# Electronic Supplementary Information

## A chemoselective oxidation of monosubstituted ethylene glycol: Facile synthesis of optically active α-hydroxy acids

**Kiran Chinthapally[a,b] and Sundarababu Baskaran*[a]**

*Department of Chemistry, Indian Institute of Technology Madras, Chennai 600 036, India.*
*Fax: 0091-44-22570545; Tel: 0091-44-22574218.*

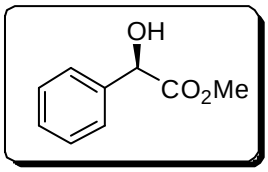
**E-mail: sbhaskar@iitm.ac.in**

## Table of Contents:

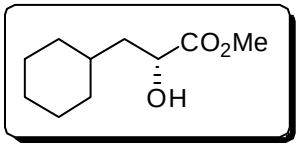
**General Information:**

All other reagents were used as received from either Aldrich or Lancaster chemical companies. Reactions requiring inert atmosphere were carried out under argon atmosphere. Infrared (IR) spectra were recorded on a JASCO 400 FT-IR spectrometer. $^{1}H$ NMR spectra were measured on Bruker AVANCE 400 MHz spectrometer. Chemical shifts were reported in ppm from tetramethylsilane in the case of $CDCl_3$ as an internal standard. $^{13}C$ NMR spectra were recorded on Bruker 100 MHz spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. The high-resolution mass spectra (HRMS) were performed on Micromass QTOF micro mass spectrometer equipped with a Harvard apparatus syringe pump. Optical rotations were measured on a JASCO P-2000 polarimeter. For thin layer chromatography (TLC) analysis throughout this work, E-merck precoated TLC plates (silica gel 60 F254 grade, 0.25 mm) were used. Acme (India) silica gel (100-200 mesh) was used for column chromatography. The enantiomeric excess was determined by chiral HPLC analyses using DAICEL's CHIRALPAK ODH, OJH and ASH columns with hexanes/isopropyl alcohol mixtures as eluent.

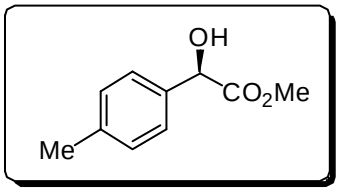
**General experimental procedure for the selective oxidation of vicinal diols to α-hydroxy acids:** To a stirred solution of compound **1** (138 mg, 1 mmol) in acetone (6 mL) and 5% aqueous $NaHCO_3$ solution (2.6 mL) at 0 °C was added KBr (12 mg, 0.1 mmol) followed by TEMPO (172 mg, 1.1 mmol). To this mixture at 0 °C, 4% NaOCl (3.7 mL, 2.0 mmol) was added dropwise and the resultant mixture was stirred at 0 °C. After 1.5 h aq 5% $NaHCO_3$ solution (3.7 mL) was added, solvent was removed under reduced pressure and the aqueous layer was washed with ether (2 x 7 mL) to remove TEMPO impurities. Then the aqueous layer was acidified to pH 6 with 1N hydrochloric acid at 0 °C and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were washed with water, brine and dried over anhydrous $Na_2SO_4$. The organic layer was concentrated under reduced pressure and the crude compound was treated with diazomethane in ether to furnish the corresponding methyl ester **2.** The crude compound **2** on column chromatographic purification over silica gel using 8-10% EtOAc in hexane as solvent gradient afforded the pure methyl ester **2** (159 mg, 96%) as a white solid.



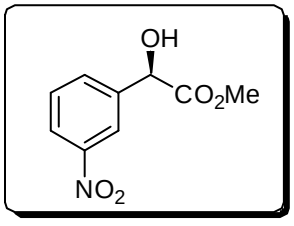

**(R)-methyl 2-hydroxy-2-phenylacetate (2).** $[\alpha]^{32}_{D}$ = –150.07 (c 1, $CHCl_3$); **IR (KBr disc):** 3438, 2953, 2924, 1732, 1493, 1454, 1437, 1214, 1176, 1090, 1065, 1028, 1005, 976, 925, 900; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.43–7.31 (m, 5H), 5.18 (d, *J* = 4.8 Hz, 1H), 3.73 (s, 3H), 3.61 (d, *J* = 3.6 Hz, 1H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 174.20, 138.3, 128.7, 128.6, 126.6, 73.0, 53.1; **HRMS** ($C_9H_{10}O_3Na$, ESI): calculated 189.0528, $[M+Na]^+$, found 189.0531. HPLC analysis of the compound **2** (Daicel OJ-H, 10% IPA/hexane, flow rate 0.3 mL/min, λ = 254 nm, 98% ee): $t_R$ 45.81 min (major enantiomer) and 51.55 min (minor enantiomer).




**(*R*)-methyl 3-cyclohexyl-2-hydroxypropanoate(4).** $[\alpha]^{32}_{D}$ = –12.2 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3455, 2920, 2849, 1735, 1444, 1210, 1140, 1092, 1014, 975, 752; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 4.27–4.22 (m, 1H), 3.78 (s, 3H), 2.74, (d, *J* = 3.6Hz, 1H), 1.85–1.82 (m, 1H), 1.73–1.51 (m, 7H), 1.30–1.16 (m, 3H), 0.97–0.91 (m, 2H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 176.5, 68.6, 52.5, 42.3, 34.1, 33.8, 32.4, 26.6, 26.4, 26.1; **HRMS** ($C_{10}H_{18}O_3Na$, ESI): calculated 209.1154, $[M+Na]^+$, found 209.1155: HPLC analysis of the analysis O-Bz derivative of the compound **4** (Daicel OJ-H, 1% IPA/hexane, flow rate 0.4 mL/min, λ = 254 nm, 62% ee): $t_R$ 15.5 min (major enantiomer) and 16.67 min (minor enantiomer).

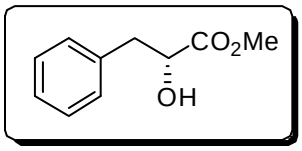



**(*R*)-methyl 2-hydroxy-2-p-tolylacetate(6).** $[\alpha]^{32}_{D}$ = –137.22 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3457, 2952, 1739, 1513, 1438, 1221, 1191, 1083, 980; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.3 (d, *J* = 8Hz, 2H), 7.18 (d, *J* = 8.8Hz, 2H), 5.14 (d, *J* = 5.2Hz, 1H), 3.75 (s, 3H), 3.47 (d, *J* = 5.2Hz, 1H), 2.35 (s, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 174.4, 138.4, 135.5, 129.4, 126.7, 72.9, 53.0, 21.3; **HRMS** ($C_{10}H_{12}O_3Na$, ESI): calculated 203.0684, $[M+Na]^+$, found 203.0687: HPLC analysis of the compound **6** (Daicel OJ-H, 10% IPA/hexane, flow rate 0.3 mL/min, λ = 254 nm, >99 % ee): $t_R$ 39.162 min (major enantiomer).

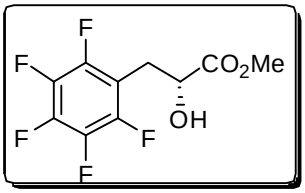



**(*R*)-methyl 2-hydroxy-2-(3-nitrophenyl)acetate(8).** $[\alpha]^{24}_{D}$ = –129.16 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3430, 2950, 1736, 1528, 1348; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 8.34 (t, *J* = 2Hz, 1H),

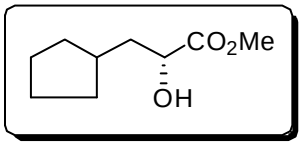
8.19 (ddd, $J$ = 0.8, 2.0, 8.0Hz, 1H), 7.80 (d, $J$ = 7.6Hz, 1H), 7.56 (t, $J$ = 8Hz, 1H), 5.30 (s, 1H), 3.80 (s, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 173.2, 148.5, 140.3, 132.7, 129.7, 123.6, 121.9, 71.9, 53.7; **HRMS** ($C_9H_9NO_5Na$, ESI): calculated 234.0378, $[M+Na]^+$, found 234.0383: HPLC analysis of the compound **8** (Daicel OD-H, 1% IPA/hexane, flow rate 0.8 mL/min, λ = 254 nm, 97% ee): $t_R$ 54.6 min (major enantiomer) and 58.62 min (minor enantiomer).




**(*R*)-methyl 2-hydroxy-3-phenylpropanoate(10).** $[\alpha]^{32}_D$ = +3.25 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3486, 3029, 2953, 2925, 2851, 1738, 1495, 1440, 1272, 1218, 1096, 1026, 748, 701; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.32–7.20 (m, 5H), 4.47–4.43 (m, 1H), 3.77 (s, 3H), 3.13 (dd, $J$ = 4.4, 14 Hz, 1H), 2.96 (dd, $J$ = 6.8, 13.6Hz, 1H), 2.69 (d, $J$ = 6Hz, 1H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 174.7, 136.5, 129.6, 128.6, 127.1, 71.4, 52.6, 40.7; **HRMS** ($C_{10}H_{12}O_3Na$, ESI): calculated 203.0684, $[M+Na]^+$, found 203.0681: HPLC analysis of the compound **10** (Daicel OJ-H, 10% IPA/hexane, flow rate 0.3 mL/min, λ = 254 nm, 40% ee): $t_R$ 41.65 min (major enantiomer) and 46.01 min (minor enantiomer).

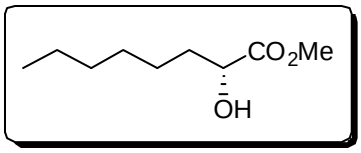



**(*R*)-methyl 2-hydroxy-3-(perfluorophenyl)propanoate(12).** $[\alpha]^{32}_D$ = +15.46 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3473, 2959, 1739, 1656, 1506, 1444, 1274, 1219, 1106, 1037, 982, 946, 730; **$^1$H NMR (500 MHz, $CDCl_3$):** δ 4.38 (q , $J$ = 5.5, 7.5Hz, 1H), 3.82 (s, 3H), 3.20 (dd, $J$ = 5.5, 14Hz, 1H), 3.04 (dd, $J$ = 7.5, 14Hz, 1H); **$^{13}$C NMR (125 MHz, $CDCl_3$):** 174.1, 145.6 (dddd, $J$ = 4.2, 8.3, 11.0, 245.2Hz, 2C), 139.9 (dtt, $J$ = 5.6, 13.4, 251.2Hz, 1C), 138.7–136.4 (m, 2C), 110.2 (td, $J$ = 3.8Hz, 18.4Hz, 1C), 69.1, 53.1, 27.8; **$^{19}$F NMR (470 MHz, $CDCl_3$):** -142.62–-142.67 (m, 2F), -156.09 (q, $J$ = 20.7, 35.7Hz, 1F), -162.68–-162.79 (m, 2F); **HRMS** ($C_{10}H_7O_3Na$, ESI): calculated 293.0213, $[M+Na]^+$, found 293.0210: HPLC analysis of the compound **12** (Daicel OJ-H, 10% IPA/hexane, flow rate 1 mL/min, λ = 254 nm, 40% ee): $t_R$ 6.18 min (minor enantiomer) and 7.47 min (major enantiomer).

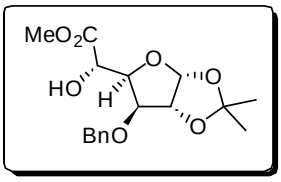



**(*R*)-methyl 3-cyclopentyl-2-hydroxypropanoate(14).** $[\alpha]^{32}_D$ = –7.091 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3476, 2946, 2864, 1736, 1443, 1212, 1157, 1095, 1019; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 4.20–4.16 (m, 1H), 3.77 (s, 3H), 2.69 (s, 1H), 2.05–1.97 (m, 1H), 1.86–1.68 (m, 4H),

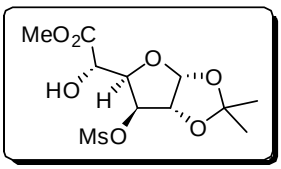
1.67-1.48 (m, 4H), 1.15-1.05 (m, 2H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 176.2, 70.3, 52.5, 40.9, 36.3, 33.1, 32.4, 25.2, 25.0; **HRMS** ($C_9H_{16}O_3Na$, ESI): calculated 195.0997, $[M+Na]^+$, found 195.0993: HPLC analysis of the analysis O-Bz derivative of the compound **14** (Daicel OJ-H, 1% IPA/hexane, flow rate 0.5 mL/min, λ = 254 nm, 69% ee): $t_R$ 17.55 min (major enantiomer) and 20.70 min (minor enantiomer).




**(*R*)-methyl 2-hydroxyoctanoate(16).** $[\alpha]^{32}_D$ = –5.82 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3476, 2925, 2860, 1736, 1450, 1212, 1132, 1083, 725; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 4.19–4.14 (m, 1H), 3.76 (s, 3H), 2.85 (d, *J* = 5.6Hz, 1H), 1.79–1.71 (m, 1H), 1.66–1.63 (m, 1H), 1.42–1.32 (m, 8H), 0.87–0.83 (m, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 175.9, 70.6, 52.5, 34.5, 31.7, 29.0, 24.8, 22.6, 14.1; **HRMS** ($C_9H_{18}O_3Na$, ESI): calculated 197.1154, $[M+Na]^+$, found 197.1151: HPLC analysis of the analysis O-Bz derivative of the compound **16** (Daicel OJ-H, 1% IPA/hexane, flow rate 0.5 mL/min, λ = 254 nm, 81% ee): $t_R$ 14.9 min (major enantiomer) and 17.75 min (minor enantiomer).

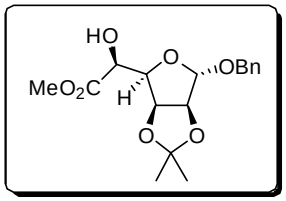



**(*S*)-methyl 2-((3a*R*,5*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2 dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-2-hydroxyacetate (18).** $[\alpha]^{28}_D$ = –30.98 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3463, 2984, 1739, 1445, 1378, 1214, 1162, 1077, 1024, 858, 744 ; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.37–7.30 (m, 5H), 6.02 (d, *J* = 4Hz, 1H), 4.67–4.60 (m, 2H), 4.58–4.50 (m, 2H), 4.39 (dd, *J* = 3.6, 6Hz, 1H), 4.14 (d, *J* = 4Hz, 1H), 3.74 (s, 3H), 3.42 (d, *J* = 9.6Hz, 1H), 1.48 (s, 3H), 1.32 (s, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 173.2, 136.7, 128.7, 128.3, 128.1, 112.2, 105.5, 83.3, 82.3, 79.8, 72.7, 69.9, 52.6, 26.9, 26.4; **HRMS** ($C_{17}H_{22}O_7Na$, ESI): calculated 361.1263, $[M+Na]^+$, found 361.1268.

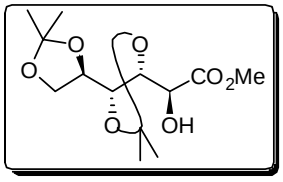



**(S)-methyl 2-((3aR,5R,6S,6aR)-2,2-dimethyl-6-(methylsulfonyloxy)tetrahydrofuro[2,3-d][1,3]dioxol-5-yl)-2-hydroxyacetate (20).** $[\alpha]^{25}_D$ = –14.71 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3514, 3056, 2987, 1737, 1442, 1365, 1264, 1219, 1179, 1164, 1087, 1022, 973, 958, 926, 852, 735; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 6.02 (d, *J* = 3.6Hz, 1H), 5.08 (d, *J* = 2.4Hz, 1H), 4.79 (d, *J* = 3.6Hz, 1H), 4.33–4.29 (m, 2H), 3.86 (s, 3H), 3.11 (s, 3H), 1.48 (s, 3H), 1.31 (s, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 173.5, 113.1, 105.6, 83.2, 82.3,

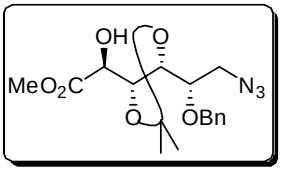
79.3, 68.1, 53.4, 38.2, 26.7, 26.4; **HRMS** ($C_{11}H_{18}O_9NaS$, ESI): calculated 349.0569, $[M+Na]^+$, found 349.0566.



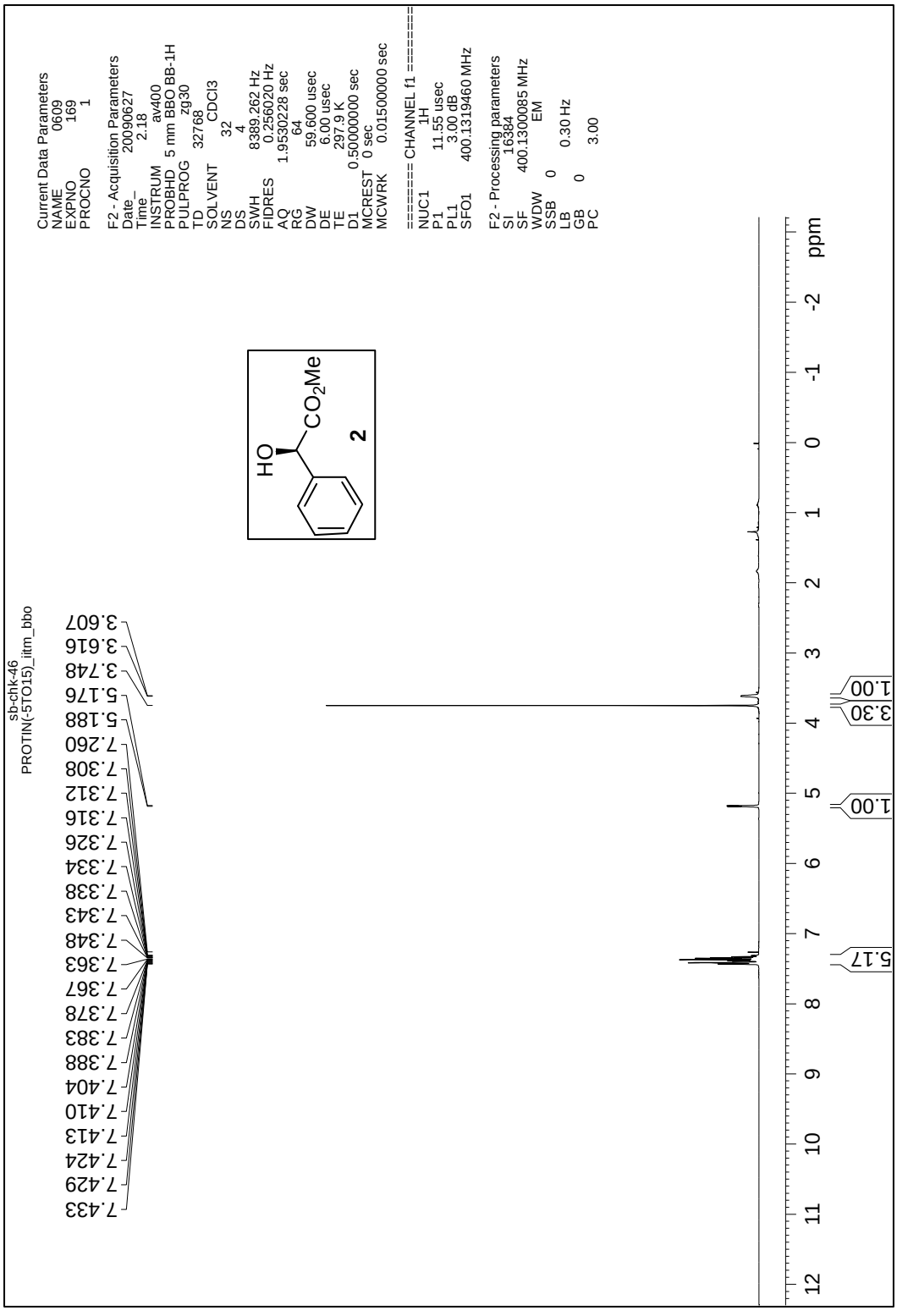
**(S)-methyl 2-((3aS,4R,6S,6aS)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-2-hydroxyacetate (22).** $[\alpha]^{25}_D$ = –37.69 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3504, 3056, 2988, 2955, 2870, 1736, 1669, 1497, 1440, 1375, 1263, 1216, 1106, 1018, 895, 862, 823, 738; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 7.33–7.19 (m, 5H), 4.88 (d, *J* = 11.6Hz, 1H), 4.76 (d, *J* = 4.4Hz, 2H), 4.58–4.52 (m, 3H), 3.90 (dd, *J* = 4.4, 7.6Hz, 1H), 3.75 (s, 3H), 3.24 (d, *J* = 7.6Hz, 1H), 1.48 (s, 3H), 1.28 (s, 3H); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 173.1, 137.2, 128.4, 128.2, 127.9, 114.9, 101.0, 80.1, 79.8, 77.5, 71.2, 70.3, 52.6, 25.7, 25.5; **HRMS** ($C_{17}H_{22}O_7Na$, ESI): calculated 361.1263, $[M+Na]^+$, found 361.1266.



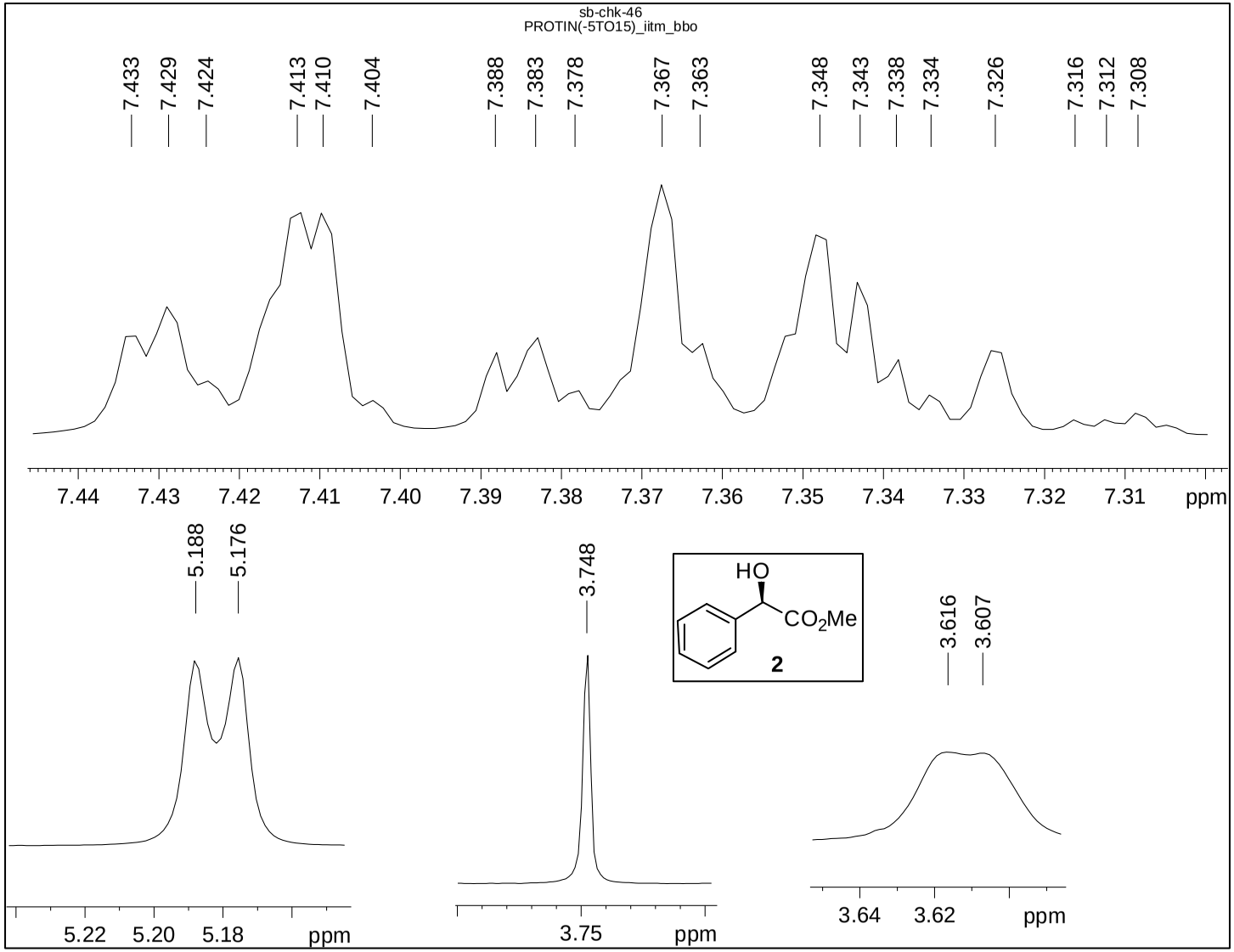
**(*S*)-methyl 2-hydroxy-2-((4*R*,4'*R*,5*R*)-2,2,2',2'-tetramethyl-4,4'-bi(1,3-dioxolan)-5-yl)acetate(24).** $[\alpha]^{28}_D$ = +28.07 (*c* 1, $CHCl_3$); **IR (KBr disc):** 3473, 2987, 2935, 2014, 1743, 1493, 1372, 1213, 1150, 1067, 987, 899, 843, 789; **$^1$H NMR (400 MHz, $CDCl_3$):** δ 4.45 (bs, 1H), 4.22 (dd, *J* = 3.2, 6.8Hz, 1H), 4.13 (dd, *J* = 5.6,8.4Hz, 1H), 4.03–3.92 (m, 3H), 3.78 (s, 3H), 3.33 (bs, 1H), 1.37 (s, 3H), 1.36 (s, 3H), 1.35 (s, 3H), 1.30 (s, 3H) ); **$^{13}$C NMR (100 MHz, $CDCl_3$):** 172.2, 110.1, 110.0, 82.3, 77.5, 76.8, 71.3, 67.9, 52.7, 27.2, 26.9, 26.5, 25.4; **HRMS** ($C_{13}H_{22}O_7Na$, ESI): calculated 313.1263, $[M+Na]^+$, found 313.1260.



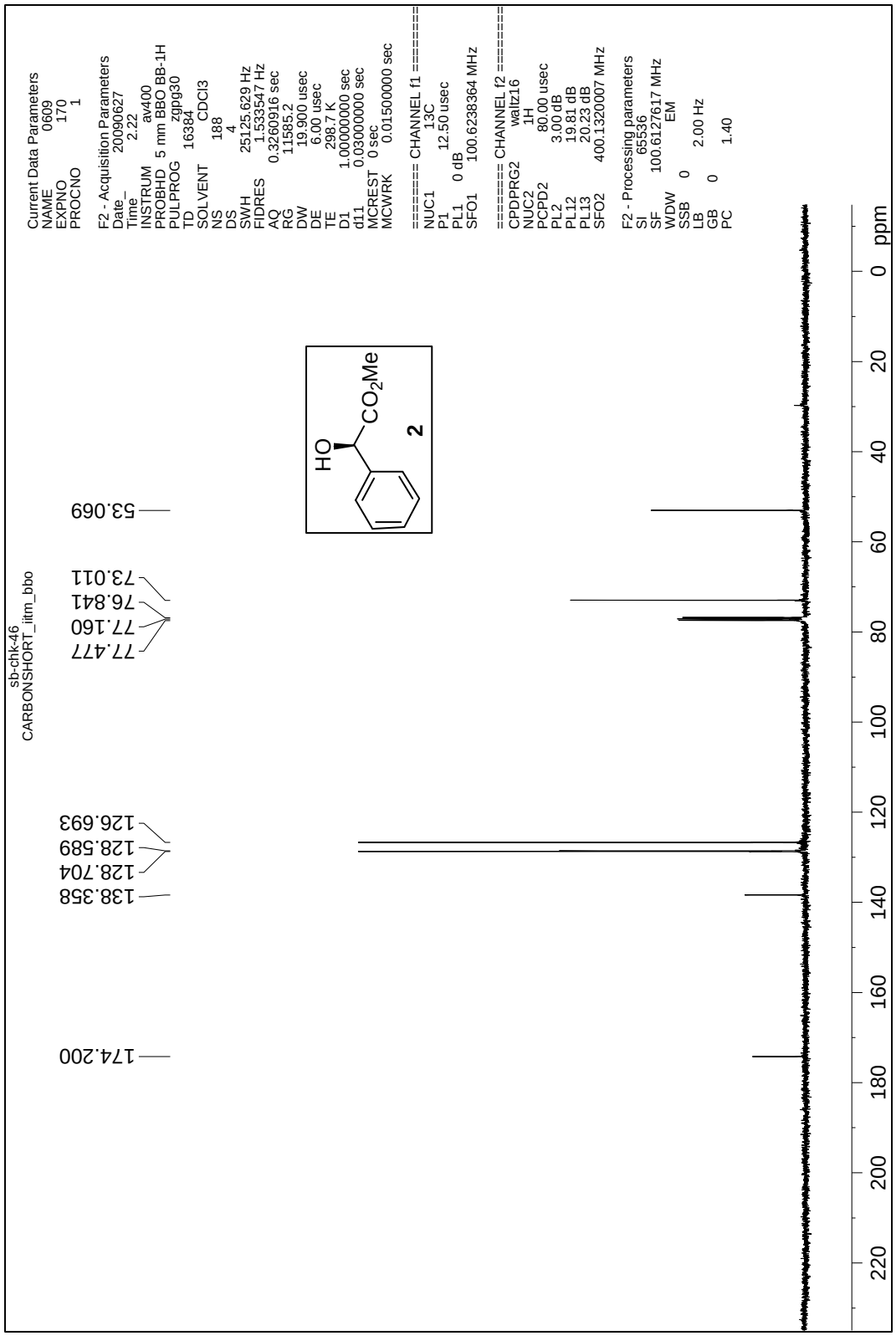
(*S*)-methyl 2-((4*R*,5*R*)-5-((*S*)-2-azido-1-(benzyloxy)ethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-hydroxyacetate(26). $[\alpha]^{26}_D$ = +30.34 (*c* 1, $CHCl_3$); IR (KBr disc): 3465, 3018, 2925, 2870, 2102, 1742, 1637, 1449; $^1$H NMR (400 MHz, $CDCl_3$): δ 7.37–7.30 (m, 5H), 4.67 (dd, *J* = 11.6Hz, 2H), 4.33 (d, *J* = 3.6Hz, 1H), 4.25 (t, *J* = 4Hz, 2H), 3.76 (s, 3H), 3.69–3.65 (m, 1H), 3.50–3.48 (m, 2H), 1.39 (s, 3H), 1.38 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): 172.3, 137.4, 128.7, 128.4, 128.2, 110.1, 78.7, 76.6, 76.5, 73.7, 71.4, 52.9, 51.6, 27.0; HRMS ($C_{17}H_{24}N_3O_6$, ESI): calculated 366.1665, $[M]^+$, found 366.1650.



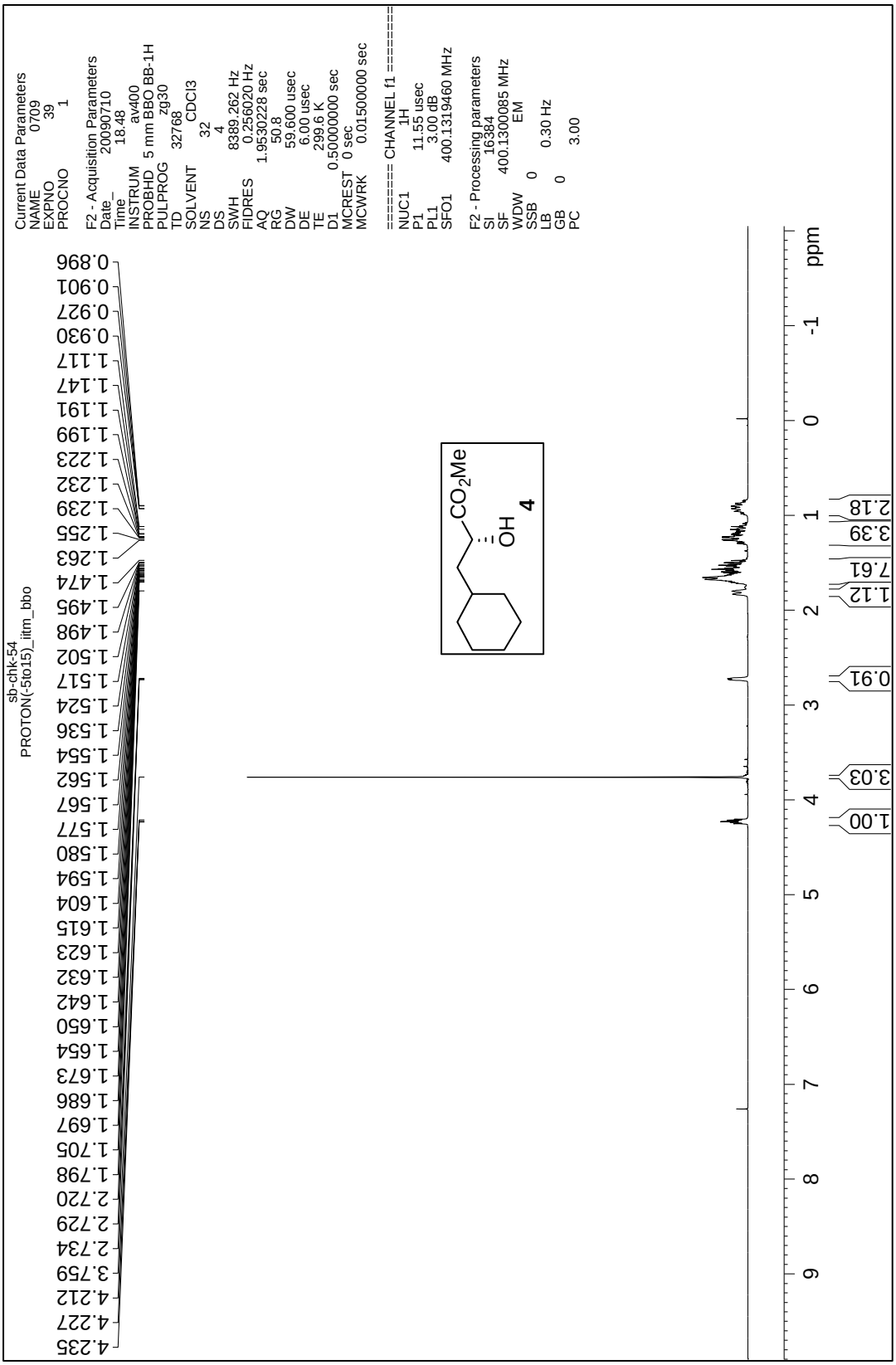

$^{1}$H NMR spectrum of Compound **2**



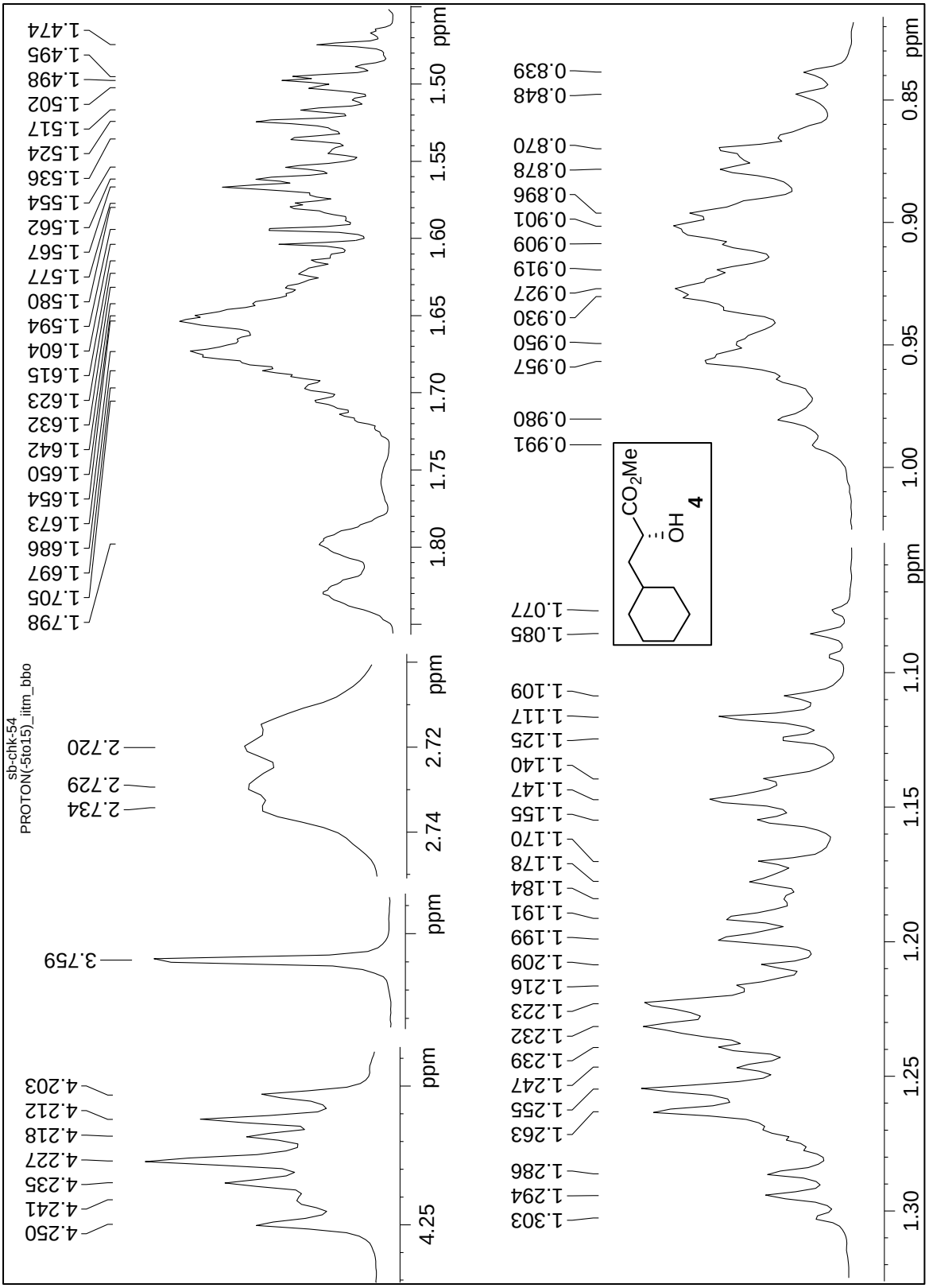

Expanded $^{1}$H NMR spectrum of Compound **2**



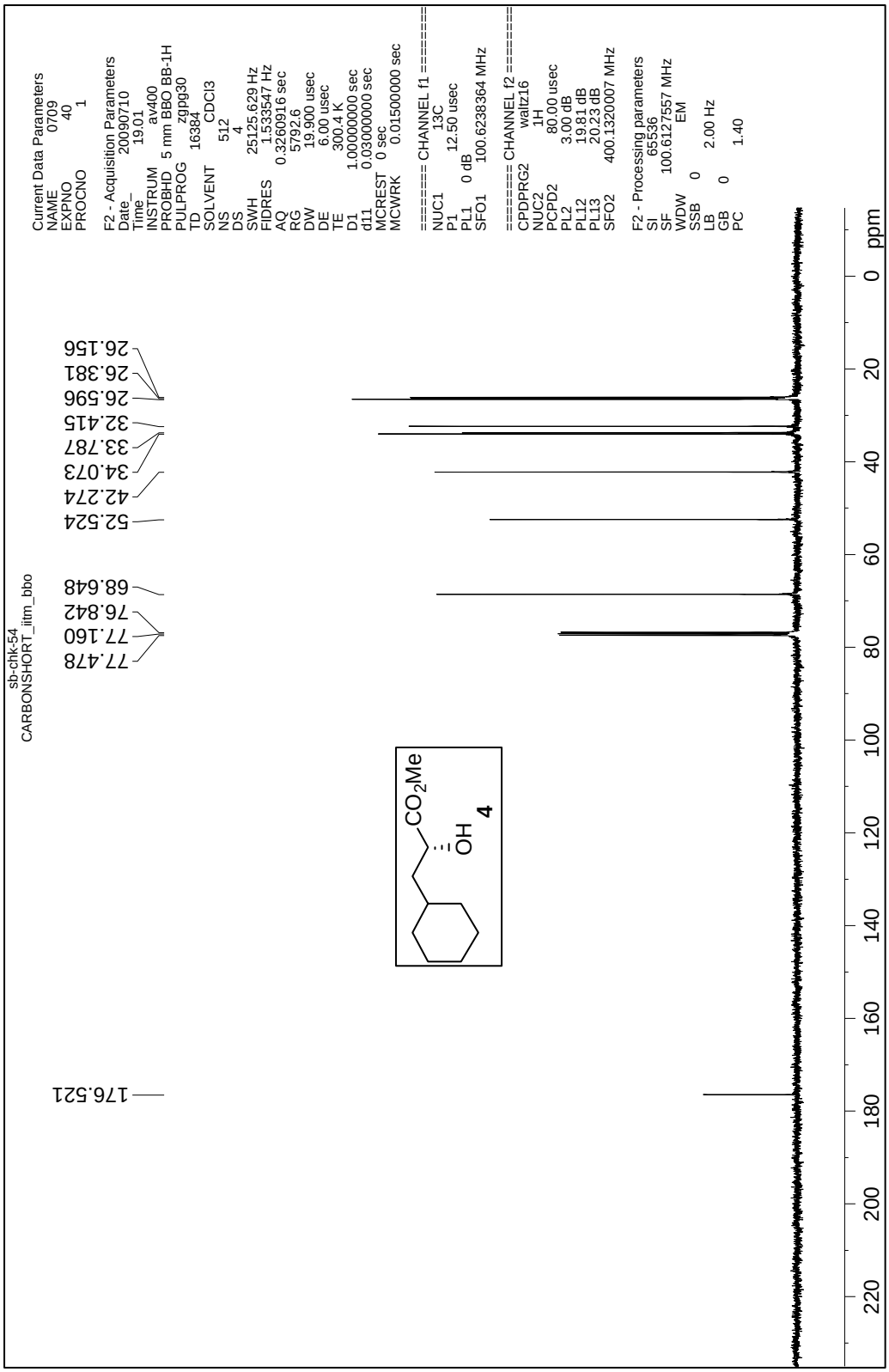

$^{13}$C NMR spectrum of Compound **2**



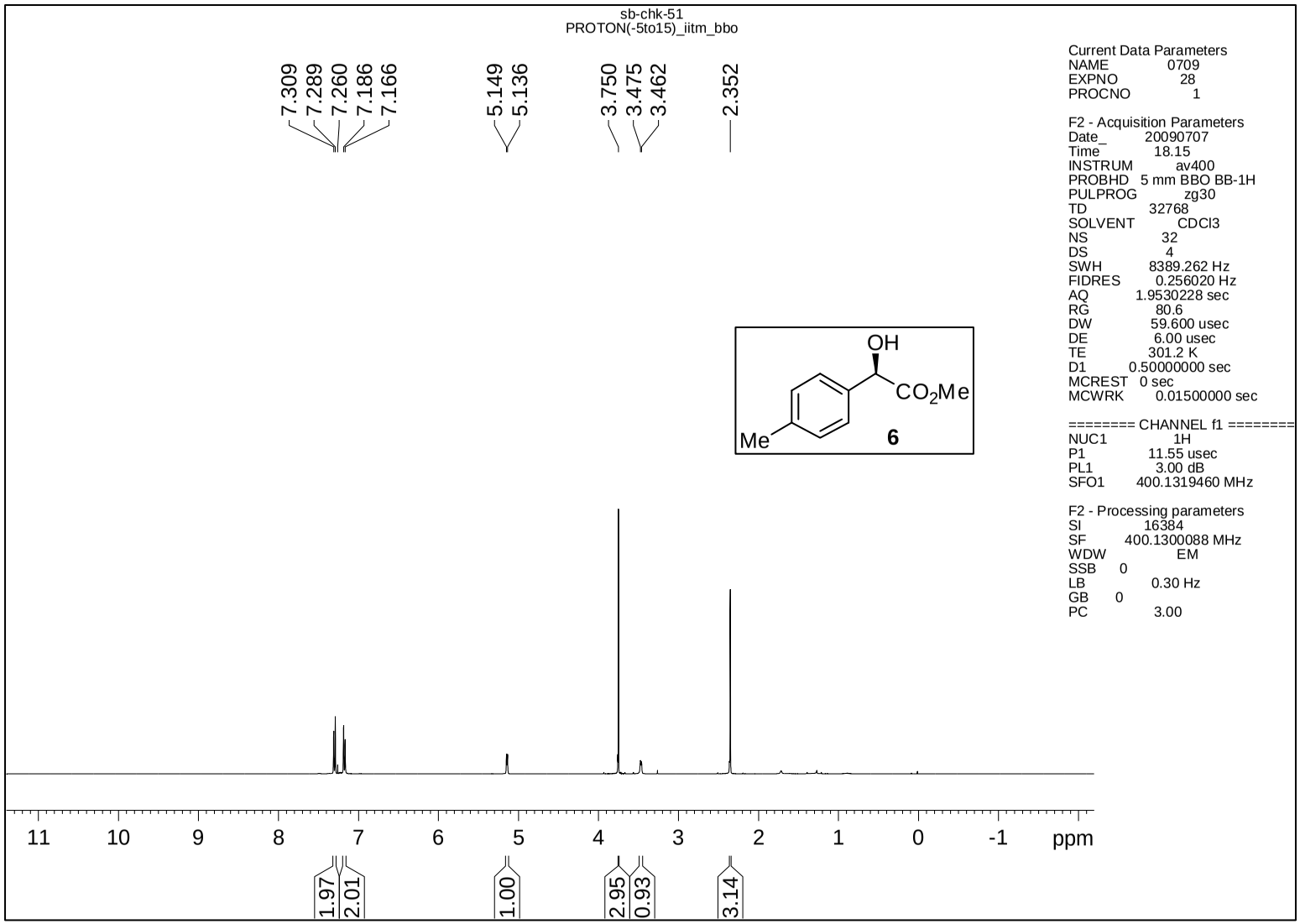

$^{1}$H NMR spectrum of Compound **4**



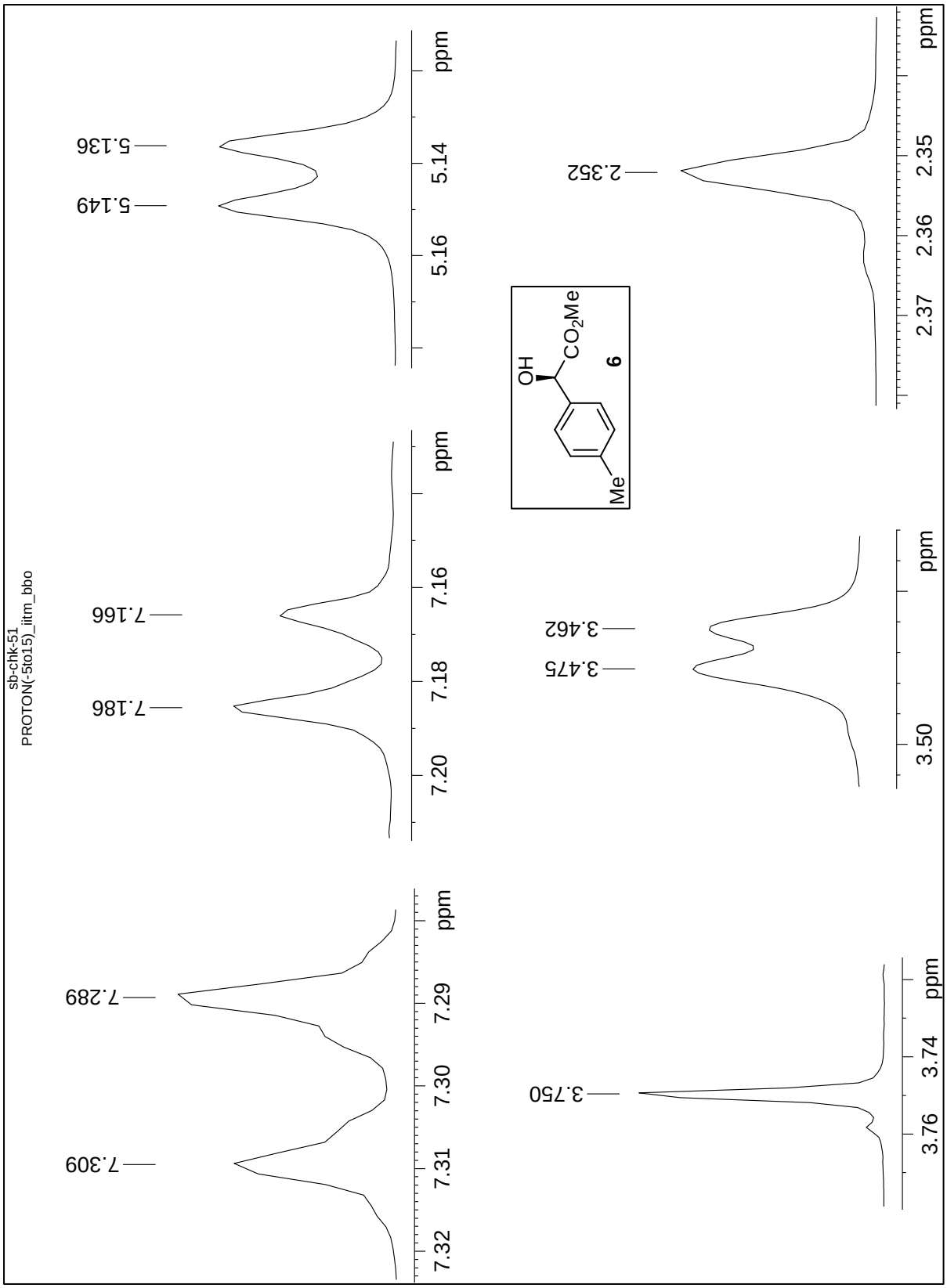

Expanded $^{1}$H NMR spectrum of Compound **4**



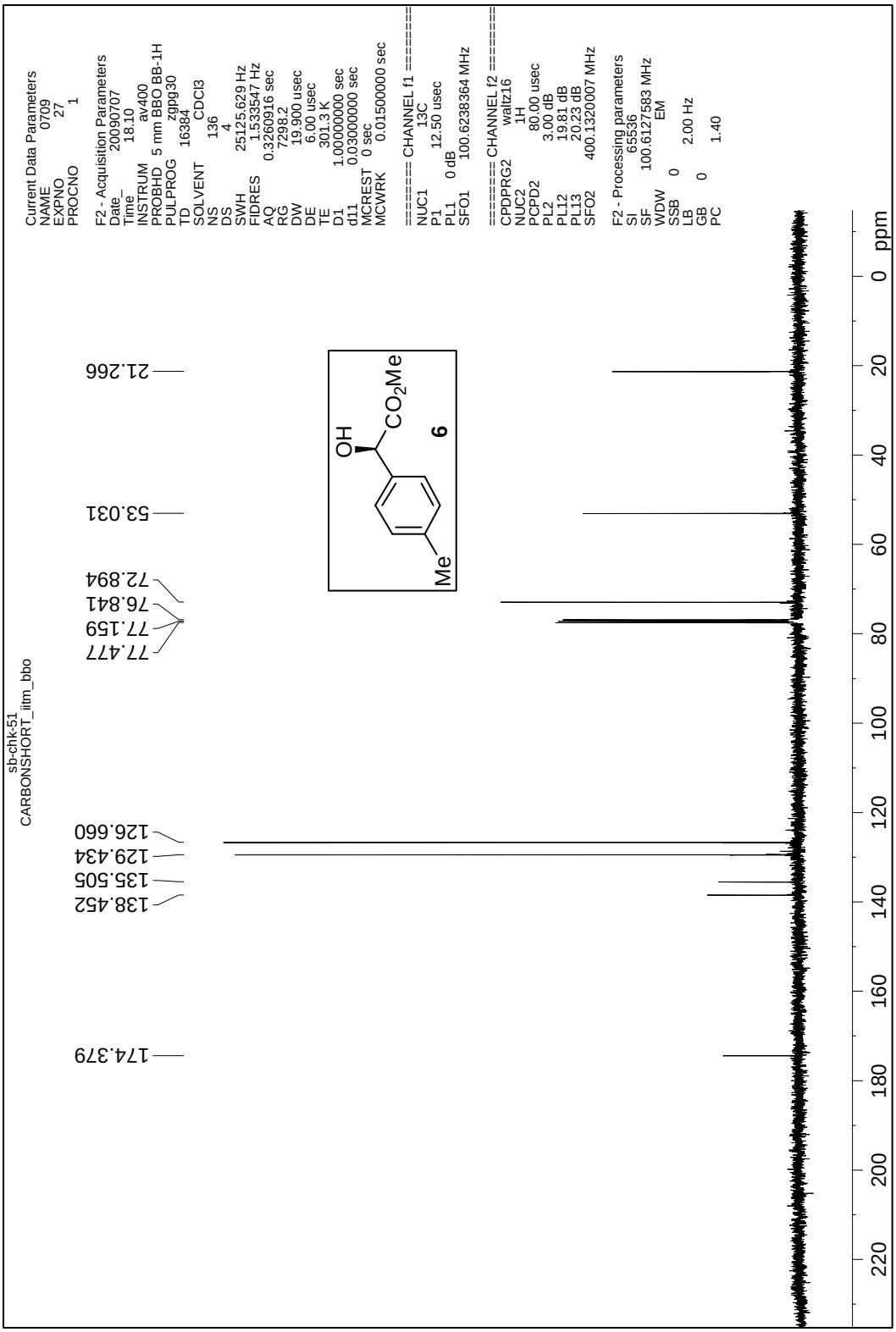

$^{13}$C NMR spectrum of Compound **4**



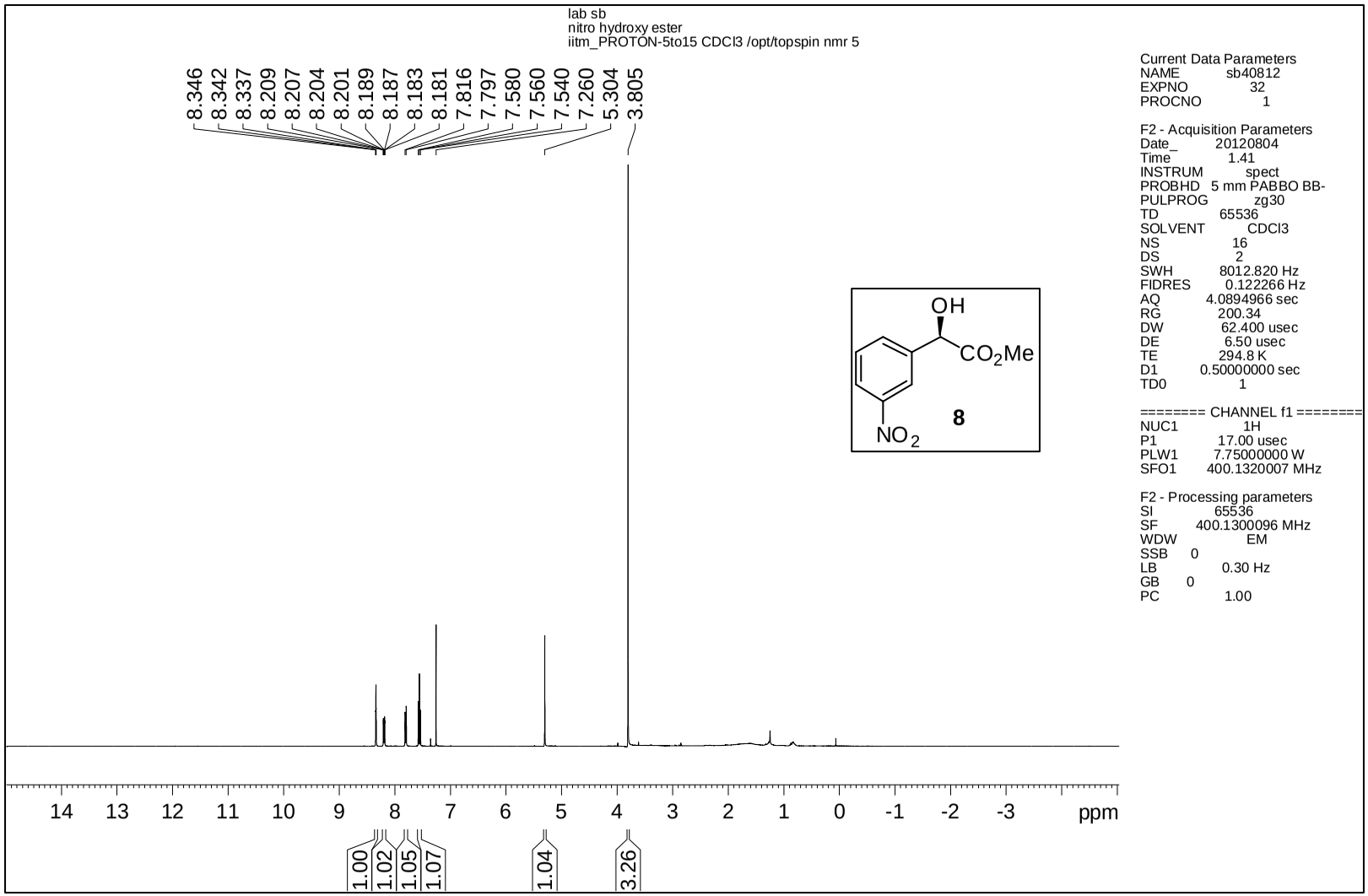

$^{1}$H NMR spectrum of Compound **6**



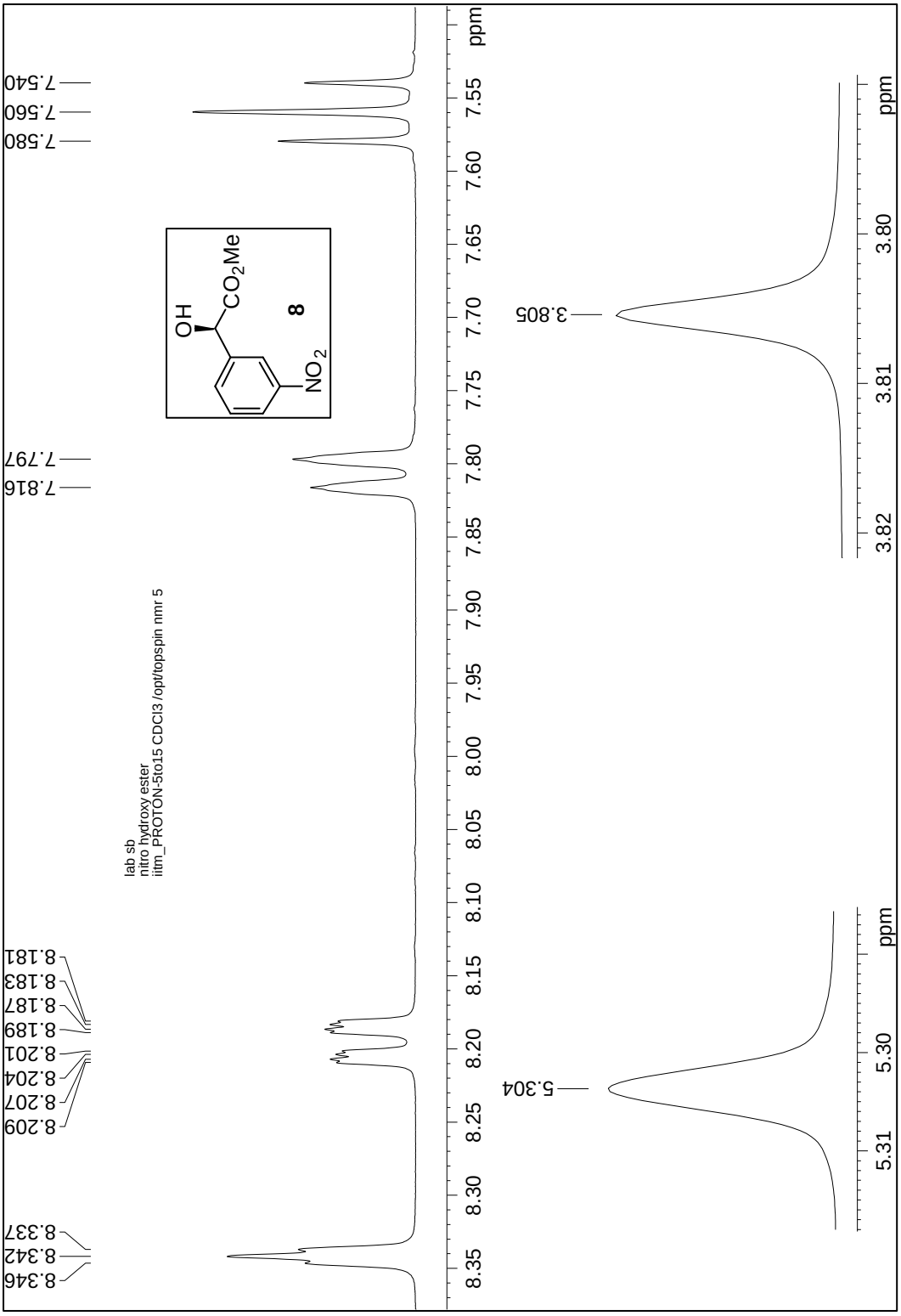

Expanded $^{1}$H NMR spectrum of Compound **6**



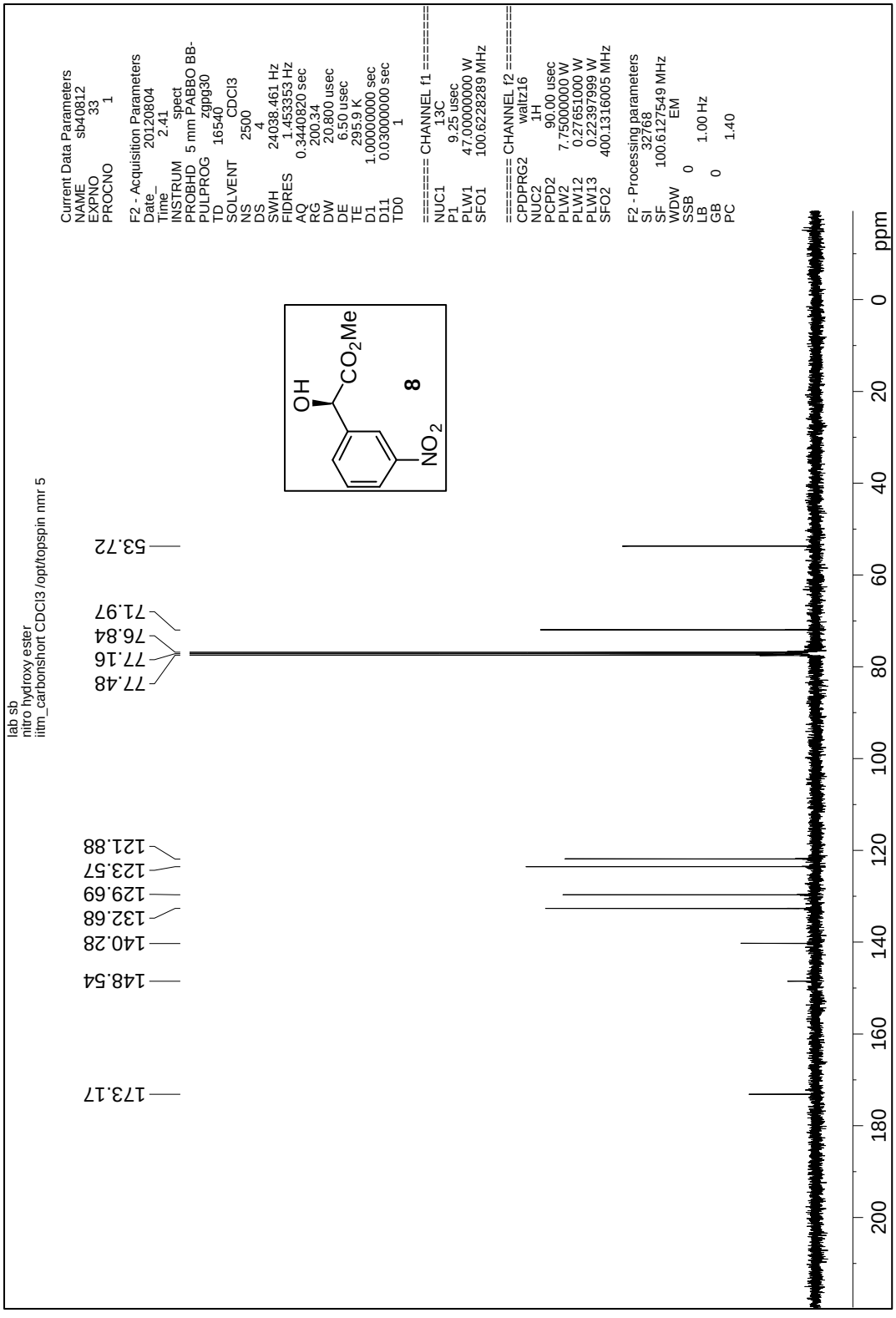

$^{13}$C NMR spectrum of Compound **6**



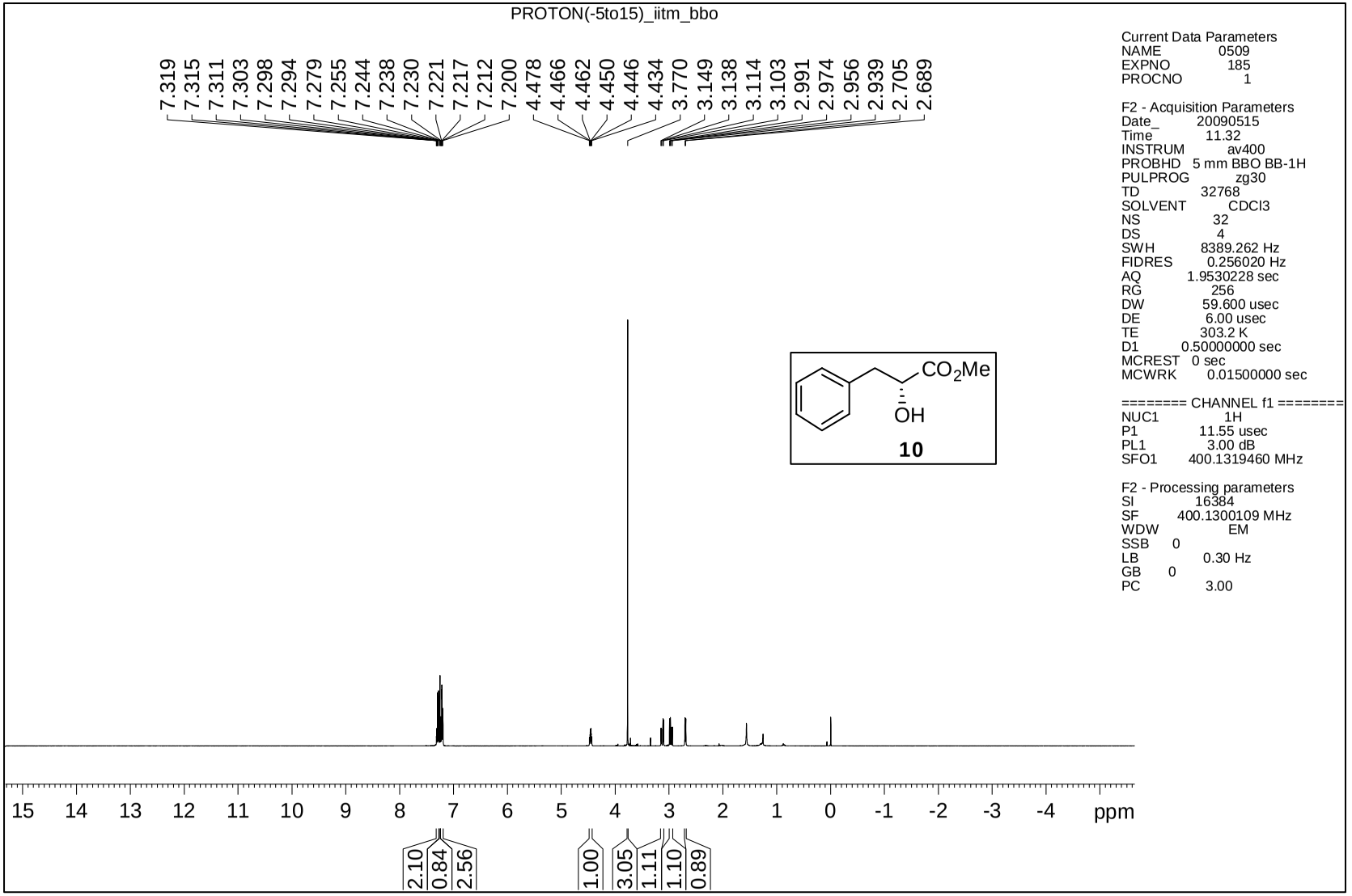

$^{1}$H NMR spectrum of Compound **8**



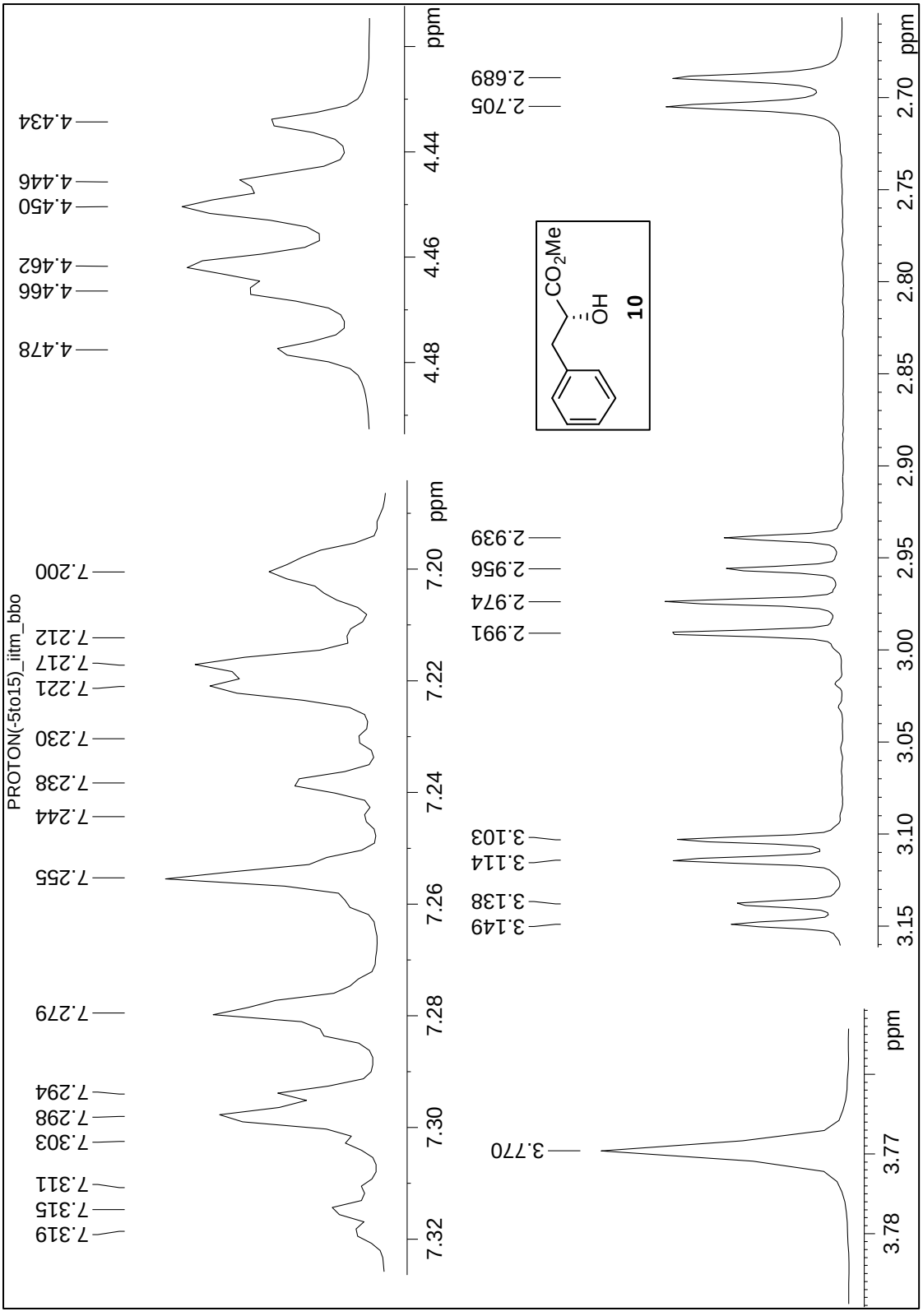

Expanded $^{1}$H NMR spectrum of Compound **8**



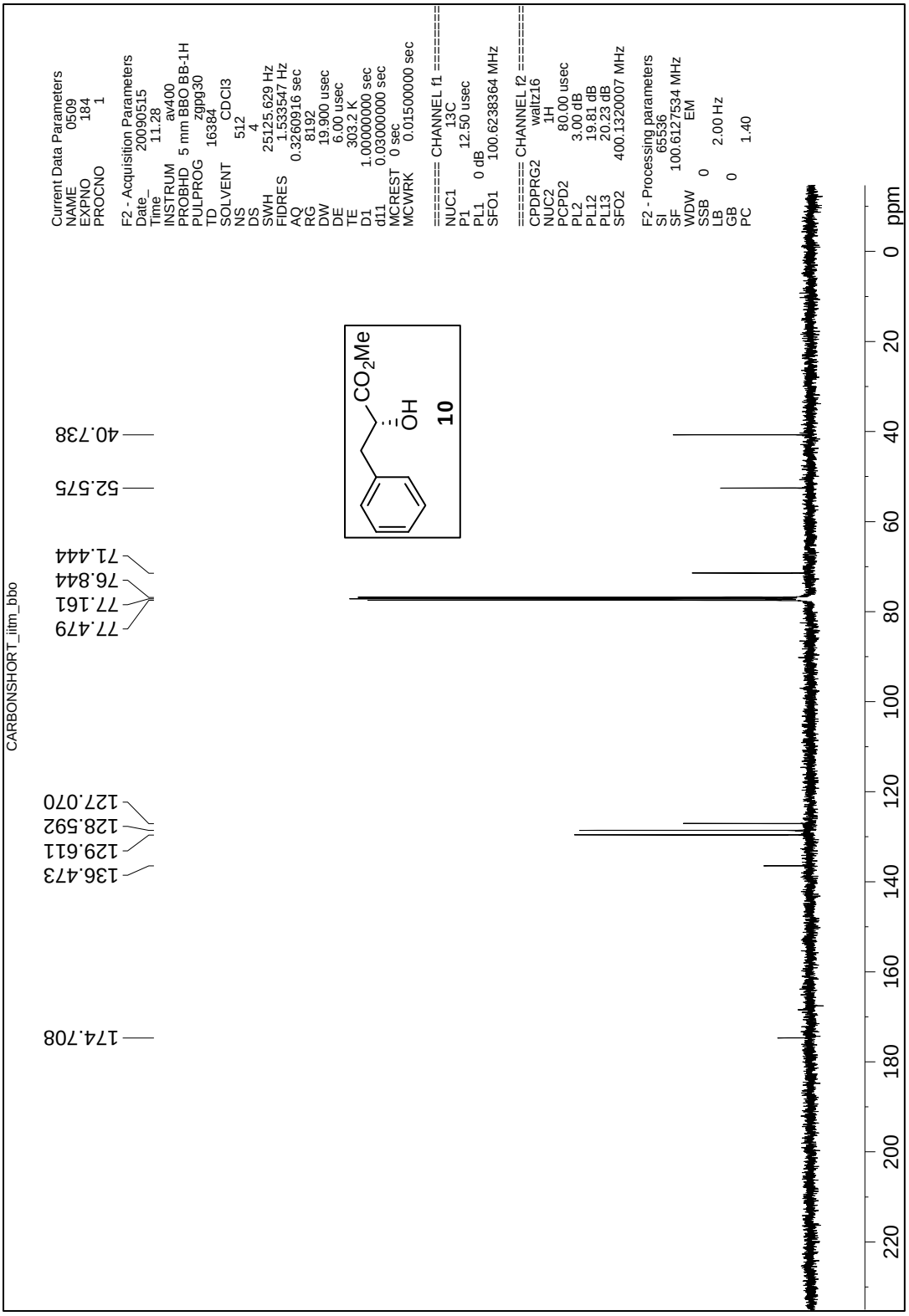

$^{13}$C NMR spectrum of Compound **8**



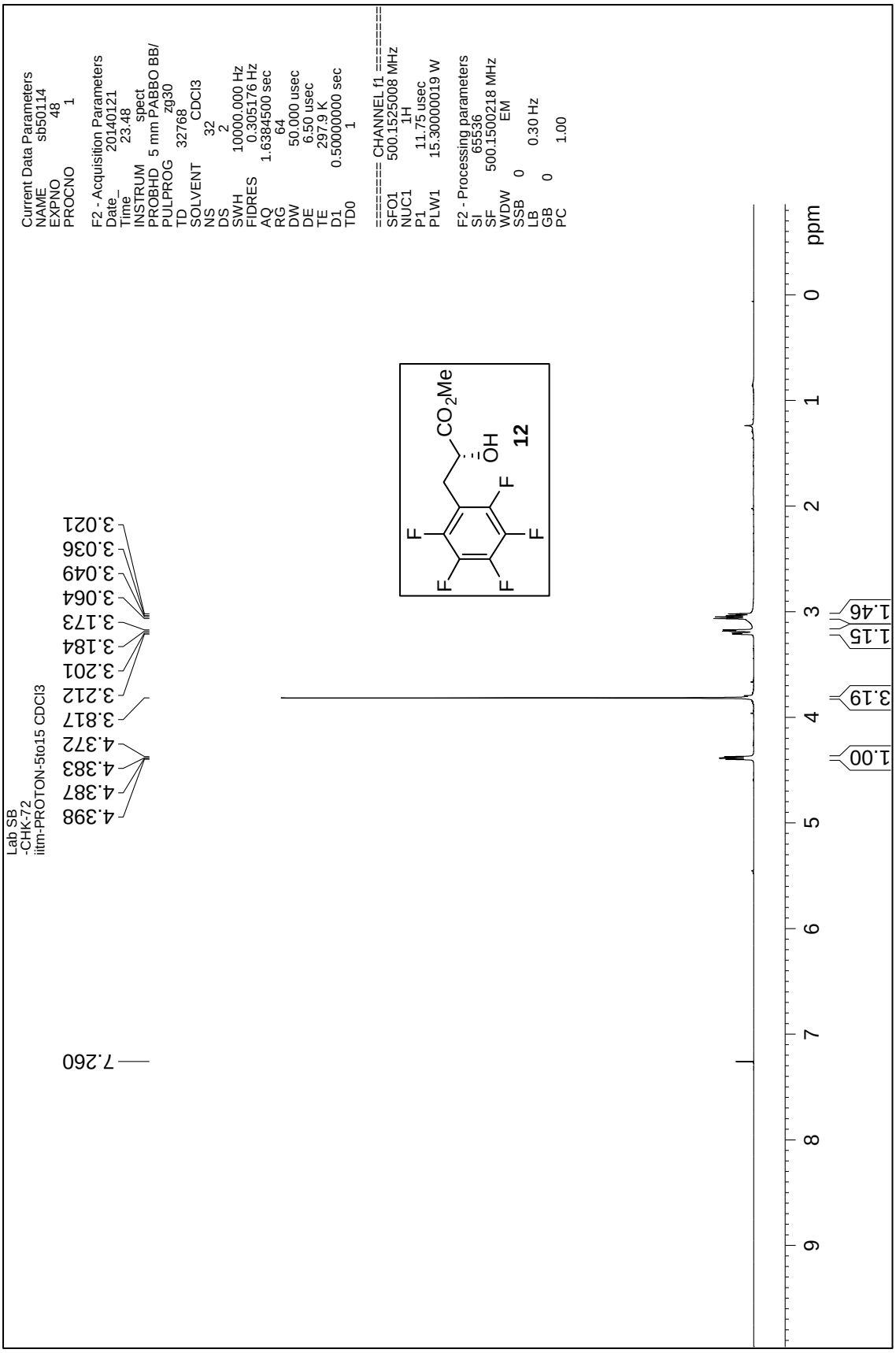

$^{1}$H NMR spectrum of Compound **10**



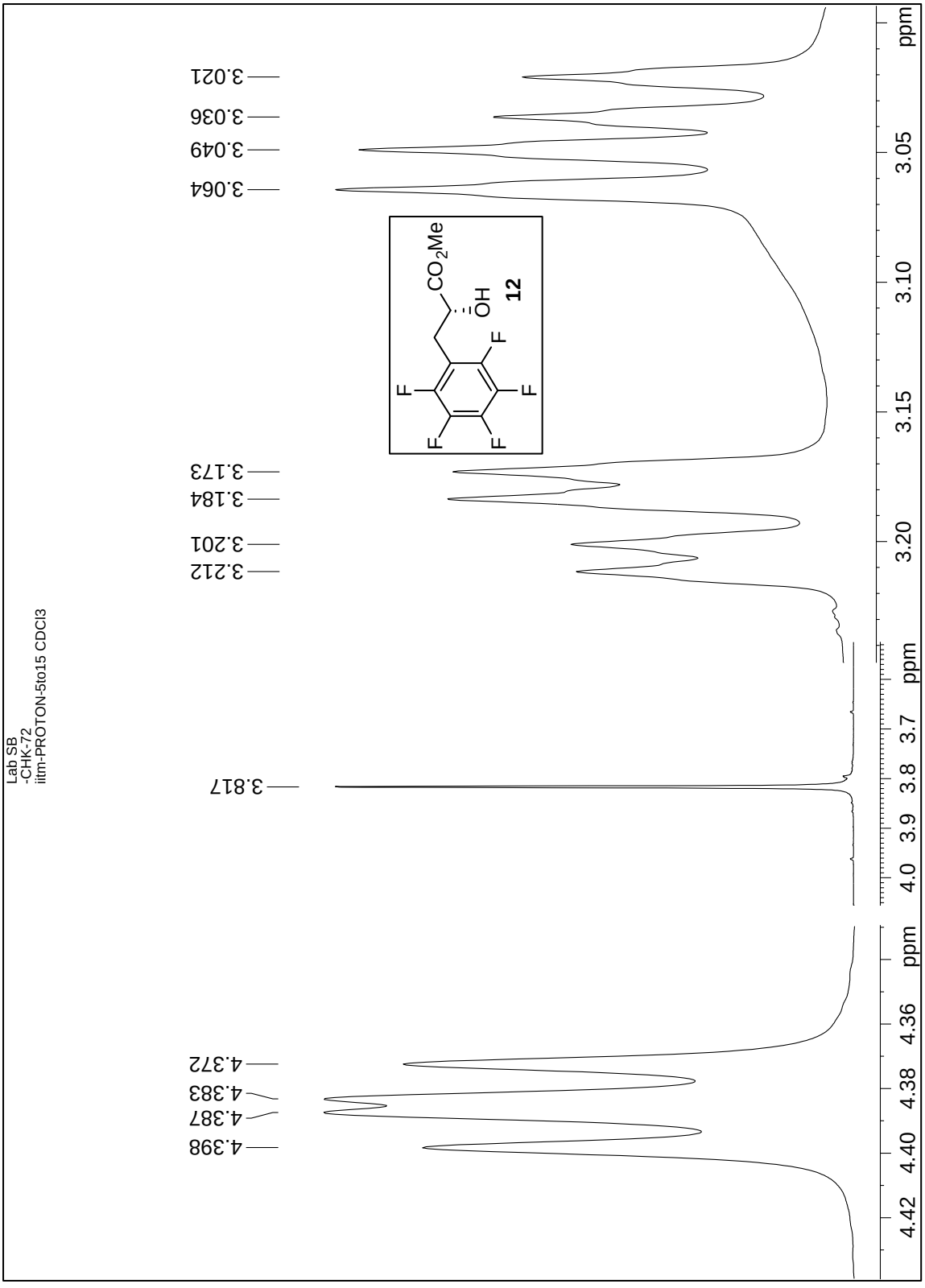

Expanded $^{1}$H NMR spectrum of Compound **10**



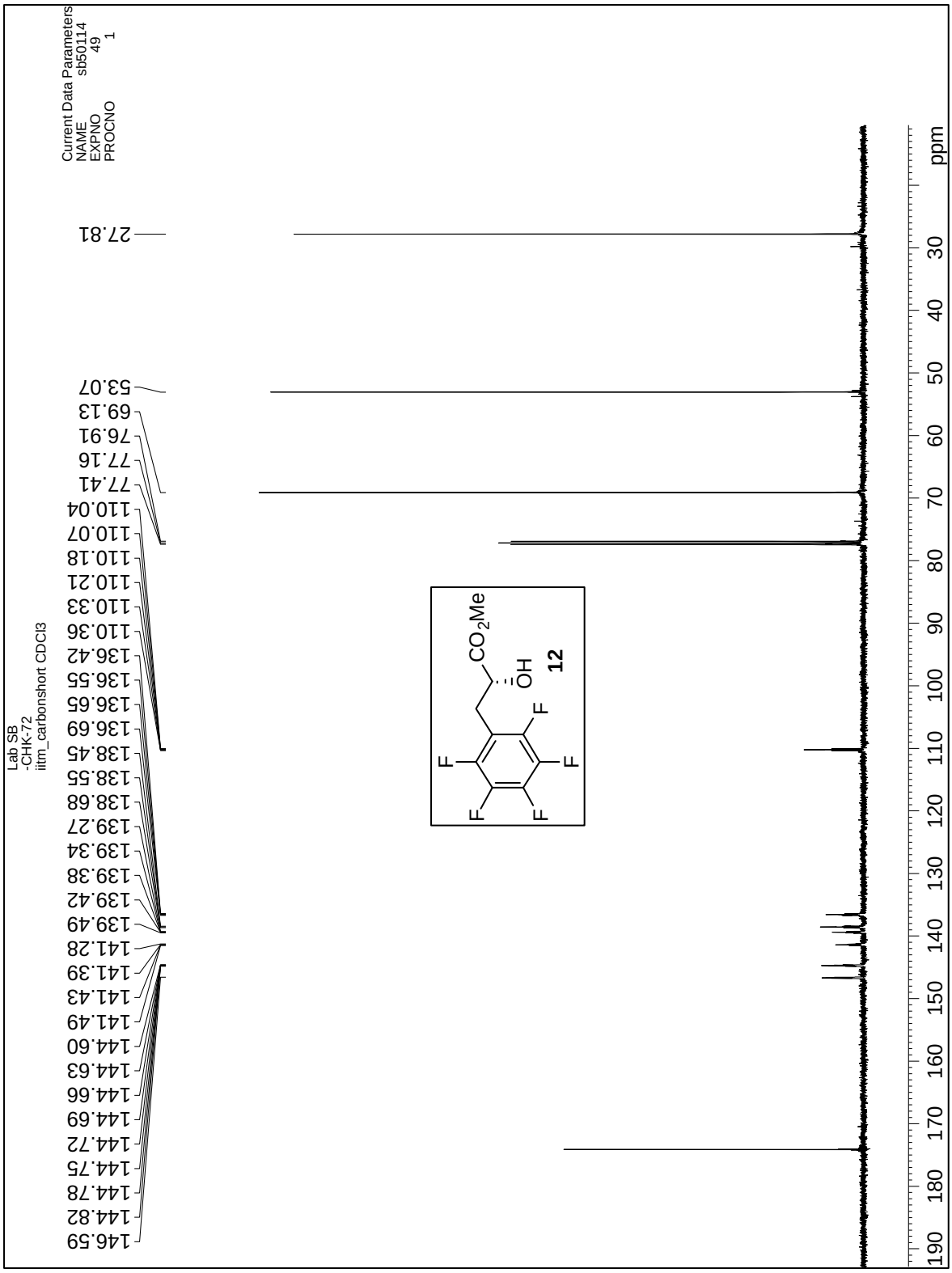

$^{13}$C NMR spectrum of Compound **10**



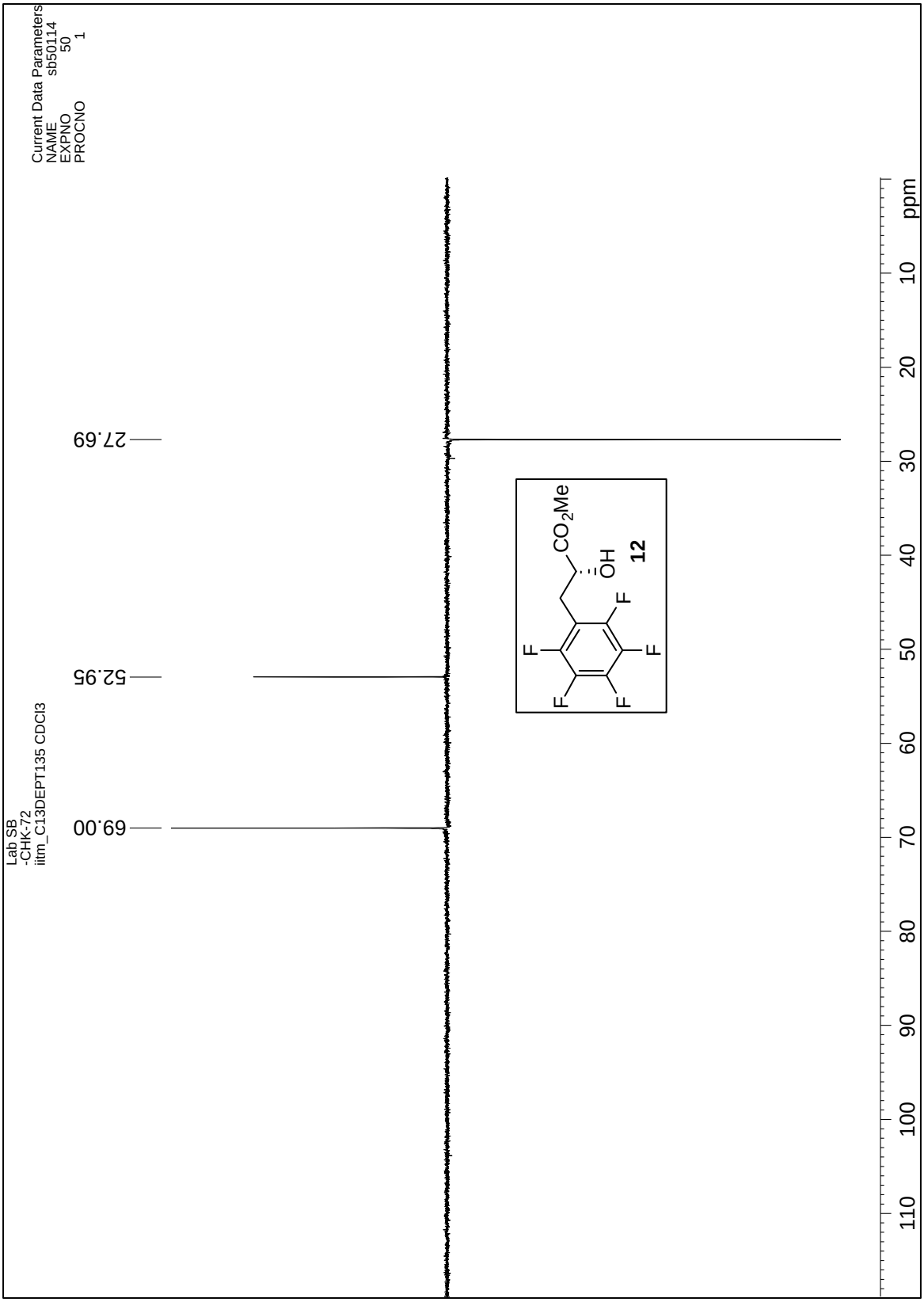

$^{1}$H NMR spectrum of Compound **12**



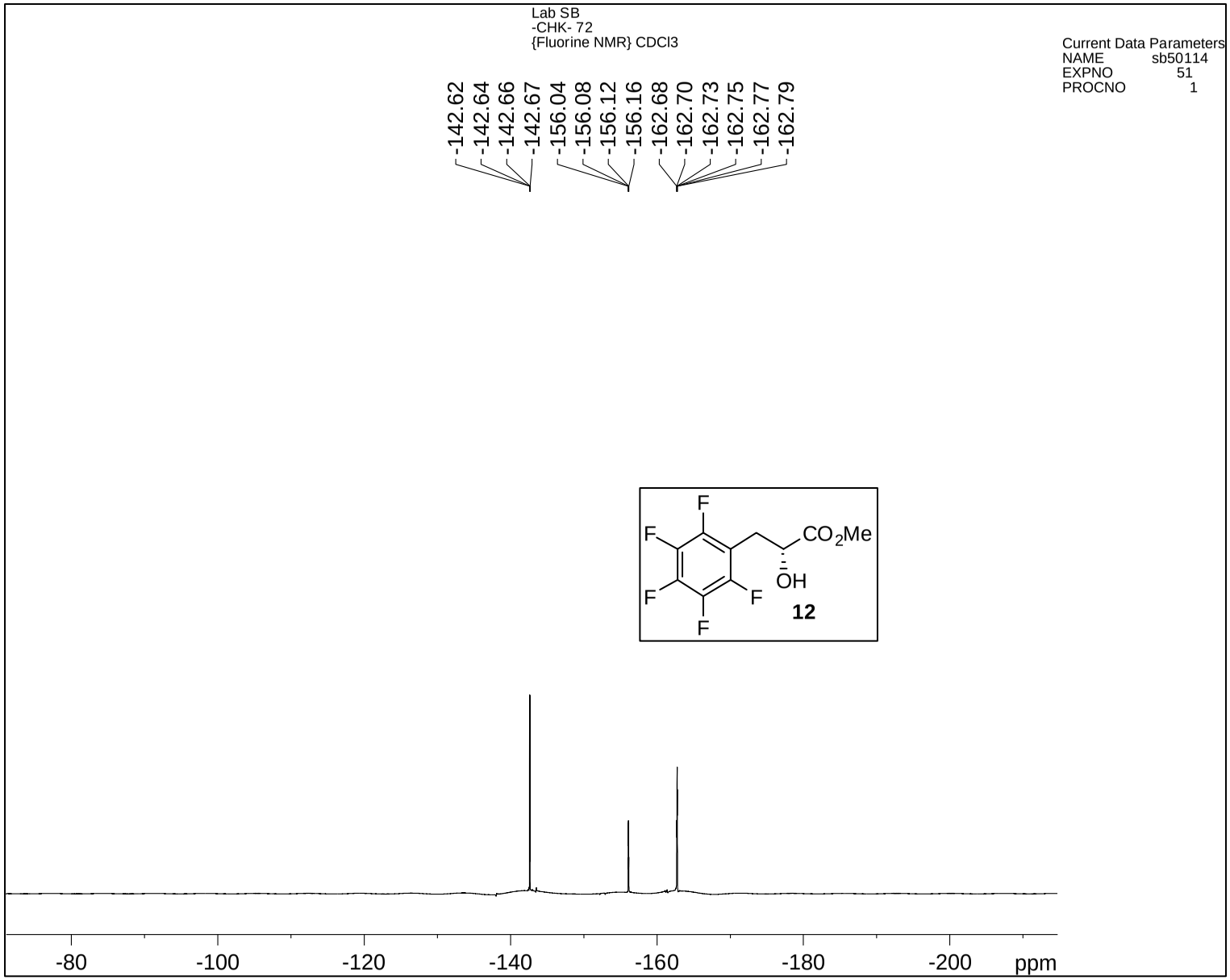

Expanded $^{1}$H NMR spectrum of Compound **12**



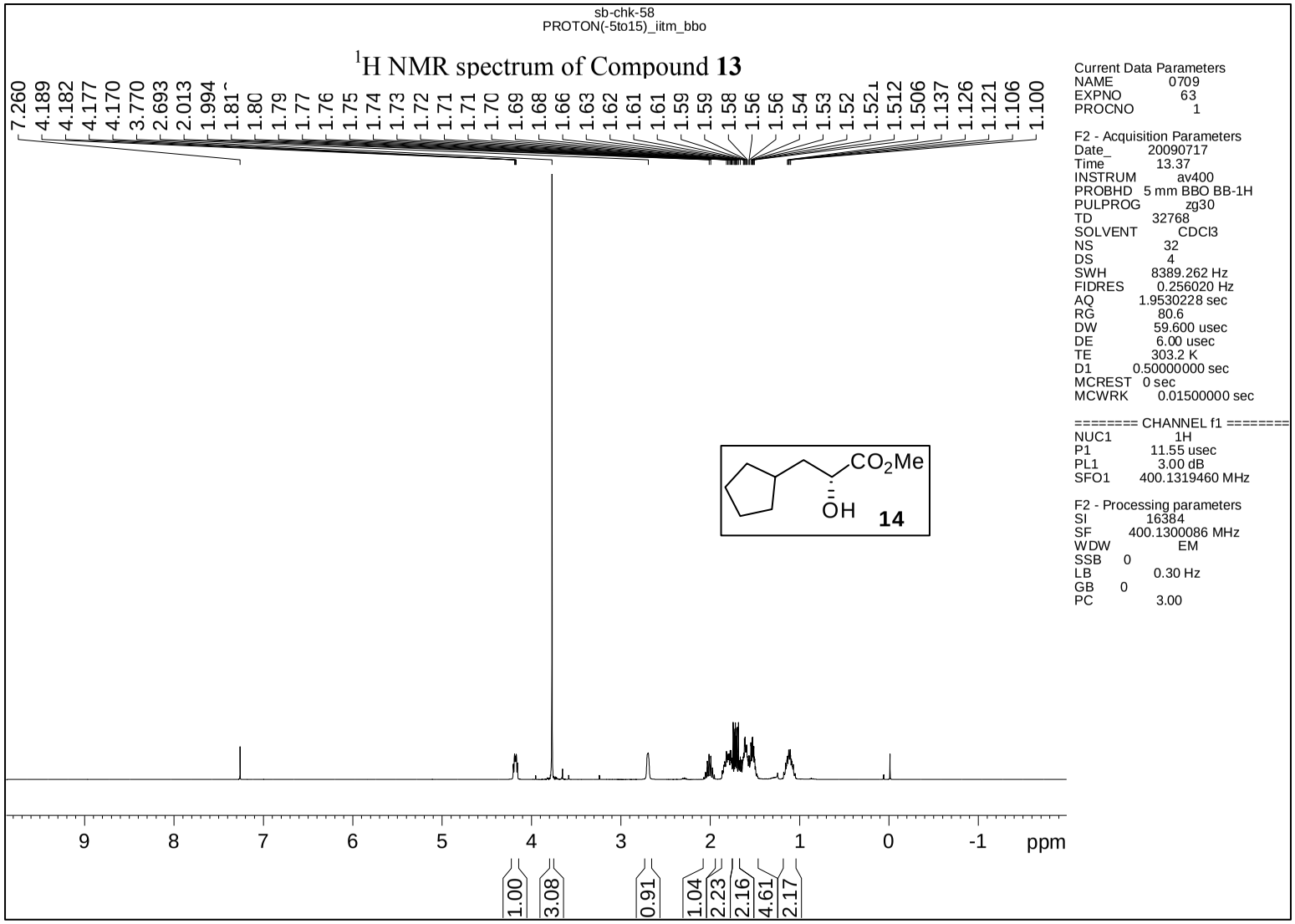

$^{13}$C NMR spectrum of Compound **12**




DEPT spectrum of Compound **12**

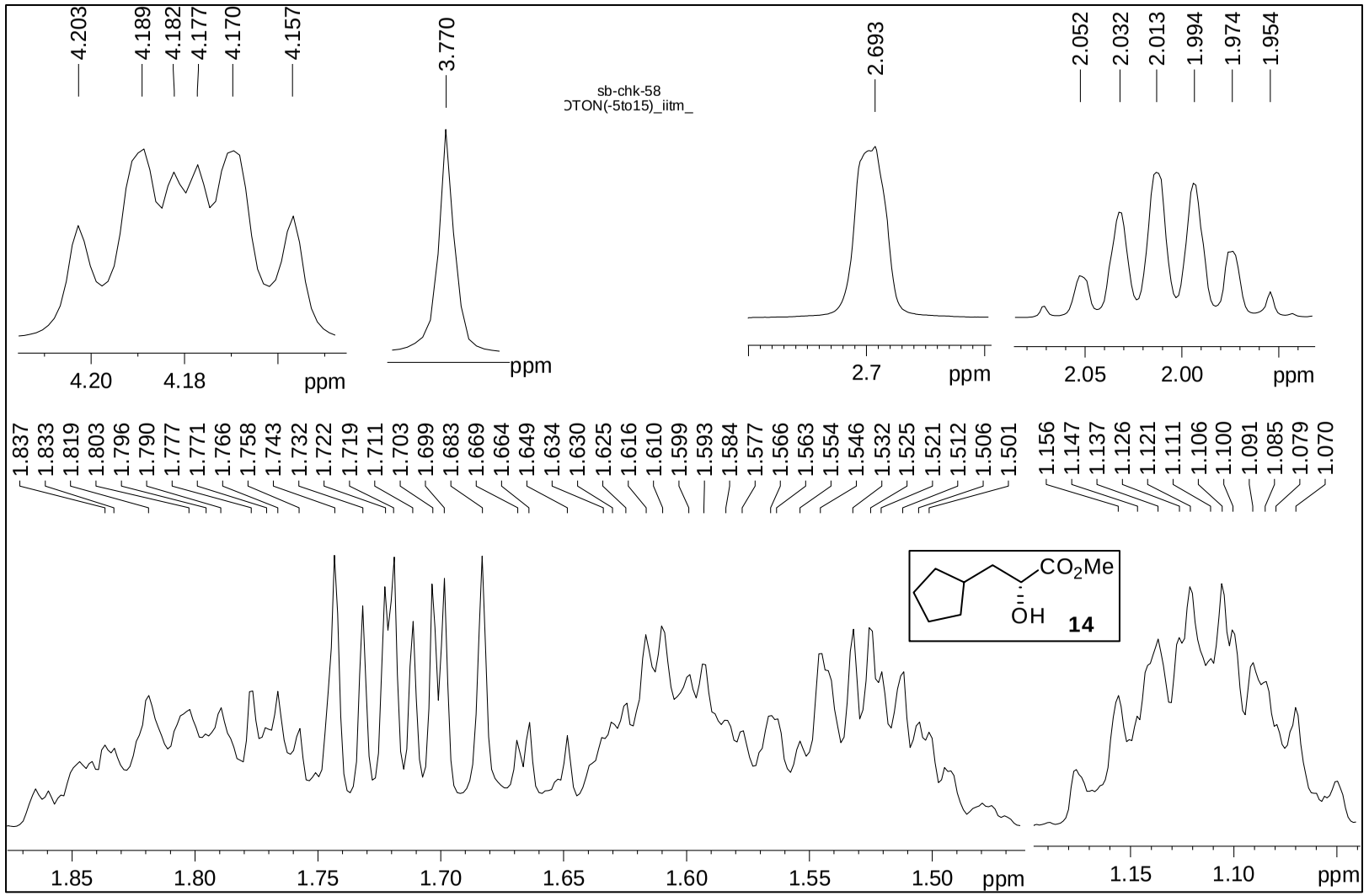



$^{19}$F spectrum of Compound **12**

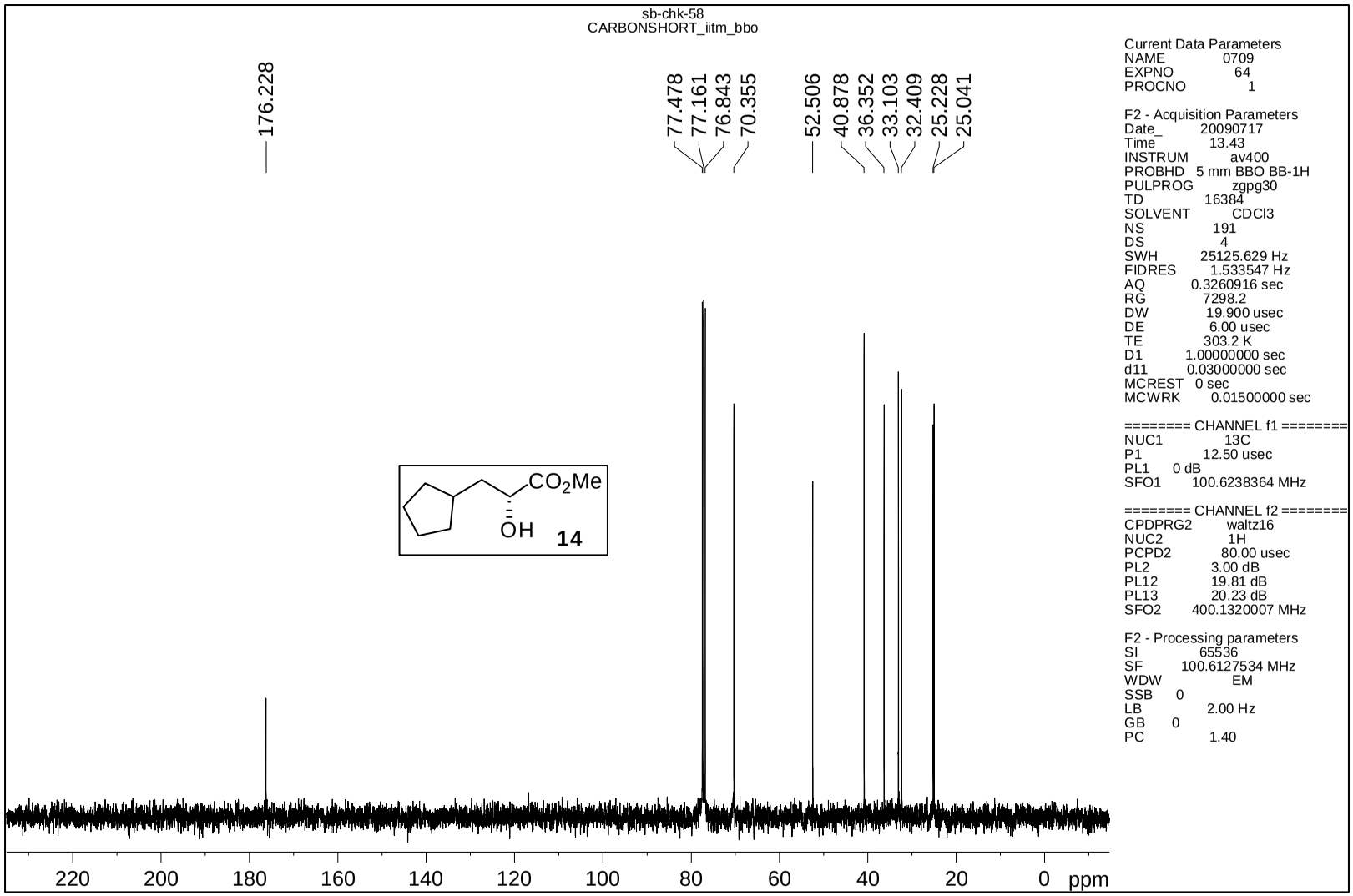



$^1$H NMR spectrum of Compound **13**

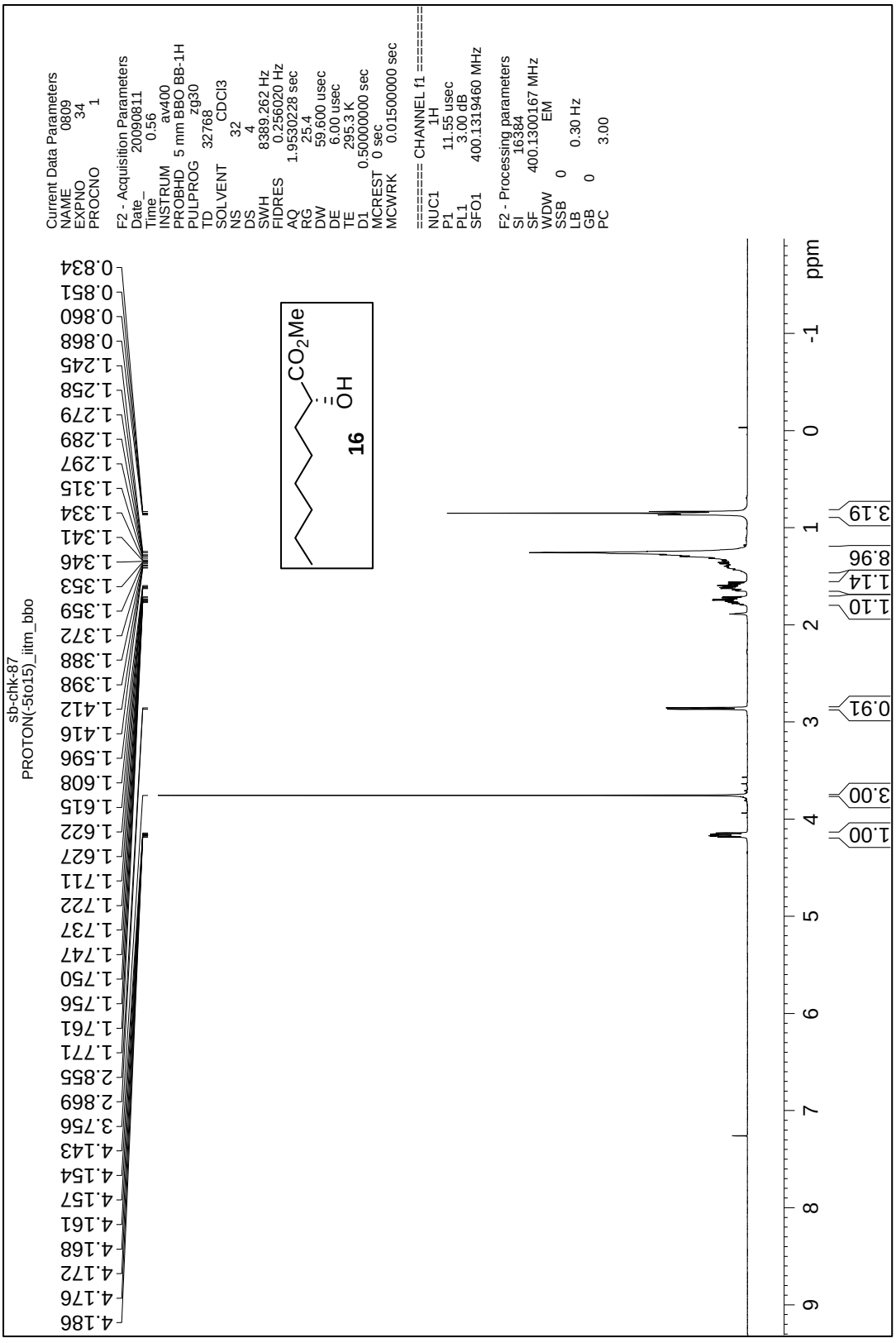
$^1$H NMR spectrum of Compound **14**



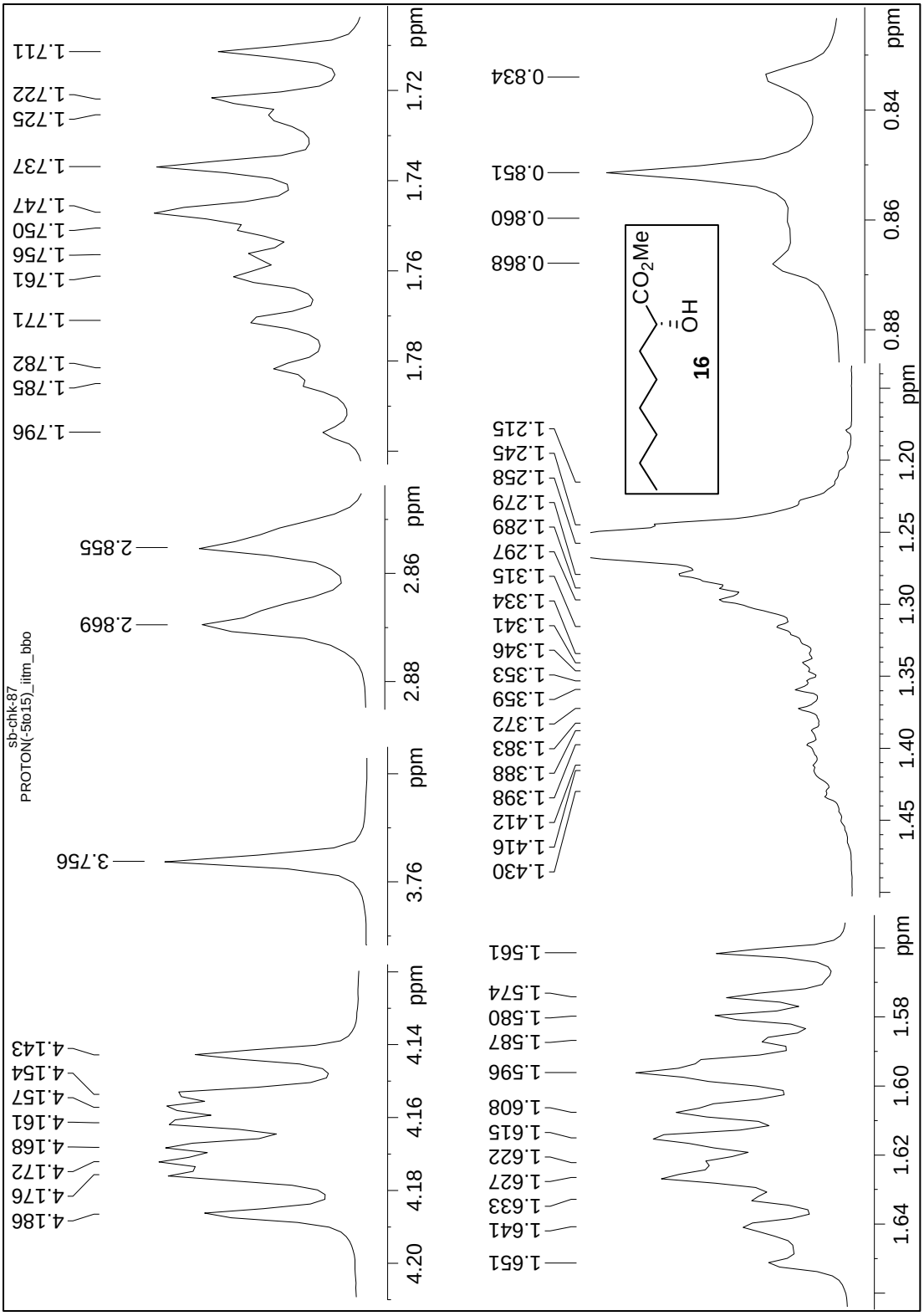

Expanded $^{1}$H NMR spectrum of Compound **14**



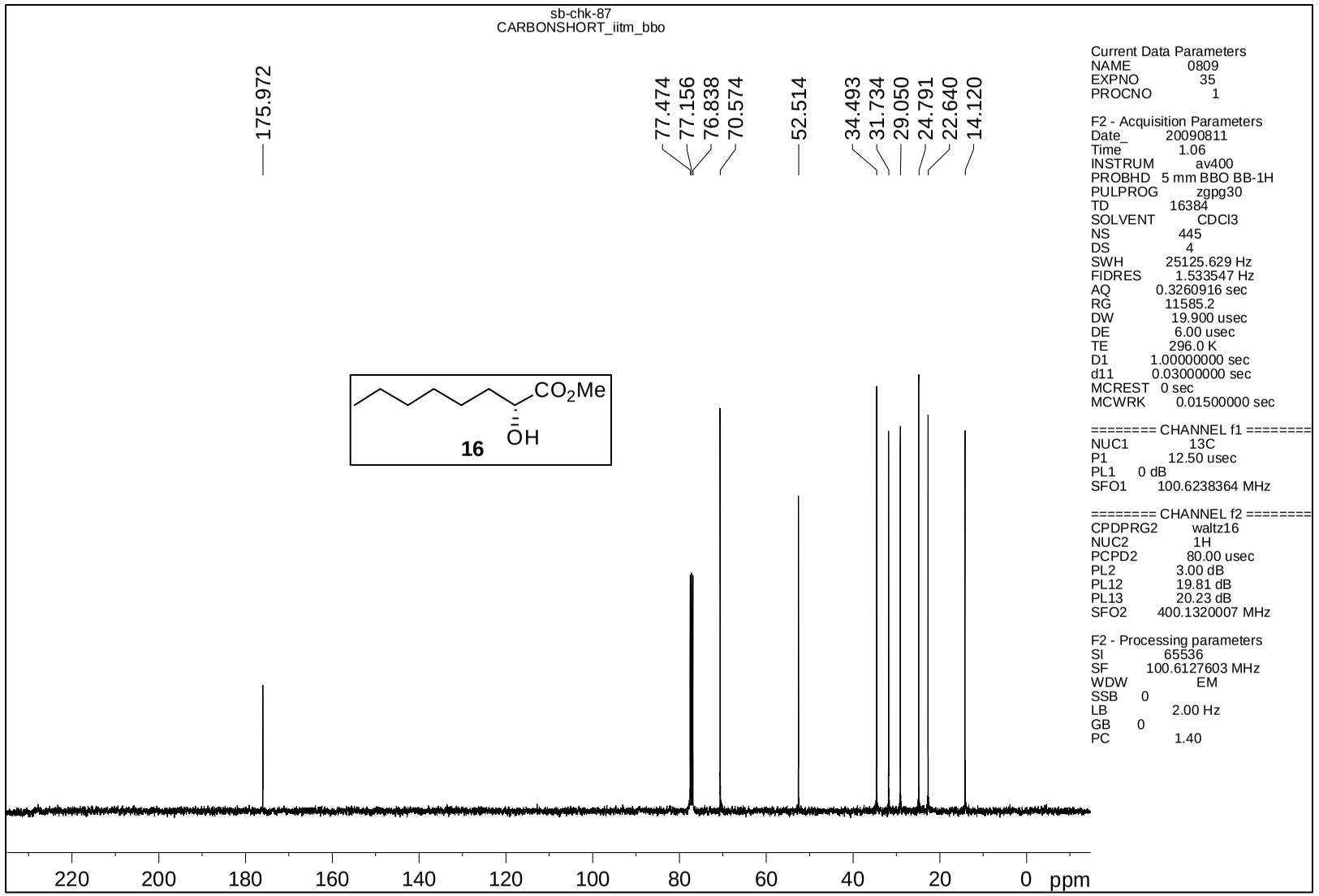

$^{13}$C NMR spectrum of Compound **14**



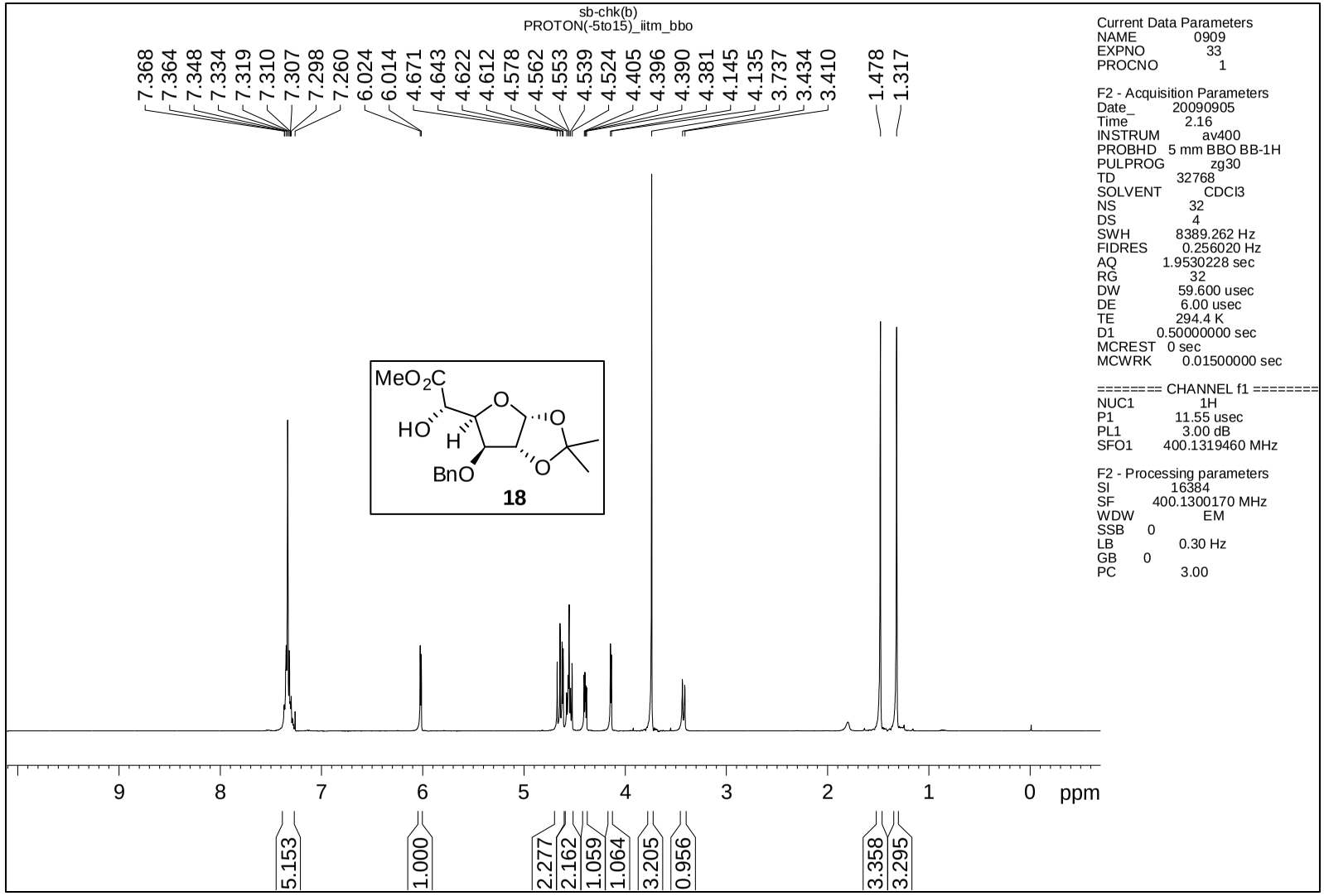

$^{1}$H NMR spectrum of Compound **16**



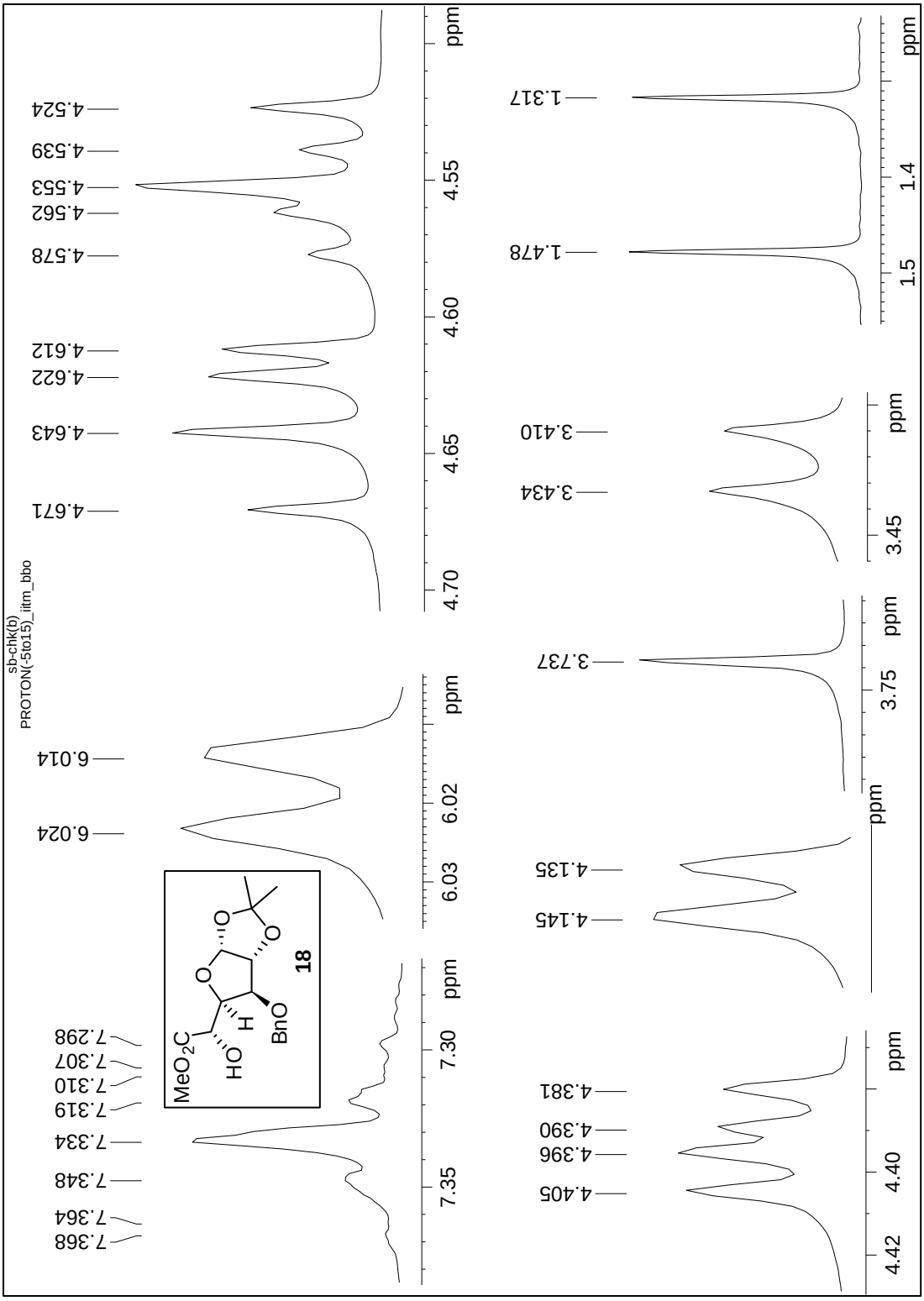

Expanded $^{1}$H NMR spectrum of Compound **16**



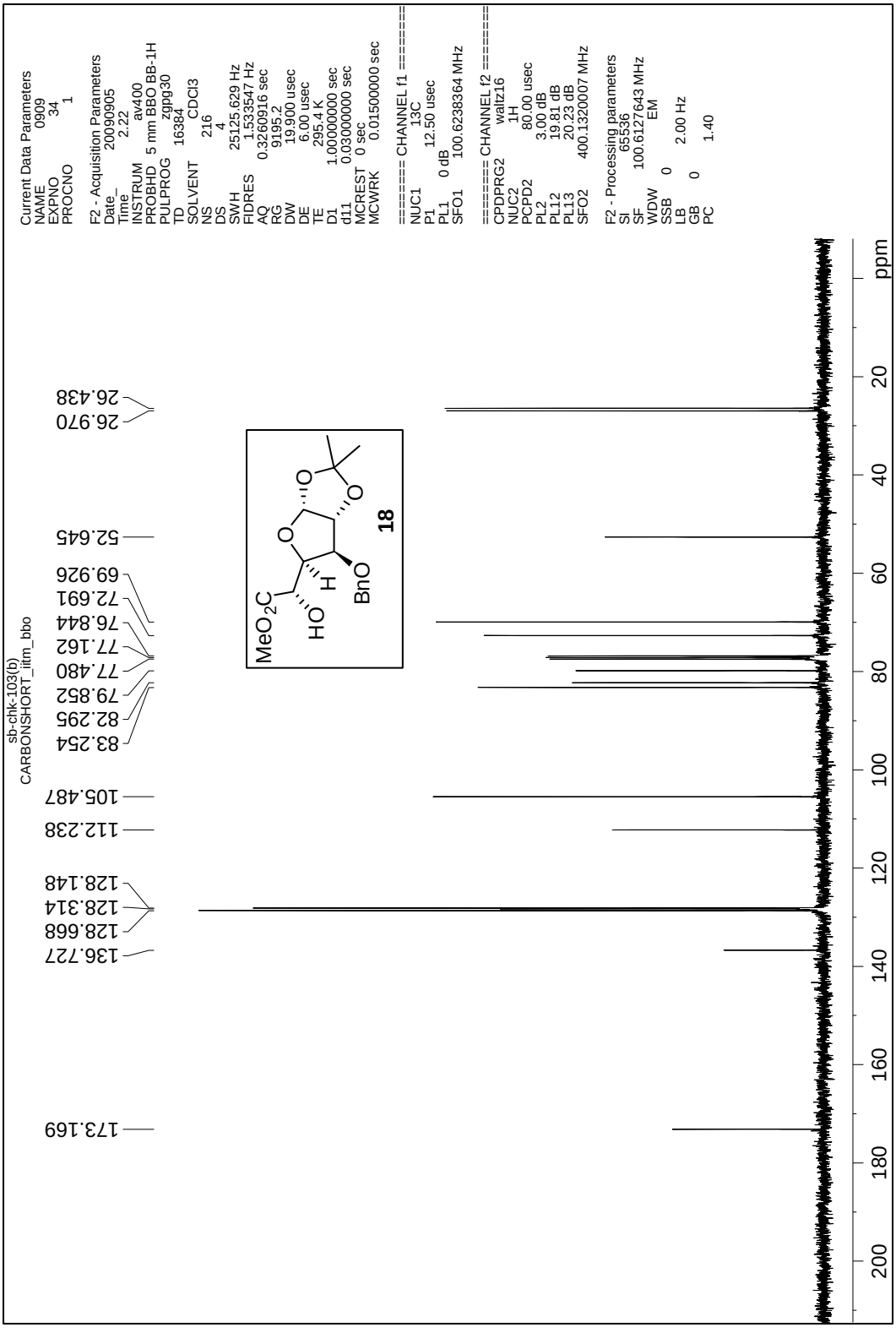

$^{13}$C NMR spectrum of Compound **16**



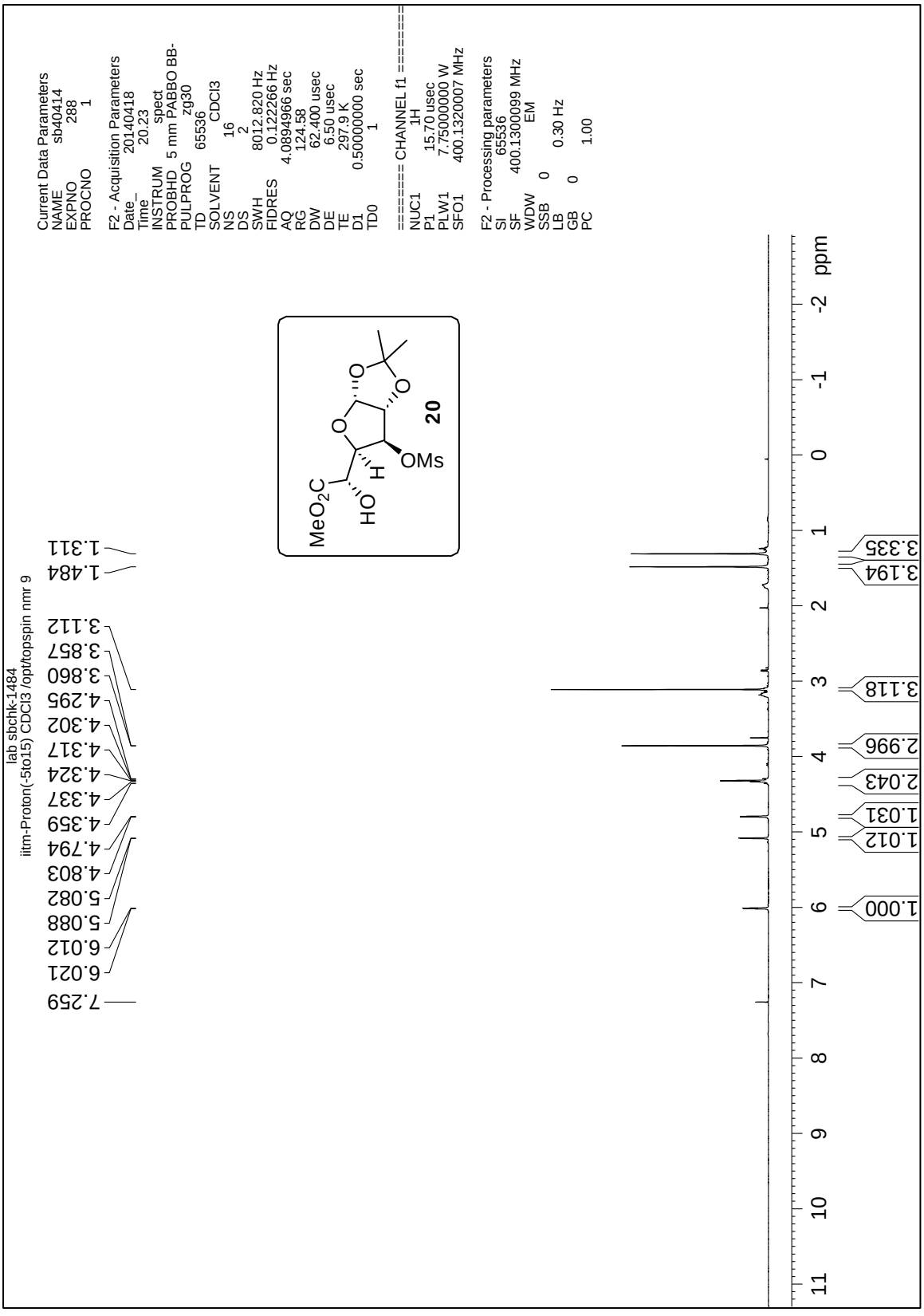

$^{1}$H NMR spectrum of Compound **18**



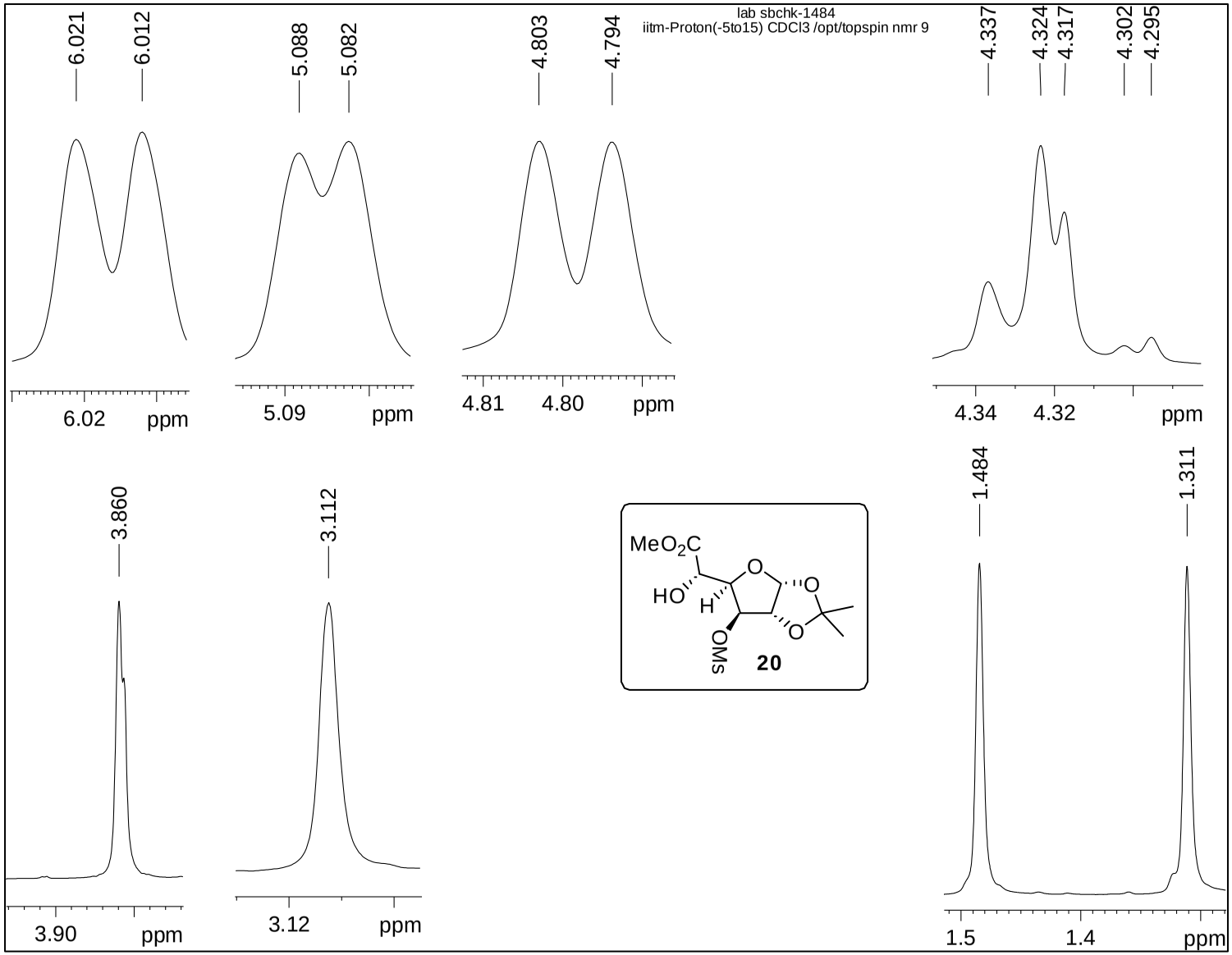

Expanded $^{1}$H NMR spectrum of Compound **18**



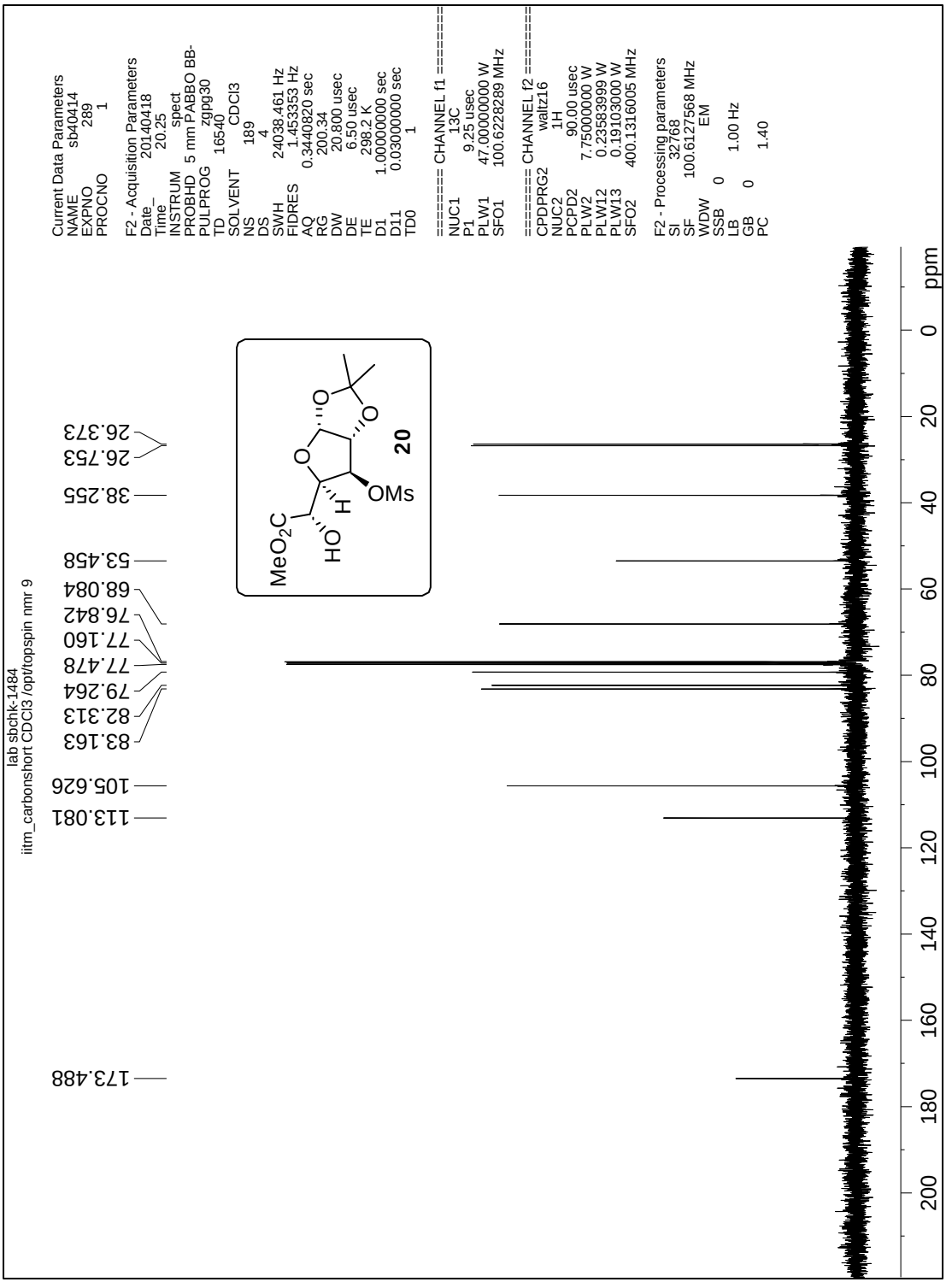

$^{13}$C NMR spectrum of Compound **18**



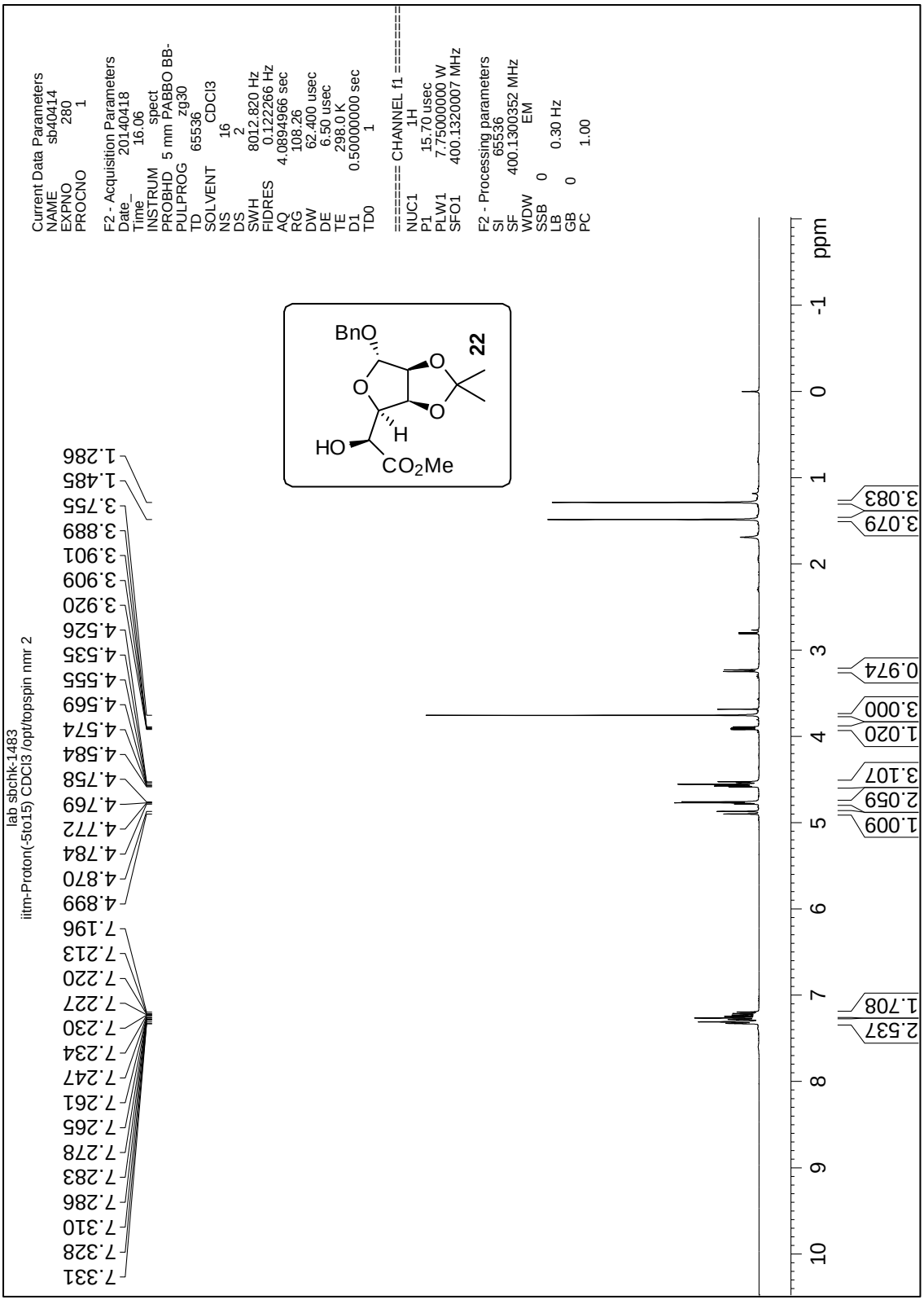

$^1$H NMR spectrum of Compound **20**



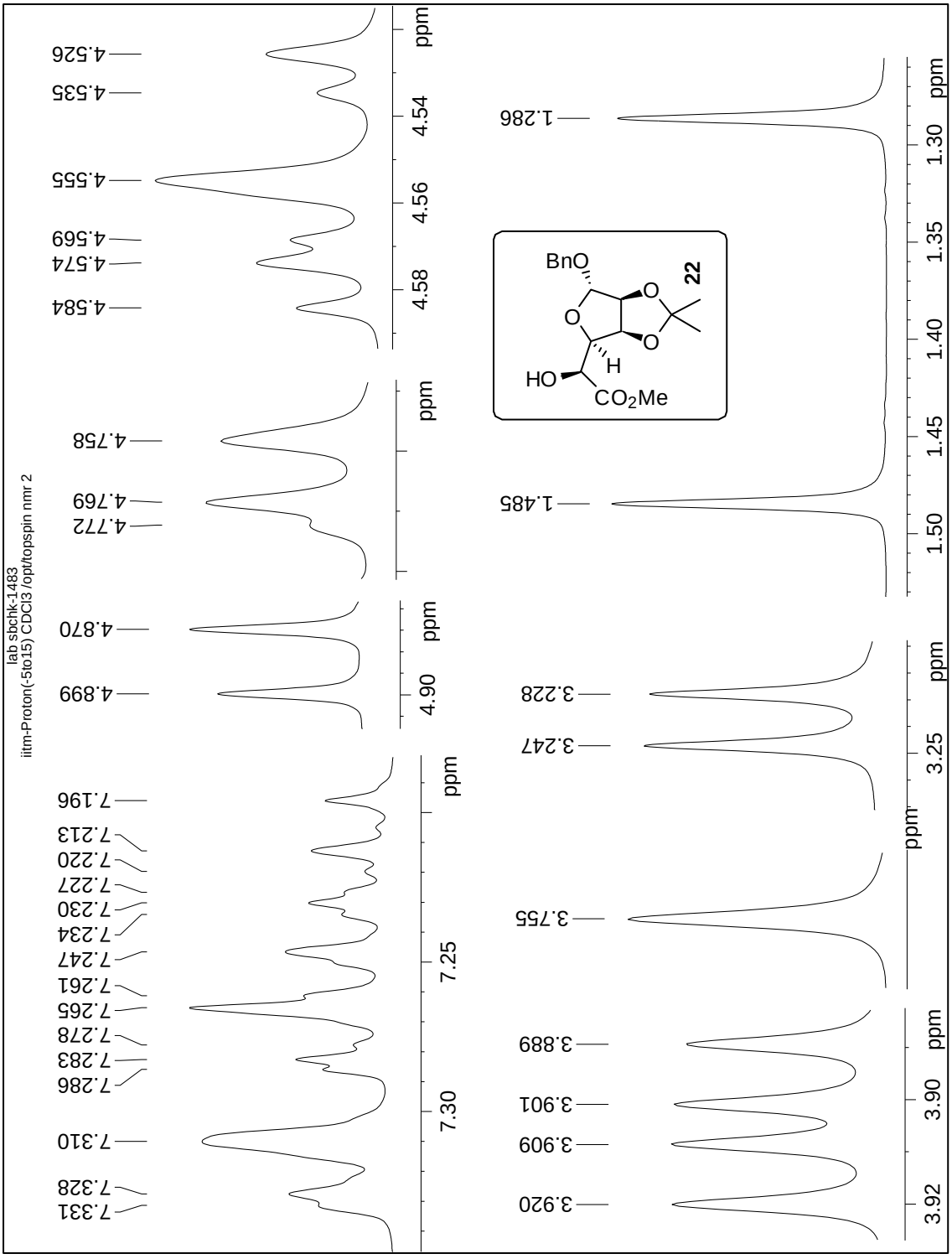

Expanded $^{1}$H NMR spectrum of Compound **20**



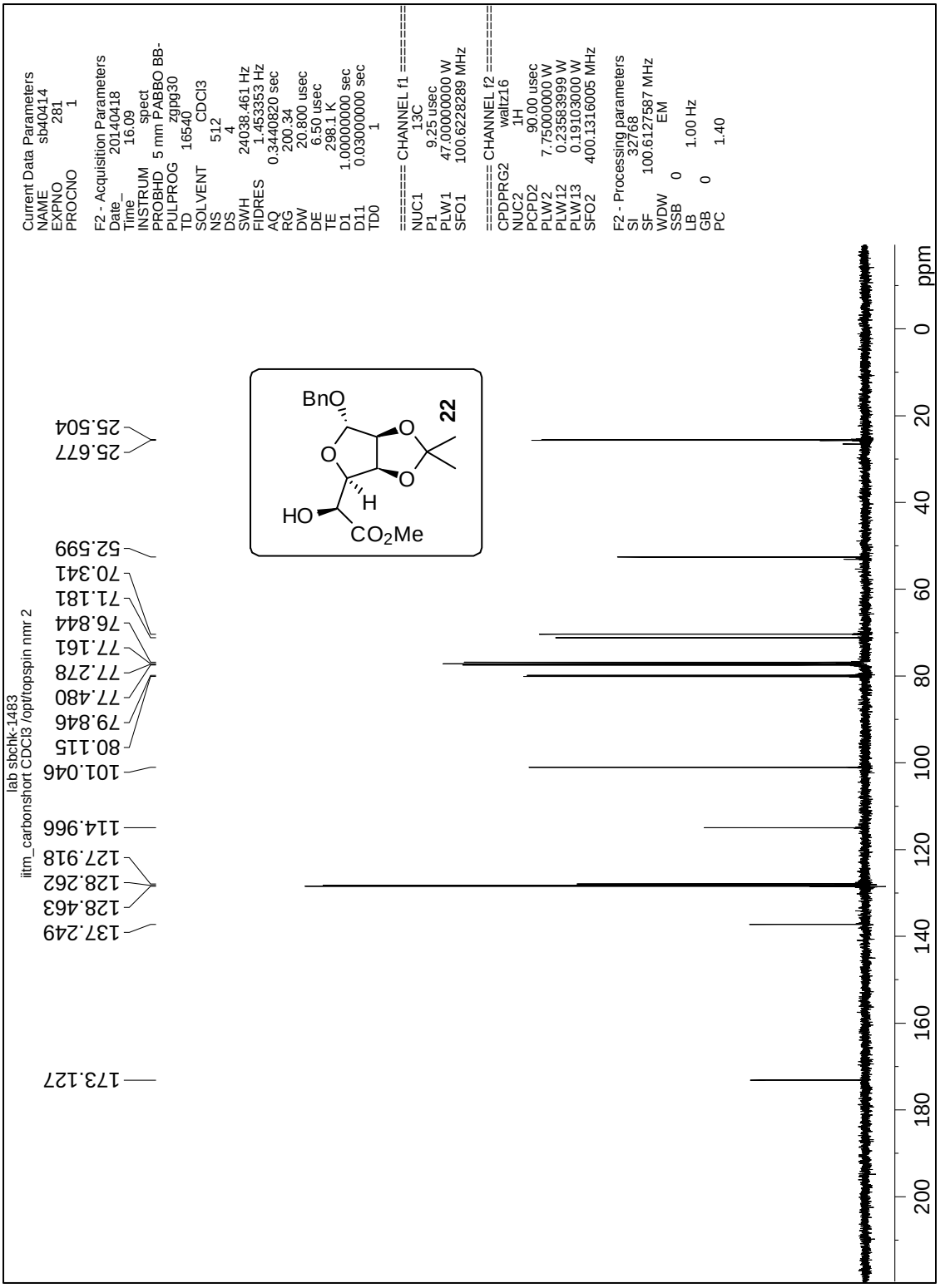

$^{13}$C NMR spectrum of Compound **20**



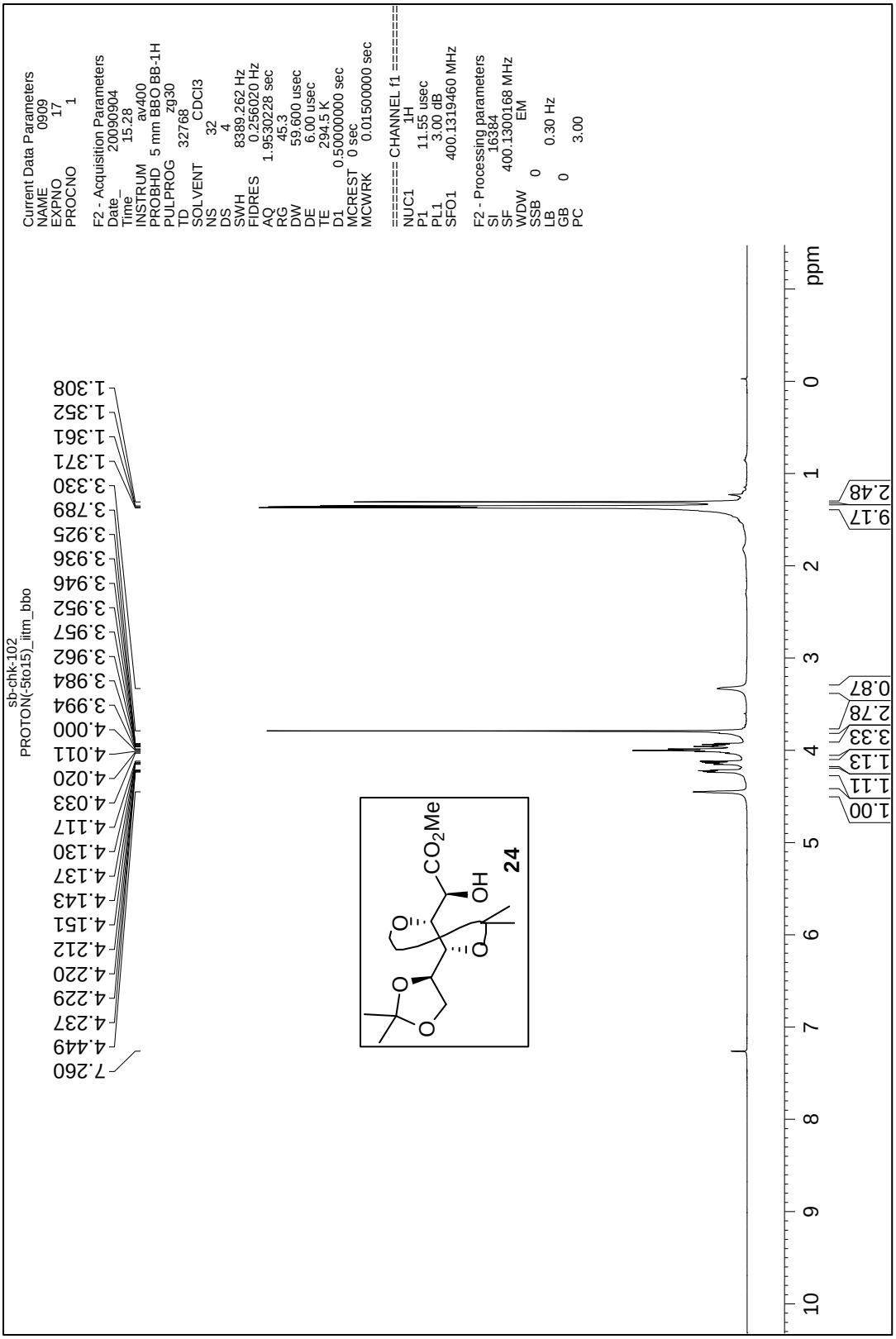

$^{1}$H NMR spectrum of Compound **22**



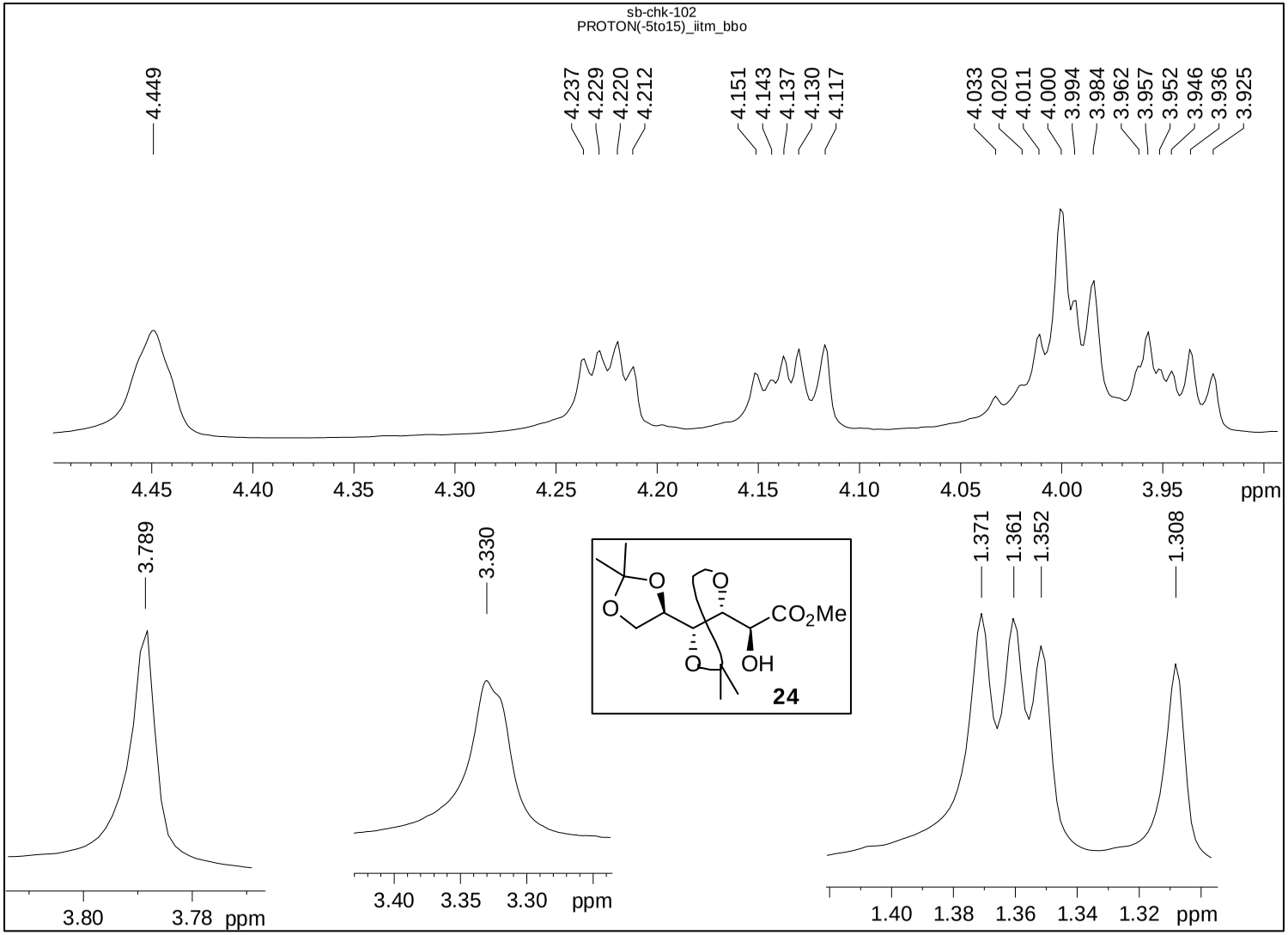

Expanded $^{1}$H NMR spectrum of Compound **22**



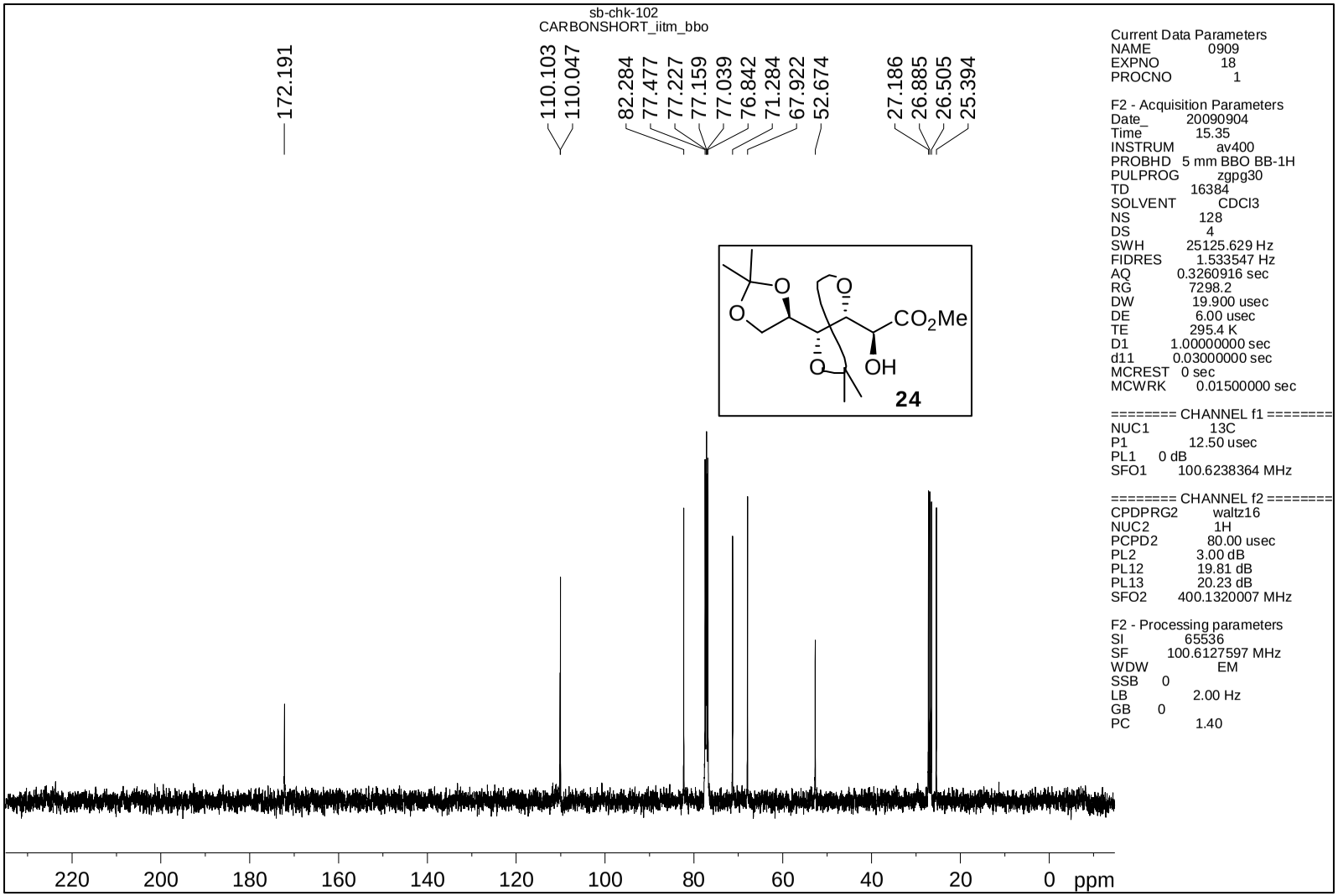

$^{13}$C NMR spectrum of Compound **22**



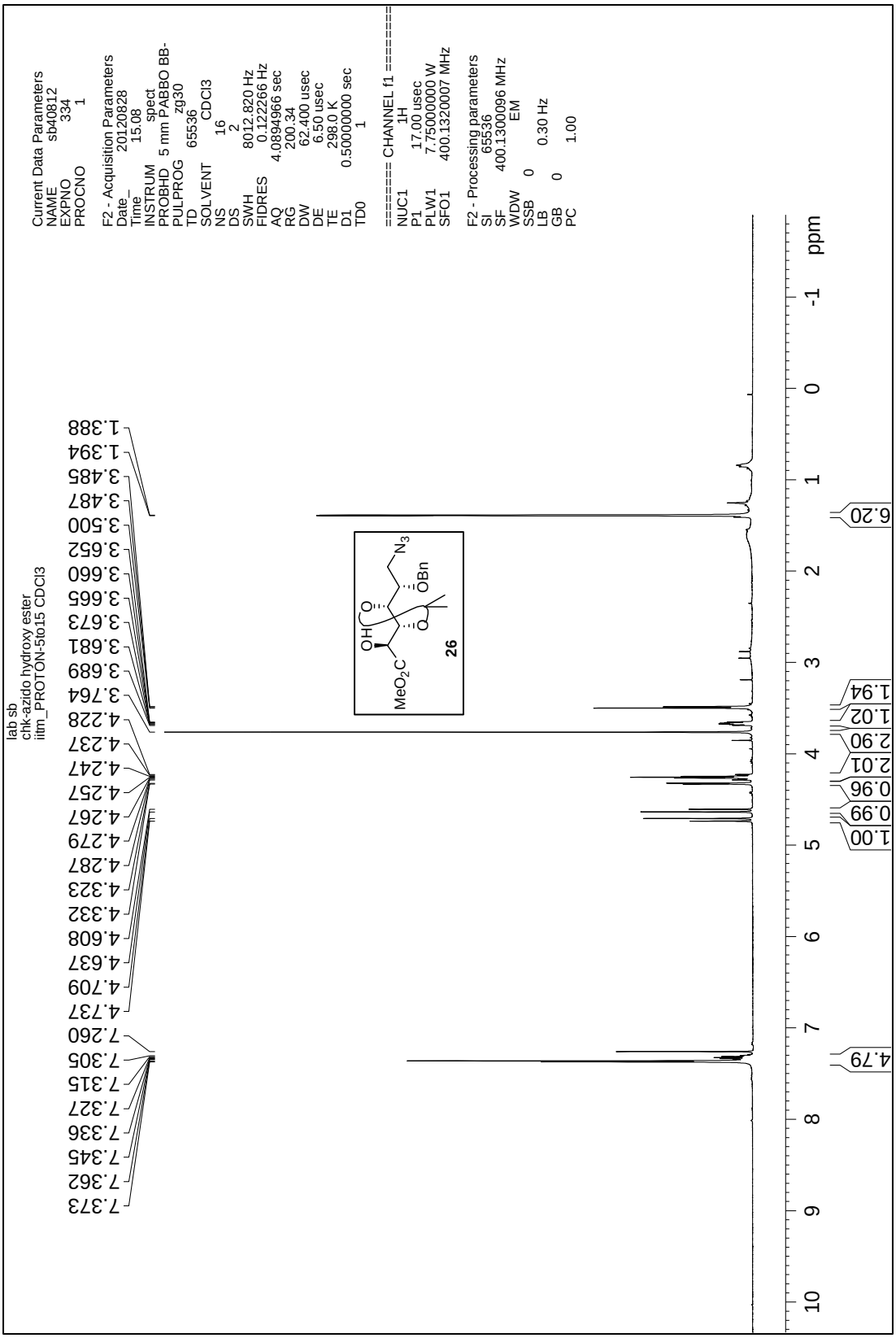

$^1$H NMR spectrum of Compound **24**



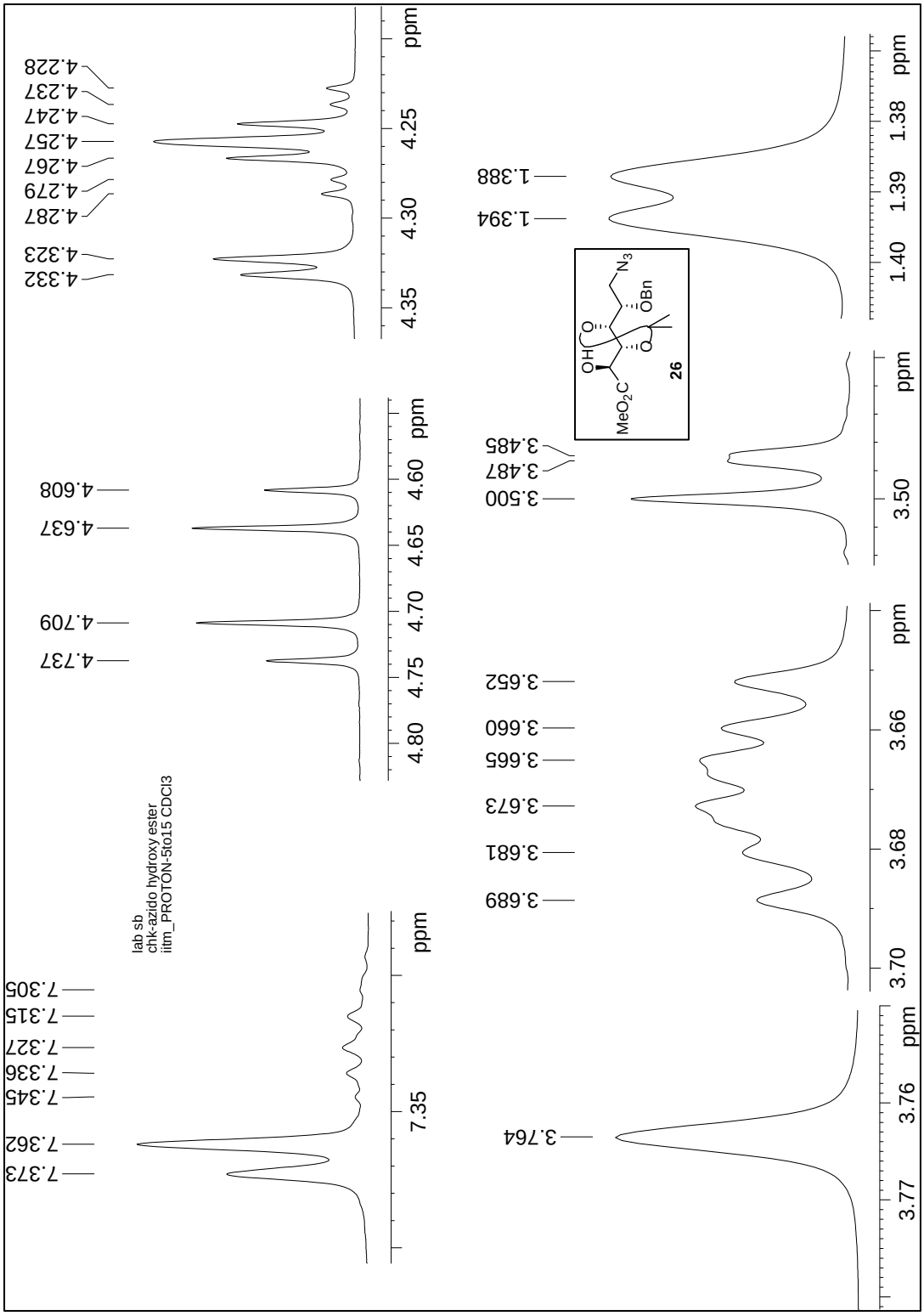

Expanded $^{1}$H NMR spectrum of Compound **24**



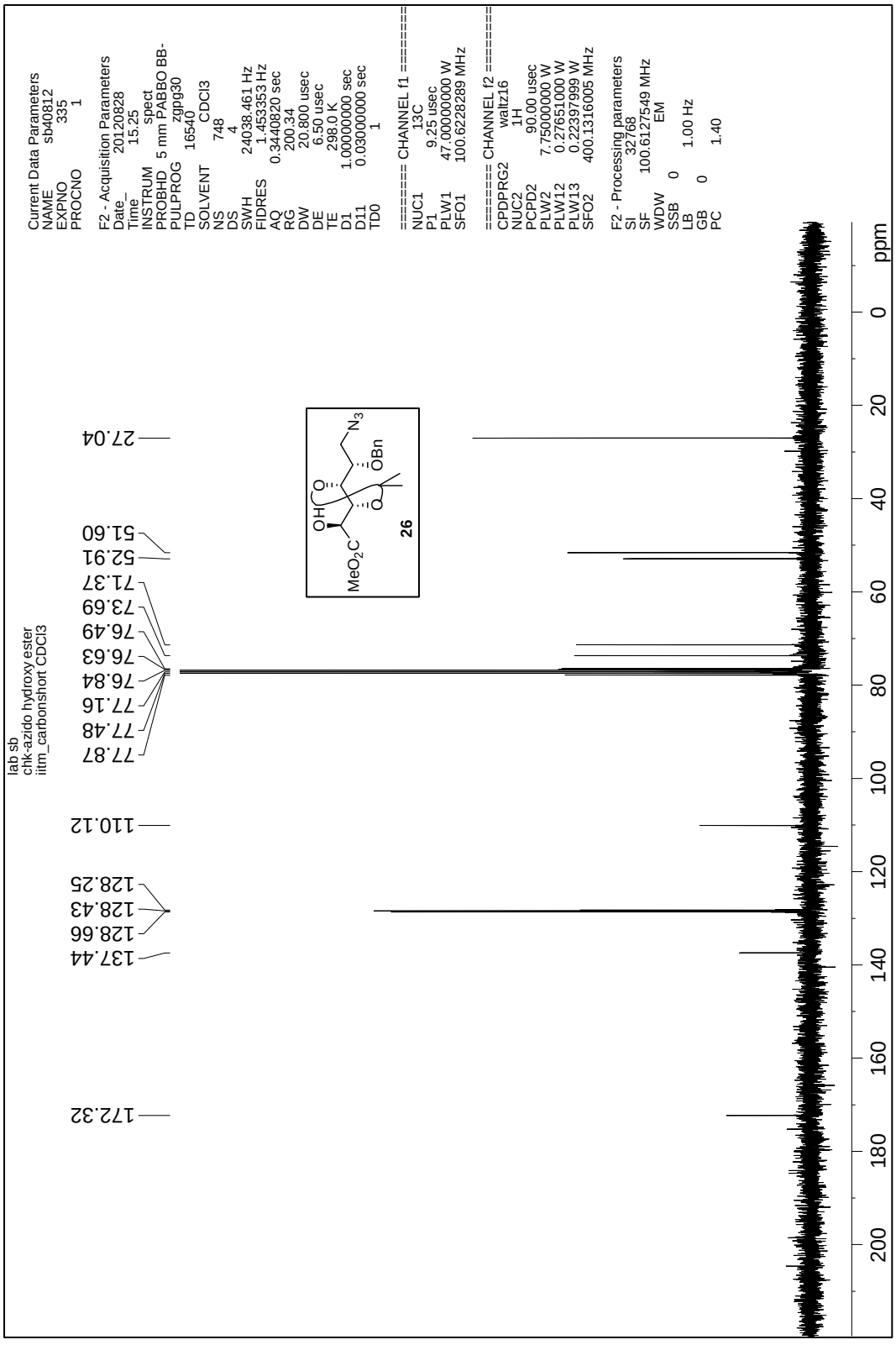

$^{13}$C NMR spectrum of Compound **24**




$^1$H NMR spectrum of Compound **26**




Expanded $^{1}$H NMR spectrum of Compound **26**




$^{13}$C NMR spectrum of Compound **26**