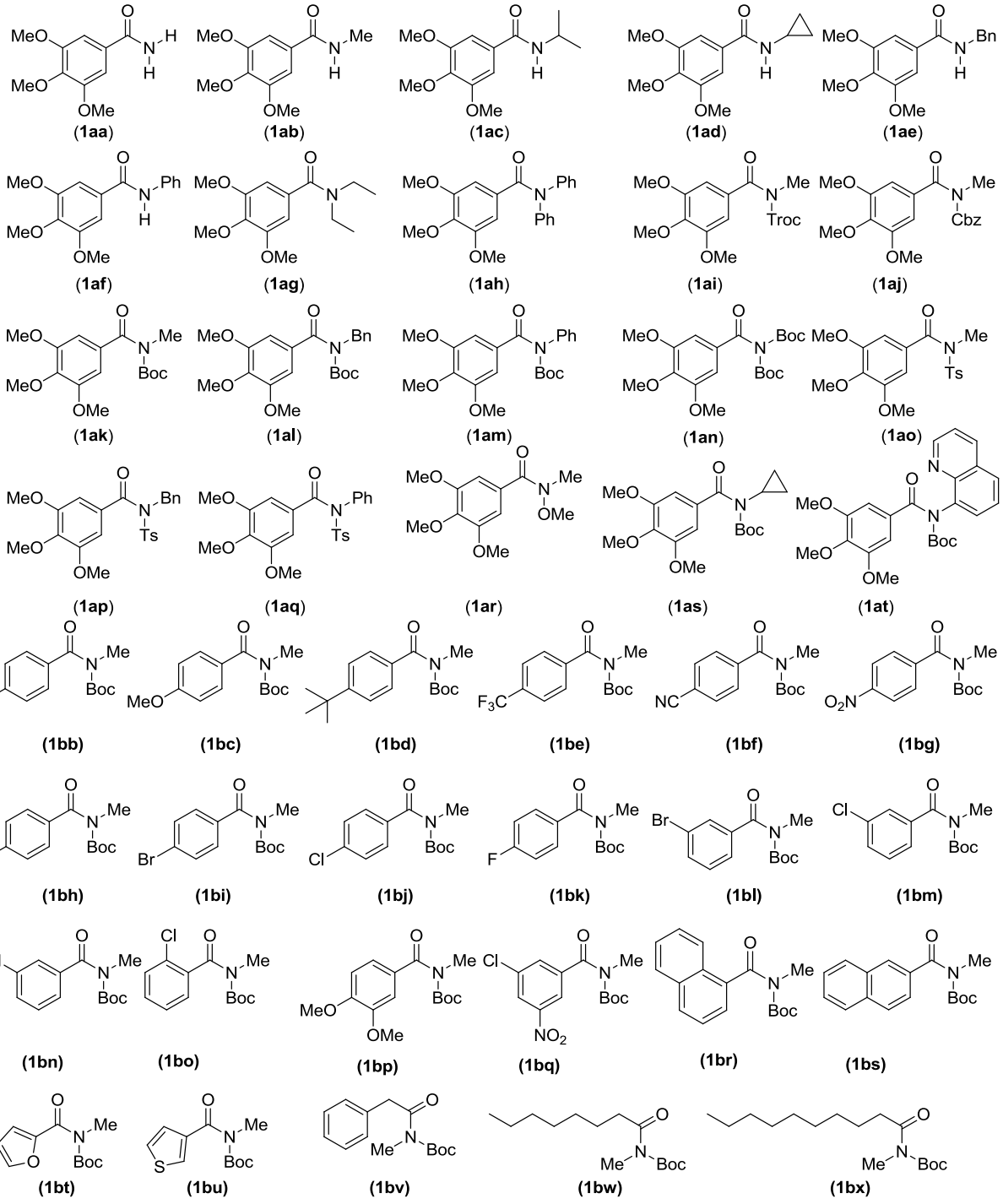
Supporting Information

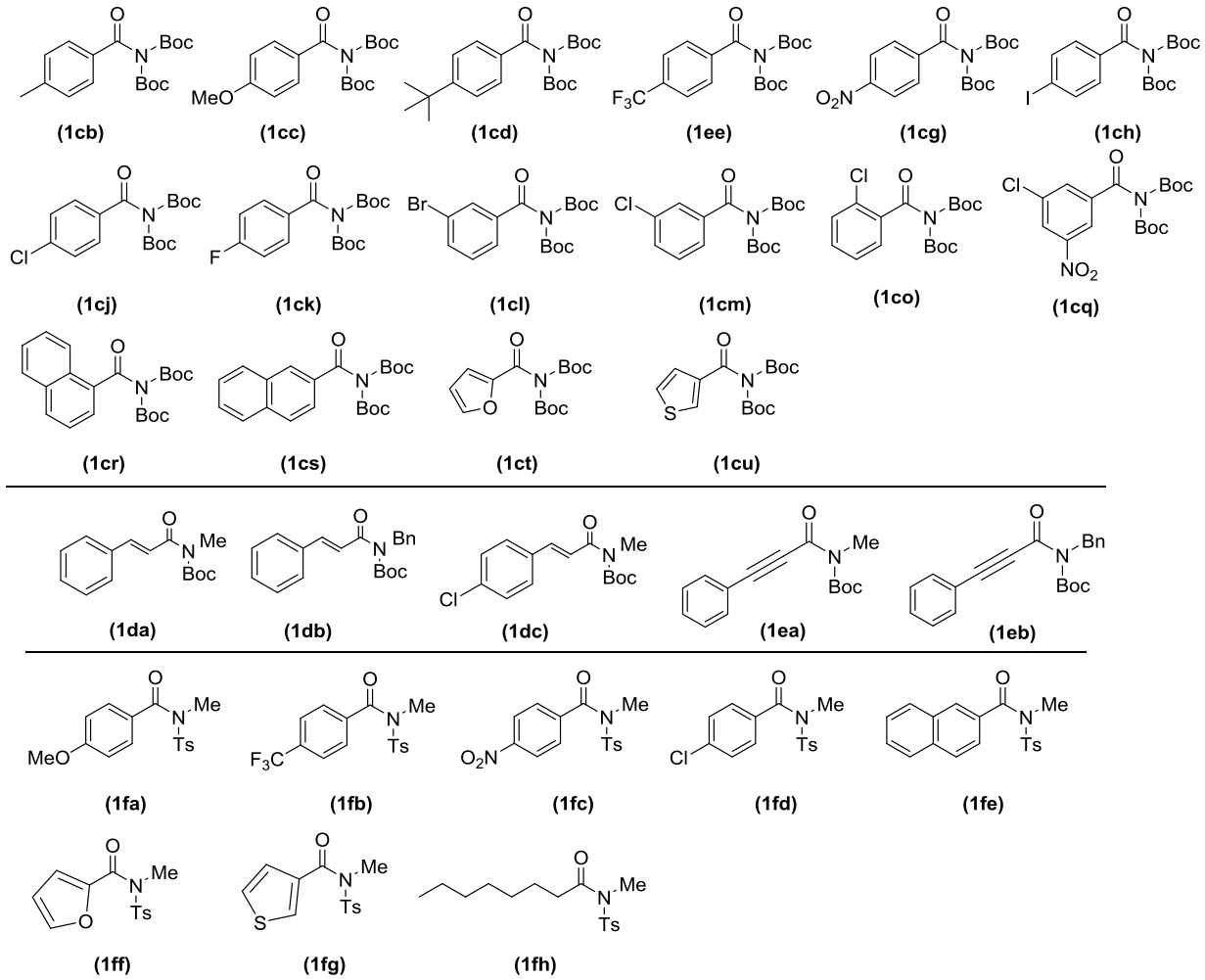
Controlled Reduction of Activated Primary and Secondary Amides into Aldehydes with Diisobutylaluminum Hydride (DIBAL-H)

Sadaf Azeez,[a#] Popuri Sureshbabu,[a#] Shahulhameed Sabiah[b] and Jeyakumar Kandasamy[a]*

[a]Department of Chemistry, Indian Institute of Technology (BHU), Varanasi, Uttar Pradesh-221005; Email: jeyakumar.chy@iitbhu.ac.in
[b]Department of Chemistry, Pondicherry University, Pondicherry-605014

1.Structure of starting materials:-

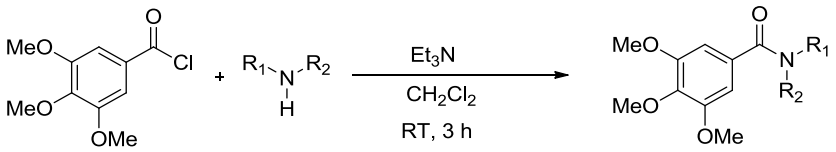




2. General Methods. Solvents, chemicals, amides **1aa** and **1ab** and reducing agents were obtained from commercial sources. DIBAL-H was obtained from Sigma-Aldrich (Catalog No: 215007). Dry THF, toluene and ether were used for the reduction reactions. The reactions were carried out under an argon atmosphere. TLC was performed using pre-coated E. Merck (*TLC silica gel 60 F254*) plates. TLCs were visualized under ultraviolet light (UV) with 254 nm of wavelength and/or by using iodine chamber. The ^{1}H and ^{13}C NMR spectra were obtained on *Bruker Avance 500 MHz NMR spectrometer* while Mass spectra (HRMS) were obtained on UHD Q-Tof (ESI-TOF) using *water's Quattro Micro V 4.1* mass spectrometer. $CDCl_3$ peak in proton (^{1}H) NMR is graduated to 7.26 ppm and 77.00 ppm for ^{13}C NMR spectra. The low temperatures were attained using a low-temperature reaction bath *Eyela PSL-1810* (Made in Japan) instrument.

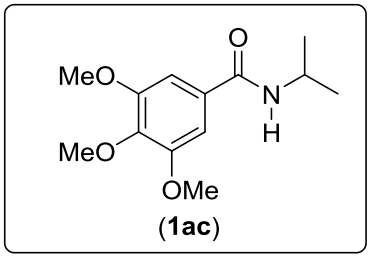
3. Experimental procedures for the synthesis of amides

3.1 Synthesis of amides 1aa-1ah and 1at:

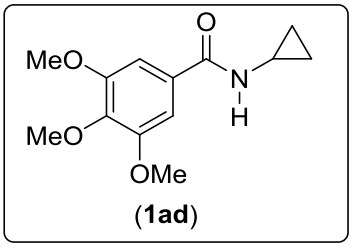


The amides were prepared using the literature procedure.[1a] 3,4,5-Trimethoxybenzoyl chloride (2.3 g, 10.0 mmol, 1 equiv.) and Et_3N (3.5 mL, 25 mmol, 2.5 equiv.) was stirred in DCM (20 mL) at 0 °C to which corresponding amine (10 mmol, 1 equiv.) was added dropwise at 0 °C. The resulting mixture was stirred at room temperature for 3 hours, and diluted with DCM (25 mL) and washed with water and brine. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude residue was purified by silica gel (100-200 mesh) column chromatography (ethyl acetate/hexane) to obtain the secondary and tertiary amides.

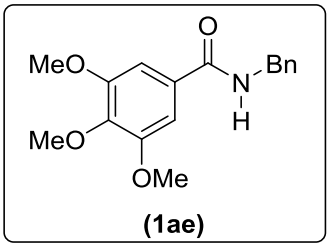
***N*-Isopropyl-3,4,5-trimethoxybenzamide (1ac):** Obtained as a white solid (mp 152–154 °C), R_f = 0.42 (hexane:EtOAc-60:40), Yield 78% (1.97 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.96 (s, 2H), 5.95 (s, 1H), 4.29-4.22 (m, 1H), 3.88 (s, 6H), 3.85 (s, 3H), 1.25 (d, J = 6.6 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 166.3, 153.1, 140.7, 130.4, 104.3, 60.8, 56.3, 42.0, 22.7. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{13}H_{20}NO_4$: 254.1392, found 254.1393.



***N*-Cyclopropyl-3,4,5-trimethoxybenzamide (1ad):** Obtained as a white solid (mp 147–148 °C), R_f = 0.47 (hexane:EtOAc- 60:40), Yield 76% (1.90 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.96 (s, 2H), 6.41 (s, 1H), 3.87 (s, 6H) 3.85 (s, 3H), 2.86 (s, 1H), 0.83 (d, J = 4.6 Hz, 2H), 0.61 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.6, 153.0, 140.7, 129.8, 104.2, 60.8, 56.2, 23.2, 6.6. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{13}H_{18}NO_4$: 252.1236, found 252.1240.

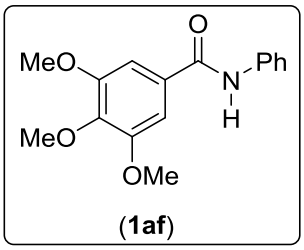


***N*-Benzyl-3,4,5-trimethoxybenzamide (1ae)**[1b]: Obtained as a white solid (mp 140 °C), R_f = 0.51 (hexane:EtOAc-60:40), Yield 79% (2.37 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.37–7.32 (m, 4H), 7.29 (d, J = 4.0 Hz, 1H), 7.02



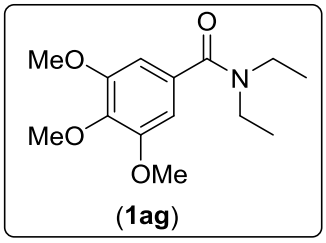
(s, 2H), 6.54 (s, 1H), 4.62 (d, J = 5.4 Hz, 2H), 3.86 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 167.0, 153.1, 140.9, 138.1, 129.7, 128.7, 127.8, 127.5, 104.3, 60.8, 56.2, 44.1.

3,4,5-Trimethoxy-*N*-phenylbenzamide (1af)[1c]: Obtained as a white solid (mp 141–142 °C), R_f = 0.52 (hexane:EtOAc-60:40), Yield 86% (2.47 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.03 (s, 1H), 7.63 (d, J = 7.7 Hz, 2H), 7.35 (t, J = 7.8 Hz, 2H), 7.15 (d, J = 7.4 Hz, 1H), 7.05 (s, 2H), 3.87 (d, J = 8.0 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 165.6, 153.2, 141.0, 137.8, 130.4, 129.0, 124.5, 120.2, 104.4, 60.8, 56.2.



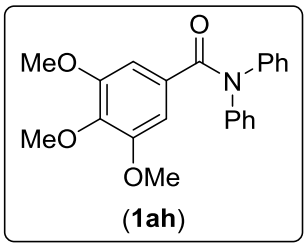
(**1af**)

***N*,*N*-Diethyl-3,4,5-trimethoxybenzamide (1ag)**[1b]: Obtained as a white solid (mp 53–54 °C), R_f = 0.54 (hexane:EtOAc-60:40), Yield 82% (2.18 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.55 (dd, J = 4.1, 1.5 Hz, 2H), 3.82 (dd, J = 4.3, 1.7 Hz, 6H), 3.81 (dd, J = 4.5, 1.8 Hz, 3H), 3.37 (m, 4H), 1.25–1.07 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 170.8, 153.1, 138.5, 132.5, 103.4, 60.7, 56.0, 43.2, 39.2, 14.2, 12.7.



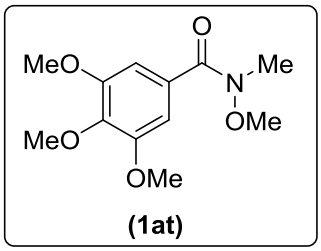
(**1ag**)

3,4,5-Trimethoxy-*N*,*N*-diphenylbenzamide (1ah): Obtained as a white solid (mp 42–44 °C), R_f = 0.48 (hexane:EtOAc-60:40), Yield 76% (2.75 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.31 (t, J = 7.8 Hz, 4H), 7.22–7.14 (m, 6H), 6.71 (s, 2H), 3.81 (s, 3H), 3.64 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.8, 152.4, 144.1, 139.7, 130.4, 129.1, 127.3, 126.3, 107.2, 60.8, 55.9. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{22}H_{22}NO_4$: 364.1549, found 364.1537.



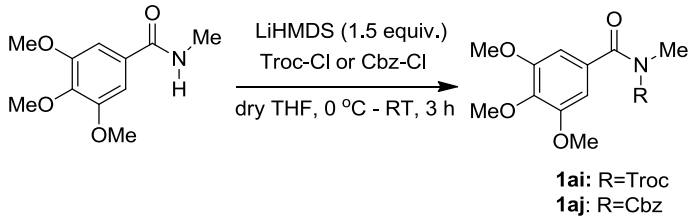
(**1ah**)

***N*,3,4,5-Tetramethoxy-*N*-methylbenzamide (1at)**[1b]: Obtained as a colorless liquid, R_f = 0.51 (hexane:EtOAc-60:40), Yield 79% (2.01 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.97 (s, 2H), 3.88 (d, J = 1.7 Hz, 9H), 3.59 (s, 3H), 3.36 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.0, 152.5, 139.8, 128.8, 105.6, 60.9, 60.6, 55.9, 33.7.



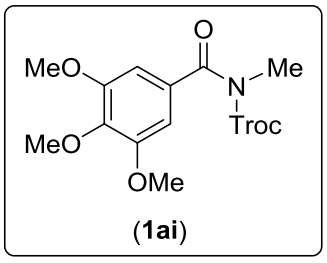
(1at)

3.2 Synthesis of amides 1ai and 1aj:



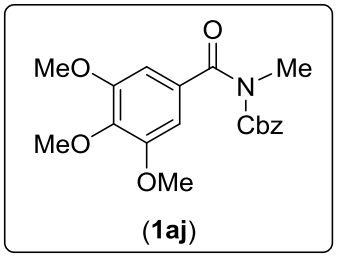
To a stirred solution of 3,4,5-trimethoxy-*N*-methylbenzamide (5 mmol, 1.125 g) in THF (20 mL) was added lithium bis(trimethylsilyl)amide (LiHMDS, 1 M solution in THF, 7.5 mmol, 7.5 mL) at 0 °C. The resulting mixture was allowed to stir for 15 min after which 2,2,2-trichloroethoxycarbonyl chloride (Troc-Cl, 10 mmol, 1.4 mL) or benzyl chloroformate (Cbz-Cl, 10 mmol, 1.4 mL) was added slowly and allowed the reaction to stir at room temperature for 3h. After completion, the reaction mixture was quenched with aqueous 1 M HCl solution (20 mL), diluted with EtOAc (60 mL) and washed brine. The organic layer was dried over anhydrous sodium sulfate and concentrated. The crude residue was purified by silica gel (100-200 mesh) column chromatography (ethyl acetate/hexane: 10/90) to obtain the title compounds.

2,2,2-Trichloroethyl methyl(3,4,5-trimethoxybenzoyl)carbamate (1ai): Obtained as a colorless liquid, R_f = 0.51 (hexane:EtOAc-90:10), Yield 72% (1.4 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.86 (d, J = 9.9 Hz, 2H), 4.71 (d, J = 9.9 Hz, 2H), 3.86 (s, 9H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.6, 153.4, 153.0, 141.5, 131.0, 105.7, 94.1, 74.6, 60.8, 56.3, 33.5. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{14}H_{17}Cl_3NO_6$: 400.0121, found 400.0107.



(**1ai**)

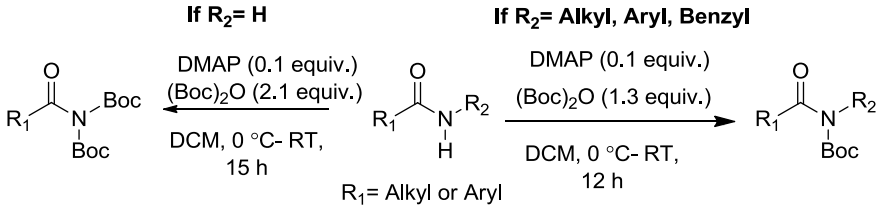
Benzyl methyl(3,4,5-trimethoxybenzoyl)carbamate (1aj): Obtained as a pale yellow liquid, R_f = 0.67 (hexane:EtOAc-90:10), Yield 87% (1.56 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.30–7.27 (m, 3H), 7.06–7.00 (m, 2H), 6.71 (s, 2H), 5.03 (s, 2H), 3.86 (s, 3H), 3.74 (s, 6H), 3.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.7, 155.0, 152.8, 140.8, 134.4, 131.7, 128.5, 128.4, 128.2, 105.0, 68.6, 60.8, 56.0, 33.1. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{19}H_{22}NO_6$: 360.1447, found 360.1436.



(**1aj**)

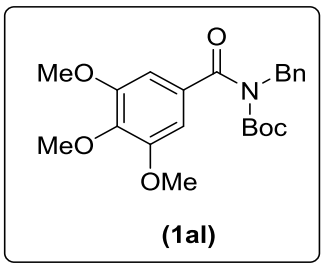
3.3 Synthesis of *N*-Boc Amides:

The amides **1bb-1bn, 1bp-bx, 1da, 1an and 1cb-1cu** were prepared using the literature procedure.[1d] Analytical data and the NMRs spectra of these amides were already reported by us (*J. Org. Chem.* **2019,** *84*, 11823-11838). The preparation and characterization of other *N*-Boc amides **1al, 1am, 1ar, 1as, 1bo, 1db, 1dc, 1ea** and **1eb** are described below.



Primary or secondary amide (5.0 mmol, 1.0 equiv.) and DMAP (65 mg, 0.5 mmol, 0.1 equiv.) were dissolved in dichloromethane (10 mL) and stirred at room temperature. In the case of primary amide, 1.3 equiv. of di-*tert*-butyl dicarbonate (Boc_2O) (1.5 mL, 6.5 mmol) was added and the reaction mixture was stirred for 12 h. In the case of secondary amide, 2.1 equiv. of di-*tert*-butyl dicarbonate (Boc_2O) (2.4 mL) was added and was stirred for 15 hours. After completion, the reaction mixture was quenched with a saturated solution of sodium bicarbonate solution (20 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was washed with water and brine. After that the organic layer was dried over anhydrous sodium sulfate and concentrated. The crude residue was purified by silica gel (100-200 mesh) column chromatography (ethyl acetate/hexane) to obtain the corresponding *N*-Boc amides.

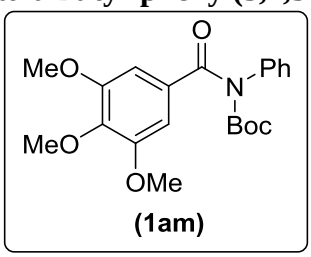
***tert*-Butyl benzyl(3,4,5-trimethoxybenzoyl)carbamate (1al)**[1e]: Obtained as a colorless liquid,



(1al)

R_f = 0.24 (hexane:EtOAc-80:20), Yield 73% (1.46 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.42 (d, J = 7.5 Hz, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.28 (s, 1H), 6.77 (s, 2H), 4.95 (s, 2H), 3.86 (s, 3H), 3.83 (s, 6H), 1.18 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.7, 153.5, 152.8, 140.7, 137.7, 132.6, 128.4, 128.1, 127.4, 105.0, 83.0, 60.9, 56.1, 49.1, 27.4.

***tert*-Butyl phenyl(3,4,5-trimethoxybenzoyl)carbamate (1am)**: Obtained as a colorless liquid.

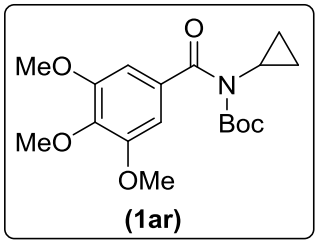


(1am)

R_f = 0.27 (hexane:EtOAc-80:20), Yield 71% (1.37 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.40 (t, J = 7.7 Hz, 2H), 7.33–7.28 (m, 1H), 7.25–

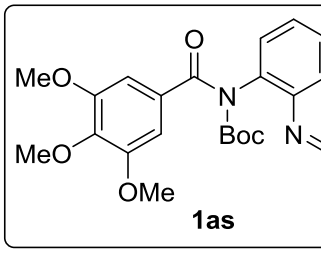
7.21 (m, 2H), 6.97 (s, 2H), 3.88 (s, 3H), 3.85 (s, 6H), 1.30 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.9, 153.3, 152.8, 141.2, 139.1, 131.4, 129.0, 127.5, 127.4, 105.8, 83.3, 60.8, 56.1, 27.5.

***tert*-Butyl cyclopropyl(3,4,5-trimethoxybenzoyl)carbamate (1ar):** Obtained as white solid (mp 110–112 °C), R_f = 0.30 (hexane:EtOAc-80:20), Yield 62% (1.1 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.25 (s, 2H), 3.90 (s, 6H), 3.89 (s, 3H), 1.66 (s, 1H), 1.59 (s, 9H), 1.50 (s, 3H), 1.25 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 165.4, 152.7, 148.7, 141.7, 127.0, 106.6, 81.1, 60.8, 56.1, 28.1, 27.6, 9.5. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{18}H_{26}NO_6$: 352.1760, found 352.1757.



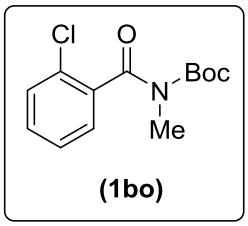
(1ar)

***tert*-Butyl quinolin-8-yl(3,4,5-trimethoxybenzoyl)carbamate (1as):** Obtained as a white solid (mp 136–138 °C), R_f = 0.37 (hexane:EtOAc-80:30), Yield 73% (1.59 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.92–8.87 (m, 1H), 8.17 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.83–7.79 (m, 1H), 7.64 (dd, *J* = 7.3, 1.0 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.23 (s, 2H), 3.88 (s, 3H), 3.81 (s, 6H), 1.26 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 172.6, 153.4, 152.7, 150.3, 144.0, 140.8, 137.1, 136.0, 132.1, 129.02, 128.9, 128.1, 126.2, 121.5, 106.1, 82.9, 60.8, 56.05, 27.5. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{24}H_{27}N_2O_6$: 439.1869, found 439.1860.



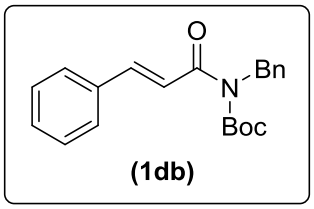
1as

***tert*-Butyl (2-chlorobenzoyl)(methyl)carbamate (1bo):** Obtained as a liquid, R_f = 0.67 (hexane:EtOAc-90:10), Yield 74% (0.995 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.36–7.26 (m, 4H), 3.33 (s, 3H), 1.16 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.7, 152.2, 138.5, 130.0, 129.7, 129.2, 127.6, 126.6, 83.3, 31.3, 27.3. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$: calcd for $C_{13}H_{16}ClNNaO_3$: 292.0716, found 292.0723.



(1bo)

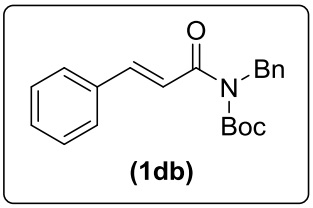
***tert*-Butyl benzyl(cinnamoyl)carbamate (1db)[1f]:** Obtained as a white solid (mp 89–91°C), R_f = 0.52 (hexane:EtOAc-95:05), Yield 73% (1.23 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 15.6 Hz, 1H), 7.60–7.56 (m, 2H), 7.53 (d, *J* = 15.6 Hz, 1H), 7.41–7.35 (m, 3H), 7.33–7.28 (m, 4H), 7.26–7.23 (m,



(1db)

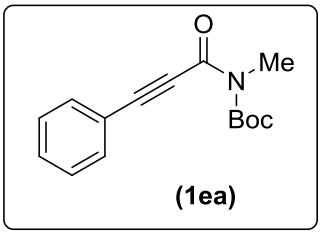
1H), 4.98 (s, 2H), 1.43 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.8, 153.2, 143.5, 138.2, 135.0, 129.9, 128.7, 128.2, 128.1, 127.5, 127.0, 121.2, 83.3, 47.8, 27.9.

***tert*-Butyl (E)-(3-(4-chlorophenyl)acryloyl)(methyl)carbamate (1dc):** Obtained as a white solid (mp 85–86 °C), R_f = 0.54 (hexane:EtOAc-95:05), Yield 74% (1.09 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.60 (d, J = 15.6 Hz, 1H), 7.48 (dd, J = 12.0, 10.0 Hz, 3H), 7.35–7.31 (m, 2H), 3.22 (s, 3H), 1.54 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 168.7, 153.4, 141.3, 135.6, 133.6, 129.2, 128.9, 122.0, 83.1, 31.8, 28.0, 27.4. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{15}H_{19}ClNO_3$: 296.1053, found 296.1058.



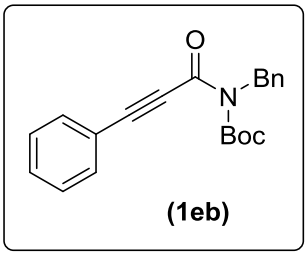
(1db)

***tert*-Butyl methyl(3-phenylpropioloyl)carbamate (1ea):** Obtained as a white solid (mp 68–69 °C), R_f = 0.56 (hexane:EtOAc-95:05), Yield 78% (1.01 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.58–7.54 (m, 2H), 7.44–7.39 (m, 1H), 7.38–7.33 (m, 2H), 3.22 (s, 3H), 1.55 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 154.0, 152.0, 132.4, 130.1, 128.4, 120.6, 92.7, 83.9, 83.4, 31.1, 28.0. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{15}H_{18}NO_3$: 260.1287, found 260.1278.



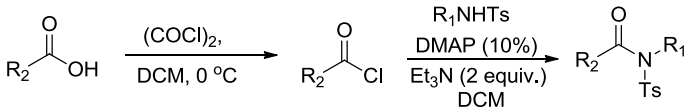
(1ea)

***tert*-Butyl Benzyl(3-phenylpropioloyl)carbamate (1eb):** Obtained as a white solid (mp 76–78 °C), R_f = 0.57 (hexane:EtOAc-95:05), Yield 77% (1.29 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.60–7.56 (m, 2H), 7.42 (d, J = 7.4 Hz, 1H), 7.37 (dd, J = 8.1, 6.6 Hz, 2H), 7.35–7.26 (m, 5H), 4.97 (s, 2H), 1.47 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.9, 151.7, 137.2, 132.5, 130.2, 128.4, 128.3, 127.8, 127.3, 120.5, 93.1, 84.1, 83.3, 47.2, 27.8. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{21}H_{22}NO_3$: 336.1600, found 336.1587.



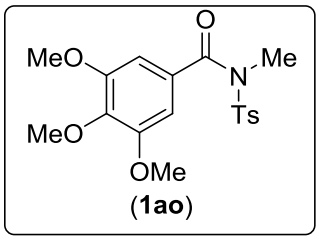
(1eb)

3.4 Synthesis of *N*-tosyl Amides:

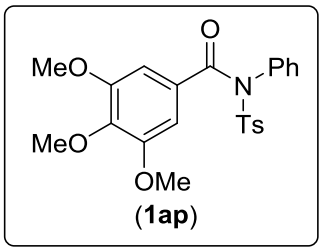


To a stirred solution of carboxylic acid (5.0 mmol) in DCM (10 mL) were added oxalyl chloride (0.6 mL, 6 mmol, 1.2 equiv.) and DMF (two drops) at 0 °C. The reaction mixture was stirred until gas evolution stopped. After completion, the reaction mixture was concentrated and was used directly for the next step. To a stirred mixture of the sulfonamide (R_1NHTs, 5 mmol, 1.0 equiv.), DMAP (65 mg, 0.5 mmol) and Et_3N (1.4 mL, 10 mmol) in DCM (10 mL) was added a solution of acyl chloride in DCM (5 ml) at 0 °C. The resulting mixture was stirred at room temperature for 2 h and diluted with DCM (20 mL), washed with 5% HCl, brine and H_2O. The organic layer was dried over anhydrous sodium sulfate and concentrated. The crude product was purified by silica gel (100-200 mesh) column chromatography (ethyl acetate/hexane) to obtain the corresponding *N*-tosyl carboxylic amides.

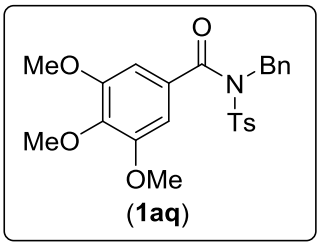
3,4,5-Trimethoxy-*N*-methyl-*N*-tosylbenzamide(1ao): Obtained as a white solid (mp 113–115 °C), R_f = 0.30 (hexane:EtOAc-80:20), Yield 82% (1.55 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.83 (d, J = 8.3 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 6.78 (d, J = 1.2 Hz, 2H), 3.88 (s, 3H), 3.84 (s, 6H), 3.29 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.1, 152.8, 144.8, 141.3, 135.1, 129.5, 129.1, 128.4, 106.1, 60.9, 56.2, 35.8, 21.6. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{18}H_{22}NO_6S$: 380.1168, found 380.1156.



3,4,5-Trimethoxy-*N*-phenyl-*N*-tosylbenzamide (1ap): Obtained as a white solid (mp 130 °C), R_f = 0.32 (hexane:EtOAc-80:20), Yield 81% (1.78 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.80 (d, J = 8.3 Hz, 2H), 7.33–7.28 (m, 5H), 7.20 7.16 (m, 2H), 6.72 (s, 2H), 3.77 (s, 3H), 3.64 (s, 6H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.1, 152.3, 144.7, 141.1, 137.9, 135.2, 130.0, 129.3, 129.1, 129.1, 129.0, 127.7, 107.5, 60.7, 55.9, 21.6. HRMS (ESI-TOF) *m/z*: $[M + H]^+$: calcd for $C_{23}H_{24}NO_6S$: 442.1324, found 442.1318.

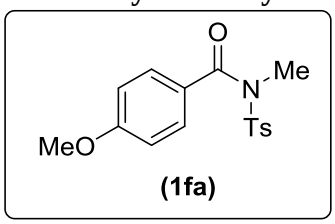


***N*-Benzyl-3,4,5-trimethoxy-*N*-tosylbenzamide (1aq):** Obtained as a white solid (mp 127–128 °C), R_f = 0.34 (hexane: EtOAc-80:20), Yield 80% (1.82 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.70 (d, J = 8.3 Hz, 2H), 7.32–7.22 (m, 8H), 6.65 (s, 2H), 4.99 (s, 2H), 3.84 (s, 3H), 3.66 (s, 6H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.2, 152.7, 144.6, 141.0, 136.6, 135.9, 129.3, 129.3, 128.7, 128.6, 127.6, 127.5, 105.6, 60.8, 55.9, 51.8, 21.6. HRMS (ESI-TOF) m/z: $[M + H]^+$: calcd for $C_{24}H_{26}NO_6S$: 456.1481, found 456.1473.



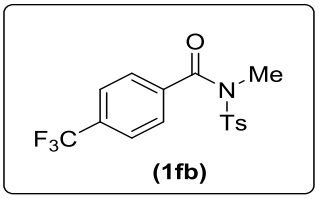
(**1aq**)

4-Methoxy-*N*-methyl-*N*-tosylbenzamide (1fa)[1g]: Obtained as a white solid (mp solid 40–41 °C), R_f = 0.53 (hexane:EtOAc-80:20), Yield 86% (1.37 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.82 (d, J = 8.3 Hz, 2H), 7.61 (d, J = 8.9 Hz, 2H), 7.32 (d, J = 8.1 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 3.84 (s, 3H), 3.23 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.2, 162.9, 144.6, 135.0, 131.3, 129.5, 128.3, 126.3, 113.5, 55.4, 35.7, 21.5.



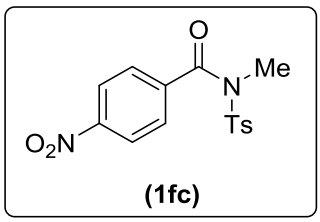
(**1fa**)

***N*-Methyl-*N*-tosyl-4-(trifluoromethyl)benzamide (1fb)**[1g]: Obtained as a white solid (mp 127–129 °C), R_f = 0.47 (hexane:EtOAc-80:20), Yield 77% (1.37 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.76–7.72 (m, 2H), 7.67 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 3.27 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 170.2, 145.3, 138.2, 134.8, 133.29 (q, J = 32.5 Hz), 129.8, 128.6, 128.1, 125.22 (q, J = 3.7 Hz), 123.59 (q, J = 271.25 Hz), 34.9, 21.6.



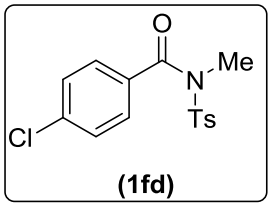
(**1fb**)

***N*-Methyl-4-nitro-*N*-tosylbenzamide (1fc)**[1g]: Obtained as a white solid (mp 117–119 °C), R_f = 0.44 (hexane:EtOAc-80:20), Yield 74% (1.23 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.28–8.22 (m, 2H), 7.71–7.64 (m, 4H), 7.35 (d, J = 8.2 Hz, 2H), 3.26 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.5, 149.3, 145.5, 140.9, 134.6, 129.9, 129.1, 128.0, 123.2, 34.5, 21.6.



(**1fc**)

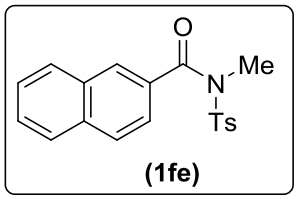
4-Chloro-*N*-methyl-*N*-tosylbenzamide (1fd)[1h]: Obtained as a white solid (mp 103–104 °C), R_f = 0.55 (hexane:EtOAc-80:20), Yield 80% (1.29 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.79–7.75 (m, 2H), 7.54–7.49 (m, 2H), 7.41–7.37 (m, 2H),



(**1fd**)

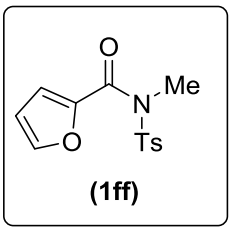
7.33 (d, J = 8.0 Hz, 2H), 3.24 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 170.6, 145.0, 138.3, 134.8, 133.0, 130.0, 129.7, 128.5, 128.2, 35.3, 21.6.

***N*-Methyl-*N*-tosyl-2-naphthamide (1fe)**[1g]: Obtained as a white solid (mp 106–107 °C), R_f = 0.59 (hexane:EtOAc-80:20), Yield 78% (1.32 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.06 (d, J = 1.1 Hz, 1H), 7.90–7.83 (m, 5H), 7.63–7.52 (m, 3H), 7.32 (d, J = 8.4 Hz, 2H), 3.34 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.5, 144.8, 135.1, 134.7, 132.1, 131.6, 129.5, 129.4, 128.8, 128.3, 128.1, 128.1, 127.7, 126.8, 124.5, 35.6, 21.5.



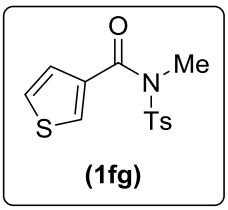
(1fe)

***N*-Methyl-*N*-tosylfuran-2-carboxamide (1ff)**[1g]: Obtained as a colorless liquid, R_f = 0.57 (hexane:EtOAc-85:15), Yield 77% (1.07 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.91 (d, J = 8.3 Hz, 2H), 7.58–7.52 (m, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.20 (dd, J = 3.6, 0.6 Hz, 1H), 6.54–6.49 (m, 1H), 3.48 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.5, 146.4, 145.9, 144.7, 135.4, 129.4, 128.4, 120.2, 112.1, 34.6, 21.6.



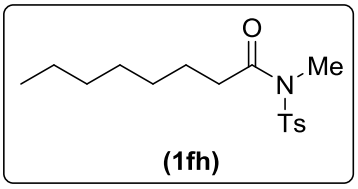
(1ff)

***N*-Methyl-*N*-tosylthiophene-3-carboxamide (1fg)**[1g]: Obtained as a colorless liquid, R_f = 0.55 (hexane:EtOAc-85:15), Yield 76% (1.12 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.88–7.80 (m, 2H), 7.36–7.27 (m, 3H), 3.36 (s, 2H), 2.44 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 165.9, 144.8, 135.5, 135.1, 131.5, 129.5, 128.2, 127.6, 125.8, 35.4, 21.5.



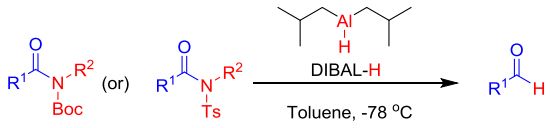
(1fg)

***N*-Methyl-*N*-tosyloctanamide (1fh)**[1g]**:** Obtained as a colorless liquid, R_f = 0.54 (hexane:EtOAc-85:15), Yield 72% (1.11 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.76 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 3.29 (s, 3H), 2.65–2.58 (m, 2H), 2.43 (s, 3H), 1.59–1.51 (m, 2H), 1.28–1.19 (m, 8H), 0.85 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 173.3, 144.7, 136.4, 129.8, 127.3, 36.4, 32.9, 31.5, 28.8, 24.5, 22.5, 21.5, 14.0.

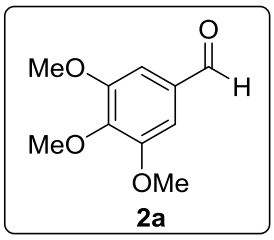


(1fh)

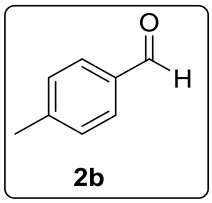
4.1 General procedure for the reduction of amides into aldehydes with DIBAL-H.



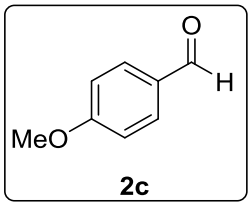
To a stirred solution of *N*-Boc or *N*-Ts amides (1 mmol) in dry toluene (3 mL) was added DIBAL-H (1M in toluene, 1.0 mL, 1.0 mmol) at -78 °C over 1-2 min under an argon atmosphere. The resulting mixture was allowed to stir for 30 min at the same temperature. After the completion, the reaction mixture was quenched by aqueous 1.0 molar sodium potassium L(+)-tartrate (5 mL) and stirred for 1 hr at 0 °C and allowed to warm to room temperature. The resulting mixture was extracted with EtOAc (20 mL) and washed with water and brine. The organic layer was dried over saturated Na_2SO_4 and concentrated. The crude residue was purified by silica gel column chromatography (ethyl acetate/hexane) to obtain the aldehydes.



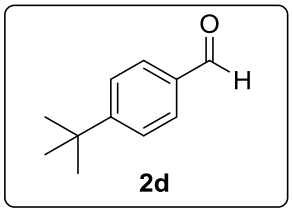
3,4,5-Trimethoxybenzaldehyde (2a)[1i]: Obtained as a white solid (mp 72–74 °C), R_f = 0.37 (hexane: EtOAc-80:20), Yield 90% (176 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.87 (m, 1H), 7.12 (s, 2H), 3.93 (d, J = 4.0 Hz, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.9, 153.6, 143.6, 131.6, 106.7, 60.9, 56.2.



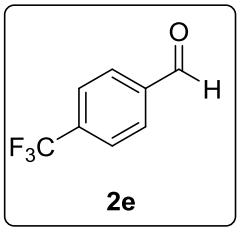
4-Methylbenzaldehyde (2b)[1j]: Obtained as a pale yellow liquid, R_f = 0.52 (hexane:EtOAc-90:10), Yield 86% (103 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.95 (s, 1H), 7.76 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.9, 145.4, 134.1, 129.7, 129.6, 21.7.



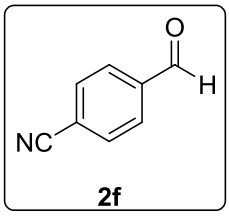
4-Methoxybenzaldehyde (2c)[1j]: Obtained as a pale yellow liquid, R_f = 0.55 (hexane: EtOAc-90:10),; Yield 86% (117 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.86 (s, 1H), 7.81 (d, J = 8.5 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 3.89–3.82 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.6, 164.5, 131.8, 129.8, 114.2, 55.4.



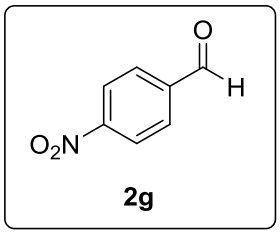
4-(*tert*-Butyl)benzaldehyde (2d)[1i]: Obtained as a white solid (mp 237–238 °C). R_f = 0.57 (hexane:EtOAc-90:10), Yield 84% (136 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.98 (s, 1H), 7.82 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.3 Hz, 2H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.0, 158.4, 134.0, 129.6, 125.9, 35.3, 31.0.



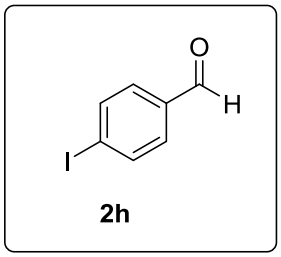
4-(Trifluoromethyl)benzaldehyde (2e)[1j]: Obtained as a pale yellow liquid, R_f = 0.62 (hexane:EtOAc-90:10), Yield 87% (151 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.09 (s, 1H), 8.00 (d, J = 8.5 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.0, 138.6, 135.59 (q, J = 32.5 Hz), 129.8, 126.08 (q, J = 3.75 Hz), 123.43 (q, J = 21.25 Hz).



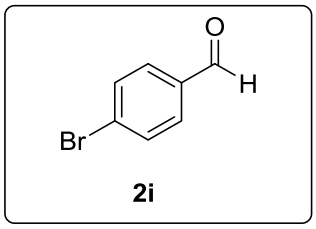
4-Cyanobenzaldehyde (2f)[1j]: Obtained as a white solid (mp 100–102 °C), R_f = 0.60 (hexane:EtOAc-90:10), Yield 89% (116 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.08 (s, 1H), 7.99 (d, J = 7.9 Hz, 2H), 7.84 (d, J = 7.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.5, 138.7, 132.8, 129.8, 117.6, 117.5.



4-Nitrobenzaldehyde (2g)[1j]: Obtained as a yellow solid (mp 104–105 °C), R_f = 0.31 (hexane:EtOAc-90:10), Yield 80% (120 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.16 (s, 1H), 8.39 (d, J = 8.7 Hz, 2H), 8.07 (d, J = 8.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.2, 151.1, 140.0, 130.4, 124.2.

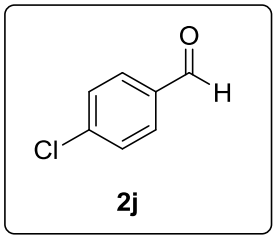


4-Iodobenzaldehyde (2h)[1i]: Obtained as a pale yellow solid (mp 75–76 °C), R_f = 0.56 (hexane:EtOAc-90:10), Yield 85% (197 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.94 (s, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.60–7.54 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.3, 138.3, 135.5, 130.7, 102.7.



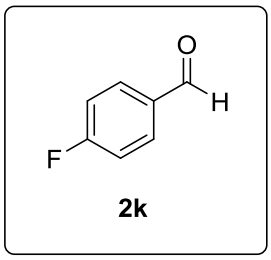
2i

4-Bromobenzaldehyde (2i)[1i]: Obtained as a white solid (mp 55–56 °C), R_f = 0.54 (hexane:EtOAc-90:10), Yield 87% (160 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.97 (s, 1H), 7.74 (t, J = 7.6 Hz, 2H), 7.71–7.64 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.0, 135.0, 132.4, 130.9, 129.7.



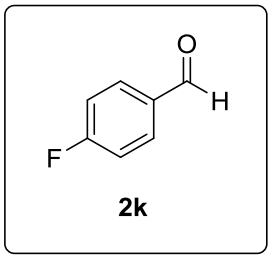
2j

4-Chlorobenzaldehyde (2j)[1j]: Obtained as a white solid (mp 47–48 °C), R_f = 0.52 (hexane: EtOAc-90:10), Yield 86% (120 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.98 (s, 1H), 7.84–7.81 (m, 2H), 7.54–7.48 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.8, 140.9, 134.7, 130.8, 129.4.



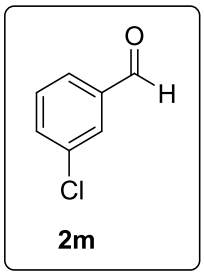
2k

4-Fluorobenzaldehyde (2k)[1k]: Obtained as a colorless liquid, R_f = 0.50 (hexane:EtOAc-90:10), Yield 85% (105 mg). 1H NMR (500 MHz, CDCl3) δ = 9.96 (s, 1H), 7.90 (dd, J = 8.8, 5.4 Hz, 2H), 7.20 (t, J = 8.5 Hz, 2H).^{13}C NMR (125 MHz, CDCl3) δ = 190.4, 166.49 (d, J = 255 MHz), 132.94 (d, J = 2.5 Hz), 132.19 (d, J = 10 Hz), 116.30 (d J = 22.5 MHz).



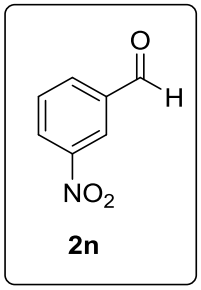
2k

3-Bromobenzaldehyde (2l)[1k]: Obtained as a yellow liquid, R_f = 0.47 (hexane:EtOAc-90:10), Yield 88% (162 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.93 (s, 1H), 8.00 (d, J = 19.7 Hz, 1H), 7.76 (d, J = 7.9 Hz, 2H), 7.46–7.32 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.7, 137.9, 137.2, 132.2, 130.6, 128.3, 123.3.

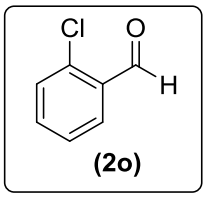


2m

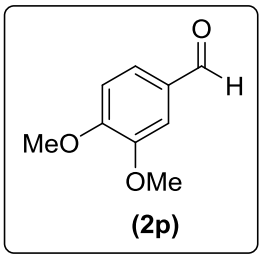
3-Chlorobenzaldehyde (2m)[1i]: Obtained as a liquid, R_f = 0.46 (hexane: EtOAc-90:10), Yield 87% (122 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.95 (s, 1H), 7.85–7.79 (m, 1H), 7.76–7.72 (m, 1H), 7.57 (ddd, J = 8.0, 2.1, 1.1 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.7, 137.7, 135.3, 134.2, 130.3, 129.1, 127.8.



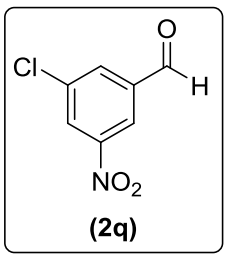
3-Nitrobenzaldehyde (2n)[11]: Obtained as a yellow solid (mp 57–59 °C), R_f = 0.34 (hexane:EtOAc-90:10), Yield 85% (128 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.12 (s, 1H), 8.73–8.70 (m, 1H), 8.49 (ddd, *J* = 8.1, 2.2, 1.0 Hz, 1H), 8.23 (dt, *J* = 7.6, 1.1 Hz, 1H), 7.77 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 189.6, 148.7, 137.3, 134.5, 130.3, 128.5, 124.4.



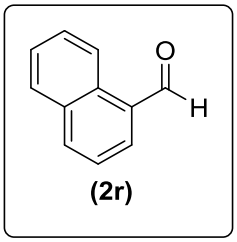
2-Chlorobenzaldehyde (2o)[11i]: Colorless liquid, Rf = 0.52 (hexane:EtOAc-90:10), Yield 81% (113 mg). ^{1}H NMR (500 MHz, CDCl3) δ = 10.44 (s, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.51–7.47 (m, 1H), 7.42 (dd, J = 14.1, 4.5 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, CDCl3) δ = 189.6, 137.7, 135.0), 132.3, 130.4, 129.2, 127.1.



3,4-dimethoxybenzaldehyde (2p)[11]: Obtained as a pale yellow solid (mp 43-45 °C), R_f = 0.31 (hexane: EtOAc-80:20), Yield 80% (133 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.85 (s, 1H), 7.45 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.41 (d, *J* = 1.8 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 3.96 (s, 3H), 3.94 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.8, 154.5, 149.6, 130.1, 126.8, 110.4, 109.0, 56.1, 55.9.

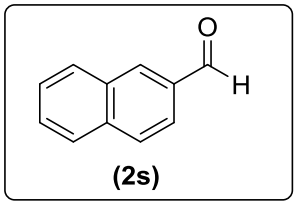


3-Chloro-5-Nitrobenzaldehyde (2q): Obtained as a pale yellow liquid, R_f = 0.37 (hexane:EtOAc-90:10), Yield 83% (153 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.04 (s, 1H), 8.36 (d, *J* = 1.9 Hz, 1H), 8.04 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 188.4, 135.4, 133.0, 132.9, 132.7, 126.3. HRMS (ESI-TOF) m/z: $[M+H]^+$: calcd for $C_7H_5ClNO_3$: 185.9958, found185.9964.

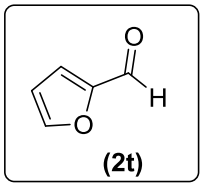


1-Naphthaldehyde (2r)[11]: Obtained as a colorless liquid, R_f = 0.52 (hexane:EtOAc-90:10), Yield 78% (122 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.40 (s, 1H), 9.29–9.23 (m, 1H), 8.09 (d, *J* = 8.2 Hz, 1H), 7.98 (dd, *J* = 7.0, 1.3 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.69 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.64–7.57 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.4, 136.5,

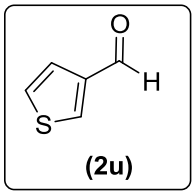
135.2, 133.6, 131.3, 130.4, 129.0, 128.4, 126.9, 124.8.



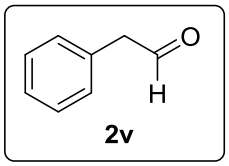
2-Naphthaldehyde (2s)[1i]: Obtained as a white solid (mp 61–62 °C), R_f = 0.53 (hexane:EtOAc-90:10), Yield 84% (131 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.17 (s, 1H), 8.35 (s, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.94 (ddd, J = 22.0, 11.0, 4.7 Hz, 3H), 7.65 (t, J = 7.5 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.2, 136.4, 134.5, 134.1, 132.6, 129.5, 129.1, 128.0, 127.0, 122.7.



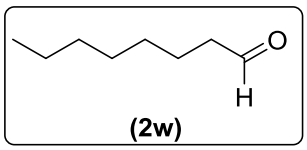
Furan-2-carbaldehyde (2t)[1l]: Obtained as colorless oil, R_f = 0.47 (hexane: EtOAc-90:10), Yield 87% (83 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.66 (s, 1H), 7.69 (s, 1H), 7.25 (d, J = 3.6 Hz, 1H), 6.60 (d, J = 3.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 177.7, 152.9, 147.9, 120.9, 112.5.



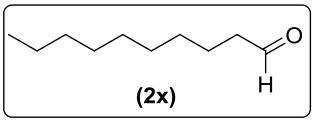
Thiophene-3-carbaldehyde (2u)[1l]: Obtained as colorless oil, R_f = 0.45 (hexane:EtOAc-90:10), Yield 85% (95 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.96–9.90 (m, 1H), 8.12 (dd, J = 2.9, 1.1 Hz, 1H), 7.55 (dd, J = 5.1, 0.8 Hz, 1H), 7.38 (ddd, J = 5.1, 2.9, 0.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 184.8, 143.0, 136.6, 127.3, 125.3.



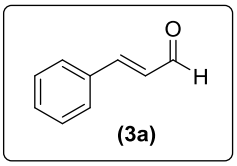
Phenylacetaldehyde (2v)[1m]**:** Obtained as colorless liquid, R_f = 0.45 (hexane:EtOAc-90:10), Yield 51% (61 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.76 (s, 1H), 7.38 (t, J = 7.4 Hz, 2H), 7.34–7.29 (m, 1H), 7.23 (dd, J = 7.8, 1.0 Hz, 2H), 3.70 (d, J = 2.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.4, 131.8, 129.5, 128.9, 127.4, 50.5.



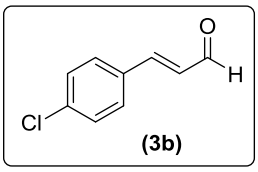
Octanal (2w)[1j]: Obtained as a colorless liquid, R_f = 0.42 (hexane:EtOAc-90:10), Yield 69% (88 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.74 (s, 1H), 2.40 (t, J = 6.1 Hz, 2H), 1.62 (d, J = 6.2 Hz, 2H), 1.28 (dd, J = 12.2, 3.8 Hz, 8H), 0.86 (t, J = 5.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 202.9, 43.8, 31.5, 29.0, 28.9, 22.5, 22.0, 14.0.



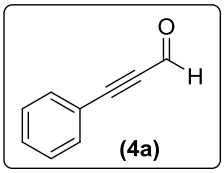
Decanal (2x)[1j]: Obtained as a colorless liquid, R_f = 0.44 (hexane:EtOAc-90:10), Yield 68% (106 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.76 (s, 1H), 2.41 (td, J = 7.4, 1.9 Hz, 2H), 1.67–1.57 (m, 2H), 1.32–1.24 (m, 12H), 0.87 (t, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 202.9, 43.9, 31.8, 29.3, 29.3, 29.2, 29.1, 22.6, 22.0, 14.0.



Cinnamaldehyde (4a)[1n]: Obtained as a pale yellow liquid, R_f = 0.54 (hexane:EtOAc-90:10), Yield 89% (117 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.70 (d, J = 7.7 Hz, 1H), 7.57 (dd, J = 6.4, 2.7 Hz, 2H), 7.50–7.41 (m, 4H), 6.72 (dd, J = 15.9, 7.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.7, 152.8, 134.0, 131.2, 129.1, 128.6, 128.5.

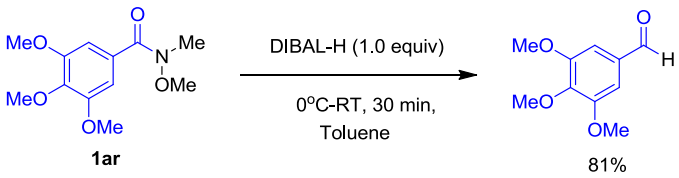


(E)-3-(4-chlorophenyl)acrylaldehyde (4b)[1n]: Pale yellow solid (mp 59–61 °C), R_f = 0.57 (hexane:EtOAc-90:10), Yield 86% (142 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.69 (d, J = 7.6 Hz, 1H), 7.52–7.47 (m, 2H), 7.45–7.37 (m, 3H), 6.68 (dd, J = 15.9, 7.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.3, 151.0, 137.2, 132.4, 129.5, 129.3, 128.8.



3-Phenylpropiolaldehyde (5a)[1o]: Obtained as a pale yellow liquid, R_f = 0.61 (hexane:EtOAc-90:10), Yield 90% (117 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.40 (s, 1H), 7.62–7.55 (m, 2H), 7.50–7.44 (m, 1H), 7.42–7.33 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 176.6, 133.1, 131.1, 128.6, 119.2, 94.9, 88.3.

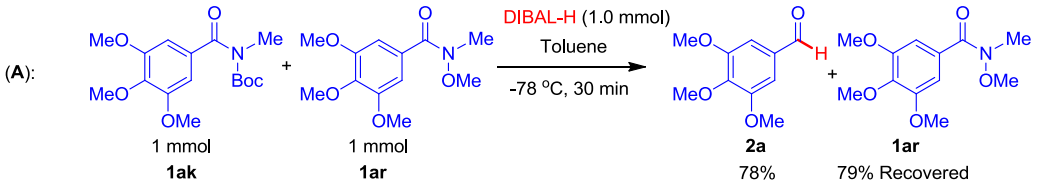
4.2 Procedure for the reduction of Weinreb amide 1ar with DIBAL-H.



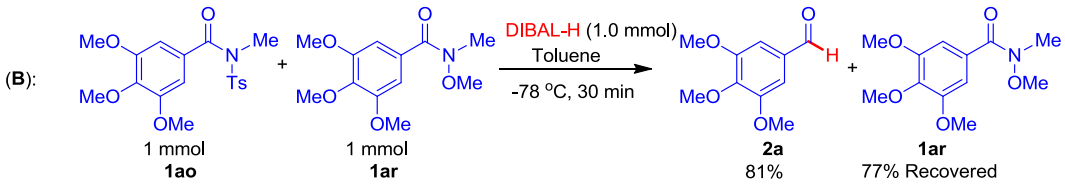
To a stirred solution of Weinreb amide **1ar** (255 mg, 1 mmol) in dry toluene (3 mL) was added DIBAL-H (1M in toluene, 1.0 mL, 1.0 mmol) at 0°C over 1-2 min under an argon atmosphere. The resulting mixture was allowed to reach room temperature and stirred for 30 min. After the completion, the reaction mixture was quenched by aqueous 1.0 molar sodium potassium L(+)-tartrate (5 mL) and stirred for 1 hr at 0 °C and allowed to warm to room temperature. The

resulting mixture was extracted with EtOAc (20 mL) and washed with water and brine. The organic layer was dried over saturated Na_2SO_4 and concentrated. The crude residue was purified by silica gel column chromatography (ethyl acetate/hexane) to obtain the aldehyde **2a** in 81% yield, 157 mg.

4.3 Procedures of the control experiments

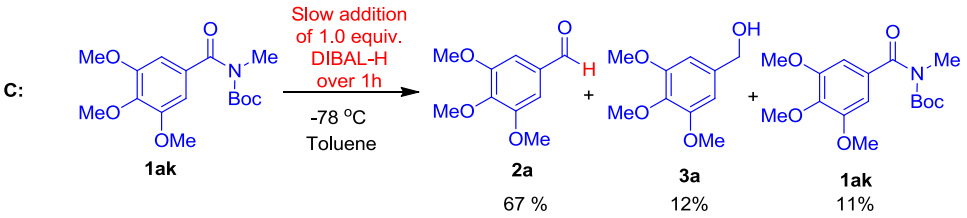


A: To a stirred solution of **1ak** (325 mg, 1 mmol) and **1at** (255 mg, 1 mmol) in dry toluene (5 mL) was added DIBAL-H (1M in toluene, 1.0 mL, 1.0 mmol) at -78 °C over 1-2 min under an argon atmosphere. The resulting mixture was allowed to stir for 30 min at the same temperature. After the completion, the reaction mixture was quenched by aqueous 1.0 molar sodium potassium L(+)-tartrate (5 mL) and stirred for 1 hr at 0 °C and allowed to warm to room temperature. The resulting mixture was extracted with EtOAc (20 mL) and washed with water and brine. The organic layer was dried over saturated Na_2SO_4 and concentrated. The crude residue was purified by silica gel column chromatography (ethyl acetate/hexane) to obtain the aldehyde **2a** in 78% (153 mg) along with 79% (202 mg) of Weinreb amide **1ar**.

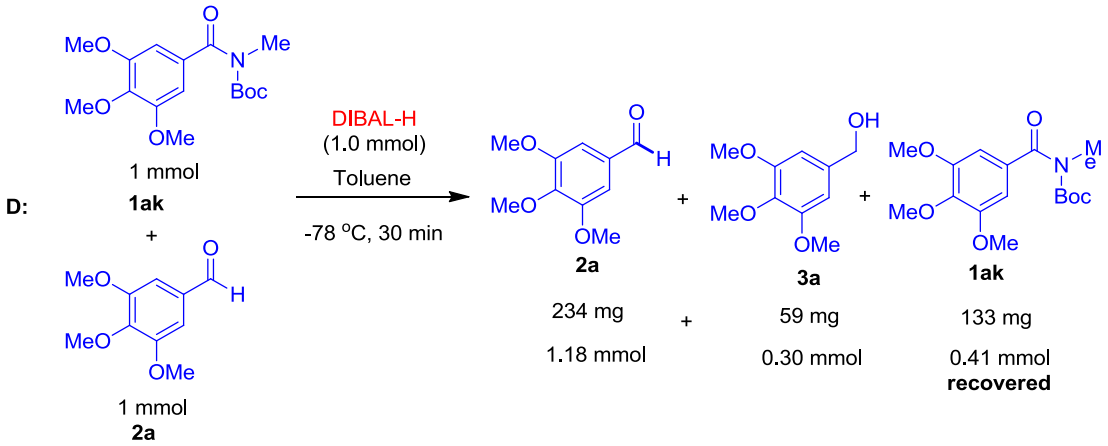


B: To a stirred solution of **1ak** (379 mg, 1 mmol) and **1at** (255 mg, 1 mmol) in dry toluene (5 mL) was added DIBAL-H (1M in toluene, 1.0 mL, 1.0 mmol) at -78 °C over 1-2 min under an argon atmosphere. The resulting mixture was allowed to stir for 30 min at the same temperature. After the completion, the reaction mixture was quenched by aqueous 1.0 molar sodium potassium L(+)-tartrate (5 mL) and stirred for 1 hr at 0 °C and allowed to warm to room temperature. The resulting mixture was extracted with EtOAc (20 mL) and washed with water and brine. The organic layer was dried over saturated Na_2SO_4 and concentrated. The crude

residue was purified by silica gel column chromatography (ethyl acetate/hexane) to obtain the aldehyde **2a** in 78% (159 mg) along with 77% (197 mg) of Weinreb amide **1ar**.



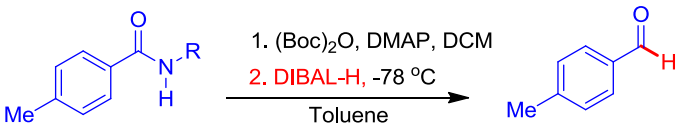
C: To a stirred solution of **1ak** (325 mg, 1 mmol) in dry toluene (3 mL) was added DIBAL-H (1M in toluene, 1.0 mL, 1.0 mmol) at -78 °C over 60 min using syringe under an argon atmosphere. The resulting mixture was allowed to stir for 30 min at the same temperature. After the completion, the reaction mixture was quenched by aqueous 1.0 molar sodium potassium L(+)-tartrate (5 mL) and stirred for 1 hr at 0 °C and allowed to warm to room temperature. The resulting mixture was extracted with EtOAc (20 mL) and washed with water and brine. The organic layer was dried over saturated Na_2SO_4 and concentrated. The crude residue was purified by silica gel column chromatography (ethyl acetate/hexane) to obtain the aldehyde **2a** in 67% (131 mg) along with alcohol **3a** 12% (23 mg) and amide **1ak** 11% (36 mg).



D: To a stirred solution of **1ak** (379 mg, 1 mmol) and **2a** (196 mg, 1 mmol) in dry toluene (5 mL) was added DIBAL-H (1M in toluene, 1.0 mL, 1.0 mmol) at -78 °C over 1-2 min under an argon atmosphere. The resulting mixture was allowed to stir for 30 min at the same temperature.

After the completion, the reaction mixture was quenched by aqueous 1.0 molar sodium potassium L(+)-tartrate (5 mL) and stirred for 1 hr at 0 °C and allowed to warm to room temperature. The resulting mixture was extracted with EtOAc (20 mL) and washed with water and brine. The organic layer was dried over saturated Na_2SO_4 and concentrated. The crude residue was purified by silica gel column chromatography (ethyl acetate/hexane) to obtain the aldehyde **2a** in 234 mg (1.18 mmol) along with alcohol **3a** 59 mg (0.3 mmol) and amide **1ak** 133 mg (0.41 mmol).

4.4 Procedure for the gram scale reaction



N,4-Dimethylbenzamide **1b** (1.5 g, 10.0 mmol) and DMAP (130 mg, 1.0 mmol, 0.1 equiv.) were stirred in dichloromethane to which 1.3 equiv. of di-*tert*-butyl dicarbonate (Boc_2O) (3.0 mL, 13.0 mmol) was added. The resulting mixture was allowed to stir for 15 h at room temperature. After that, the reaction was quenched with a saturated solution of sodium bicarbonate solution (40 mL) and extracted with EtOAc (3 × 40 mL). The organic layer was washed with water and brine and was dried over anhydrous sodium sulfate and concentrated. The crude residue was purified by silica gel (100-200 mesh) column chromatography (ethyl acetate/hexane) to obtain the corresponding *N*-Boc amide **1bb** in 2.15 g (86%) as colorless liquid. Further, The *N*-Boc amide was dissolved in dry toluene (20 ml) and stirred at -78^{o}C to which DIBAL-H (1M in toluene, 9.0 mL) was added dropwise over 5 minutes. The resulting mixture was allowed to stir for 45 minutes at the same temperature. After the completion, the reaction mixture was quenched by aqueous 1.0 molar sodium potassium L(+)-tartrate (35 mL) and stirred for 2 hr at 0 °C-rt. Further, the resulting mixture was extracted with EtOAc (100 mL*2) and ethyl acetate layer washed was washed with water and brine, dried over saturated Na_2SO_4 and concentrated. The crude residue was purified by silica gel column chromatography (ethyl acetate/hexane) to obtain the aldehyde **2a** in 0.856 g (84%) as a colorless liquid.

A similar procedure was adopted for the gram scale reduction of *N*-methylbenzamide **1c** (1.35 g, 10 mmol). The Boc protection was performed with 2.2 equiv. of di-*tert*-butyl dicarbonate (Boc_2O) (5.0 mL) for 20 hours in dichloromethane to obtain **1cb** in 2.7 g (81%) as a white solid.

The amide **1cb** was subjected to the reduction with DIBAL-H (1M in toluene, 9.0 mL) as described above to obtain the aldehyde **2a** in 0.804 g (83%) as a colorless liquid.

5. References

1. (a) L. Song, G.-M. Cao, W.-J. Zhou, J.-H.Ye, Z. Zhang, X.-Y. Tian, J. Li, and D.-G. Yu, *Org. Chem. Front*., 2018, **5,** 2086−2090; (b) A. S. Kumar, B. Thulasiram, S. B. Laxmi, V. S. Rawat and B. Sreedhar, *Tetrahedron*, 2014, **70,** 6059-6067; (c) A. Stefanachi, G. F. Mangiatordi, P. Tardia, D. Alberga, F. Leonetti, M. Niso, N. A. Colabufo, C. Adamo, O. Nicolotti and S. Cellamare, *Chem. Biol. Drug Des*., 2016, **88,** 820–831; (d) S. Shi and M. Szostak, *Org. Lett.* 2016, **18,** 5872−5875; (e) N. A. Weires, E. L. Baker and N. K. Garg, *Nat. Chem*., 2016, **8,** 75-79. (f) L. Hie, E. L. Baker, S. M. Anthony, J. N. Desrosiers, C. Senanayake and Garg, N. K. *Angew. Chem. Int. Ed.*, 2016, **55,** 15129-15132; (g) C. Wang, L. Huang, F. Wang and G. Zou, *Tetrahedron Lett.*, 2018, **59,** 2299–2301; (h) Y. Inamoto, Y. Kaga, Y. Nishimoto, M. Yasuda and A. Baba, *Org. Lett*., 2013, **15,** 3452-3455; (i) P. Hu, M. Tan, L. Cheng, H. Zhao, R. Feng, W.-J. Gu and W. Han, *Nat. Commun*., 2019, **10,** 2425–2433; (j) C. L. Bailey, A. Y. Joh, Z. Q. Hurley, C. L. Anderson and B. Singaram, *J. Org. Chem*., 2016, **81,** 3619−3628; (k) B. Liu, L. Cheng, P. Hu, F. Xu, D. Li, W.-J. Gua and W. Han, *Chem. Commun*., 2019, **55,** 4817—4820; (l) Z. Bazyar and M. Hosseini-Sarvari, *J. Org. Chem*., 2019, **84,** 13503−13515. (m) M. W. Robinson, K. S. Pillinger, I. Mabbett, D. A. Timms and A. E. Graham, *Tetrahedron*, 2010, **66,** 8377-8382; (n) A. Bhowmik, and R. A. Fernandes, *Org. Lett*., 2019, **21,** 9203−9207; (o) P. Xiao, Z. Tang, K. Wang, H. Chen, Q. Guo, Y. Chu, L. Gao and Z. Song, *J. Org. Chem.*, 2018, **83,** 1687−1700.

6. [1]H and 13C NMR Spectra of the Amides:

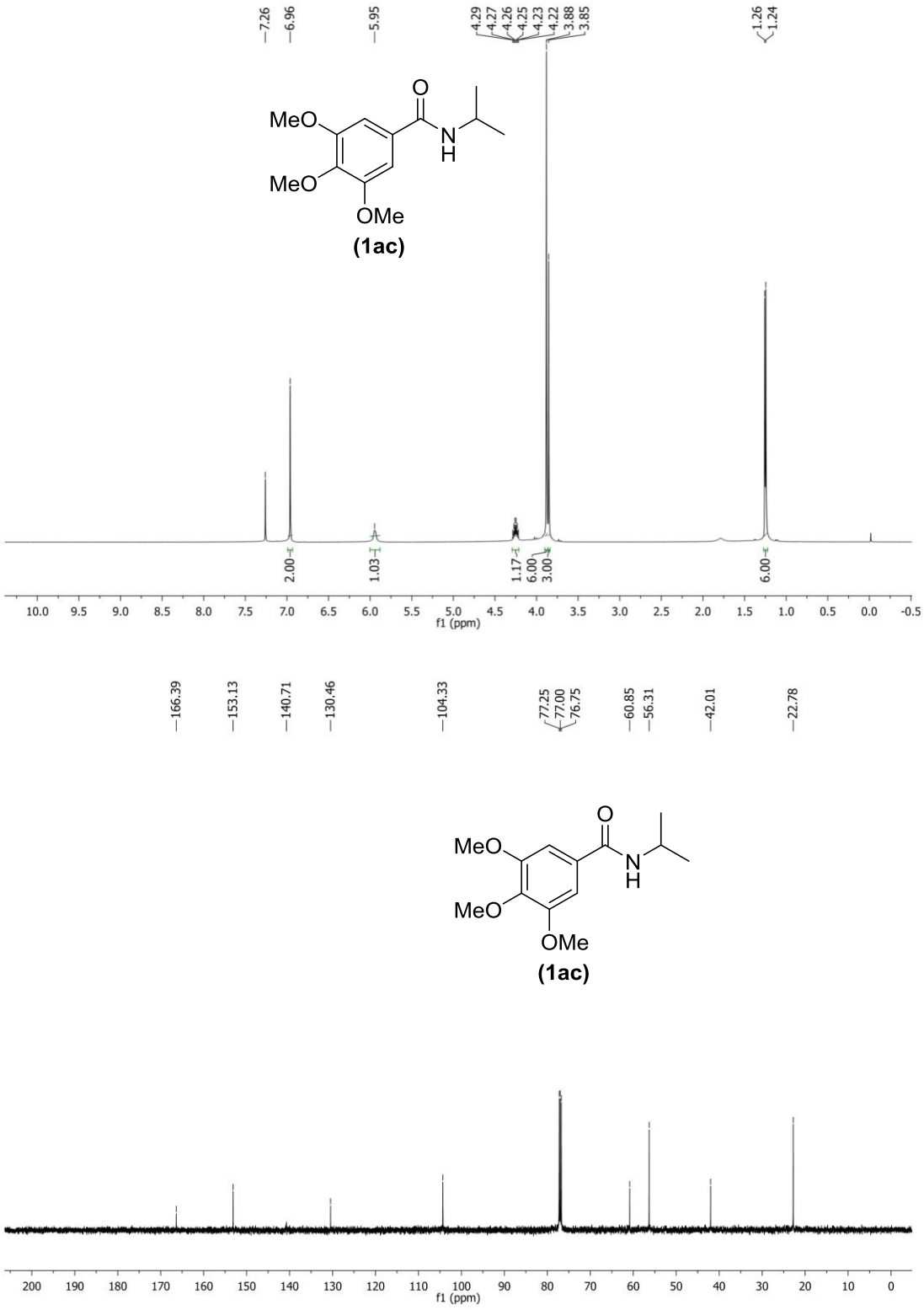


Figure SI.1 [1]H and [13]C NMR of product **1ac** in **$CDCl_3$**.

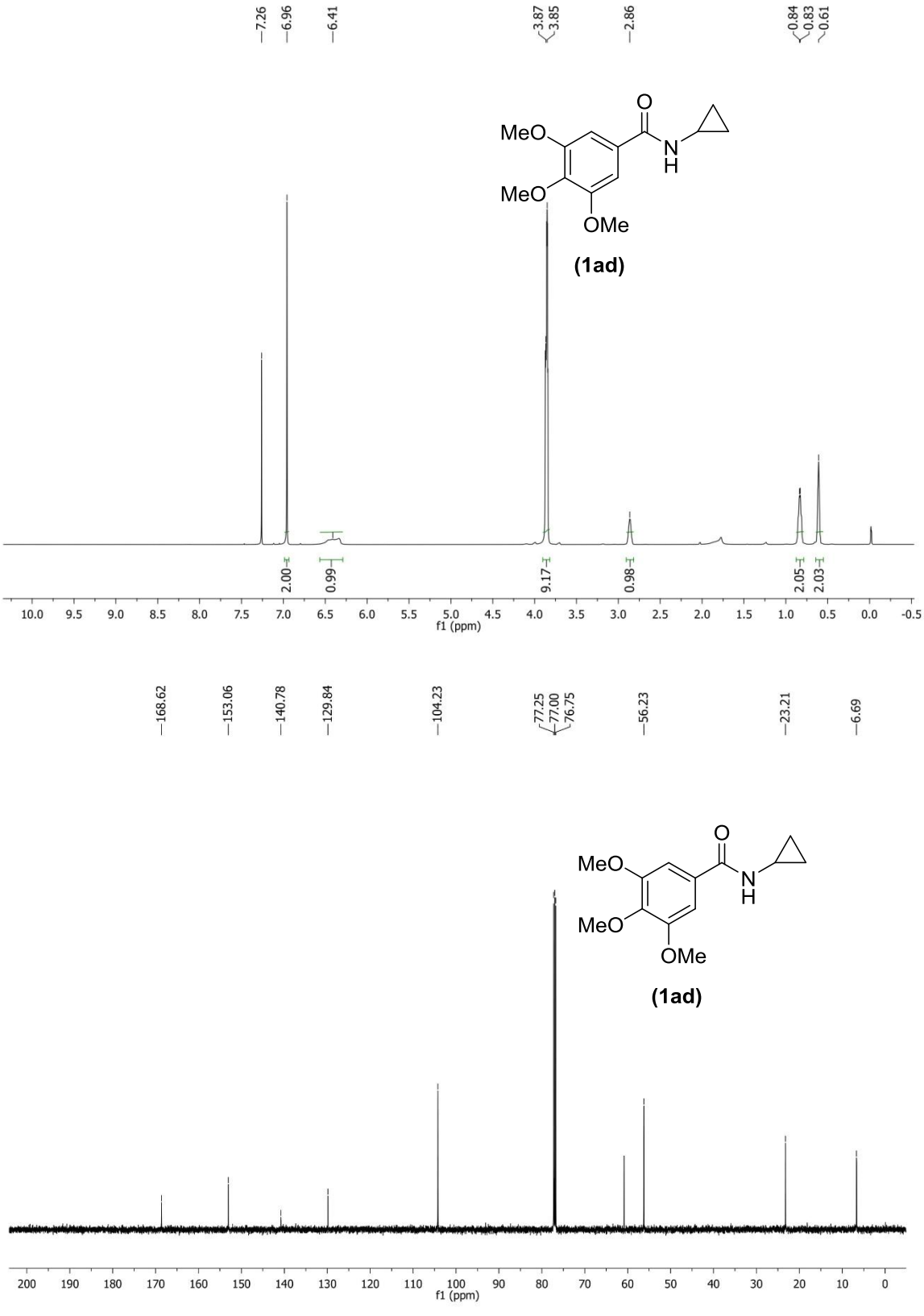


Figure SI.2 ^{1}H and ^{13}C NMR of product **1ad** in **$CDCl_3$**.

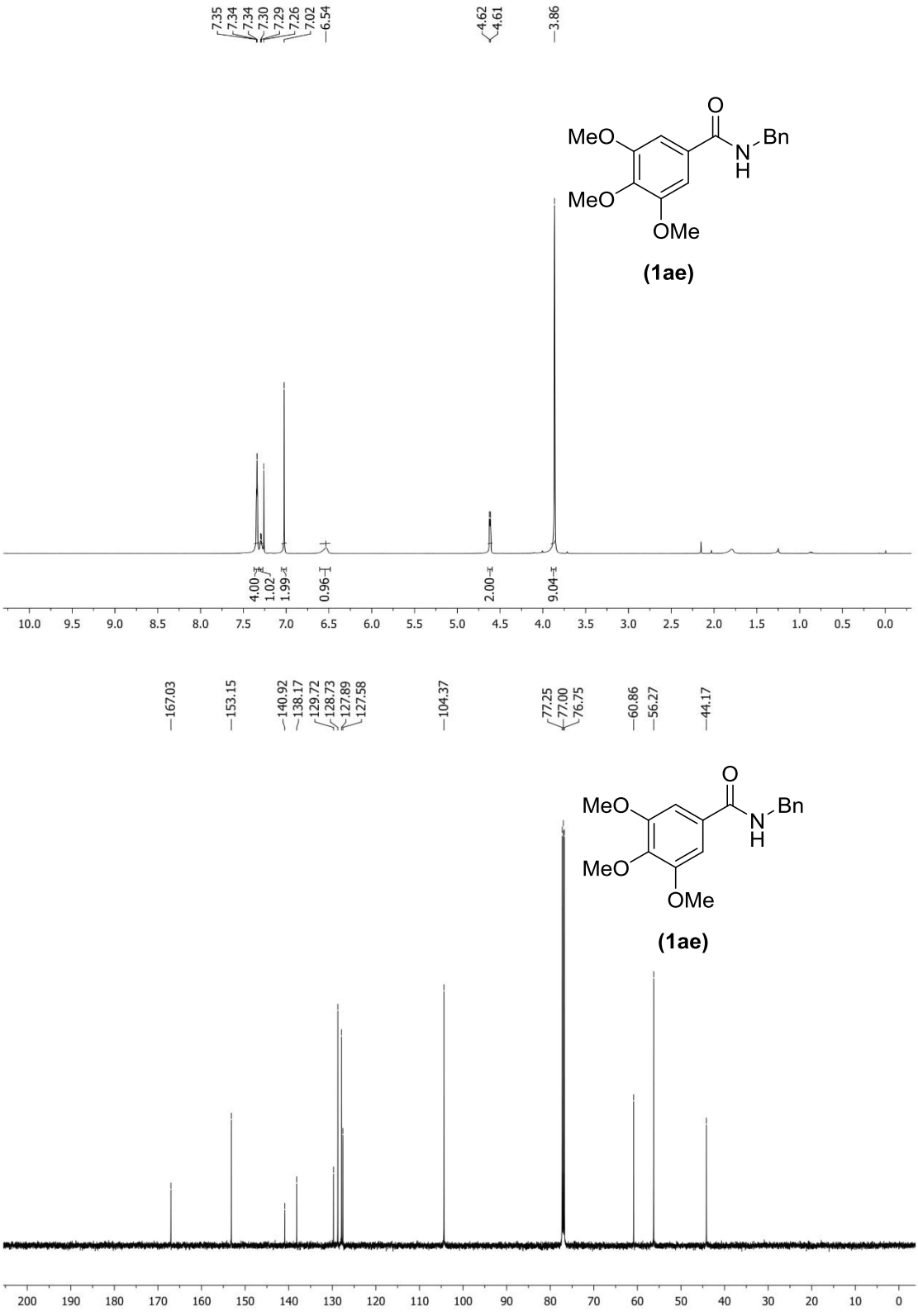


Figure SI.3 ^{1}H and ^{13}C NMR of product **1ae** in **$CDCl_3$**.

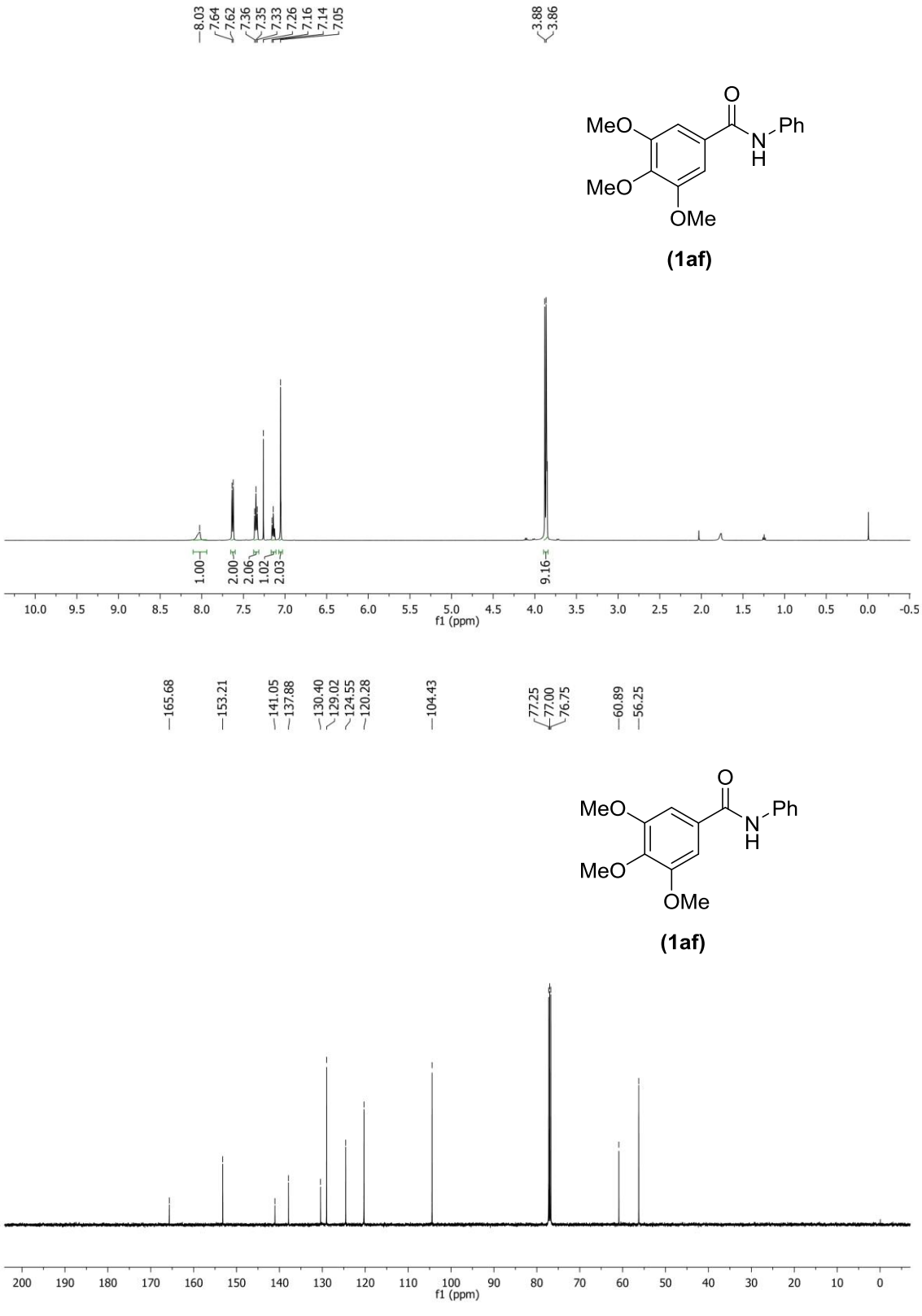


Figure SI.4 ^{1}H and ^{13}C NMR of product **1af** in **$CDCl_3$**.

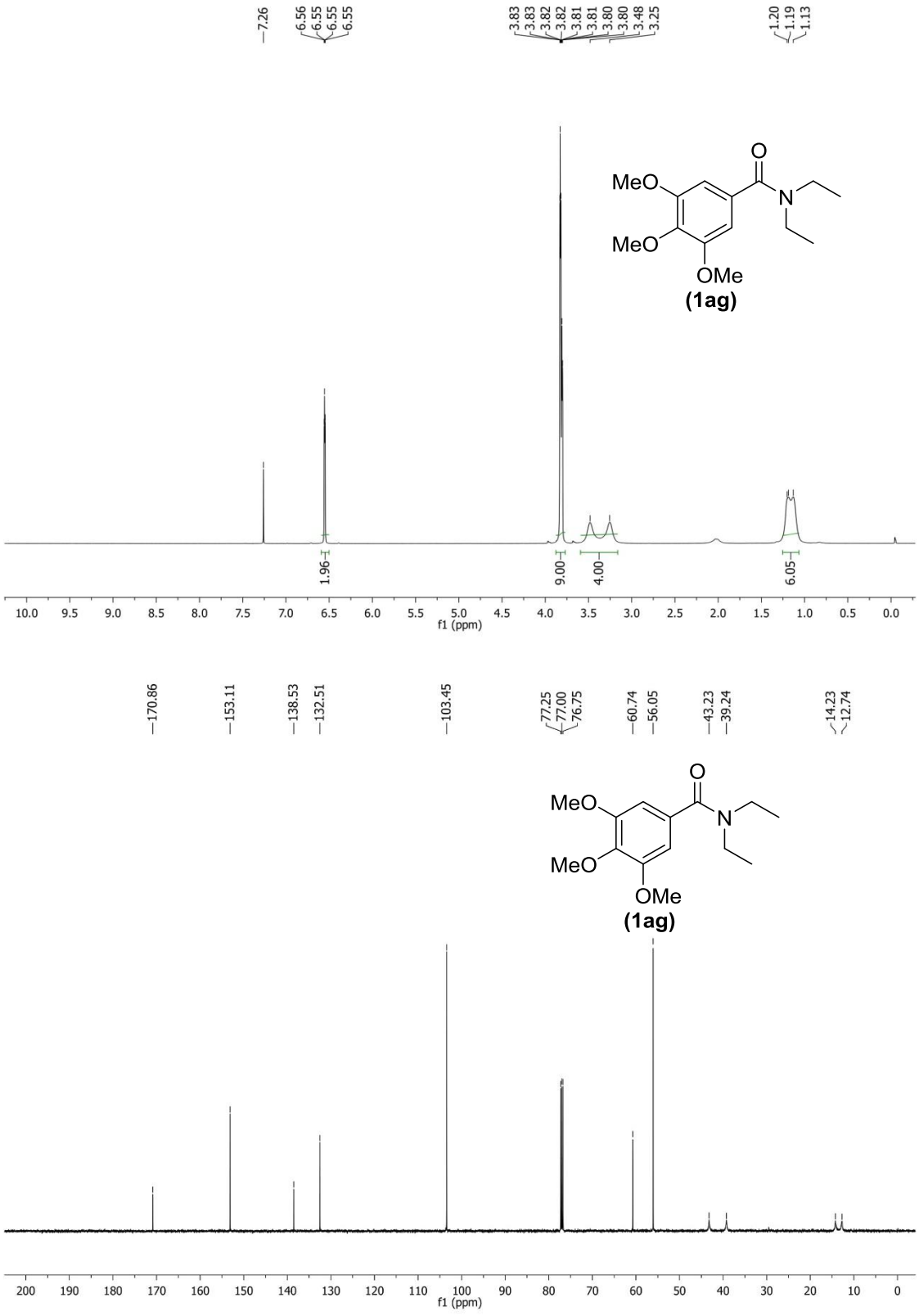


Figure SI.5 ^{1}H and ^{13}C NMR of product **1ag** in **$CDCl_3$**.

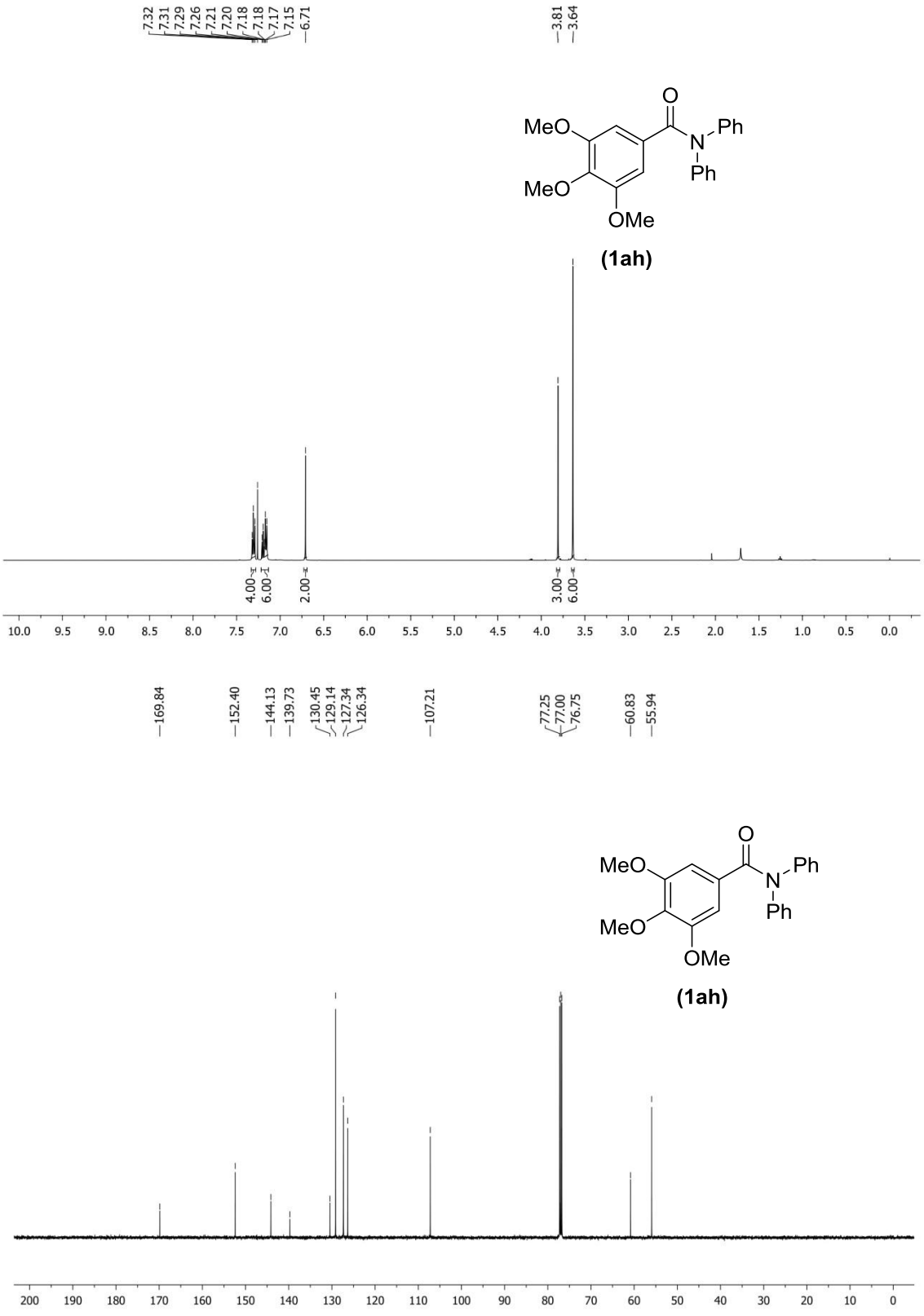


Figure SI.6 ^{1}H and ^{13}C NMR of product **1ah** in **$CDCl_3$**.

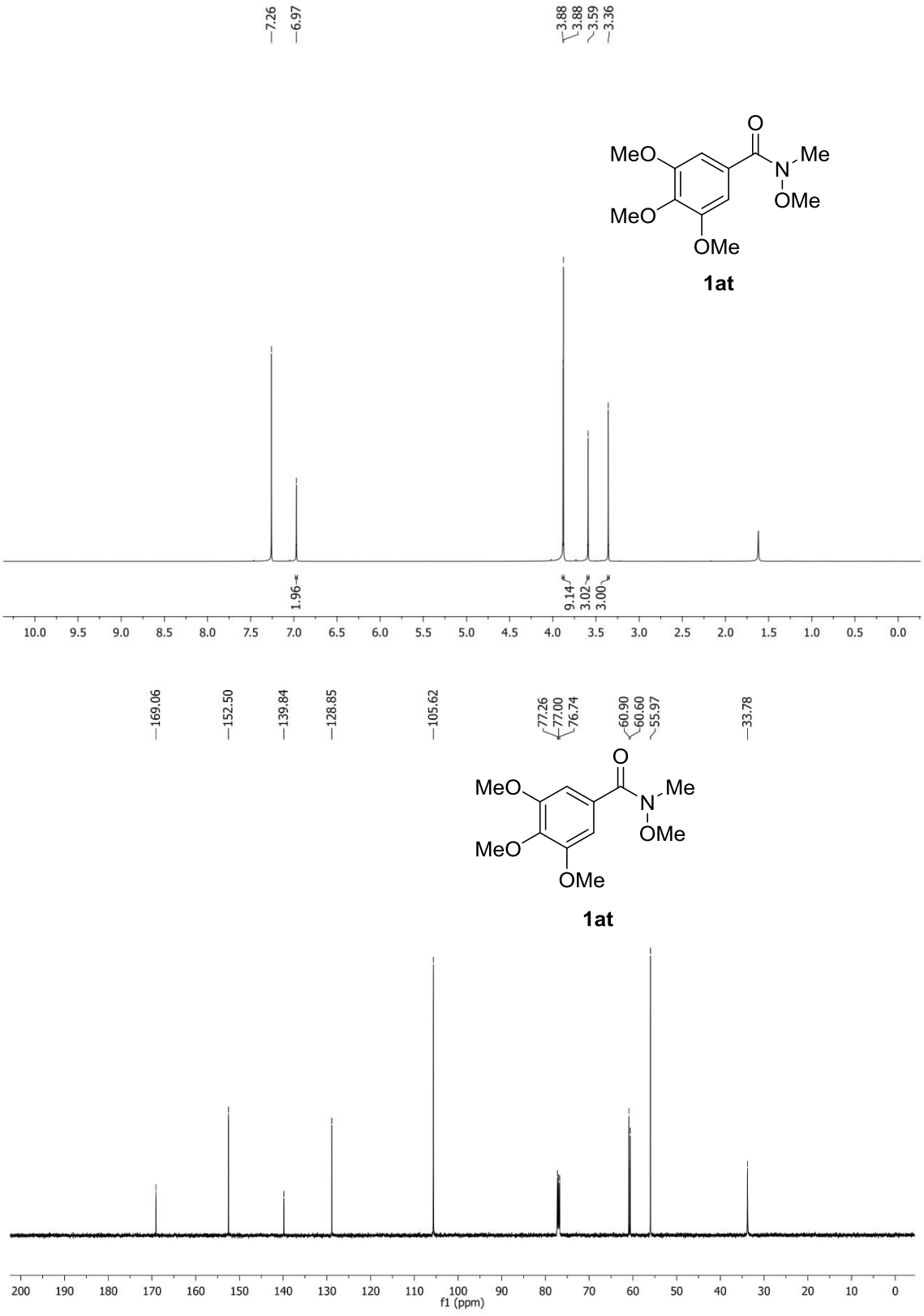


Figure SI.7 ^{1}H and ^{13}C NMR of product **1at** in **$CDCl_3$**.

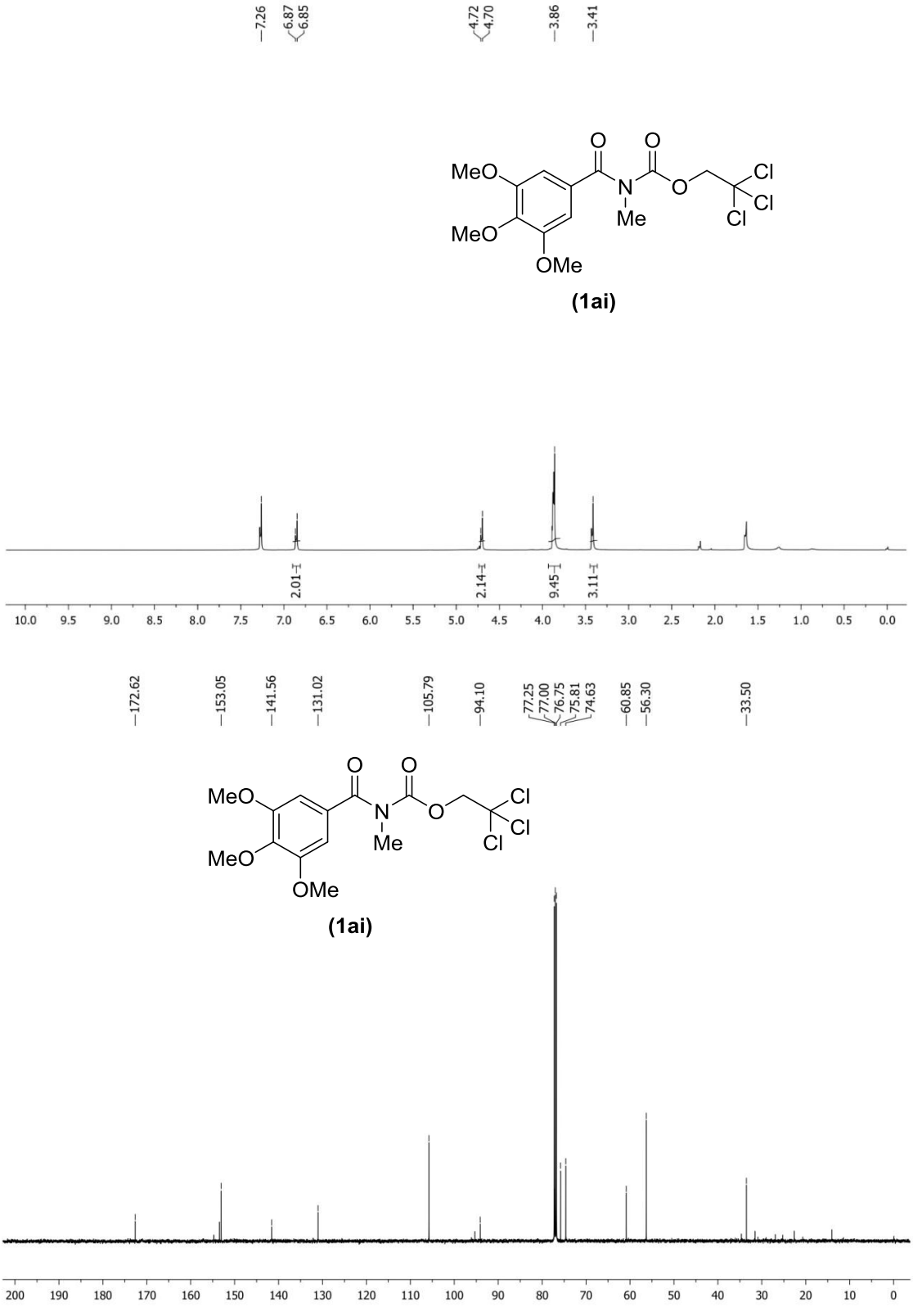


Figure SI.8 ^{1}H and ^{13}C NMR of product **1ai** in **$CDCl_3$**.

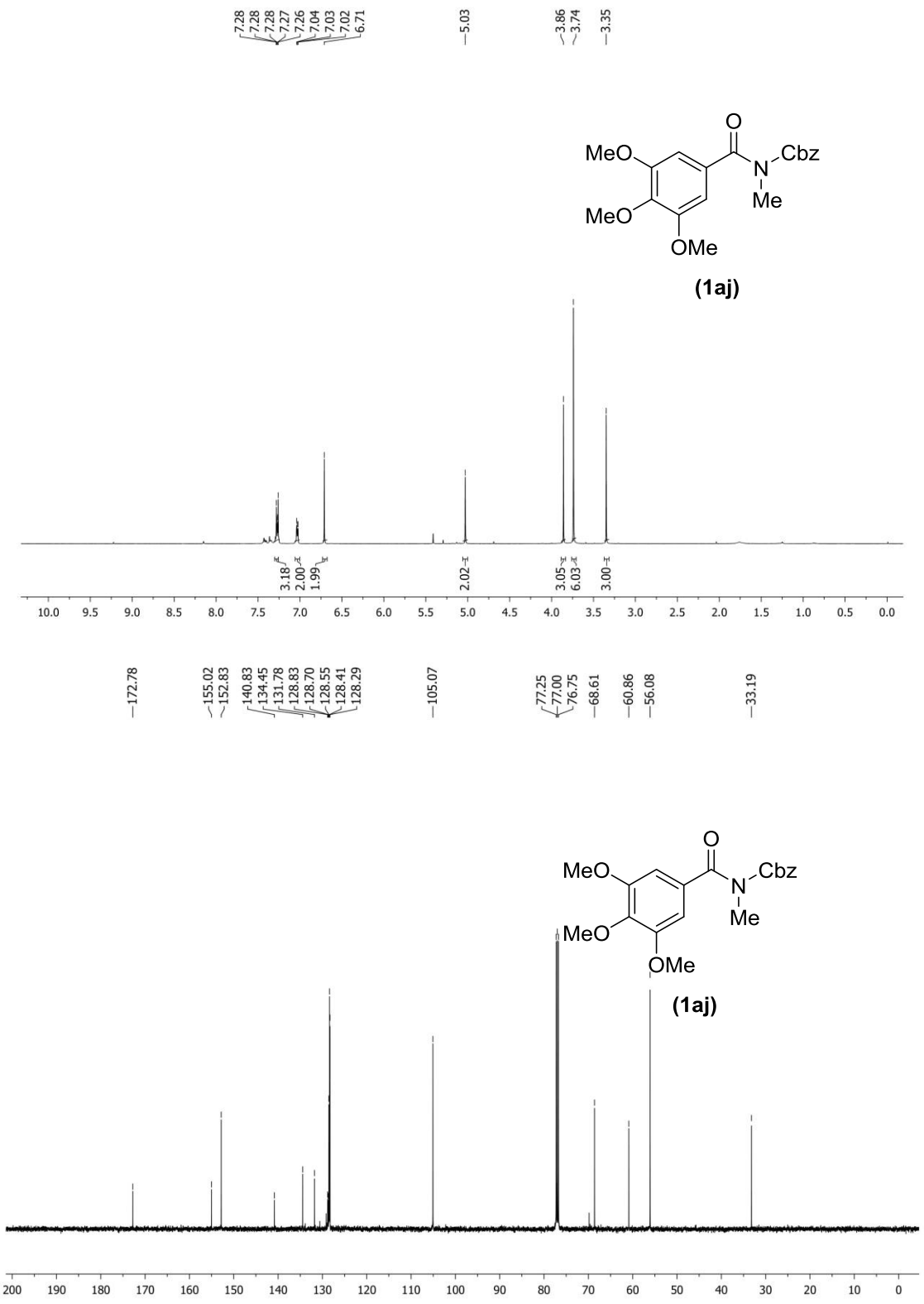


Figure SI.9 ^{1}H and ^{13}C NMR of product **1aj** in **$CDCl_3$**.

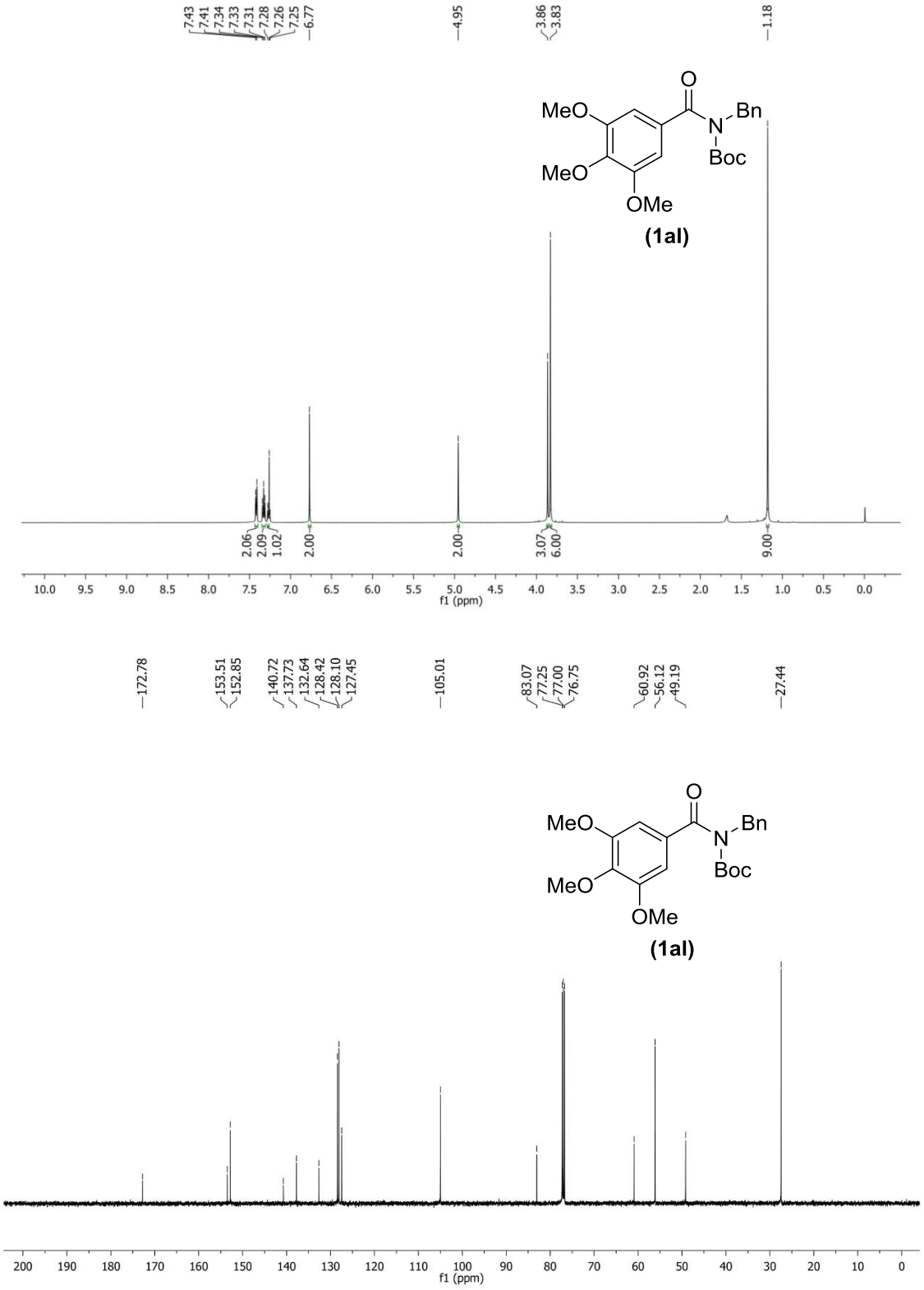


Figure SI.10 ^{1}H and ^{13}C NMR of product **1al** in **$CDCl_3$**.

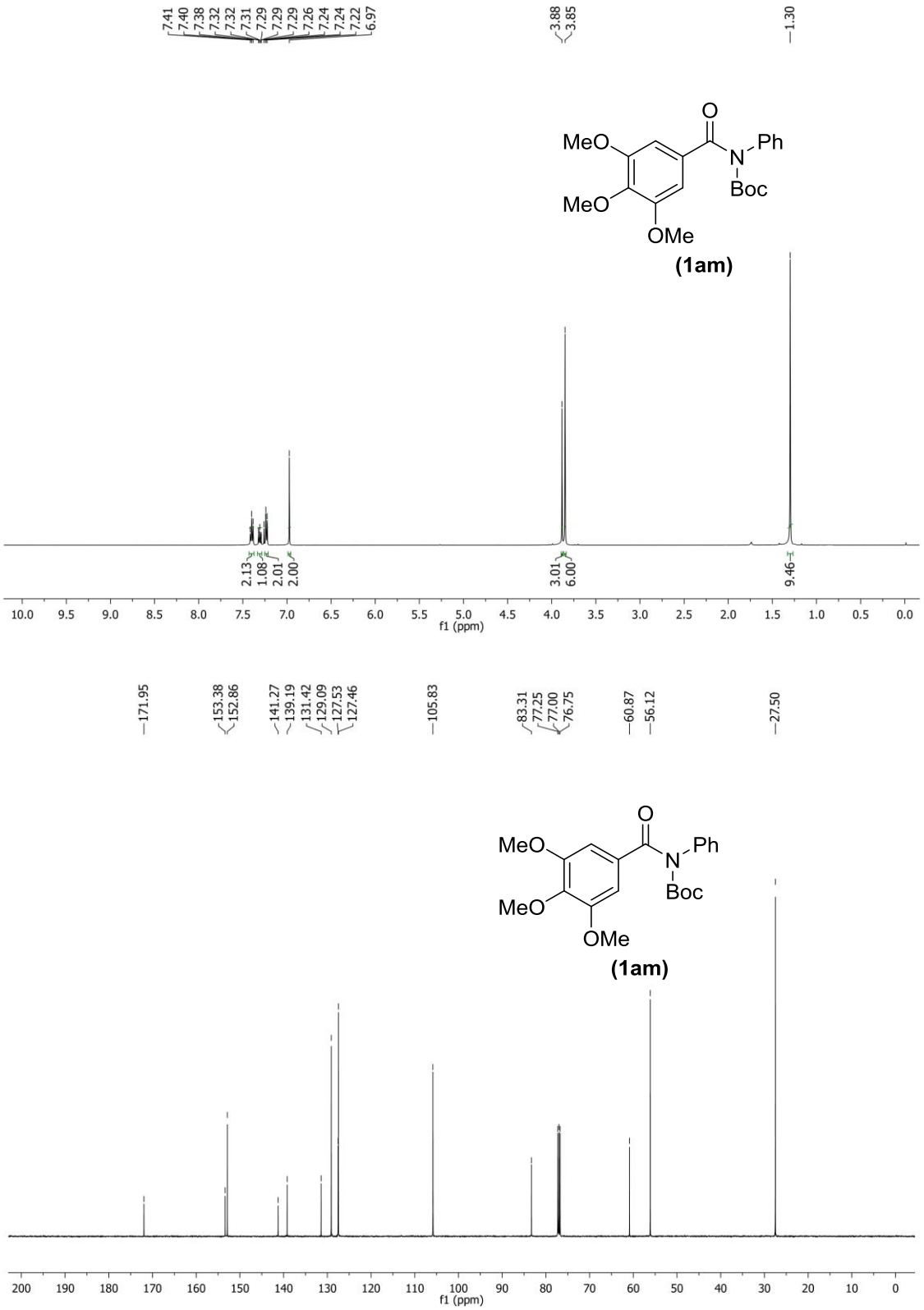


Figure SI.11 ^{1}H and ^{13}C NMR of product **1am** in **$CDCl_3$**.

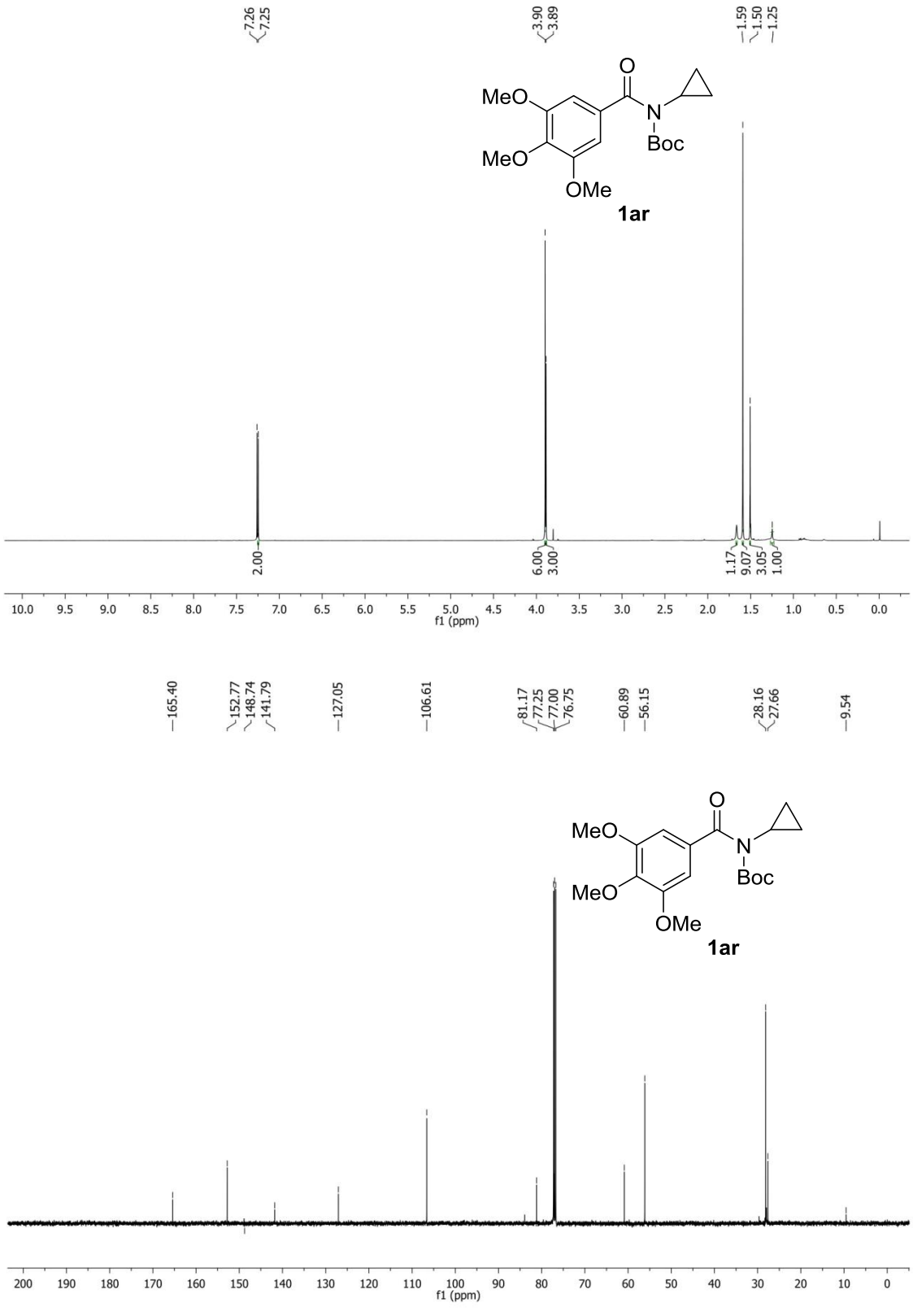


Figure SI.12 ^{1}H and ^{13}C NMR of product **1ar** in $CDCl_3$.

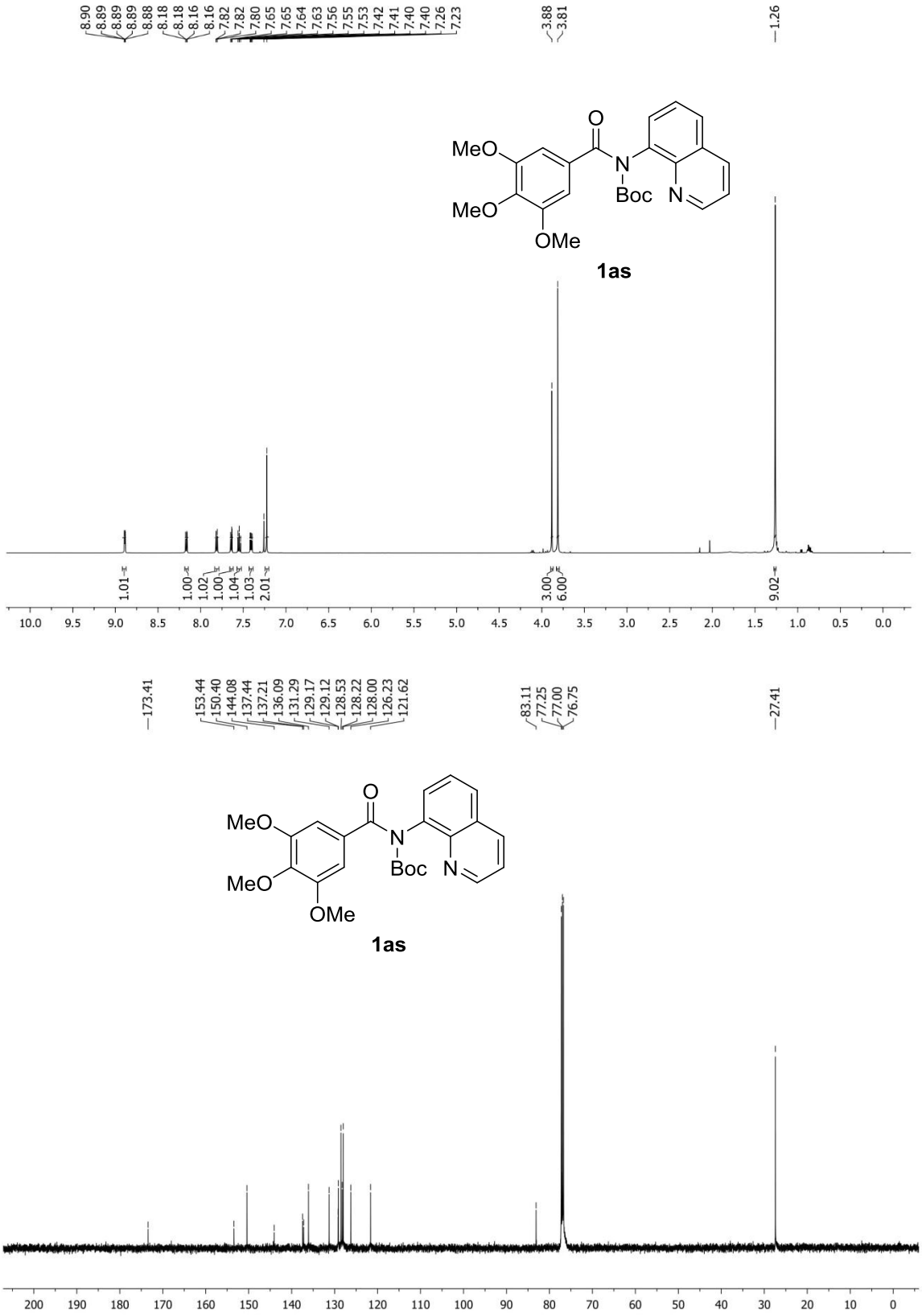


Figure SI.13 ^{1}H and ^{13}C NMR of product **1as** in **$CDCl_3$**.

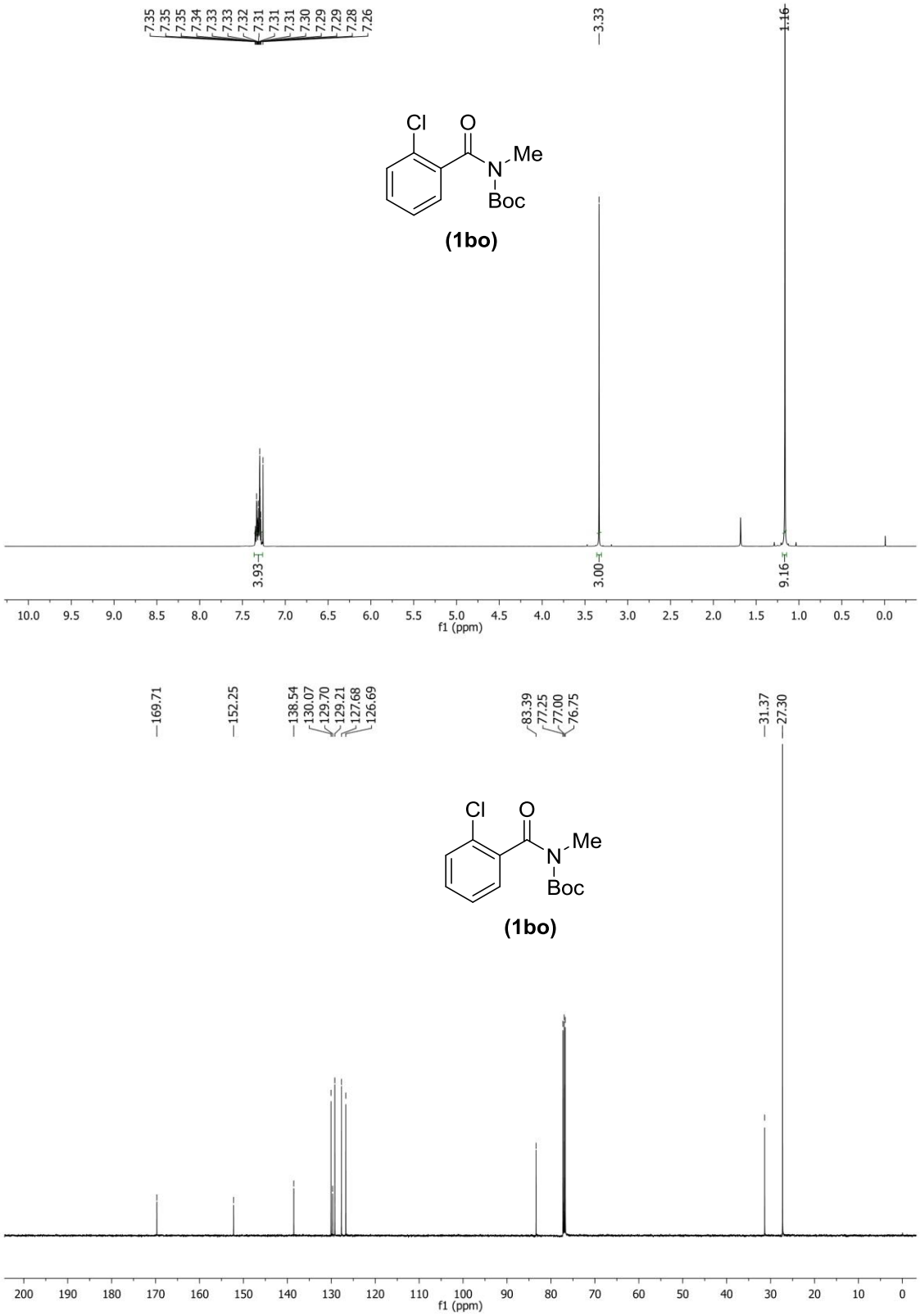


Figure SI.14 ^{1}H and ^{13}C NMR of product **1bo** in **$CDCl_3$**.

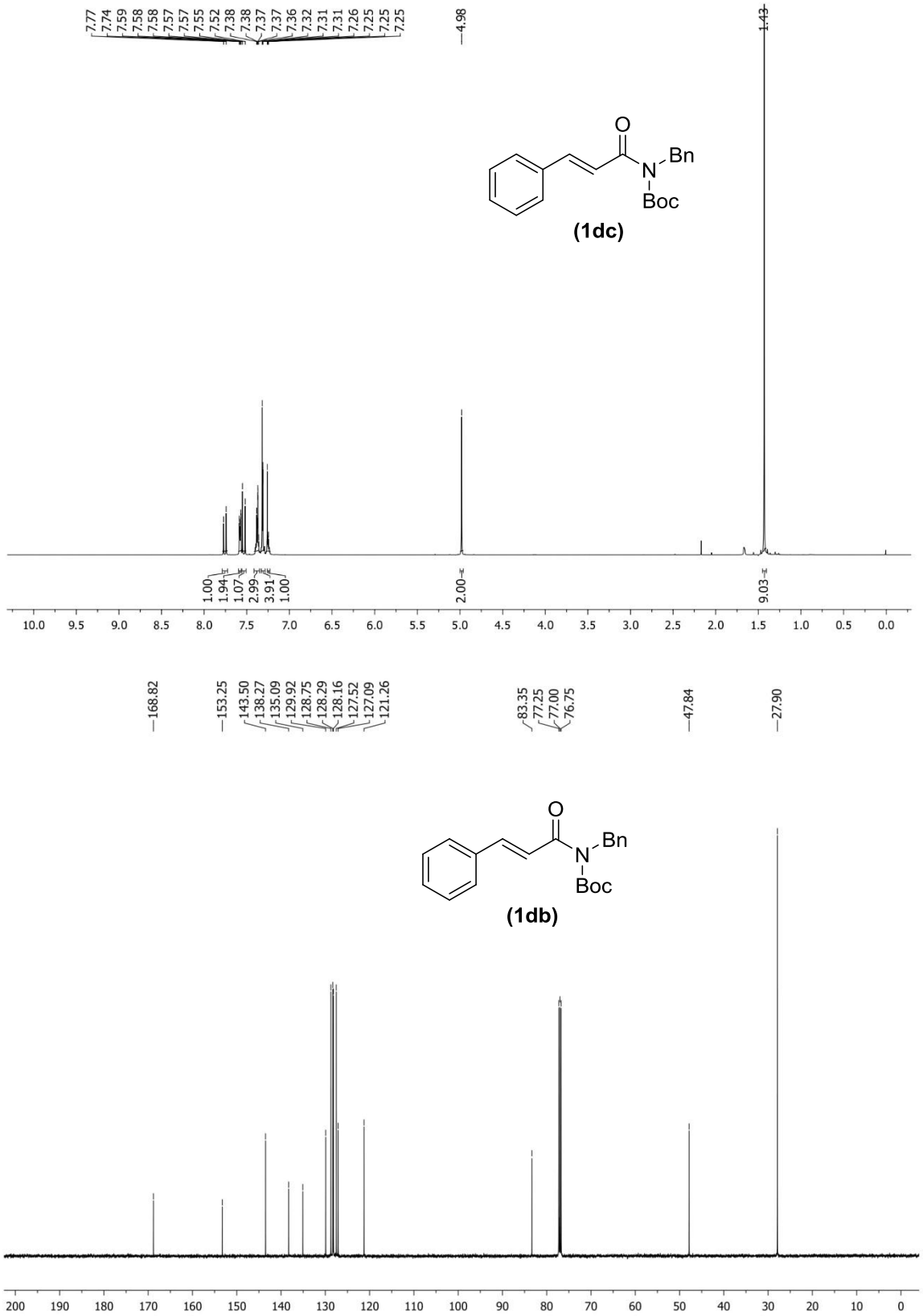


Figure SI.15 ^{1}H and ^{13}C NMR of product **1db** in **$CDCl_3$**.

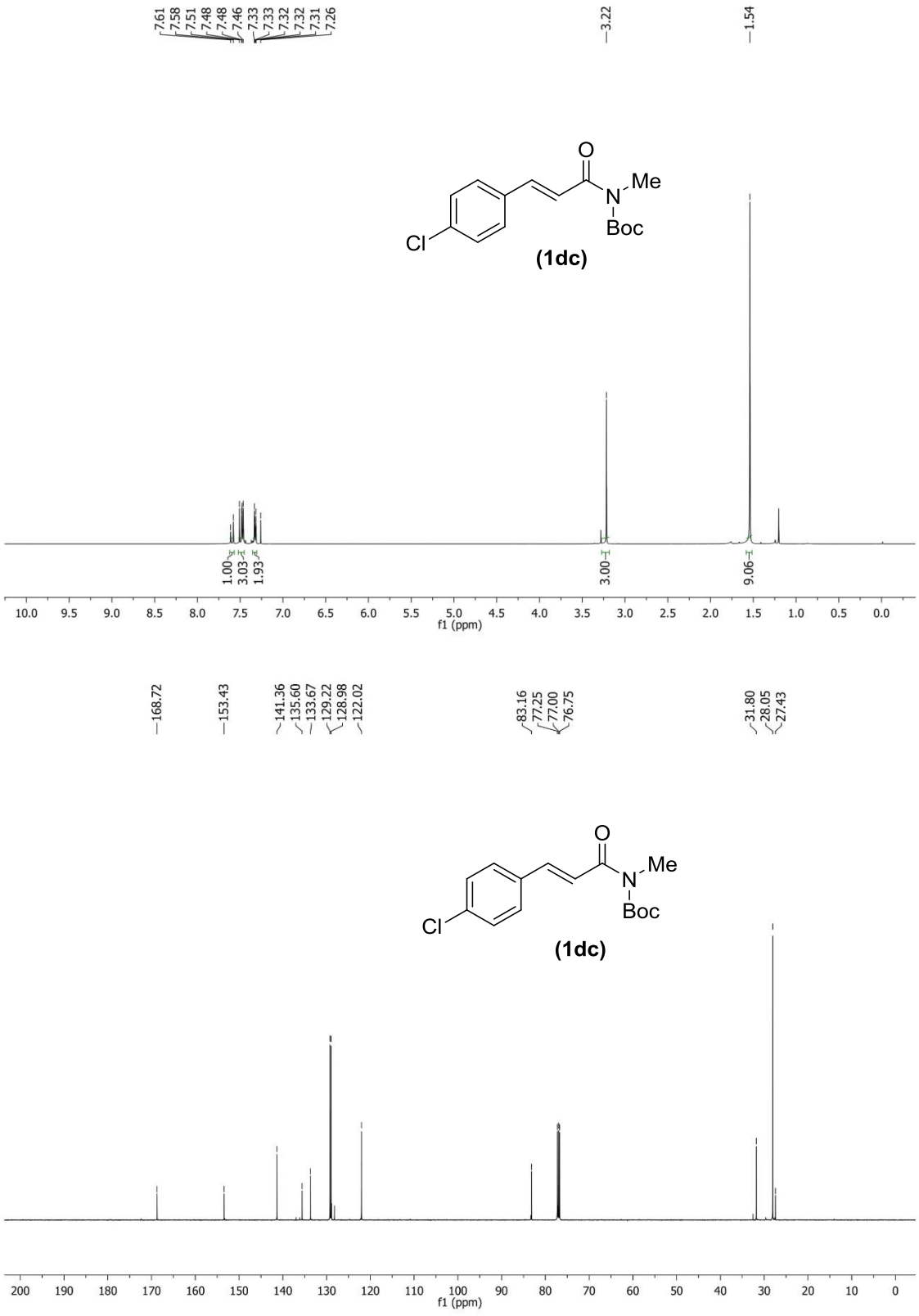


Figure SI.16 ^{1}H and ^{13}C NMR of product **1dc** in **$CDCl_3$**.

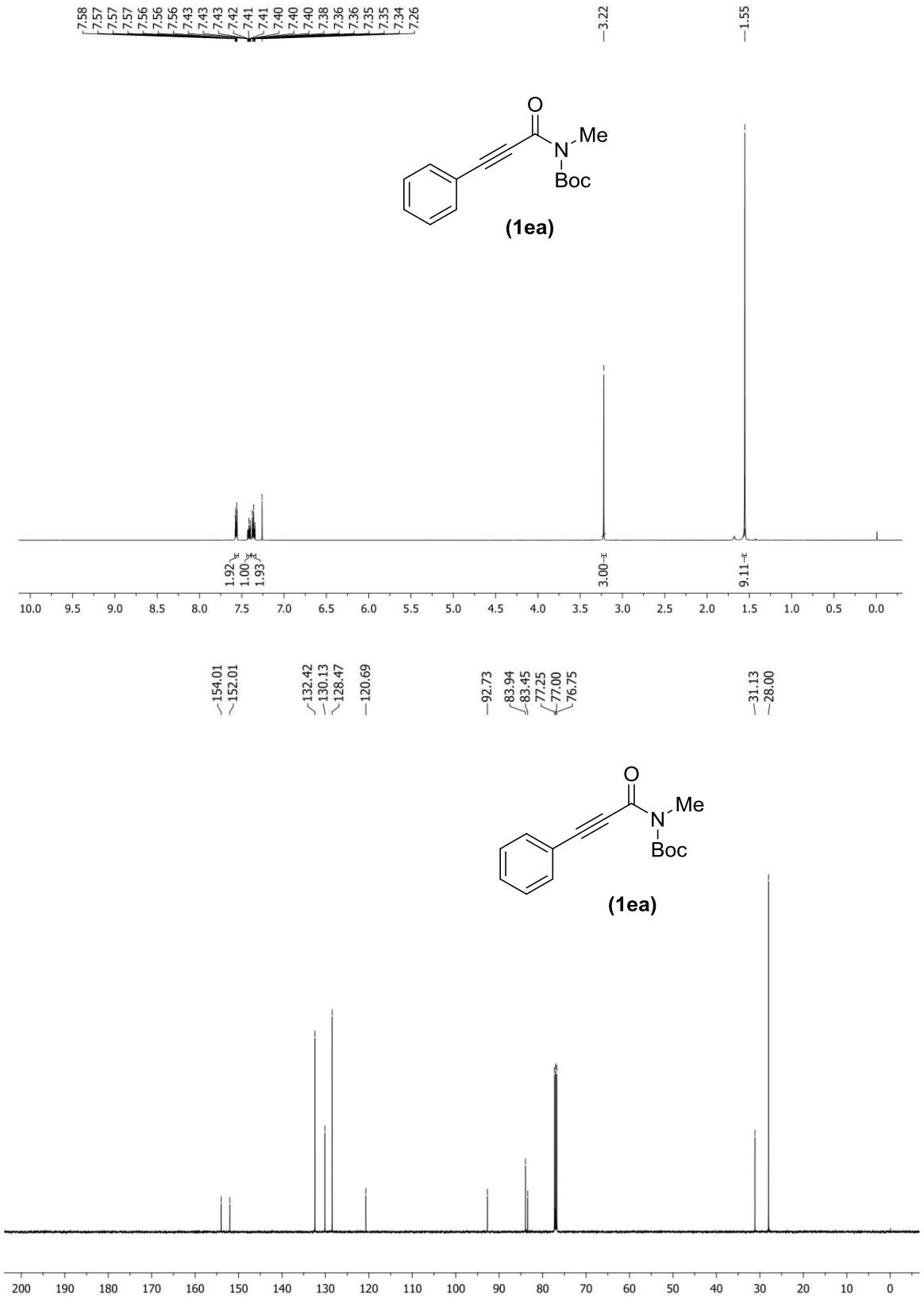


Figure SI.17 ^{1}H and ^{13}C NMR of product **1ea** in **$CDCl_3$**.

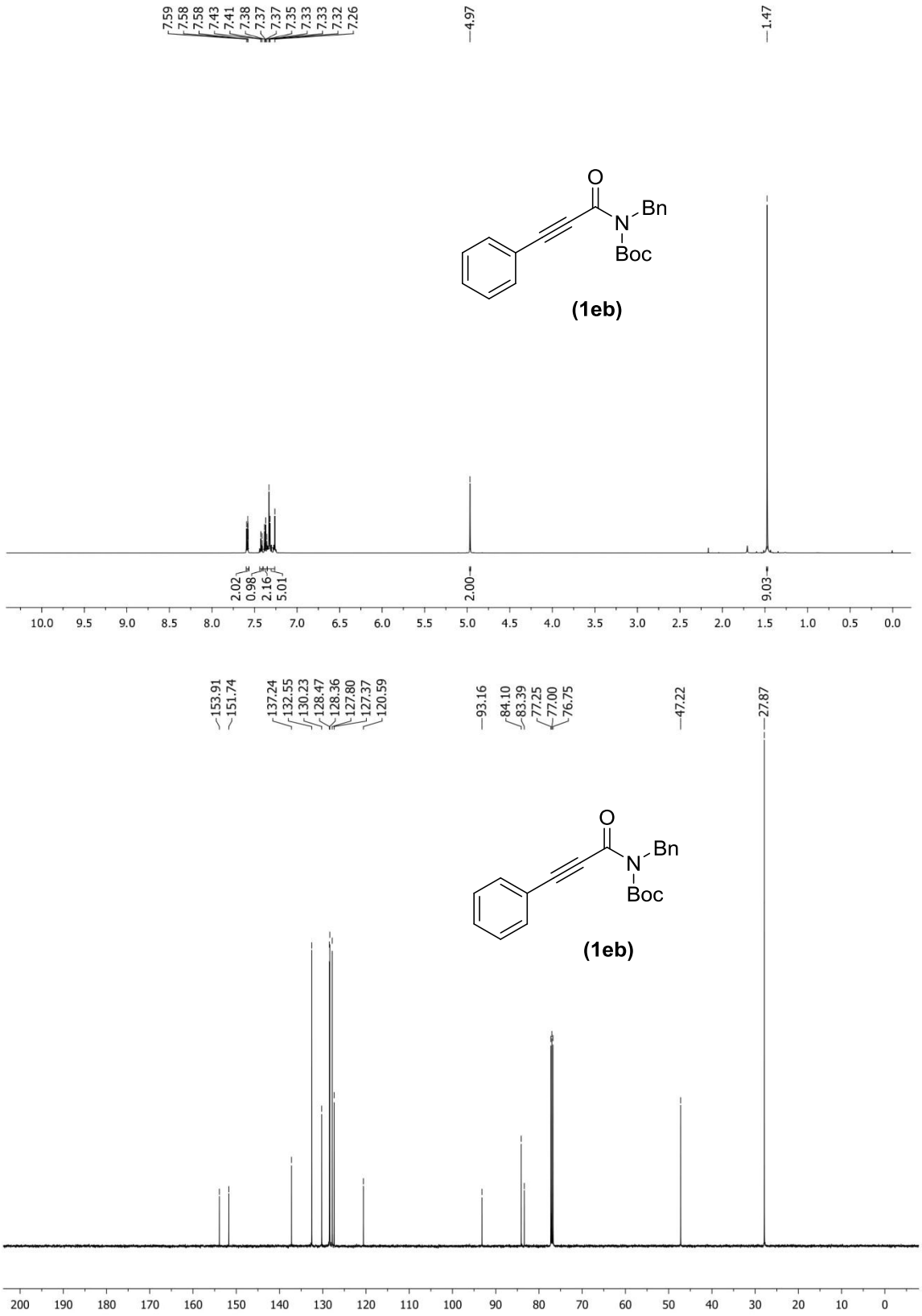


Figure SI.18 ^{1}H and ^{13}C NMR of product **1eb** in **$CDCl_3$**.

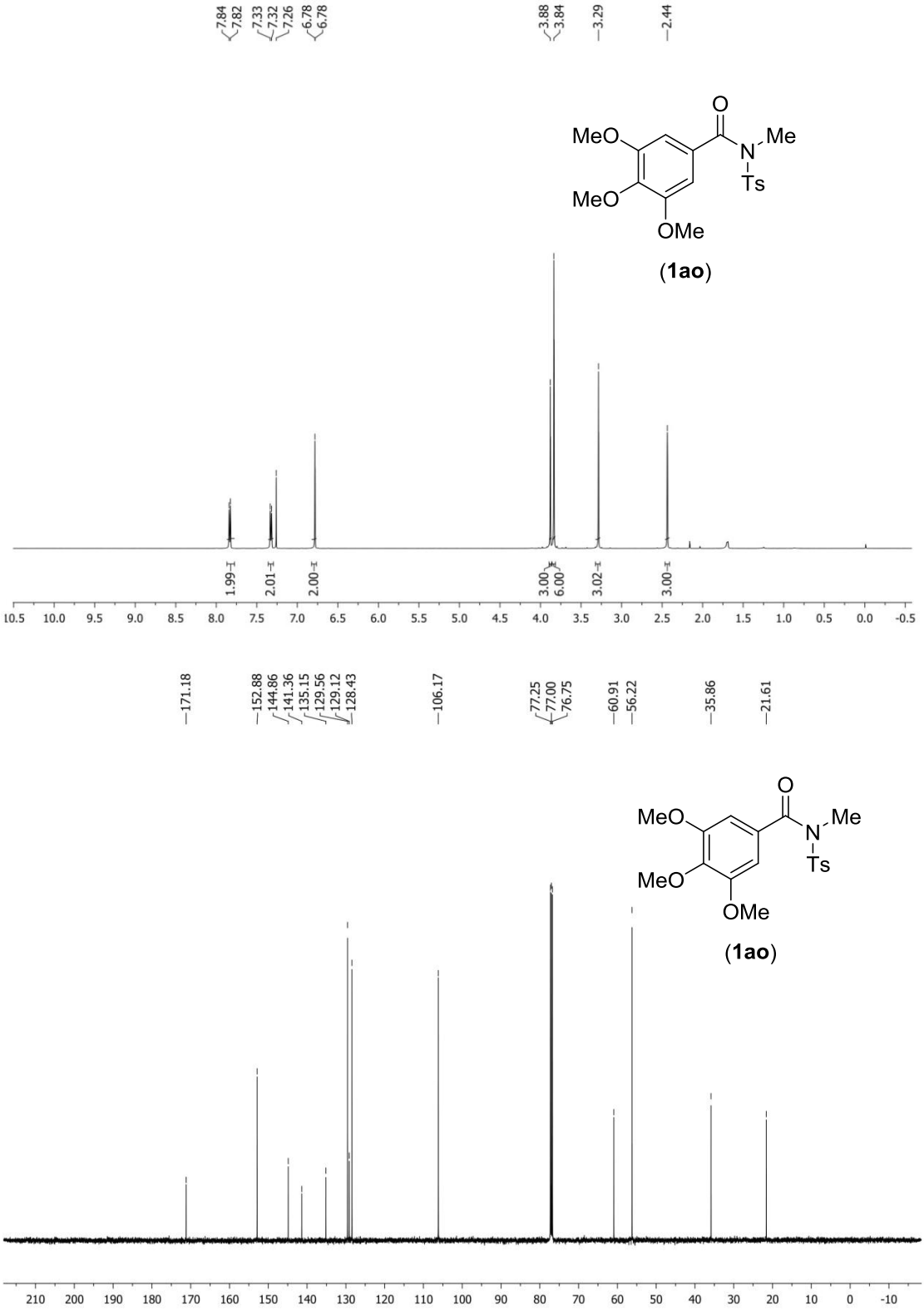


Figure SI.19 ^{1}H and ^{13}C NMR of product **1ao** in **$CDCl_3$**.

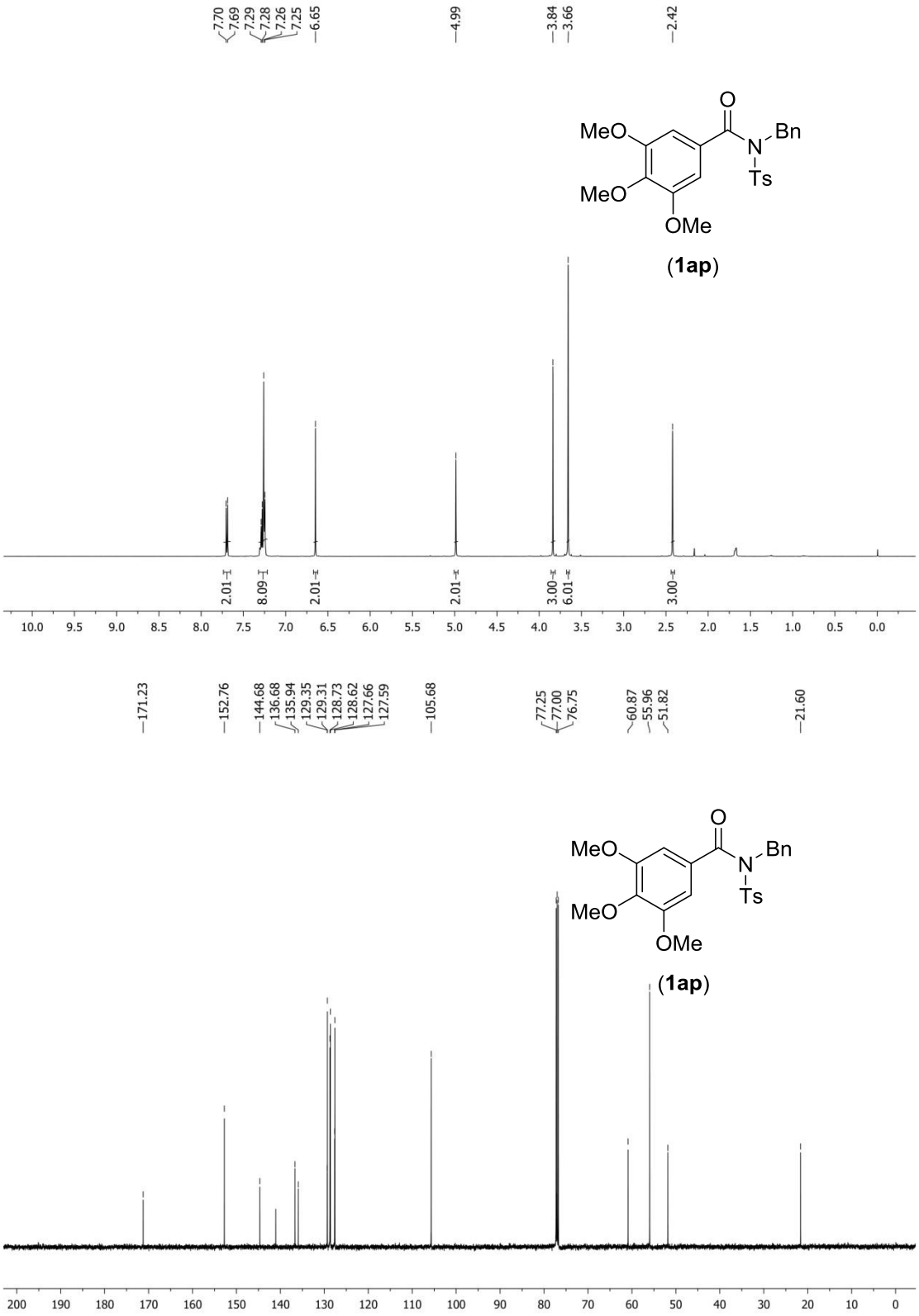


Figure SI.20 ^{1}H and ^{13}C NMR of product **1ap** in $\mathbf{CDCl_3}$.

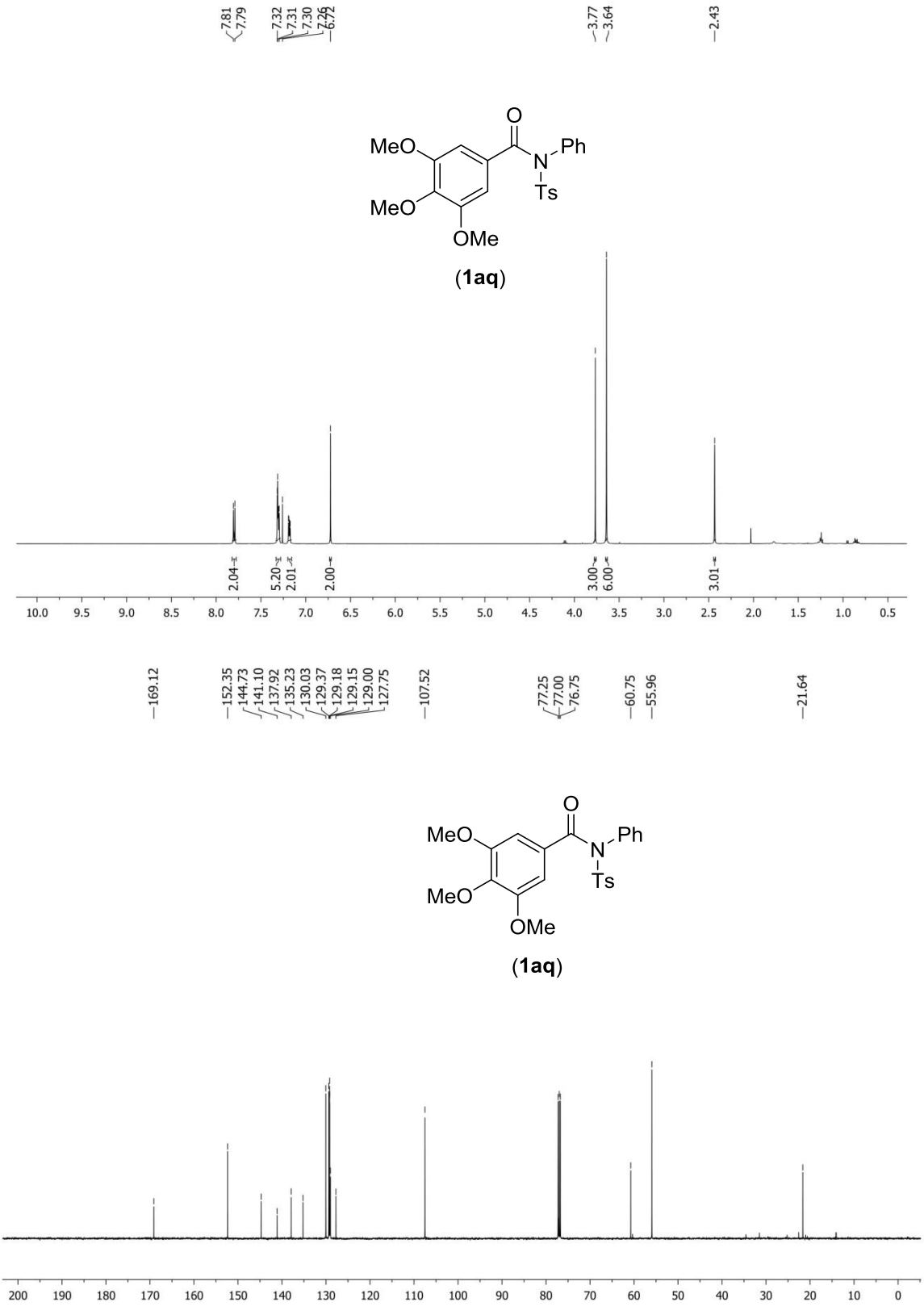


Figure SI.21 ^{1}H and ^{13}C NMR of product **1aq** in **$CDCl_3$**.

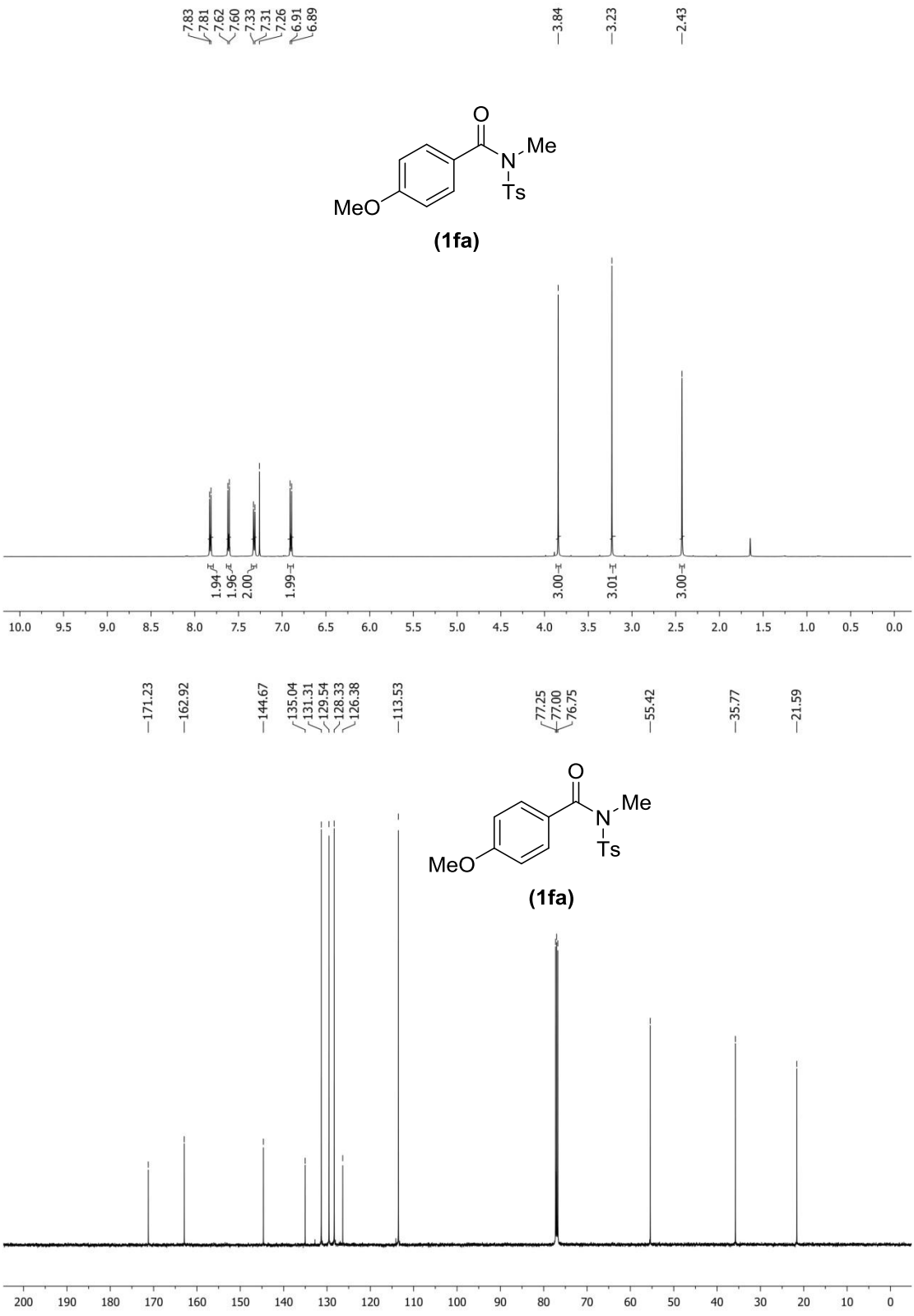


Figure SI.22 ^{1}H and ^{13}C NMR of product **1fa** in **$CDCl_3$**.

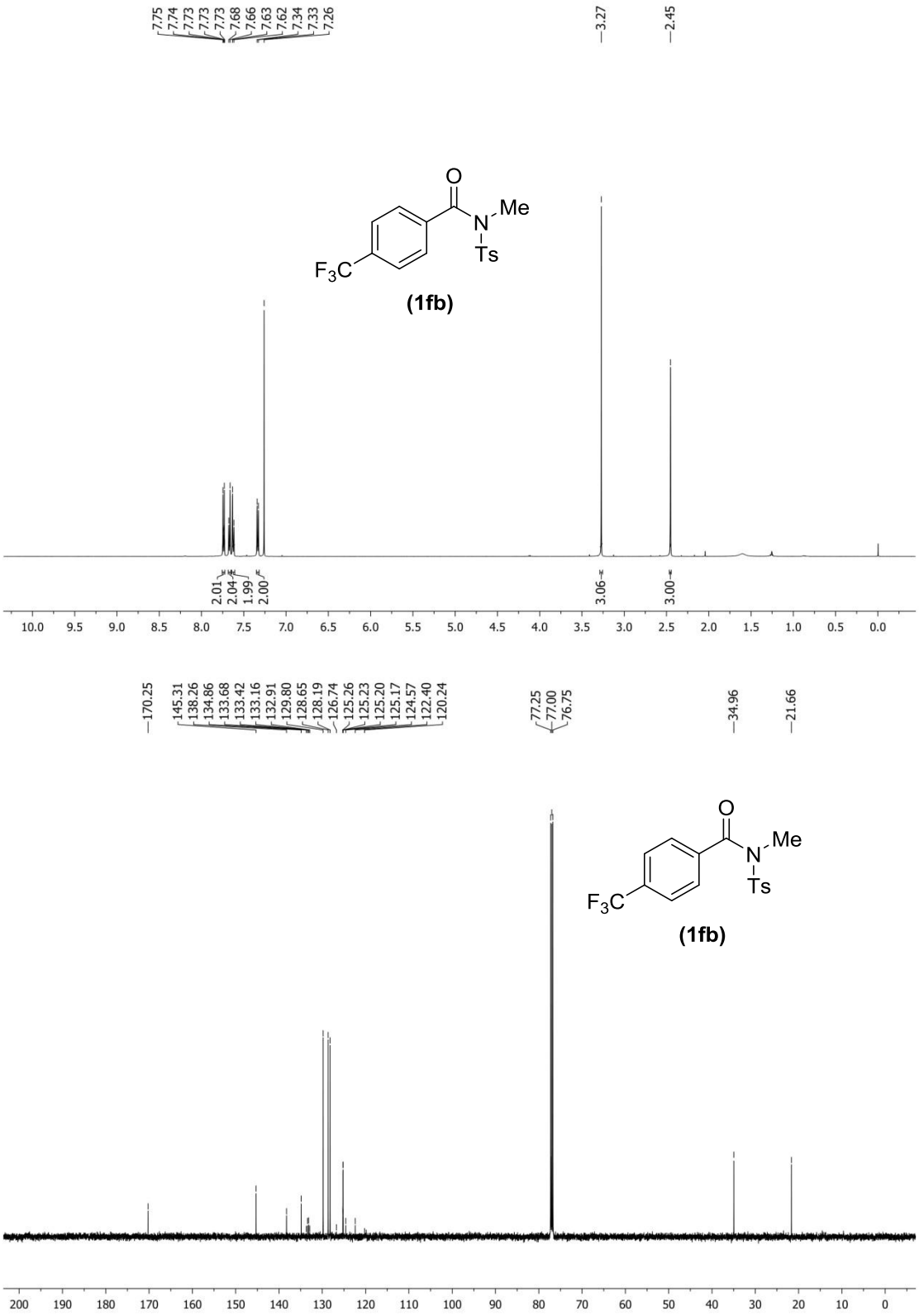


Figure SI.23 ^{1}H and ^{13}C NMR of product **1fb** in **$CDCl_3$**.

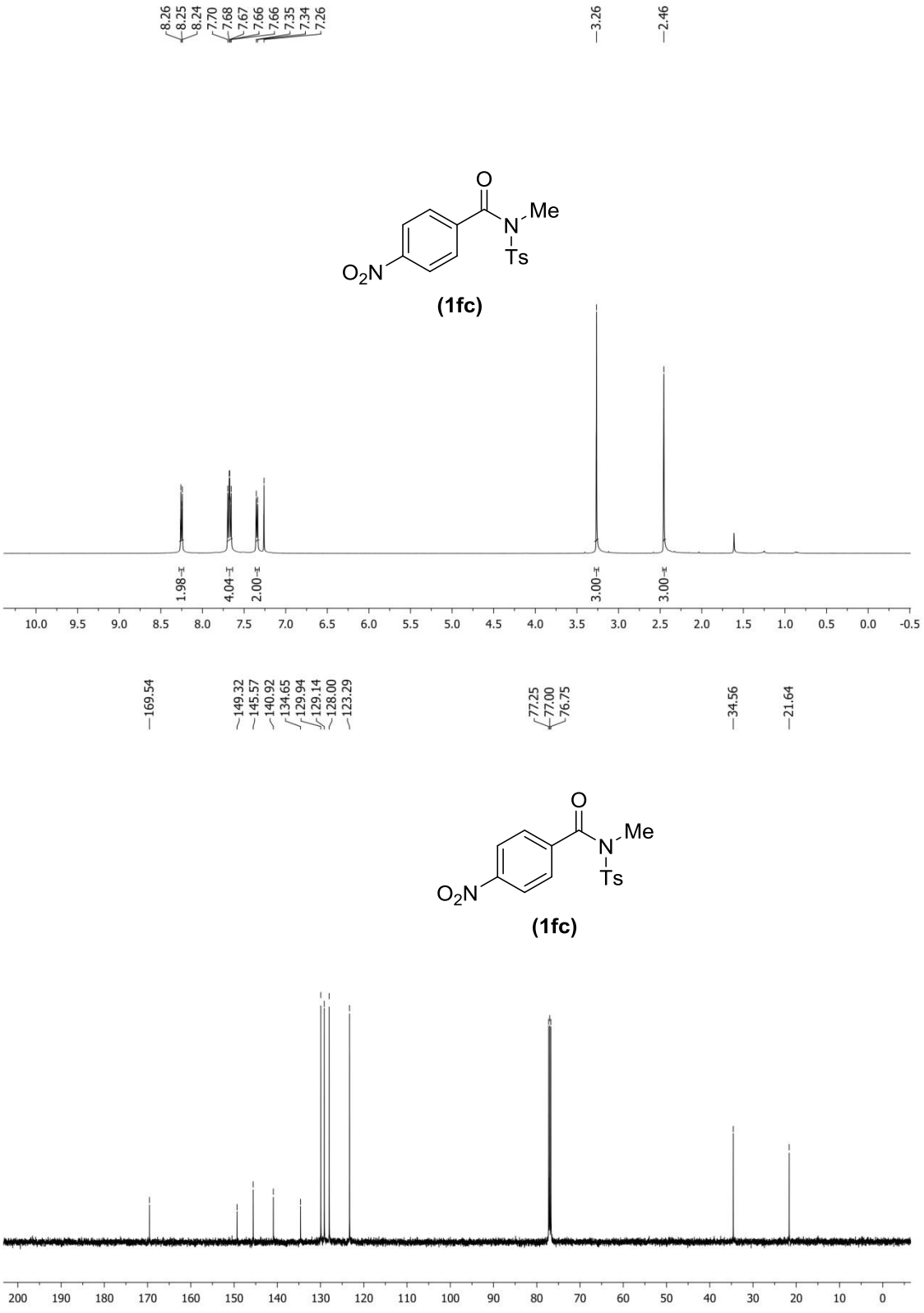


Figure SI.24 ^{1}H and ^{13}C NMR of product **1fc** in **$CDCl_3$**.

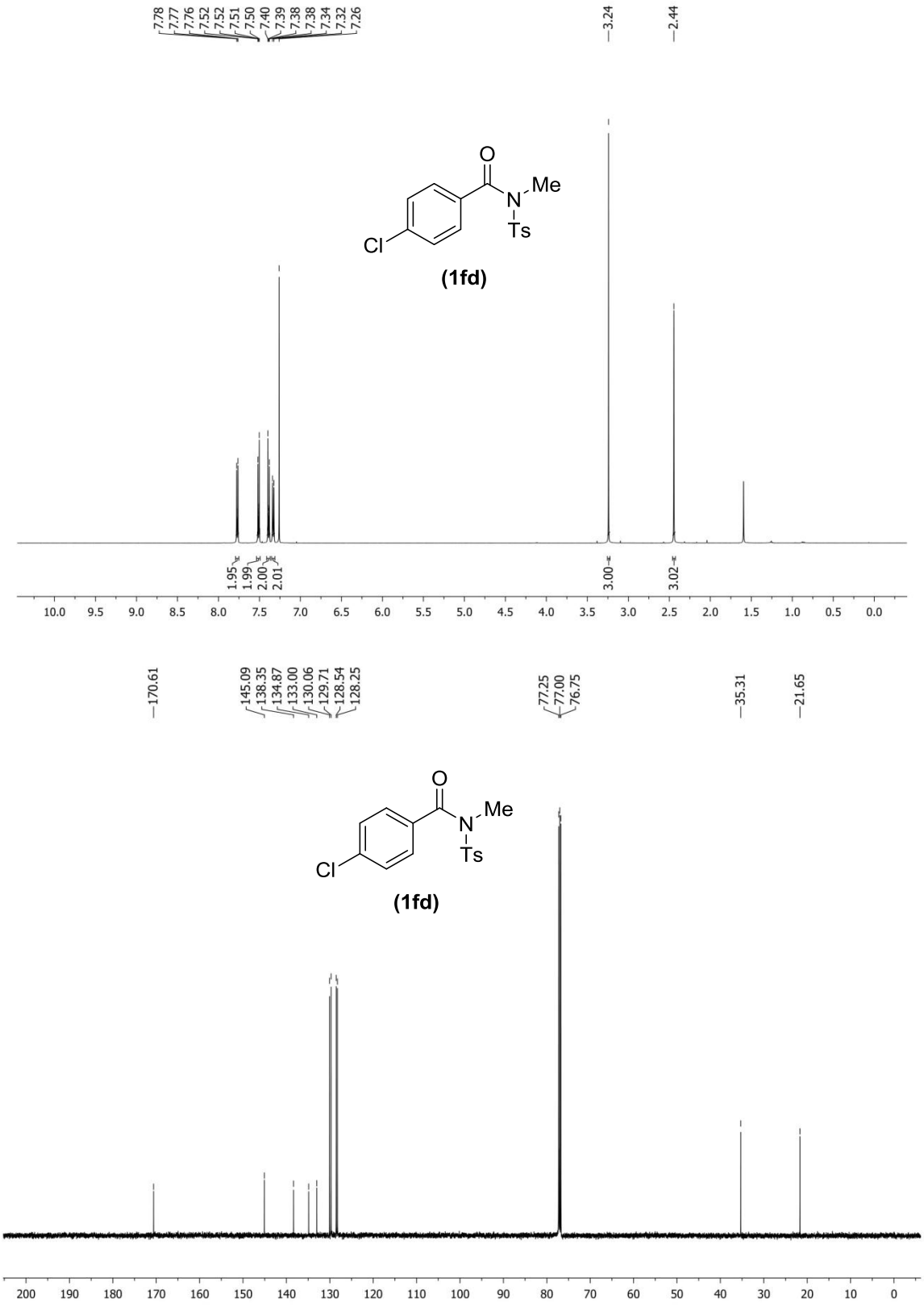


Figure SI.24 ^{1}H and ^{13}C NMR of product **1fd** in **$CDCl_3$**.

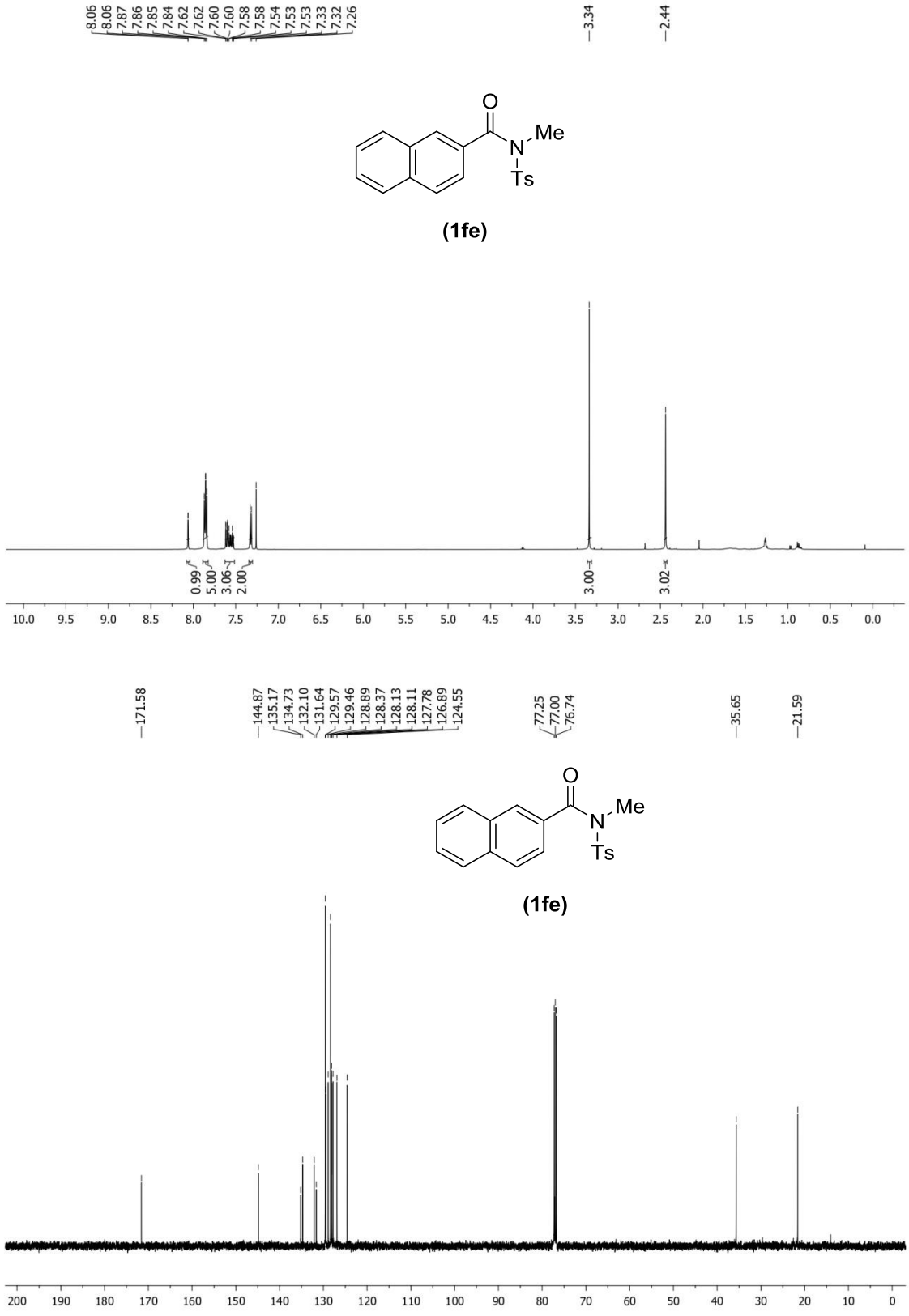


Figure SI.26 ^{1}H and ^{13}C NMR of product **1fe** in **$CDCl_3$**.

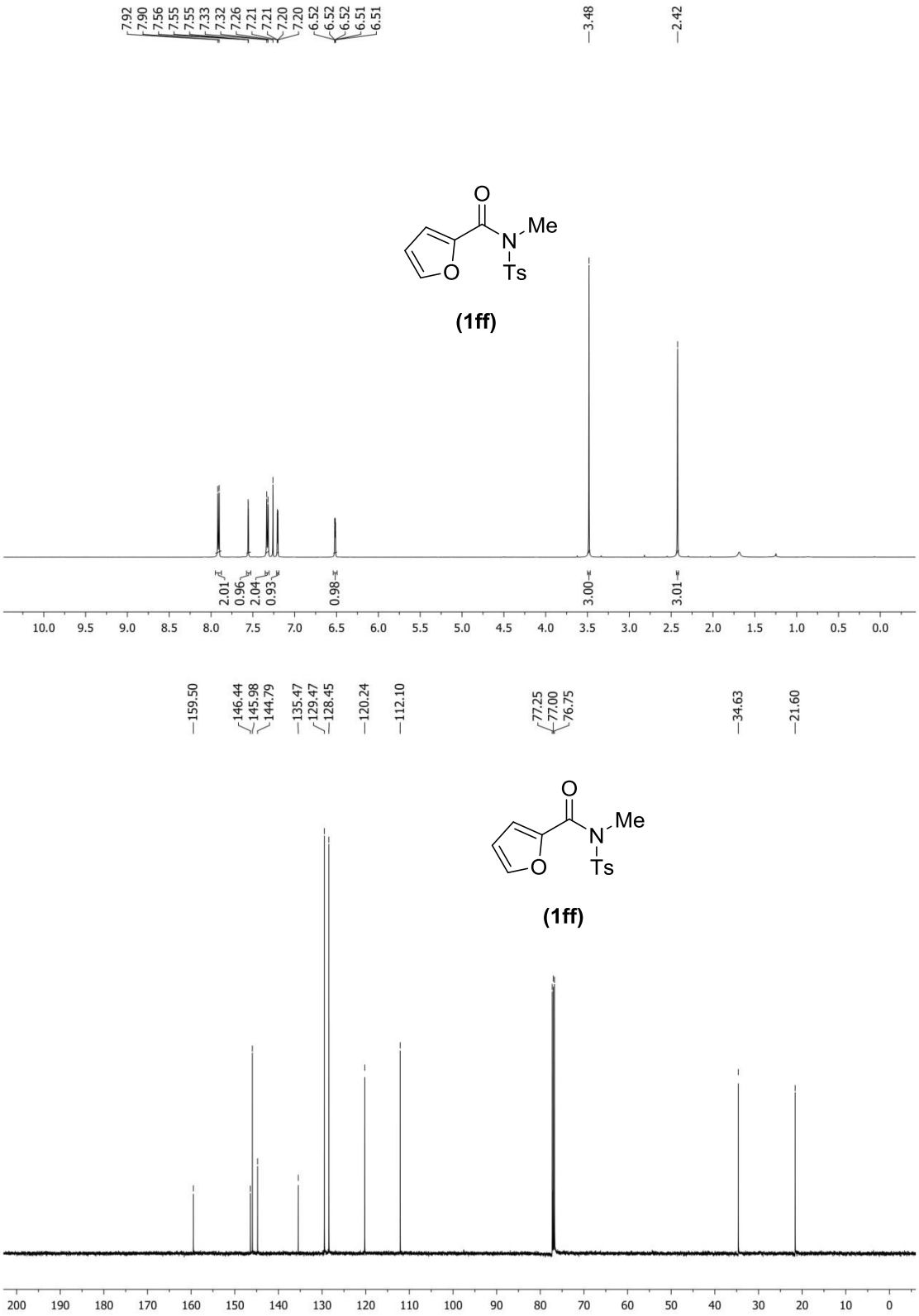


Figure SI.27 ^{1}H and ^{13}C NMR of product **1ff** in **$CDCl_3$**.

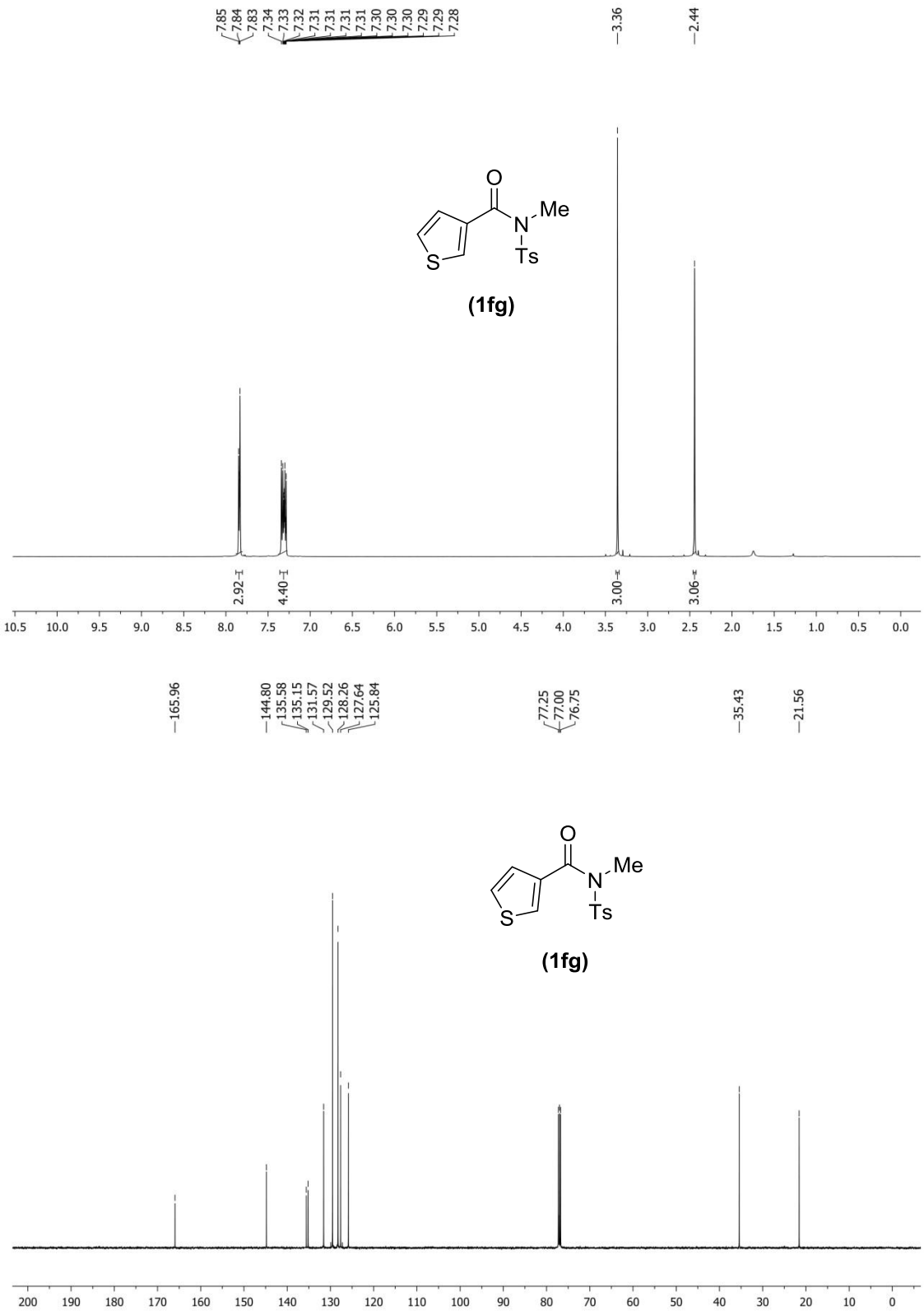


Figure SI.28 ^{1}H and ^{13}C NMR of product **1fg** in **$CDCl_3$**.

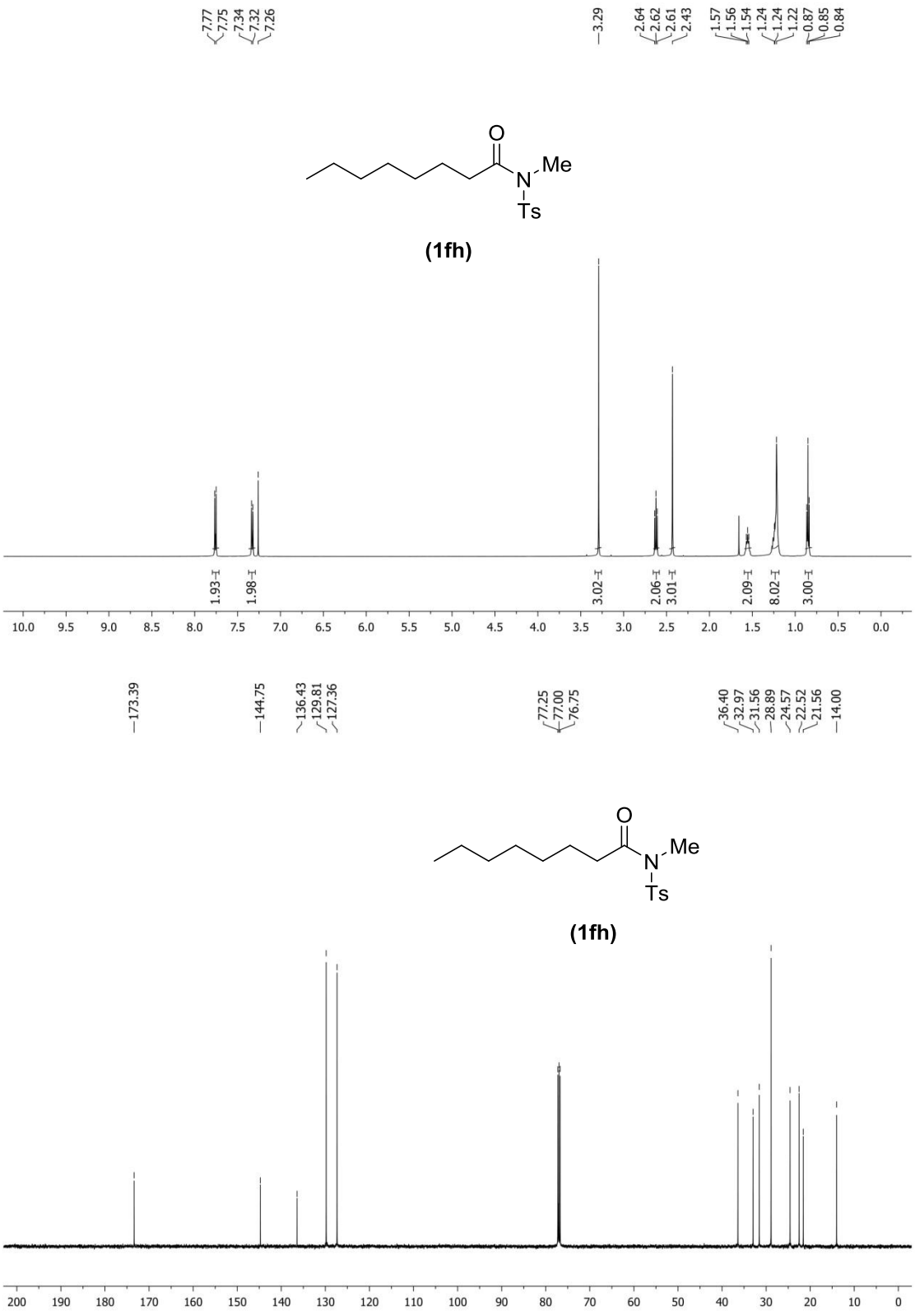


Figure SI.29 ^{1}H and ^{13}C NMR of product **1fh** in $CDCl_3$.

7. ^{1}H and ^{13}C NMR Spectra of the Aldehydes:

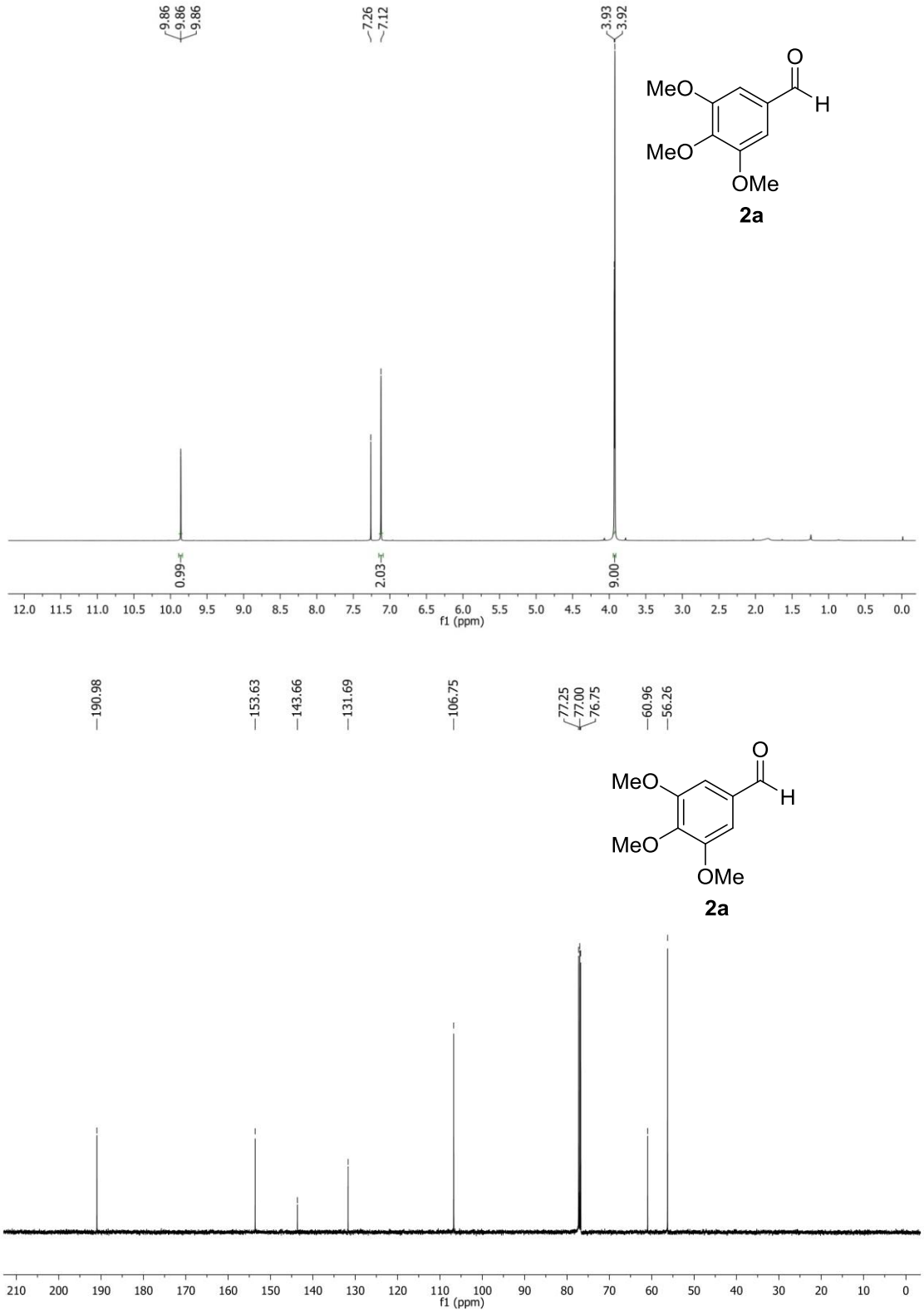


Figure SI.30 ^{1}H and ^{13}C NMR of product **2a** in **$CDCl_3$**.

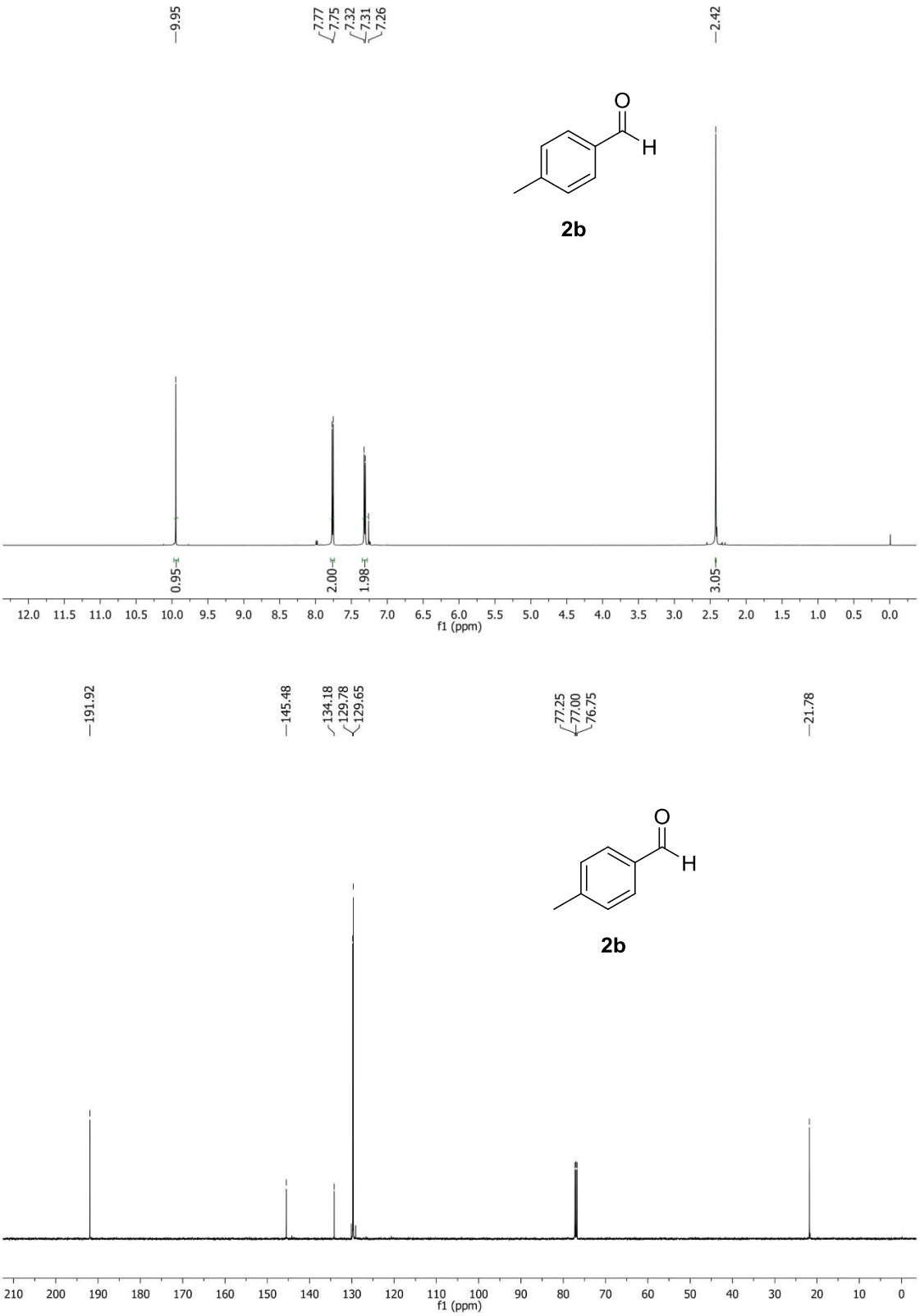


Figure SI.31 ^{1}H and ^{13}C NMR of product **2b** in **$CDCl_3$**.

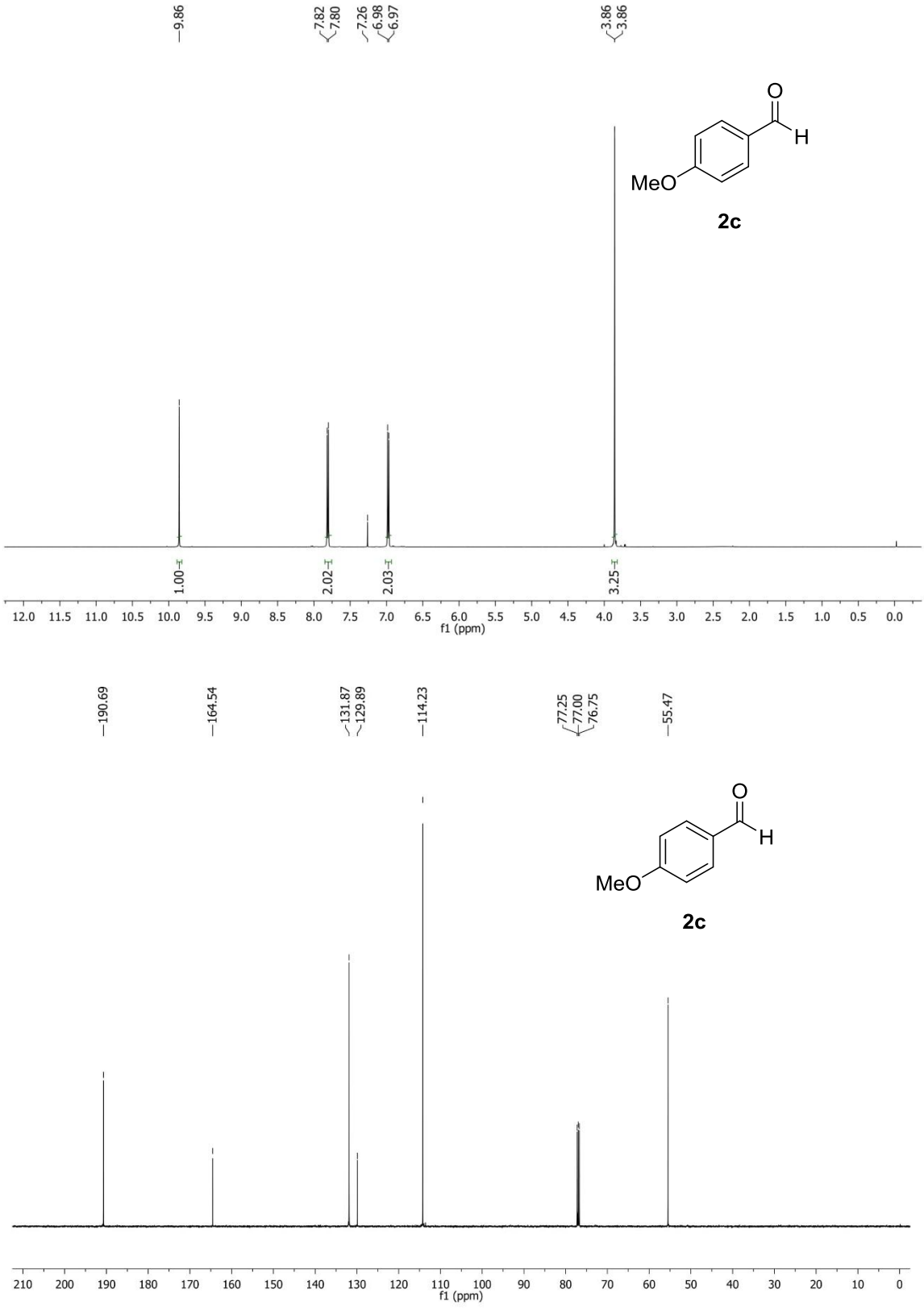


Figure SI.32 ^{1}H and ^{13}C NMR of product **2c** in **$CDCl_3$**.

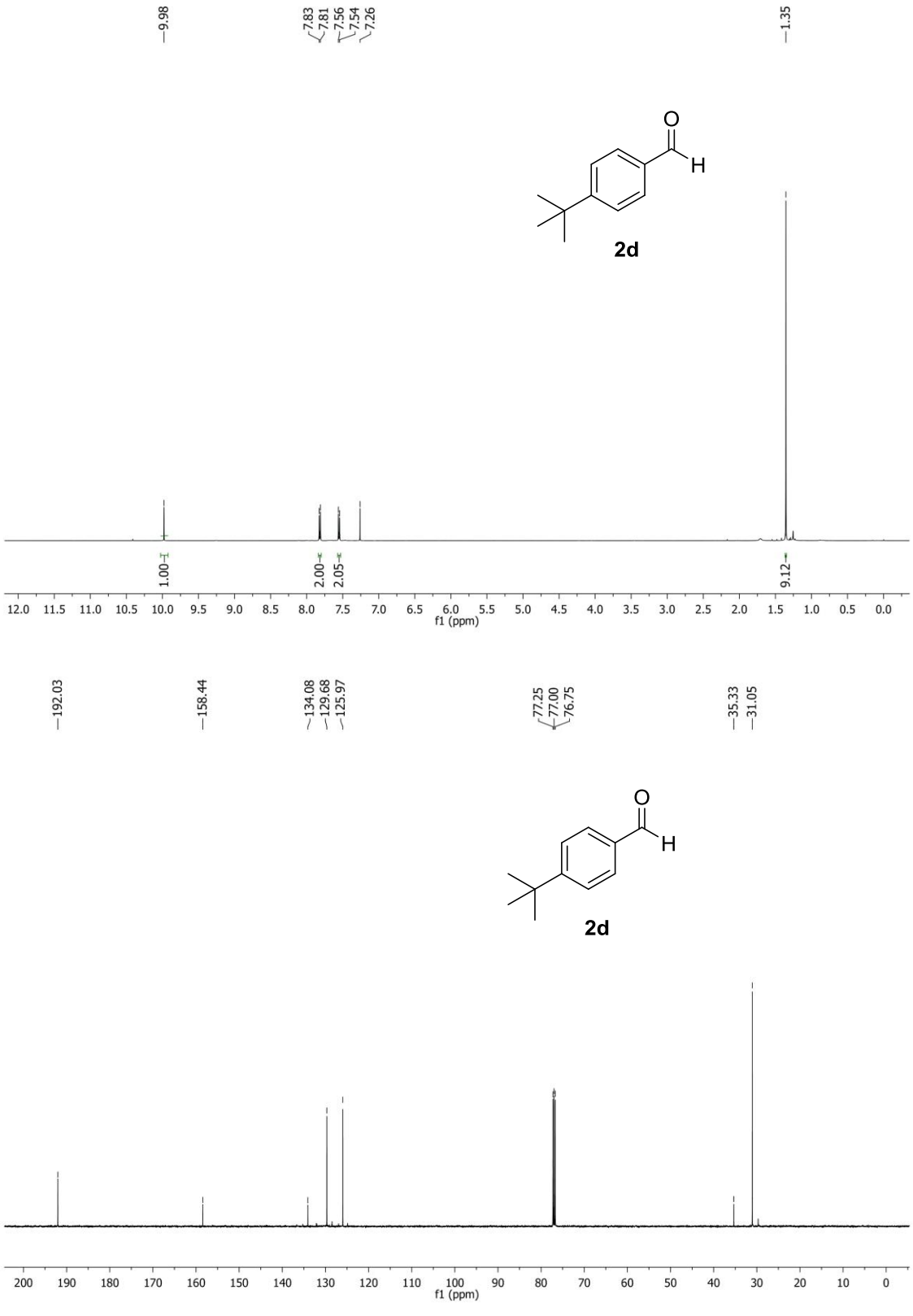


Figure SI.33 ^{1}H and ^{13}C NMR of product **2d** in **$CDCl_3$**.

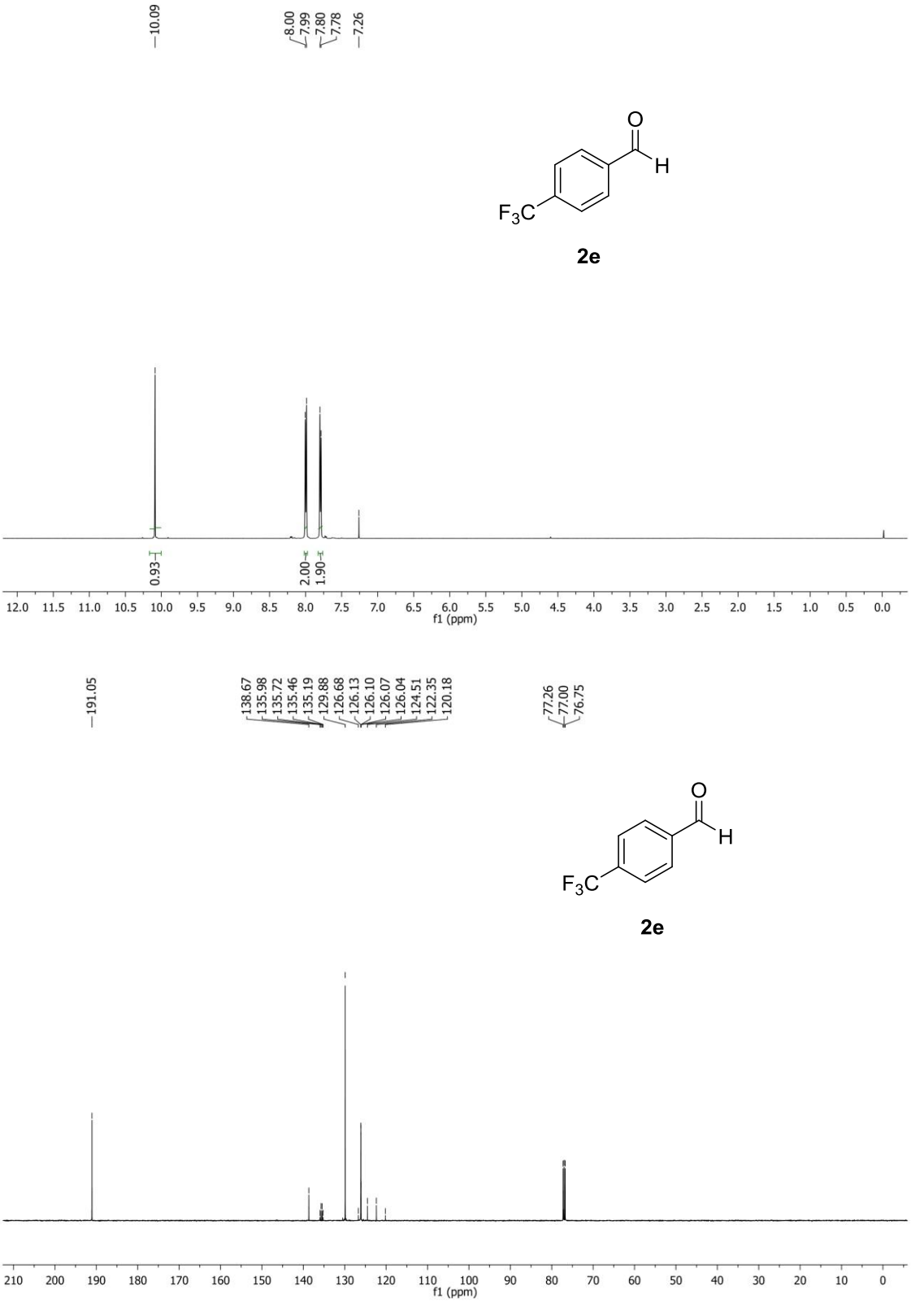


Figure SI.34 ^{1}H and ^{13}C NMR of product **2e** in **$CDCl_3$**.

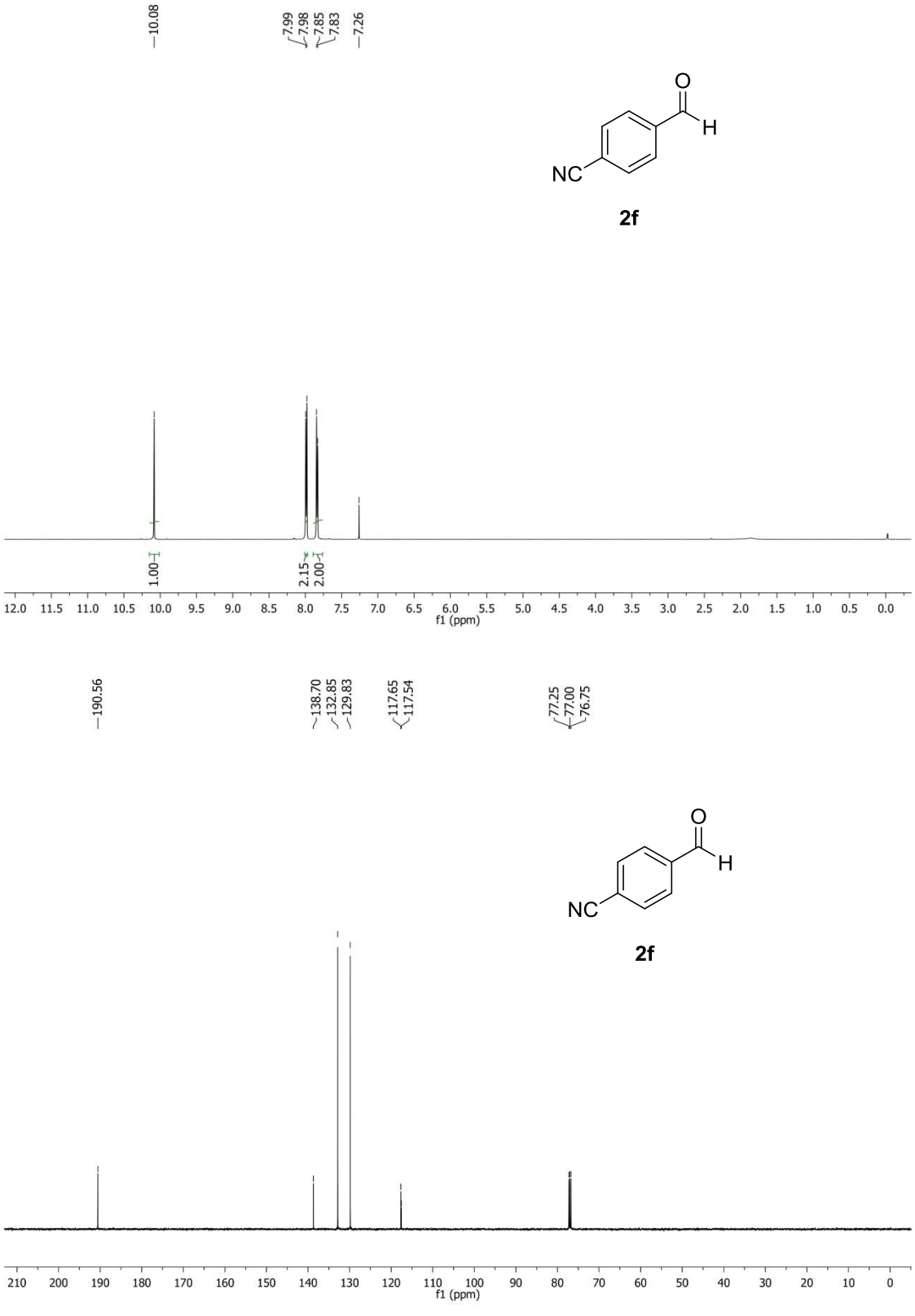


Figure SI.35 ^{1}H and ^{13}C NMR of product **2f** in **$CDCl_3$**.

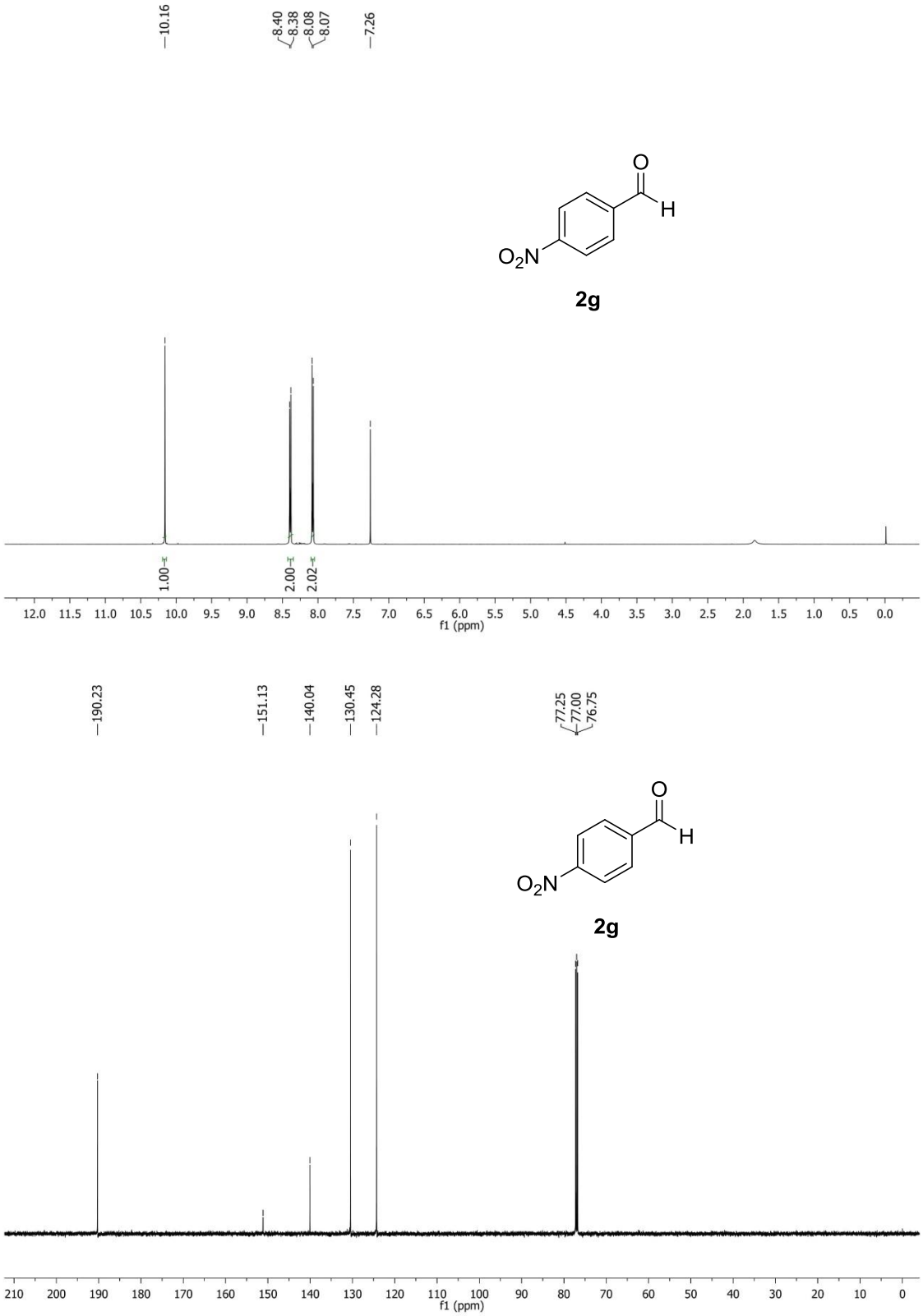


Figure SI.36 ^{1}H and ^{13}C NMR of product **2g** in **$CDCl_3$**.

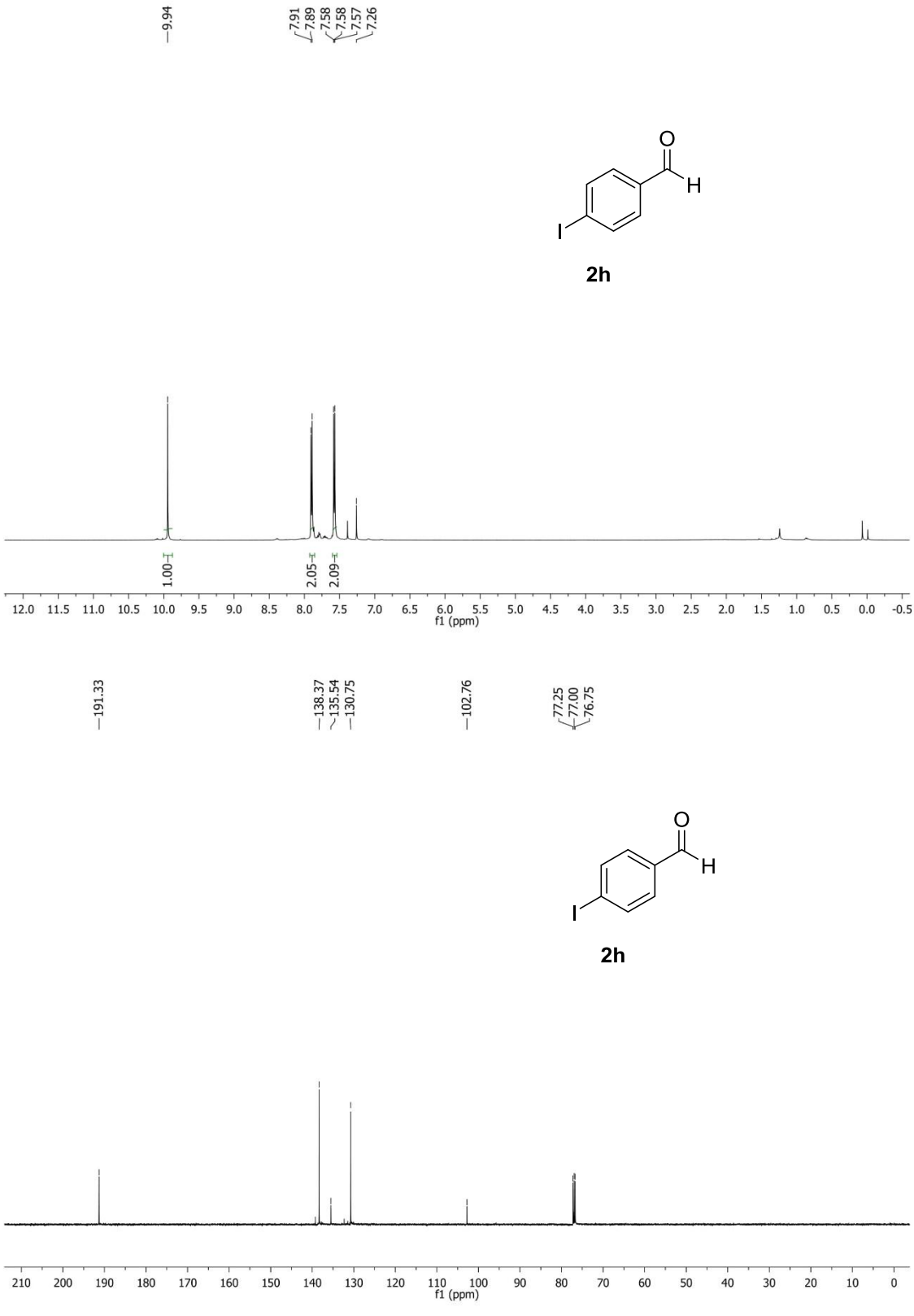


Figure SI.37 ^{1}H and ^{13}C NMR of product **2h** in **$CDCl_3$**.

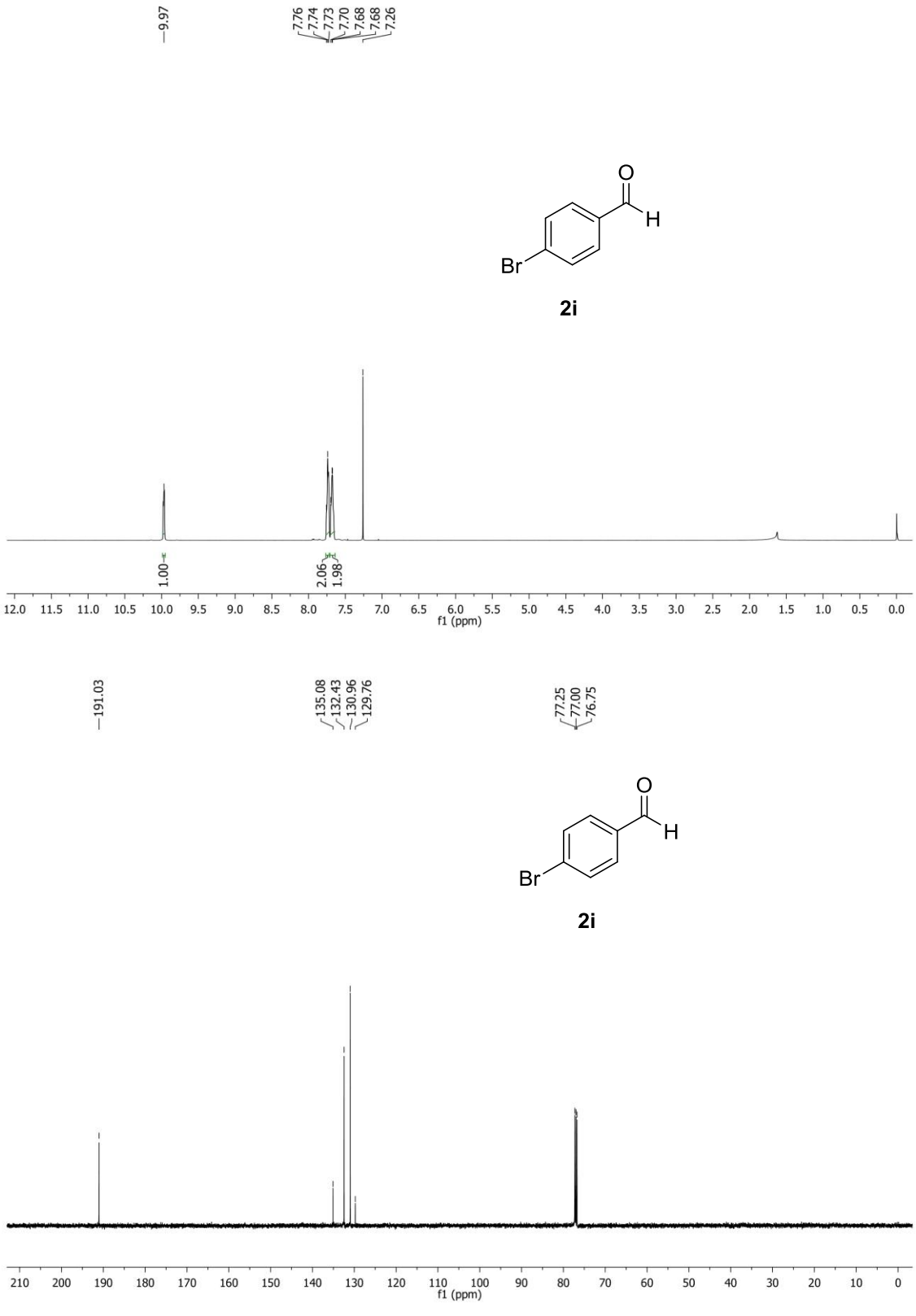


Figure SI.38 ^{1}H and ^{13}C NMR of product **2i** in **$CDCl_3$**.

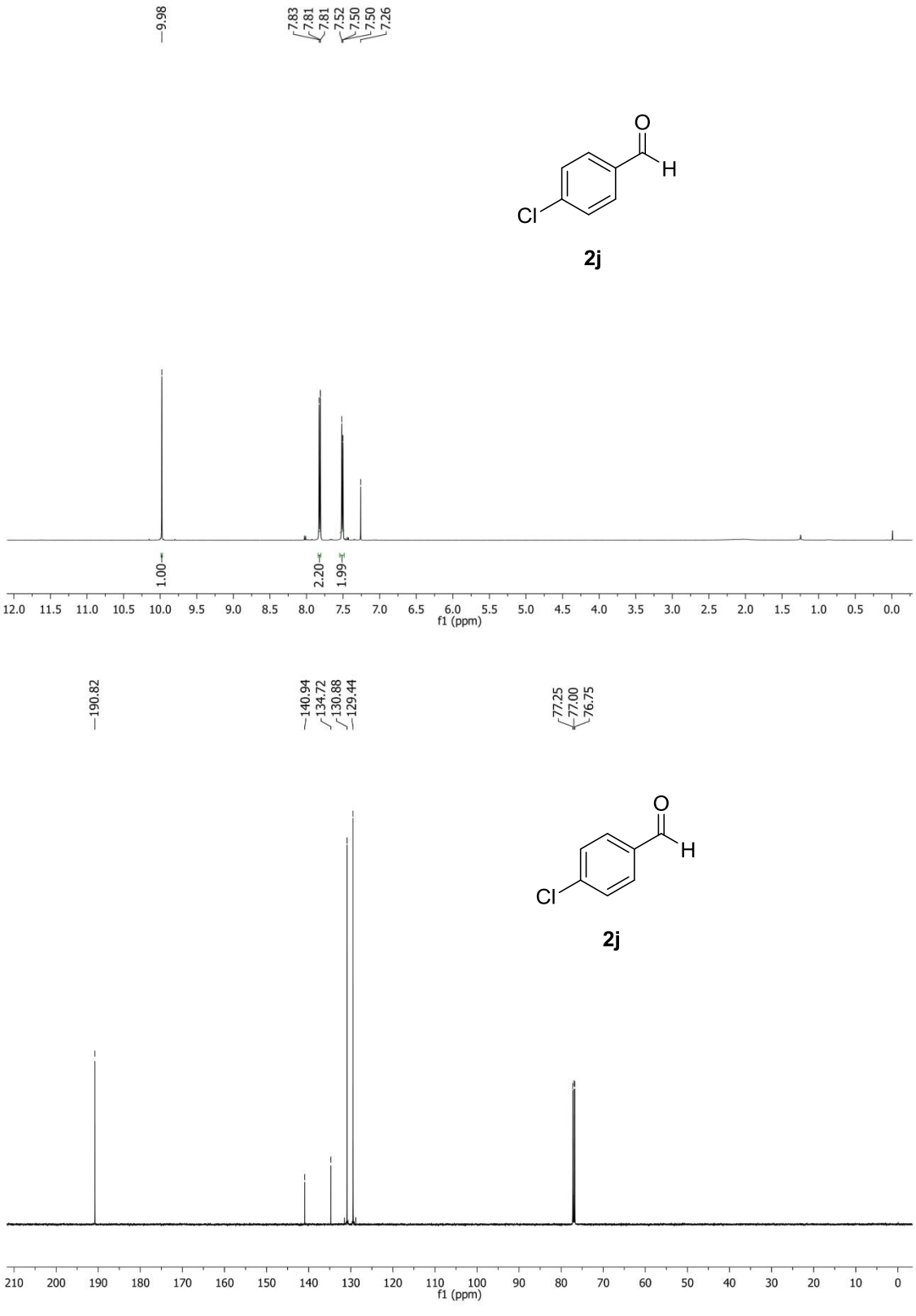


Figure SI.39 ^{1}H and ^{13}C NMR of product **2j** in **$CDCl_3$**.

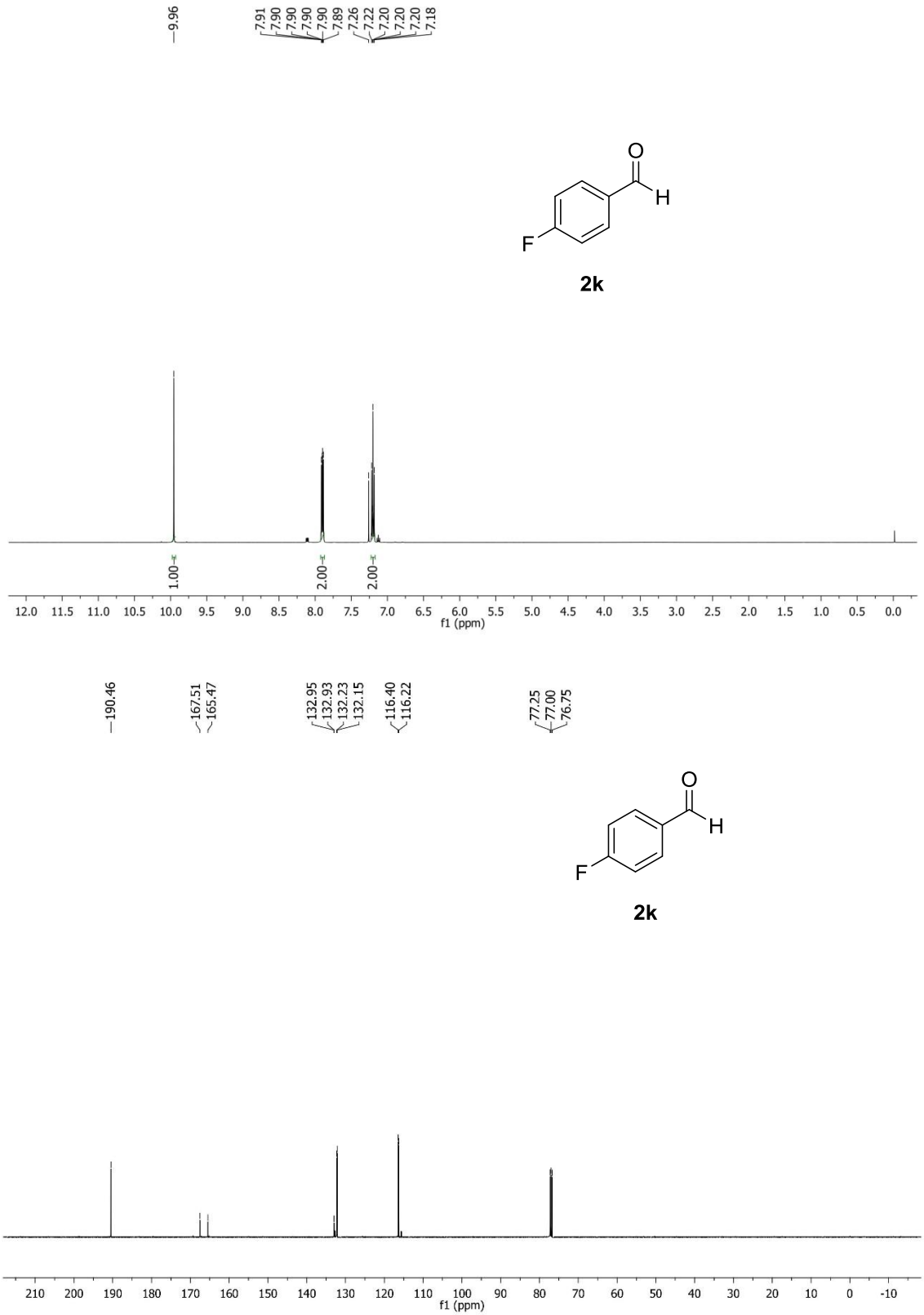


Figure SI.40 ^{1}H and ^{13}C NMR of product **2k** in **$CDCl_3$**.

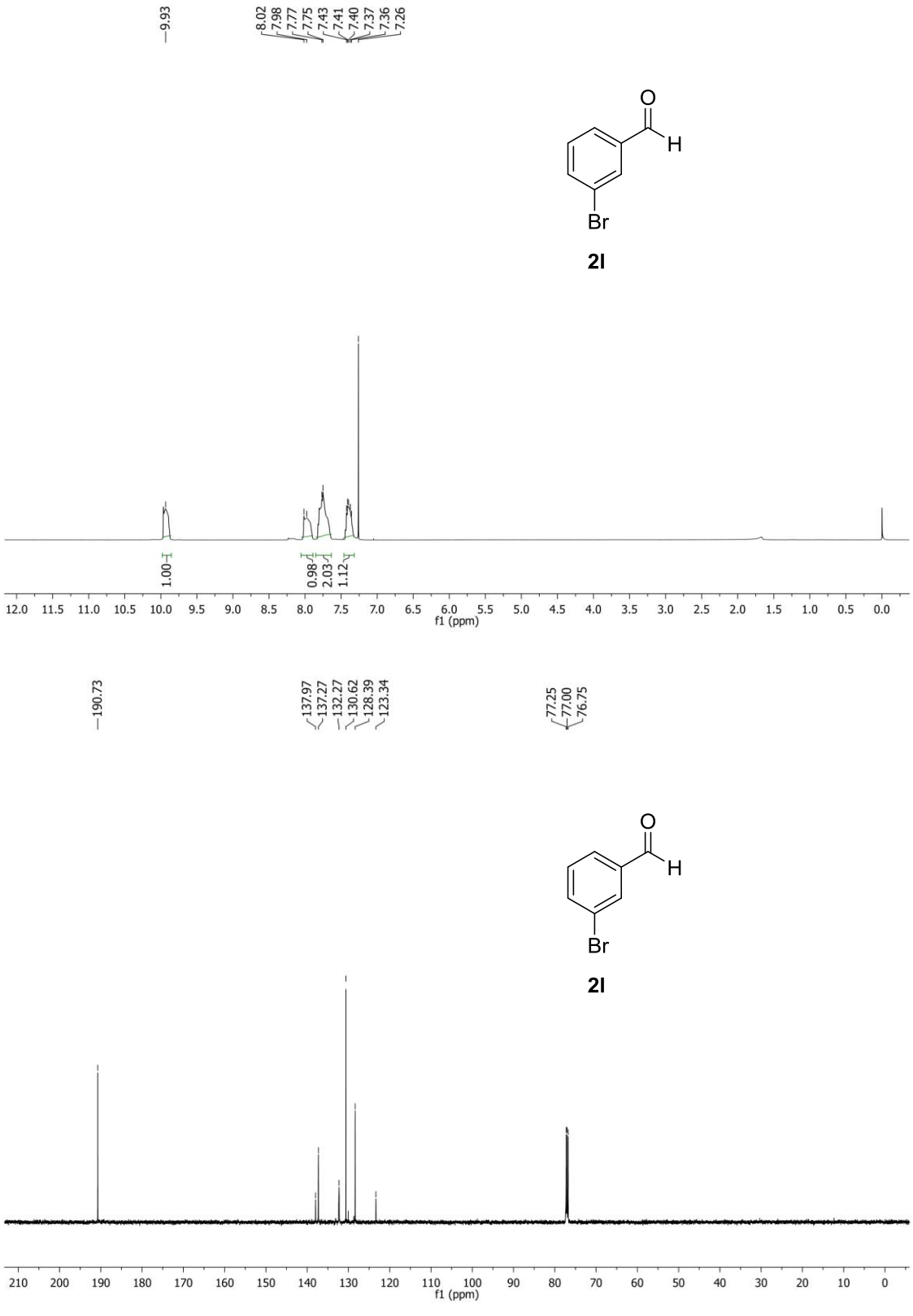


Figure SI.41 ^{1}H and ^{13}C NMR of product **2l** in **$CDCl_3$**.

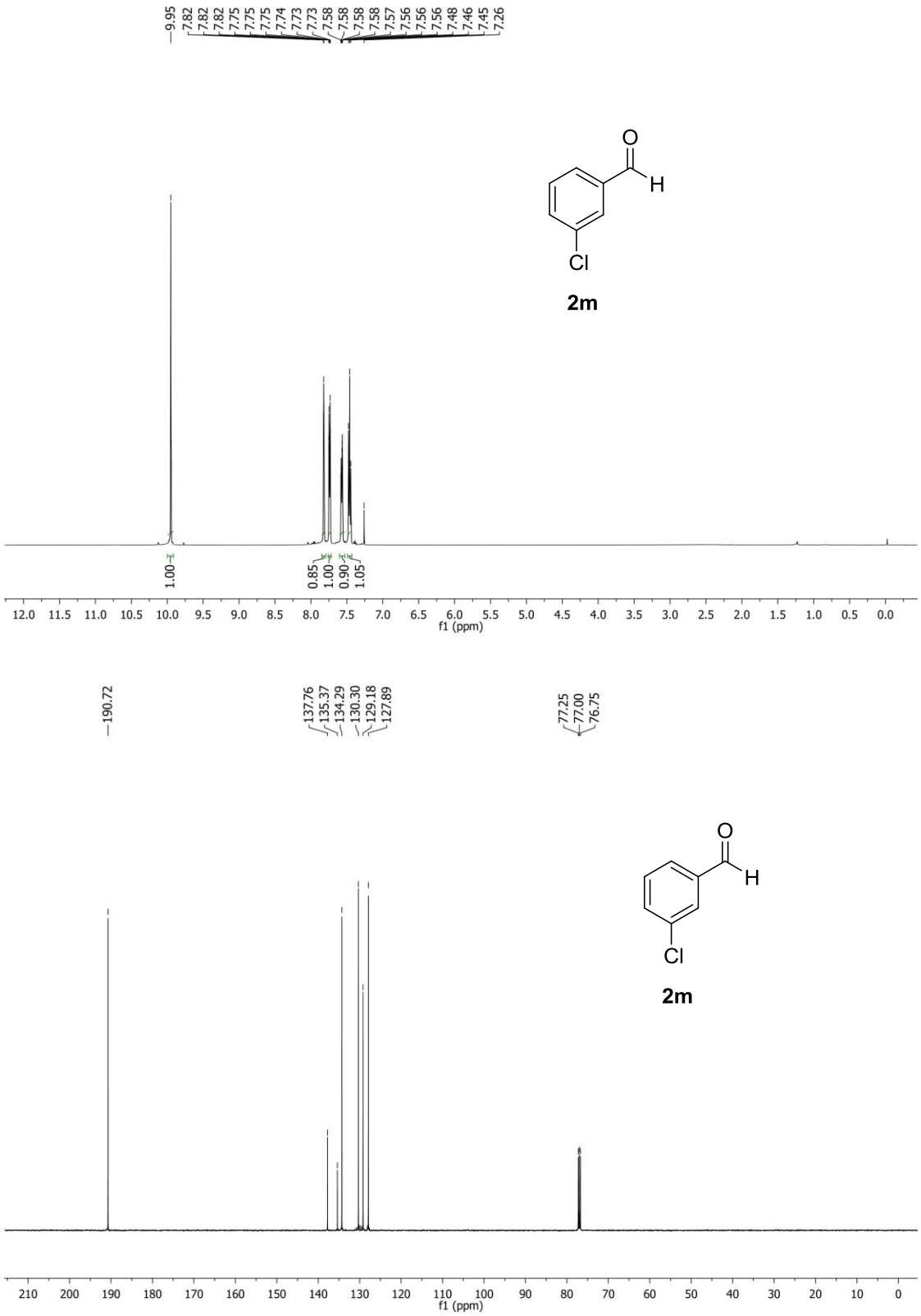


Figure SI.42 ^{1}H and ^{13}C NMR of product **2m** in **$CDCl_3$**.

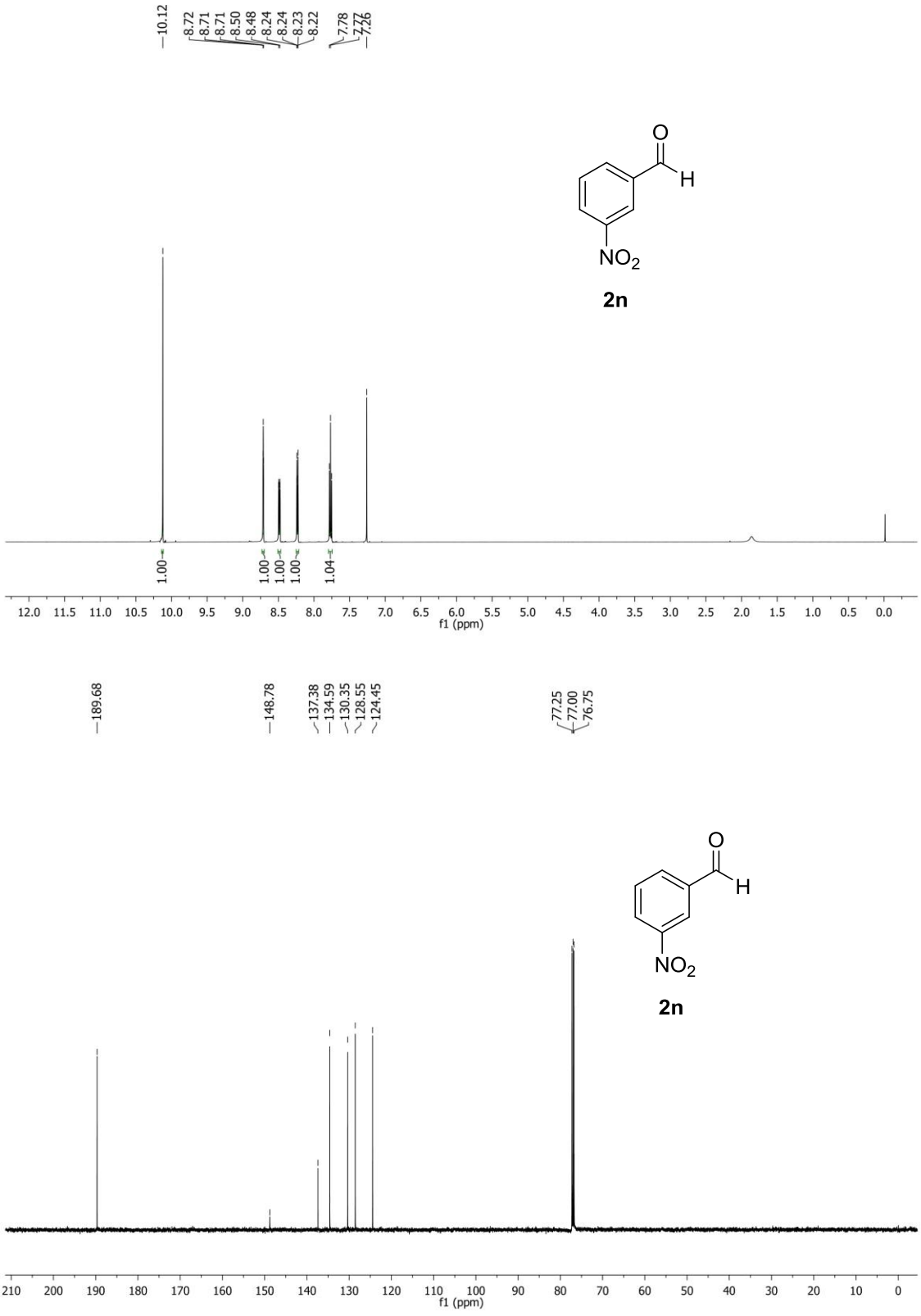


Figure SI.43 ^{1}H and ^{13}C NMR of product **2n** in **$CDCl_3$**.

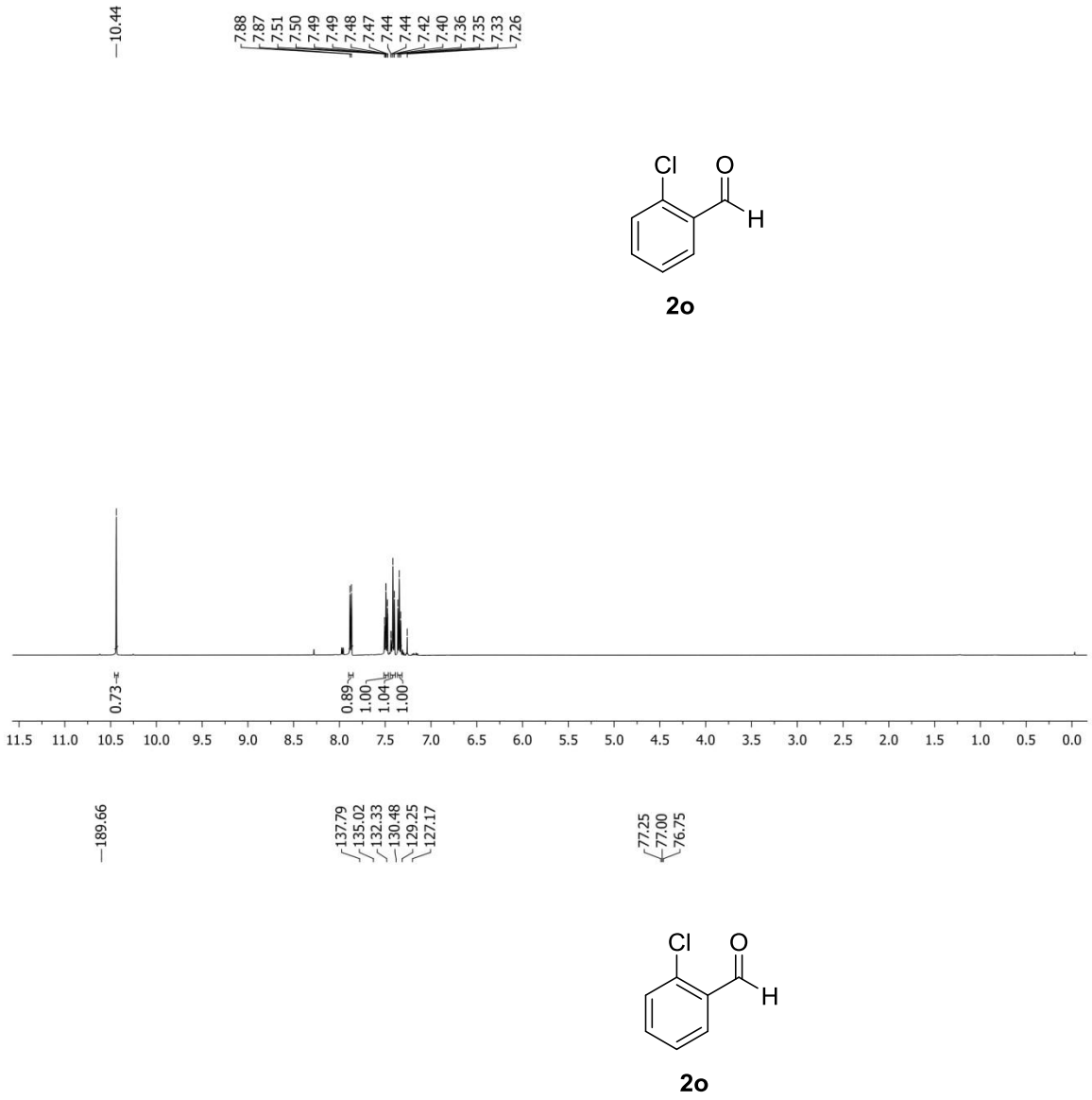


Figure SI.44 ^{1}H and ^{13}C NMR of product **2o** in **$CDCl_3$**.

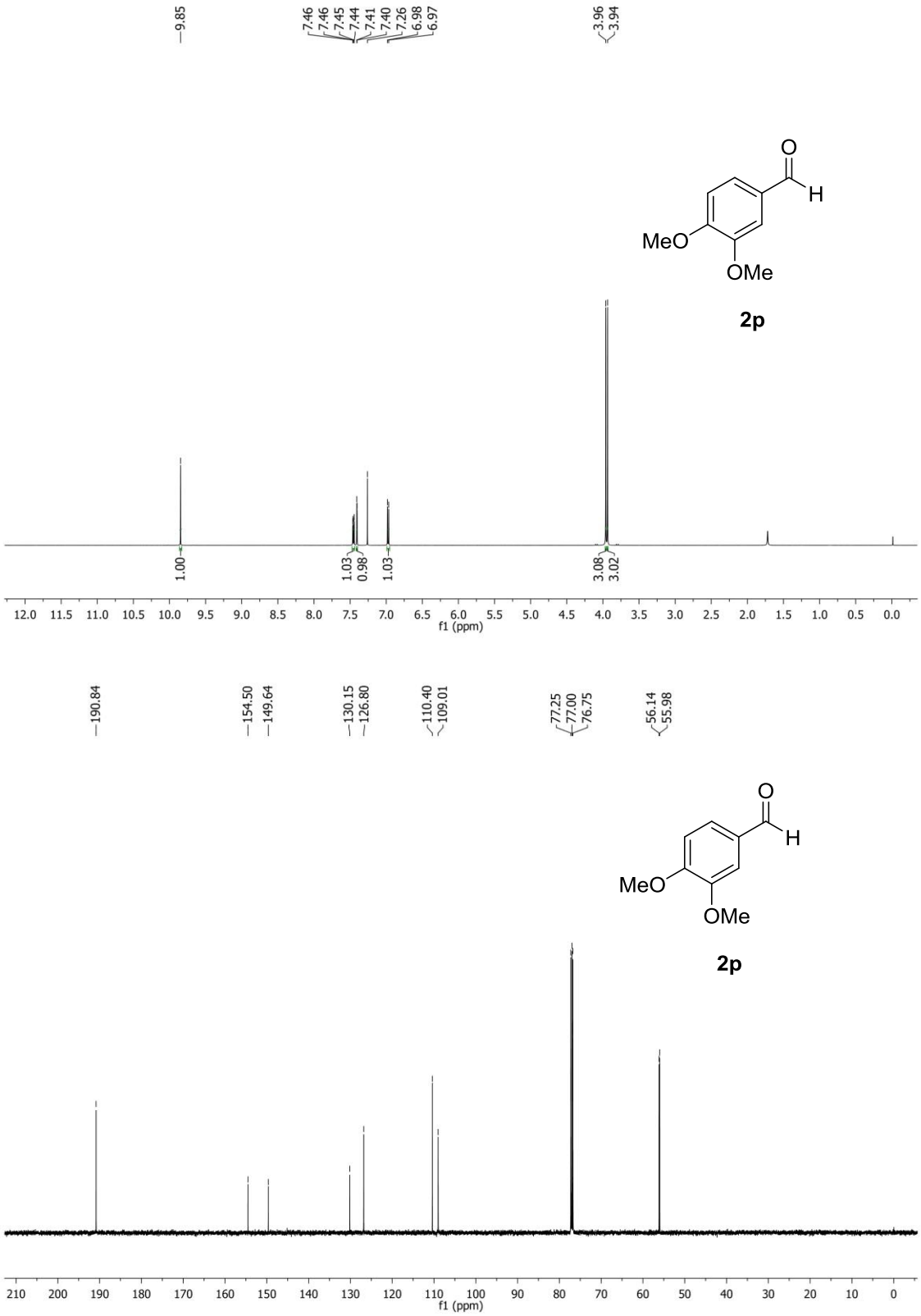


Figure SI.45 ^{1}H and ^{13}C NMR of product **2p** in **$CDCl_3$**.

Figure SI.46 ^{1}H and ^{13}C NMR of product **2q** in **$CDCl_3$**.

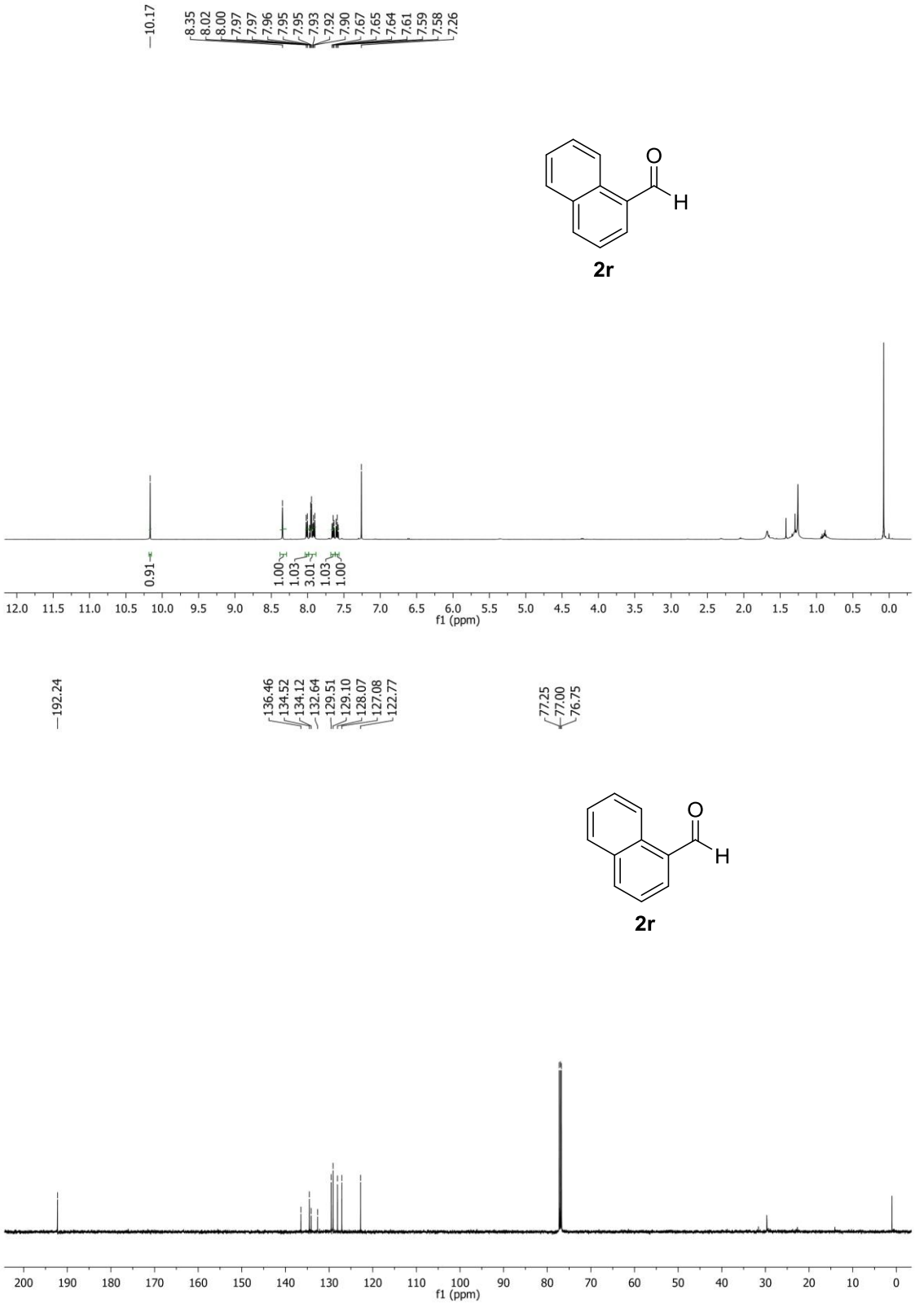
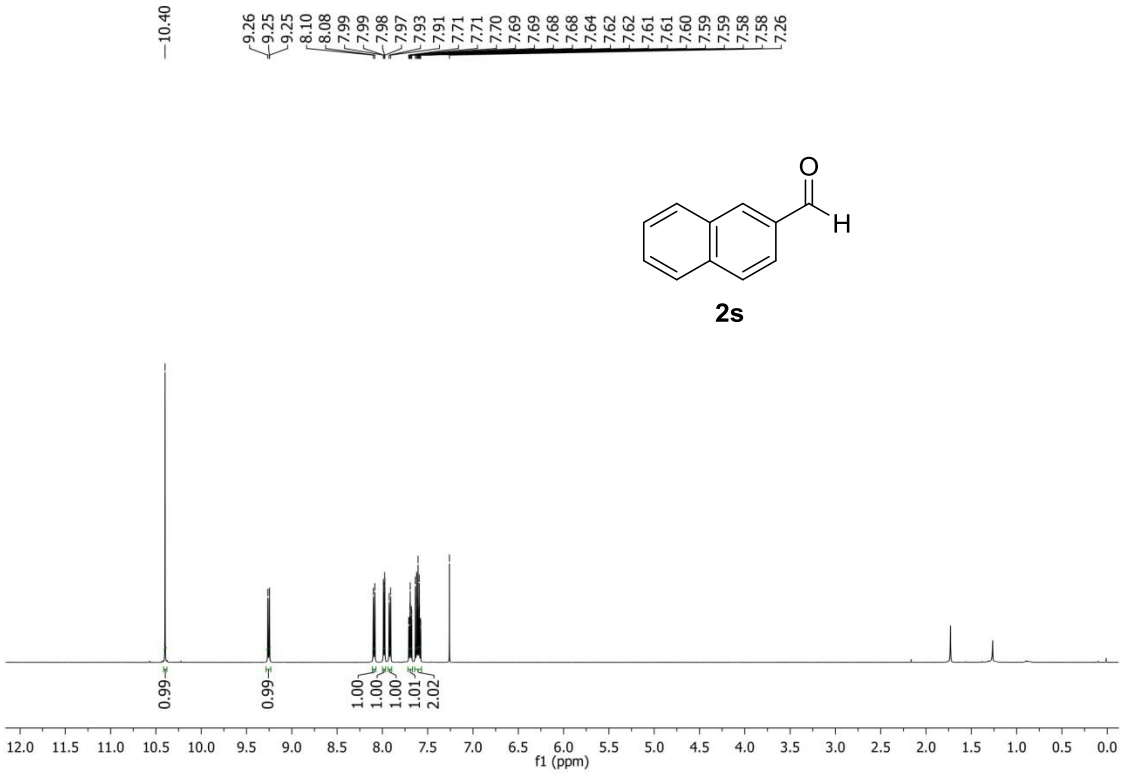


Figure SI.47 ^{1}H and ^{13}C NMR of product **2r** in **$CDCl_3$**.



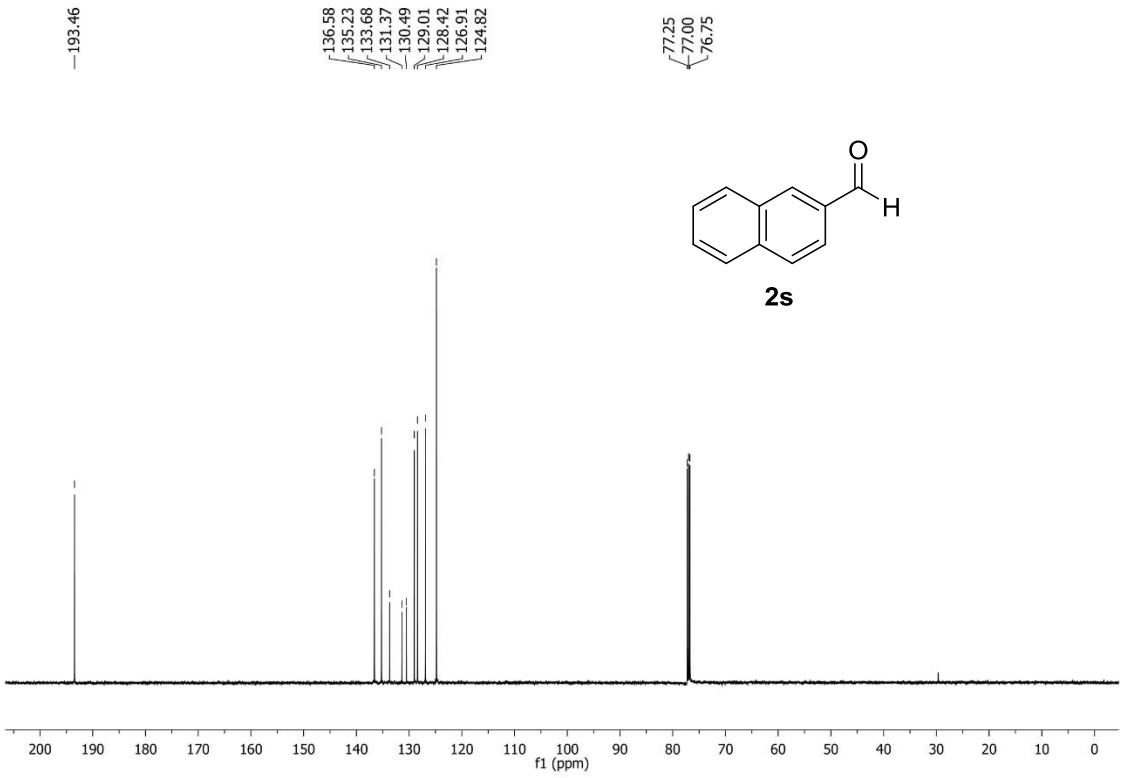


Figure SI.48 ^{1}H and ^{13}C NMR of product **2s** in **$CDCl_3$**.

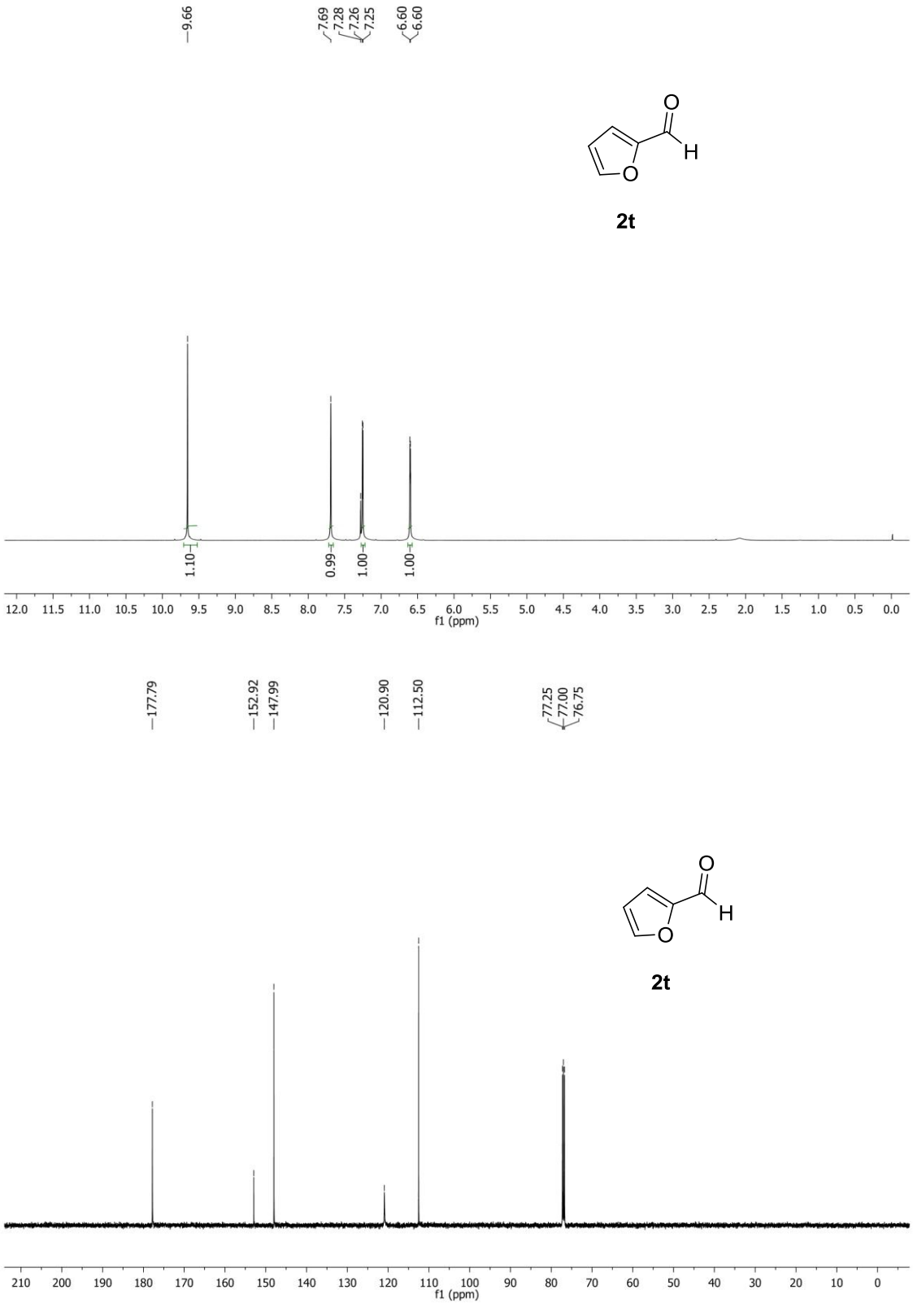


Figure SI.49 ^{1}H and ^{13}C NMR of product **2t** in **$CDCl_3$**.

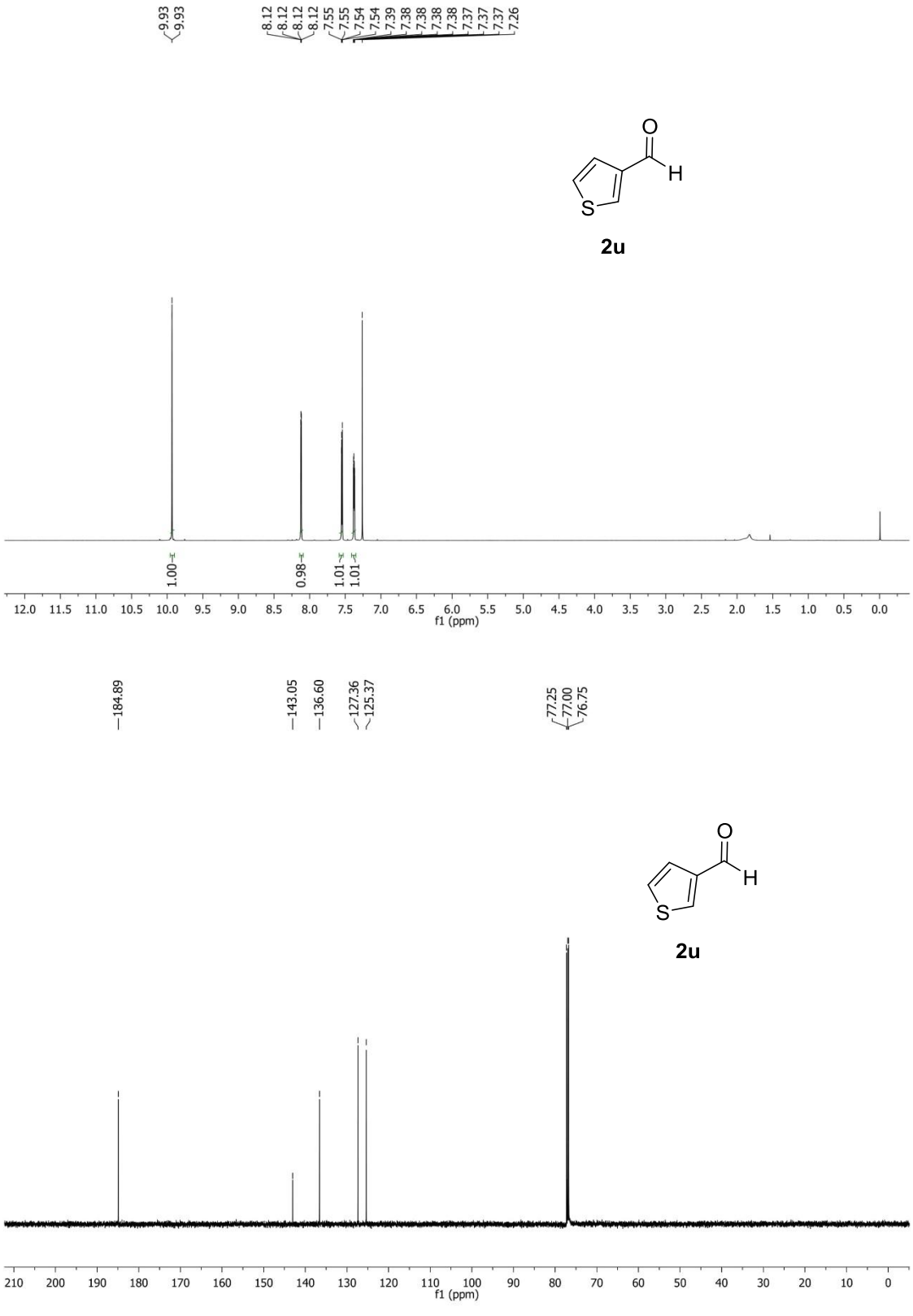


Figure SI.50 ^{1}H and ^{13}C NMR of product **2u** in **$CDCl_3$**.

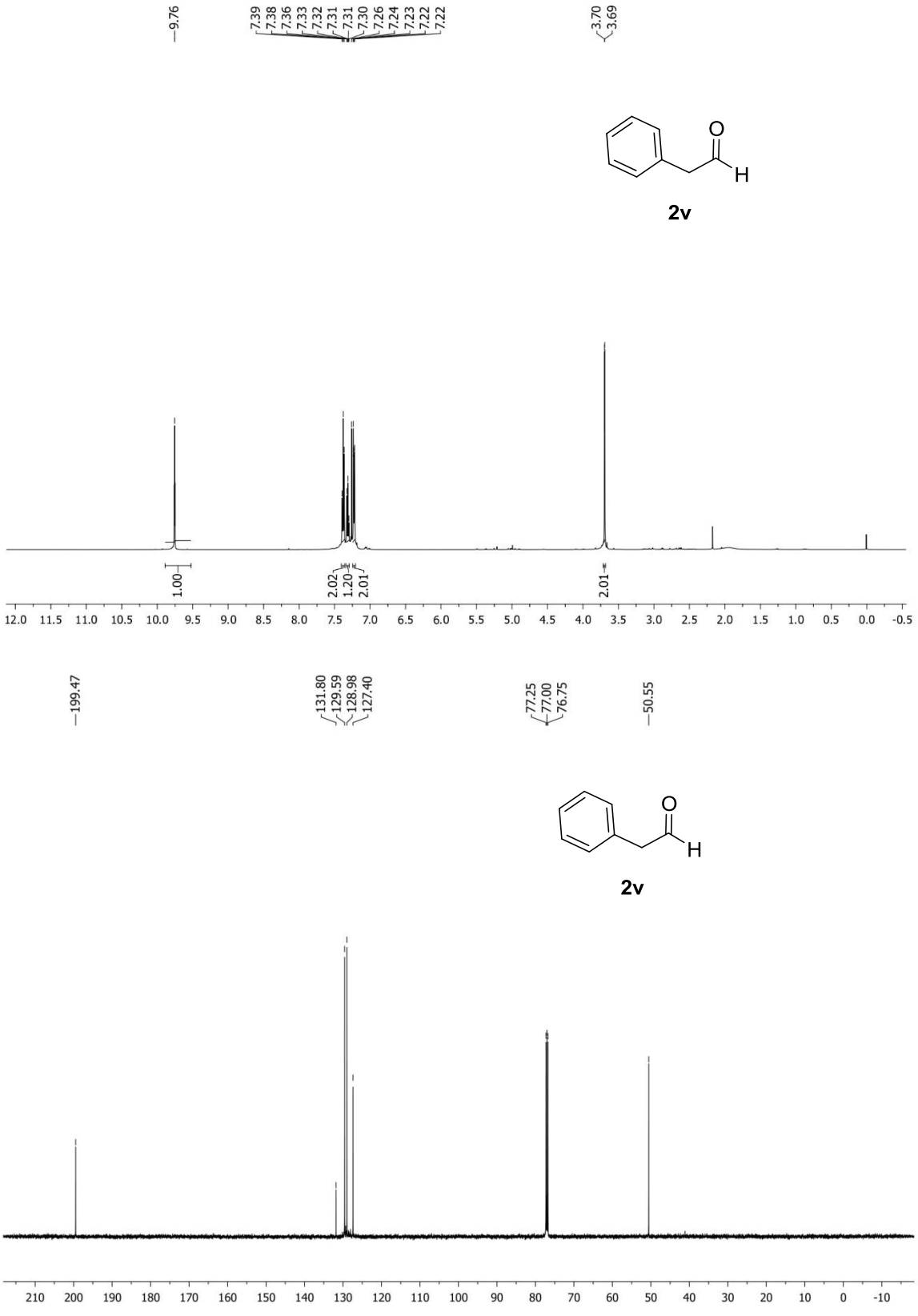


Figure SI.51 ^{1}H and ^{13}C NMR of product **2v** in **$CDCl_3$**.

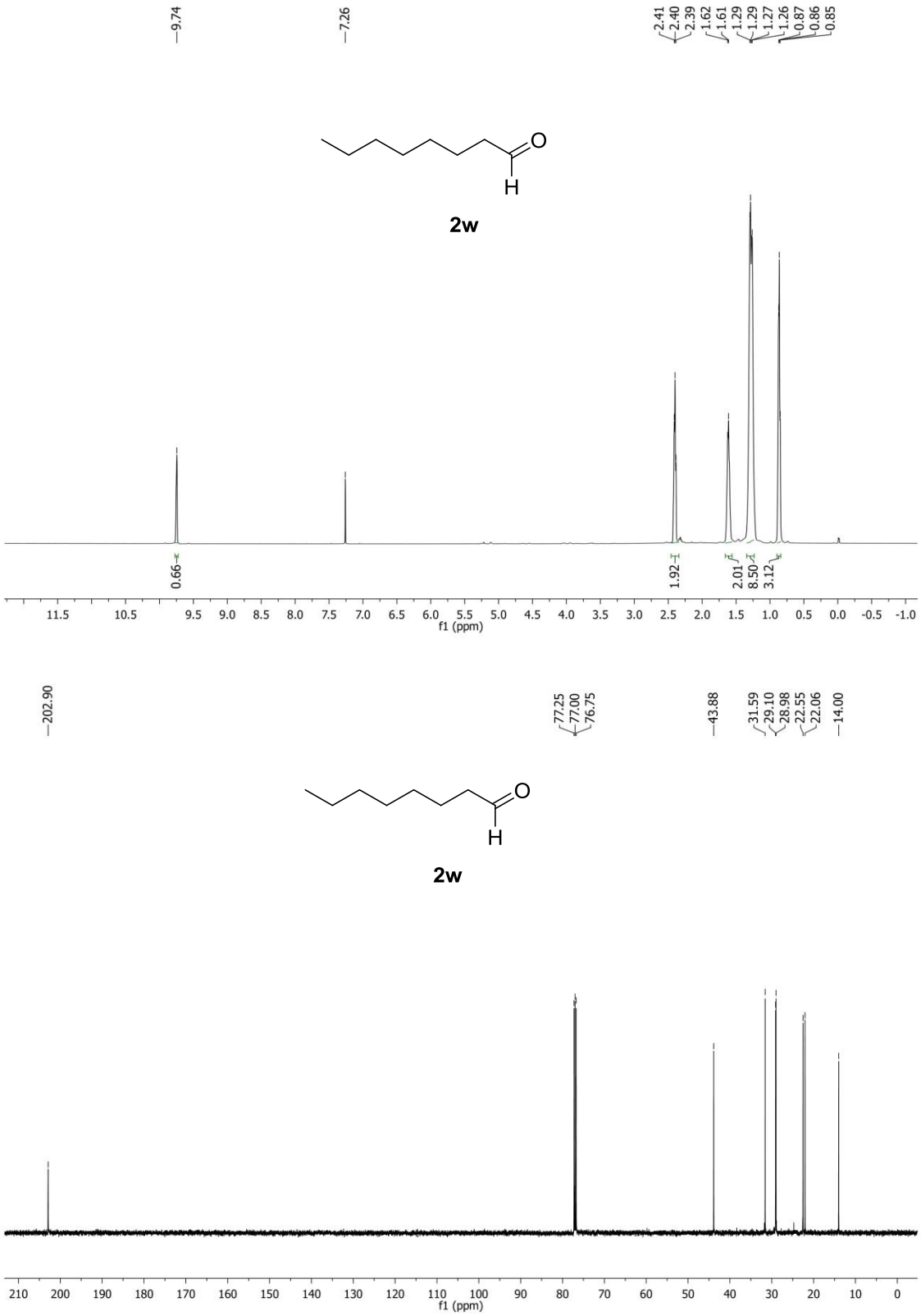


Figure SI.52 ^{1}H and ^{13}C NMR of product **2w** in **$CDCl_3$**.

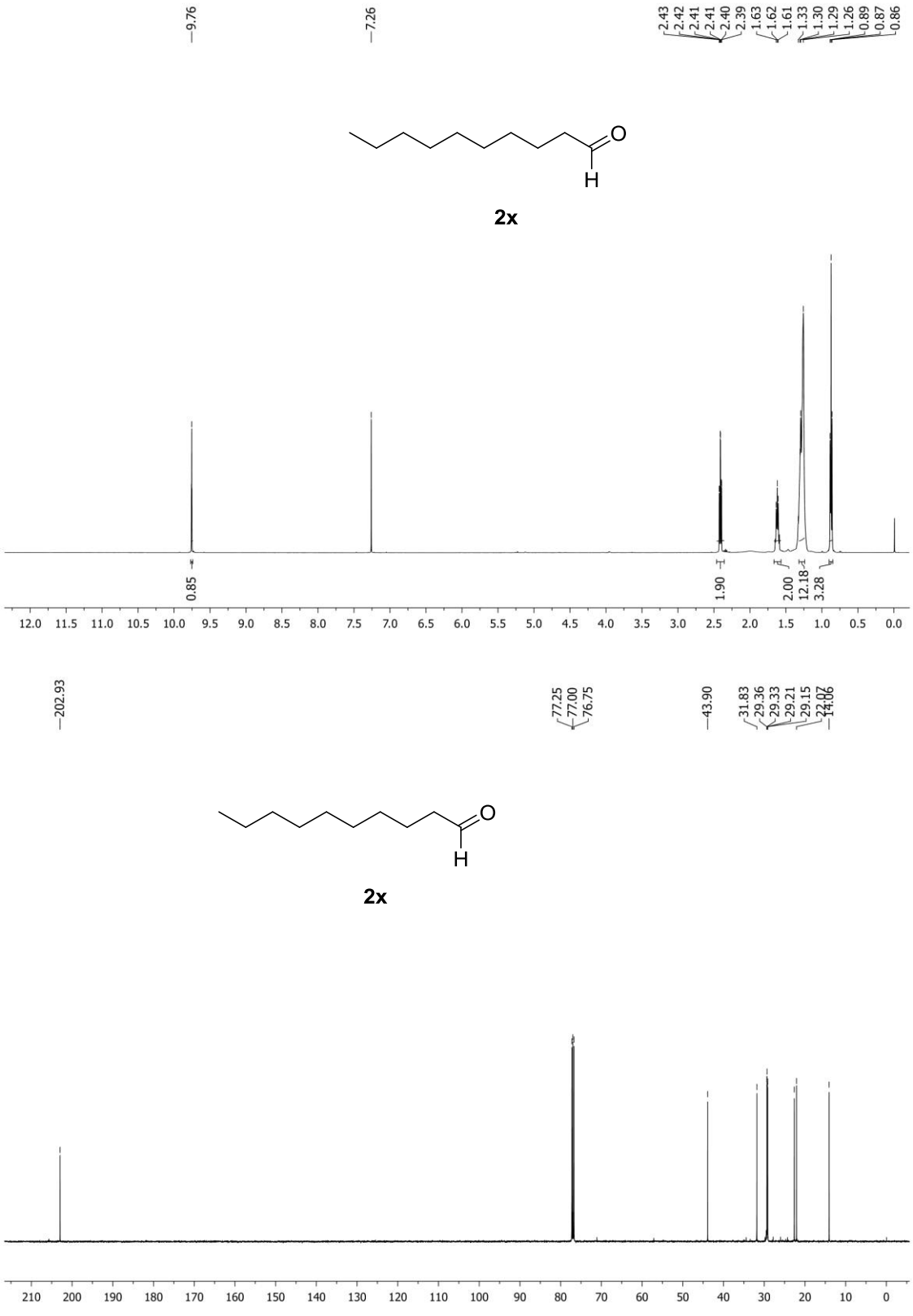


Figure SI.53 ^{1}H and ^{13}C NMR of product **2x** in **$CDCl_3$**.

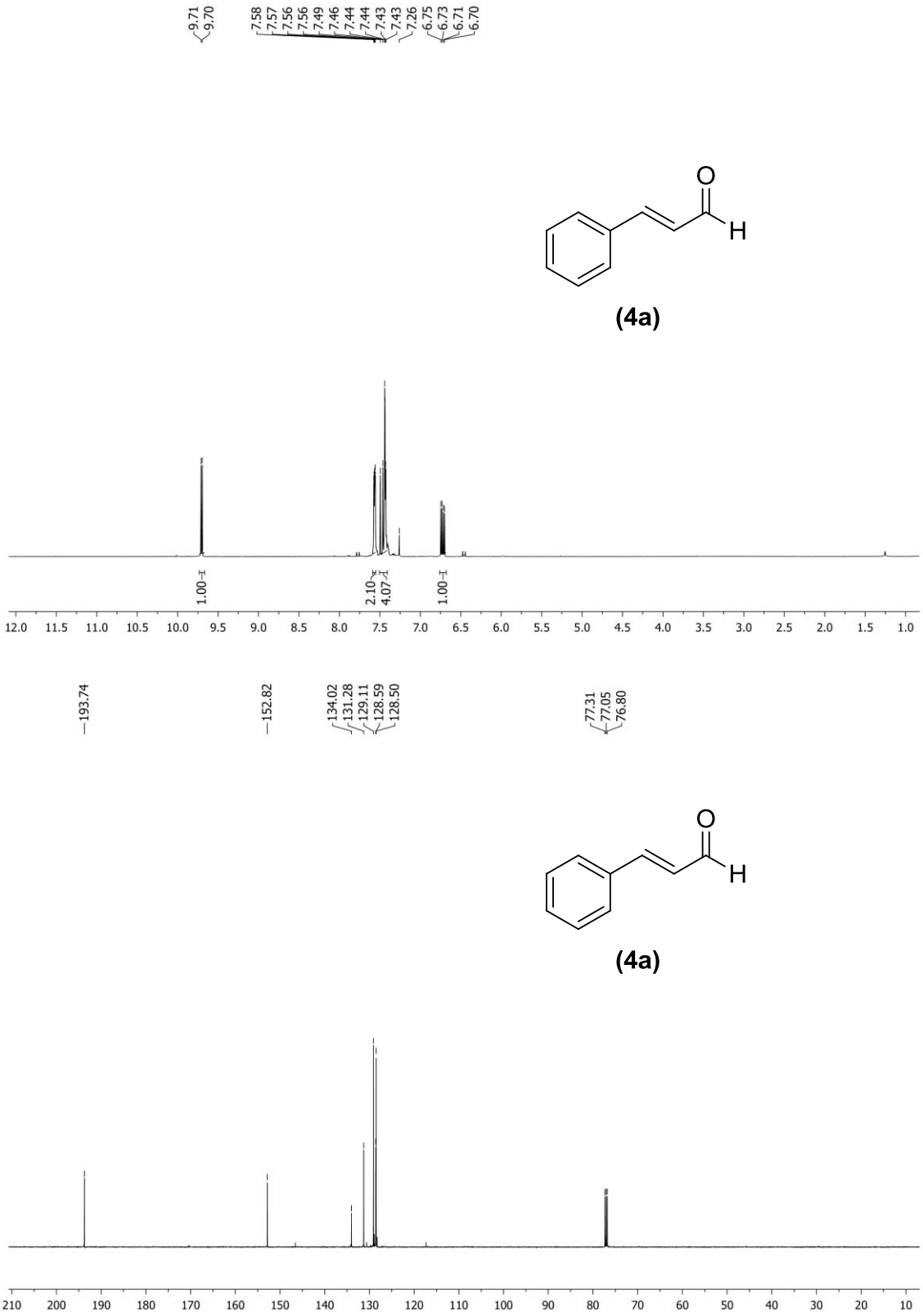


Figure SI.54 ^{1}H and ^{13}C NMR of product **4a** in **$CDCl_3$**.

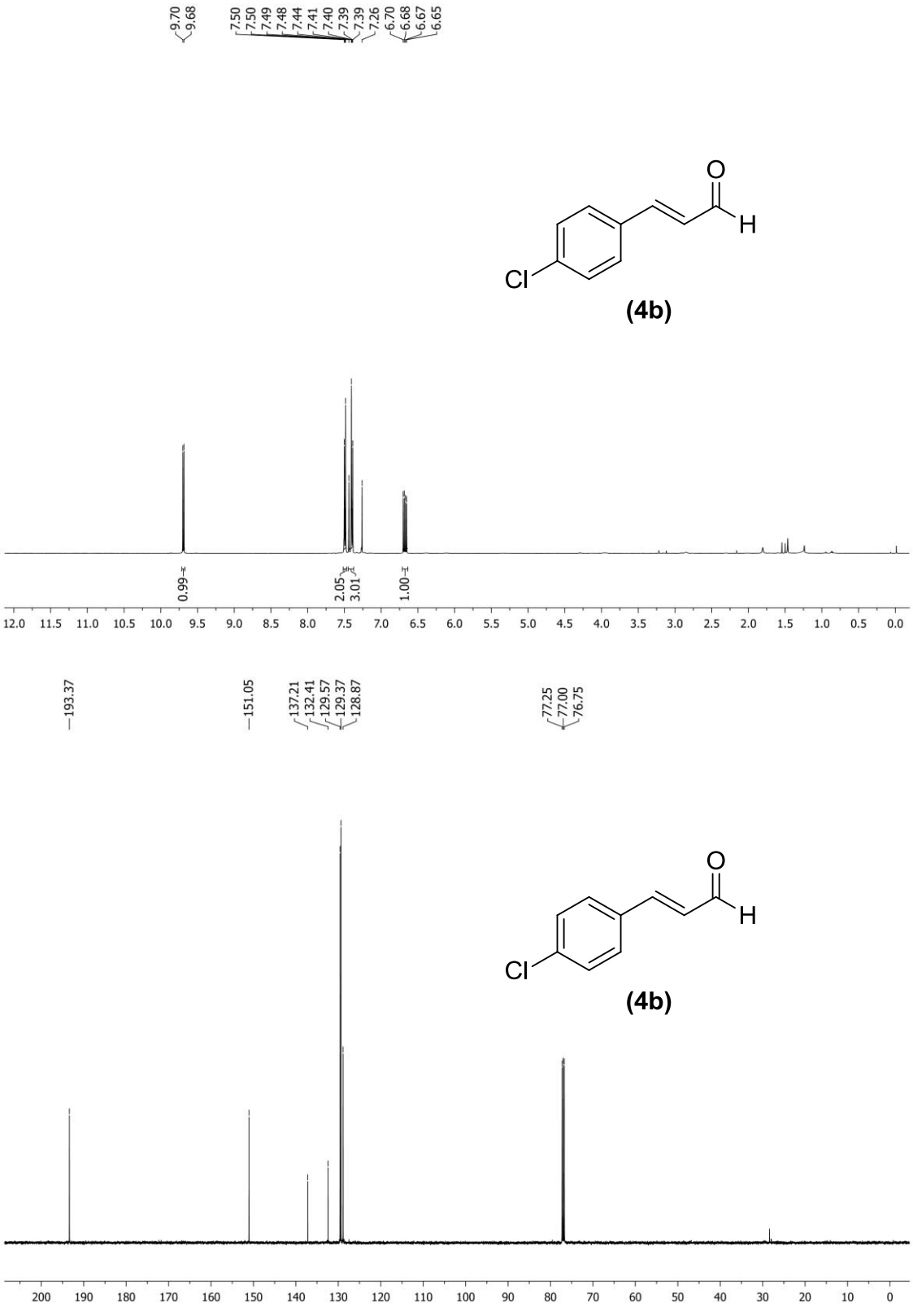


Figure SI.55 ^{1}H and ^{13}C NMR of product **4b** in **$CDCl_3$**.

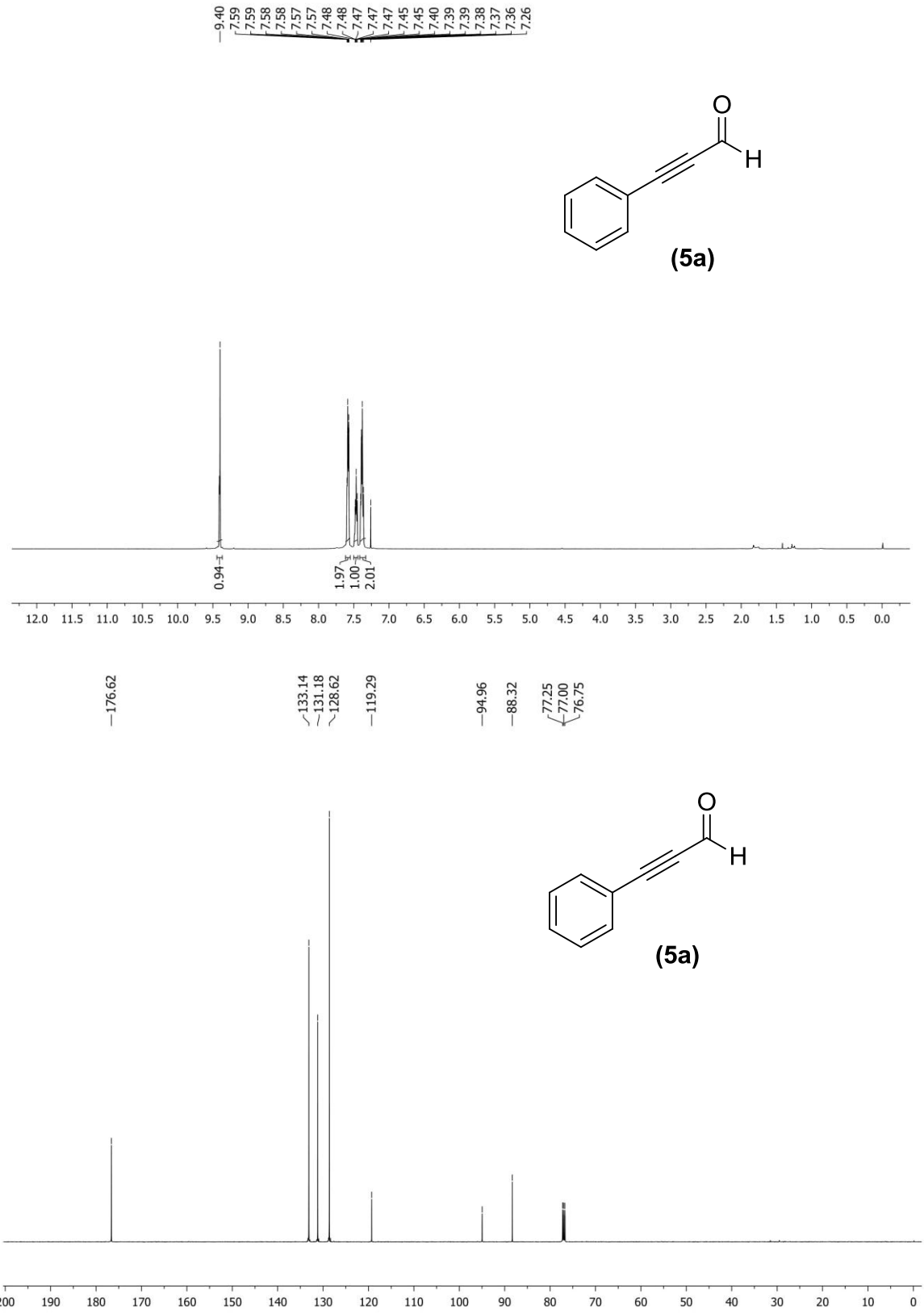


Figure SI.56 ^{1}H and ^{13}C NMR of product **5a** in **$CDCl_3$**.