Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Aniline mediated oxidative C-C bond cleavage of α-alkoxy aldehydes in air and a model reaction for the synthesis of α-(D)-amino acid derivatives

Supporting information

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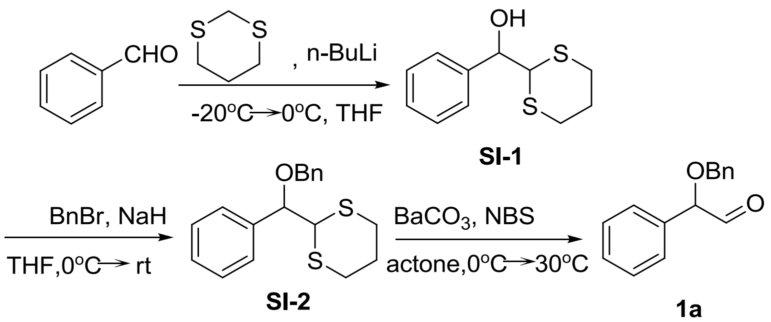
1. General Information

All reagents and materials were purchased from commercial sources unless otherwise noted. All anhydrous solvents were prepared with standard procedures. Reactions were monitored by thin-layer chromatography (TLC) using commercial silica gel 60 F254 aluminum plates. Flash chromatography was performed using silica gel of particle size 0.040-0.063 mm. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on Bruker AV400 spectrometers. Chemical shifts were reported in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ = 7.26, singlet). ^{1}H NMR splitting patterns are labeled as abbreviations s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), m (multiplets) and br (broad). The determination of *ee* was performed via chiral phase HPLC analysis using HPLC Chiralcel OD-H column. Optical rotations were measured using a 0.5 mL cell with a 10 mm path length on Optical Activity automatic polarimeter. The HR-ESI-MS data were measured on a Bruker Apex IV FTICR spectrometer.

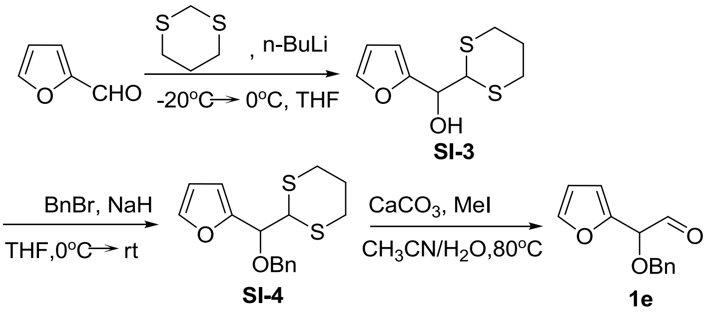
2. Preparation of α-alkoxy aldehydes

Procedure A for the synthesis of α-benzyloxy aldehydes (1a, 1c, 1d, 1f, 1h, 1i, 1j)[1]



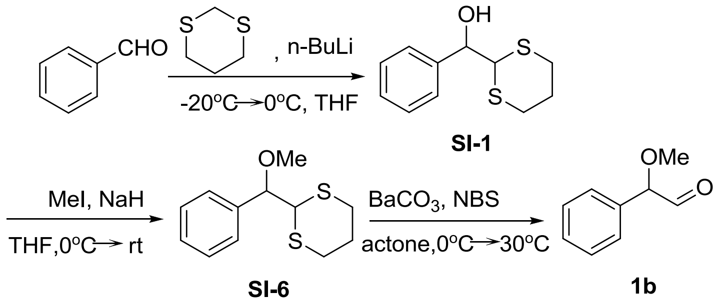
To a solution of 1,3-dithiane (3.17 g, 26 mmol) in 25 mL anhydrous THF at -20 ℃ was added slowly 11.9 mL n-butyllithium (2.2 M in hexane, 26 mmol) and stirred for 1 h. Arylaldehyde (2.24 mL, 22 mmol) dissolved in THF was added dropwise, and the reaction mixture was stirred at 0 ℃ for 24 h. After quenching by saturated aqueous NH_4Cl, the solvent was removed under vacuo. Then the product was extracted with CH_2Cl_2 and dried over $NaSO_4$. Purification by column chromatography on silica gel (petroleum ether: ethyl acetate = 5:1) afforded **SI-1** as light yellow oil, 3.74 g, 76%. **SI-1** (3.74 g, 16 mmol) in 25 mL anhydrous THF cooled to 0 ℃ was added NaH (60%, 1.25 g, 31 mmol) and BnBr (3.9 mL, 33mmol). The reaction was then warmed to room temperature, stirring for 2 h. Methanol was added and the mixture was concentrated followed by column chromatography on silica gel (petroleum ether: ethyl acetate = 10:1) to afford **SI-2** as yellow oil, 4.76 g, 91%. To a solution of **SI-2** (540 mg, 1.7 mmol) in acetone (34 mL) was added $BaCO_3$ (4.23 g, 21 mmol) at 0 ℃. A solution of N-bromo-succinimide (590 mg, 3.3 mmol) in acetone (70 mL) was added and the mixture was stirred at 30 ℃ for 2 h. After decomposition of excessive N-bromosuccinimide by addition of saturated aqueous $NaHCO_3$, the solution was filtered and concentrated, extracted with ethyl acetate by three times. The organic layer was combined and then dried over anhydrous sodium sulfate. After evaporation in vacuo, the residue was purified by chromatography on silica gel (dichloromethane: hexane = 1:1), to give **1a** as colorless oil, 319 mg, 83% yield.

Procedure B for the synthesis of 2-(benzyloxy)-2-(furanyl)acetaldehyde (1e)[1-2]



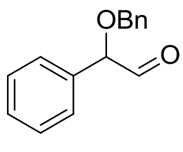
SI-4 was obtained as in procedure A. To a solution of **SI-4** (238 mg, 0.78 mmol) in MeCN (16 mL) and H_2O (4 mL) was added $CaCO_3$ (386 mg, 3.9 mmol) and MeI (2.5 mL, 40.0 mmol). The reaction mixture was stirred at 80 ℃ for 8 h, then concentrated under reduced pressure, and extracted with CH_2Cl_2 for three times. The combined organic extracts were washed with brine, dried over MgSO4 and concentrated. The residue was purified by column chromatography (dichloromethane: hexane = 8:1) to give aldehyde **1e** as yellow oil, 56 mg, 33%.

Procedure C for the synthesis of α-methyloxy aldehydes (1b, 1g)



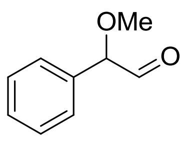
SI-1 was obtained as in procedure A. **SI-1** (217 mg, 0.96 mmol) in 10 mL anhydrous THF cooled to 0 ℃ was added NaH (60%, 73 mg, 1.8 mmol) and MeI (298 μL, 4.8 mmol). The reaction was then warmed to room temperature, stirring for 1 h. Methanol was added and the mixture was concentrated followed by column chromatography on silica gel (petroleum ether: ethyl acetate = 4:1) to afford **SI-6** as yellow oil, 166 mg, 72%. **1b** was obtained from **SI-6** as procedure A.

3. Characterization of Substrates



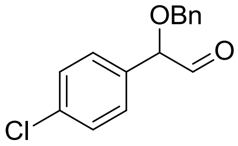
2-(benzyloxy)-2-phenylacetaldehyde (1a):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.63 (s, 1H), 7.36 (m, 10H), 4.80 (s, 1H), 4.68 (d, J = 11.8 Hz, 1H), 4.55 (d, J = 11.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 197.5, 136.2, 133.2, 128.2, 128.1, 127.7, 127.3, 127.2, 126.8, 84.7, 70.3. These data correspond to previously reported literature[1a].



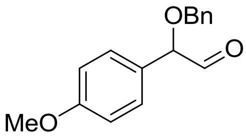
2-methoxy-2-phenylacetaldehyde (1b):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (d, *J* = 1.5 Hz, 1H), 7.38 (m, 5H), 4.64 (s, 1H), 3.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.3, 133.8, 129.0, 129.0, 127.5, 88.2, 57.3. These data correspond to previously reported literature[1a].



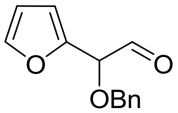
2-(benzyloxy)-2-(4-chlorophenyl)acetaldehyde (1c):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (d, *J* = 1.7 Hz, 1H), 7.36 (m, 9H), 4.76 (d, *J* = 1.6 Hz, 1H), 4.67 (d, *J* = 11.8 Hz, 1H), 4.55 (d, *J* = 11.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.2, 136.7, 135.0, 132.6, 129.30, 128.8, 128.7, 128.3, 128.1, 84.7, 71.4. HRMS (ESI) m/z calcd for $C_{15}H_{13}ClNaO_2$ $[M + Na]^+$: 283.0496, found: 283.0503.



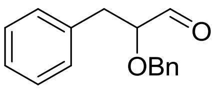
2-(benzyloxy)-2-(4-methoxyphenyl)acetaldehyde (1d):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (s, 1H), 7.32 (m, 7H), 6.95 (d, *J* = 7.9 Hz, 2H), 4.75 (s, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.52 (d, *J* = 11.6 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 198.3, 160.2, 137.1, 129.1, 128.6, 128.1, 128.0, 125.9, 114.6, 85.0, 70.8, 55.3. HRMS (ESI) m/z calcd for $C_{16}H_{16}NaO_3$ $[M + Na]^+$: 279.0992, found: 279.1000.



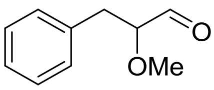
2-(benzyloxy)-2-(furanyl)acetaldehyde (1e):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.71 (d, *J* = 1.2 Hz, 1H), 7.49 (d, *J* = 1.0 Hz, 1H), 7.34 (m, 5H), 6.46 (d, *J* = 3.2 Hz, 1H), 6.42 (dd, *J* = 3.2, 1.9 Hz, 1H), 4.87 (s, 1H), 4.68 (d, *J* = 11.8 Hz, 1H), 4.53 (d, *J* = 11.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.4, 147.6, 144.2, 136.7, 128.6, 128.2, 111.4, 110.7, 78.6, 71.0. HRMS (ESI) m/z calcd for $C_{13}H_{12}NaO_3$ $[M + Na]^+$: 239.0679, found: 239.0679.



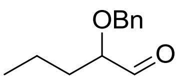
2-(benzyloxy)-3-phenylpropanal (1f):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (d, *J* = 1.9 Hz, 1H), 7.25 (m, 10H), 4.59 (d, *J* = 11.8 Hz, 1H), 4.47 (d, *J* = 11.8 Hz, 1H), 3.97 (ddd, *J* = 8.4, 4.7, 1.9 Hz, 1H), 3.03 (dd, *J* = 14.2, 4.7 Hz, 1H), 2.93 (dd, *J* = 14.2, 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 203.1, 137.1, 136.5, 129.6, 128.5, 128.0, 127.9, 126.8, 84.2, 72.8, 36.7. These data correspond to previously reported literature[3].



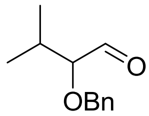
2-methoxy-3-phenylpropanal (1g):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (d, *J* = 1.9 Hz, 1H), 7.28 (m, 5H), 3.80 (ddd, *J* = 7.9, 4.9, 1.9 Hz, 1H), 3.40 (s, 3H), 3.01 (dd, *J* = 14.3, 4.9 Hz, 1H), 2.91 (dd, *J* = 14.3, 8.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 203.3, 136.4, 129.4, 128.5, 126.8, 86.5, 58.6, 36.4. These data correspond to previously reported literature[4].



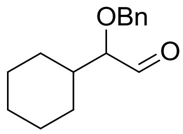
2-(benzyloxy)pentanal (1h):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (d, *J* = 2.1 Hz, 1H), 7.32 (m, 5H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.53 (d, J = 11.7 Hz, 1H), 3.76 (ddd, J = 7.5, 5.5, 2.1 Hz, 1H), 1.65 (m, 2H), 1.46 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 203.9, 137.4, 128.5, 128.1, 128.0, 83.3, 72.5, 32.1, 18.1, 13.9. HRMS (ESI) m/z calcd for $C_{12}H_{16}NaO_2$ $[M + Na]^+$: 215.1043, found: 215.1041.



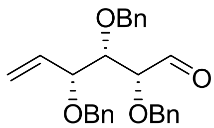
2-(benzyloxy)-3-methylbutanal (1i):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.66 (d, J = 2.7 Hz, 1H), 7.31 (m, 5H), 4.68 (d, J = 11.8 Hz, 1H), 4.49 (d, J = 11.8 Hz, 1H), 3.47 (dd, J = 5.8, 2.7 Hz, 1H), 2.09 (m, 1H), 0.99 (t, J = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 204.5, 137.5, 128.5, 128.0, 128.0, 88.1, 72.9, 30.0, 18.5, 17.6. HRMS (ESI) m/z calcd for $C_{12}H_{17}O_2$ $[M + H]^+$: 193.1223, found: 193.1219.



2-(benzyloxy)-2-cyclohexylacetaldehyde (1j):

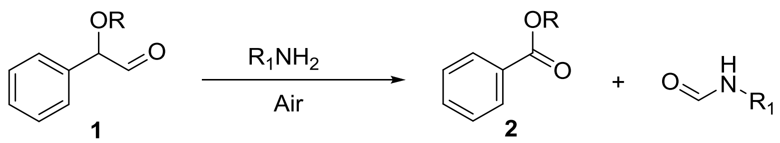
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.66 (d, J = 2.8 Hz, 1H), 7.33 (m, 5H), 4.67 (d, J = 11.8 Hz, 1H), 4.47 (d, J = 11.8 Hz, 1H), 3.49 (dd, J = 5.7, 2.8 Hz, 1H), 1.77 (m, 4H), 1.64 (m, 2H), 1.20 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 204.7, 137.5, 128.5, 128.0, 128.0, 87.8, 72.9, 39.6, 28.8, 28.0, 26.2, 26.0, 25.9. HRMS (ESI) m/z calcd for $C_{15}H_{20}NaO_2$ $[M + Na]^+$: 255.1356, found: 255.1358.



(2R,3S,4R)-2,3,4-Tris(benzyloxy)hex-5-enal (1k)[5]:

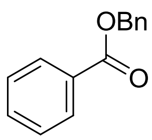
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (d, J = 0.7 Hz, 1H), 7.29 (m, 15H), 5.82 (ddd, J = 16.9, 10.8, 7.7 Hz, 1H), 5.27 (m, 2H), 4.71 (dd, J = 11.7, 2.3 Hz, 2H), 4.58 (d, J = 11.7 Hz, 1H), 4.54 (d, J = 11.5 Hz, 1H), 4.49 (d, J = 11.8 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.15 (d, J = 5.0 Hz, 1H), 3.87 (dd, J = 4.4, 0.7 Hz, 1H), 3.80 (t, J = 4.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 201.6, 137.8, 137.7, 137.2, 134.8, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 127.9, 127.6, 119.4, 82.4, 81.8, 80.0, 74.5, 73.3, 71.0. These data correspond to previously reported literature[5].

4. General Procedure for oxidative C-C bond cleavage reaction



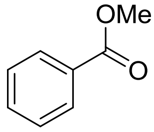
To a round-bottom flask charged with 2-(benzyloxy)-2-phenylacetaldehyde **1a** (86 mg, 0.38 mmol) in solution of toluene (4 mL) was added aniline **3f** (40 mg, 0.37 mmol). The reaction mixture was stirred at 50 ℃ for 2 h with a reflux condenser open to air. The solvent was then removed under vacuo, and the residue was purified by column chromatography on silica gel (dichloromethane: hexane = 2:3) to afford **2a** as yellow oil, 65 mg, 81%.

5. Characterization of products



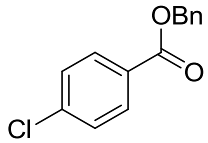
Benzyl benzoate (2a):

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (m, 2H), 7.57 (m, 1H), 7.42 (m, 7H), 5.39 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.6, 135.3, 132.2, 129.3, 128.9, 127.8, 127.6, 127.4, 127.3, 65.9. These data correspond to previously reported literature[6].



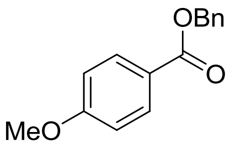
Methyl benzoate (2b):

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 7.3 Hz, 2H), 7.54 (d, J = 7.2 Hz, 1H), 7.43 (t, J = 6.9 Hz, 2H), 3.91 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.1, 132.9, 130.2, 129.6, 128.4, 52.1.These data correspond to previously reported literature[7].



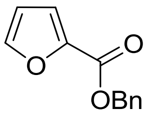
Benzyl 4-chlorobenzoate (2c):

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, J = 7.8 Hz, 2H), 7.41 (m, 7H), 5.36 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.6, 139.5, 135.8, 131.1, 128.8, 128.7, 128.6, 128.4, 128.3, 67.0. These data correspond to previously reported literature[8].



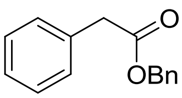
Benzyl 4-methoxybenzoate (2d):

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (m, 2H), 7.44 (m, 2H), 7.35 (m, 3H), 6.91 (m, 2H), 5.33 (s, 2H), 3.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.2, 163.5, 136.4, 131.8, 128.6, 128.4, 128.1, 128.1, 127.8, 122.6, 113.6, 66.4, 55.4. These data correspond to previously reported literature[8].



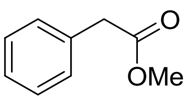
Benzyl furan-2-carboxylate (2e):

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 0.8 Hz, 1H), 7.43 (dd, J = 7.8, 1.2 Hz, 2H), 7.37 (m, 3H), 7.20 (d, J = 3.5 Hz, 1H), 6.49 (dd, J = 3.5, 1.7 Hz, 1H), 5.34 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.6, 146.5, 144.6, 135.6, 128.6, 128.4, 128.4, 118.2, 111.9, 66.6. These data correspond to previously reported literature[9].



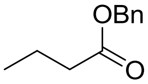
Benzyl 2-phenylacetate (2f):

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (m, 10H), 5.13 (s, 2H), 3.67 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.4, 135.9, 133.9, 129.3, 128.6, 128.6, 128.2, 128.1, 127.1, 66.6, 41.4. These data correspond to previously reported literature[10].



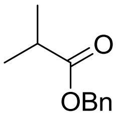
Methyl 2-phenylacetate (2g):

1H NMR (400 MHz, CDCl3): δ 7.30 (m, 5H), 3.69 (s, 3H), 3.63 (s, 2H). 13C NMR (101 MHz, CDCl3): δ 172.1, 134.0, 129.3, 128.6, 127.1, 52.1, 41.2. These data correspond to previously reported literature[11].



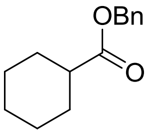
Benzyl butyrate (2h):

1H NMR (400 MHz, CDCl3): δ 7.33 (m, 5H), 5.11 (s, 2H), 2.34 (t, J = 7.4 Hz, 2H), 1.67 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H). 13C NMR (101 MHz, CDCl3): δ 173.5, 136.2, 128.6, 128.2, 66.06, 36.2, 18.5, 13.7. These data correspond to previously reported literature[12].



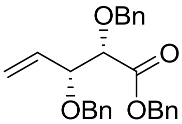
benzyl isobutyrate (2i):

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (m, 5H), 5.11 (s, 2H), 2.60 (dt, *J* = 14.0, 7.0 Hz, 1H), 1.19 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.0, 136.3, 128.5, 128.1, 128.0, 66.0, 34.0, 19.0. These data correspond to previously reported literature[13].



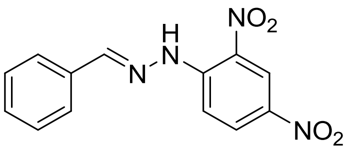
benzyl cyclohexanecarboxylate (2j):

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (m, 5H), 5.10 (s, 2H), 2.35 (tt, *J* = 11.4, 3.6 Hz, 1H), 1.93 (dd, *J* = 13.1, 2.6 Hz, 2H), 1.75 (m, 2H), 1.63 (m, 1H), 1.46 (m, 2H), 1.25 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 175.9, 136.4, 128.5, 128.1, 128.0, 65.9, 43.2, 29.0, 25.8, 25.5. These data correspond to previously reported literature[14].



(2S,3R)-benzyl 2,3-bis(benzyloxy)pent-4-enoate (2k):

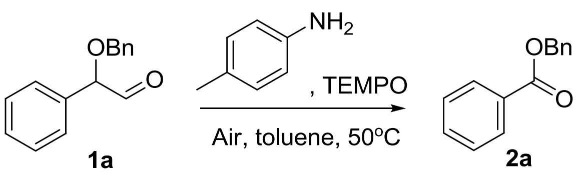
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (m, 15H), 5.94 (ddd, *J* = 17.4, 10.5, 8.0 Hz, 1H), 5.31 (dd, *J* = 13.8, 7.7 Hz, 2H), 5.21 (d, *J* = 12.2 Hz, 1H), 5.11 (d, *J* = 12.2 Hz, 1H), 4.84 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 12.2 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.39 (d, *J* = 12.2 Hz, 1H), 4.20 (dd, *J* = 7.9, 4.4 Hz, 1H), 4.09 (d, *J* = 4.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0, 138.0, 137.3, 135.5, 134.2, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 127.9, 127.9, 127.6, 119.8, 81.0, 80.6, 73.0, 70.6, 66.7. HRMS (ESI) m/z calcd for $C_{26}H_{26}NaO_4$ $[M + Na]^+$: 425.1723, found: 425.1720.



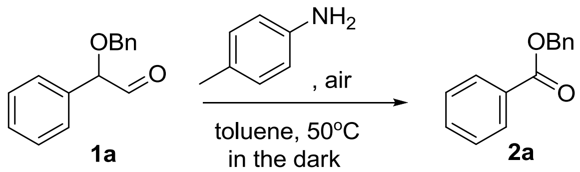
1-benzylidene-2-(2,4-dinitrophenyl)hydrazine(2l)[15]:

^{1}H NMR (400 MHz, DMSO) δ 11.68 (s, 1H), 8.87 (d, *J* = 2.6 Hz, 1H), 8.72 (s, 1H), 8.39 (dd, *J* = 9.6, 2.6 Hz, 1H), 8.12 (d, *J* = 9.6 Hz, 1H), 7.80 (dd, *J* = 7.2, 2.3 Hz, 2H), 7.50 (dd, *J* = 8.4, 3.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 149.4, 144.5, 137.1, 133.8, 130.6, 129.8, 129.5, 129.0, 127.4, 123.0, 116.8. These data correspond to previously reported literature[16].

6. Procedure for mechanistic study

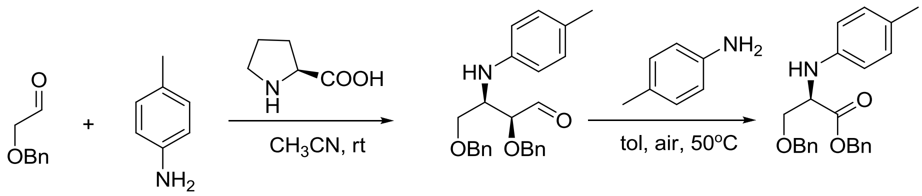


To a round-bottom flask charged with 2-(benzyloxy)-2-phenylacetaldehyde **1a** (64 mg, 0.28 mmol) in solution of toluene (4 mL) was added aniline **3f** (30 mg, 0.28 mmol) and 2,2,6,6-Tetramethyl-1-piperidinyloxy (22 mg, 0.14 mmol). The reaction mixture was stirred at 50 ℃ for 2 h with a reflux condenser open to air. Column chromatography on silica gel (dichloromethane: hexane = 2:3) gave recovered **1a**.



To an aluminium-foil paper wrapped round-bottom flask charged with 2-(benzyloxy)-2-phenylacetaldehyde **1a** (130 mg, 0.57 mmol) in solution of toluene (5 mL) was added aniline **3f** (62 mg, 0.58 mmol). The reaction mixture was stirred at 50 ℃ for 2 h with a reflux condenser open to air. The solvent was then removed under vacuo, and the residue was purified by column chromatography on silica gel (dichloromethane: hexane = 2:3) to afford **2a**, 25 mg, 18%.

7. One pot operation for Mannich reaction/Oxidative cleavage to serine derivative



To a flask containing 2-(benzyloxy)-acetaldehyde **4** (148 mg, 0.98 mmol) and 4-methyl aniline **3f** (35 mg, 0.33 mmol) in anhydrous CH_3CN (1.3 mL) was added 30% mol of L-proline (11.4 mg, 0.099 mmol). After 48 h of vigorous stirring, the reaction was quenched by addition of phosphate buffer (pH ≈ 7.0), and the aqueous phase was extracted three times with CH_2Cl_2. The combined organic layers were dried with $NaSO_4$. After concentrating, the crude Mannich reaction mixture was dissolved in toluene (3 mL) followed by addition of 4-methyl aniline **3f** (70 mg, 0.65 mmol). The reaction was stirred at 50 ℃ for 5 h with a reflux condenser open to air. Then solvent was removed under vacuo, and the residue was purified by column chromatography on silica gel (dichloromethane: hexane = 6:1) to afford **6** as dark yellow oil, 39 mg, 32%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (m, 10H), 6.96 (d, *J* = 8.1 Hz, 2H), 6.53 (d, *J* = 8.4 Hz, 2H), 5.18 (d, *J* = 12.3 Hz, 1H), 5.13 (d, *J* = 12.3 Hz, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.47 (d, *J* = 12.2 Hz, 1H), 4.25 (br, 1H), 3.88 (dd, *J* = 9.3, 3.8 Hz, 1H), 3.78 (dd, *J* = 9.3, 4.1 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 144.3, 137.6, 135.6, 129.8, 128.5, 128.4, 128.3, 128.2, 127.8, 127.8, 127.6, 114.0, 73.4, 70.2, 67.0, 57.4, 20.4.The *ee* of **6** was 97% as determined by chiral-phase HPLC analysis (Chiralcel OD-H, hexanes/i-PrOH = 70: 30, flow rate 1 mL/min, λ = 254 nm): minor isomer: t_R = 6.500 min; major isomer: t_R = 10.642 min; $[\alpha]_D^{25}$ -13.3 °(c = 1.5, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{24}H_{26}NO_3$ $[M + H]^+$: 376.1907, found: 376.1900.

1. (a)H. Nagano, H. Ohkouchi and T. Yajima, *Tetrahedron*, 2003, **59**, 3649-3663; (b)C. W. Ong and C. Y. Yu, *Tetrahedron*, 2003, **59**, 9677-9682.
2. K. P. Jang, S. Y. Choi, Y. K. Chung and E. Lee, *Org. Lett.*, 2011, **13**, 2476-2479.
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7. S. Seo, J. B. Taylor and M. F. Greaney, *Chem. Commun.*, 2012, **48**, 8270-8272.
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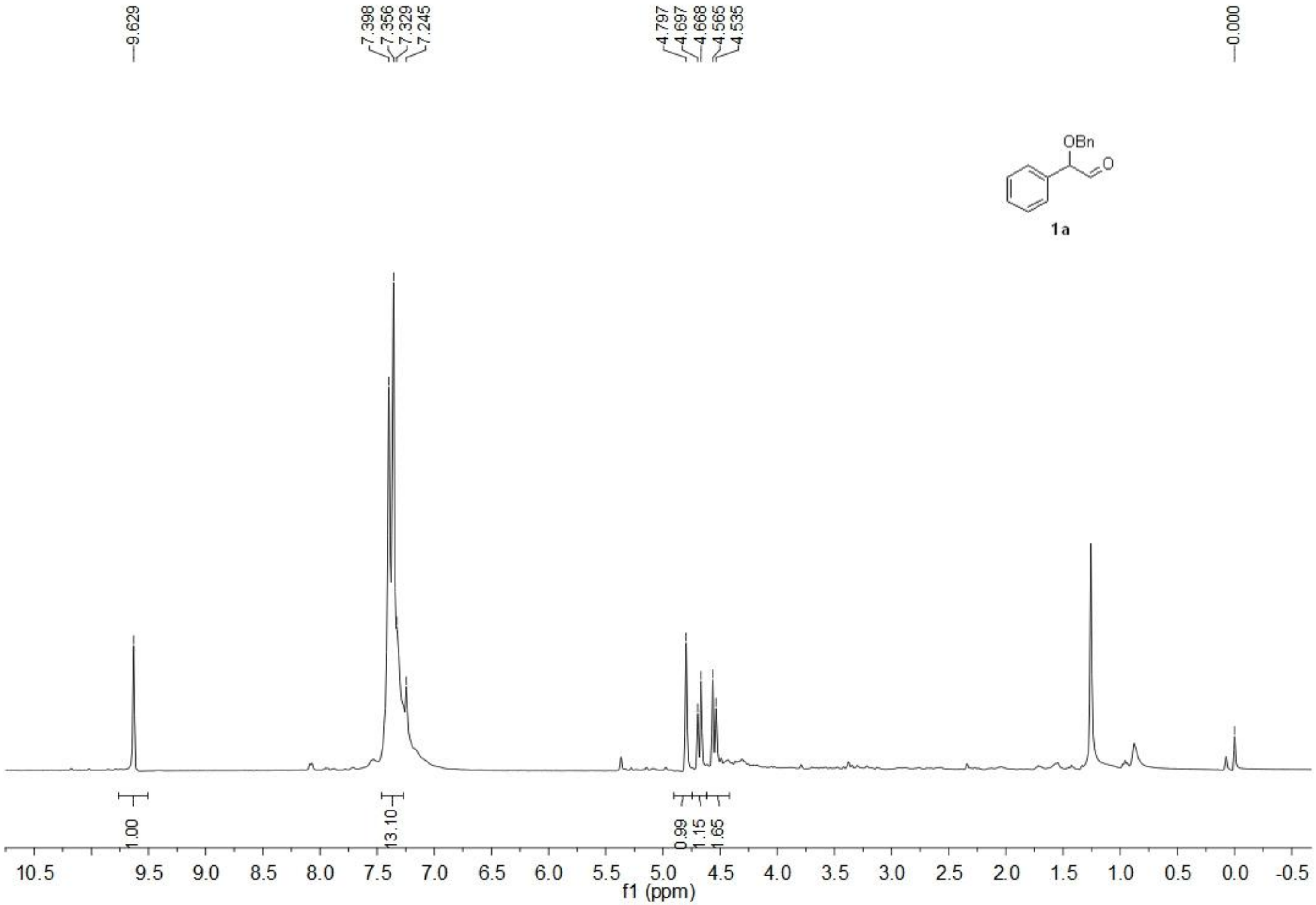
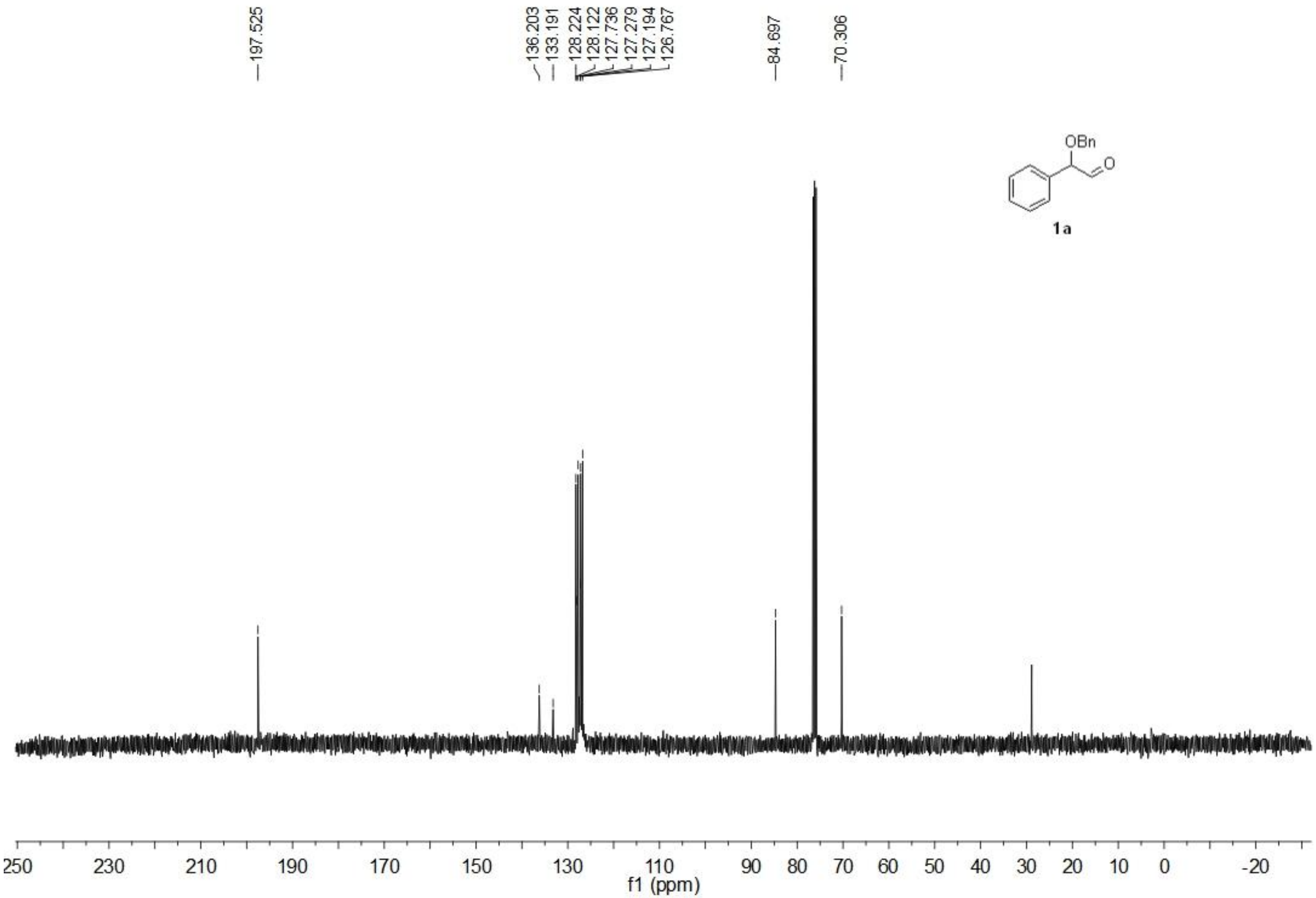
12. A. A. Poeylaut-Palena, S. A. Testero and E. G. Mata, *Chem. Commun.*, 2011, **47**, 1565-1567.
13. T. Takahashi, M. Yoshimura, H. Suzuka, T. Maegawa, Y. Sawama, Y. Monguchi and H. Sajiki, *Tetrahedron*, 2012, **68**, 8293-8299.
14. K. Ishihara, M. Niwa and Y. Kosugi, *Org. Lett.*, 2008, **10**, 2187-2190.
15. N. Havare and D. A. Plattner, *Org. Lett.*, 2012, **14**, 5078-5081.
16. F. DeRosa, L. K. Keefer and J. A. Hrabie, *J. Org. Chem.*, 2008, **73**, 1139-1142.

8. ^{1}H NMR and ^{13}C NMR spectra for substrates and products

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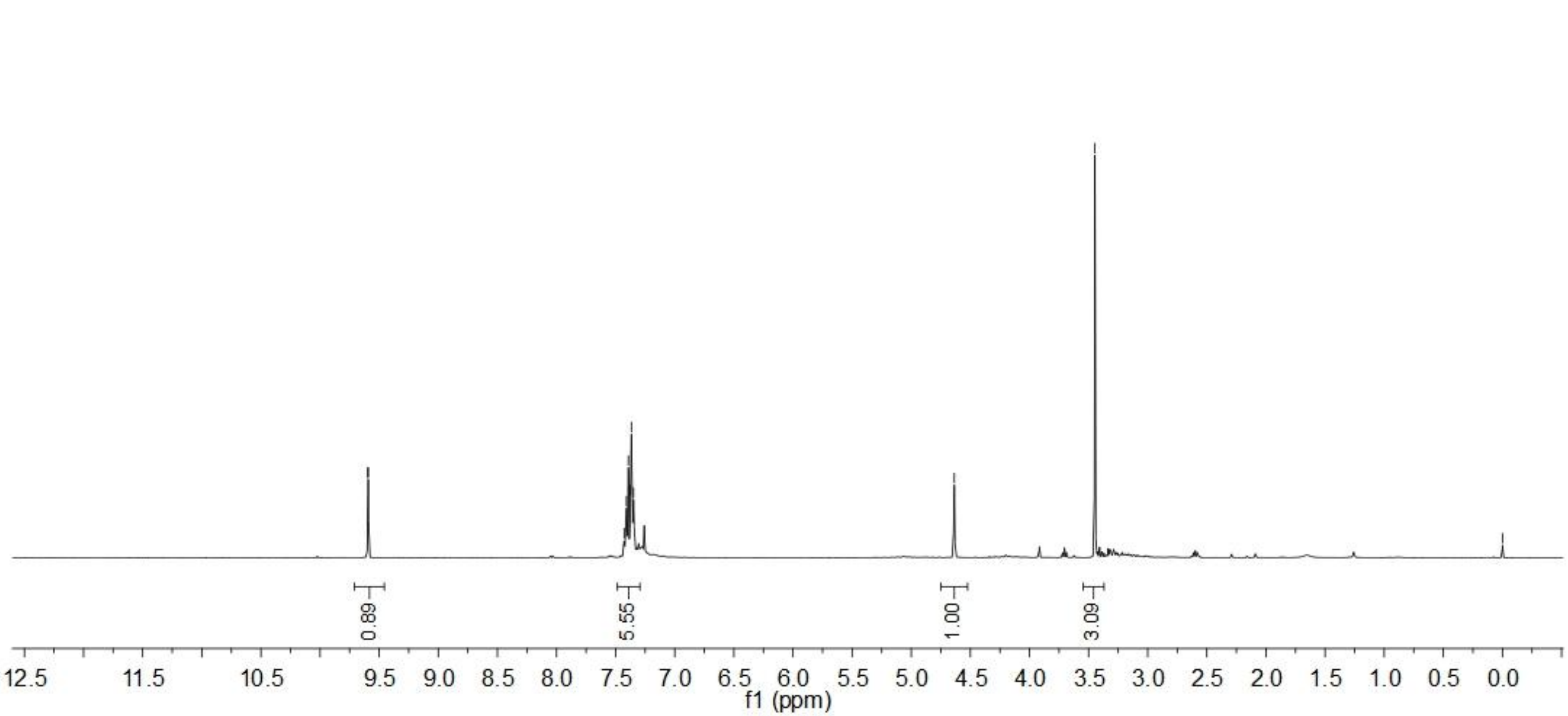
O
250
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-20
f1 (ppm)

1a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5.55
1.00
3.09
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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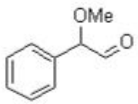
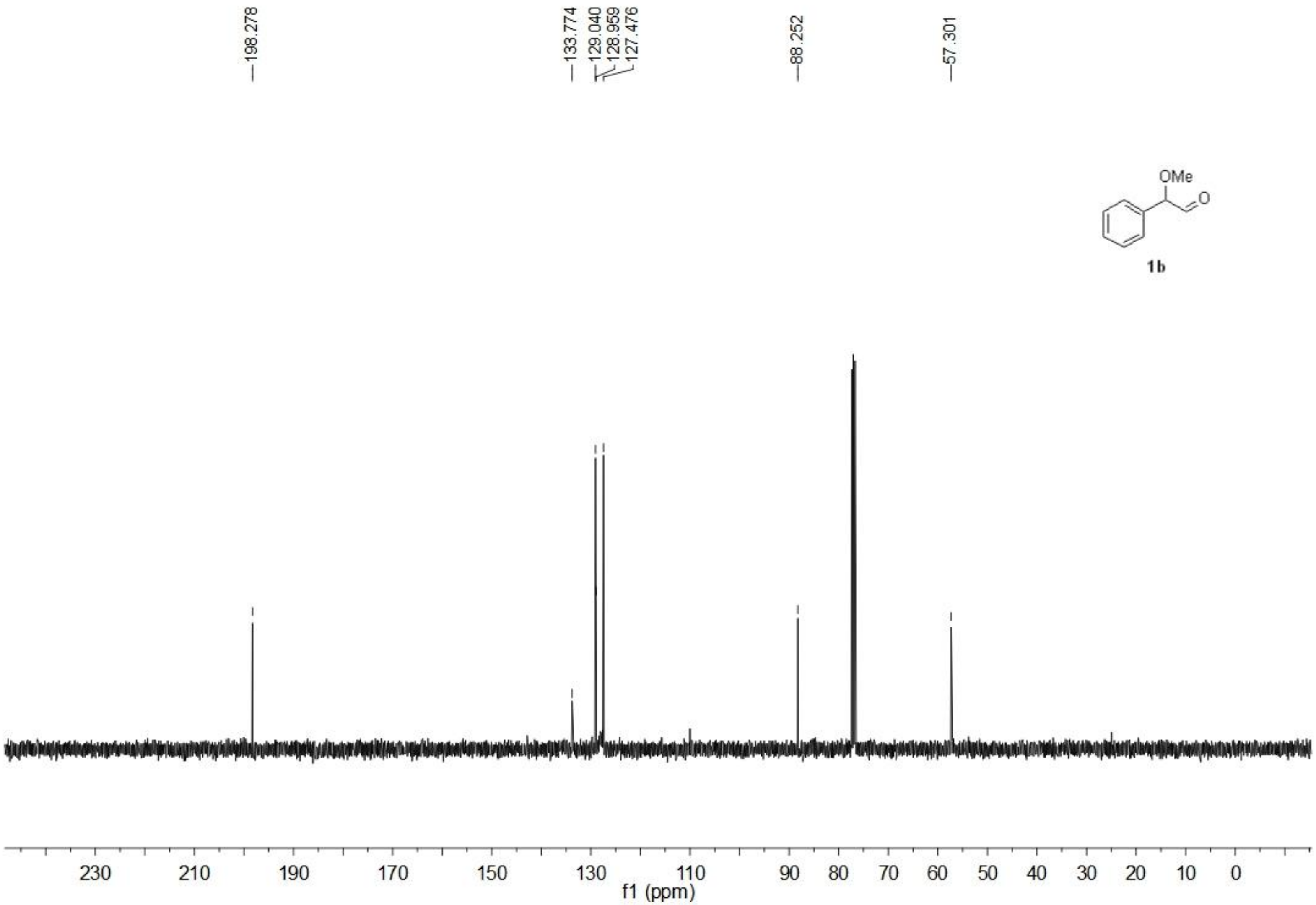
f1 (ppm)


OMe
O

1b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O
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150
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90
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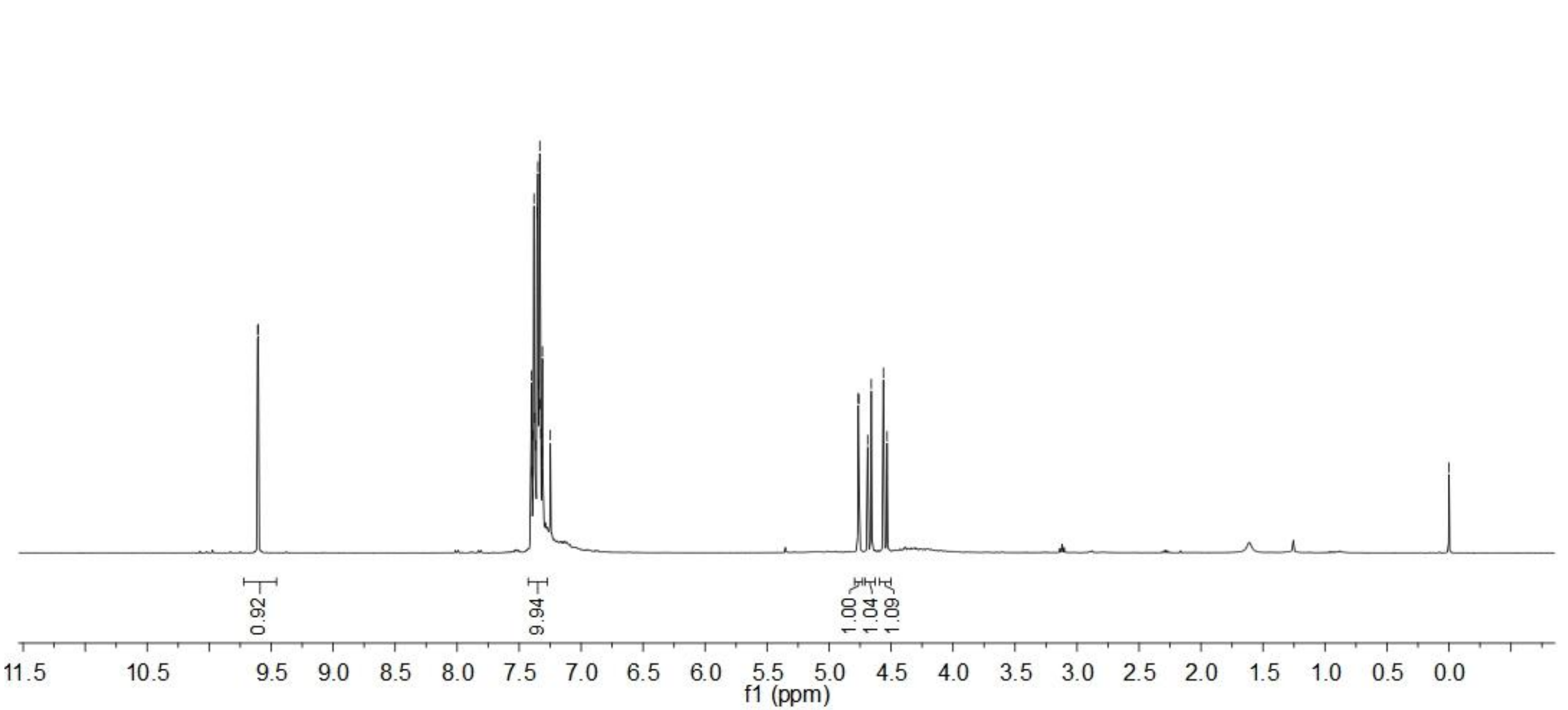
50
40
30
20
10
0
f1 (ppm)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7.324
7.316
7.312
7.248
4.764
4.760
4.688
4.659
4.561
4.532
0.000
0.92
9.94
1.00
1.04
1.09
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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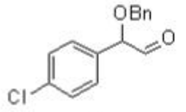
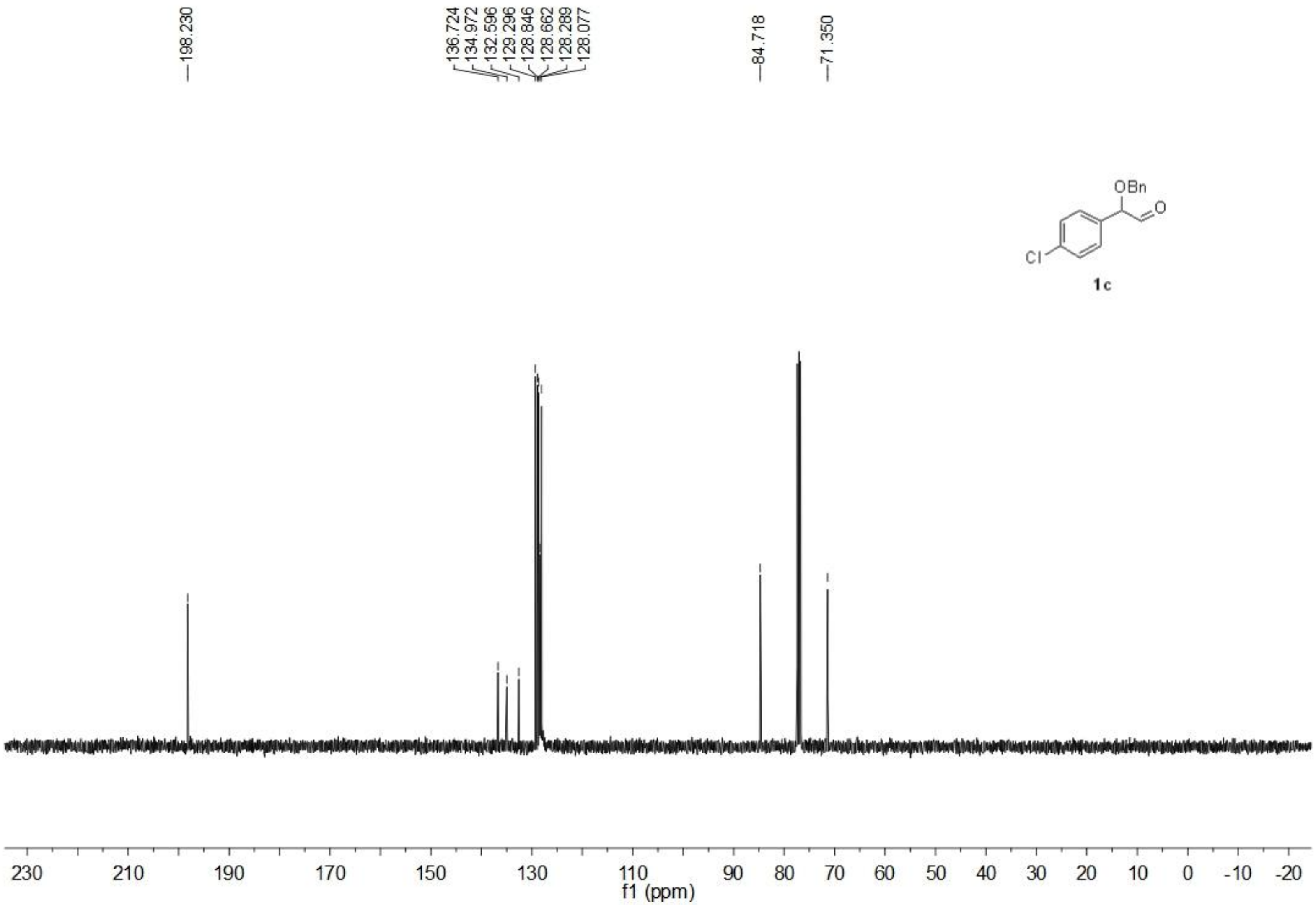
f1 (ppm)


OBn
O
Cl

1c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Cl
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130
110
90
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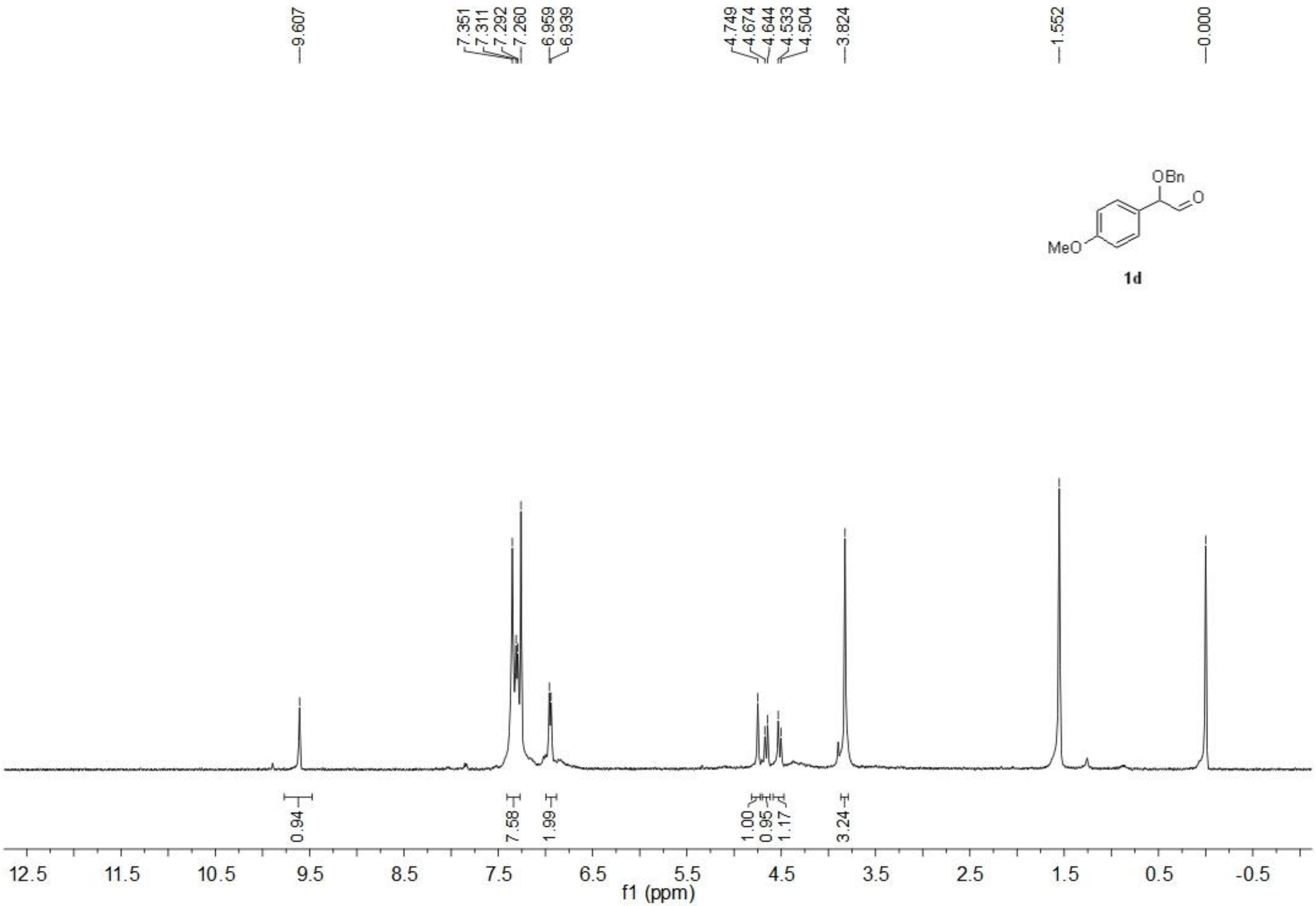
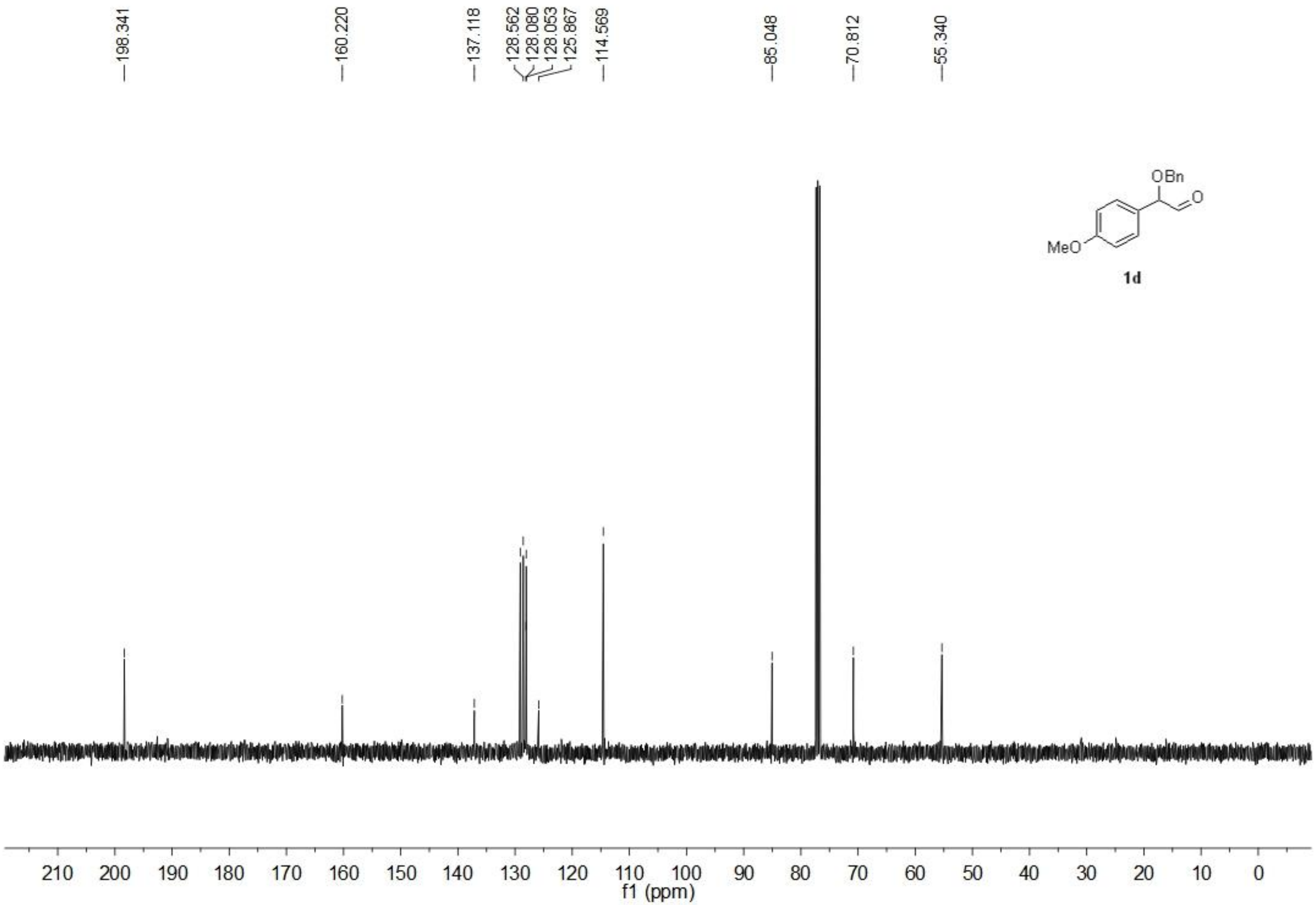
0
-10
-20
f1 (ppm)

1c

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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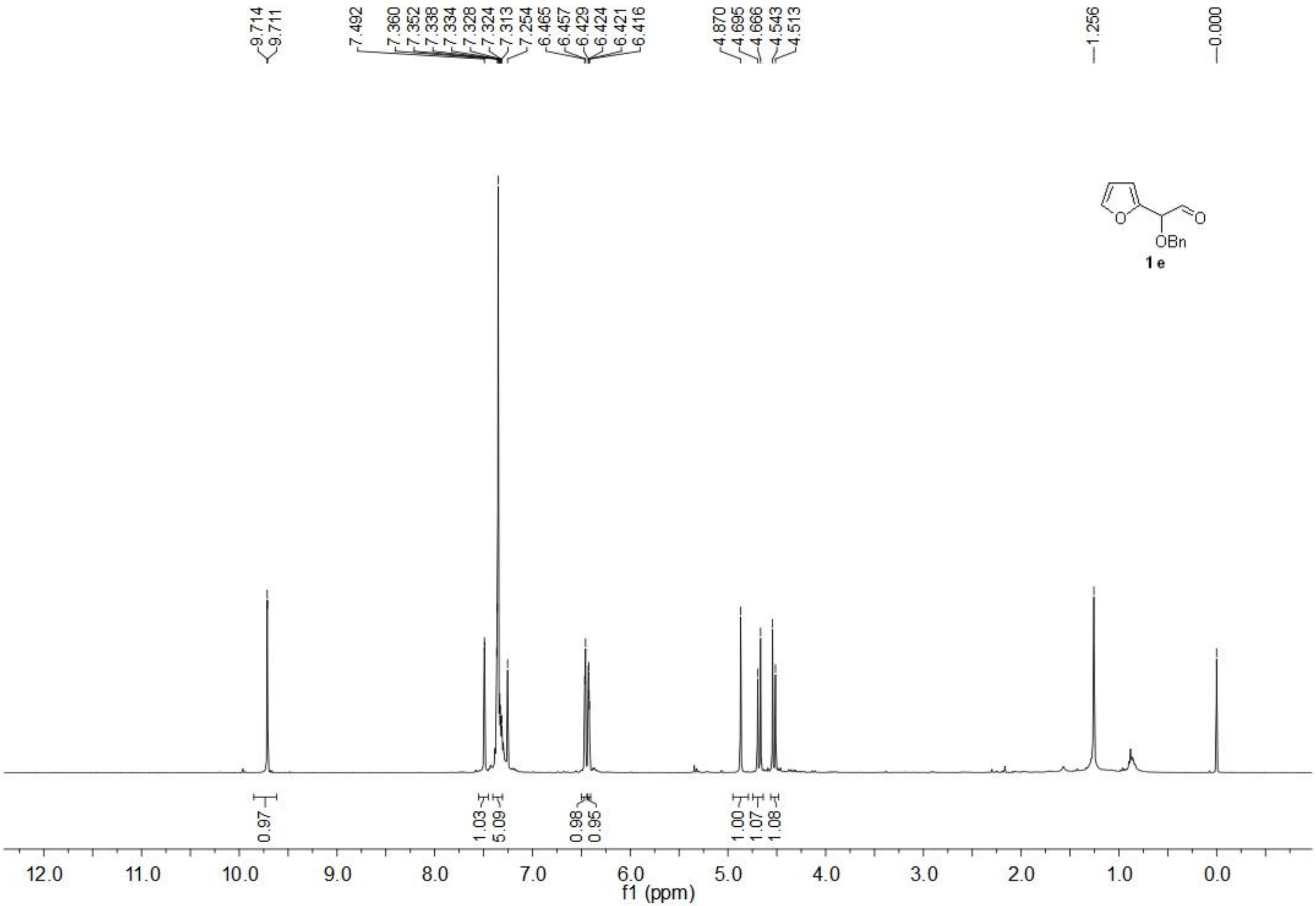
1d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6.457
6.429
6.424
6.421
6.416
4.870
4.695
4.666
4.543
4.513
1.256
0.000
O
O
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1 e
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0.98
0.95
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1.08
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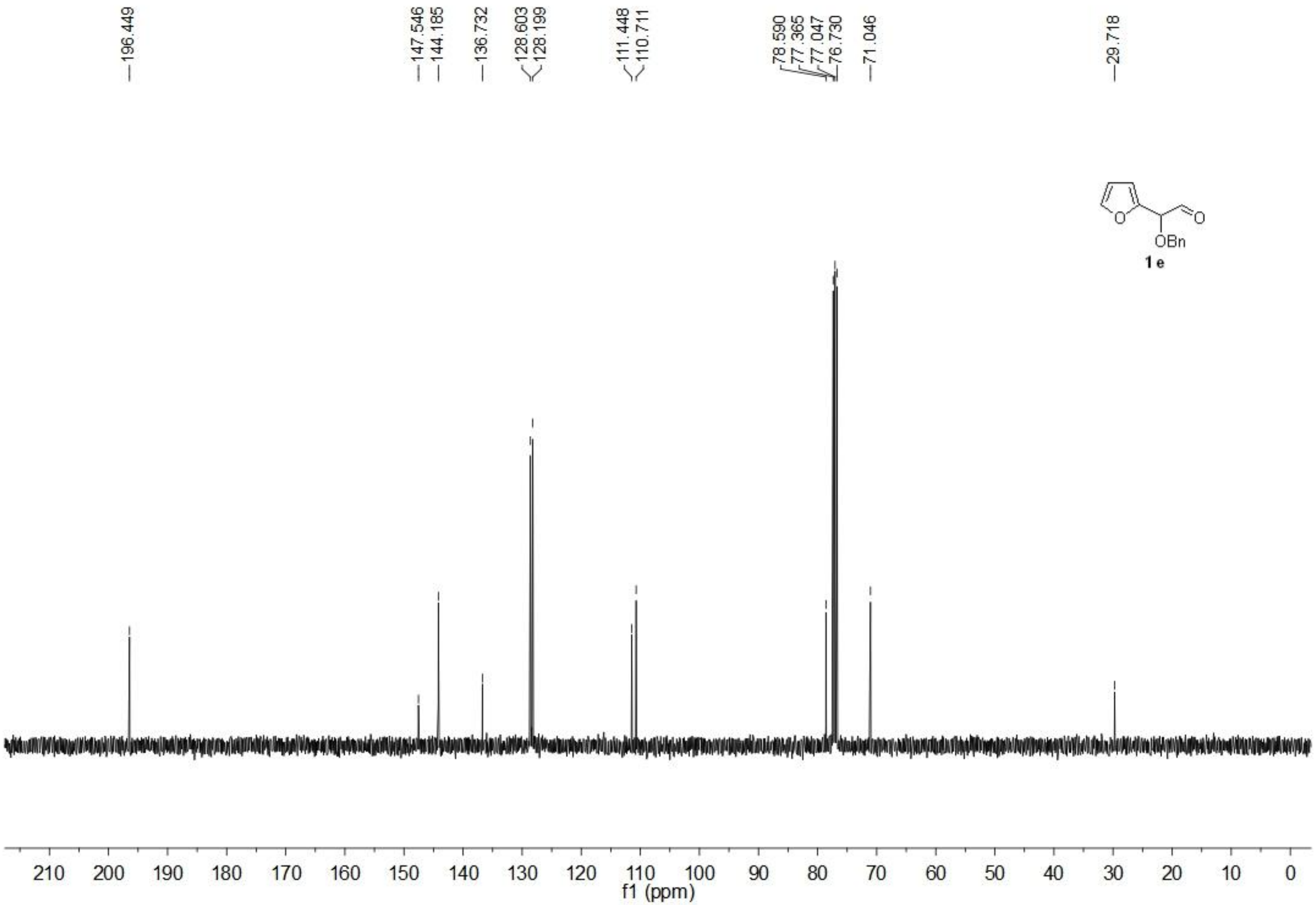
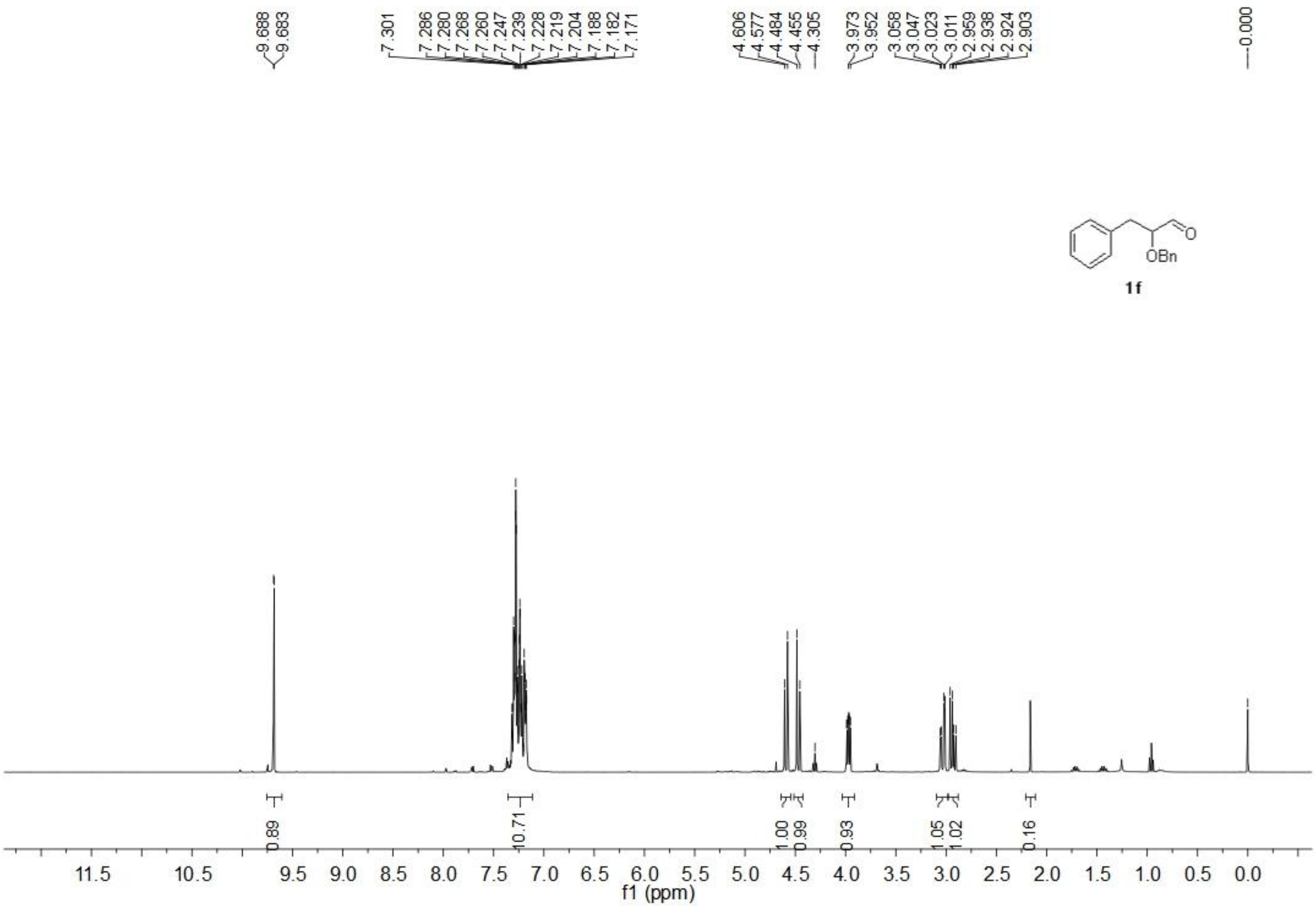
f1 (ppm)

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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4.455
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2.903
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0.93
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0.16
11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
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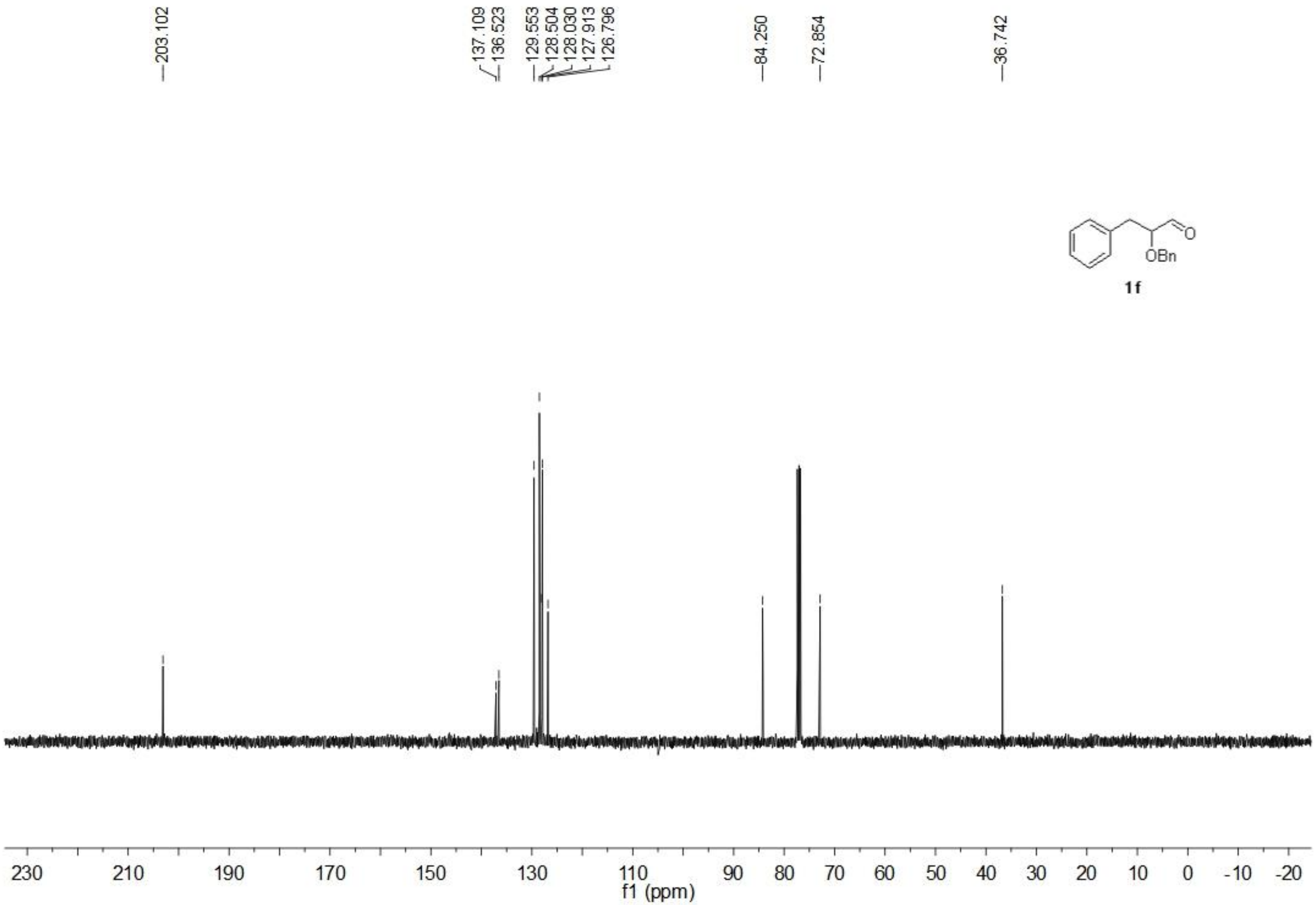
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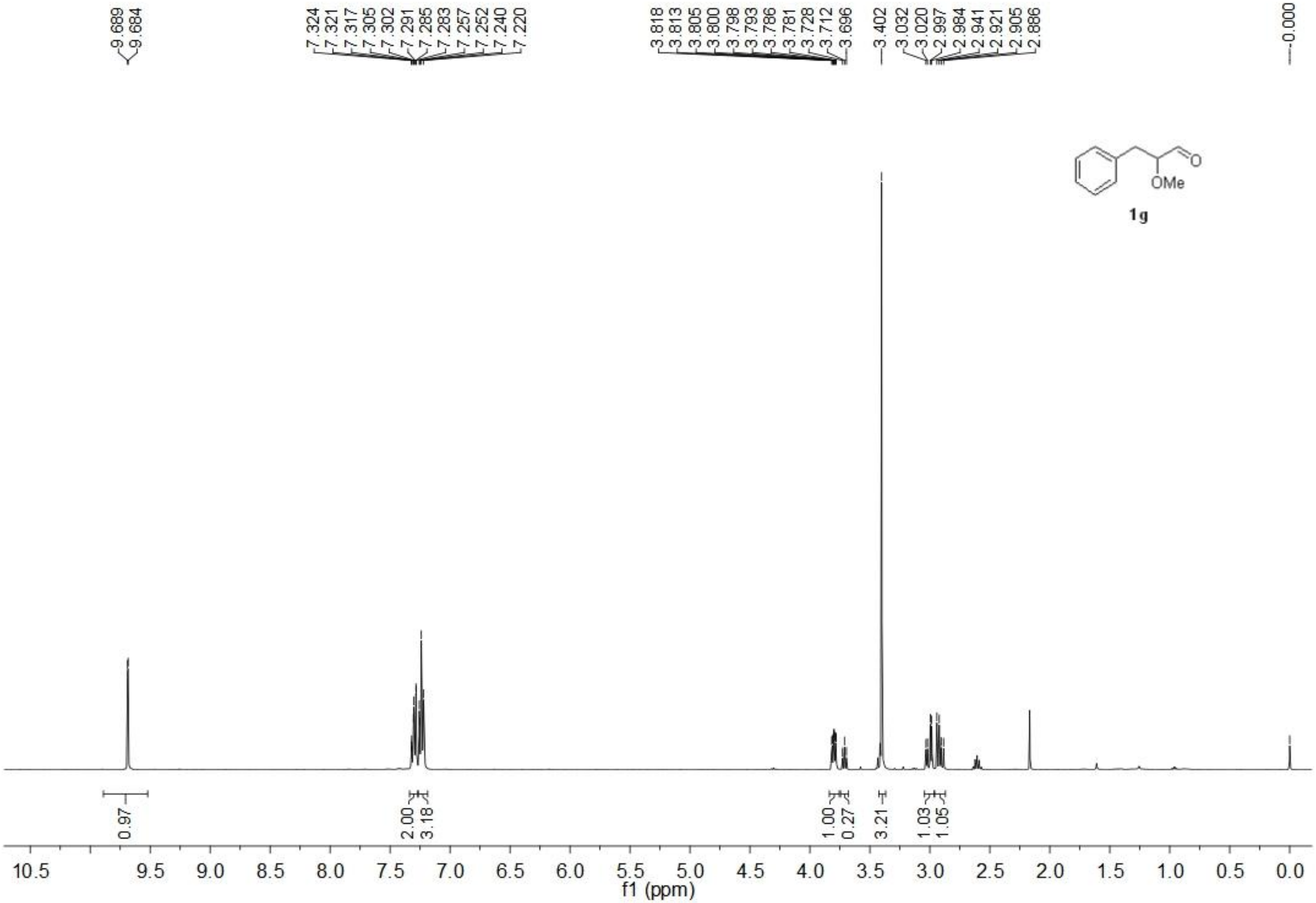
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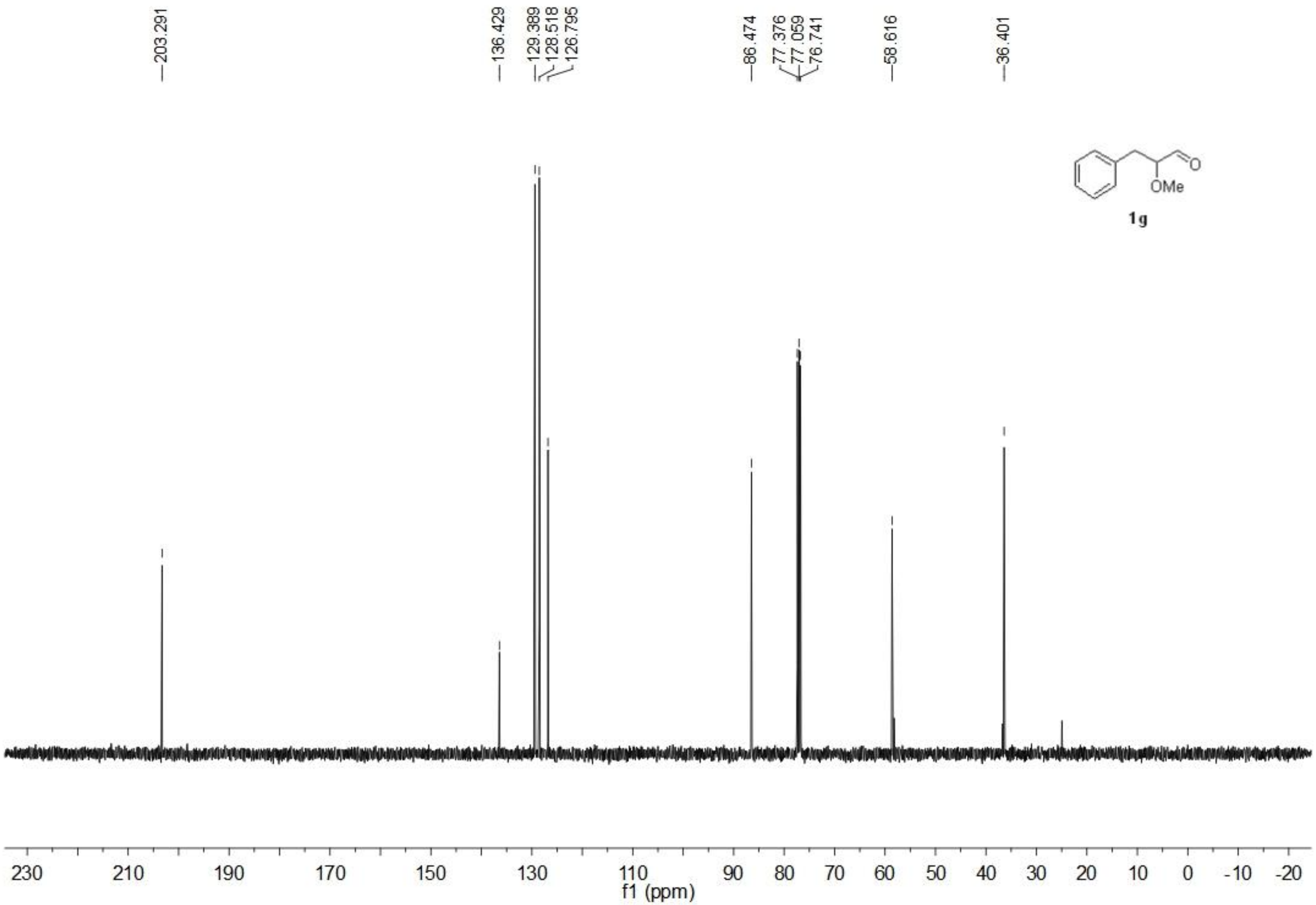
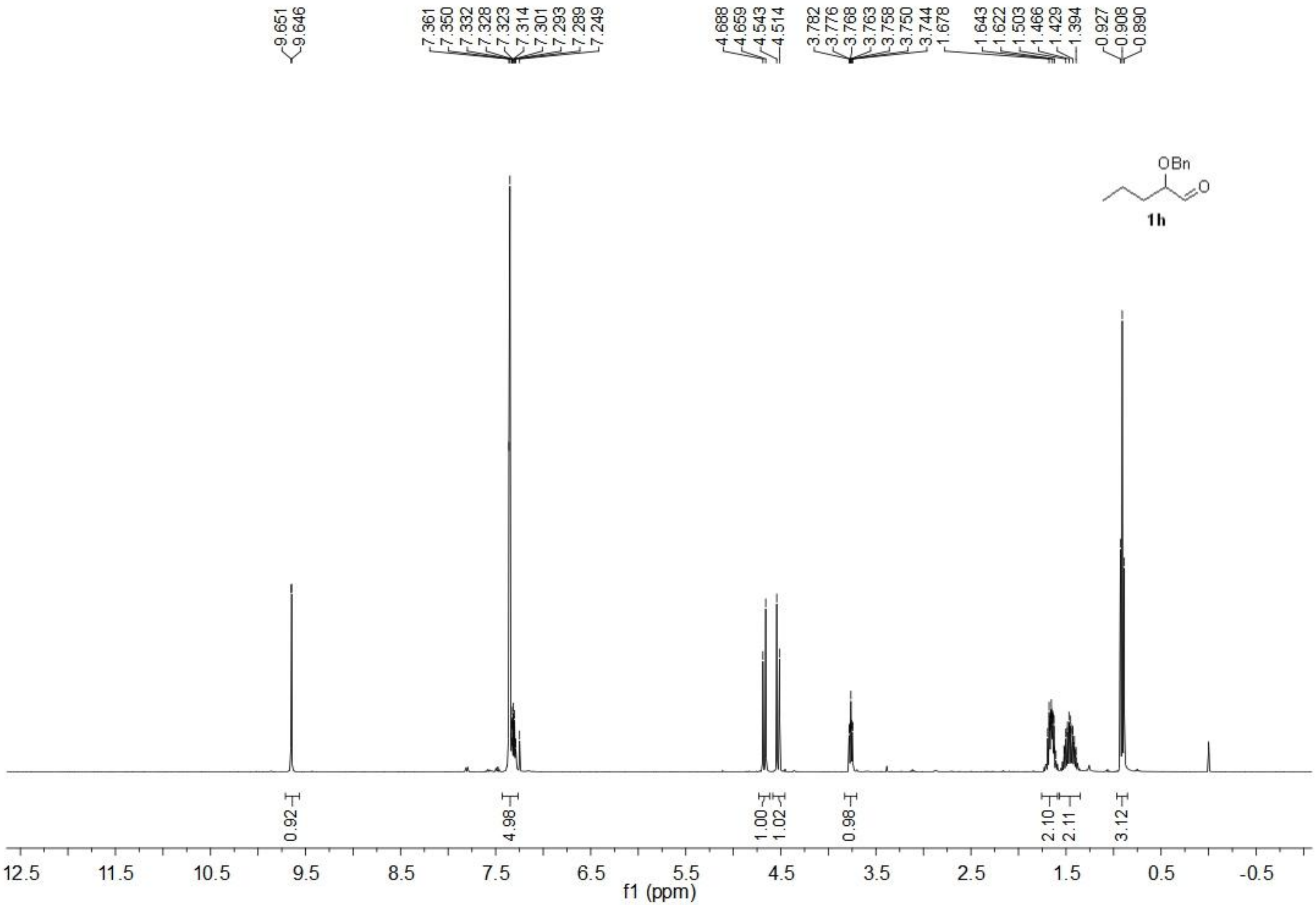
f1 (ppm)

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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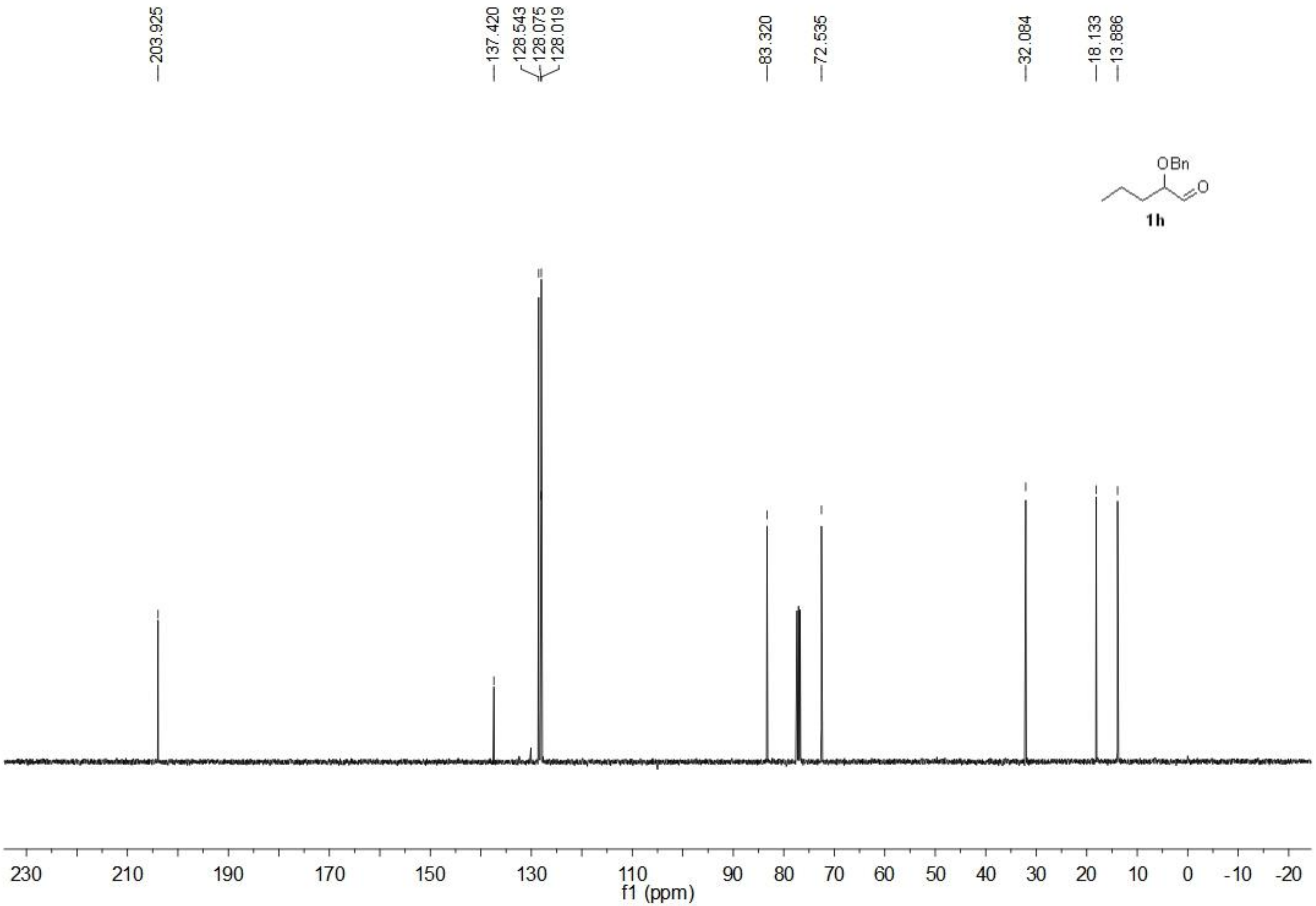
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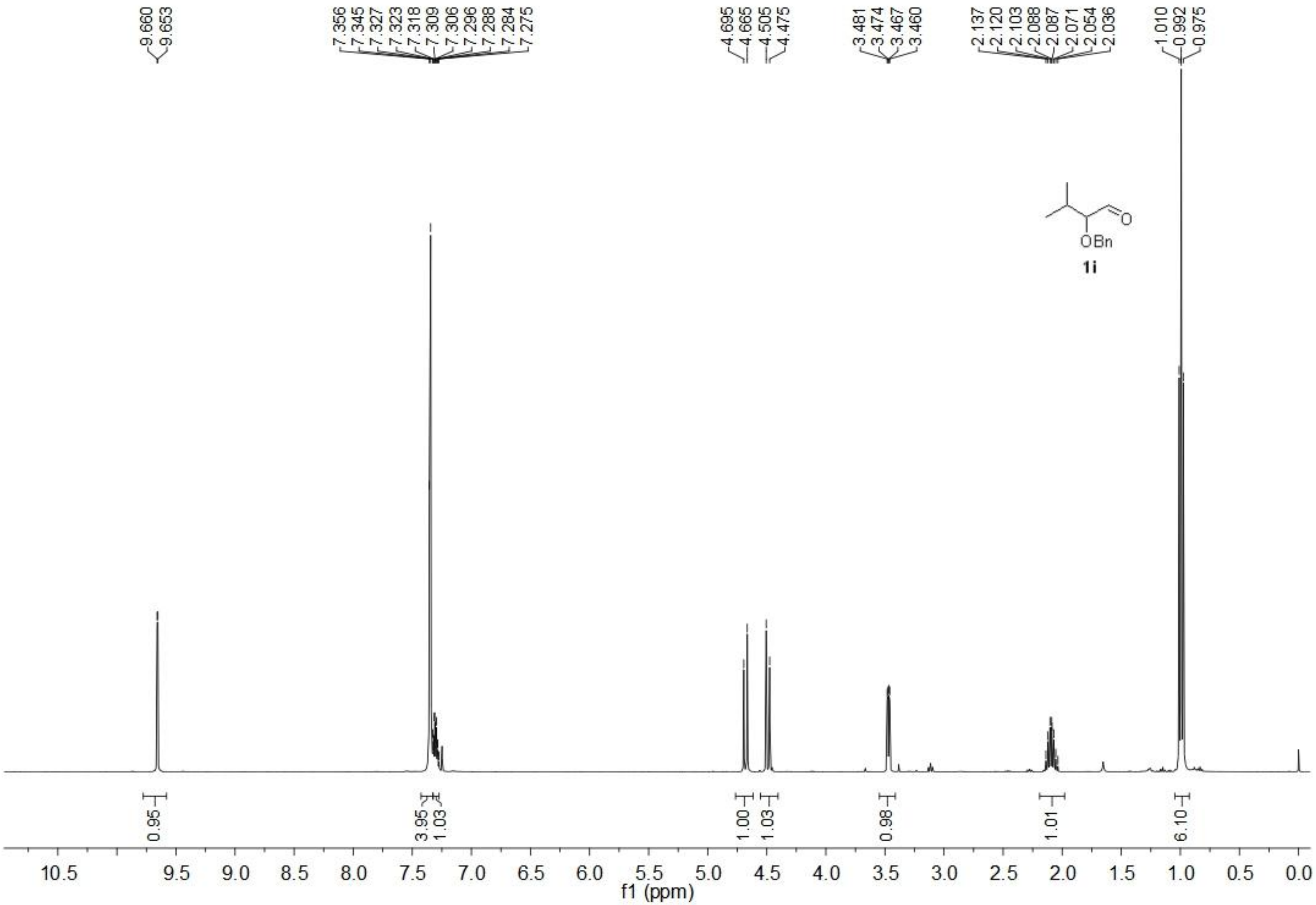
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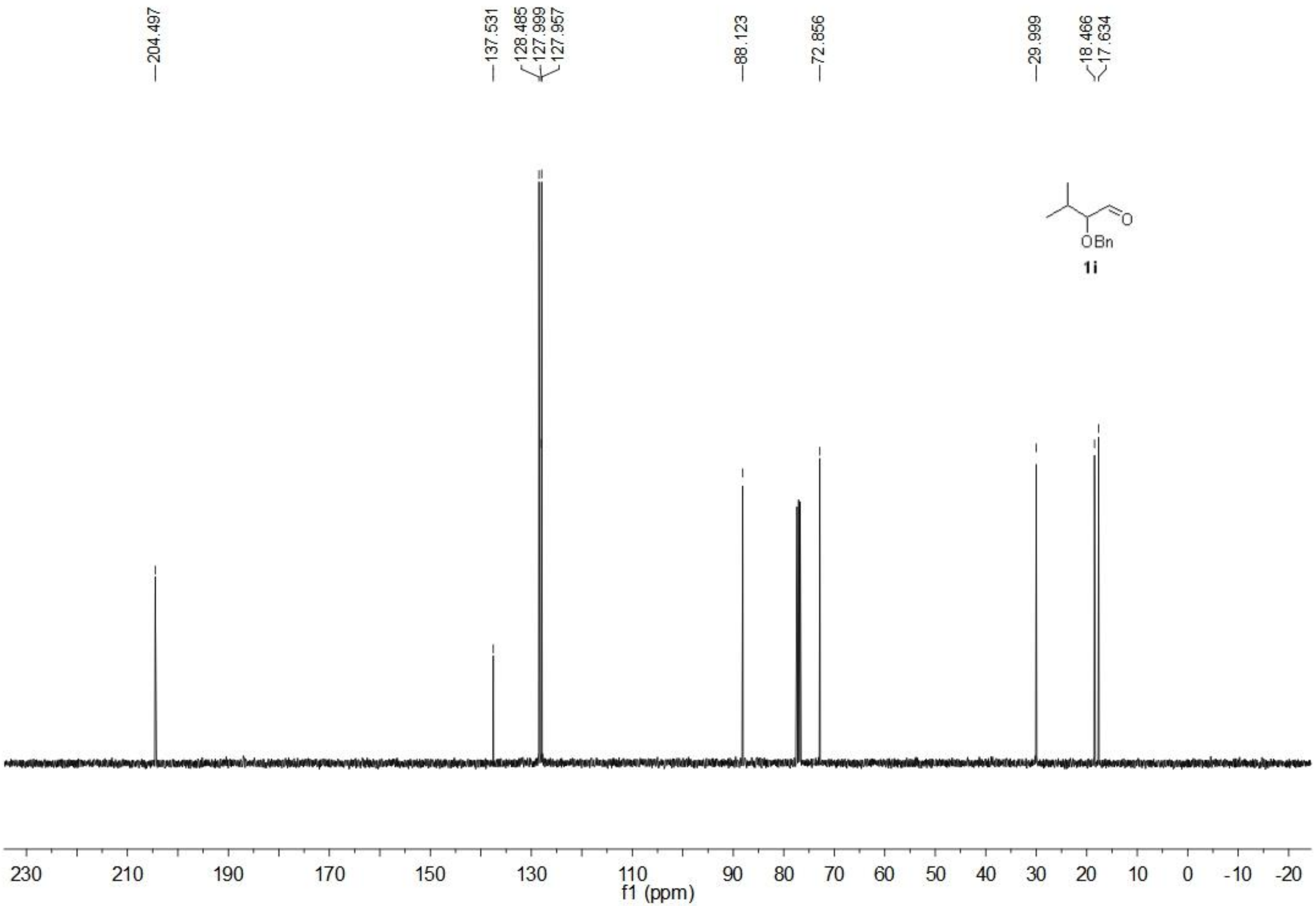
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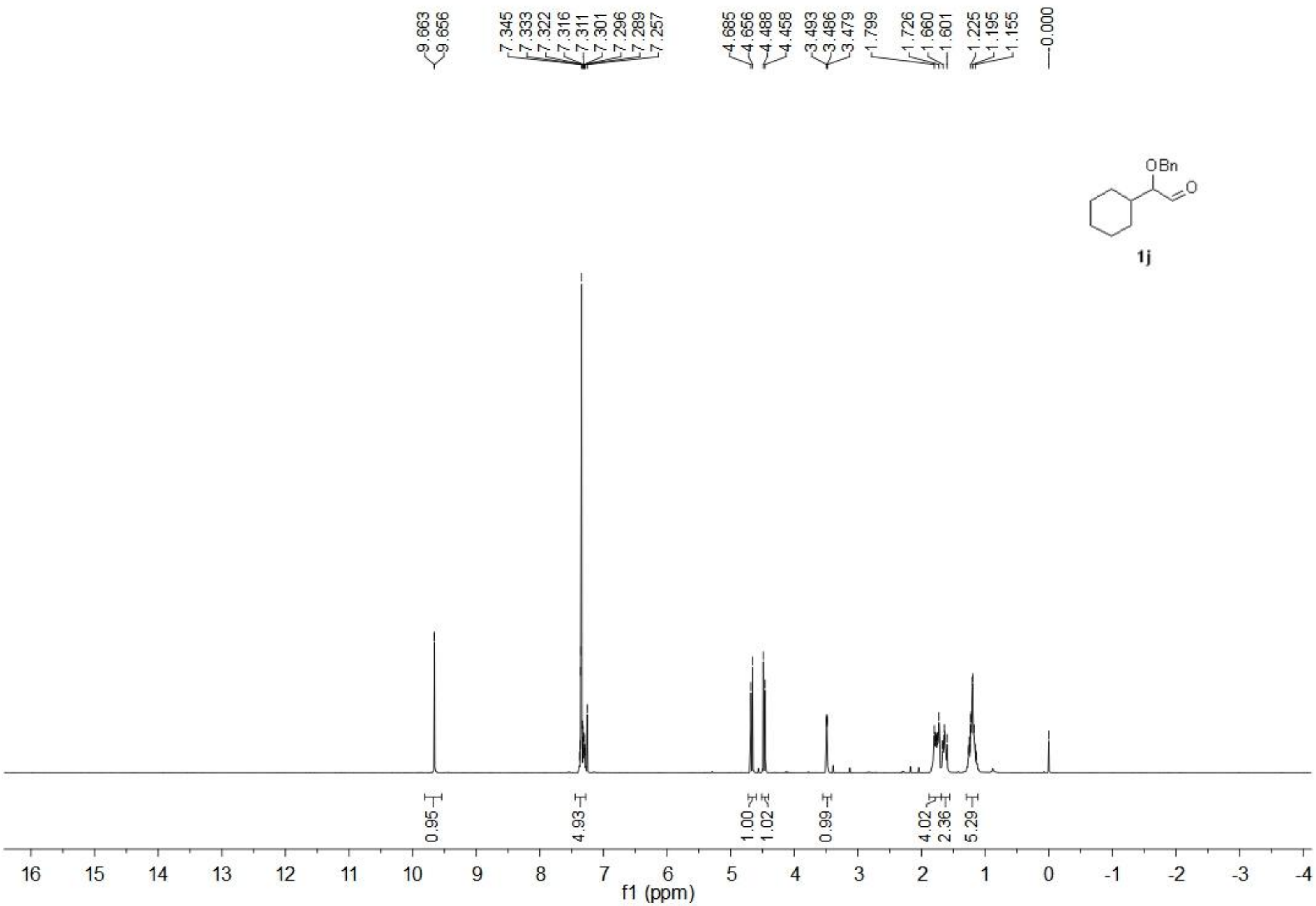
f1 (ppm)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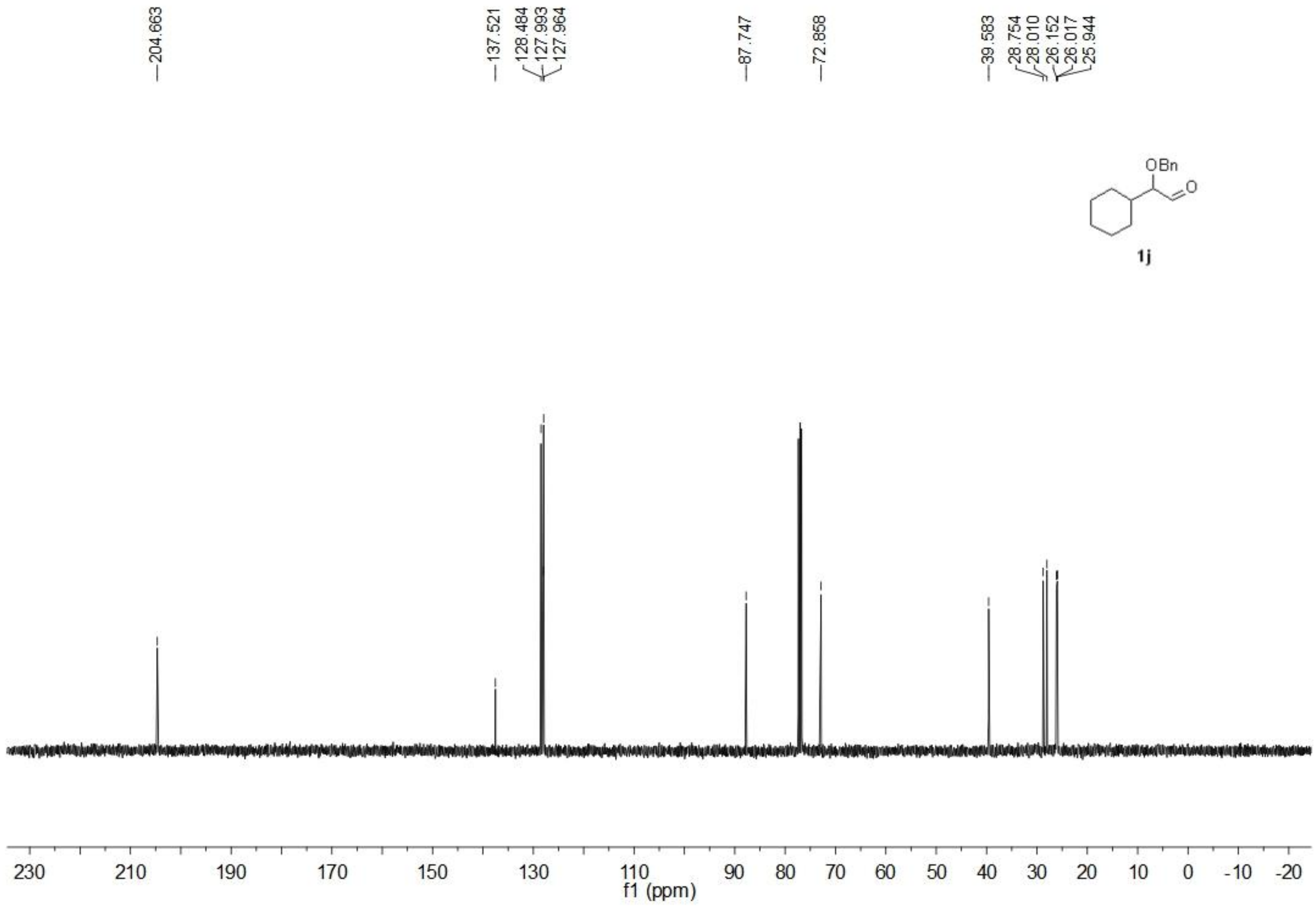
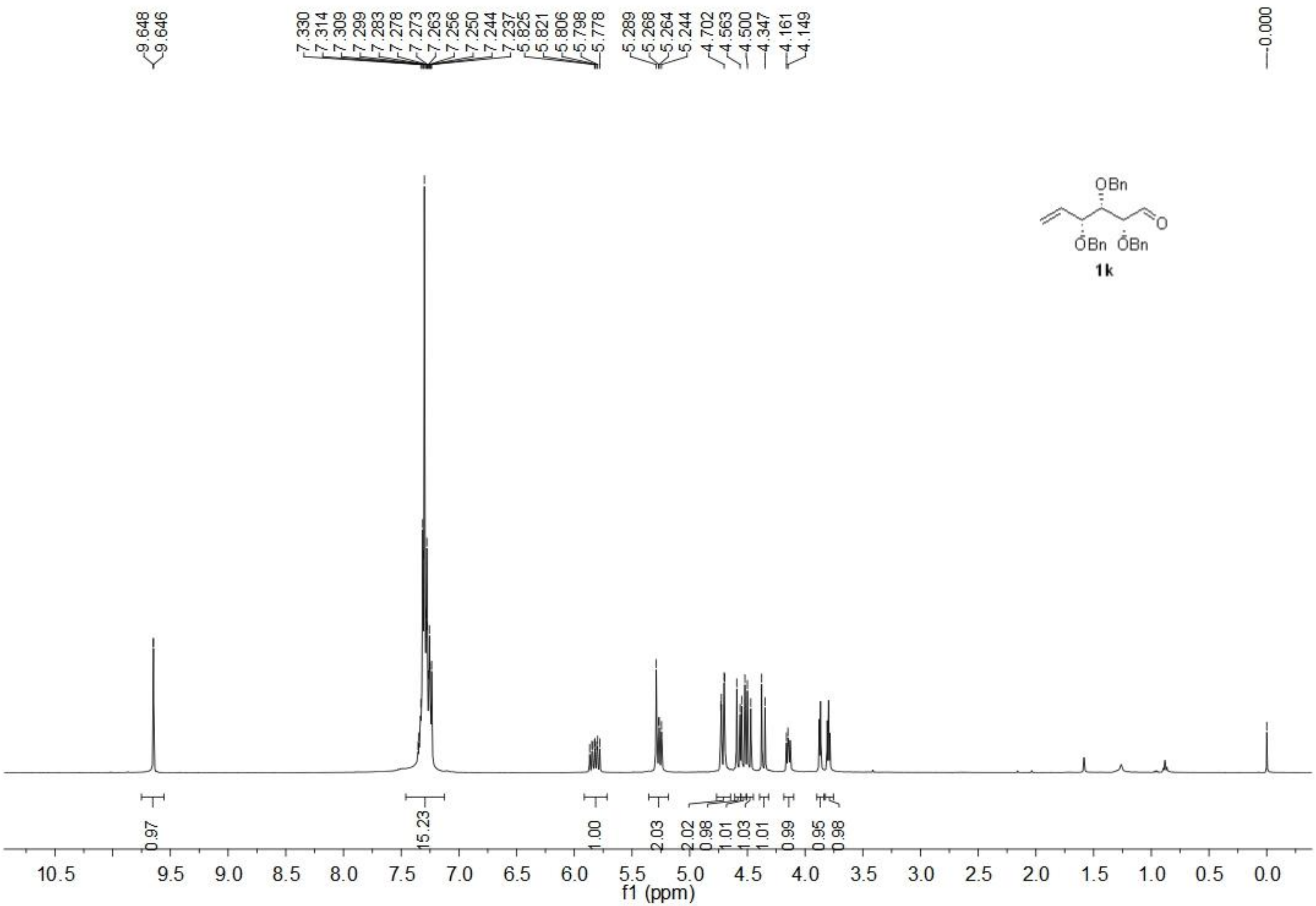
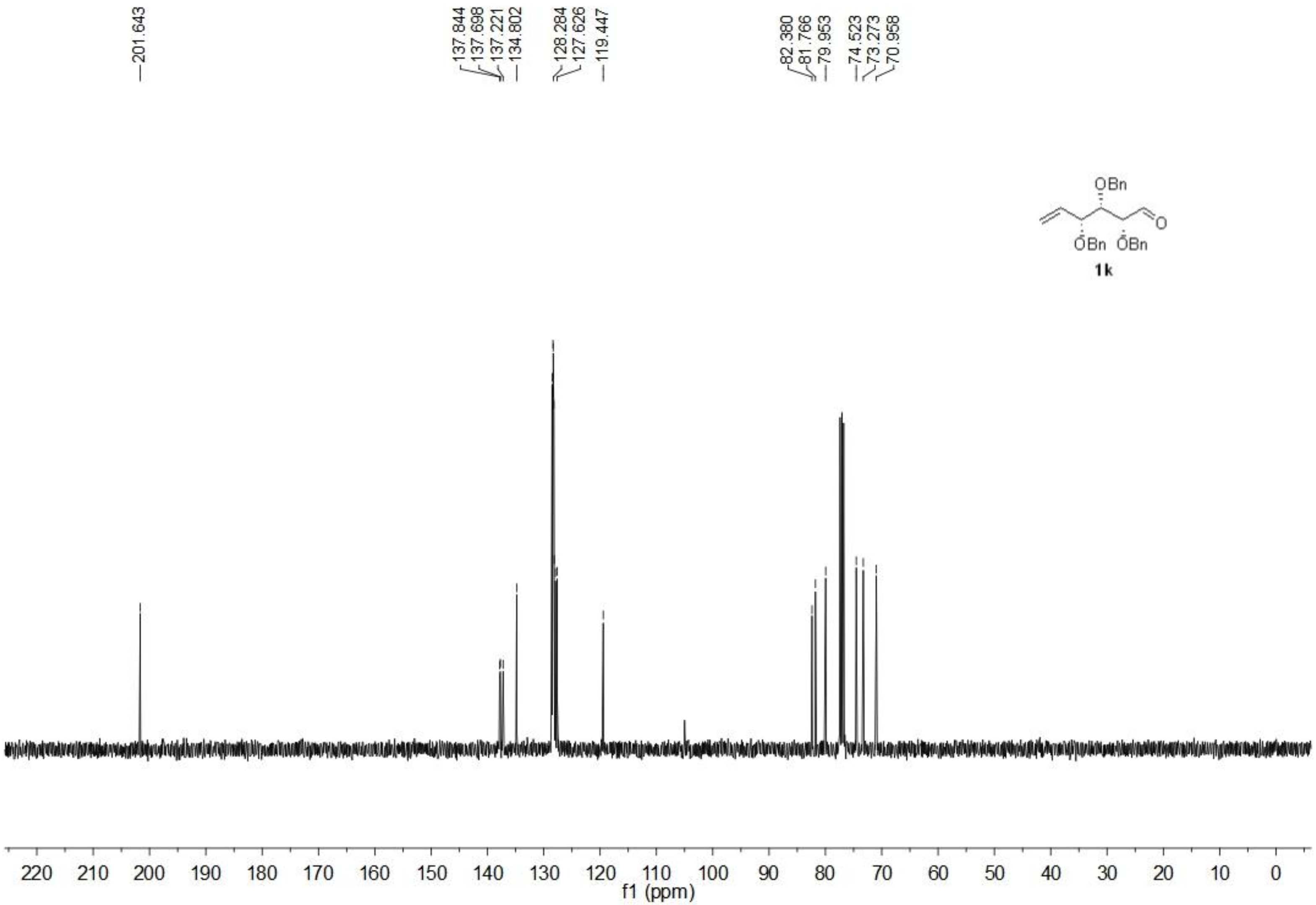
4.656
4.488
4.458
3.493
3.486
3.479
1.799
1.726
1.660
1.601
1.225
1.195
1.155
0.000
OBn
O
0.95
4.93
1.00
1.02
0.99
4.02
2.36
5.29
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

1j

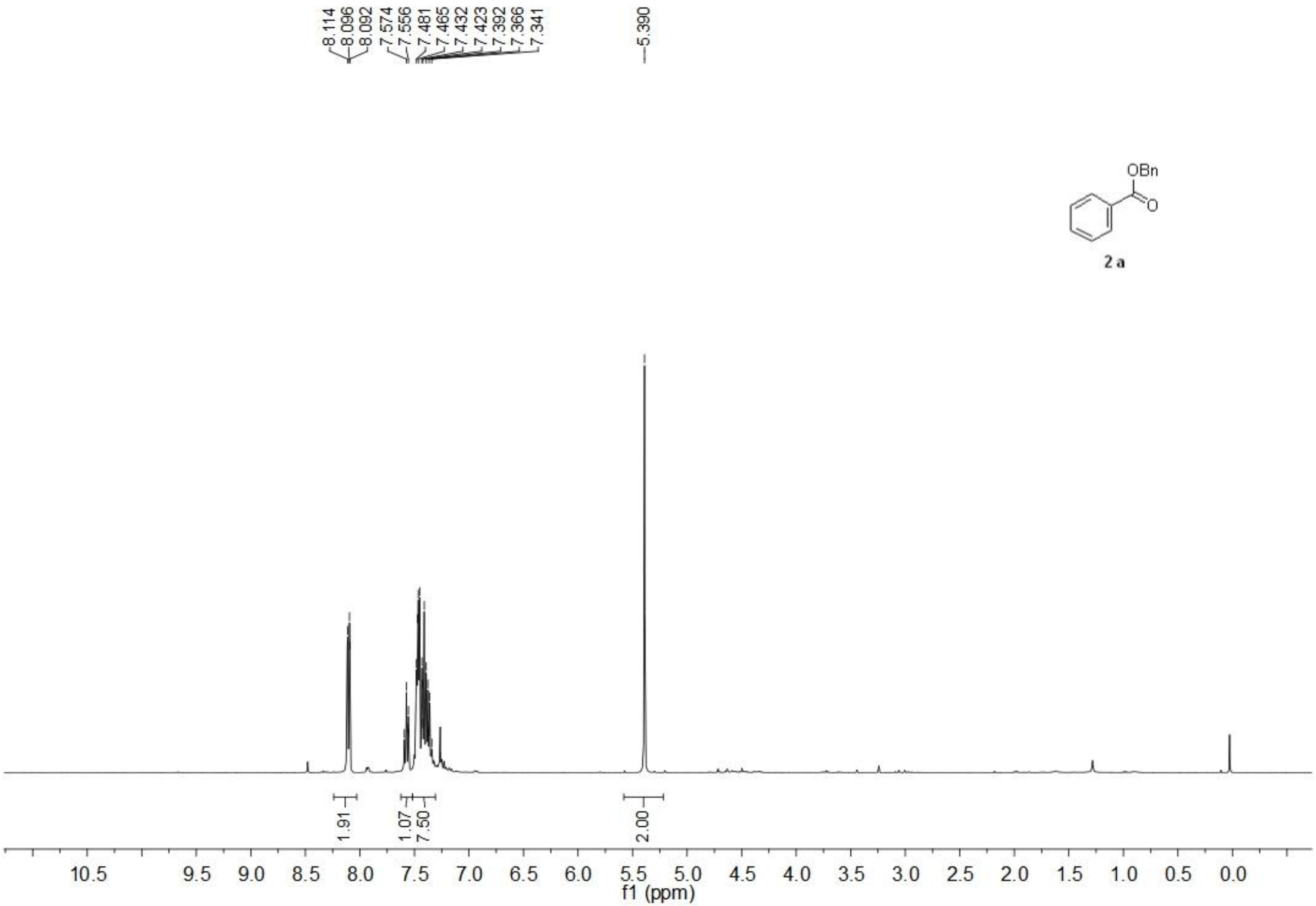

204.663
137.521
128.484
127.993
127.964
87.747
72.858
39.583
28.754
28.010
26.152
26.017
25.944
OBn
O
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

1j

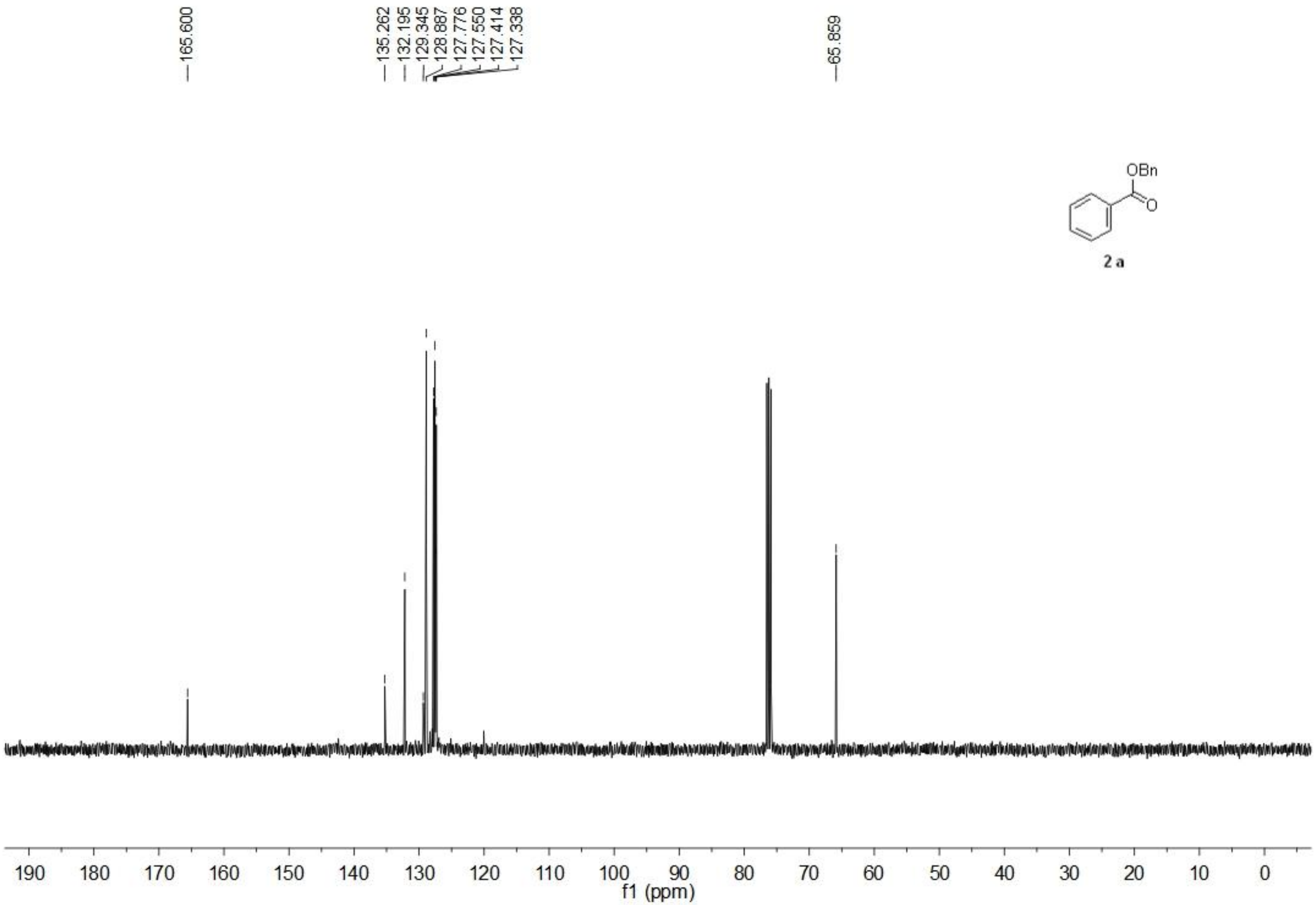

9.648
9.646
7.330
7.314
7.309
7.299
7.283
7.278
7.273
7.263
7.256
7.250
7.244
7.237
5.825
5.821
5.806
5.798
5.778
5.289
5.268
5.264
5.244
4.702
4.563
4.500
4.347
4.161
4.149
0.000
OBn
O
OBn OBn
1k
0.97
15.23
1.00
2.03
2.02
0.98
1.01
1.03
1.01
0.99
0.95
0.98
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


201.643
137.844
137.698
137.221
134.802
128.284
127.626
119.447
82.380
81.766
79.953
74.523
73.273
70.958
OBn
O
OBn OBn
1k
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

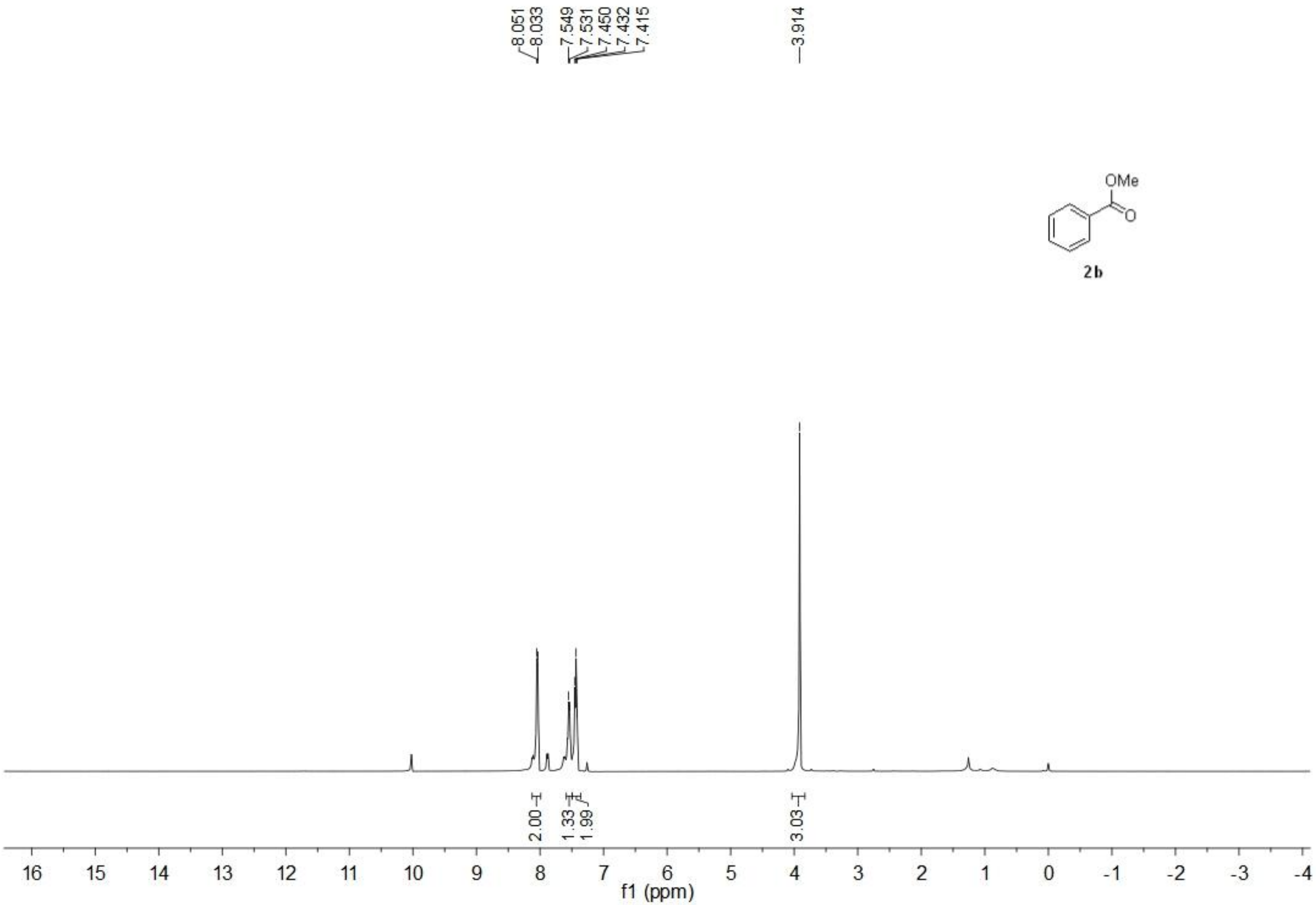
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry



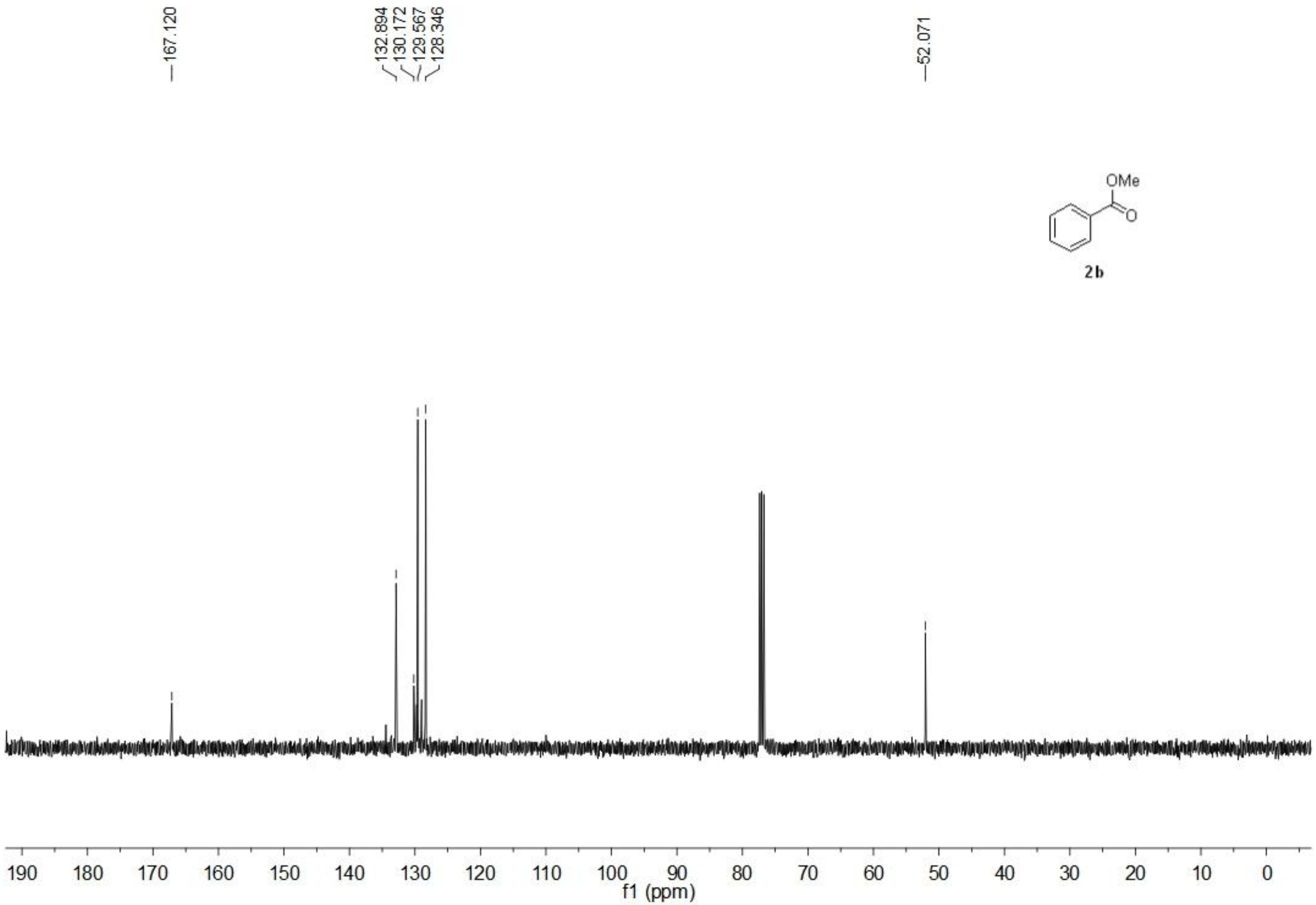
2 a

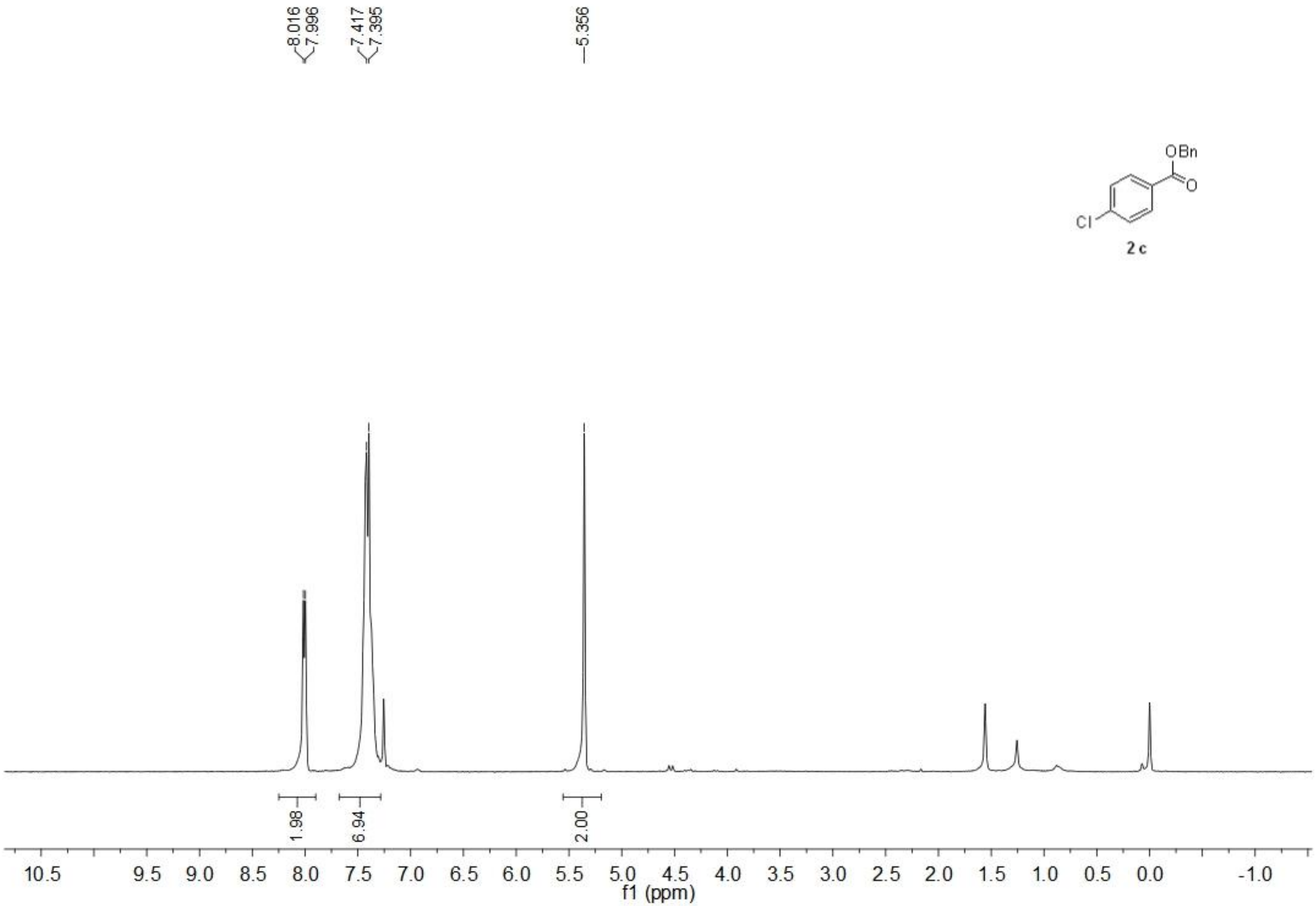

165.600
135.262
132.195
129.345
128.887
127.776
127.550
127.414
127.338
65.859
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
OBn
O

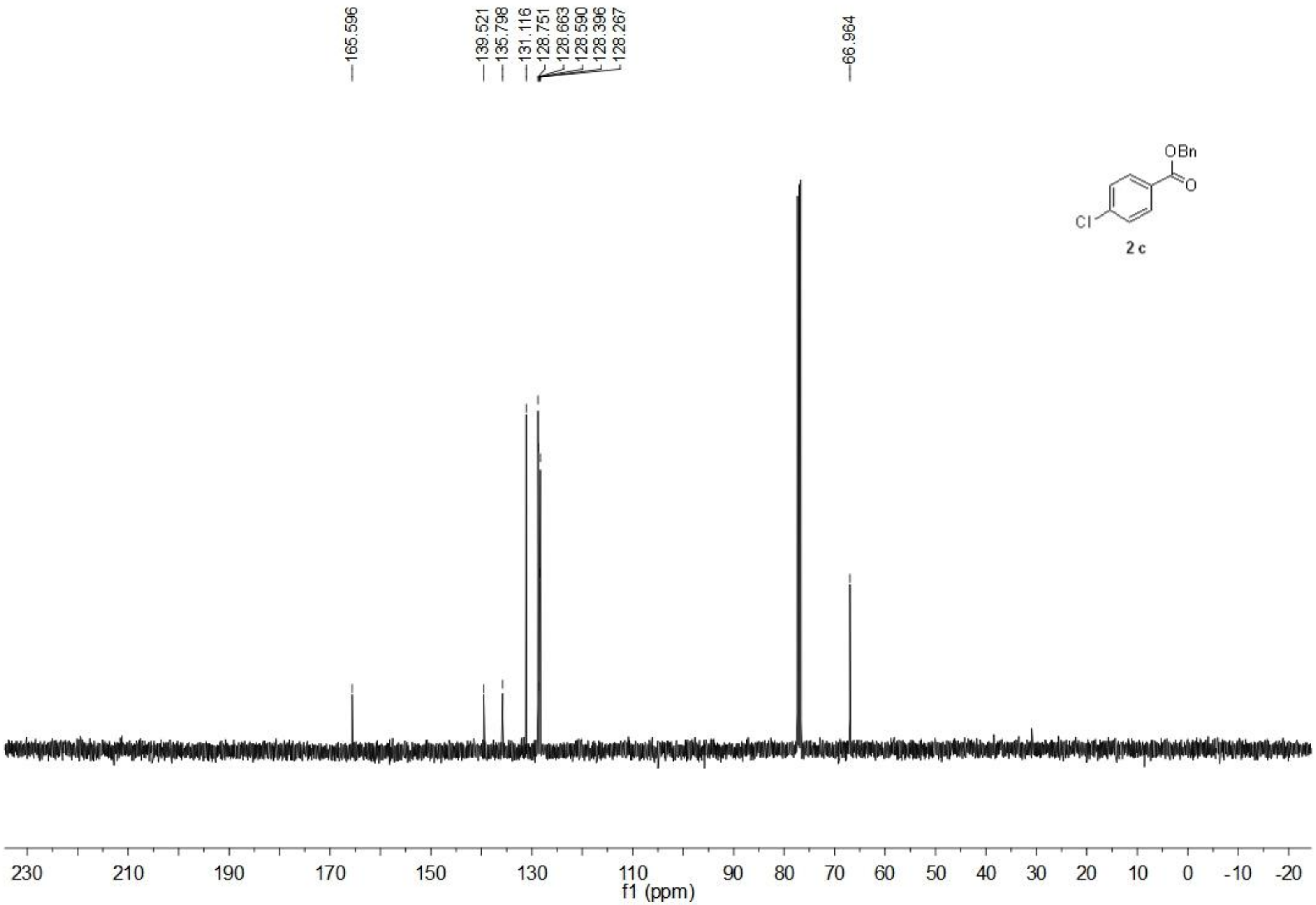
2 a


8.051
8.033
7.549
7.531
7.450
7.432
7.415
3.914
2.00
1.33
1.99
3.03
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)
OMe
O

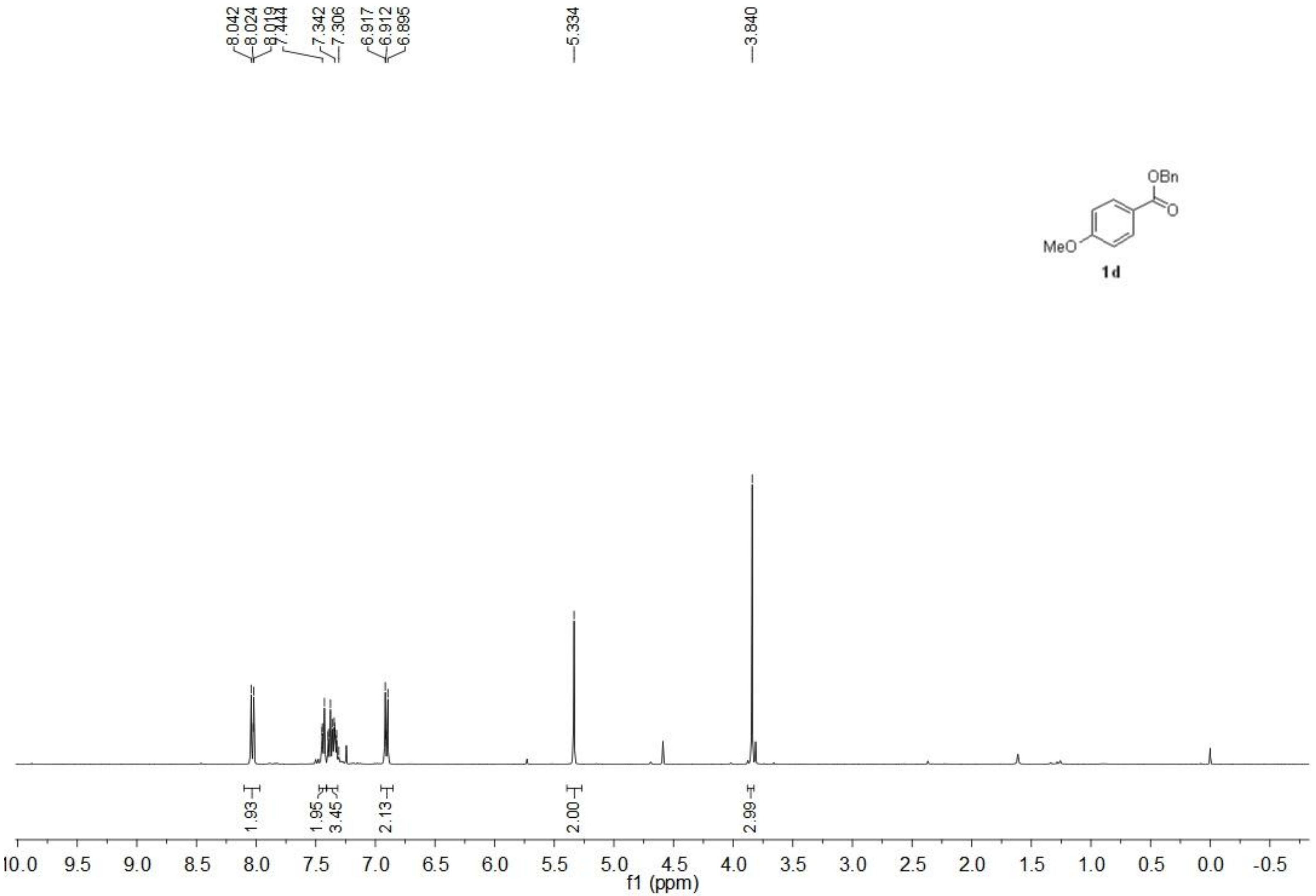
2b

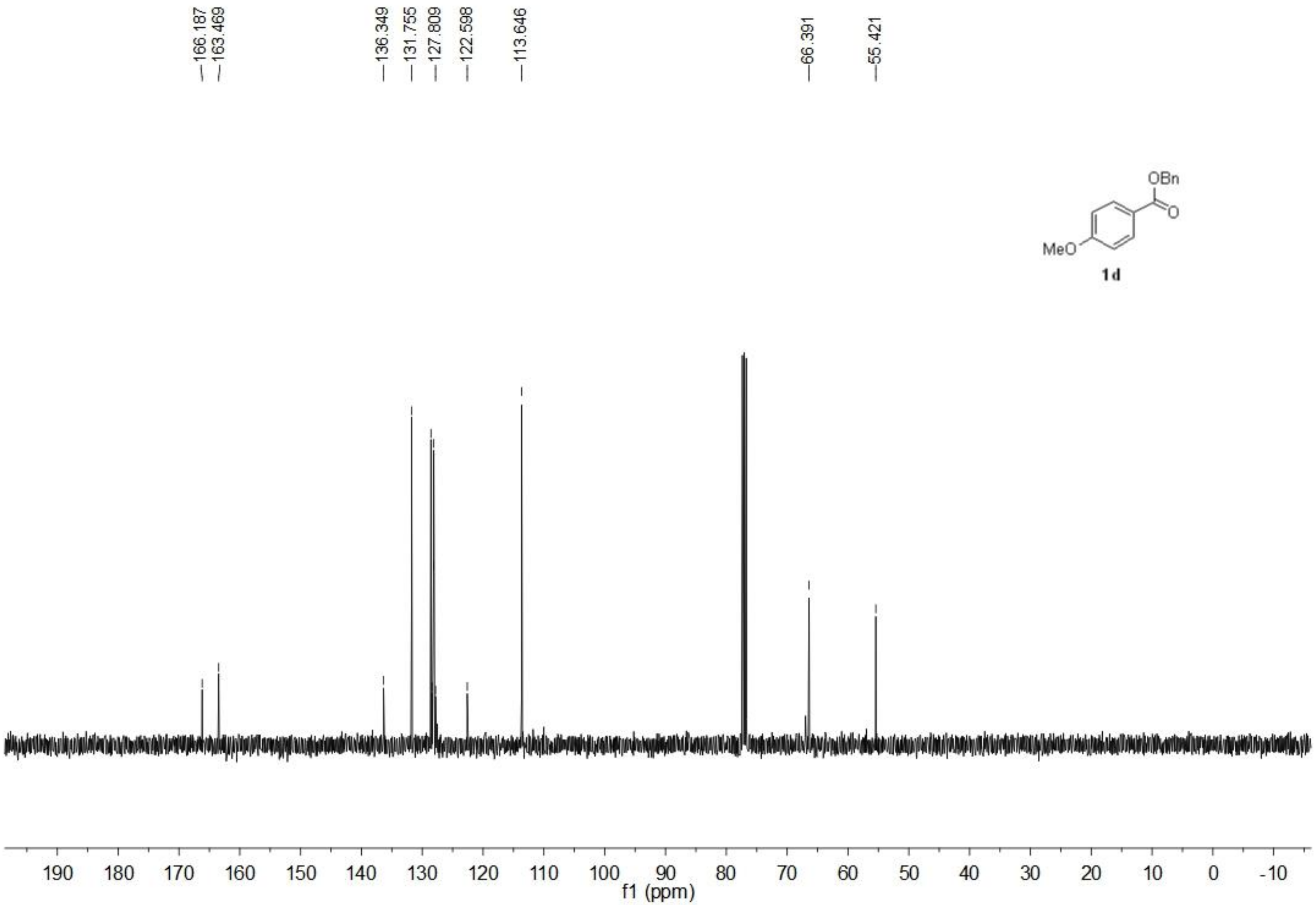

167.120
132.894
130.172
129.567
128.346
52.071
OMe
O
2b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

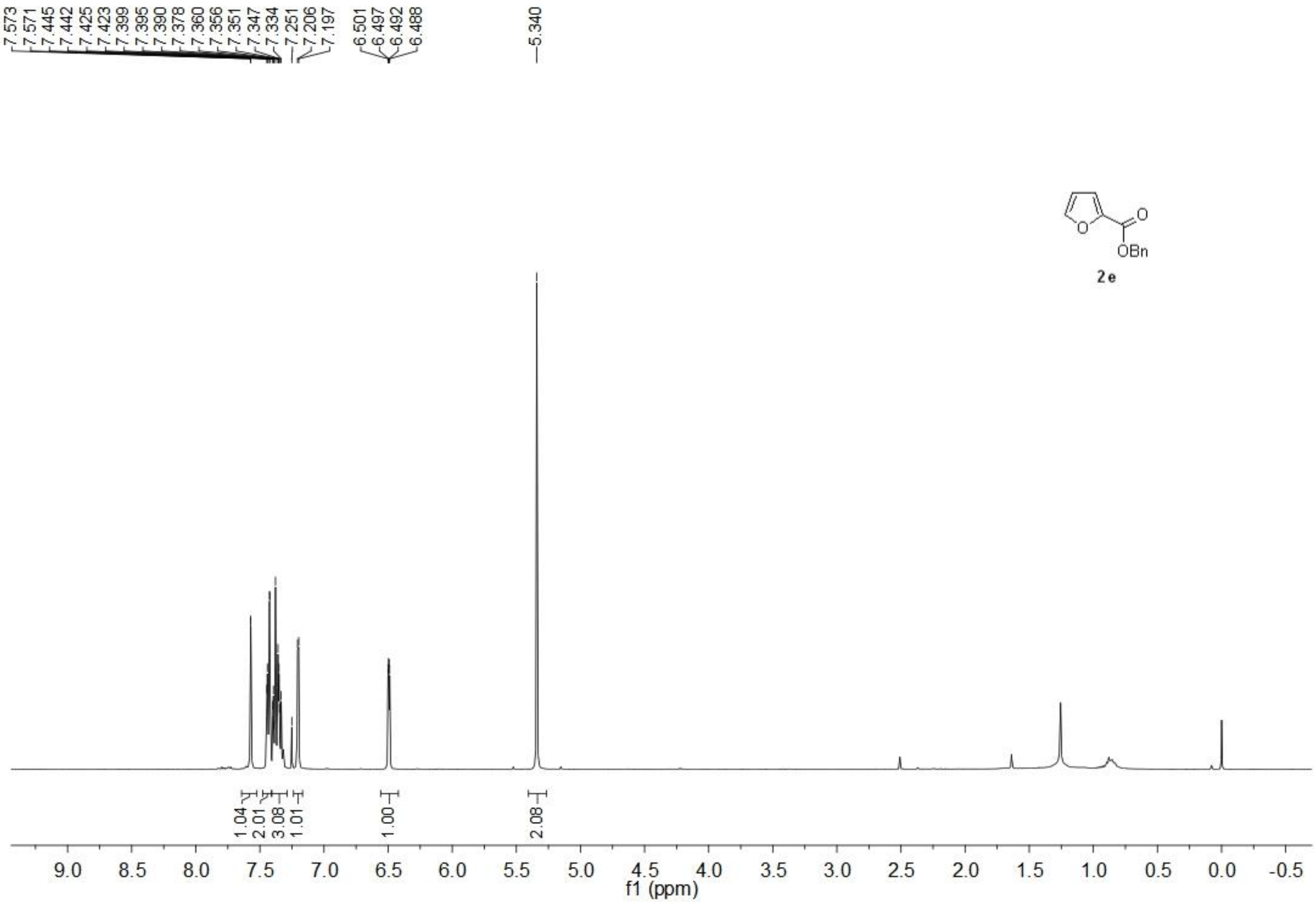

8.016
7.996
7.417
7.395
5.356
OBn
O
Cl
2c
1.98
6.94
2.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-1.0
f1 (ppm)


165.596
139.521
135.798
131.116
128.751
128.663
128.590
128.396
128.267
66.964
OBn
O
Cl
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)

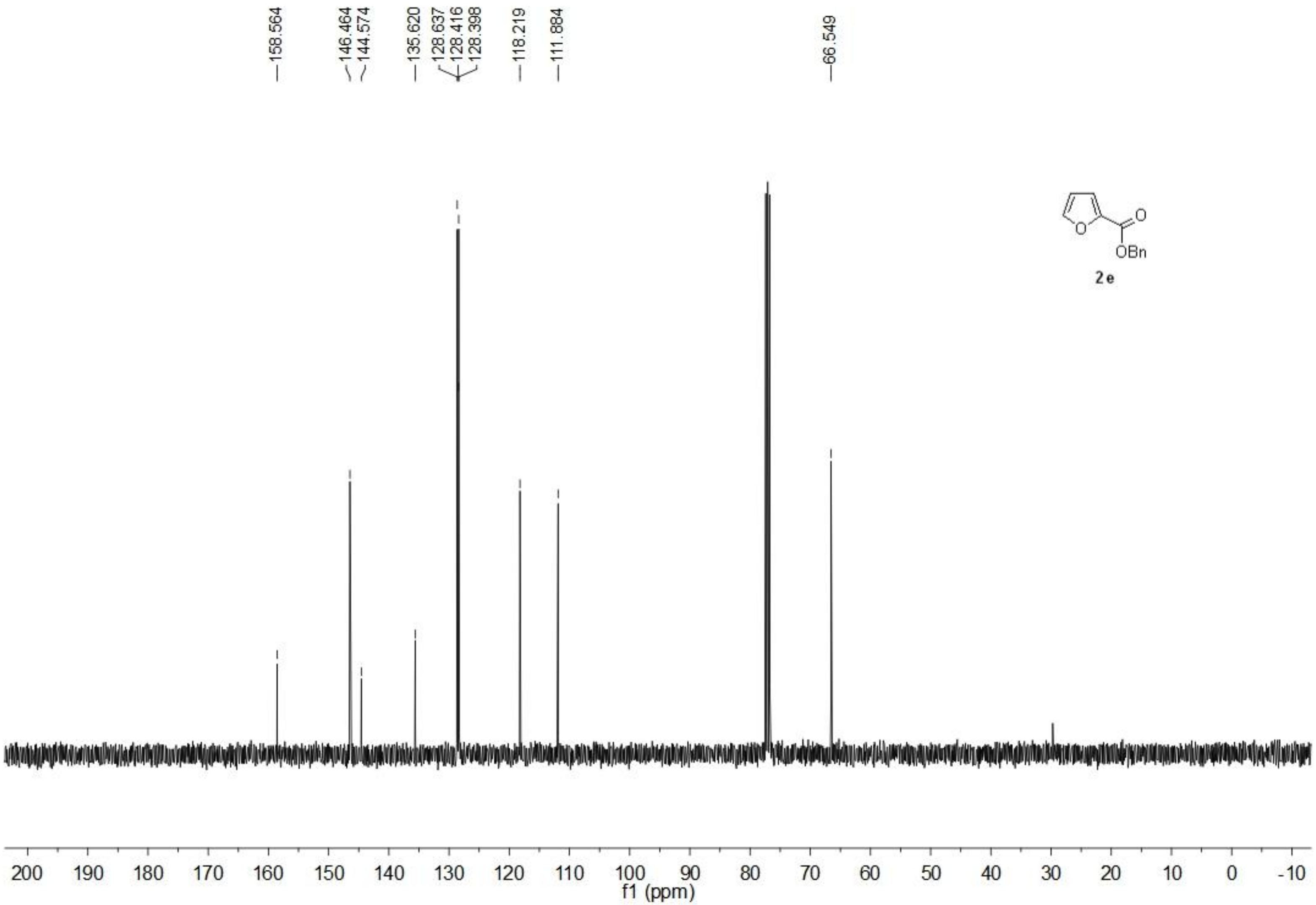
2c


8.042
8.024
8.019
7.444
7.342
7.306
6.917
6.912
6.895
5.334
3.840
OBn
O
MeO
1d
1.93
1.95
3.45
2.13
2.00
2.99
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

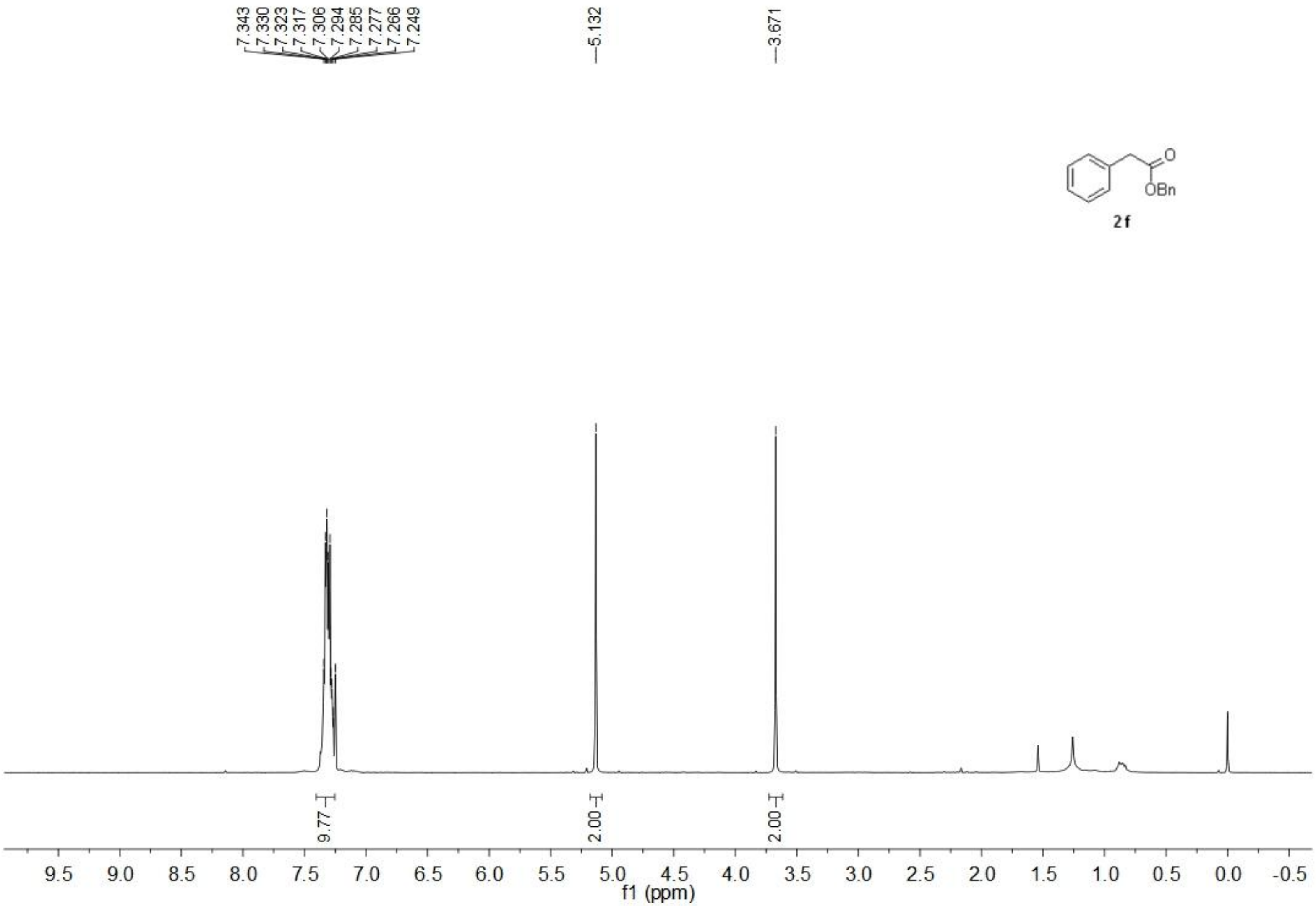

166.187
163.469
136.349
131.755
127.809
122.598
113.646
66.391
55.421
OBn
O
MeO
1d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.573
7.571
7.445
7.442
7.425
7.423
7.399
7.395
7.390
7.378
7.360
7.356
7.351
7.347
7.334
7.251
7.206
7.197
6.501
6.497
6.492
6.488
5.340
O
OBn
1.04
2.01
3.08
1.01
1.00
2.08
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

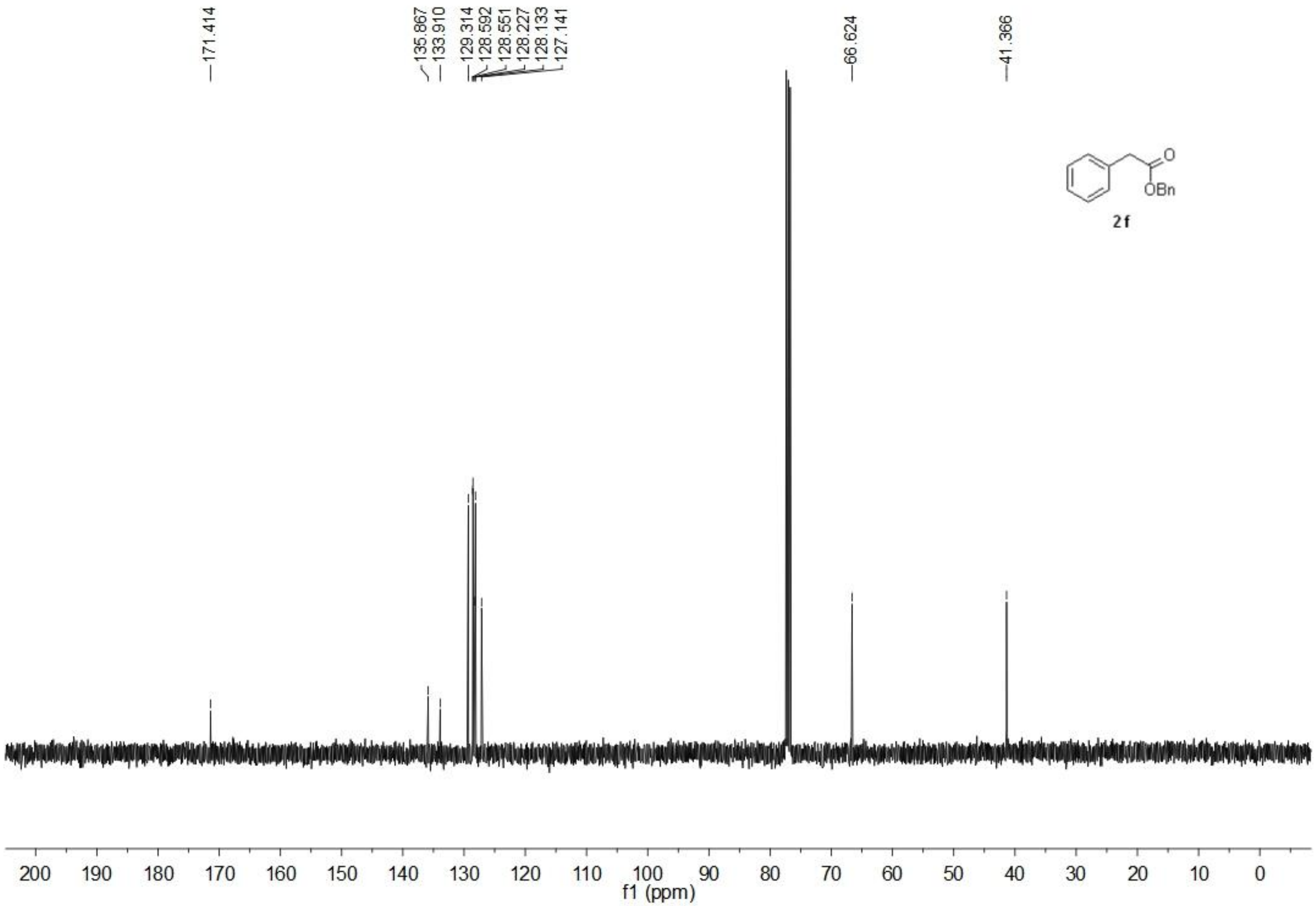
2e

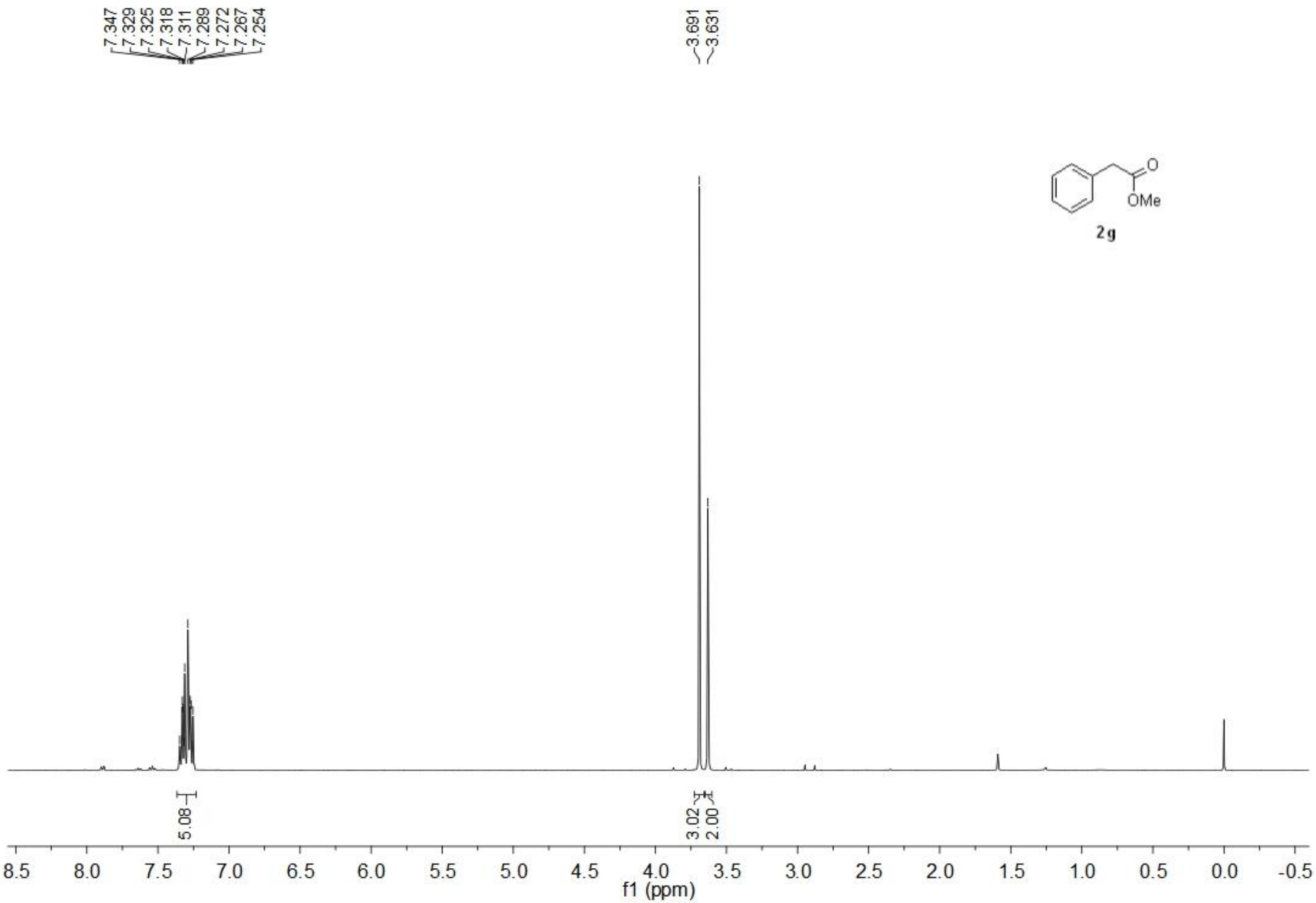

158.564
146.464
144.574
135.620
128.637
128.416
128.398
118.219
111.884
66.549
O
O
OBn
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

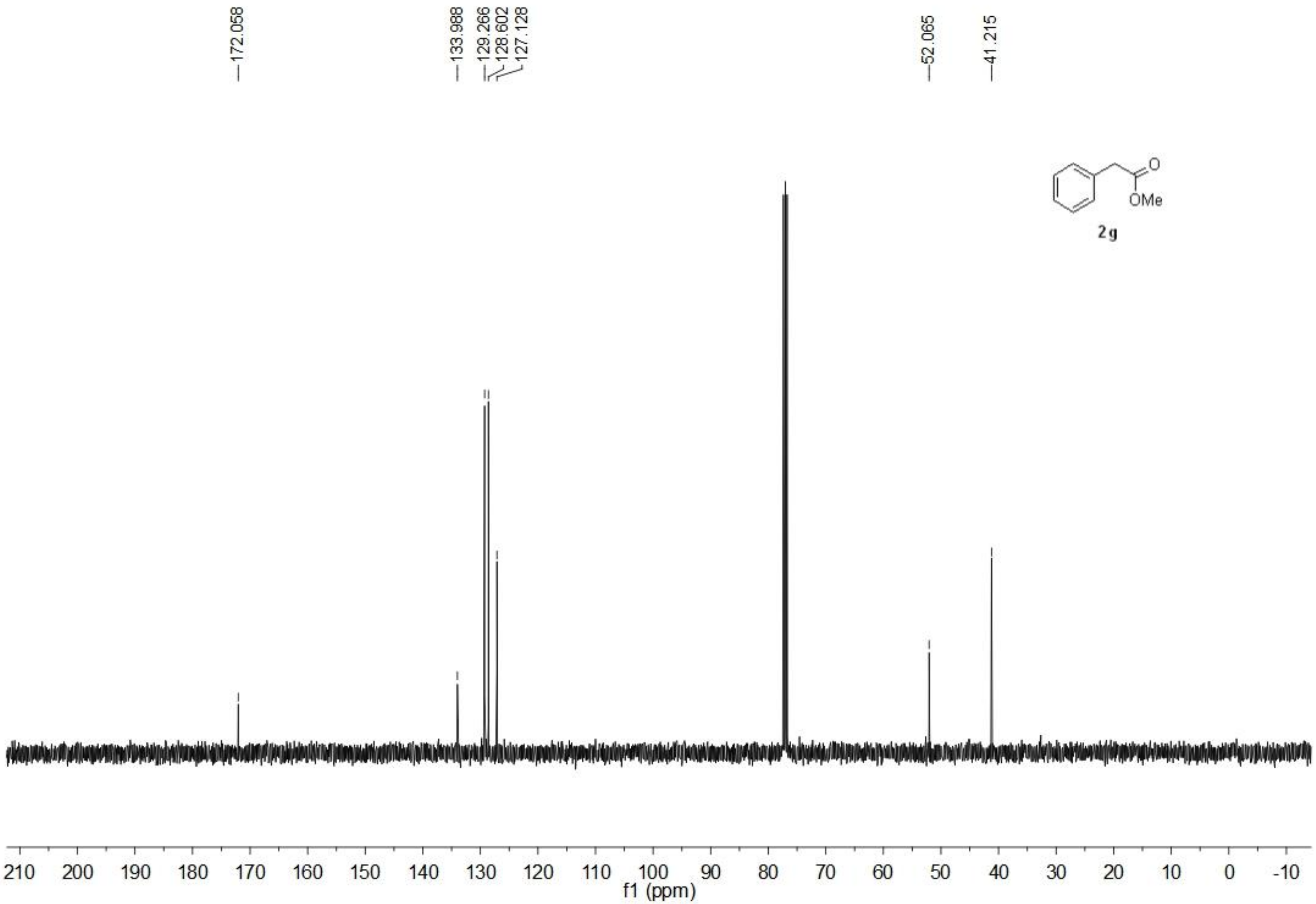
2e

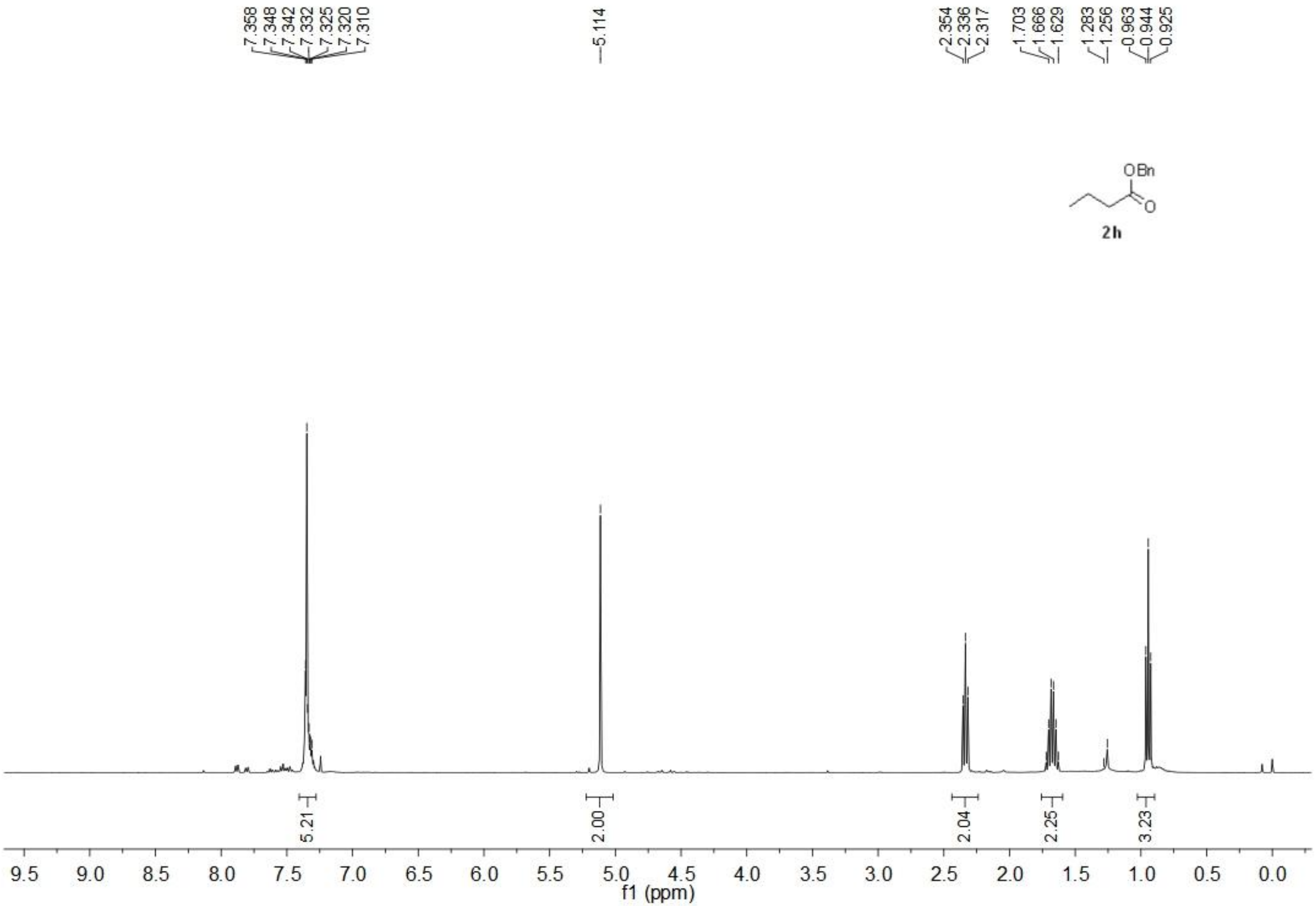

7.343
7.330
7.323
7.317
7.306
7.294
7.285
7.277
7.266
7.249
5.132
3.671
9.77
2.00
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
O
OBn

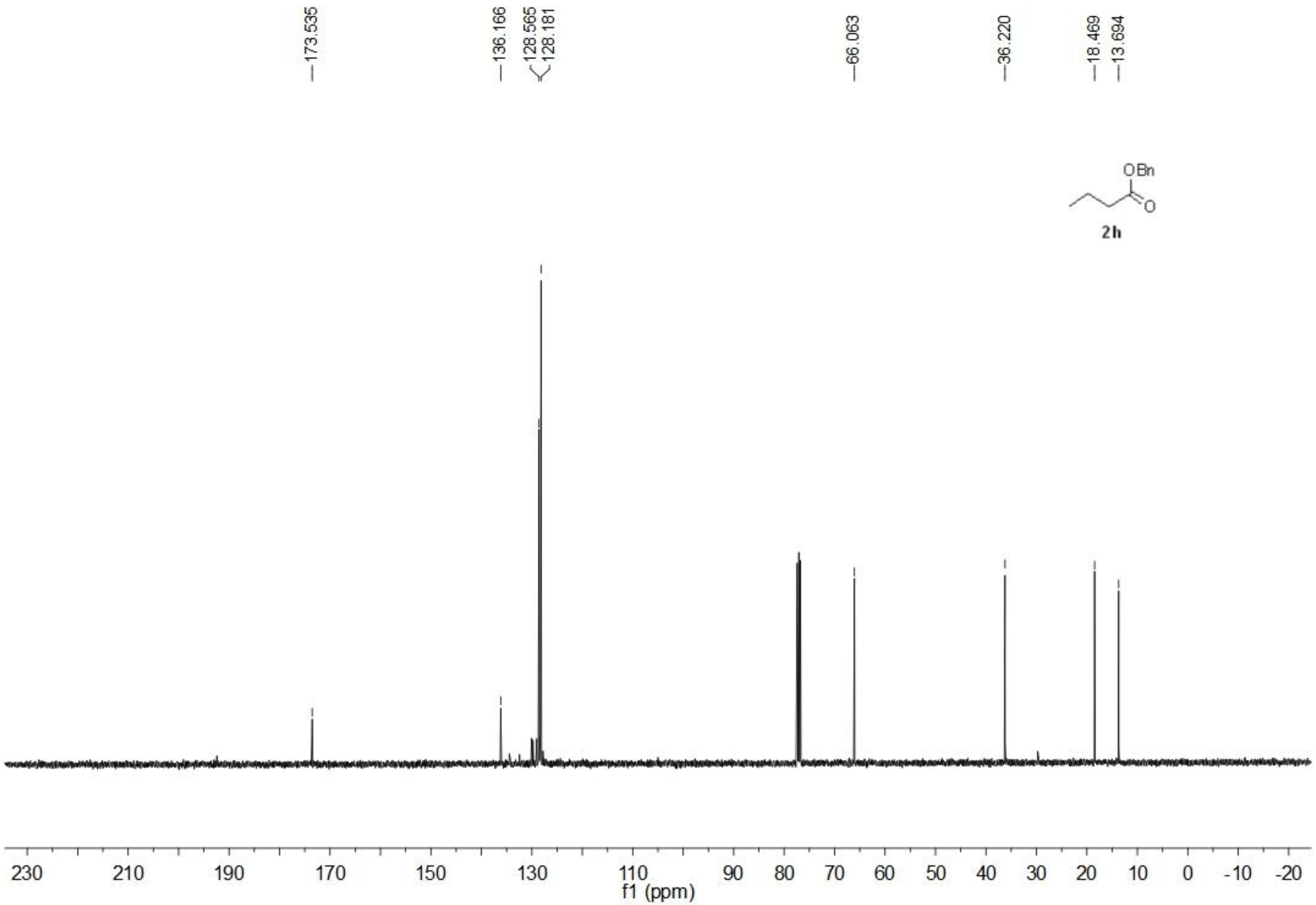
2f

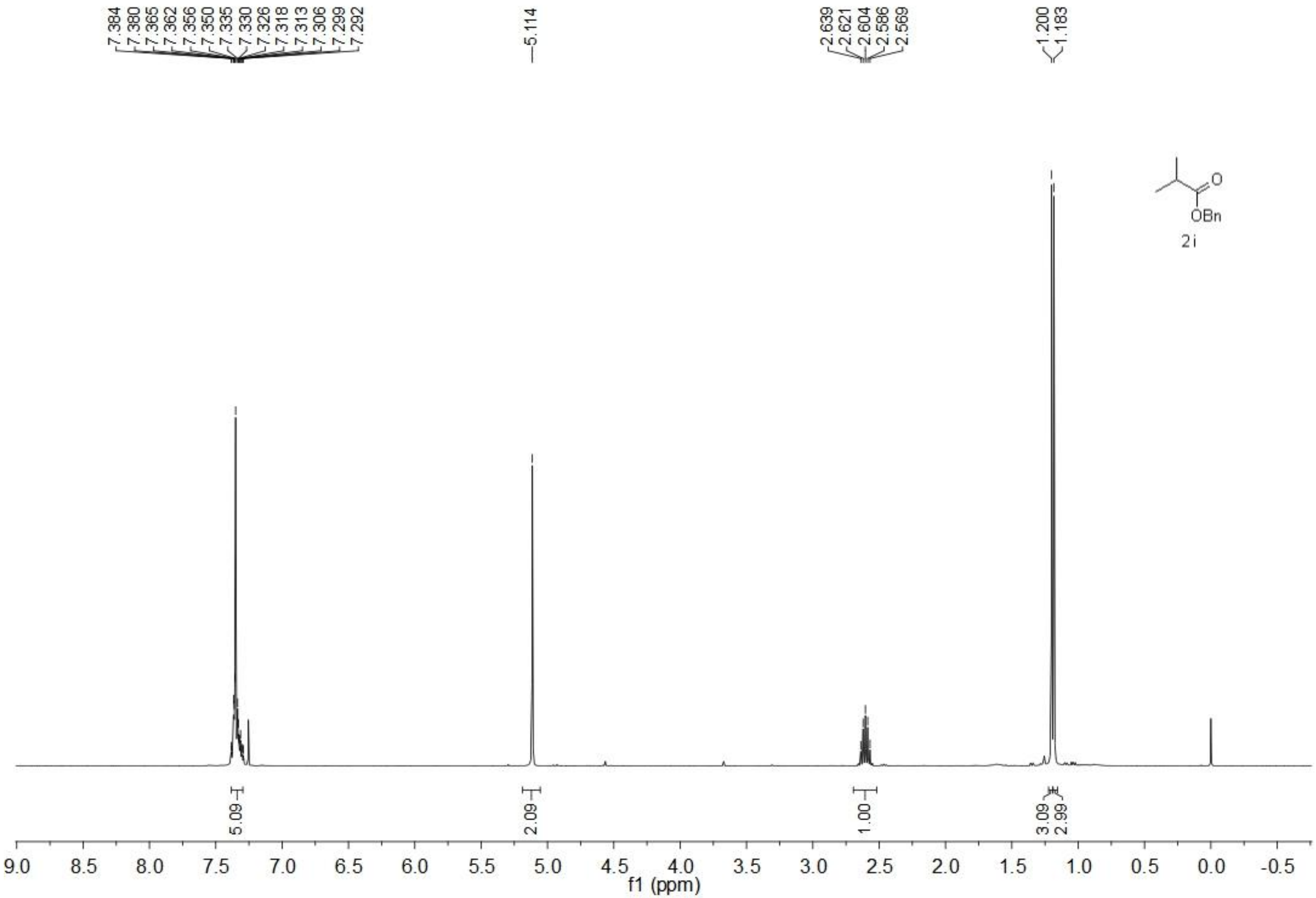

171.414
135.867
133.910
129.314
128.592
128.551
128.227
128.133
127.141
66.624
41.366
O
OBn
2f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.347
7.329
7.325
7.318
7.311
7.289
7.272
7.267
7.254
3.691
3.631
O
OMe
2g
5.08
3.02
2.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


172.058
133.988
129.266
128.602
127.128
52.065
41.215
O
OMe
2g
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.358
7.348
7.342
7.332
7.325
7.320
7.310
5.114
2.354
2.336
2.317
1.703
1.666
1.629
1.283
1.256
0.963
0.944
0.925
OBn
O
2h
5.21
2.00
2.04
2.25
3.23
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


173.535
136.166
128.565
128.181
66.063
36.220
18.469
13.694
OBn
O
2h
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)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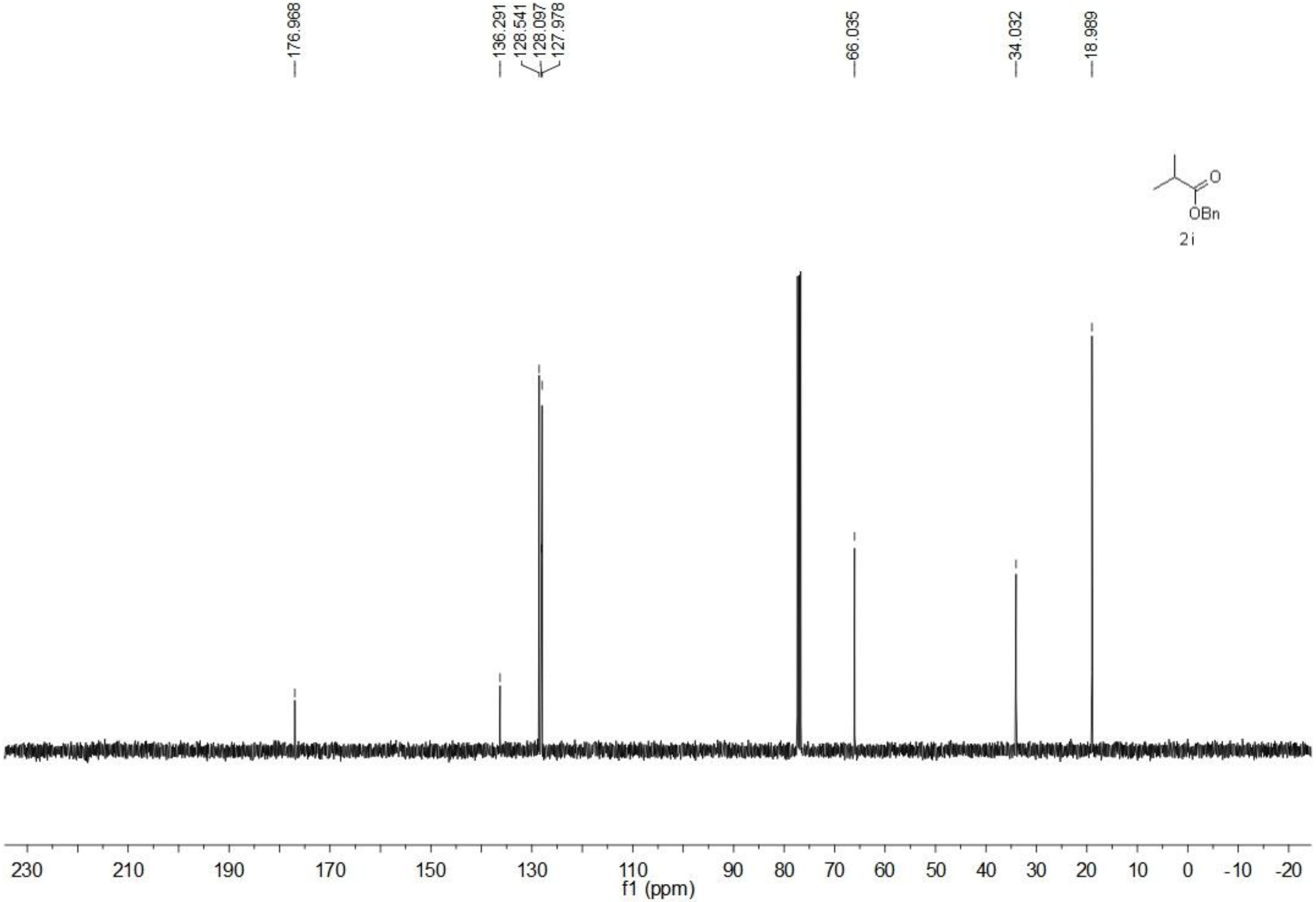
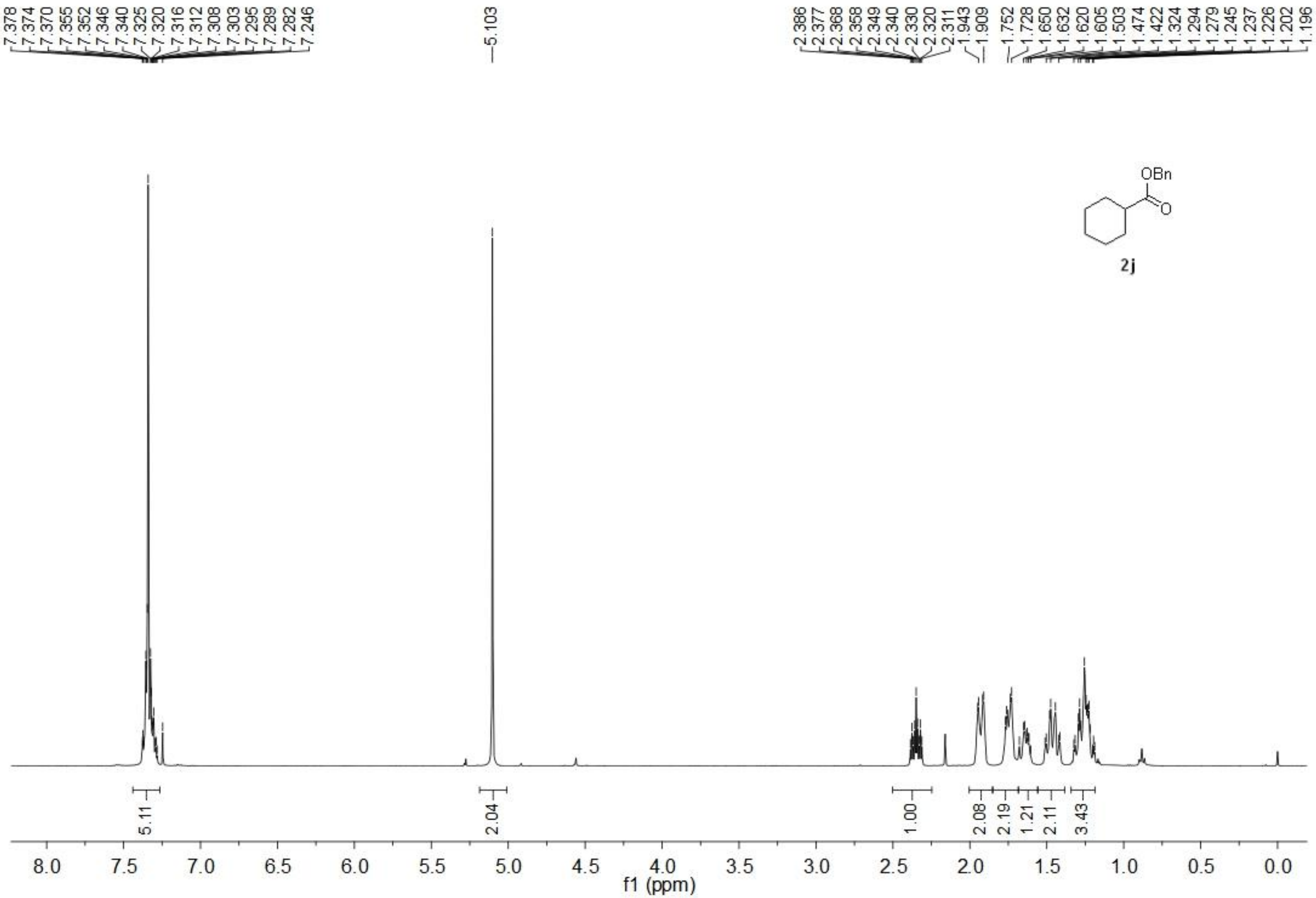
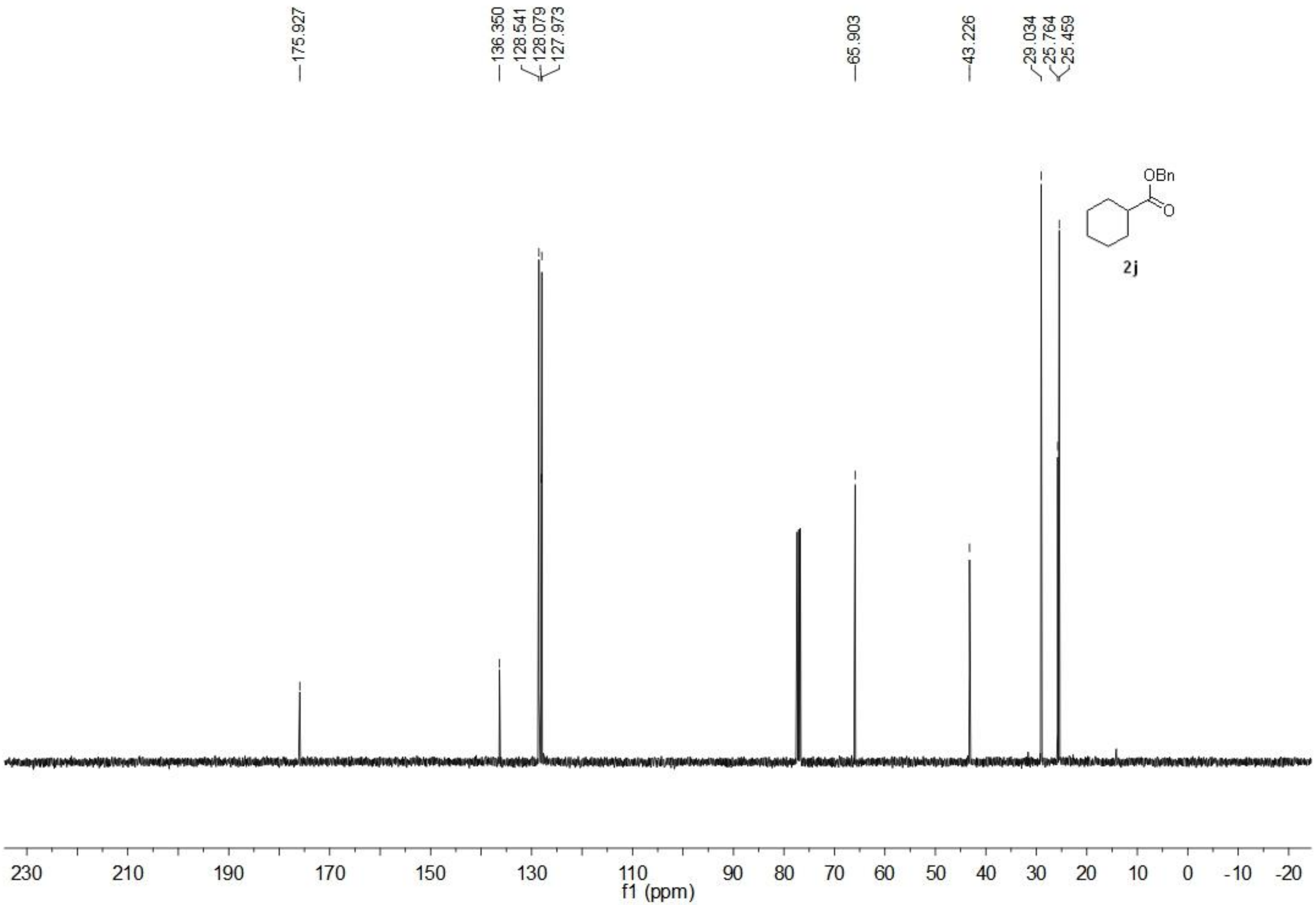
7.365
7.362
7.356
7.350
7.335
7.330
7.326
7.318
7.313
7.306
7.299
7.292
5.114
2.639
2.621
2.604
2.586
2.569
1.200
1.183
OBn
O
2i
5.09
2.09
1.00
3.09
2.99
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


176.968
136.291
128.541
128.097
127.978
66.035
34.032
18.989
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)
O
OBn

2i


7.378 7.374 7.370 7.355 7.352 7.346 7.340 7.325 7.320 7.316 7.312 7.308 7.303 7.295 7.289 7.282 7.246
5.103
2.386 2.377 2.368 2.358 2.349 2.340 2.330 2.320 2.311 1.943 1.909
1.752 1.728 1.650 1.632 1.620 1.605 1.503 1.474 1.422 1.324 1.294 1.279 1.245 1.237 1.226 1.202 1.196
OBn
O
2j
5.11
2.04
1.00
2.08
2.19
1.21
2.11
3.43
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


175.927
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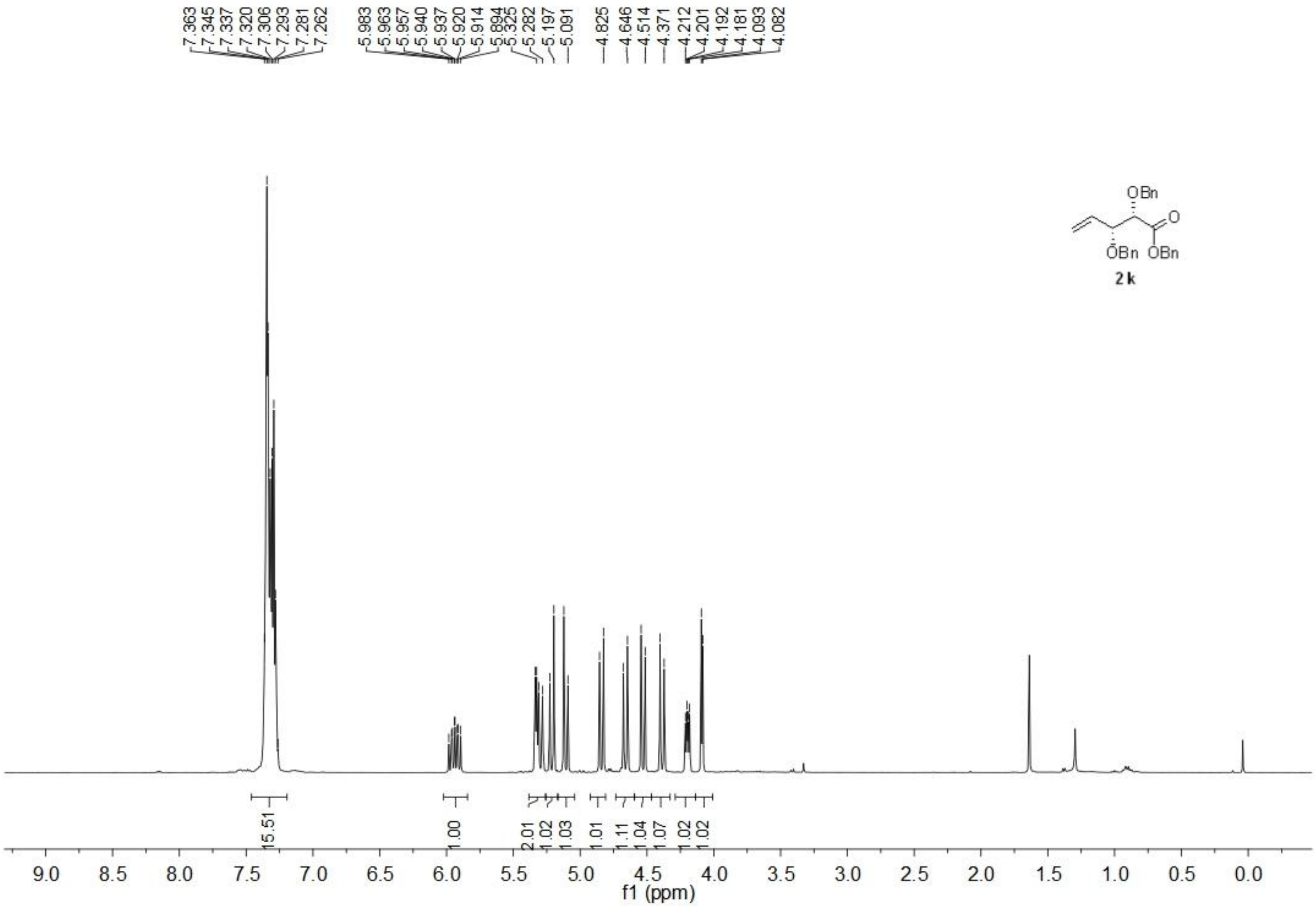
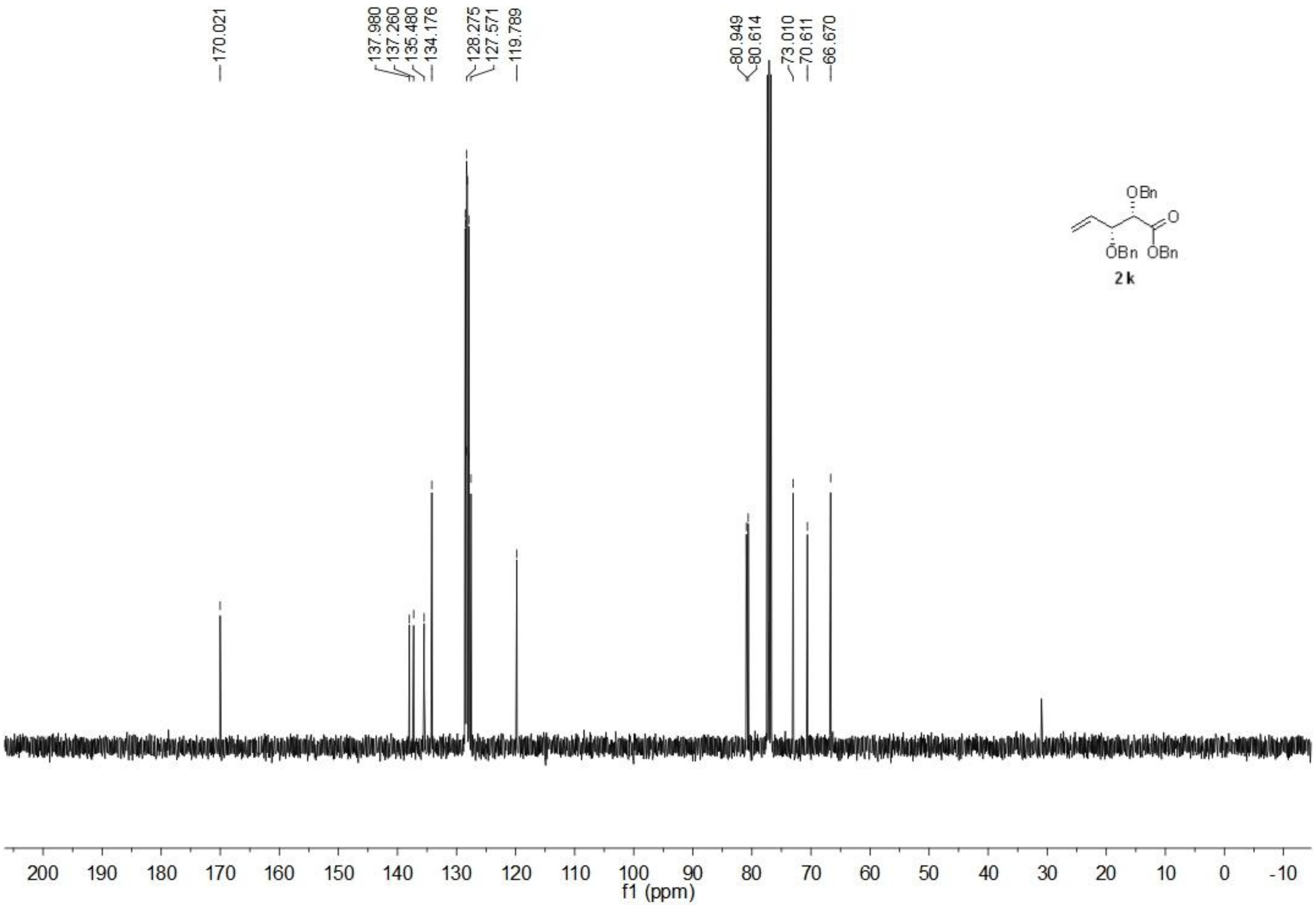
128.541
128.079
127.973
65.903
43.226
29.034
25.764
25.459
OBn
O
2j
230
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
-10
-20
f1 (ppm)


7.363
7.345
7.337
7.320
7.306
7.293
7.281
7.262
5.983
5.963
5.957
5.940
5.937
5.920
5.914
5.894
5.325
5.282
5.197
5.091
4.825
4.646
4.514
4.371
4.212
4.201
4.192
4.181
4.093
4.082
OBn
O
OBn OBn
2k
15.51
1.00
2.01
1.02
1.03
1.01
1.11
1.04
1.07
1.02
1.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


170.021
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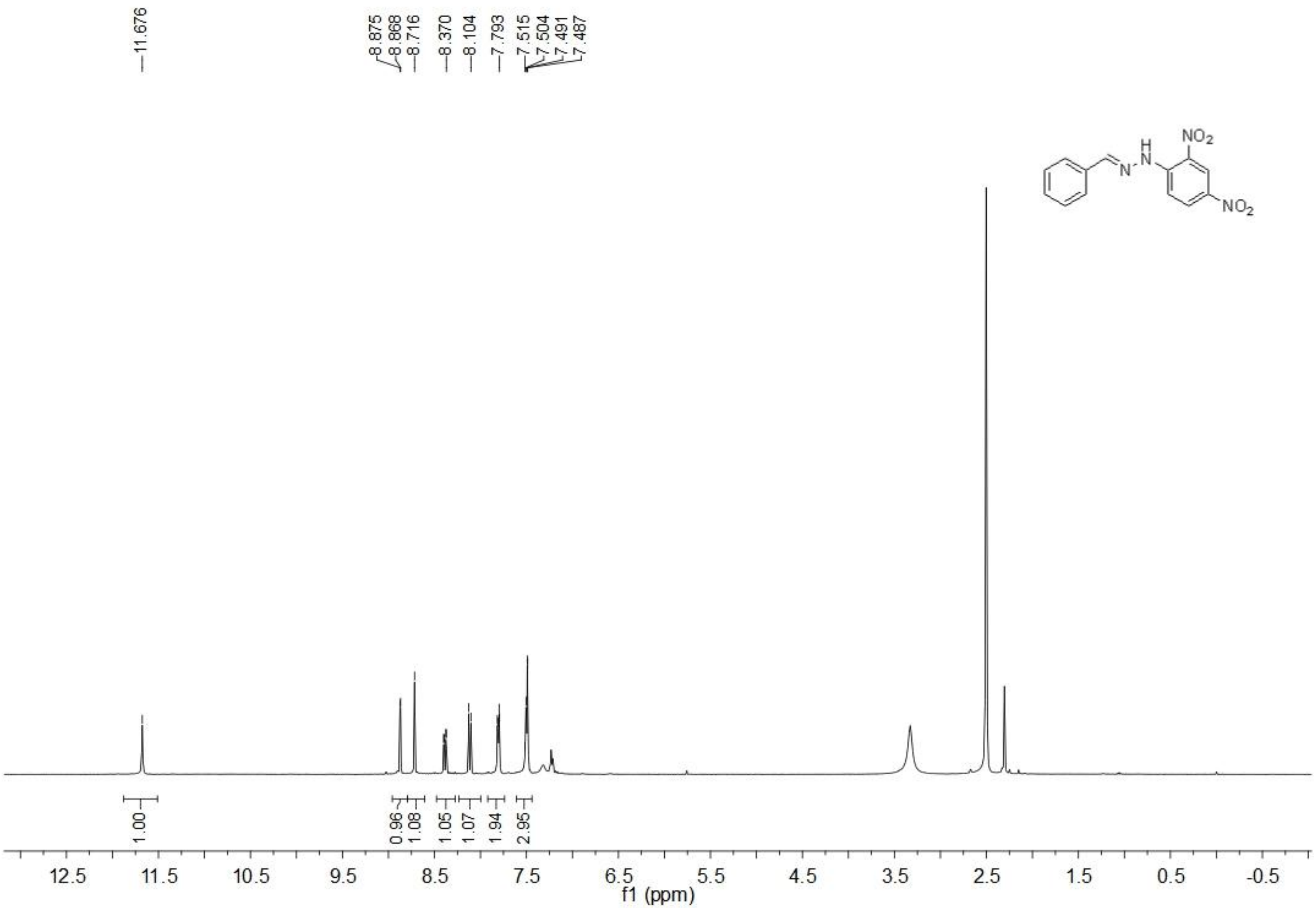
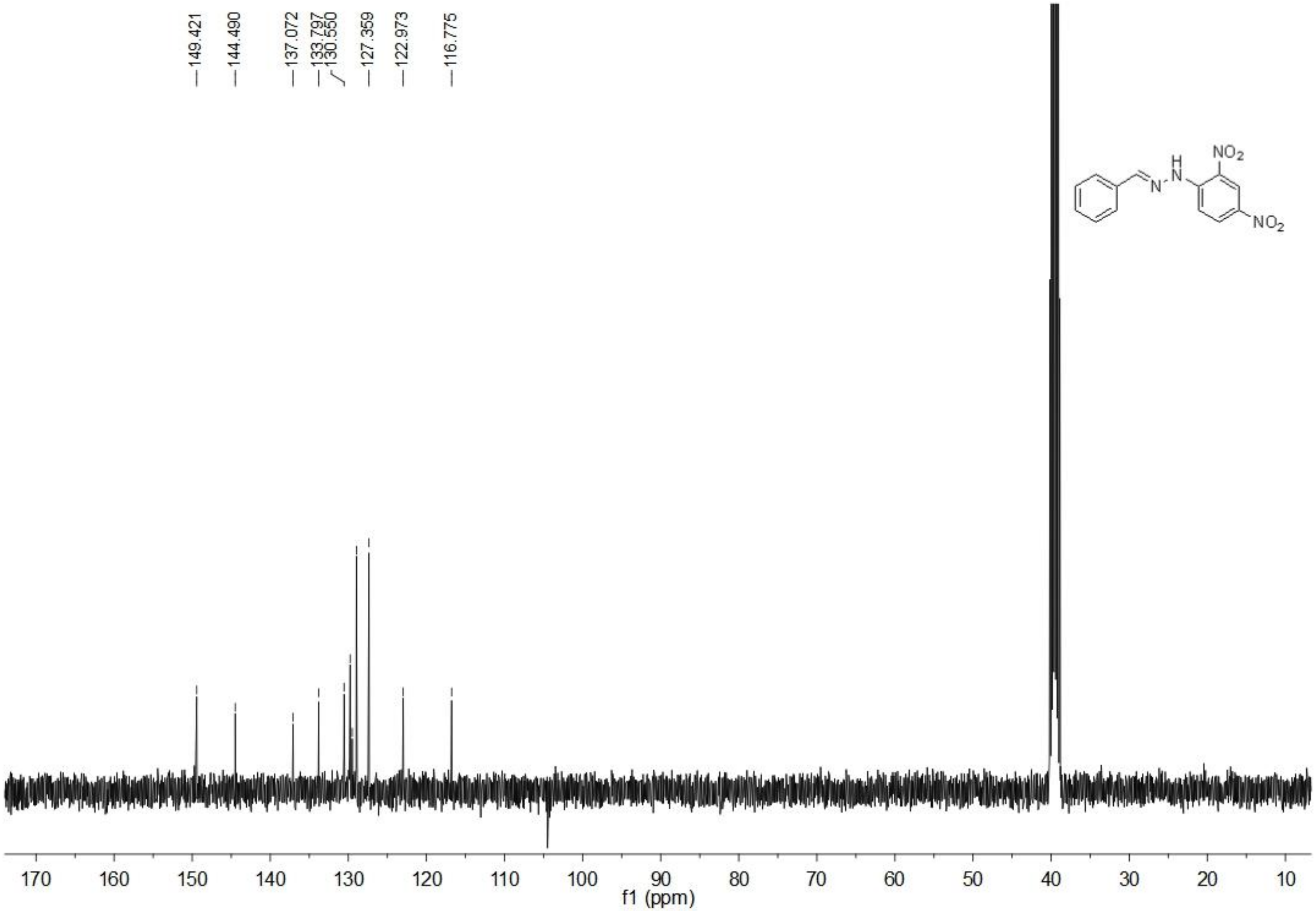
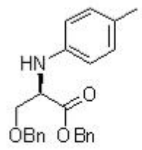
137.260
135.480
134.176
128.275
127.571
119.789
80.949
80.614
73.010
70.611
66.670
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
OBn
O
OBn
OBn

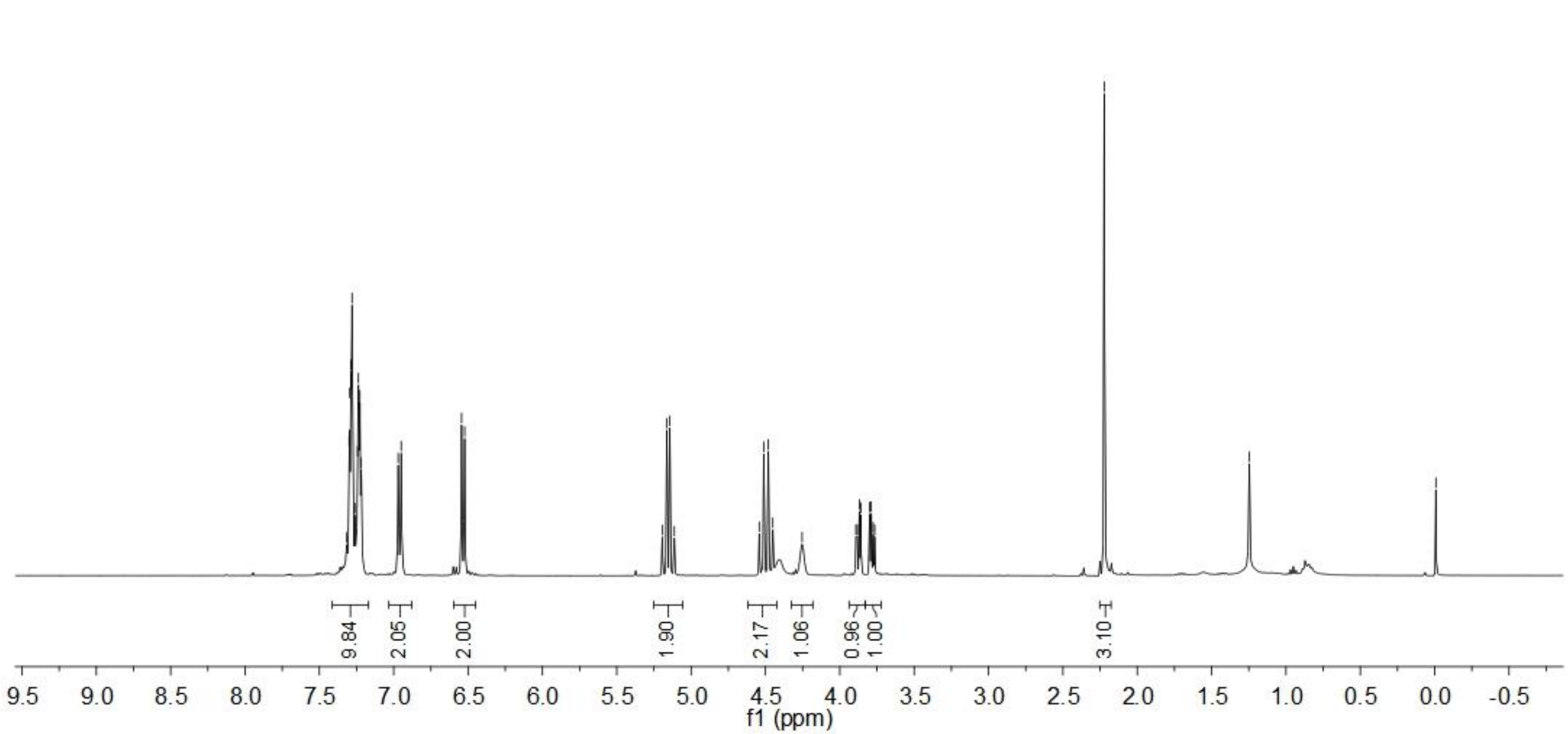
2k


11.676
8.875
8.868
8.716
8.370
8.104
7.793
7.515
7.504
7.491
7.487
H
N
N
NO2
NO2
1.00
0.96
1.08
1.05
1.07
1.94
2.95
12.5
11.5
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)


149.421
144.490
137.072
133.797
130.550
127.359
122.973
116.775
NO2
H
N
N
NO2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


HN
O
OBn
OBn

6


7.316
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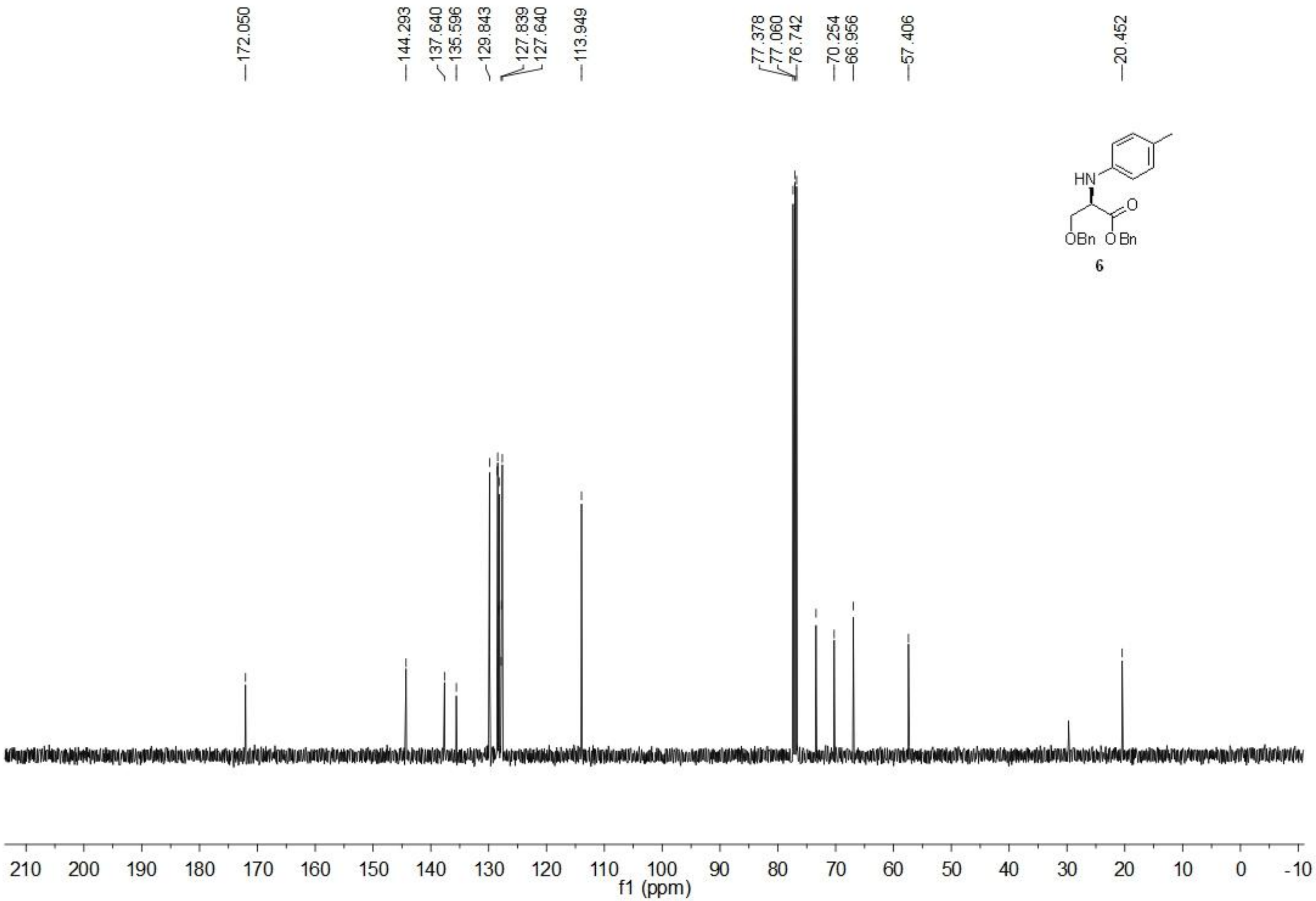
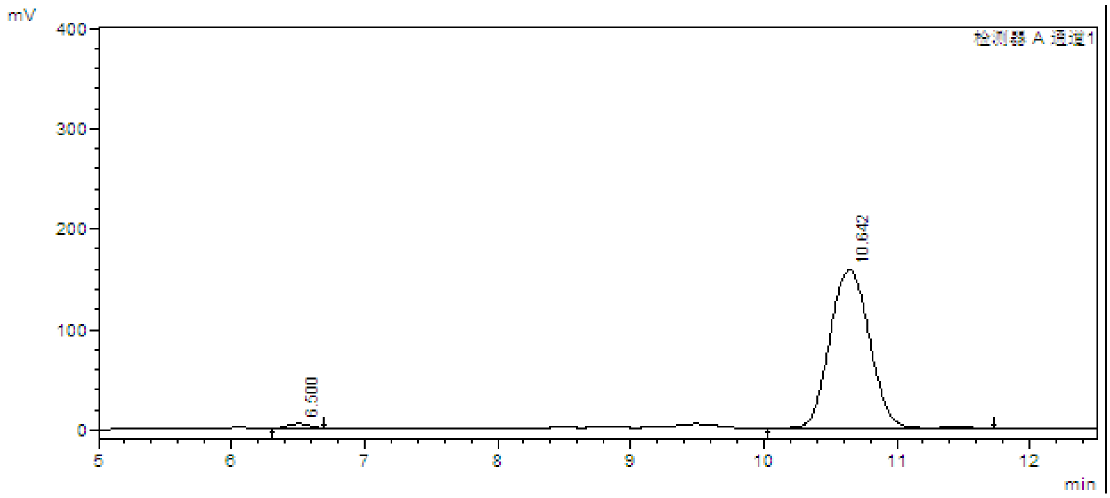
7.287
7.280
7.261
7.243
7.237
7.233
7.227
7.219
6.970
6.950
6.544
6.523
5.194
5.163
5.144
5.113
4.511
4.481
4.451
4.254
3.892
3.883
3.869
3.859
3.799
3.789
3.776
3.766
2.222
1.246
-0.008
9.84
2.05
2.00
1.90
2.17
1.06
0.96
1.00
3.10
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

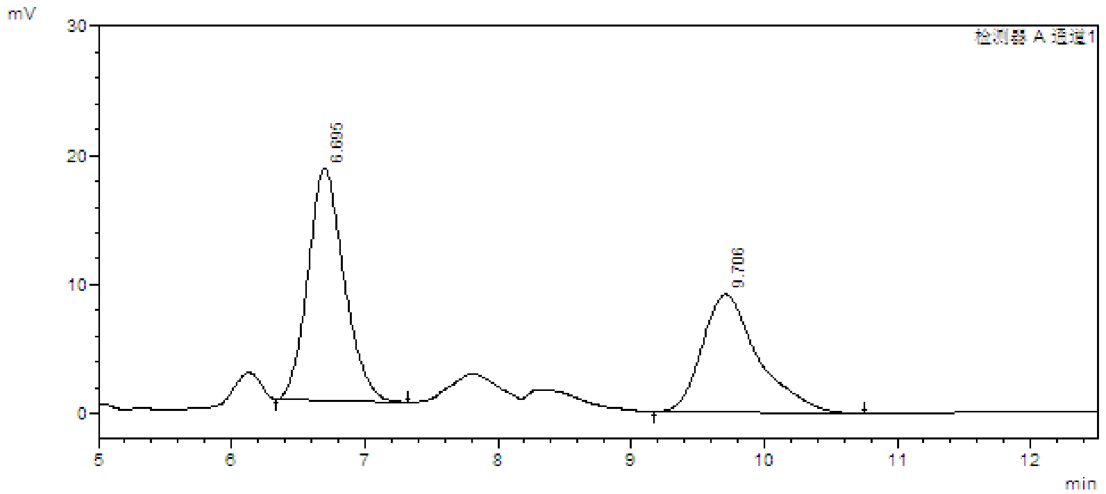

172.050
144.293
137.640
135.596
129.843
127.839
127.640
113.949
77.378
77.060
76.742
70.254
66.956
57.406
20.452
HN
O
OBn
O Bn
6
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

9. HPLC spectra for *ee* determination



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	6.500	61685	4859	1.823	2.984
2	10.642	3322834	157977	98.177	97.016
Total		3384518	162835	100.00	100.00



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	6.695	339139	17976	55.869	66.281
2	9.706	267887	9145	44.131	33.719
Total		607025	27122	100.00	100.00