ELECTRONIC SUPPORTING INFORMATION

Tetramethyl Orthosilicate (TMOS) as a Reagent for Direct Amidation of Carboxylic Acids

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Cover Page and Contents

CAUTION!!! TMOS CARRIES THE HAZARD CODE H330, MEANING IT IS FATAL IF INHALED.

General Experimental.

Reagents: Amines used were purchased from commercial sources, distilled under reduced pressure from CaH_2 and stored in Schlenk tubes over activated 4Å molecular sieves. Carboxylic acids were purchased from commercial sources and used without further purification. Tetramethylorthosilicate (TMOS) and tetraethylorthosilicate (TEOS) were purchased from commercial sources and used without further purification.

Solvents: Toluene (≥99.5% AnalaR NORMAPUR®), THF (≥99.5% AnalaR NORMAPUR®) and n-Hexane (≥95% GPR RECTAPUR®) were used as received.

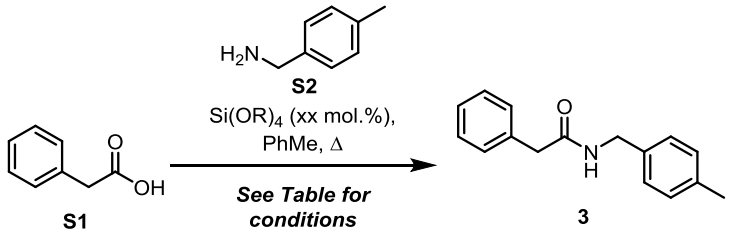
Experimental techniques: Reactions were carried out in triplicate under an inert atmosphere of nitrogen in standard 10 or 25 mL round bottomed flasks fitted with a reflux condenser and a Teflon coated stirrer bar. Reactions were simultaneously brought to reflux on a stirrer hotplate using three 10 or 25 mL DrySyn® heating blocks. All volatiles were removed *in vacuo* by rotary evaporation. Kieselgel-60 F254 pre-coated aluminium backed plates were used for analytical Thin Layer Chromatography visualised using UV light (254 nm) and chemical staining with potassium permanganate. 4Å molecular sieves were pre-activated in a glassware oven at 120 °C overnight.

Characterisation: IR spectra of were recorded on a ATR-IR spectrometer. ^{1}H NMR (400 MHz), ^{13}C NMR (101MHz) and ^{29}Si NMR (80 MHz) spectra were recorded in $CDCl_3$ at 298K on a Bruker AV-400 spectrometer. Chemical shifts (δ) are reported in ppm relative to solvent signals (δ = 7.26 and 77.16 ppm for $CDCl_3$). Coupling constants (*J*) are quoted in Hz. Abbreviations used for multiplicity are as follows: s – singlet, d – doublet, t – triplet, q – quartet, app. quint – apparent quintet, br – broad, m – multiplet. Melting points were measured using a Lambda Photometrics MPA 100 OptiMelt melting point apparatus and are uncorrected. High resolution mass spectra were recorded by the Imperial College Department of Chemistry Mass Spectrometry Service. Optical rotations $[\propto]_D^T$ are reported in

10^{-1} deg·cm^2·g^{-1}; concentrations (c) are quoted in g/100 mL; D refers to the D-line of sodium (589 nm); temperatures (T) are given in degrees Celsius (°C), (+) and (–) indicate the sign of the optical rotation. Chiral analytical HPLC was performed on a 25 cm × 4.6 mm ChiralPak AD or ODH column. All solvents for HPLC were HiPerSolv grade and used as received.

Optimization of TMOS loading.

Table 1. Orthosilicate mediated direct amidation of phenylacetic acid with 4-methylbenzylamine to give amide **3**.



Entry [a,b]	*Reagent*	*mol%*	*%Conversion*
1	-	-	11
2	TEOS	25	45
3	TEOS	100	70
4	TEOS	200	85
5	TMOS	25	52
6	TMOS	100	77
7	TMOS	200	**100 (100)**[c]

[a] Reaction conditions: toluene, reflux, 1h, N_2; [**S1**] = 0.2 M, [**S2**] = 0.2 M. [b] All reactions were performed in triplicate, the variation in observed percentage conversions are ±1%. [c] Figure in parentheses is % isolated yield after work-up.

Experimental Procedures and Characterizing Data for Compounds.

General Procedure 1 (**GP1**: 200 mol% TMOS amidations @ 0.2 M[†]).

Amine (2 mmol), carboxylic acid (2 mmol), toluene (9.4 mL) and tetramethylorthosilicate (592 μL, 4 mmol, 200 mol%) were charged into a 25 mL two-necked round bottomed flask fitted with a reflux condenser. This mixture was purged under a flow of nitrogen for 5 minutes after which the mixture was heated to reflux. Once complete, the volatiles were removed under reduced pressure, THF (10 mL) was added and the resulting solution was transferred to a separating funnel. Aqueous K_2CO_3 solution (30 mL, 0.3 M, 9 mmol) was added, then solid NaCl was added until saturation was observed. The resulting

two phase system was separated, the aqueous phase extracted with THF (2 x 15 mL), and the combined organics were dried over sodium sulphate, filtered and evaporated.

General Procedure 2 (**GP2**: 250 mol% TMOS amidations @ 0.5 $M^{\dagger}$).

Amine (5 mmol), carboxylic acid (5 mmol), toluene (8.15 mL) and tetramethylorthosilicate (1.85 mL, 12.5 mmol, 250 mol%) were charged into a 25 mL round bottomed flask fitted with a reflux condenser. This mixture was purged under a flow of nitrogen for 5 minutes after which the mixture was heated to reflux. Once complete, the volatiles were removed under reduced pressure, THF (25 mL) was added and the resulting solution was transferred to a separating funnel. Aqueous K_2CO_3 solution (75 mL, 0.3 M, 22.5 mmol) was added, then solid NaCl was added until saturation was observed. The resulting two phase system was separated, the aqueous phase was extracted with THF (2 x 10 mL), and the combined organics were dried over sodium sulphate, filtered and evaporated.

General Procedure 3 (**GP3**: 250 mol% TMOS amidations @ 2.0 $M^{\dagger}$ with azeotropic removal of methanol).

Amine (10 mmol), carboxylic acid (10 mmol), toluene (1.31 mL) and tetramethylorthosilicate (3.69 mL, 25 mmol, 250 mol%) were charged into a 10 mL round bottomed flask fitted with a reflux condenser attached to a B14-B19 adapter loosely filled with glass wool and 1g of activated 4Å molecular sieves. This mixture was purged under a flow of nitrogen for 5 minutes after which the mixture was heated to reflux. Once complete, the mixture was transferred to a separating funnel, diluted with THF (50 mL), and aqueous K_2CO_3 solution (150 mL, 0.3 M, 45 mmol) was added. Solid NaCl was added until saturation was observed, the resulting two phase system was separated, the aqueous phase was extracted with THF (2 x 15 mL), and the combined organics were dried over sodium sulphate, filtered and evaporated.

General procedure 4 (**GP4**: Mole scale preparation, 250 mol% TMOS amidation @ 2.0 M[†] with fractional distillation of methanol).

Amine (1 mole), carboxylic acid (1 mole), toluene (131 mL) and tetramethylorthosilicate (369 mL, 2.5 moles, 250 mol%) were charged into a 1 L round bottomed flask fitted with a Vigreux column, thermometer, take-off adaptor, condenser and a 100 mL receiver flask. This mixture was purged under a flow of nitrogen for 5 minutes after which the mixture was heated to reflux. Once complete, the reaction mixture was diluted with THF (1.5 L), and aqueous K_2CO_3 solution (2000 mL, 2.89 M, 5.79 moles) was added. This mixture was stirred at room temperature for 4 hours, filtered through a course frit and the solids were washed with THF (2 x 100 mL). The organics were removed *in vacuo* and the resulting solid was dissolved inCH_2Cl_2 (1 L) and transferred to a separating funnel containing water (1 L). The resulting two phase sytem was separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 100 mL). The organics were combined, dried over magneisum sulphate, filtered and evaporated.

Modified work-up Procedure A (W/U A) for removal of aliphatic amines from incomplete amidations.

To the combined organics was added aqueous HCl solution (10 mL, 1.0 M, 10 mmol), and the aqueous phase was saturated with solid NaCl. The layers were separated, the aqueous phase was extracted with THF (2 x 10 mL), the combined organics were diluted with CH_2Cl_2 (15 mL), dried over sodium sulphate, filtered and evaporated.

Modified work-up procedure B (W/U B) for removal of aliphatic amines from incomplete amidations.

To the combined organics was added aqueous HCl solution (30 mL, 1.0 M, 30 mmol), and the aqueous phase was saturated with solid NaCl. The layers were separated, the aqueous phase was extracted with THF (2 x 15 mL), the combined organics were diluted with CH_2Cl_2 (30 mL), dried over sodium sulphate, filtered and evaporated.

Modified work-up procedure C (W/U C) for removal of anilines from incomplete amidations.

Following either GP2, GP3 or GP4 after evaporation, the impure amide was triturated with hexane, 3 x 10 mL.

Photos of resulting two-phase system post addition of solid NaCl

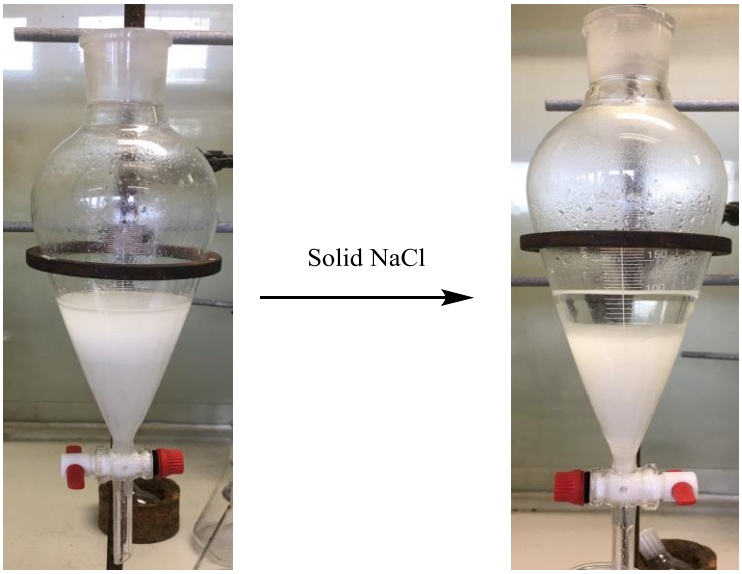
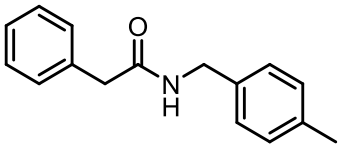


Figure 2 – After addition of aqueous K_2CO_3 to post-reaction mixture

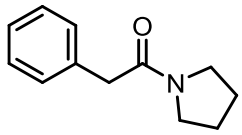
Figure 1 - Post addition of solid NaCl and the resulting two-phase system

***N*-(4-Methylbenzyl)-2-phenylacetamide (3)**



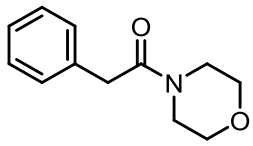
Following **GP1** amide **3** (478 mg, 100%) was isolated as a white solid: R_f = 0.61 (EtOAc); m.p. 139.0 - 139.3°C, ATR-FTIR ν_{max}/cm^{-1} 3236, 1636; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 2H), 7.31 – 7.26 (m, 3H), 7.12 – 7.07 (m, 4H), 5.93 (br s, 1H), 4.36 (d, *J* = 5.7 Hz, 2H), 3.59 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 137.2, 135.2, 135.0, 129.5, 129.4, 129.1, 127.6, 127.4, 43.9, 43.4, 21.1.; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{16}H_{18}NO$ 240.1388, Found 240.1395.

2-Phenyl-1-(pyrrolidin-1-yl)ethan-1-one (4)



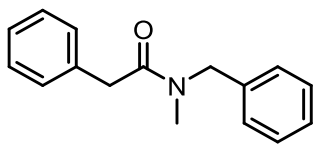
Following **GP1** compound **4**[1] (371 mg, 98%) was isolated as a colourless oil: R_f = 0.37 (EtOAc); ATR-FTIR ν_{max}/cm^{-1} 1642; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.25 – 7.21 (m, 3H), 3.71 (s, 2H), 3.62 (s, 4H), 3.46 – 3.44 (m, 2H), 3.42 – 3.39 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 134.8, 128.8, 128.6, 126.9, 66.8, 66.5, 46.5, 42.2, 40.9; HRMS (ES$^+$, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{12}H_{16}NO$ 190.1232, Found 190.1240.

1-Morpholino-2-phenylethan-1-one (5)



Following **GP1** compound **5** (394 mg, 96%) was isolated as a white solid: R_f = 0.36 (EtOAc); m.p. 66.4 - 67.6 °C, (lit. m.p. 65 – 67 °C)[2]; ATR-FTIR ν_{max}/cm^{-1} 1642; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 2H), 7.21 – 7.14 (m, 3H), 3.65 (s, 2H), 3.55 (s, 4H), 3.40 – 3.37 (m, 2H), 3.35 – 3.32 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 134.6, 128.5, 128.3, 126.6, 66.5, 66.2, 46.2, 41.9, 40.5; HRMS (ES$^+$, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{12}H_{16}NO_2$ 206.1181, Found 206.1187.

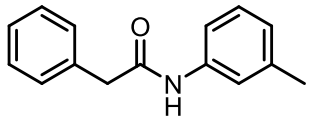
***N*-Benzyl-*N*-methyl-2-phenylacetamide (6)**



Following **GP1** and **W/U A** compound **6**[3] (388 mg, 81%) was isolated as a colourless oil: R_f = 0.60 (EtOAc); ATR-FTIR ν_{max}/cm^{-1} 1637; ^{1}H NMR (400 MHz, $CDCl_3$, mixture of two rotamers 1.4:1) δ (Major rotamer) 7.36 – 7.09 (m, 10H), 4.61 (s, 2H), 3.78 (s, 2H), 2.90 (s, 3H). (Minor rotamer) 7.36 – 7.09 (m, 10H), 4.52 (s, 2H), 3.75 (s, 2H), 2.95 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 171.2,

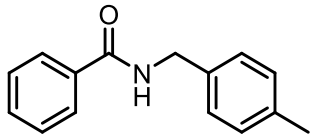
137.4, 136.6, 135.2, 135.1, 129.0, 128.9, 128.9, 128.8, 128.7, 128.2, 127.8, 127.5, 126.9, 126.9, 126.5, 53.8, 51.1, 41.3, 41.0, 35.3, 34.1; HRMS (ES^+, TOF): m/z $[M+H]^+$ calcd. For $C_{16}H_{18}NO$ 240.1388, Found 240.1384.

2-Phenyl-*N*-(*m*-tolyl)acetamide (7)



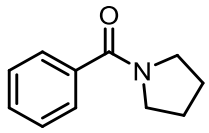
Following **GP2** and **W/U C** compound **7** (946 mg, 84%) was isolated as a white solid: R_f = 0.73 (EtOAc); m.p. 86.7 – 87.0 °C, (lit. m.p. 85 – 87 °C)[4]; ATR-FTIR ν_{max}/cm^{-1} 3285, 1656; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.38 (m, 2H), 7.35 – 7.32 (m, 3H), 7.27 (s, 1H), 7.21-7.12 (m, CON-H, Ar-H, 3H), 6.90 (d, *J* = 7.1 Hz, 1H), 3.73 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 139.0, 137.7, 134.6, 129.6, 129.4, 128.9, 127.8, 125.4, 120.6, 117.0, 45.0, 21.6; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{15}H_{16}NO$ 226.1232, Found 226.1227.

***N*-(4-Methylbenzyl)benzamide (8)**



Following **GP1** compound **8** (441mg, 98%) was isolated as a white solid: R_f = 0.66 (EtOAc); m.p. 139.7-140.1 °C (lit. m.p. 140-141 °C)[5]; ATR-FTIR ν_{max}/cm^{-1} 3306, 1631; ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.77 (m, 2H), 7.51 – 7.46 (m, 1H), 7.42-7.38 (m, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.60 (br s, 1H), 4.58 (d, *J* = 5.6 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 137.4, 135.3, 134.6, 131.5, 129.5, 128.6, 128.0, 127.1, 44.0, 21.2; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{15}H_{16}NO$ 226.1232, Found 226.1243.

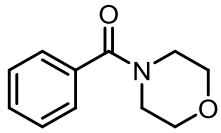
Phenyl(pyrrolidin-1-yl)methanone (9)



Following **GP1** compound **9**[6] (343 mg, 98%) was isolated as a colourless oil: R_f = 0.45 (EtOAc); ATR-FTIR ν_{max}/cm^{-1} 1615; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.45 (m, 2H), 7.49 – 7.32 (m, 3H), 3.61 (t, *J* = 7.0 Hz, 2H), 3.38 (t, *J* = 6.6 Hz, 2H), 1.94 (app. quint, *J* = 6.5 Hz, 2H), 1.83 (app. quint, *J* = 6.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 137.1, 129.7, 128.2, 127.0, 49.5, 46.1, 26.3, 24.4; HRMS (ES$^+$, TOF): *m*/*z* [M+H]$^+$ calcd. for $C_{11}H_{14}NO$ 176.1075, Found 176.1072.

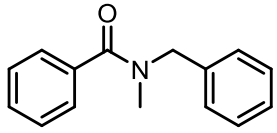
Following **GP4** compound **9** (157.8 g, 90%), isolated as an orange/brown oil: spectroscopic data for compound **9** as above.

Morpholino(phenyl)methanone (10)



Following **GP1** compound **10** (367 mg, 96%) was isolated as a white solid: R_f = 0.44 (EtOAc); m.p. 73.0-74.2 °C (lit. m.p. 73-75 °C)[7]; ATR-FTIR ν_{max}/cm^{-1} 1621; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.39 (m, 5H), 3.85 – 3.35 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 135.4, 130.0, 128.7, 127.2, 67.0, 48.3, 42.7; HRMS (ES$^+$, TOF): *m*/*z* [M+H]$^+$ calcd. for $C_{11}H_{14}NO_2$ 192.1025, Found 192.1034.

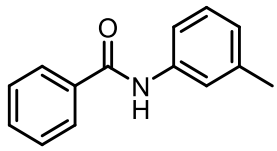
***N*-Benzyl-*N*-methylbenzamide (11)**



Following **GP3** and **W/U B** compound **11**[8] (1.98 g, 88%) was isolated as a colourless oil: R_f = 0.60 (EtOAc); ATR-FTIR ν_{max}/cm^{-1} 1629; ^{1}H NMR (400 MHz, $CDCl_3$, Mixture of rotamers 1:1) δ 7.47 –

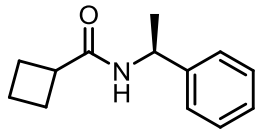
7.26 (m, 18H), 7.17 (bs, 2H) 4.76 (s, 2H), 4.51 (s, 2H), 3.03 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$, Mixture of rotamers) δ 172.0, 171.3, 136.9, 136.5, 136.1, 129.4, 128.6, 128.2, 128.0, 127.4, 126.8, 126.7, 54.9, 50.6, 36.8, 33.0; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{15}H_{16}NO$ 226.1232, Found 226.1232.

_N_-(_m_-Tolyl)benzamide (12)



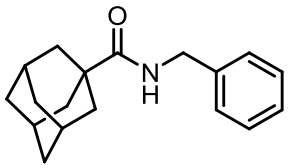
Following a modified **GP3** using two equivalents of benzoic acid and **W/U C** compound **12** (2.11 g, 100%) was isolated as a white solid: R_f = 0.71 (EtOAc); m.p. 124.3 °C - 124.8 °C (lit. m.p. 124-125 °C)[9]; ATR-FTIR ν_{max}/cm^{-1} 3261, 1646; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.85 (m, 3H, Ar-H, CON-H), 7.57 – 7.52 (m, 1H), 7.51 (bs, 1H), 7.50-7.45 (m, 2H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.25 (t, *J* = 7.8 Hz, 1H), 6.98 – 6.96 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 139.2, 138.0, 135.2, 131.9, 129.0, 128.9, 127.1, 125.5, 121.0, 117.4, 21.6. HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{14}H_{14}NO$ 212.1075, Found 212.1075.

(_S_)-N-(1-Phenylethyl)cyclobutanecarboxamide (14)



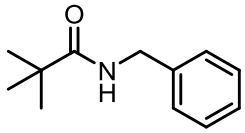
Following **GP1** on a 1 mmol scale yielded compound **14** (203 mg, 100%) as a white solid: R_f = 0.36 (Petroleum ether : EtOAc, 1:1); m.p. 119 – 120°C; $[\alpha]_D^{20}$= -107 (c 0.54, $CHCl_3$); ATR-FTIR ν_{max}/cm^{-1} 3297, 1639; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.24 (m, 5H), 5.53 (s, 1H), 5.13 (app. quint, *J* = 7.1 Hz, 1H), 2.98 (app. quintet, *J* = 8.6, 1H), 2.33 – 2.21 (m, 2H), 2.19 – 2.07 (m, 2H), 2.00 – 1.81 (m, 2H), 1.48 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 143.5, 128.8, 127.5, 126.3, 48.6, 40.1, 25.4, 25.4, 21.9, 18.3; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{13}H_{18}NO$ 204.1388, Found 204.1387.

***N*-Benzyl-(1-adamantane)-carboxamide (15)**



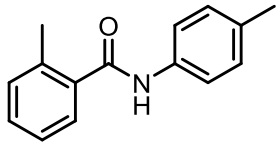
Following **GP1** and **W/U A** compound **15** (483 mg, 90%) was isolated as a white solid: R_f = 0.66 (EtOAc); m.p. 169.7-170.0 °C (lit. m.p. 169-171 °C)[10]; ATR-FTIR ν_{max}/cm^{-1} 3339, 1631; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.24 (m, 5H), 5.86 (s, 1H), 4.44 (d, *J* = 5.6 Hz, 2H), 2.04 (s, 3H), 1.89 (s, 6H), 1.76 – 1.68 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.9, 138.9, 128.8, 127.8, 127.5, 43.5, 40.8, 39.5, 36.7, 28.3; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. For $C_{18}H_{24}NO$ 270.1858, Found 270.1869.

***N*-Benzylpivalamide** (**16**)



Following **GP1** compound **16** (384 mg, 99%) was isolated as a white solid: R_f = 0.75 (EtOAc); m.p. 81-82°C (lit. m.p. 80-82°C)[11]; ATR-FTIR ν_{max}/cm^{-1} 3297, 1633; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 5H), 6.12 (s, 1H), 4.40 (d, *J* = 5.6 Hz, 2H), 1.21 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.4, 138.8, 128.7, 127.6, 127.3, 43.5, 38.7, 27.6; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. For C_{12} $H_{18}NO$ 192.1388, Found 192.1390.

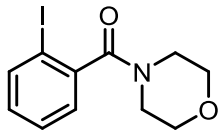
2-Methyl-*N*-(*p*-tolyl)benzamide (17)



Following **GP3** using two equivalents of *o*-toluic acid compound **17** (1.58 g, 78%) was isolated as a white solid: R_f = 0.85 (EtOAc); m.p. 143-144 °C (lit. m.p. 143.5-144 °C)[12]; ATR-FTIR ν_{max}/cm^{-1} 3226, 1651; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (bs, N-*H*, 1H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 7.6 Hz,

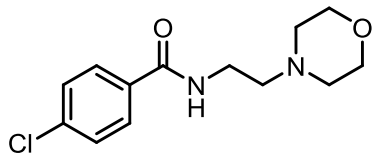
1H), 7.32m, 1H), 7.22 – 7.12 (m, 4H), 2.43 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 136.5, 136.3, 135.6, 134.0, 131.1, 130.0, 129.5, 126.7, 125.7, 120.1, 20.9, 19.8; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{15}H_{16}NO$ 226.1232, Found 226.1231.

(2-Iodophenyl)(morpholino)methanone (18)



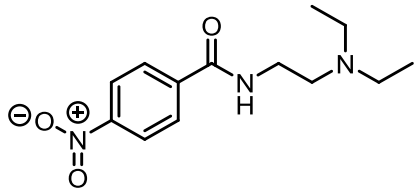
Following **GP1** on a 0.4 mmol scale compound **18** (110 mg, 87%) was isolated as a light brown solid: R_f = 0.20 (Petroleum ether : EtOAc, 1:1); m.p. 71-74 °C (lit. m.p.82-83 °C)[13]; ATR-FTIR ν_{max}/cm^{-1} 1637; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.40 (td, *J* = 7.5, 1.1 Hz, 1H), 7.20 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.09 (ddd, *J* = 8.0, 7.5, 1.7 Hz, 1H), 3.90 – 3.74 (m, 5H), 3.62 – 3.56 (m, 1H), 3.23 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 141.9, 139.4, 130.5, 128.6, 127.2, 92.6, 66.9, 66.8, 47.4, 42.1; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{11}H_{13}NO_2{}^{127}I$ 317.9991, Found 317.9948.

4-Chloro-*N*-(2-morpholinoethyl)benzamide (19)



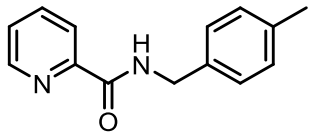
Following **GP1** compound **19** (536 mg, 100%) was isolated as a white solid: R_f = 0.60 (CH_2Cl_2: MeOH, 9:1); m.p. 136.1-136.7 °C (lit. m.p. 134-136 °C)[7]; ATR-FTIR ν_{max}/cm^{-1} 3277, 1636; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.6 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 2H), 6.77 (br s, 1H), 3.73 – 3.70 (m, 4H), 3.53 (q, *J* = 5.8 Hz, 2H), 2.59 (t, *J* = 6.0 Hz, 2H), 2.50 – 2.48 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 137.7, 133.1, 128.9, 128.5, 67.1, 56.9, 53.4, 36.2; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{13}H_{18}{}^{35}ClN_2O_2$ 269.1057, Found 269.1062.

***N*-(2-(Diethylamino)ethyl)-4-nitrobenzamide (20)**



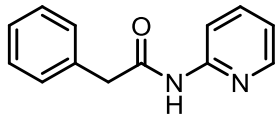
Following **GP1**, compound **20**[14] (525 mg, 99%) was isolated as a viscous yellow oil: R_f 0.33 (CH_2Cl_2 : MeOH, 9:1); ATR-FTIR ν_{max}/cm^{-1} 3316, 1647; ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.9 Hz, 2H), 7.91 (d, *J* = 8.9 Hz, 2H), 7.47 (br s, 1H), 3.44 (q, *J* = 5.4 Hz, 2H), 2.61 – 2.58 (m, 2H), 2.50 (q, *J* = 7.1 Hz, 4H), 0.96 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 149.3, 140.2, 128.1, 123.6, 51.3, 46.7, 37.6, 11.7; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{13}H_{20}N_3O_3$ 266.1505, Found 266.1510.

***N*-(4-Methylbenzyl)picolinamide (21)**



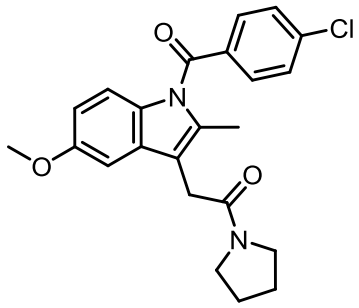
Following **GP1** on a 0.81 mmol scale compound **21** (153 mg, 84%) was isolated as a yellow solid. R_f = 0.6 (1:1 PE:EtOAc); m.p. 79 – 81 °C (lit m.p. 83 – 84 °C)[15] ; ATR-FTIR ν_{max}/cm^{-1} 3382, 1669 ; ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 8.36 (brs, 1H), 8.26 (*app* dt, *J* = 7.8, 1.1 Hz, 1H), 7.87 (td, *J* = 7.8, 1.8 Hz, 1H), 7.44 (ddd, *J* = 7.8, 4.8, 1.2 Hz, 1H) , 7.29 (d, *J* = 7.8 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 4.65 (d, *J* = 6 Hz, 2H), 2.36 (s, 3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 149.9, 148.1, 137.3, 137.2, 135.2, 129.4, 127.9, 126.2, 122.3, 43.3, 21.2; HRMS (ES^+, TOF): *m*/*z* *z* $[M+H]^+$ calcd. for $C_{14}H_{15}N_2O$ 227.1184, Found 227.1185.

2-Phenyl-*N*-(pyridin-2-yl)acetamide (22)



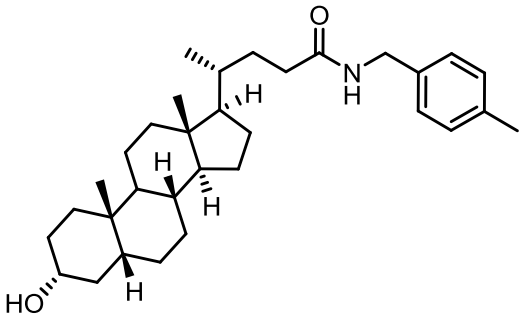
2-Aminopyridine (1.06 mmol, 100 mg), phenylacetic acid (2.12 mmol, 228 mg) and TMOS (2.65 mmol, 391 μL) were refluxed in toluene (2 mL) for 16 h. After such time the reaction mixture was worked up as described in **GP1** to yield an oily brown solid, and the crude product was trituated with cold Et_2O (x3) to yield **22** (120 mg, 53%) as a light brown solid. R_f = 0.6 (1:1 PE:EtOAc); m.p 116 – 117 °C (lit m.p (121 – 122 °C)[2]; ATR-FTIR ν_{max}/cm^{-1} 3236, 1660; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 8.20 (m, 2H), 7.92 (br s, 1H), 7.69 (m, 1H), 7.41 – 7.30 (m, 5H), 7.03 – 6.99 (m, 1H), 3.76 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 151.3, 147.9, 138.5, 134.0, 129.6, 129.4, 127.9, 120.1, 114.1, 45.2; HRMS (ES^+, TOF): *m/z* $[M+H]^+$ calcd. for $C_{13}H_{13}N_2O$ 213.1028, found 213.1021.

2-(1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)-1-(pyrrolidin-1-yl)ethan-1-one (23)



Following **GP1** on a 0.28 mmol scale compound **23** (98 mg, 86%) was isolated as a white solid: R_f = 0.27 (Petroleum ether : EtOAc, 1:1); m.p. 159 – 160 °C; ATR-FTIR ν_{max}/cm^{-1} 1682, 1637; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.06 (d, *J* = 2.5 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 1H), 6.64 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.83 (s, 3H), 3.66 (s, 2H), 3.52 – 3.47 (m, 4H), 2.39 (s, 3H), 2.01 – 1.94 (m, 2H), 1.89 – 1.82 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 168.5, 156.1, 139.3, 135.4, 134.1, 131.3, 131.1, 131.0, 129.2, 114.9, 113.4, 111.7, 101.9, 55.9, 47.0, 46.3, 31.7, 26.5, 24.4, 13.7; HRMS (ES^+, TOF): *m/z* $[M+H]^+$ calcd. for $C_{23}H_{24}N_2O_3Cl$ 411.1475, Found 411.1460.

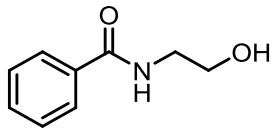
(4*R*)-4-((3*R*,5*R*,8*R*,10*S*,13*R*,14*S*,17*R*)-3-Hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(4-methylbenzyl)pentanamide (24)



Lithocholic acid (100 mg, 0.27 mmol), 4-methylbenzylamine (34 µl, 0.27 mmol) and TMOS (159 µl, 1.08 mmol) were refluxed in PhMe (1 ml) for 5 h. After such time TLC analysis showed complete consumption of the starting materials and the appearance of a new product spot (R_f = 0.73, 50:50 PE:EtOAc). Upon cooling to room temperature, the reaction material was concentrated under reduced pressure and the crude material was taken up in 4 ml of a 1:1 vol. solution of THF:1 M $NaOH_{(aq)}$. After stirring this mixture for 16 hours TLC analysis showed complete consumption of the spot at R_f 0.73 and the appearance of a new spot. This reaction mixture was worked up by saturation of the aqueous phase with $NaCl_{(s)}$ followed by collection of the clear THF organic phase. The organic phase was dried and concentrated to yield compound **24** (120 mg, 93%), as a white solid. R_f = 0.33 (1:1 PE:EtOAc); m.p. 222 – 223 °C; $[\alpha]_D^{20}$ = +104 (c 0.26, $CHCl_3$); ATR-FTIR ν_{max}/cm^{-1} 3416, 3351, 1638; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (t, *J* = 6.0 Hz, 1H), 7.11 (s, 4H), 4.46 (d, *J* = 4.5 Hz, 1H), 4.20 – 4.17 (m, 2H), 3.41 – 3.32 (m, 1H), 2.26 (s, 3H), 2.18 – 1.99 (m, 2H), 1.92 (d, *J* = 10.2 Hz, 1H), 1.85 – 1.48 (m, 8H), 1.37 – 1.29 (m, 7H), 1.24 – 0.97 (m, 10H), 0.89 (s, 3H), 0.87 (s, 3H), 0.60 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.5, 136.8, 135.7, 128.8, 127.2, 69.9, 56.1, 55.6, 42.3, 41.7, 41.6, 40.2[1], 39.5[1], 36.3, 35.4, 35.2, 34.9, 34.3, 32.4, 31.6, 30.5, 27.8, 26.9, 26.2, 23.9, 23.3, 20.7, 20.5, 18.3, 11.9; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{32}H_{50}NO_2$ 480.3842, Found 480.3839.

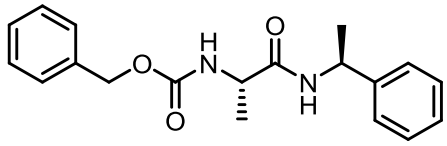
[1] Resonances overlapped with the DMSO solvent peak, they were assigned through $^1J_{CH}$ ^{1}H-^{13}C HSCQ correlations.

***N*-(2-Hydroxyethyl)benzamide (25)**



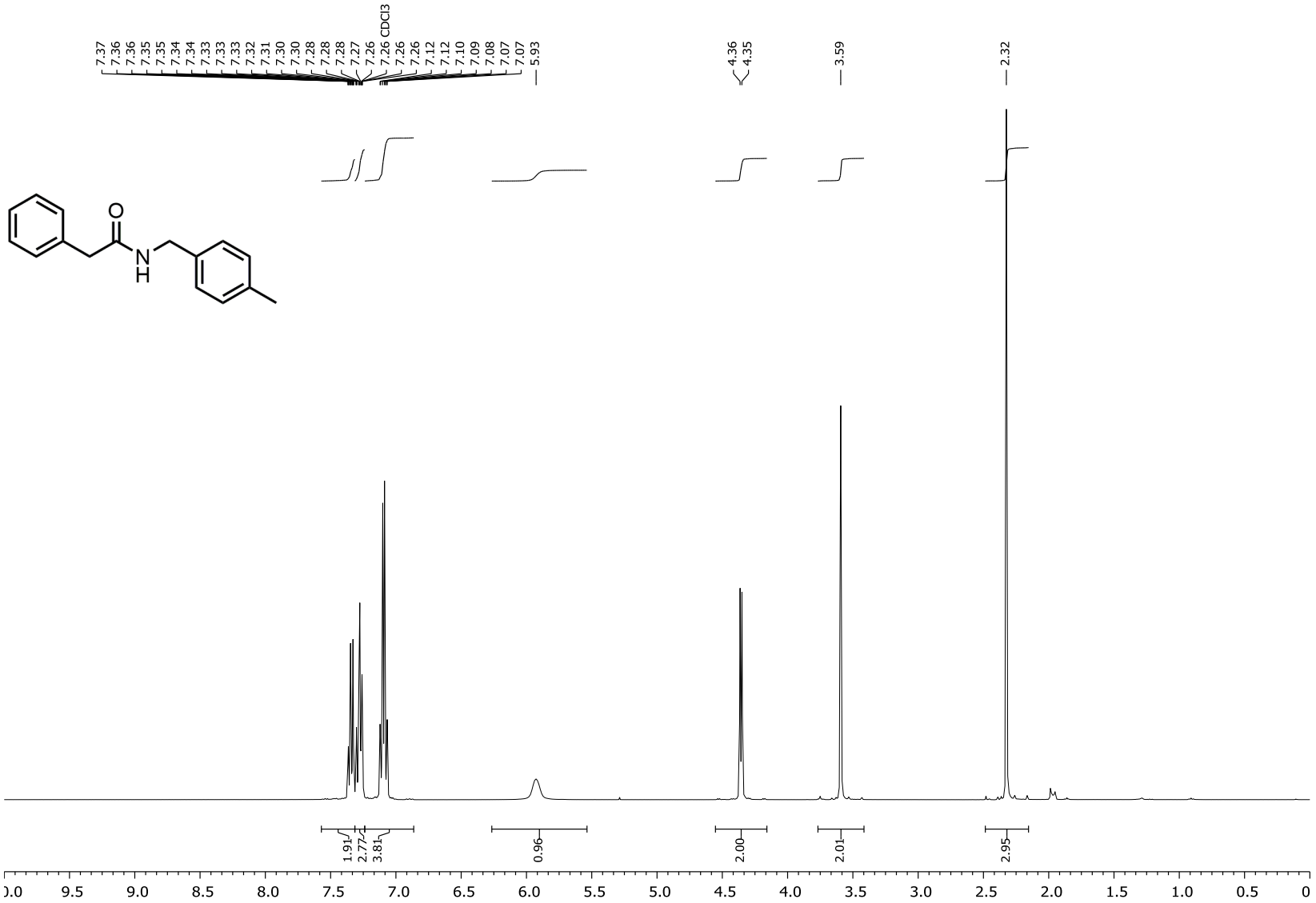
Following **GP1** compound **25** (264 mg, 80%) was isolated as a white solid: R_f = 0.29 (EtOAc); m.p. 59.7 – 60.5 °C (lit. m.p. 60 °C)[16]; ATR-FTIR ν_{max}/cm^{-1} 3314, 1633; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 2H), 7.46 (tt, *J* = 6.8, 1.2 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.24 (br s, 1H), 4.04 (s, 1H), 3.72 (s, 2H), 3.54 (q, *J* = 5.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 134.1, 131.7, 128.6, 127.1, 61.8, 42.9; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_9H_{12}NO_2$ 166.0868, Found 166.0866.

Benzyl ((*S*)-1-oxo-1-(((*S*)-1-phenylethyl)amino)propan-2-yl)carbamate (26)

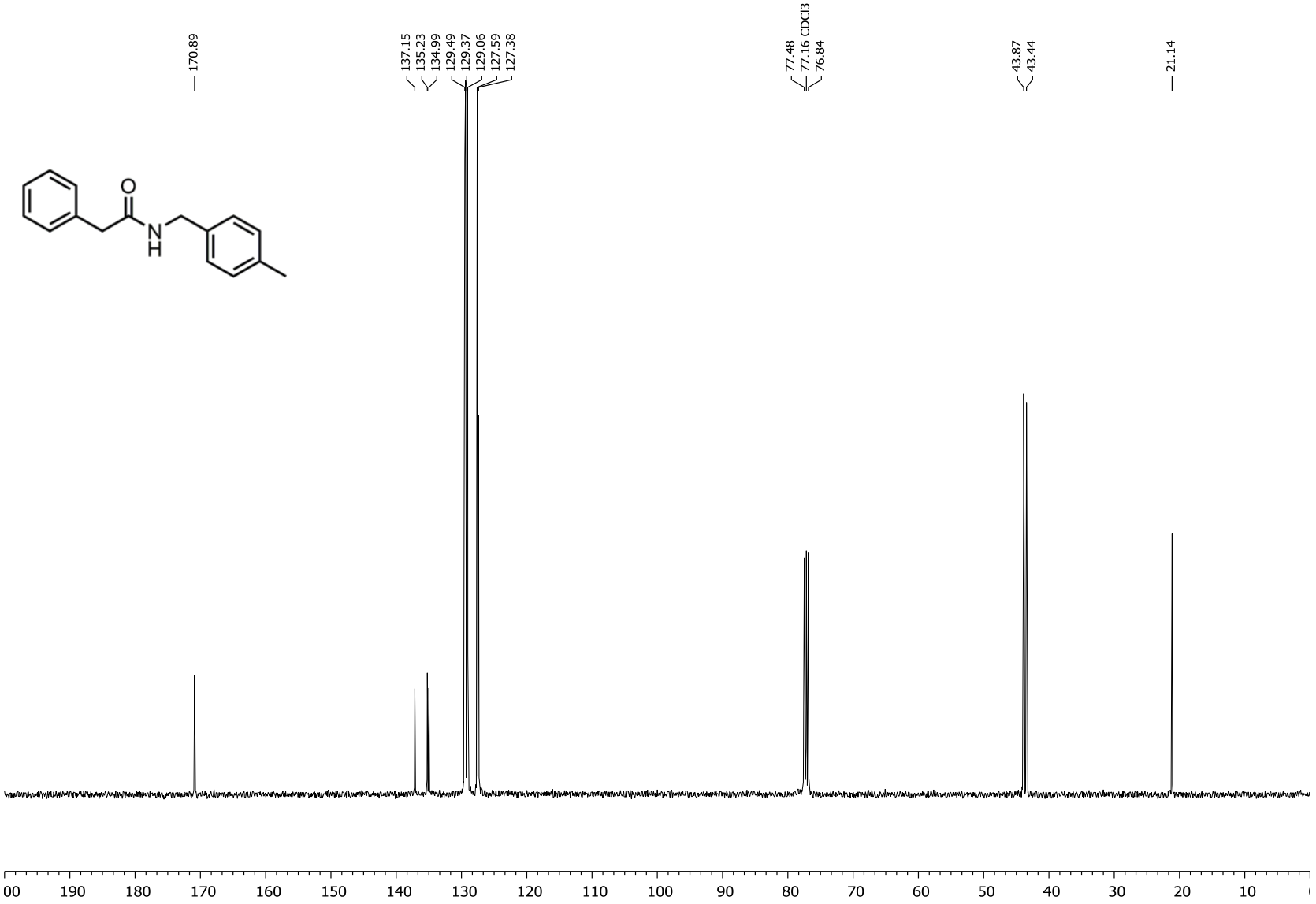


Following **GP1** on a 0.53 mmol scale compound **26** (150 mg, 87%) was isolated as a white solid: R_f = 0.52 (Petroleum ether : EtOAc, 1:1); m.p. 150 – 151 °C; ATR-FTIR ν_{max}/cm^{-1} 3298,1646; $[\alpha]_D^{20}$= -36 (c 0.26, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 10H), 6.56 (bs, 1H), 5.49 (bs, 1H), 5.11 – 5.04 (m, 3H), 4.28 – 4.23 (m, 1H), 1.44 (d, *J* = 6.9 Hz, 3H), 1.35 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 156.2, 143.1, 136.3, 128.8, 128.7, 128.4, 128.1, 127.5, 126.1, 67.1, 50.7, 48.9, 22.0, 18.8; HRMS (ES^+, TOF): *m*/*z* $[M+H]^+$ calcd. for $C_{19}H_{23}N_2O_3$ 327.1709, Found 327.1709.

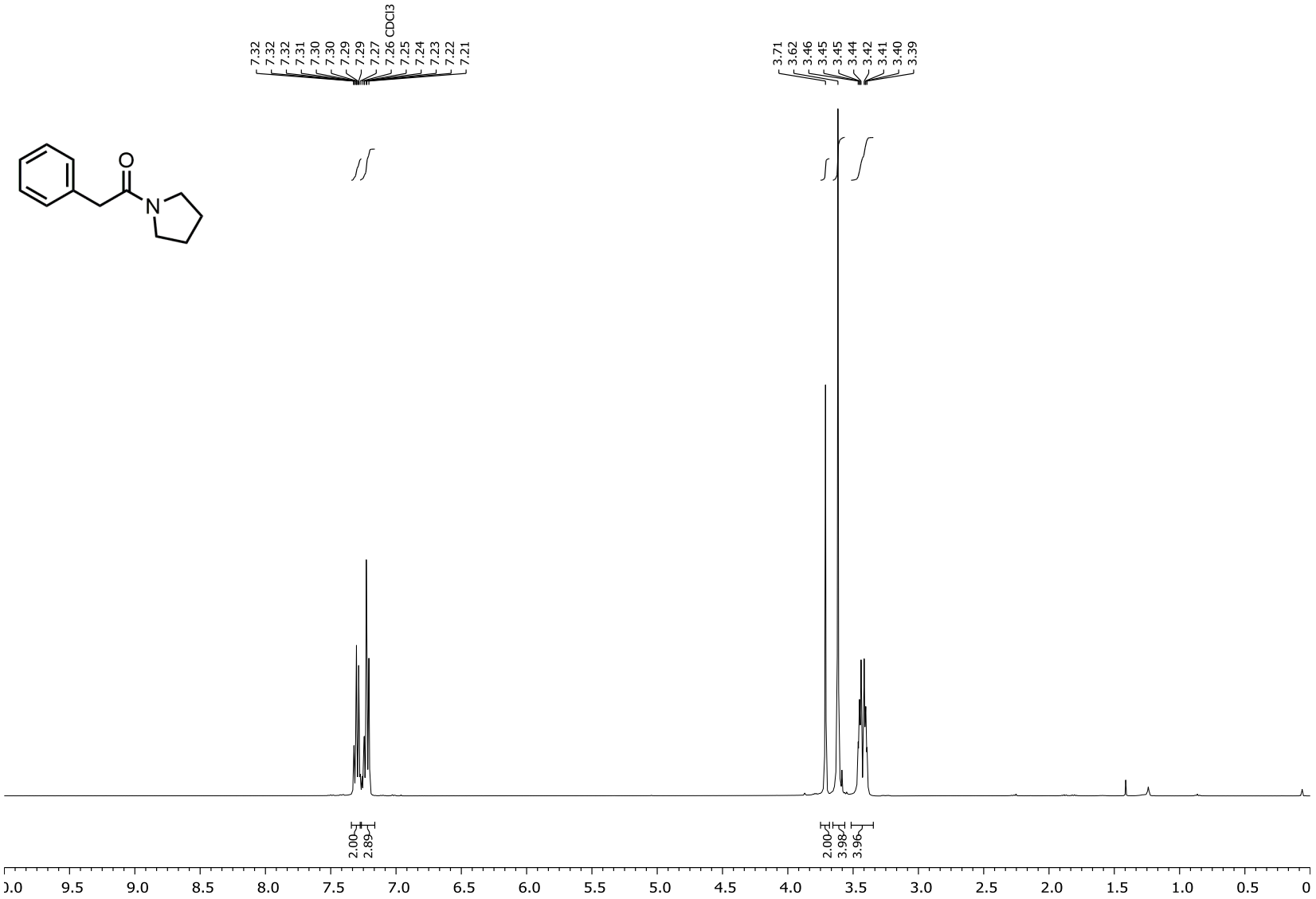
^{1}H NMR spectrum of *N*-(4-methylbenzyl)-2-phenylacetamide (**3**) (400 MHz, $CDCl_3$)



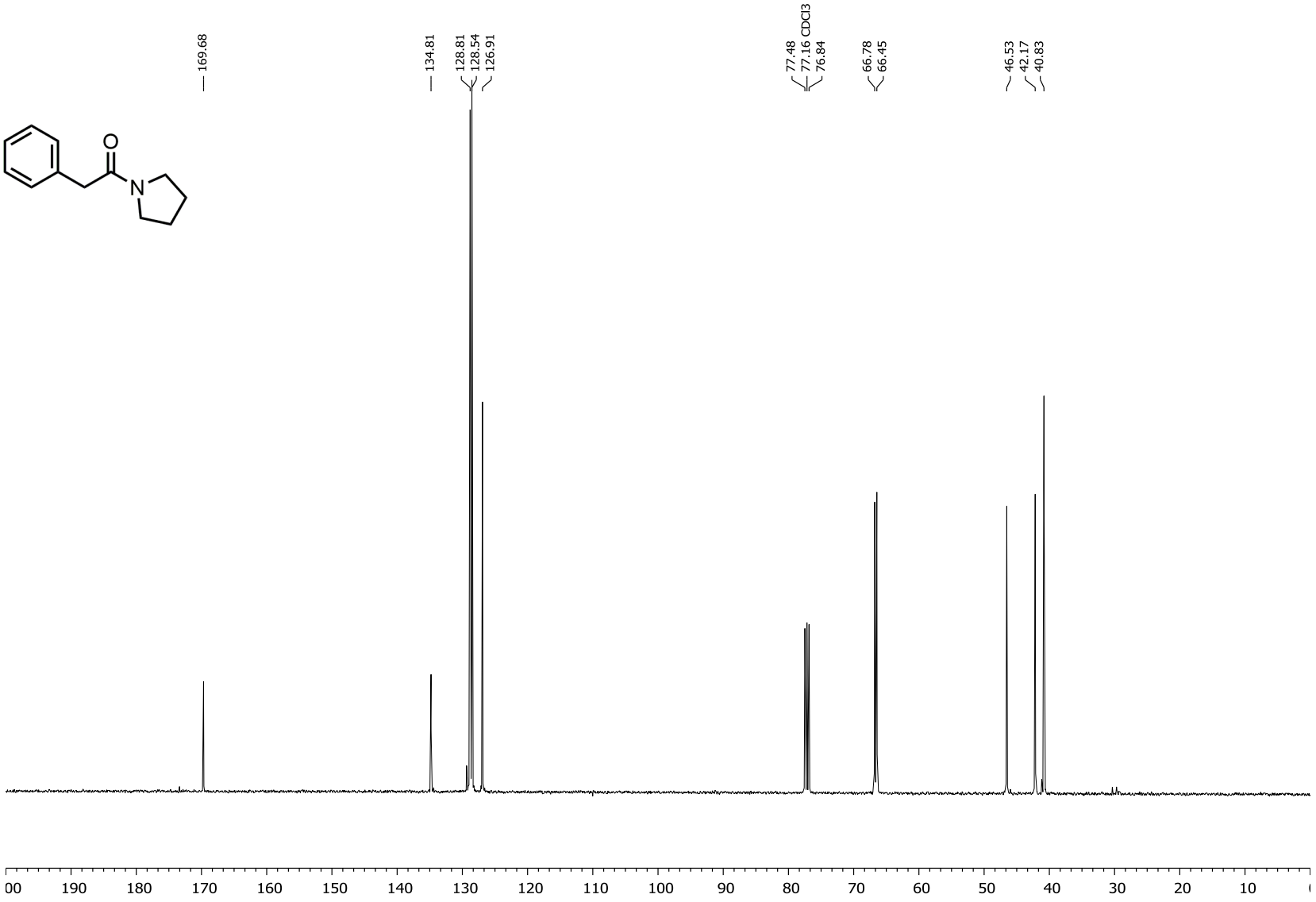
^{13}C NMR spectrum of of *N*-(4-methylbenzyl)-2-phenylacetamide (**3**) (101 MHz, $CDCl_3$)



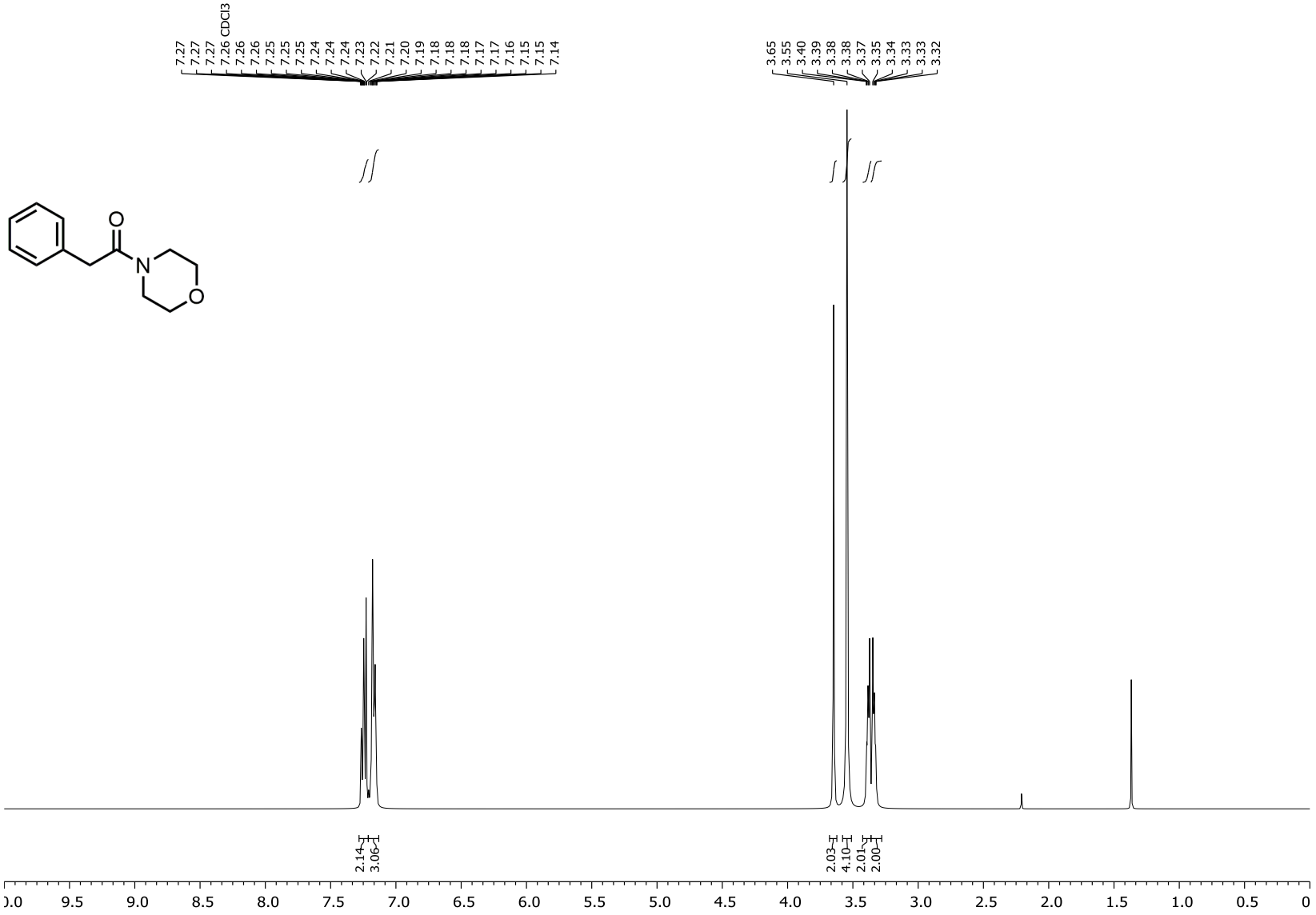
^{1}H NMR spectrum of 2-phenyl-1-(pyrrolidin-1-yl)ethan-1-one (**4**) (400 MHz, $CDCl_3$)



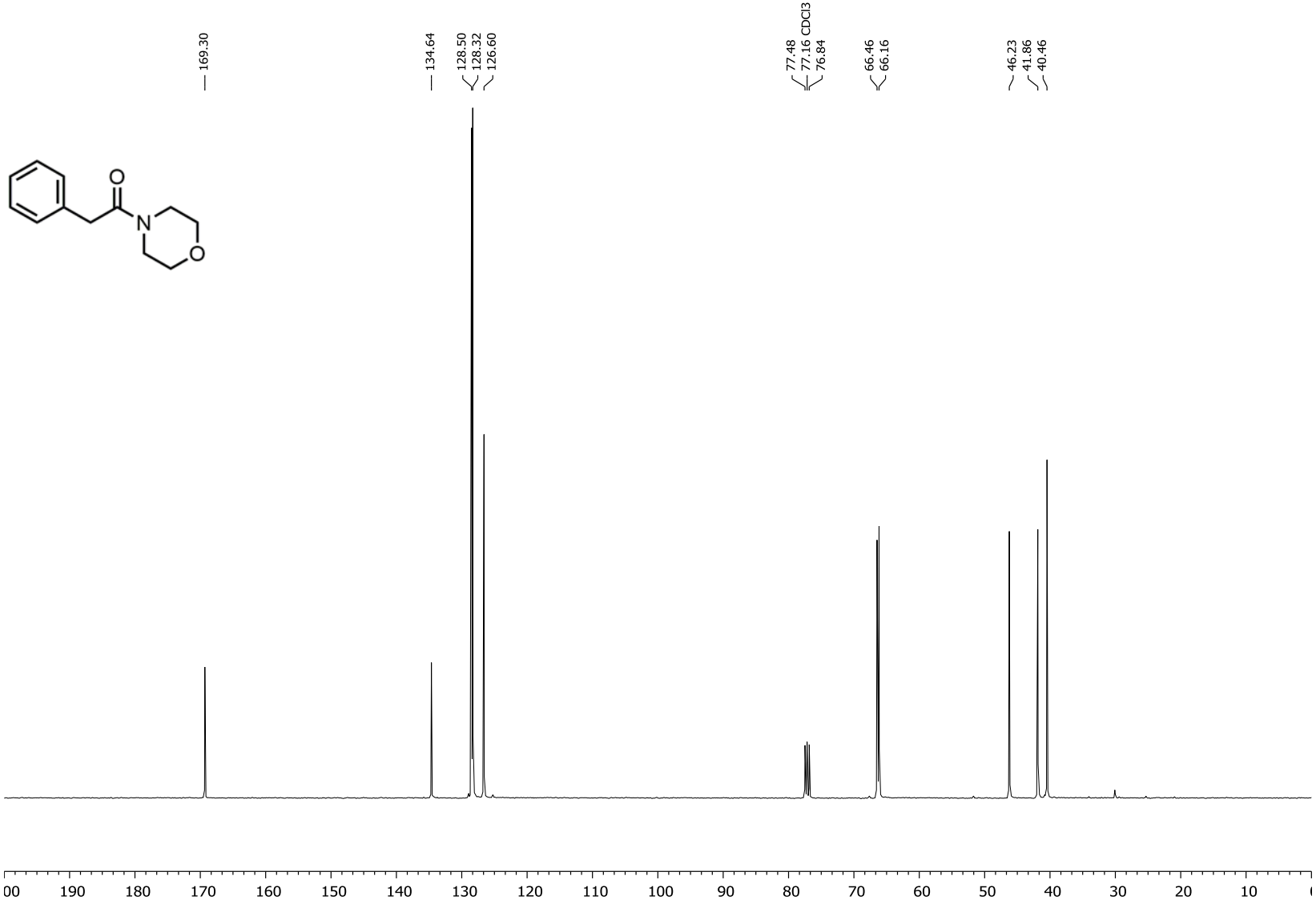
^{13}C NMR spectrum of 2-phenyl-1-(pyrrolidin-1-yl)ethan-1-one (**4**) (101 MHz, $CDCl_3$)



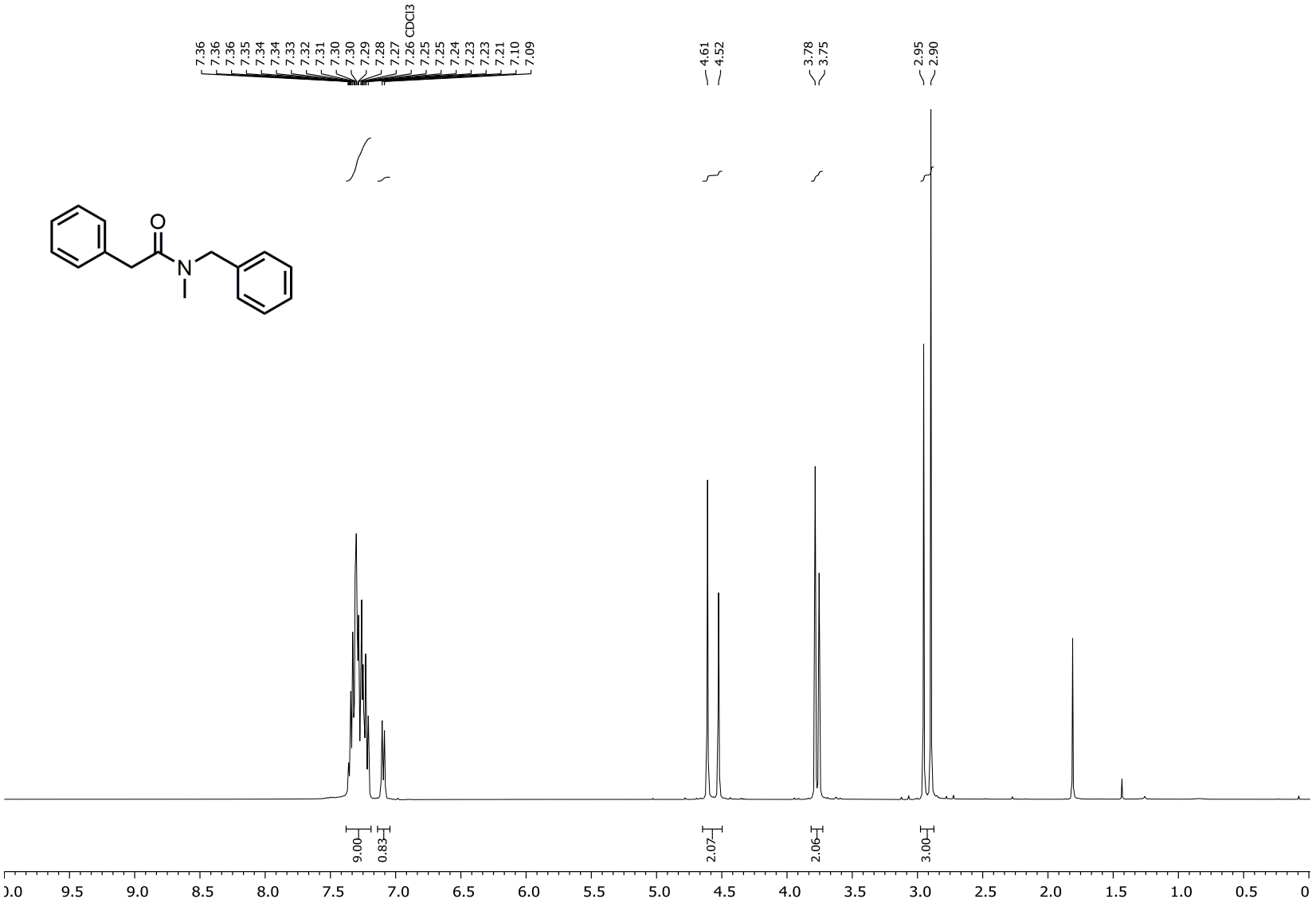
^{1}H NMR spectrum of 1-morpholino-2-phenylethan-1-one (**5**) (400 MHz, $CDCl_3$)



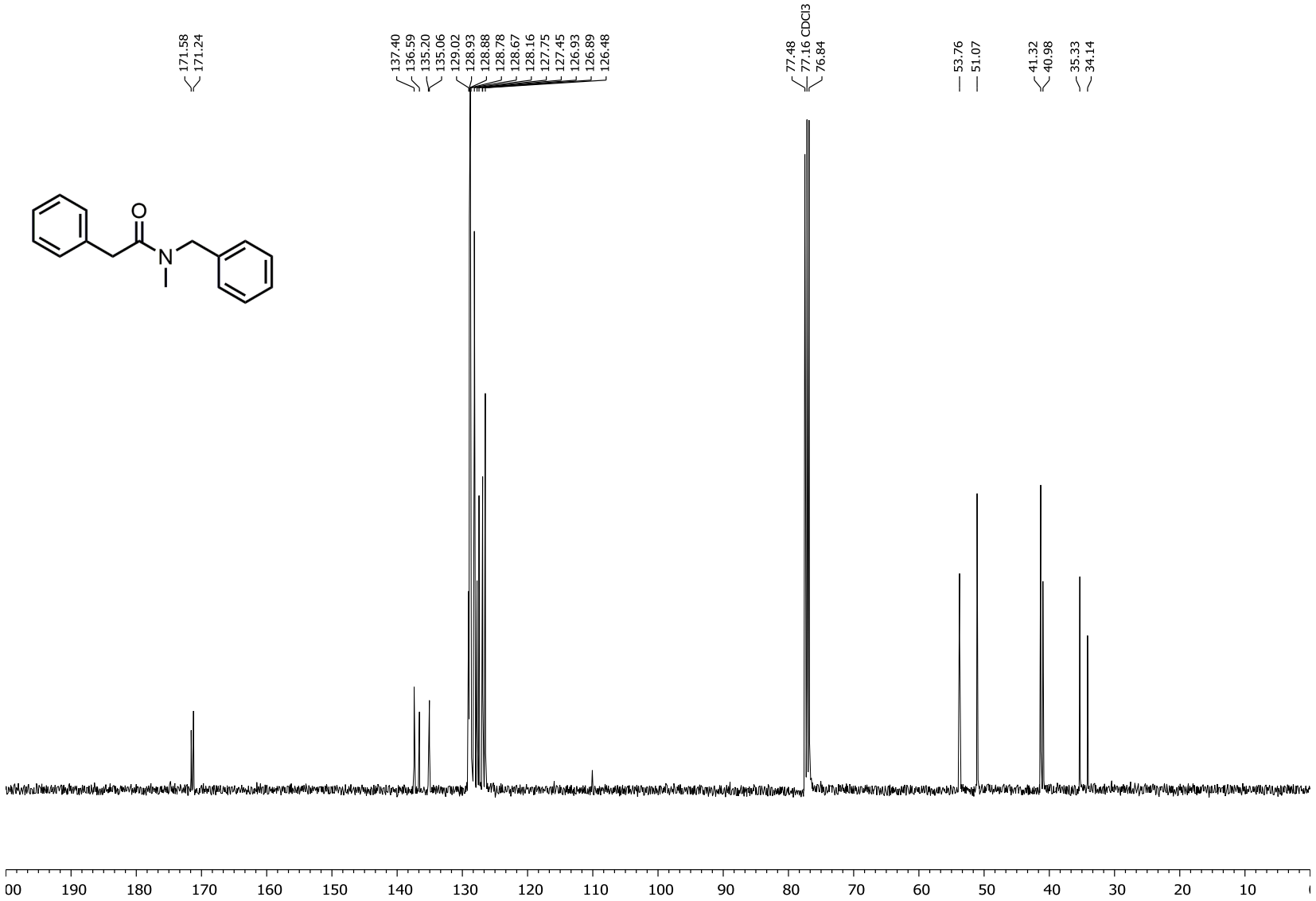
^{13}C NMR spectrum of 1-morpholino-2-phenylethan-1-one (**5**) (101 MHz, $CDCl_3$)



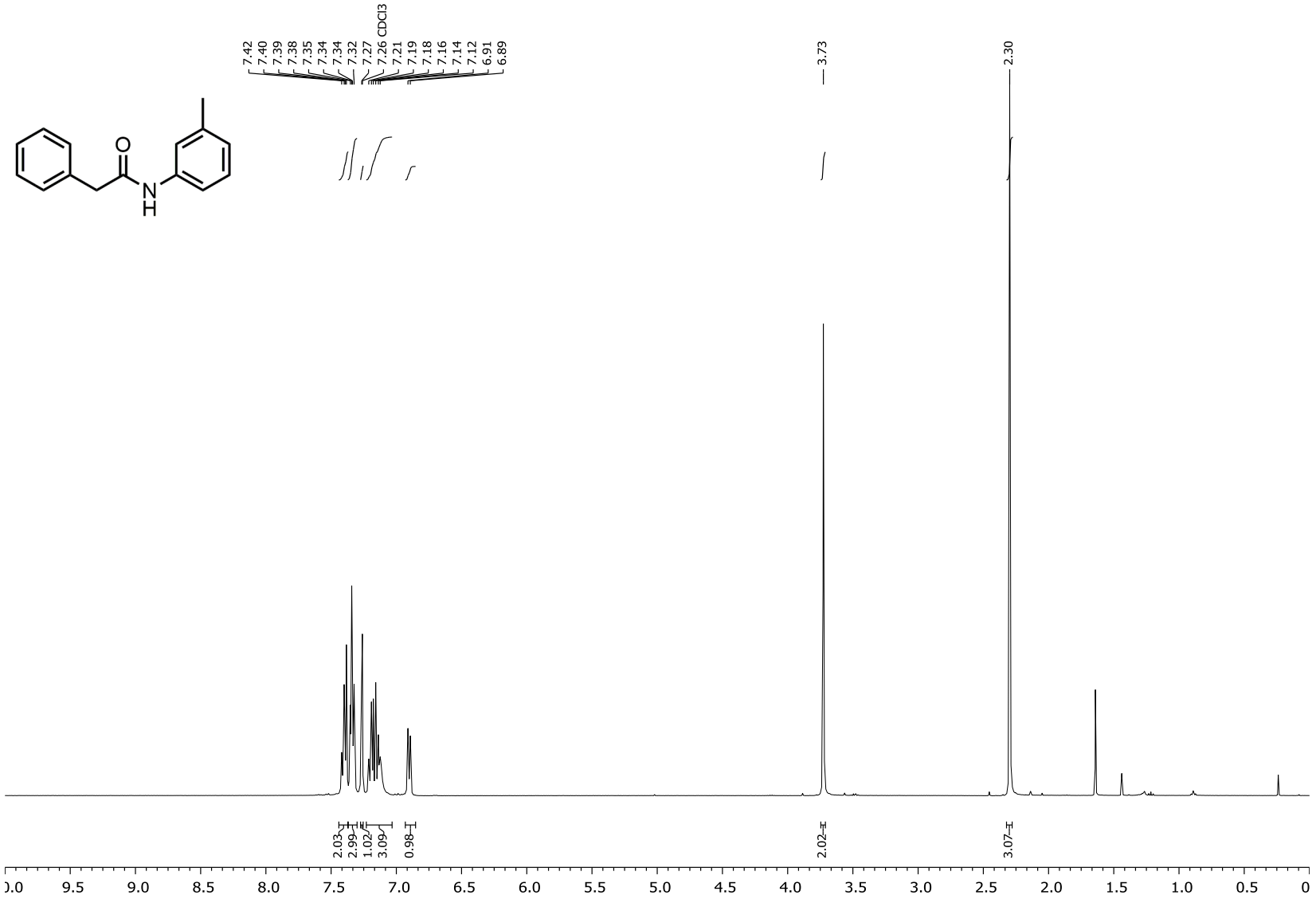
^{1}H NMR spectrum of *N*-benzyl-*N*-methyl-2-phenylacetamide (**6**) (400 MHz, $CDCl_3$)



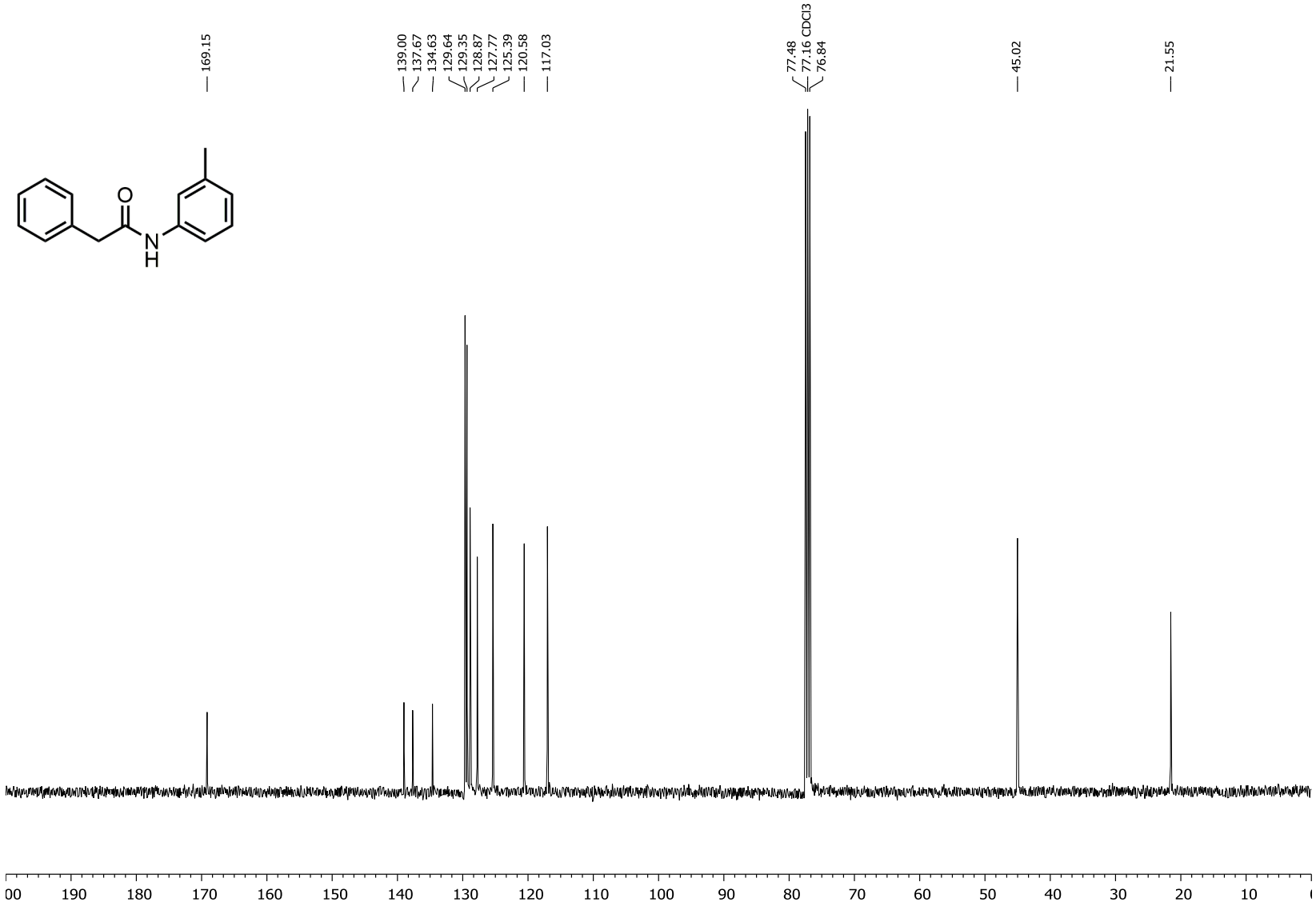
^{13}C NMR spectrum of *N*-benzyl-*N*-methyl-2-phenylacetamide (**6**) (101 MHz, $CDCl_3$)



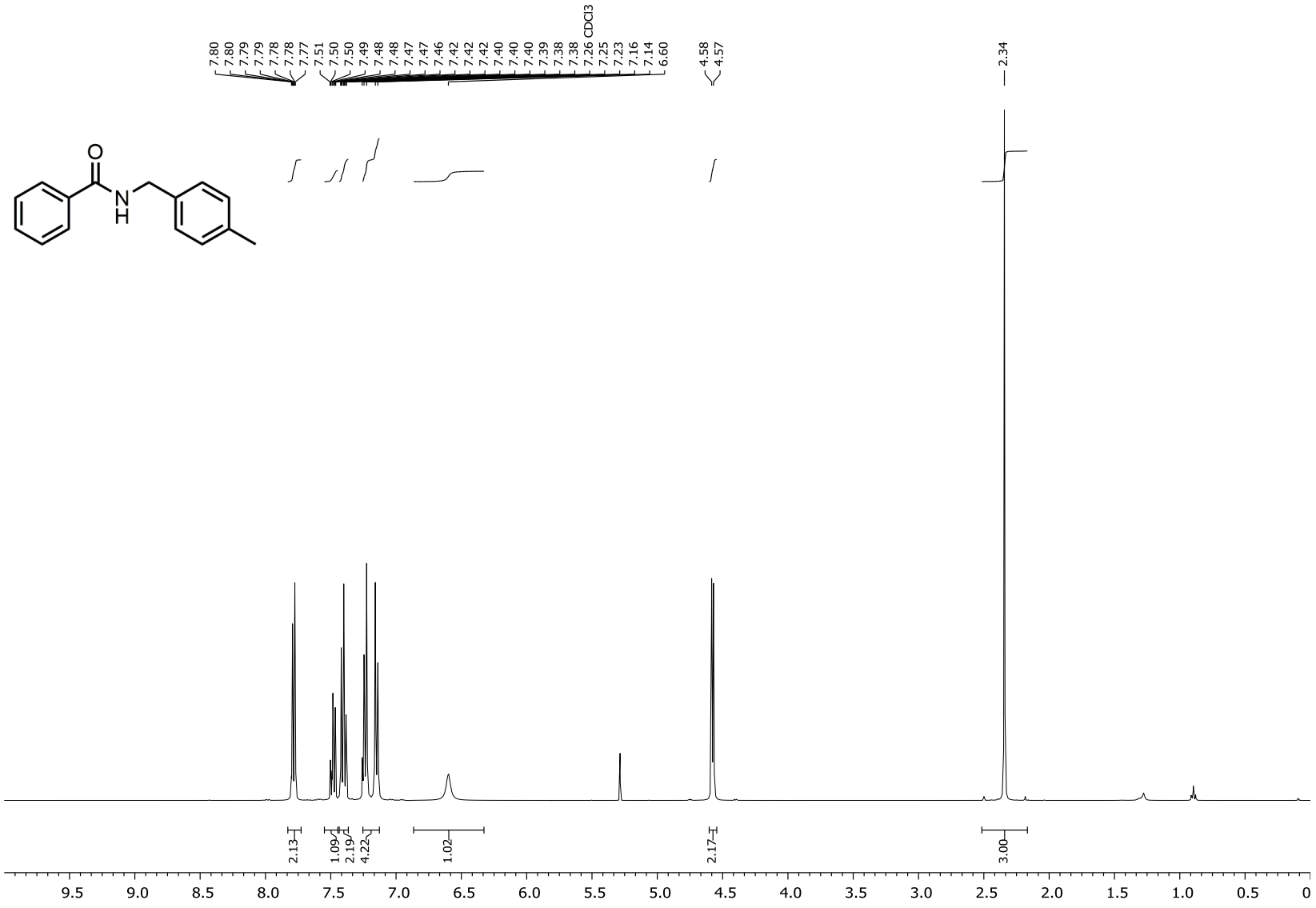
^{1}H NMR spectrum of 2-phenyl-*N*-(*m*-tolyl)acetamide (**7**) (400 MHz, $CDCl_3$)



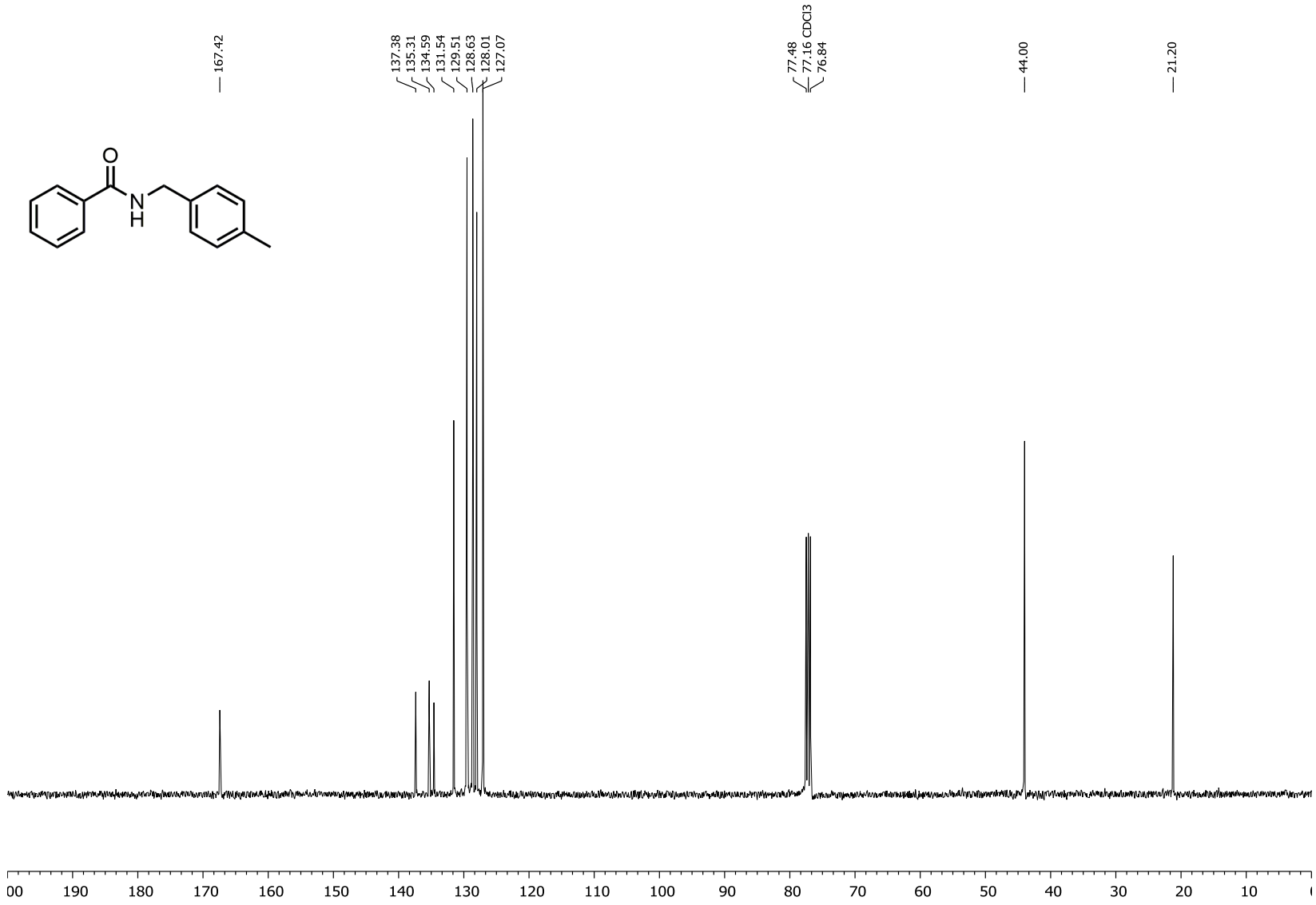
^{13}C NMR spectrum of 2-phenyl-*N*-(*m*-tolyl)acetamide (**7**) (101 MHz, $CDCl_3$)



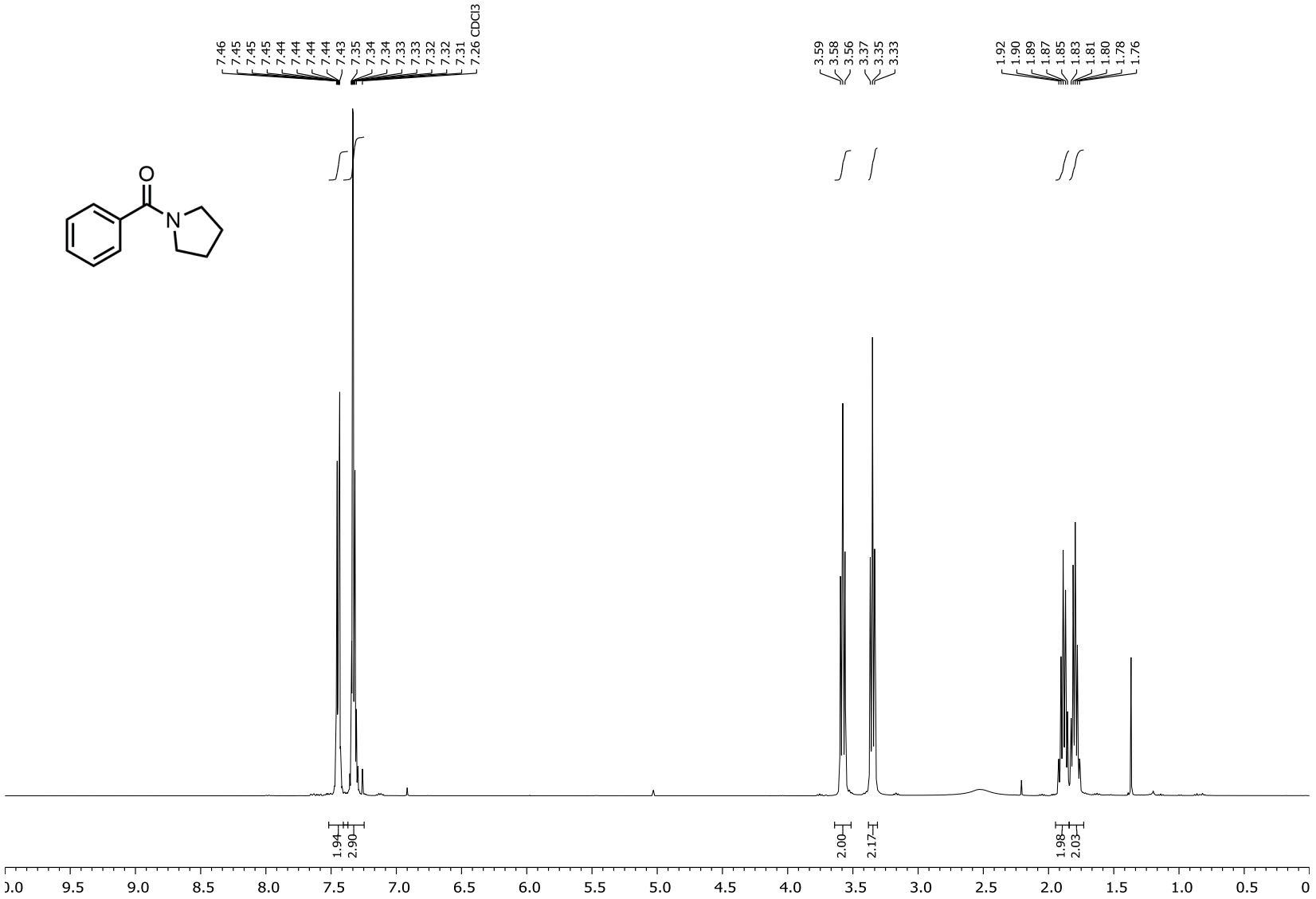
^{1}H NMR spectrum of *N*-(4-methylbenzyl)benzamide (**8**) (400 MHz, $CDCl_3$)



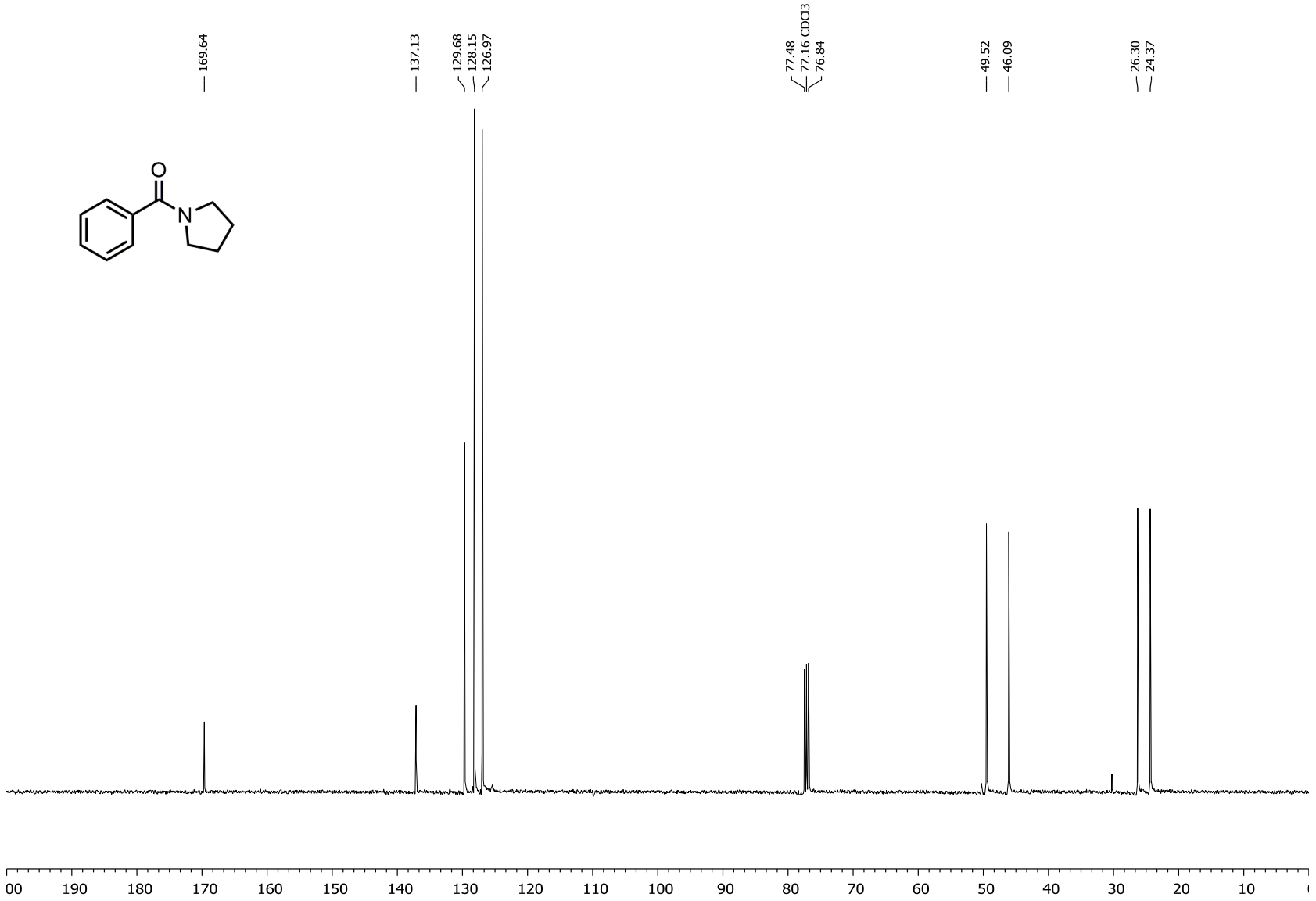
^{13}C NMR spectrum of *N*-(4-methylbenzyl)benzamide (**8**) (101 MHz, $CDCl_3$)



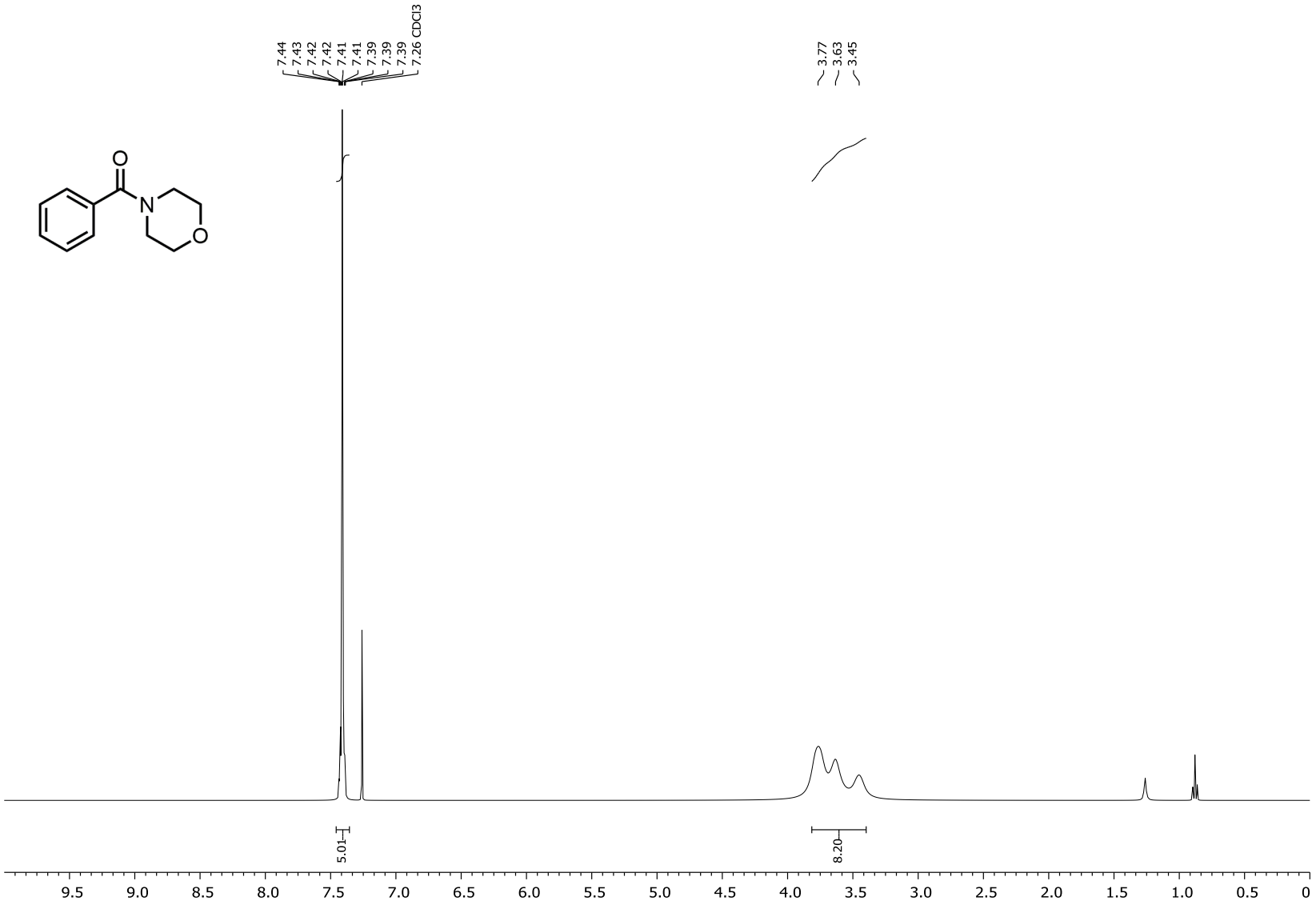
^{1}H NMR spectrum of phenyl(pyrrolidin-1-yl)methanone (**9**) (400 MHz, $CDCl_3$)



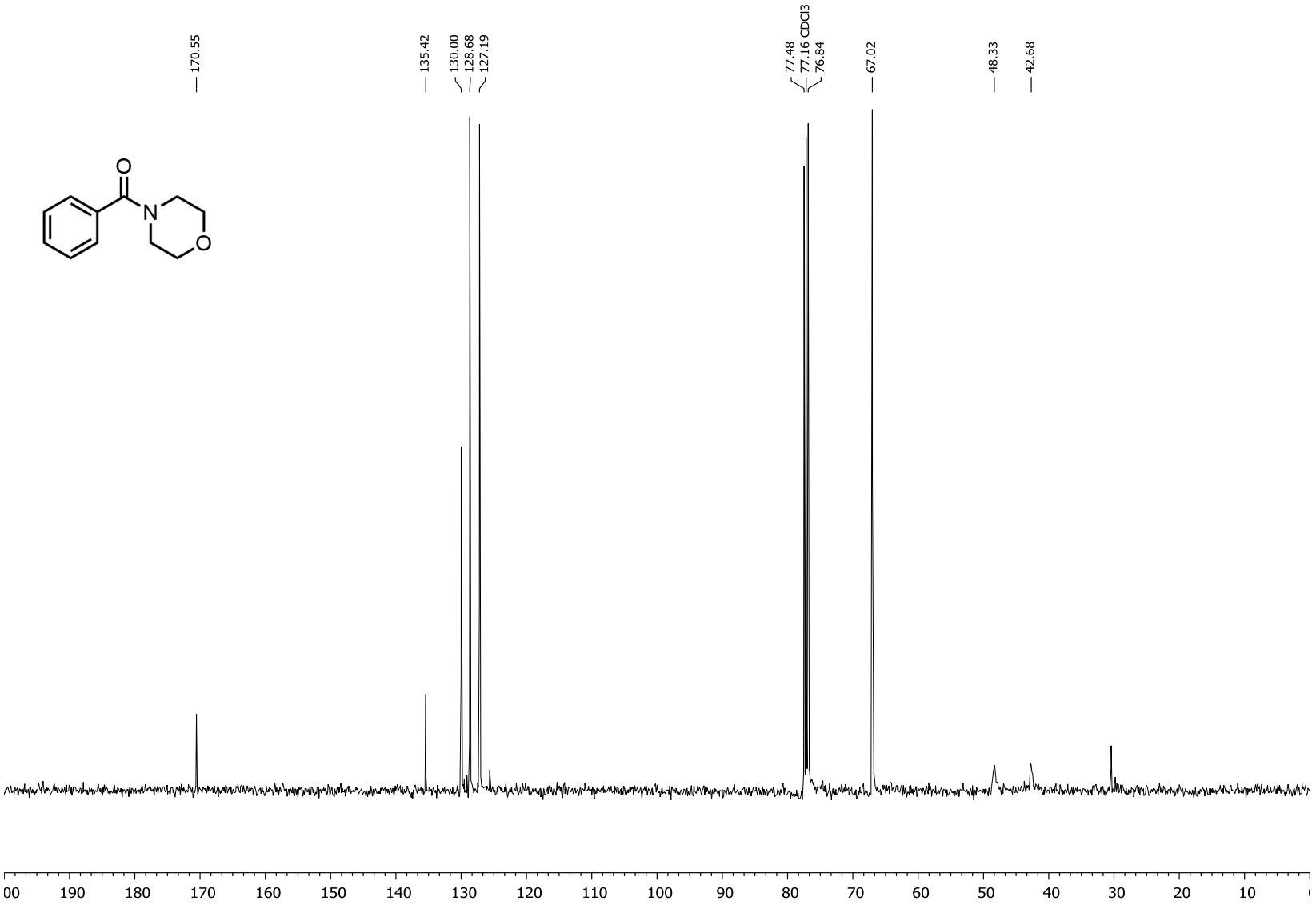
^{13}C NMR spectrum of phenyl(pyrrolidin-1-yl)methanone (**9**) (101 MHz, $CDCl_3$)



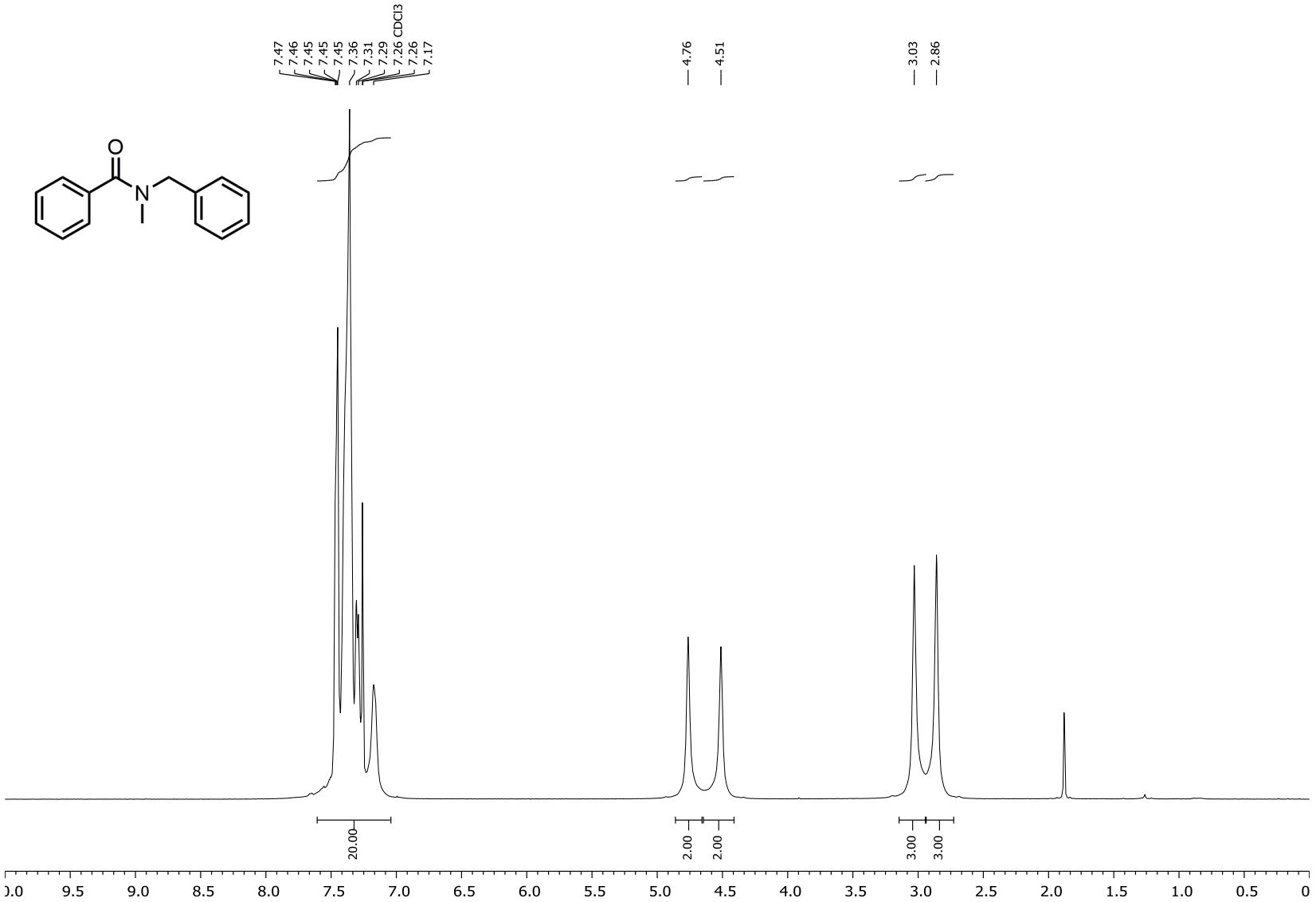
^{1}H NMR spectrum of morpholino(phenyl)methanone (**10**) (400 MHz, $CDCl_3$)



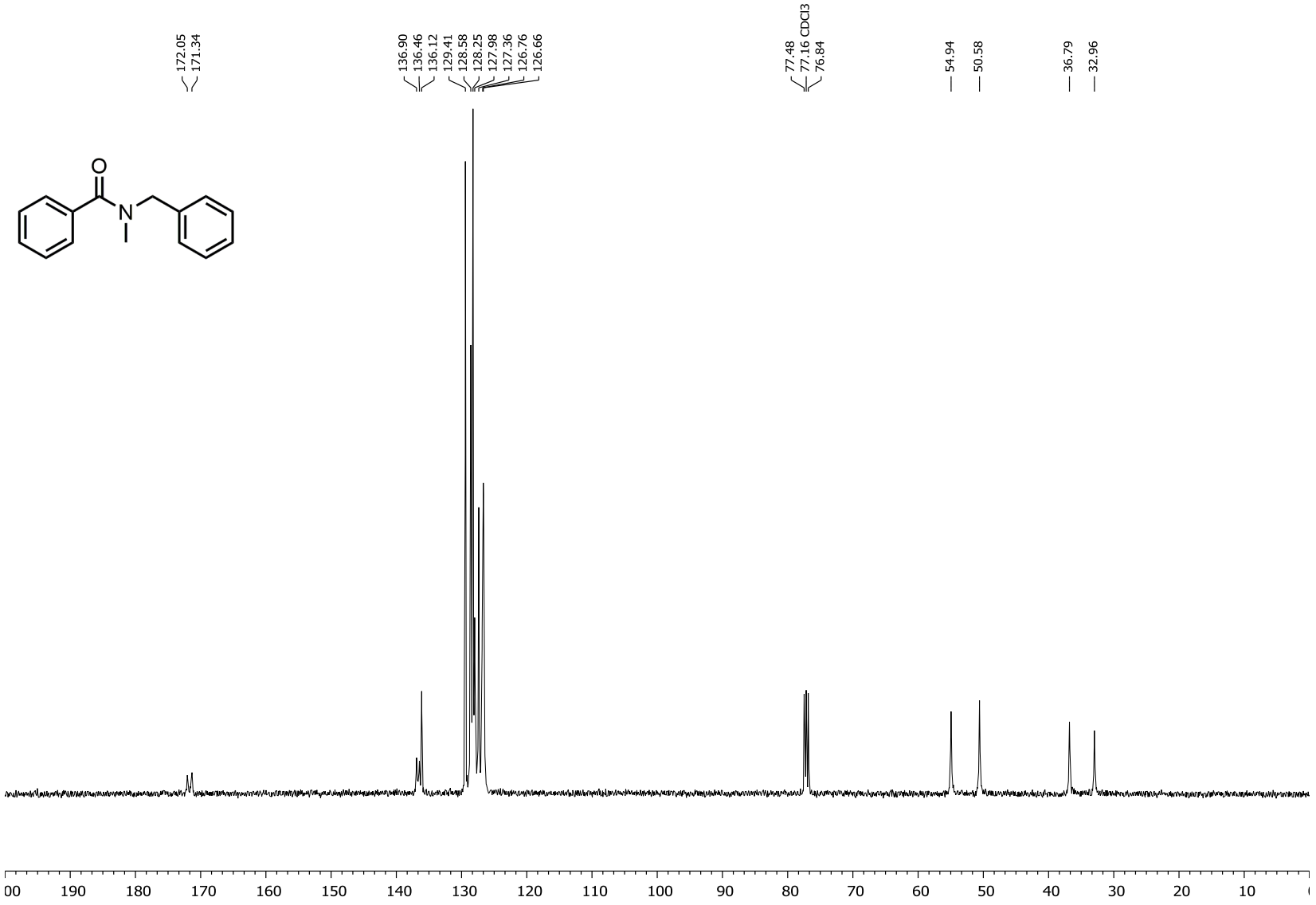
^{13}C NMR spectrum of morpholino(phenyl)methanone (**10**) (101 MHz, $CDCl_3$)



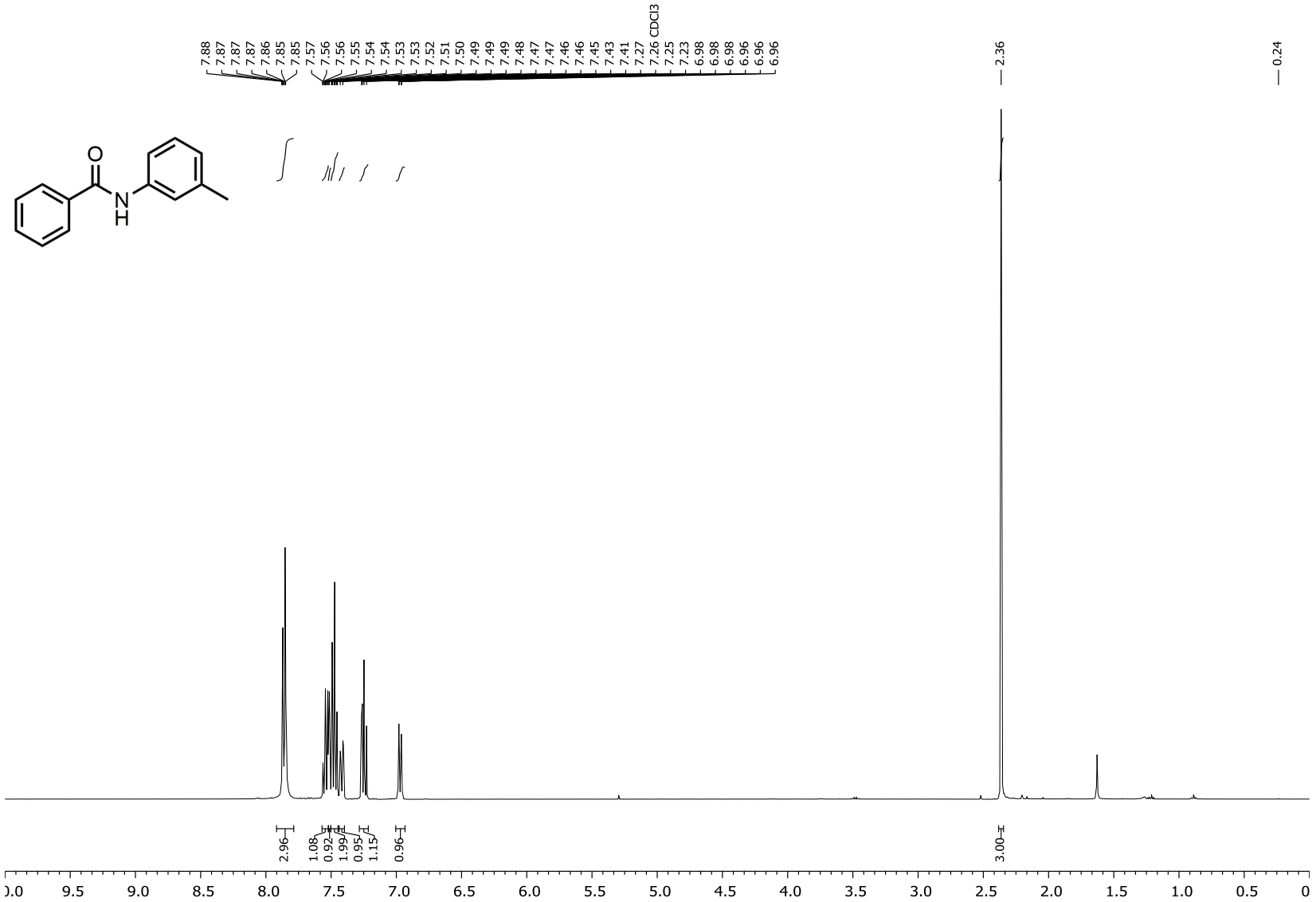
^{1}H NMR spectrum of *N*-benzyl-*N*-methylbenzamide (**11**) (400 MHz, $CDCl_3$)



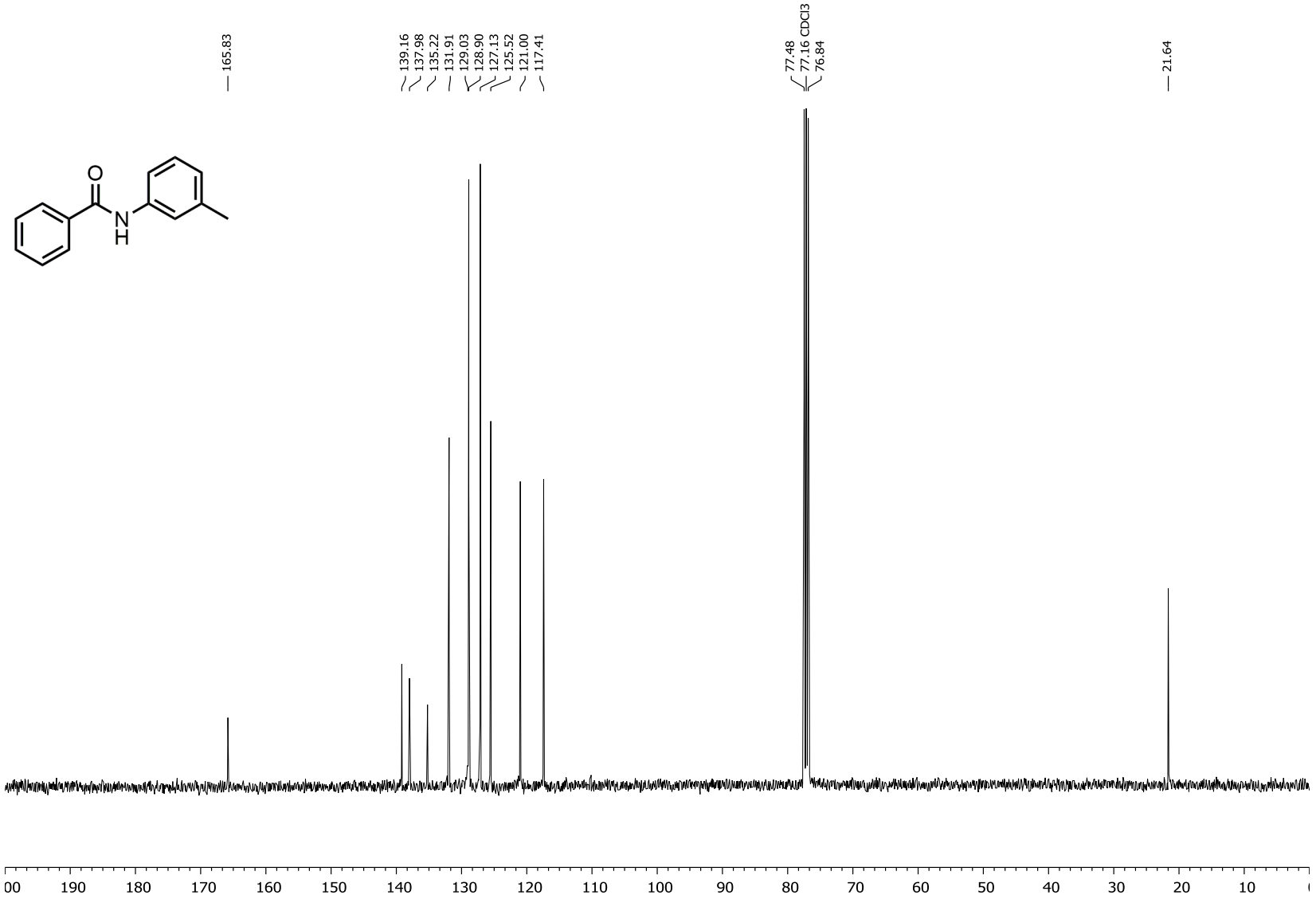
^{13}C NMR spectrum of *N*-benzyl-*N*-methylbenzamide (**11**) (101 MHz, $CDCl_3$)



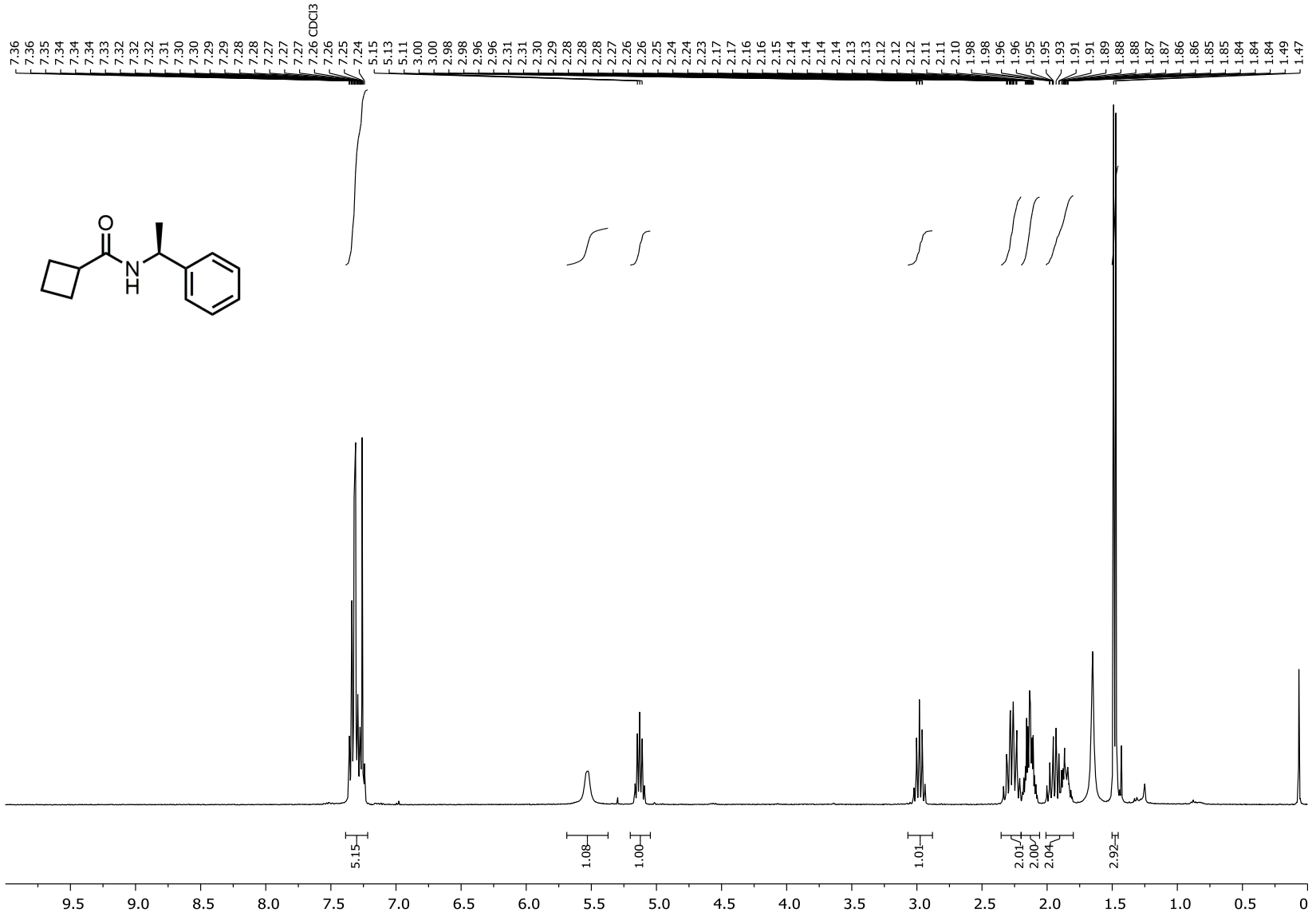
^{1}H NMR spectrum of *N*-(*m*-tolyl)benzamide (**12**) (400 MHz, $CDCl_3$)



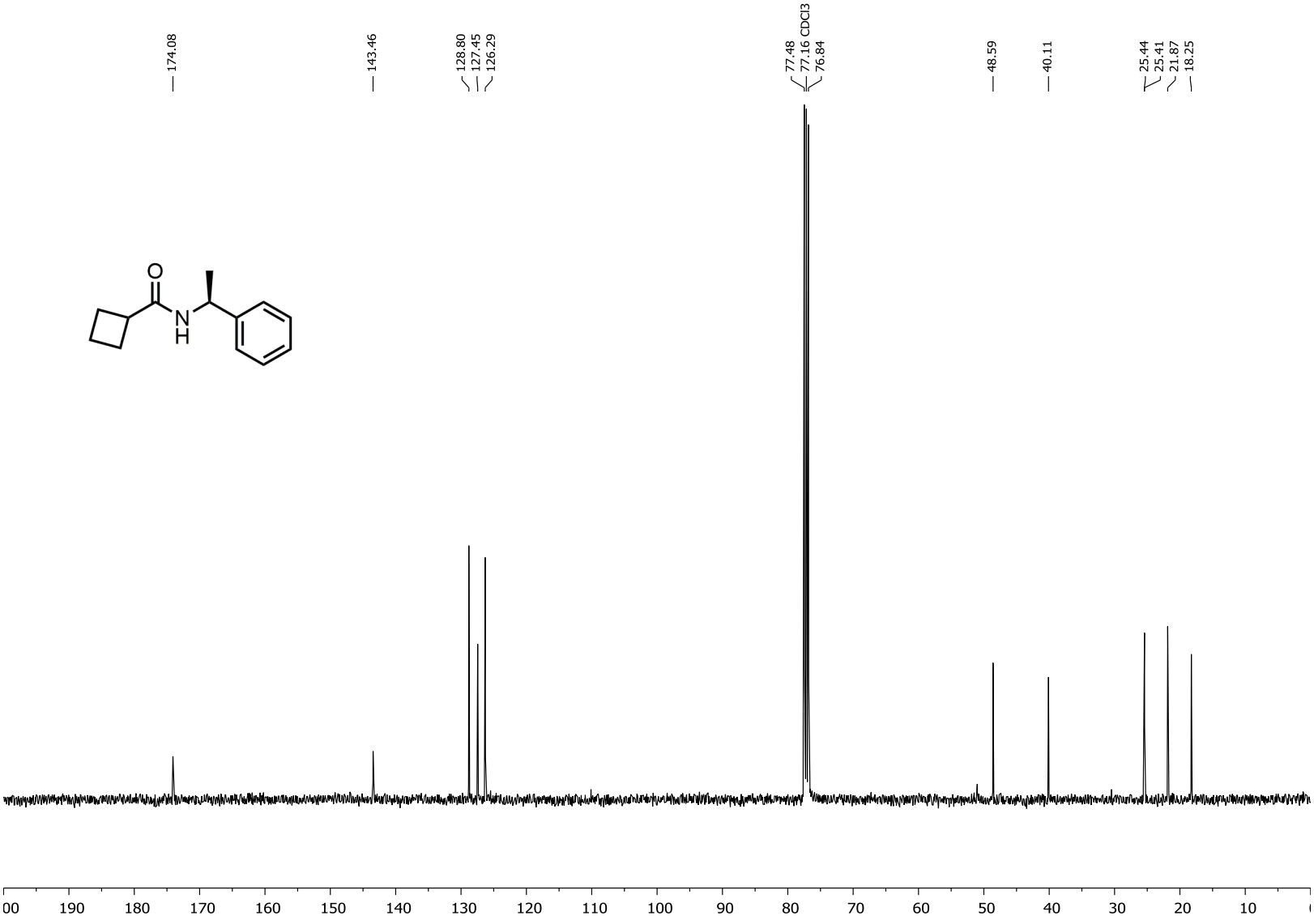
^{13}C NMR spectrum of *N*-(*m*-tolyl)benzamide (**12**) (101 MHz, $CDCl_3$)



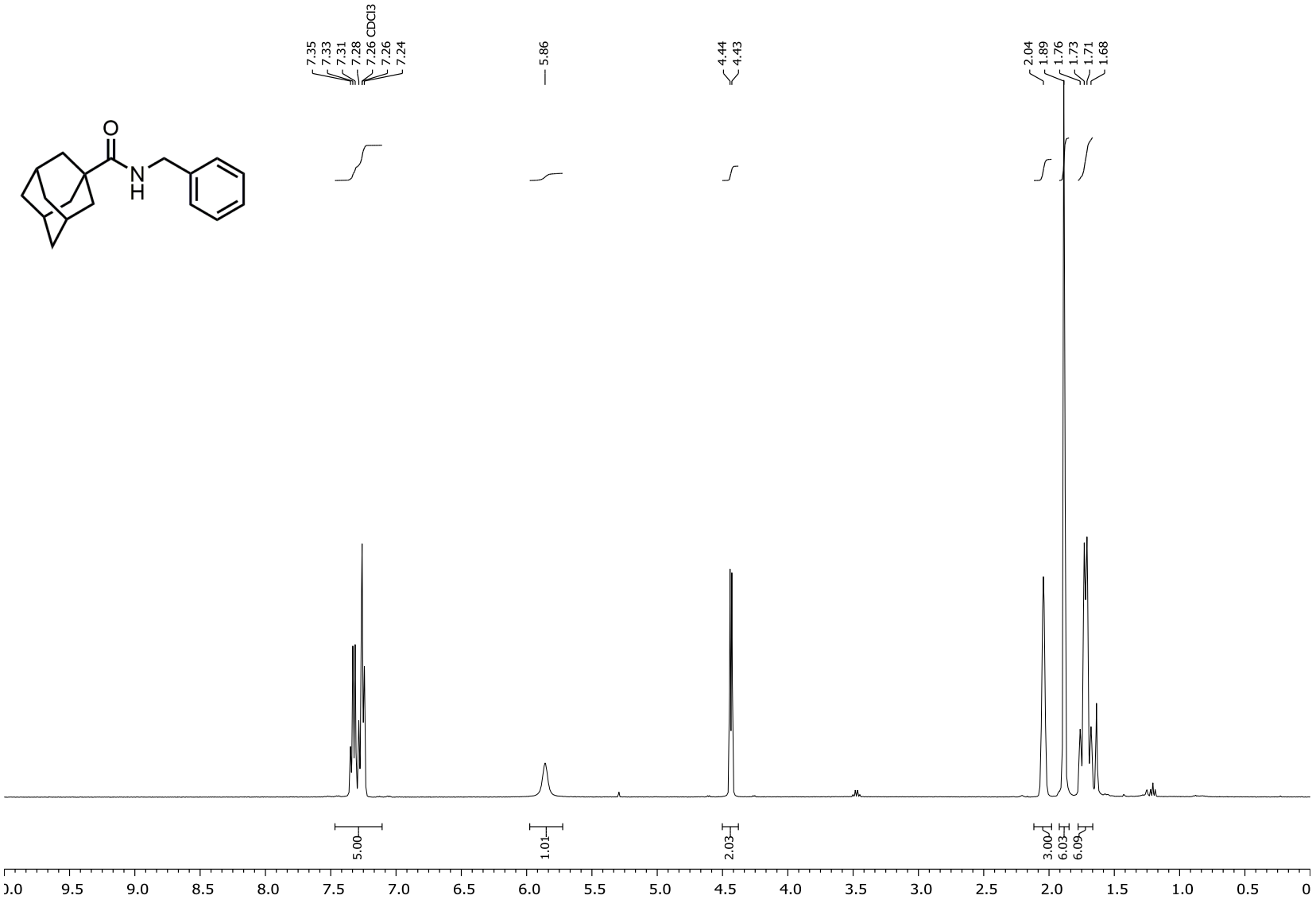
^{1}H NMR spectrum of (*S*)-N-(1-phenylethyl)cyclobutanecarboxamide (**14**) (400 MHz, $CDCl_3$)



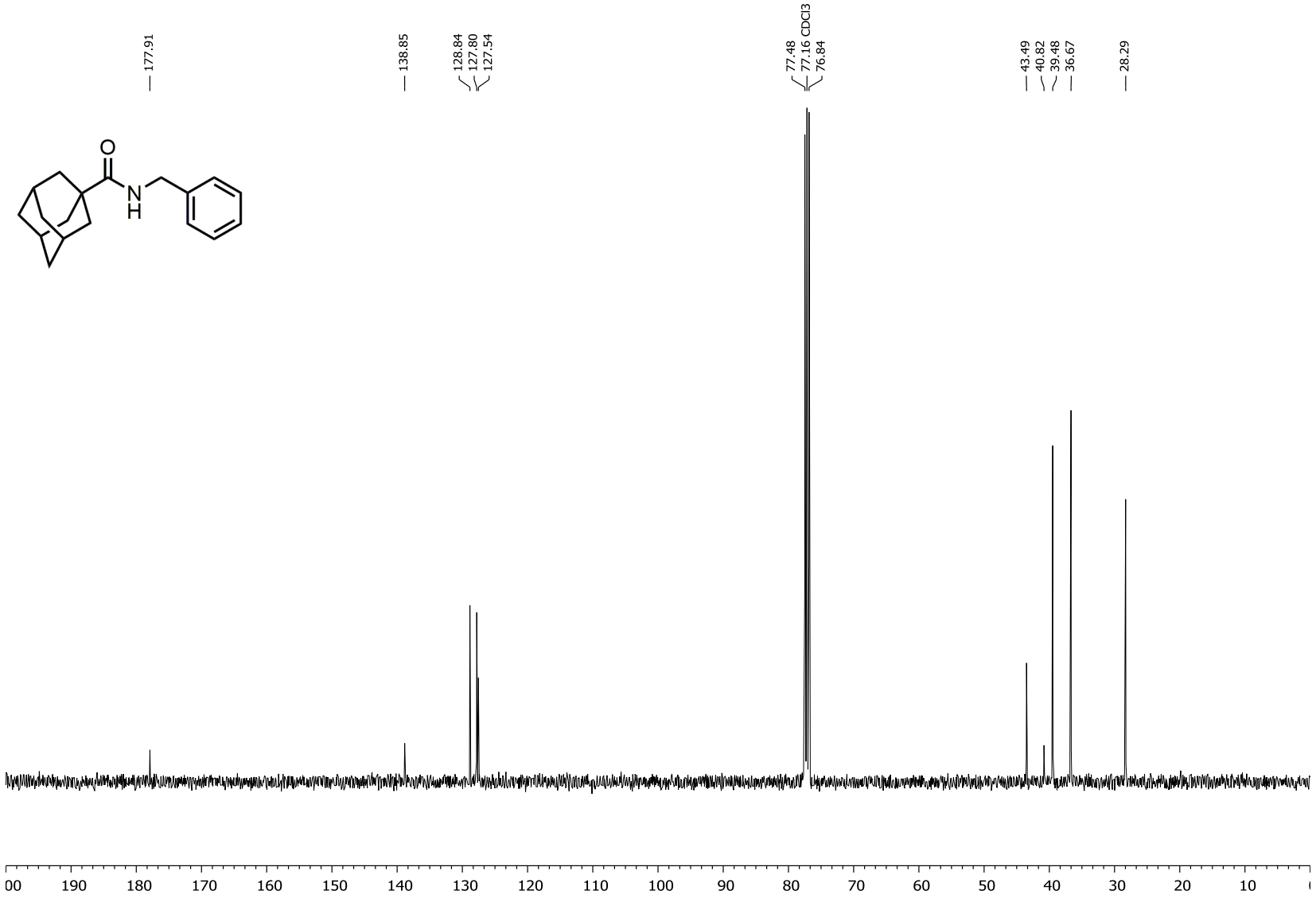
^{13}C NMR spectrum of (*S*)-*N*-(1-phenylethyl)cyclobutanecarboxamide (**14**) (101 MHz, $CDCl_3$)



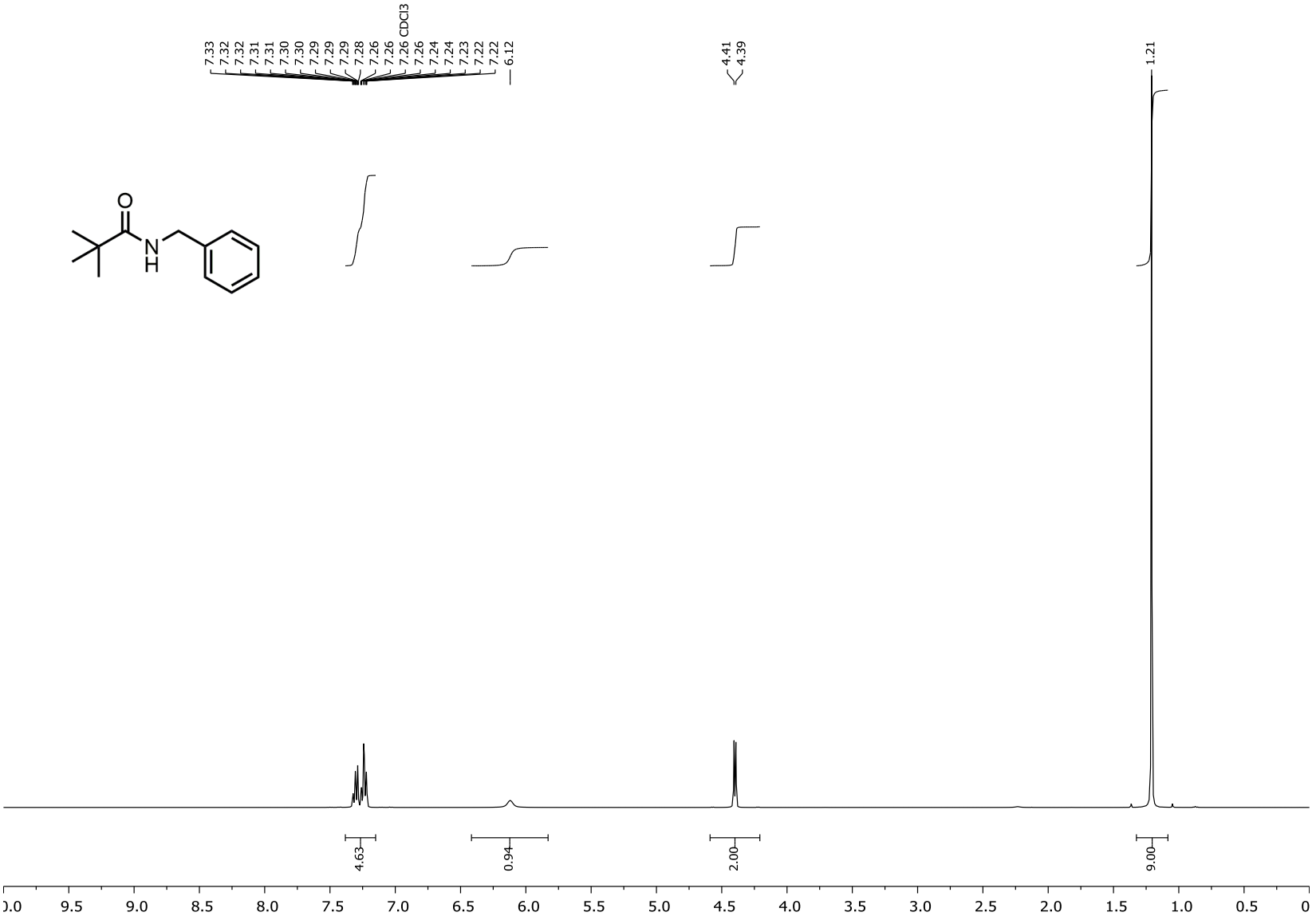
^{1}H NMR spectrum of *N*-benzyl-(1-adamantane)-carboxamide (**15**) (400 MHz, $CDCl_3$)



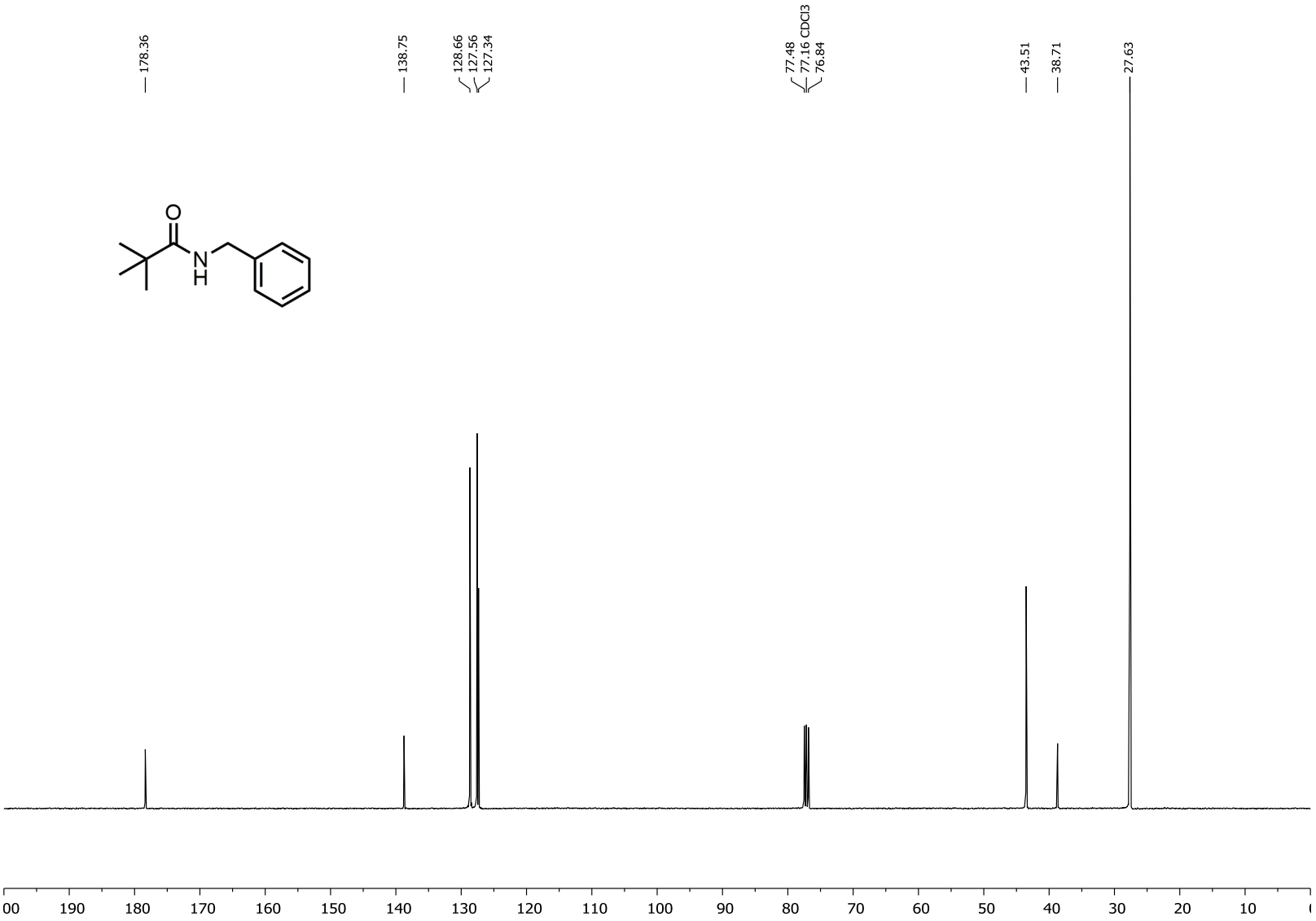
^{13}C NMR spectrum of *N*-benzyl-(1-adamantane)-carboxamide (**15**) (101 MHz, $CDCl_3$)



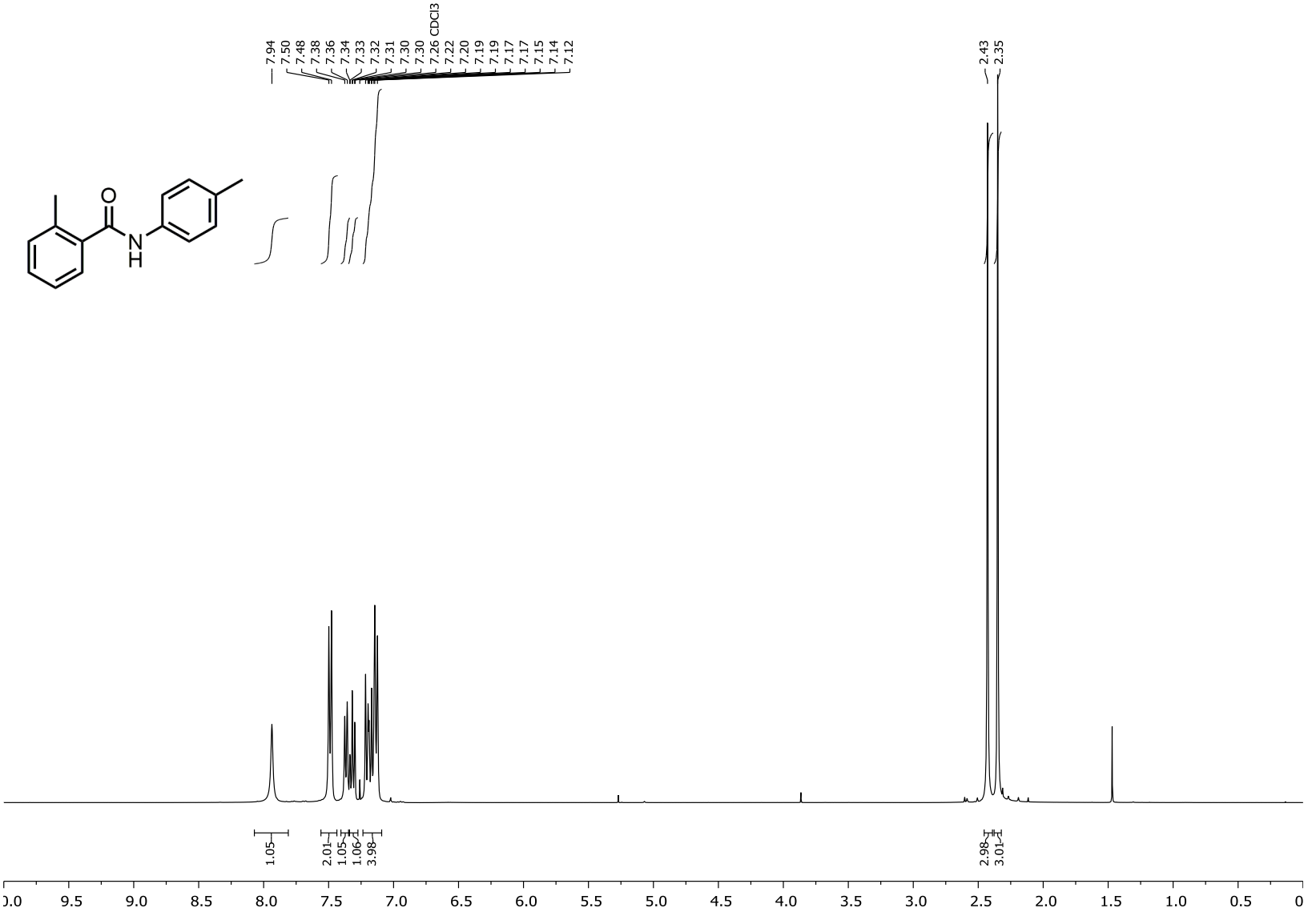
^{1}H NMR spectrum of *N*-benzylpivalamide (**16**) (400 MHz, $CDCl_3$)



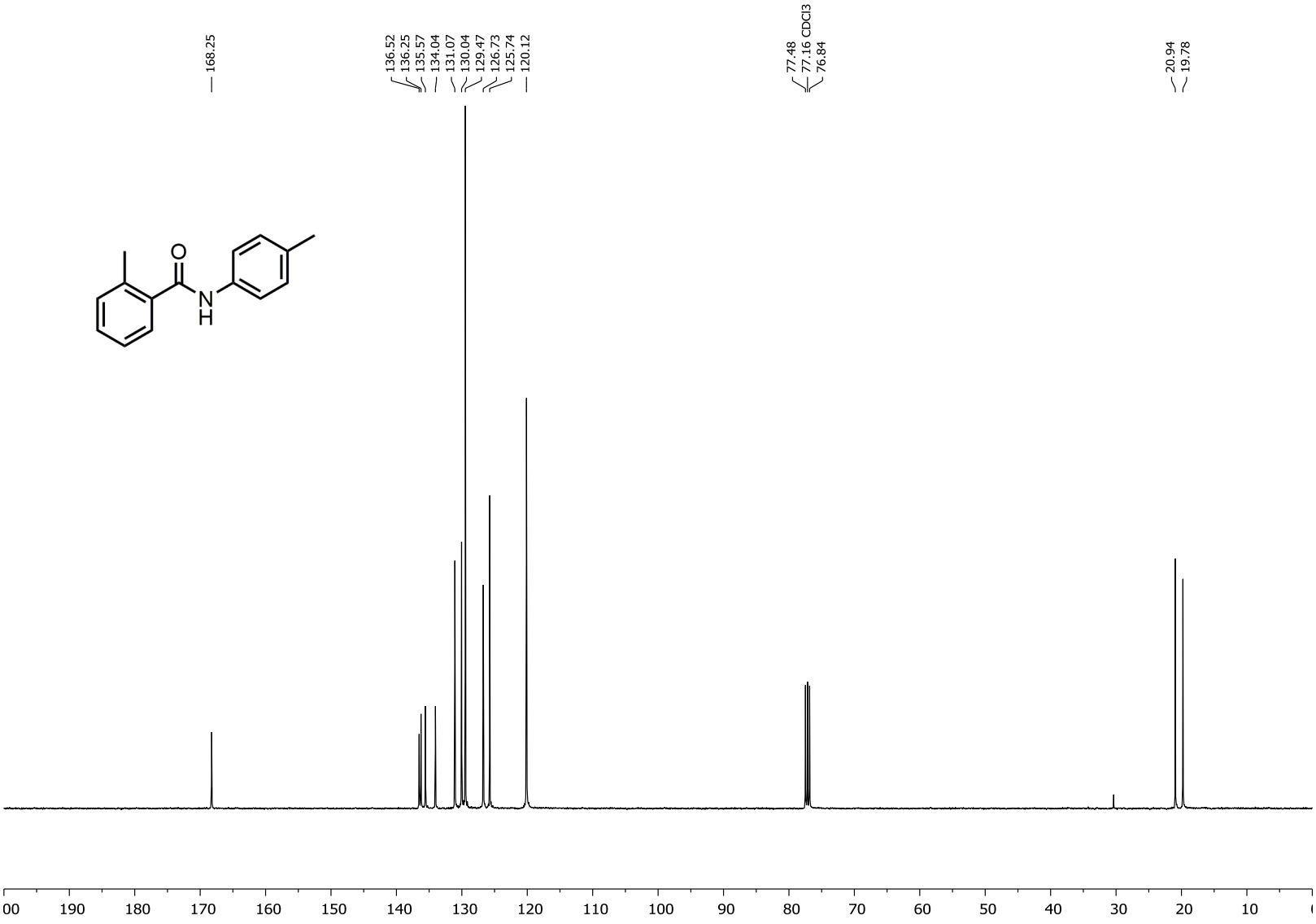
^{13}C NMR spectrum of *N*-benzylpivalamide (**16**) (101 MHz, $CDCl_3$)



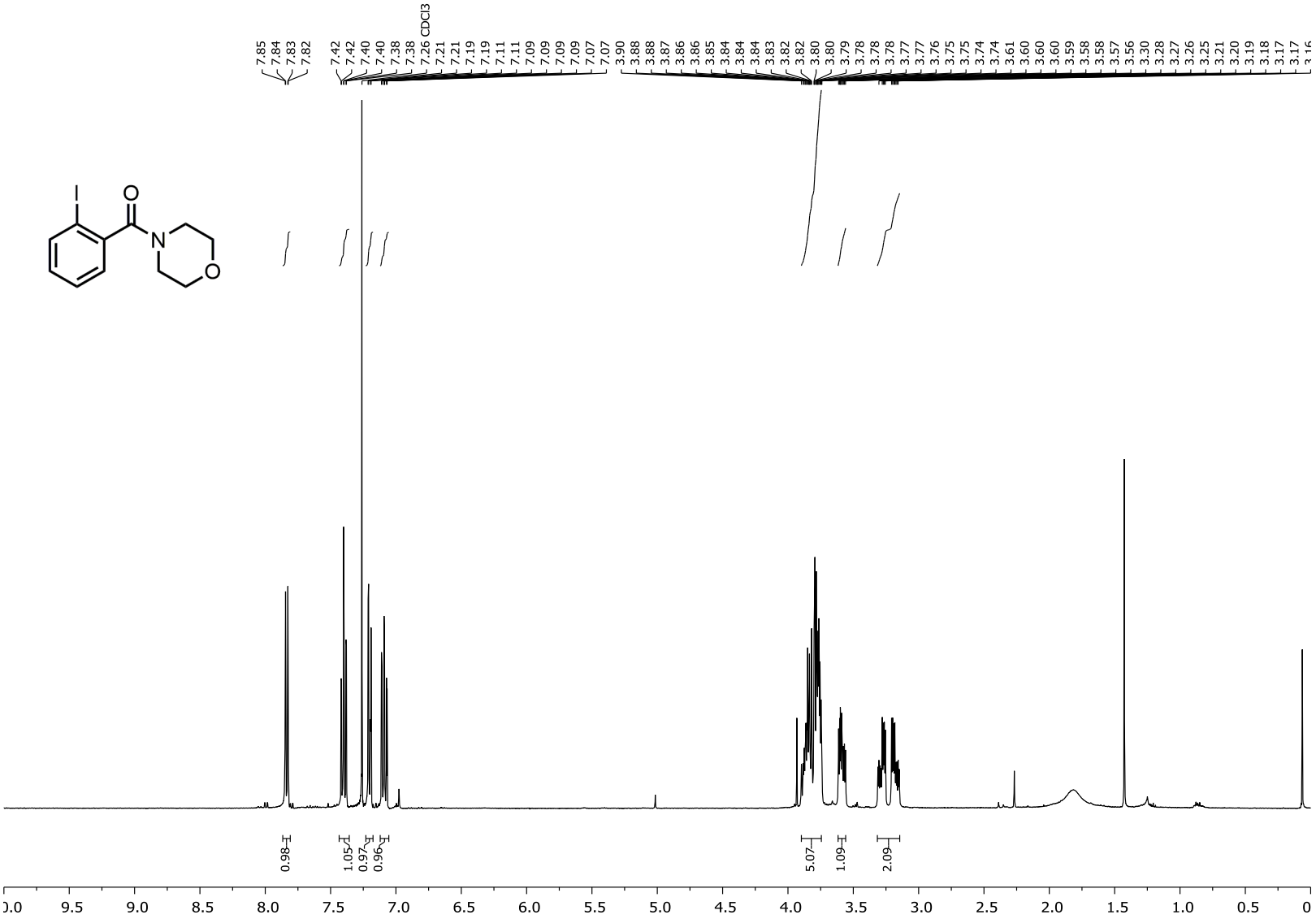
^{1}H NMR spectrum of 2-methyl-*N*-(*p*-tolyl)benzamide (**17**) (400 MHz, $CDCl_3$)



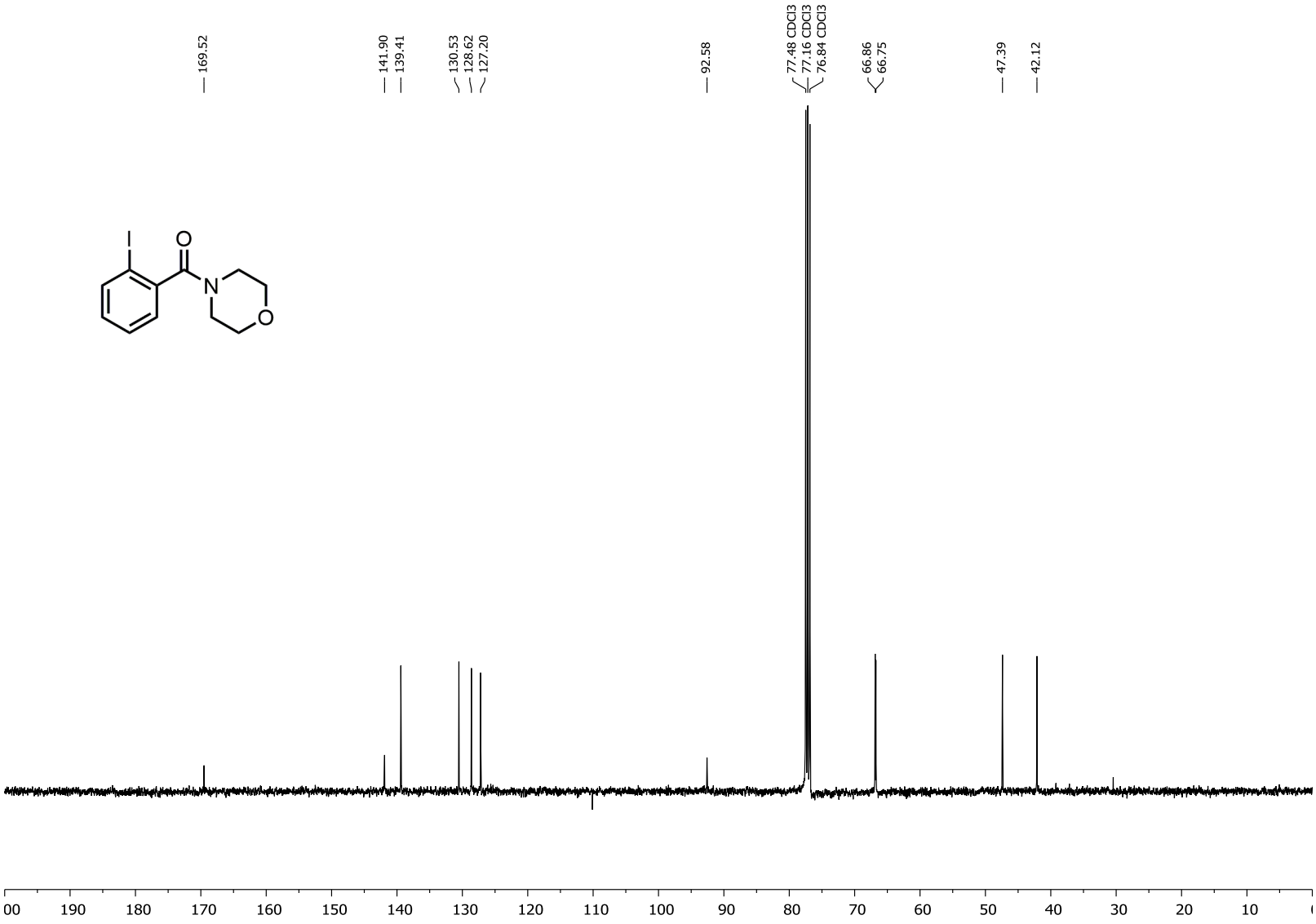
^{13}C NMR spectrum of 2-methyl-*N*-(*p*-tolyl)benzamide (**17**) (101 MHz, $CDCl_3$)



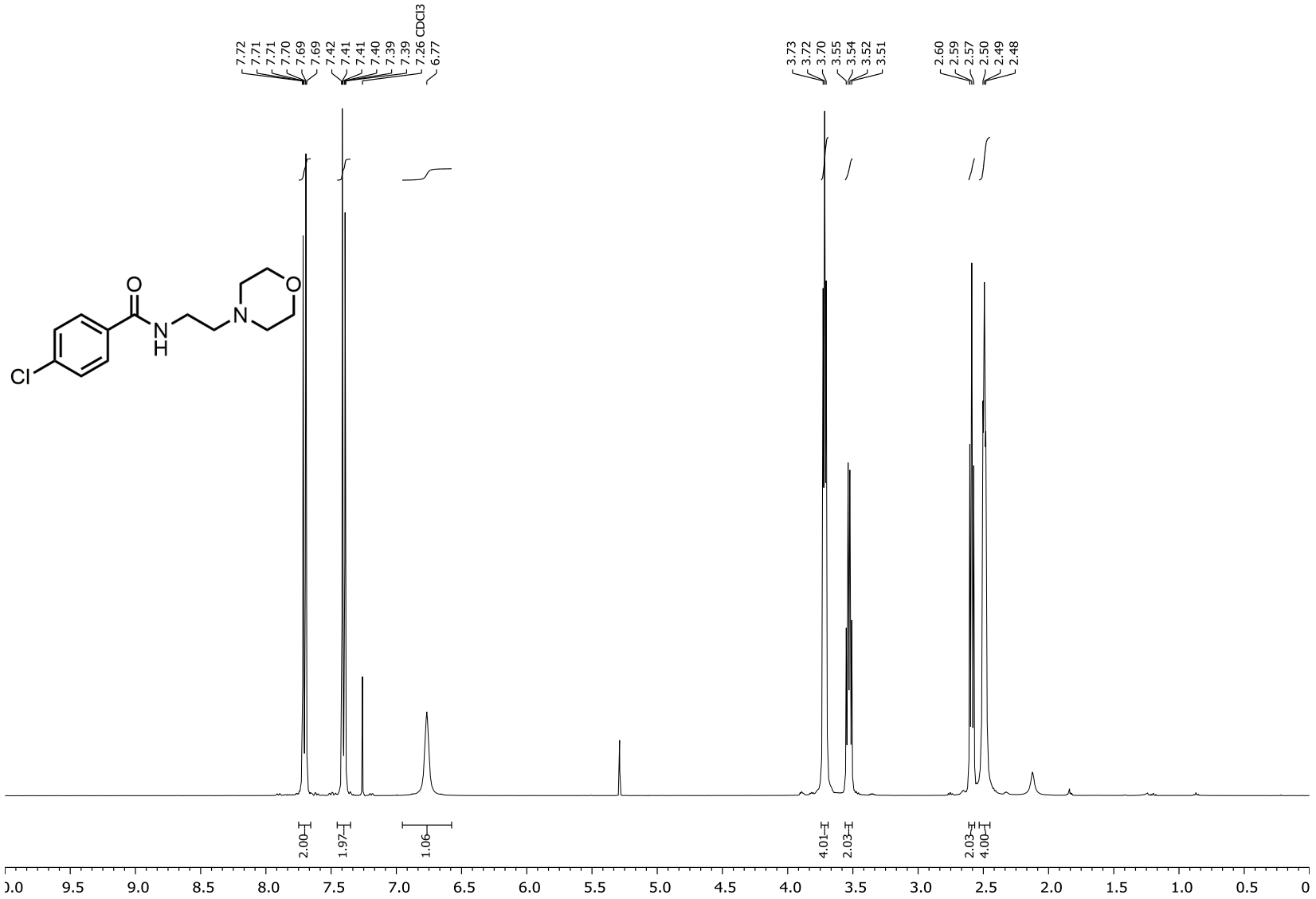
^{1}H NMR spectrum of (2-iodophenyl)(morpholino)methanone (**18**) (400 MHz, $CDCl_3$)



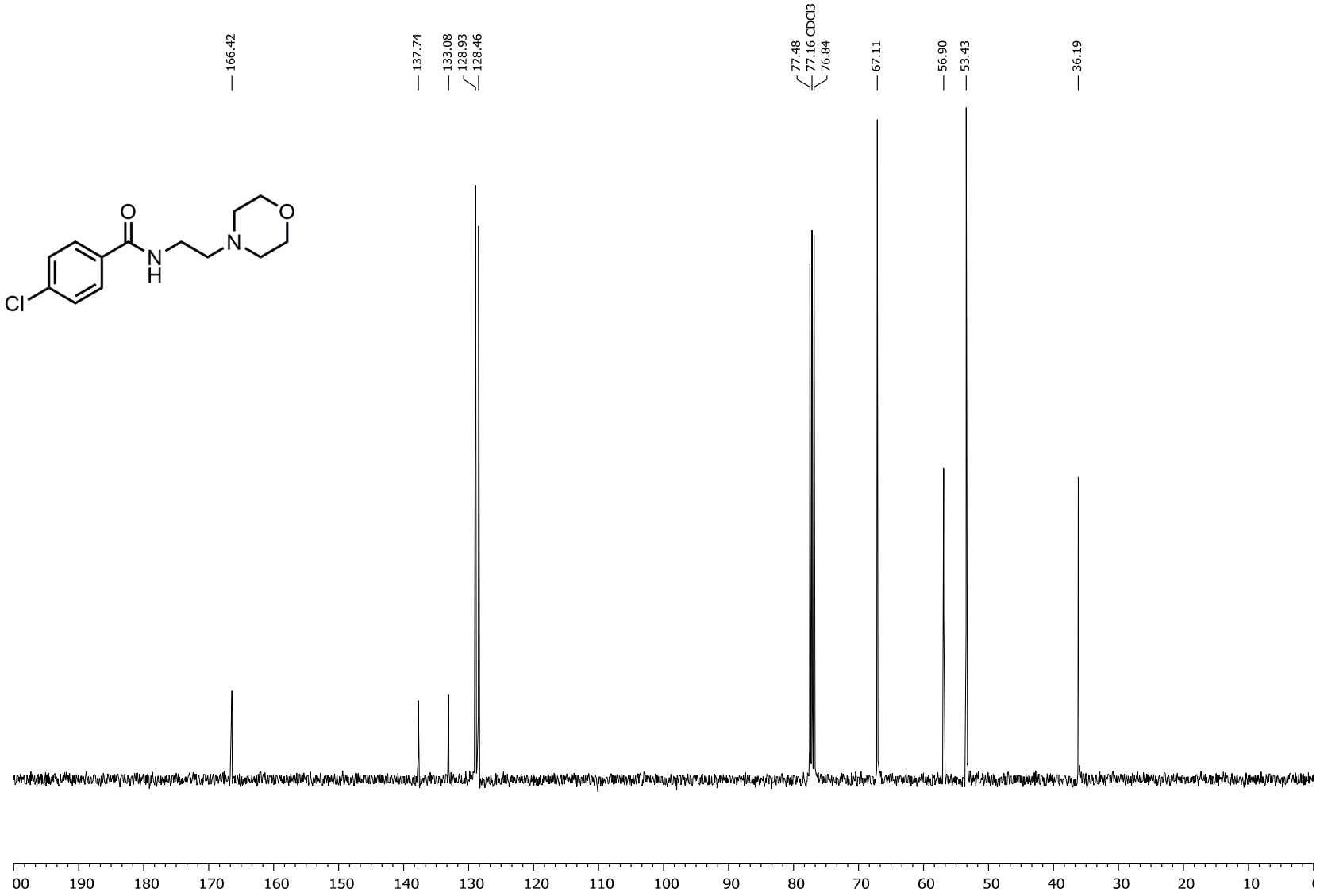
^{13}C NMR spectrum of (2-iodophenyl)(morpholino)methanone (**18**) (101 MHz, $CDCl_3$)



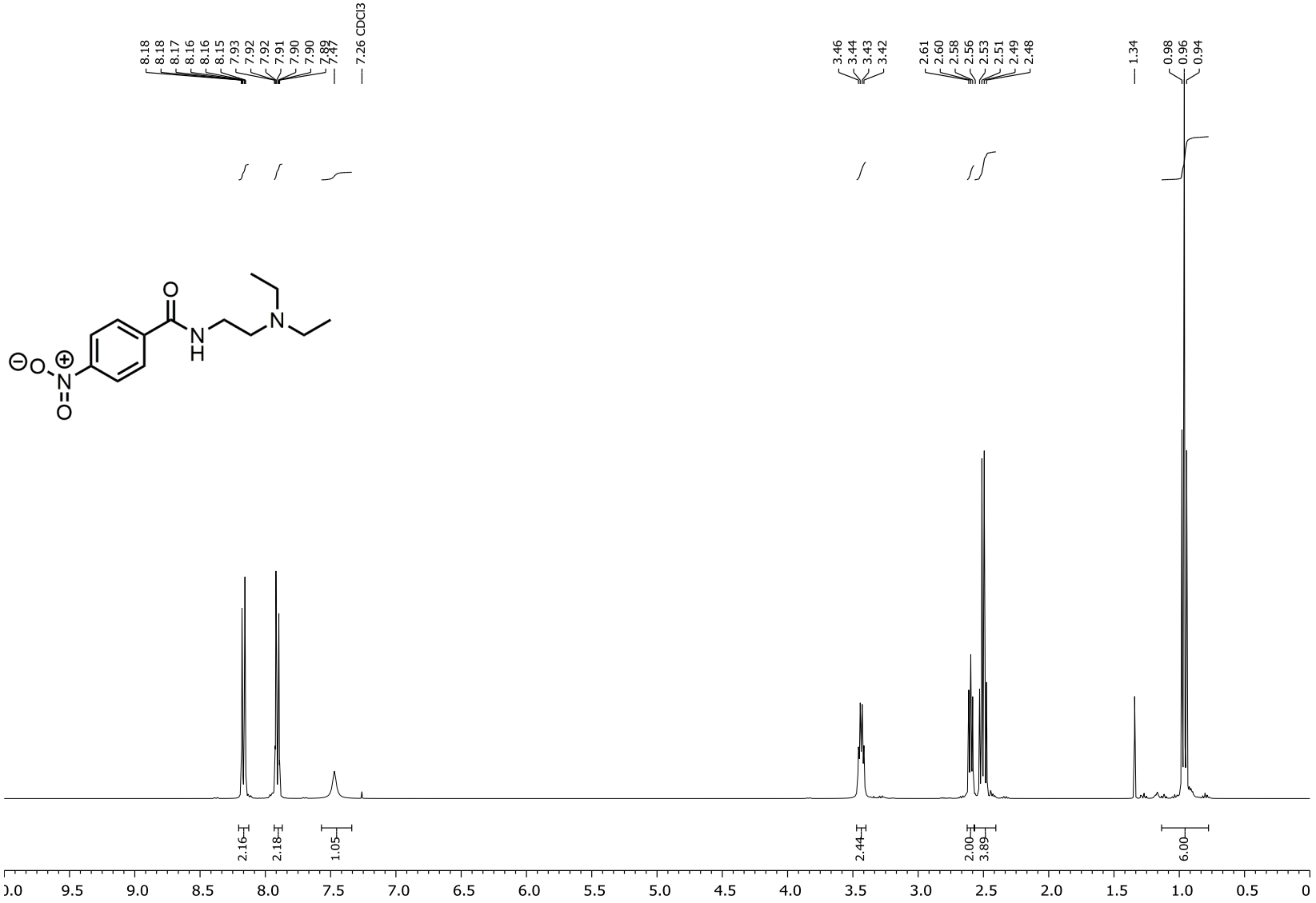
^{1}H NMR spectrum of 4-chloro-*N*-(2-morpholinoethyl)benzamide (**19**) (400 MHz, $CDCl_3$)



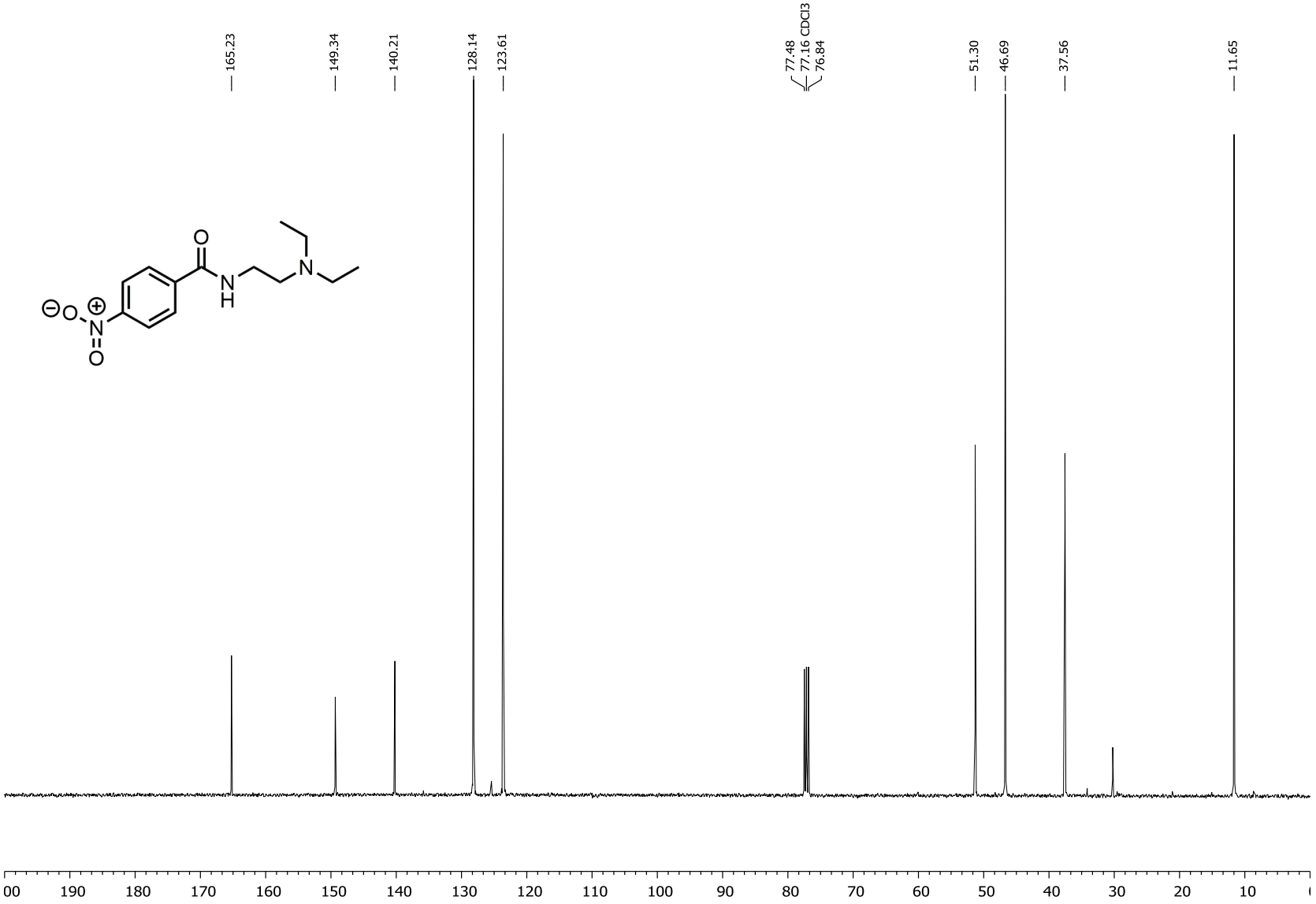
^{13}C NMR spectrum of 4-chloro-*N*-(2-morpholinoethyl)benzamide (**19**) (101 MHz, $CDCl_3$)



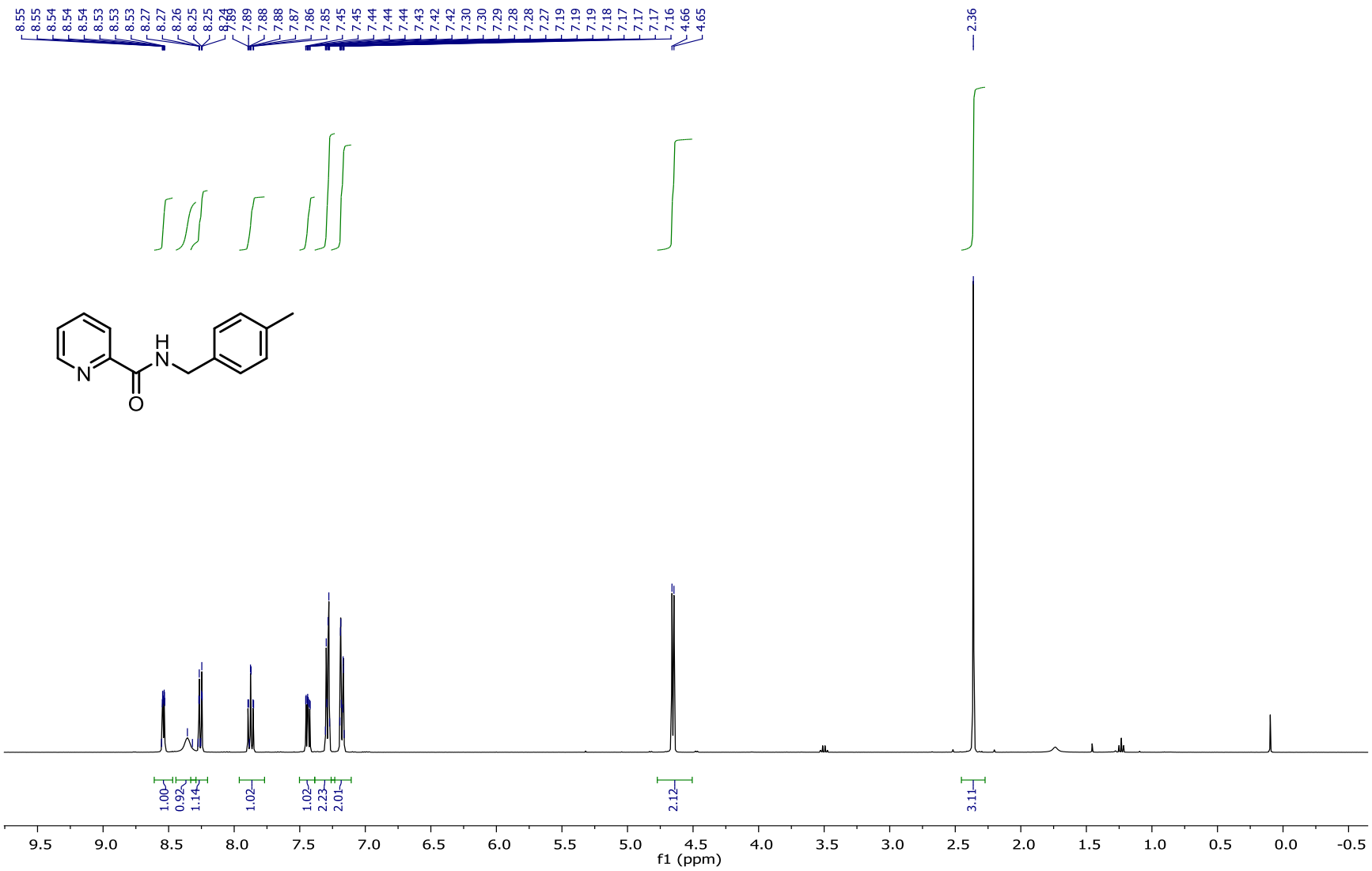
^{1}H NMR spectrum of *N*-(2-(diethylamino)ethyl)-4-nitrobenzamide (**20**) (400 MHz, $CDCl_3$)



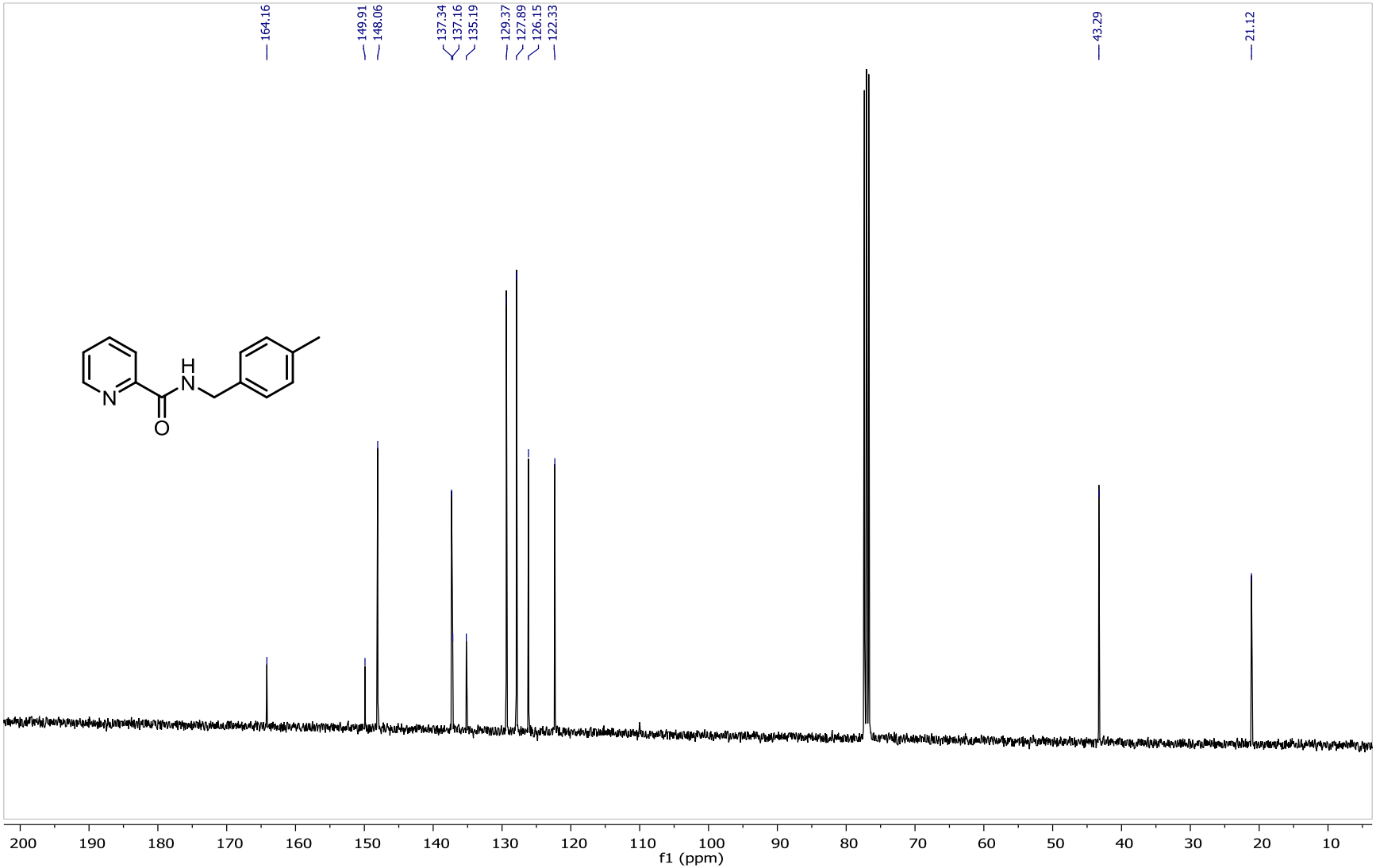
^{13}C NMR spectrum of *N*-(2-(diethylamino)ethyl)-4-nitrobenzamide (**20**) (101 MHz, $CDCl_3$)



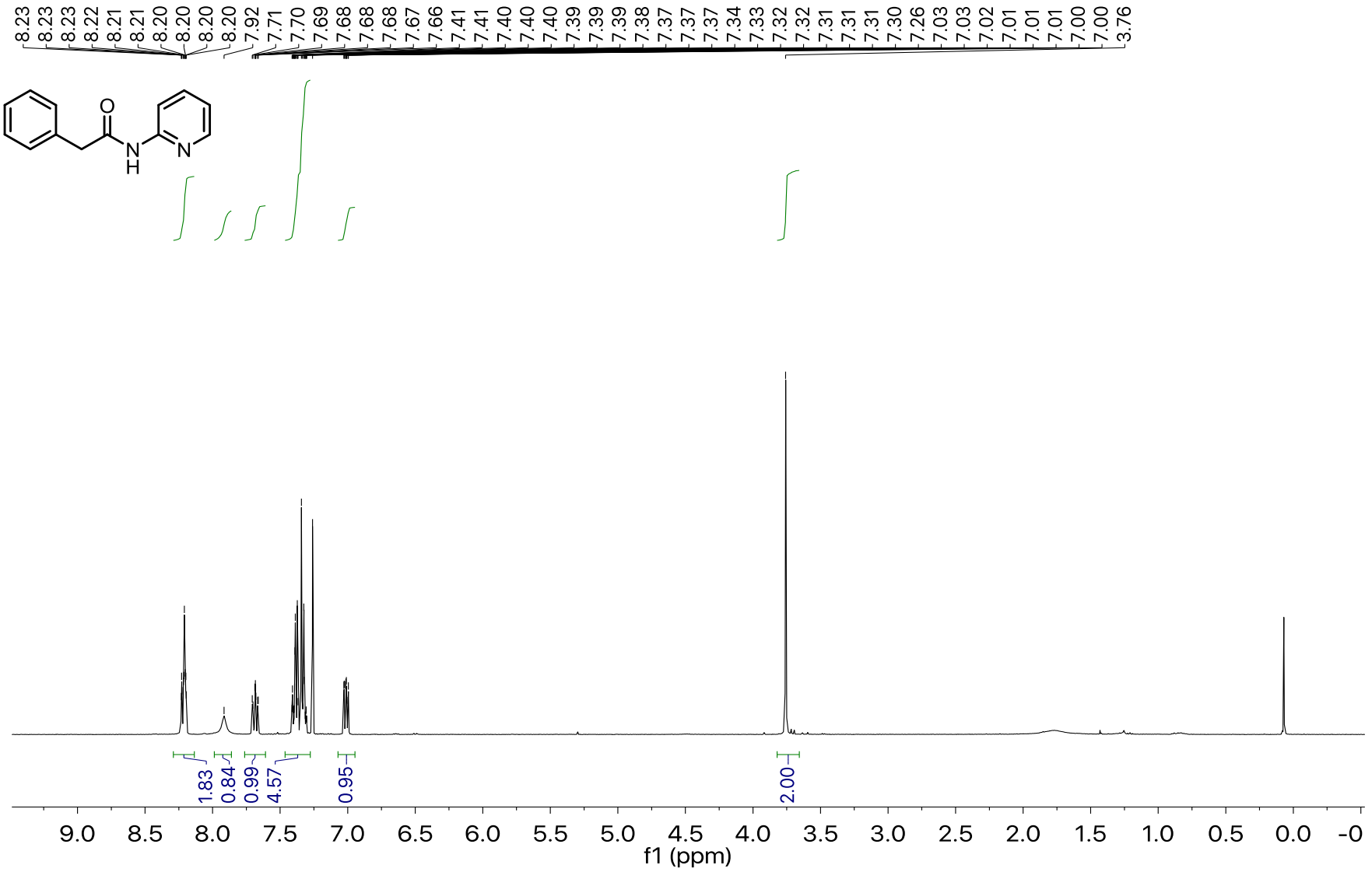
^{1}H NMR spectrum of *N*-(4-methylbenzyl)picolinamide (**21**) (400 MHz, $CDCl_3$)



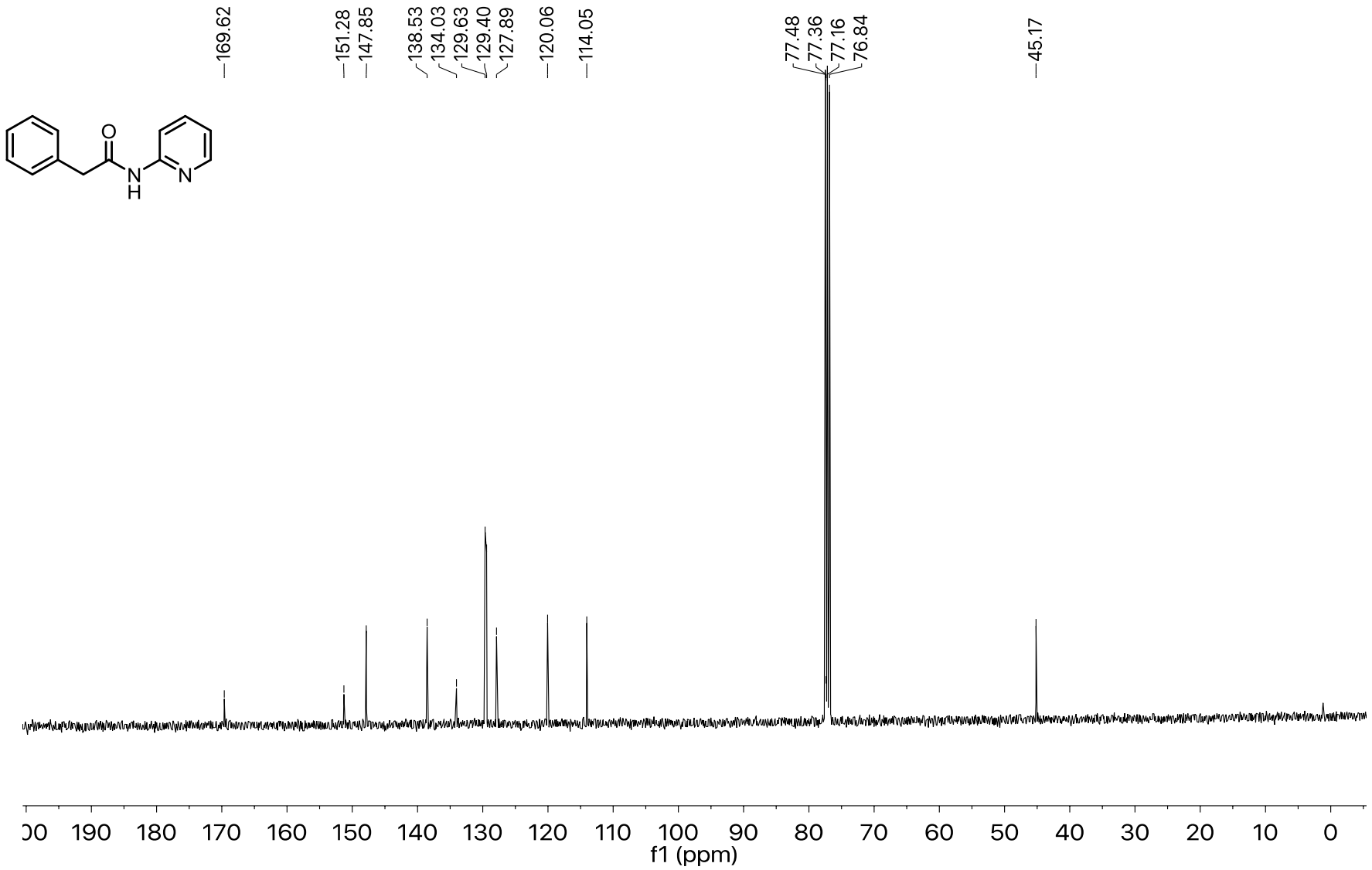
^{13}C NMR spectrum of *N*-(4-methylbenzyl)picolinamide (**21**) (101 MHz, $CDCl_3$)



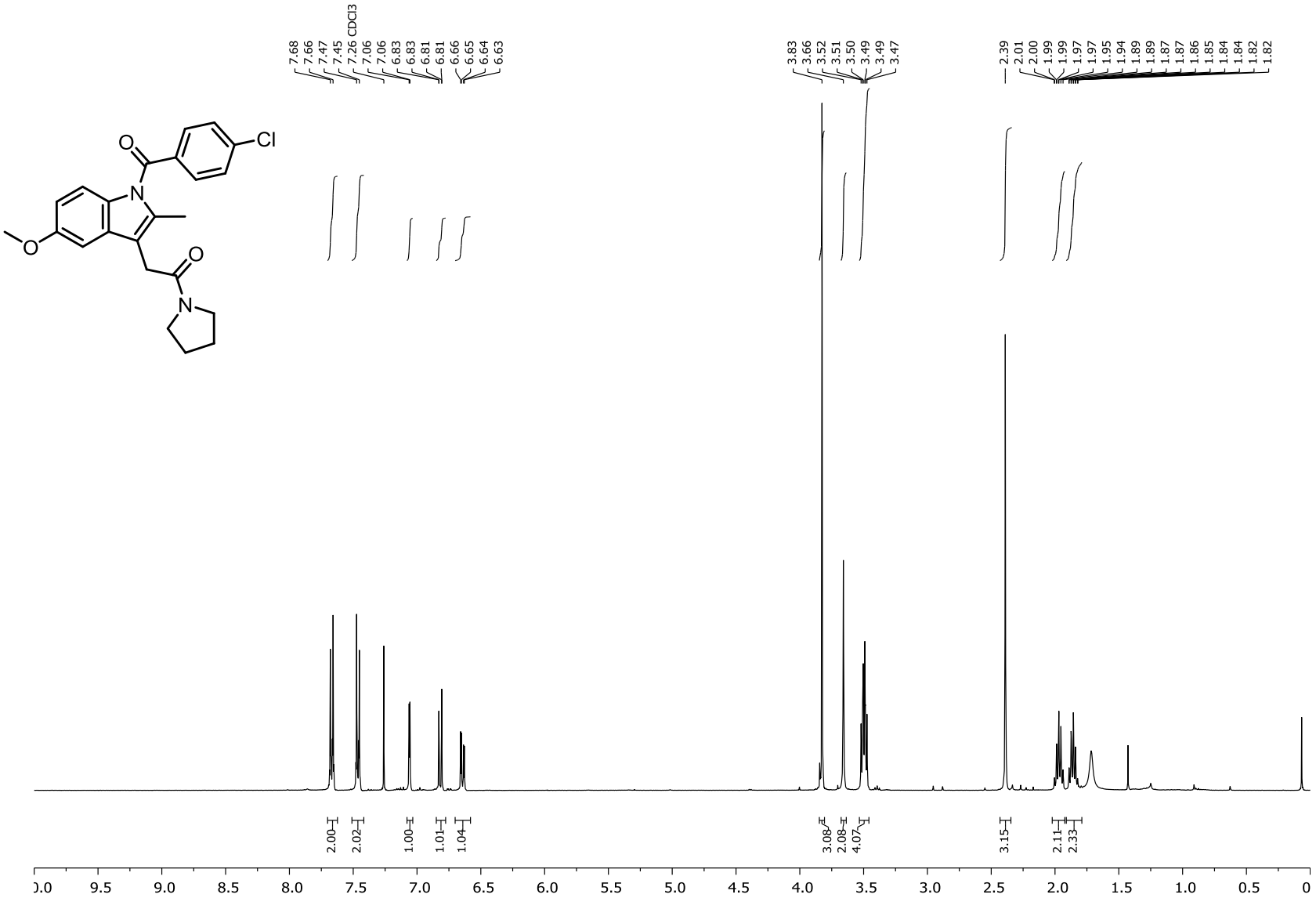
^{1}H NMR spectrum of 2-phenyl-*N*-(pyridin-2-yl)acetamide (**22**) (400 MHz, $CDCl_3$)



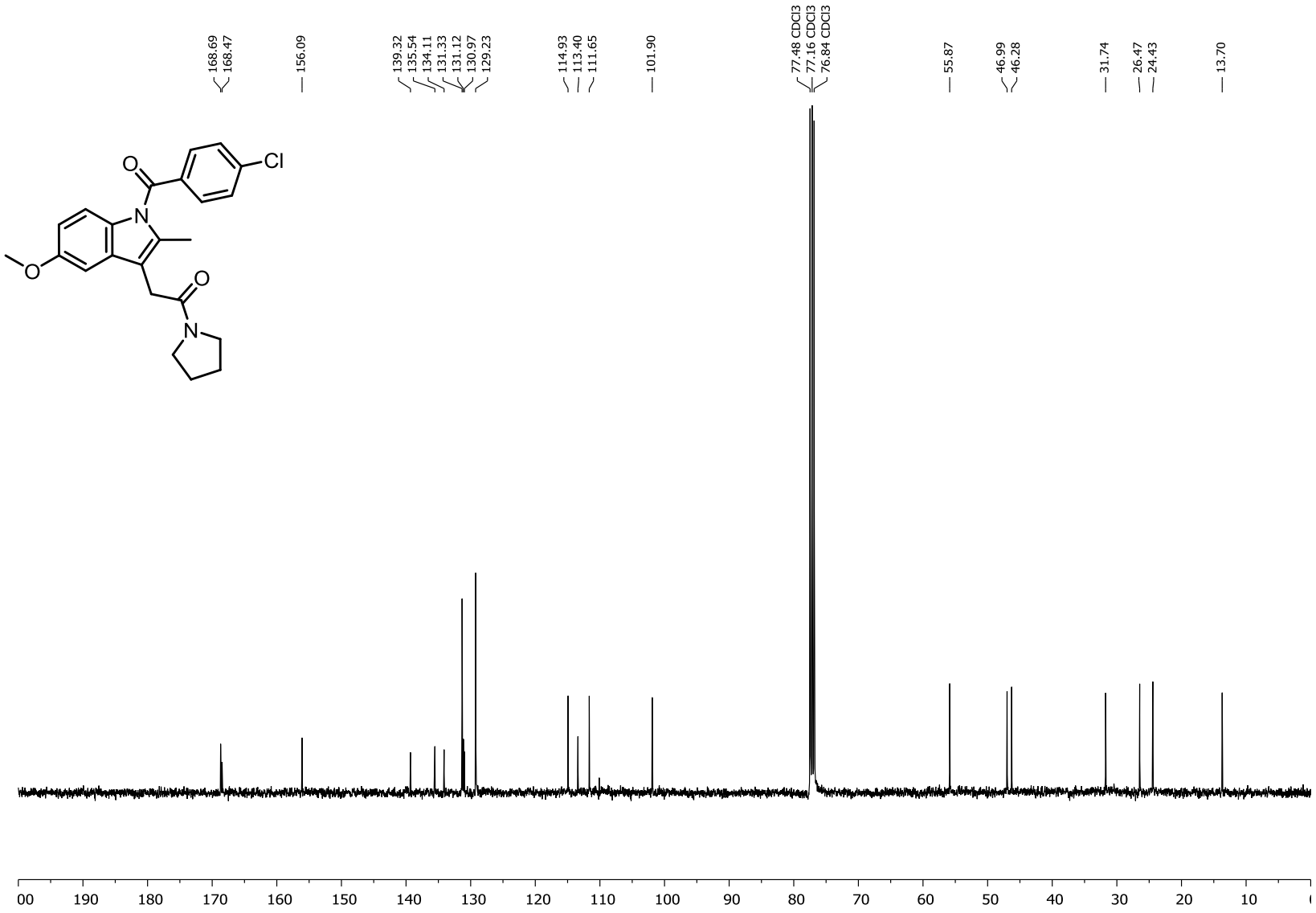
^{13}C NMR spectrum of 2-phenyl-*N*-(pyridin-2-yl)acetamide (**22**) (100 MHz, $CDCl_3$)



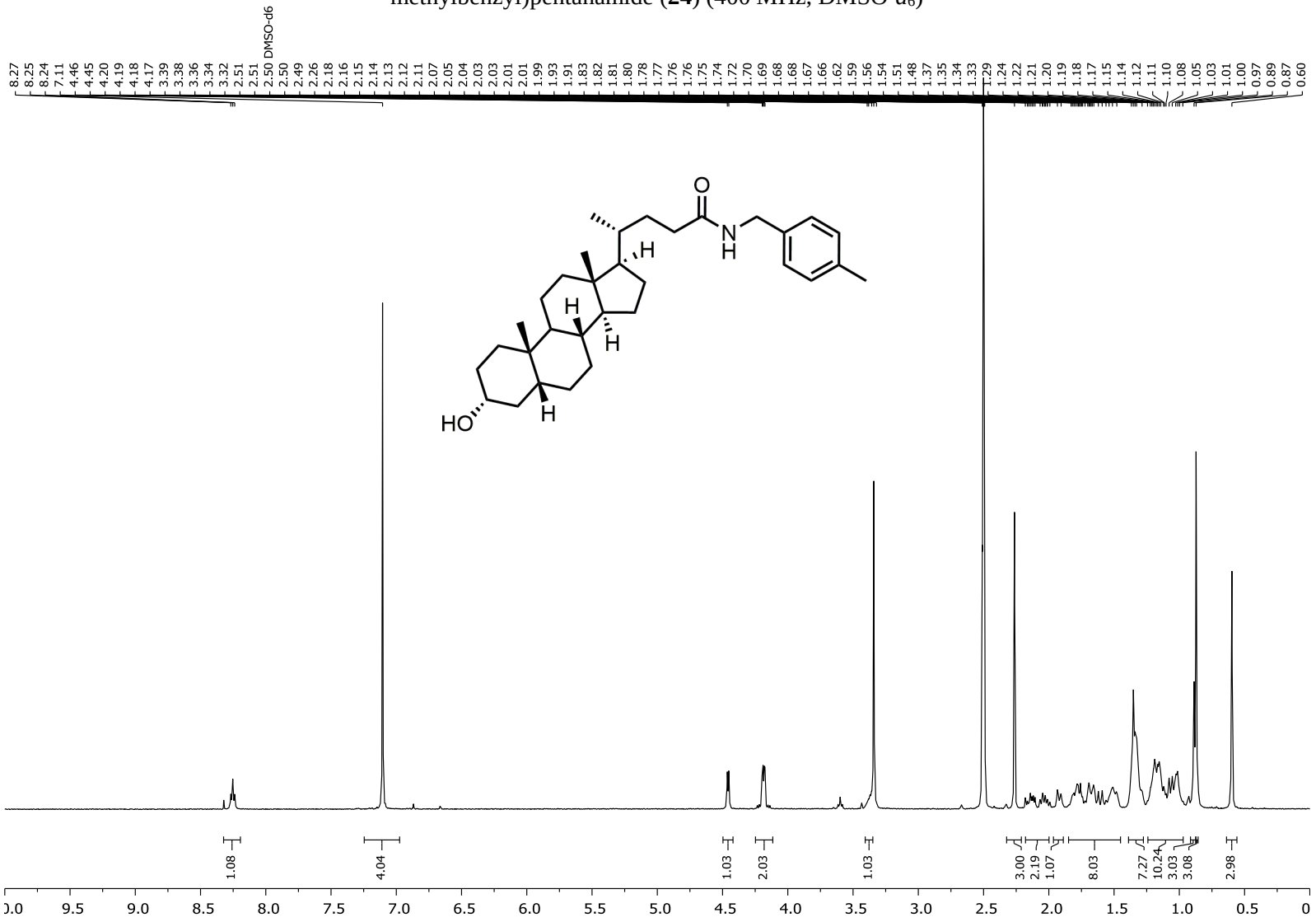
^{1}H NMR spectrum of 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)-1-(pyrrolidin-1-yl)ethan-1-one (**23**) (400 MHz, $CDCl_3$)



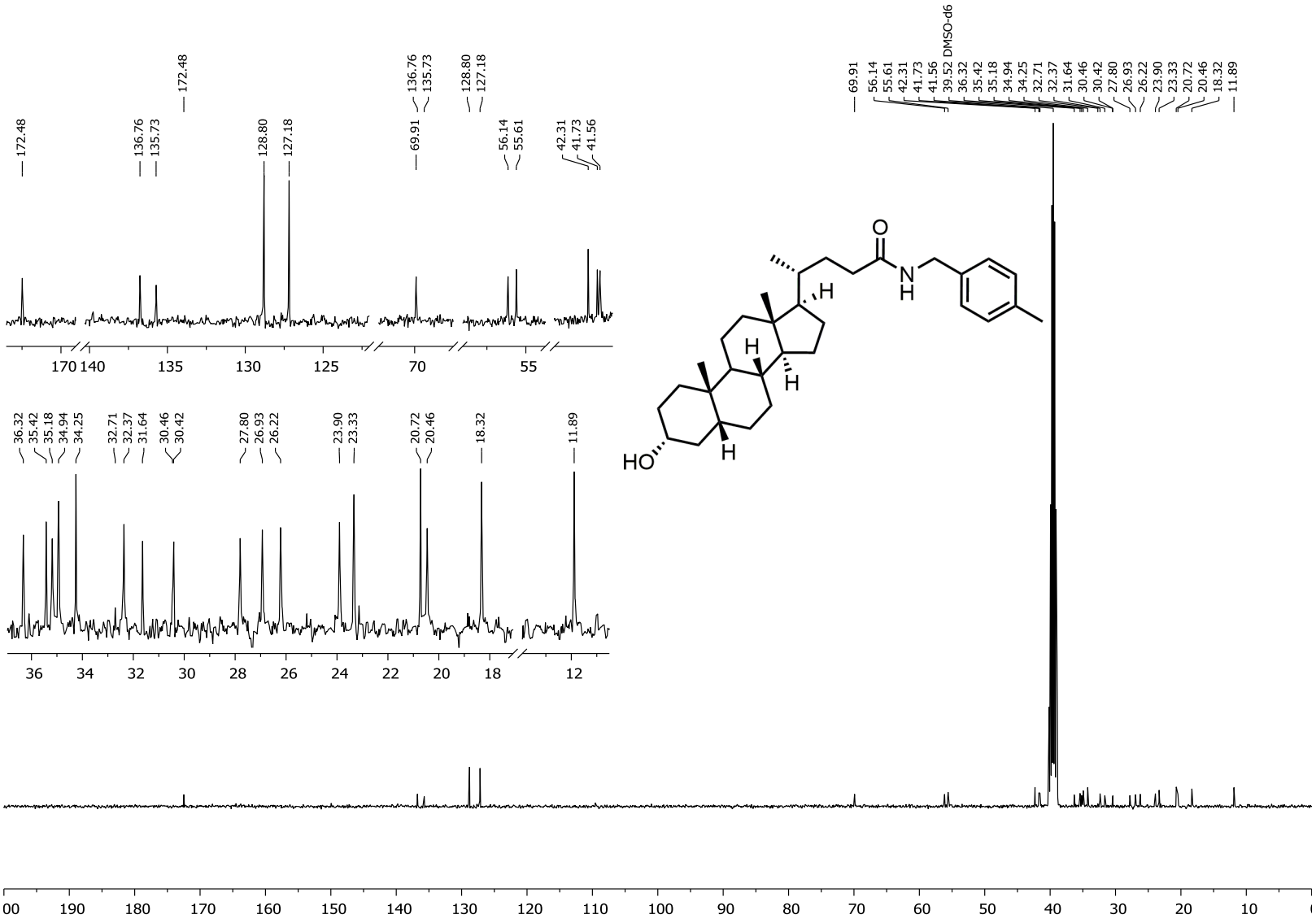
^{13}C NMR spectrum of 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)-1-(pyrrolidin-1-yl)ethan-1-one (**23**) (101 MHz, $CDCl_3$)



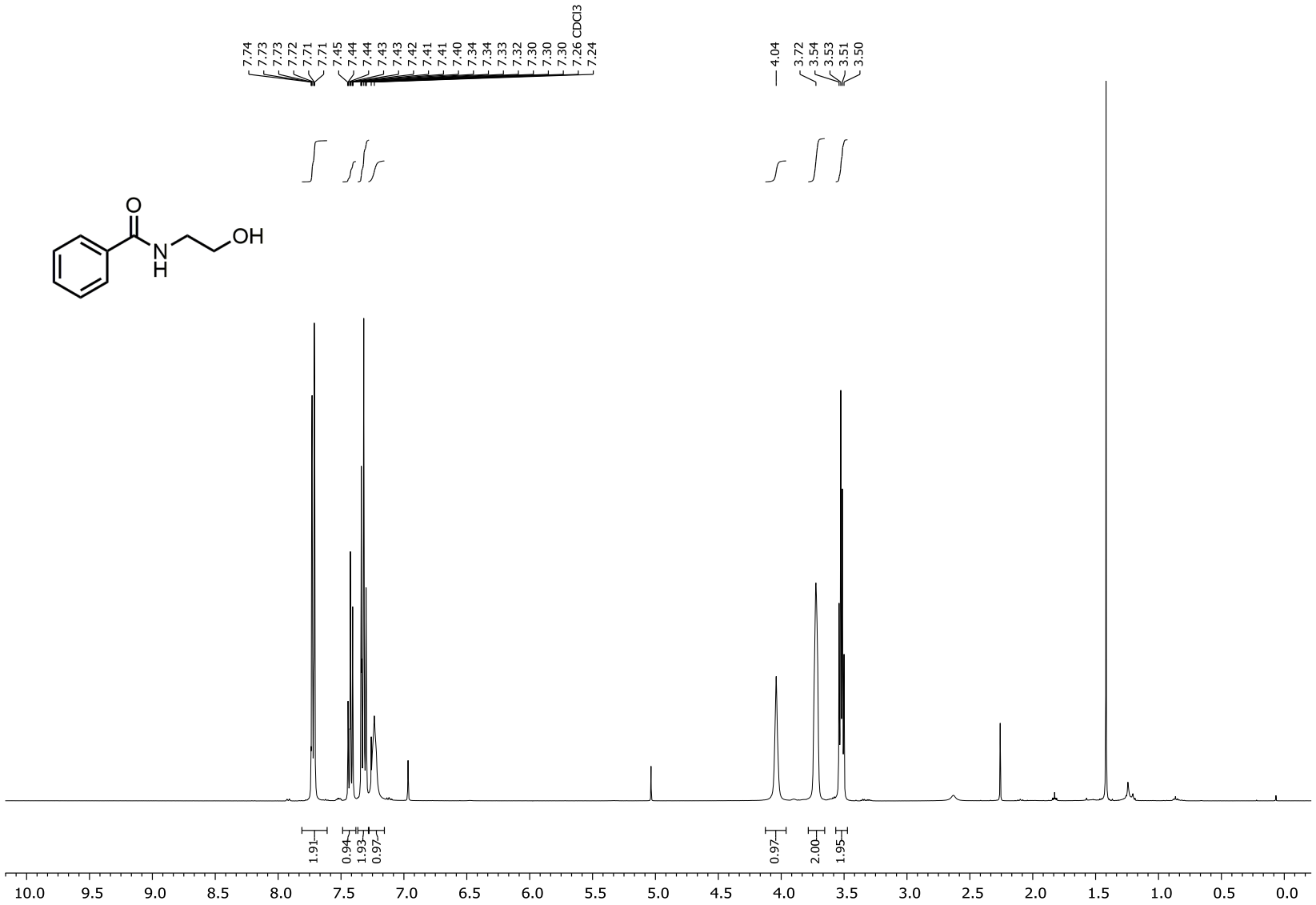
^{1}H NMR spectrum of (4*R*)-4-((3*R*,5*R*,8*R*,10*S*,13*R*,14*S*,17*R*)-3-hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(4-methylbenzyl)pentanamide (**24**) (400 MHz, DMSO-d_6)



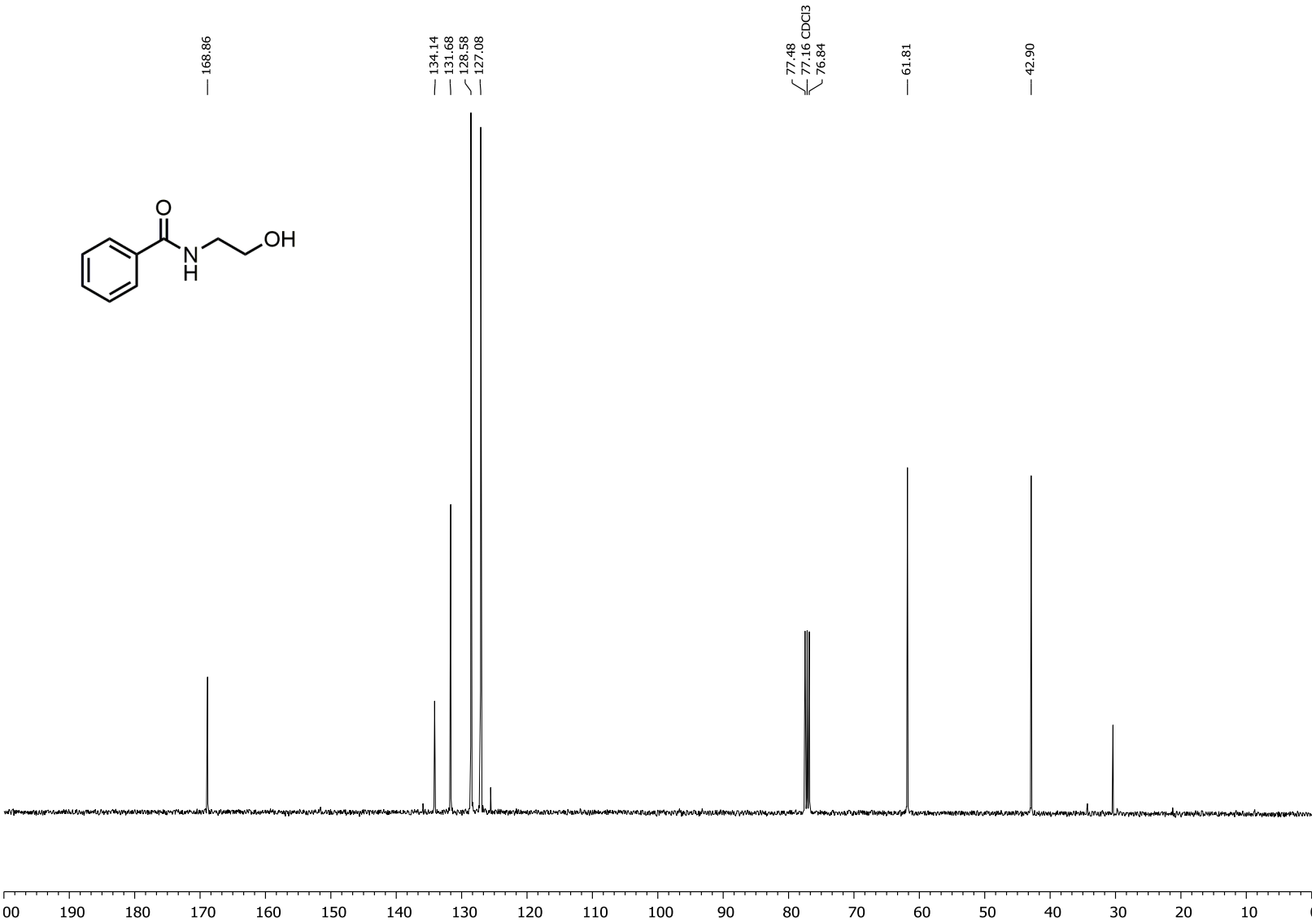
^{13}C NMR spectrum of (4*R*)-4-((3*R*,5*R*,8*R*,10*S*,13*R*,14*S*,17*R*)-3-hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(4-methylbenzyl)pentanamide (**24**) (101 MHz, DMSO-d_6)



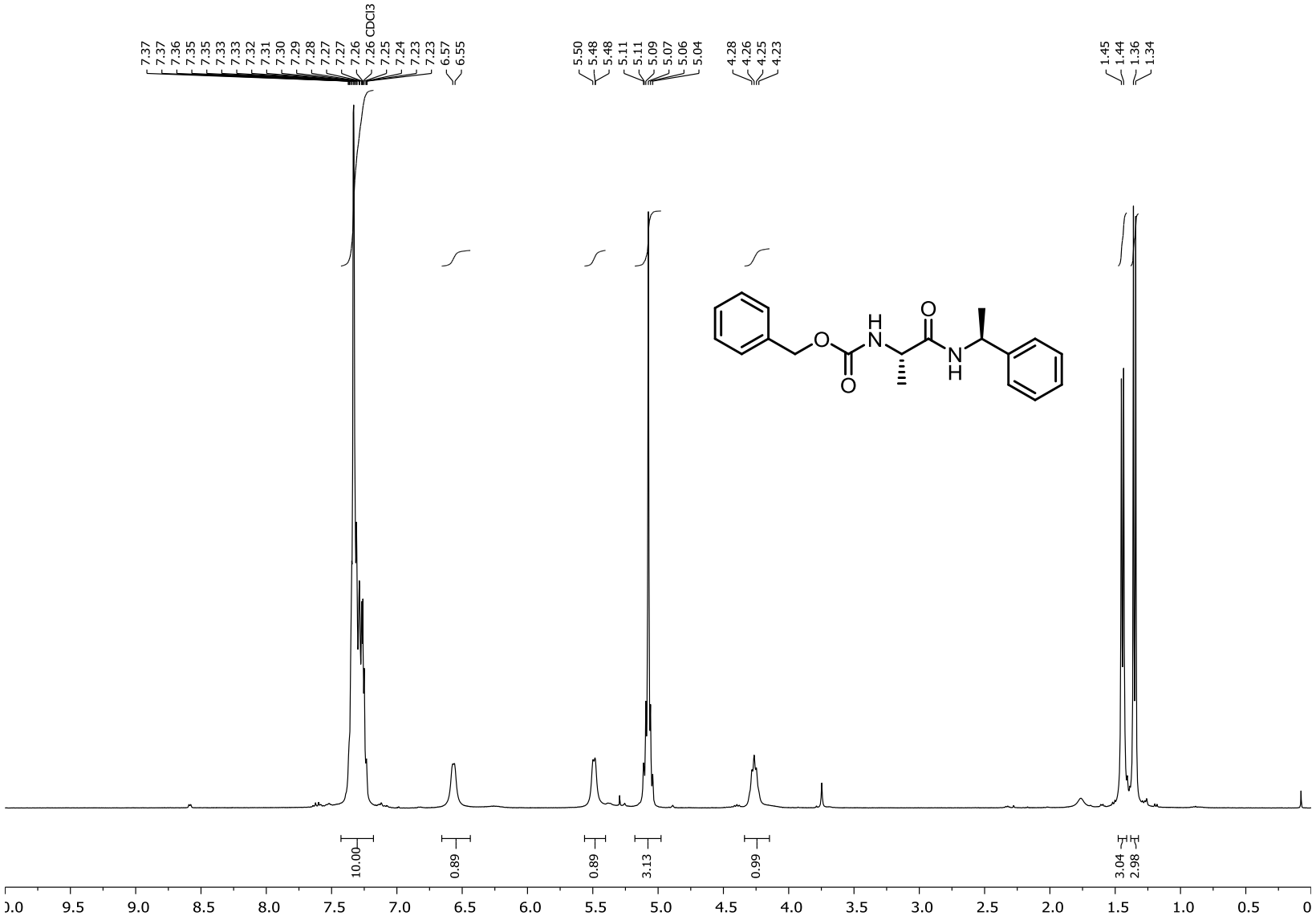
^{1}H NMR spectrum of *N*-(2-hydroxyethyl)benzamide (**25**) (400 MHz, $CDCl_3$)



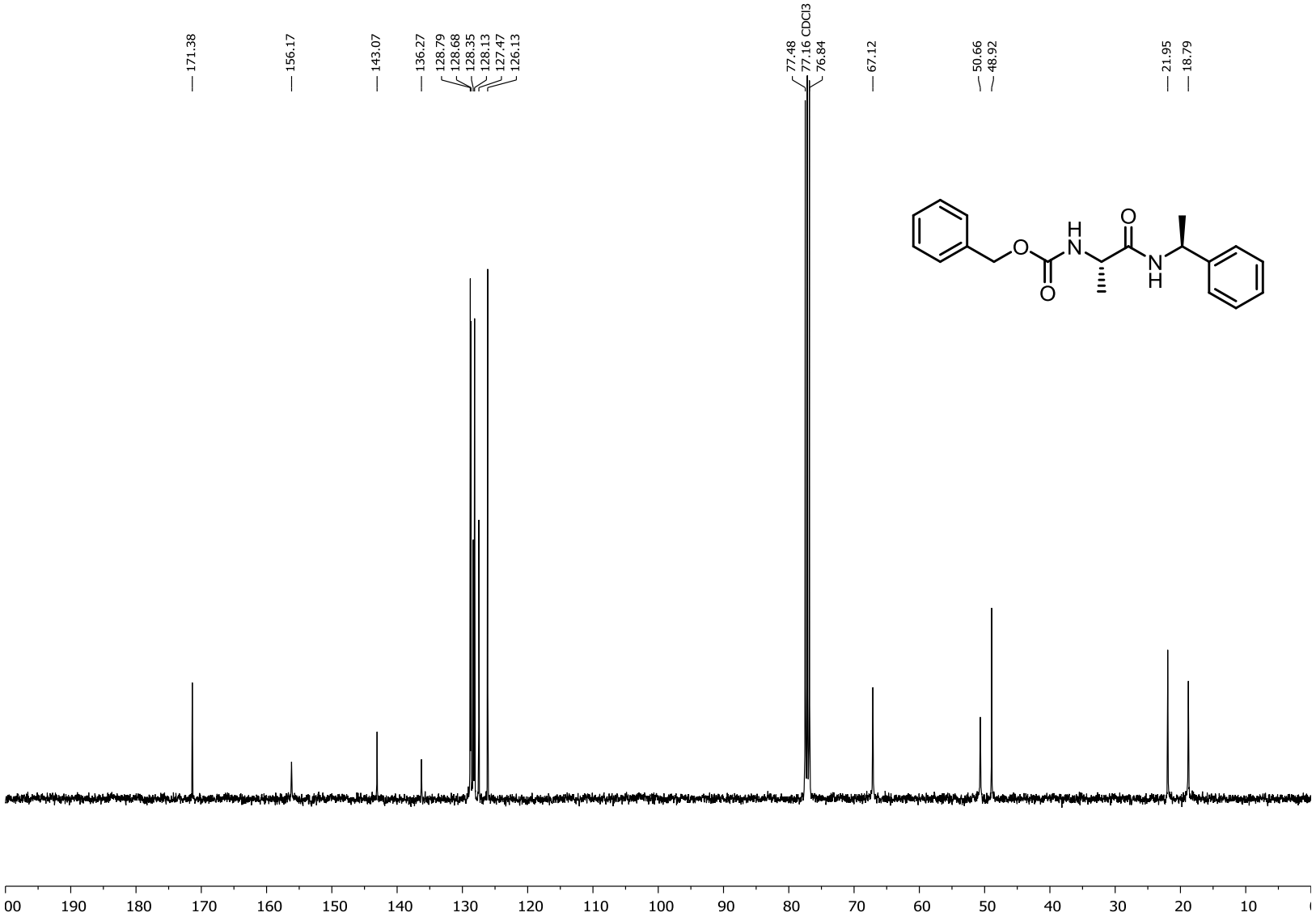
^{13}C NMR spectrum of *N*-(2-hydroxyethyl)benzamide (**25**) (101 MHz, $CDCl_3$)



^{1}H NMR spectrum of benzyl ((*S*)-1-oxo-1-(((*S*)-1-phenylethyl)amino)propan-2-yl)carbamate (**26**) (400 MHz, $CDCl_3$)

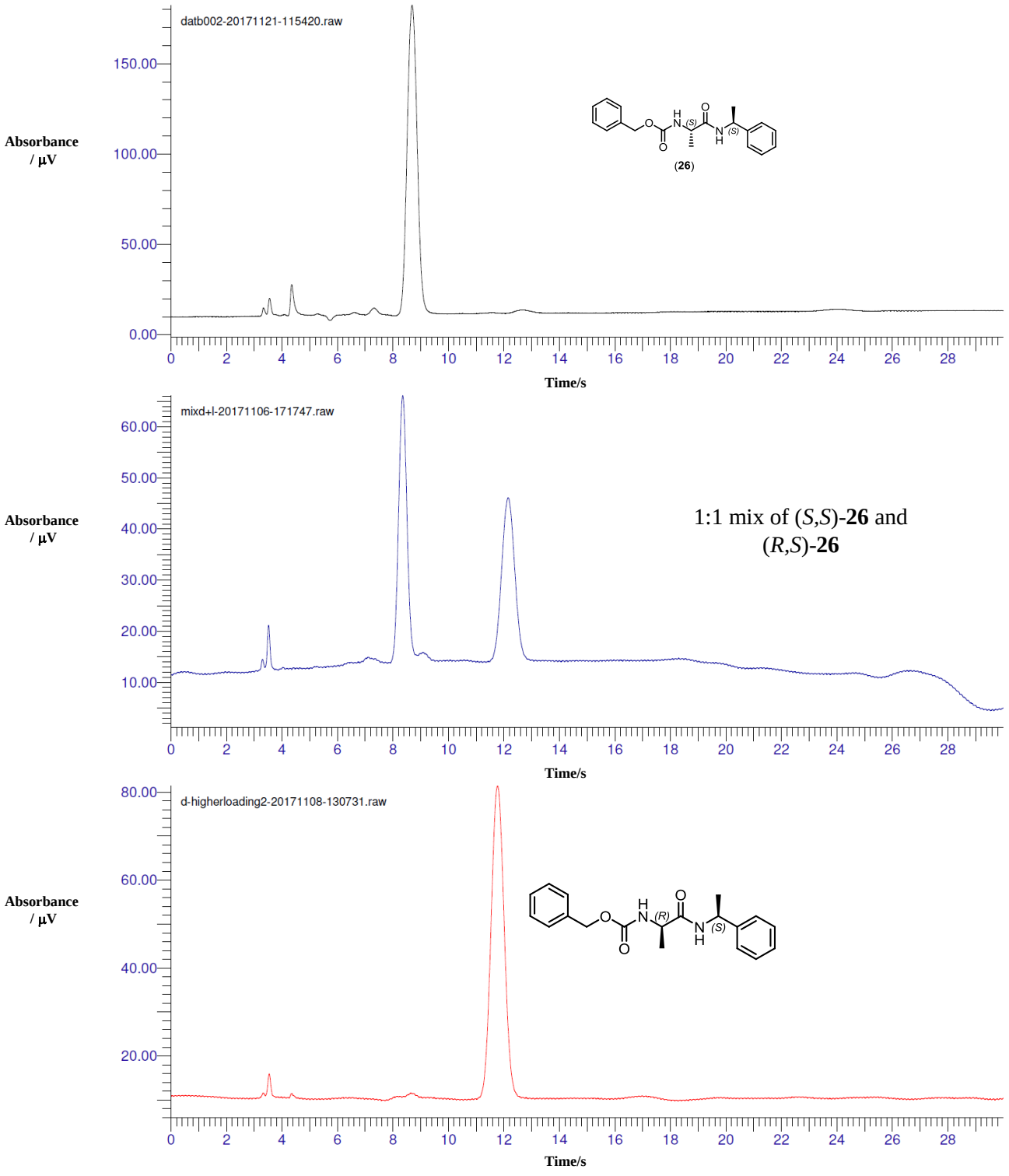


^{13}C NMR spectrum of benzyl ((*S*)-1-oxo-1-(((*S*)-1-phenylethyl)amino)propan-2-yl)carbamate (**26**) (101 MHz, $CDCl_3$)

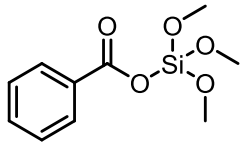


HPLC analyses of stereochemical purity of amides (*S,S*)-26 through comparison with (*R,S*)-26. (Normal Phase analytical HPLC, Column: Chiralpak AD, λ = 220nm, 20% IPA in hexane @ 0.8 ml/min over 30 min) R_t (*S,S*)-**26** = 8.26 min, R_t (*R,S*)-**26** = 12.15 min

1



***In situ* observation of the *de facto* acylating agent benzoyltrimethoxysilane (13), by ^{1}H, ^{13}C, and ^{29}Si NMR**



Benzoic acid (2.44 g, 20 mmol), tetramethylorthosilicate (2.96 mL, 20 mmol) and toluene (7.04 mL) was charged into a two-necked 25 mL flask fitted with a glass stopper, reflux condenser and a Teflon coated stirrer bar. This mixture was purged under a flow of nitrogen for 5 minutes after which the mixture was heated to reflux. The refluxing solution was sampled after 1 hour via syringe, the solvent was removed *in vacuo*, the resulting white solid was dissolved in $CDCl_3$ and NMR spectra were recorded.

Comparison of ^{1}H NMR data for *in situ* observed (13) and authentic (13)

Proton	Observed (13) δ / ppm (400 MHz, $CDCl_3$)	Authentic (13) δ / ppm (400 MHz, $CDCl_3$)[17]
(*ortho* – H)	8.12 - 8.10 (obscured)	8.12 - 8.07
(*para* – H)	7.54 – 7.51 (obscured)	7.65 - 7.55
(*meta* – H)	7.43 – 7.39 (obscured)	7.51 – 7.42
(OCH_3)	3.73	3.74

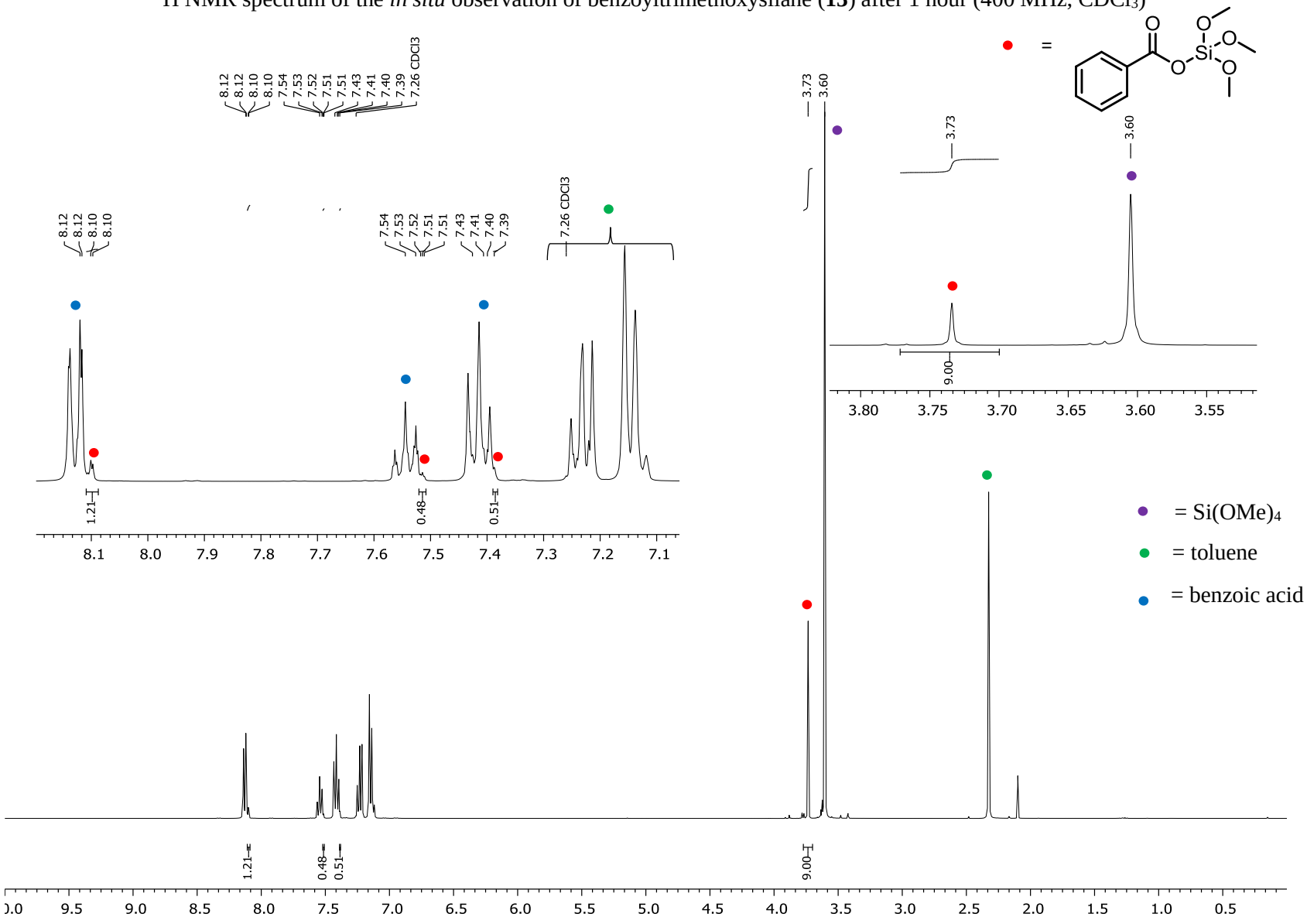
Comparison of ^{13}C NMR data for *in situ* observed (13) and authentic (13)

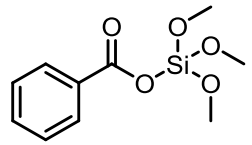
Carbon	Observed (13) δ / ppm (101 MHz, $CDCl_3$)	Authentic (13) δ / ppm (100 MHz, $CDCl_3$)[17]
C=O	164.9	164.9
(*para* – C)	133.5	133.5
(*ortho*– C)	130.5	130.4
(*ortho*– C)	obscured	129.9
(*ortho*– C)	obscured	128.4
($O\underline{C}H_3$)	51.8	51.9

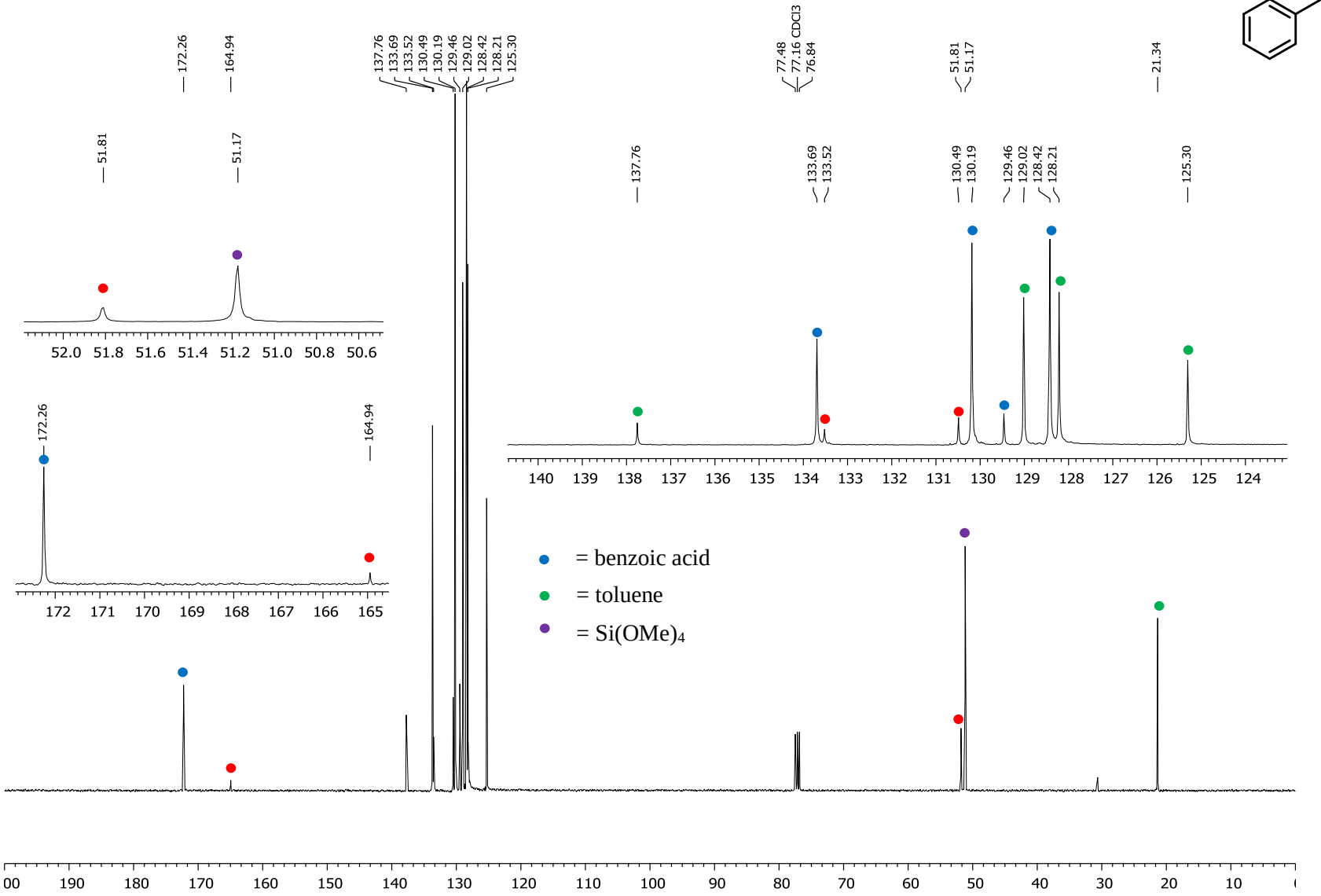
Comparison of ^{29}Si NMR data for *in situ* observed (13) and authentic (13)

Silicon	Observed (13) δ / ppm (80 MHz, $CDCl_3$)	Authentic (13) δ / ppm (80 MHz, CD_2Cl_2)[17]
$PhCO_2\underline{Si}(OMe)_3$	-82.2	-82.4

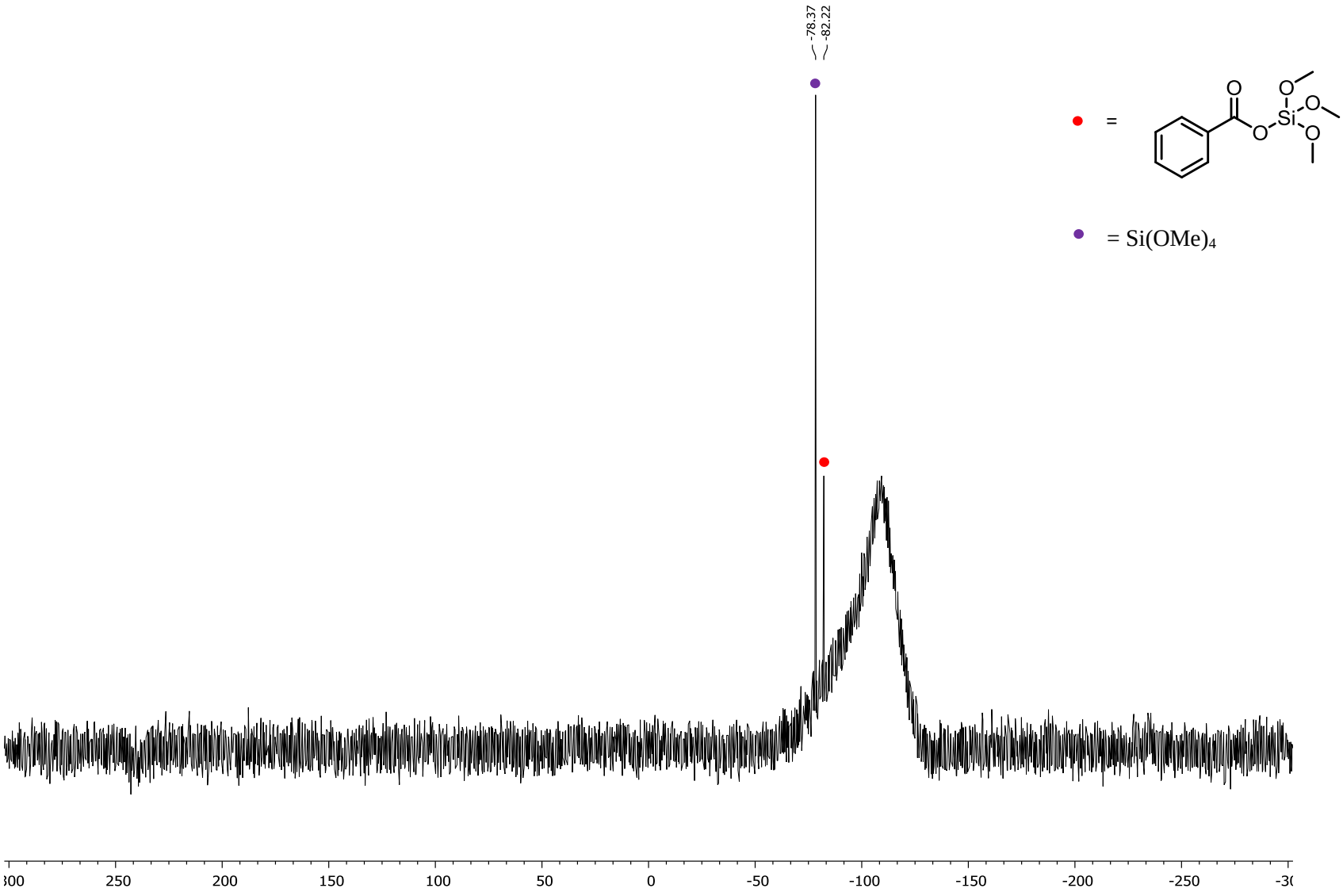
^{1}H NMR spectrum of the *in situ* observation of benzoyltrimethoxysilane (**13**) after 1 hour (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of the *in situ* observation of benzoyltrimethoxysilane (**13**) after 1 hour (101 MHz, $CDCl_3$) ● = 

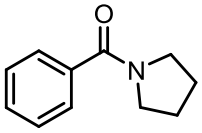


^{29}Si NMR spectrum of the *in situ* observation of benzoyltrimethoxysilane (**13**) after 1 hour (80 MHz, $CDCl_3$)



Green Metric calculations

Phenyl(pyrrolidin-1-yl)methanone (9)

 Synthesised following **GP4**.

		Equivalents used	Molarity (mol / L)	MW (g / mol)	mmol	g	Density g / mL[††]	Volume (mL)
Reactants	Benzoic acid	1.00	2.00	122.12	1000.00	122.12		
	pyrrolidine	1.00	2.00	71.12	1000.00	71.12	0.85	83.47
	TMOS	2.50		152.22	2500.00	380.55	1.03	369.47
Auxiliary materials	Toluene			92.14	1229.80	113.32	0.87	131.00
	aq.K_2CO_3		2.89	138.21	5788.00	2000.00	1.00	2000.00
	THF			72.11	20959.13	1511.30	0.89	1700.00
	DCM			84.93	15918.99	1622.40	1.35	1200.00
	Water			18.02	55493.90	1000.00	1.00	1000.00
	$MgSO_4$					20.00		
Product	phenyl(pyrrolidin-1-yl)methanone (**9**)	1.00		175.23	1000.00	157.8		
Calculations	Sum reactants					573.80		
	Sum all materials - product					6840.81		
	Yield (decimal)					0.90		
	AE %					30.54		
	RME %					27.49		
	PMI					43.38		
	RME/AE %					90.00		
	E-Factor					42.38		

Footnotes:

† Reaction molarity is defined by total volume of TMOS + toluene.

†† Aqueous K_2CO_3 density assumed as 1 g / mL

References:

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