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Internal Lewis Acid Assisted Benzoic Acid Catalysis

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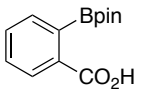
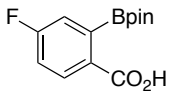
General Methods: Methylene chloride, toluene, and DMF were purified by passage through a bed of activated alumina.[1] Purification of reaction products was carried out by flash chromatography using Aldrich 60 Å (40 - 63 μm). Analytical thin layer chromatography was performed on EMD Chemicals 0.25 μm silica gel 60-F_{254} plates. Visualization was accomplished with UV light and potassium permanganate or ceric ammonium molybdate stains followed by heating. Melting points (**mp**) were obtained on a Thermo Scientific Mel-temp apparatus and are uncorrected. Infrared spectra (**IR**) were obtained on a Perkin Elmer Spectrum 100R spectrophotometer. Infrared spectra were obtained by preparing a KBr pellet containing the title compound. Proton nuclear magnetic resonances (**^{1}H NMR**) were recorded in deuterated solvents on a Bruker Avance DPX 400 (400 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm, δ) using the solvent as internal standard ($CHCl_3$, δ 7.26 and DMSO, δ 2.50) ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), or quartet (q). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m) or broad (br). Coupling constants are reported in Hertz (Hz). Proton-decoupled carbon (**^{13}C-NMR**) spectra were recorded on a Bruker Avance DPX 400 (100 MHz) spectrometer and are reported in ppm using the solvent as an internal standard ($CHCl_3$, δ 77.0; DMSO, δ 39.5). Proton decoupled fluorine (^{19}F-NMR) spectra were recorded on a Bruker Avance DPX 400 spectrometer and are reported in ppm using

$CF_3C_6H_4CH_3$ as an external standard (-63.72). Boron spectra (^{11}B-NMR) were recorded on a Bruker Avance DPX 500 spectrometer and are reported in ppm using BF_3•OEt_2 as an external standard (0.00). Electrospray mass spectra (**ESI-MS**) were obtained using a Bruker MicrOTOF Mass Spectrometer. Gas Chromatography (**GC**) analysis data were obtained on Agilent 6850 Series GC System with a 7673 Series Injector. An HP-1 capillary 30 m column was employed (19091Z-413E). 2-carboxybenzene boronic acid and (2-(methoxycarbonyl)phenyl)boronic acid was purchased from Boron Molecular and used without further purification. 2-Amino-4-(trifluoromethyl)benzoic acid was purchased from TCI America and used without further puridication. Unless otherwise noted, all other commercially available reagents and solvents were purchased from Aldrich and used without further purification.

Procedures for the preparation of boronate catalysts 8a-8d, 10b, 11:



8a: 2-carboxybenzene boronic acid (2.00g , 12.0 mmol) and pinacol (1.43 g, 12.1 mmol) were added to a 100 mL flame-dried flask equipped with a Dean Stark trap and a reflux condensor. Toluene (25 mL) was then added to the reaction pot and the heterogeneous mixture was heated reflux with vigorous stirring for 24 h. The reaction mixture was then allowed to cool to room temperature and the solvent was removed *in vacuo*. Excess pinacol was removed by trituration of the resulting white solid in ether. This afforded **8a** as a white powder, 2.89 g (97%), decomposed 331.2 – 333.6 ºC; IR (KBr) 2975, 1679, 1451, 1152, 1088 cm^{-1}; ^{1}H NMR (400 MHz, DMSO d_6) δ 7.38 (d, 1H, J = 7.2 Hz); 7.33-7.24 (m, 2H); 7.13 (m, 1H); 1.09 (s, 12H); ^{13}C NMR (100 MHz, DMSO d_6) δ 173.1, 138.1, 130.1, 128.7, 125.7, 122.2, 77.66 25.5 (the carbon bonded to boron was not seen due to broadening)[2]; ^{11}B NMR (160 MHz, DMSO d_6) δ 10.4 (br s); HRMS (ESI): Mass calculated for $C_{13}H_{16}BO_4$ $[M–H]^–$, 247.1147. Found $[M–H]^–$, 247.1147.

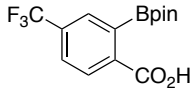


8b: The esterification was carried out as previously reported.[3] 2-Bromo-4-fluorobenzoic acid (1.00 g, 4.6 mmol) was dissolved in MeOH (6 mL), concentrated HCl (50 µL) was added, and the reaction mixture was heated to 65 ºC for 24 h. After allowing to cool to room temperature, the reaction mixture as extracted with methylene chloride (3 x 50 mL), washed with $NaHCO_3$, washed with brine, dried with Na_2SO_4, and concentrated to afford methyl 2-bromo-4-fluorobenzoate as a clear oil (850 mg, 80 %); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, 1H, J = 8.8, 6.0 Hz); 7.40 (dd, 1H, J = 8.0, 2.4 Hz); 7.07 (ddd, 1H, J = 10.4, 7.6, 2.4 Hz); 3.92 (s, 3H).

This borylation procedure was performed on a similar compound.[4] An oven-dried 50 mL schlenk flask was brought into the glove box and methyl 2-bromo-4-fluorobenzoate (500 mg, 2.15 mmol), bis(pinacolato)diboron (589 mg, 2.36 mmol, 1.1 eq.), $PdCl_2$(dppf)•DCM (89 mg, 0.108 mmol, 5 mol %), and KOAc (645 mg 6.45 mmol, 3.0 eq.) were added. The reaction flask was sealed with a septum and removed from the glove box. The reaction flask was purged with nitrogen (3x) and dioxane (11.2 mL) was added. The reaction mixture was then heated to 80 ºC for 24 h under a nitrogen atmosphere. After cooling to room temperature the reaction mixture was filtered through celite, and the solid was

washed with ethyl acetate (100 mL). The filtrate was then washed with water (2 x 100 mL), washed with brine, and dried with $MgSO_4$. After concentrating, the crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford methyl 4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate as a clear oil (546 mg, 91 %); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, 1H, *J* = 8.4 Hz, 5.2 Hz); 7.14 (dd, 1H, *J* = 8.8 Hz, 2.8 Hz); 7.07 (dt, 1H, *J* = 8.4 Hz, 2.4 Hz); 3.90 (s, 3H); 1.42 (s, 12 H).

The methyl 4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (100 mg, 0.376 mmol) was added to an 8 mL vial and dissolved in THF (2.0 mL) under an argon atmosphere. Aqueous LiOH (2 M, 0.50 mL, 1 mmol) was then added at 23 ºC and the reaction mixture was allowed to stir at 23 ºC for ~1 h (monitored by TLC). After the reaction reached completion the reaction mixture was diluted with water, acidified, and extracted with ethyl acetate (3 x 50 mL). The organic layer was then washed with brine and dried with $MgSO_4$. The solvent was removed to afford **8b** (74 mg, 77%) as a white solid, mp 136.2 – 137.9 ºC; IR (KBr) 2980, 1675 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-8.00 (m, 1H); 7.17 (d, 1H, *J* = 7.2 Hz); 7.15-7.05 (m, 1H); 1.39 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 164.5 (d, *J* = 250 Hz), 131.2, 129.8, 117.2 (d, *J* = 20 Hz), 115.3 (d, *J* = 22 Hz), 82.43, 24.6 (the carbon bonded to boron was not seen due to broadening)[2]; ^{19}F NMR (376 MHz, $CDCl_3$) δ –105.7; ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.1 (br s); HRMS (ESI): Mass calculated for $C_{13}H_{15}BFO_4$ $[M–H]^–$, 265.1047. Found $[M–H]^–$, 265.1045.



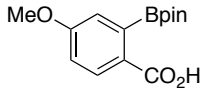
8c: A modified version of the previously published procedure was used.[5] 2-Amino-4-(trifluoromethyl)benzoic acid (2.05 g, 10.0 mmol, 1 eq.) was dissolved in a mixture of acetic acid (6 mL), 48 % HBr (4 mL), and water (4 mL) and cooled to -10º C. A solution of sodium nitrite (690 mg, 10.0 mmol, 1 eq.) in water (2 mL) was added dropwise over 5 min. The temperature was raised to 0 ºC and allowed to stir at this temperature for 3 h. The resulting slurry was added dropwise *via* syringe to a solution of CuBr (1.435 g, 10.0 mmol, 1 eq.) in 48% HBr (5 mL) at 60 ºC over 20 min. After the addition the reaction mixture was heated for 1 h at 60 ºC. The reaction mixture was then allowed to cool to 23 ºC and poured into ice cold water (200 mL). The resulting precipitate was collected in vacuo and washed with water (100 mL). The solid was then stirred in boiling DCM for 5 min and the solid was removed by vacuum filtration. The filtrate was concentrated to afford 2-bromo-4-(trifluoromethyl)benzoic acid as a tan solid (1.884 g, 70 %); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, 1H, *J* = 8.0 Hz); 7.98 (s, 1H); 7.68 (d, 1H, *J* = 8.0 Hz).

This methylation procedure has been previously reported was followed.[6] 2-bromo-4-(trifluoromethyl)benzoic acid (422 mg, 1.57 mmol) was dissolved in DMF (4.2 mL) under an argon atmosphere. Potassium carbonate (240 mg, 1.73 mmol, 1.1 eq.) and iodomethane (120 µL, 1.88 mmol, 1.2 eq.) were then added. The reaction mixture was stirred at 23 ºC for 24 h then poured into water (100 mL). The water was extracted with ethyl acetate (3 x 40 mL) and the organic layers were washed with $NaHCO_3$, washed with water, washed with brine, dried with Na_2SO_4, and concentrated to afford methyl 2-

bromo-4-(trifluoromethyl)benzoate as a orange oil (427 mg, 96 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H); 7.87 (d, 1H, *J* = 8.0 Hz); 7.62 (d, 1H, *J* = 8.0 Hz), 3.97 (s, 3 H).

This borylation procedure was performed on a similar compound.[4] An oven-dried 25 mL schlenk flask was brought into the glove box and methyl 2-bromo-4-(trifluoromethyl)benzoate (300 mg, 1.06 mmol), bis(pinacolato)diboron (290 mg, 1.16 mmol, 1.1 eq.), $PdCl_2$(dppf)•DCM (44 mg, 0.053 mmol, 5 mol %), and KOAc (318 mg, 3.18 mmol, 3.0 eq.) were added. The reaction flask was sealed with a septum and removed from the glove box. The reaction flask was purged with nitrogen (3x) and dioxane (5.6 mL) was added. The reaction mixture was then heated to 80 ºC for 24 h under a nitrogen atmosphere. After cooling to room temperature the reaction mixture was filtered through celite, and the solid was washed with ethyl acetate (100 mL). The filtrate was then washed with water (2 x 100 mL), washed with brine, and dried with $MgSO_4$. After concentrating, the product was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford methyl 4-(trifluoromethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate as a light yellow oil (317 mg, 91 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, 1H, *J* = 8.4 Hz); 7.74 (s, 1H); 7.70-7.65 (m, 1H), 3.95 (s, 3 H), 1.43 (s, 12H).

Methyl 4-(trifluoromethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (100 mg, 0.303 mmol) was added to an 8 mL vial and dissolved in THF (2 mL) under an argon atmosphere. Aqueous LiOH (2 M, 0.50 mL, 1 mmol) was then added at 23 ºC and the reaction mixture was allowed to stir at 23 ºC for ~1 h (monitored by TLC). After the reaction reached completion the reaction mixture was diluted with water, acidified, and extracted with ethyl acetate (3 x 50 mL). The organic layer was then washed with brine and dried with $MgSO_4$. The solvent was removed to afford **8c** as a white solid (85 mg, 85%), mp 133.3 – 136.4 ºC; IR (KBr) 2990, 1696, 1500, 1360, 1309, 1137, 1076 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.45 (br s, 1H); 8.15 (d, 1H, *J* = 8.0 Hz); 7.77 (s, 1H); 7.19 (d, 1H, *J* = 8.0 Hz); 1.42 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 135.8, 134.4 (q, *J* = 33 Hz), 130.1, 129.4 (m), 126.3 (q, *J* = 3 Hz), 123.8 (q, *J* = 271 Hz), 84.8, 24.9 (the carbon bonded to boron was not seen due to broadening)[2]; ^{19}F NMR (376 MHz, $CDCl_3$) δ –63.20; ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.8 (br s); HRMS (ESI): $C_{14}H_{15}BF_3O_4$ $[M–H]^-$, 315.1015. Found $[M–H]^-$, 315.1013.

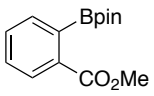


8d: The *o*-borylation procedure reported on a similar compound by Leigh and coworkers was followed.[7] N,N,N'-trimethylethylenediamine (0.82 mL, 6.4 mmol) was dissolved in dry THF (16 mL) under an argon atmosphere and cooled to -20 ºC. nBuLi (1.3 M, 4.8 mL, 6.2 mmol) was added dropwise at -20 ºC and allowed to stir at -20 ºC for 15 min. Freshly distilled aldehyde (0.73 mL, 6.0 mmol) was then added at -20 ºC and allowed to stir at -20 ºC for an additional 15 min. An additional volume of nBuLi (1.3 M, 13.9 mL, 18 mmol) was added at -20 ºC and the reaction mixture was stirred at -20 ºC for 24 h. The solution was then cooled to -78 ºC and a solution of triisopropyl borate (8.3 mL, 36 mmol, 6.0 eq) in toluene (10 mL) was added. The reaction mixture was stirred at -78 ºC for 1 h, allowed to warm to 23 ºC, and stirred for an additional 2 h. The resulting slurry was then poured into 1 M HCl solution

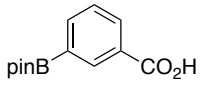
(50 mL) and stirred at 23 ºC for 30 min. The layers were separated and the aqueous layer was extracted with ether (3 x 75 mL). The organic layer was washed with brine, dried with $MgSO_4$, and concentrated to give a yellow oil. The product was purified by silica gel chromatography (5 % MeOH in methylene chloride). Crystallization of the pure product by dissolution in hot ethyl acetate and the addition of cold hexanes afforded 2-Formyl-4-methoxyphenyl boronic acid (549 mg, 47%) as a white solid. ^{1}H NMR (400 MHz, DMSO d_6) δ 9.97 (s, 1H); 8.23 (br s, 1H); 7.85 (d, 1H, *J* = 8.8 Hz); 7.10-7.04 (m, 2 H); 3.85 (s, 3H).

A modified oxidation procedure described by Lindsey *et. al* was followed.[8] 2-Formyl-4-methoxyphenyl boronic acid (400 mg, 2.22 mmol) was dissolved in a 2.5 M NaOH solution (3.6 mL) and a solution of $KMnO_4$ (350 mg, 2.22 mmol) in H_2O (13 mL) was added at 23 ºC for 4 h. The reaction mixture was then filtered through celite. The filtrate was acidified, extracted with ethyl acetate (3 x 80 mL), dried with Na_2SO_4, and concentrated to give 2-carboxy-4-methoxyphenyl boronic acid as light yellow foam (195 mg, 45%). ^{1}H NMR (400 MHz, MeOD d_4) δ 7.90 (d, 1H, *J* = 8.8 Hz); 6.99-6.90 (m, 2H); 3.86 (s, 3H).

2-Carboxy-4-methoxyphenyl boronic acid (110 mg, 0.561 mmol) and pinacol (70 mg, 0.589 mmol) were added to a flame-dried round bottom flask equipped with Dean Stark trap and a reflux condensor. Toluene (6 mL) was added and the reaction mixture was stirred in refluxing toluene for 20 h. The reaction mixture was allowed to cool to 23 ºC and the toluene was removed *in vacuo* to afford a yellow solid. Ether (5 mL) was added to the reaction flask and stirred for 30 min. The filtrate was concentrated to afford **8d** (141mg, 90%) as a white solid, mp 170.2 – 172.5 ºC; IR (KBr) 2981, 1675, 1604, 1560, 1411, 1228, 1145 cm^{-1}; ^{1}H NMR (400 MHz, DMSO d_6) δ 7.79 (d, 1H, 8.6 Hz); 6.98 (dd, 1H, *J* = 8.6, 2.4 Hz); 8.66 (d, 1H, *J* = 2.4 Hz); 3.82 (s, 3H); 1.29 (s, 12H); ^{13}C NMR (100 MHz, DMSO d_6) δ 168.7, 161.9, 130.2, 126.2, 116.4, 113.8, 83.0, 55.3, 24.6 (the carbon bonded to boron was not seen due to broadening)[2]; ^{11}B NMR (160 MHz, DMSO d_6) δ 29.6 (br s); HRMS (ESI): $C_{14}H_{18}BO_5$ [M–H]$^-$, 277.1247. Found [M–H]$^-$, 277.1246.



10b: (2-(methoxycarbonyl)phenyl)boronic acid (500 mg, 2.78 mmol), pincaol (328 mg, 2.78 mmol), and toluene (5 mL) were added to a flame-dried 25 mL round bottom flask equipped with a Dean Stark trap and a reflux condensor. The contents were then heated to reflux for 24 h under a nitrogen atmosphere. After cooling to 23 ºC, the contents were concentrated and the product was purified by silica gel column chromatography (15% ethyl acetate in hexanes) to afford methyl 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate as a colorless oil (648 mg, 89 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.91 (m, 1H); 7.53-7.46 (m, 2H); 7.45-7.37 (m, 1H); 3.91 (s, 3H); 1.419 (s, 12H).

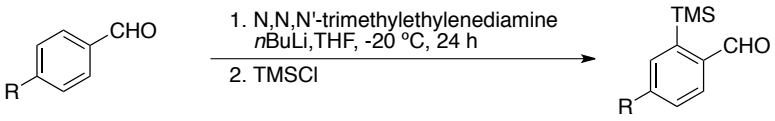


11: This borylation procedure was performed on a similar compound.[4] An oven-dried 10 mL schlenk flask was brought into the glove box and methyl 3-bromobenzoate (100.0 mg, 0.465 mmol),

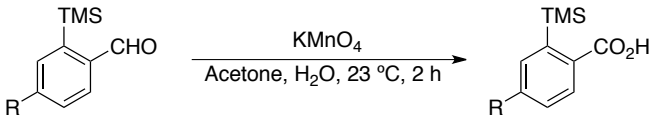
bis(pinacolato)diboron (127 mg, 0.508 mmol, 1.1 eq.), $PdCl_2$(dppf)•DCM (20 mg, 0.024 mmol, 5 mol %), and KOAc (140 mg, 1.40 mmol, 3.0 eq.) were added. The reaction flask was sealed with a septum and removed from the glove box. The reaction flask was purged with nitrogen (3x) and dioxane (2.4 mL) was added. The reaction mixture was then heated to 80 ºC for 24 h under a nitrogen atmosphere. After cooling to room temperature the reaction mixture was filtered through celite, and the solid was washed with ethyl acetate (100 mL). The filtrate was then washed with water (2 x 100 mL), washed with brine, and dried with $MgSO_4$. After concentrating, the product was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford methyl 4-(trifluoromethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate as a light yellow oil (114 mg, 93 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H); 8.12 (d, 1H, J = 12.4 Hz); 7.98 (d, 1H, J = 12.0 Hz); 7.45 (t, 1H, 12.0 Hz); 3.92 (s, 3H); 1.36 (s, 12H).

Methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (114 mg, 0.435 mmol) was added to an 8 mL vial and dissolved in THF (2 mL) under an argon atmosphere. Aqueous LiOH (2 M, 0.50 mL, 1 mmol) was then added at 23 ºC and the reaction mixture was allowed to stir at 23 ºC for 18 h (monitored by TLC). After the reaction reached completion the reaction mixture was diluted with water, acidified, and extracted with ethyl acetate (3 x 50 mL). The organic layer was then washed with brine and dried with $MgSO_4$. The solvent was removed to afford **11** as a white solid (79 mg, 73%); ^{1}H NMR (400 MHz, DMSO d_6) δ 12.94 (br s, 1H); 8.26 (s, 1H); 8.05 (d, 1H, J = 7.6 Hz); 7.88 (d, 1H, J = 7.2 Hz); 7.52 (t, 1H, J = 7.6 Hz); 1.31 (s, 12H). ^{11}B NMR (160 MHz, DMSO d_6) δ 29.8 (br s).

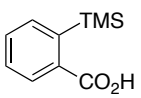
General Procedure for the preparation of silicate benzoic acids 7a-7d:



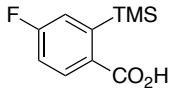
The *ortho*-lithiation procedure developed by Comins and Brown was followed.[9] N,N,N'-trimethylethylenediamine (0.82 mL, 6.4 mmol) was dissolved in dry THF (16 mL) under an argon atmosphere and cooled to -20 ºC. nBuLi (1.3 M, 4.8 mL, 6.2 mmol) was added dropwise at -20 ºC and allowed to stir at -20 ºC for 15 min. Freshly distilled aldehyde (0.73 mL, 6.0 mmol) was then added at -20 ºC and allowed to stir at -20 ºC for an additional 15 min. An additional volume of nBuLi (1.3 M, 13.9 mL, 18 mmol) was added at -20 ºC and the reaction mixture was stirred at -20 ºC for 24 h. The reaction mixture was then cooled to -40 ºC and freshly distilled TMSCl (4.57 mL, 36 mmol) was added dropwise. The reaction mixture was stirred at -40 ºC for 30 min and 23 ºC for 30 min before being quenched by pouring into 50 mL of 1M HCl. The mixture was extracted with ether, washed with brine and dried with $MgSO_4$. The yellow residue was purified via column chromatography (0% to 5% ethyl acetate in hexanes) to afford the pure product as a colorless oil.



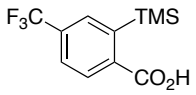
The oxidation procedure developed by Schultz *et al.* was followed.[10] The 2-trimethylsilylbenzaldehyde was (2.6 mmol) added to a 50 mL flask and dissolved in mixture of acetone (7.2 mL) and water (1.2 mL). The solution was cooled to 0 ºC and $KMnO_4$ (0.50 g, 3.2 mmol) was added slowly with rapid stirring. After 5 min the reaction mixture was allowed to warm to 23 ºC and stirred at 23 ºC. After completion of the reaction (monitored by TLC, about 1.5 h), acetone was removed *in vacuo* and the concentrate was dissolved in concentrated Na_2SO_3 and filtered through celite. The solid was washed with DCM (100 mL) and water (50 mL). The filtrate was acidified (pH ~ 2.5) and extracted with DCM (3 x 50 mL), dried with Na_2SO_4, and concentrated to afford the pure 2-trimethylsilylbenzoic acid.



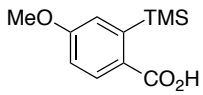
7a: 74 % - 2 steps. white solid, mp 93.0 – 94.5 ºC; IR (KBr) 2948, 1690, 1588, 1471, 1409, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 12.53 (br s, 1H); 8.19 (d, 1H, J = 7.6 Hz); 7.75 (d, 1H, J = 7.6 Hz); 7.58 (dt, 1H, J = 7.6 Hz, J = 1.6 Hz); 7.48 (dt, 1H, J = 7.6 Hz, J = 1.6 Hz); 0.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 144.0, 135.8, 134.3, 132.6, 131.1, 129.1, 0.5; HRMS (ESI): Mass calculated for $C_{10}H_{14}SiO_2Na$ $[M+Na]^+$, 217.0655. Found $[M+Na]^+$, 217.0644.



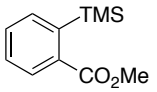
7b: 49 % - 2 steps. white solid, mp 109.8 – 111.7 ºC; IR (KBr) 2954, 1698, 1576, 1423, 1312, 1252, 1212, 1130 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.37 (br s, 1H); 8.22 (dd, 1H, *J* = 8.4 Hz, *J* = 5.2 Hz); 7.40 (dd, 1H, *J* = 9.2 Hz, *J* = 2.8 Hz); 7.12 (m, 1H); 0.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 165.6 (d, *J* = 255 Hz), 148.68 (d, J = 5 Hz), 134.0 (d, *J* = 9 Hz) 130.1 (d, *J* = 3 Hz), 122.8 (d, *J* = 20 Hz), 115.8 (d, *J* = 22 Hz), 0.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –105.9; HRMS (ESI): Mass calculated for $C_{10}H_{13}SiFNaO_2$ $[M+Na]^+$, 235.0561. Found $[M+Na]^+$, 235.0553.



7c: 86 % - 2 steps. white solid, mp 129.5 – 130.8 ºC; IR (KBr) 2955, 1705, 1482, 1411, 1321, 1264, 1136, 1077 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.28 (br s, 1H); 8.27 (d, 1H, *J* = 8.2 Hz); 7.96 (s, 1H); 7.73 (d, 1H, *J* = 8.2); 0.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 145.5, 137.5, 133.9 (q, *J* = 32 Hz), 132.3, 131.29, 126.0, 124.0 (q, *J* = 270 Hz), 0.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –63.2; HRMS (ESI): Mass calculated for $C_{11}H_{13}SiNaF_3O_2$ $[M+Na]^+$, 285.0529. Found $[M+Na]^+$, 285.0527.

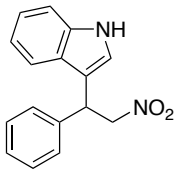


7d: 86 % - 2 steps. white solid, mp 136.8 – 138.0 ºC; IR (KBr) 2951, 1682, 1585, 1417, 1318, 1240, 1138 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.60 (br s, 1H); 8.20 (d, 1H, *J* = 8.8 Hz); 7.24 (d, 1H, *J* = 2.8 Hz); 6.93 (dd, 1H, *J* = 8.8 Hz, *J* = 2.8 Hz); 0.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 162.9.0, 146.8, 133.8, 126.4, 122.4, 112.90, 55.5, 0.5; HRMS (ESI): Mass calculated for $C_{11}H_{16}SiO_3Na$ $[M+Na]^+$, 247.0761. Found $[M+Na]^+$, 247.0754.

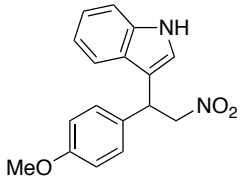


10a: The esterification procedure that was previously described was followed.[10] 2-Trimethylsilylbenzoic acid (75 mg, 0.39 mmol), potassium carbonate (133 mg, 0.958 mmol, 2.5 eq.), acetone (3.5 mL), and dimethyl sulfate (90 µL, 0.96 mmol, 2.5 eq.) were added to a flame-dried 10 mL round bottom flask equipped with a reflux condensor. The reaction mixture was then heated to 56 ºC for 24 h. After allowing to cool to 23 ºC, the reaction was quenched by the addition of water (1 mL) and stirred at 23 ºC for 1 h. The reaction mixture was extracted with ethyl acetate (3 x 20 mL), washed with $NaHCO_3$, washed with brine, and dried with Na_2SO_4. The ethyl acetate was removed *in vacuo* to afford methyl 2-trimethylsilylbenzoate as a colorless oil (72 mg, 90 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, 1H, *J* = 7.6 Hz, 1.6 Hz); 7.69 (dd, 1H, *J* = 7.2 Hz, 1.6 Hz); 7.50 (dt, 1H, *J* = 7.2 Hz, 1.6 Hz); 7.42 (dt, 1H, *J* = 7.6 Hz, 1.6 Hz); 3.91 (s, 3H); 0.326 (s, 9H). All spectral data match those that were previously reported.[10]

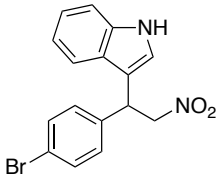
General procedure for the conjugate addition of indoles to nitroalkenes:
A dry 4 mL vial equipped with a magnetic stirbar was charged with catalyst (0.0752 mmol, 20 mol %) and nitroalkene (0.376 mmol). Methylene chloride (90 μL) was then added, followed by indole, (0.564 mmol, 1.5 equiv) and a second portion of methylene chloride (100 μL). The vial was then sealed and the reaction mixture was stirred under ambient conditions for the indicated time. The reaction mixture was then immediately purified by flash column chromatography on silica gel.



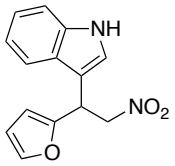
6a: Purified by column chromatography (5 to 20 % ethyl acetate in hexanes) to afford 83.2 mg (83%) of **6a** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (br s, 1H); 7.45 (app d, 1H, J = 7.6 Hz); 7.38-7.29 (m, 5H); 7.29-7.24 (m, 1H); 7.20 (app t, 1H, J = 8.0 Hz); 7.09 (app t, 1H, J = 6.8 Hz); 7.03 (app d, 1H, J = 2.0 Hz); 5.20 (app t, 1H; J = 8.0Hz); 5.07 (dd, 1H, J =12.4, 7.6 Hz); 4.95 (dd, 1H, J = 12.4, 8.4 Hz); All spectral data match those that were previously reported.[11]



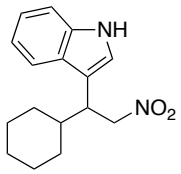
6b: Purified by column chromatography (5 to 25 % ethyl acetate in hexanes) to afford 86.3 mg (79%) of **6b** as a white crystalline solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (br s, 1H); 7.43 (app d, 1H, J = 8.0 Hz); 7.36 (app d, 1H, J = 8.0 Hz); 7.24-7.18 (m, 2H); 7.08 (app td, 1H, J = 8.0, 0.8 Hz); 7.02 (app d, 1H, J = 2.0); 6.88-6.83 (m, 2H); 5.14 (app t, J = 8.8 Hz, 1H); 5.05 (dd, J = 12.4, 8.4 Hz, 1H); 4.90 (dd, J = 12.4, 8.4 Hz, 1H); 3.78 (s, 3H). All spectral data match those that were previously reported.[11]



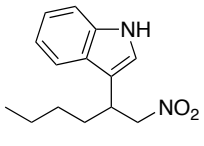
6c: Purified by column chromatography (5 to 25 % ethyl acetate in hexanes) to afford 92.1 mg (72%) of **6c** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (br s, 1H); 7.45 (app d, 2H, J = 8.4, 2.4 Hz); 7.42-7.35 (m, 2H); 7.24-7.18 (m, 3H); 7.09 (app td, 1H, J = 7.0, 1.2 Hz); 7.04-7.01 (m, 1H); 5.16 (app t, 1H, J = 7.6 Hz); 5.05 (dd, 1H, J = 12.4, 7.4 Hz); 4.91 (dd, 1H, J = 12.4, 8.8 Hz). All spectral data match those that were previously reported.[11]



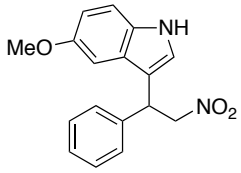
6d: Purified by column chromatography (5 to 20 % ethyl acetate in hexanes) to afford 81.5 mg (85%) of **6d** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (br s, 1H); 7.56 (app d, 1H, J = 8.0 Hz); 7.41 - 7.36 (m, 2H); 7.23 (app dt, 1H, J = 7.2 Hz, J = 1.2 Hz); 7.17-7.12 (m, 2H); 6.31 (dd, 1H, J = 3.2, 1.6); 6.17 (app d, 1H, J = 3.2 Hz); 5.26 (app t, 1H, J = 8.0 Hz); 5.06 (dd, 1H, J = 12.4, 8.0 Hz); 4.92 (dd, 1H, J = 12.4, 7.2 Hz); All spectral data match those that were previously reported.[12]



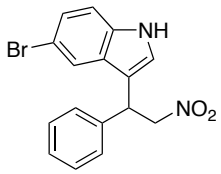
6e: Purified by column chromatography (5 to 15 % ethyl acetate in hexanes) to afford 65.4 mg (64%) of **6e** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (br s, 1H); 7.60 (m, 1H); 7.36 (m, 1H); 7.21 (m, 1H); 7.13 (m, 1H); 7.00 (s, 1H); 4.86-4.78 (m, 1H); 4.78-4.68 (m, 1H); 3.72-3.65 (m, 1H); 1.89-1.65 (m, 6H); 1.30-0.95 (m, 5 H). All spectral data match those that were previously reported.[13]



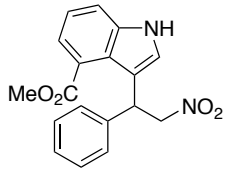
6f: Purified by column chromatography (5 to 15 % ethyl acetate in hexanes) to afford 75.6 mg (81%) of **6f** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (br s, 1H); 7.65 (m, 1H); 7.40 (m, 1H); 7.24 (m, 1H); 7.17 (m, 1H); 7.07 (m, 1H); 4.75-4.61 (m, 2H); 3.87-3.77 (m, 1H); 1.96-1.75 (m, 2H); 1.40-1.22 (4H); 0.86 (t, 3 H, *J* = 7.0 Hz); All spectral data match those that were previously reported.[14]



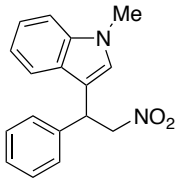
6g: Purified by column chromatography (5 to 20 % ethyl acetate in hexanes) to afford 86.2 mg (79%) of **6g** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (br s, 1H); 7.37-7.24 (m, 6H); 7.01 (app d, *J* = 2.4 Hz, 1H); 6.88 (app d, *J* = 2.4 Hz, 1H); 6.86 (br s, 1H); 5.16 (app t, *J* = 8.0 Hz, 1H); 5.06 (dd, *J* = 12.4, 7.6 Hz, 1H); 4.95 (dd, *J* = 12.4, 8.4 Hz, 1H); 3.79 (s, 3H). All spectral data match those that were previously reported[11].



6h: Purified by column chromatography (5 to 30 % ethyl acetate in hexanes) to afford 89.5 mg (69%) of **6h** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (br s, 1H); 7.55 (app d, 1H, *J* = 2.0 Hz); 7.37-7.24 (m, 7H); 7.08 (app d, 1H, *J* = 2.4 Hz); 5.13 (app t, *J* = 8.0 Hz, 1H); 5.03 (dd, *J* = 12.4, 8.0 Hz, 1H); 4.92 (dd, *J* = 12.4, 8.0 Hz, 1H); All spectral data match those that were previously reported.[15]



6i: Purified by column chromatography (5 to 35 % ethyl acetate in hexanes) to afford 51.2 mg (42%) of **6i** as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (br s, 1H); 7.60 (app dd, 1H, *J* = 7.2, 0.8 Hz); 7.52 (app dd, 1H, *J* = 8.0, 0.8 Hz); 7.31-7.19 (m, 6H); 7.08 (app dd, *J* = 2.8 Hz, 0.8 Hz, 1H); 5.83 (app t, *J* = 8.0 Hz, 1H); 5.06 (dd, *J* = 13.2, 7.4 Hz, 1H); 4.86 (dd, *J* = 13.2, 8.4 Hz, 1H); 3.85 (s, 3H); All spectral data match those that were previously reported.[16]



6j: Purified by column chromatography (5 to 15 % ethyl acetate in hexanes) to afford 15.2 mg (14%) of **6j** as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (app d, 1H, *J* = 8.0 Hz); 7.37-7.20 (m, 7H); 7.10-7.07 (m, 1H); 6.86 (s, 1H); 5.19 (app t, *J* = 8.0 Hz, 1H); 5.06 (dd, *J* = 12.4, 7.6 Hz, 1H); 4.94 (dd, *J* = 12.4, 8.4 Hz, 1H); 3.75 (s, 3H); All spectral data match those that were previously reported.[15]

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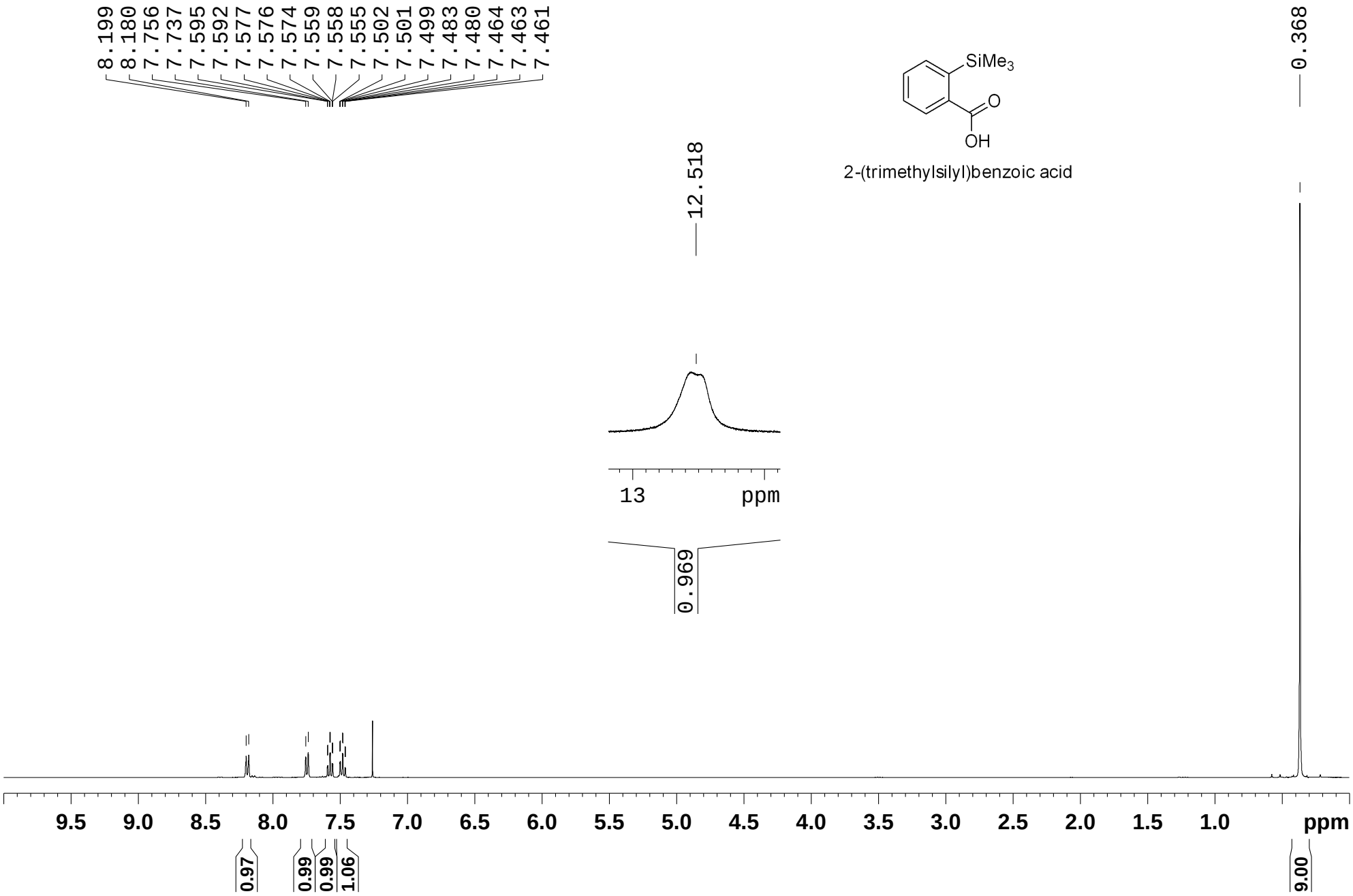
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7.499
7.483
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OH
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13
ppm
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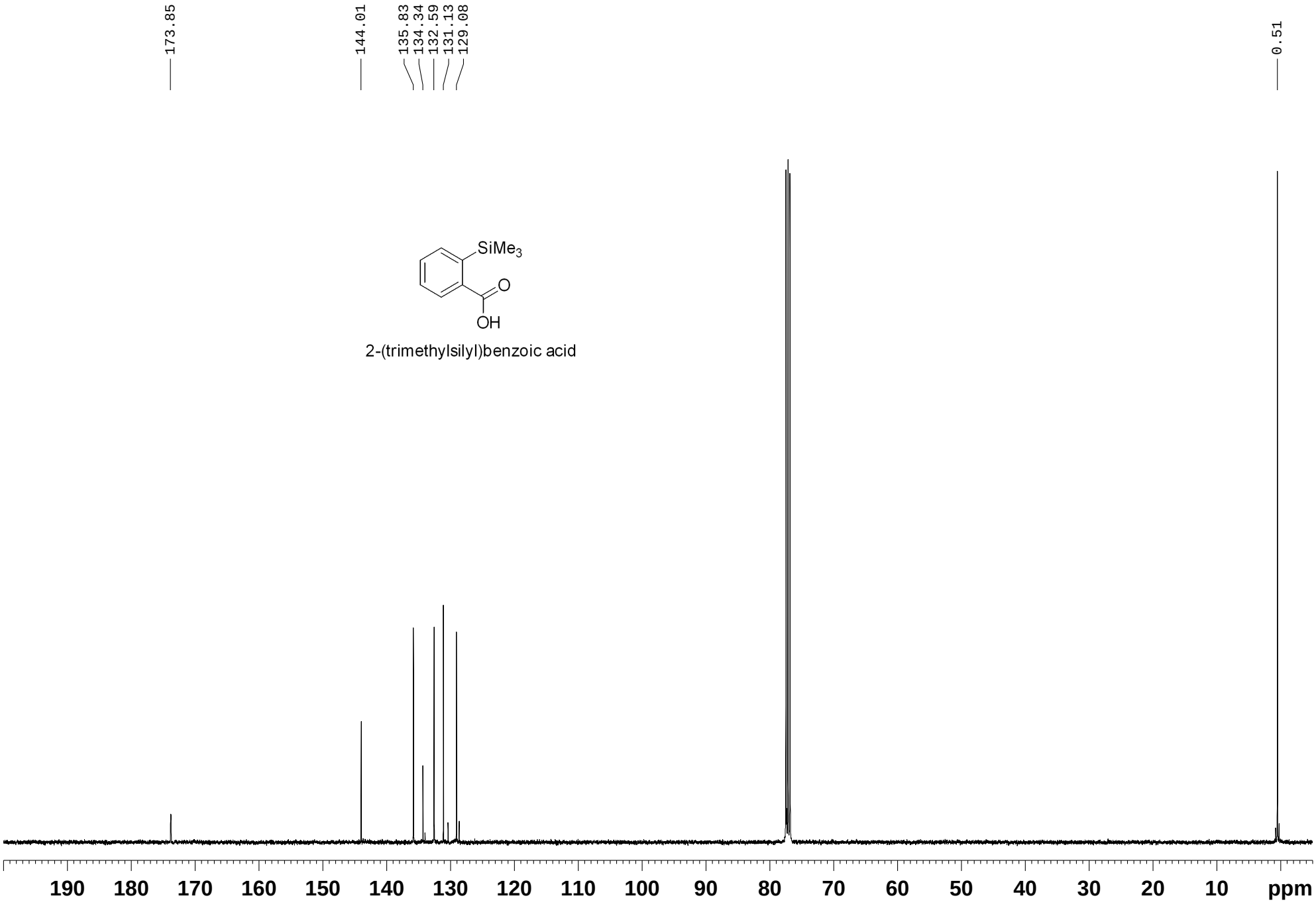
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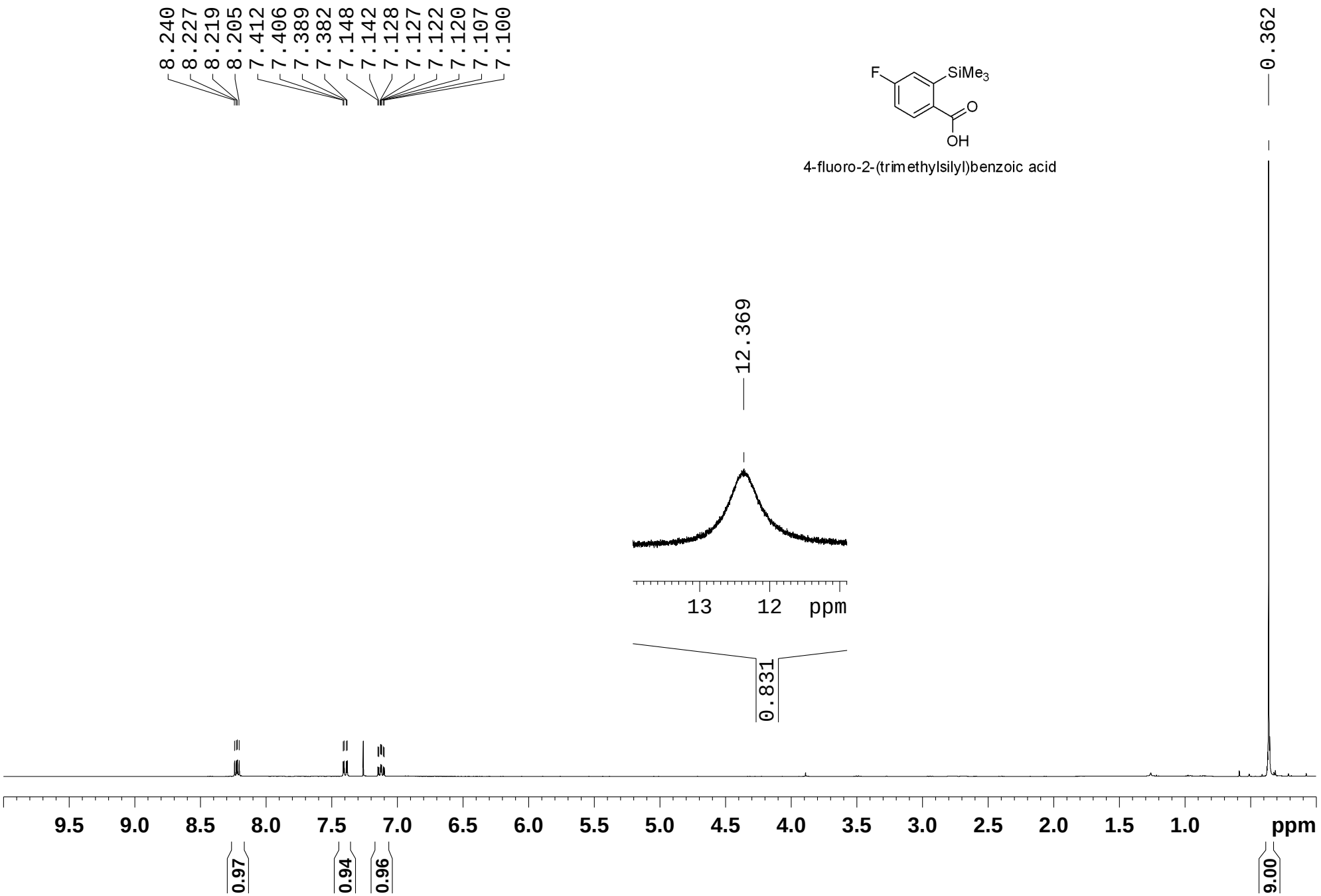
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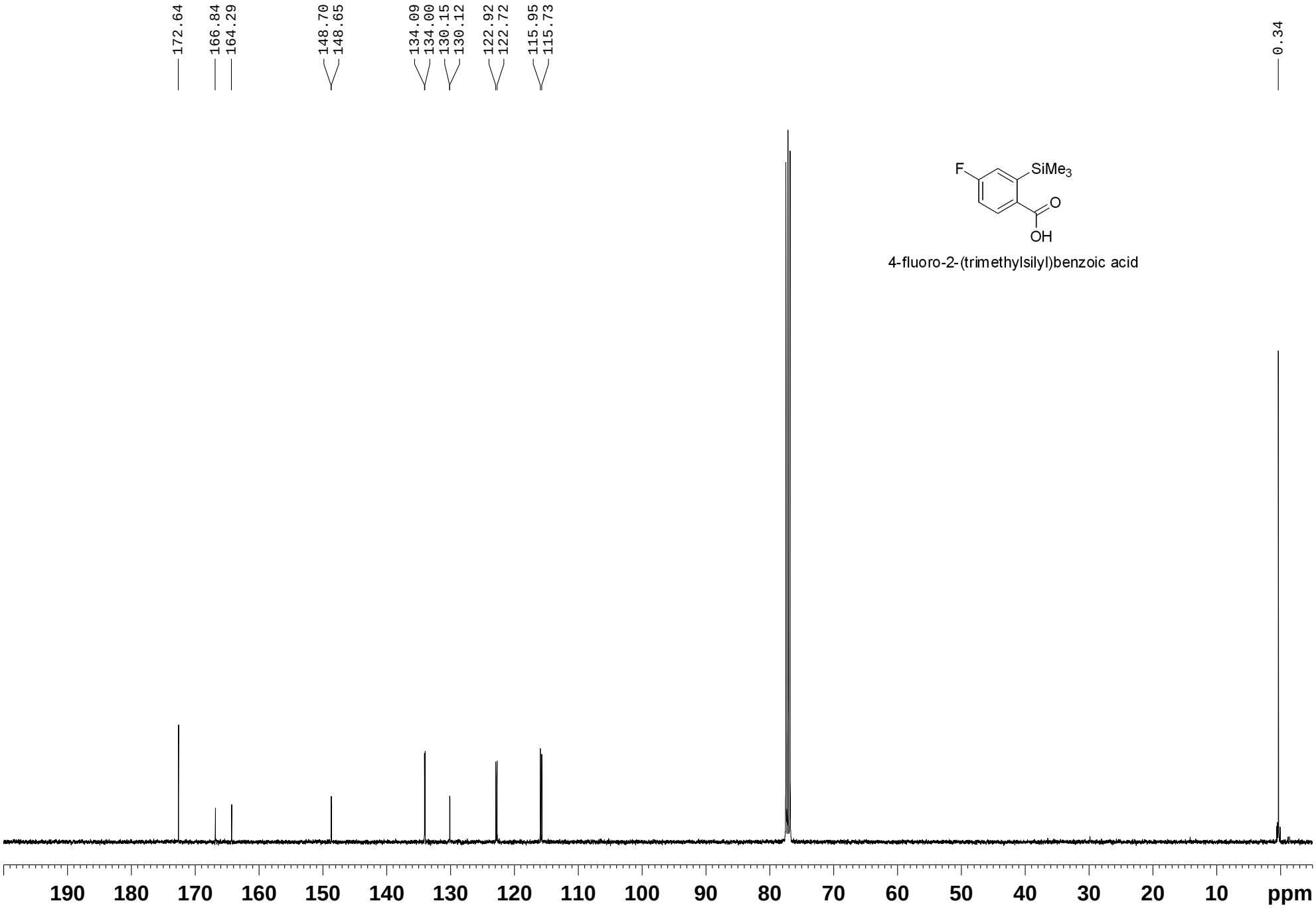
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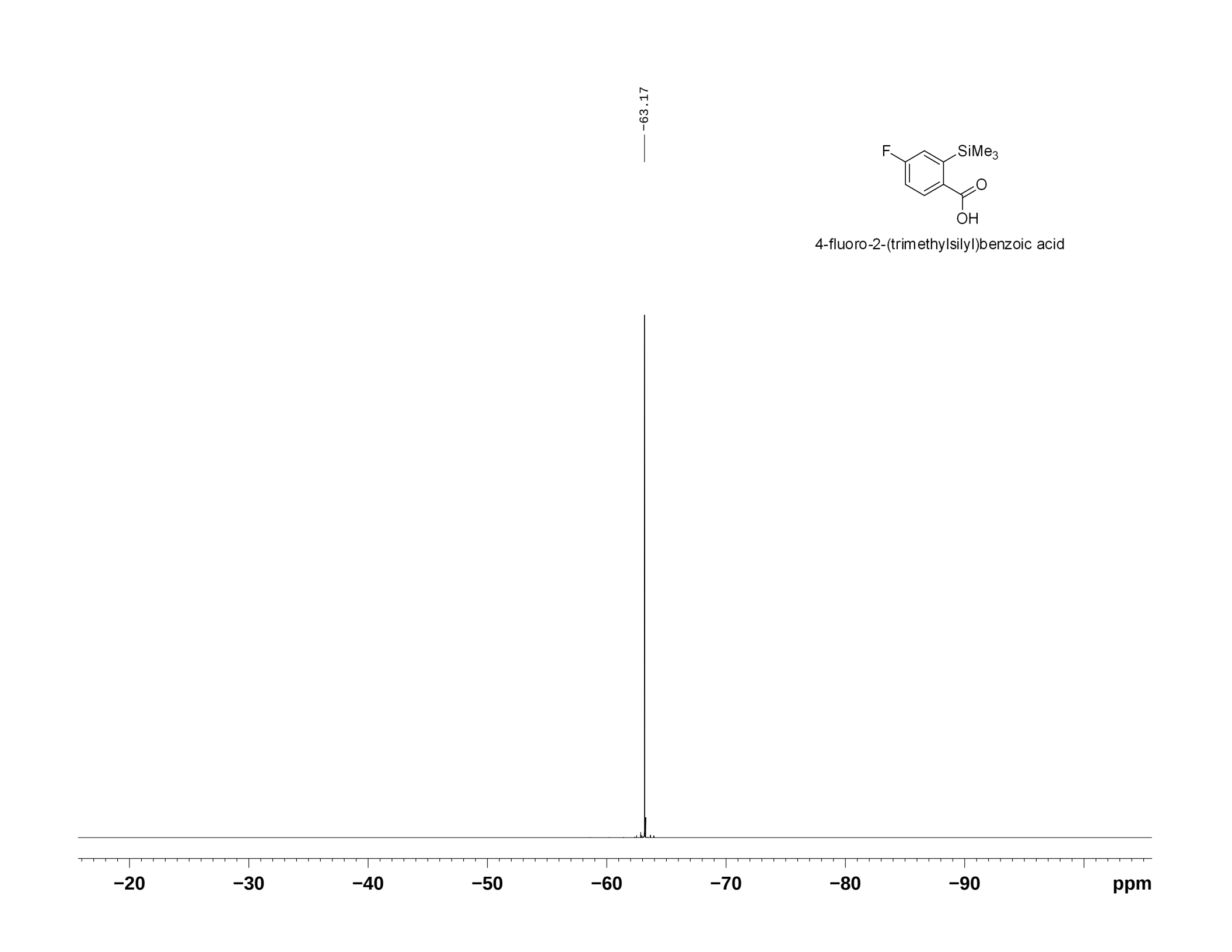
ppm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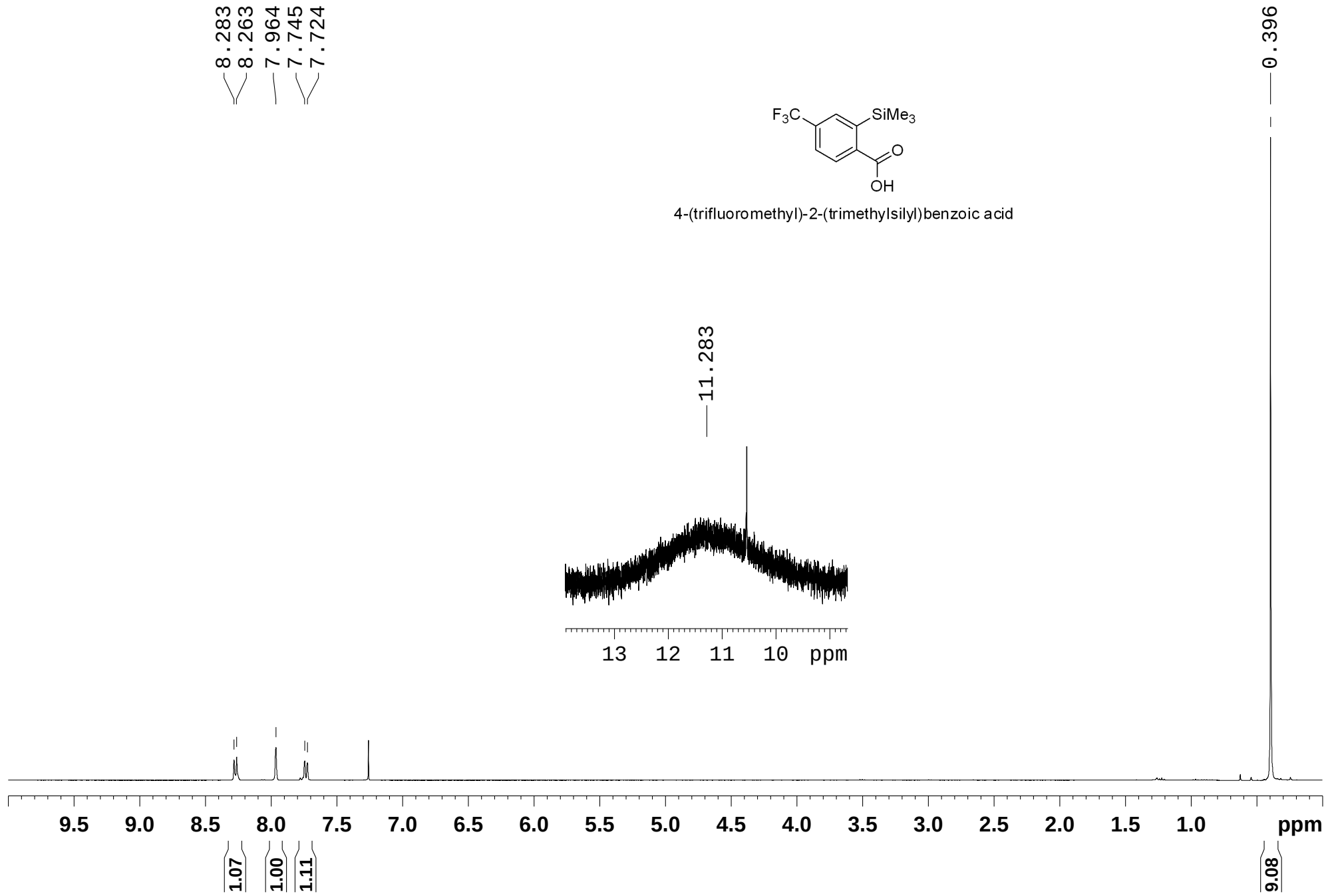
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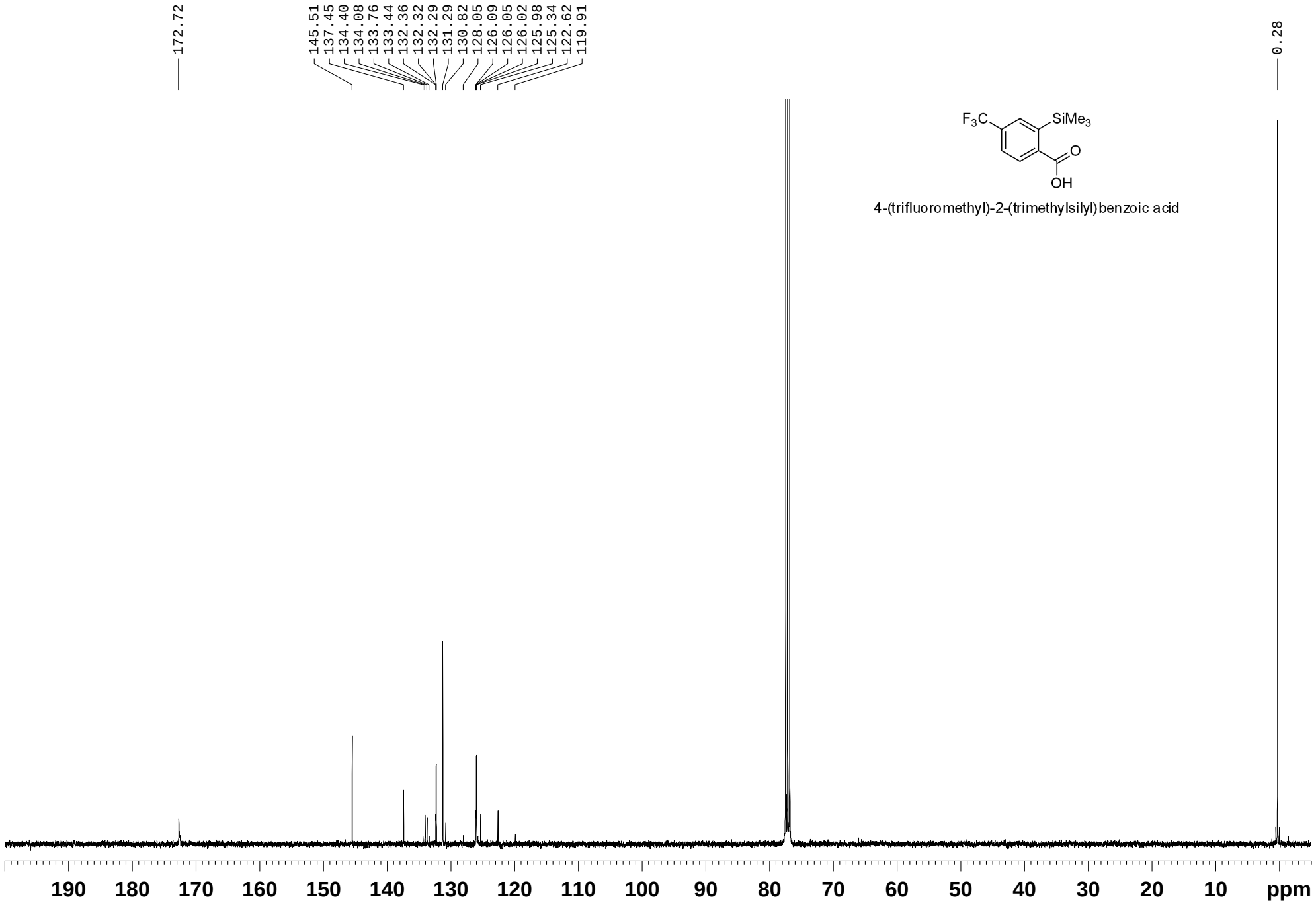
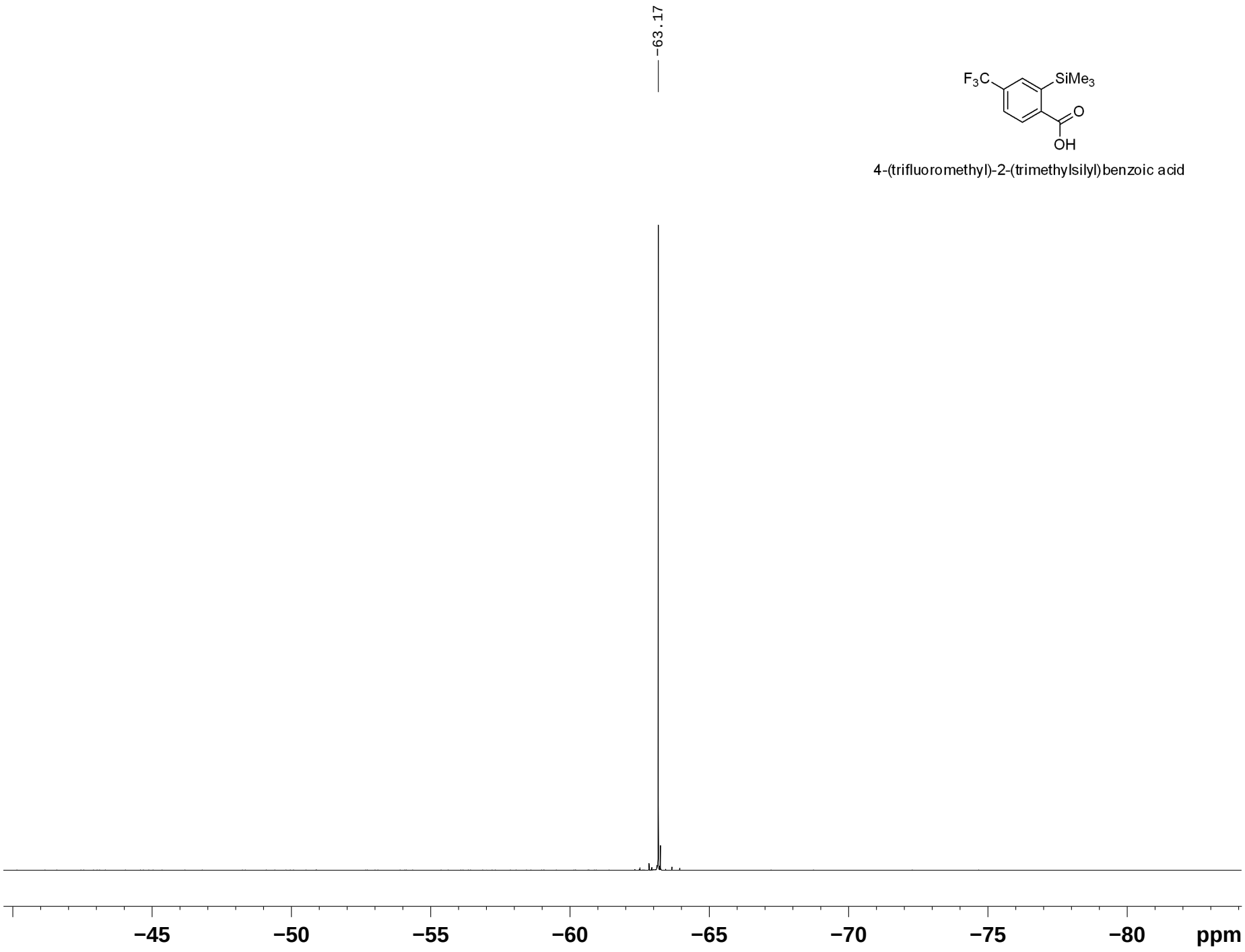
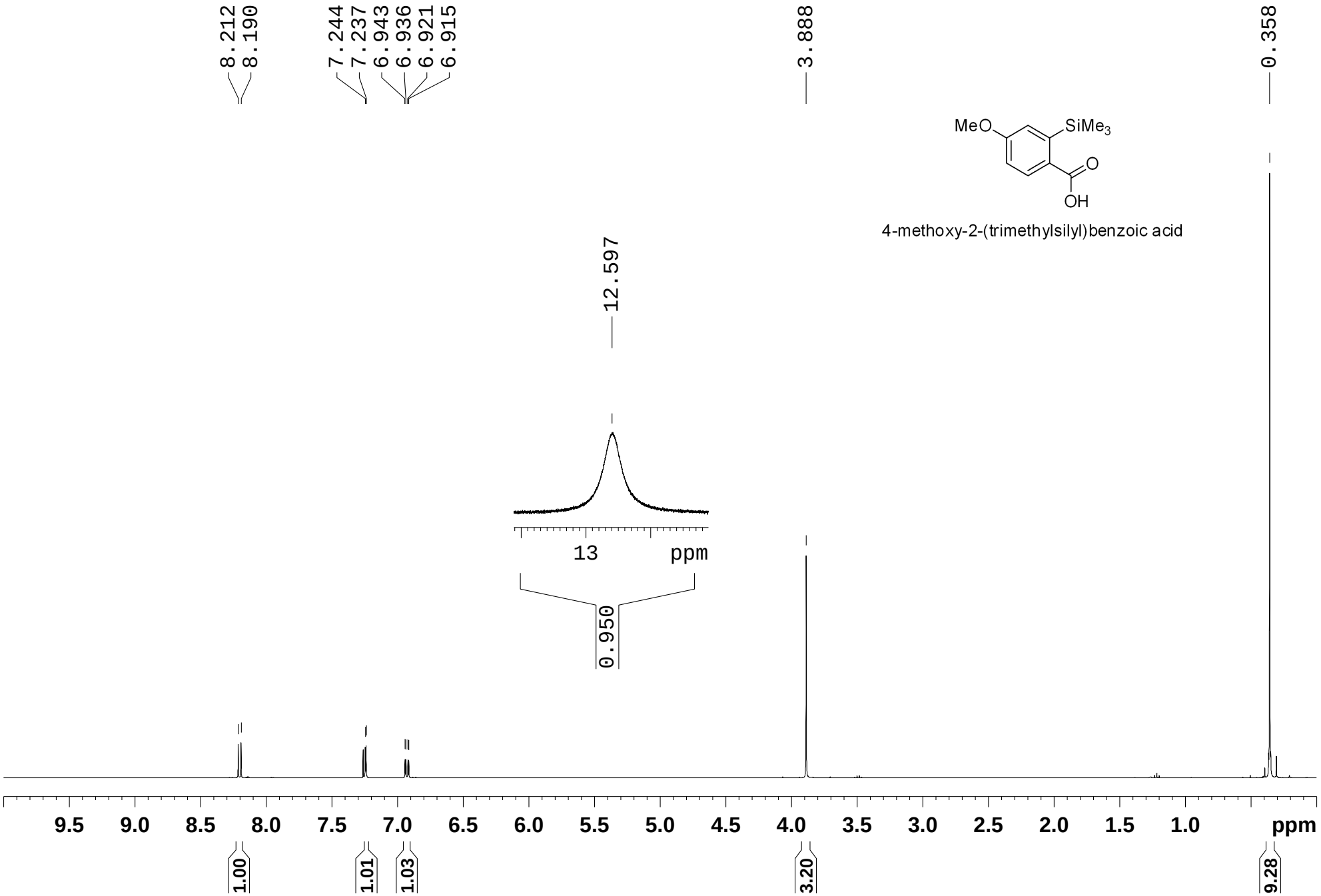
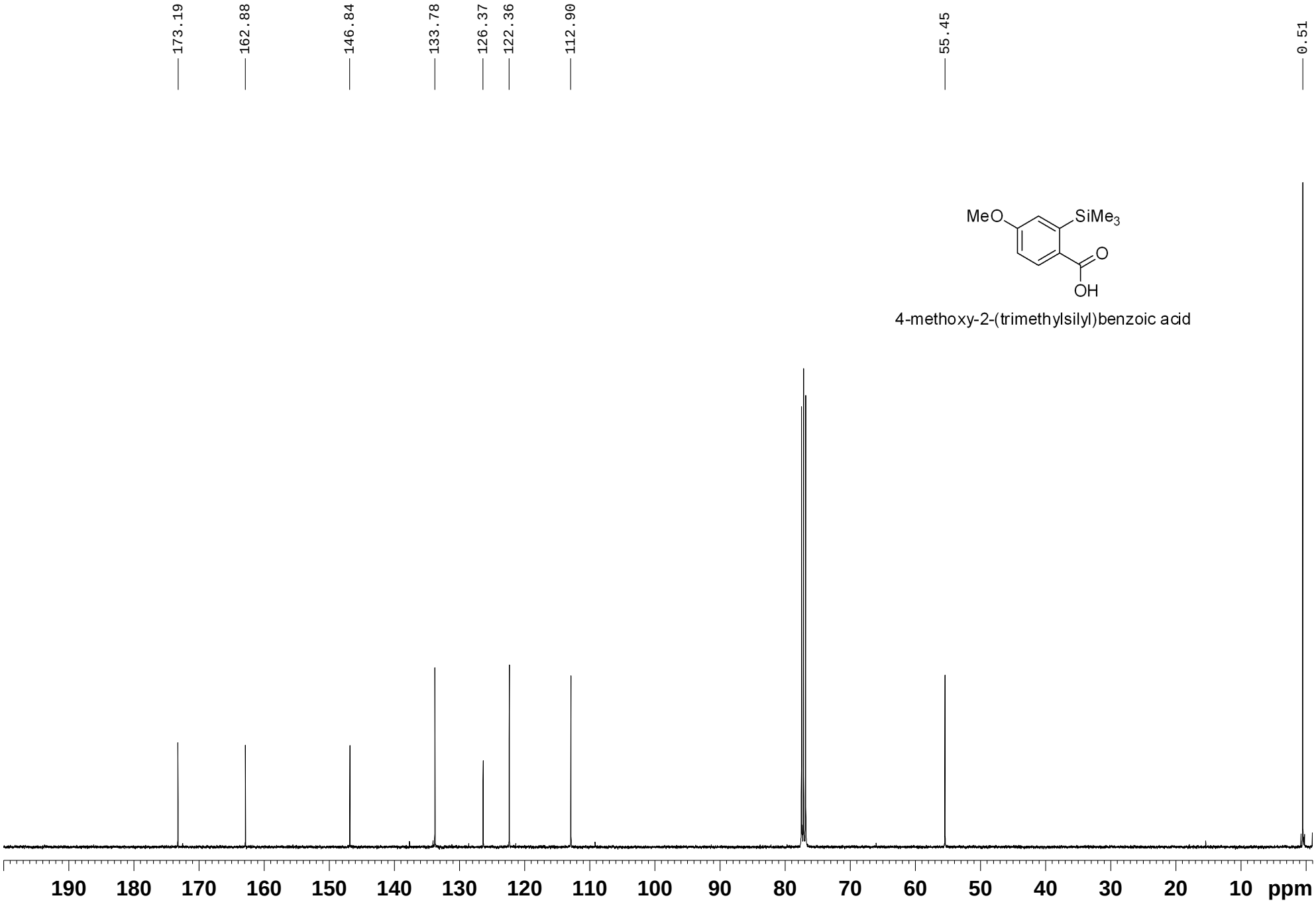
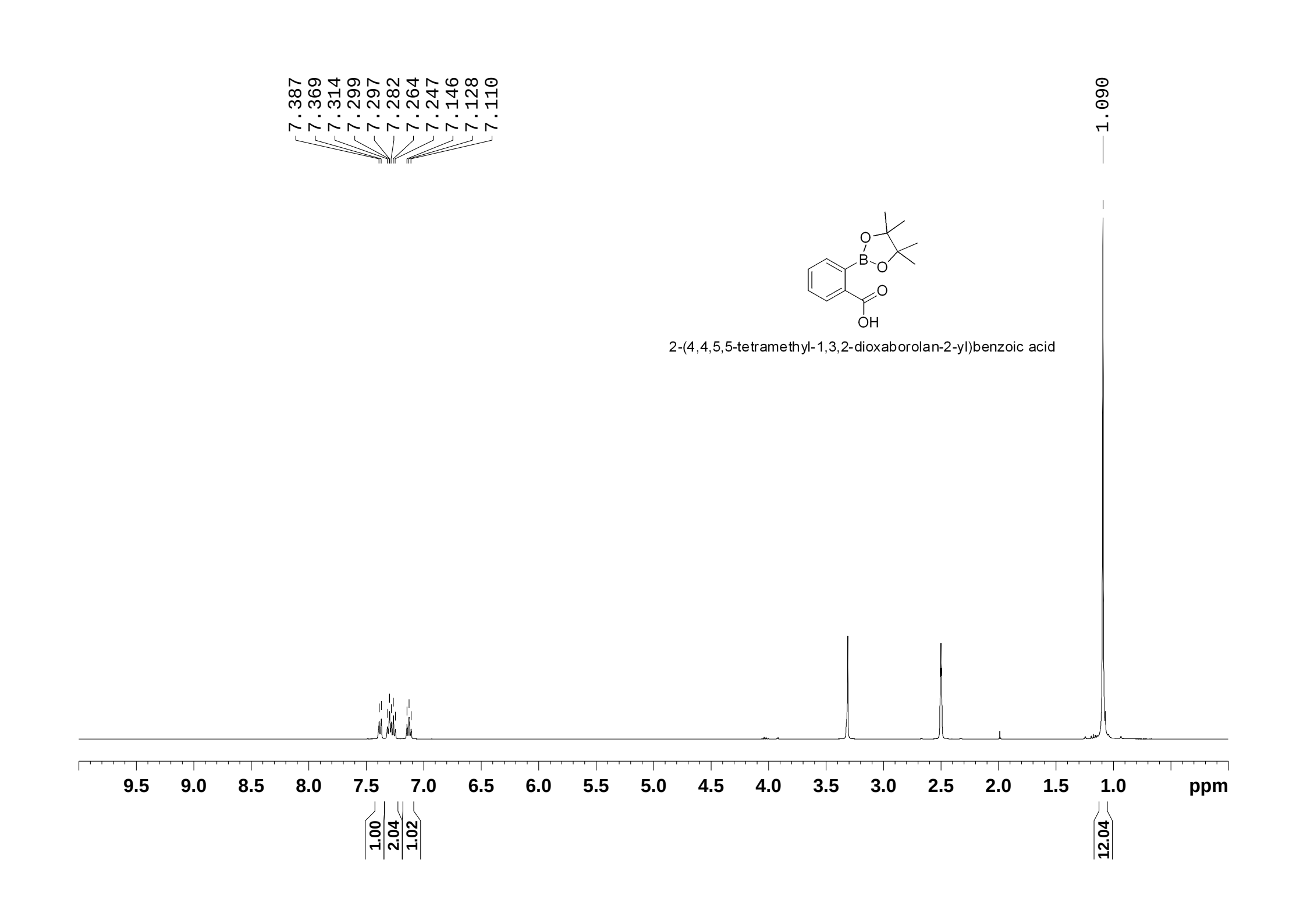
13 12 11 10 ppm
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.07
1.00
1.11
9.08

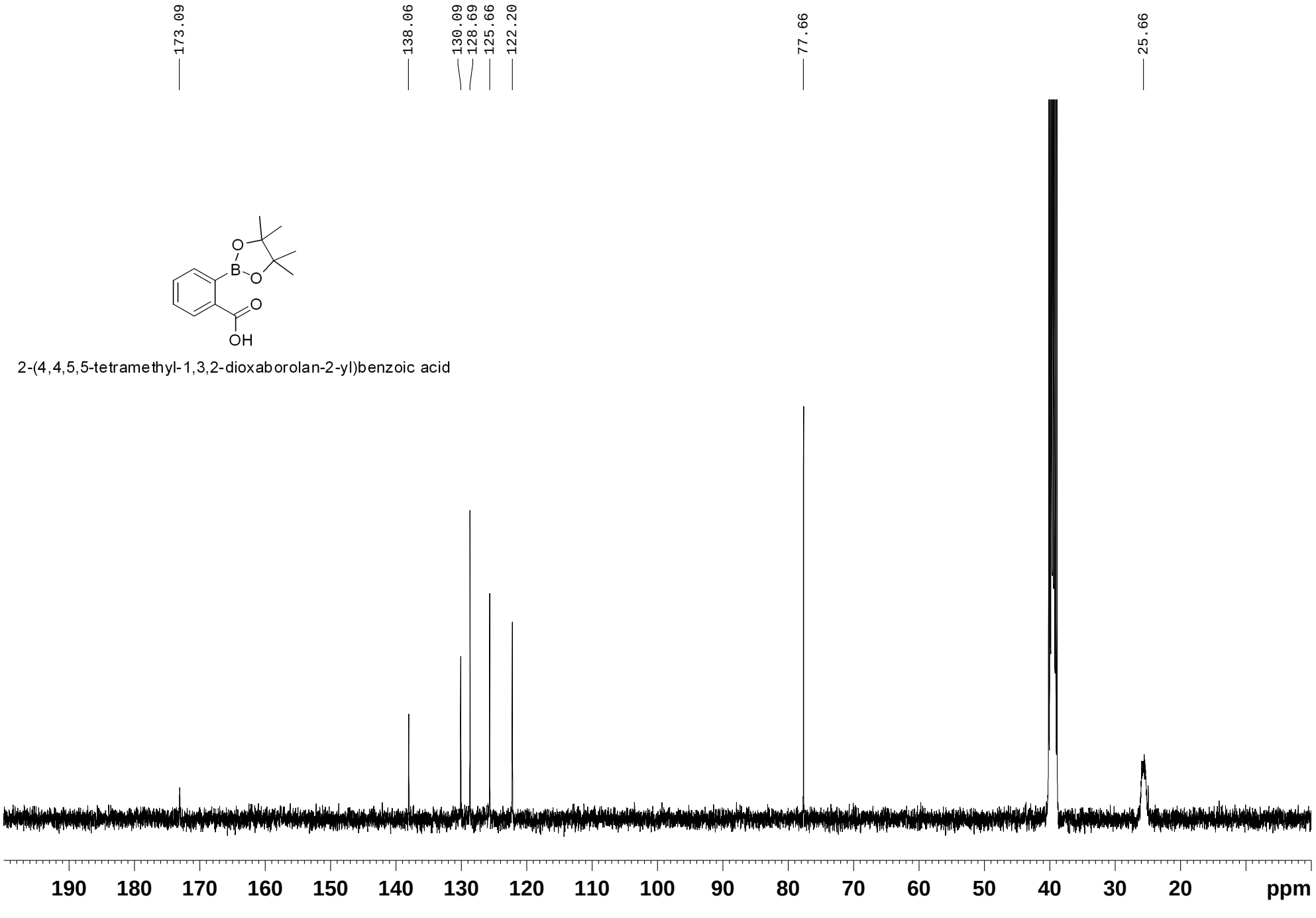

172.72
145.51
137.45
134.40
134.08
133.76
133.44
132.36
132.32
132.29
131.29
130.82
128.05
126.09
126.05
126.02
125.98
125.34
122.62
119.91
0.28
F3C
SiMe3
O
OH
4-(trifluoromethyl)-2-(trimethylsilyl)benzoic acid
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

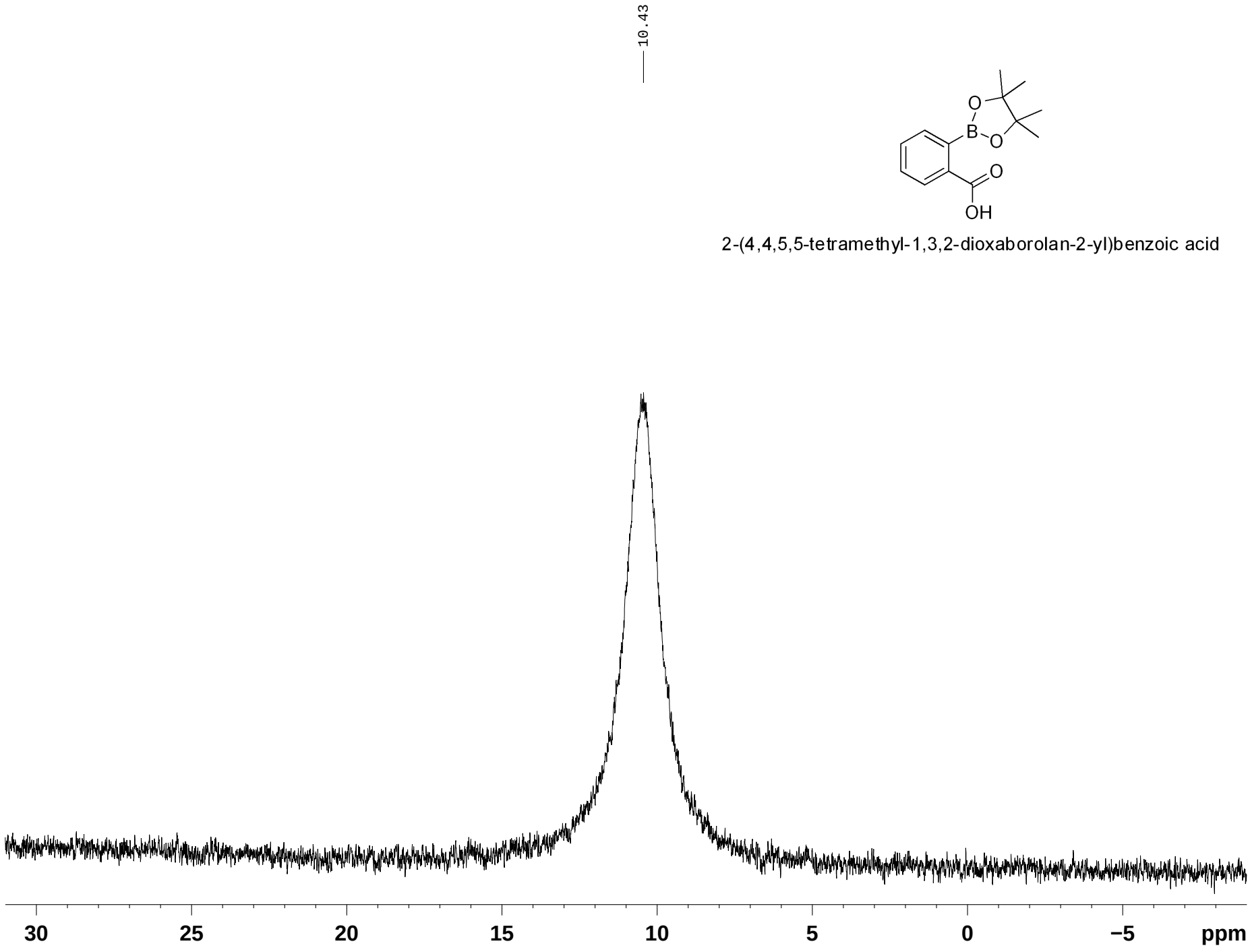

−63.17
F3C
SiMe3
O
OH
4-(trifluoromethyl)-2-(trimethylsilyl)benzoic acid
−45
−50
−55
−60
−65
−70
−75
−80
ppm


8.212
8.190
7.244
7.237
6.943
6.936
6.921
6.915
3.888
0.358
12.597
MeO
SiMe3
O
OH
4-methoxy-2-(trimethylsilyl)benzoic acid
13
ppm
0.950
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
ppm
1.00
1.01
1.03
3.20
9.28

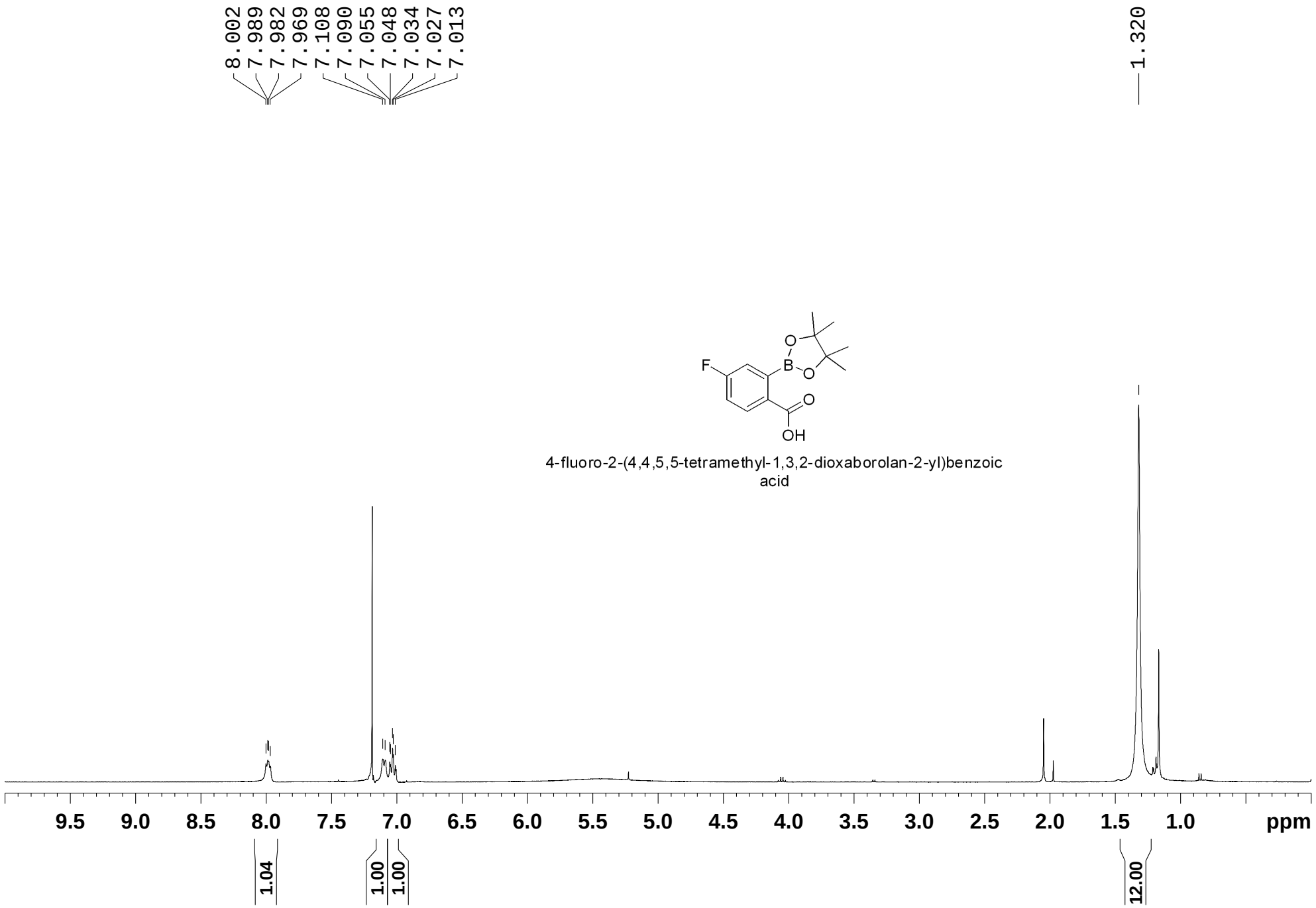

173.19
162.88
146.84
133.78
126.37
122.36
112.90
55.45
0.51
MeO
SiMe3
O
OH
4-methoxy-2-(trimethylsilyl)benzoic acid
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

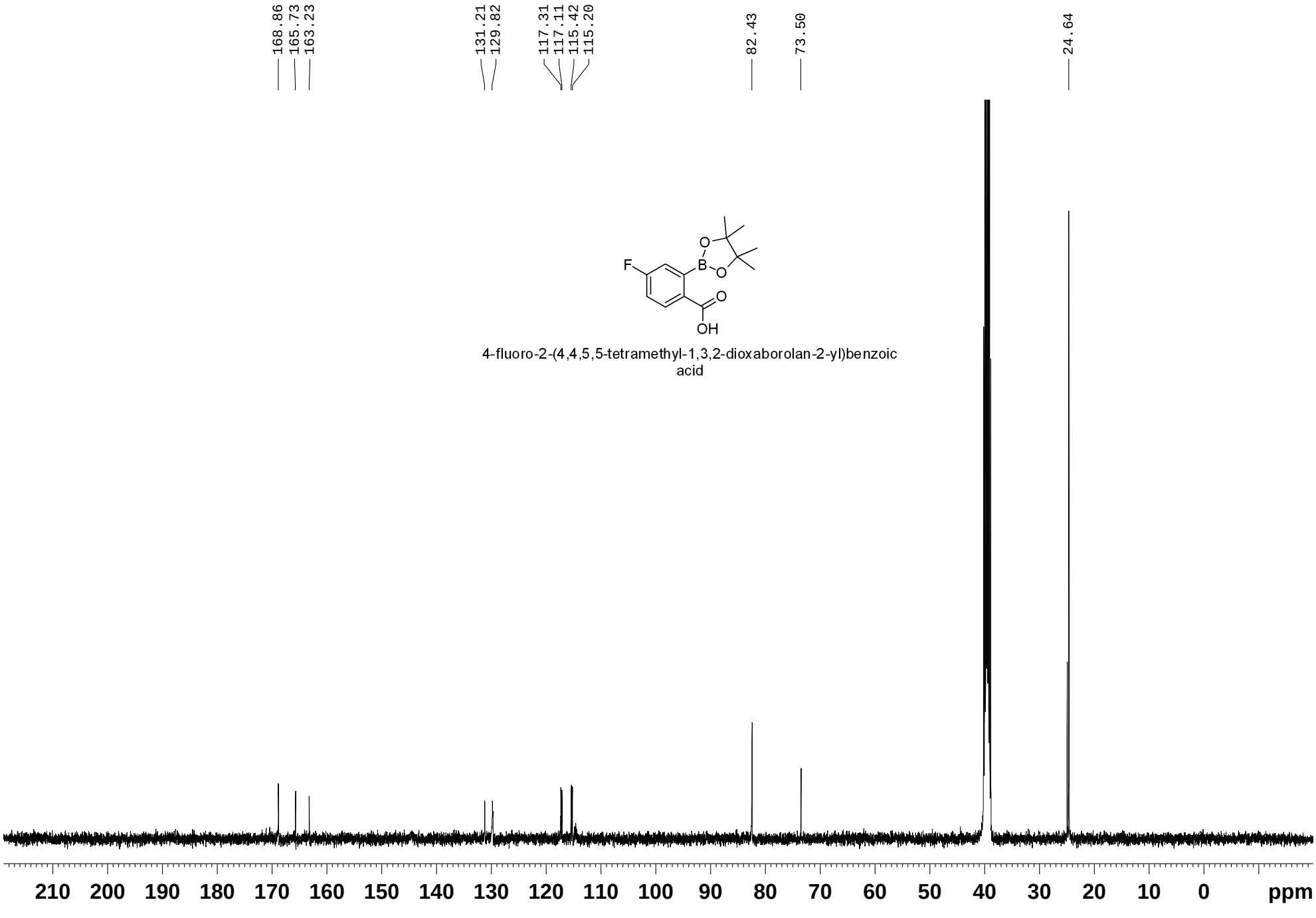

7.387
7.369
7.314
7.299
7.297
7.282
7.264
7.247
7.146
7.128
7.110
1.090
O
B
O
O
OH
2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
2.04
1.02
12.04


173.09
138.06
130.09
128.69
125.66
122.20
77.66
25.66
O
B
O
O
OH
2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

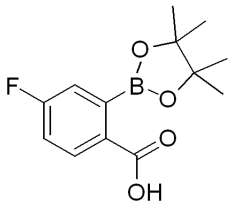


2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

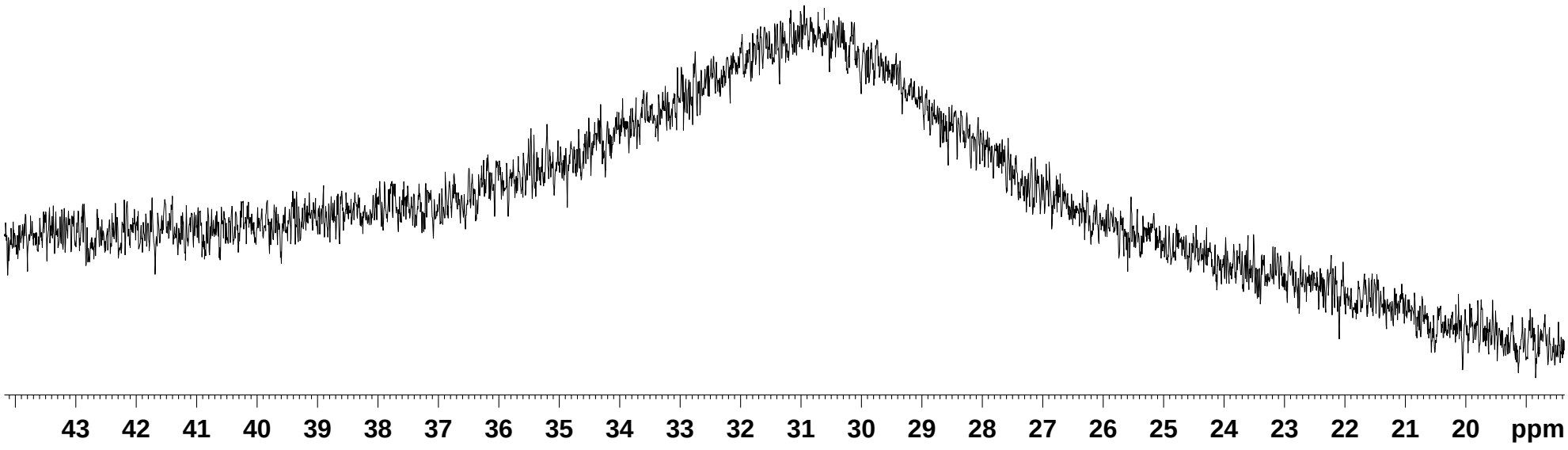

8.002
7.989
7.982
7.969
7.108
7.090
7.055
7.048
7.034
7.027
7.013
1.320
F
B
O
O
O
OH
4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.04
1.00
1.00
12.00

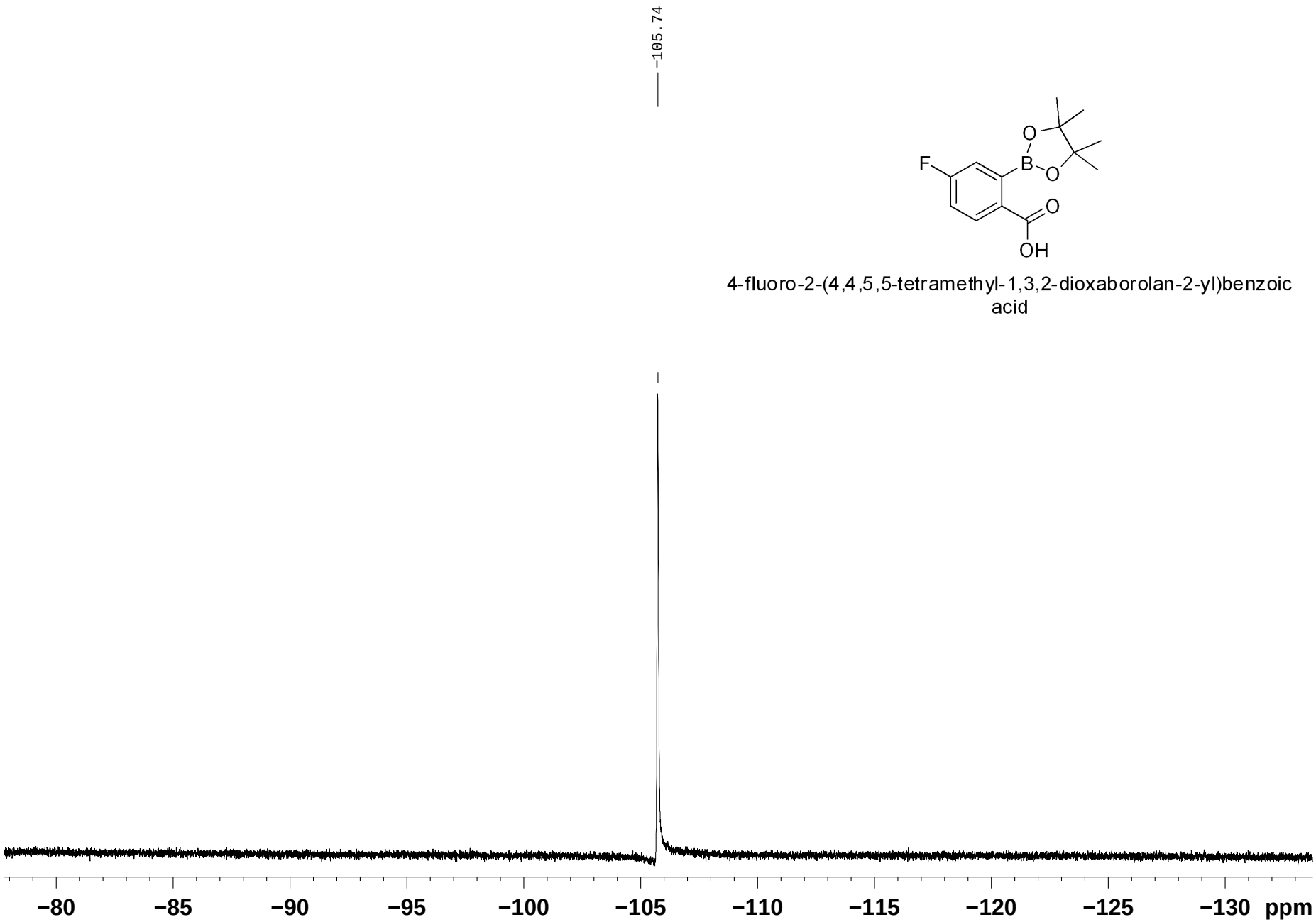

168.86
165.73
163.23
131.21
129.82
117.31
117.11
115.42
115.20
82.43
73.50
24.64
F
B
O
O
O
OH
4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

30.615

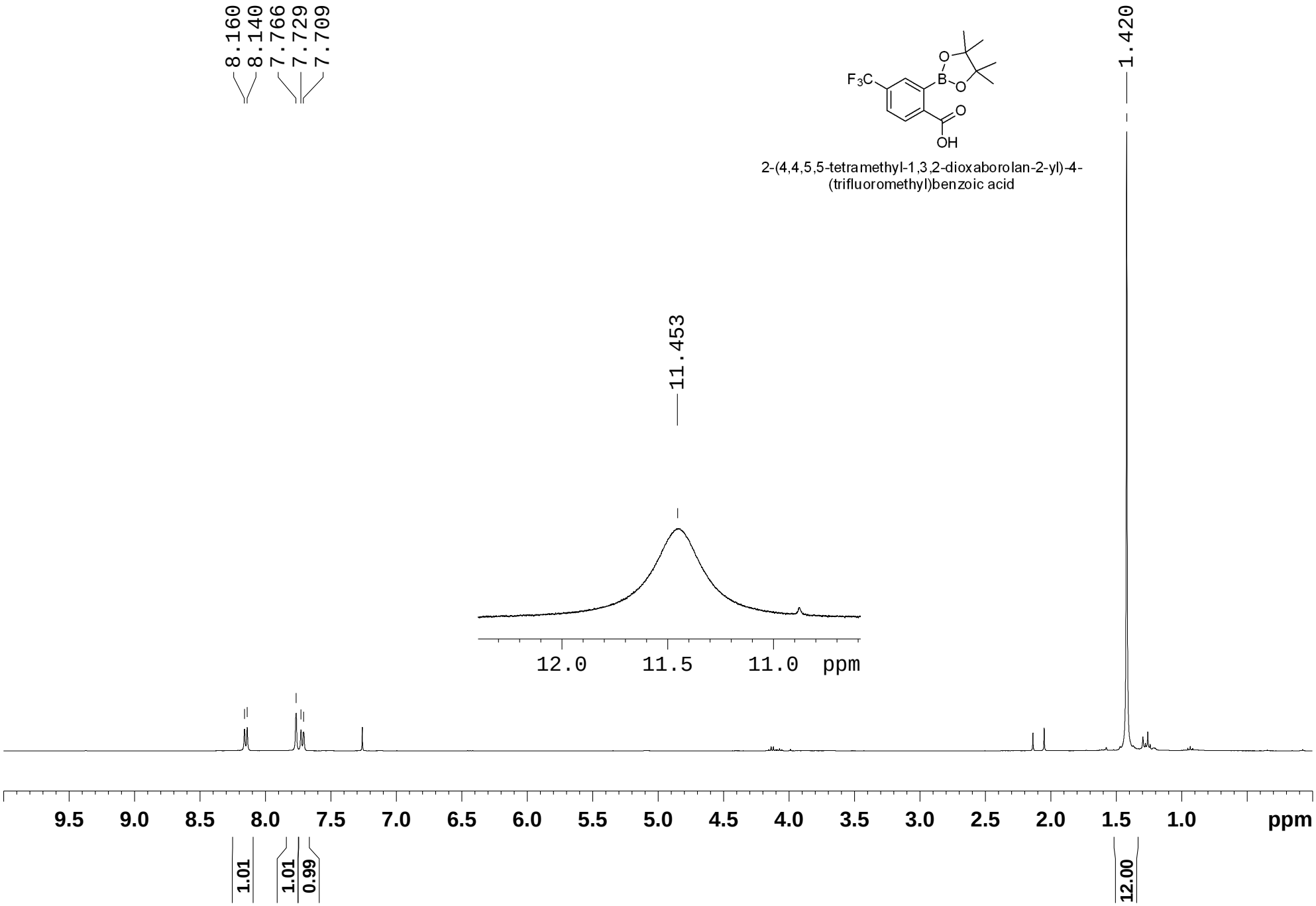


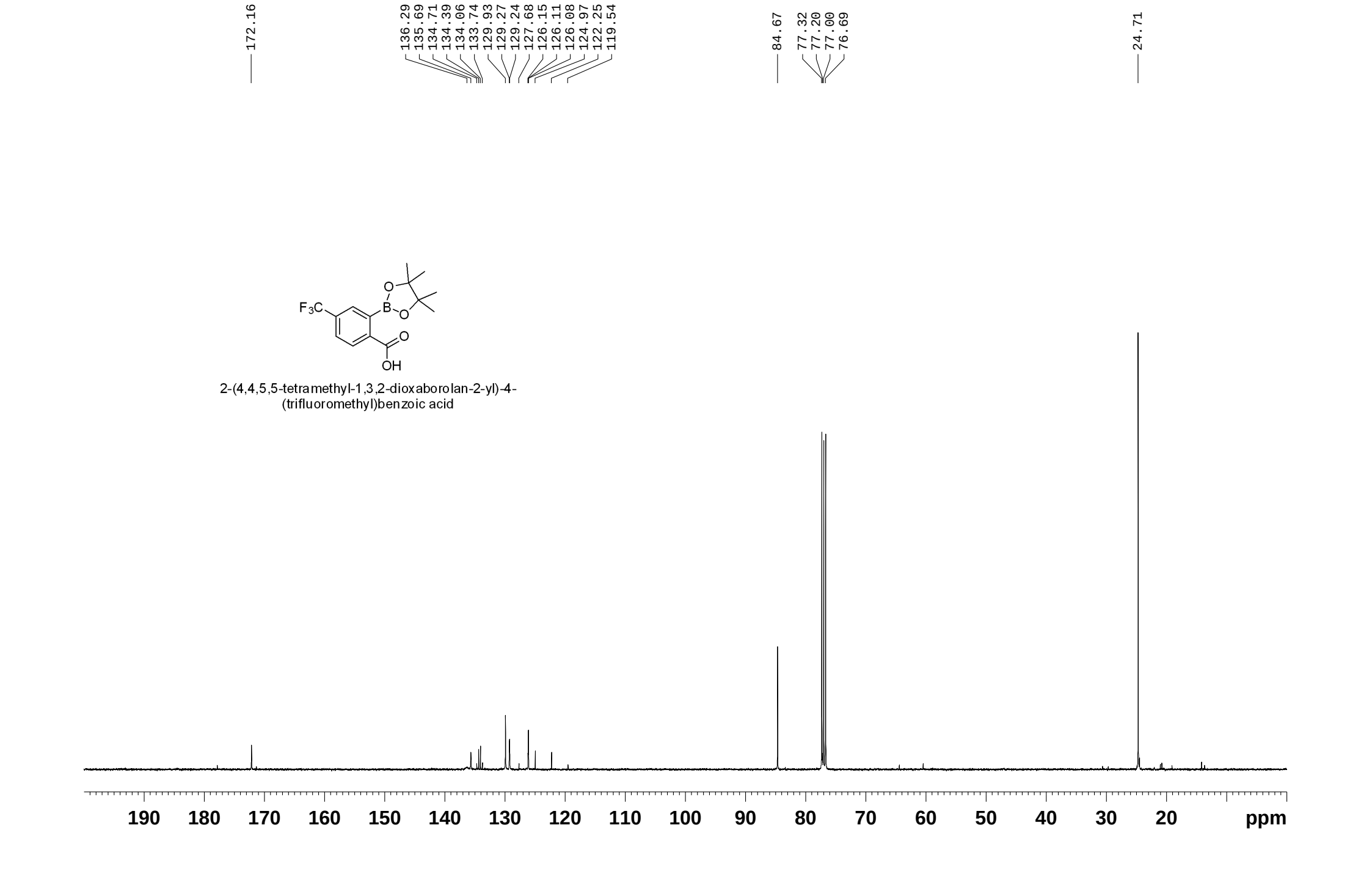
4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

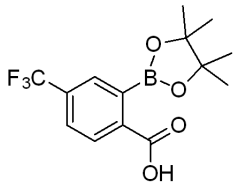




4-fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

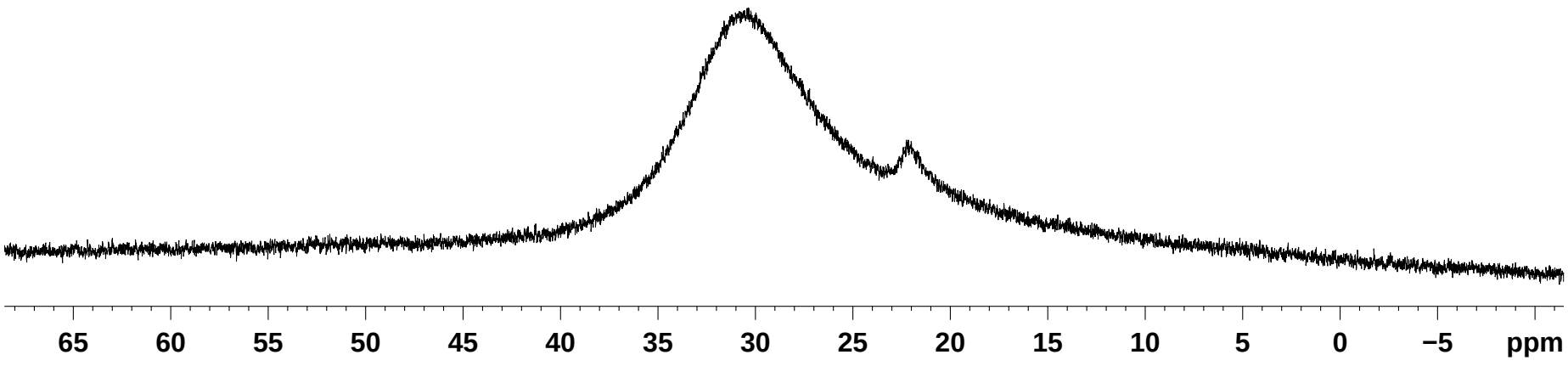

8.160
8.140
7.766
7.729
7.709
1.420
11.453
F3C
B
O
O
O
OH
2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-
(trifluoromethyl)benzoic acid
12.0
11.5
11.0
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.01
1.01
0.99
12.00

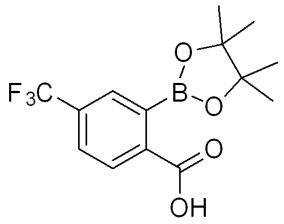

172.16
136.29
135.69
134.71
134.39
134.06
133.74
129.93
129.27
129.24
127.68
126.15
126.11
126.08
124.97
122.25
119.54
84.67
77.32
77.20
77.00
76.69
24.71
F3C
B
O
O
O
OH
2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-
(trifluoromethyl)benzoic acid
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



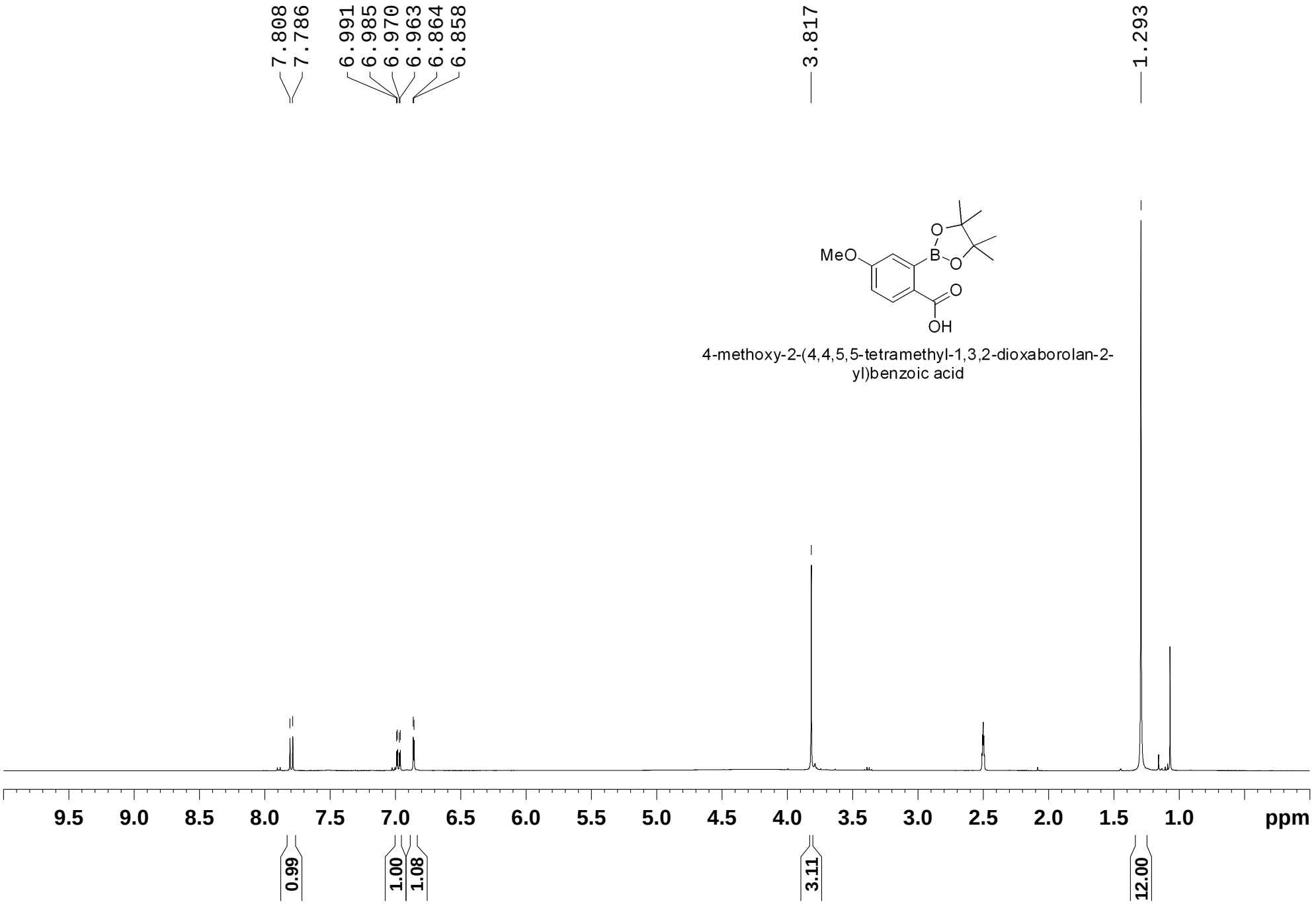
2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)benzoic acid

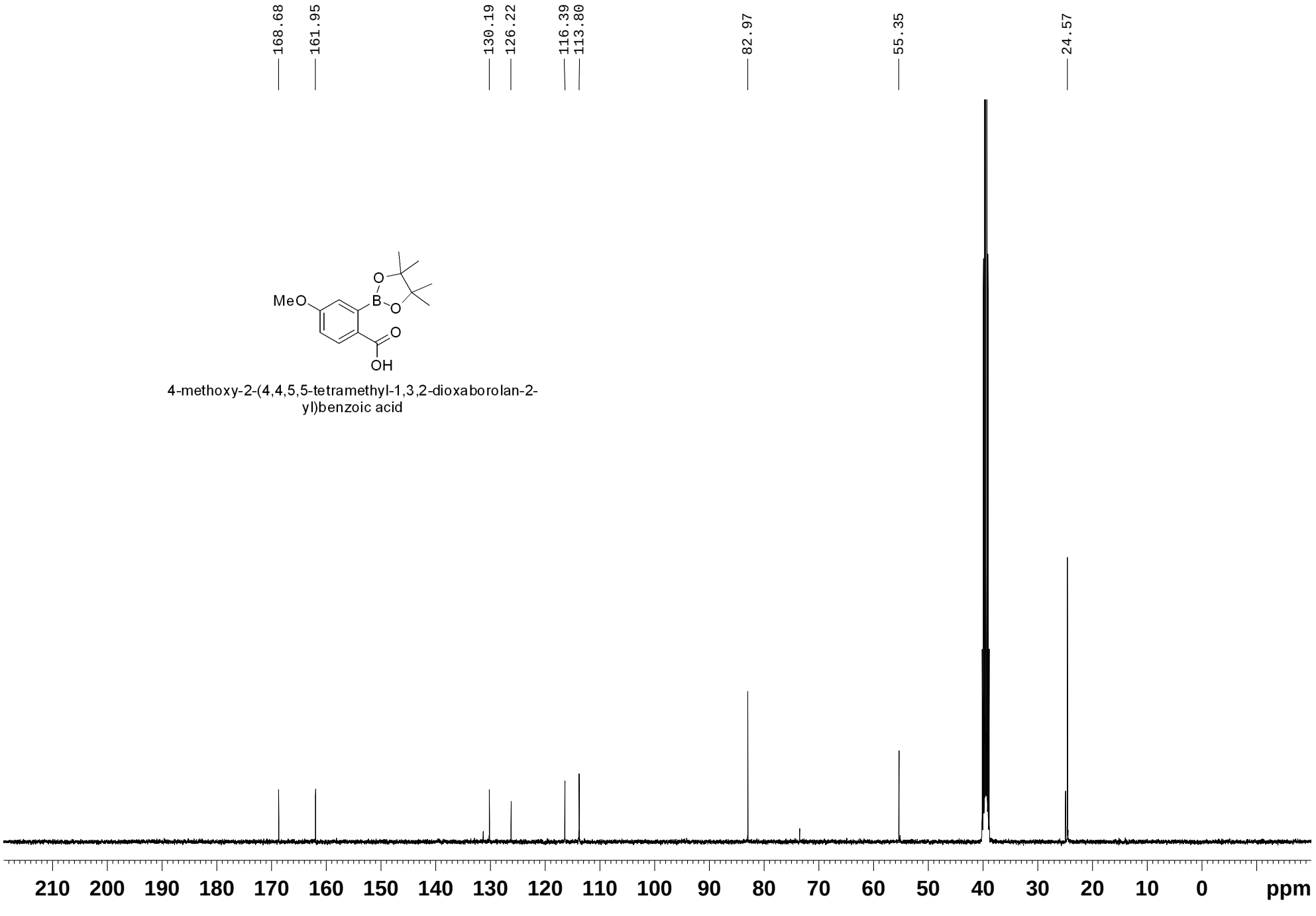
30.57



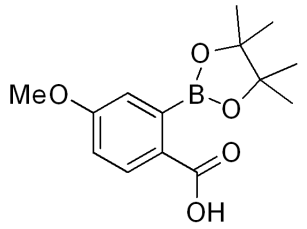


2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)benzoic acid


7.808
7.786
6.991
6.985
6.970
6.963
6.864
6.858
3.817
1.293
MeO
B
O
O
O
OH
4-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid
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
ppm
0.99
1.00
1.08
3.11
12.00


168.68
161.95
130.19
126.22
116.39
113.80
82.97
55.35
24.57
MeO
B
O
O
O
OH
4-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

29.62



4-methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid