), 1318 (m), 1269 (m), 1221 (s), 1178 (m), 1103 (s), 1069 (s), 1081 (m), 998 (m), 908 (s), 790 (m), 726 (s), 700 (s), 595 (m).

MS (ESI) m/z calcd for $C_{12}H_{13}NO_3Na$ 242.1 $[M+Na]^+$, found 242.0 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{13}NO_3$ 219.0895 $[M]^+$, found 219.0907 $[M]^+$.

(Z)-Isomer:

R_f (*n*-hexane:EtOAc = 4:1) 0.18

m.p. 83-85°C.

^{1}H NMR (400 Hz, DMSO-d^6) δ = 7.62 – 7.24 (m, 5H), 6.61 (d, J=5.4 Hz, 1H), 5.93 (m, 1H), 3.23 (s, 3H), 2.14 (s, 3H).

^{13}C NMR (101 Hz, DMSO-d^6) δ = 169.7, 166.8, 135.4, 130.3, 128.2, 127.7, 124.1, 115.2, 34.7, 20.5.

IR (ATR, ν in cm^{-1}): 3100 (w), 3016 (w), 1764 (s), 1628 (s), 1577 (w), 1432 (m), 1369 (m), 1354 (s), 1329 (m), 1219 (s), 1174 (m), 1073 (s), 1025 (m), 956 (m), 800 (m), 762 (s), 719 (s), 700 (s), 593 (m).

MS (ESI) m/z calcd for $C_{12}H_{13}NO_3Na$ 242.1 $[M+Na]^+$, found 242.0 $[M+Na]^+$.

HRMS (EI) m/z calcd for $C_{12}H_{13}NO_3$ 219.0895 $[M]^+$, found 219.0875 $[M]^+$.

3 COMPUTATIONAL DETAILS

The conformational space for each structure was explored with Grimme's extended tight-binding method (xTB)[8] and the meta-dynamics package Conformer Rotamer Ensemble Sampling Tool (CREST).[9] The default parameters were used in combination with the GFN2-FF force field.[10] As typically a large number of conformers were obtained, a clustering approach was employed to reduce the number of conformers to 30. The remaining structures were then optimized with the M06-2X functional,[11] Grimme's D3 correction (zero-damping),[12] and the triple-ζ basis set 6-311+G(d,p). Solvation by dichloromethane was accounted for with the SMD solvation model[13] and a superfine grid was used for the numerical integration of the density. Vibrational analysis verified that each structure was a minimum. Thermal corrections were obtained from unscaled harmonic vibrational frequencies at the same level of theory for a standard state of 1 mol L^{-1} and 298.15 K. Entropic contributions to free energies were obtained from partition functions evaluated with Grimme's quasi-harmonic approximation.[14] This method employs the free-rotor approximation for all frequencies below 100 cm^{-1}, the rigid-rotor-harmonic-oscillator (RRHO) approximation for all frequencies above 100 cm^{-1}, and a damping function to interpolate between the two expressions. Similar results were obtained from partition functions evaluated with Cramer's and Truhlar's quasiharmonic approximation.[15] Electronic energies were subsequently obtained from single-point calculations employing Neese's domain-based local pair-natural orbital (DLPNO) approach to the CCSD(T) method [DLPNO-CCSD(T)] with the default normalPNO settings,[16] an extrapolation to the basis set limit as implemented in ORCA using def2-TZVPP and def2-QZVPP as well as appropriate auxiliary basis sets,[17] and the SMD solvation model for dichloromethane.[13] The calculations were performed with Gaussian16[18] and ORCA.[19]

The optimized geometries for each structure as well as the associated electronic energies and thermal corrections are provided in an additional archive file.

4 NMR DATA

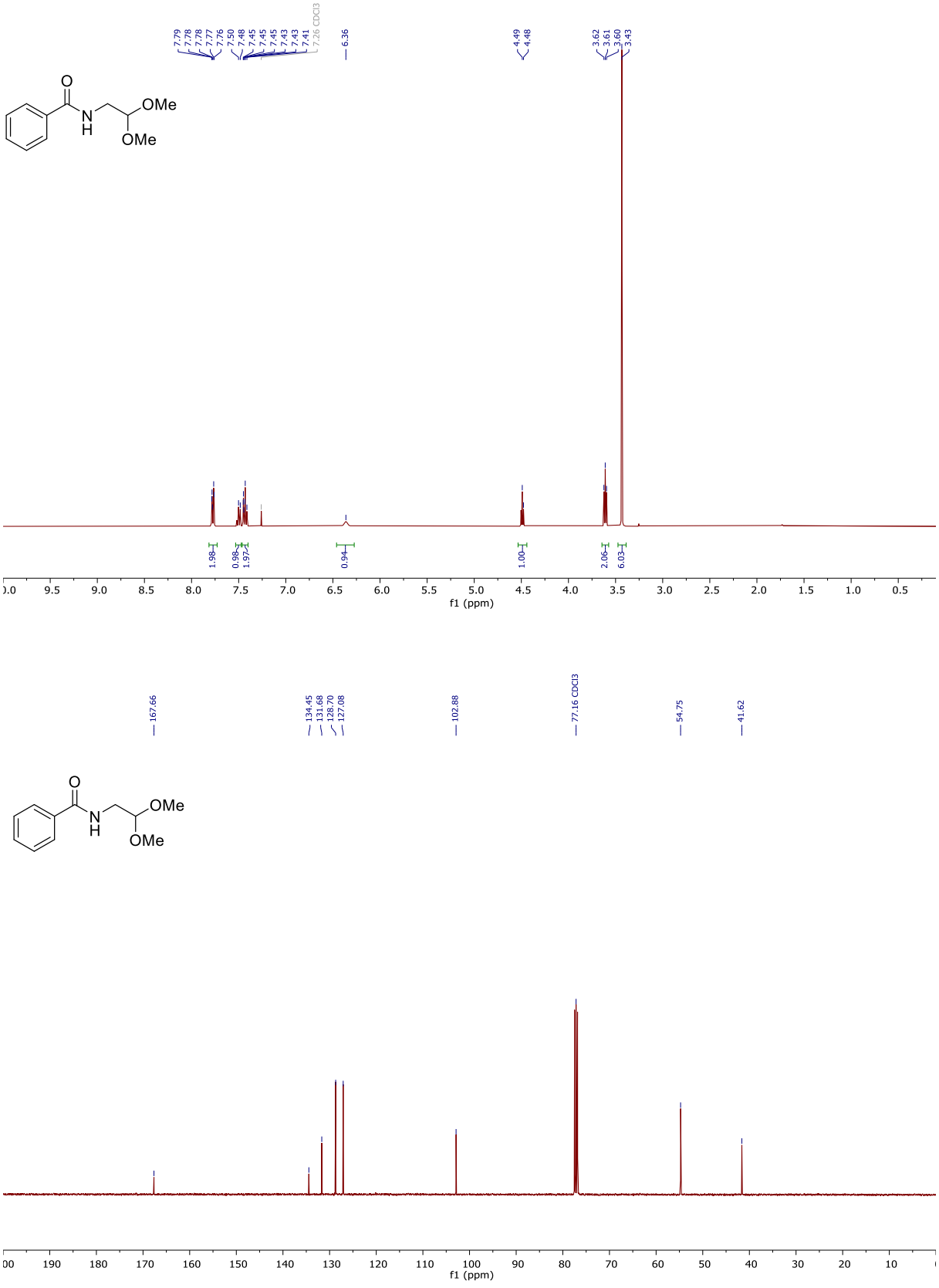


*Figure 1: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5a** in $CDCl_3$.*

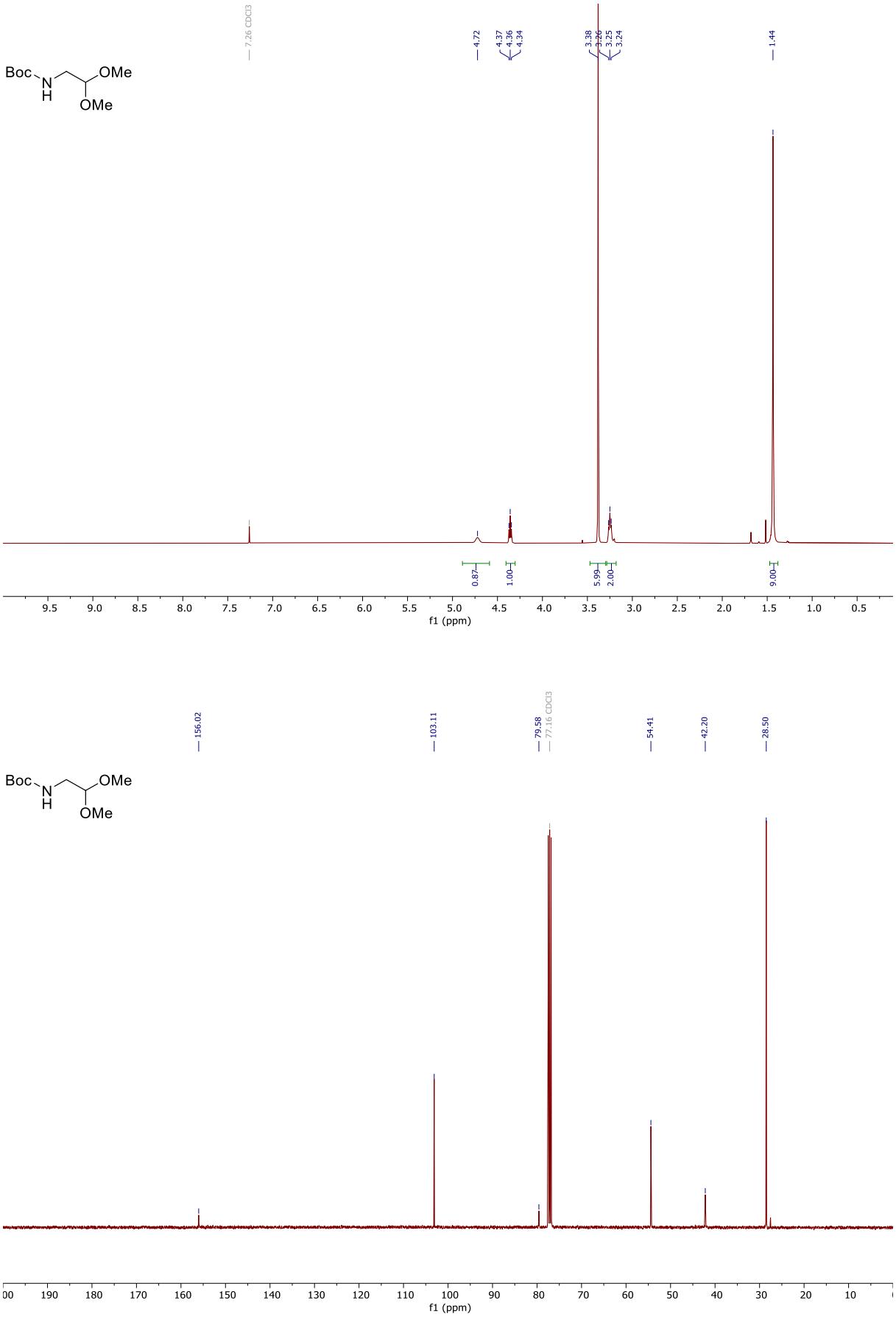


*Figure 2: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5b** in $CDCl_3$.*

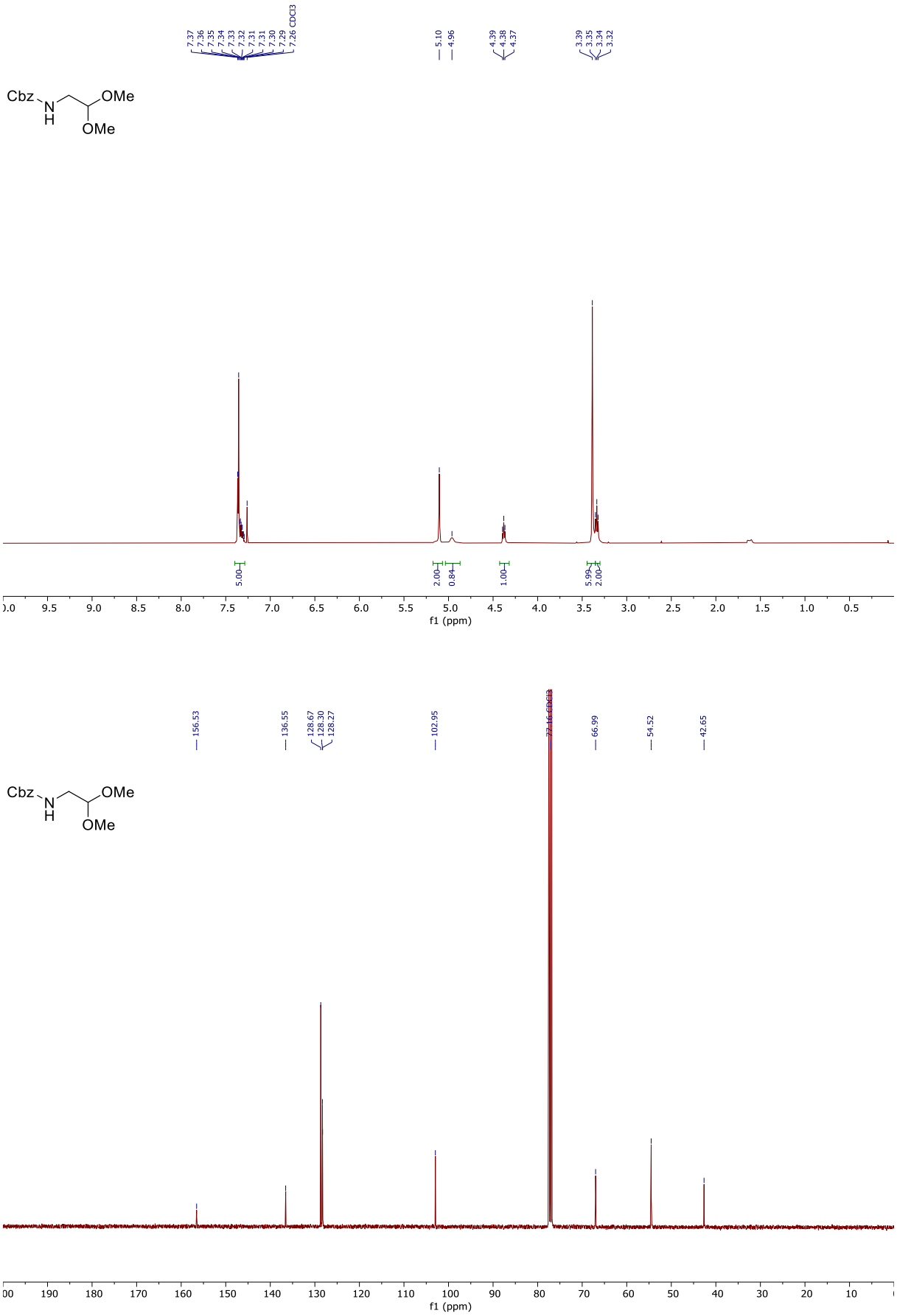


*Figure 3: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5c** in $CDCl_3$.*

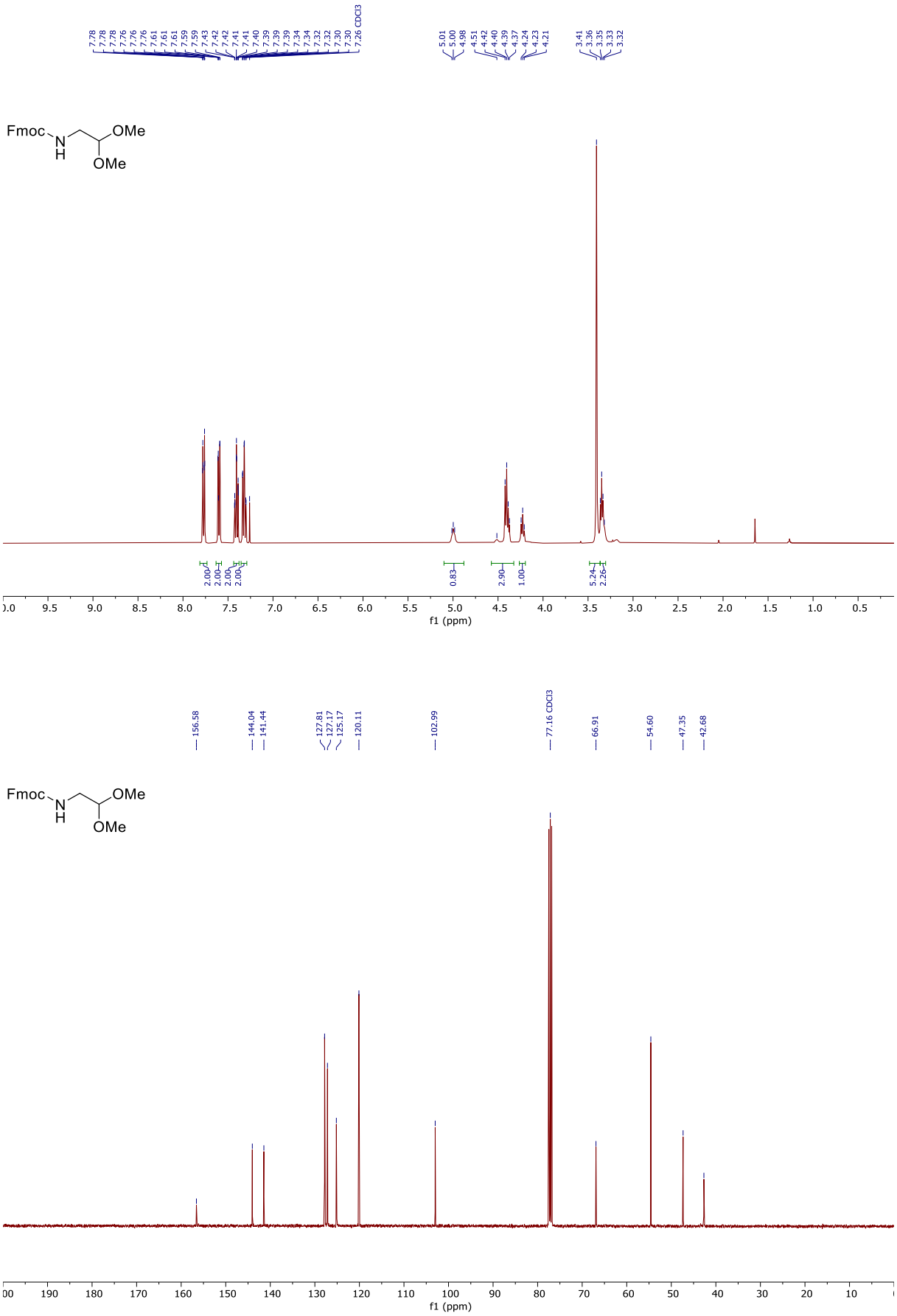


*Figure 4: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5d** in $CDCl_3$.*

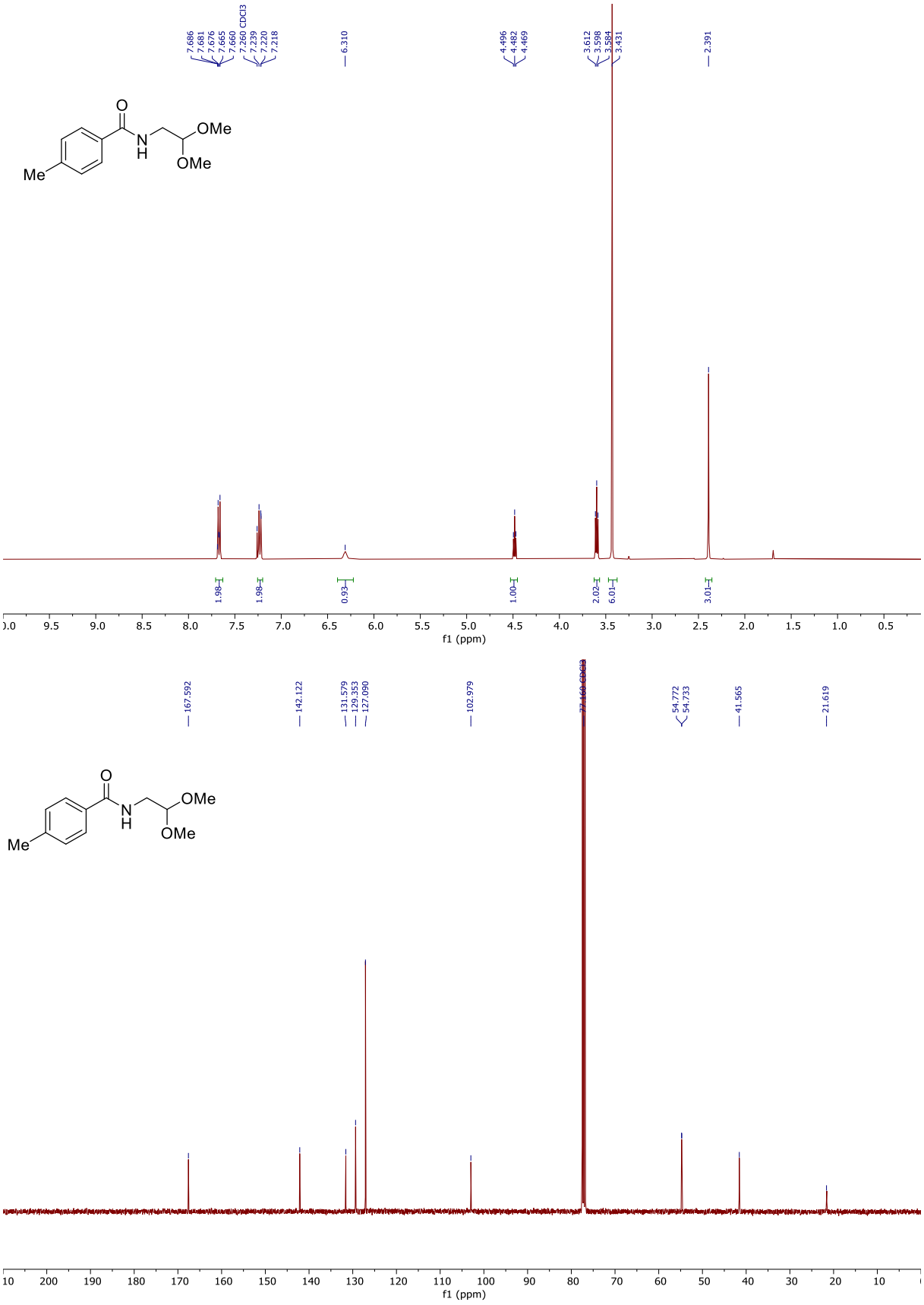


*Figure 5: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5e** in $CDCl_3$.*

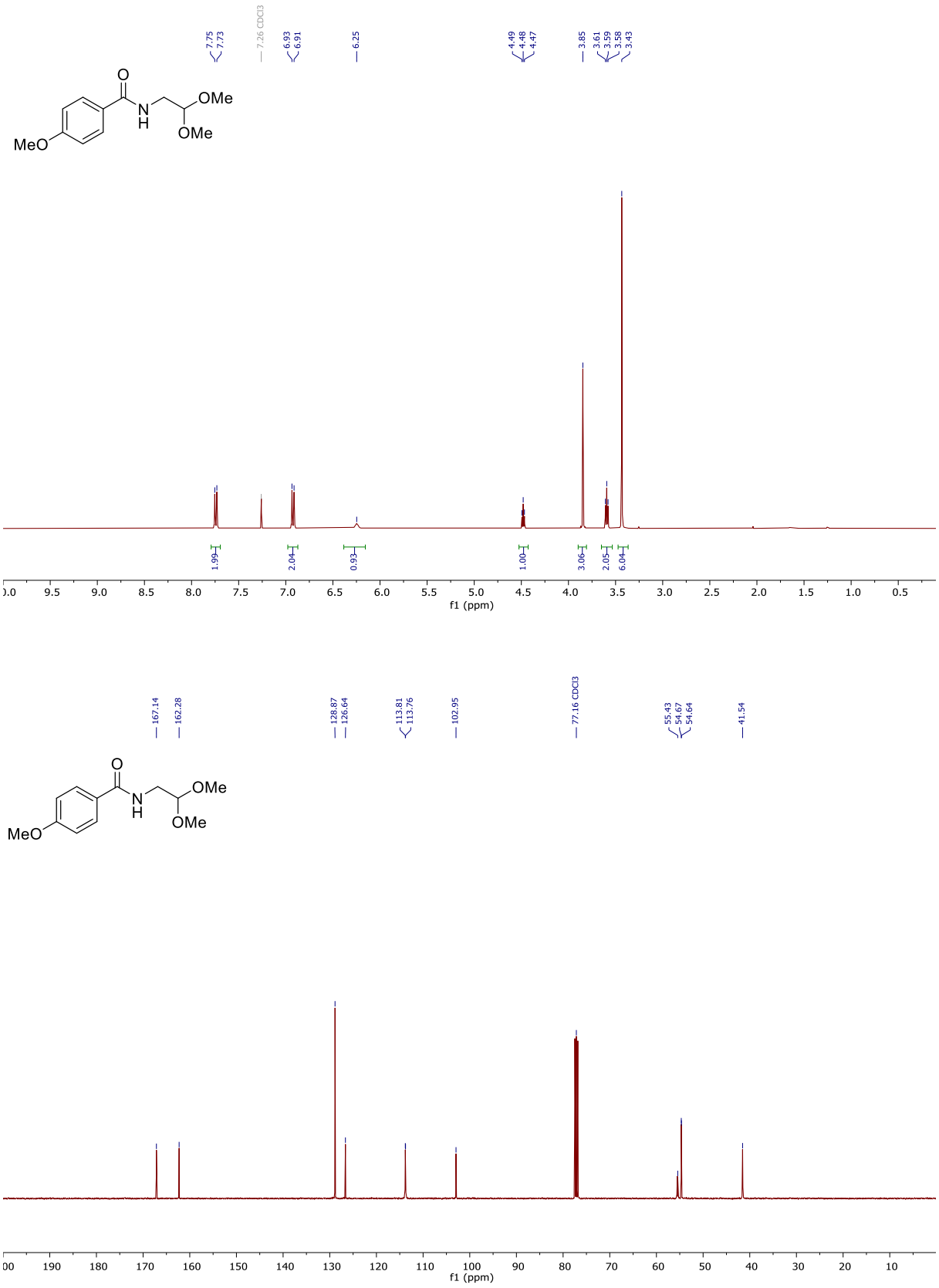


*Figure 6: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5f** in $CDCl_3$.*

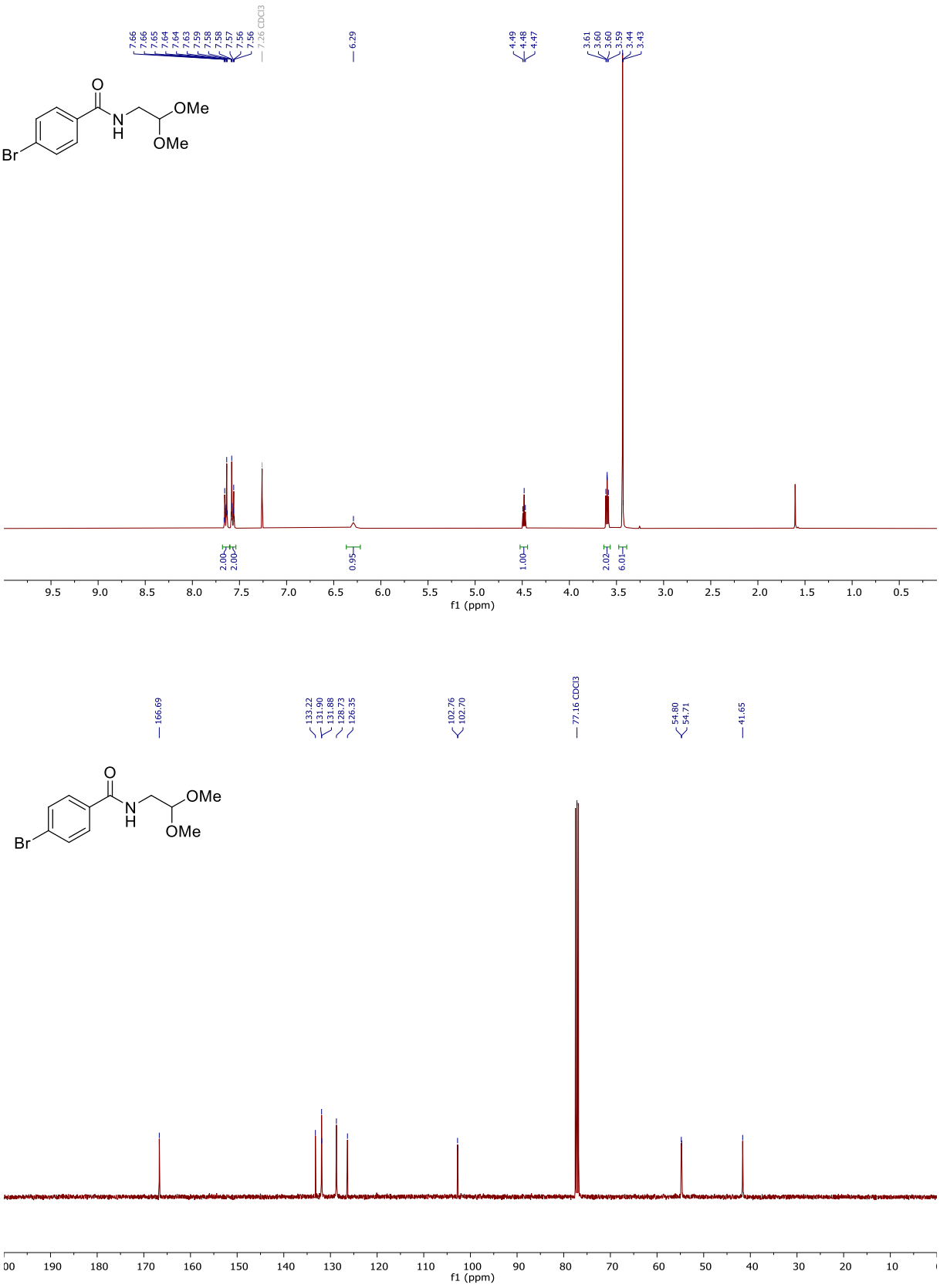
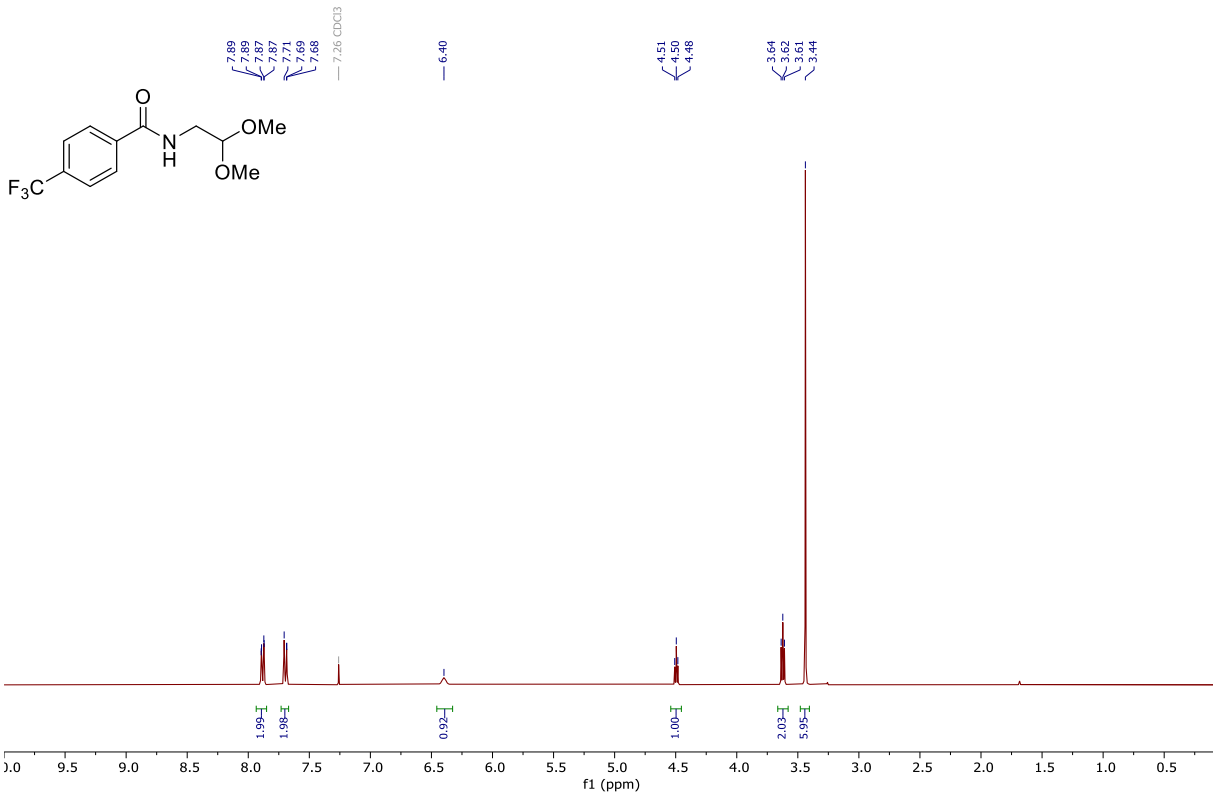
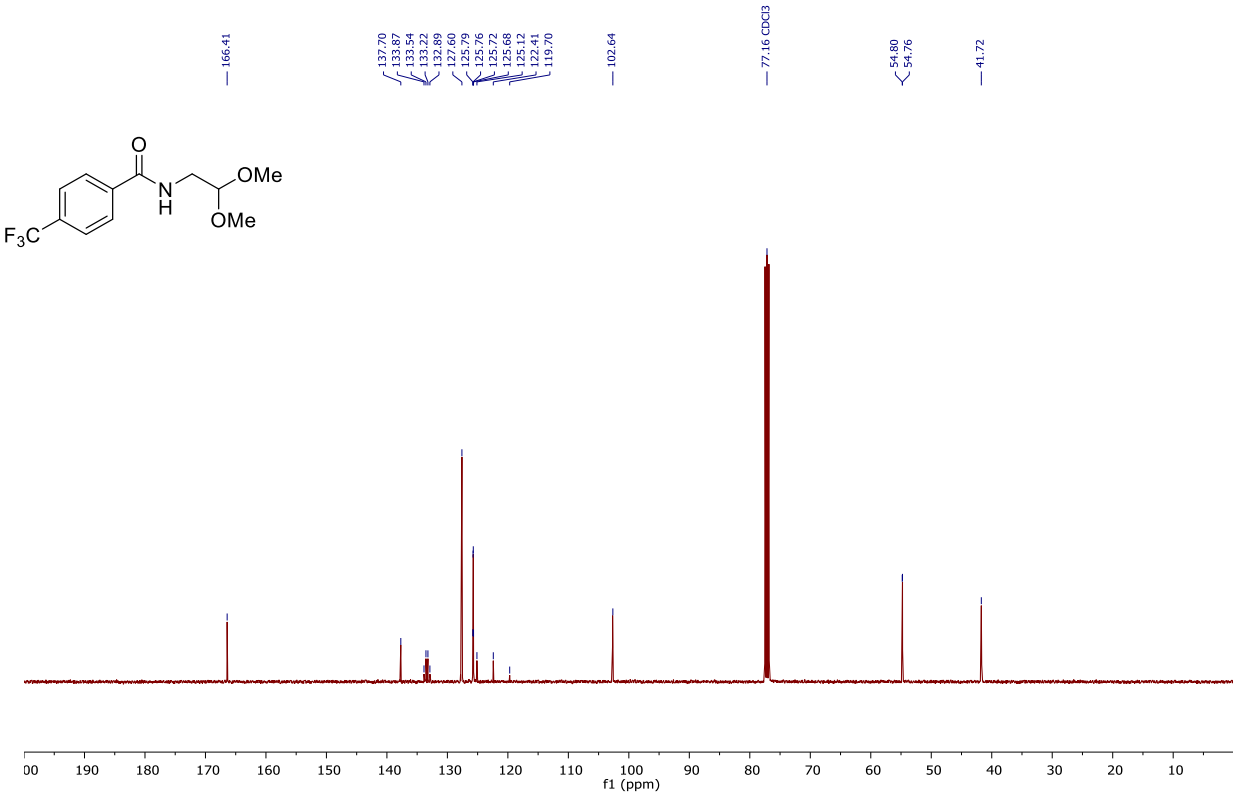


*Figure 7: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5g** in $CDCl_3$.*


7.89
7.89
7.87
7.87
7.71
7.69
7.68
7.26 CDCl3
6.40
4.51
4.50
4.48
3.64
3.62
3.61
3.44
O
N
H
OMe
OMe
F3C
1.99
1.98
0.92
1.00
2.03
5.95
f1 (ppm)


166.41
137.70
133.87
133.54
133.22
132.89
127.60
125.79
125.76
125.72
125.68
122.12
122.11
119.70
102.64
77.16 CDCl3
54.80
54.76
41.72
O
N
H
OMe
OMe
F3C
f1 (ppm)

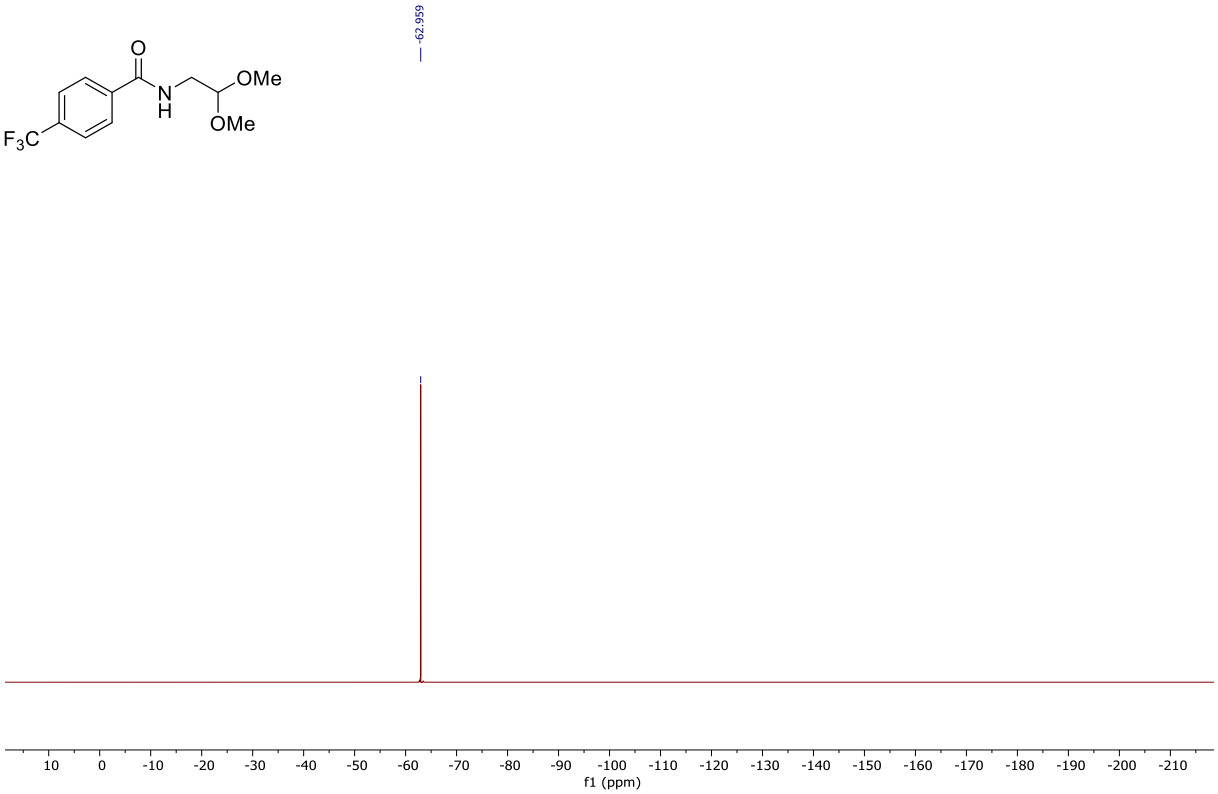


*Figure 8: ^{1}H (400 MHz), ^{13}C (126 MHz) NMR and ^{19}F (376 MHz) NMR spectra of **5h** in $CDCl_3$.*

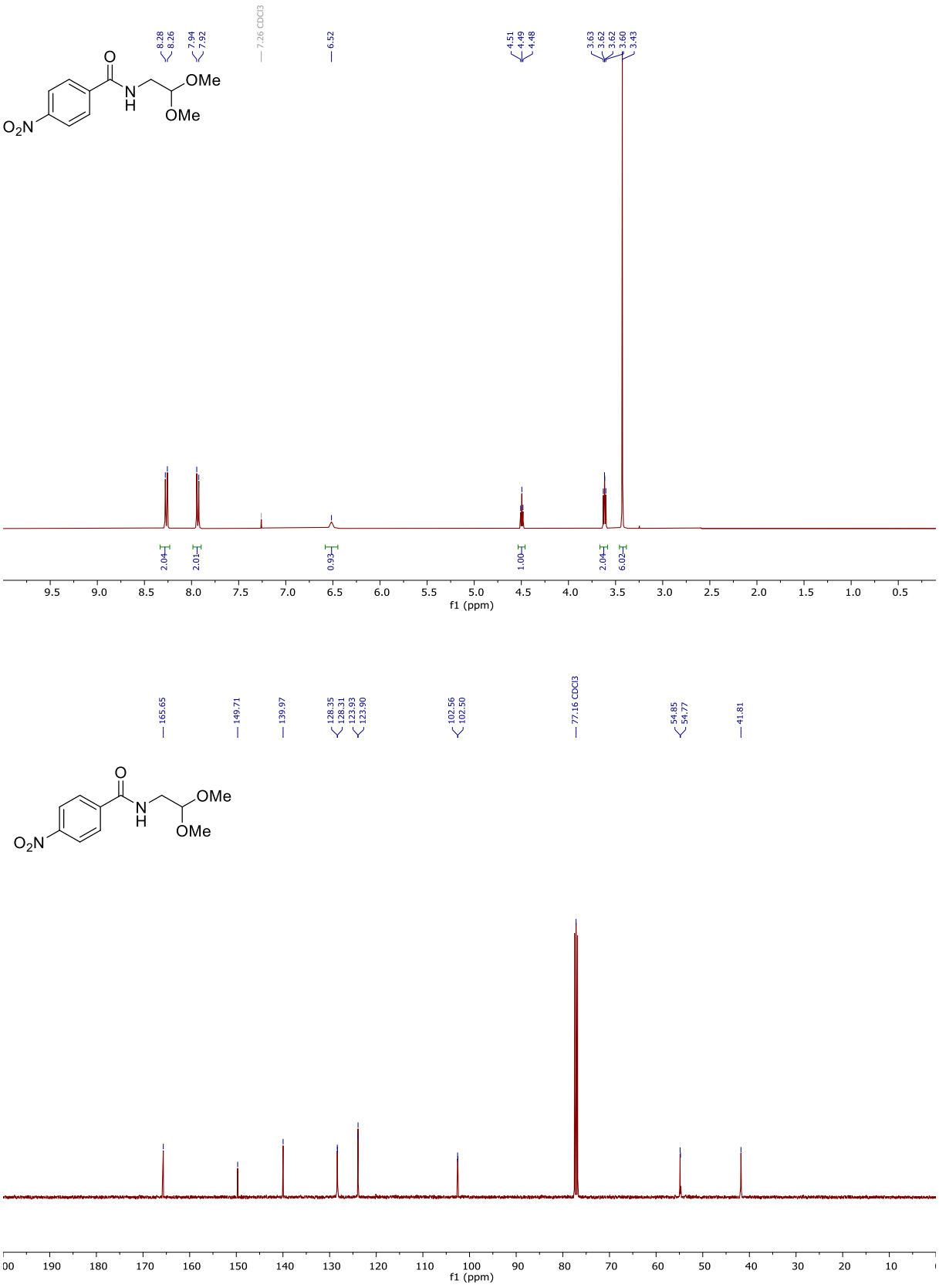


*Figure 9: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5i** in $CDCl_3$.*

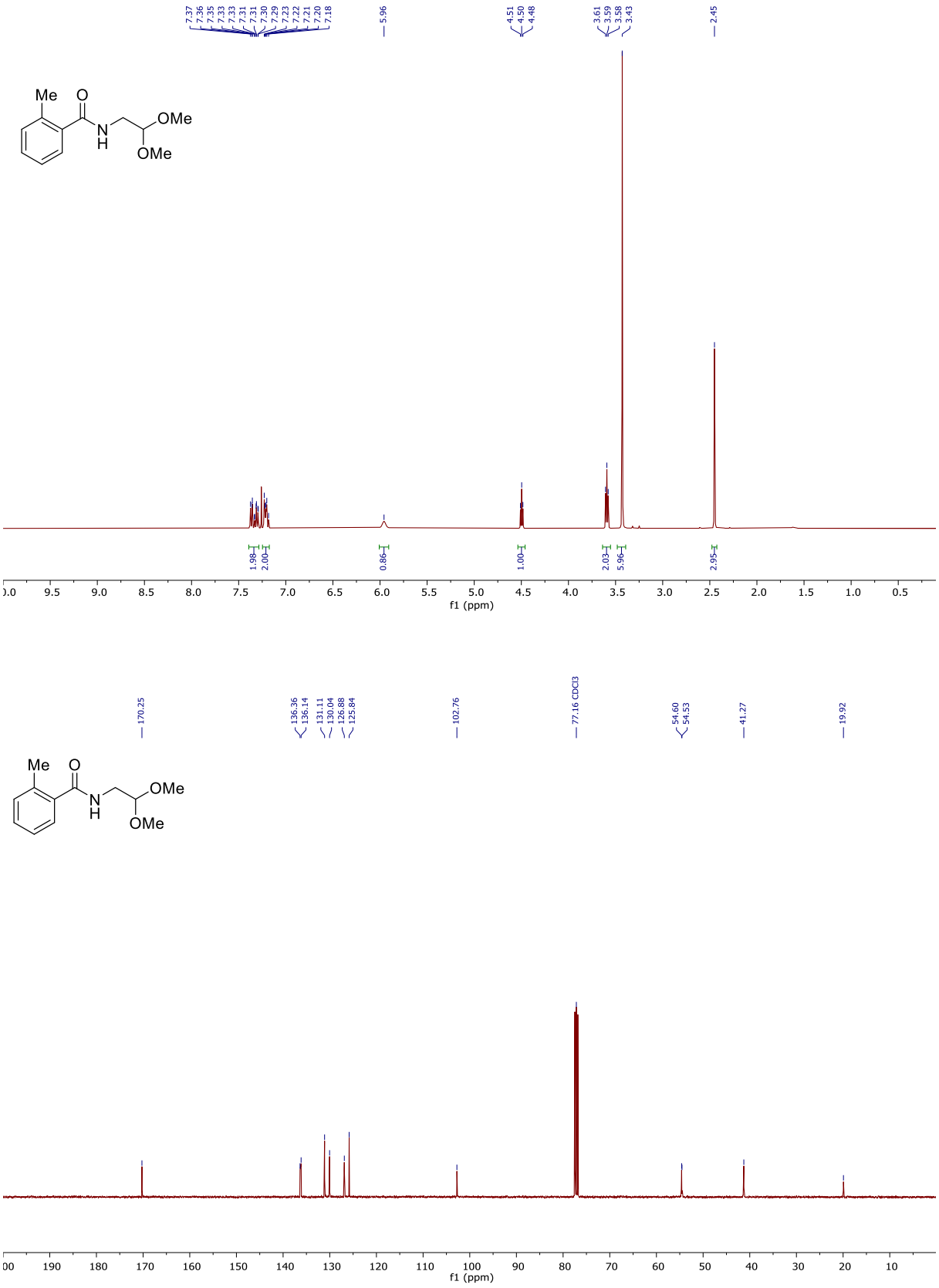


*Figure 10: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5j** in $CDCl_3$.*

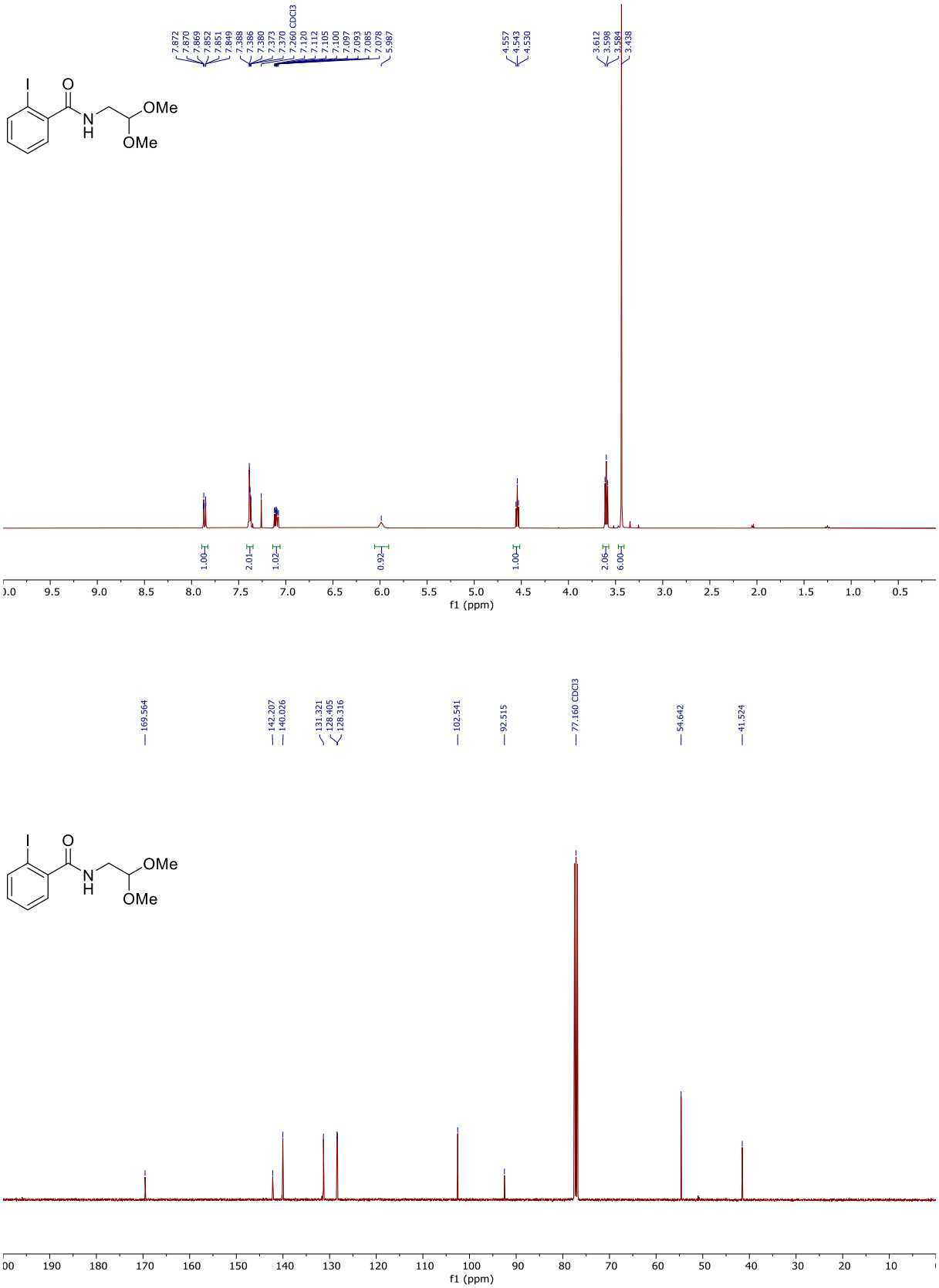


*Figure 11: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5k** in $CDCl_3$.*

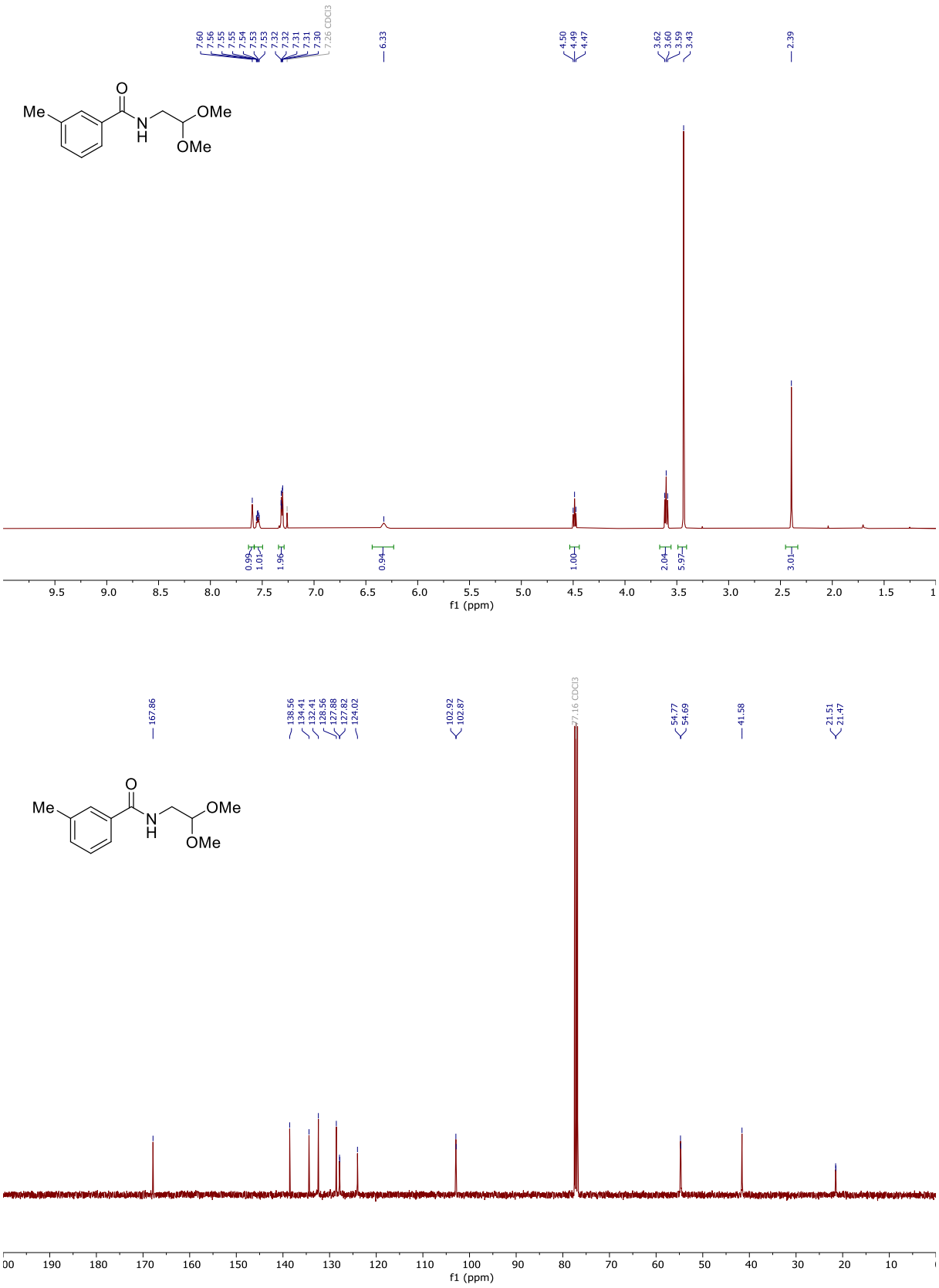


*Figure 12: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5l** in $CDCl_3$.*

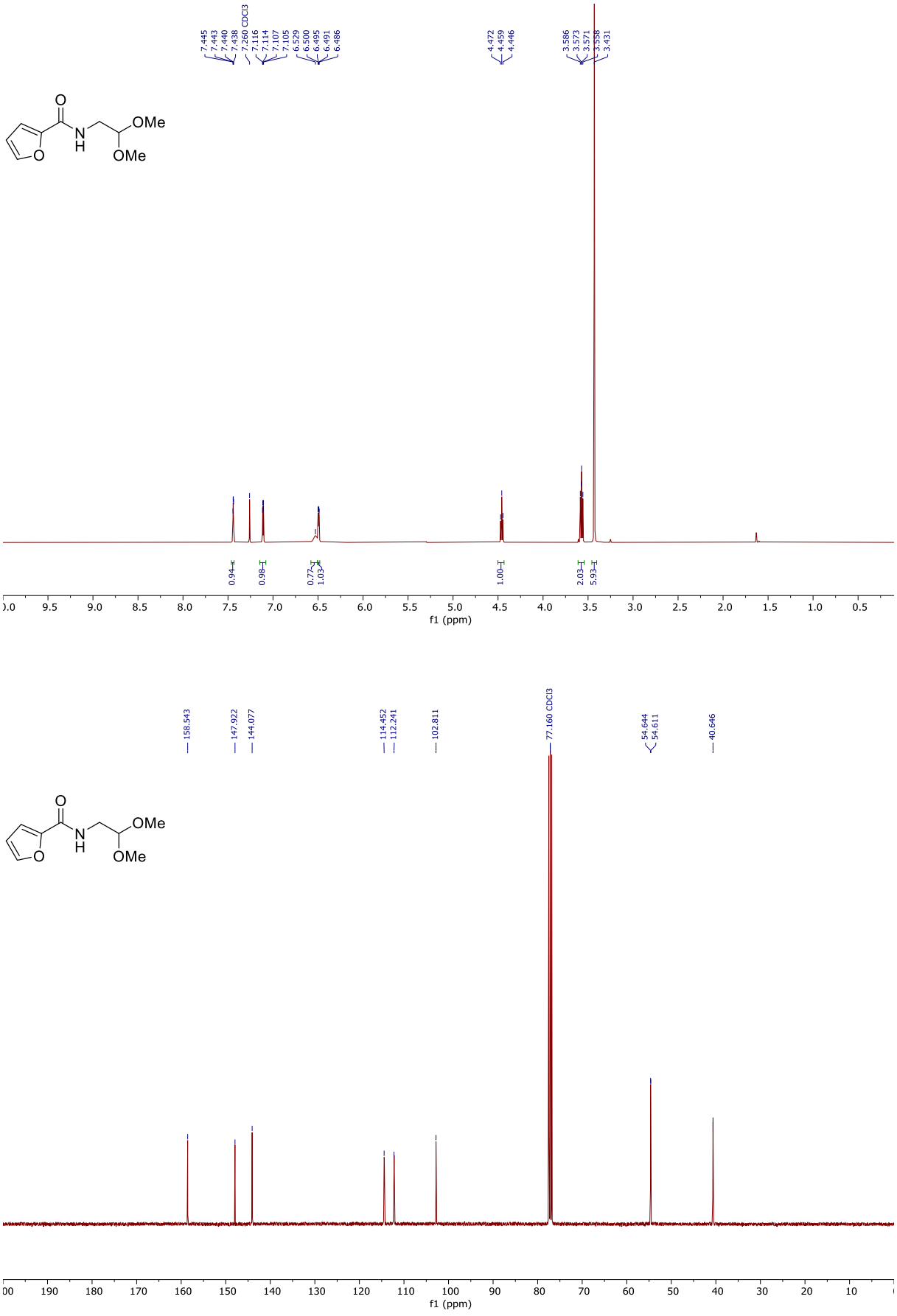


*Figure 13: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5m** in $CDCl_3$.*

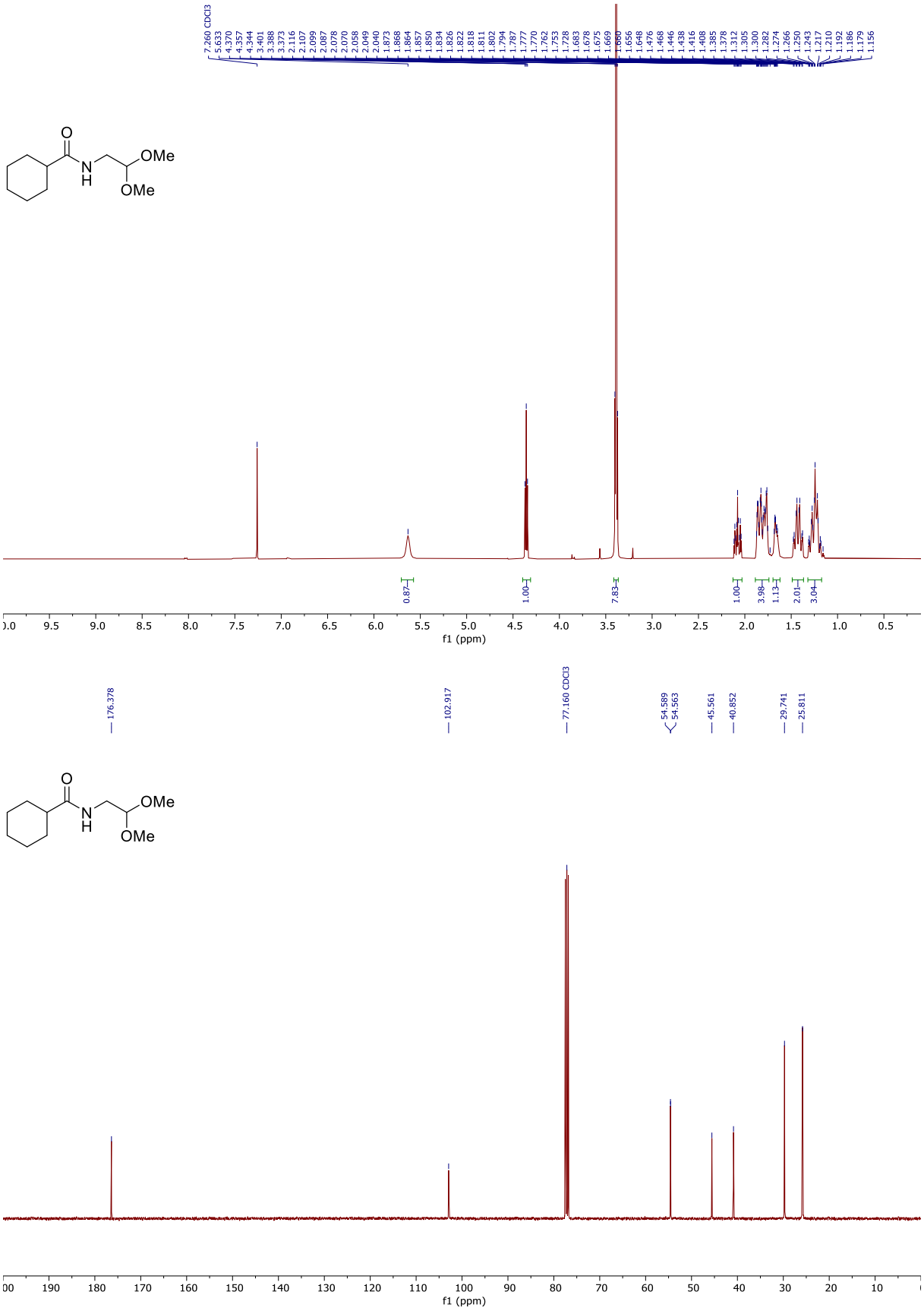


*Figure 14: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5n** in $CDCl_3$.*

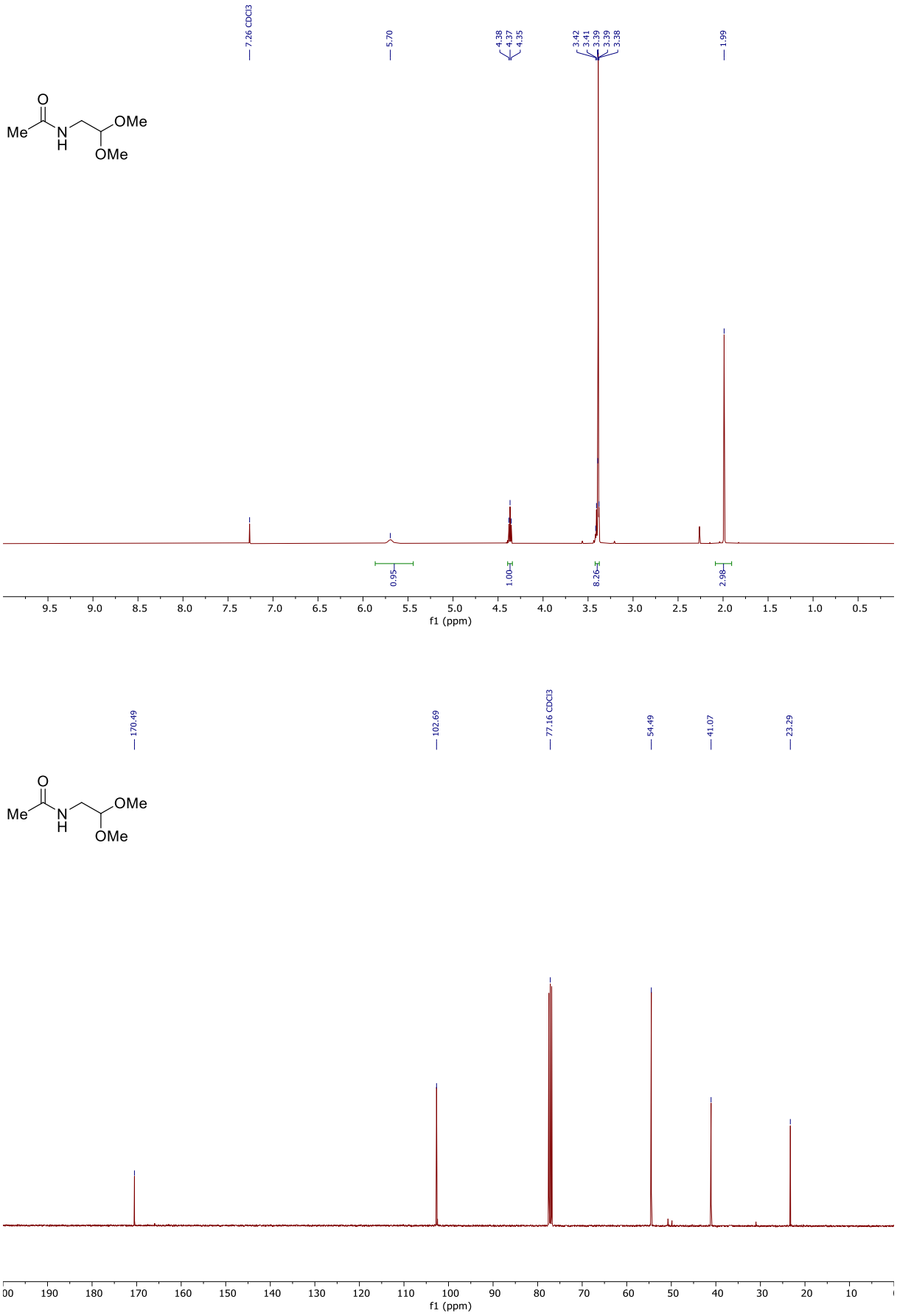


*Figure 15: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5o** in $CDCl_3$.*

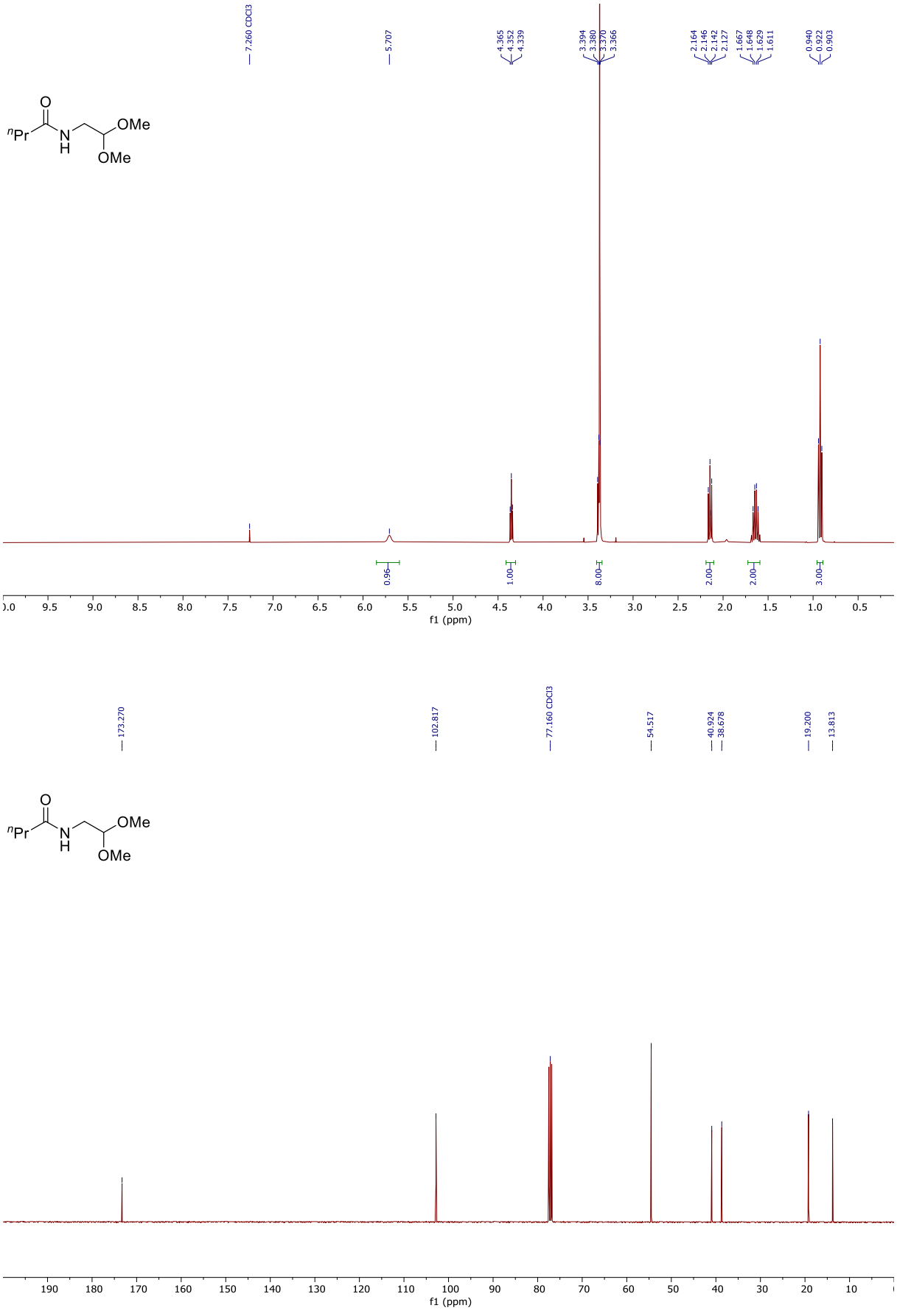


*Figure 16: ^{1}H (400 MHz) and ^{13}C (126) NMR spectra of **5p** in $CDCl_3$.*

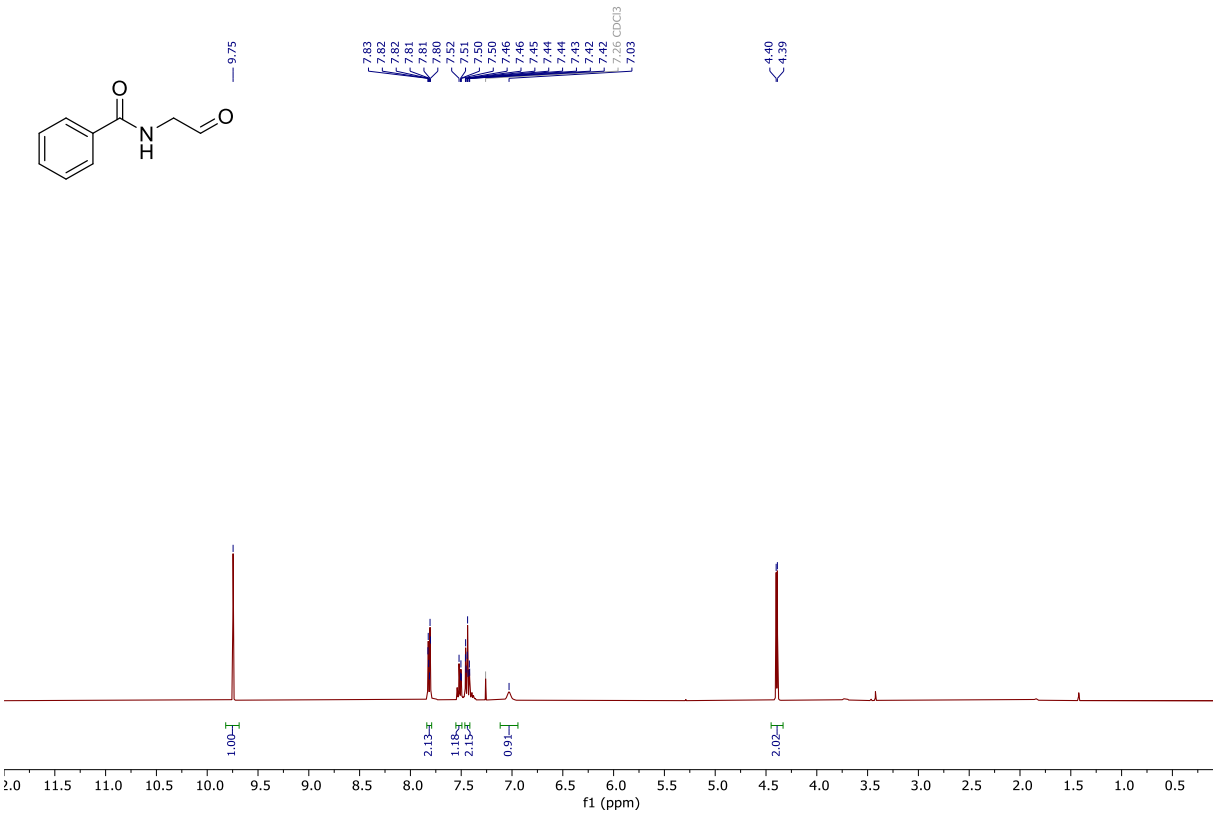


*Figure 17: ^{1}H (400 MHz) NMR spectra of **3a** in $CDCl_3$.*

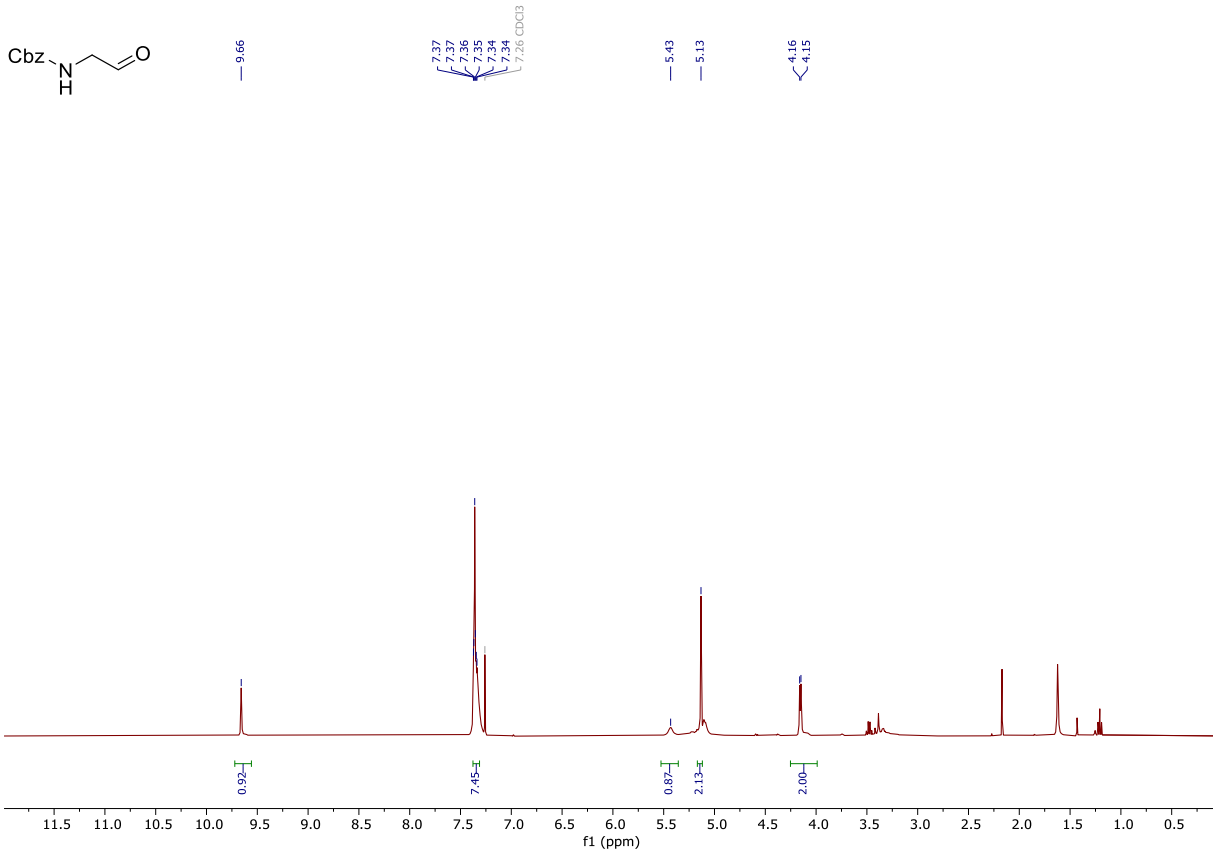


*Figure 18: ^{1}H (400 MHz) NMR spectra of **3c** in $CDCl_3$.*

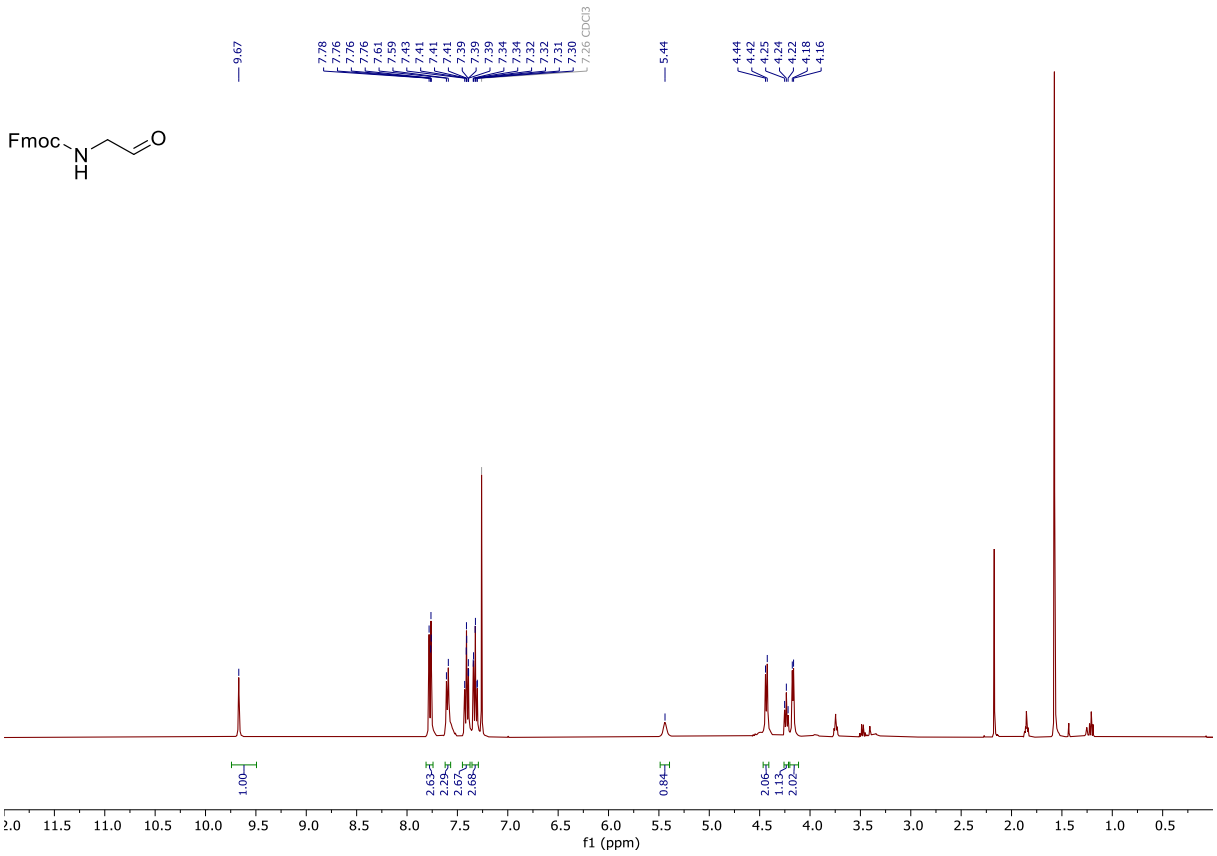


*Figure 19: ^1H (400 MHz) NMR spectra of **3d** in $CDCl_3$.*

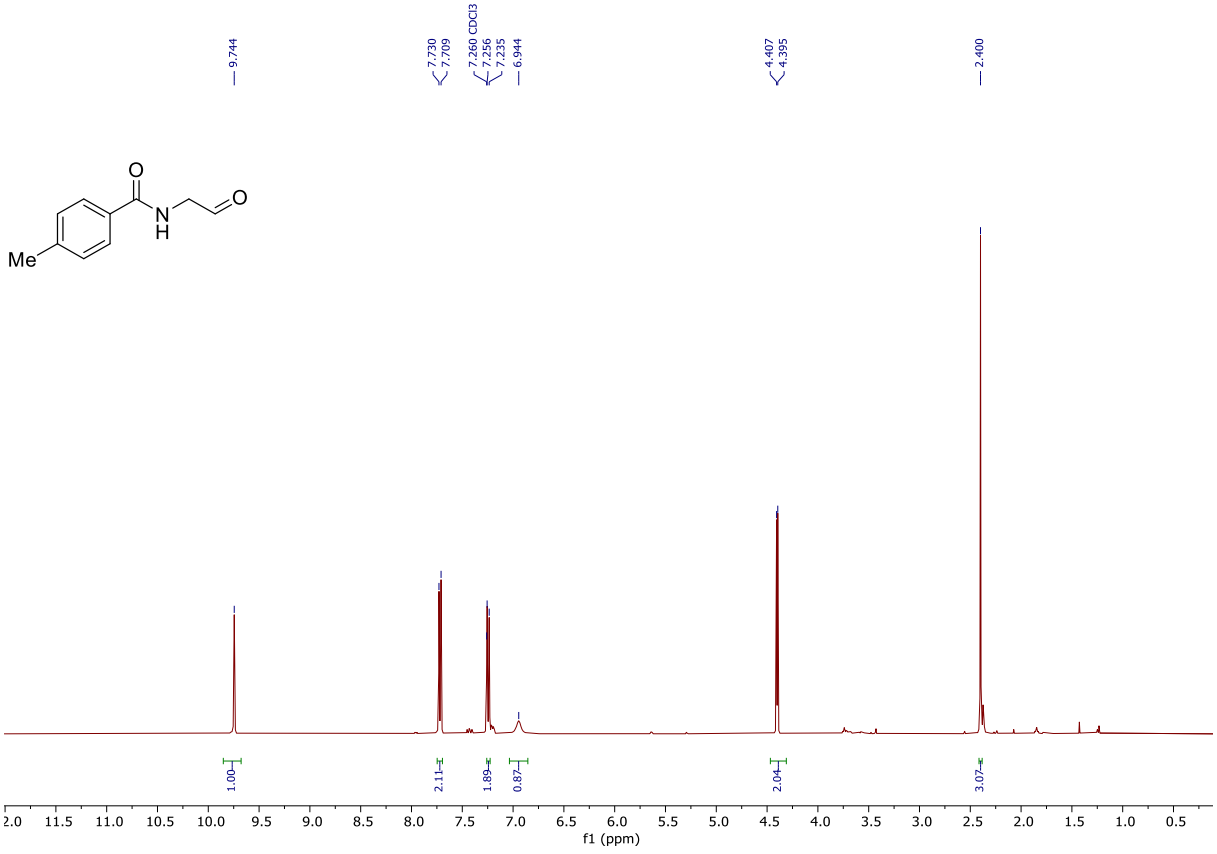


*Figure 20: ^1H (400 MHz) NMR spectra of **3e** in $CDCl_3$.*

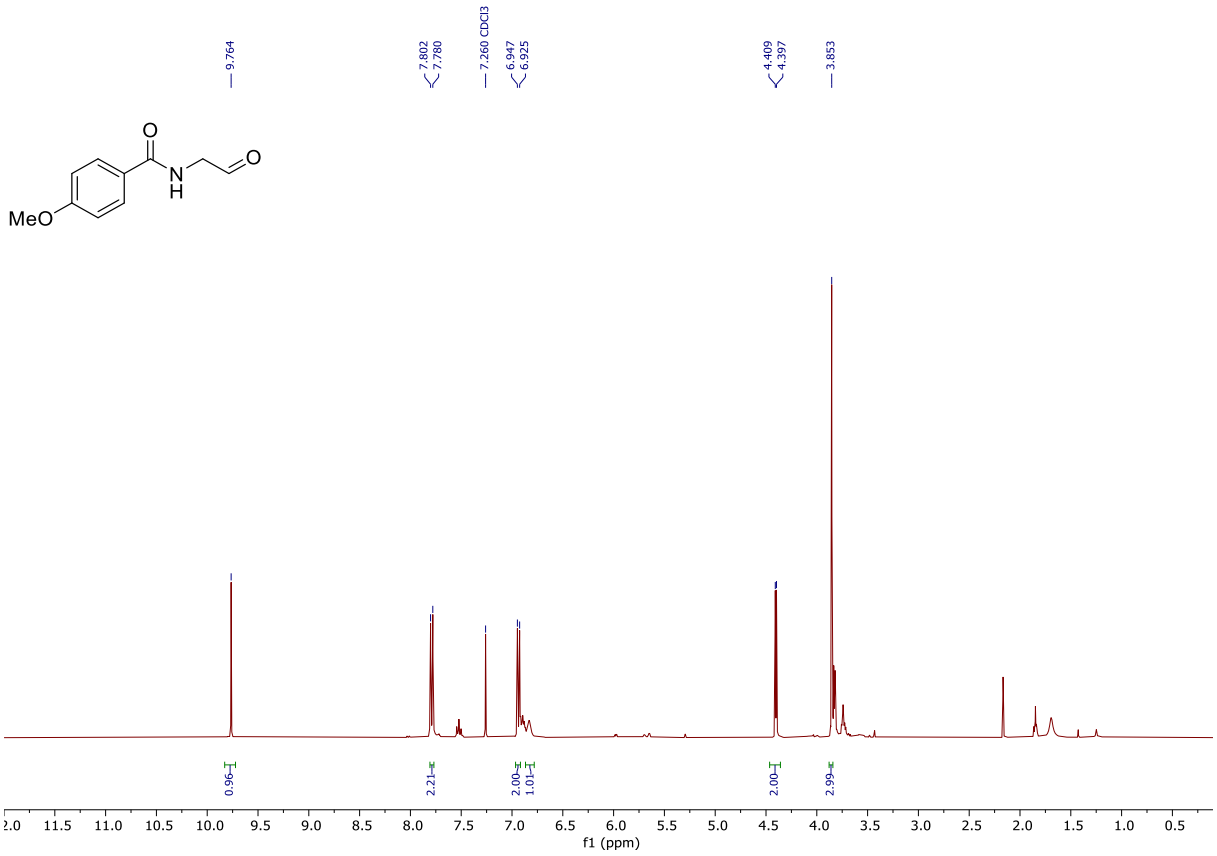


*Figure 12: ^1H (400 MHz) NMR spectra of **3f** in $CDCl_3$.*

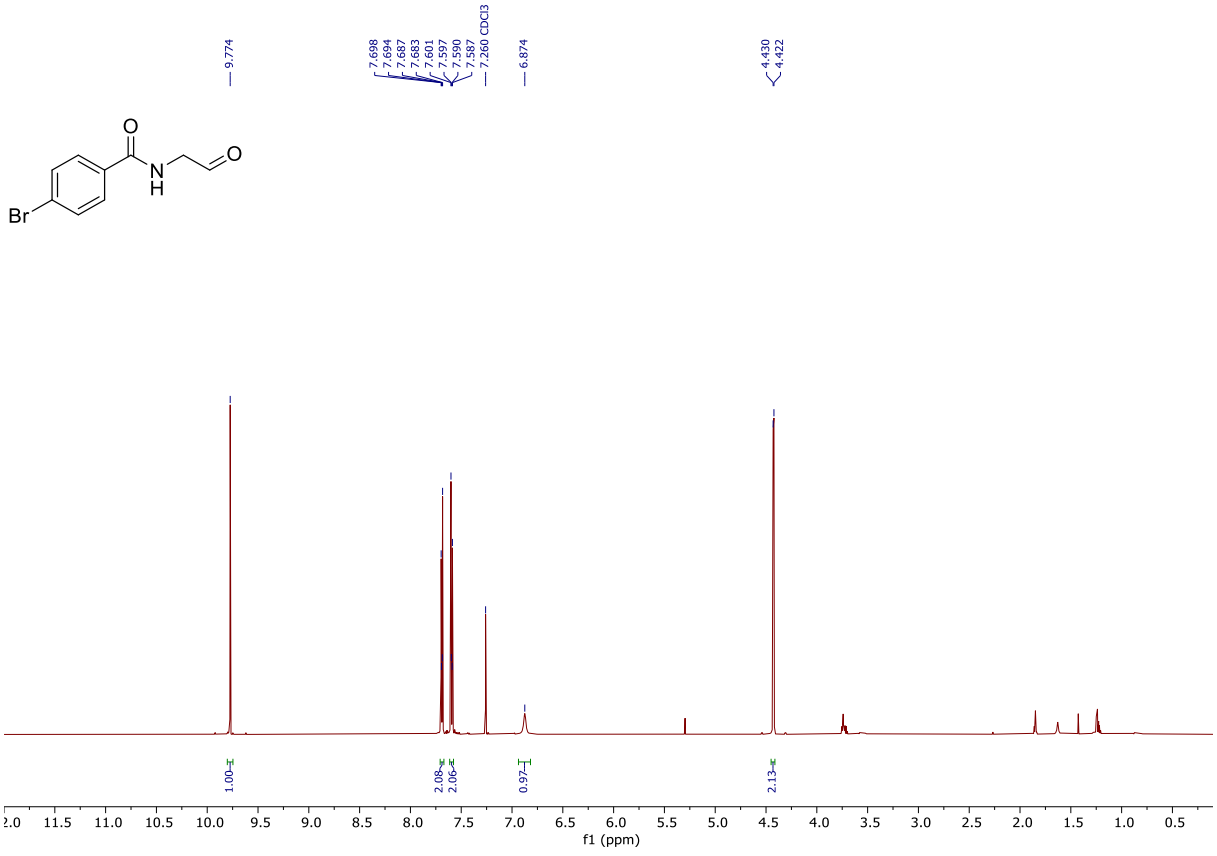


*Figure 21: ^1H (400 MHz) NMR spectra of **3g** in $CDCl_3$.*

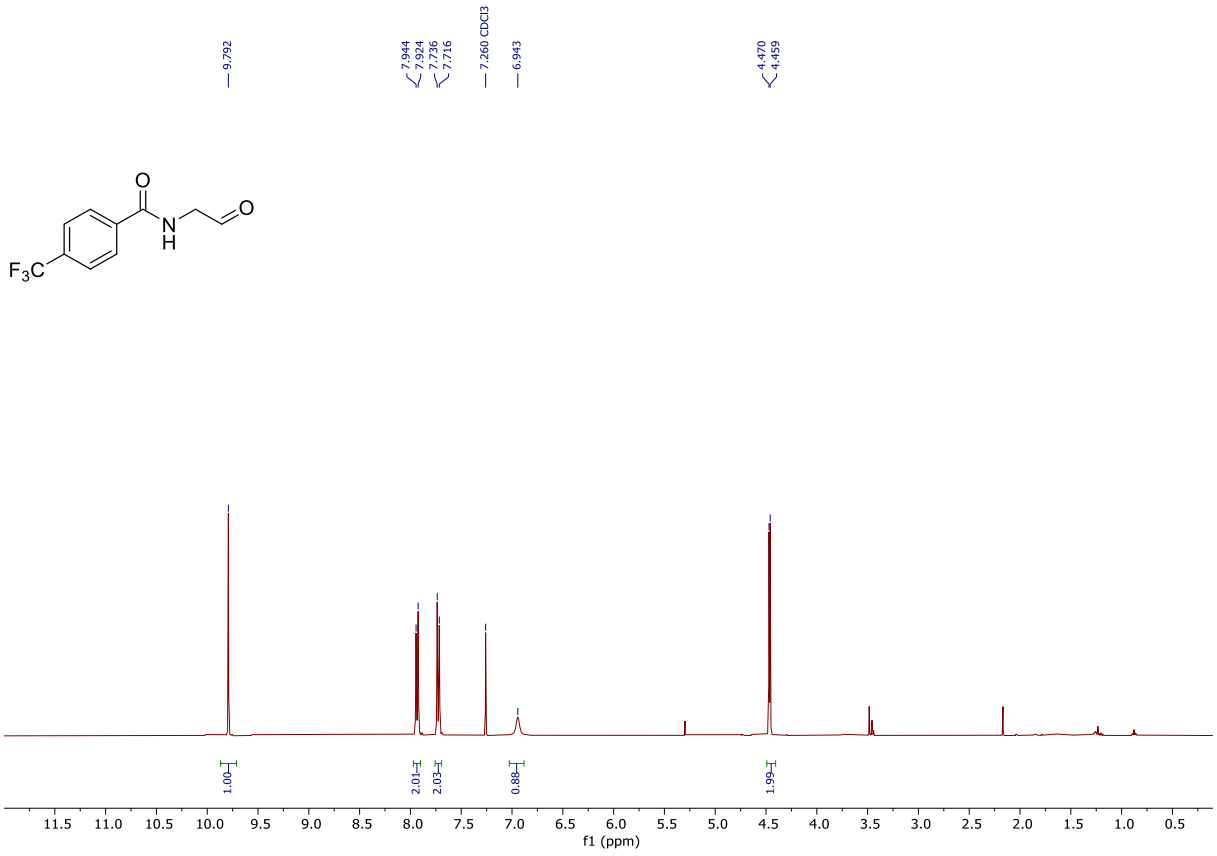


*Figure 22: ^{1}H (400 MHz) NMR spectra of **3h** in $CDCl_3$.*

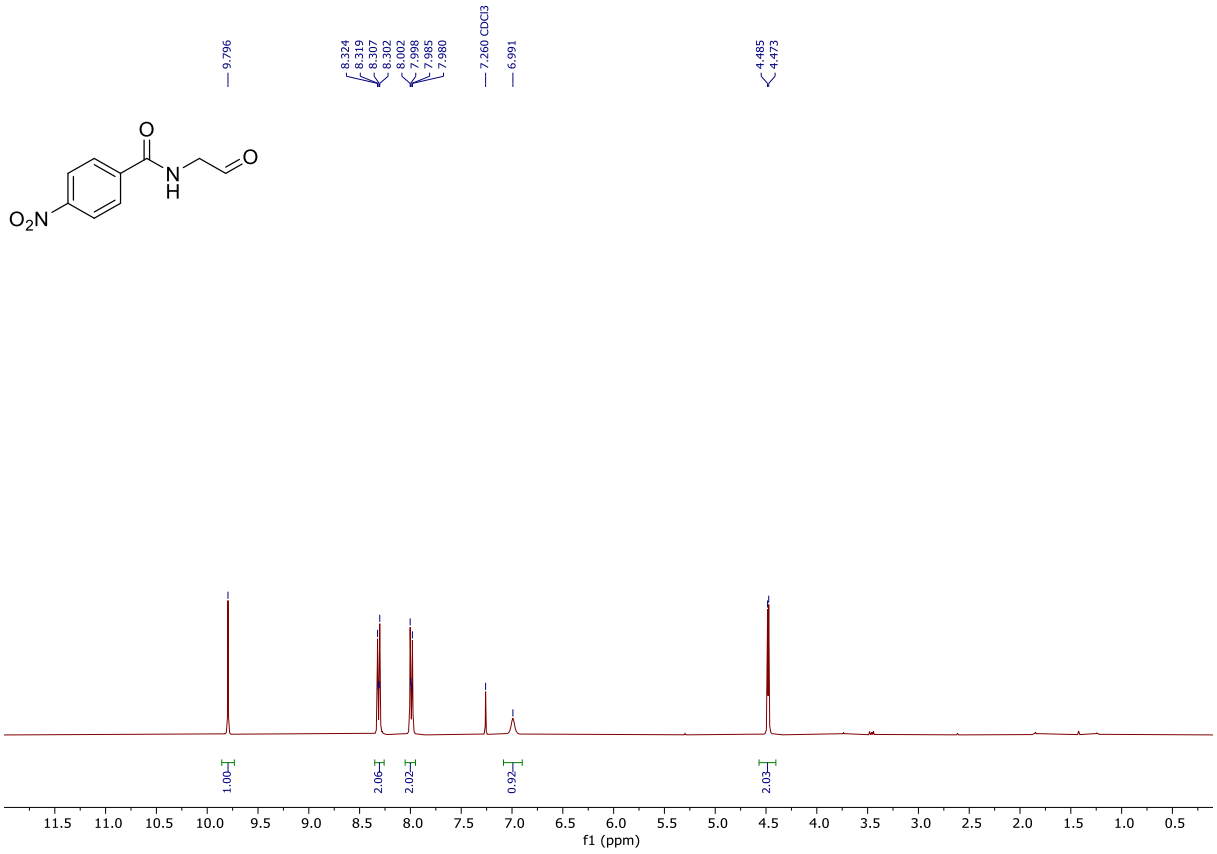


*Figure 23: ^{1}H (400 MHz) NMR spectra of **3i** in $CDCl_3$.*

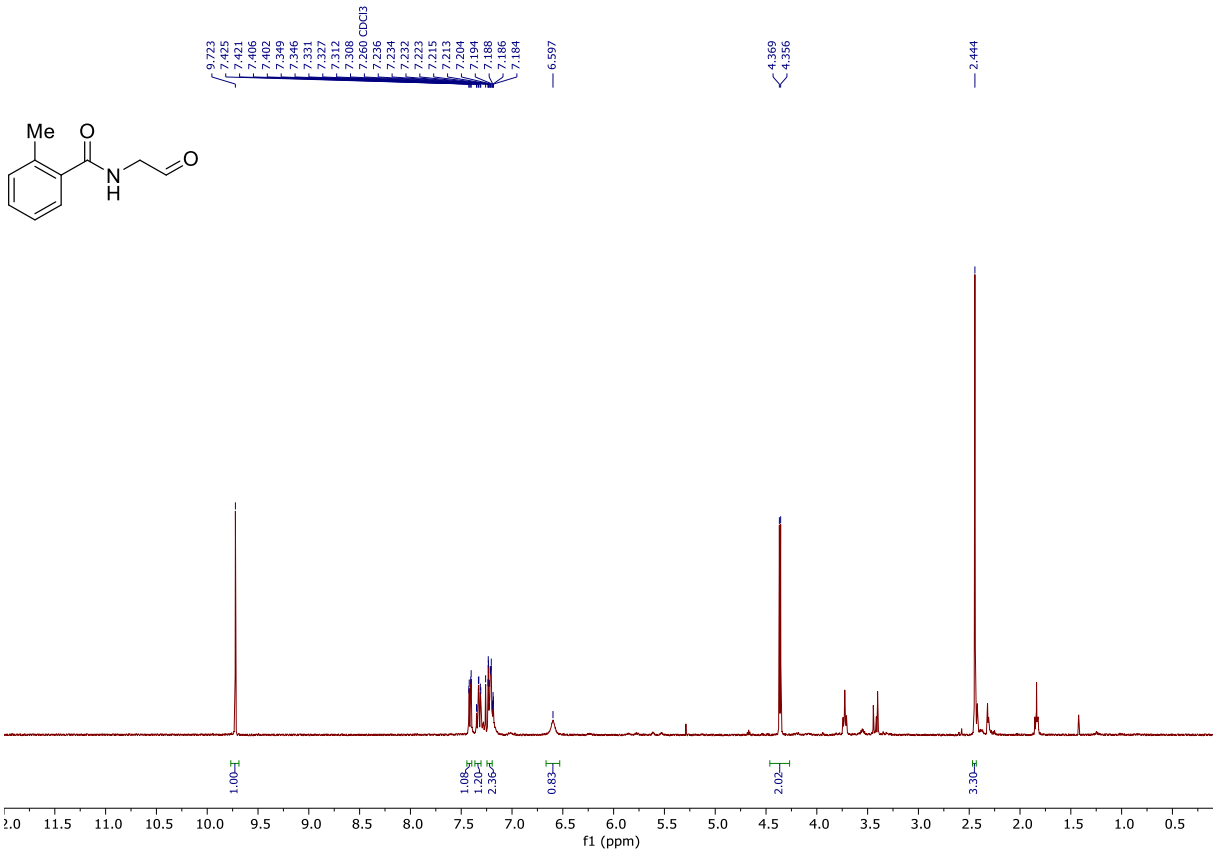


*Figure 24: ^{1}H (400 MHz) NMR spectra of **3j** in $CDCl_3$.*

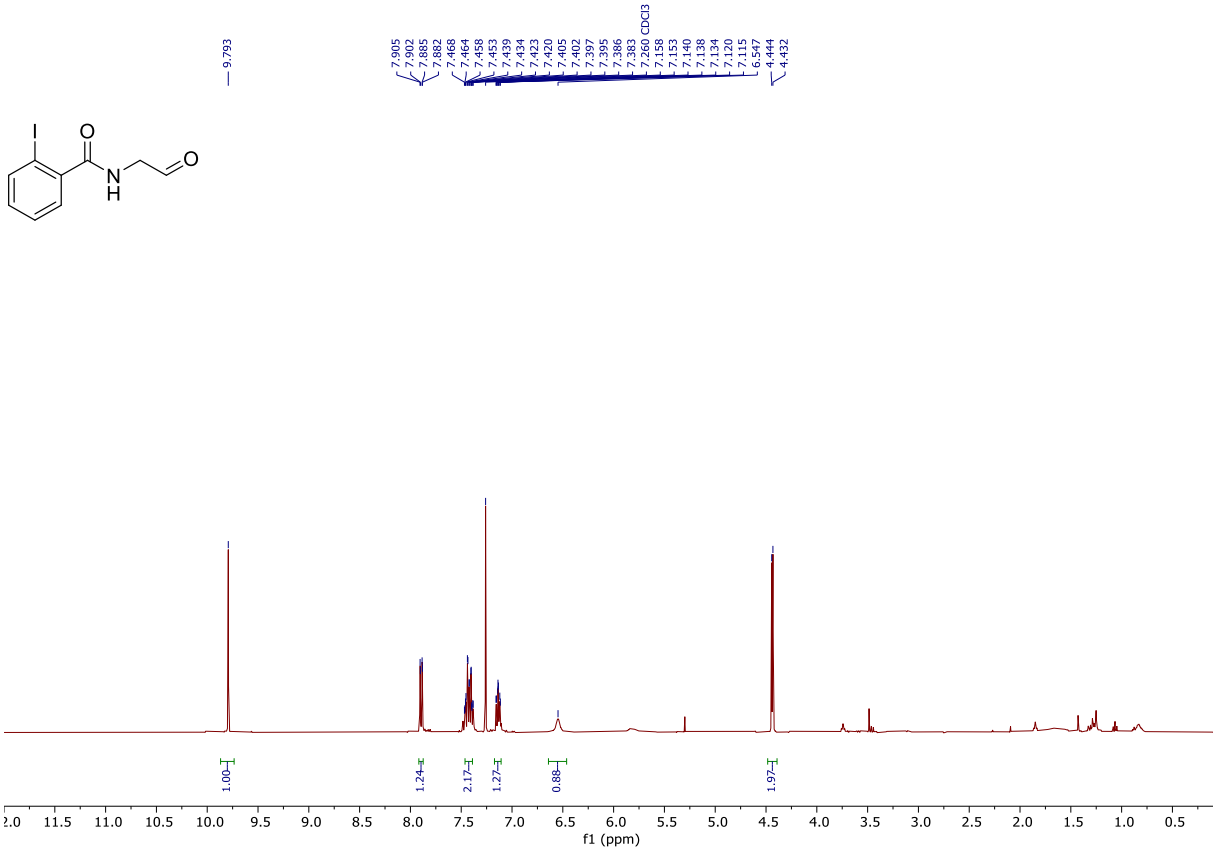


*Figure 25: ^{1}H (400 MHz) NMR spectra of **3k** in $CDCl_3$.*

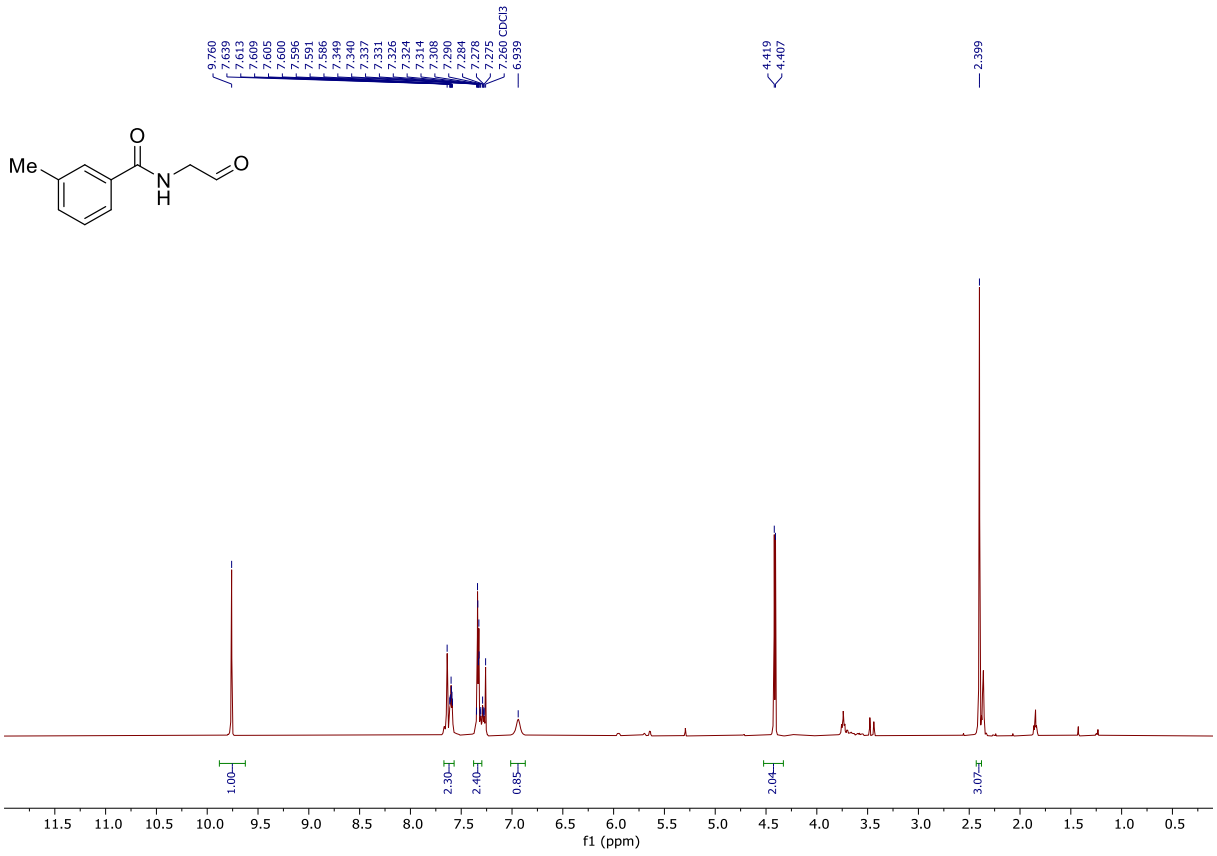


*Figure 26: ^{1}H (400 MHz) NMR spectra of **3l** in $CDCl_3$.*

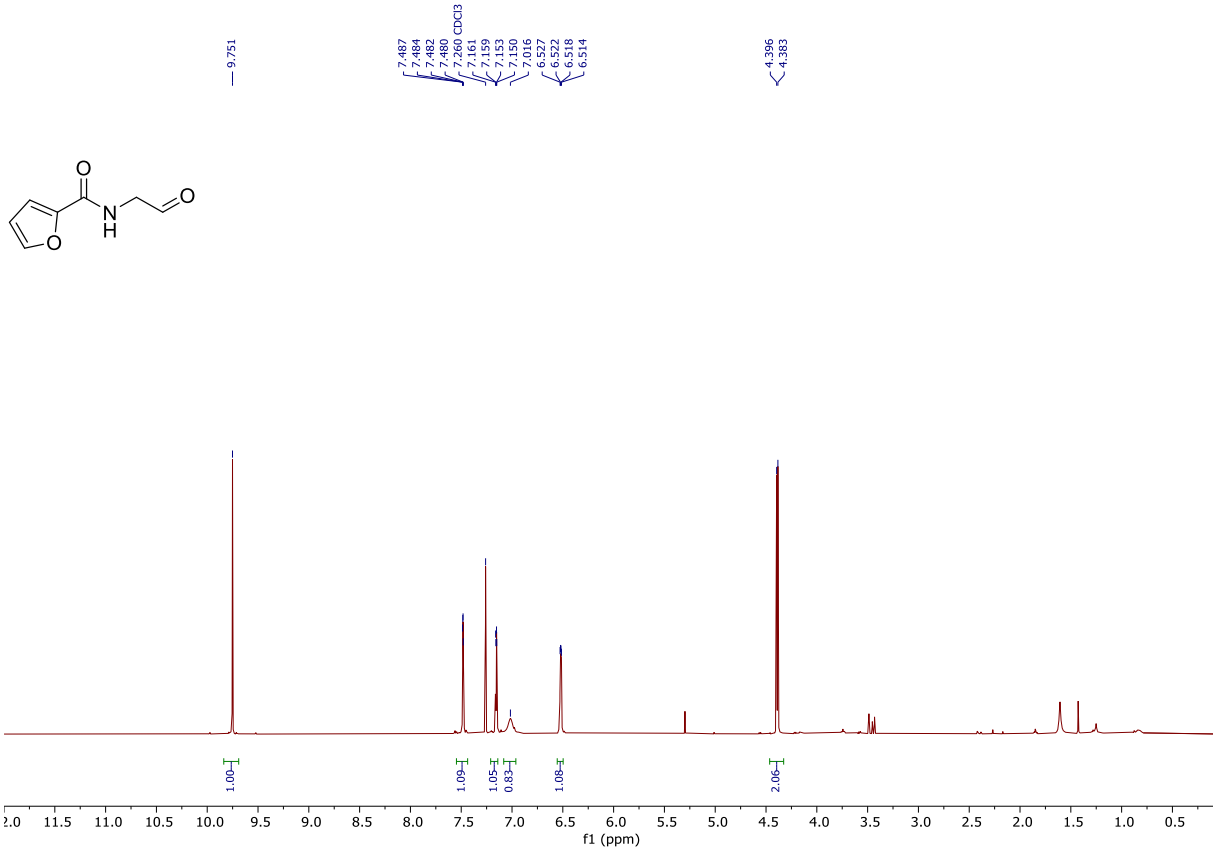


*Figure 27: ^{1}H (400 MHz) NMR spectra of **3m** in $CDCl_3$.*

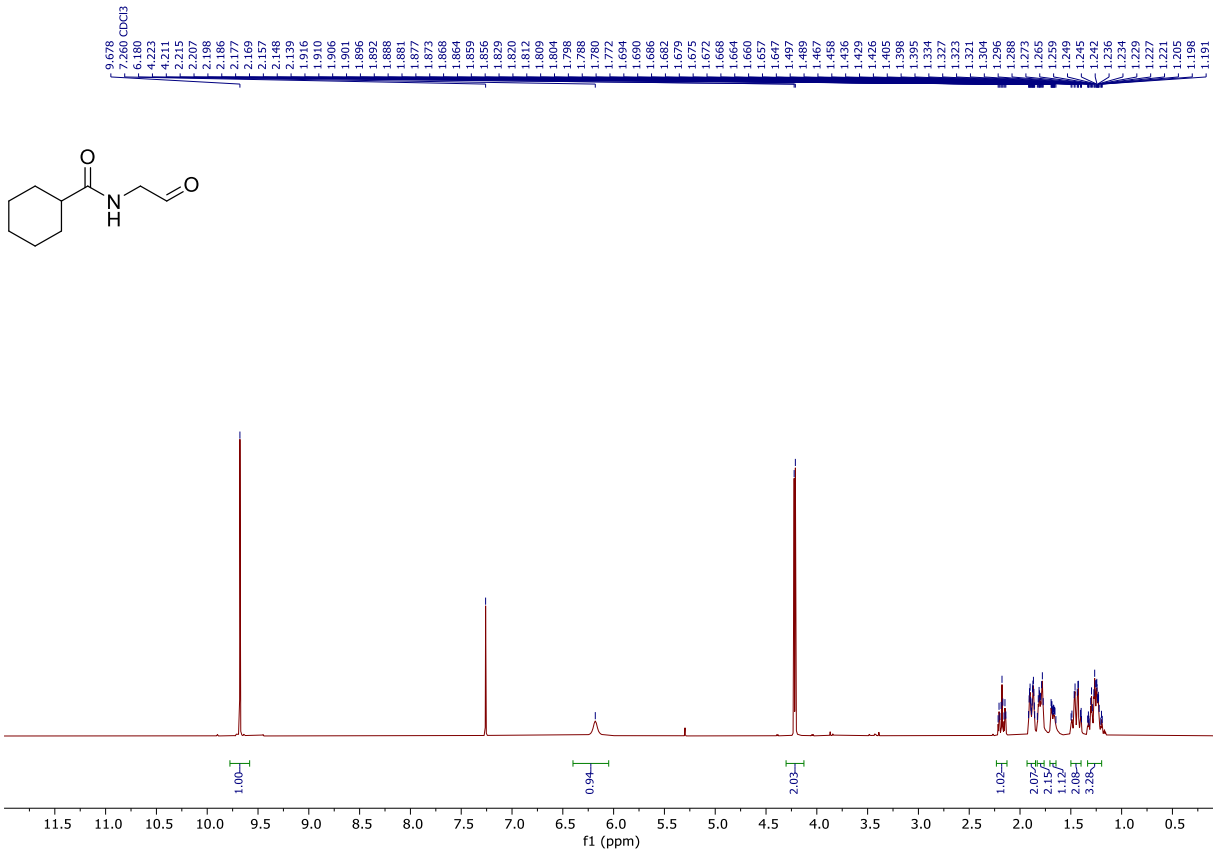


*Figure 28: ^{1}H (400 MHz) NMR spectra of **3n** in $CDCl_3$.*

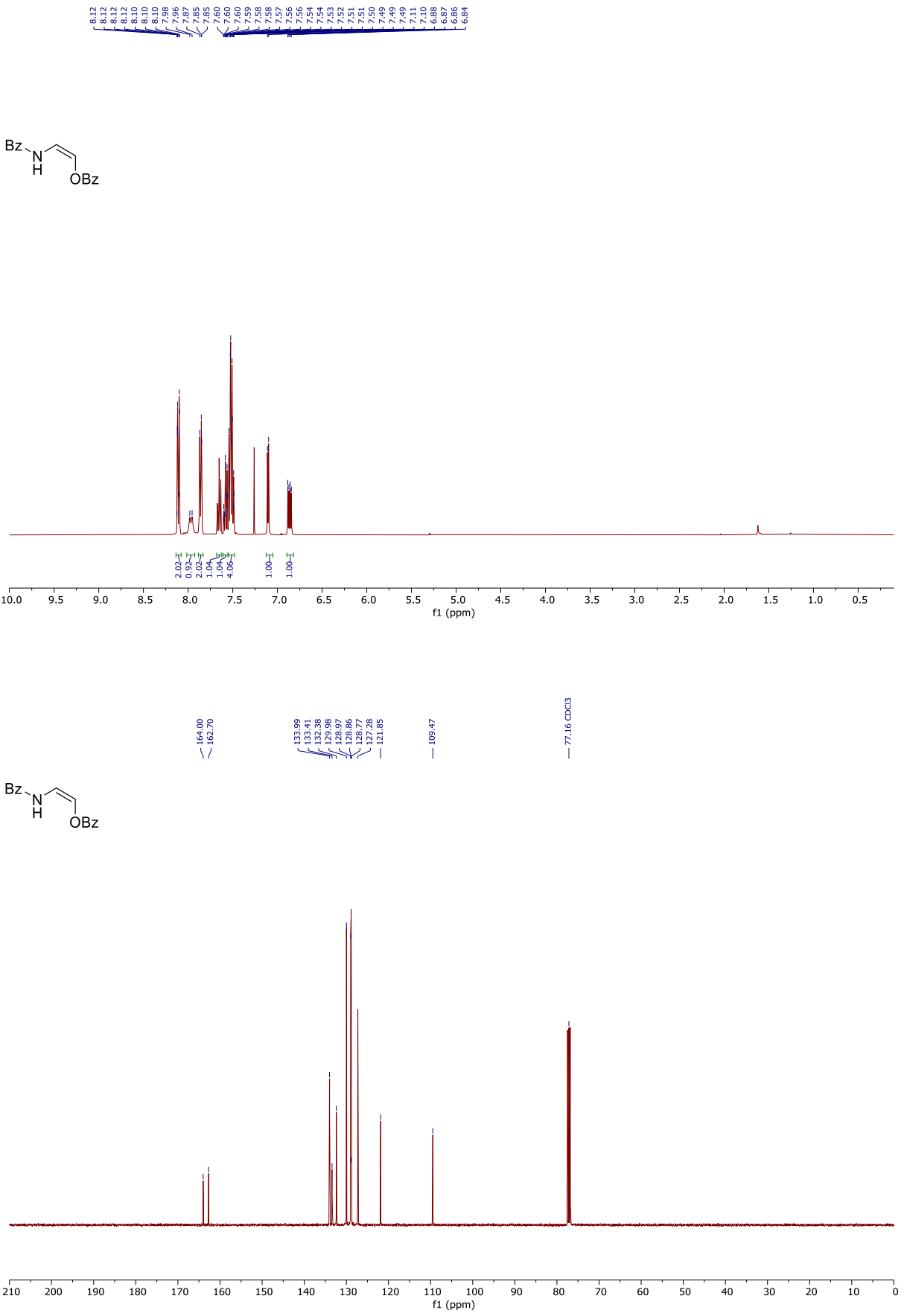


*Figure 29: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1a** in $CDCl_3$.*

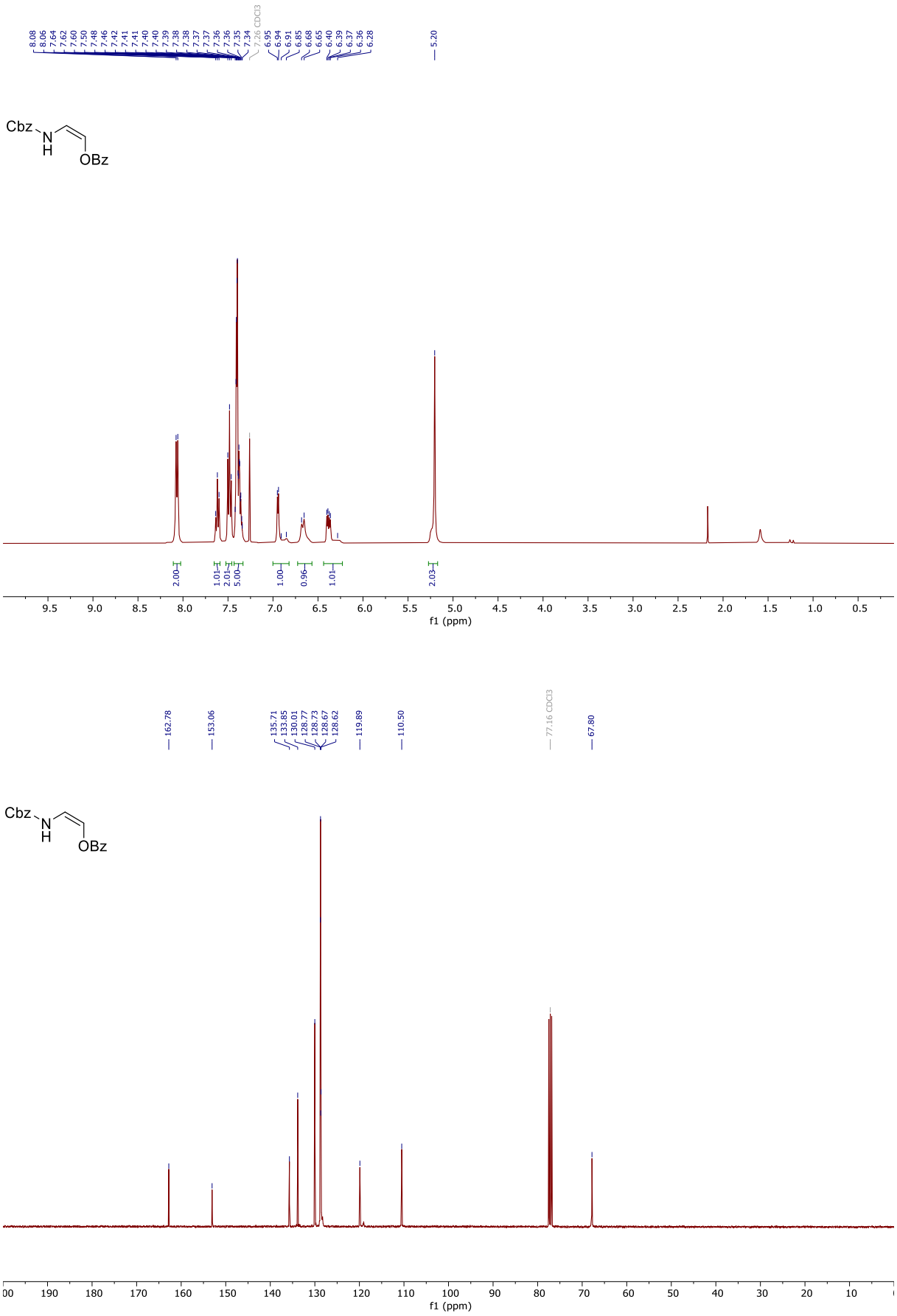


*Figure 30: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1c** in $CDCl_3$.*

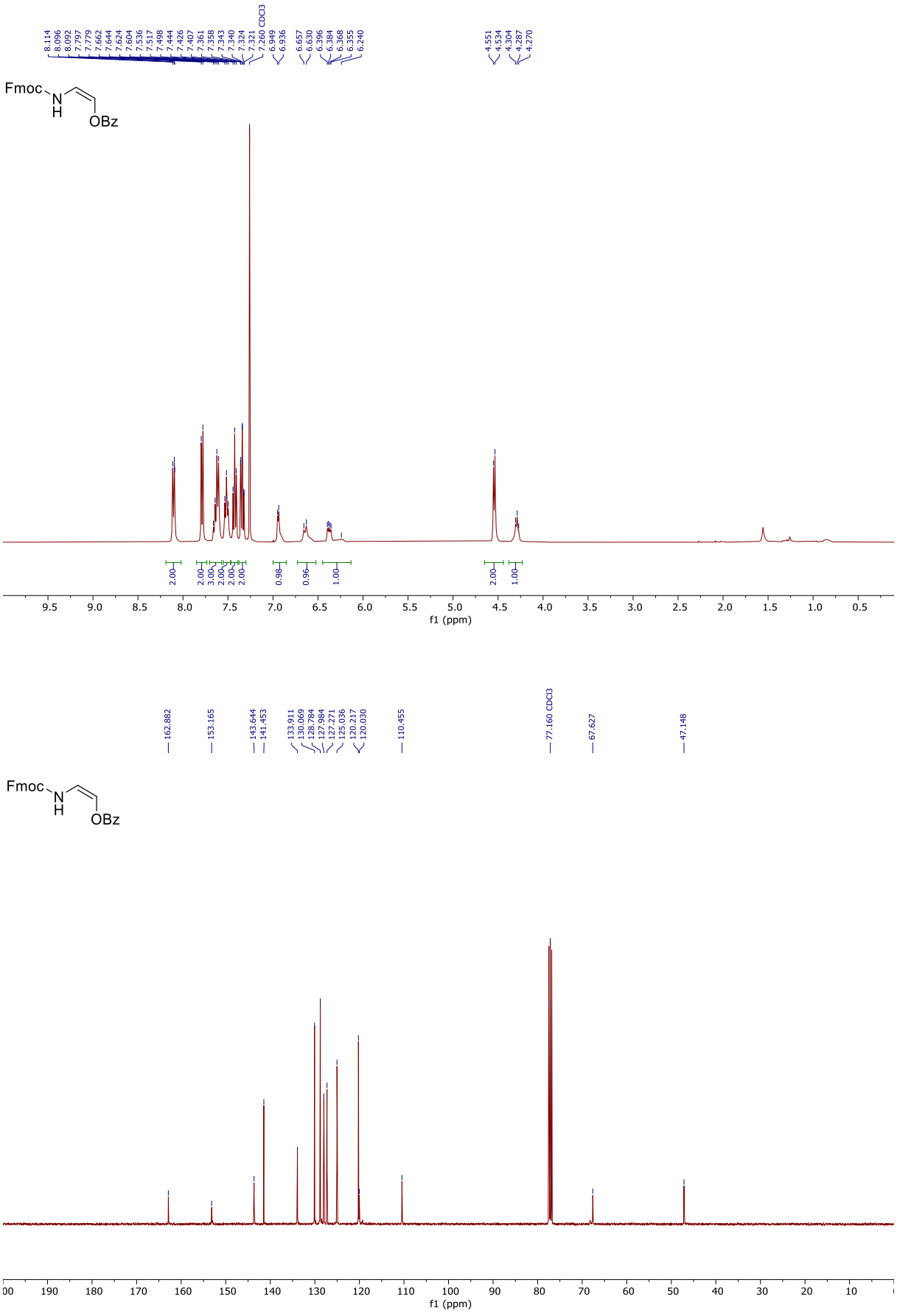


*Figure 31: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1d** in $CDCl_3$.*

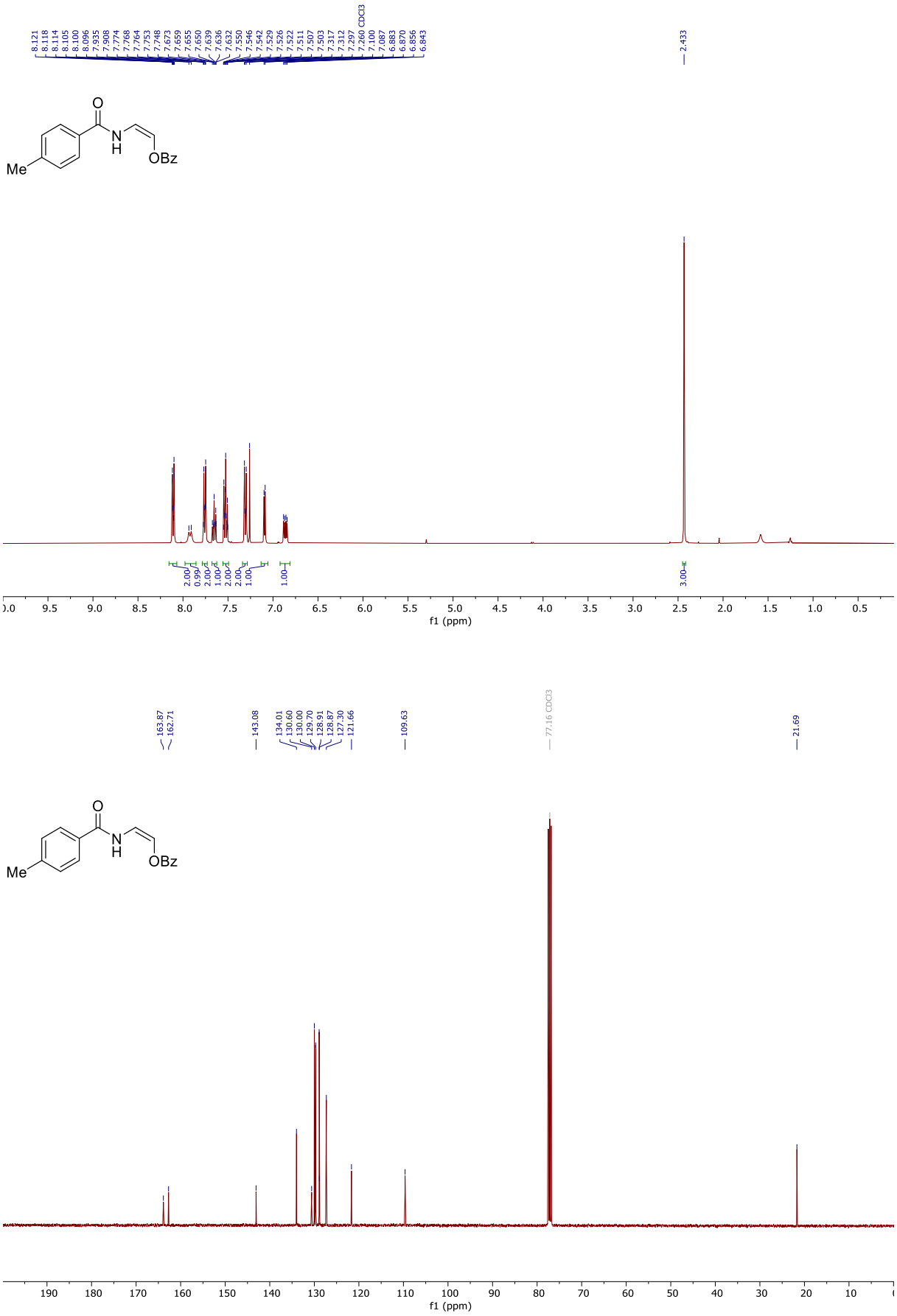


*Figure 32: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1e** in $CDCl_3$.*

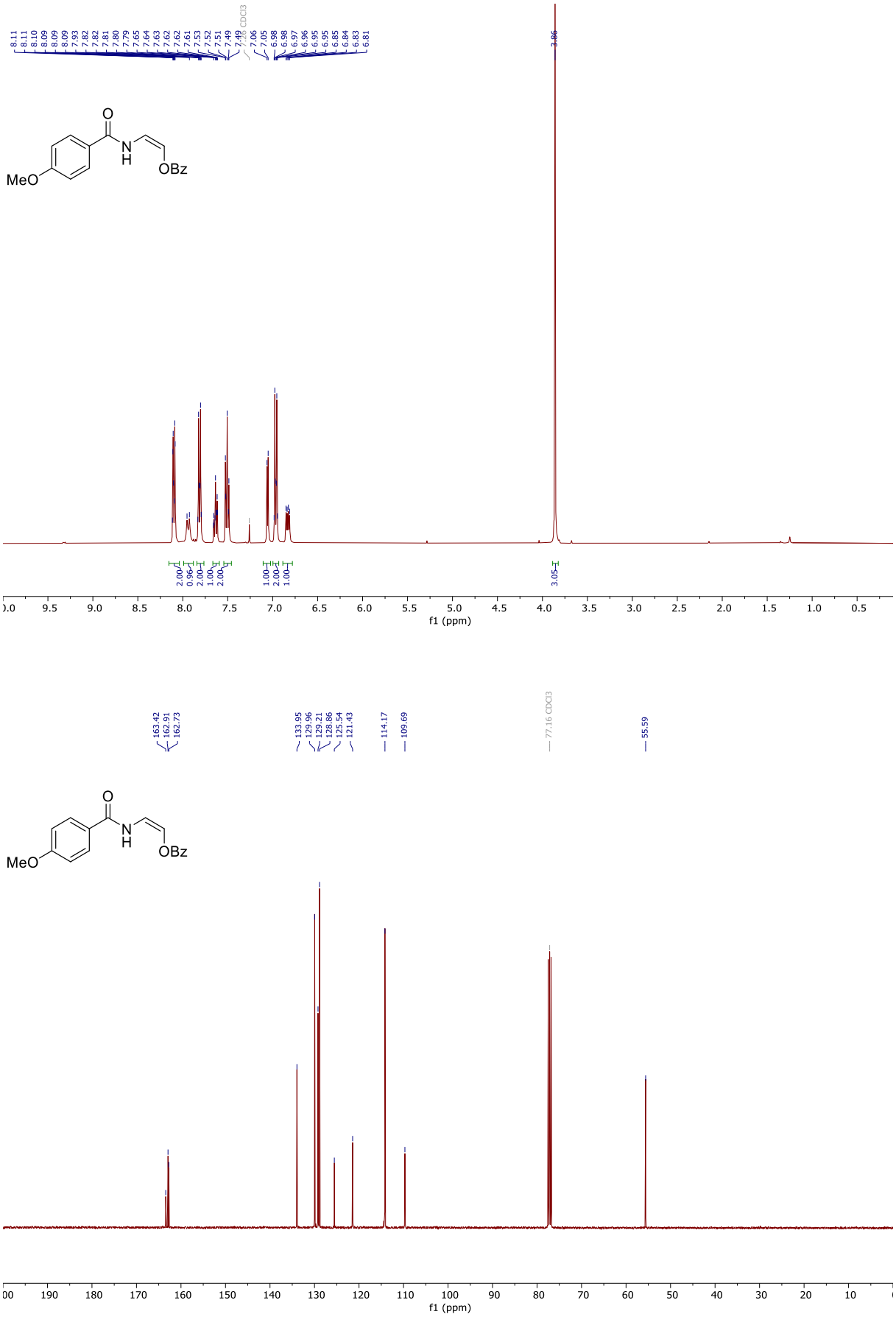


*Figure 33: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1f** in $CDCl_3$.*

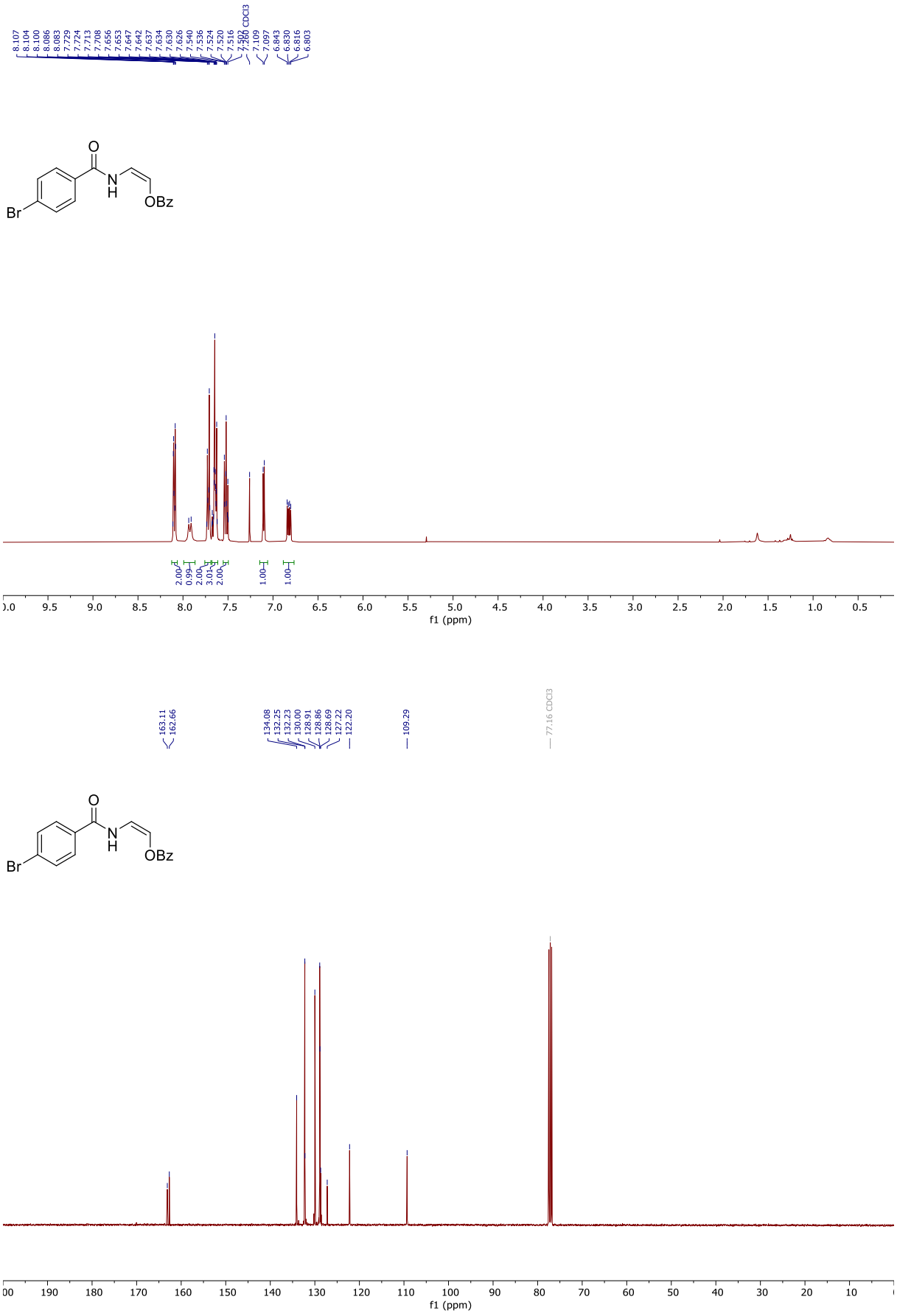
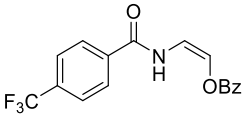
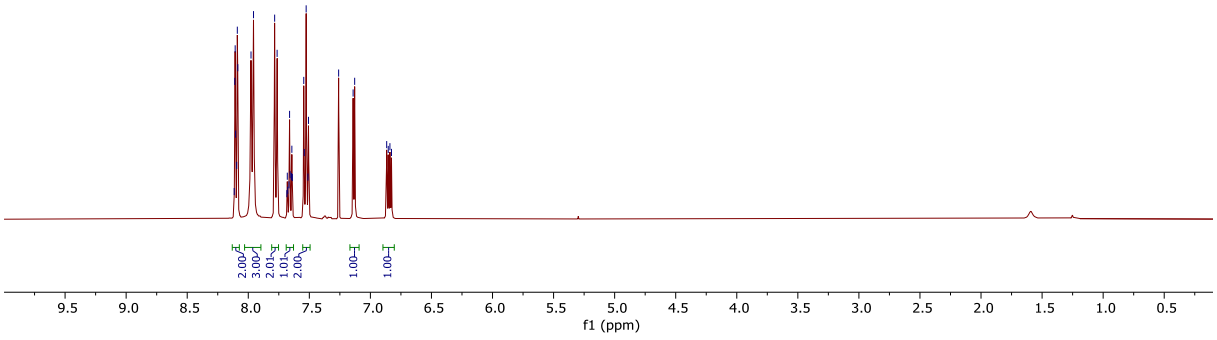
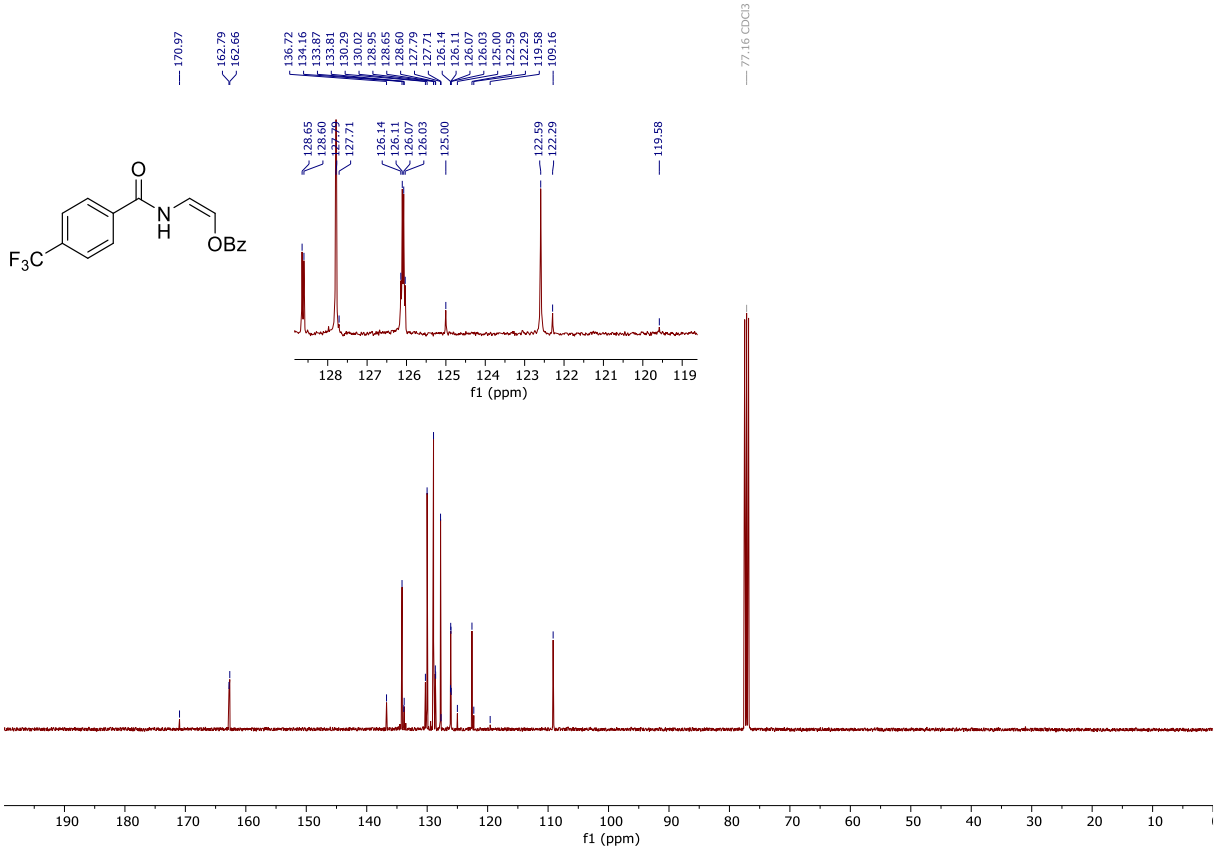


*Figure 34: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1g** in $CDCl_3$.*


8.110
8.107
8.103
8.095
8.090
8.086
7.978
7.957
7.784
7.764
7.680
7.677
7.667
7.662
7.657
7.647
7.643
7.639
7.546
7.542
7.526
7.512
7.507
7.260 CDCl3
7.142
7.129
6.867
6.854
6.840
6.827


O
N
H
OBz
F3C


2.00
3.00
2.01
1.01
2.00
1.00
1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


170.97
162.79
162.66
136.72
134.16
133.87
133.81
130.29
130.02
128.95
128.65
128.60
127.79
127.71
126.14
126.11
126.07
126.03
125.00
122.59
122.29
119.58
109.16
77.16 CDCl3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

O
N
H
OBz
F3C

128.65
128.60
127.79
127.71
126.14
126.11
126.07
126.03
125.00
122.59
122.29
119.58
128 127 126 125 124 123 122 121 120 119
f1 (ppm)

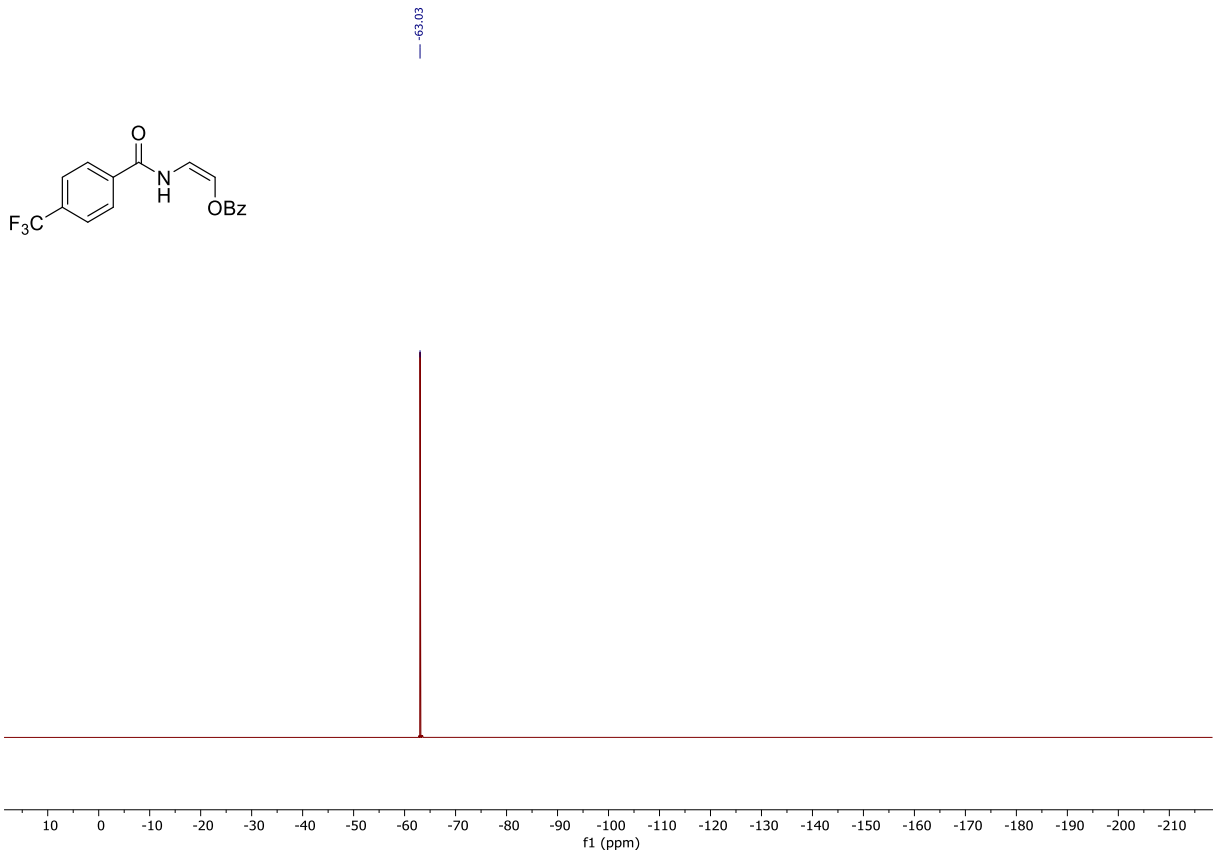


*Figure 35: ^{1}H (400 MHz), ^{13}C (101 MHz) and ^{19}F (376 MHz) NMR spectra of **1h** in $CDCl_3$.*

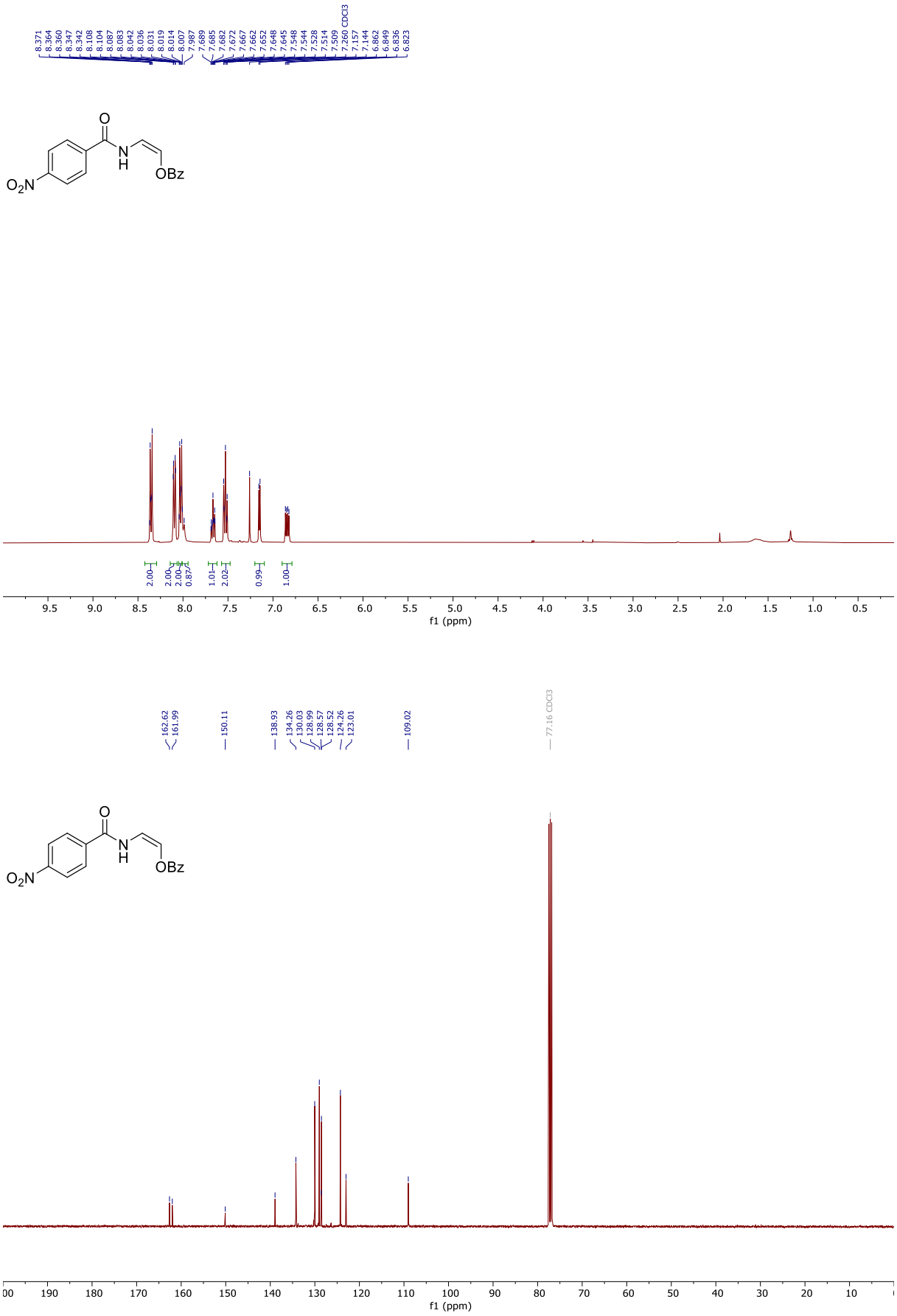


*Figure 36: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1i** in $CDCl_3$.*

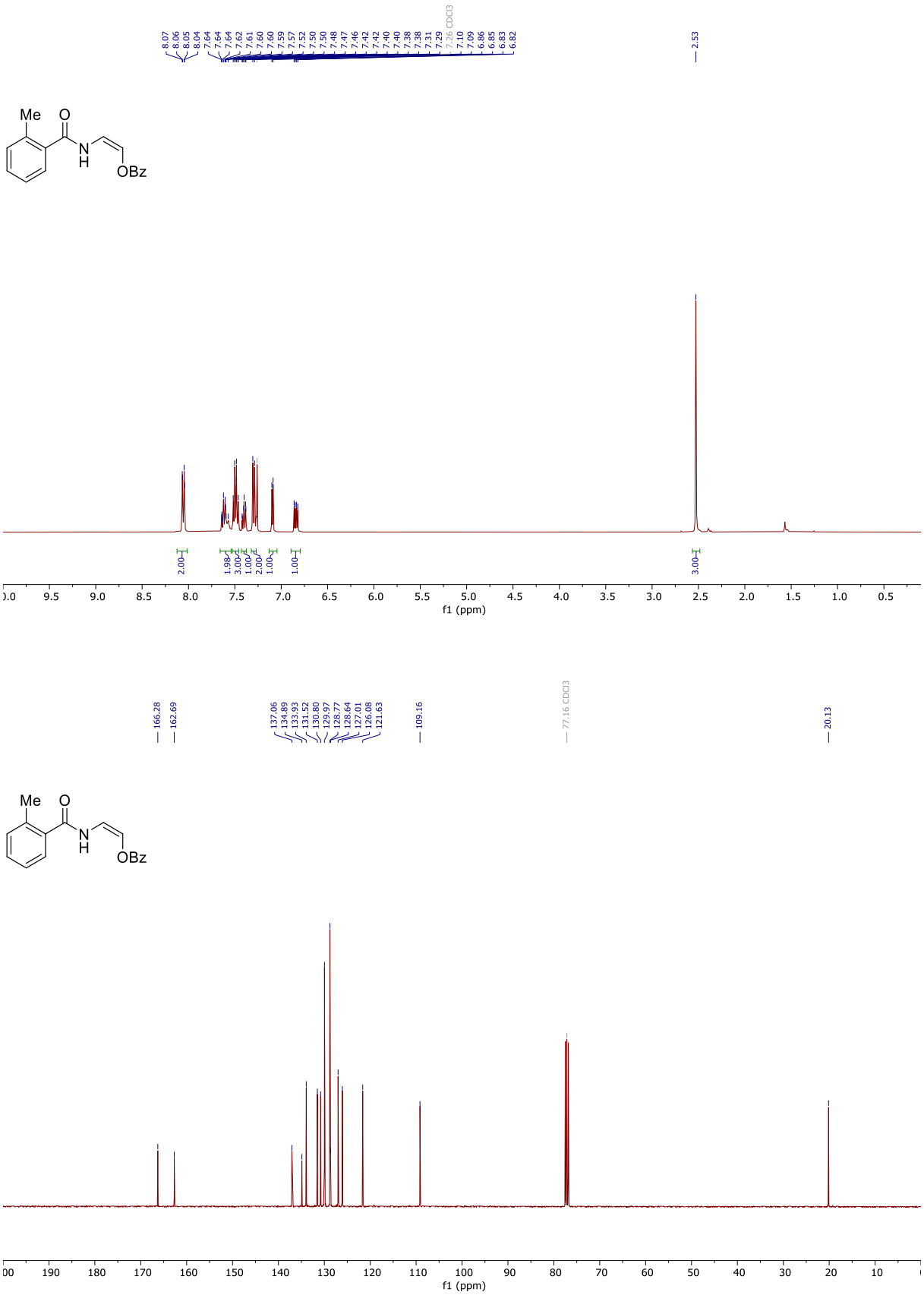
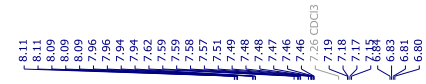
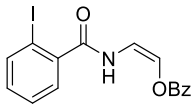
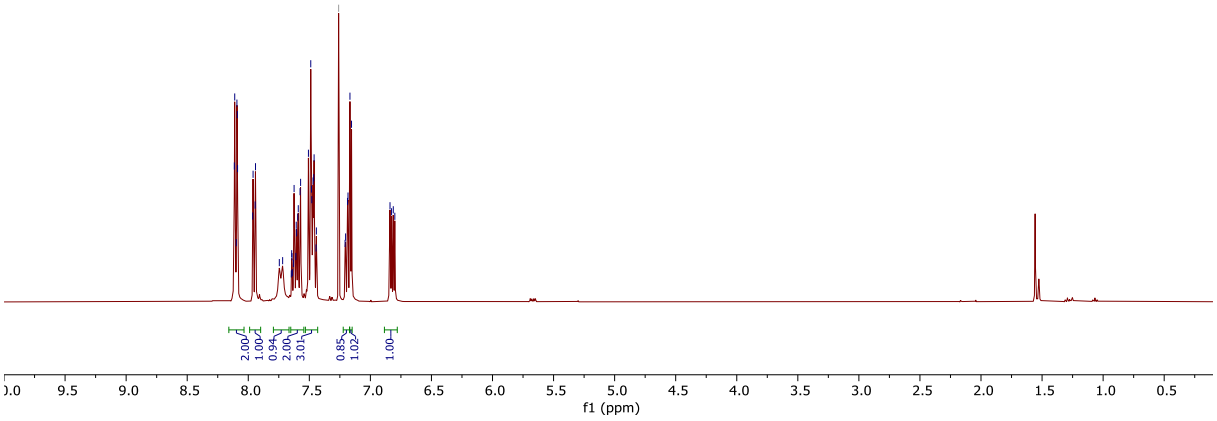


*Figure 37: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1j** in $CDCl_3$.*







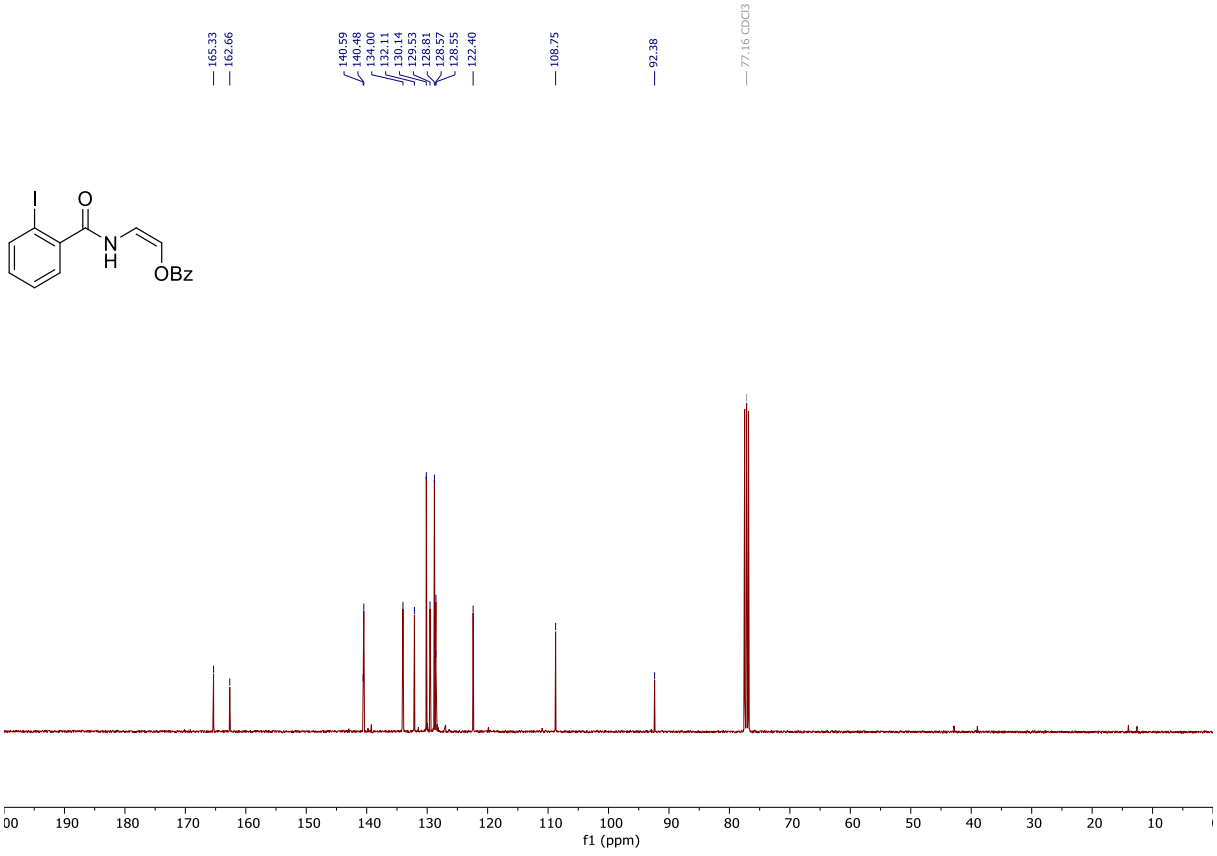


*Figure 38: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1k** in $CDCl_3$.*

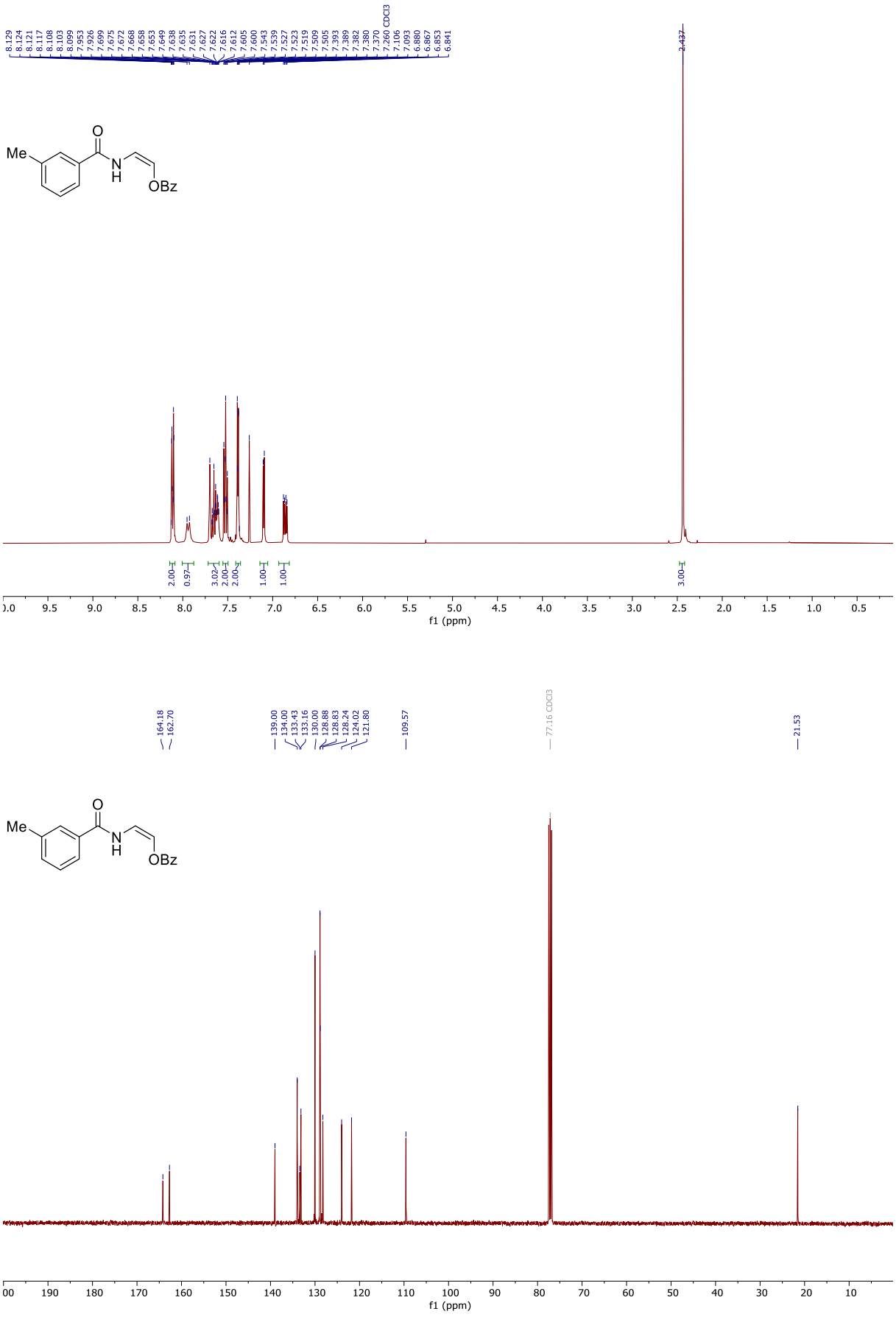
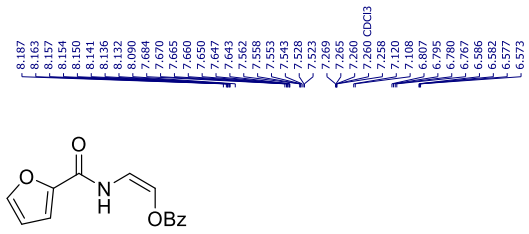
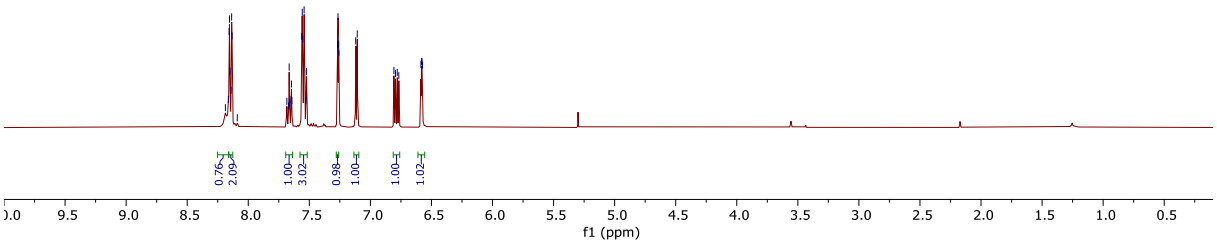
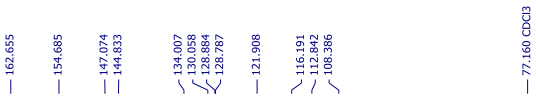
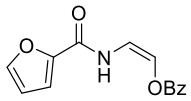


*Figure 39: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1l** in $CDCl_3$.*









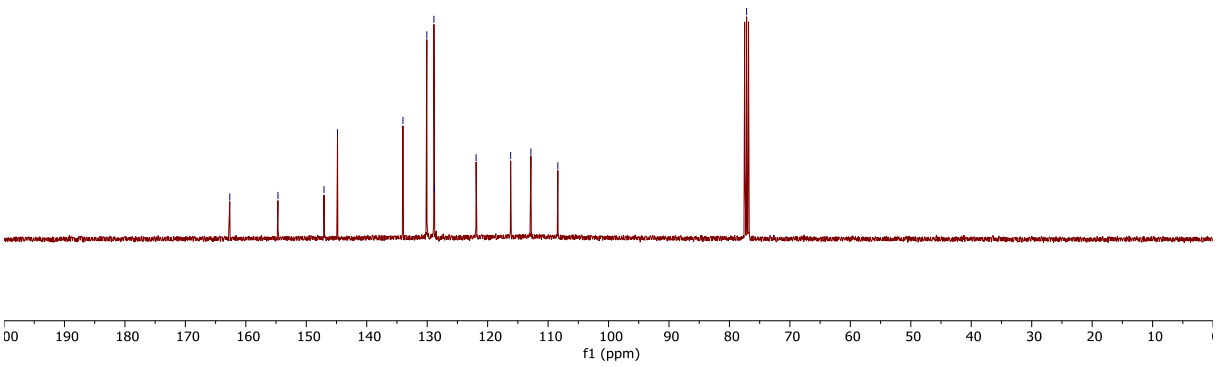


*Figure 40: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1m** in $CDCl_3$.*

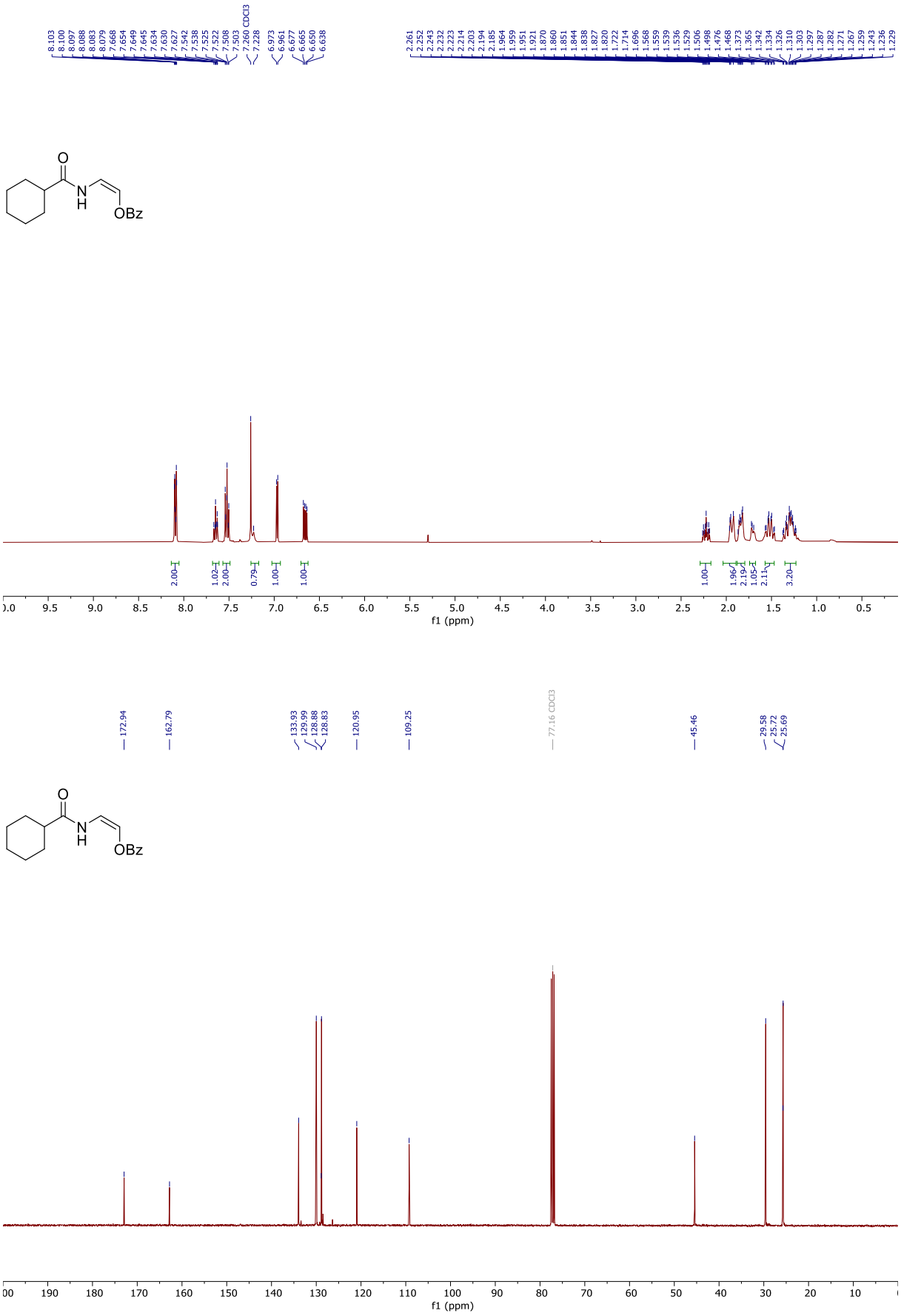


*Figure 41: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **1n** in $CDCl_3$.*

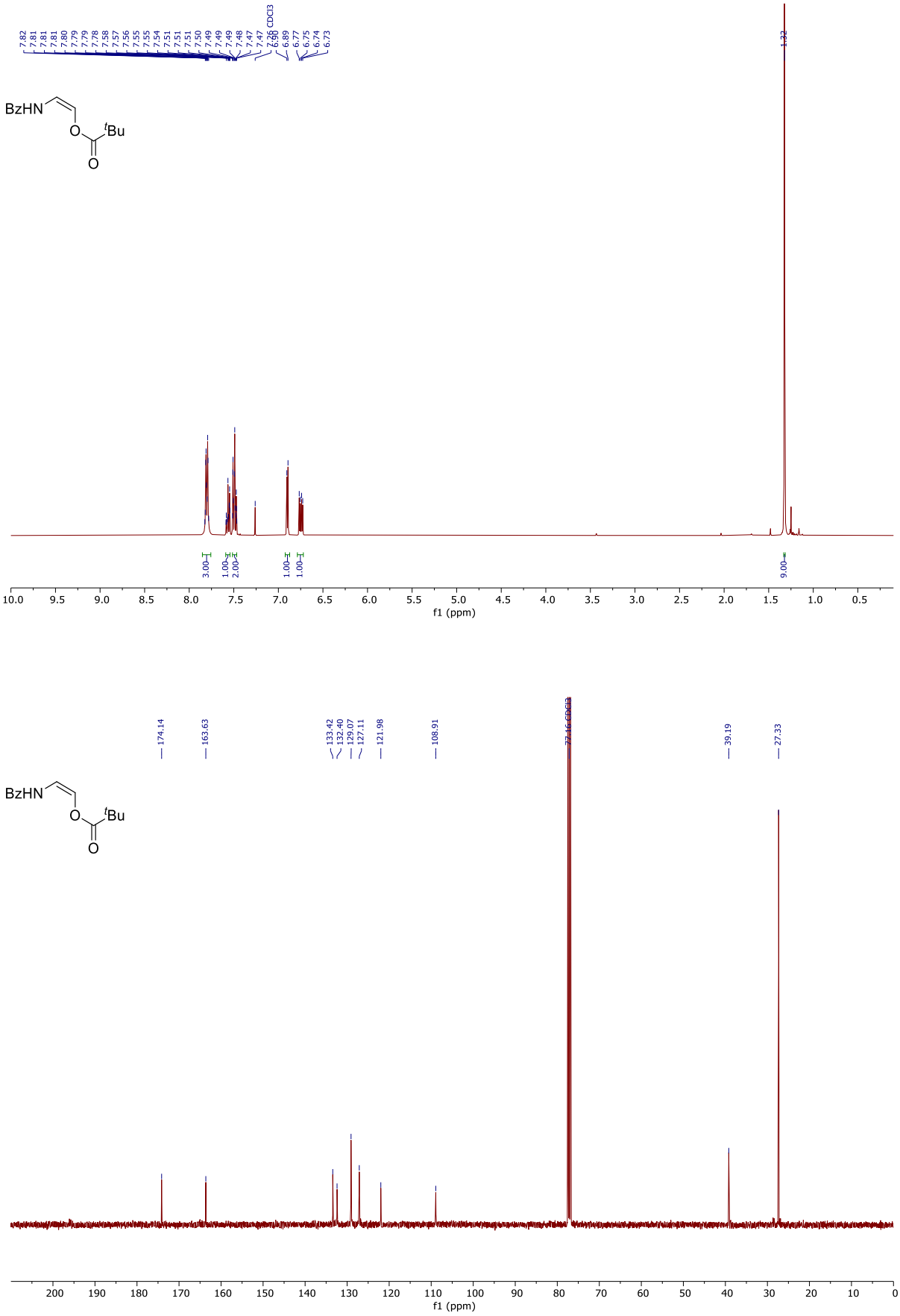


*Figure 42: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2a** in $CDCl_3$.*

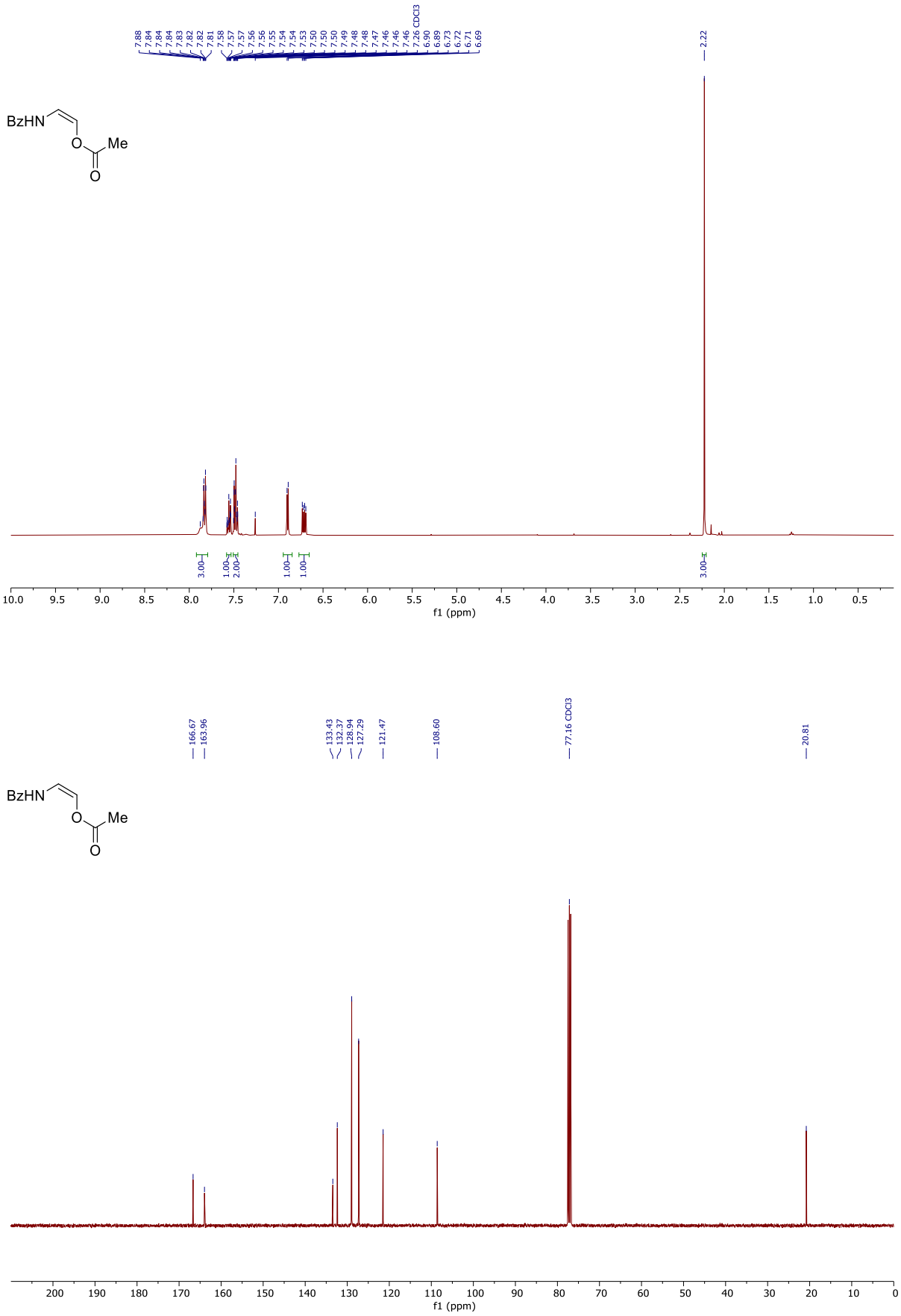


*Figure 43: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2b** in $CDCl_3$.*

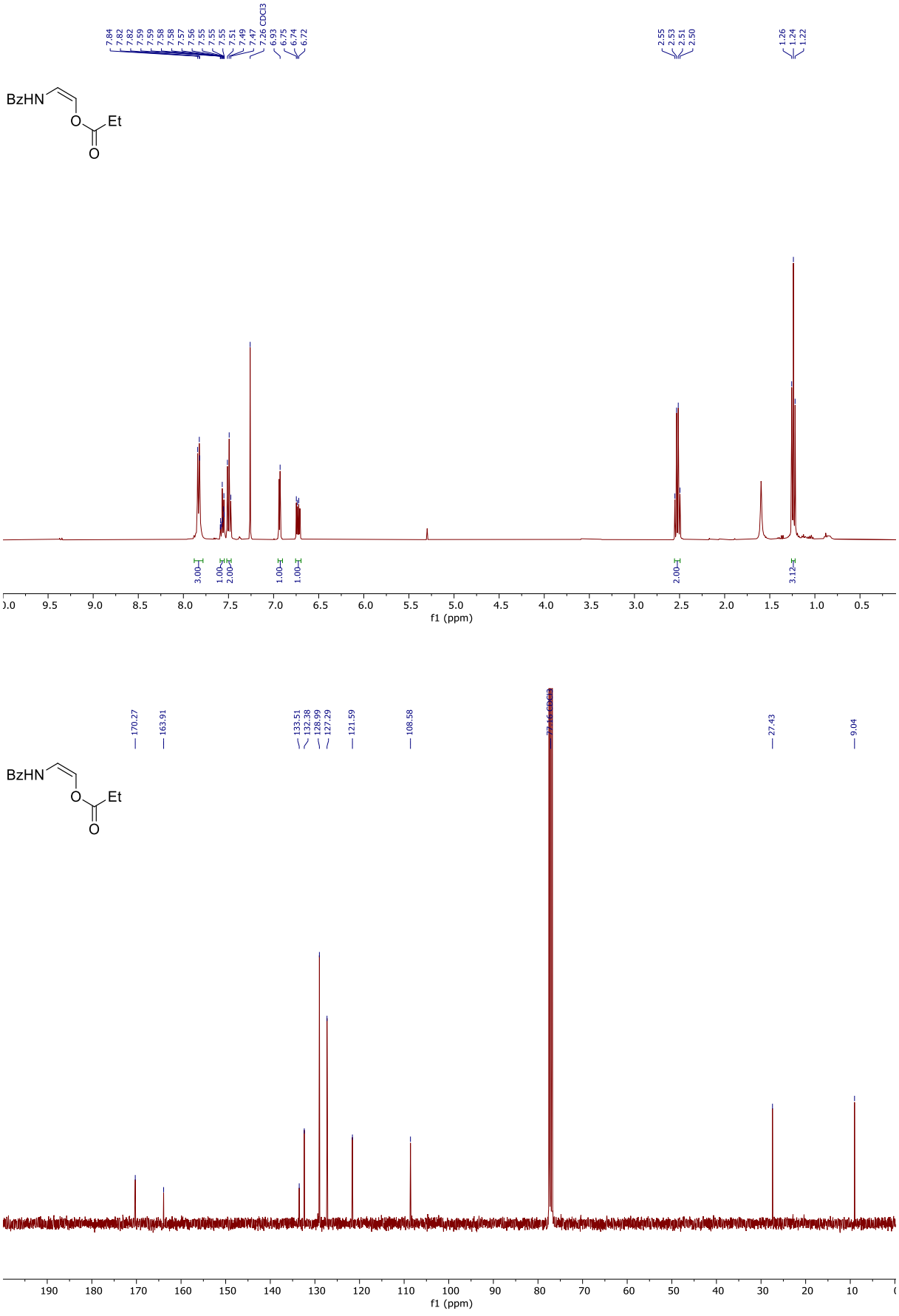


*Figure 44: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2c** in $CDCl_3$.*

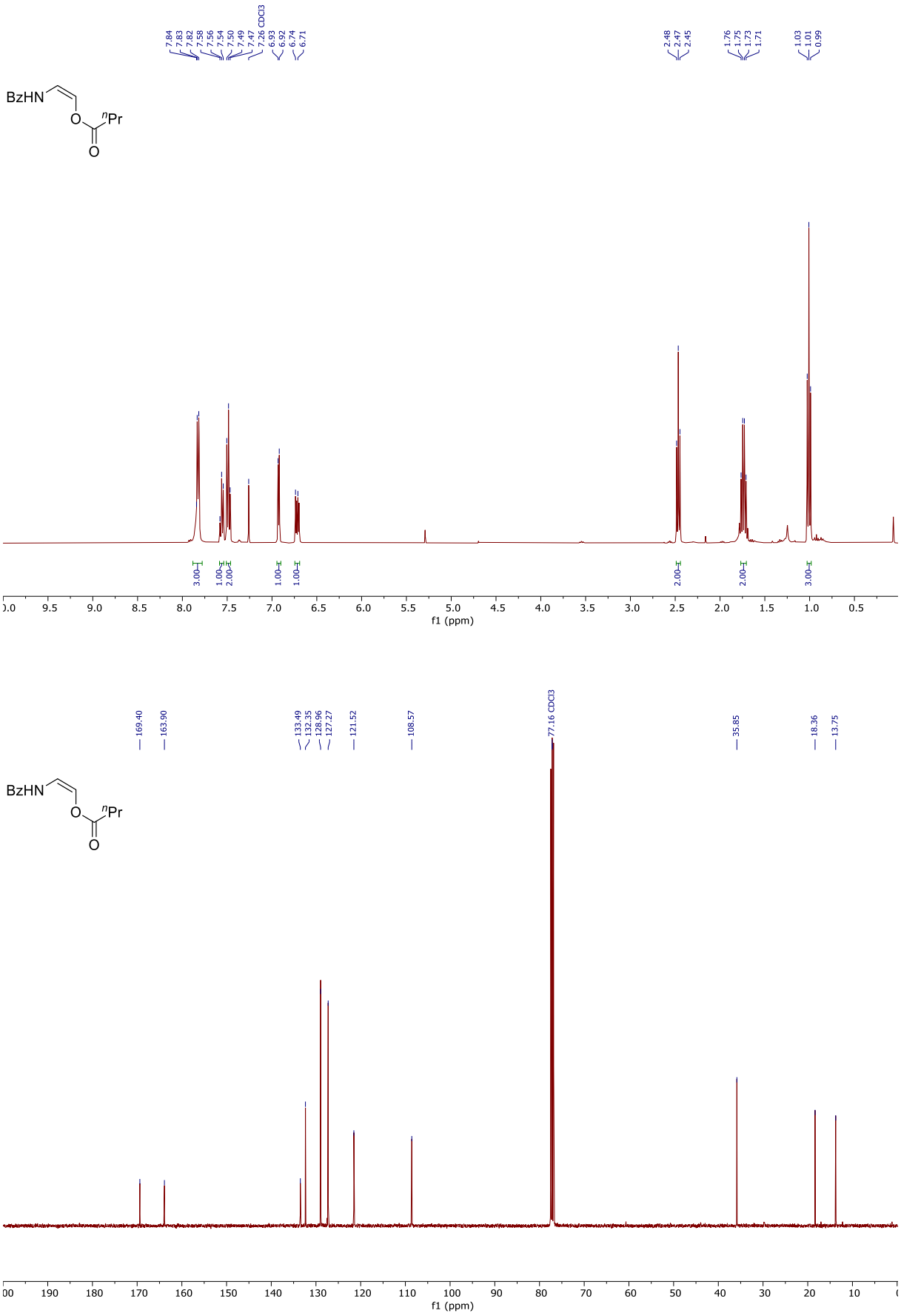


*Figure 45: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2d** in $CDCl_3$.*

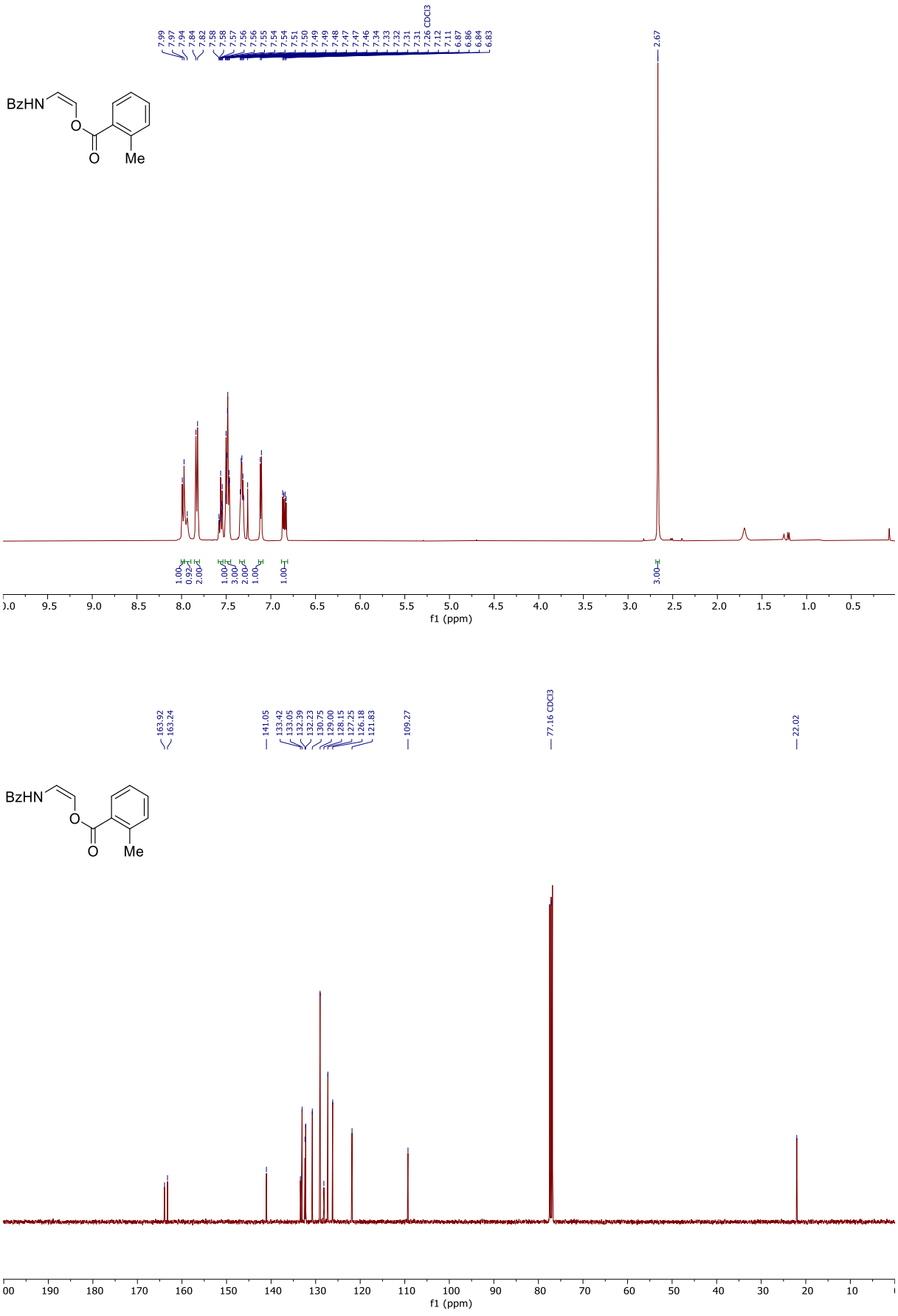


*Figure 46: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2e** in $CDCl_3$.*

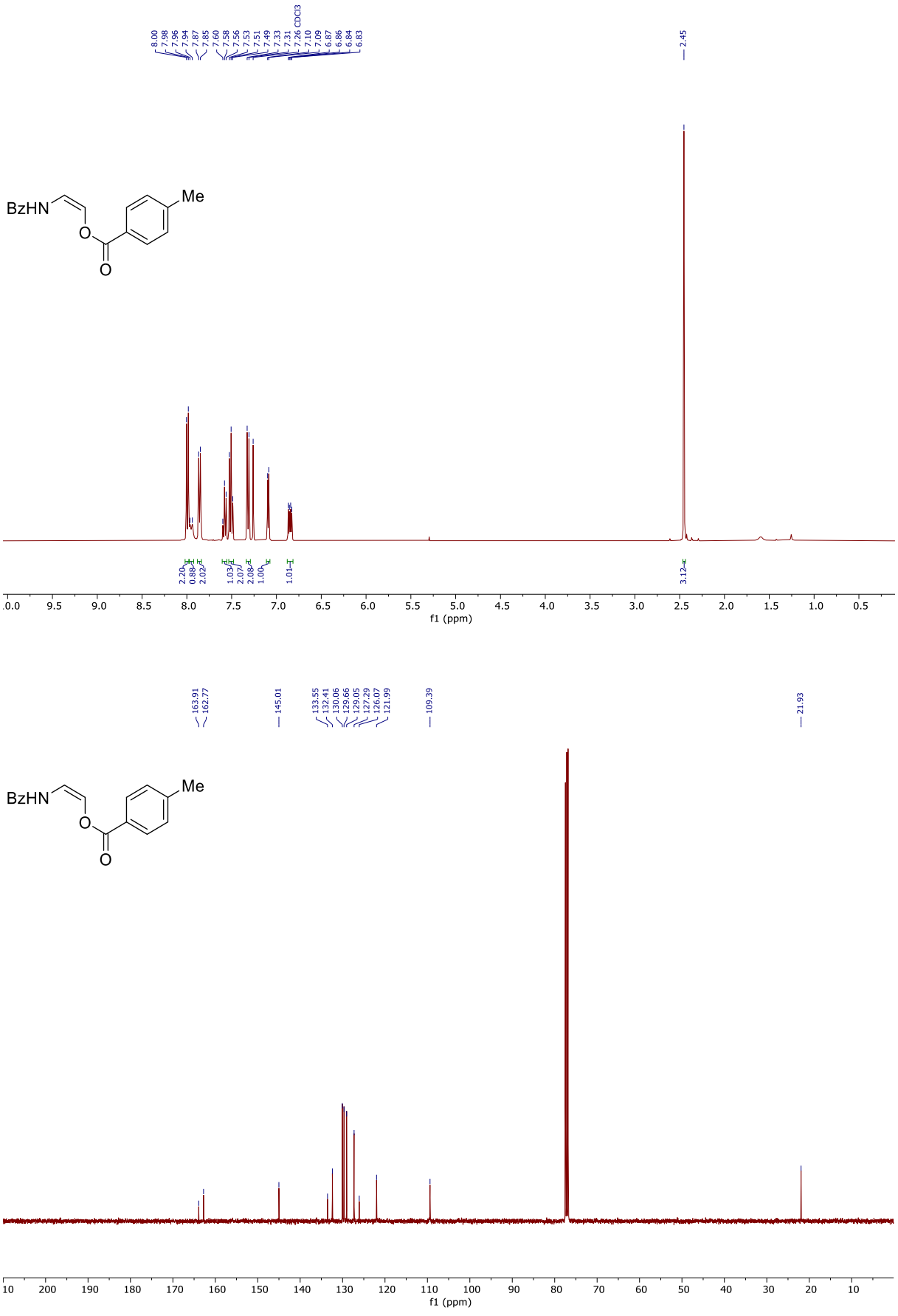


*Figure 47: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2f** in $CDCl_3$.*

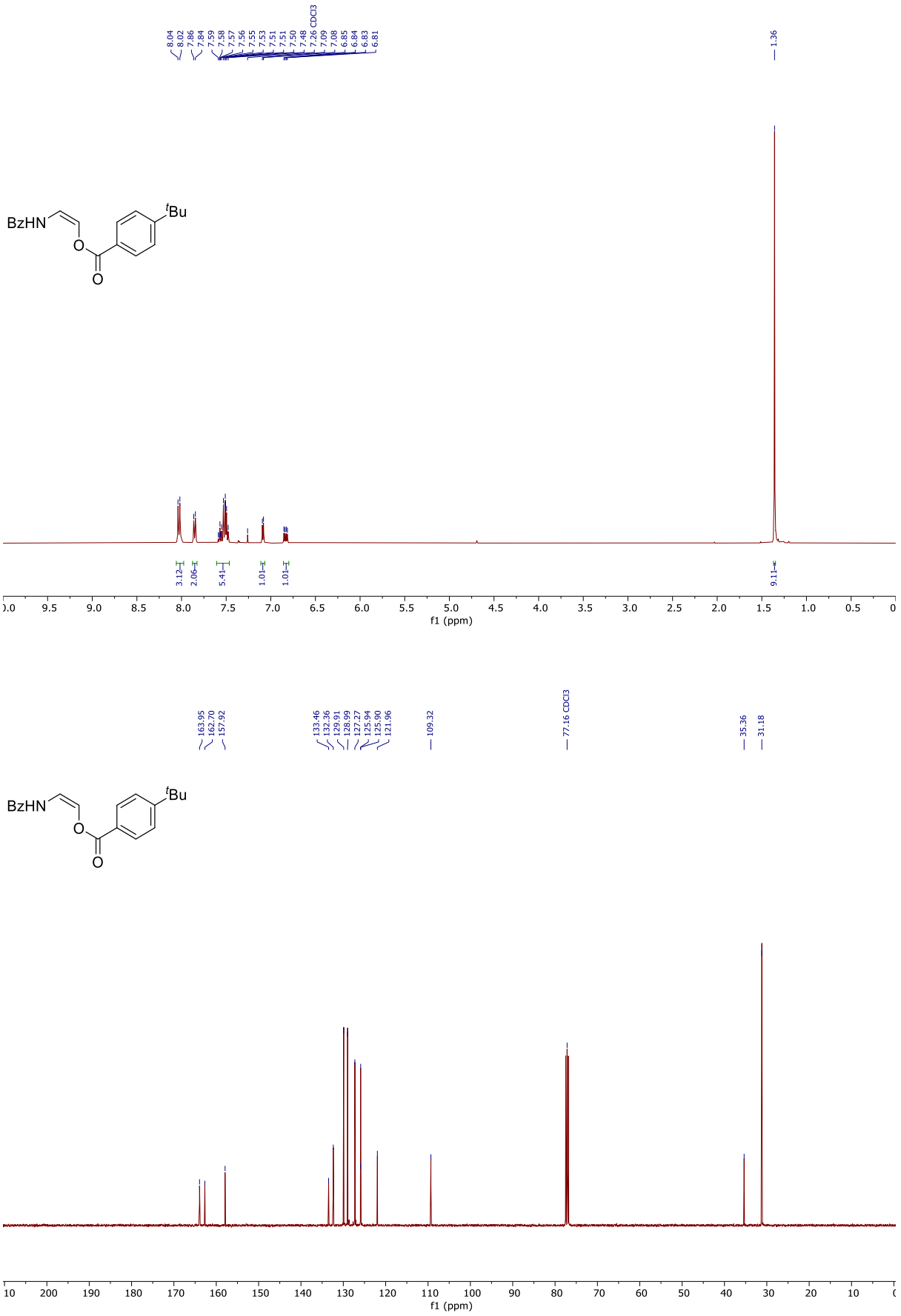


*Figure 48: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2g** in $CDCl_3$.*

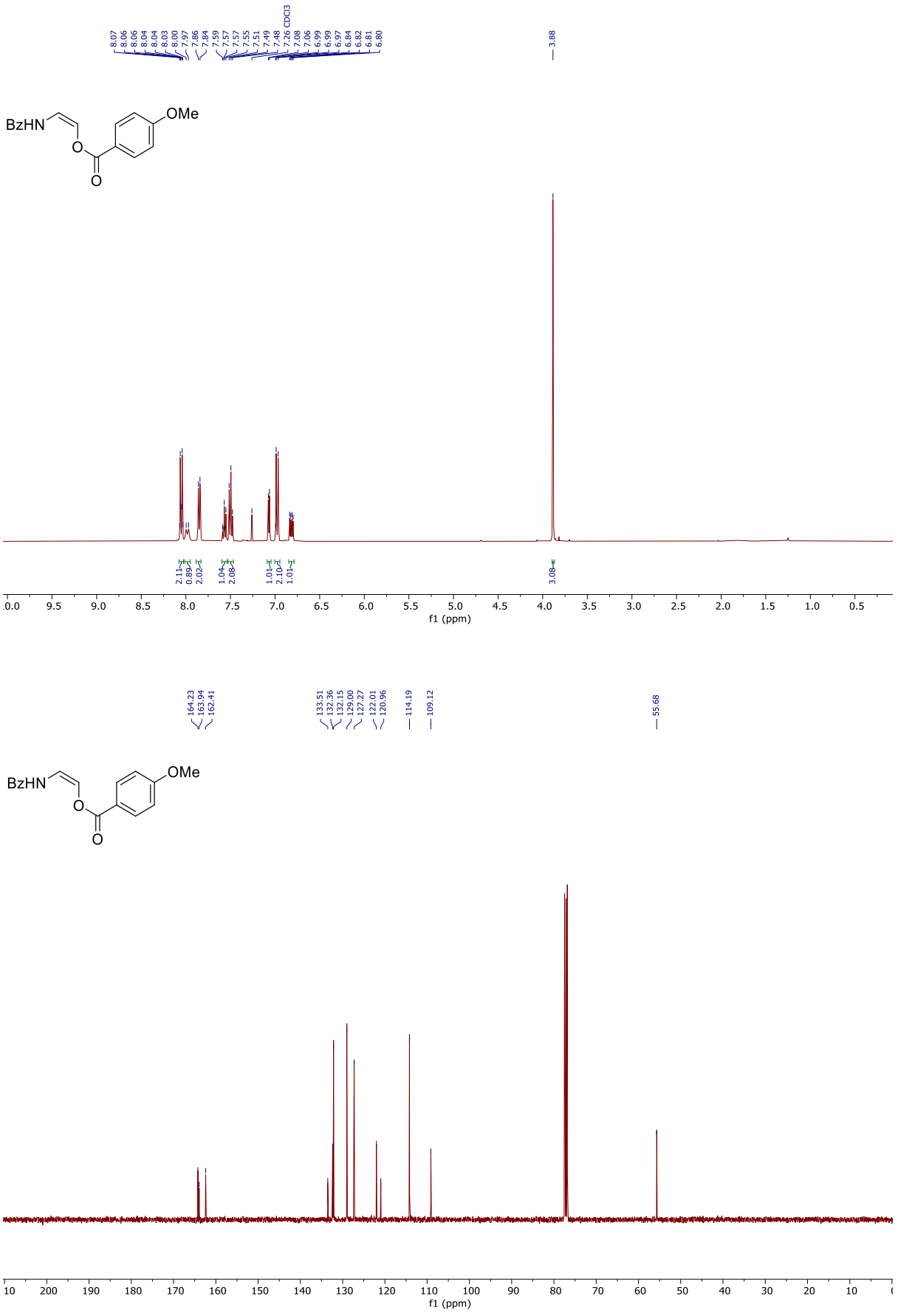
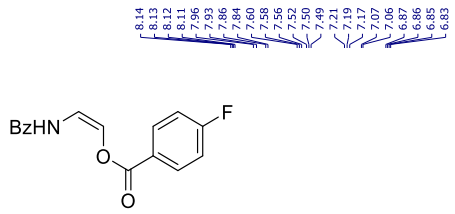
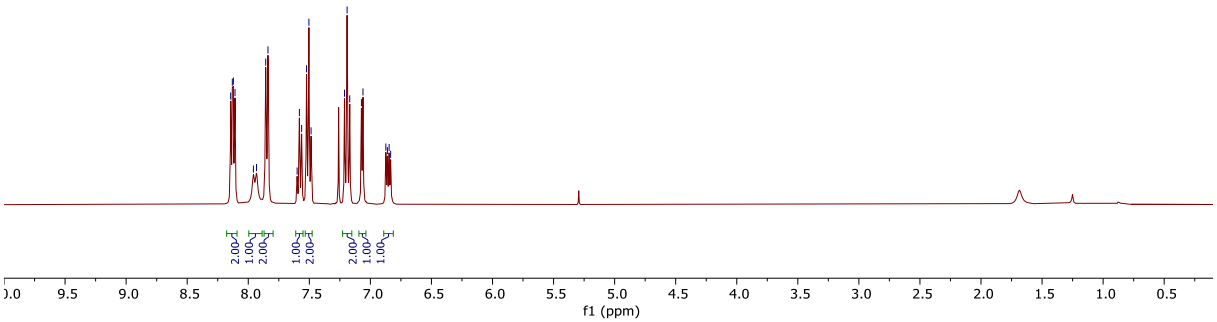
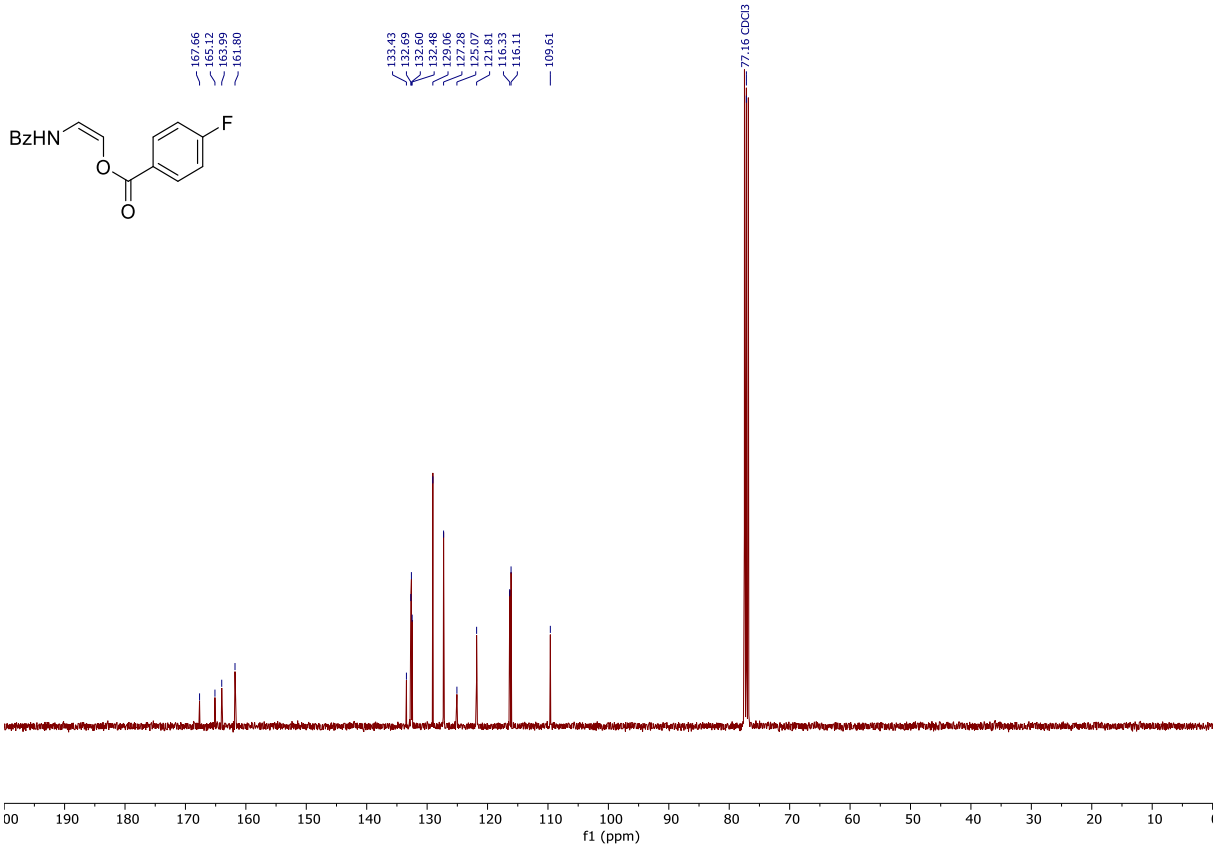


*Figure 49: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2h** in $CDCl_3$.*


8.14
8.13
8.12
8.11
7.96
7.93
7.86
7.84
7.60
7.58
7.56
7.52
7.50
7.49
7.21
7.19
7.17
7.07
7.06
6.87
6.86
6.85
6.83
BzHN
O
O
F


2.00
1.00
2.00
1.00
2.00
2.00
1.00
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


167.66
165.12
163.99
161.80
133.43
132.69
132.60
132.48
129.06
127.28
125.07
121.81
116.33
116.11
109.61
77.16 CDCl3
BzHN
O
O
F
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

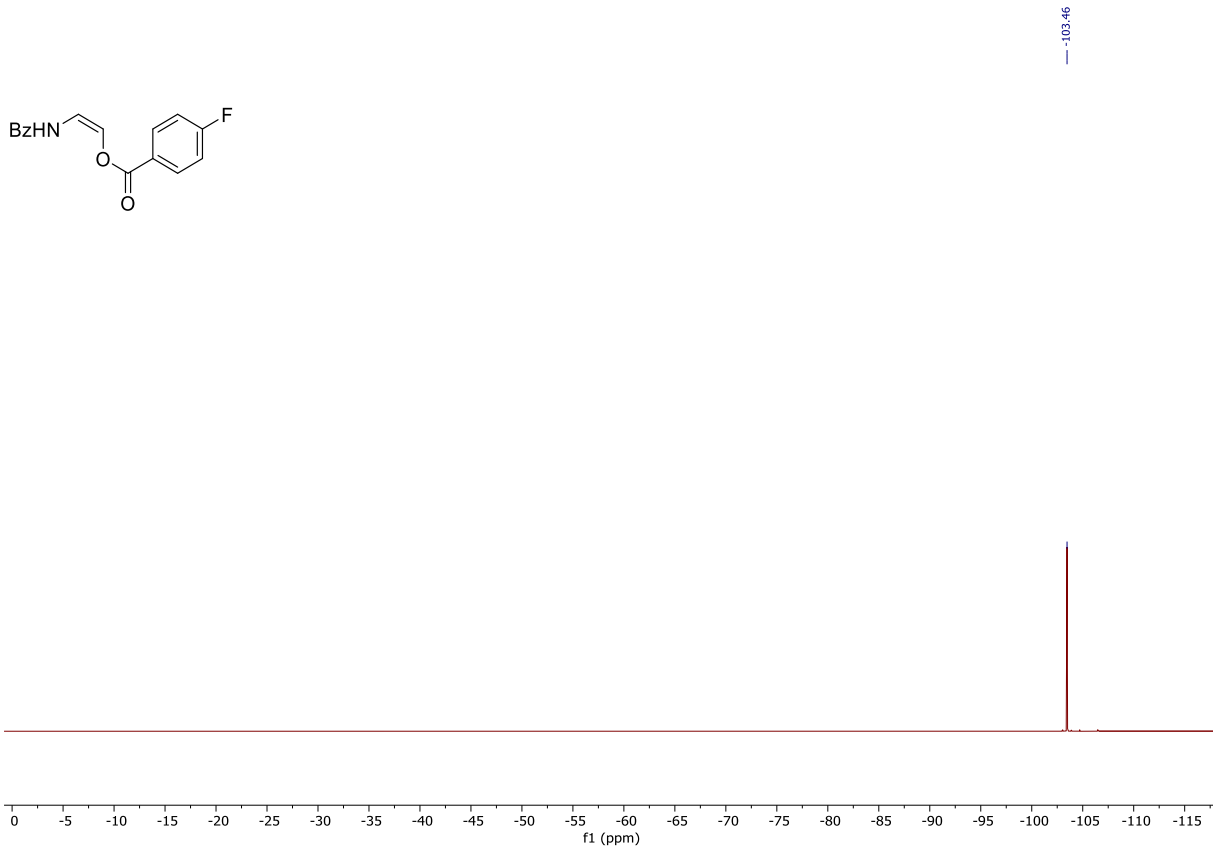


*Figure 50: ^{1}H (400 MHz), ^{13}C (101 MHz) and ^{19}F (376 MHz) NMR spectra of **2i** in $CDCl_3$.*

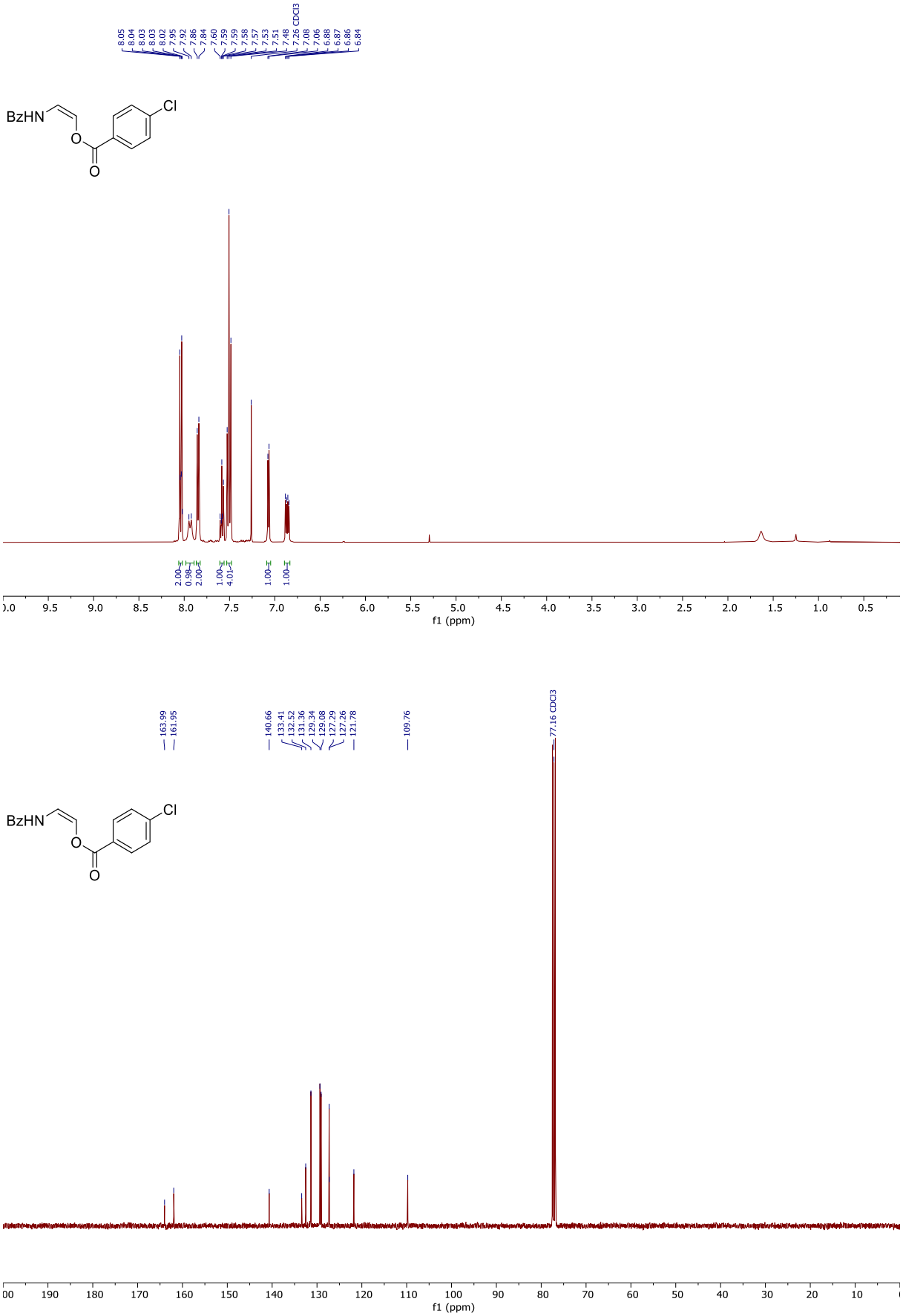


*Figure 51: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2j** in $CDCl_3$.*

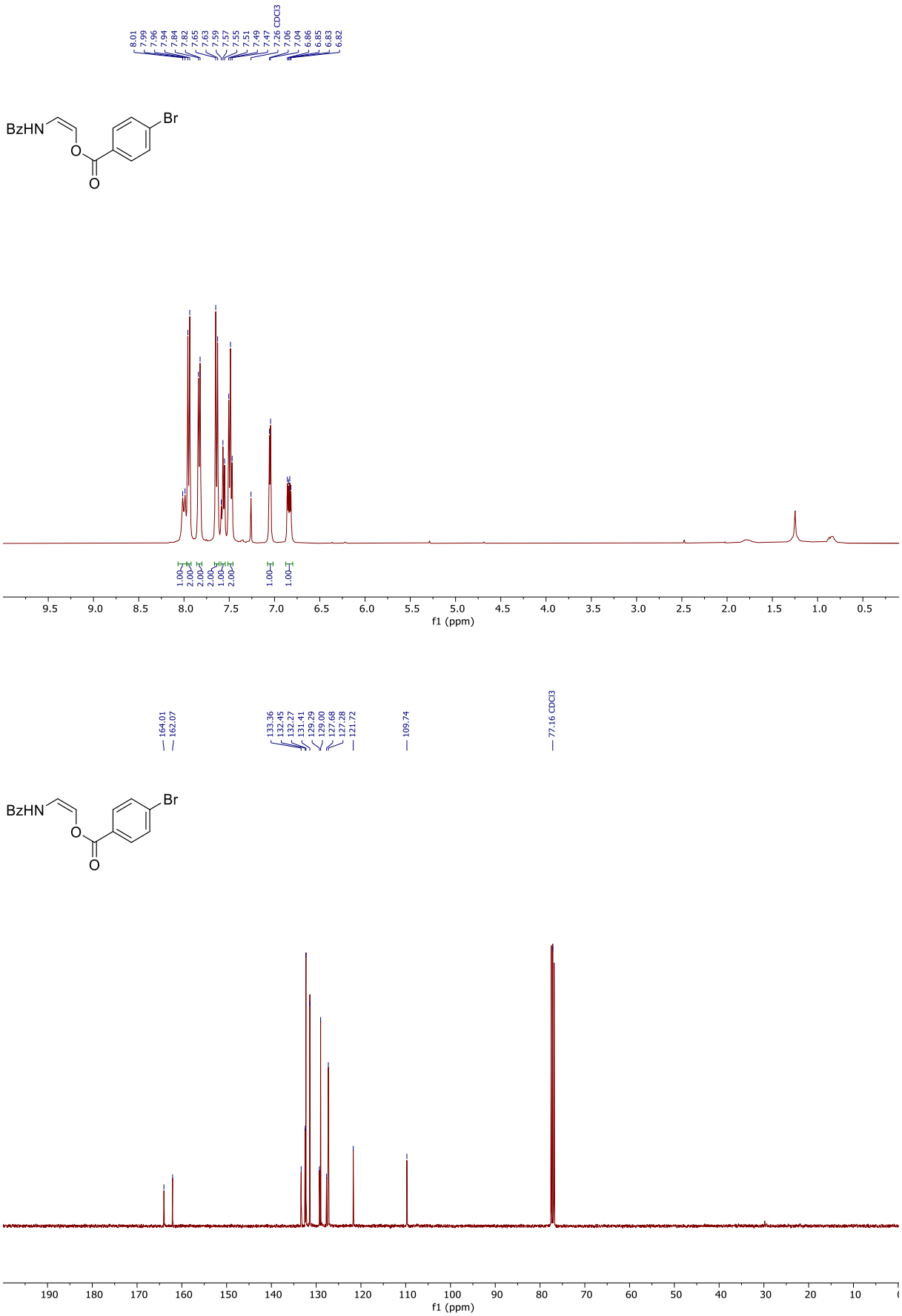
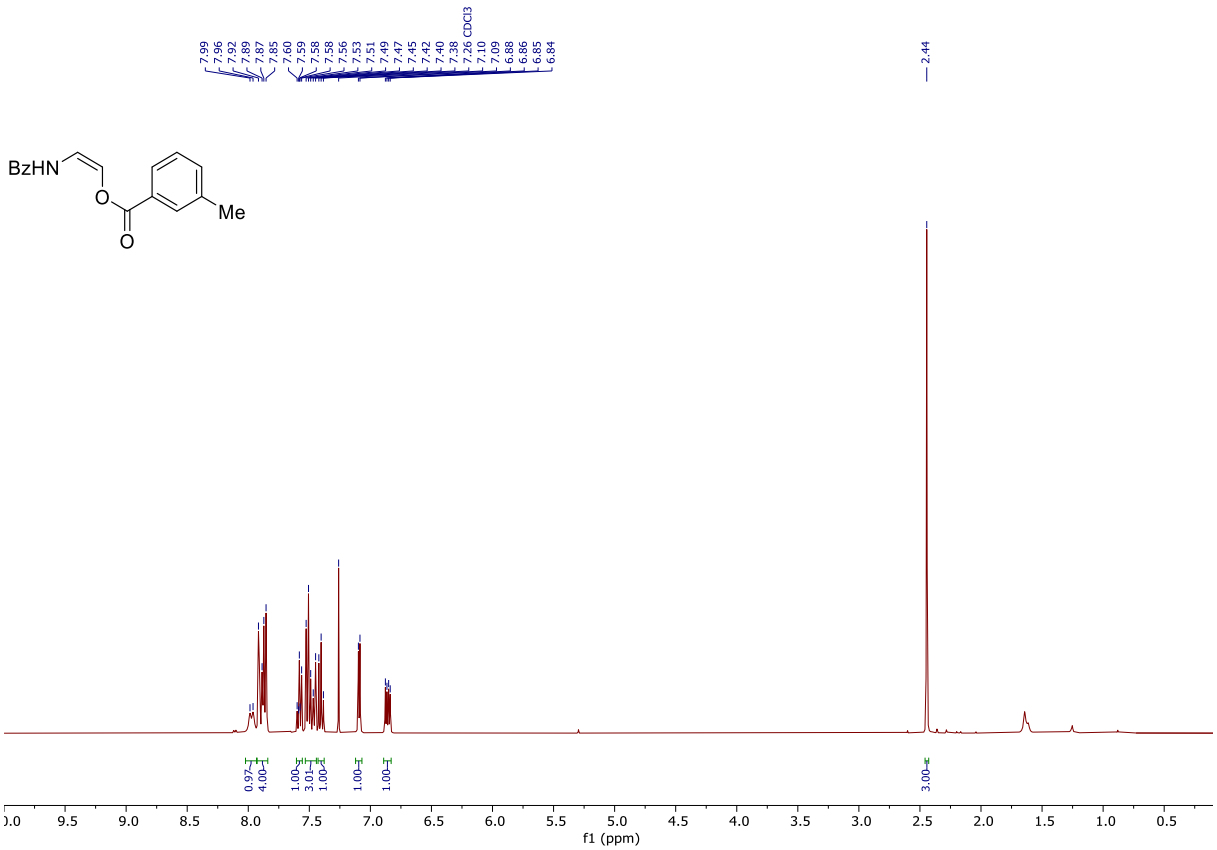


*Figure 52: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2k** in $CDCl_3$.*



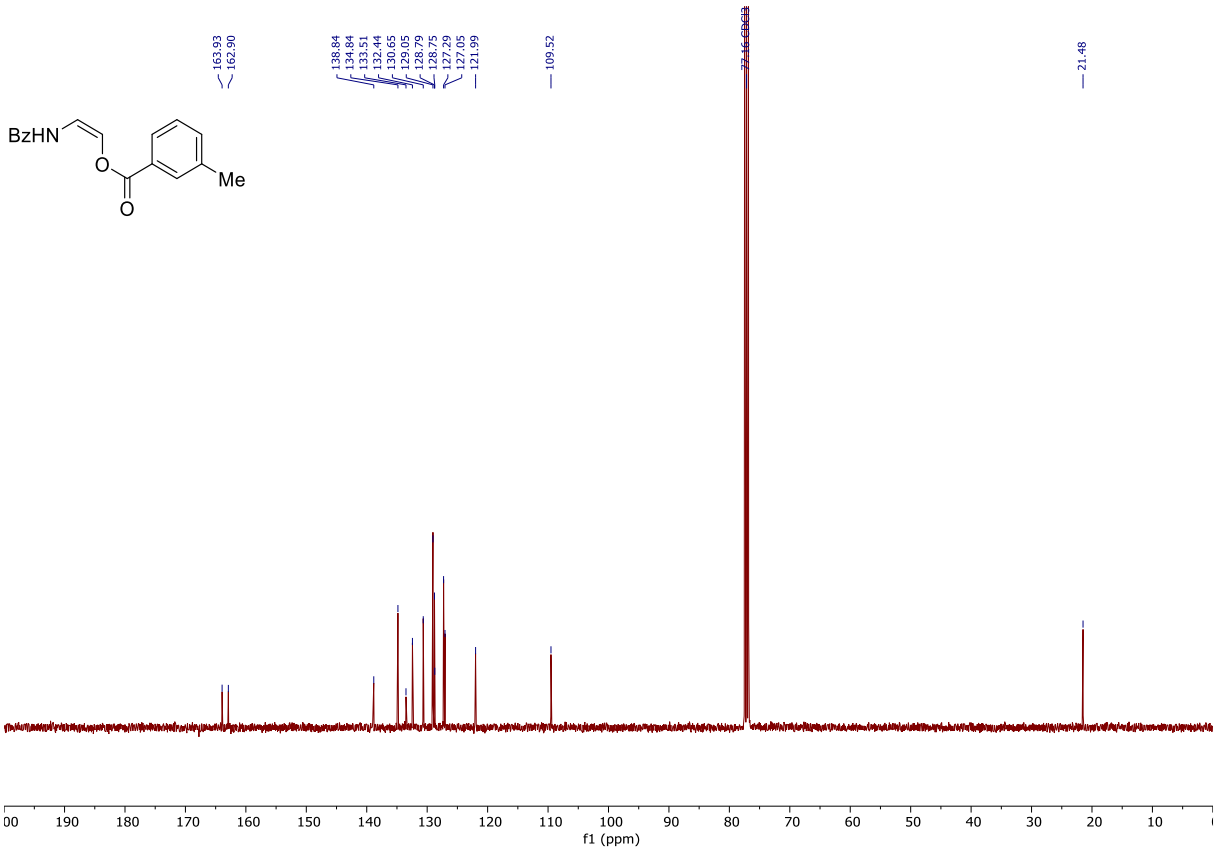


*Figure 53: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2l** in $CDCl_3$.*

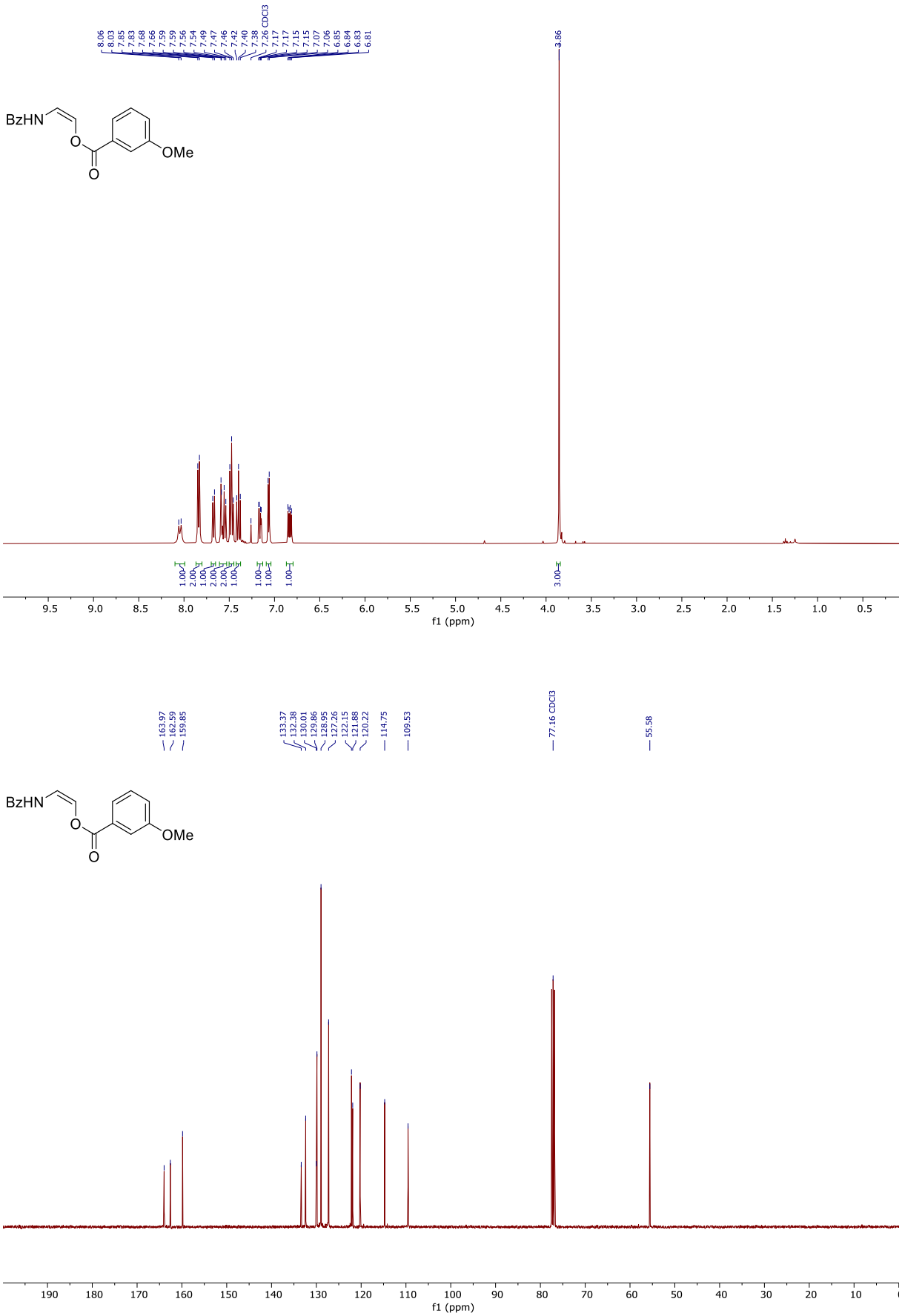


*Figure 54: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2m** in $CDCl_3$.*

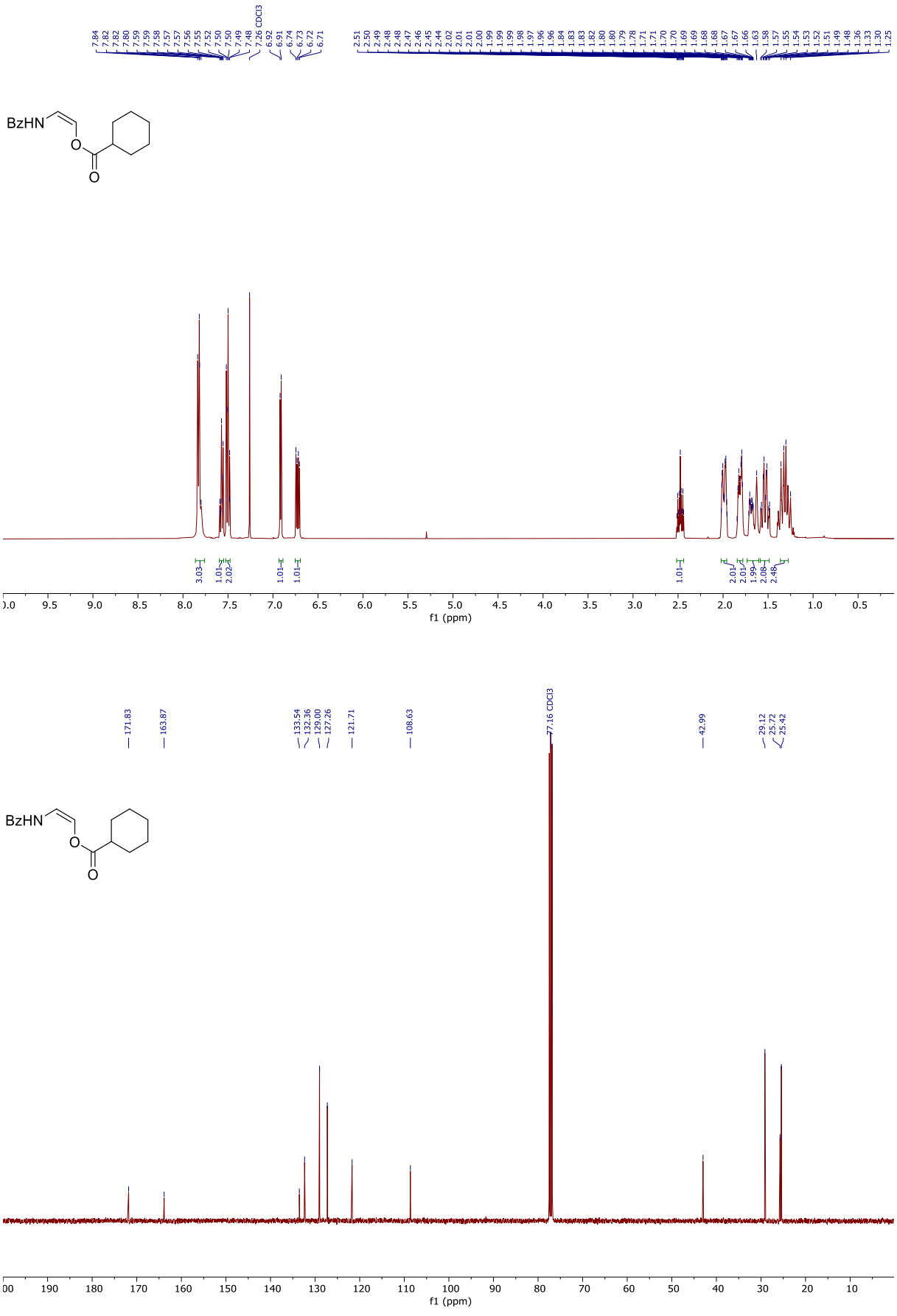


*Figure 55: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2n** in $CDCl_3$.*

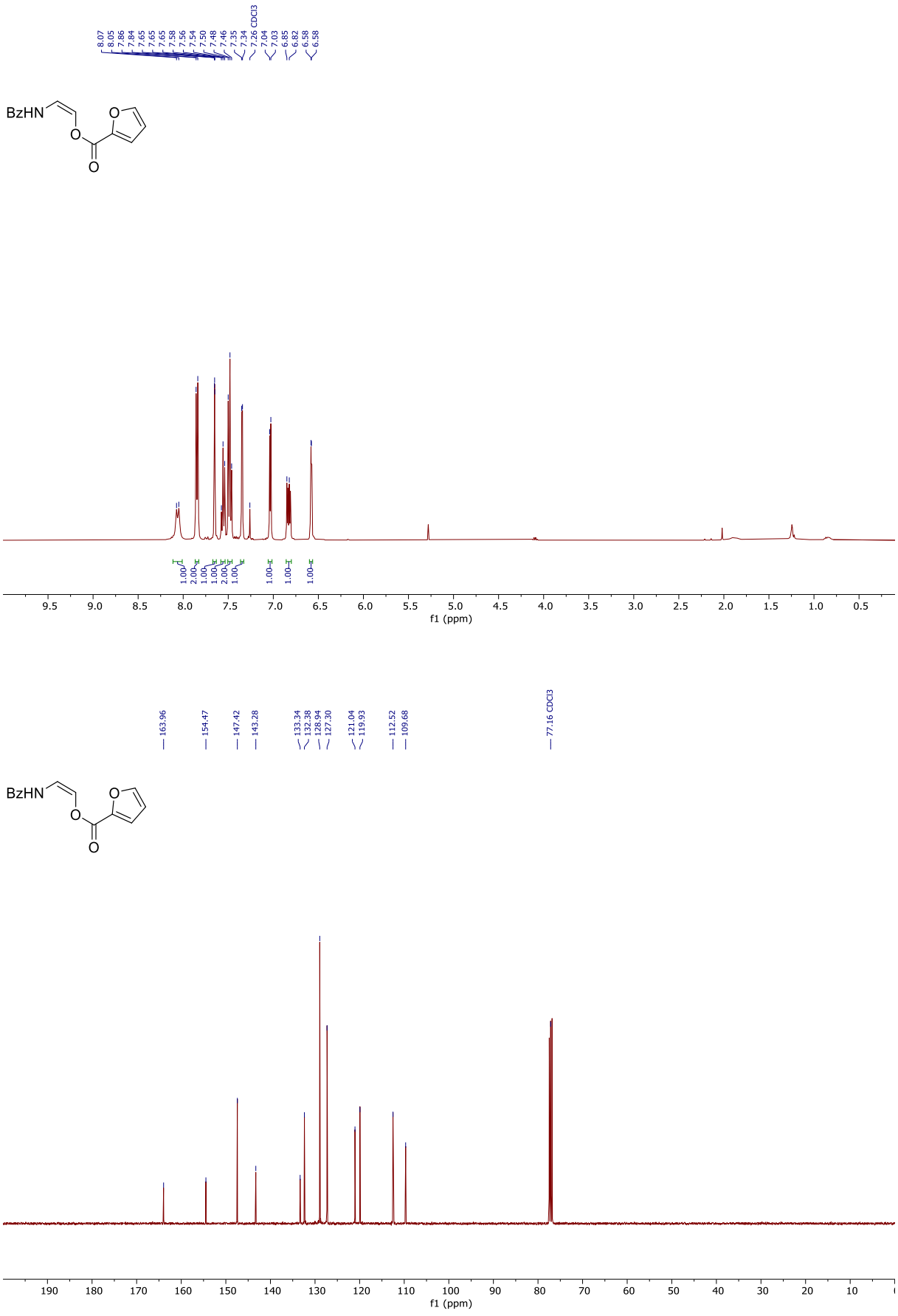


*Figure 56: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2o** in $CDCl_3$.*

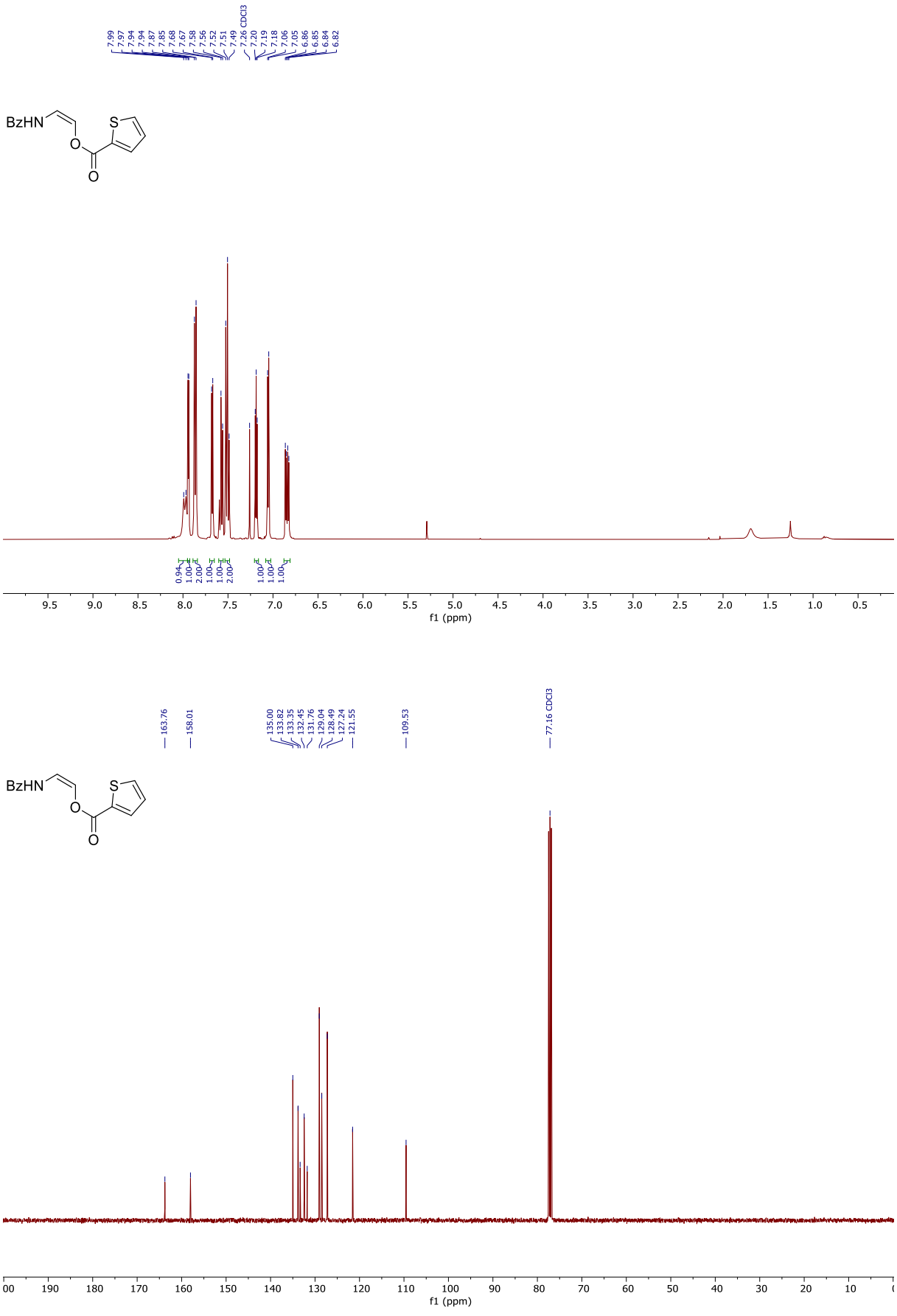
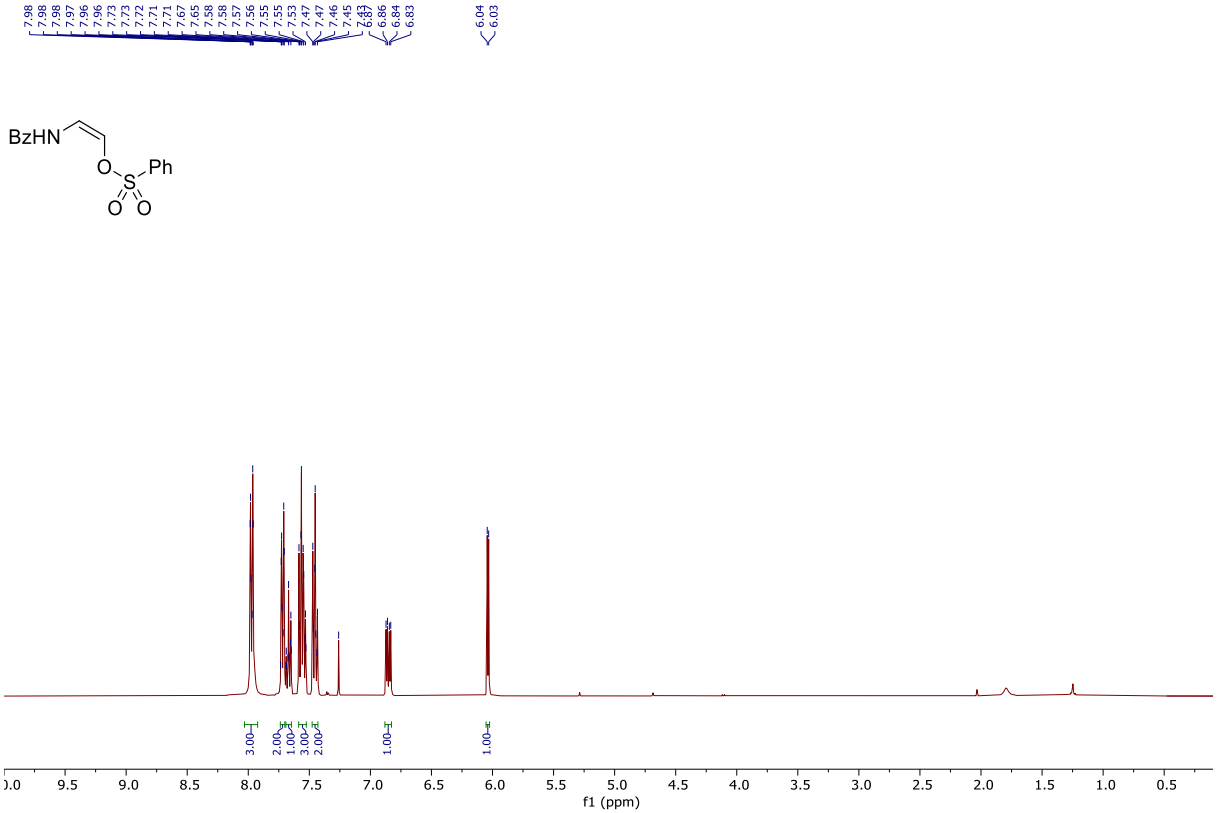


*Figure 57: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **2p** in $CDCl_3$.*



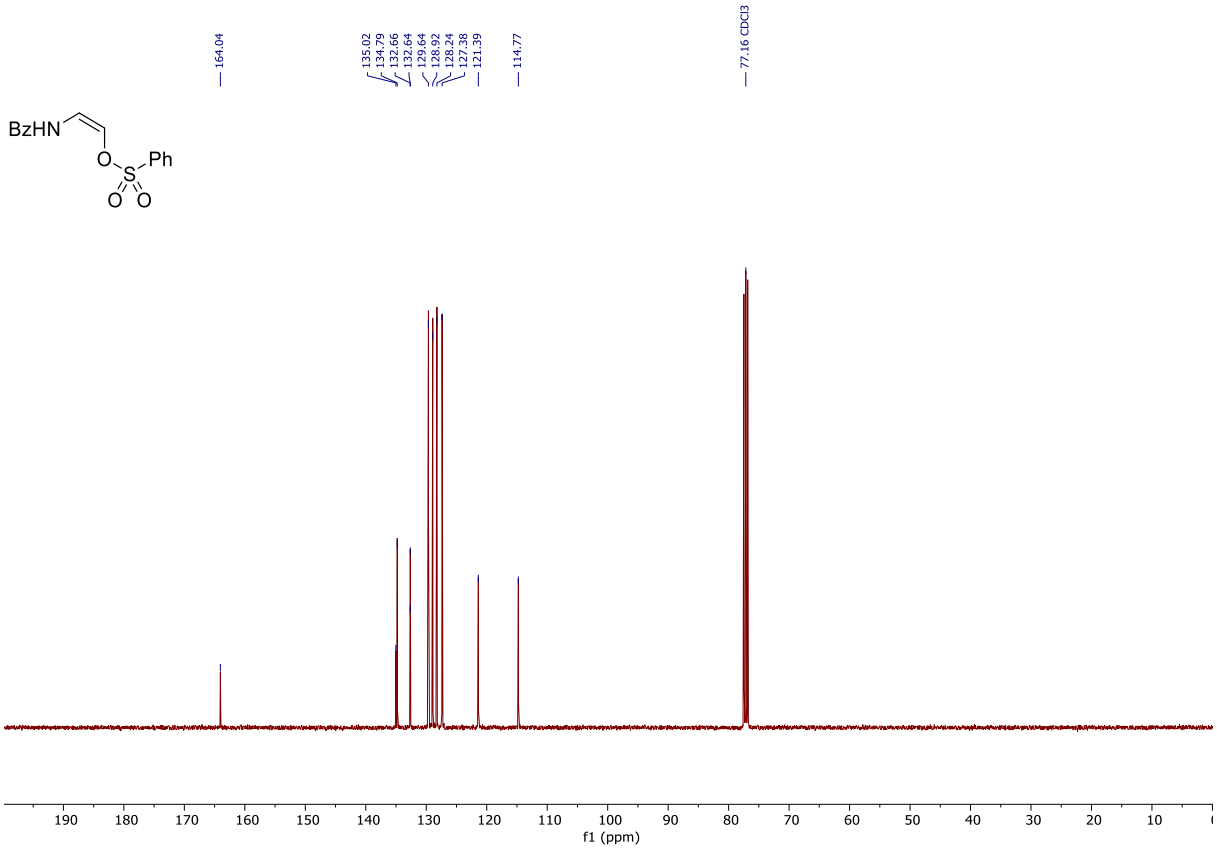


*Figure 58; ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **7a** in $CDCl_3$.*

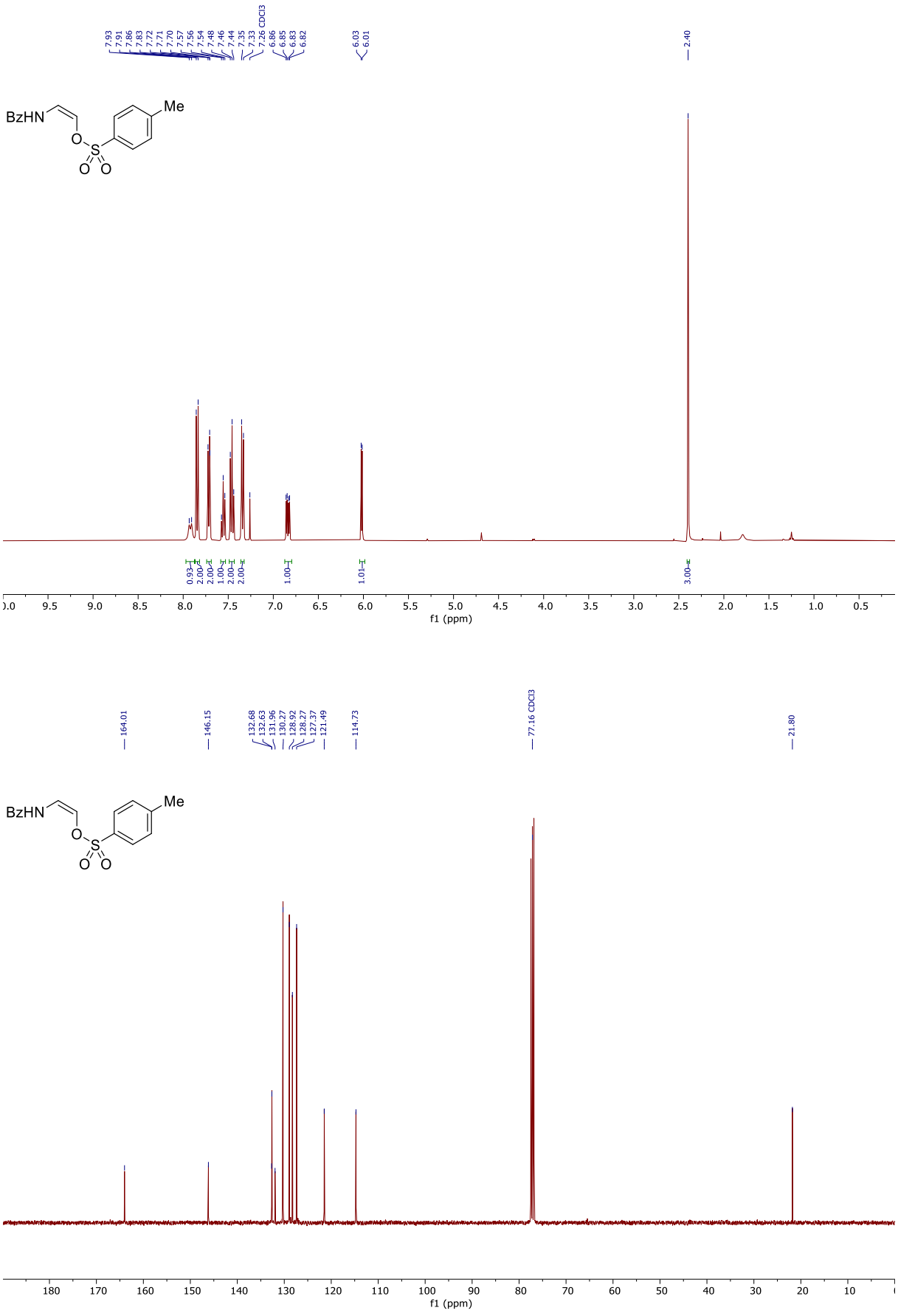
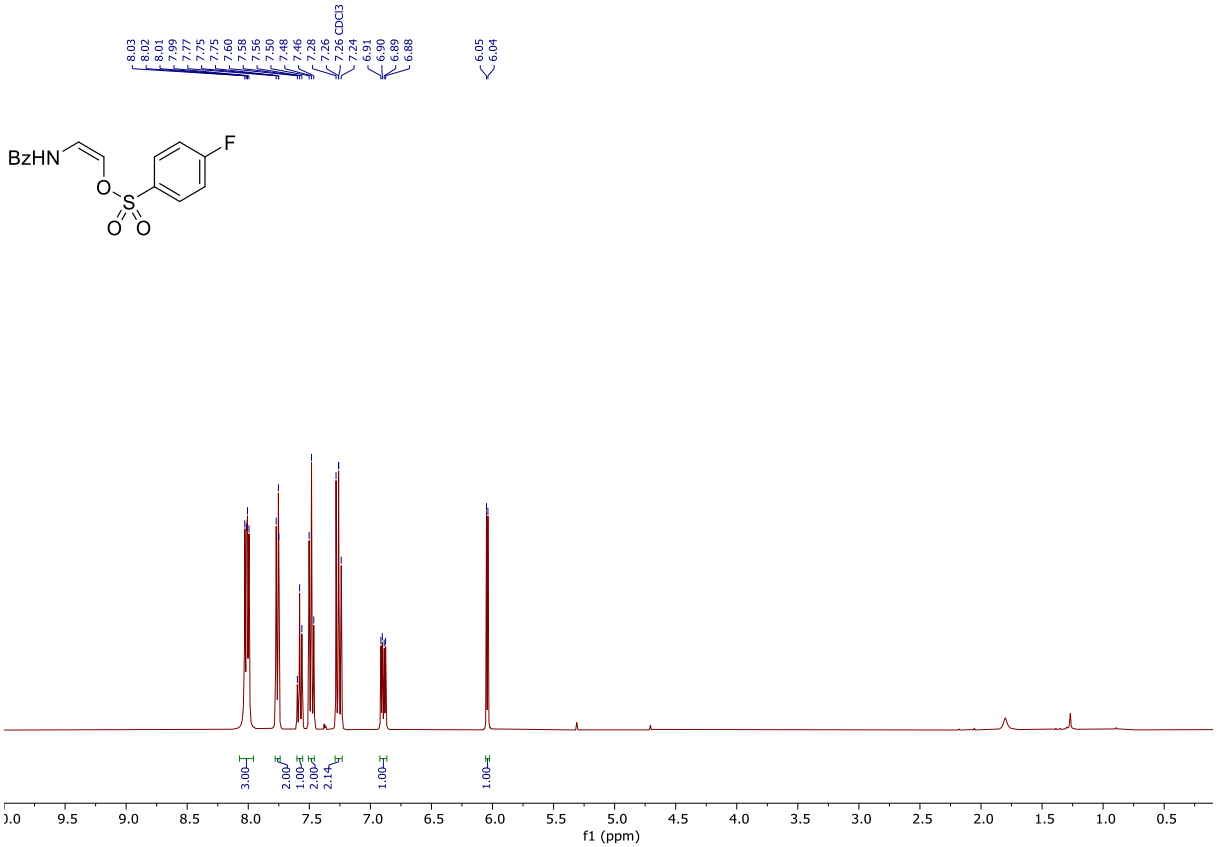
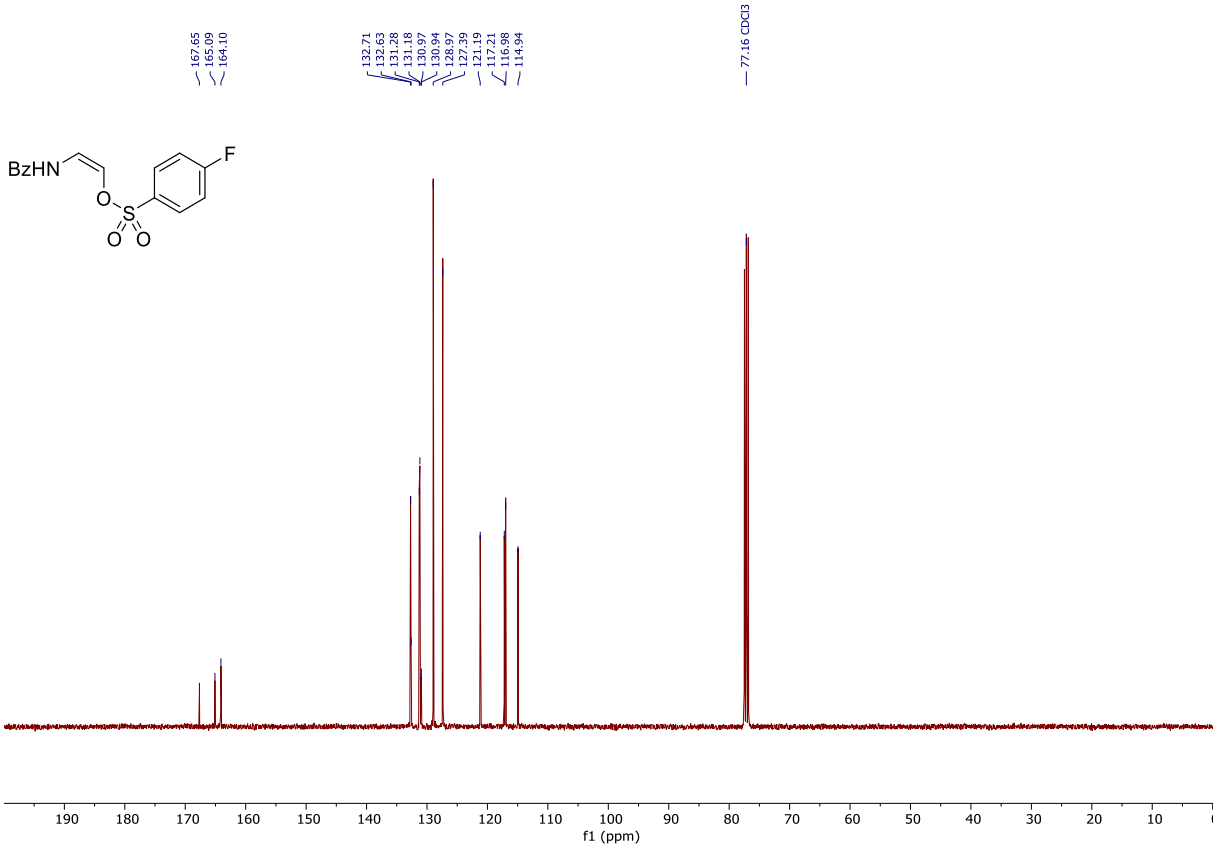


*Figure 59: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **7b** in $CDCl_3$.*


8.03
8.02
8.01
7.99
7.77
7.75
7.75
7.60
7.58
7.56
7.50
7.48
7.46
7.28
7.26
7.26 CDCl3
7.24
6.91
6.90
6.89
6.88
6.05
6.04
BzHN
O
S
O
O
F
3.00
2.00
1.00
2.00
2.14
1.00
1.00
f1 (ppm)


167.65
165.09
164.10
132.71
132.63
131.28
131.18
130.97
130.94
128.97
127.39
121.19
117.21
116.98
114.94
77.16 CDCl3
BzHN
O
S
O
O
F
f1 (ppm)

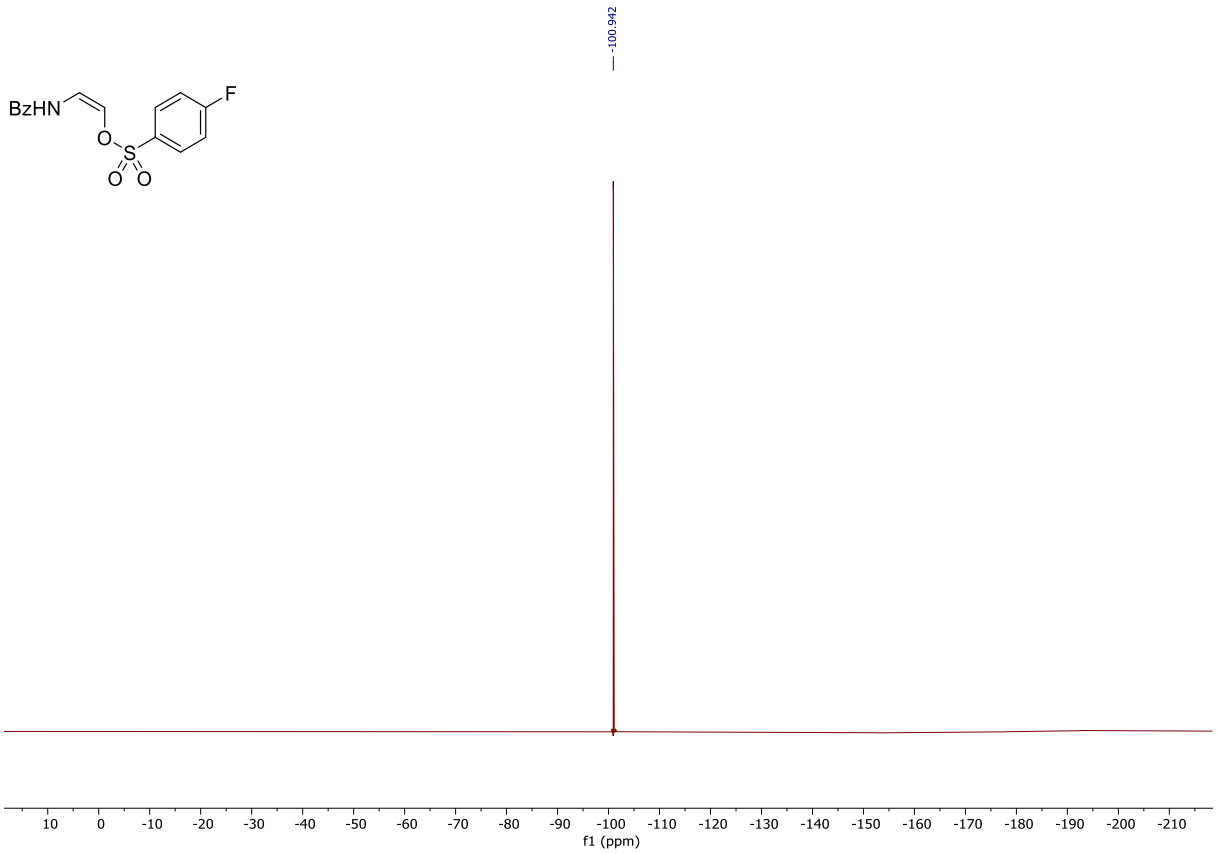


*Figure 60: ^{1}H (400 MHz), ^{13}C (101 MHz) and ^{19}F (376 MHz) NMR spectra of **7c** in $CDCl_3$.*

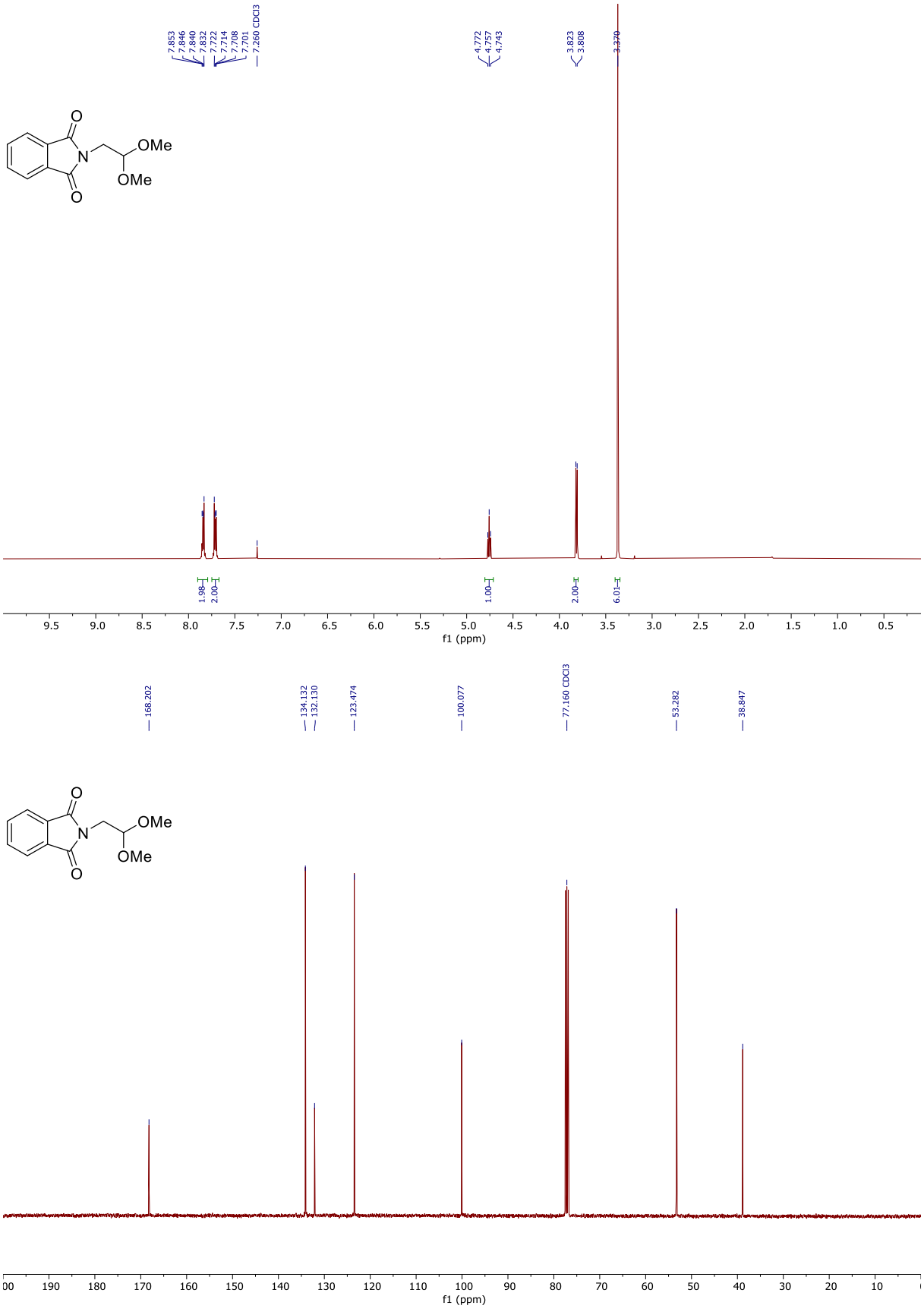


*Figure 61: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **8** in $CDCl_3$.*

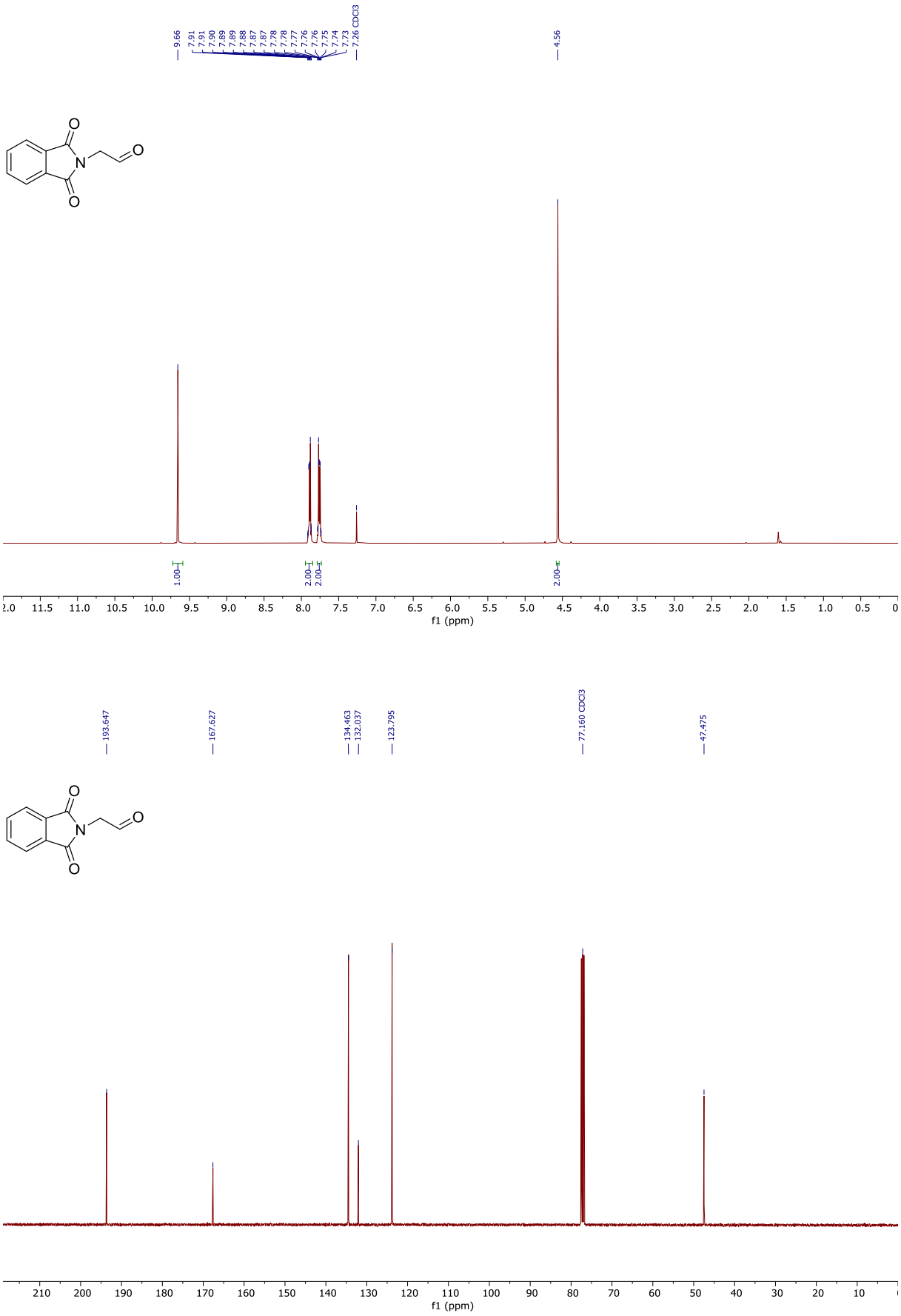


*Figure 62: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **9** in $CDCl_3$.*

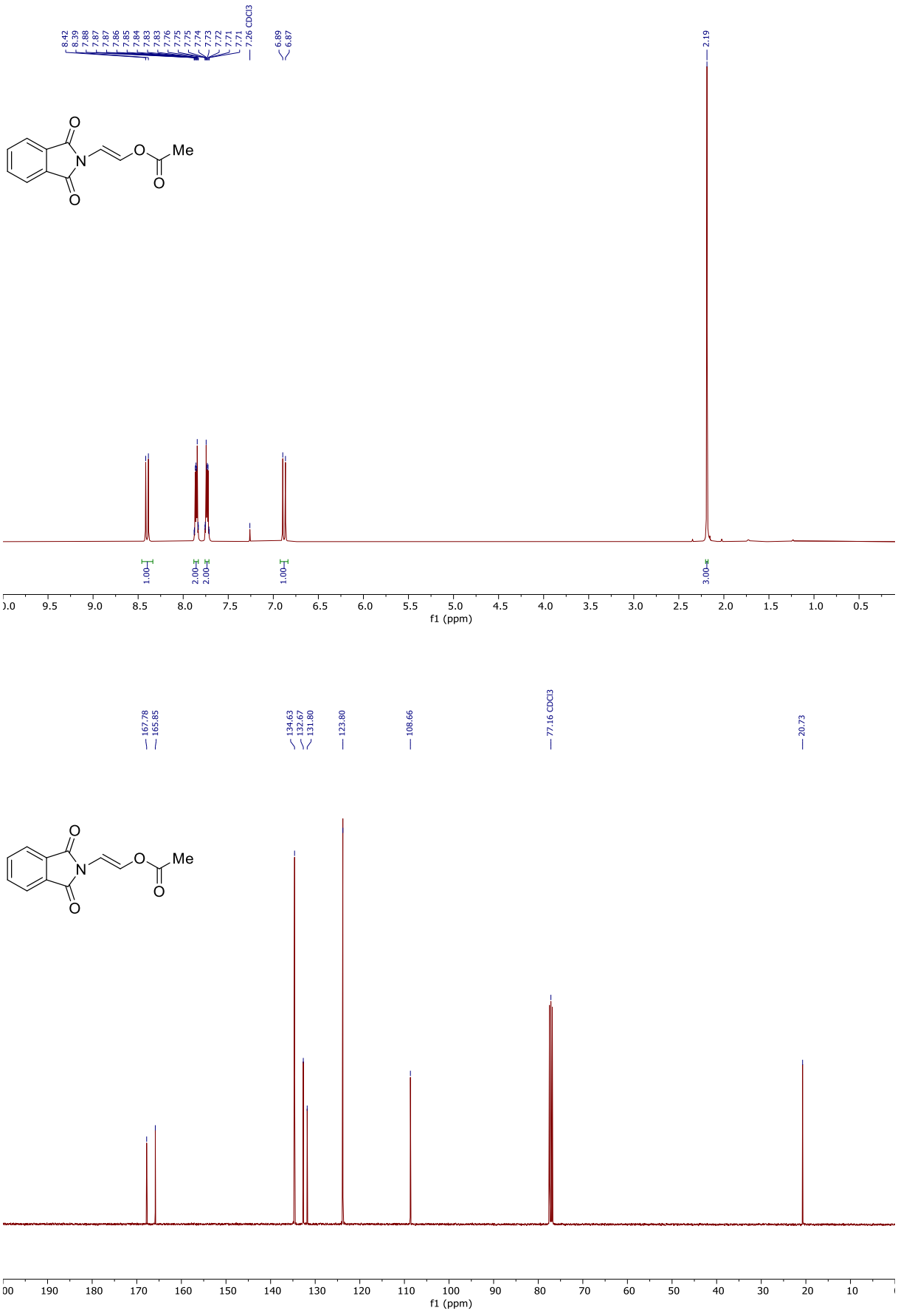


*Figure 63: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **E-10a** in $CDCl_3$.*

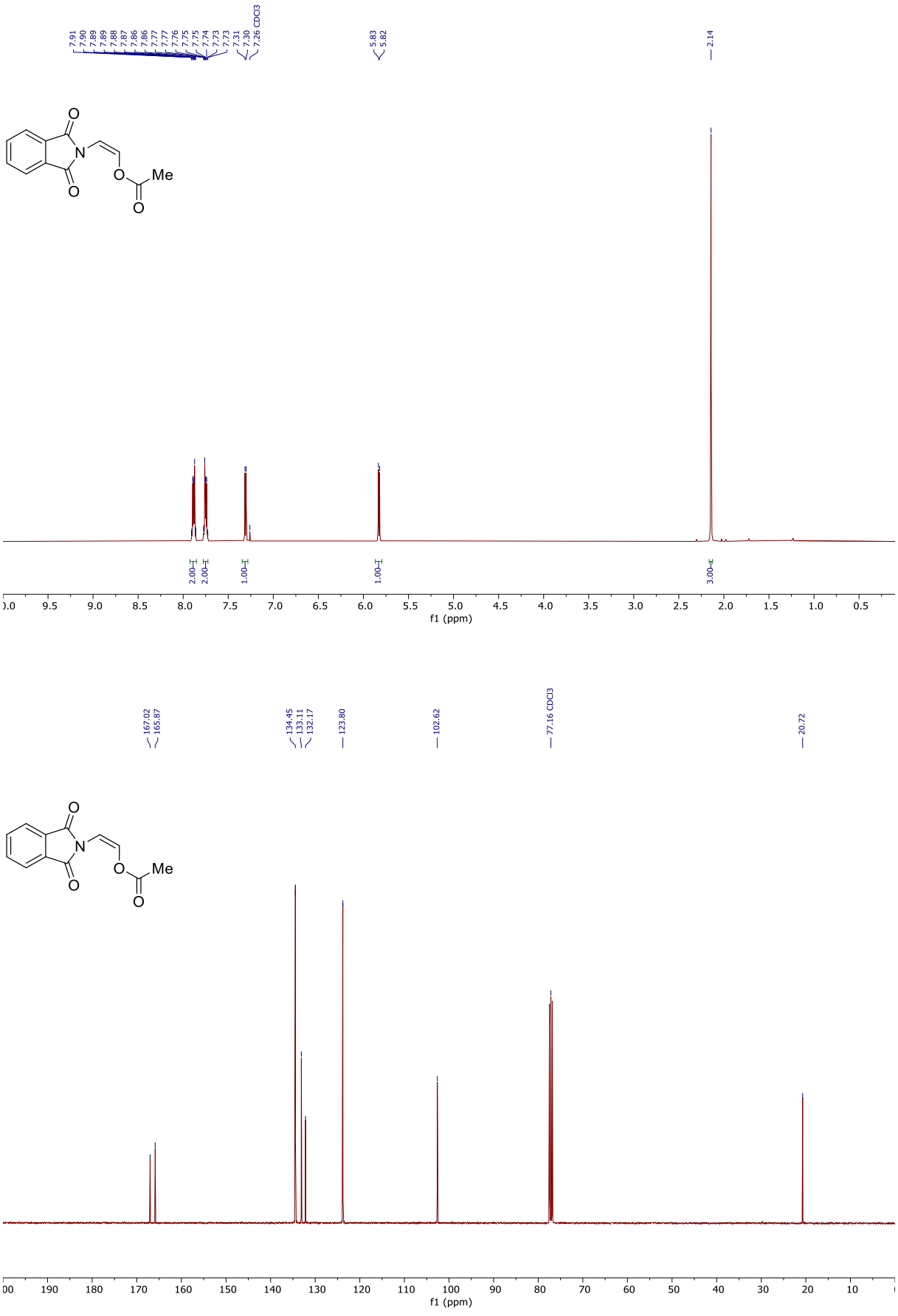


*Figure 64: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **Z-10a** in $CDCl_3$.*

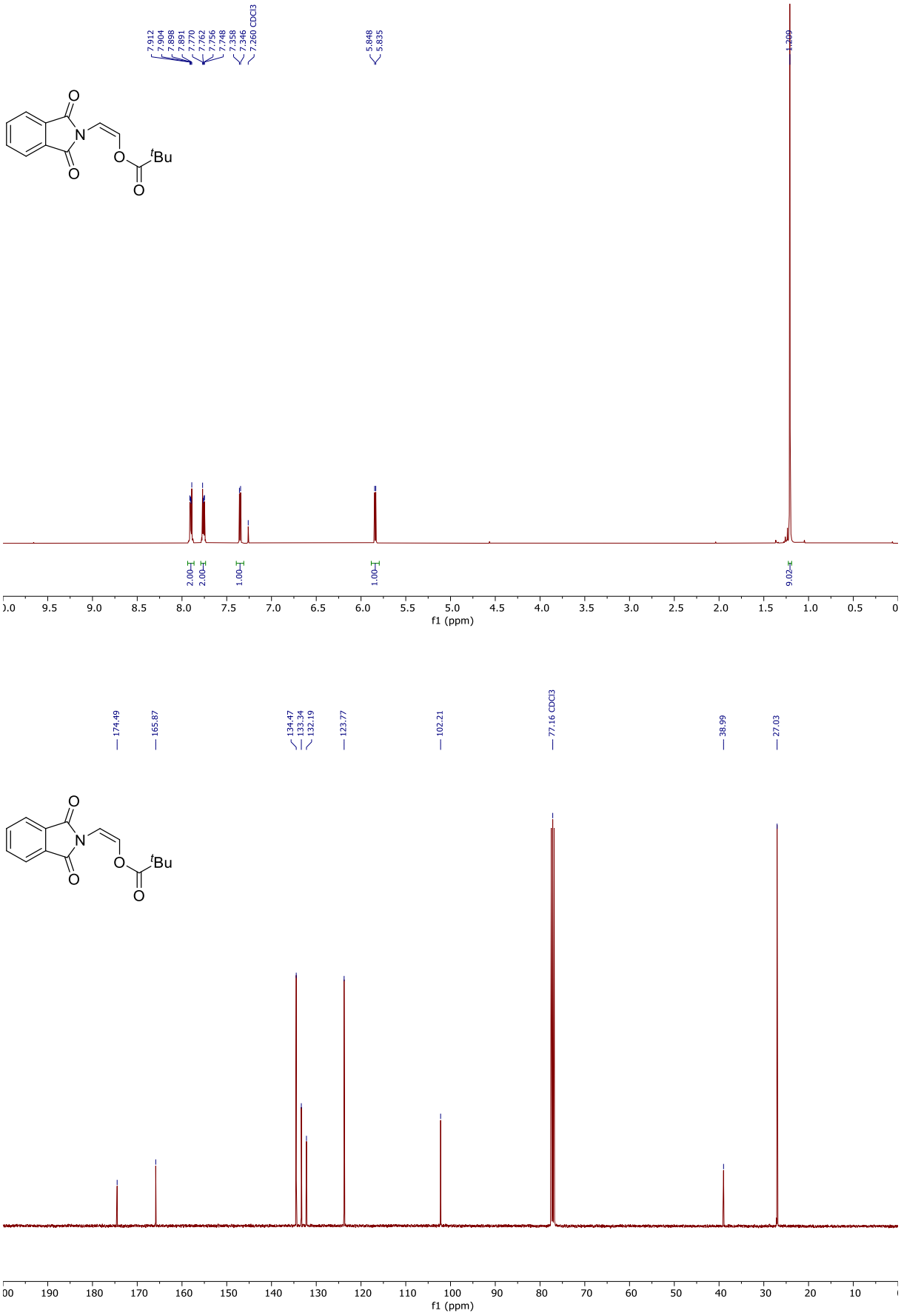


*Figure 65: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **Z-10b** in $CDCl_3$.*

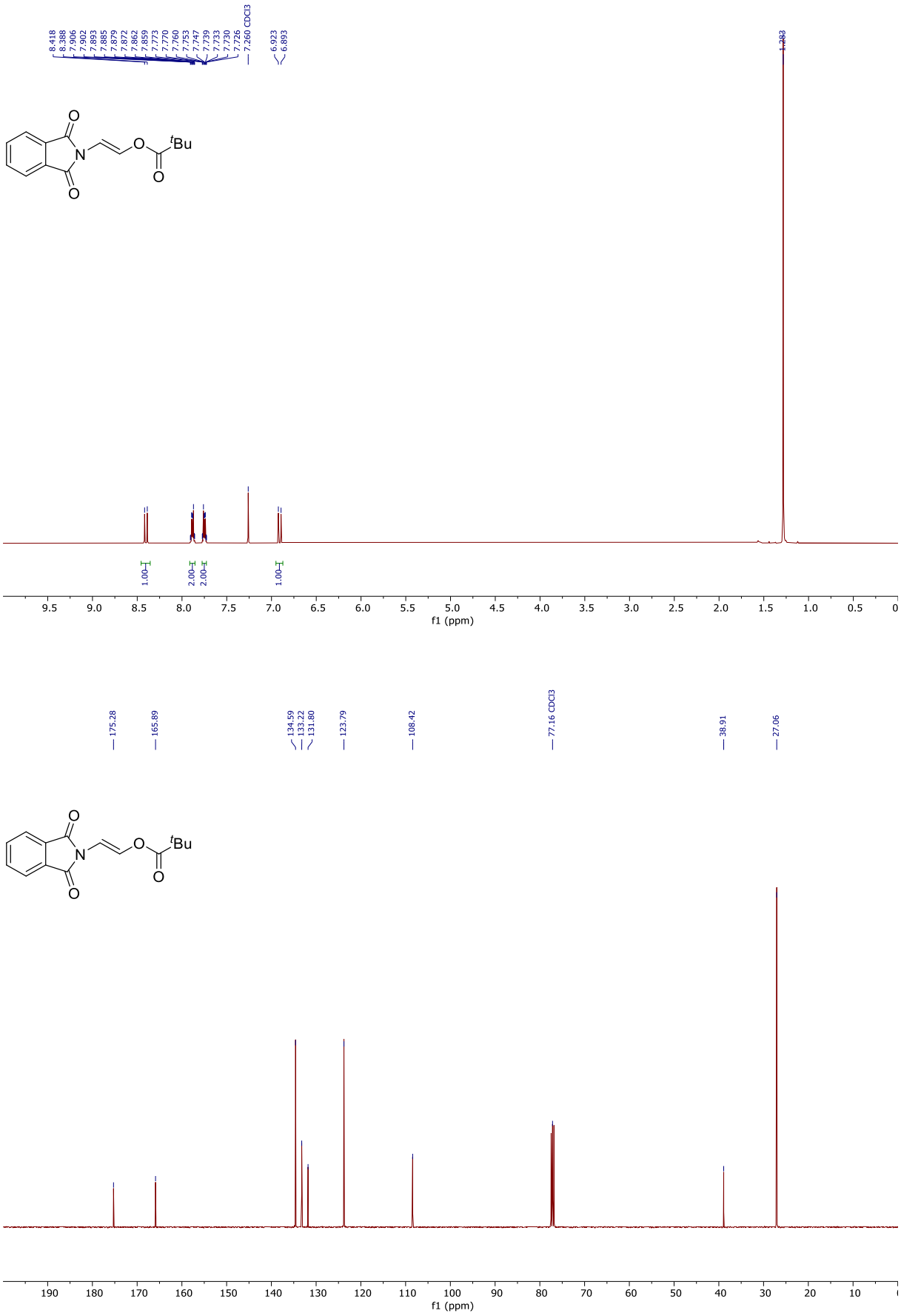


*Figure 66: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **E-10b** in $CDCl_3$.*

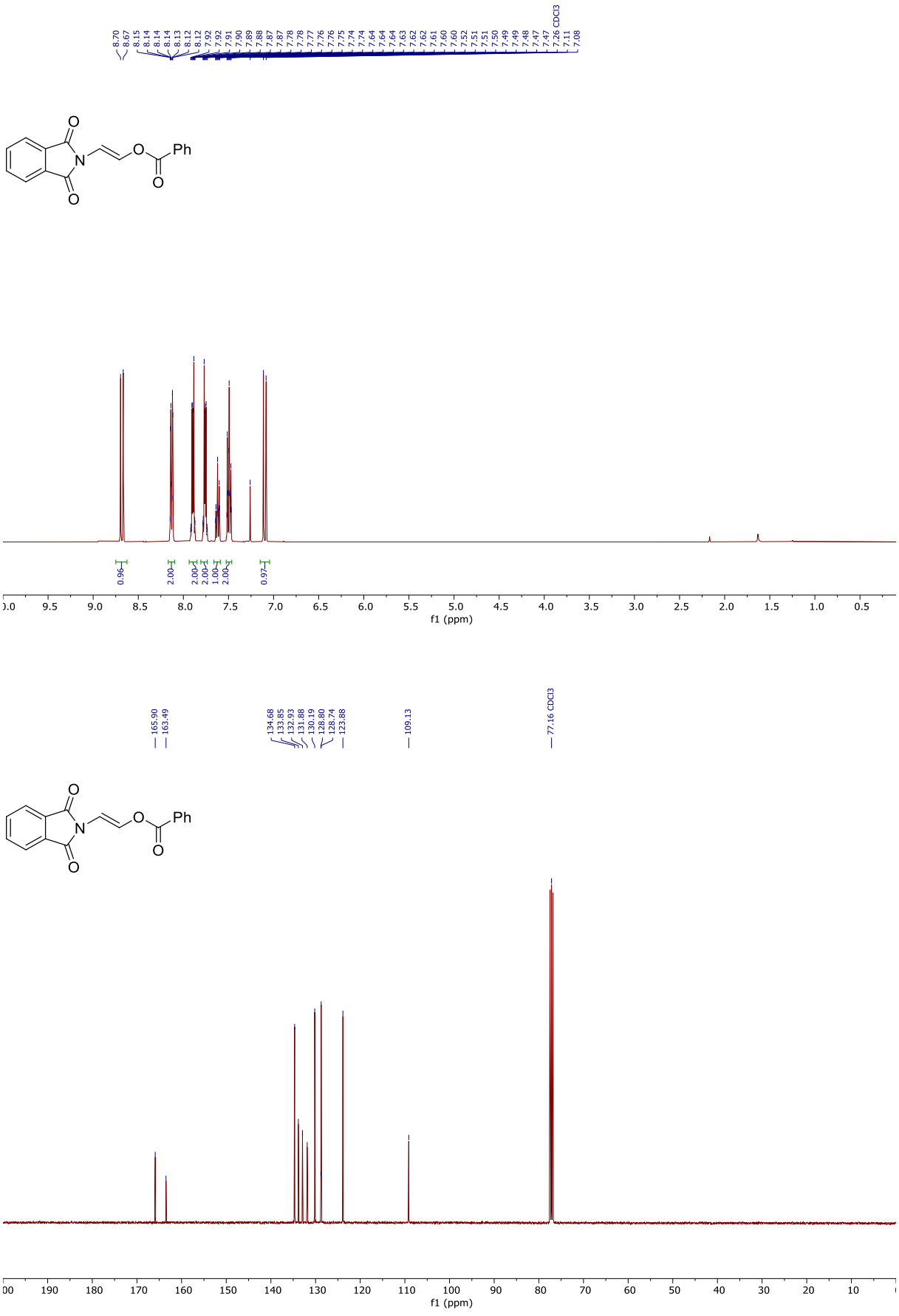


*Figure 67: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **E-10c** in $CDCl_3$.*

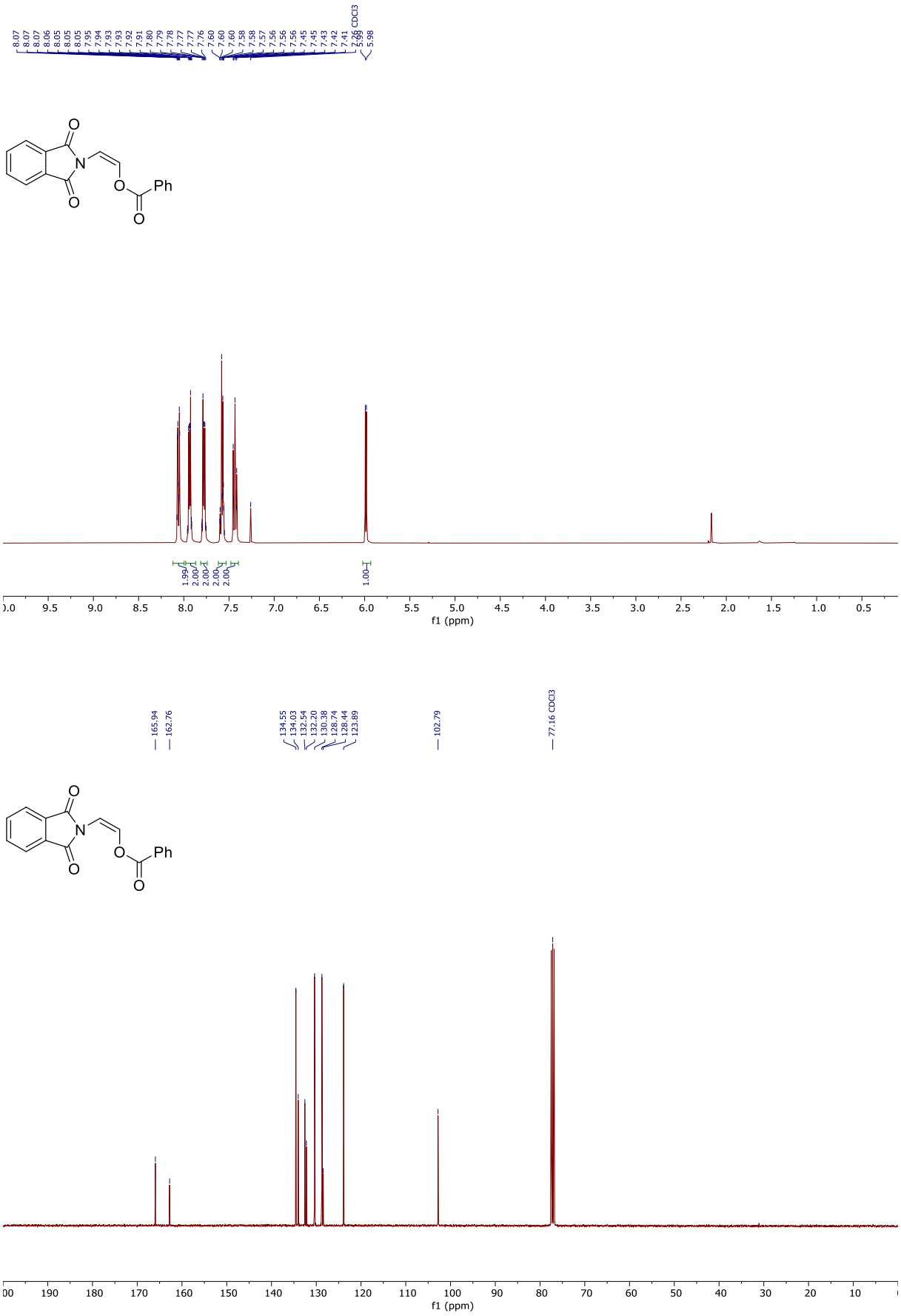


*Figure 68: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **Z-10c** in $CDCl_3$.*

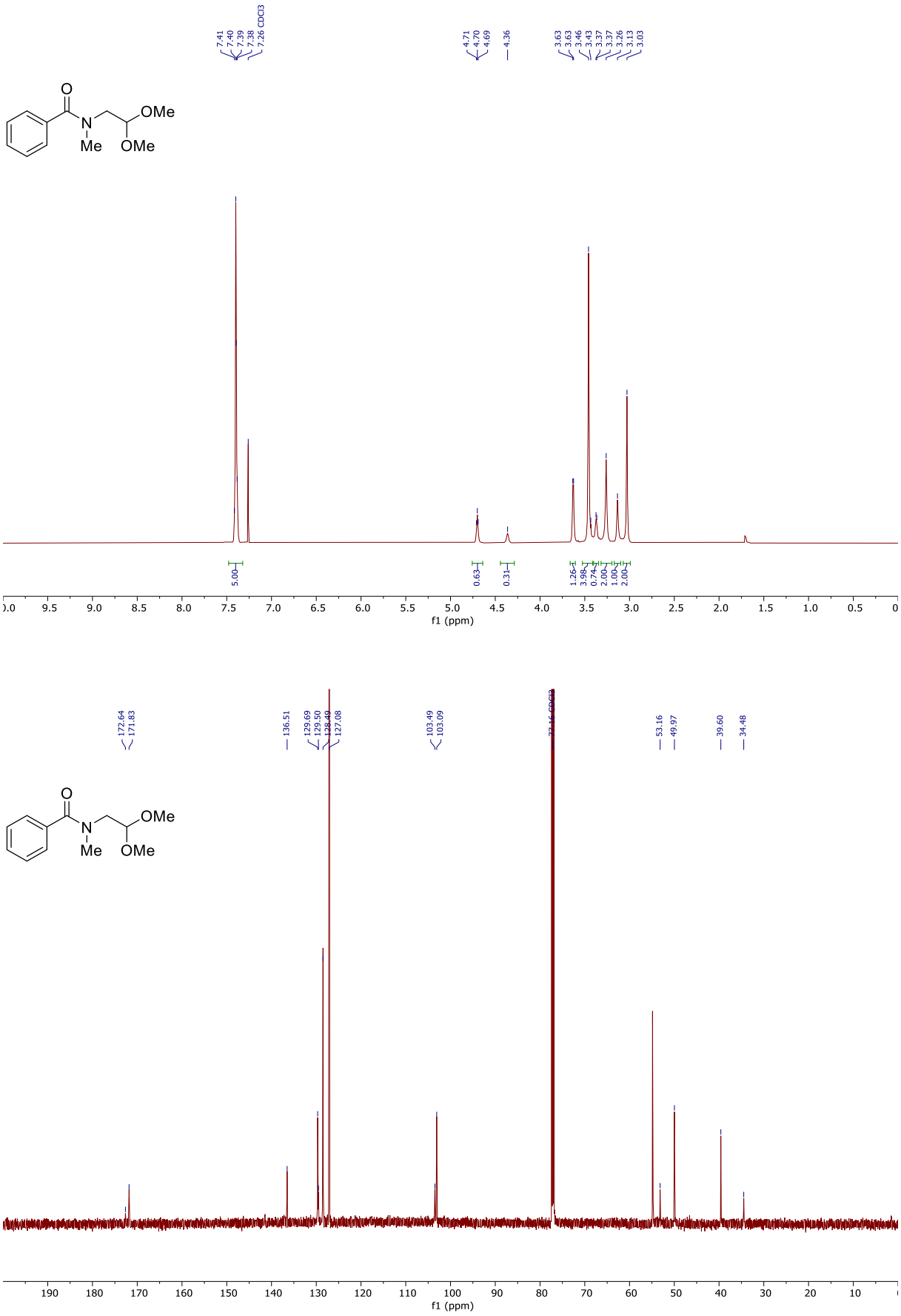


*Figure 69: ^{1}H (400 MHz) and ^{13}C (101 MHz) NMR spectra of **12** in $CDCl_3$.*

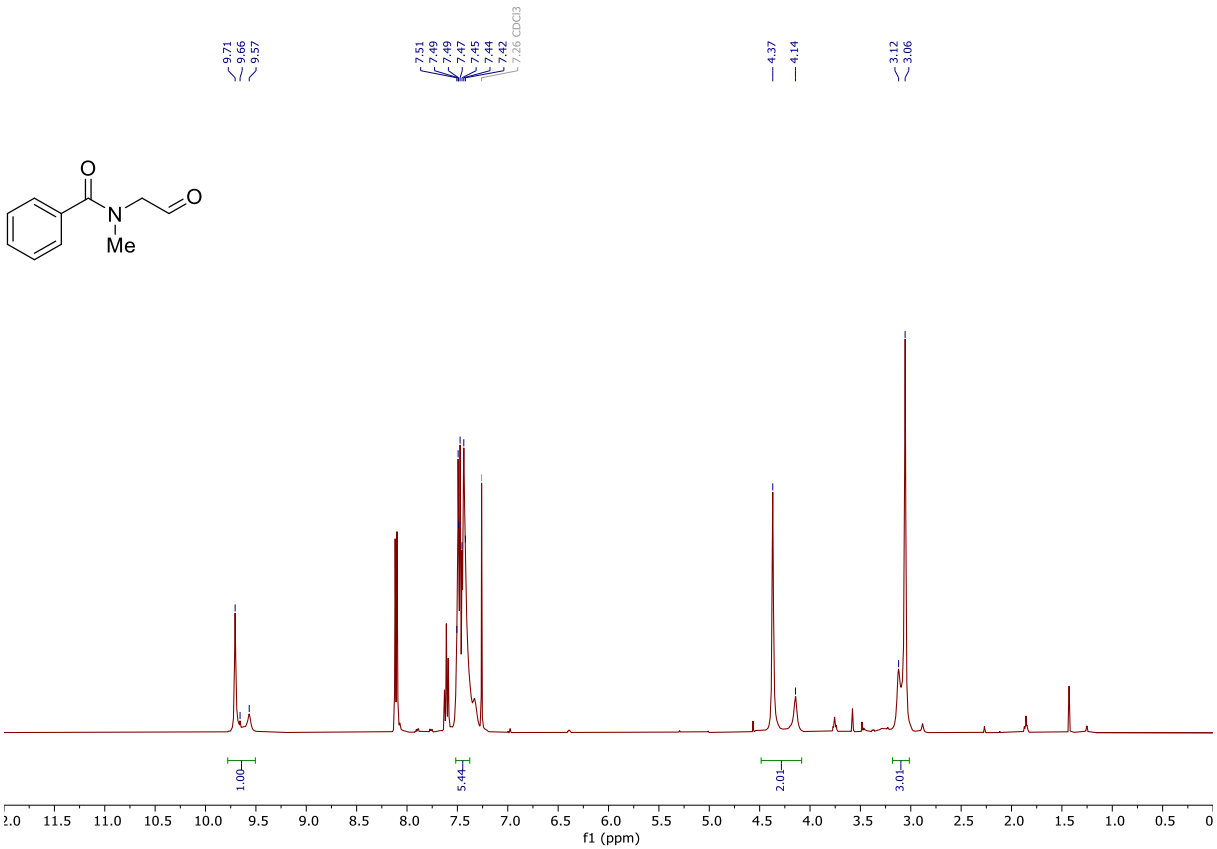


*Figure 70: ^{1}H (400 MHz) NMR spectra of **S1** in $CDCl_3$.*

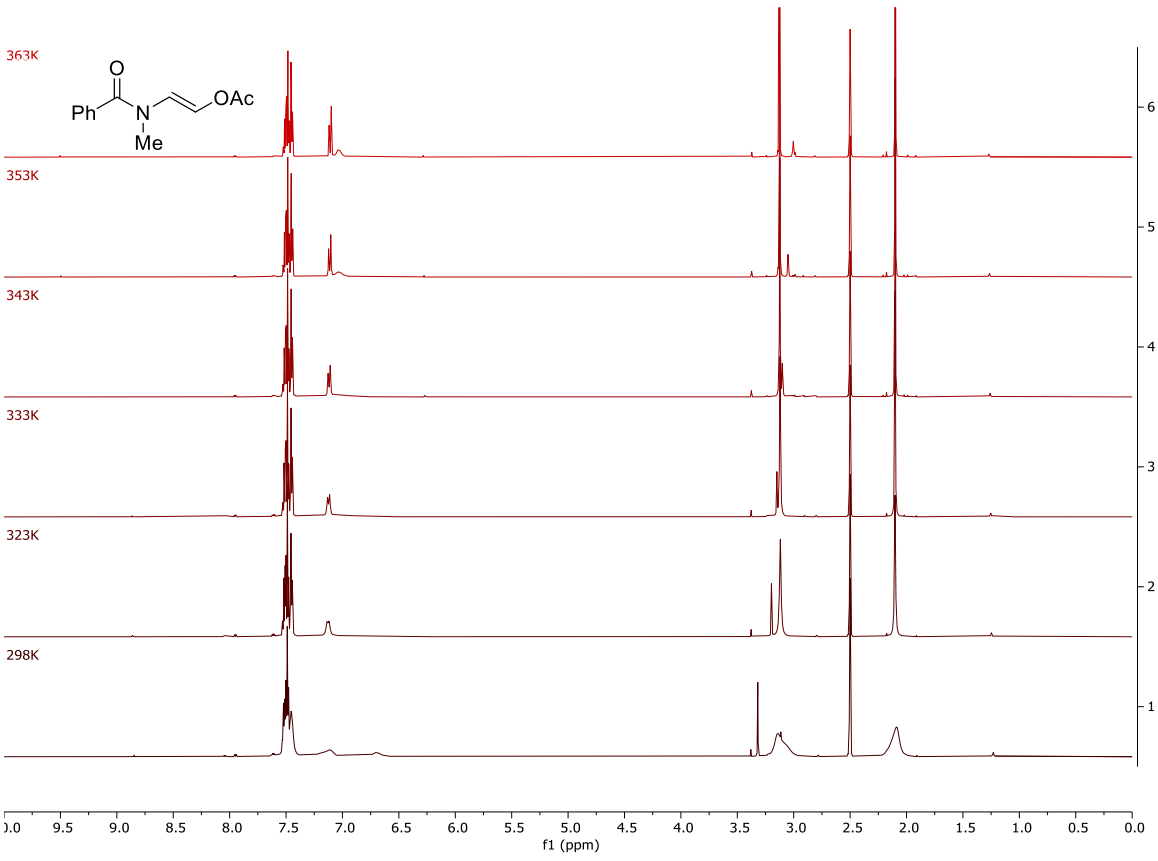
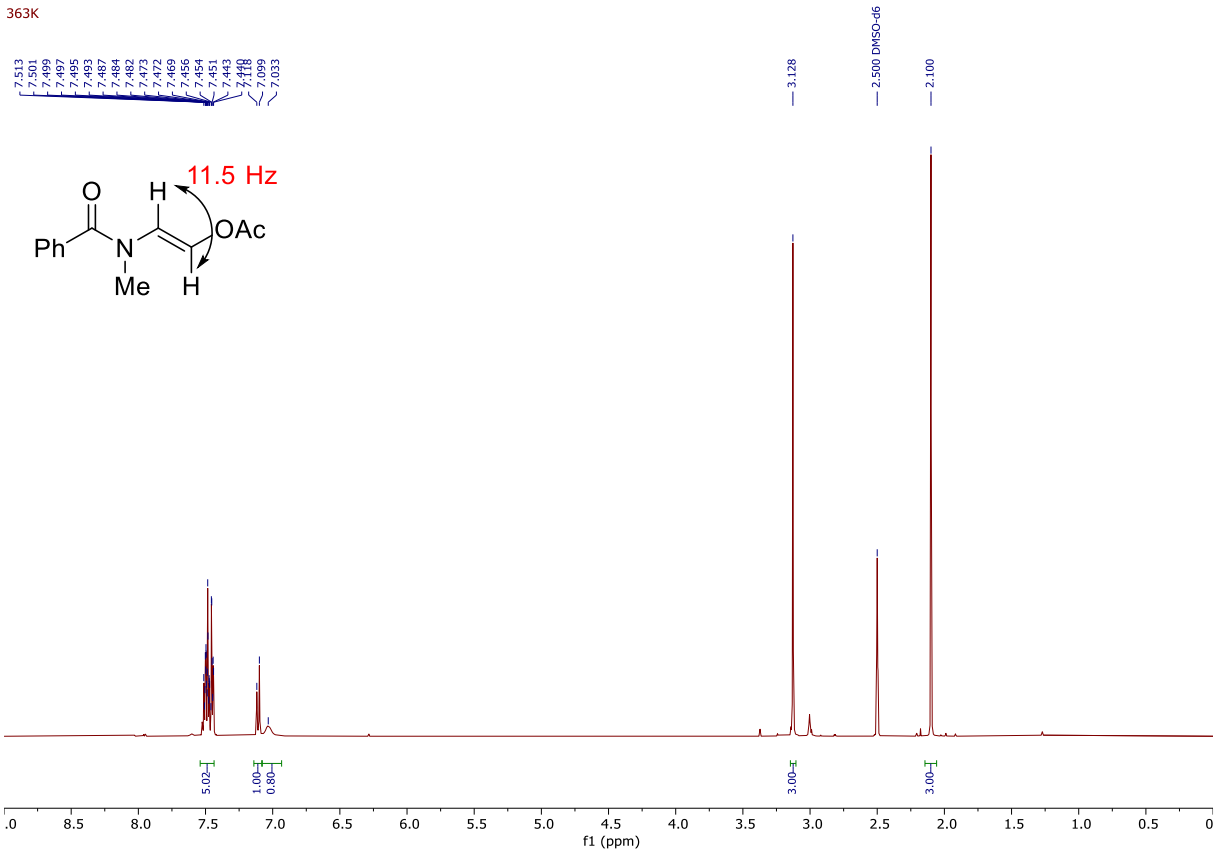


*Figure 71: ^{1}H (600 MHz) NMR spectra of **E-11** in DMSO-d^6 at different temperatures.*



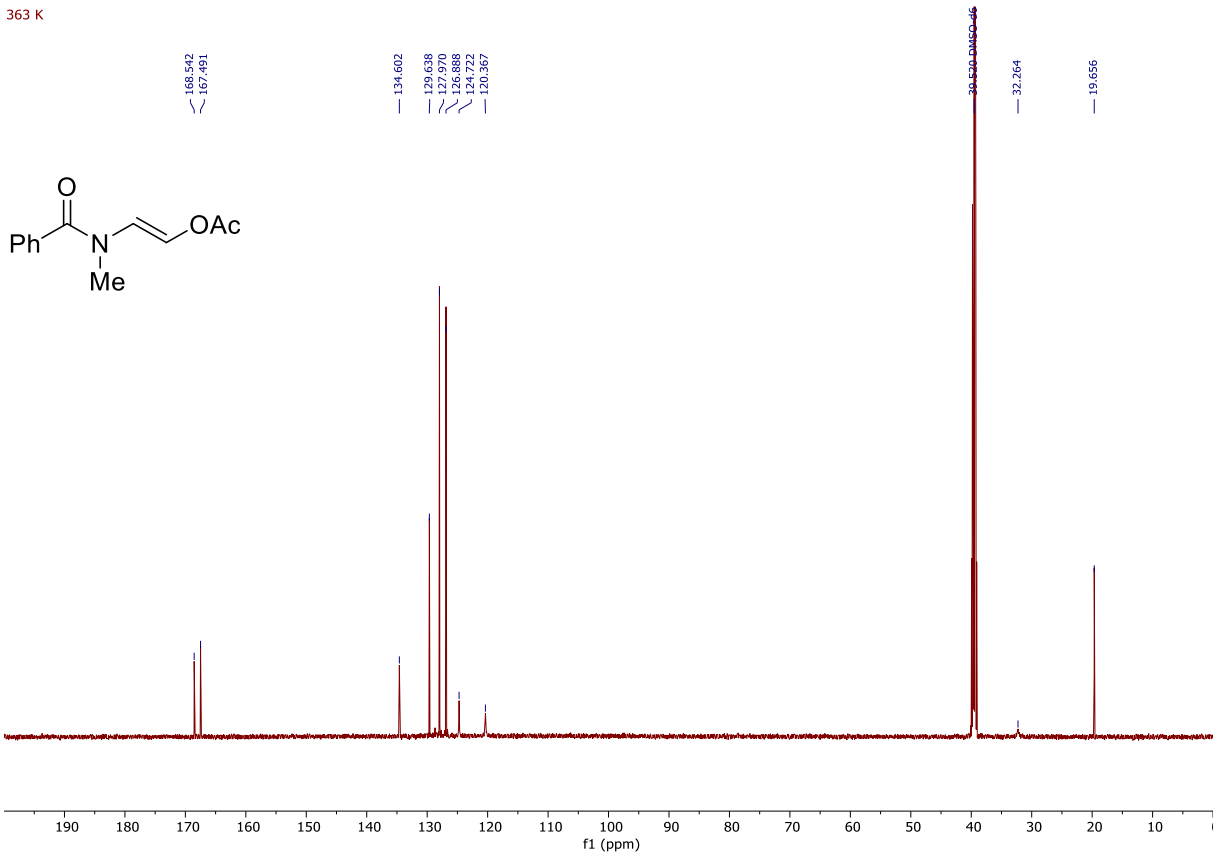


*Figure 72: ^{1}H (600 MHz) and ^{13}C (151) NMR spectra of **E-11** in DMSO-d^{6}.*

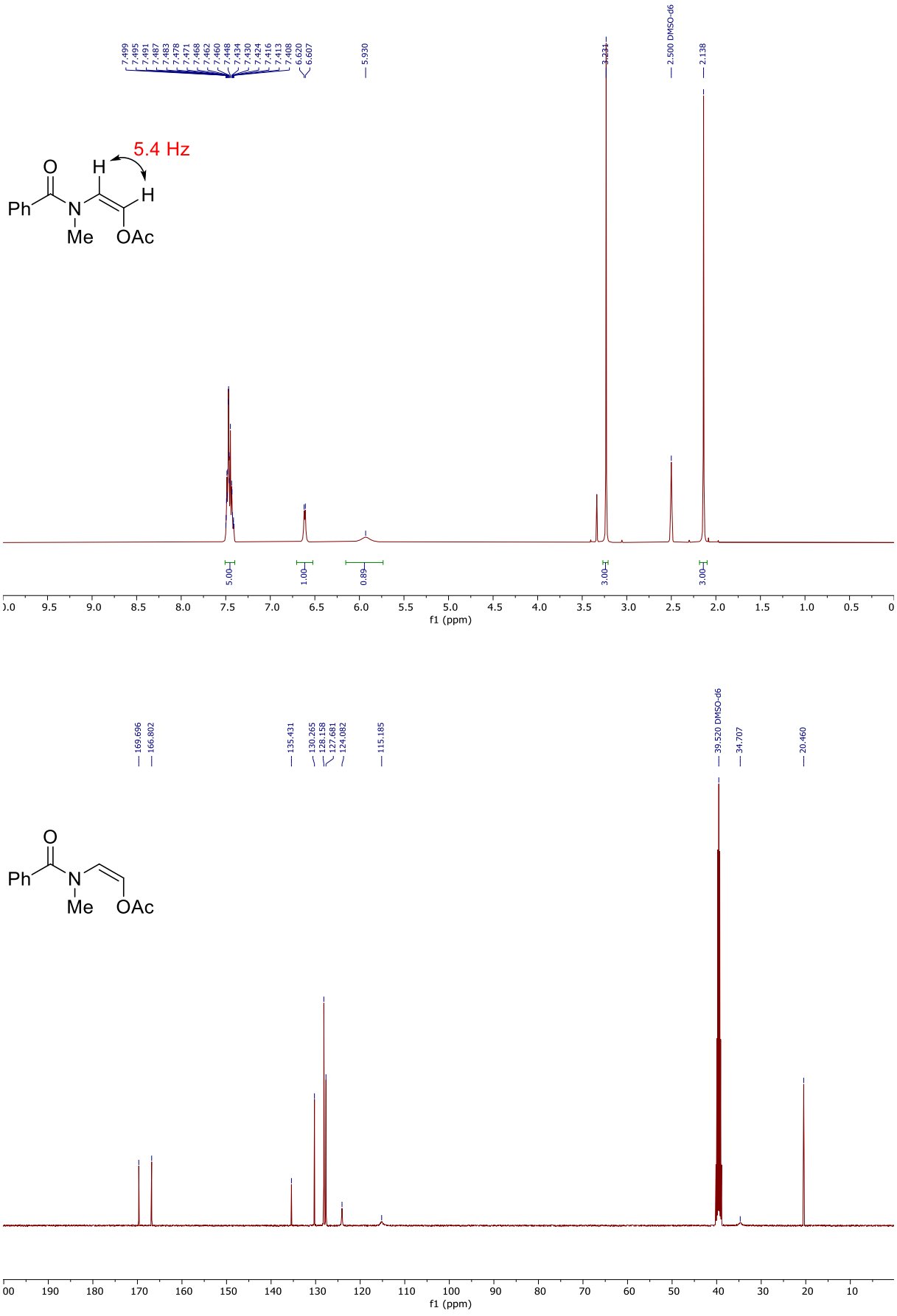


*Figure 73: ^{1}H (400 MHz) and ^{13}C (101) NMR spectra of **E-11** in DMSO-d^{6}.*

5 XRAY

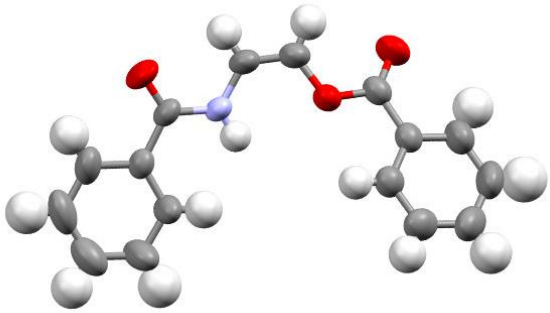


Table 1. Crystal data and structure refinement for **1a**. Displacement ellipsoids are shown at the 50% probability level.

Identification code	CCDC 2180323	
Empirical formula	$C_{16}H_{13}NO_3$	
Formula weight	267.27	
Temperature	293(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 7.9146(3)	α = 90°.
	b = 19.7402(5) Å	β = 108.761(3)°.
	c = 9.2157(3) Å	γ = 90°.
Volume	1363.32(8) $Å^3$	
Z	4	
Density (calculated)	1.302 Mg/m^3	
Absorption coefficient	0.743 mm^{-1}	
F(000)	560	
Crystal size	0.480 x 0.480 x 0.280 mm^3	
Theta range for data collection	4.480 to 61.935°.	
Index ranges	-8<=h<=9, -22<=k<=19, -10<=l<=10	
Reflections collected	5168	
Independent reflections	2126 [R(int) = 0.0275]	
Completeness to theta = 61.935°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.64017	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2126 / 0 / 182	
Goodness-of-fit on F^2	1.071	
Final R indices [I>2sigma(I)]	R1 = 0.0474, wR2 = 0.1321	
R indices (all data)	R1 = 0.0525, wR2 = 0.1386	
Extinction coefficient	0.0048(12)	
Largest diff. peak and hole	0.138 and -0.153 $e.Å^{-3}$	

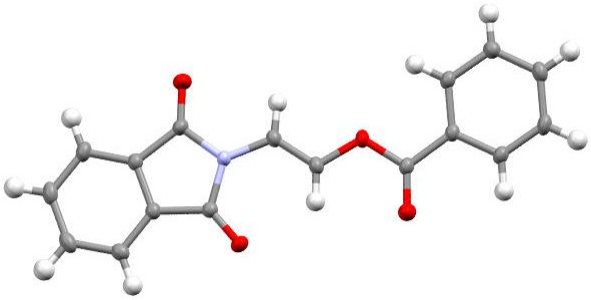


Table 2. Crystal data and structure refinement for ***E*-11c**. Displacement ellipsoids are shown at the 50% probability level.

Identification code	CCDC 2180324	
Empirical formula	$C_{17}H_{11}NO_4$	
Formula weight	293.27	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.3631(4) Å	α= 77.411(4)°.
	b = 8.3022(3) Å	v= 75.849(4)°.
	c = 11.5152(6) Å	γ = 85.663(3)°.
Volume	665.97(6) $Å^3$	
Z	2	
Density (calculated)	1.462 Mg/m^3	
Absorption coefficient	0.106 mm^{-1}	
F(000)	304	
Crystal size	0.550 x 0.180 x 0.030 mm^3	
Theta range for data collection	2.804 to 30.000°.	
Index ranges	-9<=h<=10, -10<=k<=11, -16<=l<=16	
Reflections collected	7764	
Independent reflections	3881 [R(int) = 0.0279]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.70334	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3881 / 0 / 199	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2sigma(I)]	R1 = 0.0425, wR2 = 0.1063	
R indices (all data)	R1 = 0.0615, wR2 = 0.1201	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.317 and -0.265 $e.Å^{-3}$	

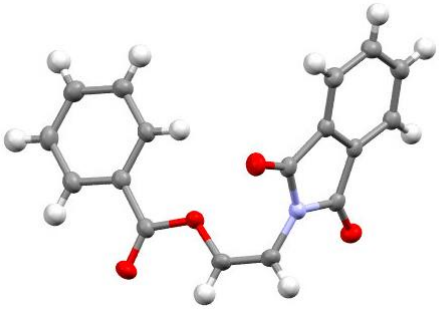


Table 3. Crystal data and structure refinement for ***Z*-11c**. Displacement ellipsoids are shown at the 50% probability level.

Identification code	CCDC 2180325	
Empirical formula	$C_{17}H_{11}NO_4$	
Formula weight	293.27	
Temperature	150(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 11.8563(4) Å	a= 90°.
	b = 13.8074(4) Å	b= 111.751(4)°.
	c = 8.8461(3) Å	g = 90°.
Volume	1345.04(8) $Å^3$	
Z	4	
Density (calculated)	1.448 Mg/m^3	
Absorption coefficient	0.870 mm^{-1}	
F(000)	608	
Crystal size	0.280 x 0.180 x 0.140 mm^3	
Theta range for data collection	4.014 to 62.580°.	
Index ranges	-13<=h<=13, -15<=k<=11, -7<=l<=10	
Reflections collected	5559	
Independent reflections	2132 [R(int) = 0.0262]	
Completeness to theta = 62.580°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.91601	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2132 / 0 / 200	
Goodness-of-fit on F^2	1.042	
Final R indices [I>2sigma(I)]	R1 = 0.0426, wR2 = 0.1155	
R indices (all data)	R1 = 0.0444, wR2 = 0.1177	
Extinction coefficient	0.0032(6)	
Largest diff. peak and hole	0.180 and -0.203 $e.Å^{-3}$	

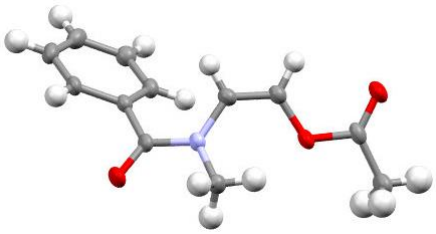


Table 3. Crystal data and structure refinement for ***Z*-12**. Displacement ellipsoids are shown at the 50% probability level.

Identification code	CCDC 2180326	
Empirical formula	$C_{12}H_{13}NO_3$	
Formula weight	219.23	
Temperature	150(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 7.5089(4) Å	a= 90°.
	b = 6.6411(4) Å	b= 106.354(6)°.
	c = 11.4915(8) Å	g = 90°.
Volume	549.87(6) $Å^3$	
Z	2	
Density (calculated)	1.324 Mg/m^3	
Absorption coefficient	0.790 mm^{-1}	
F(000)	232	
Crystal size	0.360 x 0.280 x 0.040 mm^3	
Theta range for data collection	4.009 to 62.599°.	
Index ranges	-8<=h<=8, -7<=k<=7, -13<=l<=11	
Reflections collected	2259	
Independent reflections	1457 [R(int) = 0.0357]	
Completeness to theta = 62.599°	98.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.50745	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1457 / 1 / 147	
Goodness-of-fit on F^2	1.050	
Final R indices [I>2sigma(I)]	R1 = 0.0537, wR2 = 0.1339	
R indices (all data)	R1 = 0.0555, wR2 = 0.1374	
Absolute structure parameter	0.0(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.244 and -0.269 $e.Å^{-3}$	

6 REFERENCES

[1] H. Ueda, M. Yamaguchi, H. Kameya, K. Sugimoto, H. Tokuyama, *Org. Lett.* **2014**, *16*, 4948.

[2] O. Chantarasriwong, B. Jiangchareon, C. K. Putra, W. Suwankrua, W. Chavasiri, *Tetrahedron Lett.* **2016**, *57*, 4807–4811.

[3] J. F. Hooper, S. Seo, F. R. Truscott, J. D. Neuhaus, M. C. Willis, *J. Am. Chem. Soc.* **2016**, *138*, 1630–1634.

[4] M. Marzi, D. Alloatti, G. Giannini, World Intellectual Property Patent WO 2004/005328 A2, **2004**.

[5] W. J. Greenlee, P. L. Allibone, D. S. Perlow, A. A. Patchett, E. H. Ulm, T. C. Vassil, *J. Med. Chem.* **1985**, *28*, 434-442.

[6] S.-C. Krieg, J. Grimmer, P. Kramer, M. Bolte, H. Kelm, G. Manolikakes, *Angew. Chem. Int. Ed.* **2021**, *60*, 23667–23671; *Angew. Chem.* **2021**, *133*, 23859–23864.

[7] P. S. Naidu, P. J. Bhuyan, *Tetrahedron Lett.* **2012**, *53*, 426–428.

[8] C. Bannwarth, E. Caldeweyher, S. Ehlert, A. Hansen, P. Pracht, J. Seibert, S. Spicher, S. Grimme, *Wiley Interdiscip. Rev.: Comput. Mol. Sci.* **2021**, *11*, e1493.

[9] a) S. Grimme, *J. Chem. Theory Comput.* **2019**, *15*, 2847–2862; b) P. Pracht, F. Bohle, S. Grimme, *Phys. Chem. Chem. Phys.* **2020**, *22*, 7169–7192.

[10] S. Spicher, S. Grimme, *Angew. Chem. Int. Ed.* **2020**, *59*, 15665–15673; *Angew.Chem.* **2020**, *132*, 15795–15803 .

[11] Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215–241.

[12] S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.* **2010**, *132*, 154104.

[13] A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378–6396.

[14] S. Grimme, *Chem. Eur. J.* **2012**, *18*, 9955–9964.

[15] R. F. Ribeiro, A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2011**, *115*, 14556–14562.

[16] a) F. Neese, A. Hansen, D. G. Liakos, *J. Chem. Phys.* **2009**, *131*, 064103; b) F. Neese, F. Wennmohs, A. Hansen, *J. Chem. Phys.* **2009**, *130*, 114108; c) C. Riplinger, B. Sandhoefer, A. Hansen, F. Neese, *J. Chem. Phys.* **2013**, *139*, 134101; d) C. Riplinger, F. Neese, *J. Chem. Phys.* **2013**, *138*, 034106.

[17] a) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297–3305; b) A. Hellweg, C. Hättig, S. Höfener, W. Klopper, *Theor. Chem. Acc.* **2007**, *117*, 587–597.

[18] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, Williams, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, D. J. Fox, Wallingford, CT, **2016**.

[19] a) F. Neese, *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2012**, *2*, 73–78; b) F. Neese, *Wiley Interdiscip. Rev. Comput. Mol. Sci.* **2018**, *8*, e1327.