Supplementary Information

Nickel-Catalyzed C-O/N-H, C-S/N-H, and C-CN/N-H Annulation of Aromatic Amides with Alkynes: C-O, C-S, and C-CN Activation

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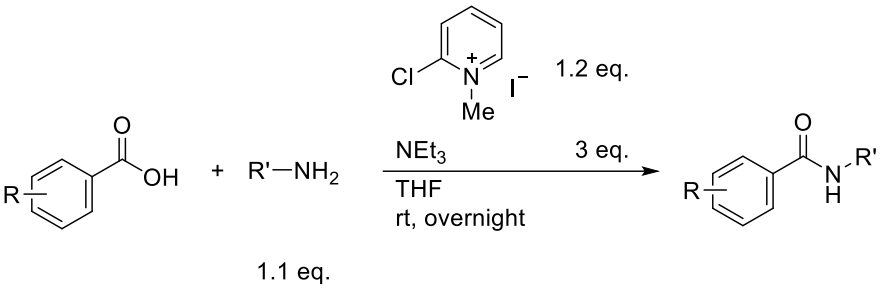
General Information

^{1}H, ^{2}H, ^{13}C and ^{19}F NMR spectra were recorded on a JEOL ECZ-400S spectrometer (except for ^{13}C NMR spectrum of **1a-*d***) or a JEOL ECS-400 spectrometer (^{13}C NMR spectrum of **1a-*d***). The chemical shifts in ^{1}H NMR spectra were recorded relative to tetramethylsilane (δ: 0.0) or DMSO *d6* (δ: 2.50). The chemical shifts in ^{2}H NMR spectra were recorded relative to $CDCl_3$ (δ: 7.26). The chemical shifts in ^{13}C NMR spectra were recorded relative to $CDCl_3$ (δ: 77.0) or DMSO *d6* (δ: 39.52). The chemical shifts in ^{19}F NMR spectra were recorded relative to $CFCl_3$ (δ: 0.0). Data are recorded as follows: chemical shifts in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad singlet, m = multiplet, c = complex), coupling constant (Hz), and integration. Infrared spectra (IR) were recorded on a JASCO FT/IR-4000 spectrometer using ATR method. Absorption data are reported in reciprocal centimeters from 800 to 3500 cm^{-1} with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained using a SHIMDZU QP-2010 spectrometer with a quadrupole mass analyzer at 70 eV. Data are recorded as follows: mass/charge ratio and relative intensity to base peak at 100 %. High-resolution mass spectra (HRMS) were obtained using a JEOL JMS-T100LP spectrometer with a time-of-flight mass analyzer. Elemental analyses were performed by the Elemental Analysis Section of Osaka University. Melting points were determined on a Stanford Research Systems MPA100 apparatus equipped with a digital thermometer and are uncorrected. Preparative gel permeation chromatography (GPC) were carried out on a JAI LC-5060 equipped with two JAIGEL-2HR columns connected in series. Column chromatography was performed with SiO_2 (Silicycle Siliaflash F60 (230-400 mesh)) or NH_2-modified SiO_2 (Kanto Chemical, Silica gel 60 (spherical) NH_2 (40-50μm)).

Materials

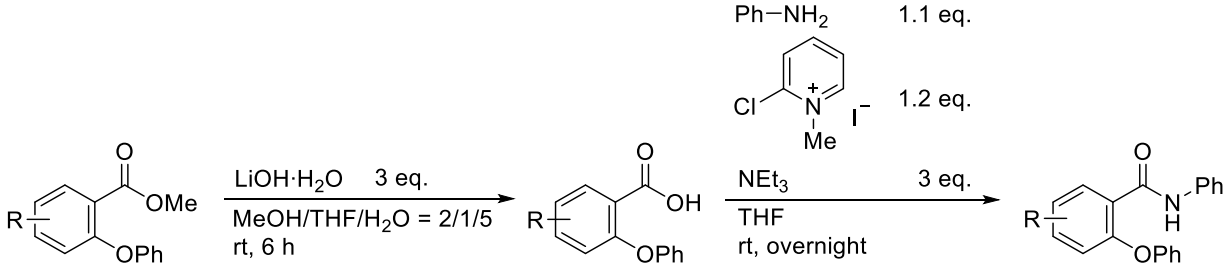
Toluene (super dehydrated), 1,4-dioxane (super dehydrated), DMF (super dehydrated), DMSO (super dehydrated), $Ni(cod)_2$, PPh_3, dppe, dttbpy, Li*O*^{t}Bu, Na*O*^{t}Bu and K*O*^{t}Bu were purchased and used as received. Diphenyl acetylene (**2a**) was purchased and recrystalyzed from hexane before use. 3-Hexyne (**2f**) and 1-phenyl-1-pentyne (**2g**) were purchased and distilled over CaH_2 before use. 1,2-bis(4-methoxyphenyl)ethyne (**2b**)[1], 1,2-bis(4-(trifluoromethyl)phenyl)ethyne (**2c**)[2], 1,2-bis(4-fluorophenyl)ethyne (**2d**)[2], 1,2-di(thiophen-2-yl)ethyne (**2e**)[3] and 2-cyano-*N*-phenylbenzamide (**1r**)[4] were prepared according to the reported procedure. Other starting materials were prepared as described below.

General Procedure A: Synthesis of Amides from Carboxylic Acids.



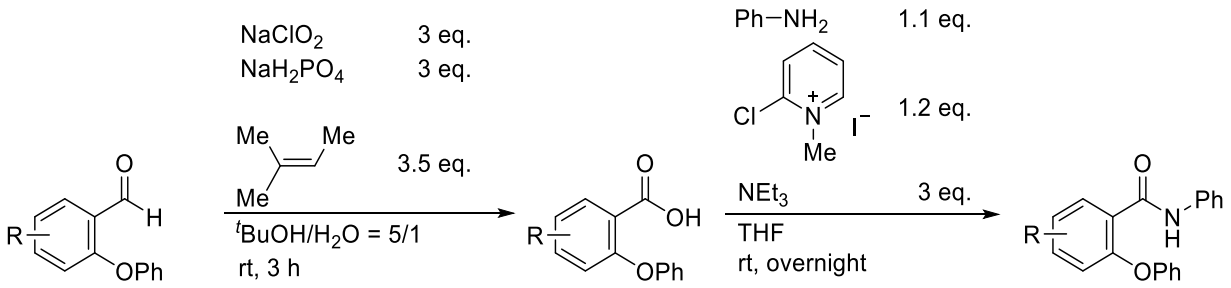
To a solution of carboxylic acid (1 eq.), aniline (1.1 eq.) and NEt_3 (3 eq.) in THF (0.5 M), 2-chloro-1-methylpyridinium iodide (1.2 eq.) was added. After stirring overnight at room temperature, the volatiles were removed under reduced pressure. EtOAc and sat. $NaHCO_3$ aq. were then added and the organic layer was separated. The organic layer was washed with 1N HCl aq. and dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by silica-gel flash column chromatography or by recrystallization.

General Procedure B: Synthesis of Amides from Esters.



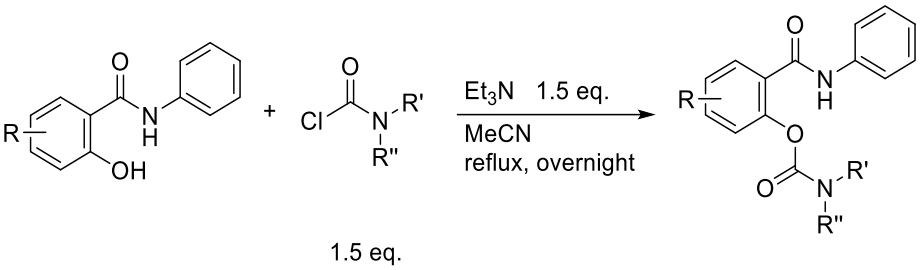
The mixture of the ester and $LiOH{\cdot}H_2O$ (3 eq.) in MeOH/THF/H_2O = 2/1/5 (0.15 M) was stirred at room temparature for 6 h. After removing the volatiles under reduced pressure, 1N HCl aq. and Et_2O were added and the organic layer was separated. The aqueous layer was extracted with Et_2O and the combined organic layer was dried over Na_2SO_4. After removing the volatiles by evaporation, the resulting crude material was used for subsquent amidation by following general procedure A without further purification.

General Procedure C: Synthesis of Amides from Aldehydes.



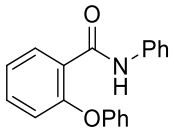
To a solution of the aldehyde in ^{t}BuOH/H_2O = 5/1 (0.33 M), NaH_2PO_4 (3 eq.), 2-methyl-2-butene (3.5 eq.) and $NaClO_2$ (3 eq.) were added) and the resulting mixture was stirred at room temparature for 3 h. After removing the volatiles under reduced pressure, 1N HCl aq. and Et_2O were added and the organic layer was dried over Na_2SO_4. After removing the volatiles in vacuo, the resulting crude material was used for subsquent amidation reactions with aniline following general procedure A without further purification.

General Procedure D: Synthesis of Carbamates.



A solution conta of the salicylanilide, dimethylcarbamoyl chloride (1.5 eq.), Et_3N (1.5 eq.) and MeCN (0.25 M) were stirred reflux overnight. After the reaction, EtOAc and 1N HCl aq were added and the organic layer was dried over Na_2SO_4. After the volatile was removed under reduced pressure, the resulting crude mixture was purified by silica-gel flash column chromatography or recrystallization.

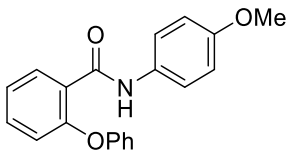
2-Phenoxy-*N*-phenylbenzamide (1a) [CAS: 140437-02-1]



1a was prepared from 2-phenoxy benzoic acid (10.5 g, 49.0 mmol) and aniline (5.04 g, 54.1 mmol) following general procedure A. The product was obtained in 64% yield (9.10 g, 31.5 mmol) as a white solid by recrystallization from EtOH.

Mp = 97.4-97.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.88 (dd, *J* = 8.2 Hz, 0.9 Hz, 1H), 7.06-7.13 (c, 3H), 7.19-7.26 (c, 2H), 7.29-7.34 (m, 2H), 7.38-7.44 (c, 3H), 7.59-7.63 (m, 2H), 8.33 (dd, *J* = 7.9 Hz, 1.7 Hz, 1H), 9.63 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 118.4, 119.4, 120.3, 123.9, 124.1, 124.3, 124.9, 128.9, 130.3, 132.4, 133.0, 138.1, 155.2, 155.3, 162.6. **IR** (ATR): 3348 w, 1657 m. **MS**: *m*/*z* (EI, relative intensity, %): 289 (18, M^+), 198 (14), 197 (100), 196 (14), 115 (13). **Anal.** Calcd for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.95; H, 5.14; N, 4.81.

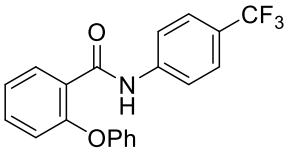
***N*-(4-methoxyphenyl)-2-phenoxybenzamide (1b)** [CAS: 349399-98-0]



1b was prepared from 2-phenoxy benzoic acid (3.24 g, 15.1 mmol) and *p*-anisidine (2.09 g, 17.0 mmol) following general procedure A. The product was obtained in 79% yield (3.79 g, 11.9 mmol) as a yellow solid by recrystallization from EtOH.

Mp = 119.9-120.6 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.76 (s, 3H), 6.82-6.89 (c, 3H), 7.09-7.11 (m, 2H), 7.19-7.25 (c, 2H), 7.37-7.42 (c, 3H), 7.50-7.54 (m, 2H), 8.32 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H), 9.50 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 55.4, 114.0, 118.4, 119.4, 122.0, 123.9, 124.2, 124.8, 130.2, 131.2, 132.3, 132.8, 155.1, 155.3, 156.3, 162.4. **IR** (ATR): 3382 w, 1660 m, 1235 s, 1216 s. **MS**: *m*/*z* (EI, relative intensity, %): 320 (12), 319 (52, M^+), 198 (14), 197 (100), 115 (11). **Anal.** Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.20; H, 5.30; N, 4.38.

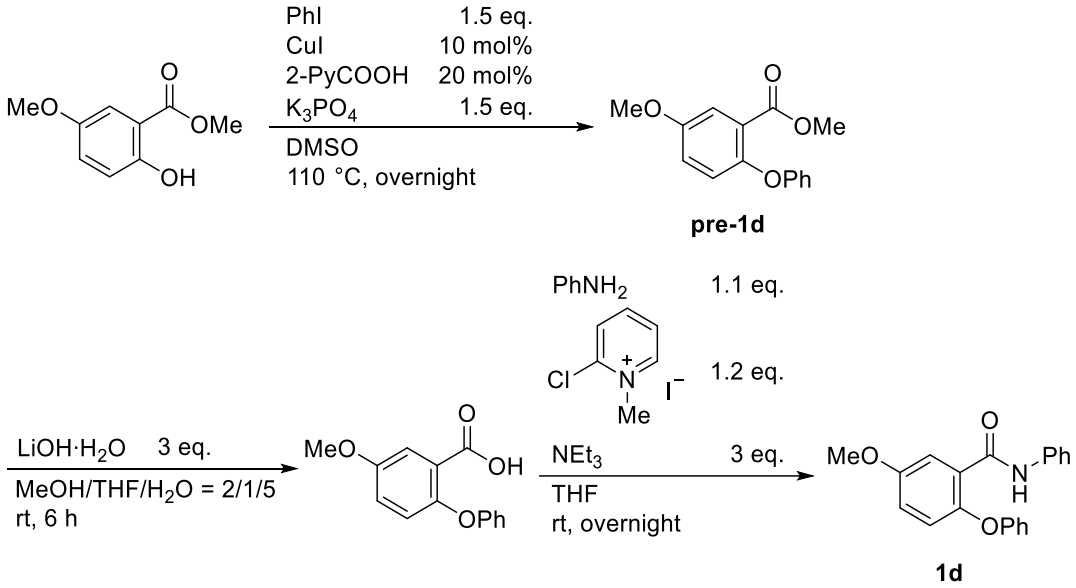
2-Phenoxy-*N*-(4-(trifluoromethyl)phenyl)benzamide (1c) [CAS: 1004245-21-9]



1c was prepared from 2-phenoxy benzoic acid (3.19 g, 14.9 mmol) and 4-aminobenzotrifluoride (2.64 g, 16.4 mmol) following general procedure A. The product was obtained in 38% yield (2.04 g, 5.71 mmol) as a white solid by recrystallization from EtOH.

Mp = 118.8-119.1 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.90 (dd, *J* = 8.2 Hz, 0.9 Hz, 1H), 7.11-7.14 (m, 2H), 7.22-7.29 (c, 2H), 7.40-7.48 (c, 3H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.74 (d, *J* = 8.5 Hz, 2H), 8.33 (dd, *J* = 7.9 Hz, 1.7 Hz, 1H), 9.82 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 118.3, 119.5, 119.9, 123.5, 124.0, 124.1 (q, *J* = 270 Hz), 125.2, 125.9 (q, *J* = 32.6 Hz), 126.2 (q, *J* = 3.8 Hz) 130.4, 132.5, 133.5, 141.2, 155.0, 155.4, 162.9. **^{19}F NMR** -62.6 (s). **IR** (ATR): 3371 w, 1678 w, 1319 s. **MS**: *m*/*z* (EI, relative intensity, %): 357 (12, M^+), 198 (15), 197 (100), 115 (12). **Anal.** Calcd for $C_{20}H_{14}F_3NO_2$: C, 67.23; H, 3.95; N, 3.92. Found: C, 67.27; H, 3.88; N, 3.92.

5-Methoxy-2-phenoxy-*N*-phenylbenzamide (1d)

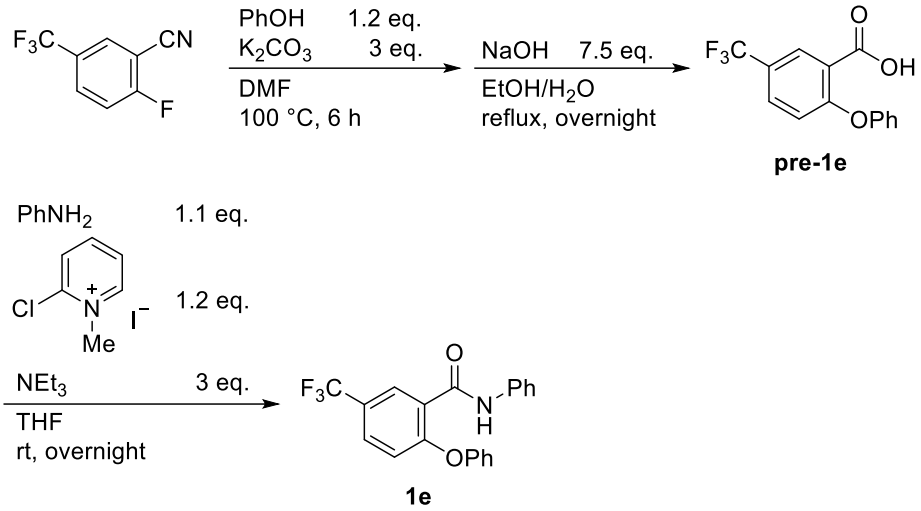


CuI (512 mg, 2.7 mmol), 2-pyridinecarboxylic acid (662 mg, 5.4 mmol) and K_3PO_4 (8.74 g, 41.1 mmol) were added to a 200 mL three-necked round-bottom flask and the flask was purged with N_2. DMSO (60 mL), methyl 5-methoxysalicylate (4.93 g, 27.1 mmol) and PhI (8.08 g, 39.6 mmol) were added to the flask and the resulting mixture was stirred overnight at 110 °C under a N_2 atmosphere. After cooling the flask to room temperature, the resulting crude mixture was suspended in EtOAc (120 mL) and the resulting suspension was filtered through a celite pad. The mixture was washed with sat. $NaHCO_3$ aq. (50 mL) and H_2O (50 mL). The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 40/1 to 10/1, R_f = 0.23 in hexane/EtOAc = 10/1) to afford methyl 5-methoxy-2-phenoxybenzoate (**pre-1d**) in 23% yield (1.59 g, 6.16 mmol) as a pale yellow oil.

1d was prepared from **pre-1d** (1.59 g, 6.16 mmol) following general procedure B. The product was obtained in 47% yield (932 mg, 2.91 mmol) as a white solid after recrystallization from Et_2O.

Mp = 76.1-76.9 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.89 (s, 3H), 6.91 (d, *J* = 8.9 Hz, 1H), 7.02 (dd, *J* = 8.9 Hz, 3.3 Hz, 1H), 7.04-7.08 (m, 2H), 7.08-7.13 (m, 1H), 7.14-7.19 (m, 1H), 7.30-7.34 (m, 2H), 7.36-7.41 (m, 2H), 7.56-7.62 (m, 2H), 7.85 (d, *J* = 3.3 Hz, 1H), 9.68 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 55.8, 114.8, 118.1, 120.2, 120.3, 121.3, 124.2, 124.3, 125.5, 128.9, 130.2, 138.0, 148.0, 156.1, 156.4, 162.3. **IR** (ATR): 3366 w, 1660 m, 1209 s. **MS**: *m*/*z* (EI, relative intensity, %): 319 (33, M^+), 228 (15), 227 (100), 184 (23). **Anal.** Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.10; H, 5.36; N, 4.44.

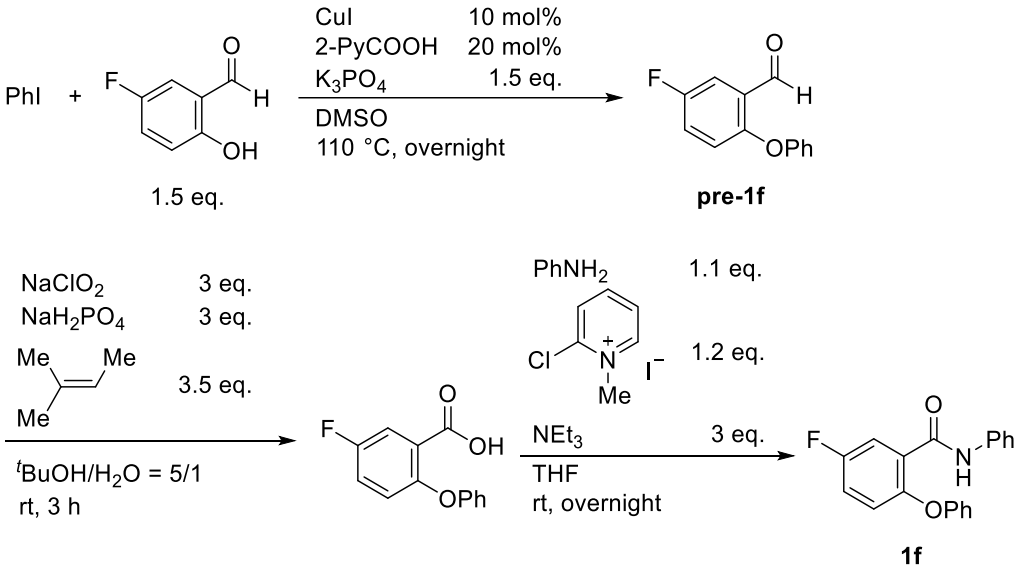
2-Phenoxy-*N*-phenyl-5-(trifluoromethyl)benzamide (1e)



2-Phenoxy-5-(trifluoromethyl)benzoic acid (**pre-1e**) was prepared from 2-fluoro-5-(trifluoromethyl)benzonitrile (5.45 g, 28.8 mmol) according to the reported procedure[5] and was then used in a subsquent amidation following general procedure A without further purification. **1e** was obtained in 34% yield (3.53 g, 9.88 mmol) as a white solid by recrystallization from Et_2O.

Mp = 100.9-101.4 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.93 (d, *J* = 8.7 Hz, 1H), 7.12-7.20 (c, 3H), 7.31-7.38 (c, 3H), 7.47-7.52 (m, 2H), 7.61-7.66 (c, 3H), 8.66 (d, *J* = 2.3 Hz, 1H), 9.64 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 117.6, 120.4, 120.5, 123.6 (q, *J* = 271 Hz), 123.8, 124.7, 125.9 (q, *J* = 33.5 Hz), 126.1, 129.1, 129.8 (q, *J* = 2.9 Hz), 130.3 (q, *J* = 3.8 Hz), 130.7, 137.7, 153.9, 158.1, 161.3. **^{19}F NMR** -62.6 (s). **IR** (ATR): 3310 w, 1648 m, 1115 s. **MS**: *m/z* (EI, relative intensity, %): 357 (19, M^+), 266 (15), 265 (100), 264 (23), 77 (11). **Anal.** Calcd for $C_{20}H_{14}F_3NO_2$: C, 67.23; H, 3.95; N, 3.92. Found: C, 67.09; H, 3.97; N, 3.97.

5-Fluoro-2-phenoxy-*N*-phenylbenzamide (1f) [CAS: 140437-19-0]



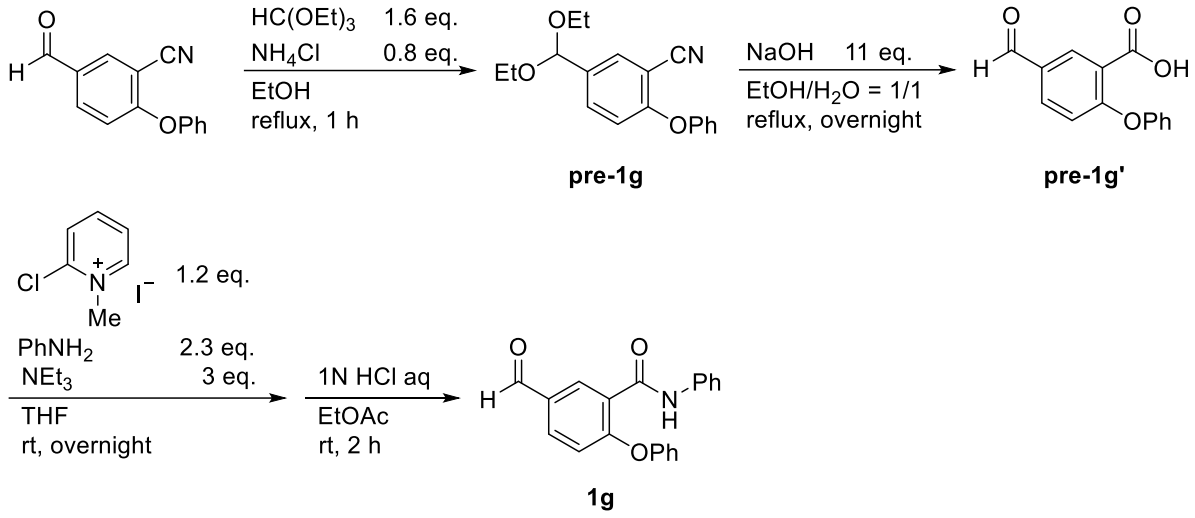
CuI (477 mg, 2.5 mmol), 2-pyridinecarboxylic acid (615 mg, 5.0 mmol) and K_3PO_4 (7.77 g, 36.6 mmol) were added to a round-bottom flask and the flask was purged with N_2. DMSO (60 mL) was added and the solution was heated at 50 °C for 10 min. PhI (5.04 g, 24.7 mmol) and 5-fluorosalicylaldehyde (5.27 g, 37.6 mmol) were added and the mixture were then stirred overnight at 110 °C under a N_2 atmosphere. After cooling the flask to room temperature, the resulting crude mixture was suspended in Et_2O (150 mL) and filtered through a Celite pad. The mixture was washed with 4N NaOH aq. (100 mL) and brine (100 mL). The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 50/1 to 20/1, R_f = 0.20 in hexane/EtOAc = 20/1) to afford 5-fluoro-2-phenoxybenzaldehyde (**pre-1f**) in 26% yield (1.41 g, 6.52 mmol) as a pale yellow oil.

1f was prepared from **pre-1f** (1.34 g, 6.20 mmol) following general procedure C. The product was obtained in 47% yield (889 mg, 2.89 mmol) as a white solid by recrystallization from EtOAc.

Mp = 119.1-119.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.90 (dd, *J* = 9.0, 4.5 Hz, 1H), 7.08-7.16 (c, 4H), 7.20-7.24 (m, 1H), 7.30-7.34 (m, 2H), 7.40-7.44 (m, 2H), 7.58-7.60 (m, 2H), 8.04 (dd, *J* = 9.3, 3.3 Hz, 1H), 9.64 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 118.5 (d, *J* = 24.9 Hz), 118.9, 119.9 (d, *J* = 23.0 Hz), 120.4, 120.6 (d, *J* = 7.7 Hz), 124.6, 124.9, 126.0 (d, *J* = 6.7 Hz), 129.0, 130.4, 137.8, 150.9 (d, *J* = 2.9 Hz),

155.6, 158.7 (d, *J* = 242 Hz), 161.3. **^{19}F NMR** -118.2 (m). **IR** (ATR): 3375 w, 1670 m, 1197 s. **MS**: *m*/*z* (EI, relative intensity, %): 307 (27, M^+), 216 (16), 215 (100), 214 (22), 159 (11), 133 (14), 93 (11), 77 (12). **Anal.** Calcd for $C_{19}H_{14}FNO_2$: C, 74.26; H, 4.59; N, 4.56. Found: C, 74.37; H, 4.51; N, 4.56.

5-Formyl-2-phenoxy-*N*-phenylbenzamide (1g)



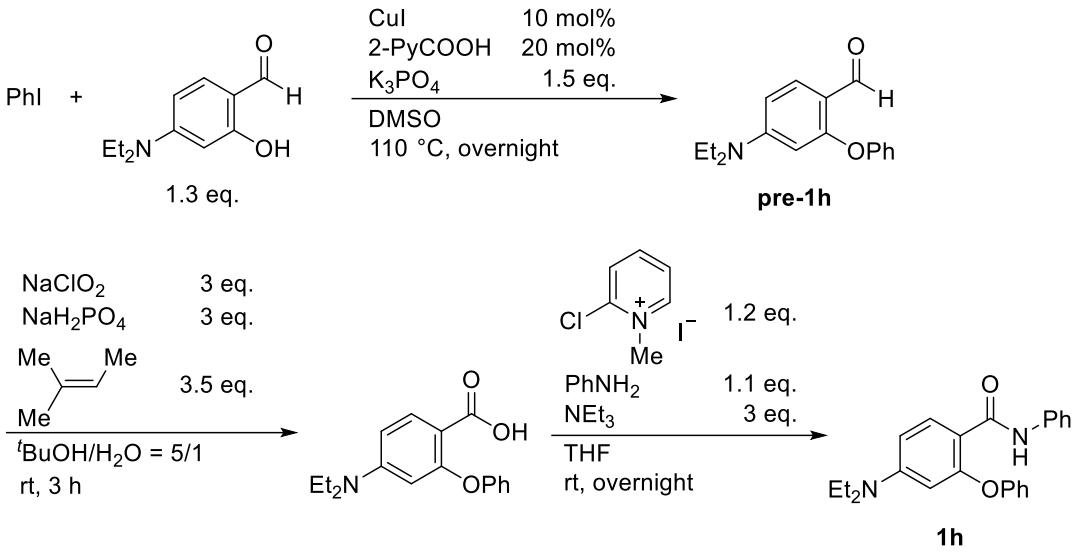
A solution of 5-formyl-2-phenoxybenzonitrile (3.15 g, 14.1 mmol)[5], triethyl orhoformate (3.41 g, 23.0 mmol) and NH_4Cl (641 mg, 12.0 mmol) in EtOH (60 mL) was stirred under reflux for 1 h. After cooling the flask to room temperature, the volatiles were removed under reduced pressure. After adding EtOAc (100 mL) and sat. $NaHCO_3$ aq (100 mL) to the mixture, the organic layer was isolated and dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 5/1, R_f = 0.37 in hexane/EtOAc = 5/1) to afford 5-(diethoxymethyl)-2-phenoxybenzonitrile (**pre-1g**) in 53% yield (2.21 g, 7.43 mmol) as a pale yellow oil..

A solution of **pre-1g** (3.94 g, 13.2 mmol) in EtOH (50 mL) and 3N NaOH aq (50 mL) was heated overnight under reflux. Et_2O (100 mL) and H_2O (100 mL) were added to the mixture and the aqueous layer was separated. The aqueous layer was acidified with 6N HCl aq and extracted with EtOAc (150 mL). The organic layer was dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The crude mixture that contained 5-formyl-2-phenoxybenzoic acid (**pre-1g'**) (1.93 g) was used in the subsequent step without further purification.

To a solution of **pre-1g'** (1.93 g, crude mixture), aniline (1.63 g, 17.5 mmol) and NEt_3 (2.26 g, 22.3 mmol) in THF (15 mL), 2-chloro-1-methylpyridinium iodide (2.31 g, 9.04 mmol) was added. After stirring the solution overnight at room temperature, the volatiles were removed under reduced pressure. 1N HCl aq (50 mL) and EtOAc (50 mL) were added and the resulting mixture was stirred at room temperature for 2 h. The organic layer was then separated and washed with 1N HCl aq. (50 mL) and sat. $NaHCO_3$ aq. (50 mL). The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by recrystallization from EtOAc to give **1g** in 35% yield (1.46 g, 4.60 mmol) from **pre-1g** as a pale yellow solid.

Mp = 130.8-131.2 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.93 (d, *J* = 8.6 Hz, 1H), 7.10-7.15 (m, 1H), 7.18-7.25 (m, 2H), 7.30-7.38 (c, 3H), 7.47-7.53 (m, 2H), 7.63-7.65 (m, 2H), 7.91 (dd, *J* = 8.6, 2.2 Hz, 1H), 8.80 (d, *J* = 2.2 Hz, 1H), 9.58 (br, 1H), 9.98 (s, 1H). **^{13}C NMR** ($CDCl_3$) δ: 117.4, 120.4, 120.6, 123.7, 124.6, 126.2, 129.0, 130.6, 131.6, 132.2, 136.3, 137.7, 153.6, 160.2, 161.4, 190.2. **IR** (ATR): 3372 w, 1693 s, 1673 m. **MS**: *m*/*z* (EI, relative intensity, %): 317 (33, M^+), 226 (16), 225 (100), 224 (43), 197 (61), 141 (14), 115 (20), 93 (10), 77 (20). **Anal.** Calcd for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N, 4.41. Found: C, 75.63; H, 4.73; N, 4.47.

4-(Diethylamino)-2-phenoxy-*N*-phenylbenzamide (1h)

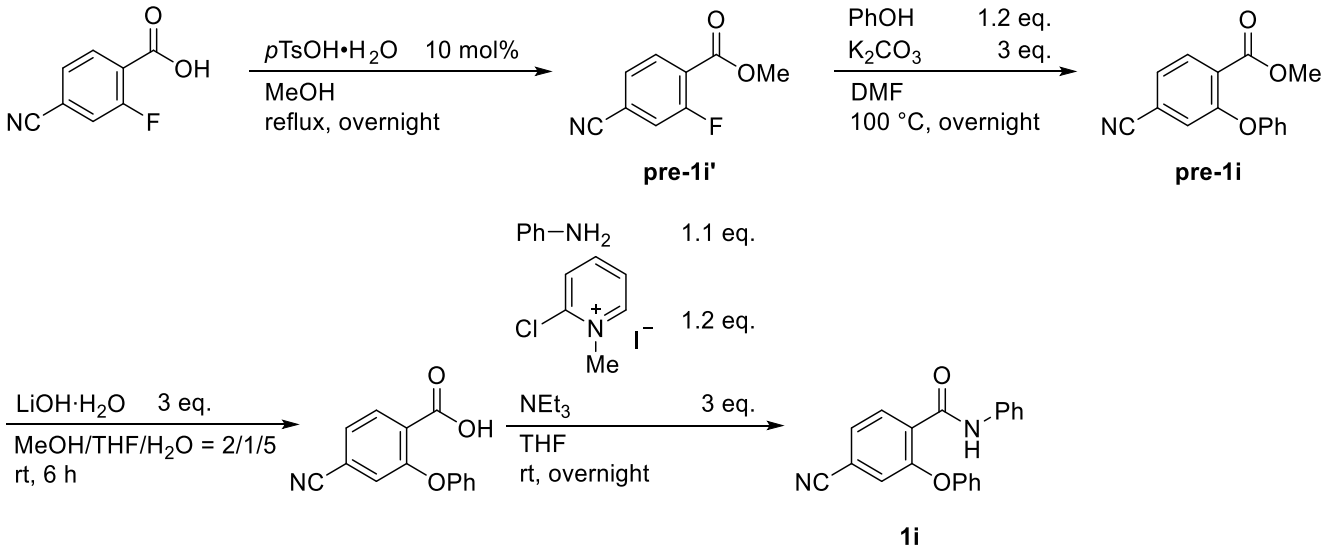


CuI (381 mg, 2.0 mmol), 2-pyridinecarboxylic acid (499 mg, 4.1 mmol) and K_3PO_4 (6.34 g, 29.9 mmol) were added to a round-bottom flask and the flask was then purged with N_2. DMSO (50 mL) was added and the resulting solution was heated at 50 °C for 10 min. PhI (4.01 g, 19.7 mmol) and 4-(diethylamino)salicylaldehyde (5.09 g, 26.3 mmol) were added and the mixture was stirred overnight at 110 °C under a N_2 atmosphere. After cooling the flask to room temperature, the resulting crude mixture was suspended in EtOAc (150 mL) and filtered through a Celite pad. The mixture was washed with sat. $NaHCO_3$ aq. (100 mL) and brine (100 mL). The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 20/1 to 5/1, R_f = 0.14 in hexane/EtOAc = 5/1). Et_2O (50 mL) and 4N NaOH aq. (50 mL) were then added to remove the remaining 4-(diethylamino)salicylaldehyde. The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, 4-(diethylamino)-2-phenoxybenzaldehyde (**pre-1h**) was obtained in 76% yield (3.96 g, 14.3 mmol) as a yellow oil.

1h was prepared from **pre-1h** (3.79 g, 14.1 mmol) following general procedure C (H_2O was used for washing instead of 1N HCl aq). The product was obtained in 13% yield (667 mg, 1.85 mmol) as a white solid by flash column chromatography on silica gel (eluent: hexane/EtOAc = 10/1 to 5/1, R_f = 0.26 in hexane/EtOAc = 5/1) followed by recrystallization from EtOAc.

Mp = 93.6-94.1 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.09 (t, *J* = 7.1 Hz, 6H), 3.27 (q, *J* = 7.1 Hz, 4H), 6.01 (d, *J* = 2.5 Hz, 1H), 6.52 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.01-7.06 (m, 1H), 7.11-7.21 (c, 3H), 7.25-7.31 (m, 2H), 7.35-7.42 (m, 2H), 7.57-7.61 (m, 2H), 8.17 (d, *J* = 9.1 Hz, 1H), 9.51 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 12.4, 44.5, 100.7, 107.4, 110.7, 118.9, 120.0, 123.4, 124.3, 128.8, 130.1, 133.7, 138.8, 151.4, 155.7, 156.6, 163.2. **IR** (ATR): 3383 w, 1659 m. **MS**: *m/z* (EI, relative intensity, %): 360 (13, M^+), 269 (19), 268 (100), 224 (19). **Anal.** Calcd for $C_{23}H_{24}N_2O_2$: C, 76.64; H, 6.71; N, 7.77. Found: C, 76.58; H, 6.83; N, 7.73.

4-Cyano-2-phenoxy-*N*-phenylbenzamide (1i)



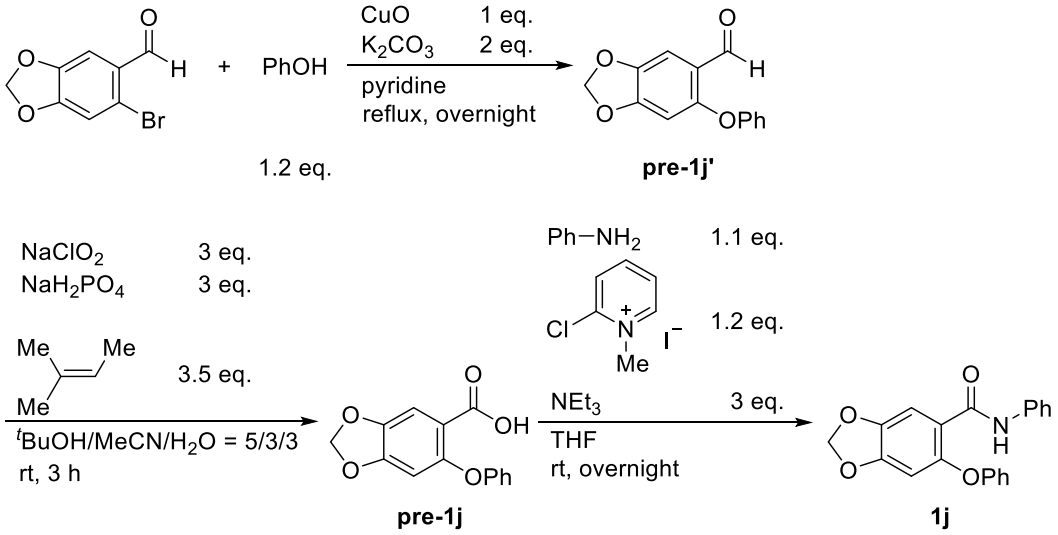
A solution of 4-cyano-2-fluorobenzoic acid (5.39 g, 32.6 mmol) and *p*-toluenesulfonic acid (619 mg, 3.3 mmol) in MeOH (65 mL) was stirred overnight under reflux. After cooling the flask to room temperature, the volatiles were removed under reduced pressure. After adding EtOAc (100 mL) and sat. $NaHCO_3$ aq (100 mL) to the mixture, the organic layer was isolated and dried over Na_2SO_4. After

removing the volatiles under reduced pressure, methyl 4-cyano-2-fluorobenzoate (**pre-1i'**) was obtained in 88% yield (5.15 g, 28.7 mmol) as a white solid and used in the subsequent step without further purification.

Pre-1i' (5.15 g, 28.7 mmol) and K_2CO_3 (12.1 g, 87.5 mmol) were added to a 200 mL three-necked round-bottom flask and the flask was purged with N_2. DMF (90 mL) and phenol (3.39 g, 36.0 mmol) were added and the resulting mixture were then stirred overnight at 100 °C under a N_2 atmosphere. After cooling the flask to room temperature, EtOAc (150 mL) and H_2O (100 mL) were added and the organic layer was separated. The organic layer was washed with 1N NaOH aq. (50 mL) and brine (50 mL). The organic layer was dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The crude mixture that contained methyl 4-cyano-2-phenoxybenzoate (**pre-1i**) (6.75 g) was used in the subsequent step following general procedure B without further purification.The product **1i** was obtained by recrystallization from acetone in 15% yield (1.40 g, 4.45 mmol) from **pre-1i'** as a white solid.

Mp = 156.7-158.3 ºC. **^{1}H NMR** (DMSO-*d6*) δ: 7.07-7.13 (c, 3H), 7.18-7.22 (m, 1H), 7.30-7.35 (m, 2H), 7.38-7.45 (c, 3H), 7.64-7.69 (m, 2H), 7.74 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 10.53 (br, 1H). **^{13}C NMR** (DMSO-*d6*) δ: 113.6, 117.7, 119.1, 119.6, 121.9, 123.9, 124.5, 127.4, 128.8, 130.2, 130.6, 133.6, 138.7, 153.9, 155.7, 163.1. **IR** (ATR): 3381 w, 2234 w, 1668 m. **MS**: *m*/*z* (EI, relative intensity, %): 314 (23, M^+), 223 (15), 222 (100), 221 (20), 77 (13). **Anal.** Calcd for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.18; H, 4.43; N, 8.73.

6-Phenoxy-*N*-phenylbenzo[*d*][1,3]dioxole-5-carboxamide (1j)

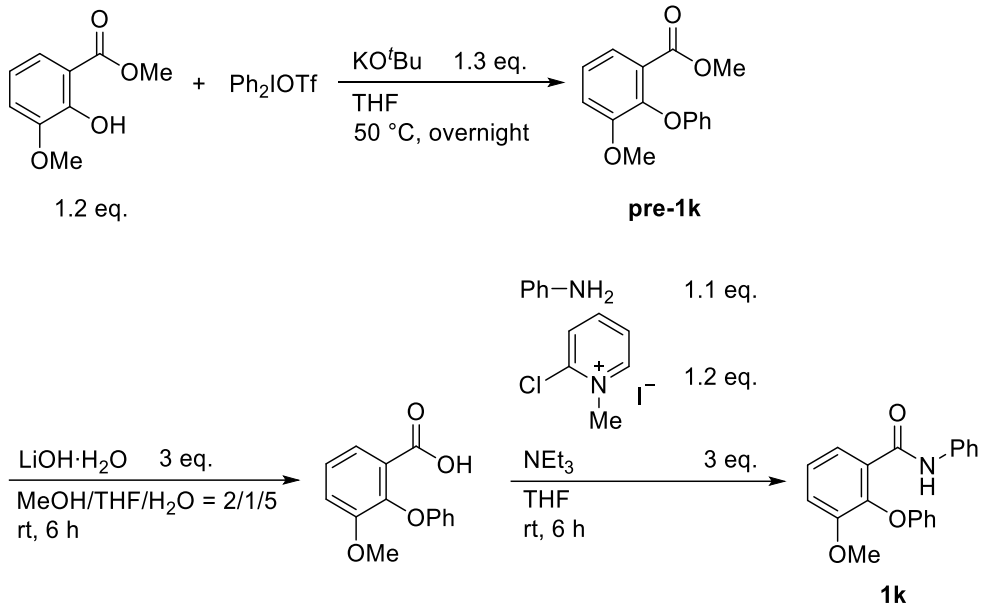


CuO (1.60 g, 20.1 mmol), K_2CO_3 (5.50 g, 39.8 mmol), 6-bromopiperonal (4.57 g, 20.0 mmol) and phenol (2.23 g, 23.7 mmol) were added to a 100 mL three-necked round-bottom flask and the flask was then purged with N_2. Pyridine (20 mL) was added and the mixture was then stirred under reflux overnight under a N_2 atmosphere. After cooling the flask to room temperature, the resulting crude mixture was suspended in toluene and filtered through a celite pad. After removing the volatiles under reduced pressure, EtOAc (100 mL) and 1N HCl aq. (100 mL) were added and the organic layer was separated. The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 5/1, R_f = 0.51 in hexane/EtOAc = 5/1). EtOAc (100 mL) and 1N NaOH aq. (100 mL) were then added to remove the remaining phenol. The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, 6-phenoxybenzo[*d*][1,3]dioxole-5-carbaldehyde (**pre-1j'**) was obtained in 82% yield (3.97 g, 16.4 mmol) as a yellow solid.

To a solution of **pre-1j'** (3.97 g, 16.4 mmol) in ^{t}BuOH (50 mL), CH_3CN (30 mL) and H_2O (30 mL), NaH_2PO_4 (5.79 g, 48.2 mmol), 2-methyl-2-butene (3.97 g, 56.6 mmol) and $NaClO_2$ (4.36 g, 48.2 mmol) were added and the resulting mixture was stirred at room temparature for 3 h. After removing the volatiles under reduced pressure, 1N HCl aq. (50 mL) and EtOAc (100 mL) were added and the organic layer was dried over Na_2SO_4. After removing the volatiles in vacuo, the resulting crude material that contained 6-phenoxybenzo[*d*][1,3]dioxole-5-carboxylic acid (**pre-1j**) (4.59 g) was used for subsquent amidation reactions with aniline following general procedure A without further purification. .The product **1j** was obtained by recrystallization from EtOAc in 52% yield (2.84 g, 8.52 mmol) from **pre-1j'** as a white solid.

Mp = 174.0-174.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.01 (s, 2H), 6.42 (s, 1H), 7.04-7.10 (c, 3H), 7.16-7.21 (m, 1H), 7.27-7.32 (m, 2H), 7.36-7.42 (m, 2H), 7.53-7.57 (m, 2H), 7.75 (s, 1H), 9.55 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 100.8, 102.3, 110.1, 118.1, 118.6, 120.2, 124.1, 124.6, 128.9, 130.3, 138.2, 144.5, 150.7, 151.3, 155.9, 162.1. **IR** (ATR): 3346 w, 1658 m, 1205 s. **MS**: *m*/*z* (EI, relative intensity, %): 334 (23), 333 (36, M^+), 242 (15), 241 (100), 211 (10), 183 (19), 155 (20), 127 (14), 77 (16). **Anal.** Calcd for $C_{20}H_{15}NO_4$: C, 72.06; H, 4.54; N, 4.20. Found: C, 71.83; H, 4.52; N, 4.23.

3-Methoxy-2-phenoxy-*N*-phenylbenzamide (1k)

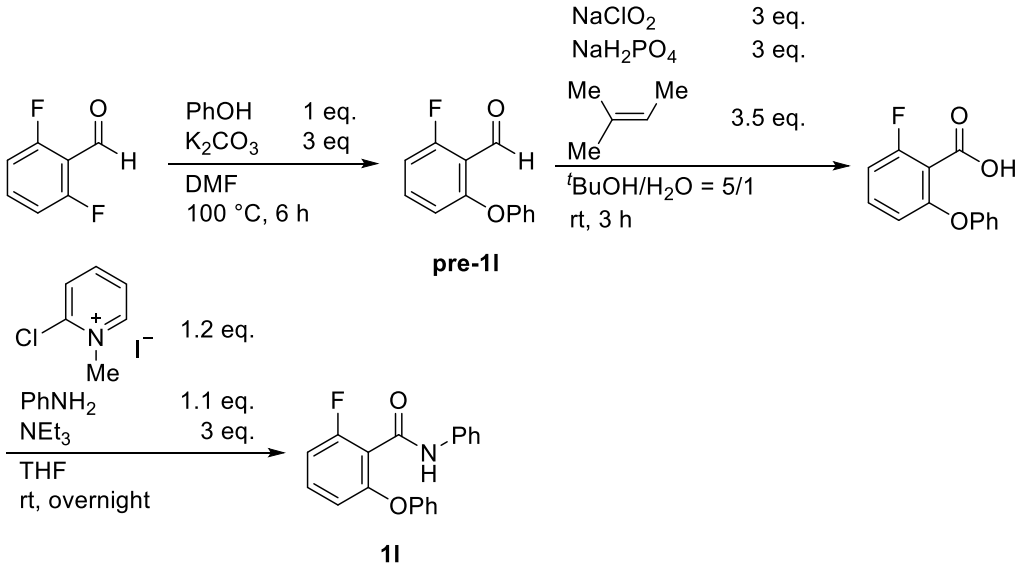


A 200ml round-botom flask was charged with methyl 3-methoxysalicylate (4.92 g, 27.0 mmol) and THF (45 mL). KO^{t}Bu (3.35 g, 29.6 mmol) was added to the stirred solution at 0 °C. After stirring for 10 min at the same temperature, diphenyliodonium trifluoromethanesulfonate (9.98 g, 23.2 mmol) was added at the same temperature. The resulting mixture was stirred overnight at room temperature. After removing the volatiles under reduced pressure, Et_2O (100 mL) and H_2O (100 mL) were added and the organic layer was separated. The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 20/1 to 5/1, R_f = 0.29 in hexane/EtOAc = 5/1) to afford methyl 3-methoxy-2-phenoxybenzoate (**pre-1k**) in 41% yield (2.42 g, 9.60 mmol) as a pale yellow solid.

1k was prepared from **pre-1k** (2.42 g, 9.60 mmol) following general procedure B. The product was obtained in 26% yield (811 mg, 2.54 mmol) as a white solid after recrystallization from acetone.

Mp = 176.8-178.0 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.76 (s, 3H), 6.90-6.94 (m, 2H), 7.03-7.11 (c, 2H), 7.17 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.27-7.32 (c, 4H), 7.36 (t, *J* = 8.2 Hz, 1H), 7.49-7.52 (m, 2H), 7.87 (dd, *J* = 8.2, 1.5 Hz, 1H), 9.30 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 56.3, 114.9, 116.0, 120.1, 123.0, 123.3, 124.3, 126.2, 128.6, 128.9, 129.8, 138.0, 140.9, 152.4, 157.2, 162.4. **IR** (ATR): 3372 w, 1662 m, 1213 s. **MS**: *m/z* (EI, relative intensity, %): 319 (26, M^+), 228 (16), 227 (100), 212 (35), 184 (16). **HRMS (DART)** Calcd for $C_{20}H_{18}NO_3$ ($[M+H]^+$): 320.12812. Found: 320.12802.

2-Fluoro-6-phenoxy-*N*-phenylbenzamide (1l)



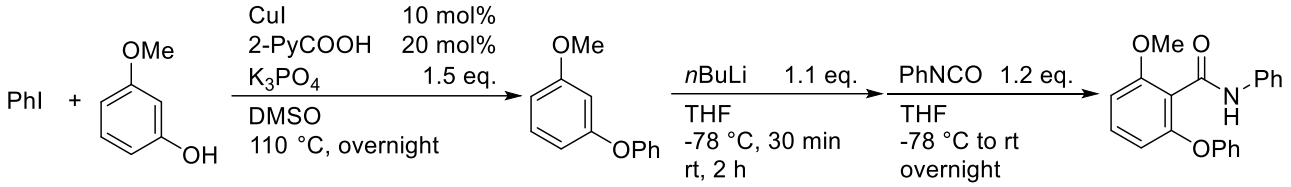
A three-necked flask was purged with N_2 and then charged with 2,6-difluorobenzaldehyde (5.09 g, 35.8 mmol), PhOH (3.49 g, 37.1 mmol), K_2CO_3 (14.7 g, 106 mmol) and DMF (70 mL). The resulting mixture were then stirred at 100 °C for 6 h under a N_2 atmosphere. After the flask was cooled to room temperature, EtOAc (100 mL) and H_2O (150 mL) were added and the organic layer

was separated. The organic layer was washed with sat. $NaHCO_3$ aq. (100 mL) and was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by bulb-to-bulb distillation (1.2 mmHg, 140-160 °C) to afford 2-fluoro-6-phenoxybenzaldehyde (**pre-1l**) in 59% yield (4.59 g, 21.2 mmol) as a yellow oil.

1l was prepared from **pre-1l** (4.59 g, 21.2 mmol) following general procedure C. The product was obtained by flash column chromatography on silica gel (eluent: hexane/EtOAc = 20/1 to 1/2, R_f = 0.14 in hexane/EtOAc = 5/1) followed by recrystallization from $CHCl_3$ in 49% yield (3.22 g, 10.5 mmol) as a white solid.

Mp = 166.5-167.9 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.70 (d, *J* = 8.5 Hz, 1H), 6.90 (t, *J* = 8.7 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 2H), 7.10-7.17 (c, 2H), 7.25-7.39 (c, 5H), 7.55 (d, *J* = 7.8 Hz, 2H), 7.84 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 111.0 (d, *J* = 22.0 Hz), 114.0 (d, *J* = 2.9 Hz), 117.3 (d, *J* = 18.2 Hz), 119.3, 120.1, 124.4, 124.7, 129.0, 130.0, 131.6 (d, *J* = 9.6 Hz), 137.6, 155.5 (d, *J* = 6.7 Hz), 156.0, 160.1, 160.7 (d, *J* = 251 Hz). **^{19}F NMR** -113.1 (dd, *J* = 9.0 Hz, 6.5 Hz). **IR** (ATR): 3289 w, 1658 m, 1234 s, 1207 m. **MS**: *m*/*z* (EI, relative intensity, %): 307 (10, M^+), 216 (14), 215 (100), 214 (48), 139 (41). **HRMS (DART)** Calcd for $C_{19}H_{15}NO_2F$ ($[M+H]^+$): 308.10813. Found: 308.10779.

2-Methoxy-6-phenoxy-*N*-phenylbenzamide (1m)

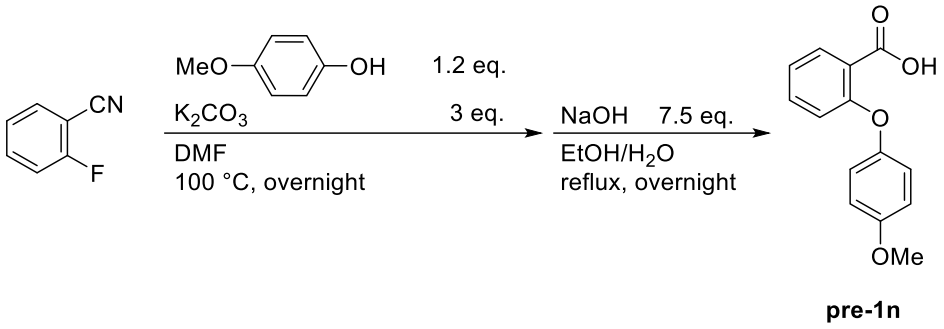


CuI (562 mg, 3.0 mmol), 2-pyridinecarboxylic acid (739 mg, 6.0 mmol) and K_3PO_4 (9.42 g, 44.3 mmol) were added to a 200 mL three-necked flask and the flask was purged with N_2. DMSO (75 mL) was added and the solution was heated at 50 °C for 10 min. PhI (6.02 g, 29.5 mmol) and 3-methoxyphenol (5.65 g, 45.5 mmol) were added and the mixture was then stirred overnight at 110 °C under a N_2 atmosphere. After cooling the flask to room temperature, the resulting crude mixture was suspended with Et_2O (150 mL) and filtered through a celite pad. The mixture was washed with 1N NaOH aq. (100 mL × 2). The organic layer was dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was dissolved in Et_2O and filtered through NH_2-modified silica gel pad to afford 1-methoxy-3-phenoxybenzene (**pre-1m**) in 90% yield (5.33 g, 26.6 mmol) as a colorless oil.

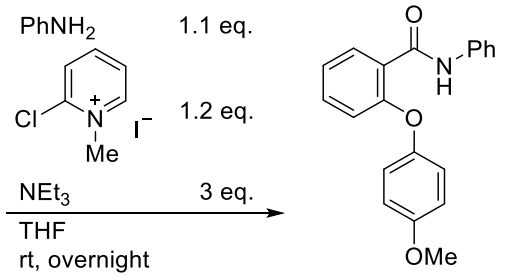
A 200 mL three-necked flask was flame-dried and purged with N_2 and charged with **pre-1m** (5.33 g, 26.6 mmol) and THF (45 mL). A 1.6 M solution of *n*BuLi (18 mL, 28.8 mmol) in hexane was slowly added to the stirred solution at -78 °C. After stirring for 30 min at the same temperature, the solution was warmed to room temperature and then stirred for 2 h. Phenyl isocyanate (3.87 g, 32.5 mmol) was added dropwise to the solution at -78 °C. After warming the solution to room temperature, the resulting mixture was stirred overnight. EtOAc (100 mL) and sat. NH_4Cl aq. (50 mL) were added and the aqueous layer was separated. The aqueous layer was extracted with EtOAc (100 mL) and the combined organic layers were dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by recrystallization from acetone to obtain **1m** in 45% yield (3.84 g, 12.0 mmol) as a white solid.

Mp = 158.4-158.6 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.87 (s, 3H), 6.53 (d, *J* = 8.2 Hz, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 7.06-7.11 (m, 2H), 7.25-7.31 (c, 5H), 7.51-7.60 (c, 3H). **^{13}C NMR** ($CDCl_3$) δ: 56.1, 106.2, 111.3, 118.8, 119.0, 119.8, 123.6, 124.2, 128.9, 129.7, 131.0, 138.0, 155.2, 156.8, 157.9, 162.7. **IR** (ATR): 1652 m, 1241 s. **MS**: *m*/*z* (EI, relative intensity, %): 319 (6, M^+), 228 (15), 227 (100), 226 (22), 213 (11), 212 (74). **Anal.** Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.14; H, 5.34; N, 4.38.

2-(4-Methoxyphenoxy)-*N*-phenylbenzamide (1n)



pre-1n

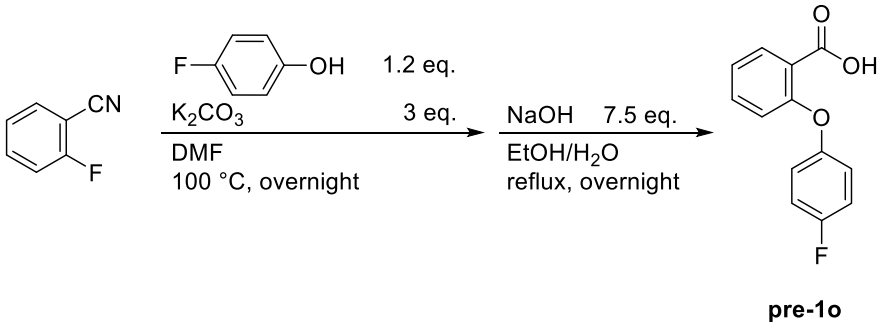


1n

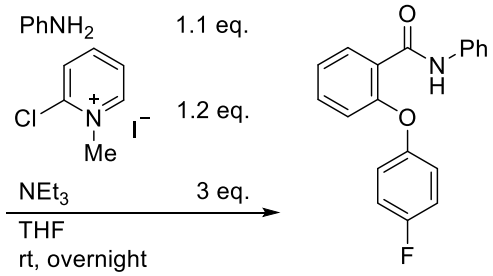
2-(4-Methoxyphenoxy)benzoic acid (**pre-1n**) was prepared from 2-fluoro-benzonitrile (4.83 g, 39.9 mmol) according to the reported procedure[5] and was then used in a subsquent amidation following general procedure A without further purification. **1n** was obtained in 56% yield (7.12 g, 22.3 mmol) as a white solid by recrystallization from EtOAc.

Mp = 100.3-100.9 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.82 (s, 3H), 6.81 (dd, *J* = 8.3 Hz, 0.8 Hz, 1H), 6.92-6.98 (m, 2H), 7.06-7.13 (c, 3H), 7.18-7.22 (m, 1H), 7.30-7.35 (m, 2H), 7.36-7.40 (m, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 8.33 (dd, *J* = 7.8 Hz, 1.8 Hz, 1H), 9.77 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 55.5, 115.2, 117.0, 120.3, 121.1, 123.1 (two overlapping peaks), 124.1, 128.8, 132.2, 132.9, 138.1, 148.0, 156.3, 156.8, 162.7. **IR** (ATR): 3373 w, 1667 m, 1208 s. **MS**: *m*/*z* (EI, relative intensity, %): 319 (22, M^+), 228 (15), 227 (100), 196 (50), 184 (29). **Anal.** Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.39; H, 5.26; N, 4.39.

2-(4-Fluorophenoxy)-*N*-phenylbenzamide (1o)



pre-1o



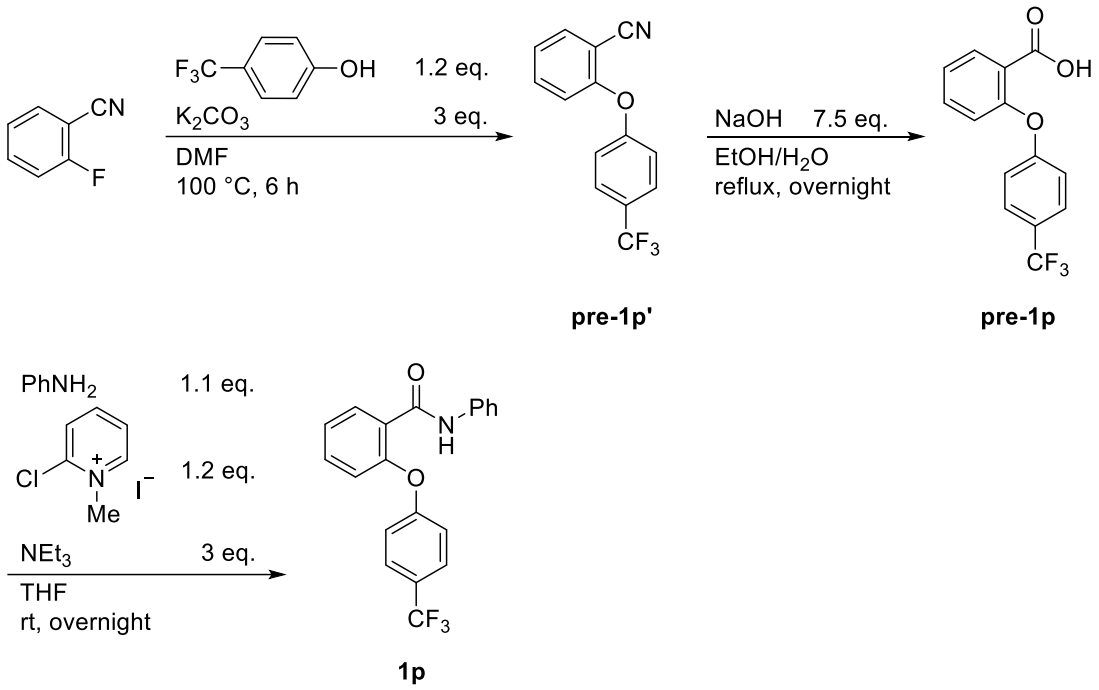
1o

2-(4-Fluorophenoxy)benzoic acid (**pre-1o**) was prepared from 2-fluoro-benzonitrile (4.86 g, 40.1 mmol) according to the reported procedure[5] and was then used in a subsquent amidation following general procedure A without further purification. **1o** was obtained in 49% yield (6.02 g, 19.6 mmol) as a white solid by recrystallization from EtOH.

Mp = 80.3-80.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.82 (dd, *J* = 8.2 Hz, 0.9 Hz, 1H), 7.06-7.13 (c, 5H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.29-7.33 (m, 2H), 7.38-7.42 (m, 1H), 7.60-7.63 (m, 2H), 8.30 (dd, *J* = 7.6 Hz, 1.8 Hz, 1H), 9.54 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 116.9 (d, *J* = 23.9

Hz), 117.7, 120.3, 121.1 (d, *J* = 8.6 Hz), 123.85, 123.91, 124.3, 128.9, 132.4, 133.0, 138.0, 150.9 (d, *J* = 2.9 Hz), 155.4, 159.6 (d, *J* = 243 Hz), 162.5. **^{19}F NMR** -117.9 (m). **IR** (ATR): 3382 w, 1667 m, 1201 s. **MS**: *m*/*z* (EI, relative intensity, %): 307 (21, M^+), 216 (15), 215 (100), 196 (19), 133 (12). **Anal.** Calcd for $C_{19}H_{14}FNO_2$: C, 74.26; H, 4.59; N, 4.56. Found: C, 74.44; H, 4.57; N, 4.60.

***N*-Phenyl-2-(4-(trifluoromethyl)phenoxy)benzamide (1p)**



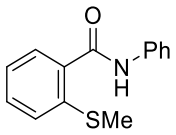
2-Fluoro-benzonitrile (6.06 g, 50.0 mmol) and K_2CO_3 (20.5 g, 149 mmol) were added to a 300 mL three-necked round-bottom flask and the flask was purged with N_2. DMF (125 mL) and 4-hydroxybenzotrifluoride (9.71 g, 59.9 mmol) were added and the resulting mixture were then stirred overnight at 100 °C under a N_2 atmosphere. After cooling the flask to room temperature, EtOAc (200 mL) and H_2O (150 mL) were added and the organic layer was separated. The organic layer was washed with 1N NaOH aq. (50 mL) and brine (100 mL). 1N HCl aq. (150 mL) was added to the combined aqueous layer and the aqueous layer was extracted with Et_2O (200 mL). The combined organic layer was dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 10/1, R_f = 0.34 in hexane/EtOAc = 10/1) followed by bulb-to-bulb distillation (2.8-3.0 mmHg, 150-170 °C) to afford 2-(4-(trifluoromethyl)phenoxy)benzonitrile (**pre-1p'**) in 35% yield (4.61 g, 17.6 mmol) as a colorless oil.

A solution of **pre-1p'** (4.61 g, 17.6 mmol) in EtOH (45 mL) and 3N NaOH aq (45 mL) was heated overnight under reflux. Et_2O (100 mL) and H_2O (100 mL) were added to the mixture and the aqueous layer was separated. The aqueous layer was acidified with 1N HCl aq and extracted with Et_2O (100 mL × 2). The organic layer was dried over Na_2SO_4 and the volatiles were removed under reduced pressure. The crude mixture was purified by flash column chromatography (eluent: hexane/EtOAc = 5/1 to 2/1, R_f = 0.43 in hexane/EtOAc = 2/1) to afford the mixture that contained 2-(4-(trifluoromethyl)phenoxy)benzoic acid (**pre-1p**) and some impurities (3.81 g).

1p was prepared from **pre-1p** (3.81 g, mixture with some impurites) with aniline (2.08 g, 22.3 mmol) following general procedure A. The product was obtained in 30% yield (1.87 g, 5.23 mmol) from **pre-1p'** as a white solid after recrystallization from Et_2O.

Mp = 102.6-103.6 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.97 (d, *J* = 8.0 Hz, 1H), 7.09-7.13 (m, 1H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.30-7.36 (c, 3H), 7.47-7.51 (m, 1H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 8.30 (dd, *J* = 7.9 Hz, 1.8 Hz, 1H), 9.21 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 118.6, 119.7, 120.3, 123.8 (q, *J* = 271 Hz), 124.5, 125.2, 125.4, 126.7 (q, *J* = 32.6 Hz), 127.7 (q, *J* = 3.6 Hz), 129.0, 132.6, 133.3, 137.8, 153.5, 158.6, 162.3. **^{19}F NMR** -62.5 (s). **IR** (ATR): 3392 w, 1664 m, 1321 s. **MS**: *m*/*z* (EI, relative intensity, %): 357 (24, M^+), 266 (20), 265 (100), 245 (11). **Anal.** Calcd for $C_{20}H_{14}F_3NO_2$: C, 67.23; H, 3.95; N, 3.92. Found: C, 67.24; H, 3.88; N, 3.87.

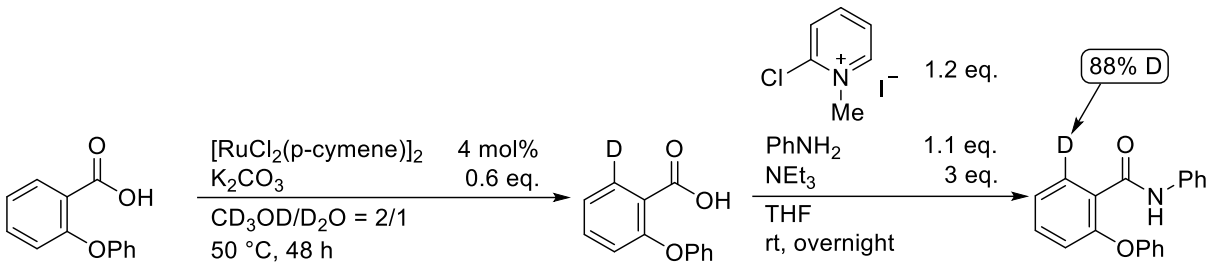
2-(Methylthio)-*N*-phenylbenzamide (1q) [CAS: 23343-16-0]



1q was prepared from 2-(methylthio)benzoic acid (2.53 g, 15.0 mmol) and aniline (1.49 g, 16.0 mmol) following general procedure A. The product was obtained in 48% yield (1.74 g, 7.15 mmol) as a white solid by recrystallization from EtOAc.

Mp = 149.1-150.3 ºC. **^{1}H NMR** ($CDCl_3$) δ: 2.48 (s, 3H), 7.12-7.17 (m, 1H), 7.23-7.28 (m, 1H), 7.33-7.39 (c, 3H), 7.40-7.44 (m, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.71 (d, *J* = 6.9 Hz, 1H), 8.34 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 17.0, 120.0, 124.5, 125.7, 128.0, 129.0, 129.1, 131.0, 135.1, 136.6, 137.9, 165.9. **IR** (ATR): 3289 w, 1650 s. **MS**: *m*/*z* (EI, relative intensity, %): 243 (4, M^+), 151 (100), 93 (76). **Anal.** Calcd for $C_{14}H_{13}NOS$: C, 69.11; H, 5.39; N, 5.76. Found: C, 68.98; H, 5.45; N, 5.75.

2-Phenoxy-*N*-phenylbenzamide-6-*d* (1a-*d*)

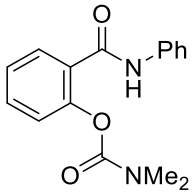


pre-1a-*d* **1a-*d***

2-Phenoxybenzoic-6-*d* acid (**pre-1a-*d***) was synthesized according to Ma's procedure.[6] $[RuCl_2(p\text{-cymene})]_2$ (241 mg, 0.39 mmol), K_2CO_3 (662 mg, 6.0 mmol) and 2-phenoxybenzoic acid (2.14 g, 10.0 mmol) were added to a 25 mL schlenk tube and the tube was then purged with N_2. After adding CD_3OD (4 mL) and D_2O (2 mL) to the flask, the resulting mixture was stirred for 48 h at 50 °C under a N_2 atmosphere. After cooling the flask to room temperature, the volatiles were removed under reduced pressure. EtOAc (50 mL) and 1N HCl aq. (50 mL) were added and the aqueous layer was separated. The aqueous layer was extracted with EtOAc (50 mL) and the combined organic layer was dried over Na_2SO_4 and the solvent removed under a vaccum. These operations were repeated twice to give the crude mixture that contained **pre-1a-*d*** was obtained, which was used in a subsequent amidation with aniline following general procedure A without further purification. **1a-*d*** was obtained by flash column chromatography on silica gel (eluent: hexane/EtOAc = 5/1, R_f = 0.34 in hexane/EtOAc = 5/1) followed by recrystallization from EtOH in 59% yield (1.68 g, 5.9 mmol) as a white solid.

^{1}H NMR ($CDCl_3$) δ: 6.88 (dd, *J* = 8.2 Hz, 1.1 Hz, 1H), 7.07-7.16 (c, 3H), 7.19-7.26 (c, 2H), 7.28-7.34 (m, 2H), 7.38-7.44 (m, 3H), 7.59-7.64 (m, 2H), 8.33 (dd, *J* = 7.9 Hz, 1.7 Hz, 0.1H), 9.63 (br, 1H). **^{2}H NMR** ($CHCl_3$) δ: 8.40. **^{13}C NMR** ($CDCl_3$) δ: 118.3 (1C), 119.4 (2C), 120.3 (2C), 123.8 (0.83C), 123.9 (0.15C), 123.97 (0.88C), 124.04 (0.13C), 124.2 (1C), 124.9 (1C), 128.9 (2C), 130.2 (2C), ((132.1 (t, *J* = 25.4 Hz) and 132.37), 1C), 133.0 (1C), 138.1 (1C), 155.1 (1C), 155.2 (1C), 162.6 (1C). **HRMS (DART)** Calcd for $C_{19}H_{15}NO_2D$ ($[M+H]^+$): 291.12383. Found: 291.12411.

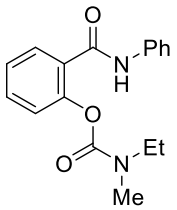
2-(Phenylcarbamoyl)phenyl dimethylcarbamate (5a) [CAS: 35410-18-5][7]



5a was prepared from salicylanilide (2.13 g, 10.0 mmol) and dimethylcarbamoyl chloride (1.62 g, 15.0 mmol) following general procedure D. The product was obtained in 97% yield (2.76 g, 9.71 mmol) as a white solid by recrystallization from hexane/EtOAc.

^{1}H NMR ($CDCl_3$) δ: 3.02 (s, 3H), 3.10 (s, 3H), 7.11-7.17 (c, 2H), 7.31-7.39 (c, 3H), 7.46-7.51 (m, 1H), 7.62 (d, *J* = 7.7 Hz, 2H), 7.78 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.59 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 36.7, 36.9, 119.5, 123.3, 124.3, 126.3, 129.0, 130.0, 130.5, 131.8, 138.1, 148.0, 155.3, 164.2. **MS**: *m*/*z* (EI, relative intensity, %): 284 (2, M^+), 195 (11), 192 (77), 72 (100). **Anal.** Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.56; H, 5.71; N, 9.75.

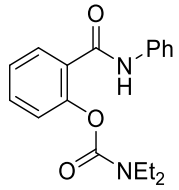
2-(Phenylcarbamoyl)phenyl ethyl(methyl)carbamate (5b)



5b was prepared from salicylanilide (2.13 g, 10.0 mmol) and *N*-ethyl-*N*-methylcarbamoyl chloride (1.82 g, 15.0 mmol) following general procedure D. The product was obtained in 93% yield (2.76 g, 9.25 mmol) as a white solid by flash column chromatography on silica gel (eluent: hexane/EtOAc = 50/1 to 5/1, R_f = 0.63 in hexane/EtOAc = 1/1) followed by recrystallization from hexane/EtOAc.

Mp = 96.8-97.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.07-1.16 (t × 2, *J* = 7.2 Hz, 3H), 2.97-3.06 (s × 2, 3H), 3.36-3.47 (q × 2, *J* = 7.2 Hz, 2H), 7.10-7.14 (c, 2H), 7.29-7.36 (c, 3H), 7.44-7.49 (m, 1H), 7.59-7.63 (c, 2H), 7.71-7.78 (m, 1H), 8.58-8.63 (br × 2, 1H). **^{13}C NMR** ($CDCl_3$) δ: 12.3, 13.0, 34.0, 34.3, 44.3, 119.4, 119.5, 123.17, 123.23, 124.2, 126.2, 126.3, 129.0, 129.86, 129.94, 130.5, 130.8, 131.66, 131.70, 138.1, 147.9, 148.0, 154.8, 155.1, 164.26, 164.33. **IR** (ATR): 3309 w, 1710 s, 1676 s, 1208 s, 1158 s. **MS**: *m*/*z* (EI, relative intensity, %): 298 (2, M^+), 207 (11), 206 (88), 195 (13), 86 (100), 58 (56). **Anal.** Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.38; H, 6.08; N, 9.32.

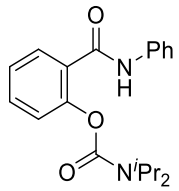
2-(Phenylcarbamoyl)phenyl diethylcarbamate (5c) [CAS: 1924681-17-3]



5c was prepared from salicylanilide (4.29 g, 20.1 mmol) and diethylcarbamoyl chloride (4.05 g, 29.9 mmol) following general procedure D. The product was obtained in 61% yield (3.85 g, 12.3 mmol) as a white solid by flash column chromatography on silica gel (eluent: hexane/EtOAc = 5/1 to 2/1, R_f = 0.11 in hexane/EtOAc = 5/1) followed by recrystallization from Et_2O.

Mp = 83.1-84.2 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.13 (t, *J* = 7.2 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H), 3.37 (q, *J* = 7.2 Hz, 2H), 3.42 (q, *J* = 7.2 Hz, 2H), 7.09-7.14 (c, 2H), 7.31-7.37 (c, 3H), 7.48 (td, *J* = 7.8 Hz, 1.6 Hz, 1H), 7.59-7.63 (m, 2H), 7.74 (td, *J* = 7.8 Hz, 1.6 Hz, 1H), 8.58 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 13.2, 14.0, 42.1, 42.4, 119.5, 123.2, 124.2, 126.3, 129.0, 129.9, 131.0, 131.7, 138.1, 147.9, 154.9, 164.4. **IR** (ATR): 3277 w, 3246 w, 1716 s, 1649 s, 1203 s, 1149 s. **MS**: *m*/*z* (EI, relative intensity, %): 312 (1, M^+), 220 (57), 100 (100), 72 (47). **HRMS (DART)** Calcd for $C_{18}H_{21}N_2O_3$ ($[M+H]^+$): 313.15467. Found: 313.15532.

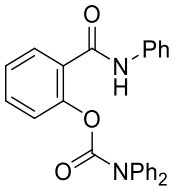
2-(Phenylcarbamoyl)phenyl diisopropylcarbamate (5d)



5d was prepared from salicylanilide (2.30 g, 10.8 mmol) and diisopropylcarbamoyl chloride (2.52 g, 15.4mmol) following general procedure D. The product was obtained in 67% yield (2.47 g, 7.26 mmol) as a white solid by recrystallization from hexane/EtOAc.

Mp = 121.8-122.0 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.19 (d, *J* = 6.8 Hz, 6H), 1.27 (d, *J* = 6.8 Hz, 6H), 3.89-3.95 (m, 1H), 4.06-4.15 (m, 1H), 7.08-7.13 (c, 2H), 7.30-7.36 (c, 3H), 7.46-7.50 (m, 1H), 7.58-7.63 (m, 2H), 7.74 (dd, *J* = 7.7 Hz, 1.6 Hz, 1H), 8.59 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 20.3, 21.3, 46.5, 47.3, 119.5, 123.2, 124.2, 126.3, 128.9, 129.9, 131.3, 131.7, 138.1, 147.8, 154.6, 164.6. **IR** (ATR): 3315 w, 1714 s, 1682 s, 1200 s, 1152 m. **MS**: *m*/*z* (EI, relative intensity, %): 340 (2, M^+), 248 (22), 128 (99), 121 (30), 93 (61), 86 (100). **Anal.** Calcd for $C_{20}H_{24}N_2O_3$: C, 70.57; H, 7.11; N, 8.23. Found: C, 70.25; H, 7.16; N, 8.23.

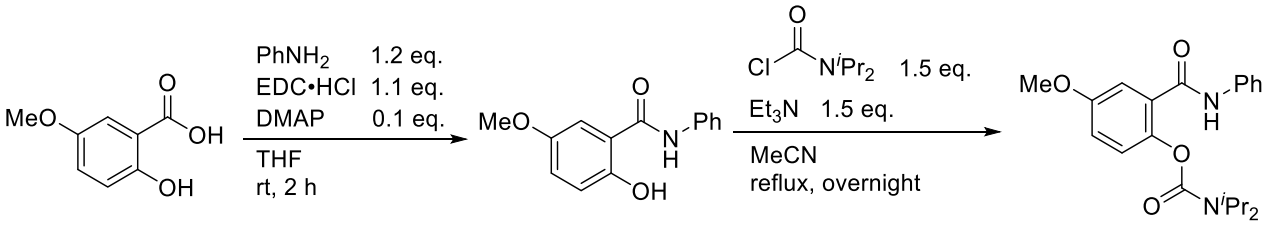
2-(phenylcarbamoyl)phenyl diphenylcarbamate (5e) [CAS: 1621339-73-8][8]



5e was prepared from salicylanilide (2.13 g, 10.0 mmol) and diphenylcarbamoyl chloride (2.30 g, 9.9 mmol) following general procedure D. The product was obtained in 84% yield (3.42 g, 8.37 mmol) as a white solid by flash column chromatography on silica gel (eluent: hexane/EtOAc = 50/1 to 3/1, R_f = 0.64 in hexane/EtOAc = 1/1).

^{1}H NMR ($CDCl_3$) δ: 7.14 (t, *J* = 7.3 Hz, 1H), 7.21-7.37 (c, 14H), 7.42-7.52 (c, 3H), 7.82 (d, *J* = 7.7 Hz, 1H), 8.08 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 120.2, 123.0, 124.5, 126.2, 126.9, 128.8, 129.1, 130.0, 130.1, 131.8, 137.7, 141.6, 147.8, 152.8, 163.8. **MS**: *m*/*z* (EI, relative intensity, %): 408 (2, M^+), 317 (10), 316 (45), 197 (15), 196 (100), 169 (48), 168 (45), 167 (23), 93 (11), 77 (24). **HRMS (DART)** Calcd for $C_{26}H_{21}N_2O_3$ ($[M+H]^+$): 409.15467. Found: 409.15563.

4-Methoxy-2-(phenylcarbamoyl)phenyl diisopropylcarbamate (5f)



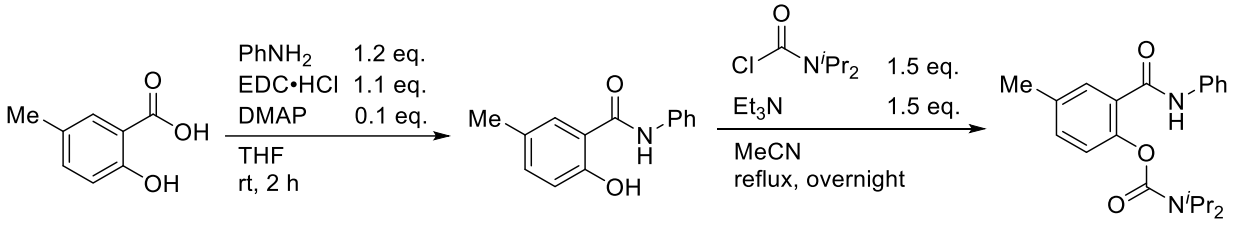
pre-5f **5f**

A mixture of 5-methoxysalicylic acid (2.52 g, 15.0 mmol), aniline (1.68 g, 18.0 mmol), EDC•HCl (3.16 g, 16.5 mmol), DMAP (0.18 g, 1.5 mmol) and THF (50 mL) were stirred at room temperature for 2 h. After the reaction, sat. $NaHCO_3$ aq. and EtOAc were added and the organic layer was separated. The organic layer was washed with 1N HCl aq. and dried over Na_2SO_4. After removing the volatiles under reduced pressure, the resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 50/1 to 10/1, R_f = 0.60 in hexane/EtOAc = 1/1) to afford the mixture that contained 2-hydroxy-5-methoxy-*N*-phenylbenzamide (**pre-5f**) and some impurities (2.15 g).

5f was prepared fr om **pre-5f** (2.15 g, mixture with some impurities) and diisopropylcarbamoyl chloride (2.16 g, 13.2 mmol) following general procedure D. The product was obtained in 15% yield (829 mg, 2.24 mmol) from 5-methoxysalicylic acid as a white solid after flash column chromatography on silica gel (eluent: hexane/EtOAc = 20/1 to 10/1, R_f = 0.54 in hexane/EtOAc = 1/1) followed by recrystallization from hexane/EtOAc.

Mp = 119.3-120.1 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.19 (d, *J* = 6.8 Hz, 6H), 1.25 (d, *J* = 6.8 Hz, 6H), 3.83 (s, 3H), 3.86-3.94 (m, 1H), 4.06-4.17 (m, 1H), 7.00 (d, *J* = 1.6 Hz, 2H), 7.08-7.13 (m, 1H), 7.23 (t, *J* = 1.6 Hz, 1H), 7.30-7.34 (m, 2H), 7.58-7.62 (m, 2H), 8.70 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 20.3, 21.3, 46.4, 47.3, 55.8, 113.5, 118.2, 119.5, 124.17, 124.22, 128.9, 131.8, 138.0, 141.1, 155.1, 157.4, 164.4. **IR** (ATR): 3317 w, 1717 s, 1680 s, 1198 s. **MS**: *m*/*z* (EI, relative intensity, %): 370 (2, M^+), 243 (11), 225 (11), 151 (16), 150 (28), 128 (100), 93 (50), 86 (98). **HRMS (DART)** Calcd for $C_{21}H_{27}N_2O_4$ ([M+H]$^+$): 371.19653. Found: 371.19733.

4-Methyl-2-(phenylcarbamoyl)phenyl diisopropylcarbamate (5g)

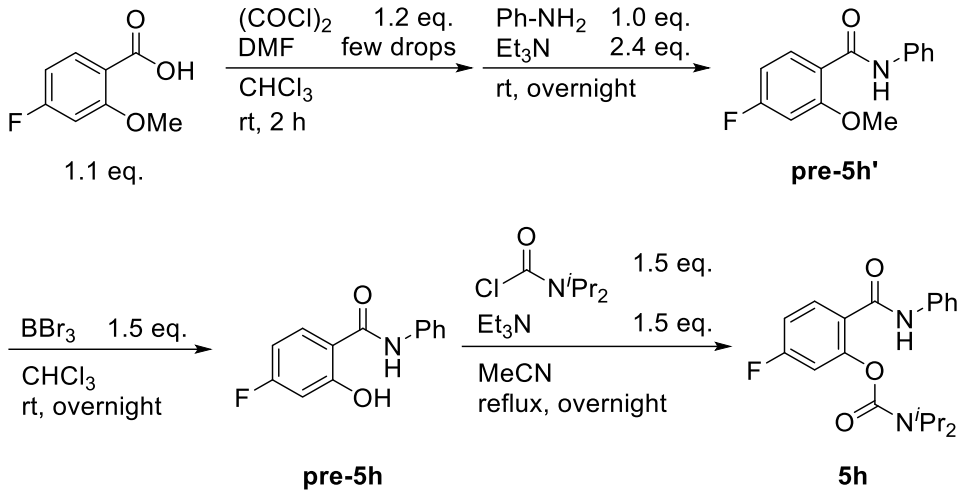


pre-5g **5g**

A mixture of 5-methylsalicylic acid (2.28 g, 15.0 mmol), aniline (1.68 g, 18.0 mmol), EDC•HCl (3.16 g, 16.5 mmol), DMAP (0.18 g, 1.5 mmol) and THF (50 mL) were stirred at room temperature for 2 h. After the reaction, sat. $NaHCO_3$ aq. and EtOAc were added and the organic layer was separated. The organic layer was washed with 1N HCl aq. and dried over Na_2SO_4. After the volatiles were removed under reduced pressure, the crude mixture that contained 2-hydroxy-5-methyl-*N*-phenylbenzamide (**pre-5g**) was obtained, which was used in the subsequent step without further purification according to general procedure D. **5g** was obtained by flash column chromatography on silica gel (eluent: hexane/EtOAc = 15/1 to 10/1, R_f = 0.69 in hexane/EtOAc = 1/1) in 11% yield (562 mg, 1.59 mmol). Further purification by recrystallization from hexane/EtOAc afforded the title compound as a white solid.

Mp = 137.5-140.5 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.18 (d, *J* = 6.8 Hz, 6H), 1.25 (d, *J* = 6.8 Hz, 6H), 2.38 (s, 3H), 3.82-3.95 (m, 1H), 4.05-4.15 (m, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 7.07-7.12 (m, 1H), 7.25-7.27 (m, 1H), 7.30-7.34 (m, 2H), 7.53 (d, *J* = 1.8 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 2H), 8.63 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 20.3, 20.7, 21.3, 46.4, 47.3, 119.5, 122.9, 124.1, 128.9, 130.2, 130.9, 132.3, 136.1, 138.1, 145.5, 154.9, 164.8. **IR** (ATR): 3315 w, 1713 m, 1679 s, 1200 s. **MS**: *m*/*z* (EI, relative intensity, %): 262 (2, M^+-92(NHPh)), 135 (34), 128 (100), 93 (67), 86 (88), 81 (15), 69 (12). **HRMS (DART)** Calcd for $C_{21}H_{27}N_2O_3$ ([M+H]$^+$): 355.20162. Found: 355.20236.

5-Fluoro-2-(phenylcarbamoyl)phenyl diisopropylcarbamate (5h)

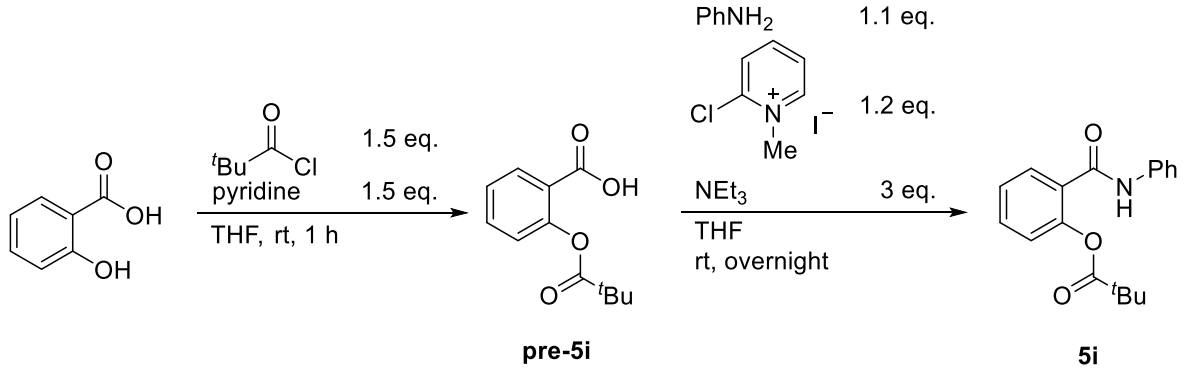


To a stirred solution of 4-fluoro-2-methoxybenzoic acid (2.73 g, 16.0 mmol) and DMF (5 drops) in $CHCl_3$ (20 mL), $(COCl)_2$ (1.5 mL, 17.5 mmol) was added dropwise. The solution was stirred at room temperature for 2 h. The solvent was then removed under reduced pressure, and the resulting residue was dissolved in $CHCl_3$. After cooling the reaction mixture to 0 °C, a solution of aniline (1.38 g, 14.8 mmol) and triethylamine (5.0 mL, 35.9 mmol) in $CHCl_3$ was added dropwise. The resulting mixture was allowed to warm to room temperature and stirred overnight. The solution containing the crude product was washed with saturated aqueous $NaHCO_3$ and $CHCl_3$. The combined organic layer was washed with 1N HCl aq. The organic phase was dried over Na_2SO_4 and the solvent was removed under vaccum. The resulting crude mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 50/1 to 10/1, R_f = 0.34 in hexane/EtOAc = 5/1) to afford the mixture that contained 4-fluoro-2-methoxy-*N*-phenylbenzamide (**pre-5h'**) and some impurities (3.75 g).

A mixture of **pre-5h'** (3.75 g, mixture with some impurities), 1.0 M solution of BBr_3 (23 mL, 23 mmol) in DCM and $CHCl_3$ (30 mL) were stirred at rt overnight. After the reaction, MeOH were added. After the volatile was removed under reduced pressure, the crude mixture that cotained 4-fluoro-2-hydroxy-*N*-phenylbenzamide (**pre-5h**) was obtained, which was used in the subsequent step according to general procedure D without further purification. **5h** was obtained by flash column chromatography on silica gel (eluent: hexane/EtOAc = 10/1 to 7/1, R_f = 0.40 in hexane/EtOAc = 3/1) in 50% yield (2.65 g, 7.39 mmol) from aniline. Further purification by recrystallization from hexane/EtOAc afforded the title compound as a white solid.

Mp = 135.3-136.0 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.20 (d, *J* = 6.8 Hz, 6H), 1.26 (d, *J* = 6.8 Hz, 6H), 3.91-3.97 (m, 1H), 4.03-4.09 (m, 1H), 6.85 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.02-7.07 (m, 1H), 7.09-7.13 (m, 1H), 7.30-7.34 (m, 2H), 7.57-7.59 (m, 2H), 7.75 (dd, *J* = 8.6 Hz, 6.3 Hz, 1H), 8.50 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 20.2, 21.3, 46.7, 47.4, 110.9 (d, *J* = 24.1 Hz), 113.6 (d, *J* = 21.2 Hz), 119.6, 124.4, 127.5 (d, *J* = 2.9 Hz), 129.0, 131.5 (d, *J* = 9.6 Hz), 137.9, 149.1 (d, *J* = 11.6 Hz), 153.9, 163.7, 163.9 (d, *J* = 252 Hz). **^{19}F NMR** ($CDCl_3$) δ: -107.7 (dd, *J* = 15.0, 7.5 Hz). **IR** (ATR): 3312 w, 1739 m, 1692 s, 1321 s. **MS**: *m/z* (EI, relative intensity, %): 358 (1, M^+), 266 (13), 139 (20), 128 (91), 93 (37), 86 (100). **HRMS (DART)** Calcd for $C_{20}H_{24}N_2O_3F$ ($[M+H]^+$): 359.17655. Found: 359.17658.

2-(Phenylcarbamoyl)phenyl pivalate (5i)



To a solution of salicylic acid (3.48 g, 25.2 mmol) and pyridine (2.38 g, 30.1 mmol) in THF (25 mL), pivaloyl chloride (3.6 mL, 29.6 mmol) was added dropwise. The solution was stirred at room temperature for 1 h. After removing the volatiles under reduced pressure, EtOAc (100 mL) and 1N HCl aq. were added and the organic layer was separated. The organic layer was dried over Na_2SO_4 and the solvent was removed under vaccum. The crude mixture that contained 2-(pivaloyloxy)benzoic acid (**pre-5i**) (5.69 g) was used in the subsequent step according to general procedure A without further purification. **5i** was obtained in 34% yield (2.58 g, 8.68 mmol) as a white solid by recrystallization from EtOAc.

Mp = 163.6-164.2 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.31 (s, 9H), 7.07 (dd, *J* = 8.1 Hz, 0.8 Hz, 1H), 7.12-7.16 (m, 1H), 7.33-7.37 (c, 3H), 7.48-7.52 (m, 1H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.79 (d, *J* = 7.7 Hz, 1.3 Hz, 1H), 7.89 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 27.0, 39.2, 119.7, 123.0, 124.5, 126.4, 129.1, 129.7, 129.8, 131.8, 137.7, 147.8, 163.8, 177.5. **IR** (ATR): 3307 w, 1750 m, 1659 m, 1109 s. **MS**: *m*/*z* (EI, relative intensity, %): 297 (9, M^+), 213 (11), 205 (37), 121 (36), 93 (100), 57 (50). **Anal.** Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.71; H, 6.44; N, 4.68.

Typical Procedure

Typical Procedure A: The reaction from biaryl ether, thioether and nitrile.

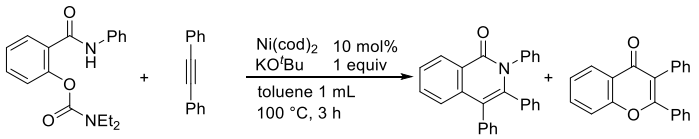
To an oven-dried 10 mL screw-capped vial in a glove box, $Ni(cod)_2$ (11 mg, 0.04 mmol), LiO^tBu (32 mg, 0.4 mmol), the amide (0.4 mmol), the alkyne (if solid) (0.6 mmol), DMSO (1 mL) or the alkyne (0.6 mmol), if a liquid, was added last in sequential order. The mixture was stirred at 40 °C for 5 h followed by cooling. The resulting mixture was filtered through a silica gel pad eluting with EtOAc and the filtrate was washed with 1N HCl aq, which was dried over Na_2SO_4. The crude mixture was concentrated under reduced pressure and analyzed by ^{1}H NMR using 1,1,1,2- tetrachloroethane as an internal standard. The resulting mixture was purified by flash column chromatography on silica gel.

Typical Procedure B: The reaction from the carbamates and the pivalate.

To an oven-dried 10 mL screw-capped vial in a glove box, $Ni(cod)_2$ (11 mg, 0.04 mmol), KO^tBu (44 mg, 0.4 mmol), the amide (0.4 mmol), the alkyne (if solid) (0.6 mmol), toluene (1 mL) or the alkyne (0.6 mmol), if a liquid, was added last in sequential order. The mixture was stirred at 0 °C for 5 h followed by cooling. The resulting mixture was filtered through a silica gel pad eluting with EtOAc and the filtrate was washed with 1N HCl aq, which was dried over Na_2SO_4. The crude mixture was concentrated under reduced pressure and analyzed by ^{1}H NMR using 1,1,2,2- tetrachloroethane as an internal standard. The resulting mixture was purified by flash column chromatography on silica gel.

Optimization studies

Table S1. screening of conditions using **5**[a].



5c **2a** 2 eq. **3aa** **6aa**

entry	base (equiv.)	solvent	temp. (°C)	time (h)	NMR yields (isolated yields)		
					3aa	**6a**	**5c**
1	KO^tBu(1.0)	DMSO	80	3	40%	12%	0%
2	KO^tBu(0.2)	DMSO	80	3	54%	10%	36%
3	KO^tBu(1.0)	DMSO	100	3	56% (56%)	17% (19%)	0%
4	KO^tBu(1.0)	DMSO	100	1	58%	16%	0%
5	KO^tBu(1.0)	DMSO	120	3	58%	17%	0%
6	Cs_2CO_3(1.0)	DMSO	80	3	0%	0%	63%
7	K_3PO_4(1.0)	DMSO	80	3	15%	trace	67%
8	KO^tBu(1.0)	DMF	80	3	77%	16%	0%
9	KO^tBu(1.0)	toluene	80	3	73%	trace	0%
10	**KO^tBu(1.0)**	**toluene**	**100**	**3**	**86%(86%)**	**trace**	**0%**

Reaction conditions: **5c** (0.15 mmol), $Ni(cod)_2$ (0.015 mmol), and base in solvent (1 mL).

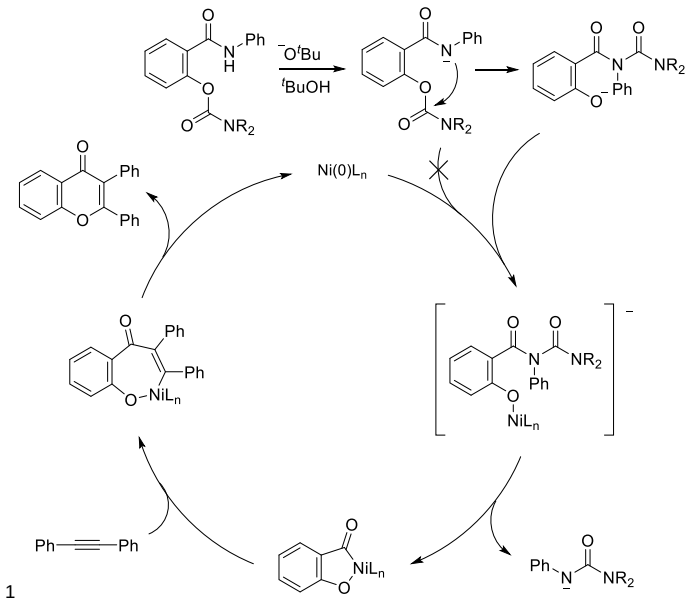
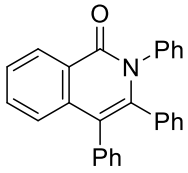


Figure S1. A plausible mechanism for the generation of **6**.

Characterization of Products

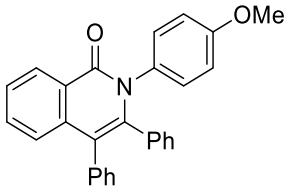
2,3,4-triphenylisoquinolin-1(2*H*)-one (3aa) [CAS: 14959-72-9]



3aa was prepared from the reaction of **1a**, **5d**, **5i**, **1q** or **1r** with **2a** following typical procedure A (**1a**, **1q**, **1r** (60 ºC)) or typical procedure B (**5d**, **5i**). The product was obtained as a white solid by flash column chromatography on silica gel (R_f = 0.14 in hexane/EtOAc = 5/1) in 88% yield (130 mg, 0.35 mmol) from **1a**, 86% yield (129 mg, 0.35 mmol) from **5d**, 24% yield (35 mg, 0.094 mmol) from **5i** or 58% yield (84 mg, 0.23 mmol) from **1q.** The product was obtained in 37% yield (54 mg, 0.15 mmol) from **1r** as a white solid by flash column chromatography on silica gel followed by GPC.

Mp = 221.2-221.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.87-6.92 (c, 5H), 7.09-7.28 (c, 11H), 7.51-7.56 (m, 1H), 7.58-7.62 (m, 1H), 8.58 (ddd, *J* = 7.9 Hz, 1.6 Hz, 0.6 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 118.7, 125.5, 125.6, 126.8, 126.9, 127.1, 127.2, 127.5, 127.9, 128.2, 128.6, 129.5, 131.0, 131.6, 132.5, 134.7, 136.3, 137.6, 139.4, 141.0, 162.6. **IR** (ATR): 3059 w, 3027 w, 1656 s. **MS**: *m*/*z* (EI, relative intensity, %): 374 (32), 373 (100, M^+), 372 (73), 180 (11), 77 (33). **Anal.** Calcd for $C_{27}H_{19}NO$: C, 86.84; H, 5.13; N, 3.75. Found: C, 86.58; H, 5.08; N, 3.76.

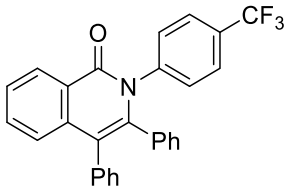
2-(4-Methoxyphenyl)-3,4-diphenylisoquinolin-1(2*H*)-one (3ba) [CAS: 1253388-47-4]



3ba was prepared from the reaction of **1b** with **2a** following typical procedure A. The product was obtained in 93% yield (152 mg, 0.38 mmol) as a pale yellow solid by flash column chromatography on silica gel (R_f = 0.29 in hexane/EtOAc = 2/1).

Mp = 214.2-216.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.67 (s, 3H), 6.69-6.73 (m, 2H), 6.86-6.93 (c, 5H), 6.99-7.03 (m, 2H), 7.10-7.21 (c, 5H), 7.24 (dd, *J* = 8.1 Hz, 0.6 Hz, 1H), 7.47-7.51 (m, 1H), 7.53-7.57 (m, 1H), 8.56 (dd, *J* = 7.9 Hz, 1.3 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 55.2, 113.8, 118.6, 125.4, 125.5, 126.7, 127.05, 127.10, 127.9, 128.2, 130.3, 130.9, 131.5, 132.1, 132.4, 134.8, 136.3, 137.5, 141.3, 158.4, 162.8, one signal is obscured by overlap with other signals. **IR** (ATR): 3058 w, 3024 w, 1656 s, 1247 s. **MS**: *m*/*z* (EI, relative intensity, %): 404 (32), 403 (100, M^+), 402 (64), 280 (10). **HRMS (DART)** Calcd for $C_{28}H_{22}NO_2$ ($[M+H]^+$): 404.16451. Found: 404.16333.

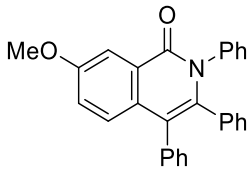
3,4-Diphenyl-2-(4-(trifluoromethyl)phenyl)isoquinolin-1(*2H*)-one (3ca) [CAS: 2151819-41-7]



3ca was prepared from the reaction of **1c** with **2a** following typical procedure A. The product was obtained in 78% yield (142 mg, 0.32 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.29 in hexane/EtOAc = 2/1) followed by flash column chromatography on NH_2-modified silica gel.

Mp = 228.0-229.6 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.86-6.93 (c, 5H), 7.12-7.31 (c, 8H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.52-7.56 (m, 1H), 7.59-7.63 (m, 1H), 8.56 (dd, *J* = 7.8 Hz, 0.9 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 119.3, 123.6 (q, *J* = 272 Hz), 125.3, 125.67 (q, *J* = 3.9 Hz), 125.75, 127.0, 127.1, 127.4, 127.6, 128.0, 128.2, 129.6 (q, *J* = 32.6 Hz) 130.1, 130.9, 131.5, 132.8, 134.2, 136.0, 137.6, 140.3, 142.7, 162.4. **^{19}F NMR** ($CDCl_3$) δ: -63.1 (s) **IR** (ATR): 3061 w, 3026 w, 1658 s, 1323 s. **MS**: *m*/*z* (EI, relative intensity, %): 442 (29), 441 (100, M^+), 440 (60), 248 (10), 145 (11). **HRMS (DART)** Calcd for $C_{28}H_{19}NOF_3$ ($[M+H]^+$): 442.14133. Found: 442.13913.

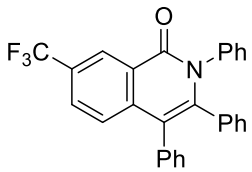
7-Methoxy-2,3,4-triphenylisoquinolin-1(*2H*)-one (3da)



3da was prepared from the reaction of **1d** or **5f** with **2a** following typical procedure A (**1d**) or typical procedure B (**5f**). The product was obtained as a white solid by flash column chromatography on silica gel (R_f = 0.06 in hexane/EtOAc = 5/1) in 87% yield (141 mg, 0.35 mmol) from **1d** or 75% yield (121 mg, 0.31 mmol) from **5d**.

Mp = 232.8-234.1 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.94 (s, 3H), 6.85-6.92 (c, 5H), 7.09-7.24 (c, 12H), 7.99 (t, *J* = 1.5 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 56.6, 108.0, 118.7, 122.8, 126.6, 126.8, 127.0, 127.1, 127.3, 127.5, 127.9, 128.5, 129.4, 131.2, 131.5, 131.6, 134.8, 136.5, 138.7, 139.6, 158.8, 162.2. **IR** (ATR): 3058 w, 1651 s. **MS**: *m*/*z* (EI, relative intensity, %): 404 (32), 403 (100, M^+), 402 (35), 388 (18), 77 (20). **Anal.** Calcd for $C_{28}H_{21}NO_2$: C, 83.35; H, 5.25; N, 3.47. Found: C, 83.04; H, 5.24; N, 3.50.

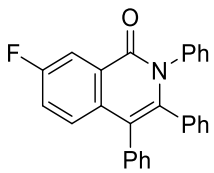
2,3,4-triphenyl-7-(trifluoromethyl)isoquinolin-1(*2H*)-one (3ea)



3ea was prepared from the reaction of **1e** with **2a** following typical procedure A (60 °C). The product was obtained in 87% yield (152 mg, 0.34 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.23 in hexane/EtOAc = 5/1).

Mp = 219.8-223.4 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.84-6.93 (c, 5H), 7.08-7.26 (c, 10H), 7.38 (d, *J* = 8.6 Hz, 1H), 7.76 (dd, *J* = 8.6 Hz, 1.6 Hz 1H), 8.83-8.85 (m, 1H). **^{13}C NMR** ($CDCl_3$) δ: 118.3, 123.9 (q, *J* = 272 Hz), 125.3, 125.9 (q, *J* = 4.2 Hz), 126.5, 127.2, 127.5, 127.9, 128.2, 128.5 (q, *J* = 3.5 Hz), 128.69 (q, *J* = 33.6 Hz), 128.73, 129.3, 130.7, 131.4, 134.2, 135.6, 138.9, 140.1, 143.4, 162.0, one signal is obscured by overlap with other signals. **^{19}F NMR** ($CDCl_3$) δ: -62.8 (s). **IR** (ATR): 3060 w, 1658 s, 1314 s. **MS**: *m*/*z* (EI, relative intensity, %): 442 (29), 441 (100, M^+), 440 (75), 180 (10), 77 (33). **HRMS (DART)** Calcd for $C_{28}H_{19}NOF_3$ ($[M+H]^+$): 442.14133. Found: 442.14097.

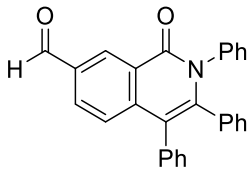
7-Fluoro-2,3,4-triphenylisoquinolin-1(*2H*)-one (3fa)



3fa was prepared from the reaction of **1f** with **2a** following typical procedure A (24 h). The product was obtained in 93% yield (141 mg, 0.36 mmol) as a pale yellow solid by flash column chromatography on silica gel (R_f = 0.49 in toluene/EtOAc = 10/1).

Mp = 227.4-229.4 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.88 (s, 5H), 7.09-7.31 (c, 12H), 8.20 (dd, *J* = 9.3 Hz, 2.2 Hz 1H). **^{13}C NMR** ($CDCl_3$) δ: 113.2 (d, *J* = 23.1 Hz), 118.3, 121.0 (d, *J* = 23.1 Hz), 127.0, 127.07, 127.12, 127.3, 127.6, 128.0, 128.2 (d, *J* = 7.7 Hz), 128.6, 129.3, 131.0, 131.4, 134.2 (d, *J* = 1.9 Hz), 134.4, 136.1, 139.2, 140.3 (d, *J* = 2.9 Hz), 161.5 (d, *J* = 249 Hz), 161.7 (d, *J* = 3.8 Hz). **^{19}F NMR** ($CDCl_3$) δ: -116.1 (m). **IR** (ATR): 3072 w, 3045 w, 1655 s. **MS**: *m*/*z* (EI, relative intensity, %): 392 (28), 391 (100, M^+), 390 (68), 180 (11), 77 (27). **HRMS (DART)** Calcd for $C_{27}H_{19}NOF$ ($[M+H]^+$): 392.14452. Found: 392.14342.

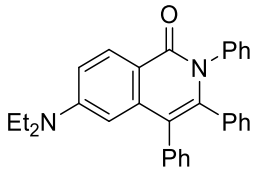
1-Oxo-2,3,4-triphenyl-1,2-dihydroisoquinoline-7-carbaldehyde (3ga)



3ga was prepared from the reaction of **1g** with **2a** following typical procedure A (60 °C). The product was obtained in 76% yield (121 mg, 0.30 mmol) as a yellow solid by flash column chromatography on silica gel (R_f = 0.31 in hexane/EtOAc = 2/1).

Mp could not be measured because the title compound was decomposed at 265 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.88-6.93 (c, 5H), 7.09-7.28 (c, 10H), 7.37 (d, *J* = 8.5 Hz, 1H), 8.07 (dd, *J* = 8.5 Hz, 1.7 Hz 1H), 8.99 (d, *J* = 1.7 Hz, 1H), 10.15 (s, 1H). **^{13}C NMR** ($CDCl_3$) δ: 118.7, 125.5, 126.6, 127.2, 127.6, 127.9, 128.2, 128.8, 129.3, 130.0, 130.6, 131.4, 133.5, 134.2, 134.5, 135.6, 138.9, 142.2, 144.6, 162.1, 191.3, one signal is obscured by overlap with other signals. **IR** (ATR): 3056 w, 1689 m, 1657 s. **MS**: *m*/*z* (EI, relative intensity, %): 402 (27), 401 (100, M^+), 400 (67), 77 (25). **HRMS (DART)** Calcd for $C_{28}H_{20}NO_2$ ($[M+H]^+$): 402.14886. Found: 402.14791.

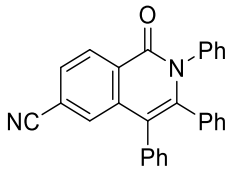
6-(Diethylamino)-2,3,4-triphenylisoquinolin-1(*2H*)-one (3ha)



3ha was prepared from the reaction of **1h** with **2a** following typical procedure A. The product was obtained in 97% yield (173 mg, 0.39 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.60 in hexane/EtOAc = 1/1).

Mp = 212.0-212.7 ºC. **^{1}H NMR** ($CDCl_3$) δ: 1.07 (t, *J* = 7.1 Hz, 6H), 3.28 (q, *J* = 7.1 Hz, 4H), 6.21 (d, *J* = 2.5 Hz, 1H), 6.83-6.92 (c, 6H), 7.05-7.22 (c, 10H), 8.36 (d, *J* = 8.9 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 12.3, 44.6, 104.7, 112.3, 114.4, 118.5, 126.5, 126.9, 127.1, 127.7, 128.3, 129.8, 130.0, 131.0, 131.6, 135.3, 137.1, 139.5, 139.8, 141.0, 150.5, 162.4, one signal is obscured by overlap with other signals. **IR** (ATR): 3059 w, 3026 w, 1636 s. **MS**: *m*/*z* (EI, relative intensity, %): 445 (22), 444 (63, M^+), 443 (10), 430 (34), 429 (100), 399 (21), 222 (11), 77 (12). **HRMS (DART)** Calcd for $C_{31}H_{29}N_2O$ ($[M+H]^+$): 445.22774. Found: 445.22615.

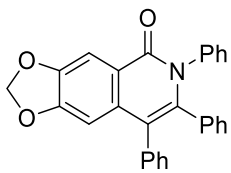
1-Oxo-2,3,4-triphenyl-1,2-dihydroisoquinoline-6-carbonitrile (3ia)



3ia was prepared from the reaction of **1i** with **2a** following typical procedure A (80 °C). The product was obtained in 52% yield (87 mg, 0.22 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.34 in hexane/EtOAc = 2/1).

Mp = 267.2-269.3 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.83-6.98 (c, 5H), 7.06-7.32 (c, 10H), 7.59 (d, *J* = 1.2 Hz, 1H), 7.68 (dd, *J* = 8.3 Hz, 1.2 Hz, 1H), 8.63 (d, *J* = 8.3 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 116.0, 117.8, 118.2, 127.2, 127.5, 127.6, 127.8, 127.9, 128.36, 128.42, 128.7, 129.1, 129.4, 130.4, 130.6, 131.3, 133.9, 134.9, 137.8, 138.8, 143.2, 161.5. **IR** (ATR): 3062 w, 3032 w, 2226 w, 1662 s. **MS**: *m*/*z* (EI, relative intensity, %): 399 (29), 398 (100, M^+), 397 (75), 77 (31). **HRMS (DART)** Calcd for $C_{28}H_{19}N_2O$ ($[M+H]^+$): 399.14919. Found: 399.14847.

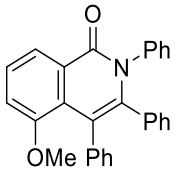
6,7,8-triphenyl-[1,3]dioxolo[4,5-*g*]isoquinolin-5(*6H*)-one (3ja)



3ja was prepared from the reaction of **1j** with **2a** following typical procedure A. The product was obtained in 82% yield (138 mg, 0.33 mmol) as a pale yellow solid by flash column chromatography on silica gel (R_f = 0.20 in hexane/EtOAc = 2/1).

Mp = 271.8-275.2 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.04 (s, 2H), 6.60 (s, 1H), 6.86-6.88 (c, 5H), 7.08-7.23 (c, 10H), 7.92 (s, 1H). **^{13}C NMR** ($CDCl_3$) δ: 101.7, 103.8, 106.0, 118.6, 121.0, 126.8, 127.0, 127.1, 127.4, 128.0, 128.5, 129.4, 131.0, 131.4, 134.7, 135.0, 136.5, 139.5, 139.8, 147.7, 152.0, 161.7. **IR** (ATR): 3058 w, 3023 w, 1647 s. **MS**: *m*/*z* (EI, relative intensity, %): 418 (19), 417 (100, M^+), 416 (65), 180 (12), 77 (25). **HRMS (DART)** Calcd for $C_{28}H_{20}NO_3$ ($[M+H]^+$): 418.14377. Found: 418.14353.

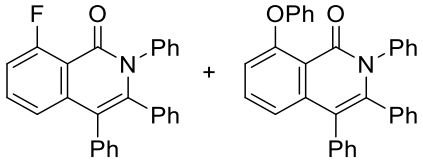
5-Methoxy-2,3,4-triphenylisoquinolin-1(*2H*)-one (3ka)



3ka was prepared from the reaction of **1k** with **2a** following typical procedure A (80 °C). The product was obtained in 54% yield (86 mg, 0.21 mmol) as a pale yellow solid by flash column chromatography on silica gel (R_f = 0.20 in hexane/EtOAc = 2/1).

Mp = 232.2-234.3 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.34 (s, 3H), 6.81-6.88 (c, 5H), 6.97-7.14 (c, 9H), 7.17-7.21 (m, 2H), 7.49 (t, *J* = 8.0 Hz, 1H), 8.24 (dd, *J* = 8.0 Hz, 1.3 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 55.9, 115.0, 116.6, 120.7, 125.3, 126.4, 126.7, 126.8, 127.38, 127.44, 127.5, 127.6, 128.5, 129.4, 130.6, 131.2, 134.8, 139.5, 140.3, 141.1, 156.2, 162.2. **IR** (ATR): 3058 w, 3026 w, 1650 s, 1268 m. **MS**: *m*/*z* (EI, relative intensity, %): 404 (19), 403 (100, M^+), 402 (21), 180 (15), 77 (25). **HRMS (DART)** Calcd for $C_{28}H_{22}NO_2$ ($[M+H]^+$): 404.16451. Found: 404.16296.

8-Fluoro-2,3,4-triphenylisoquinolin-1(*2H*)-one (3la), 8-phenoxy-2,3,4-triphenylisoquinolin-1(*2H*)-one (3la')



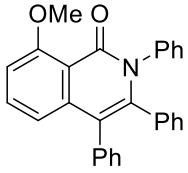
3la **3la'**

99% NMR yield (**3la**/**3la'** = 1/6)

3la and **3la'** were prepared from the reaction of **1l** with **2a** following typical procedure A (80 °C). The products were obtained as a pale yellow solid (180 mg) by flash column chromatography on silica gel (R_f = 0.06 in hexane/EtOAc = 5/1). The product yield and the ratio of products were determined by ^{1}H NMR using 1,1,2,2- tetrachloroethane as an internal standard after flash column chromatography on silica gel.

^{1}H NMR ($CDCl_3$) δ: 6.85-6.92 (c), 6.94-6.99 (m), 7.03-7.25 (c), 7.28-7.34 (m), 7.44 (t, *J* = 8.1 Hz, 1H, **3la'**), 7.49 (td, *J* = 8.2 Hz, 5.0 Hz, 1H, **3la**). **^{13}C NMR** ($CDCl_3$) for **3la'** δ: 117.6, 117.7, 117.9, 118.7, 121.1, 122.8, 126.8, 127.0, 127.14, 127.3, 127.99, 128.4, 129.5, 129.8, 130.8, 131.7, 132.8, 134.7, 136.7, 139.4, 140.7, 142.0, 157.6, 158.1, 160.3. Some peaks of **3la** are overlapped with **3la'**. Selected ^{13}C NMR peaks of **3la** are shown. δ: 127.09, 127.6, 128.03, 128.5, 129.6, 131.5. **^{19}F NMR** ($CDCl_3$) for **3la** δ: -110.2 (dd, *J* = 11.3 Hz, 4.7 Hz). **HRMS (DART)** Calcd for $C_{33}H_{24}NO_2$ (**3la'**, $[M+H]^+$): 466.18016. Found: 466.18129. Calcd for $C_{27}H_{19}NOF$ (**3la**, $[M+H]^+$): 392.14452. Found: 392.14526.

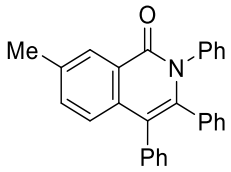
8-Methoxy-2,3,4-triphenylisoquinolin-1(2*H*)-one (3ma)



3ma was prepared from the reaction of **1m** with **2a** following typical procedure A (80 °C). The product was obtained in 75% yield (120 mg, 0.30 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.26 in hexane/EtOAc = 1/2).

Mp = 243.8-245.8 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.99 (s, 3H), 6.78 (d, *J* = 7.9 Hz, 1H), 6.87 (s, 5H), 6.94 (d, *J* = 7.9 Hz, 1H), 7.06-7.23 (c, 10H), 7.46 (t, *J* = 7.9 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 56.1, 108.4, 115.0, 117.8, 117.9, 126.6, 126.9, 127.0, 127.1, 127.8, 128.2, 129.7, 130.7, 131.6, 132.9, 134.8, 136.9, 139.6, 140.7, 141.8, 161.0, 161.3. **IR** (ATR): 3061 w, 1659 s, 1264 m. **MS**: *m*/*z* (EI, relative intensity, %): 404 (29), 403 (100, M^+), 402 (43), 387 (10), 386 (32), 375 (15), 374 (57), 372 (11), 357 (14), 180 (14), 77 (38). **HRMS (DART)** Calcd for $C_{28}H_{22}NO_2$ ($[M+H]^+$): 404.16451. Found: 404.16383.

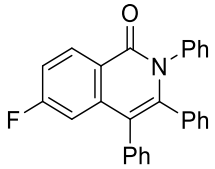
7-Methyl-2,3,4-triphenylisoquinolin-1(2*H*)-one (3na) [CAS: 1253388-60-1]



3na was prepared from the reaction of **5g** with **2a** following typical procedure B. The product was obtained in 90% yield (138 mg, 0.36 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.14 in hexane/EtOAc = 5/1).

Mp = 213.3-214.5 ºC. **^{1}H NMR** ($CDCl_3$) δ: 2.49 (s, 3H), 6.83-6.91 (c, 5H), 7.09-7.23 (c, 11H), 7.39 (dd, *J* = 8.5 Hz, 1.8 Hz, 1H), 8.37 (s, 1H). **^{13}C NMR** ($CDCl_3$) δ: 21.3, 118.7, 125.3, 125.5, 126.7, 126.96, 127.04, 127.4, 127.7, 127.8, 128.5, 129.4, 131.0, 131.5, 133.9, 134.8, 135.2, 136.5, 136.9, 139.5, 140.0, 162.5. **IR** (ATR): 3059 w, 3025 w, 1657 s. **MS**: *m*/*z* (EI, relative intensity, %): 388 (31), 387 (100, M^+), 386 (59), 180 (11), 77 (30). **HRMS (DART)** Calcd for $C_{28}H_{22}NO$ ($[M+H]^+$): 388.16959. Found: 388.16859.

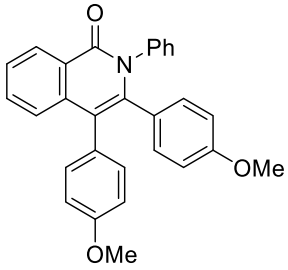
6-Fluoro-2,3,4-triphenylisoquinolin-1(2*H*)-one (3oa)



3oa was prepared from the reaction of **5h** with **2a** following typical procedure B (120 °C). The product was obtained in 75% yield (123 mg, 0.31 mmol) as a pale yellow solid by flash column chromatography on silica gel (R_f = 0.14 in hexane/EtOAc = 5/1).

Mp = 225.2-227.1 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.85-6.92 (c, 6H), 7.06-7.25 (c, 11H), 8.57 (dd, *J* = 8.9 Hz, 5.9 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 110.8 (d, *J* = 23.3 Hz), 115.5 (d, *J* = 23.3 Hz), 118.3 (d, *J* = 3.1 Hz), 122.1 (d, *J* = 1.2 Hz), 127.1, 127.2, 127.4, 127.7, 128.2, 128.6, 129.4, 130.8, 131.5 (d, *J* = 9.9 Hz), 134.5, 135.8, 139.2, 140.2 (d, *J* = 10.1 Hz), 142.4, 162.0, 165.5 (d, *J* = 252 Hz). **^{19}F NMR** ($CDCl_3$) δ: -105.8 (m). **IR** (ATR): 3060 w, 1657 s, 1327 s. **MS**: *m*/*z* (EI, relative intensity, %): 392 (27), 391 (100, M^+), 390 (83), 77 (28). **HRMS (DART)** Calcd for $C_{27}H_{19}NOF$ ($[M+H]^+$): 392.14452. Found: 392.14514.

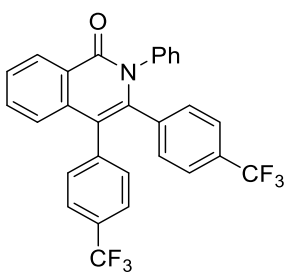
3,4-Bis(4-methoxyphenyl)-2-phenylisoquinolin-1(2*H*)-one (3ab) [CAS: 1266570-07-3]



3aa was prepared from the reaction of **1a** or **5d** with **2b** following typical procedure A (**1a**, DMF was used instead of DMSO.) or typical procedure B (**5d**). The product was obtained as a yellow solid by flash column chromatography on silica gel (R_f = 0.23 in hexane/EtOAc = 2/1) in 92% yield (159 mg, 0.37 mmol) from **1a** or 70% yield (120 mg, 0.28 mmol) from **5d**.

Mp = 246.5-247.6 ºC. **^{1}H NMR** ($CDCl_3$) δ: 3.61 (s, 3H), 3.77 (s, 3H), 6.42-6.45 (m, 2H), 6.76-6.80 (c, 4H), 7.02-7.06 (m, 2H), 7.08-7.10 (c, 2H), 7.13-7.17 (m, 1H), 7.21-7.25 (c, 2H), 7.27-7.29 (m, 1H), 7.49-7.53 (m, 1H), 7.56-7.60 (m, 1H), 8.54-8.56 (m, 1H). **^{13}C NMR** ($CDCl_3$) δ: 54.9, 55.1, 112.5, 113.4, 118.6, 125.4, 125.5, 126.7, 127.3, 127.4, 128.2, 128.6, 128.7, 129.4, 132.2, 132.4, 132.6, 138.0, 139.6, 141.0, 158.11, 158.15, 162.7. **IR** (ATR): 3064 w, 3036 w, 1652 s, 1243 s. **MS**: *m*/*z* (EI, relative intensity, %): 434 (32), 433 (100, M^+), 432 (38), 418 (10), 165 (13), 77 (13). **HRMS (DART)** Calcd for $C_{29}H_{24}NO_3$ ($[M+H]^+$): 434.17507. Found: 434.17370.

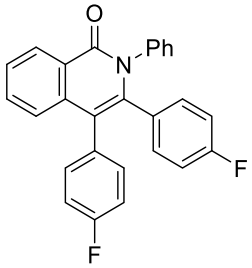
2-phenyl-3,4-bis(4-(trifluoromethyl)phenyl)isoquinolin-1(2*H*)-one (3ac)



3aa was prepared from the reaction of **1a** or **5d** with **2c** following typical procedure A (**1a**, 80 °C) or typical procedure B (**5d**). The product was obtained as a white solid by flash column chromatography on silica gel (R_f = 0.14 in hexane/EtOAc = 5/1) in 78% yield (157 mg, 0.31 mmol) from **1a** or 75% yield (154 mg, 0.30 mmol) from **5d**.

Mp = 228.2-229.9 ºC. **^{1}H NMR** ($CDCl_3$) δ: 7.03 (d, *J* = 8.0 Hz, 2H), 7.08-7.10 (m, 2H), 7.14-7.30 (c, 8H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.56-7.60 (m, 1H), 7.61-7.65 (m, 1H), 8.57-8.60 (m, 1H). **^{13}C NMR** ($CDCl_3$) δ: 117.9, 123.4 (q, *J* = 272 Hz), 123.9 (q, *J* = 272 Hz), 124.3 (q, *J* = 3.5 Hz), 125.2 (q, *J* = 3.5 Hz), 125.3, 125.7, 127.6, 128.1, 128.5, 128.9, 129.3, 129.5 (q, *J* = 32.6 Hz), 129.6 (q, *J* = 32.6 Hz), 131.3, 131.9, 133.0, 136.7, 137.9, 138.8, 139.77, 139.80, 162.3. **^{19}F NMR** ($CDCl_3$) δ: -63.5 (s), -63.1 (s). **IR** (ATR): 3067 w, 1658 s, 1323 s. **MS**: *m*/*z* (EI, relative intensity, %): 510 (33), 509 (100, M^+), 508 (83), 244 (15), 77 (47). **HRMS (DART)** Calcd for $C_{29}H_{18}NOF_6$ ($[M+H]^+$): 510.12871. Found: 510.12885.

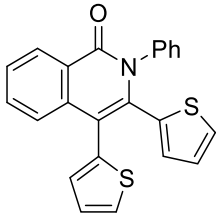
3,4-Bis(4-fluorophenyl)-2-phenylisoquinolin-1(2*H*)-one (3ad)



3ad was prepared from the reaction of **1a** or **5d** with **2d** following typical procedure A (**1a**, 24 h) or typical procedure B (**5d**). The product was obtained as a white solid by flash column chromatography on silica gel (R_f = 0.06 in hexane/EtOAc = 5/1) in 81% yield (135 mg, 0.33 mmol) from **1a** or 78% yield (129 mg, 0.32 mmol) from **5d**

Mp = 250.1-251.0 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.59-6.66 (m, 2H), 6.83-6.88 (m, 2H), 6.90-6.96 (m, 2H), 7.06-7.12 (c, 4H), 7.14-7.20 (m, 1H), 7.20-7.27 (c, 3H), 7.51-7.57 (m, 1H), 7.59-7.64 (m, 1H), 8.54-8.59 (m, 1H). **^{13}C NMR** ($CDCl_3$) δ: 114.5 (d, *J* = 21.7 Hz), 115.2 (d, *J* = 21.4 Hz), 118.1, 125.4, 125.6, 127.2, 127.8, 128.4, 128.8, 129.4, 130.7 (d, *J* = 3.7 Hz), 132.1 (d, *J* = 3.6 Hz), 132.67 (d, *J* = 8.3 Hz), 132.70, 133.1 (d, *J* = 8.1 Hz), 137.4, 139.3, 140.3, 161.4 (d, *J* = 249 Hz), 161.7 (d, *J* = 247 Hz), 162.5. **^{19}F NMR** ($CDCl_3$) δ: -115.2 (tt, *J* = 8.9 Hz, 4.6 Hz), -113.5 (tt, *J* = 9.2 Hz, 4.6 Hz). **IR** (ATR): 3069 w, 3043 w, 1653 s, 1221 s. **MS**: *m*/*z* (EI, relative intensity, %): 410 (28), 409 (100, M^+), 408 (81), 77 (26). **HRMS (DART)** Calcd for $C_{27}H_{18}NOF_2$ ($[M+H]^+$): 410.13510. Found: 410.13484.

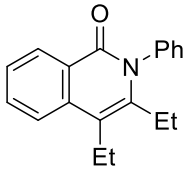
2-Phenyl-3,4-di(thiophen-2-yl)isoquinolin-1(2*H*)-one (3ae)



3ae was prepared from the reaction of **1a** or **5d** with **2e** following typical procedure A (**1a**, 60 °C) or typical procedure B (**5d**, 22 h). The product was obtained as a black solid by flash column chromatography on silica gel (R_f = 0.14 in hexane/EtOAc = 5/1) in 74% yield (113 mg, 0.29 mmol) from **1a.** The product was obtained in 48% yield (74 mg, 0.19 mmol) from **5d** by flash column chromatography on silica gel followed by GPC.

Mp = 243.7-245.1 ºC. **^{1}H NMR** ($CDCl_3$) δ: 6.58-6.62 (c, 2H), 6.93 (dd, *J* = 3.4 Hz, 1.1 Hz, 1H), 6.97 (dd, *J* = 5.1 Hz, 3.4 Hz, 1H), 7.06 (dd, *J* = 4.6 Hz, 1.6 Hz, 1H), 7.17-7.19 (c, 2H), 7.21-7.32 (c, 4H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.54-7.58 (m, 1H), 7.63-7.67 (m, 1H), 8.53 (dd, *J* = 7.9 Hz, 0.8 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 113.9, 125.6, 125.7, 126.56, 126.63, 127.6, 127.8, 127.9, 128.2, 128.7, 129.2, 129.8, 131.2, 132.8, 134.9, 136.2, 137.0, 137.5, 139.3, 162.5, one signal is obscured by overlap with other signals. **IR** (ATR): 3069 w, 1658 s. **MS**: *m*/*z* (EI, relative intensity, %): 387 (13), 386 (29), 385 (100, M^+), 384 (27), 352 (16), 326 (11), 282 (17), 253 (11), 77 (28). **HRMS (DART)** Calcd for $C_{23}H_{16}NOS_2$ ($[M+H]^+$): 386.06678. Found: 386.06574.

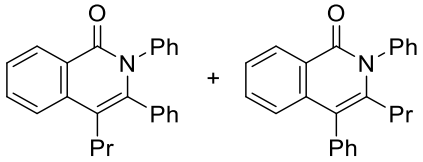
3,4-Diethyl-2-phenylisoquinolin-1(2*H*)-one (3af)



3af was prepared from the reaction of **1a, 1q, 1r** or **5d** with **2e** following typical procedure A (**1a** (60 °C), **1q**, **1r** (60 °C)) or typical procedure B (**5d**, 22 h). The product was obtained as a white solid by flash column chromatography on silica gel (R_f = 0.11 in hexane/EtOAc = 5/1) in 79% yield (89 mg, 0.32 mmol) from **1a**, 80% yield (92 mg, 0.33 mmol) from **1q** or 84% yield (93 mg, 0.34 mmol) from **5d.** The product was obtained in 27% yield (30 mg, 0.11 mmol) from **1r** as a pale yellow solid by flash column chromatography on silica gel followed by GPC.

Mp = 84.5-87.2 ºC. **^{1}H NMR** ($CDCl_3$) δ: 0.99 (t, *J* = 7.5 Hz, 3H), 1.29 (t, *J* = 7.5 Hz, 3H), 2.45 (q, *J* = 7.5 Hz, 2H), 2.82 (q, *J* = 7.5 Hz, 2H), 7.26-7.28 (m, 2H), 7.43-7.48 (m, 2H), 7.49-7.57 (c, 2H), 7.68-7.75 (c, 2H), 8.46 (dd, *J* = 7.9 Hz, 0.8 Hz, 1H). **^{13}C NMR** ($CDCl_3$) δ: 13.8, 14.7, 20.4, 23.1, 114.6, 122.6, 125.3, 125.7, 128.3, 128.5, 128.9, 129.3, 132.4, 136.8, 139.5, 140.9, 163.0. **IR** (ATR): 3064 w, 1651 s. **MS**: *m/z* (EI, relative intensity, %): 278 (16), 277 (69, M^+), 263 (21), 262 (100), 233 (13), 86 (14), 84 (21), 77 (22). **HRMS (DART)** Calcd for $C_{19}H_{20}NO$ ($[M+H]^+$): 278.15394. Found: 278.15341.

2,3-Diphenyl-4-propylisoquinolin-1(2*H*)-one (3ag) [CAS: 1253388-64-5]
2,4-Diphenyl-3-propylisoquinolin-1(2*H*)-one (3ag') [CAS: 1253388-65-6][9]



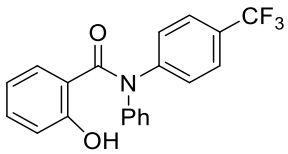
3ag **3ag'**

3ag : **3ag'** = 16 : 1

3ag and **3ag'** were prepared from the reaction of **1a** with **2g** following typical procedure A (60 °C). The products were obtained in 80% yield (109 mg, 0.32 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.11 in hexane/EtOAc = 5/1).

^{1}H NMR ($CDCl_3$) for **3ag** δ: 0.83 (t, *J* = 7.3 Hz, 3H), 1.51-1.61 (m, 2H), 2.42-2.46 (m, 2H), 6.98-7.21 (c, 10H), 7.51-7.58 (m, 1H), 7.73-7.78 (c, 2H), 8.56 (d, *J* = 7.8 Hz, 1H). Some peaks of **3ag'** are overlapped with **3ag**. Selected ^{1}H NMR peaks of **3ag'** are shown. δ: 0.40 (t, *J* = 7.3 Hz, 3H), 1.21-1.28 (m, 2H), 2.11-2.15 (m, 2H), 8.45 (d, *J* = 8.0 Hz, 1H). **^{13}C NMR** ($CDCl_3$) for **3ag** δ: 14.3, 23.7, 30.6, 115.3, 123.5, 126.1, 126.6, 127.4, 127.7, 127.8, 128.5, 128.7, 129.5, 130.4, 132.5, 135.1, 136.8, 139.7, 140.3, 162.4. **Anal.** Calcd for $C_{24}H_{21}NO$: C, 84.92; H, 6.24; N, 4.13. Found: C, 84.57; H, 6.14; N, 4.14.

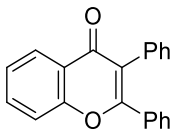
2-Hydroxy-*N*-phenyl-*N*-(4-(trifluoromethyl)phenyl)benzamide (4p)



4p was prepared from the reaction of **4p** with **2a** following typical procedure A (30 min). The product was obtained in 64% yield (91 mg, 0.25 mmol) as a yellow oil by flash column chromatography on silica gel (R_f = 0.29 in hexane/EtOAc = 5/1) followed by flash column chromatography on NH_2-modified silica gel (R_f = 0.43 in EtOAc only).

^{1}H NMR ($CDCl_3$) δ: 6.47-6.51 (m, 1H), 6.94 (dd, *J* = 8.1 Hz, 1.5 Hz, 1H), 6.97 (dd, *J* = 8.5 Hz, 0.9 Hz, 1H), 7.12-7.15 (m, 2H), 7.22-7.31 (c, 4H), 7.34-7.38 (m, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 10.51 (br, 1H). **^{13}C NMR** ($CDCl_3$) δ: 115.7, 118.21, 118.22, 123.7 (q, *J* = 272 Hz), 126.4 (q, *J* = 3.6 Hz), 127.1, 127.4, 127.5, 128.5 (q, *J* = 32.9 Hz), 129.8, 130.6, 133.9, 143.4, 146.9, 161.4, 172.7. **^{19}F NMR** ($CDCl_3$) δ: -62.9. **HRMS (DART)** Calcd for $C_{20}H_{15}NO_2F_3$ ($[M+H]^+$): 358.10494. Found: 358.10490.

2,3-Diphenyl-4*H*-chromen-4-one (6aa) [CAS: 6005-12-5][10]

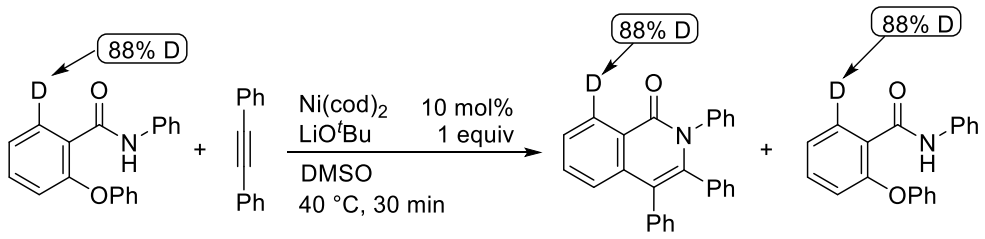


6aa was prepared from the reaction of **5c** with **2a** following typical procedure A (0.2 mmol, 80 °C, 3 h, KO^{t}Bu was used instead of LiO^{t}Bu.). The product was obtained in 11% yield (7 mg, 0.023 mmol) as a white solid by flash column chromatography on silica gel (R_f = 0.26 in hexane/EtOAc = 5/1).

^{1}H NMR ($CDCl_3$) δ: 7.21-7.24 (c, 2H), 7.27-7.37 (c, 6H), 7.40-7.46 (c, 3H), 7.54-7.56 (m, 1H), 7.69-7.74 (m, 1H), 8.29-8.32 (m, 1H).

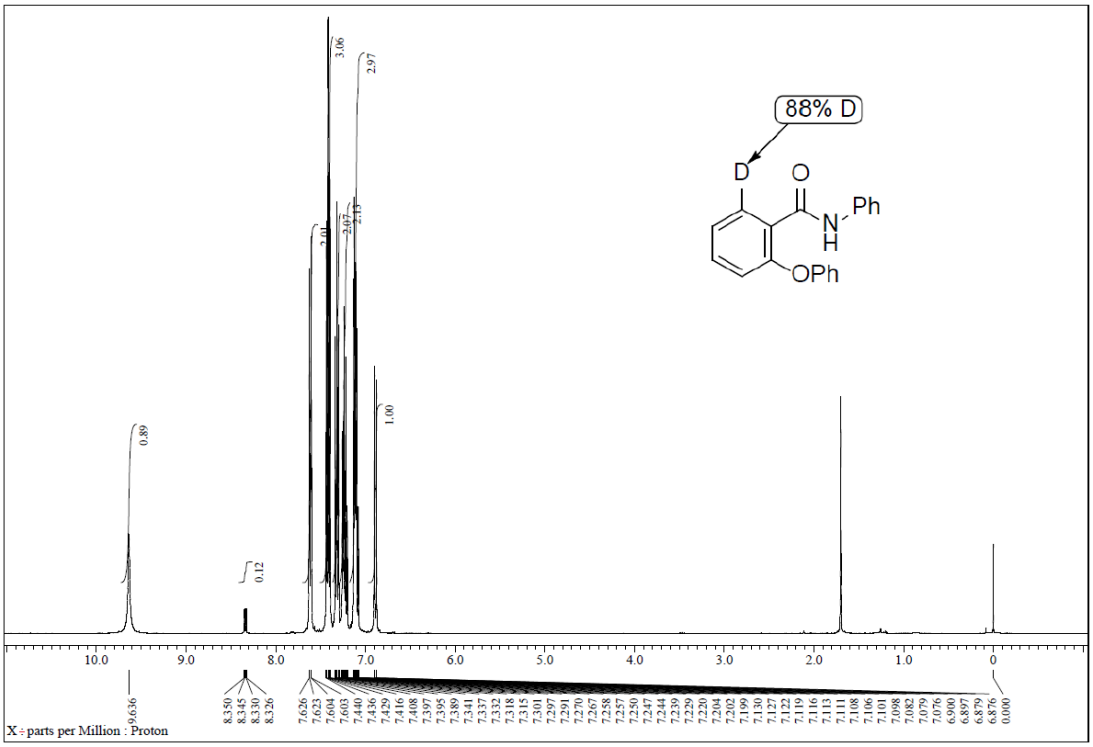
Mechanistic Studies

Labeling experiment (Scheme 5b).

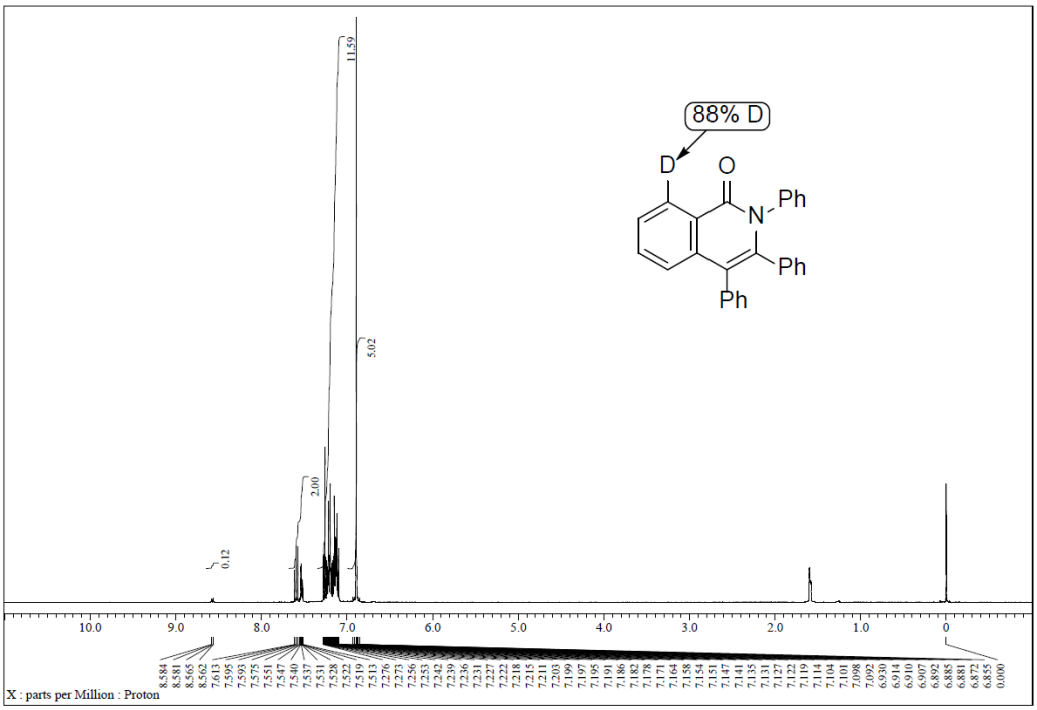


1a-*d* **2a** **3aa** 38% **1a-*d*** 50%

Compound **1a-*d*** was subjected to the typical procedure (30 min.). The resulting mixture was purified by flash column chromatography on silica gel (eluent: hexane/EtOAc = 10/1 to 5/1) to afford **3aa** (R_f = 0.31 in hexane/EtOAc = 5/1) as a white solid (56 mg, 0.15 mmol, 38%) and **1a-*d*** (R_f = 0.17 in hexane/EtOAc = 2/1) as a white solid (57 mg, 0.20 mmol, 50%).



^{1}H NMR spectrum of **1a-*d***



^{1}H NMR spectrum of **3aa**

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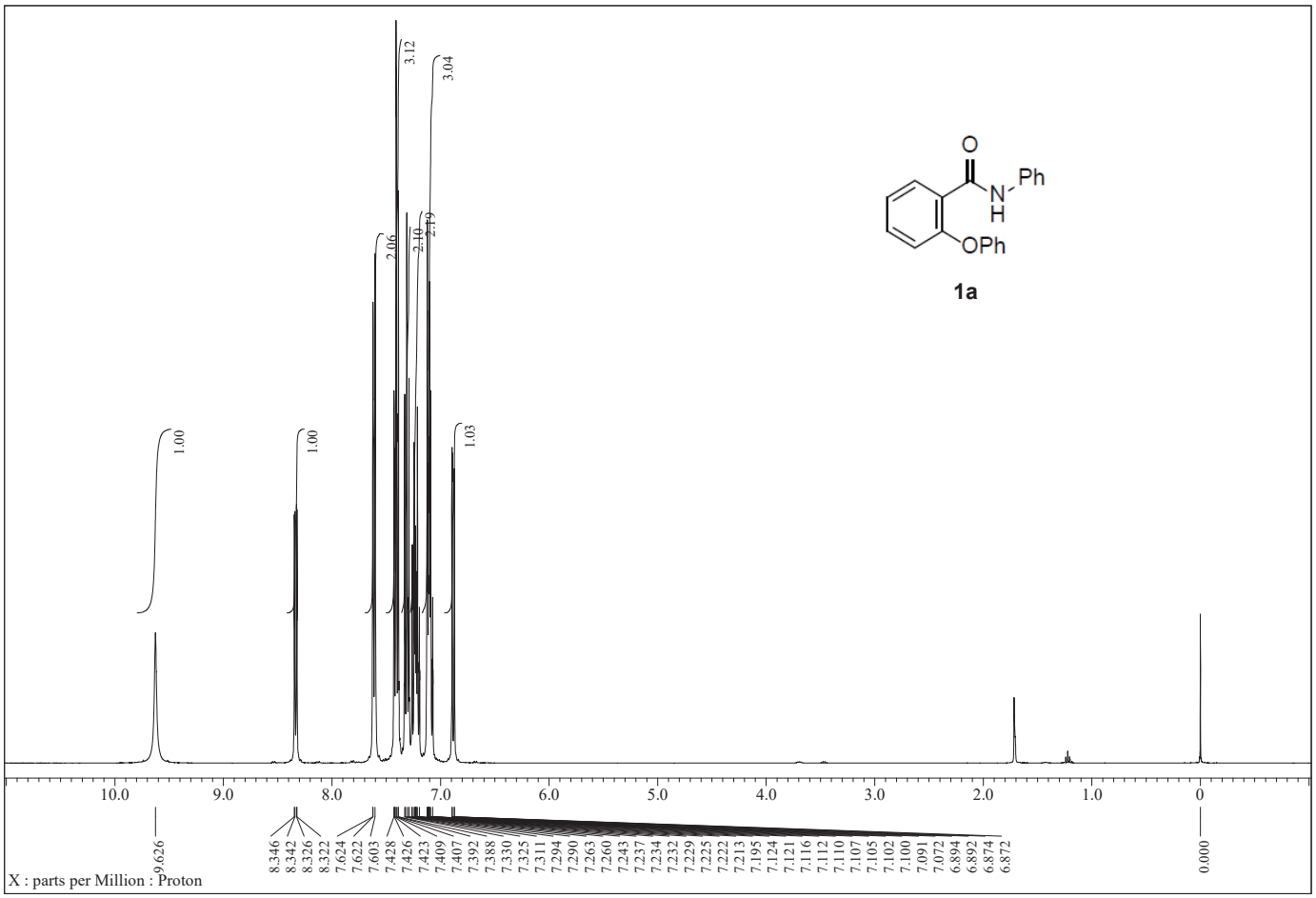
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7.0
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7.232
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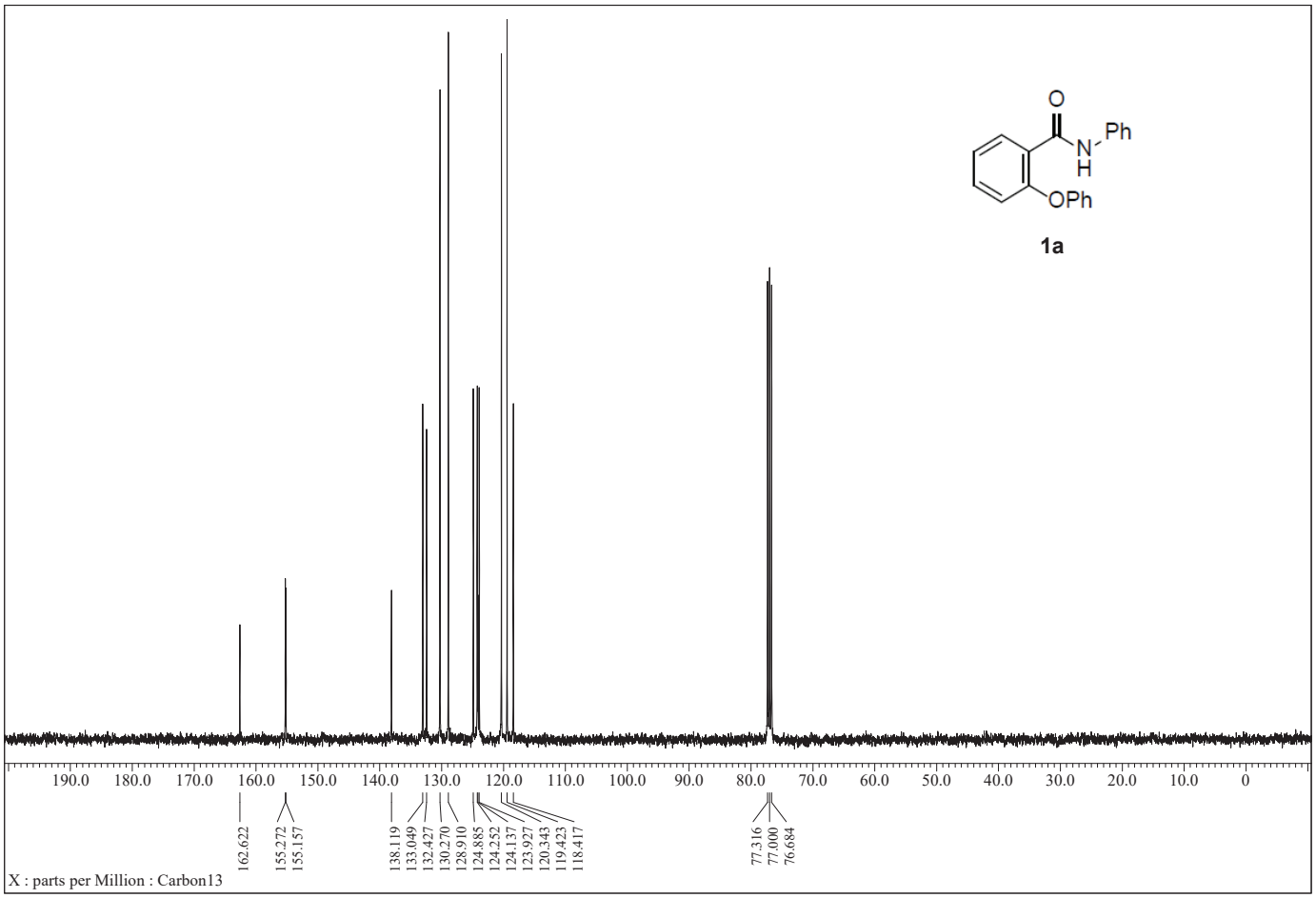
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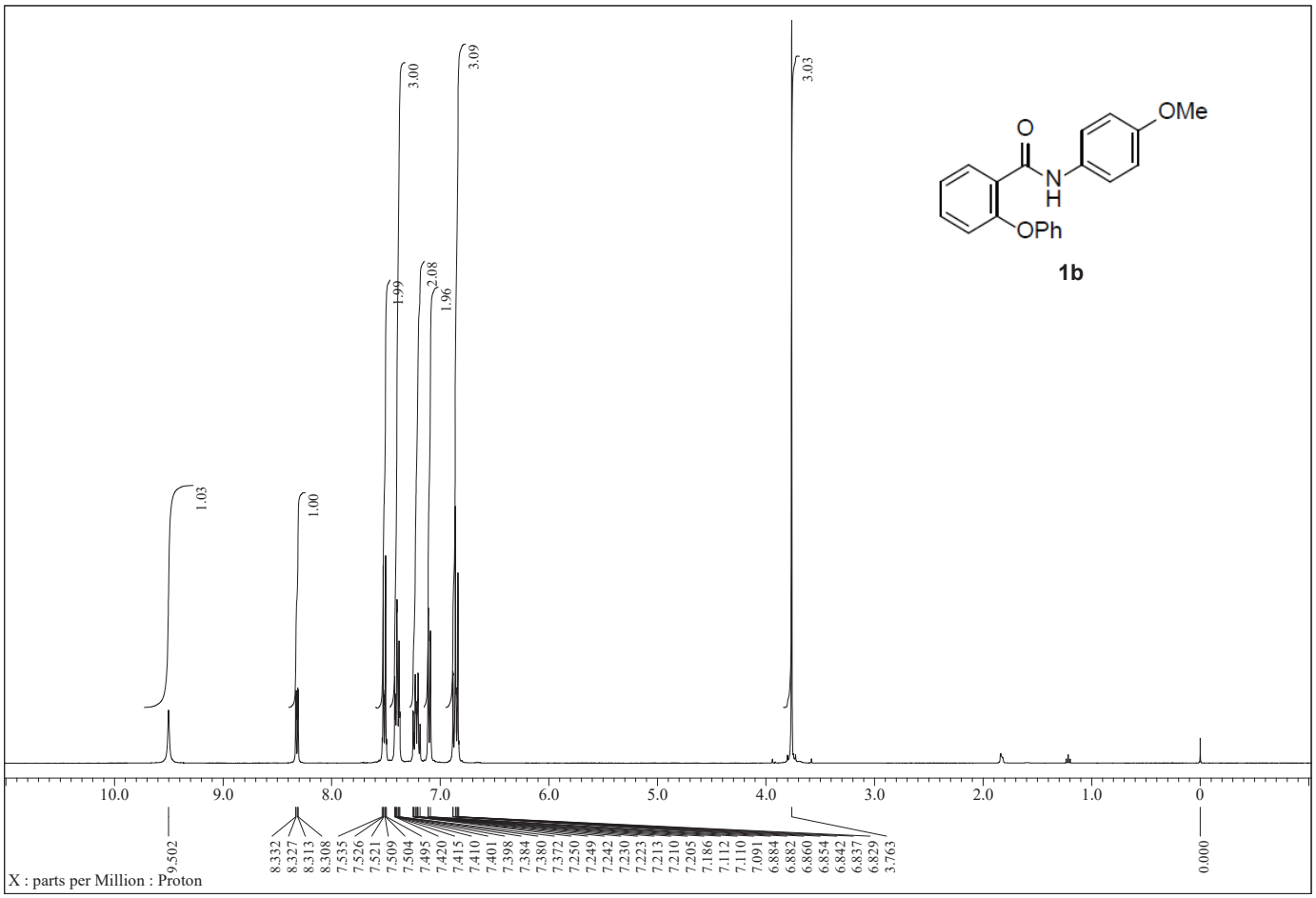
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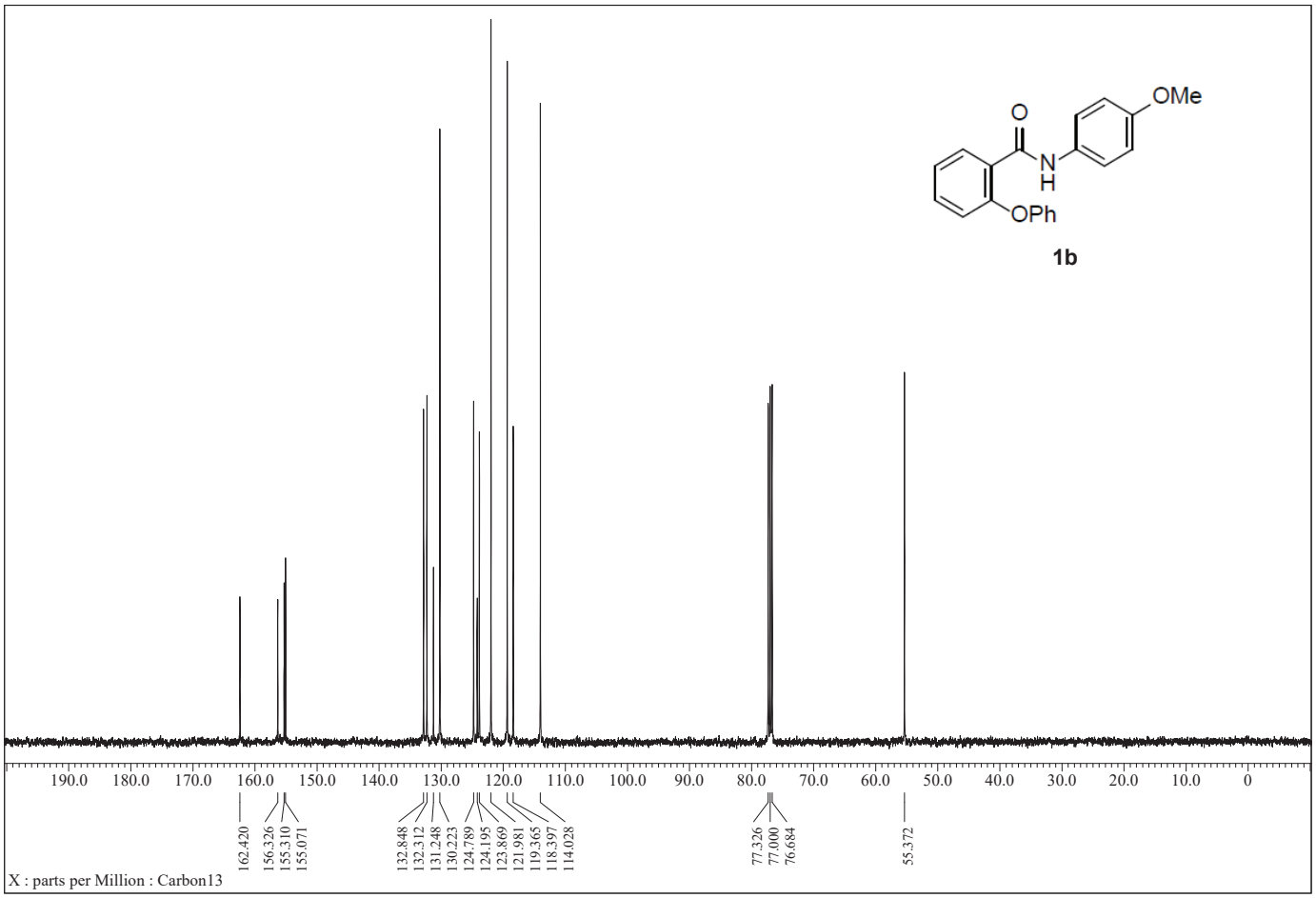
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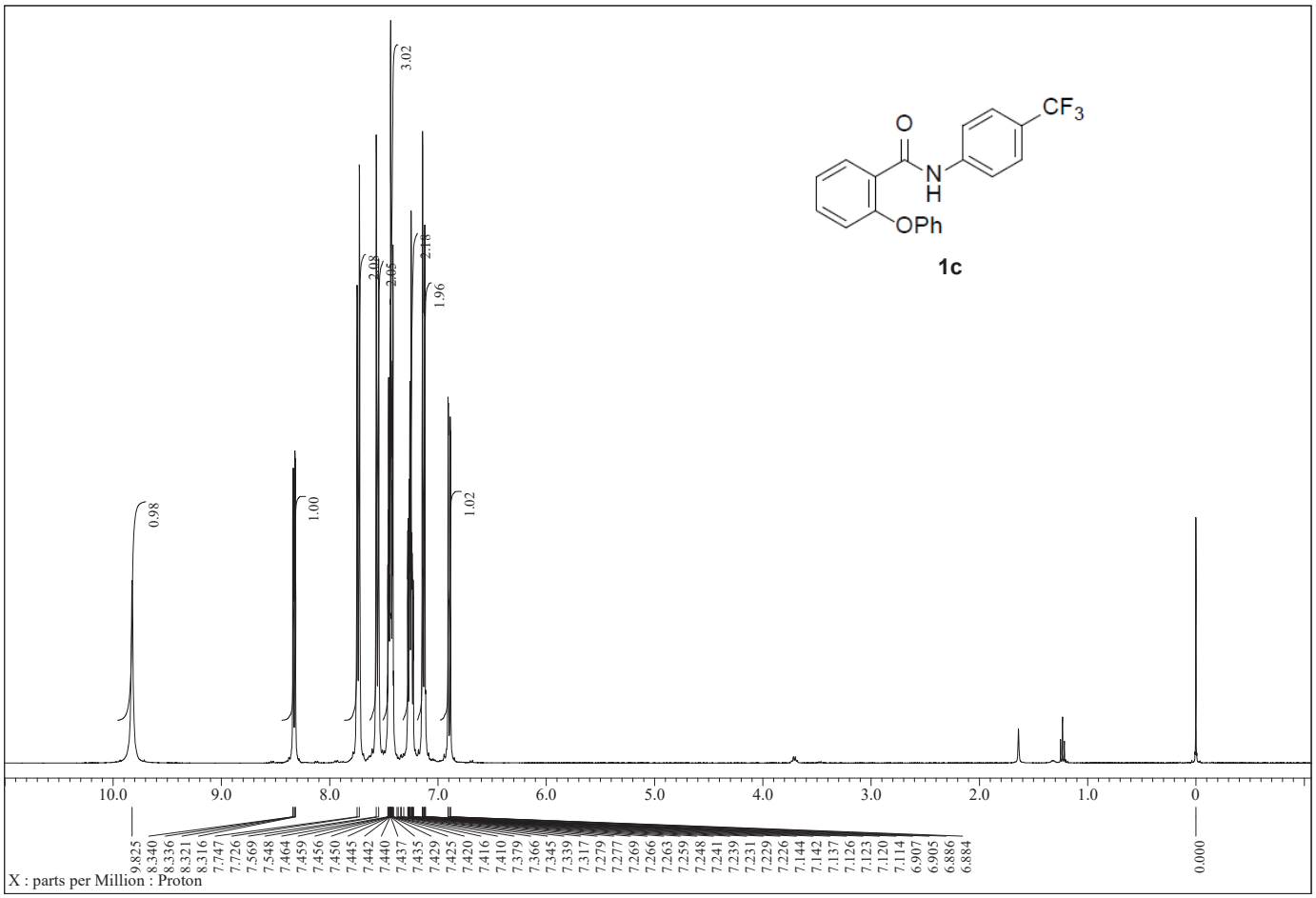
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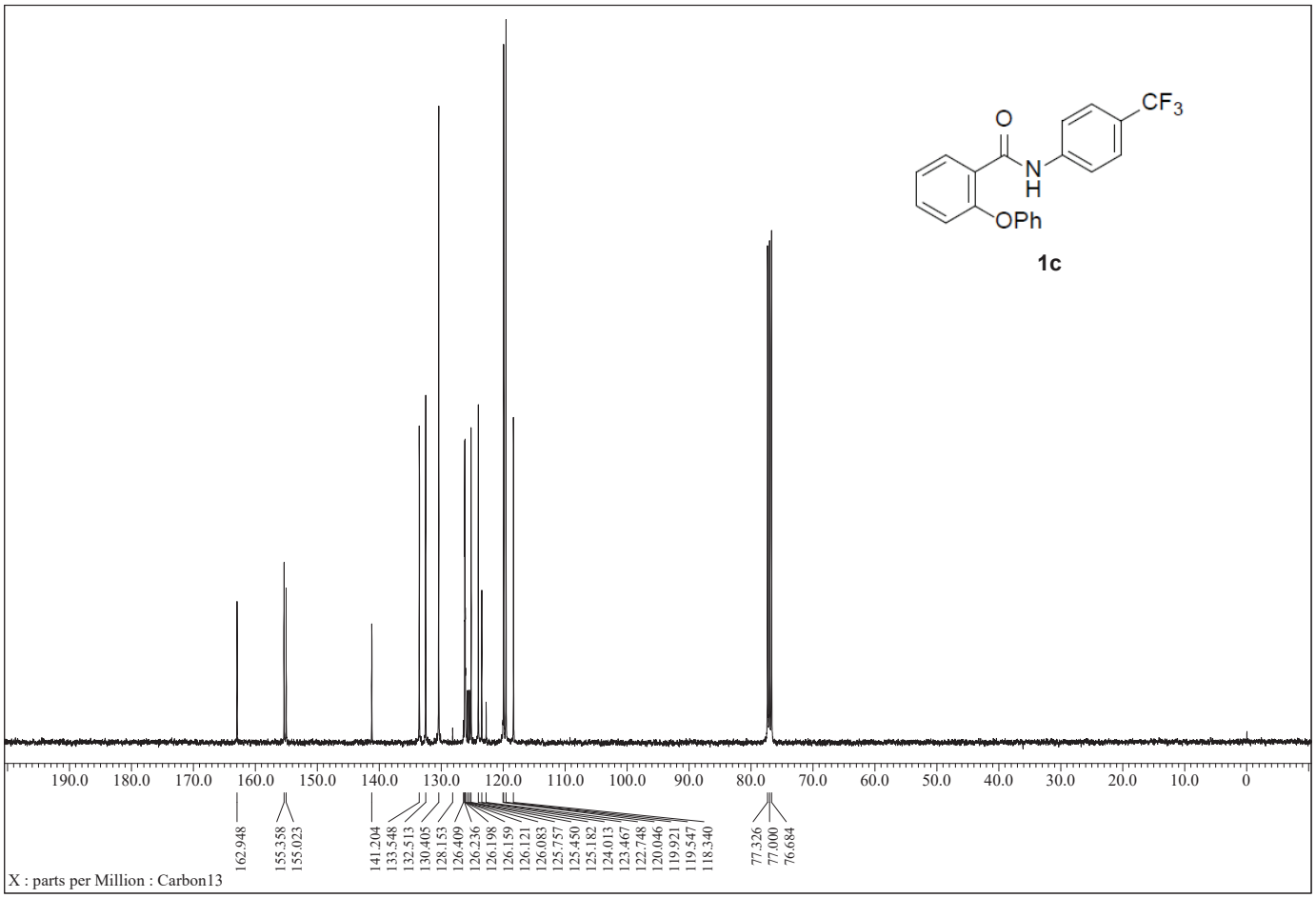
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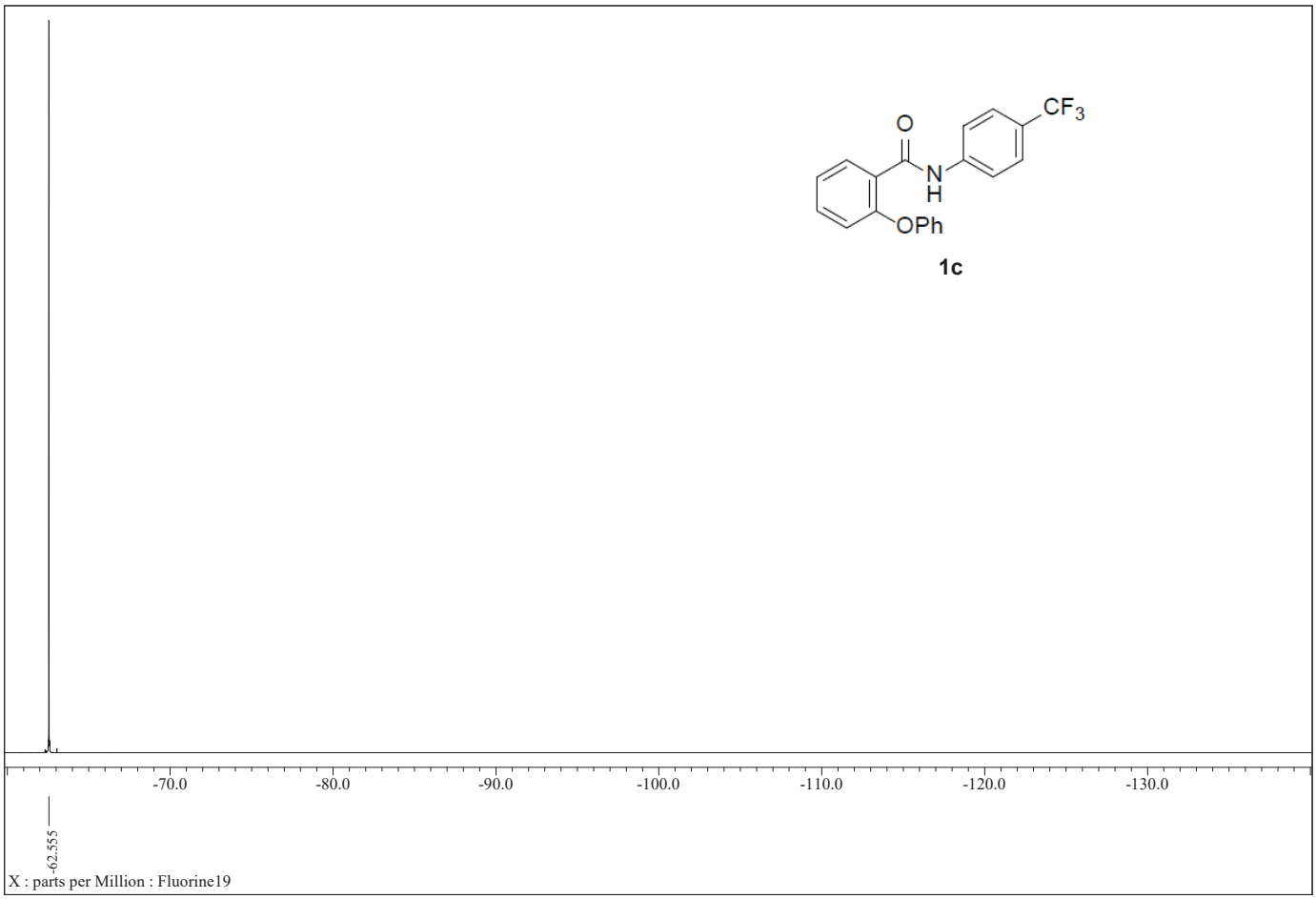
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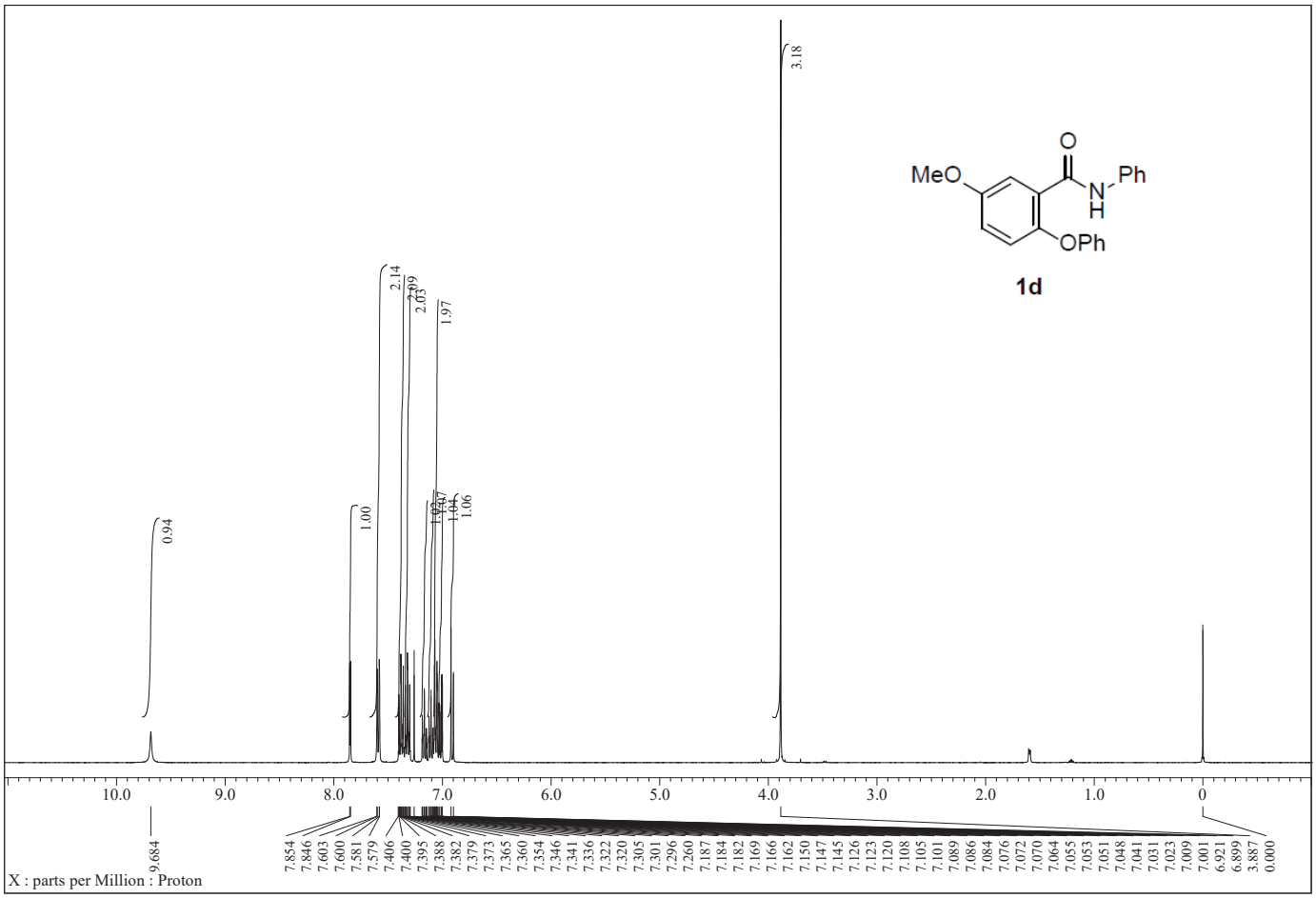
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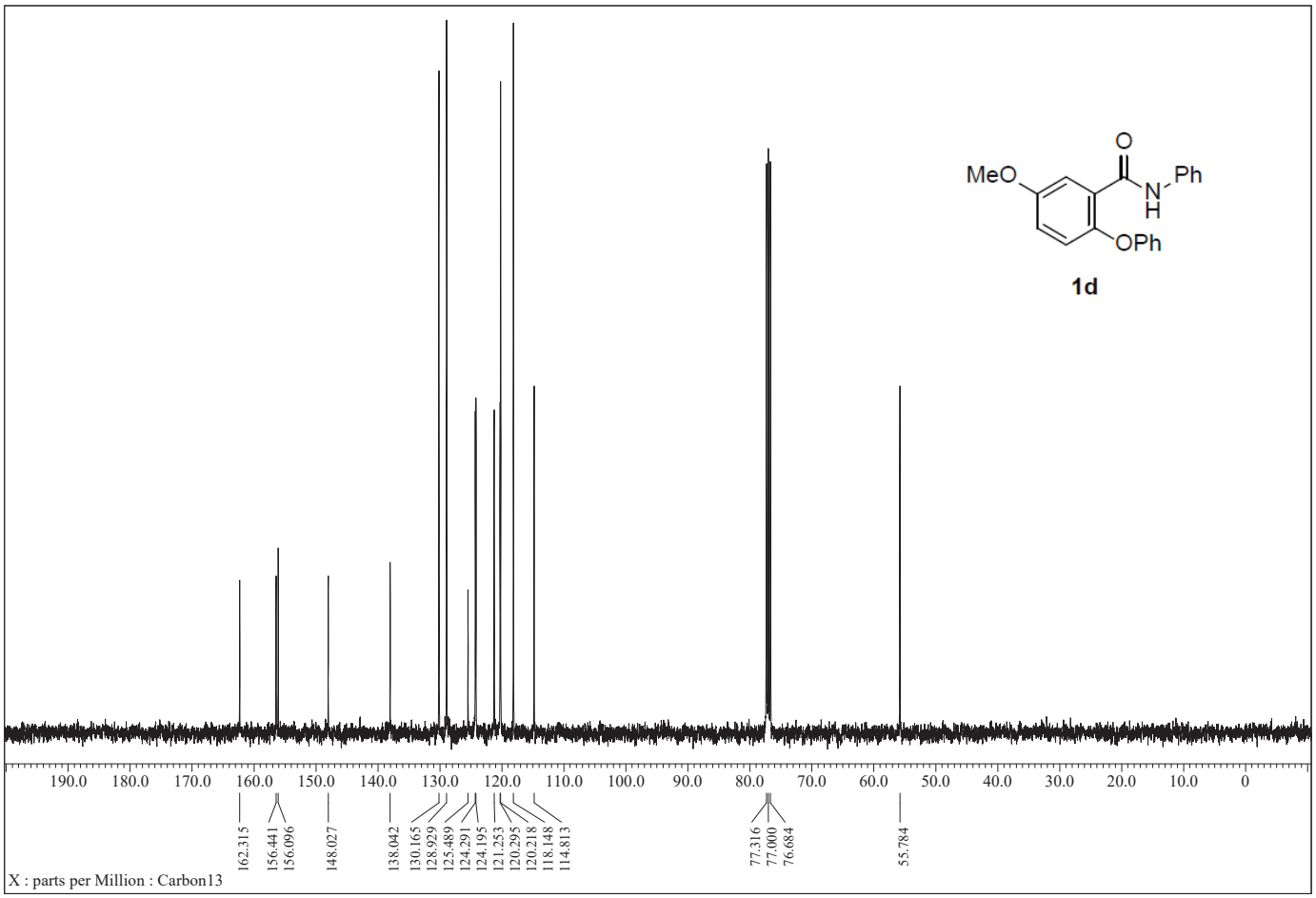
1d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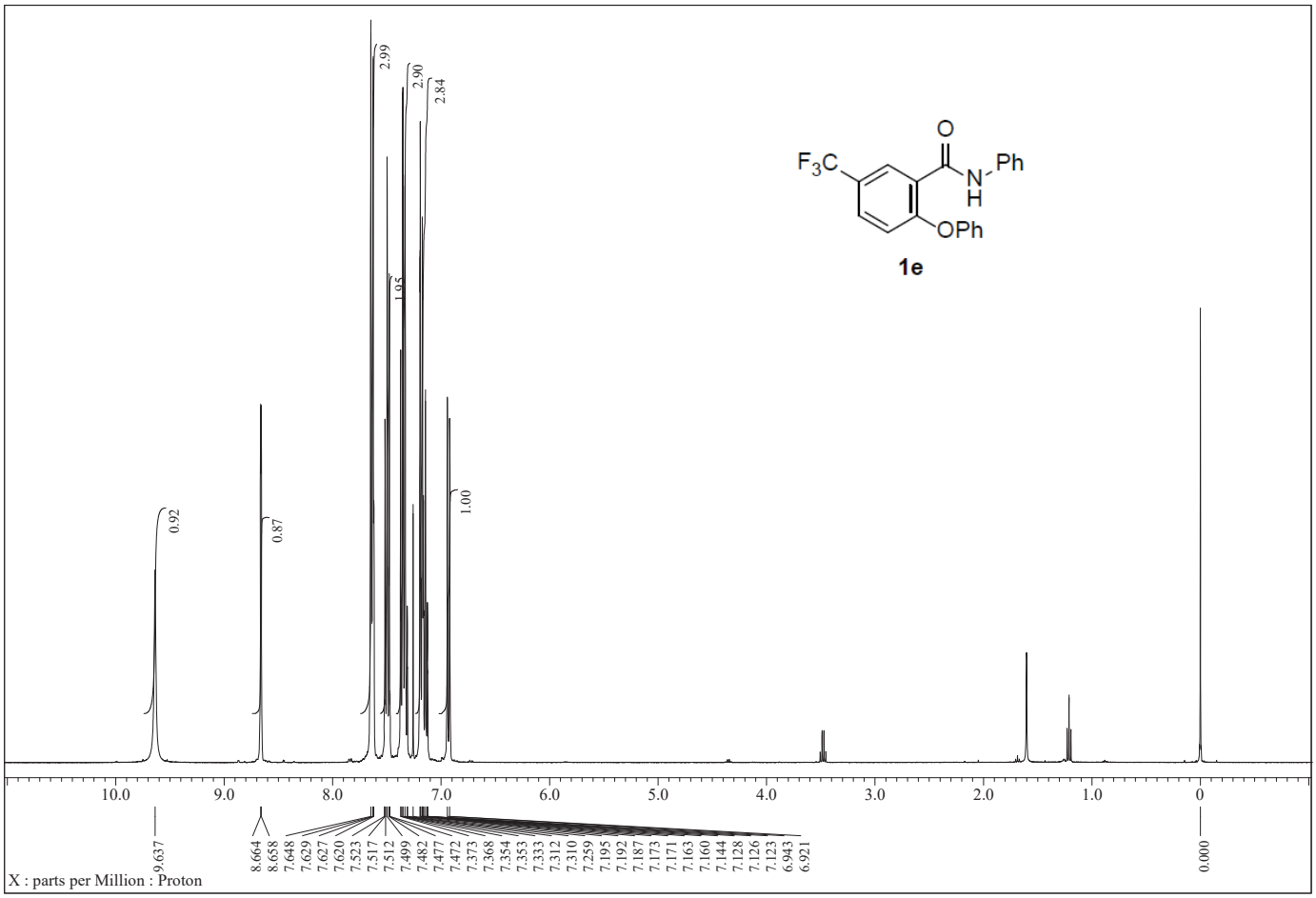
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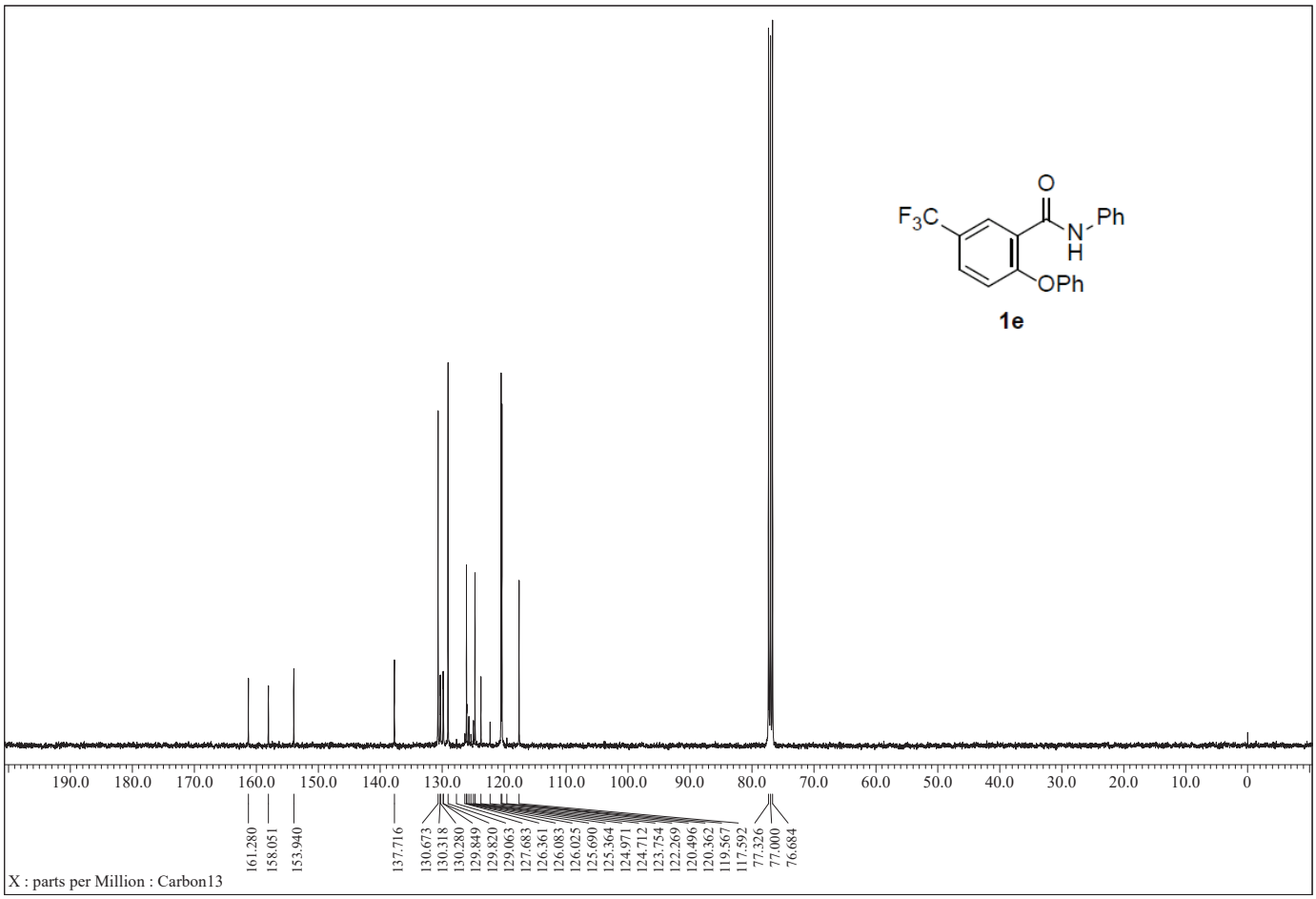
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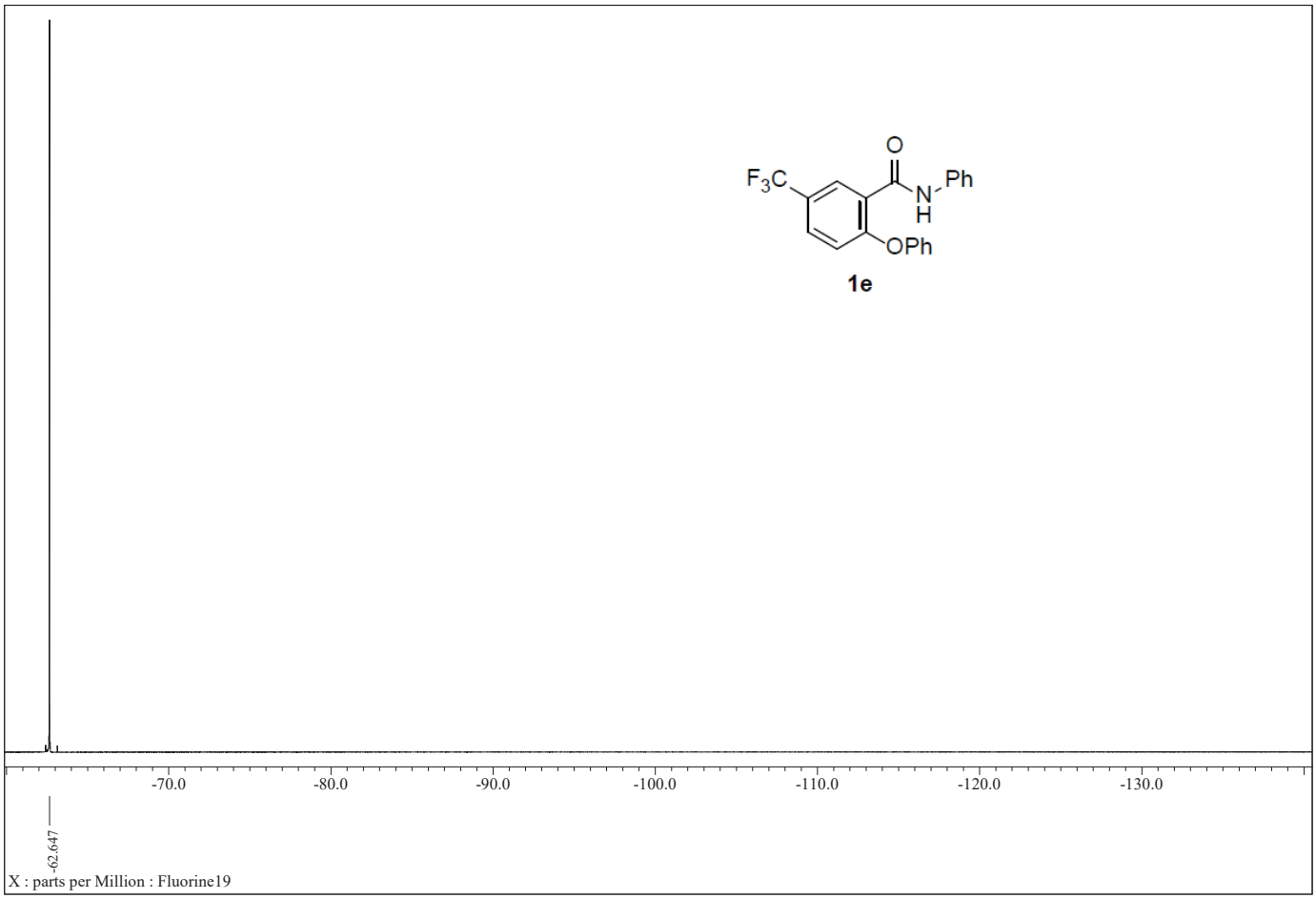
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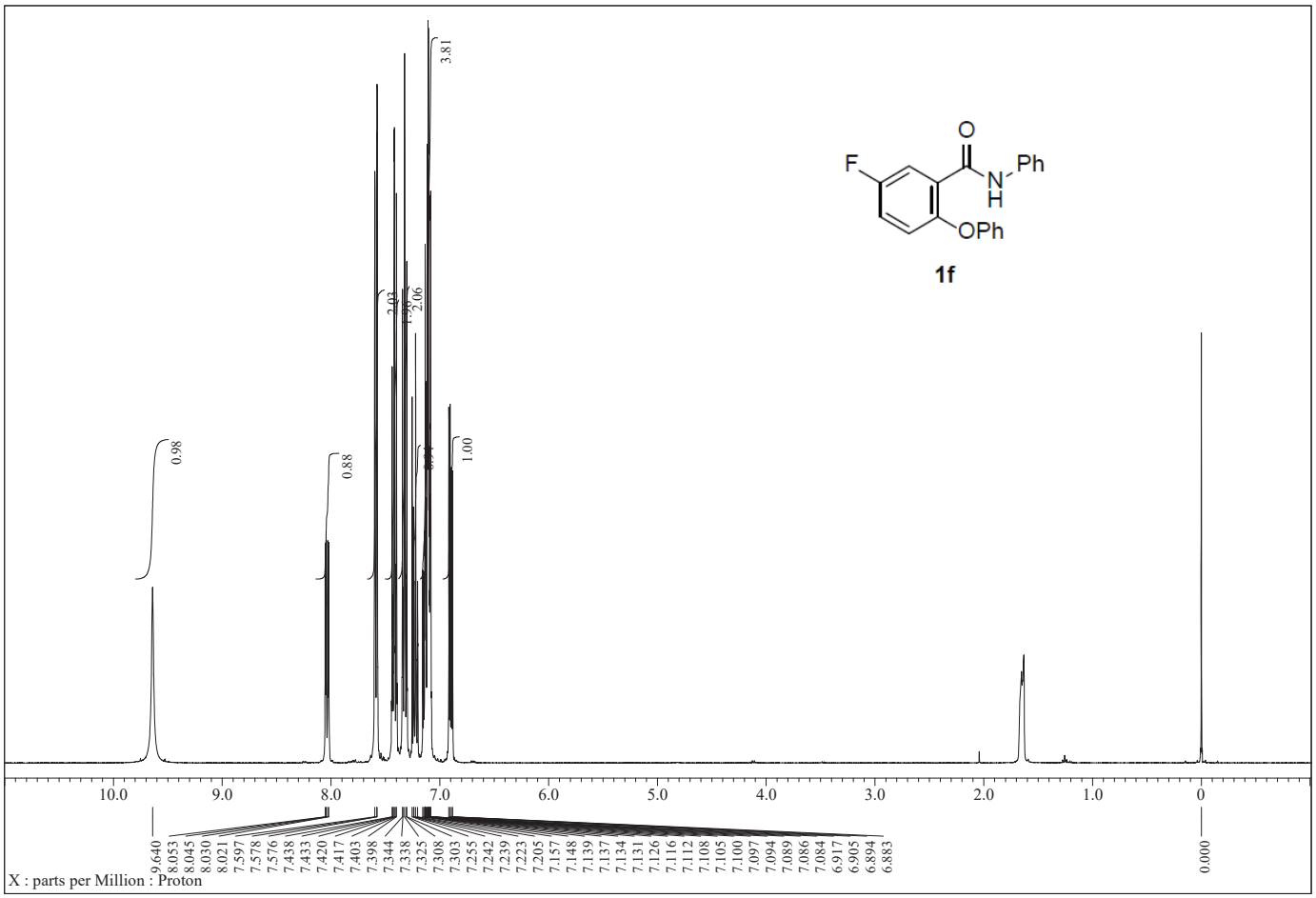
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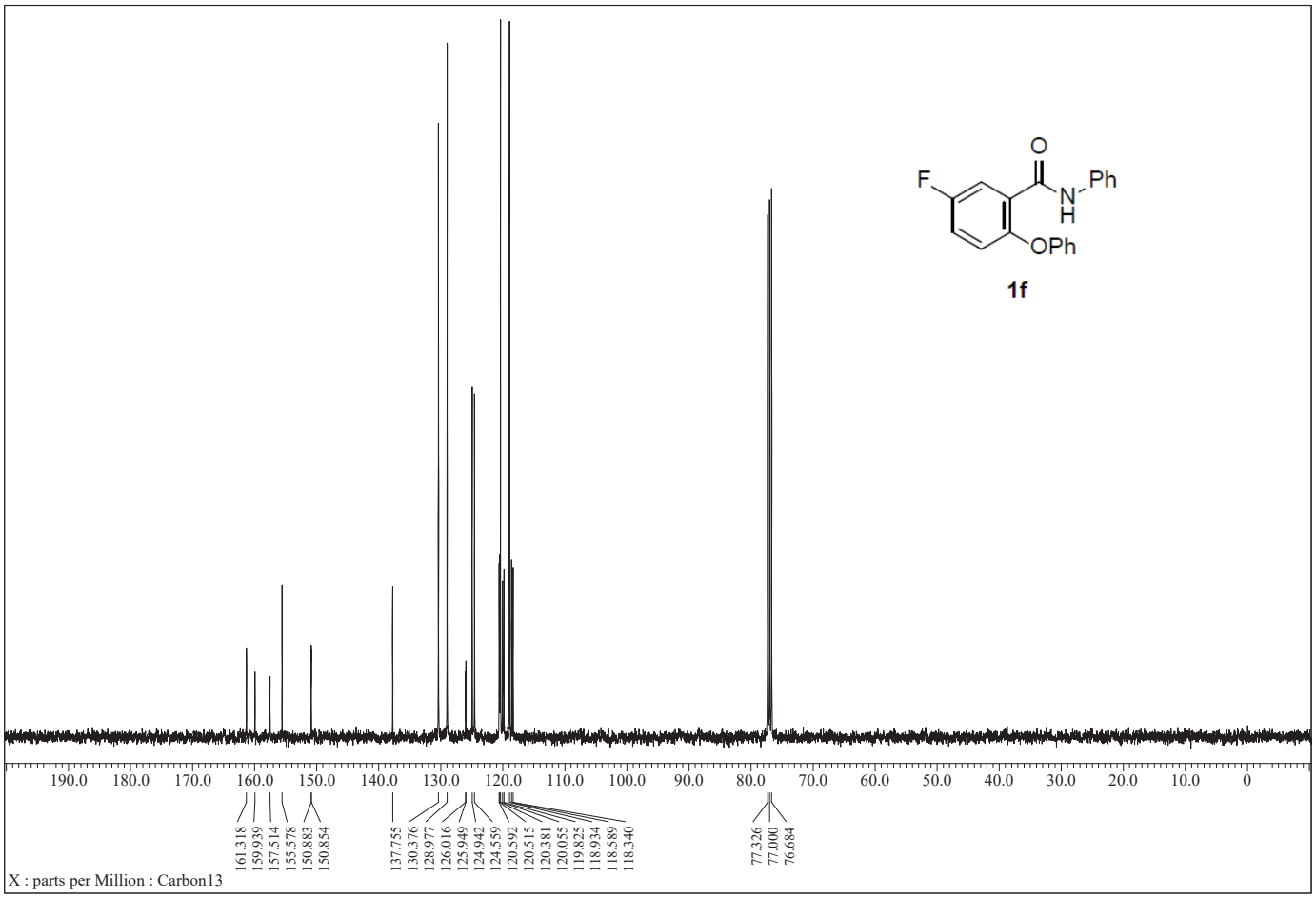
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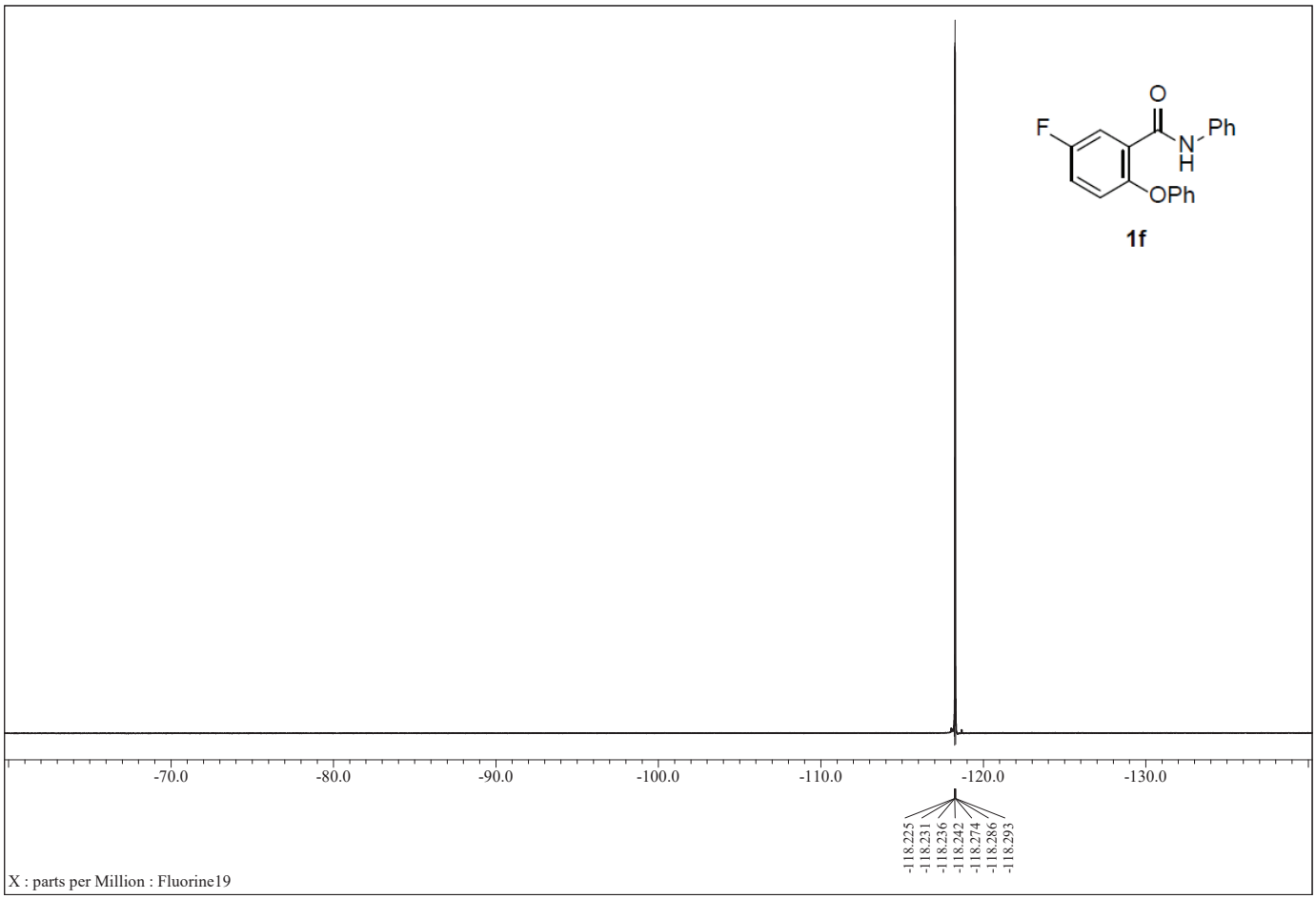
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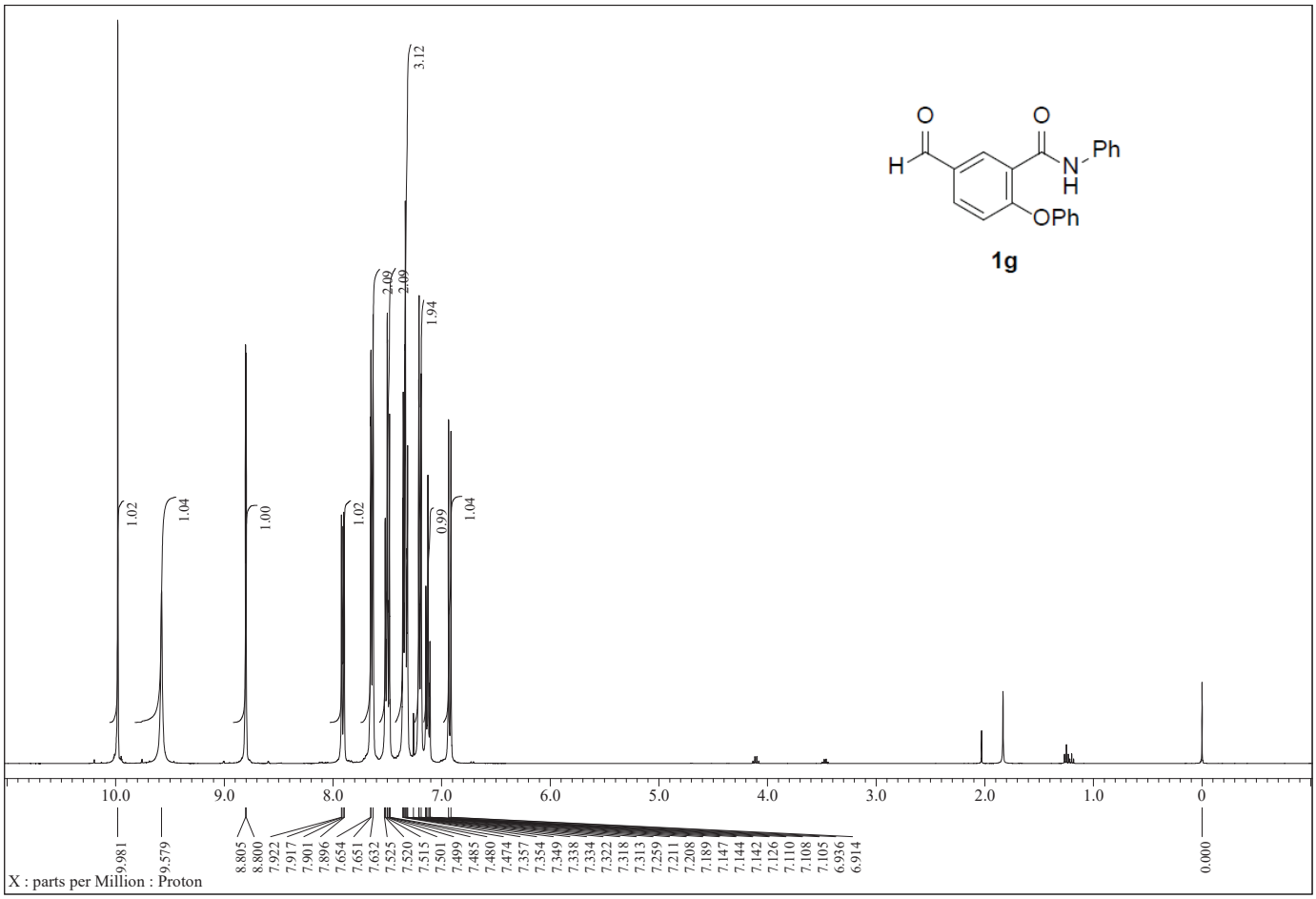
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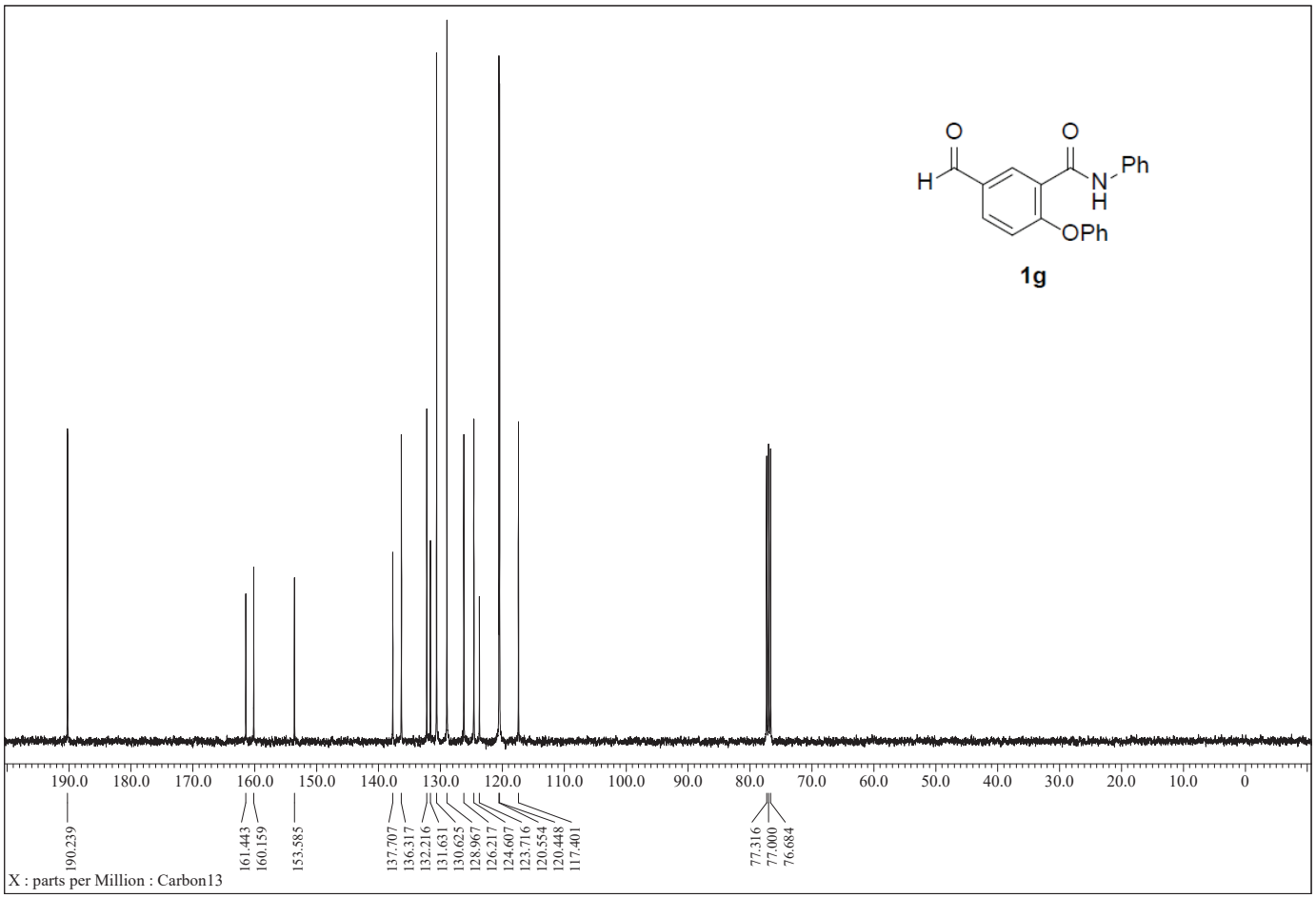
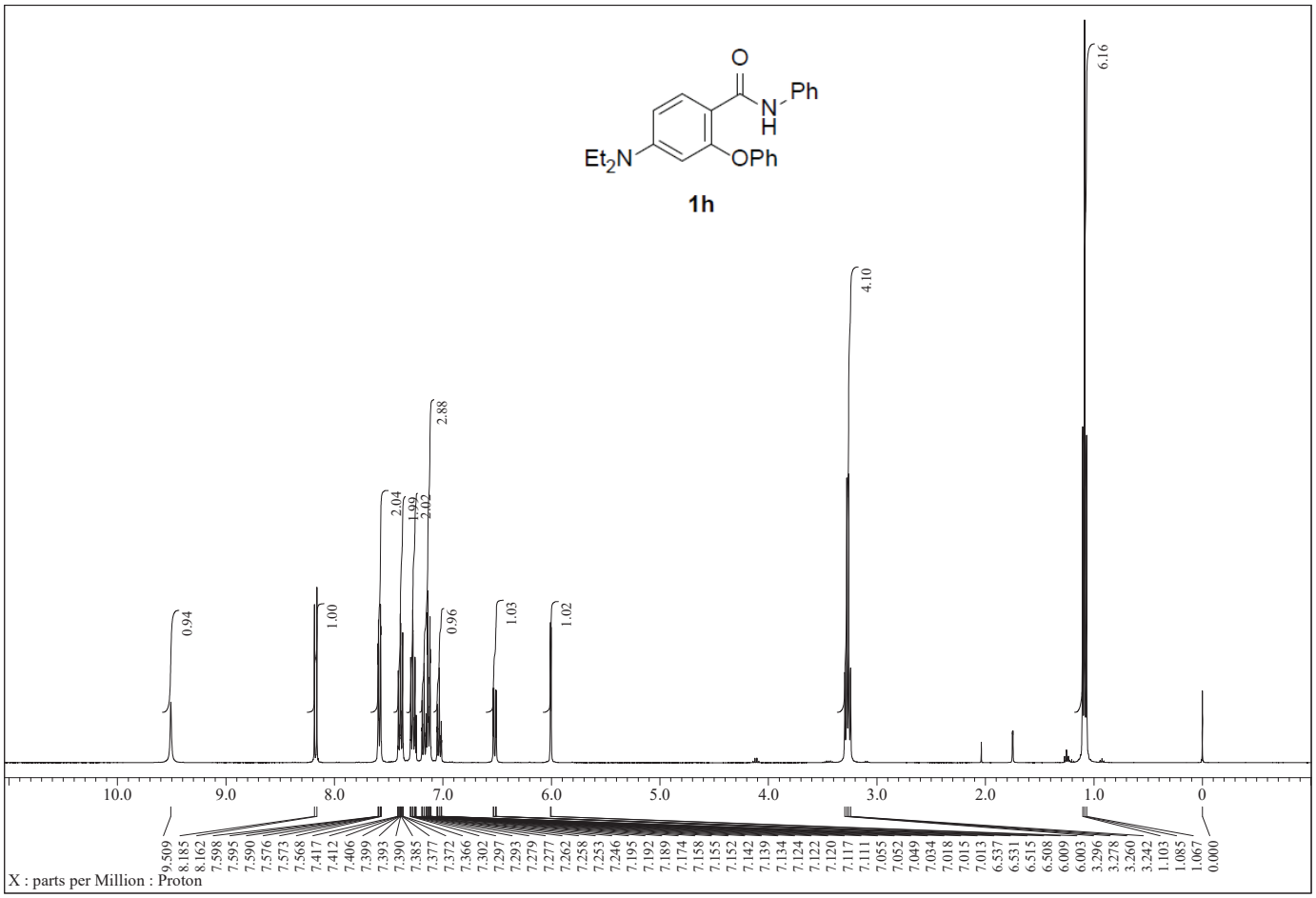
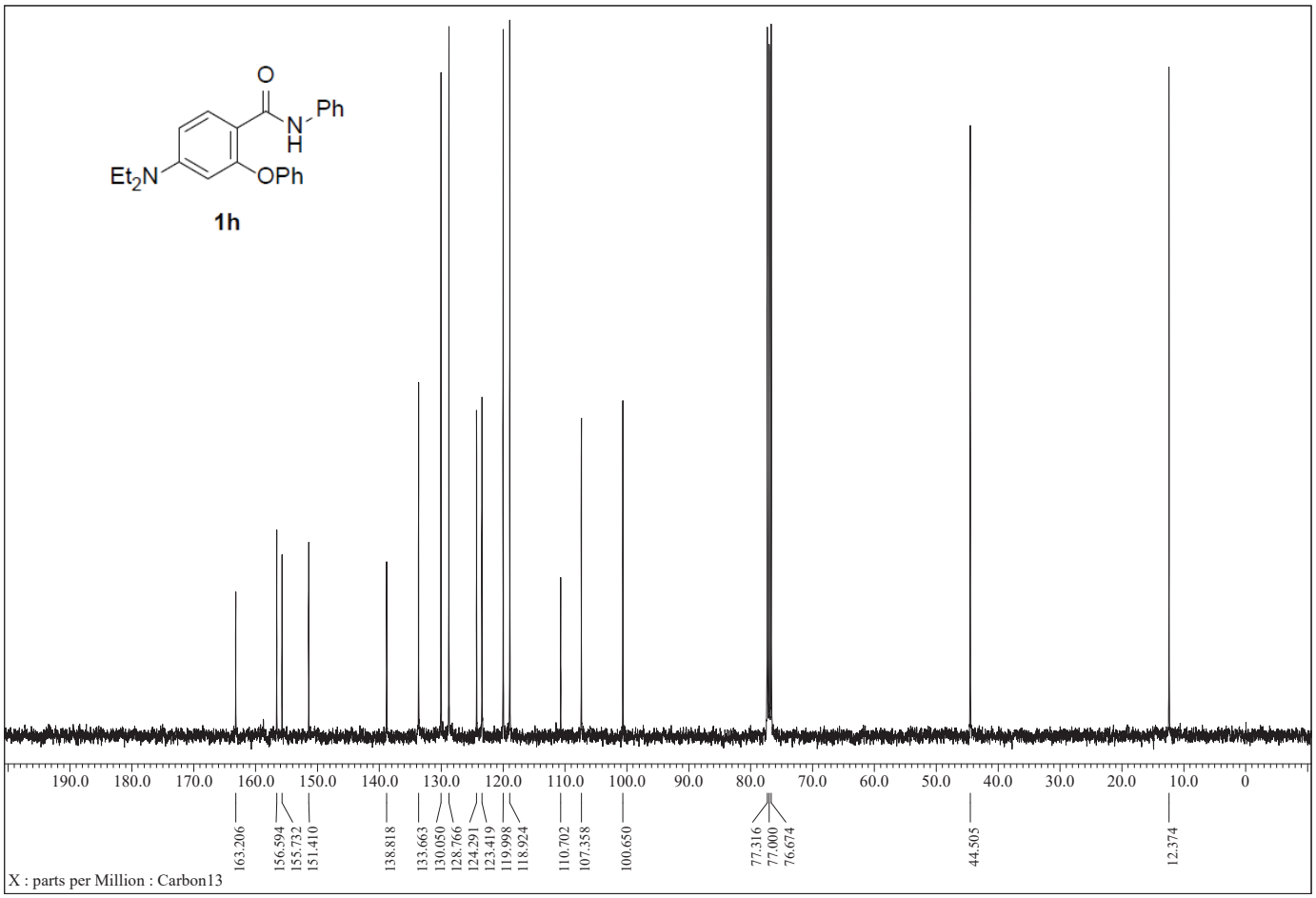
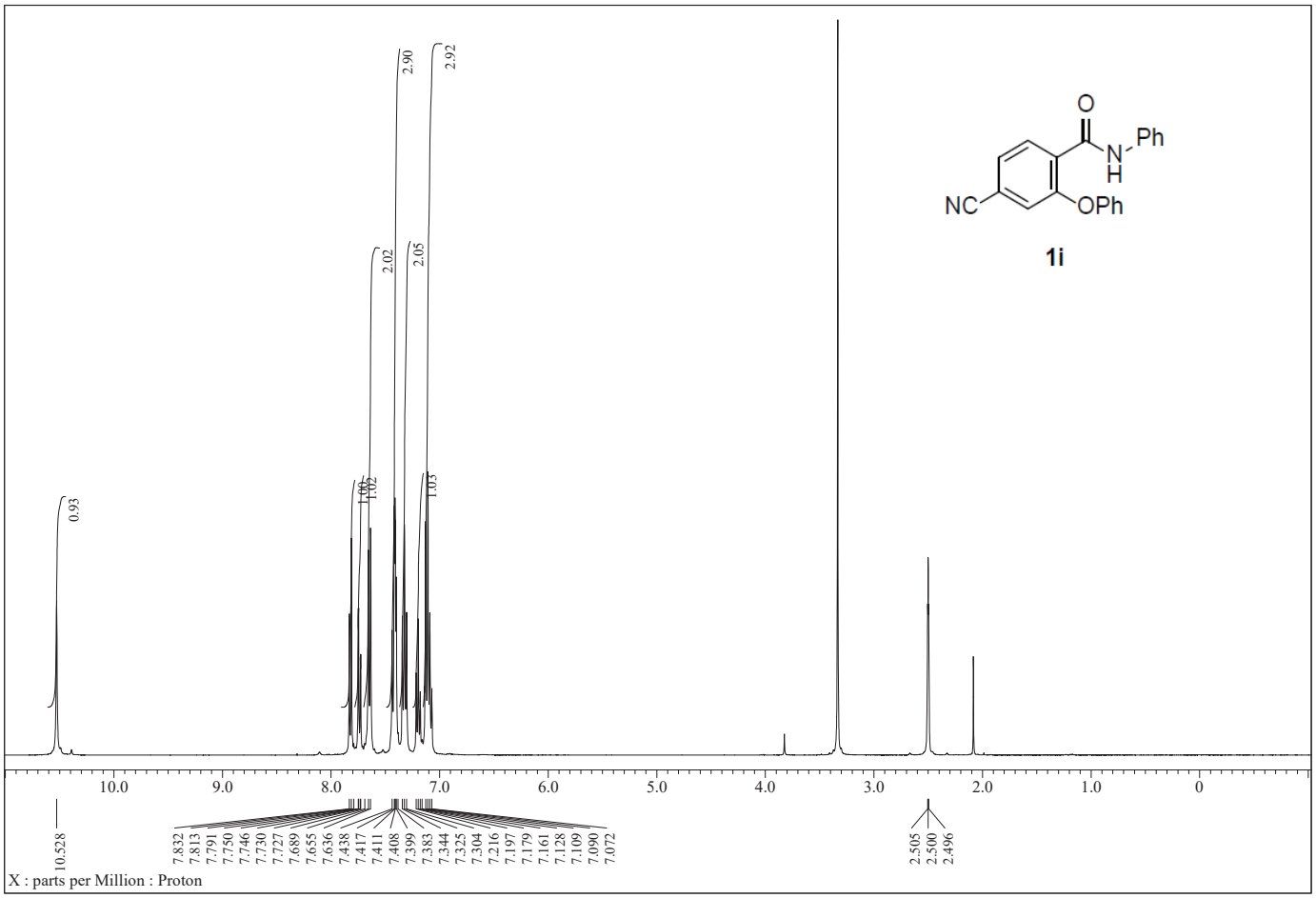
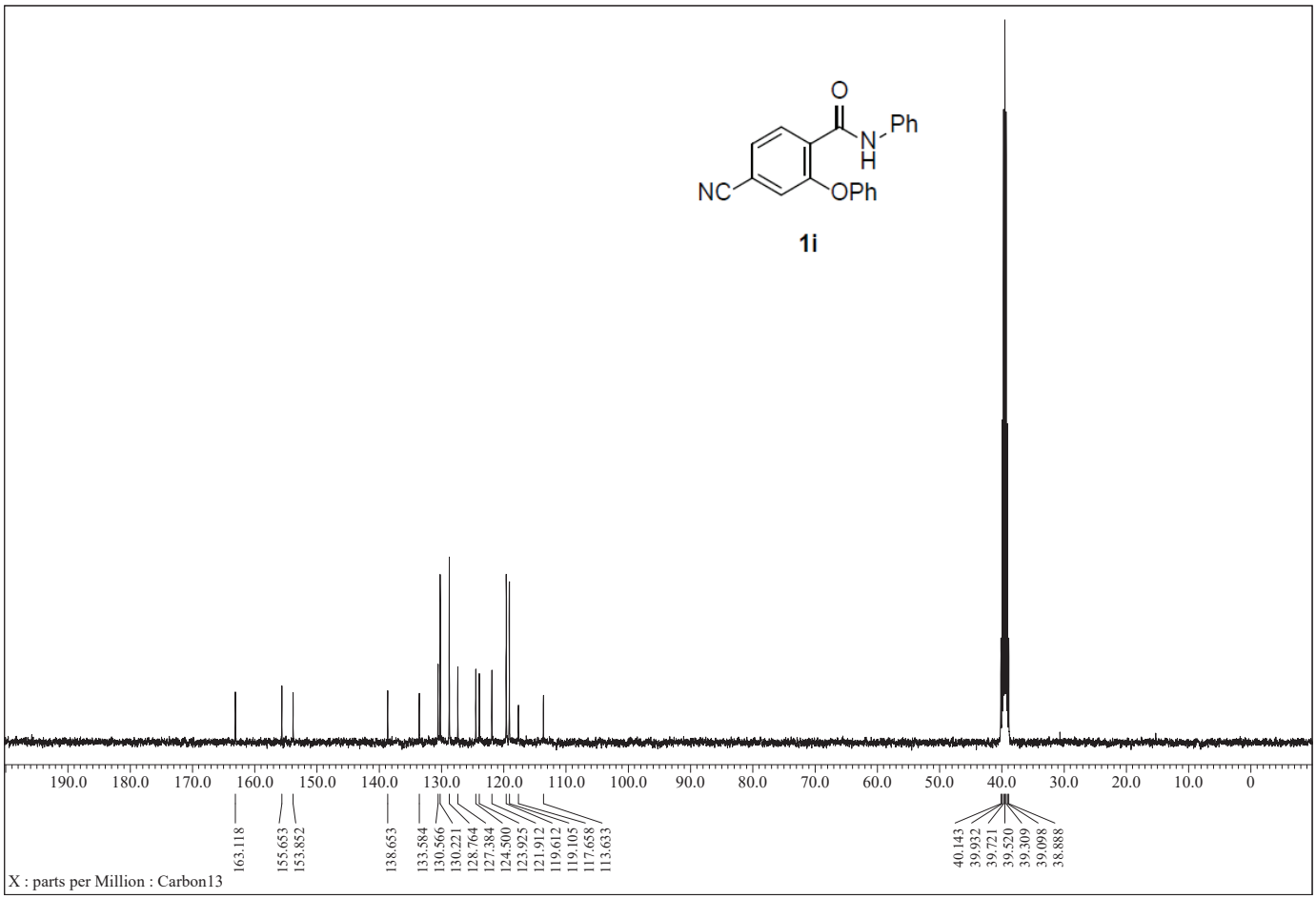
N
H
Ph
OPh
1g
3.12
2.02
2.00
1.94
1.02
1.04
1.00
1.02
0.99
1.04
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.981
9.579
8.805
8.800
7.922
7.917
7.901
7.896
7.654
7.651
7.632
7.525
7.520
7.515
7.501
7.499
7.485
7.480
7.474
7.357
7.354
7.349
7.338
7.334
7.322
7.318
7.313
7.259
7.211
7.208
7.189
7.147
7.144
7.142
7.126
7.110
7.108
7.105
6.936
6.914
0.000
X : parts per Million : Proton

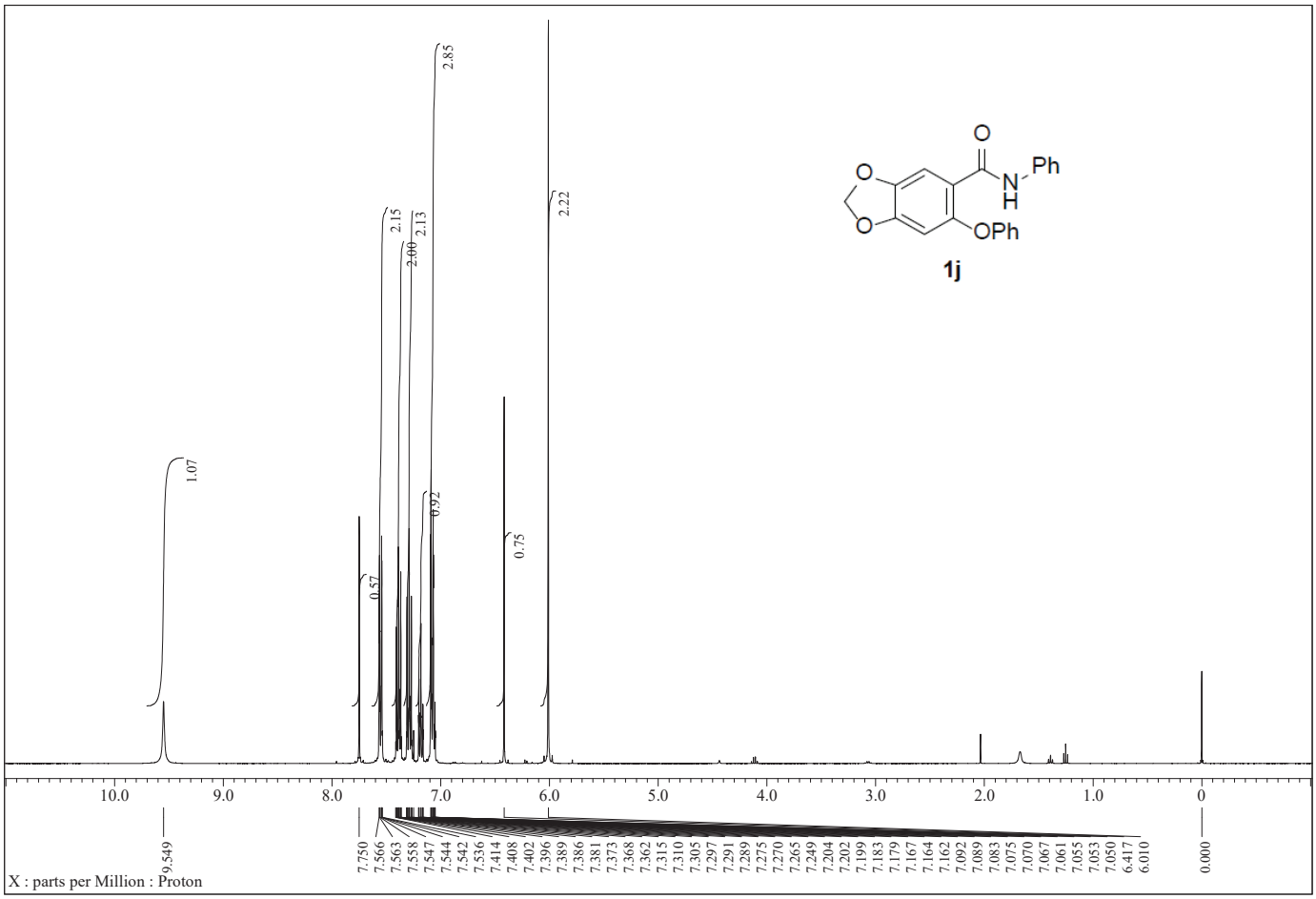

O
O
H
N
Ph
H
OPh
1g
190.239
161.443
160.159
153.585
137.707
136.317
132.216
131.631
130.625
128.967
126.217
124.607
123.716
120.554
120.448
117.401
77.316
77.000
76.684
X : parts per Million : Carbon13

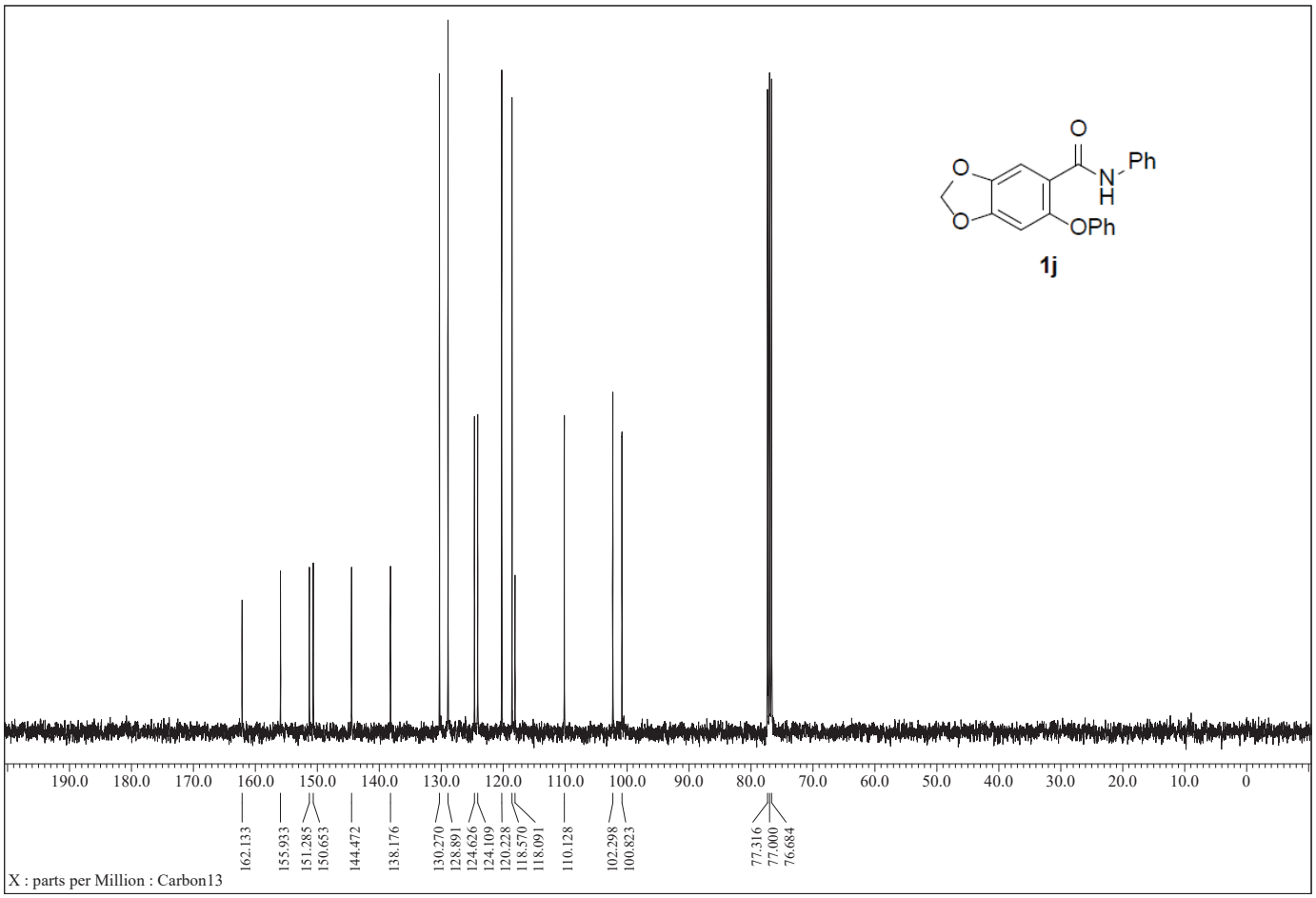

O
N
Ph
H
Et2N
OPh
1h
6.16
4.10
2.88
2.04
1.99
2.02
0.94
1.00
0.96
1.03
1.02
9.509
8.185
8.162
7.598
7.595
7.590
7.576
7.573
7.568
7.417
7.412
7.406
7.399
7.393
7.390
7.385
7.377
7.372
7.366
7.302
7.297
7.293
7.279
7.277
7.262
7.258
7.253
7.246
7.195
7.192
7.189
7.174
7.158
7.155
7.152
7.142
7.139
7.134
7.124
7.122
7.120
7.117
7.111
7.055
7.052
7.049
7.034
7.018
7.015
7.013
6.537
6.531
6.515
6.508
6.009
6.003
3.296
3.278
3.260
3.242
1.103
1.085
1.067
0.000
X : parts per Million : Proton

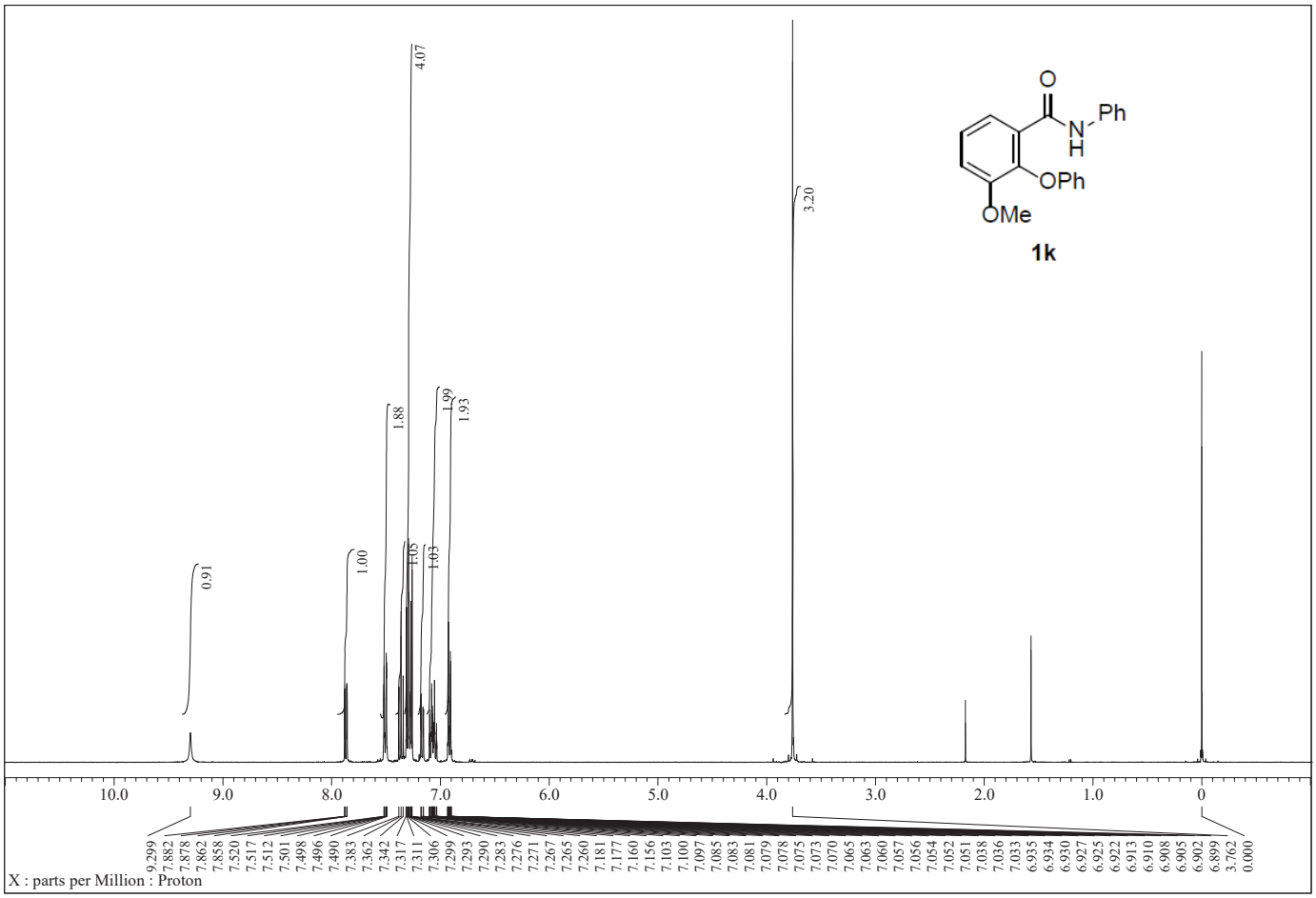

O
N
H
Ph
Et2N
OPh
1h
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
163.206
156.594
155.732
151.410
138.818
133.663
130.050
128.766
124.291
123.419
119.998
118.924
110.702
107.358
100.650
77.316
77.000
76.674
44.505
12.374
X : parts per Million : Carbon13

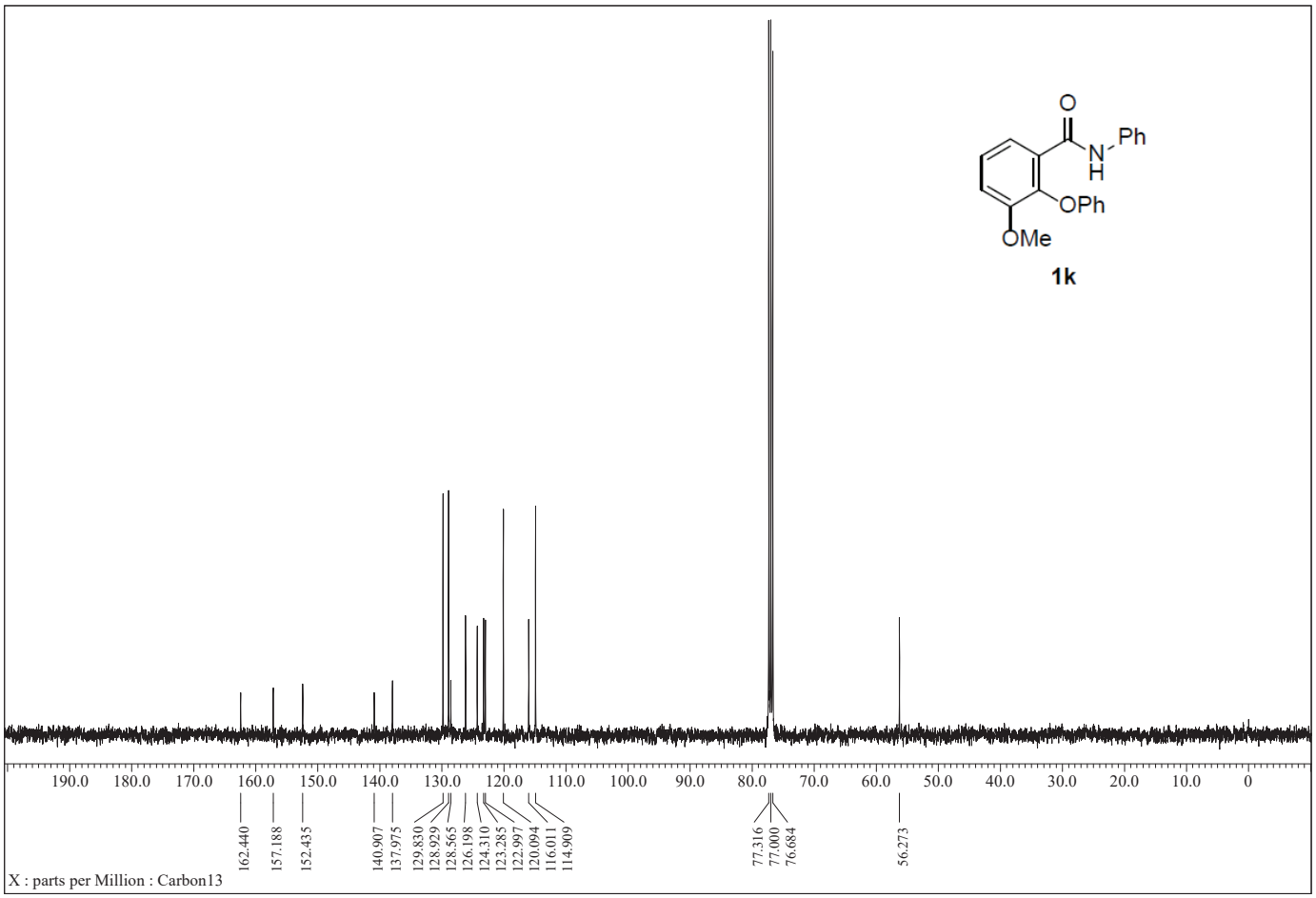

2.92
2.90
2.05
2.02
1.05
1.00
1.02
0.93
O
N
H
Ph
NC
OPh
1i
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
10.528
7.832
7.813
7.791
7.750
7.746
7.730
7.727
7.689
7.655
7.636
7.438
7.417
7.411
7.408
7.399
7.383
7.344
7.325
7.304
7.216
7.197
7.179
7.161
7.128
7.109
7.090
7.072
2.505
2.500
2.496
X : parts per Million : Proton

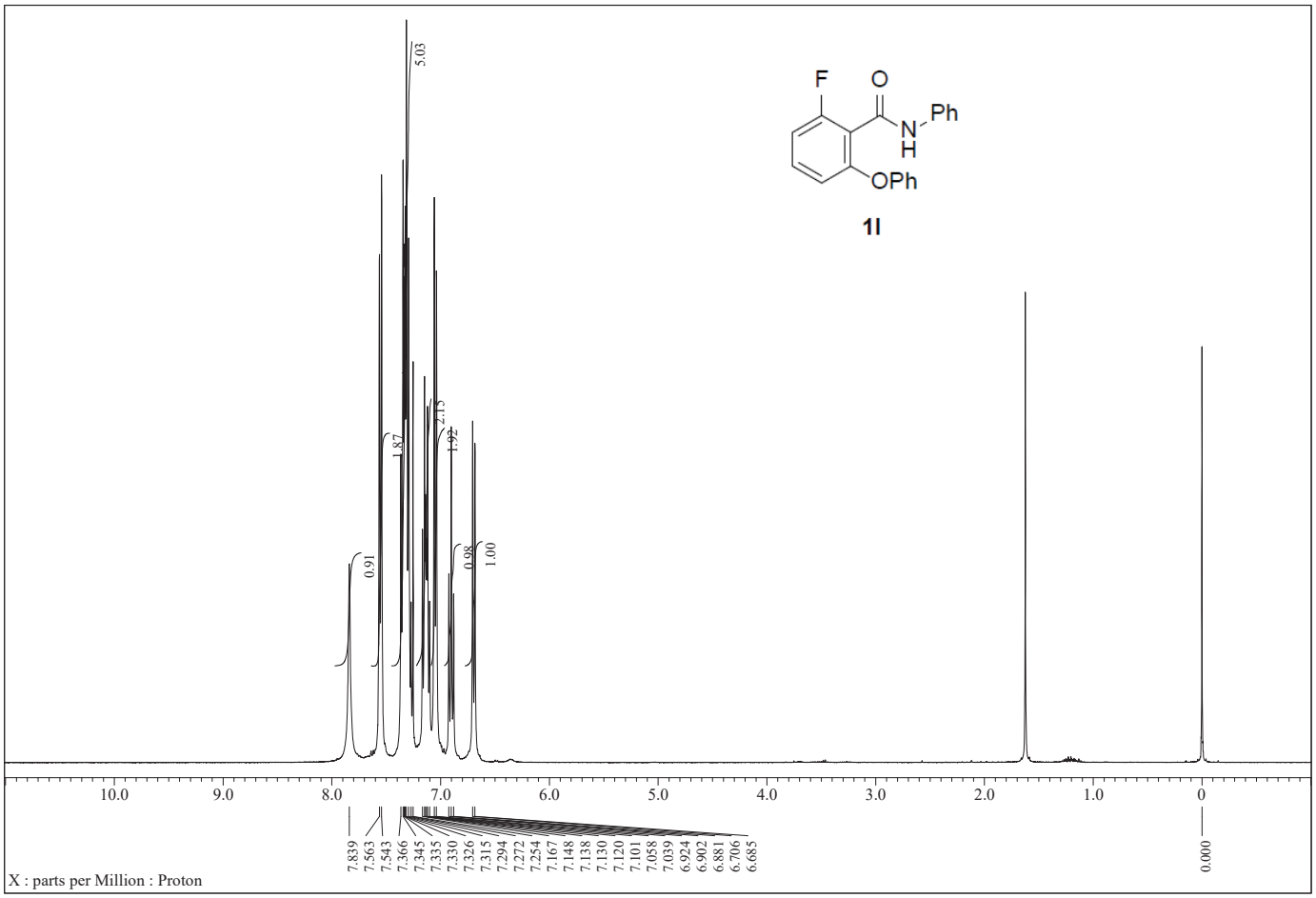

O
N
H
Ph
NC
OPh
1i
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
163.118
155.653
153.852
138.653
133.584
130.566
130.221
128.764
127.384
124.500
123.925
121.912
119.612
119.105
117.658
113.633
40.143
39.932
39.721
39.520
39.309
39.098
38.888
X : parts per Million : Carbon13

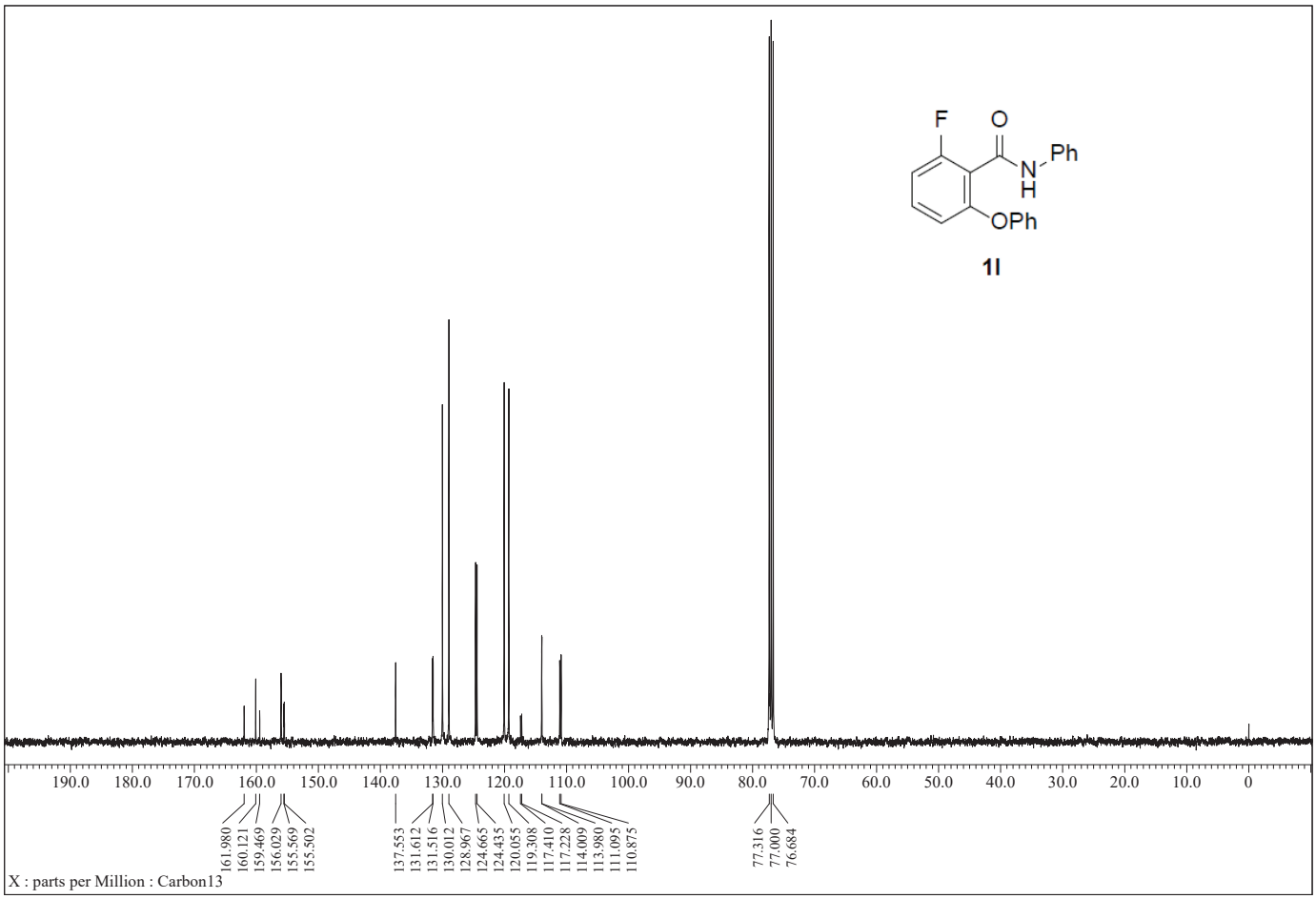

O
O
O
N
H
Ph
OPh
1j
2.85
2.22
2.15
2.13
2.00
1.07
0.92
0.75
0.57
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
9.549
7.750
7.566
7.563
7.558
7.547
7.544
7.542
7.536
7.414
7.408
7.402
7.396
7.389
7.386
7.381
7.373
7.368
7.362
7.315
7.310
7.305
7.297
7.291
7.289
7.275
7.270
7.265
7.249
7.204
7.202
7.199
7.183
7.179
7.167
7.164
7.162
7.092
7.089
7.083
7.075
7.070
7.067
7.061
7.055
7.053
7.050
6.417
6.010
0.000
X : parts per Million : Proton

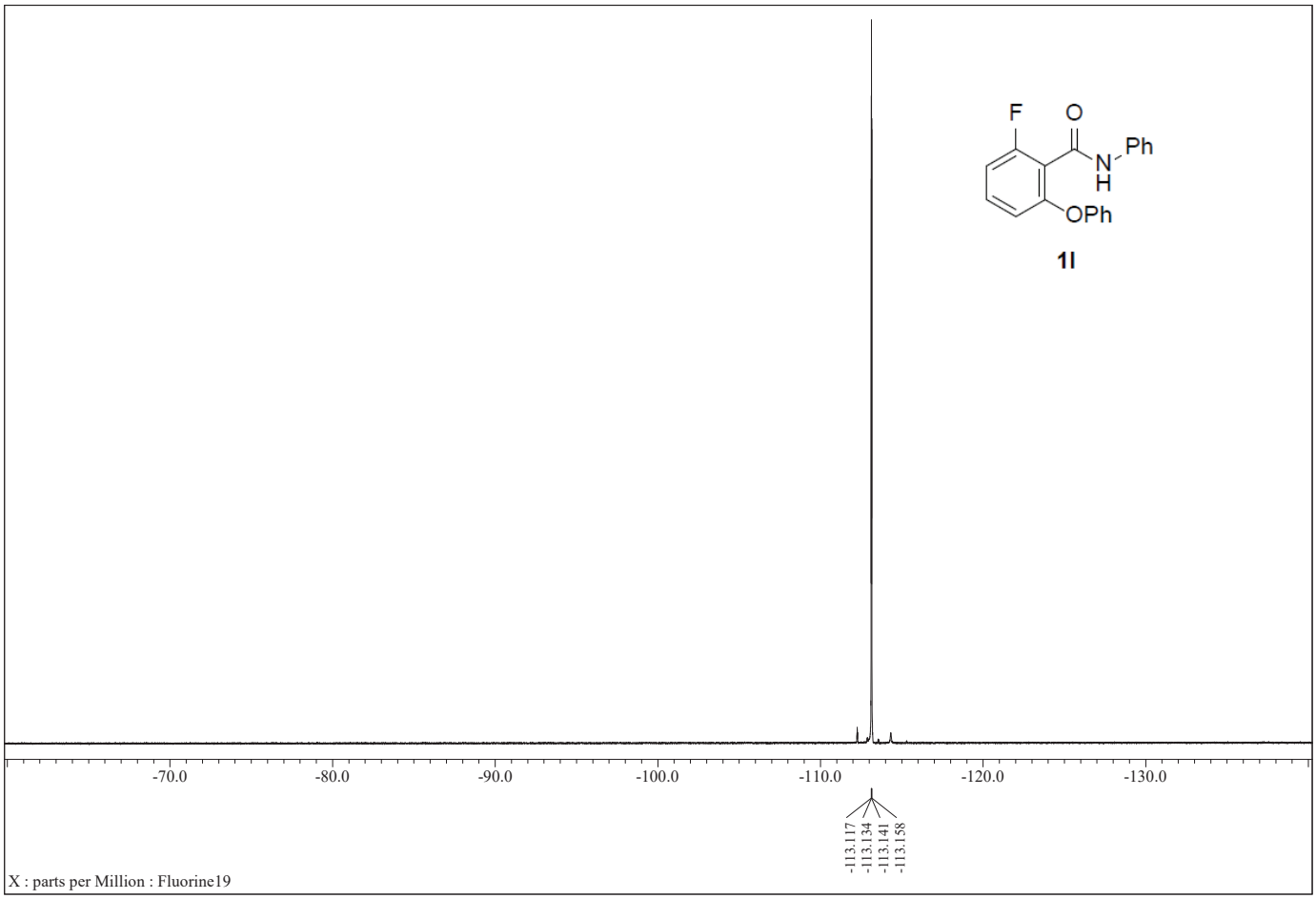

O
O
O
N
H
Ph
OPh
1j
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.133
155.933
151.285
150.653
144.472
138.176
130.270
128.891
124.626
124.109
120.228
118.570
118.091
110.128
102.298
100.823
77.316
77.000
76.684
X : parts per Million : Carbon13

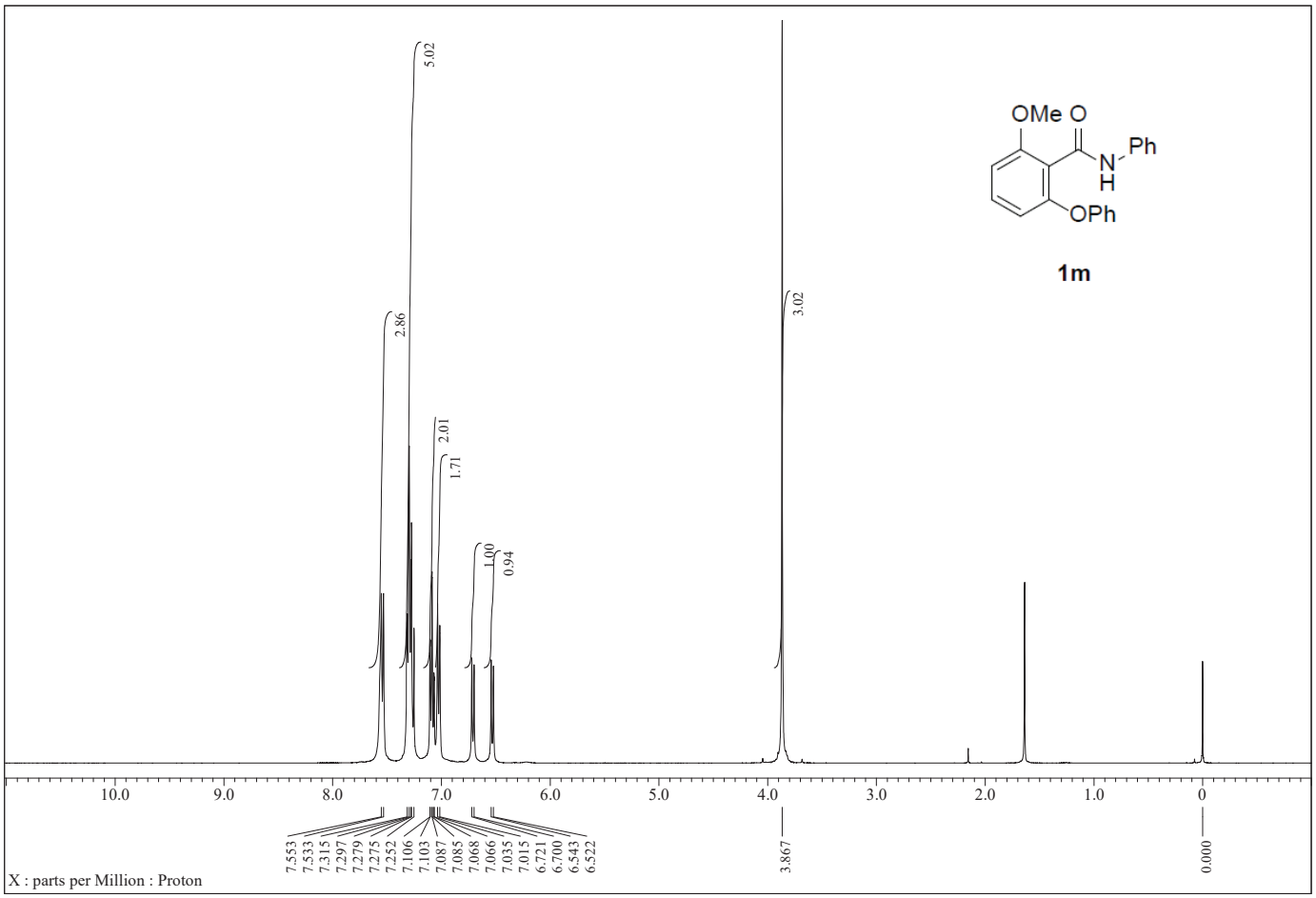

O
N
H
Ph
OPh
OMe
1k
4.07
3.20
1.88
1.99
1.93
1.00
1.05
1.03
0.91
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
9.299
7.882
7.878
7.862
7.858
7.520
7.517
7.512
7.501
7.498
7.496
7.490
7.383
7.362
7.342
7.317
7.311
7.306
7.299
7.293
7.290
7.283
7.276
7.271
7.267
7.265
7.260
7.181
7.177
7.160
7.156
7.103
7.100
7.097
7.085
7.083
7.081
7.079
7.078
7.075
7.073
7.070
7.065
7.063
7.060
7.057
7.056
7.054
7.052
7.051
7.038
7.036
7.033
6.935
6.934
6.930
6.927
6.925
6.922
6.913
6.910
6.908
6.905
6.902
6.899
3.762
0.000
X : parts per Million : Proton

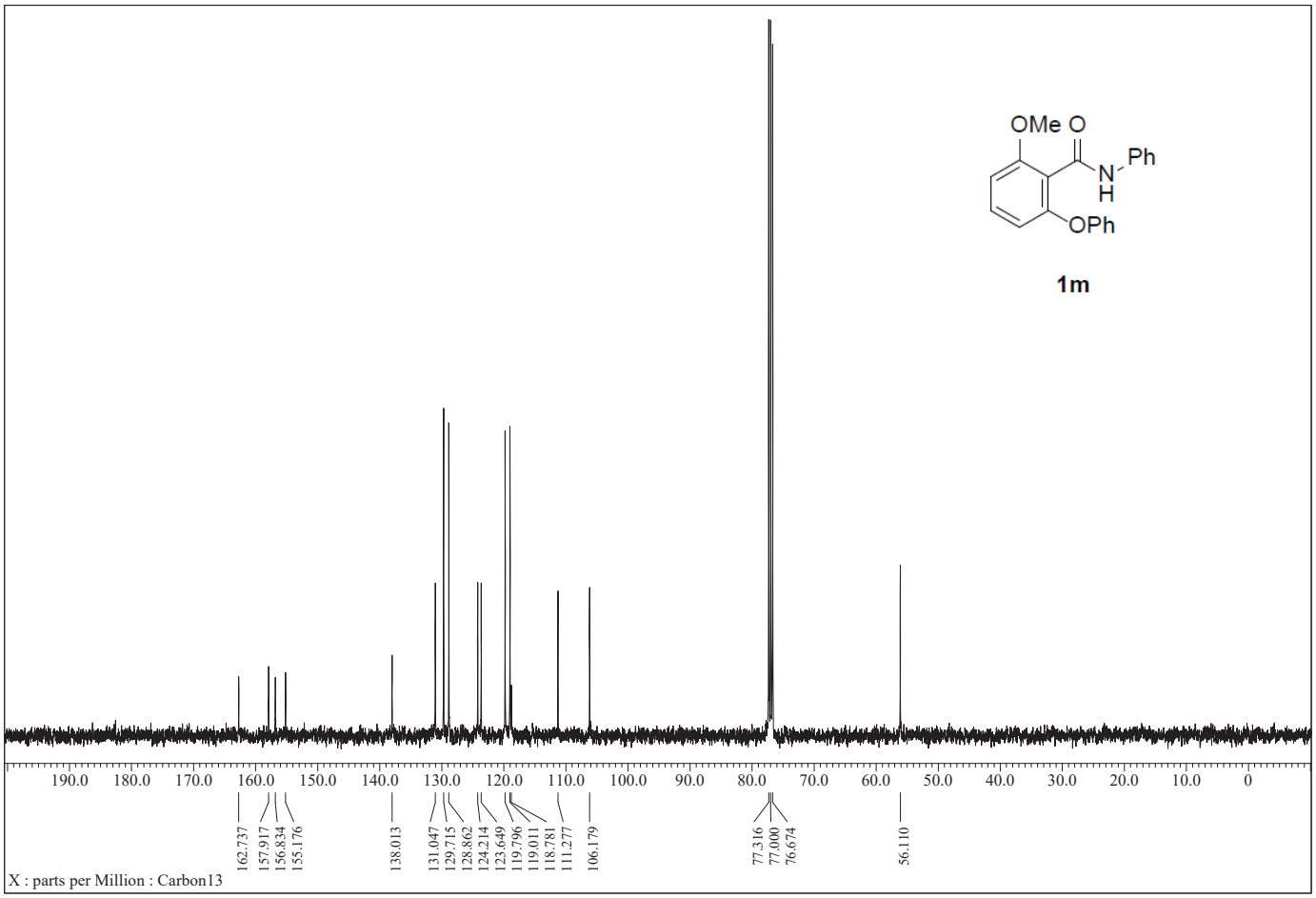

O
Ph
N
H
OPh
OMe
1k
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.440
157.188
152.435
140.907
137.975
129.830
128.929
128.565
126.198
124.310
123.285
122.997
120.094
116.011
114.909
77.316
77.000
76.684
56.273
X : parts per Million : Carbon13

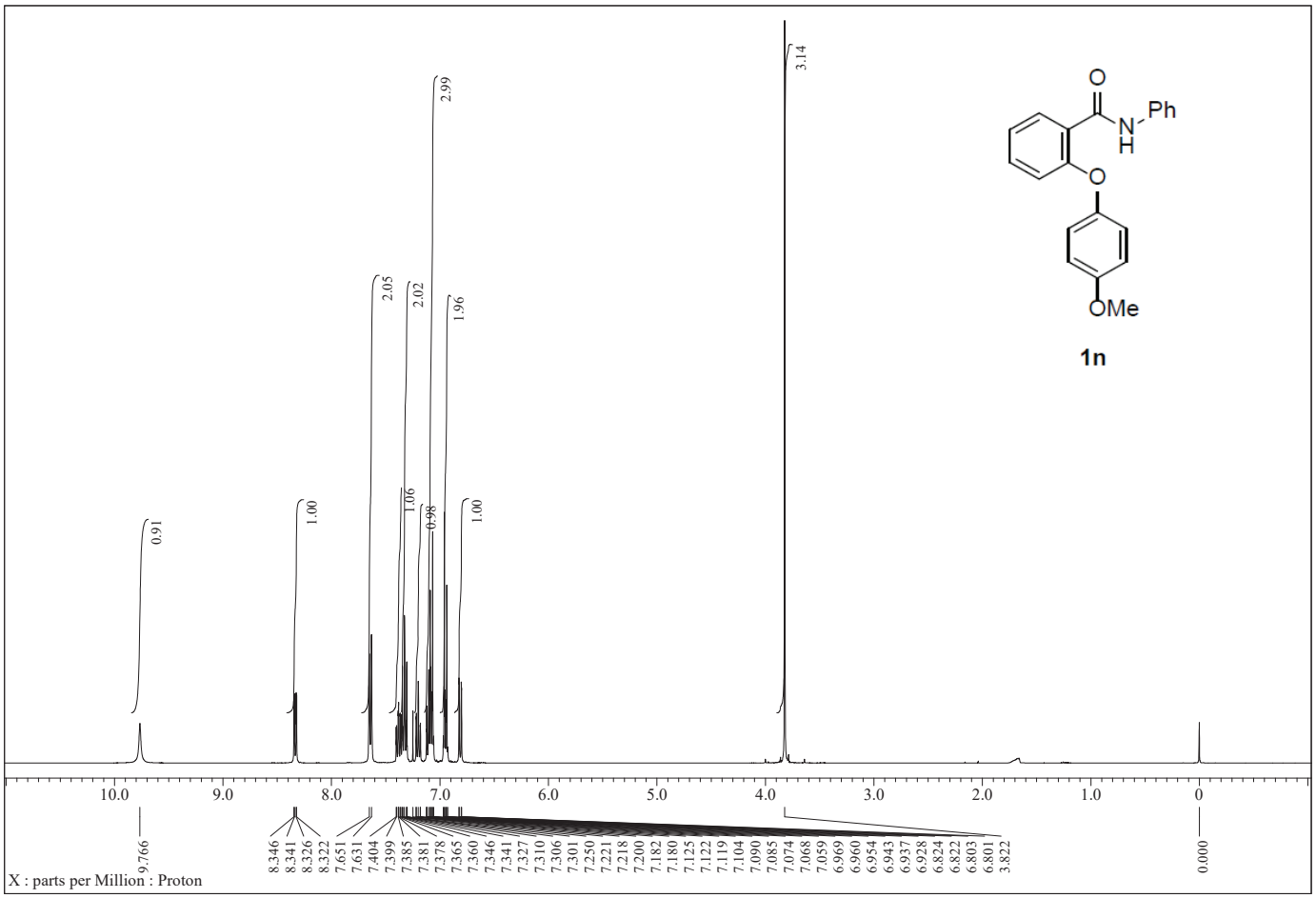

F
O
Ph
N
H
OPh
1l
5.03
1.87
2.15
1.92
0.91
0.98
1.00
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.839
7.563
7.543
7.366
7.345
7.335
7.330
7.326
7.315
7.294
7.272
7.254
7.167
7.148
7.138
7.130
7.120
7.101
7.058
7.039
6.924
6.902
6.881
6.706
6.685
0.000
X : parts per Million : Proton

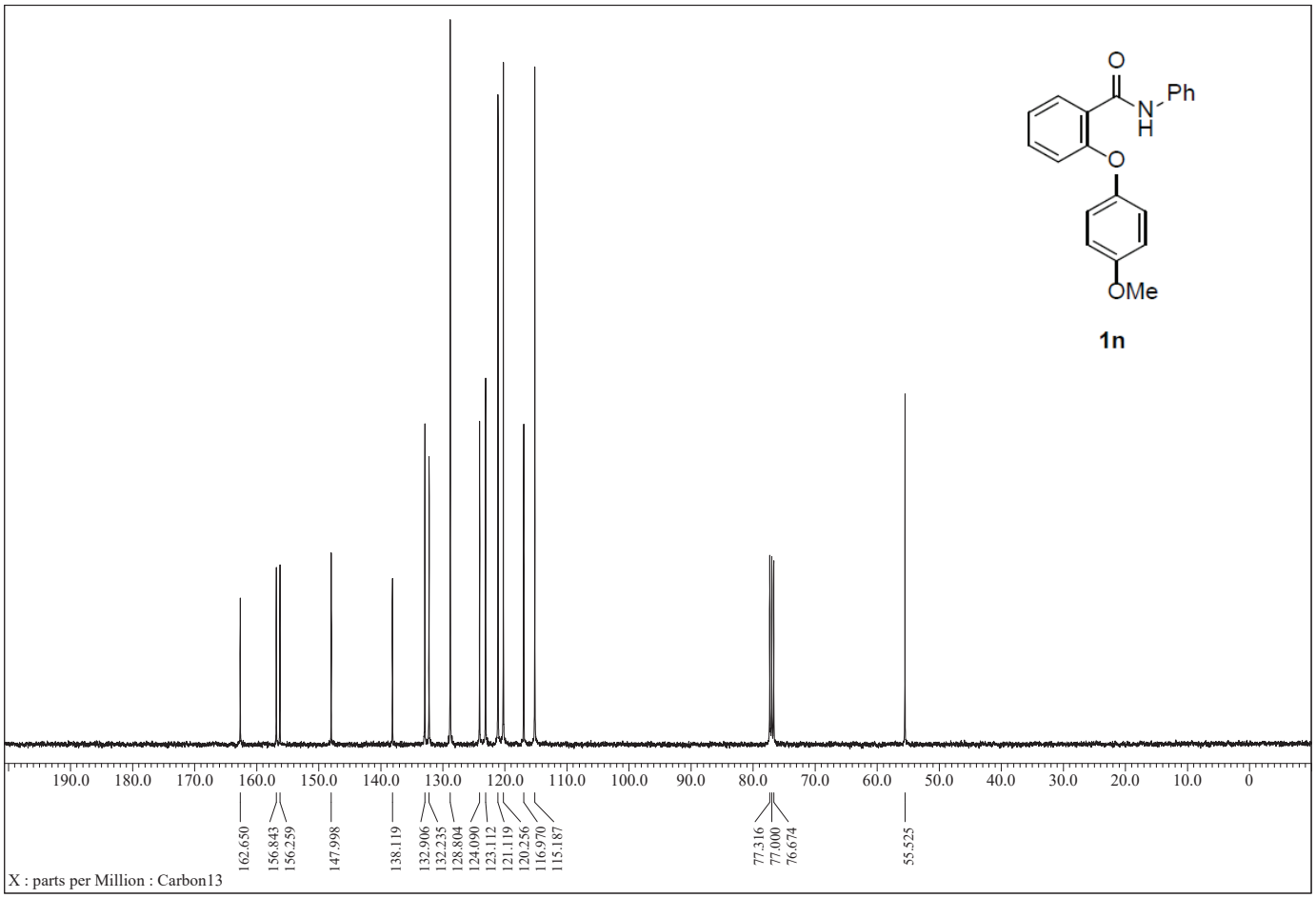

F
O
Ph
N
H
OPh
1l
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
161.980
160.121
159.469
156.029
155.569
155.502
137.553
131.612
131.516
130.012
128.967
124.665
124.435
120.055
119.308
117.410
117.228
114.009
113.980
111.095
110.875
77.316
77.000
76.684
X : parts per Million : Carbon13

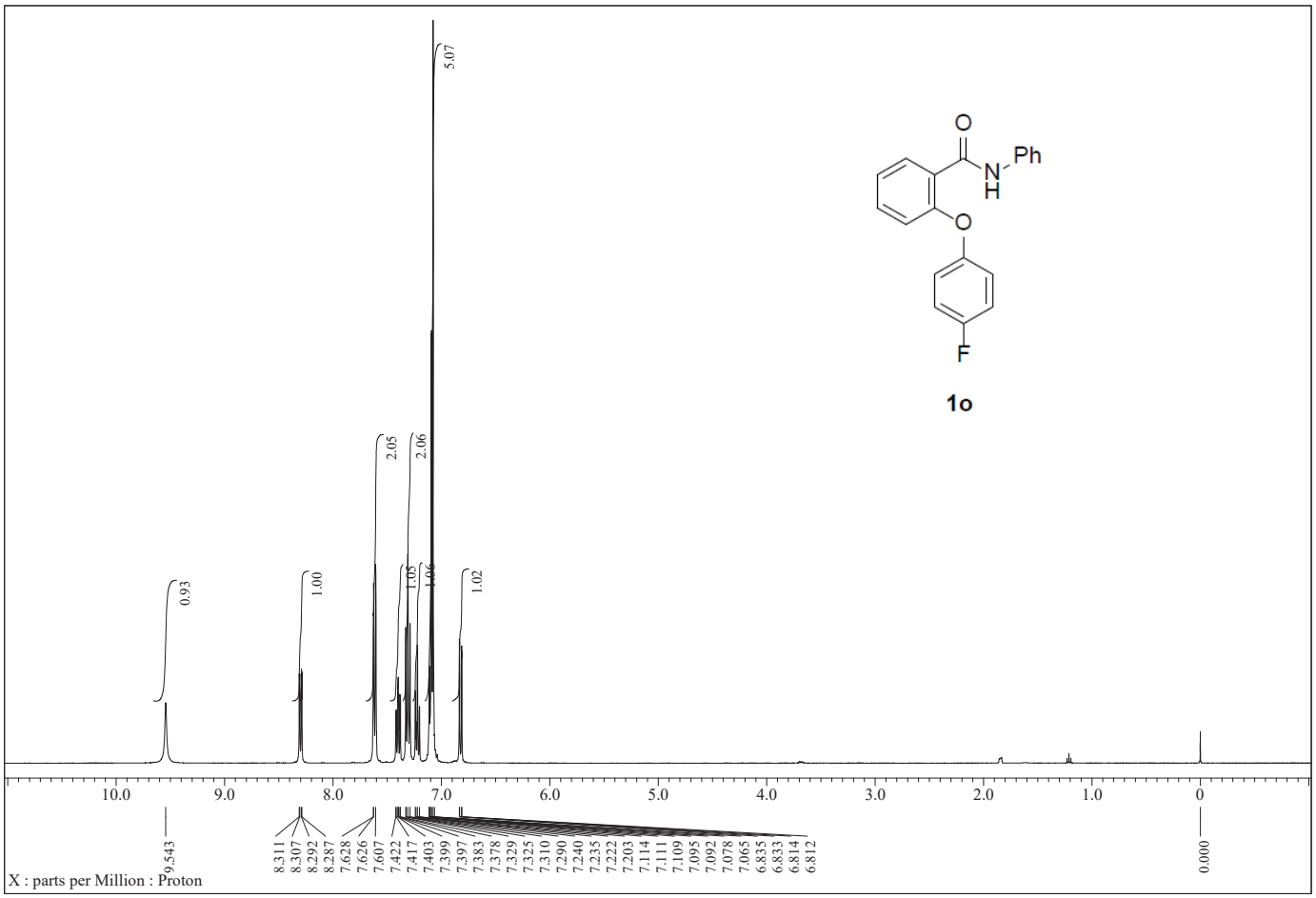

F
O
Ph
N
H
OPh
1l
-70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0
-113.117
-113.134
-113.141
-113.158
X : parts per Million : Fluorine19

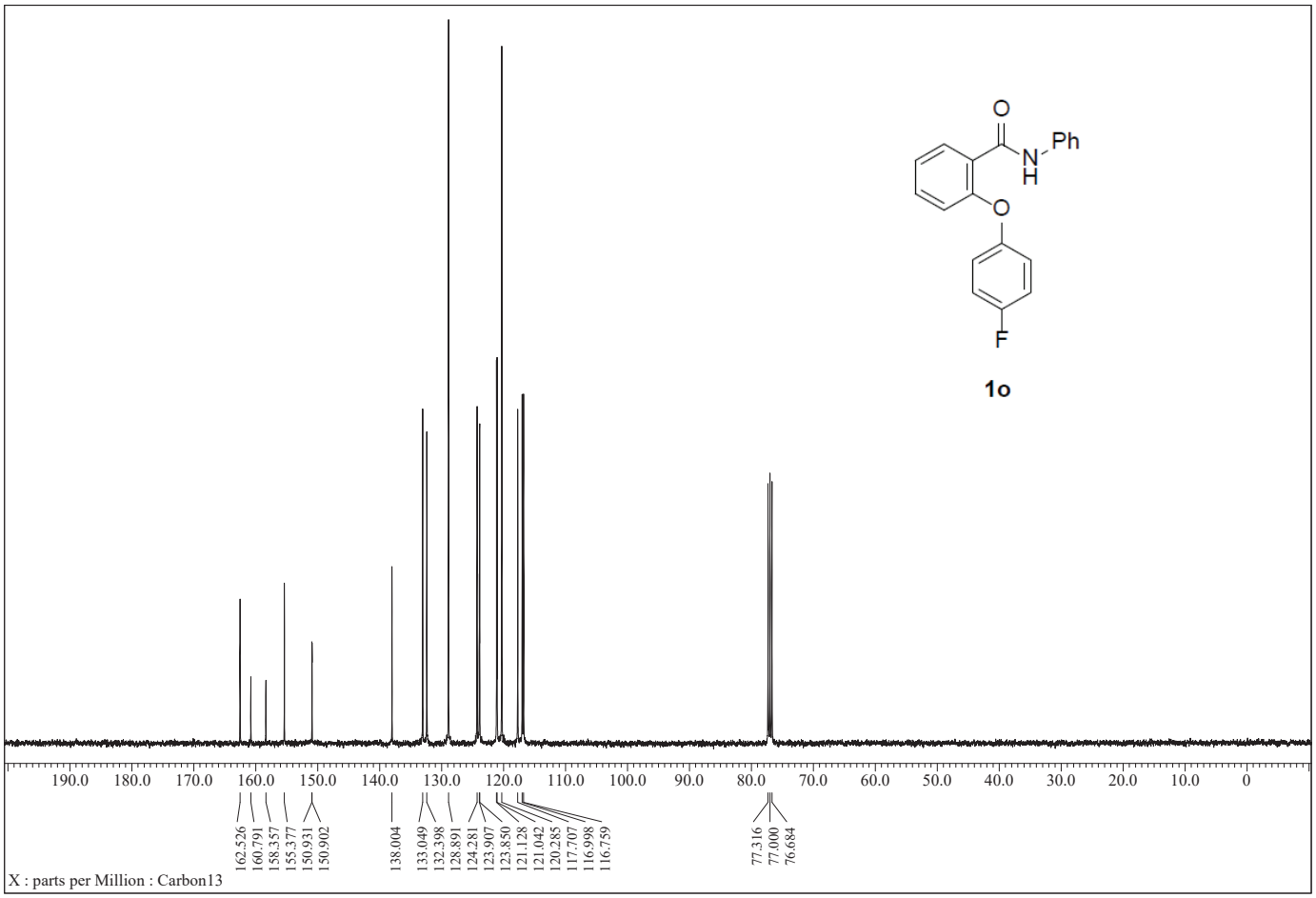

OMe O
Ph
N
H
OPh
1m
5.02
2.86
3.02
2.01
1.71
1.00
0.94
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.553
7.533
7.315
7.297
7.279
7.275
7.252
7.106
7.103
7.087
7.085
7.068
7.066
7.035
7.015
6.721
6.700
6.543
6.522
3.867
0.000
X : parts per Million : Proton

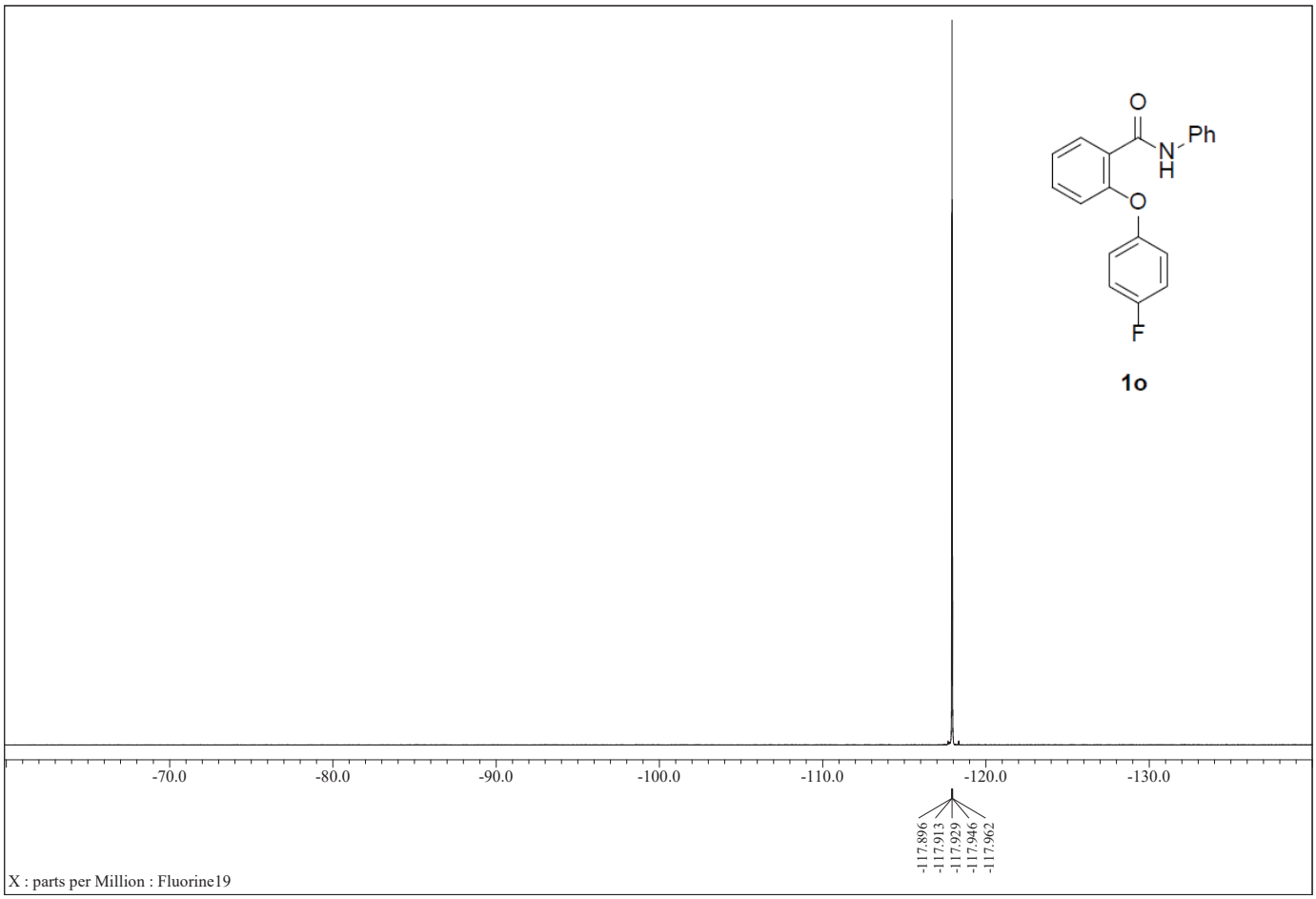

OMe O
Ph
N
H
OPh
1m
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.737
157.917
156.834
155.176
138.013
131.047
129.715
128.862
124.214
123.649
119.796
119.011
118.781
111.277
106.179
77.316
77.000
76.674
56.110
X : parts per Million : Carbon13

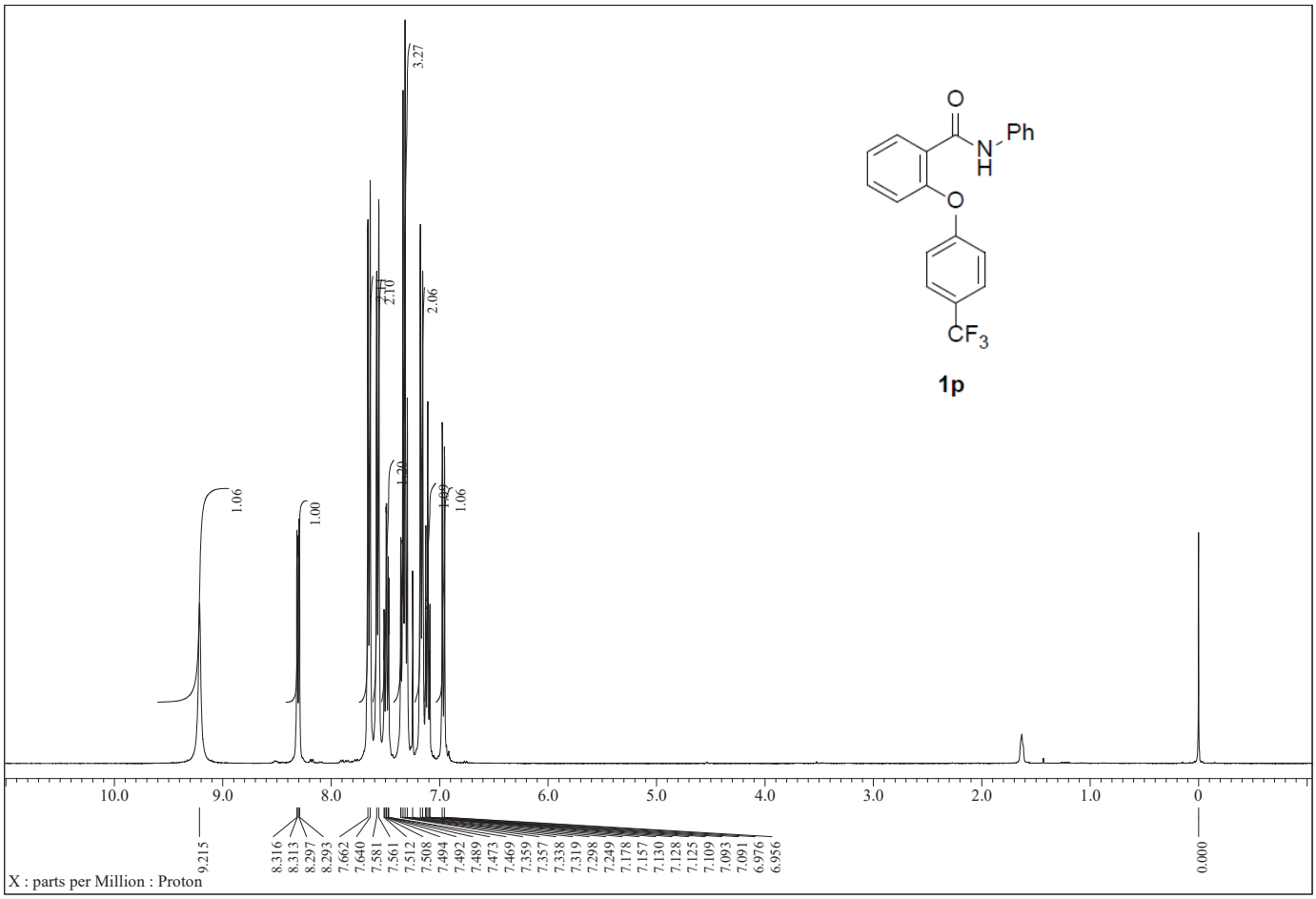

O
N
H
Ph
O
OMe
1n
3.14
2.99
2.05
2.02
1.96
1.06
1.00
0.98
1.00
0.91
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.766
8.346
8.341
8.326
8.322
7.651
7.631
7.404
7.399
7.385
7.381
7.378
7.365
7.360
7.346
7.341
7.327
7.310
7.306
7.301
7.250
7.221
7.218
7.200
7.182
7.180
7.125
7.122
7.119
7.104
7.090
7.085
7.074
7.068
7.059
6.969
6.960
6.954
6.943
6.937
6.928
6.824
6.822
6.803
6.801
3.822
0.000
X : parts per Million : Proton

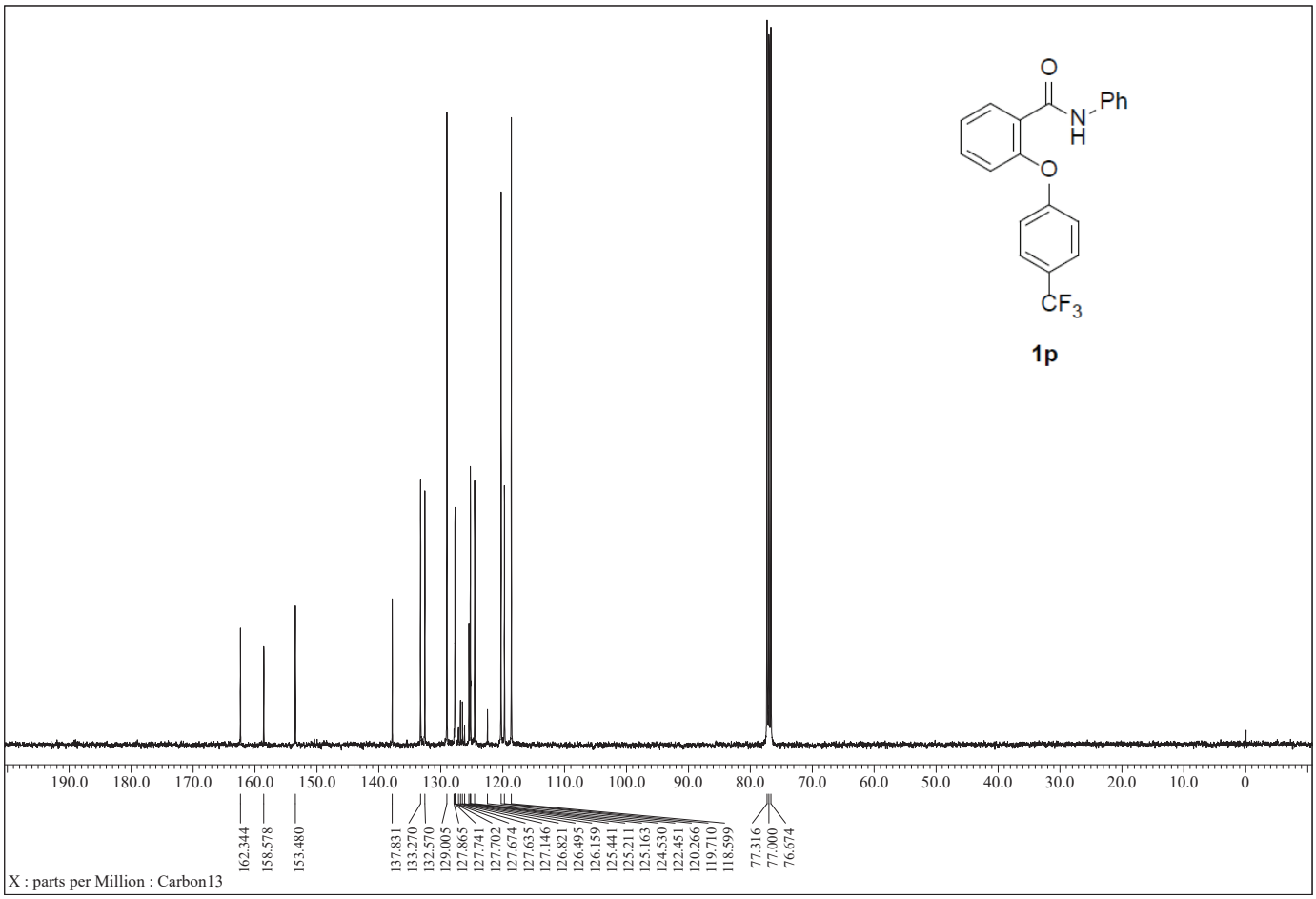

O
N
H
Ph
O
OMe
1n
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.650
156.843
156.259
147.998
138.119
132.906
132.235
128.804
124.090
123.112
121.119
120.256
116.970
115.187
77.316
77.000
76.674
55.525
X : parts per Million : Carbon13

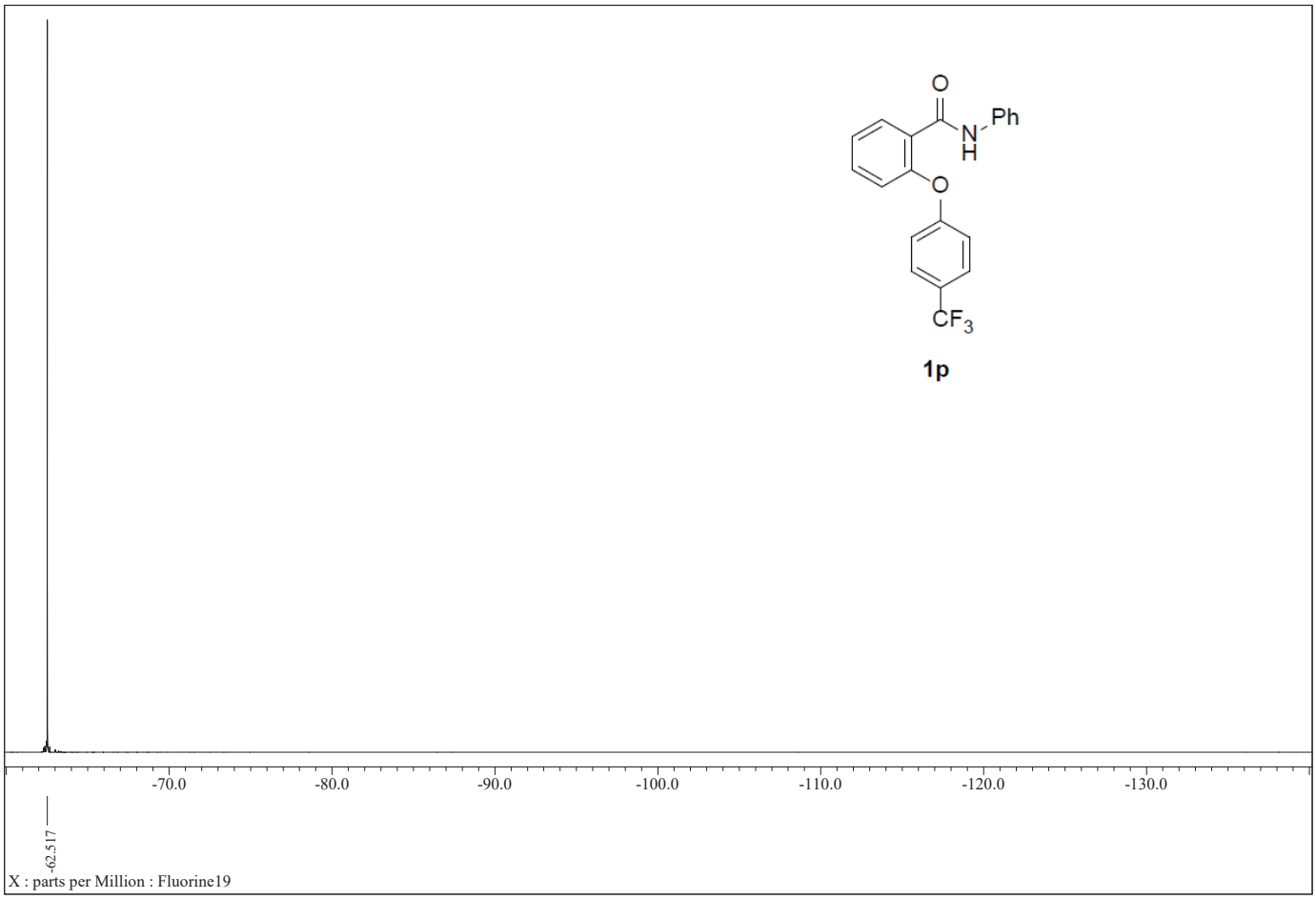

O
N
H
Ph
O
F
1o
5.07
2.05
2.06
1.05
1.06
0.93
1.00
1.02
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.543
8.311
8.307
8.292
8.287
7.628
7.626
7.607
7.422
7.417
7.403
7.399
7.397
7.383
7.378
7.329
7.325
7.310
7.290
7.240
7.235
7.222
7.203
7.114
7.111
7.109
7.095
7.092
7.078
7.065
6.835
6.833
6.814
6.812
0.000
X : parts per Million : Proton

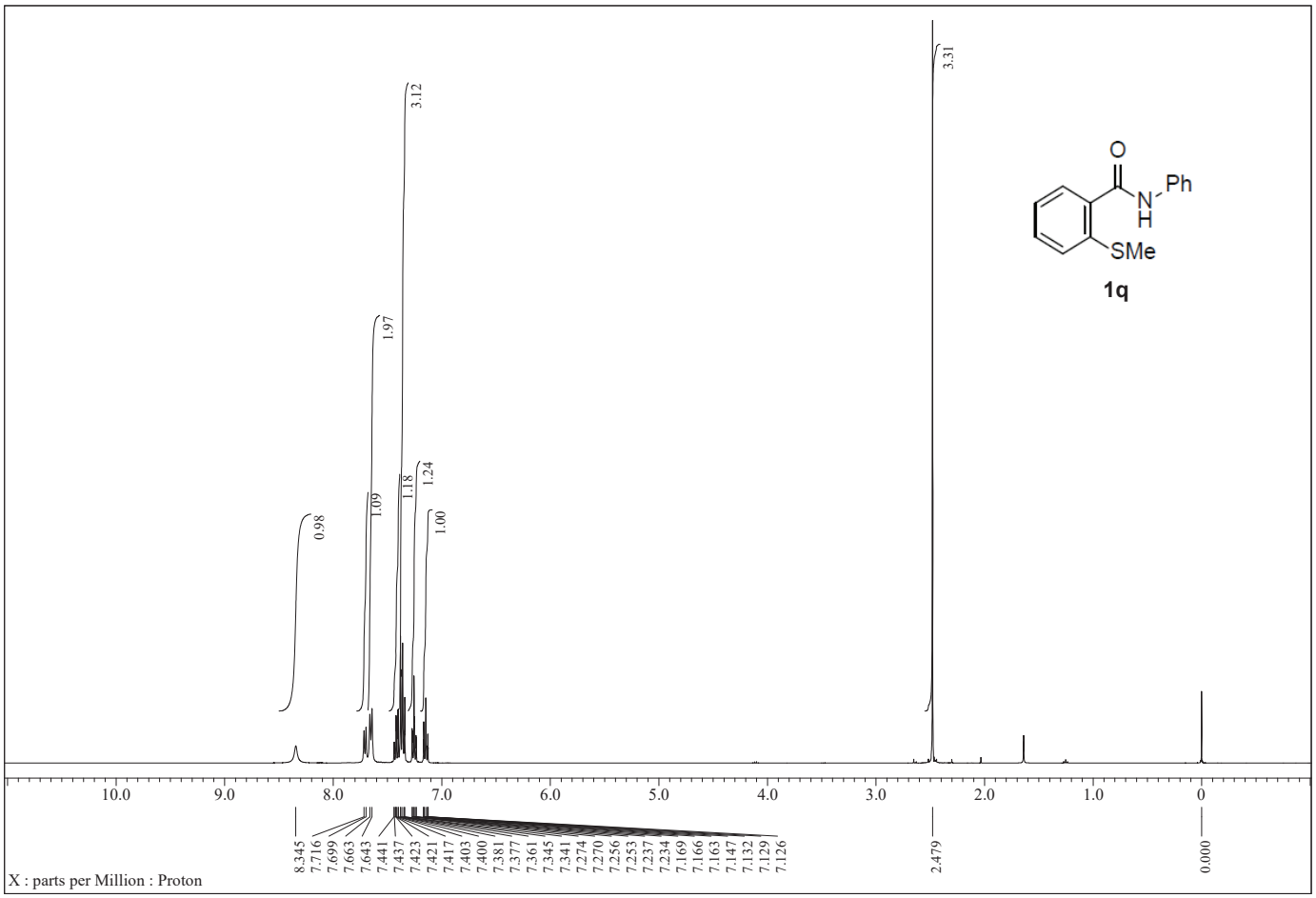

O
N
H
Ph
O
F
1o
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.526
160.791
158.357
155.377
150.931
150.902
138.004
133.049
132.398
128.891
124.281
123.907
123.850
121.128
121.042
120.285
117.707
116.998
116.759
77.316
77.000
76.684
X : parts per Million : Carbon13

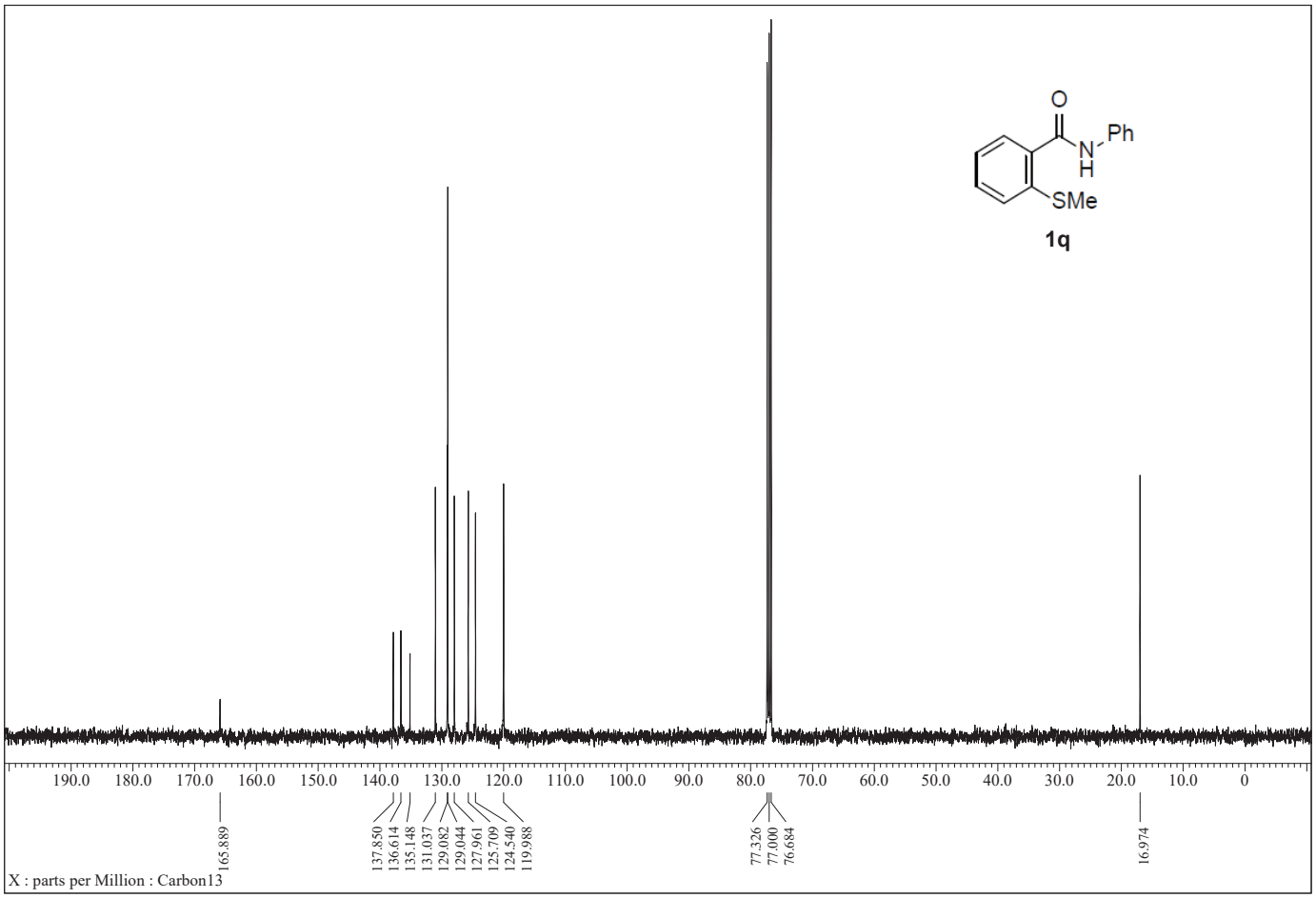

O
N
H
Ph
O
F
1o
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-117.896
-117.913
-117.929
-117.946
-117.962
X : parts per Million : Fluorine19

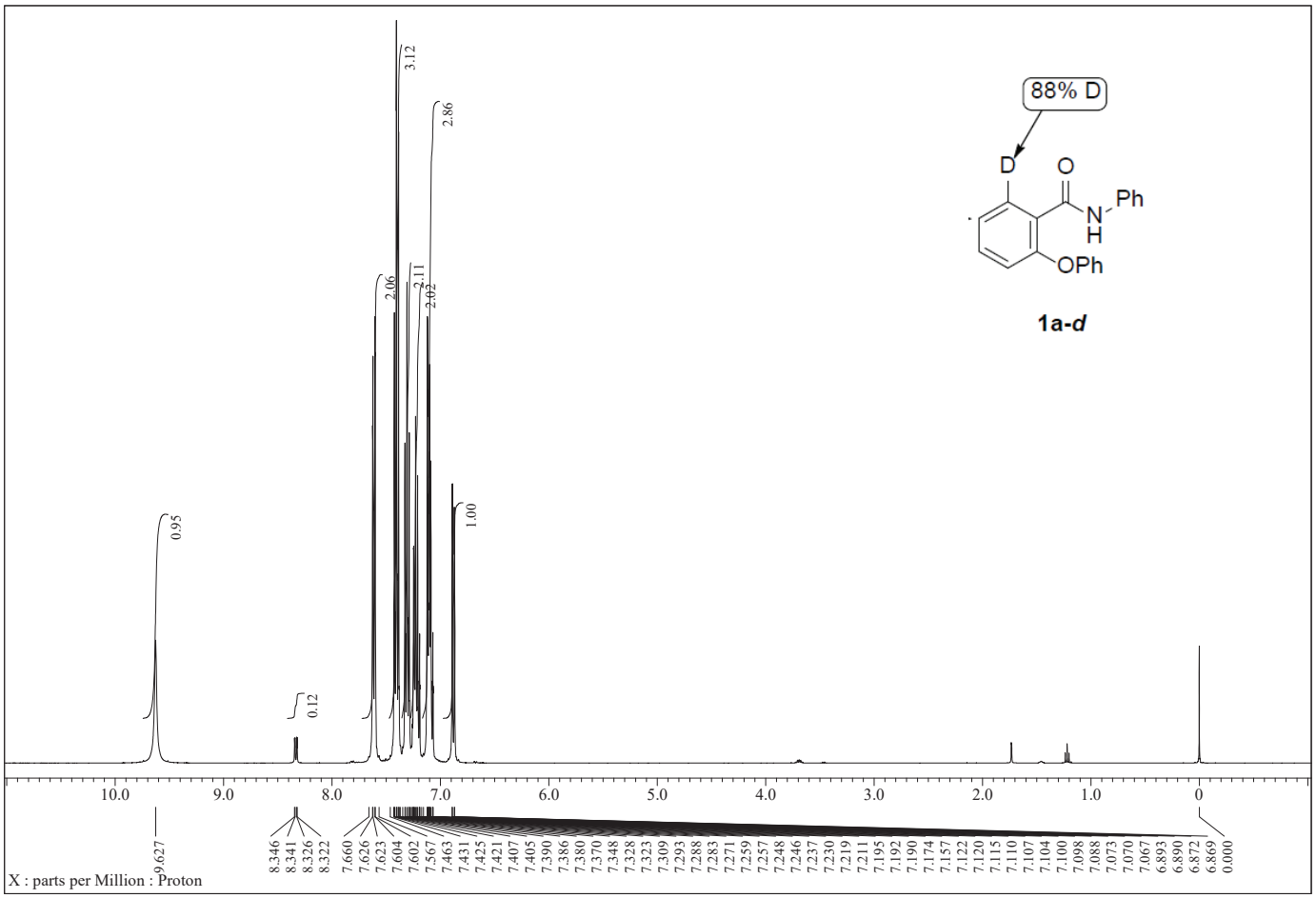

O
N
H
Ph
O
CF3
1p
3.27
2.10
2.06
1.20
1.06
1.00
1.02
1.06
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.215
8.316
8.313
8.297
8.293
7.662
7.640
7.581
7.561
7.512
7.508
7.494
7.492
7.489
7.473
7.469
7.359
7.357
7.338
7.319
7.298
7.249
7.178
7.157
7.130
7.128
7.125
7.109
7.093
7.091
6.976
6.956
0.000
X : parts per Million : Proton

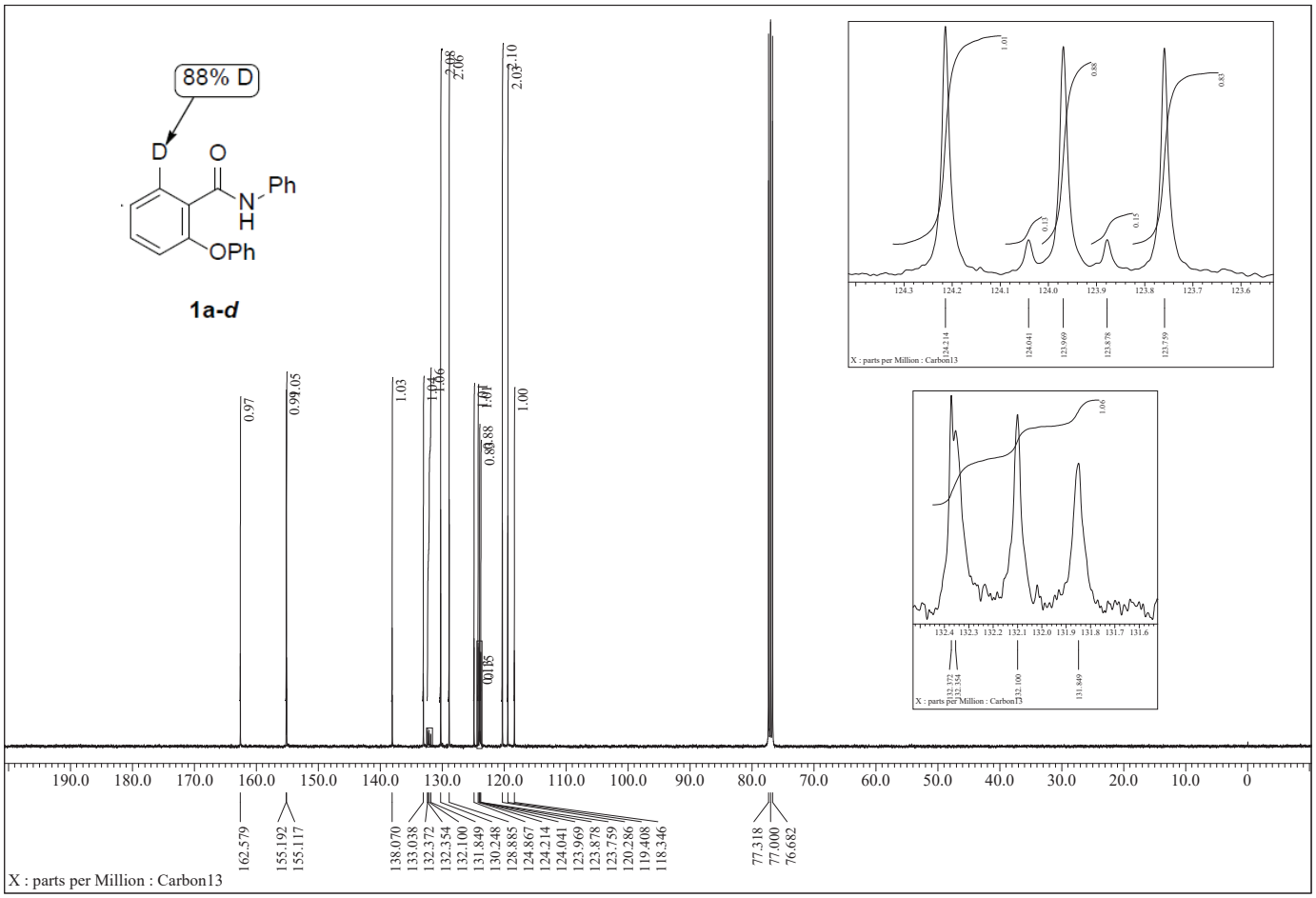

O
N
H
Ph
O
CF3
1p
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.344
158.578
153.480
137.831
133.270
132.570
129.005
127.865
127.741
127.702
127.674
127.635
127.146
126.821
126.495
126.159
125.441
125.211
125.163
124.530
122.451
120.266
119.710
118.599
77.316
77.000
76.674
X : parts per Million : Carbon13

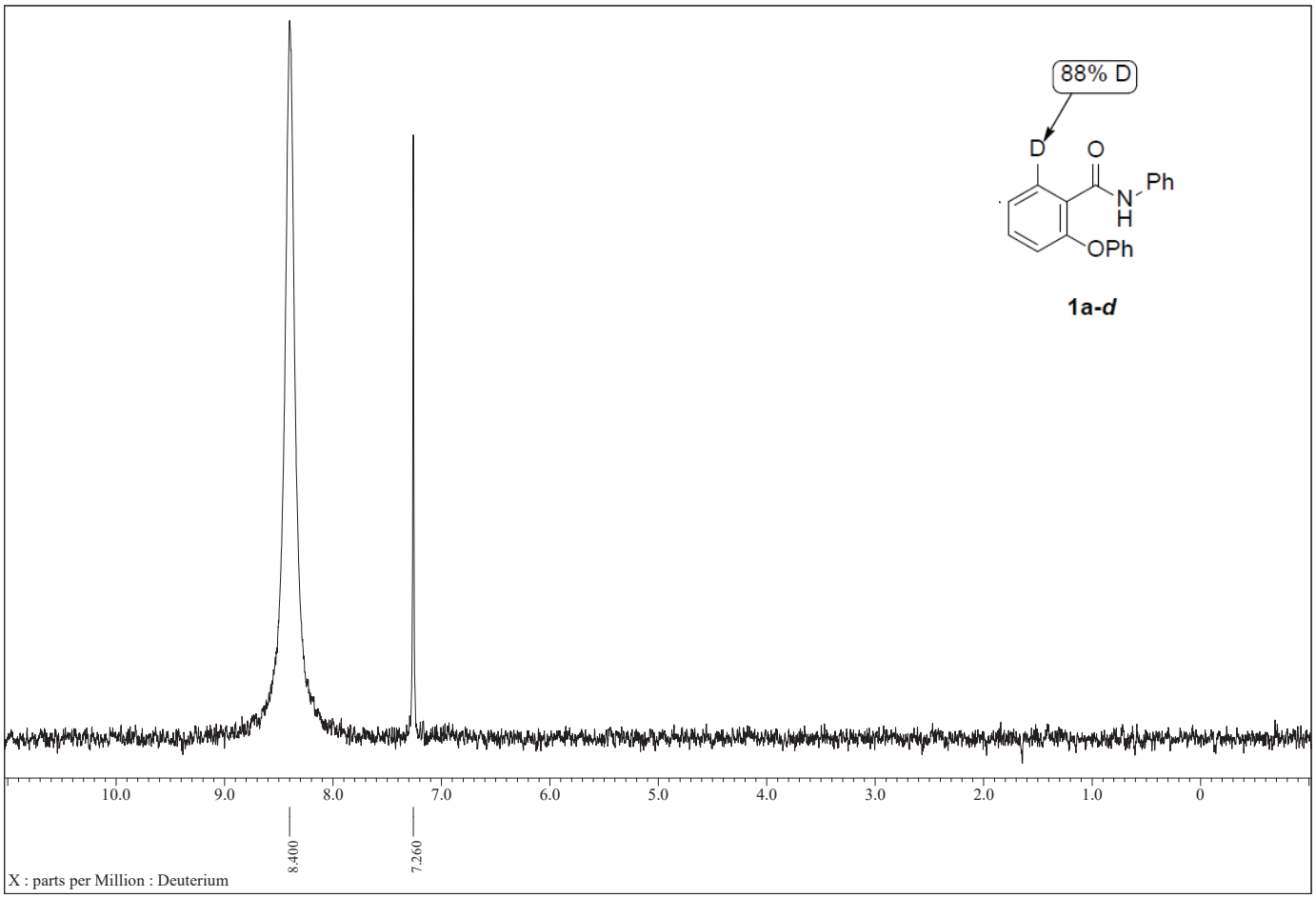

O
N
H
Ph
O
CF3
1p
-70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0
-62.517
X : parts per Million : Fluorine19

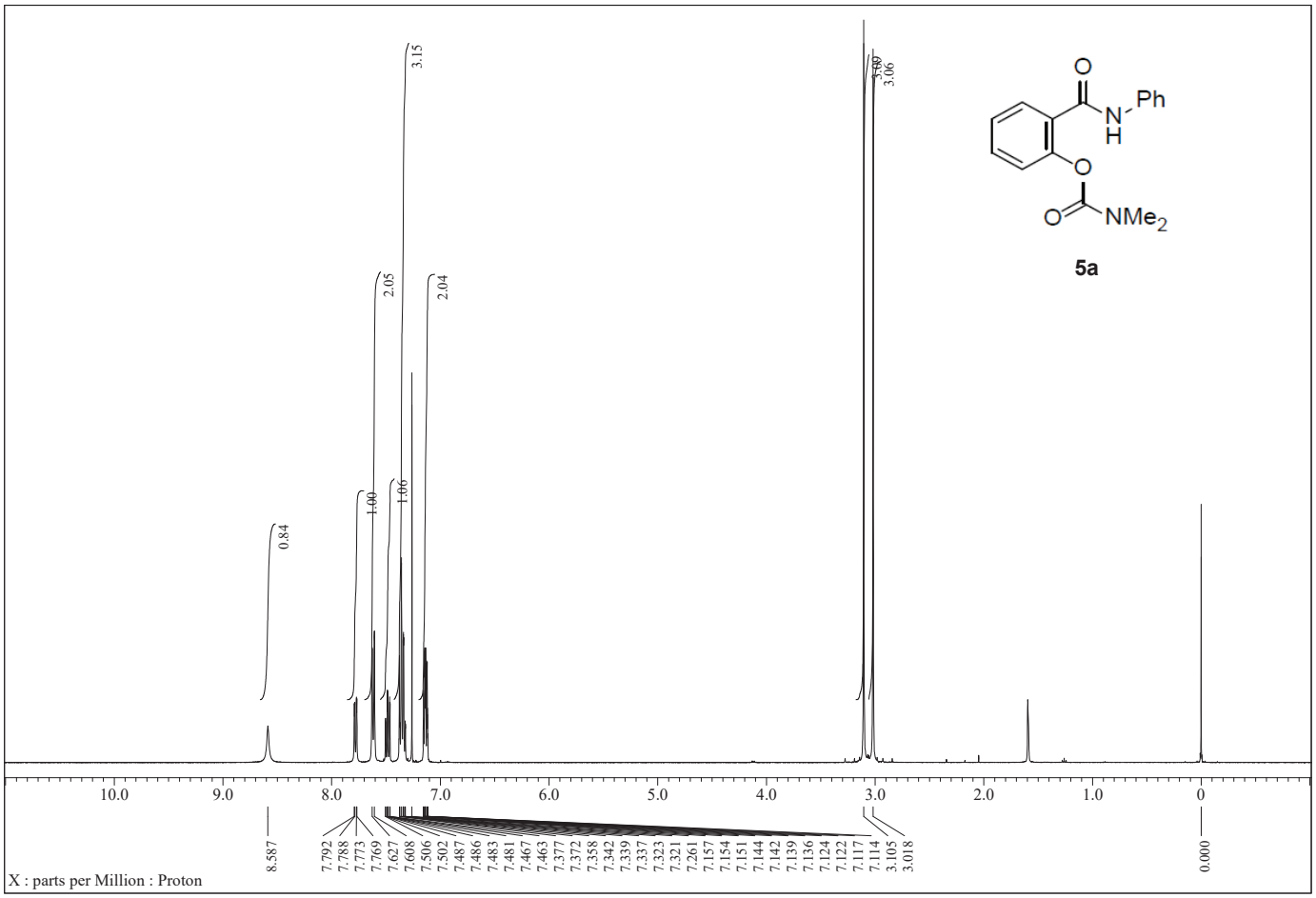

3.31
3.12
1.97
1.18
1.24
1.09
1.00
0.98
O
N
H
Ph
SMe
1q
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.345
7.716
7.699
7.663
7.643
7.441
7.437
7.423
7.421
7.417
7.403
7.400
7.381
7.377
7.361
7.345
7.341
7.274
7.270
7.256
7.253
7.237
7.234
7.169
7.166
7.163
7.147
7.132
7.129
7.126
2.479
0.000
X : parts per Million : Proton

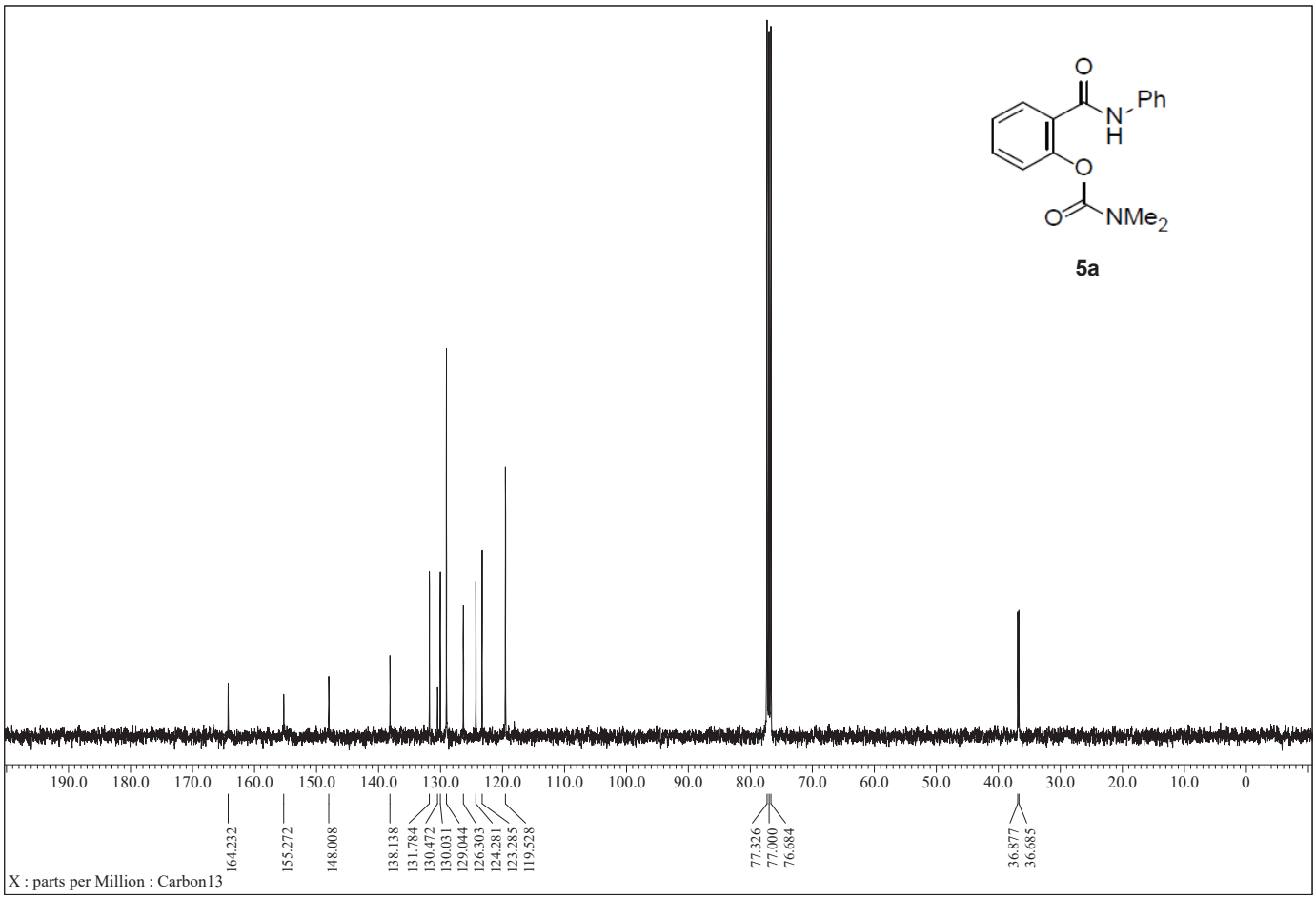

O
N
H
Ph
SMe
1q
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
165.889
137.850
136.614
135.148
131.037
129.082
129.044
127.961
125.709
124.540
119.988
77.326
77.000
76.684
16.974
X : parts per Million : Carbon13

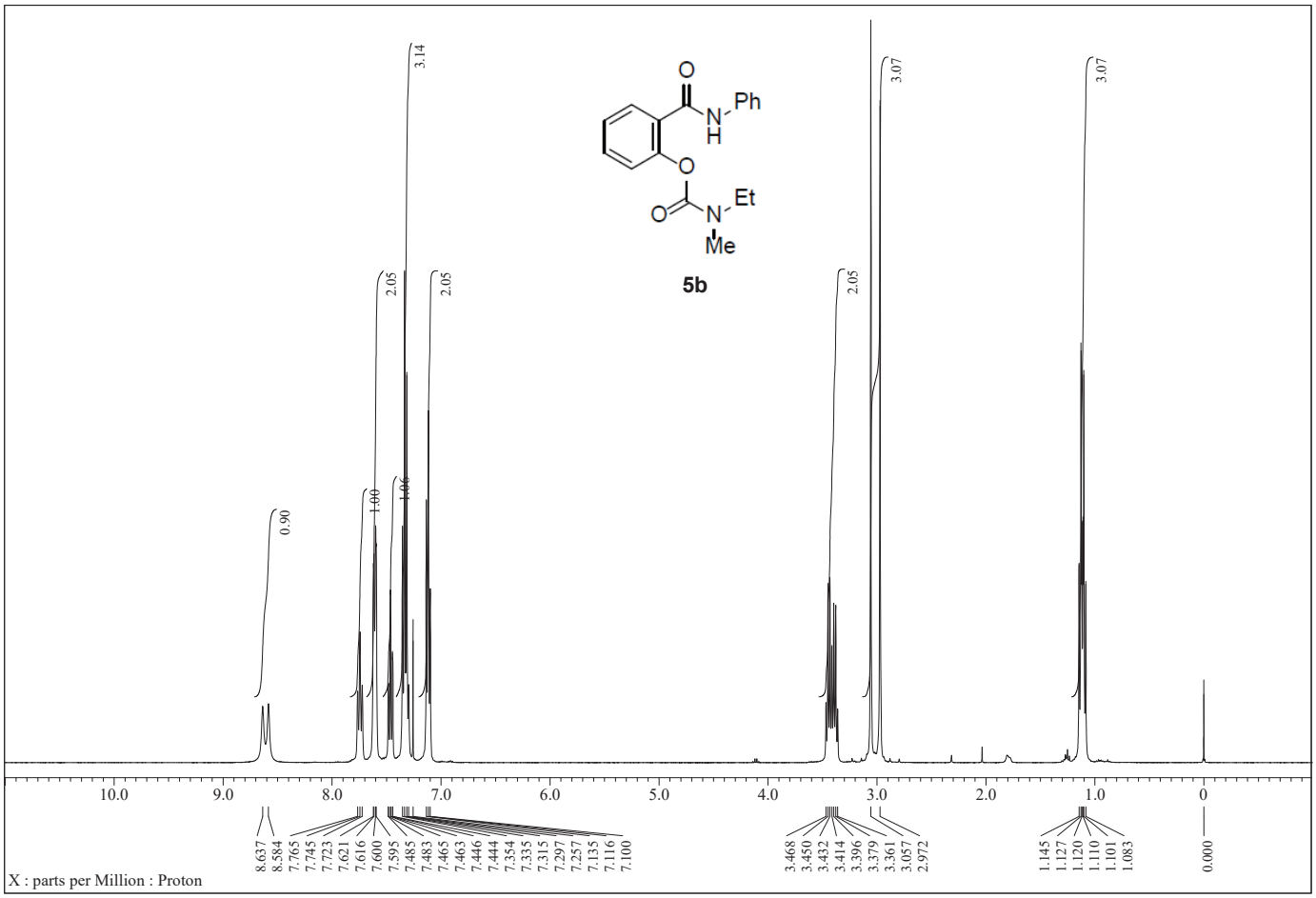

88% D
D
O
N
H
Ph
OPh
1a-d
X : parts per Million : Proton

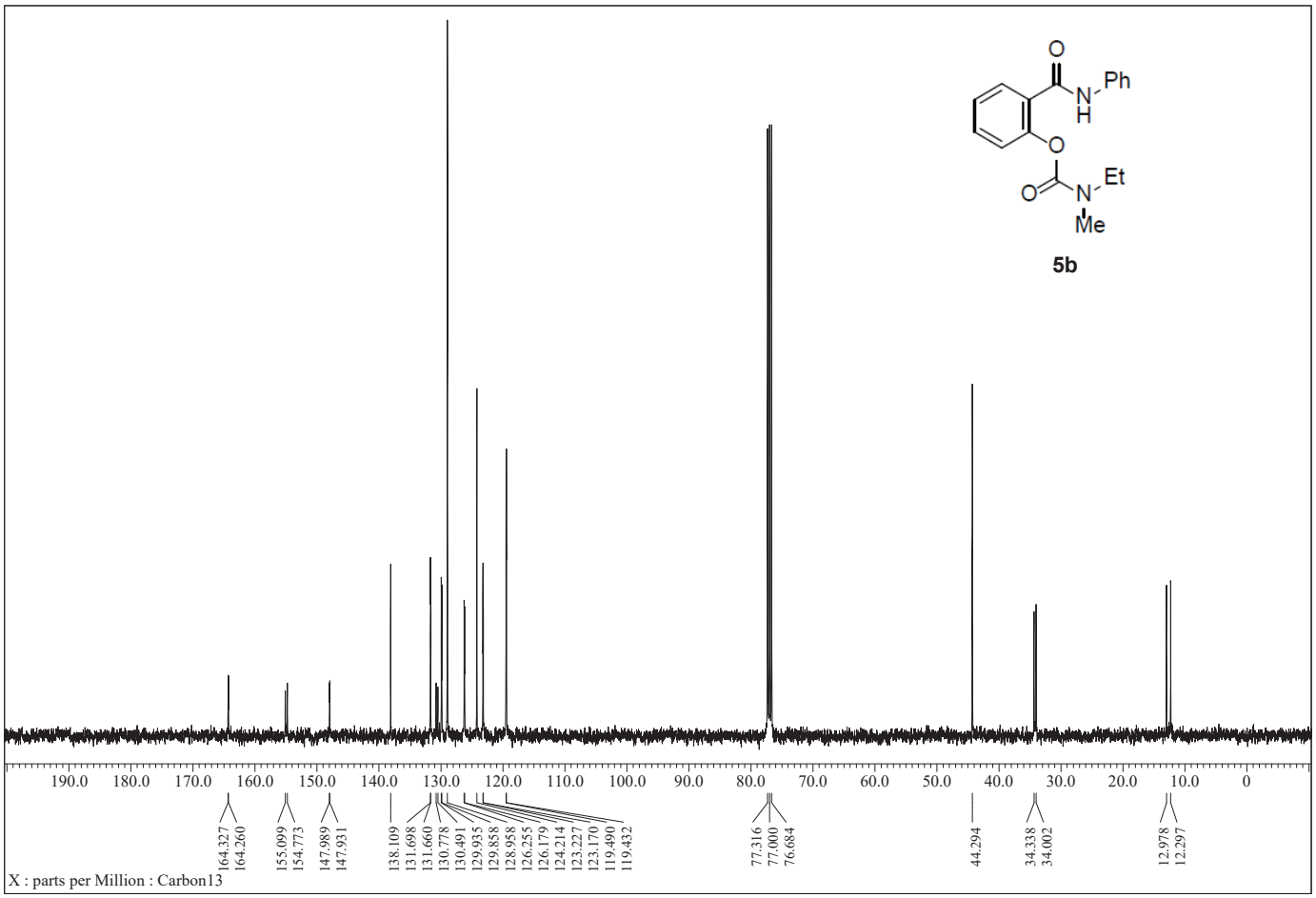

88% D
D
O
N
H
Ph
OPh
1a-d
X : parts per Million : Carbon13

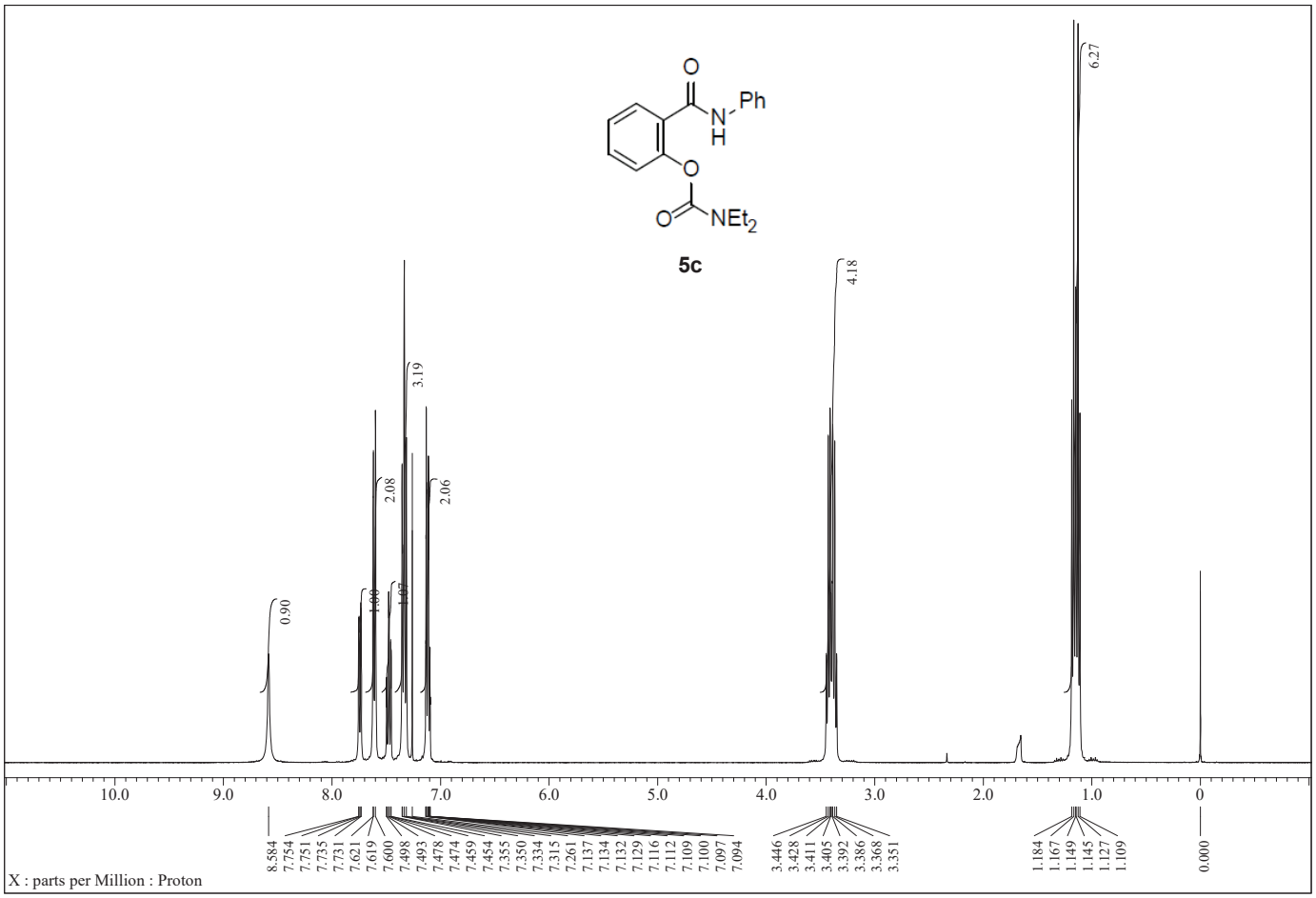

88% D
D
O
N
H
Ph
OPh
1a-d
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.400
7.260
X : parts per Million : Deuterium

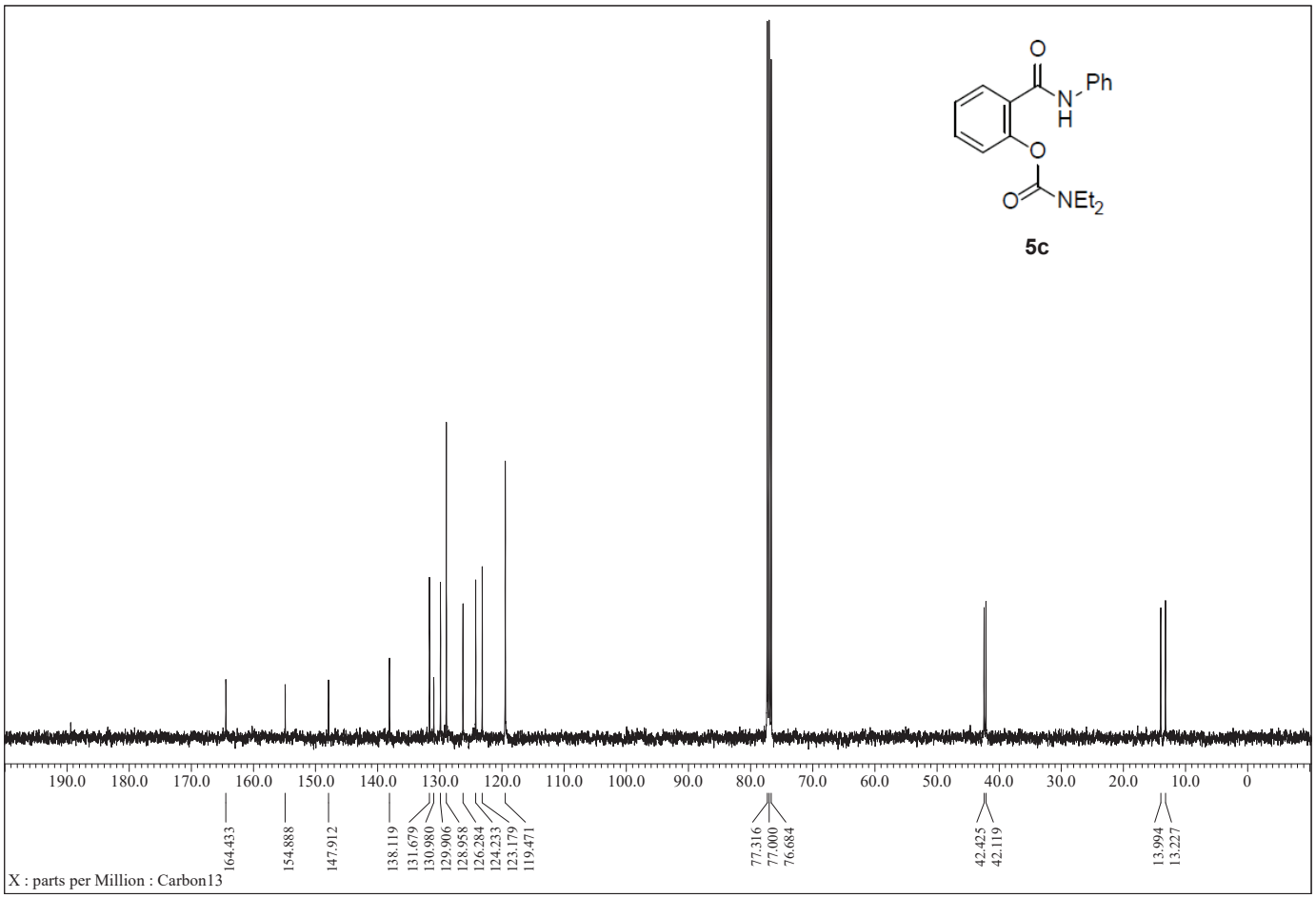

O
N
H
Ph
O
O
NMe2
5a
3.15
3.08
3.06
2.05
2.04
1.00
1.06
0.84
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.587
7.792
7.788
7.773
7.769
7.627
7.608
7.506
7.502
7.487
7.486
7.483
7.481
7.467
7.463
7.377
7.372
7.358
7.342
7.339
7.337
7.323
7.321
7.261
7.157
7.154
7.151
7.144
7.142
7.139
7.136
7.124
7.122
7.117
7.114
3.105
3.018
0.000
X : parts per Million : Proton

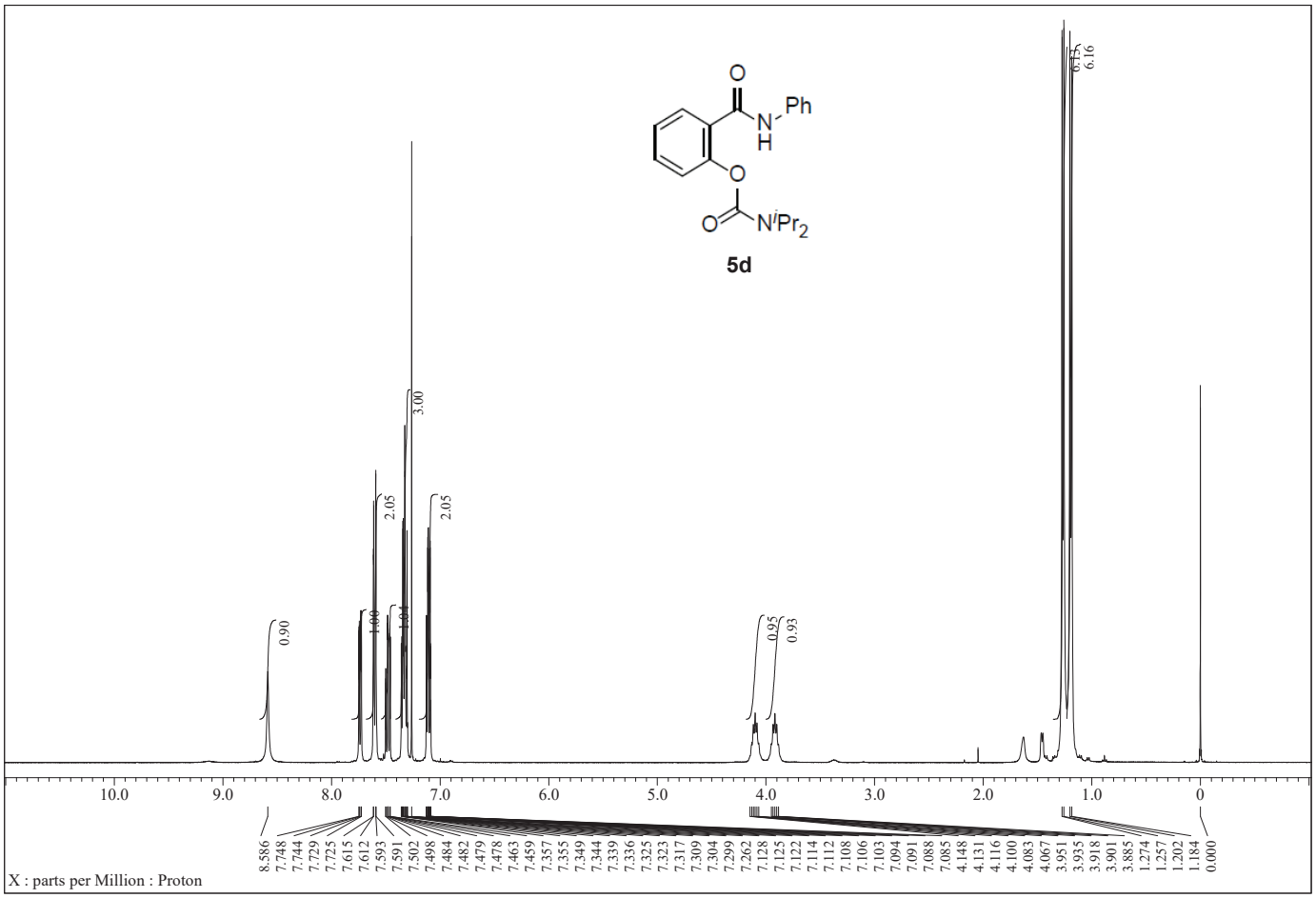

O
N
H
Ph
O
O
NMe2
5a
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
164.232
155.272
148.008
138.138
131.784
130.472
130.031
129.044
126.303
124.281
123.285
119.528
77.326
77.000
76.684
36.877
36.685
X : parts per Million : Carbon13

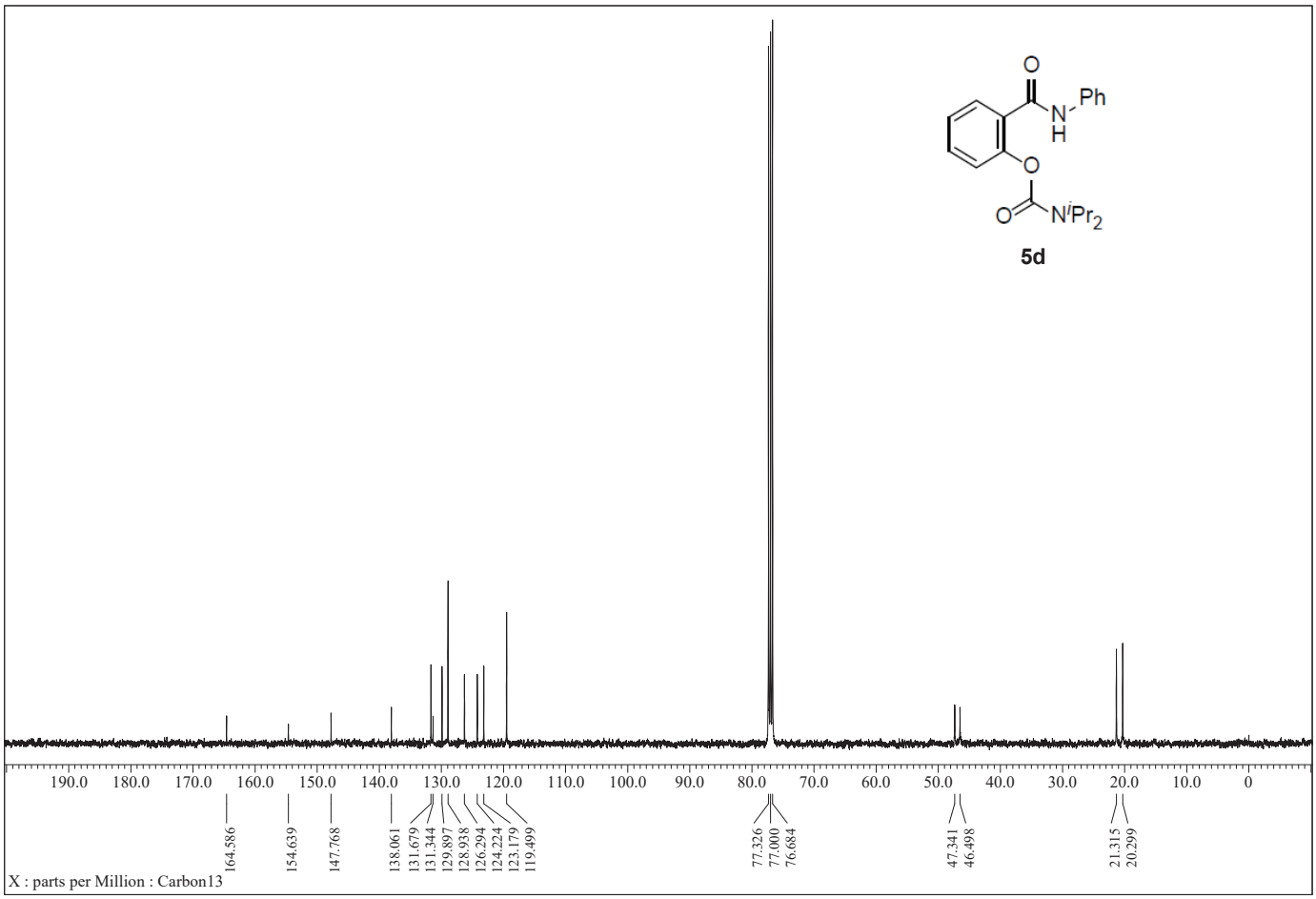

O
N
H
Ph
O
O
N
Et
Me
5b
3.14
3.07
3.07
2.05
2.05
2.05
1.00
1.06
0.90
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.637
8.584
7.765
7.745
7.723
7.621
7.616
7.600
7.595
7.485
7.483
7.465
7.463
7.446
7.444
7.354
7.335
7.315
7.297
7.257
7.135
7.116
7.100
3.468
3.450
3.432
3.414
3.396
3.379
3.361
3.057
2.972
1.145
1.127
1.120
1.110
1.101
1.083
0.000
X : parts per Million : Proton

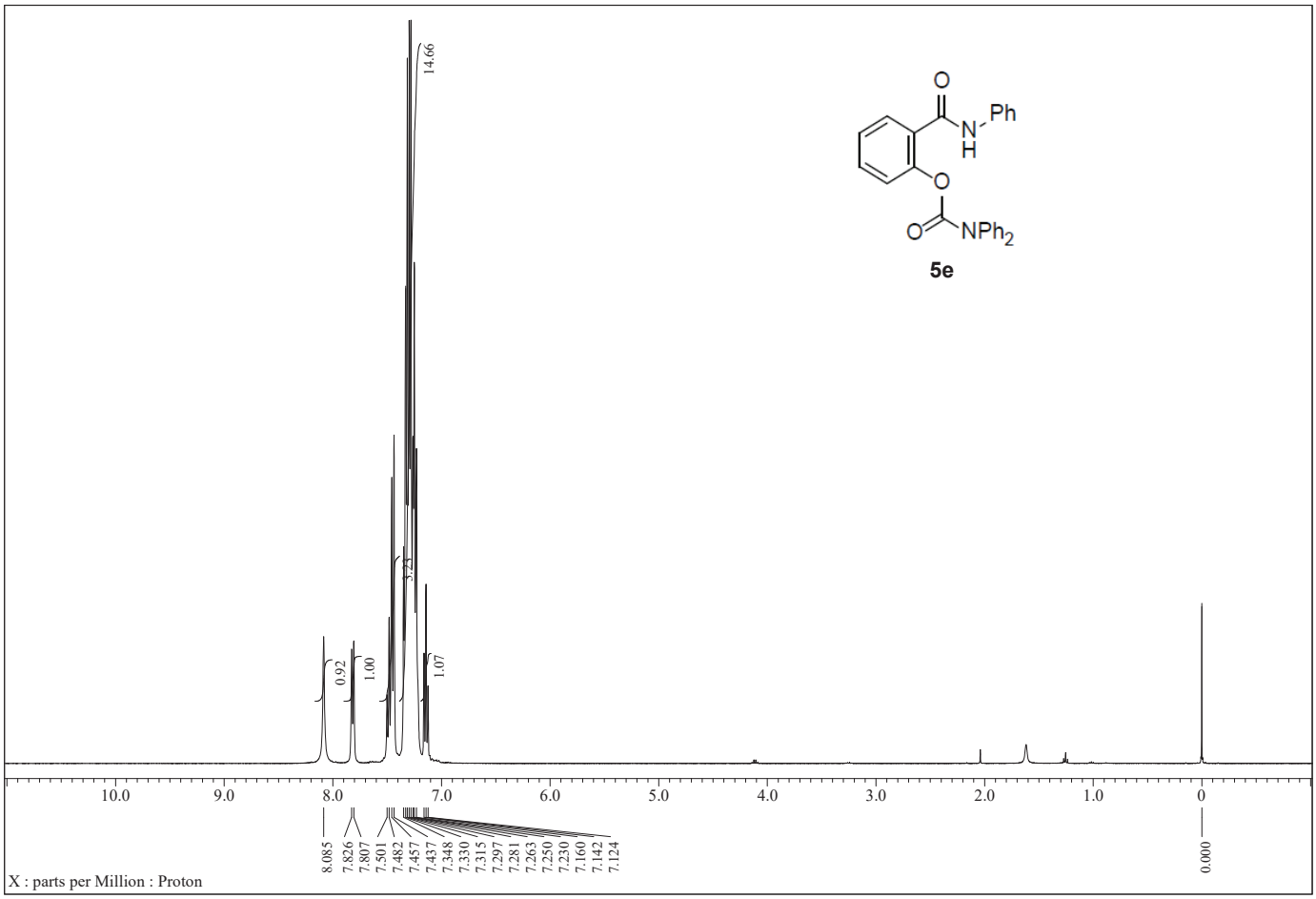

O
N
H
Ph
O
O
N
Et
Me
5b
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
164.327 164.260 155.099 154.773 147.989 147.931 138.109 131.698 131.660 130.778 130.491 129.935 129.858 128.958 126.255 126.179 124.214 123.227 123.170 119.490 119.432 77.316 77.000 76.684 44.294 34.338 34.002 12.978 12.297
X : parts per Million : Carbon13

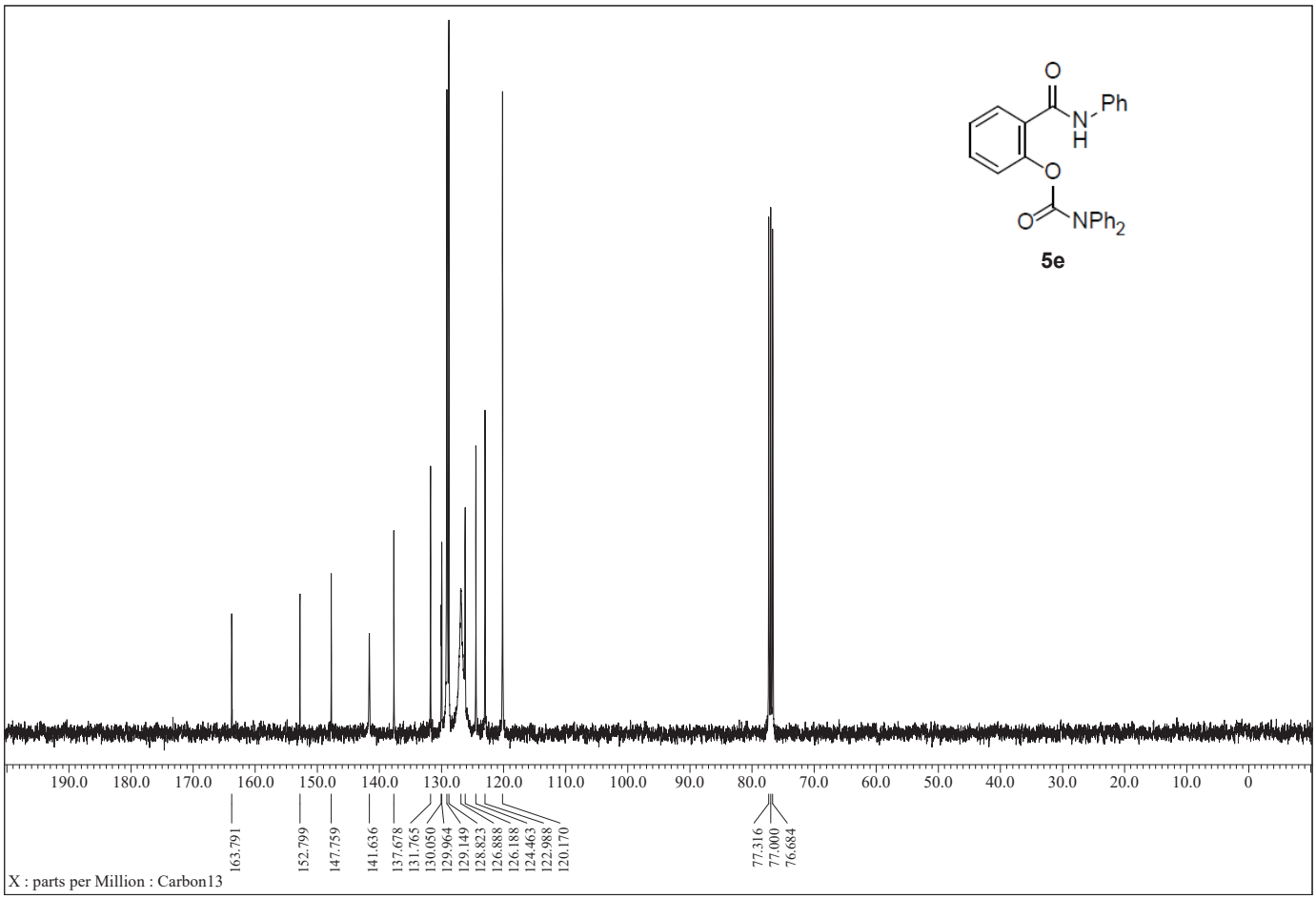

O
N
H
Ph
O
O
NEt2
5c
6.27
4.18
3.19
2.08
2.06
1.88
1.67
0.90
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.584 7.754 7.751 7.735 7.731 7.621 7.619 7.600 7.498 7.493 7.478 7.474 7.459 7.454 7.355 7.350 7.334 7.315 7.261 7.137 7.134 7.132 7.129 7.116 7.112 7.109 7.100 7.097 7.094 3.446 3.428 3.411 3.405 3.392 3.386 3.368 3.351 1.184 1.167 1.149 1.145 1.127 1.109 0.000
X : parts per Million : Proton

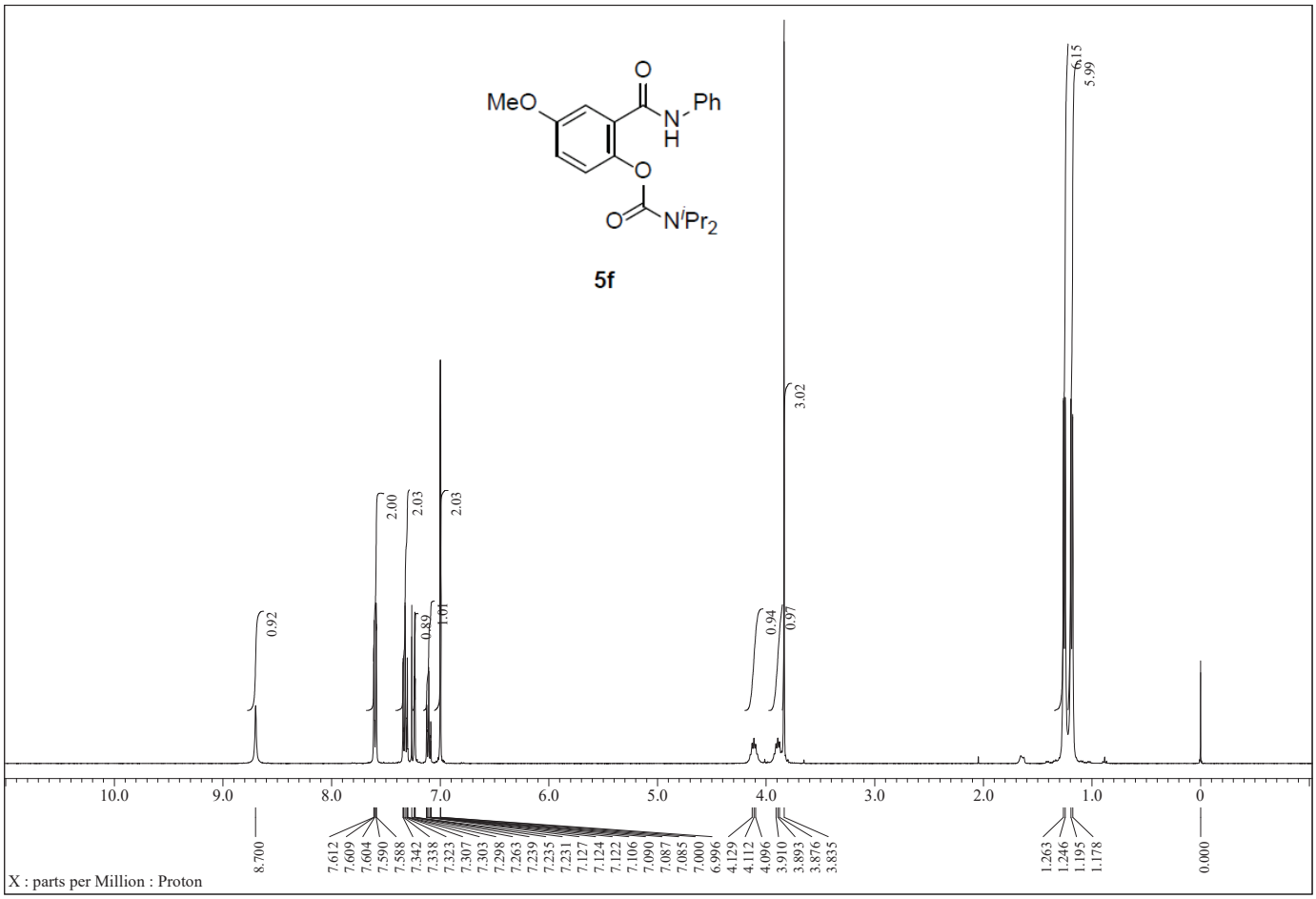

O
N
H
Ph
O
O
NEt2
5c
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
164.433
154.888
147.912
138.119
131.679
130.980
129.906
128.958
126.284
124.233
123.179
119.471
77.316
77.000
76.684
42.425
42.119
13.994
13.227
X : parts per Million : Carbon13

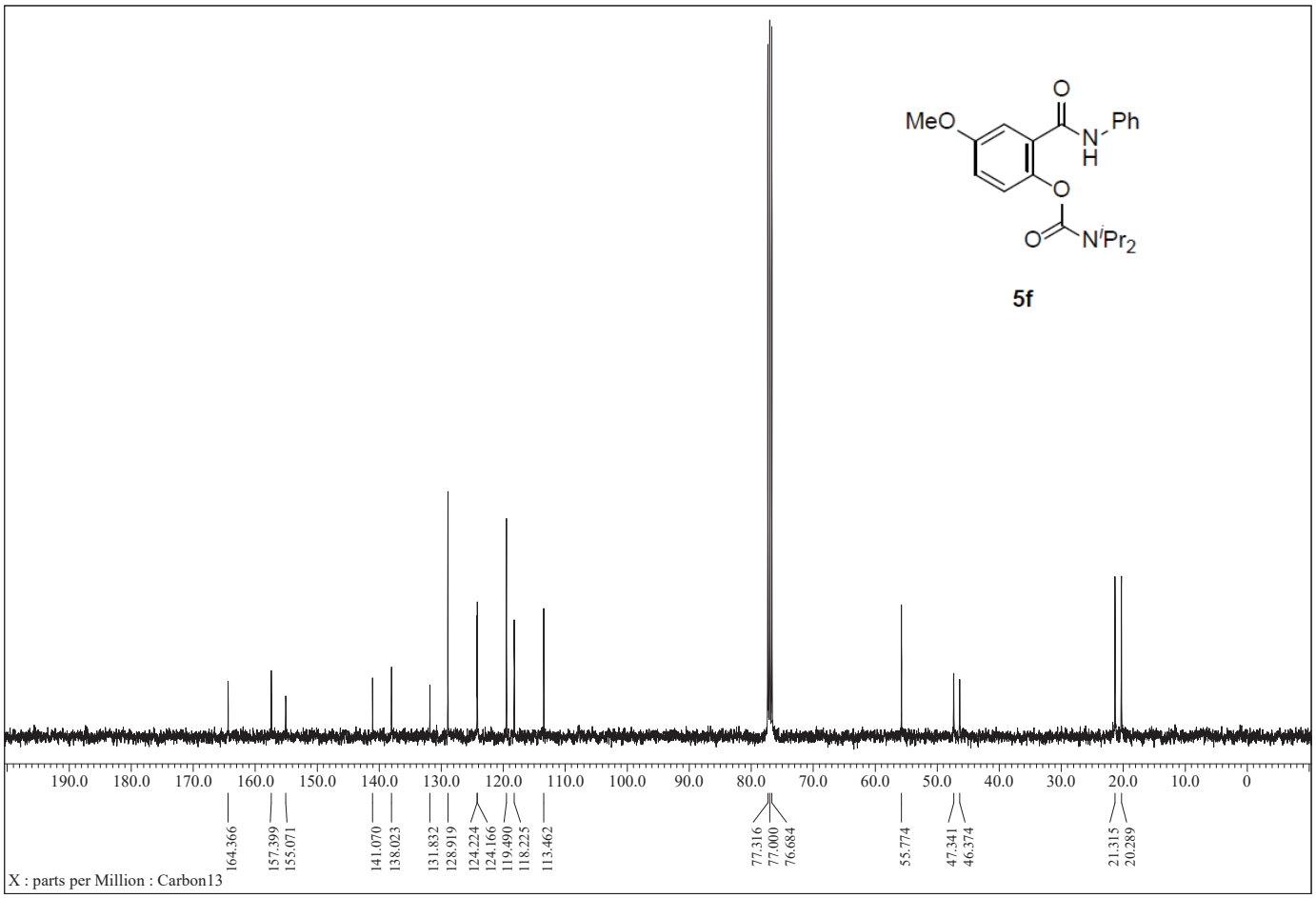

O
N
H
Ph
O
O
NiPr2
5d
6.15
6.16
3.00
2.05
2.05
1.08
1.04
0.90
0.95
0.93
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.586
7.748
7.744
7.729
7.725
7.615
7.612
7.593
7.591
7.502
7.498
7.484
7.482
7.479
7.478
7.463
7.459
7.357
7.355
7.349
7.344
7.339
7.336
7.325
7.323
7.317
7.309
7.304
7.299
7.262
7.128
7.125
7.122
7.114
7.112
7.108
7.106
7.103
7.094
7.091
7.088
7.085
4.148
4.131
4.116
4.100
4.083
4.067
3.951
3.935
3.918
3.901
3.885
1.274
1.257
1.202
1.184
0.000
X : parts per Million : Proton


O
N
Ph
H
O
O
N^{i}Pr$_2$
5d
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
164.586
154.639
147.768
138.061
131.679
131.344
129.897
128.938
126.294
124.224
123.179
119.499
77.326
77.000
76.684
47.341
46.498
21.315
20.299
X : parts per Million : Carbon13

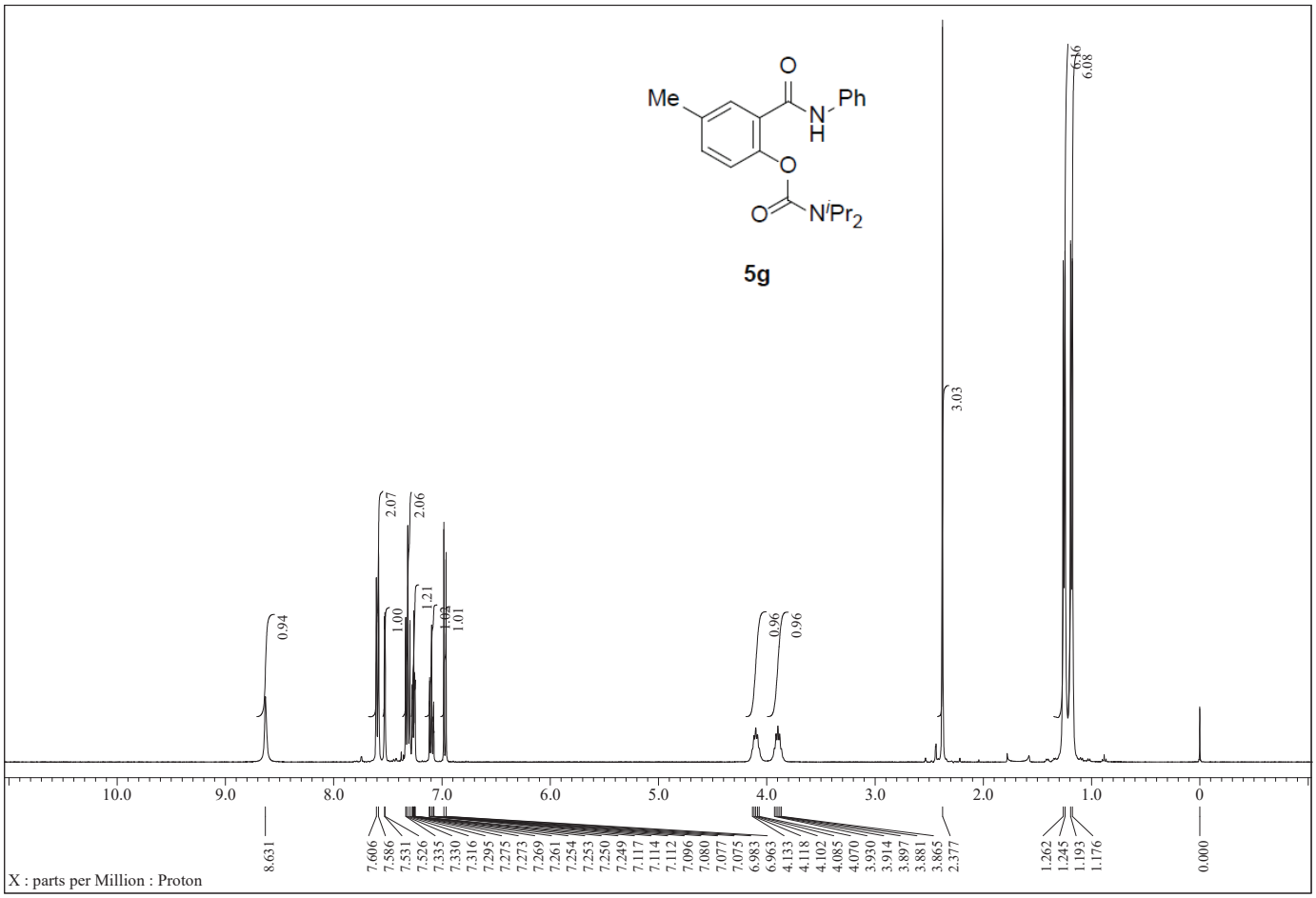

14.66
3.23
0.92
1.00
1.07
O
N
Ph
H
O
O
NPh$_2$
5e
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.085
7.826
7.807
7.501
7.482
7.457
7.437
7.348
7.330
7.315
7.297
7.281
7.263
7.250
7.230
7.160
7.142
7.124
0.000
X : parts per Million : Proton


O
N
Ph
H
O
O
NPh2
5e
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
163.791
152.799
147.759
141.636
137.678
131.765
130.050
129.964
129.149
128.823
126.888
126.188
124.463
122.988
120.170
77.316
77.000
76.684
X : parts per Million : Carbon13

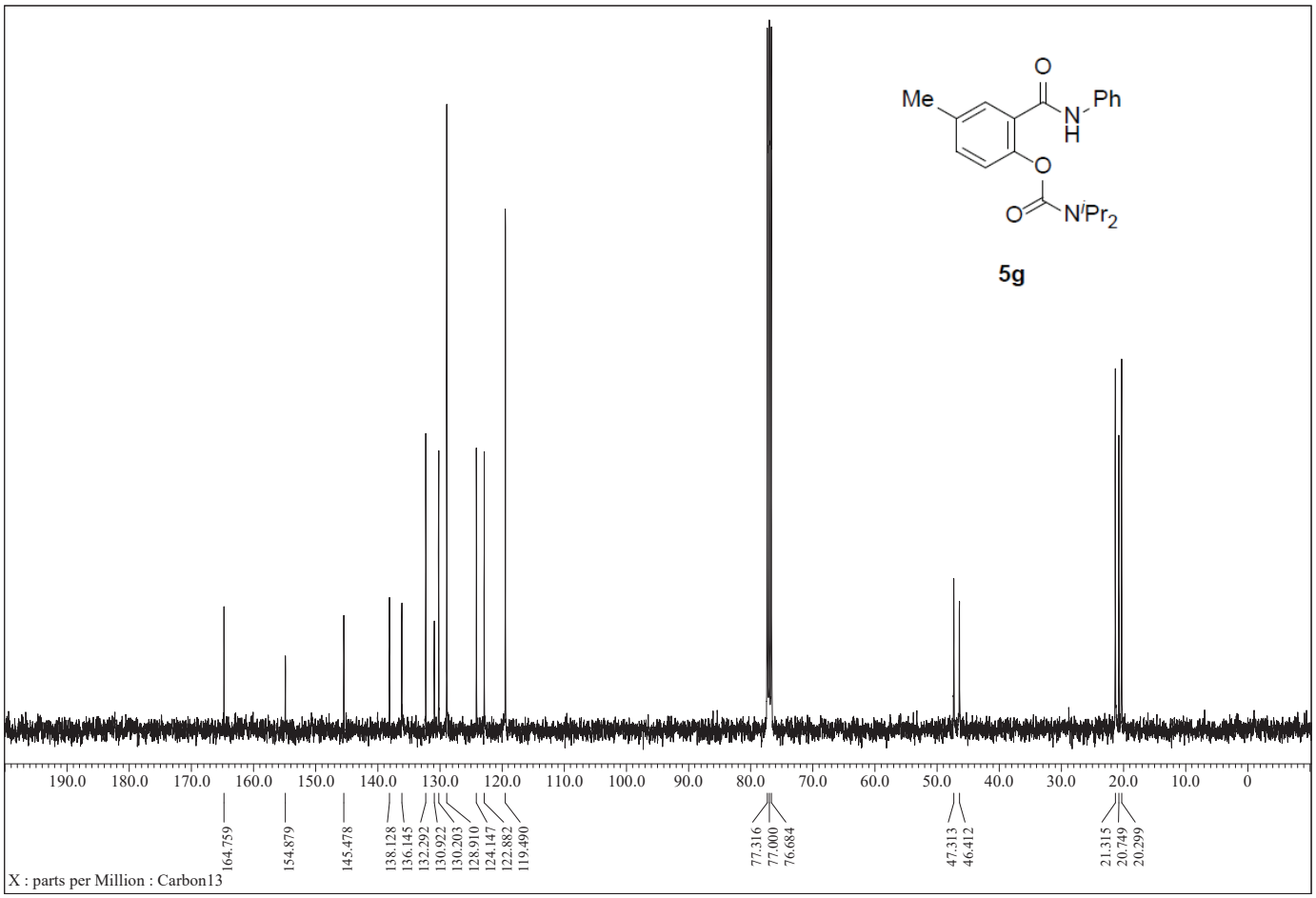

MeO
O
N
Ph
H
O
O
N^{i}Pr$_2$
5f
0.92
2.00
2.03
2.03
0.89
1.01
0.94
0.97
3.02
6.15
5.99
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.700
7.612
7.609
7.604
7.590
7.588
7.342
7.338
7.323
7.307
7.303
7.298
7.263
7.239
7.235
7.231
7.127
7.124
7.122
7.106
7.090
7.087
7.085
7.000
6.996
4.129
4.112
4.096
3.910
3.893
3.876
3.835
1.263
1.246
1.195
1.178
0.000
X : parts per Million : Proton

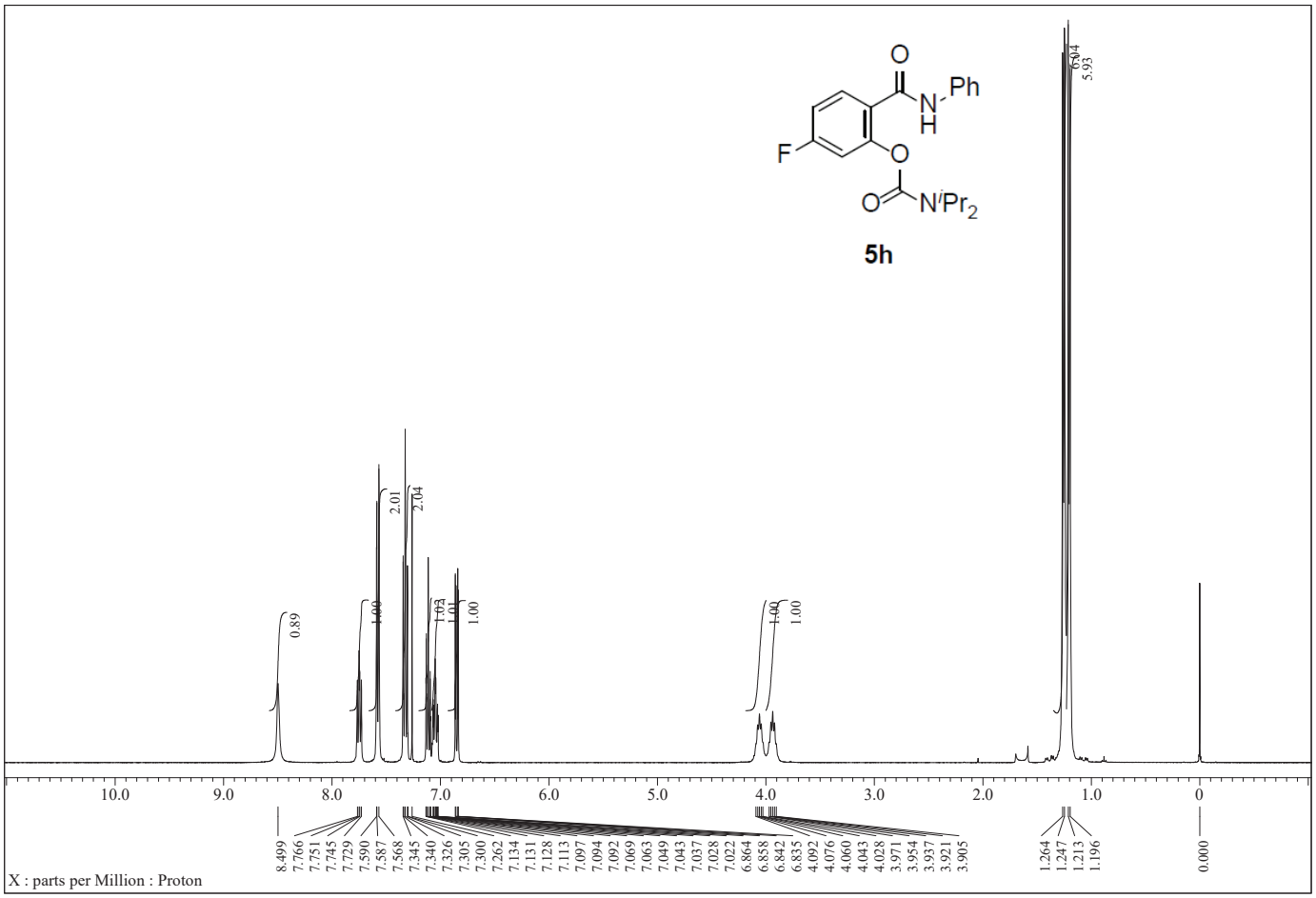

MeO
O
N
H
Ph
O
O
N^{i}Pr$_2$
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
164.366
157.399
155.071
141.070
138.023
131.832
128.919
124.224
124.166
119.490
118.225
113.462
77.316
77.000
76.684
55.774
47.341
46.374
21.315
20.289
X : parts per Million : Carbon13

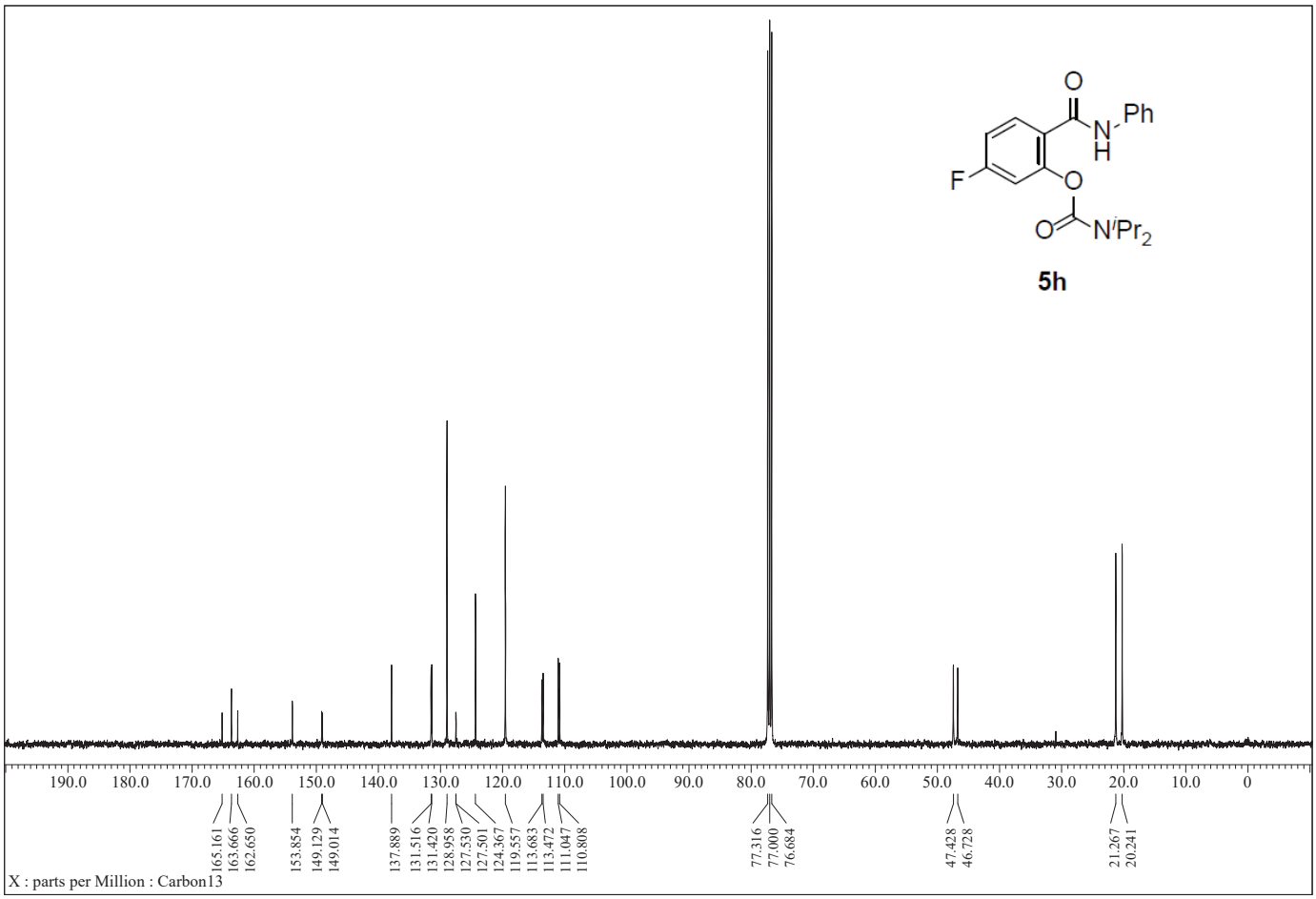
5f

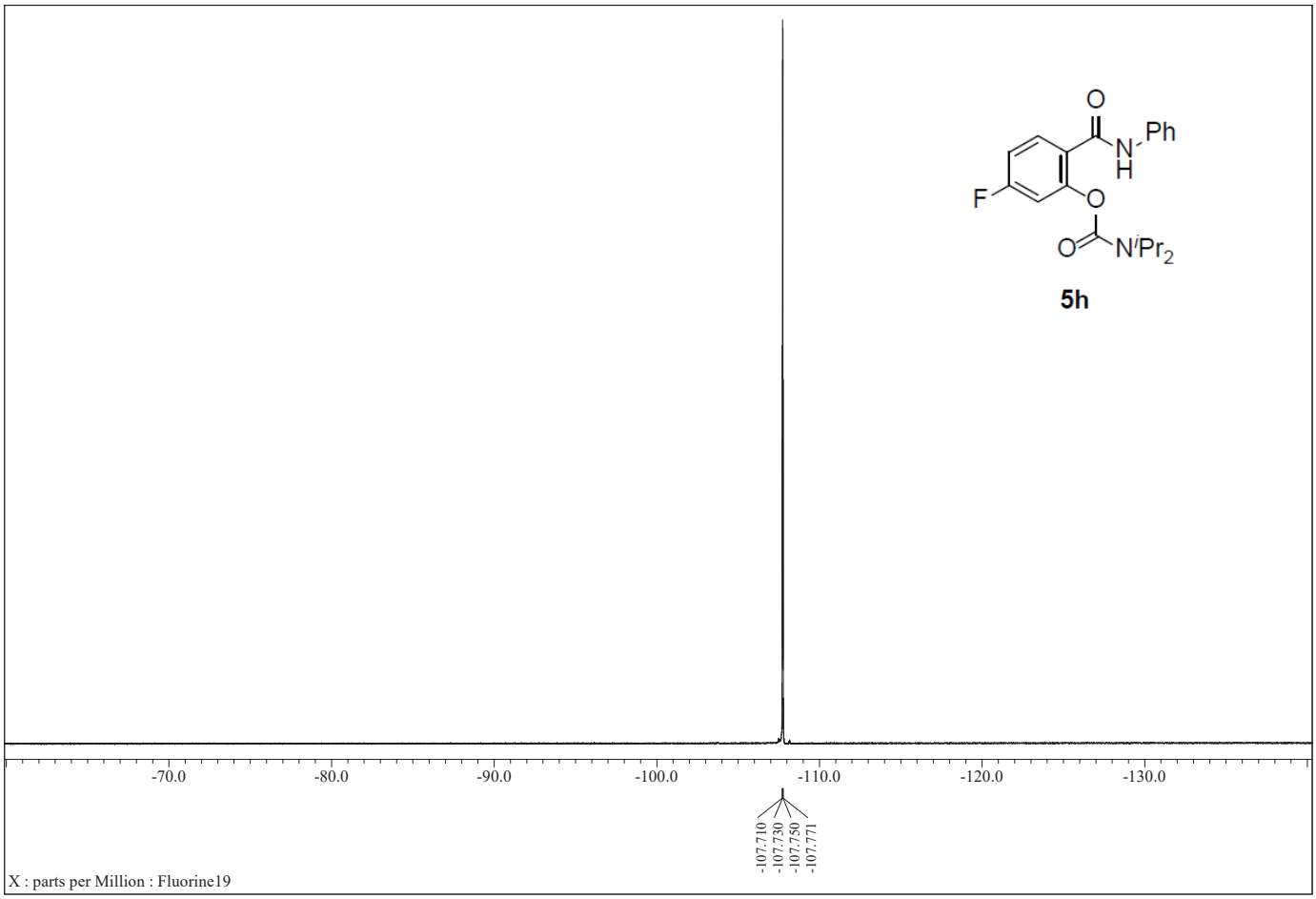

Me
O
N
H
Ph
O
O
N^{i}Pr$_2$
6.16
6.08
3.03
2.07
2.06
1.21
1.03
1.01
1.00
0.94
0.96
0.96
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.631
7.606
7.586
7.531
7.526
7.335
7.330
7.316
7.295
7.275
7.273
7.269
7.261
7.254
7.253
7.250
7.249
7.117
7.114
7.112
7.096
7.080
7.077
7.075
6.983
6.963
4.133
4.118
4.102
4.085
4.070
3.930
3.914
3.897
3.881
3.865
2.377
1.262
1.245
1.193
1.176
0.000
X : parts per Million : Proton

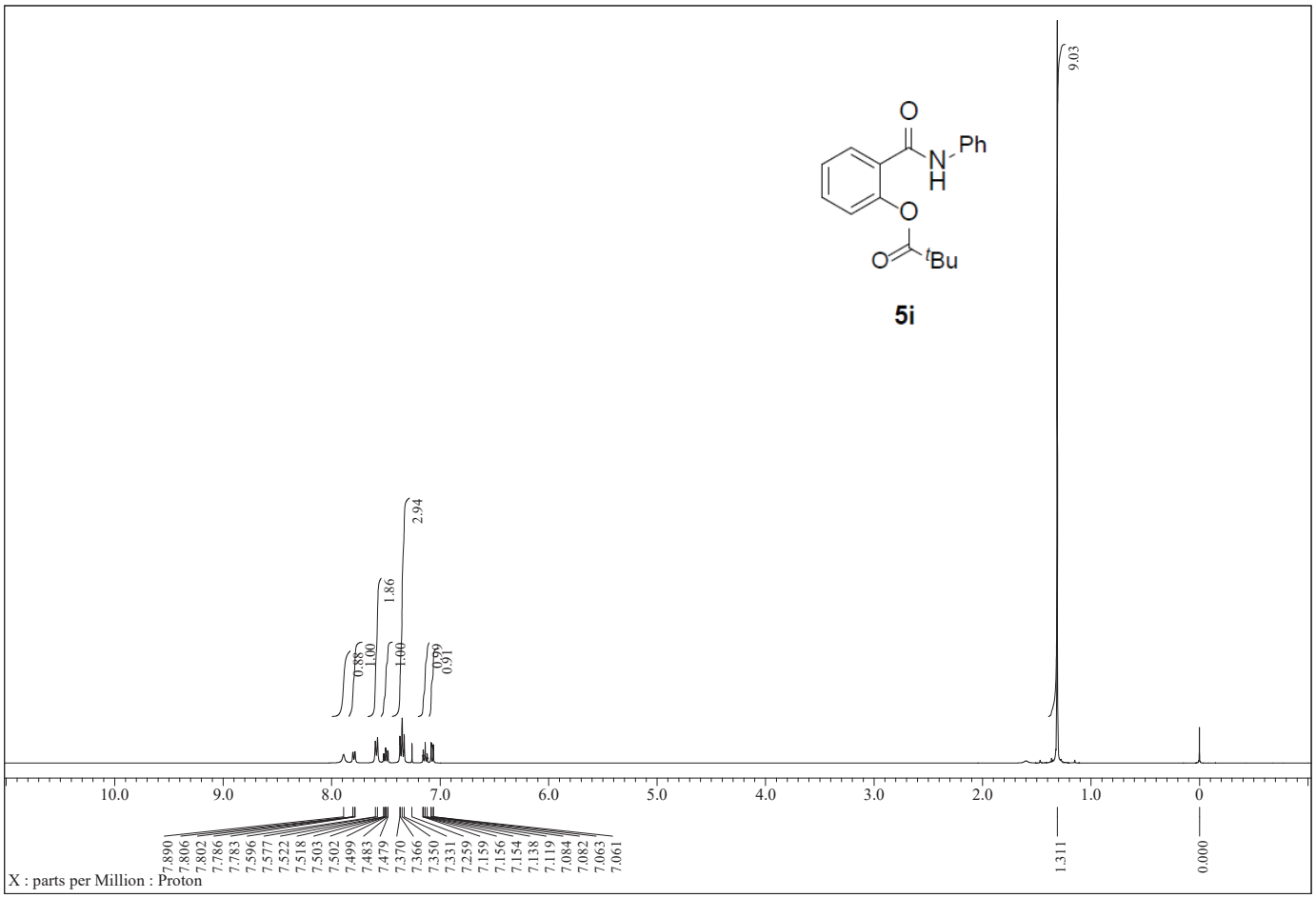
5g

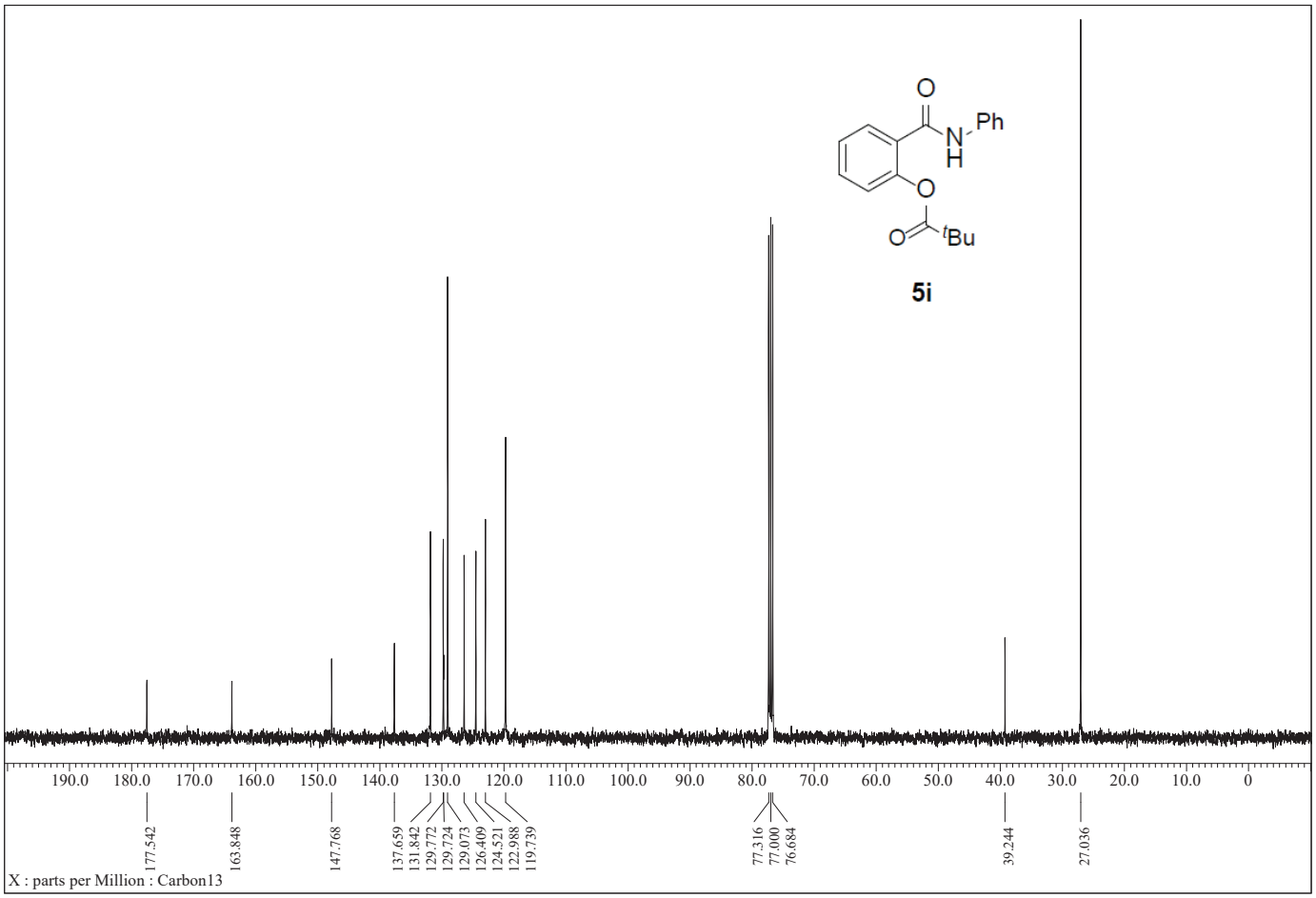

Me
O
N
H
Ph
O
O
N^{i}Pr$_2$
5g
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
164.759
154.879
145.478
138.128
136.145
132.292
130.922
130.203
128.910
124.147
122.882
119.490
77.316
77.000
76.684
47.313
46.412
21.315
20.749
20.299
X : parts per Million : Carbon13

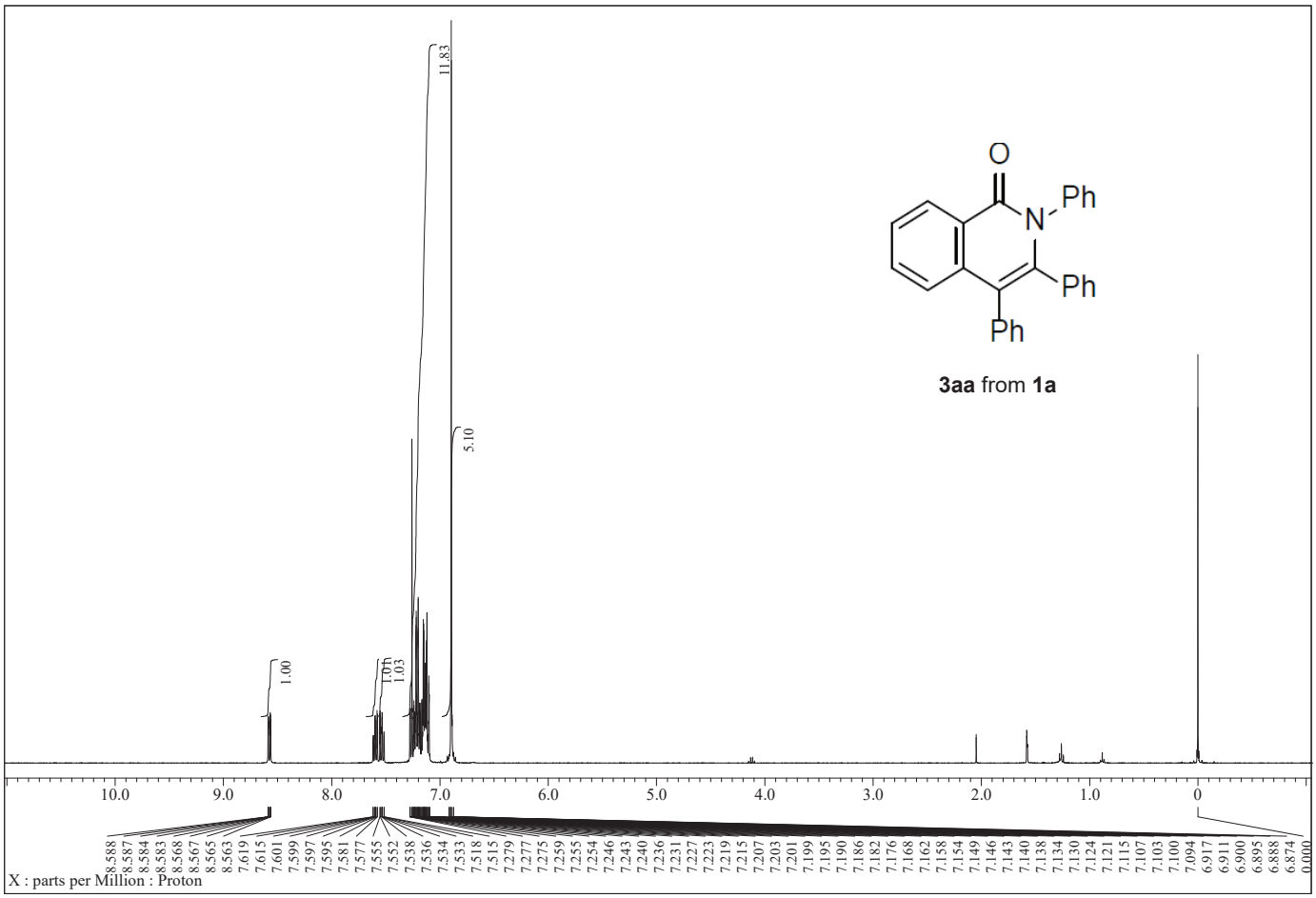

O
N
H
Ph
F
O
O
N^{i}Pr$_2$
5h
6.94
5.93
0.89
1.00
2.01
2.04
1.03
1.01
1.00
1.00
1.00
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.499
7.766
7.751
7.745
7.729
7.590
7.587
7.568
7.345
7.340
7.326
7.305
7.300
7.262
7.134
7.131
7.128
7.113
7.097
7.094
7.092
7.069
7.063
7.049
7.043
7.037
7.028
7.022
6.864
6.858
6.842
6.835
4.092
4.076
4.060
4.043
4.028
3.971
3.954
3.937
3.921
3.905
1.264
1.247
1.213
1.196
0.000
X : parts per Million : Proton

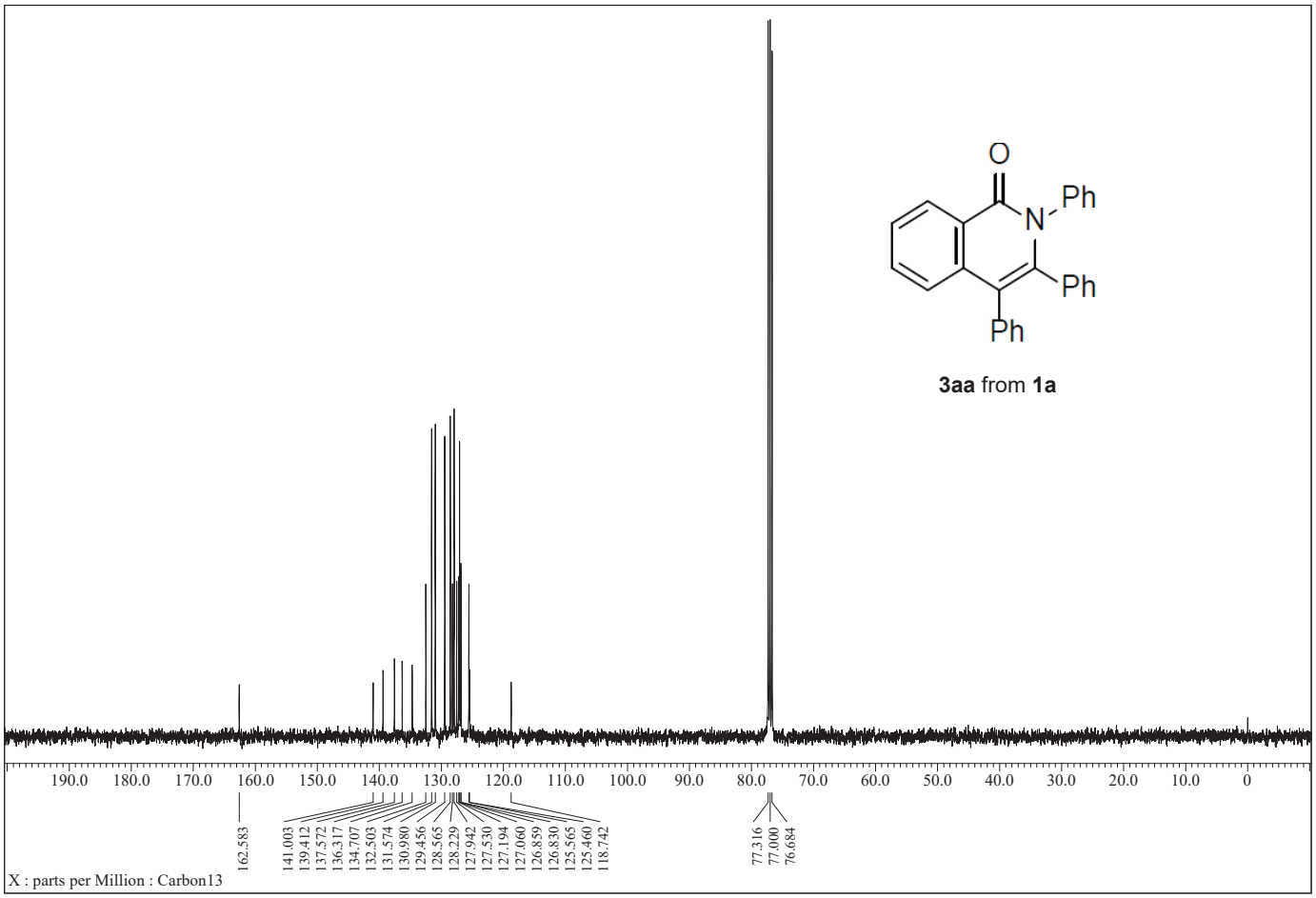

O
N
H
Ph
F
O
O
N^{i}Pr$_2$
5h
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
165.161
163.666
162.650
153.854
149.129
149.014
137.889
131.516
131.420
128.958
127.530
127.501
124.367
119.557
113.683
113.472
111.047
110.808
77.316
77.000
76.684
47.428
46.728
21.267
20.241
X : parts per Million : Carbon13

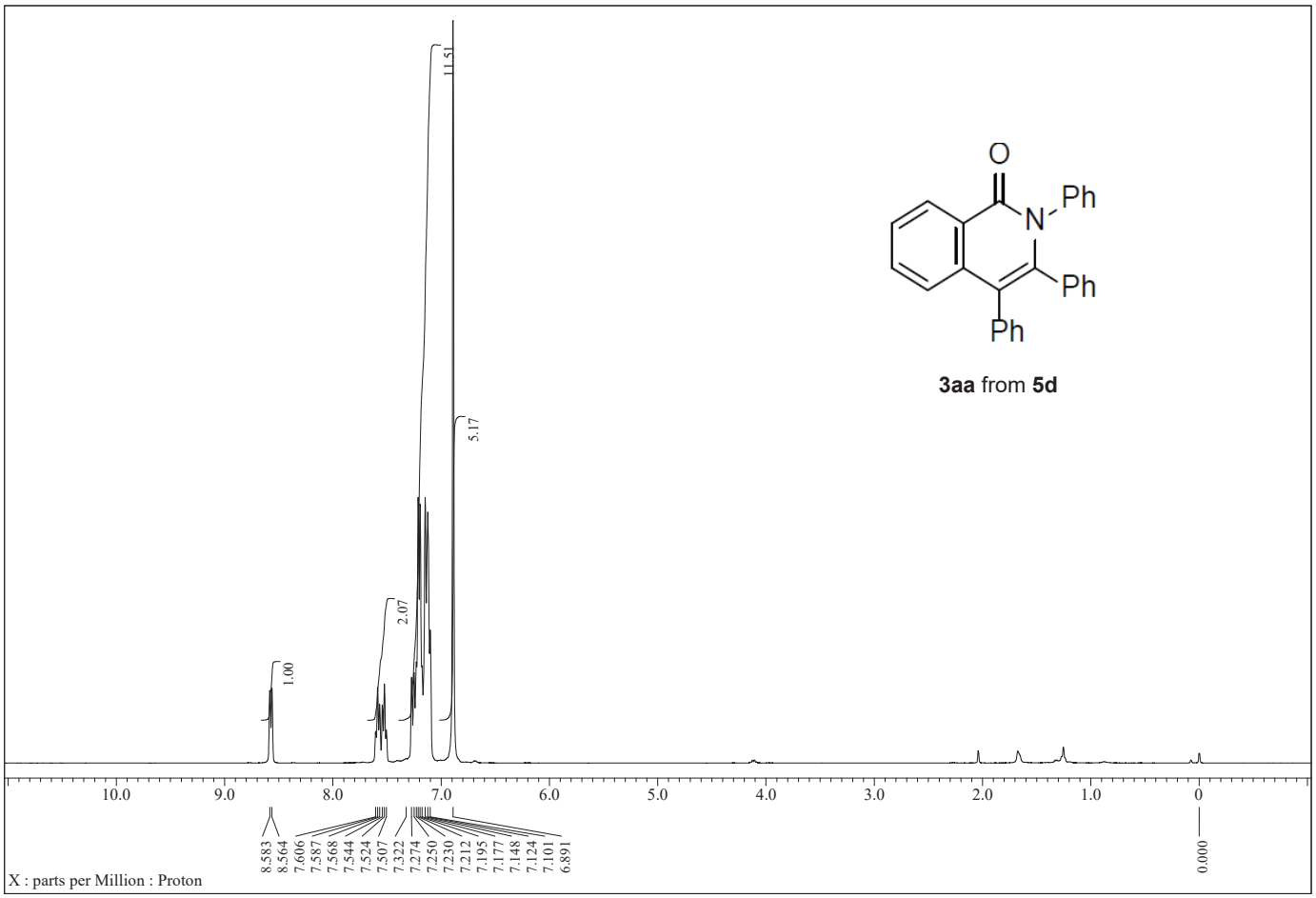

O
N
H
Ph
F
O
O
N^{i}Pr$_2$
5h
-70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0
-107.710
-107.730
-107.750
-107.771
X : parts per Million : Fluorine19


O
N
Ph
H
O
O
tBu
5i
9.03
2.94
1.86
0.88
1.00
1.00
0.79
0.91
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.890
7.806
7.802
7.786
7.783
7.596
7.577
7.522
7.518
7.503
7.502
7.499
7.483
7.479
7.370
7.366
7.350
7.331
7.259
7.159
7.156
7.154
7.138
7.119
7.084
7.082
7.063
7.061
1.311
0.000
X : parts per Million : Proton

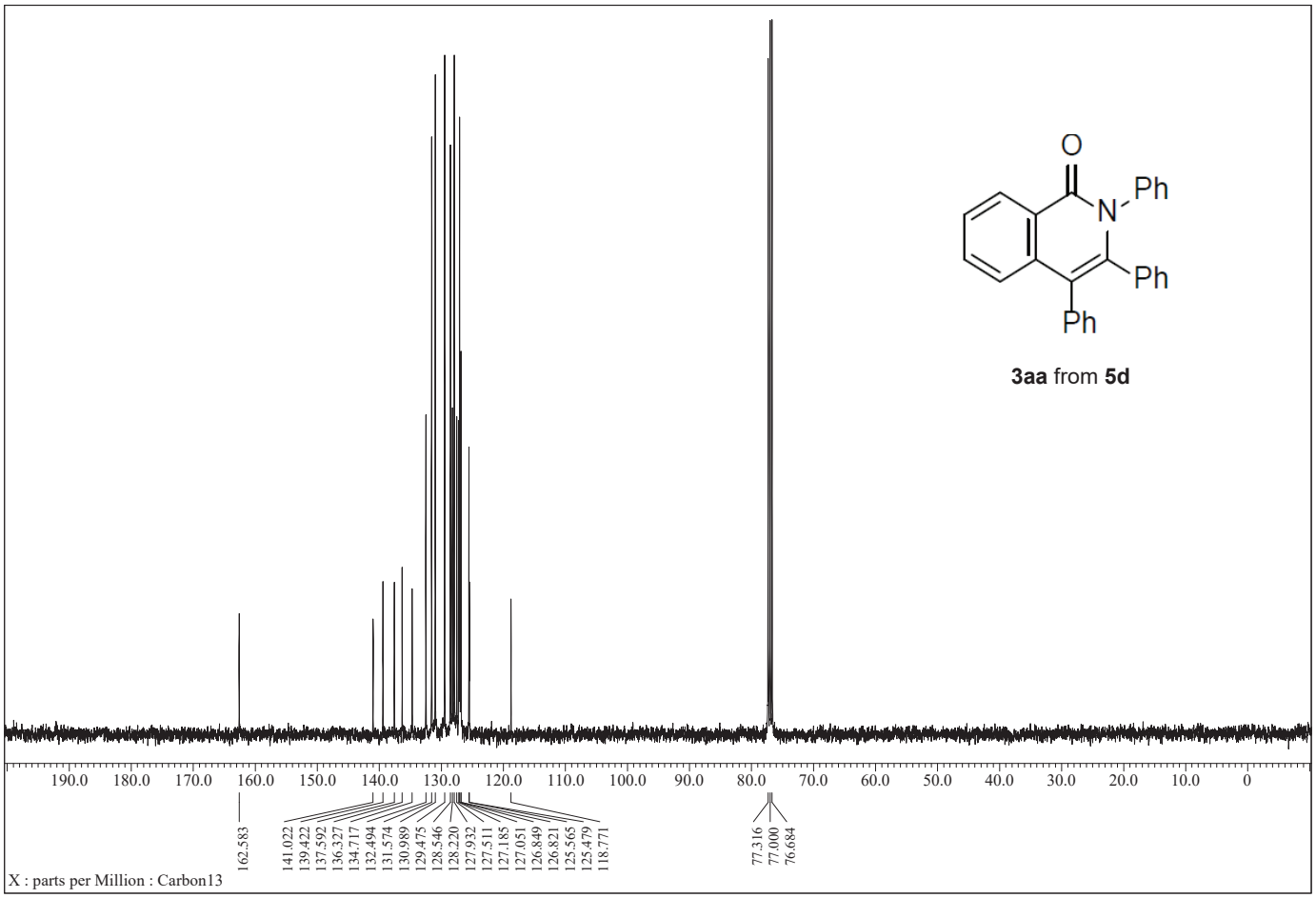

O
N
Ph
H
O
O
tBu
5i
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
177.542
163.848
147.768
137.659
131.842
129.772
129.724
129.073
126.409
124.521
122.988
119.739
77.316
77.000
76.684
39.244
27.036
X : parts per Million : Carbon13


O
N
Ph
Ph
Ph
3aa from 1a
11.83
5.10
1.00
1.01
1.03
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

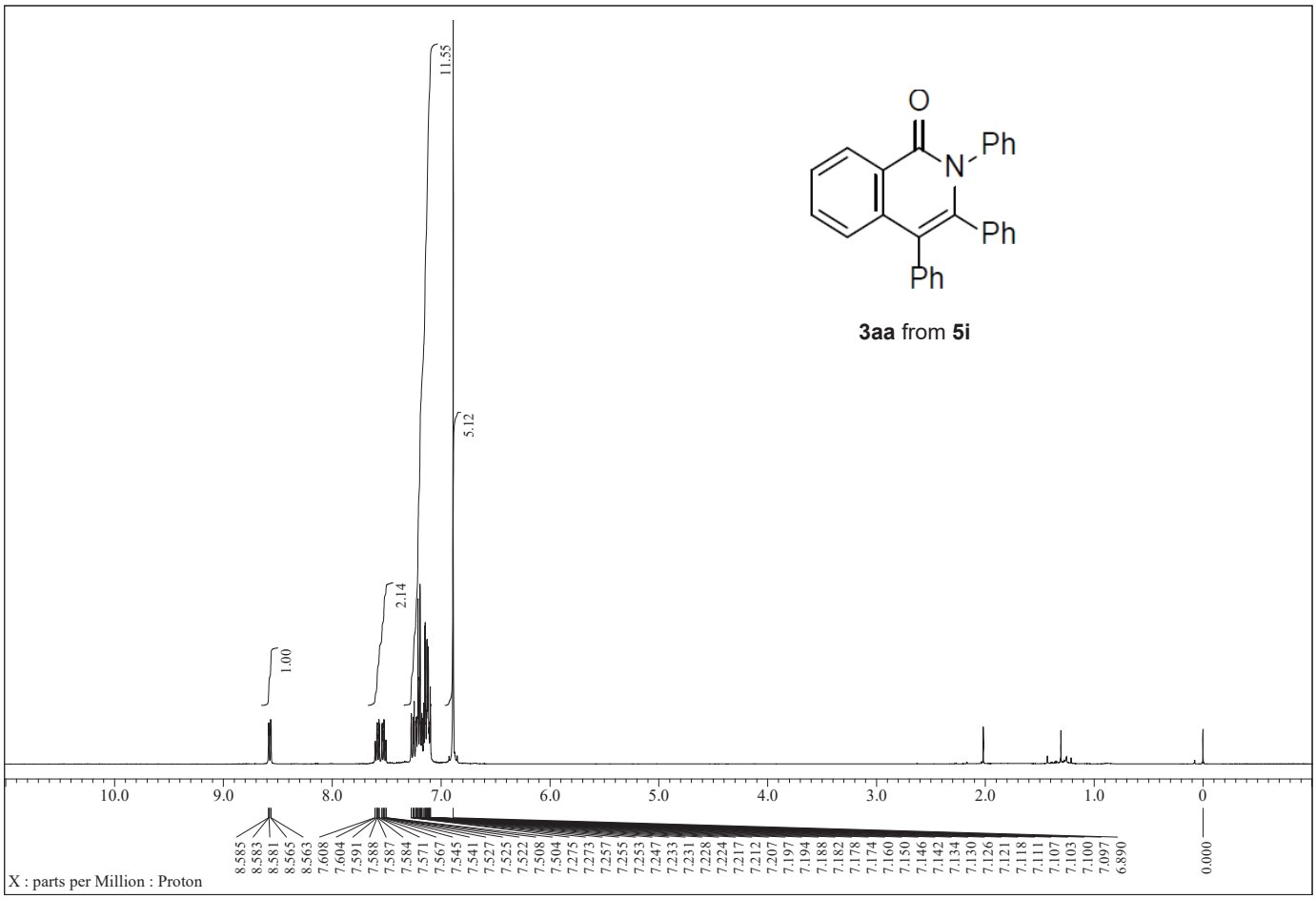

O
N
Ph
Ph
Ph
3aa from 1a
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.583
141.003
139.412
137.572
136.317
134.707
132.503
131.574
130.980
129.456
128.565
128.229
127.942
127.530
127.194
127.060
126.859
126.830
125.565
125.460
118.742
77.316
77.000
76.684
X : parts per Million : Carbon13



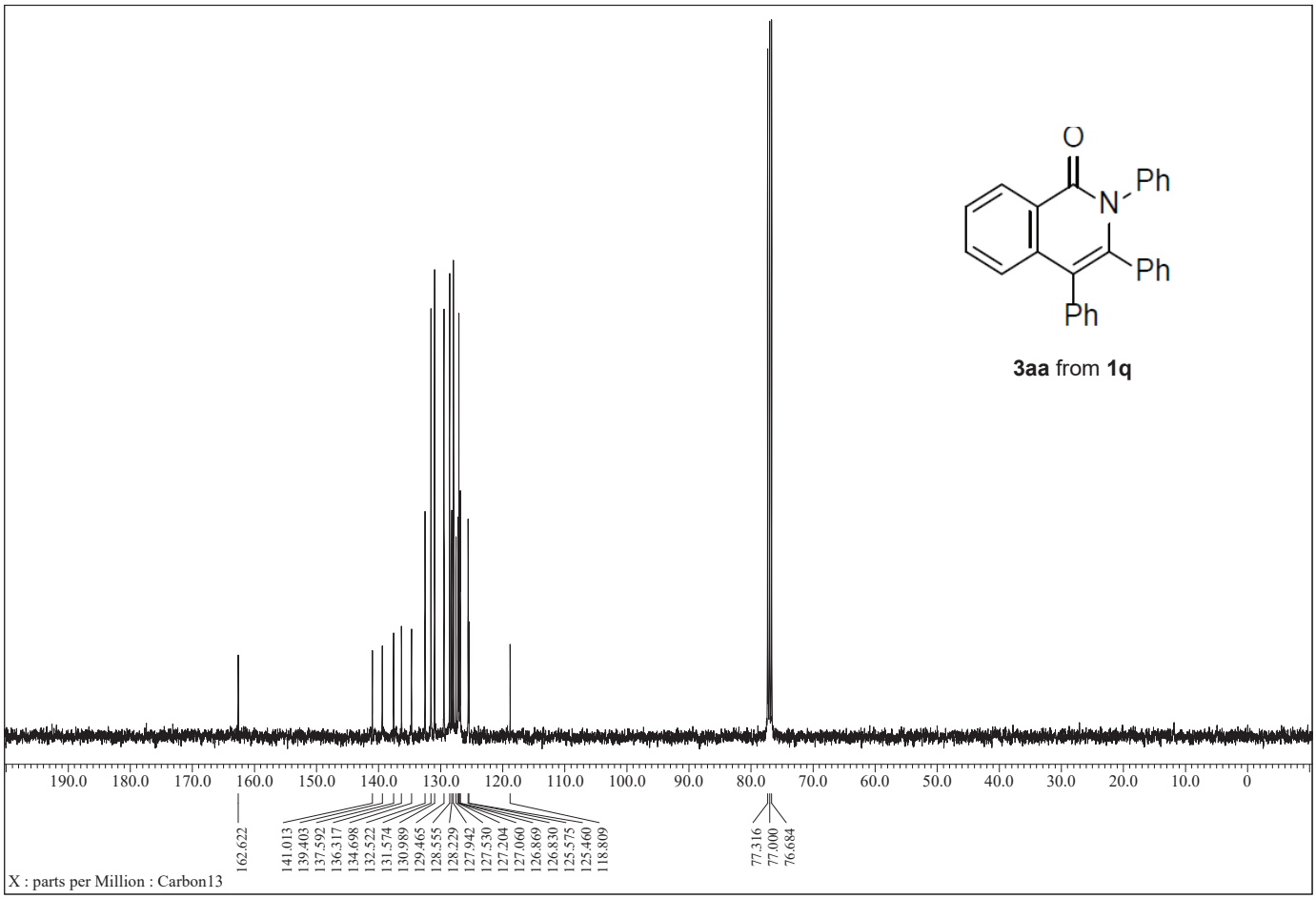
3aa from **5d**



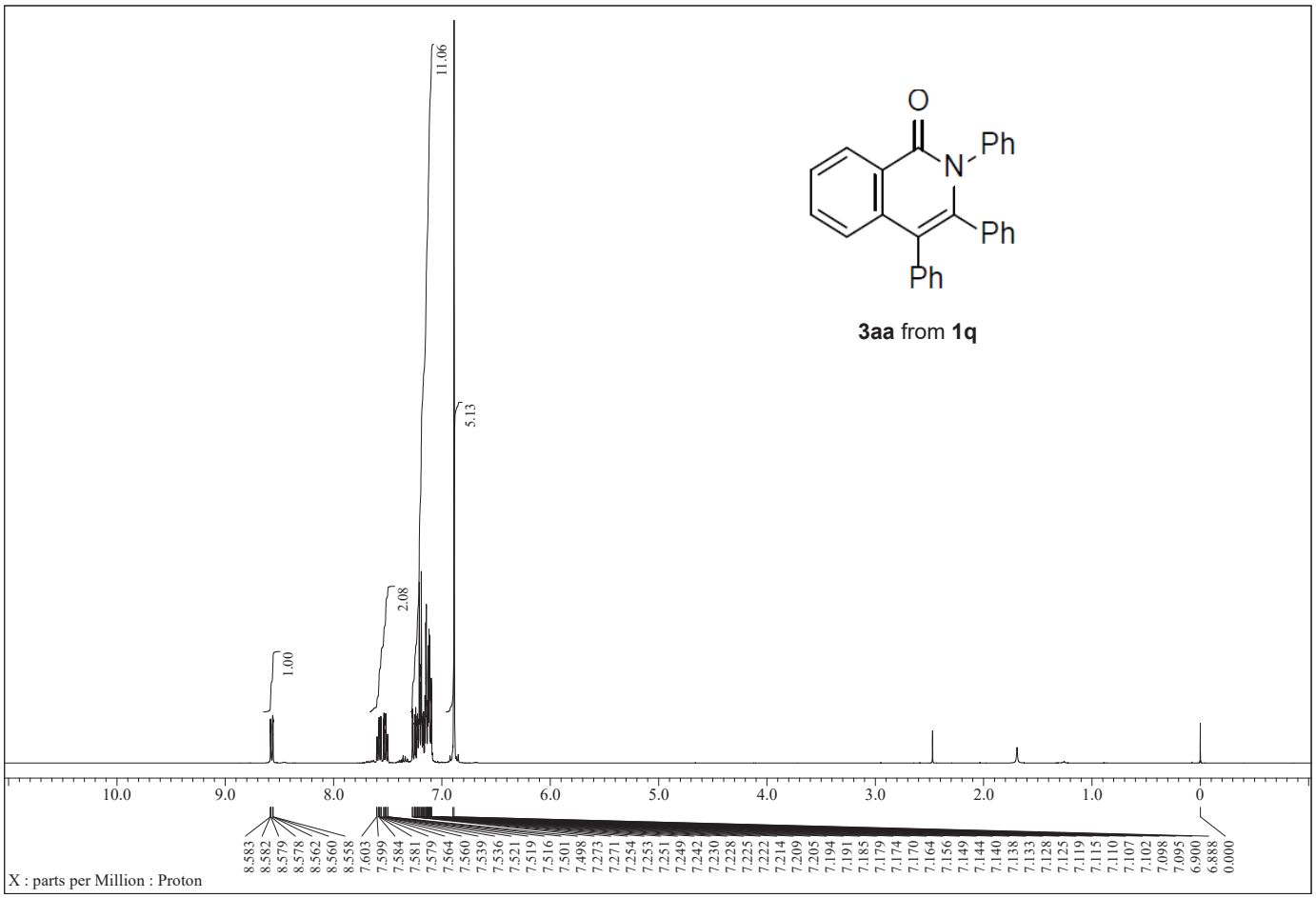
3aa from **5d**



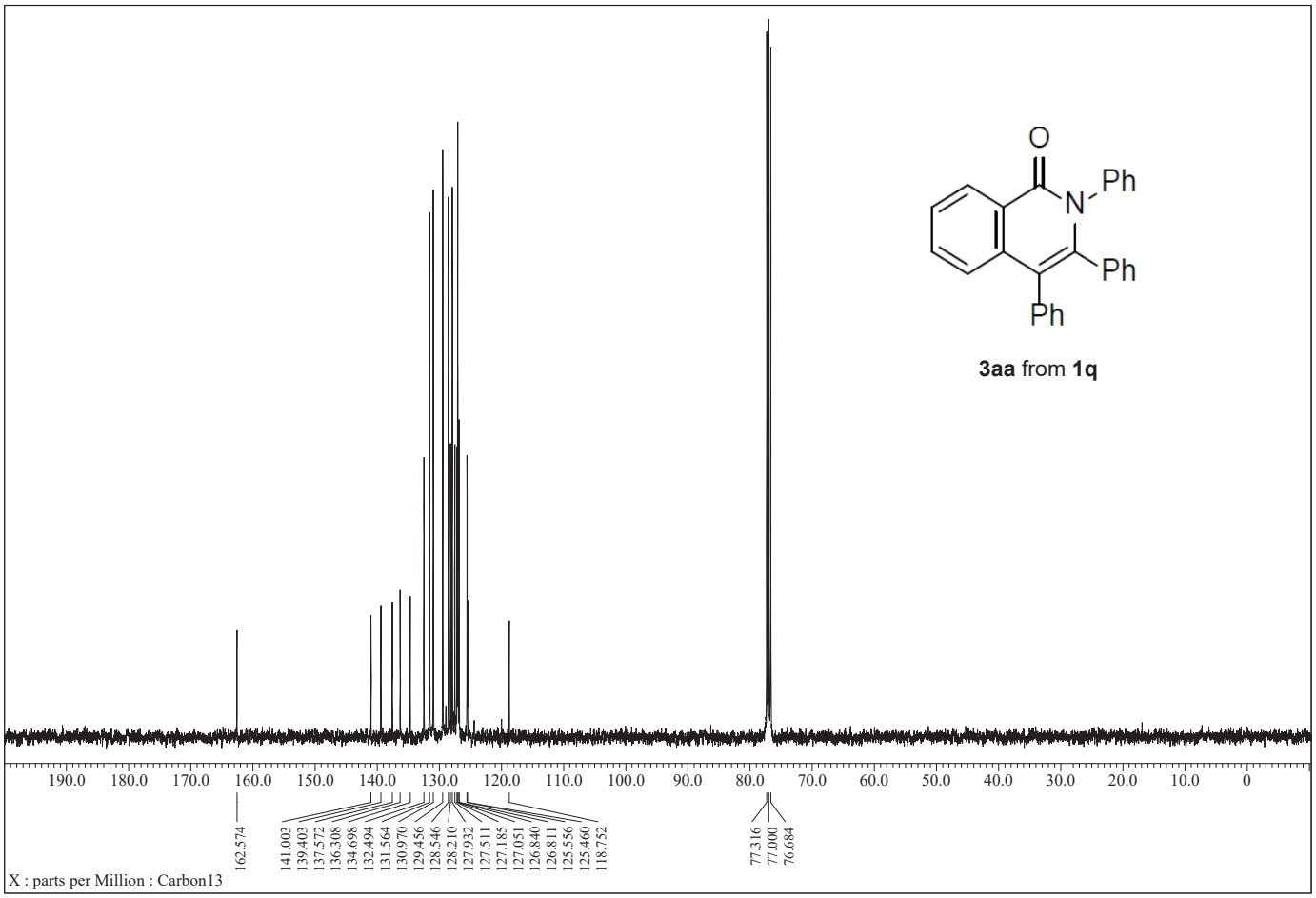
3aa from **5i**



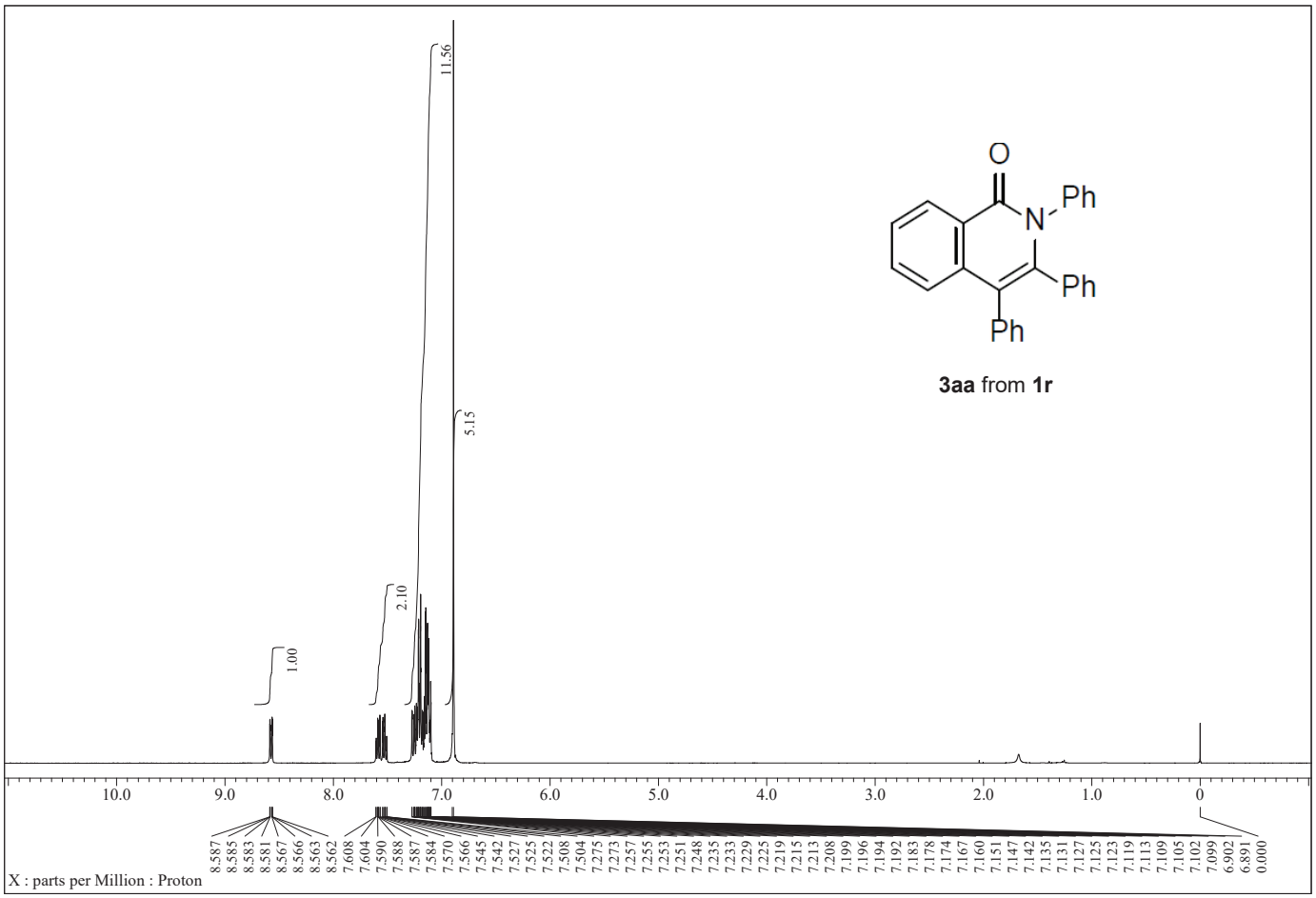
3aa from **1q**

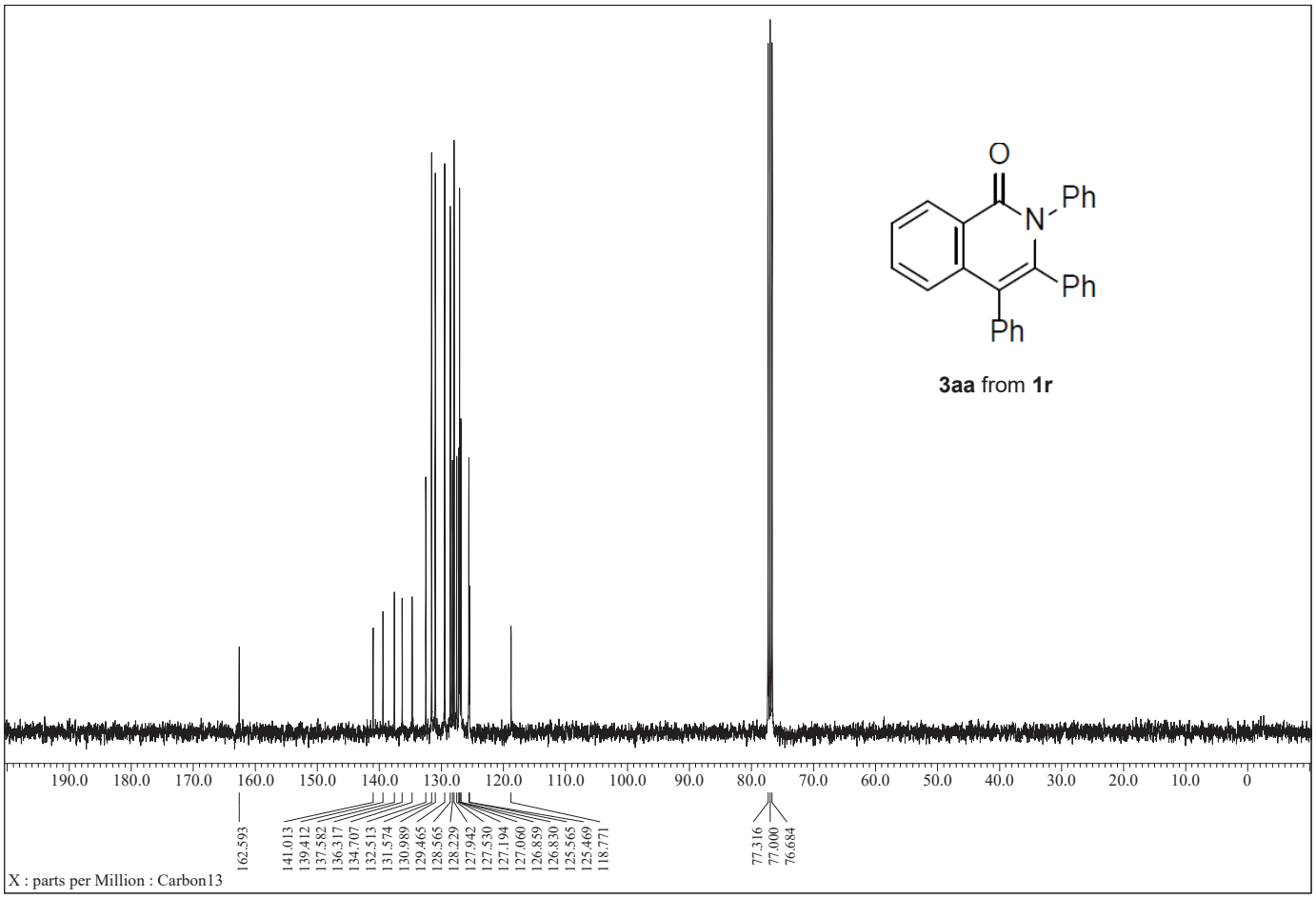


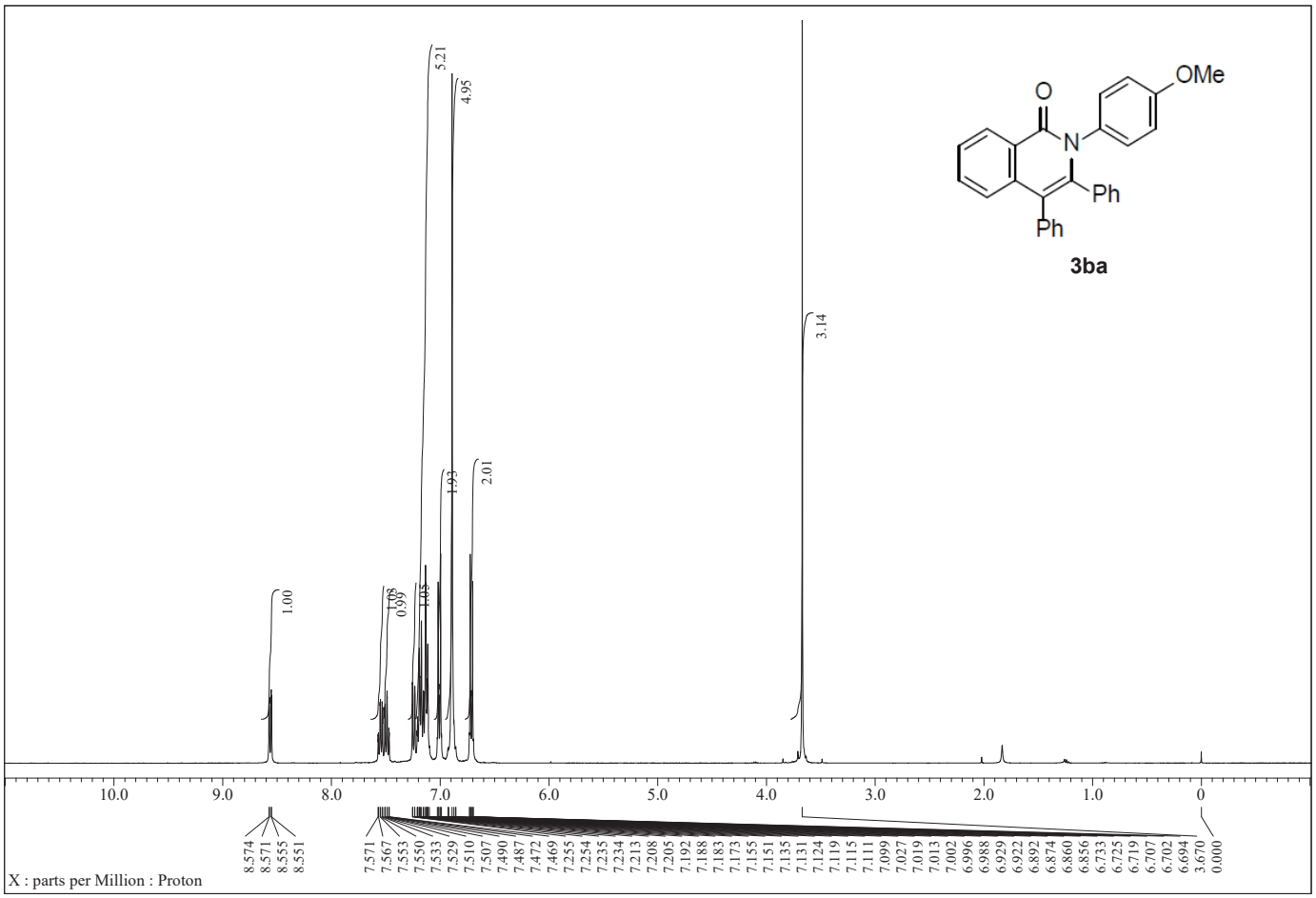
3aa from **1q**

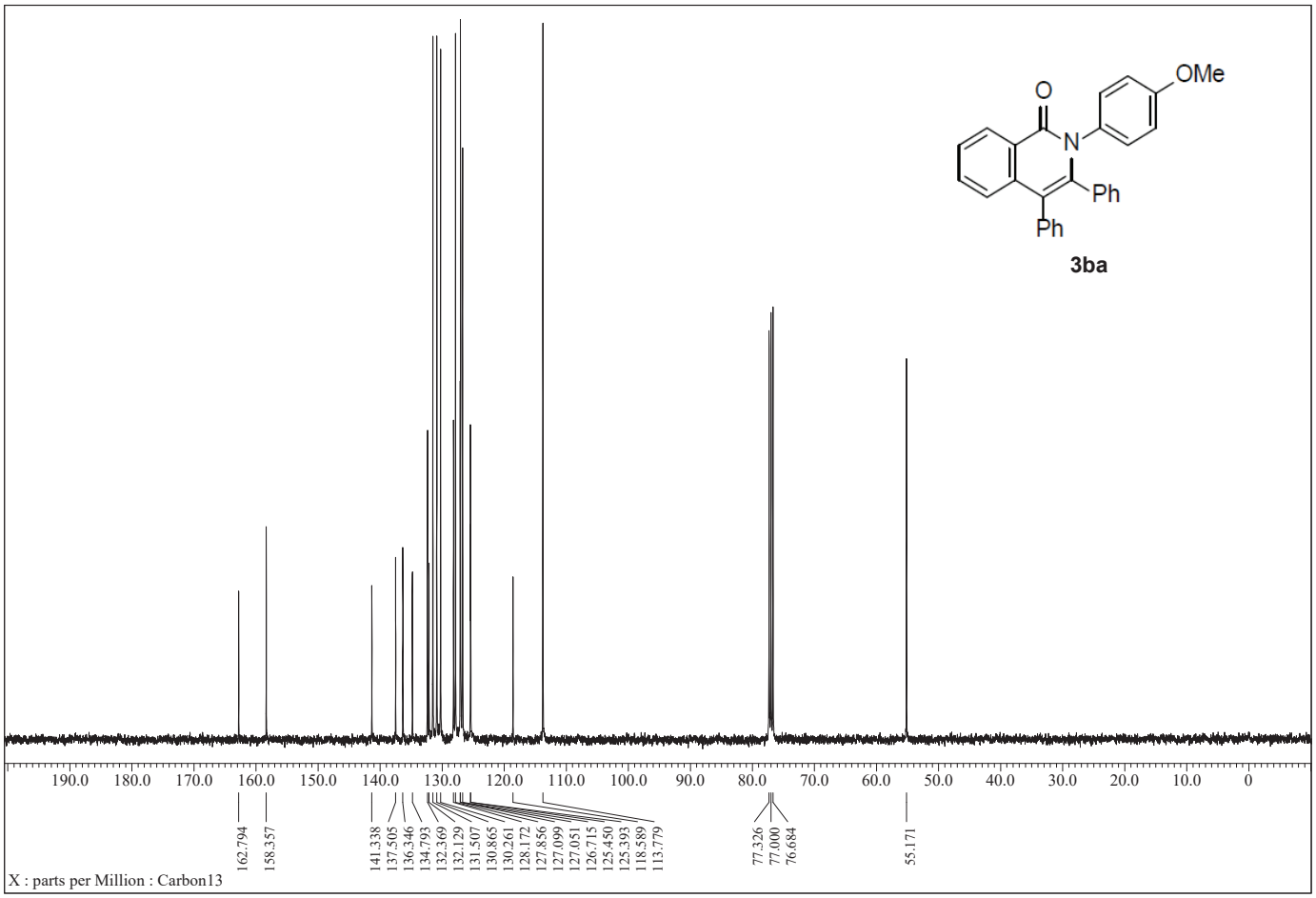


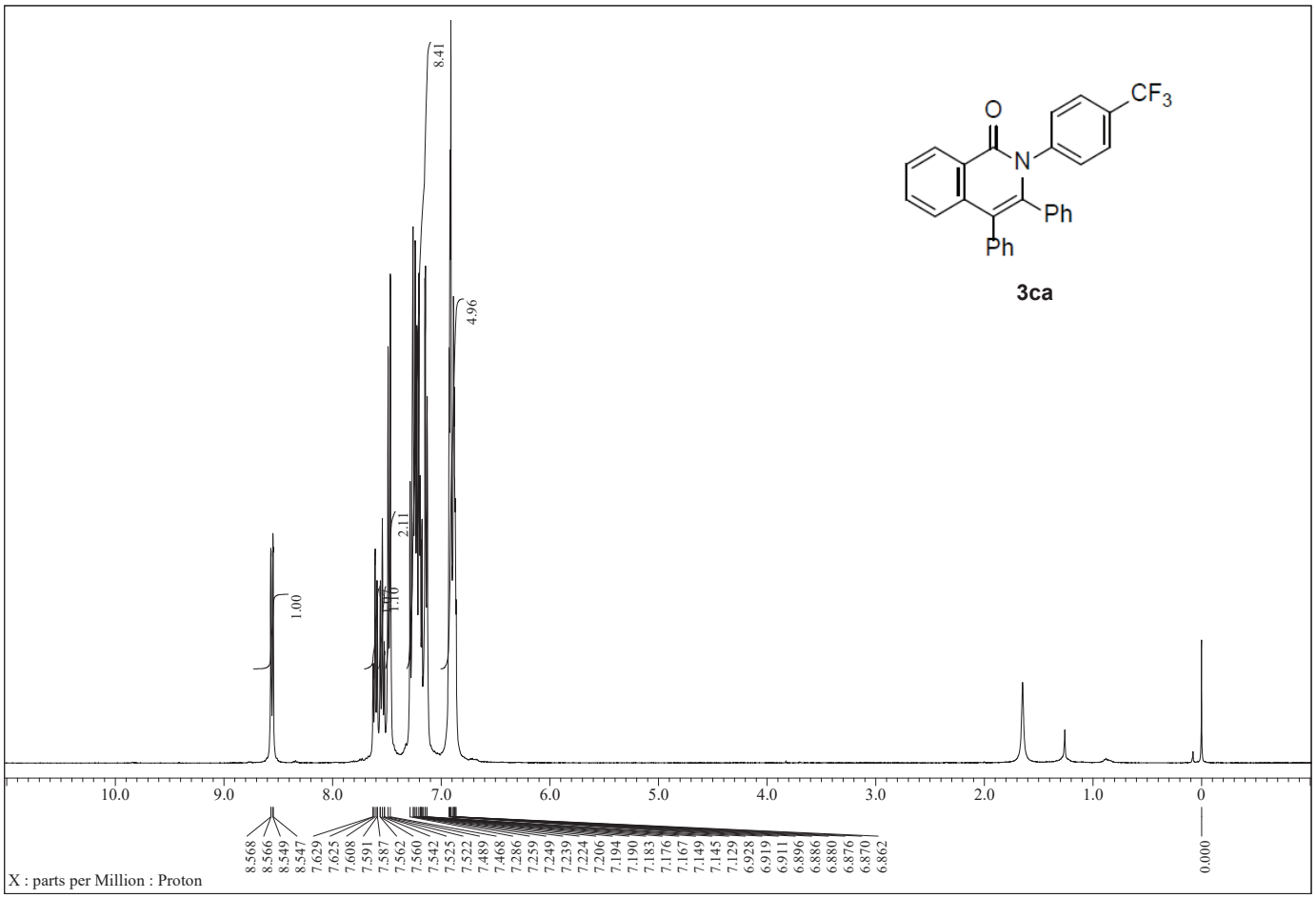
3aa from **1q**

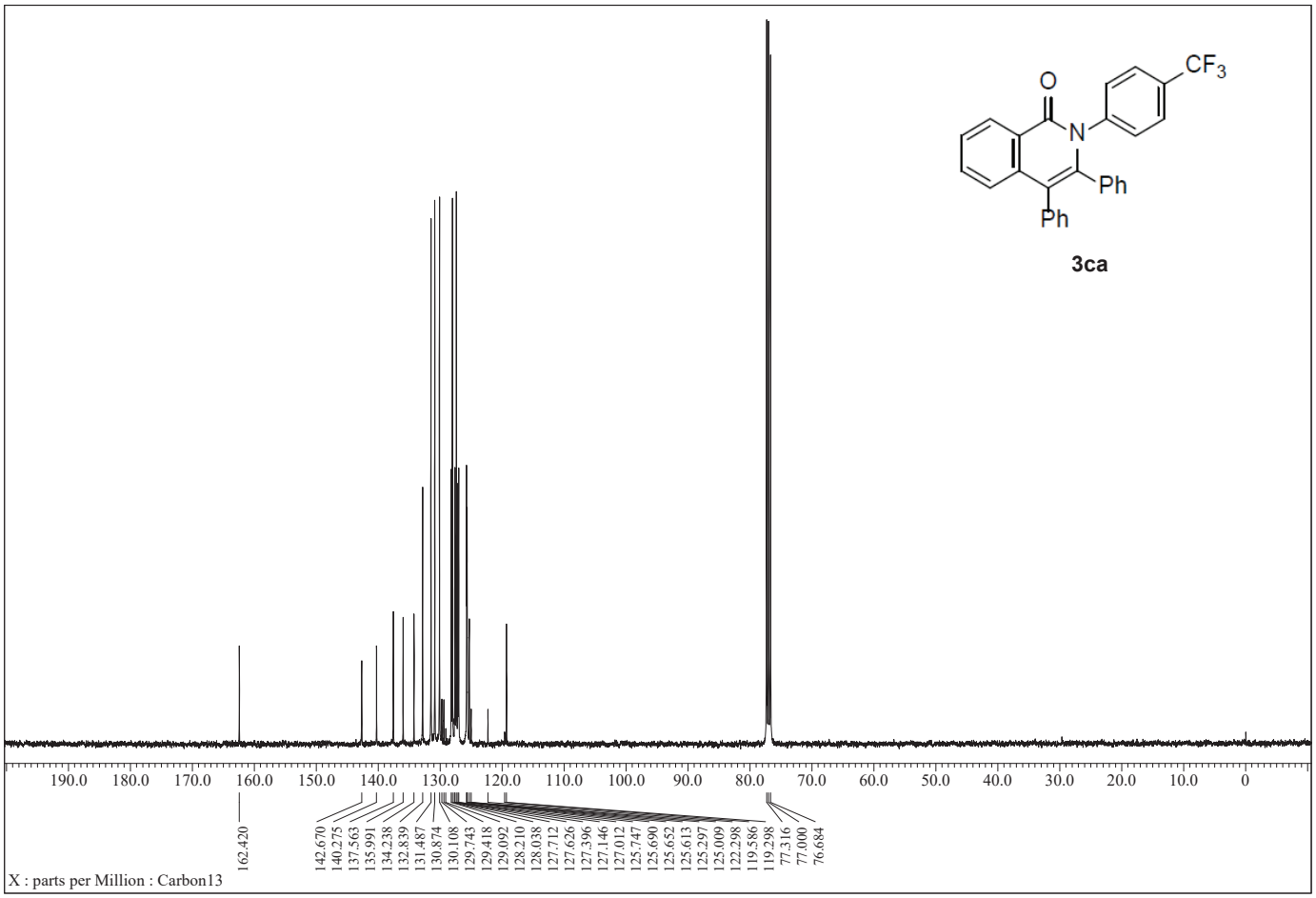

11.56
5.15
2.10
1.00
O
N
Ph
Ph
Ph
3aa from 1r
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

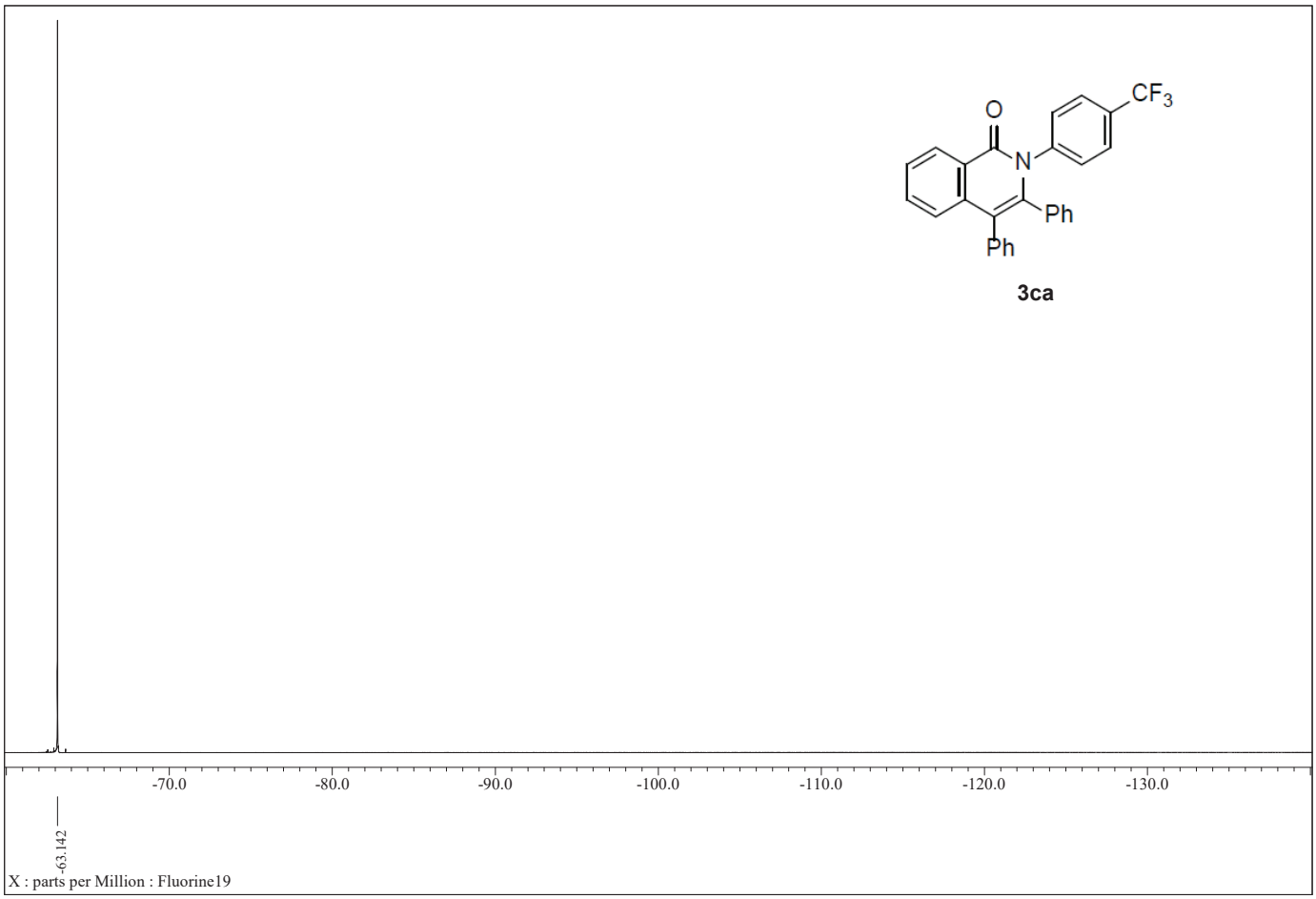

O
N
Ph
Ph
Ph
3aa from 1r
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13


OMe
O
N
Ph
Ph
3ba
5.21
4.95
3.14
2.01
1.93
1.08
0.99
1.05
1.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.574
8.571
8.555
8.551
7.571
7.567
7.553
7.550
7.533
7.529
7.510
7.507
7.490
7.487
7.472
7.469
7.255
7.254
7.235
7.234
7.213
7.208
7.205
7.192
7.188
7.183
7.173
7.155
7.151
7.135
7.131
7.124
7.119
7.115
7.111
7.099
7.027
7.019
7.013
7.002
6.996
6.988
6.929
6.922
6.892
6.874
6.860
6.856
6.733
6.725
6.719
6.707
6.702
6.694
3.670
0.000
X : parts per Million : Proton

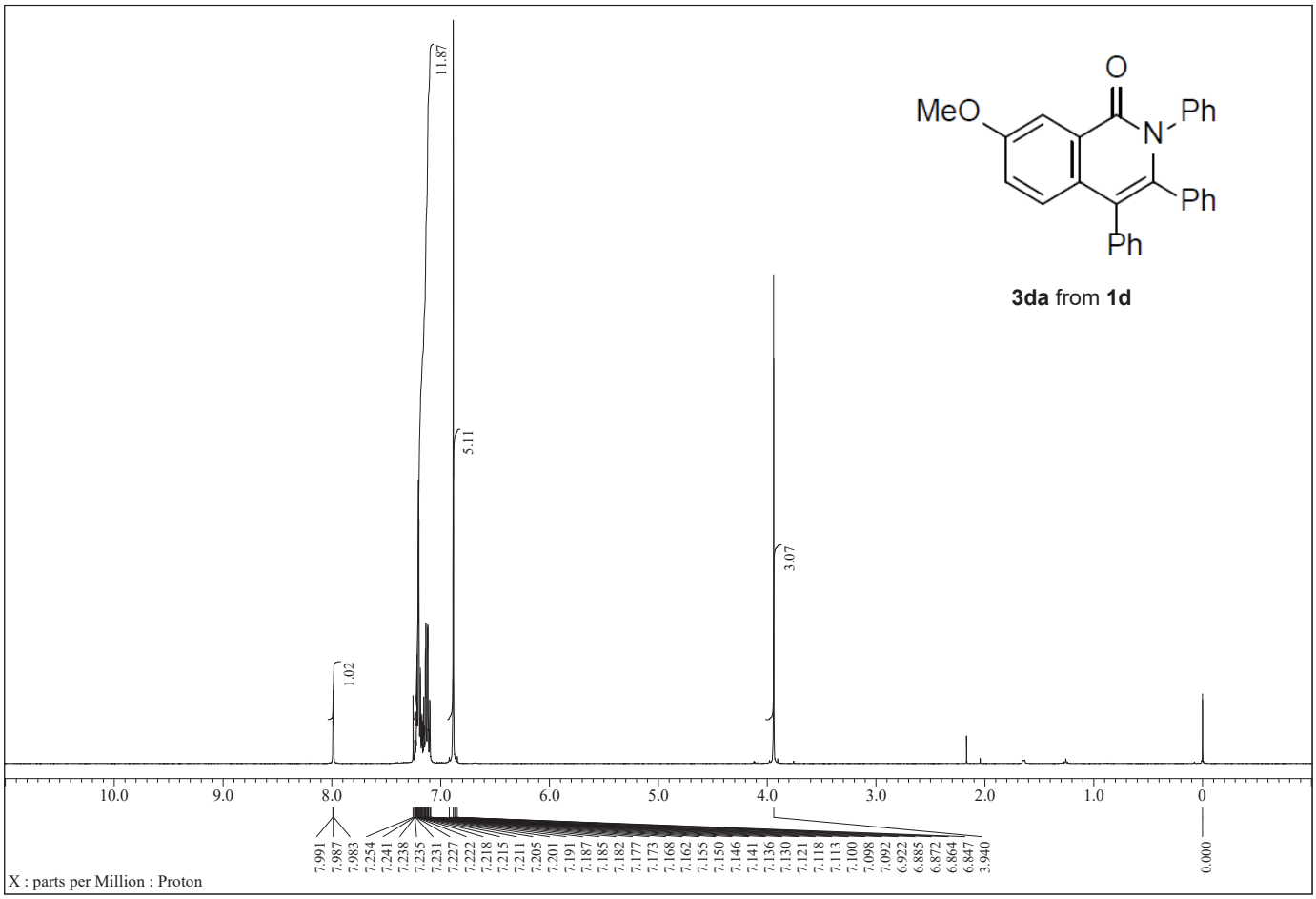

OMe
O
N
Ph
Ph
3ba
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.794
158.357
141.338
137.505
136.346
134.793
132.369
132.129
131.507
130.865
130.261
128.172
127.856
127.099
127.051
126.715
125.450
125.393
118.589
113.779
77.326
77.000
76.684
55.171
X : parts per Million : Carbon13


8.41
4.96
2.11
1.10
1.00
O
N
CF3
Ph
Ph
3ca
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.568
8.566
8.549
8.547
7.629
7.625
7.608
7.591
7.587
7.562
7.560
7.542
7.525
7.522
7.489
7.468
7.286
7.259
7.249
7.239
7.224
7.206
7.194
7.190
7.183
7.176
7.167
7.149
7.145
7.129
6.928
6.919
6.911
6.896
6.886
6.880
6.876
6.870
6.862
0.000
X : parts per Million : Proton

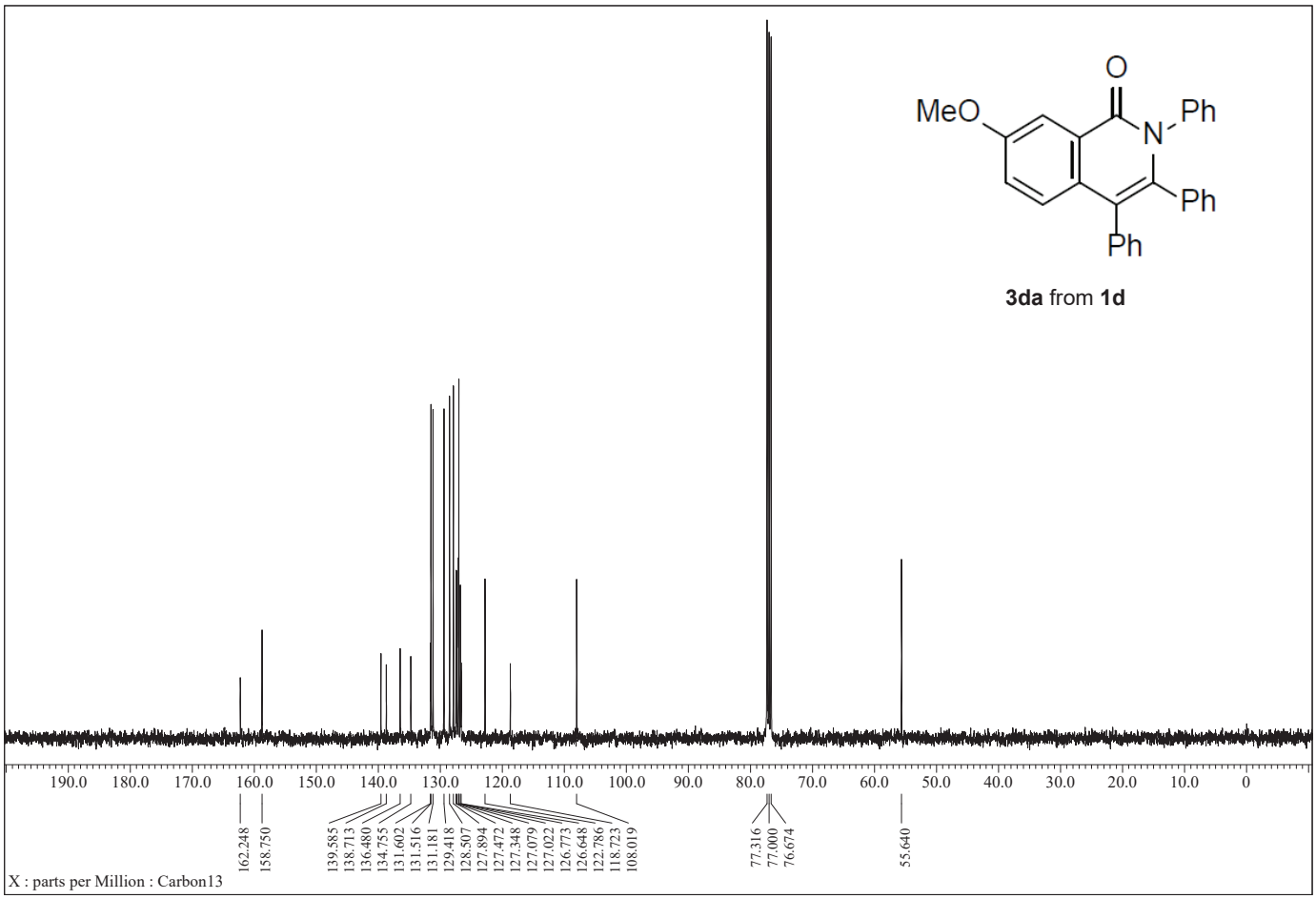

O
N
CF3
Ph
Ph
3ca
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.420
142.670
140.275
137.563
135.991
134.238
132.839
131.487
130.874
130.108
129.743
129.418
129.092
128.210
128.038
127.712
127.626
127.396
127.146
127.012
125.747
125.690
125.652
125.613
125.297
125.009
122.298
119.586
119.298
77.316
77.000
76.684
X : parts per Million : Carbon13

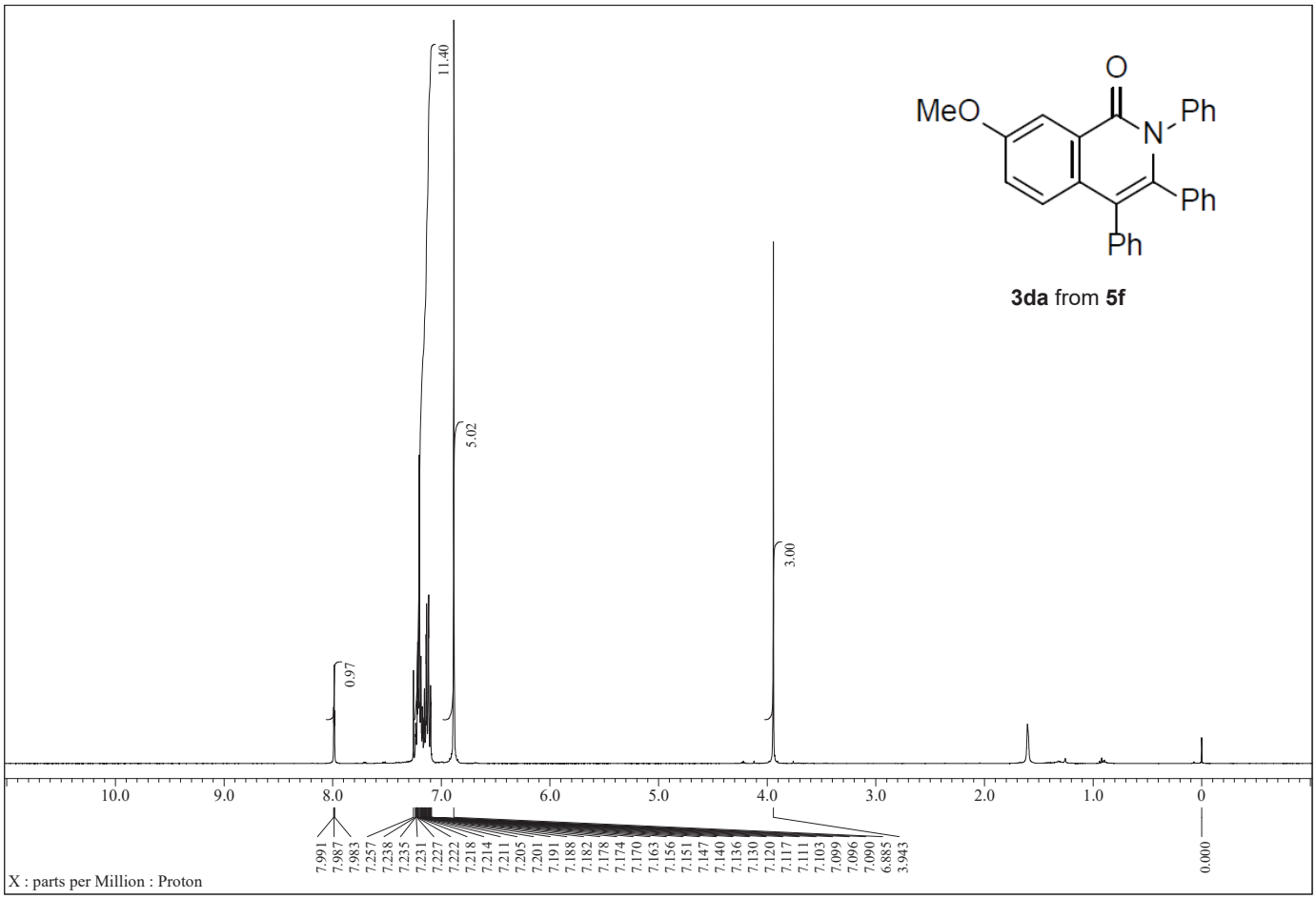


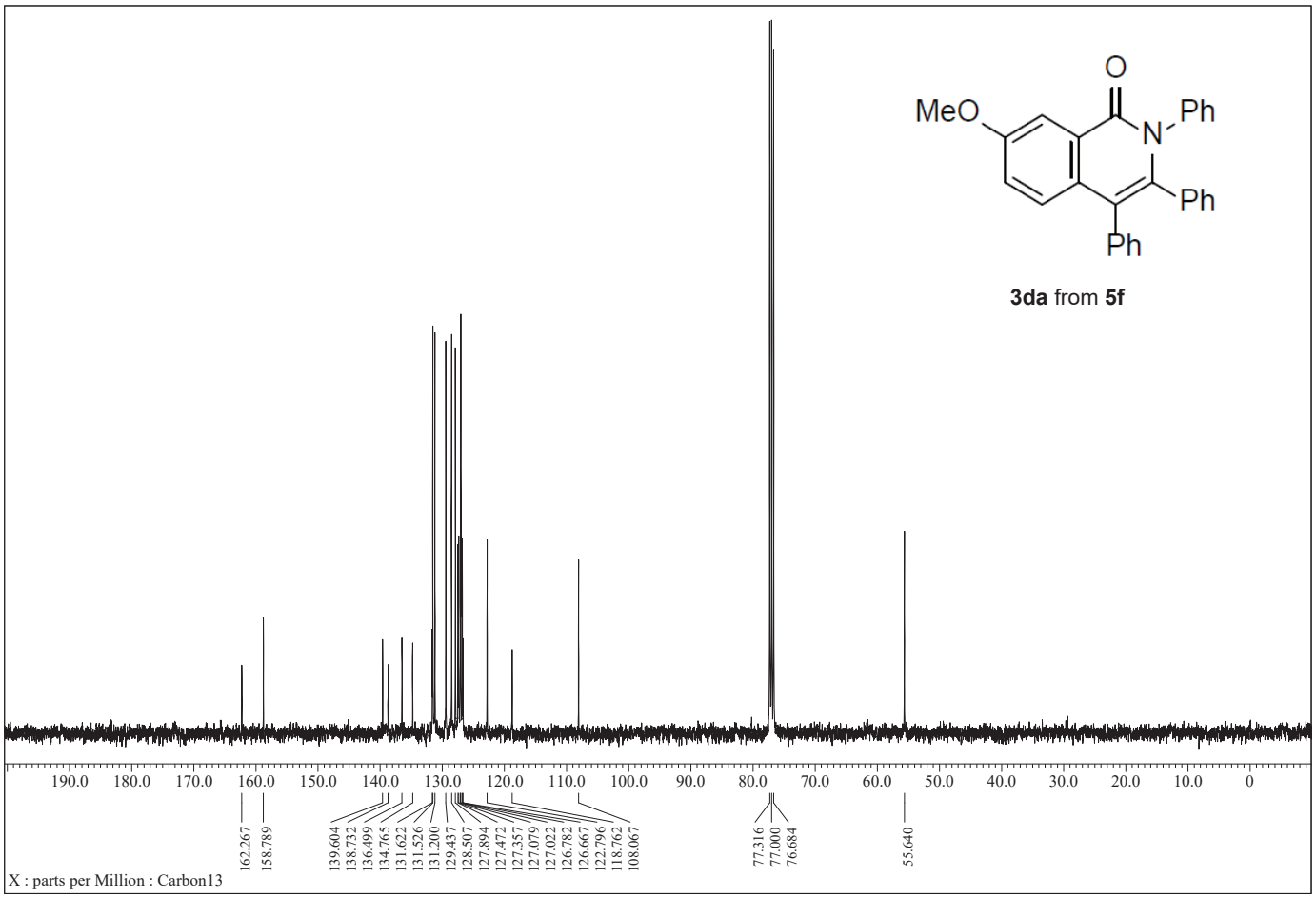
3ca

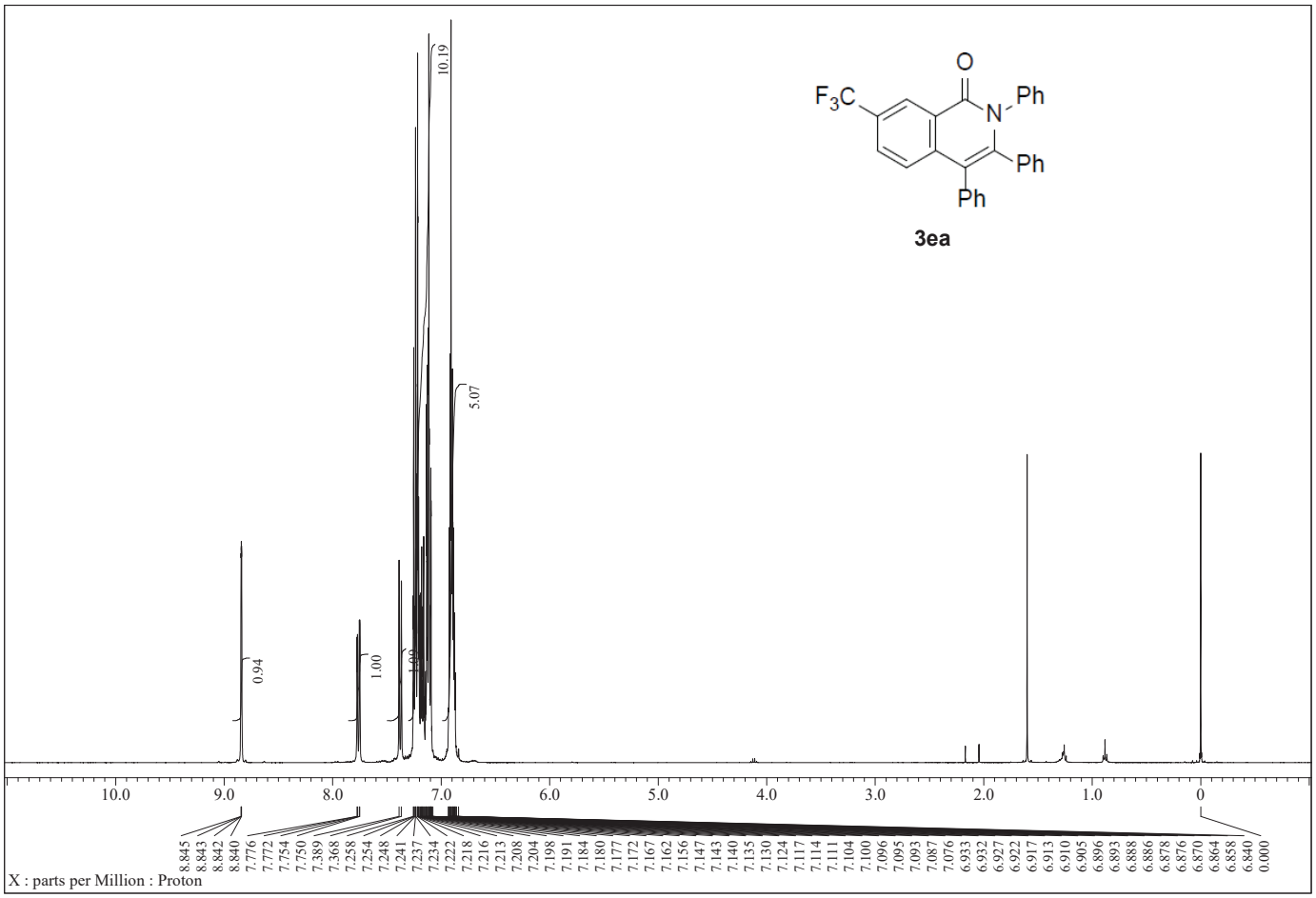


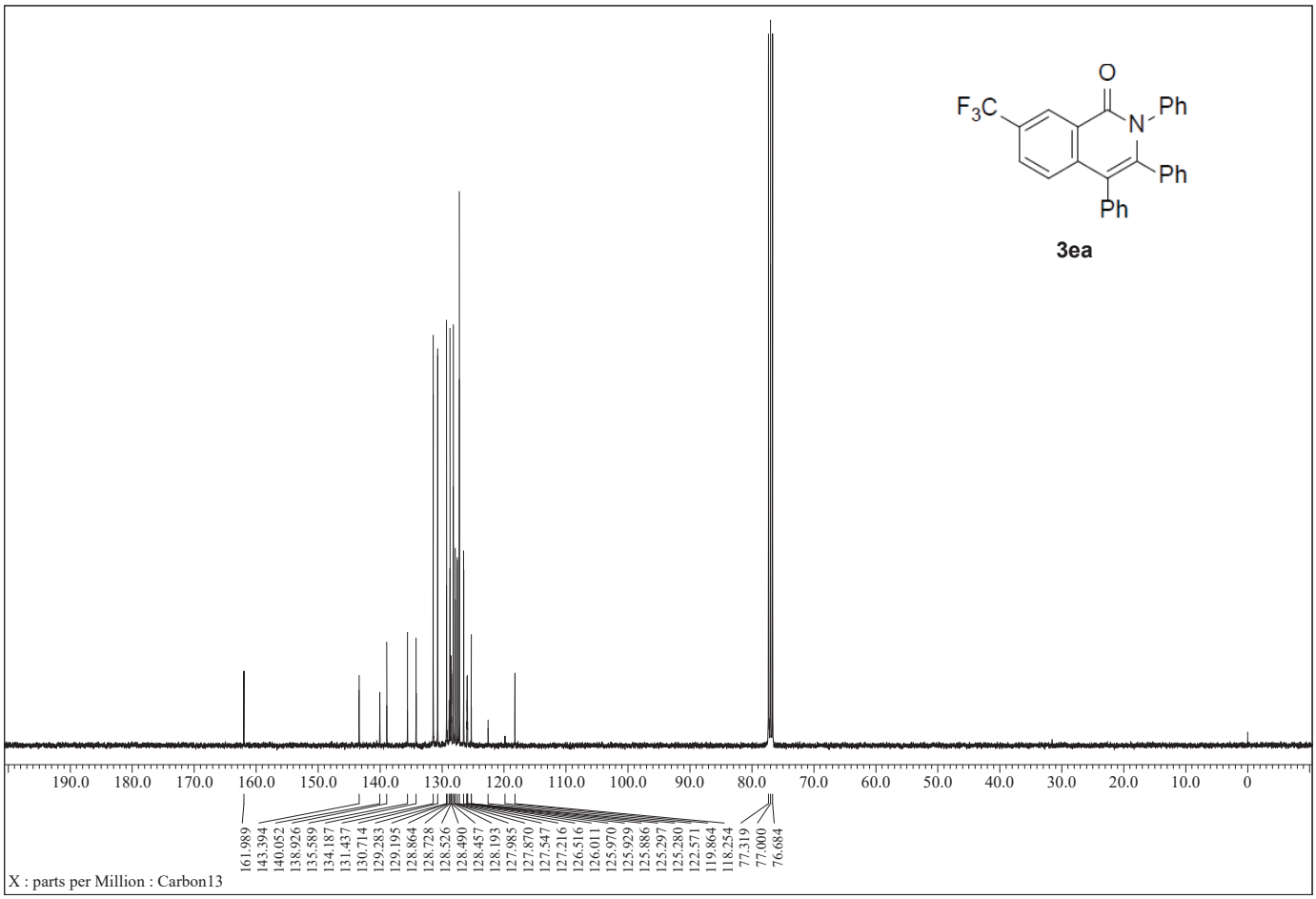
3da from **1d**

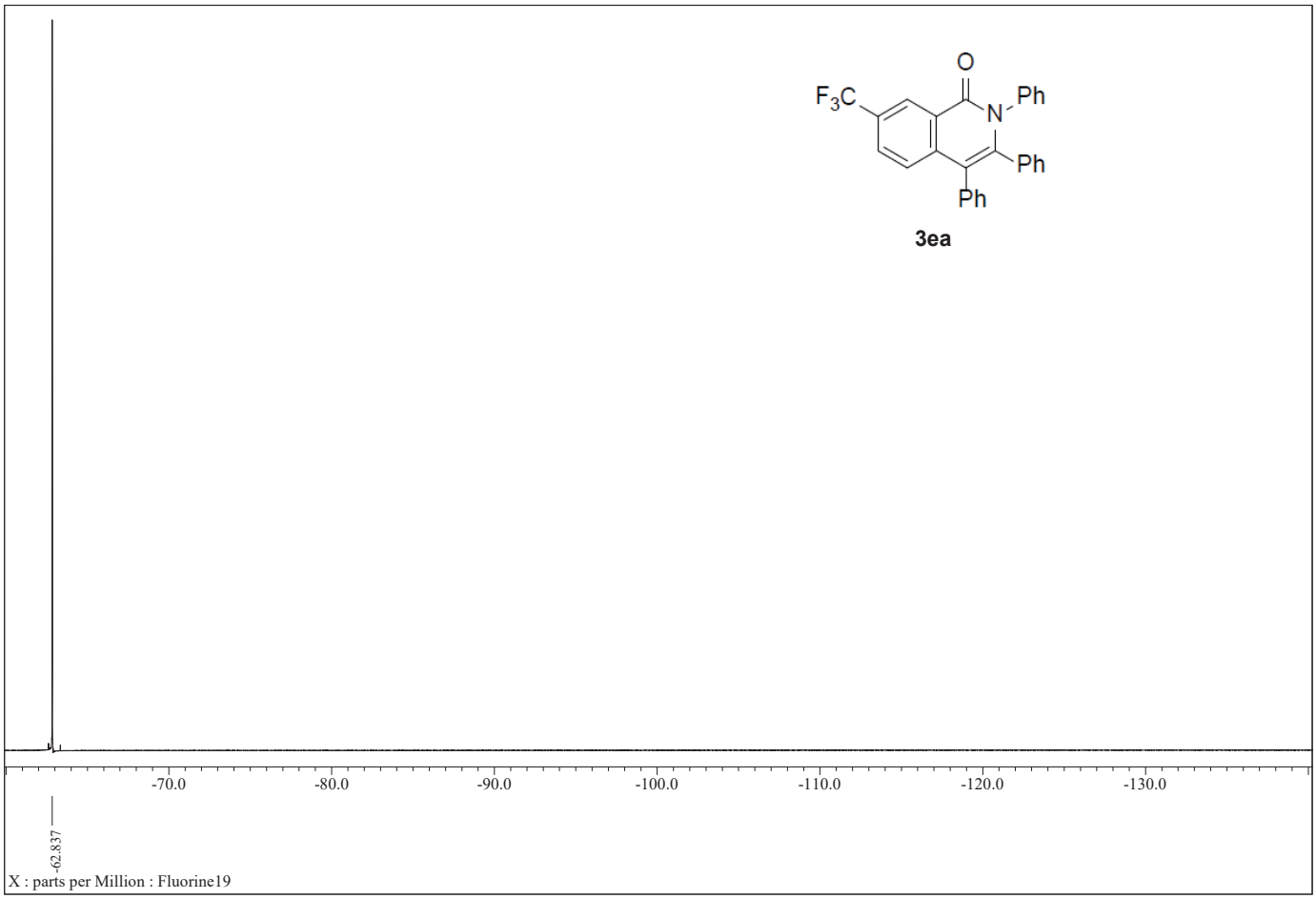

MeO
O
N
Ph
Ph
Ph
3da from 1d
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.248
158.750
139.585
138.713
136.480
134.755
131.602
131.516
131.181
129.418
128.507
127.894
127.472
127.348
127.079
127.022
126.773
126.648
122.786
118.723
108.019
77.316
77.000
76.674
55.640
X : parts per Million : Carbon13

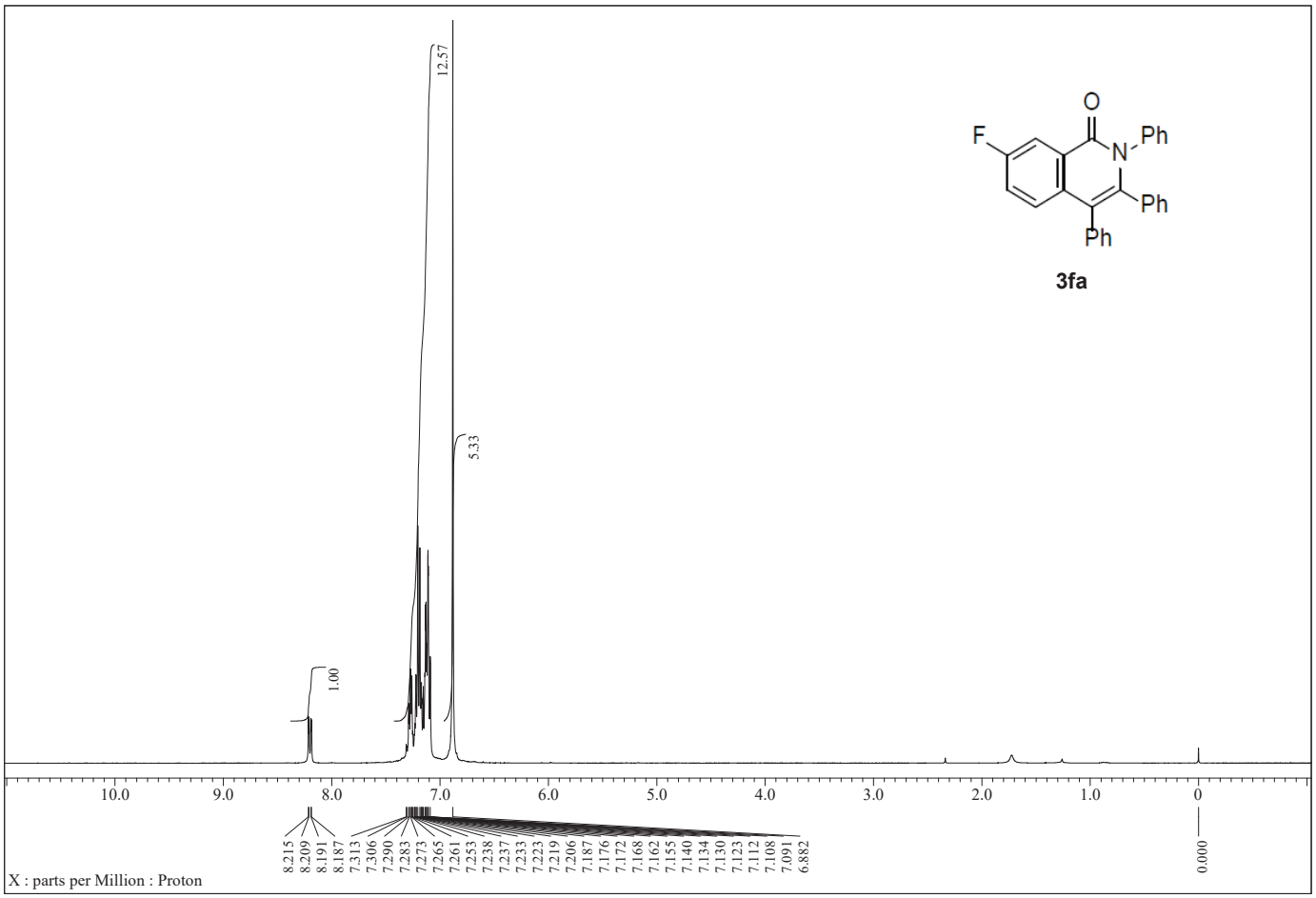

MeO
O
N
Ph
Ph
Ph
3da from 5f
11.40
5.02
3.00
0.97
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.991
7.987
7.983
7.257
7.238
7.235
7.231
7.227
7.222
7.218
7.214
7.211
7.205
7.201
7.191
7.188
7.182
7.178
7.174
7.170
7.163
7.156
7.151
7.147
7.140
7.136
7.130
7.120
7.117
7.111
7.103
7.099
7.096
7.090
6.885
3.943
0.000
X : parts per Million : Proton

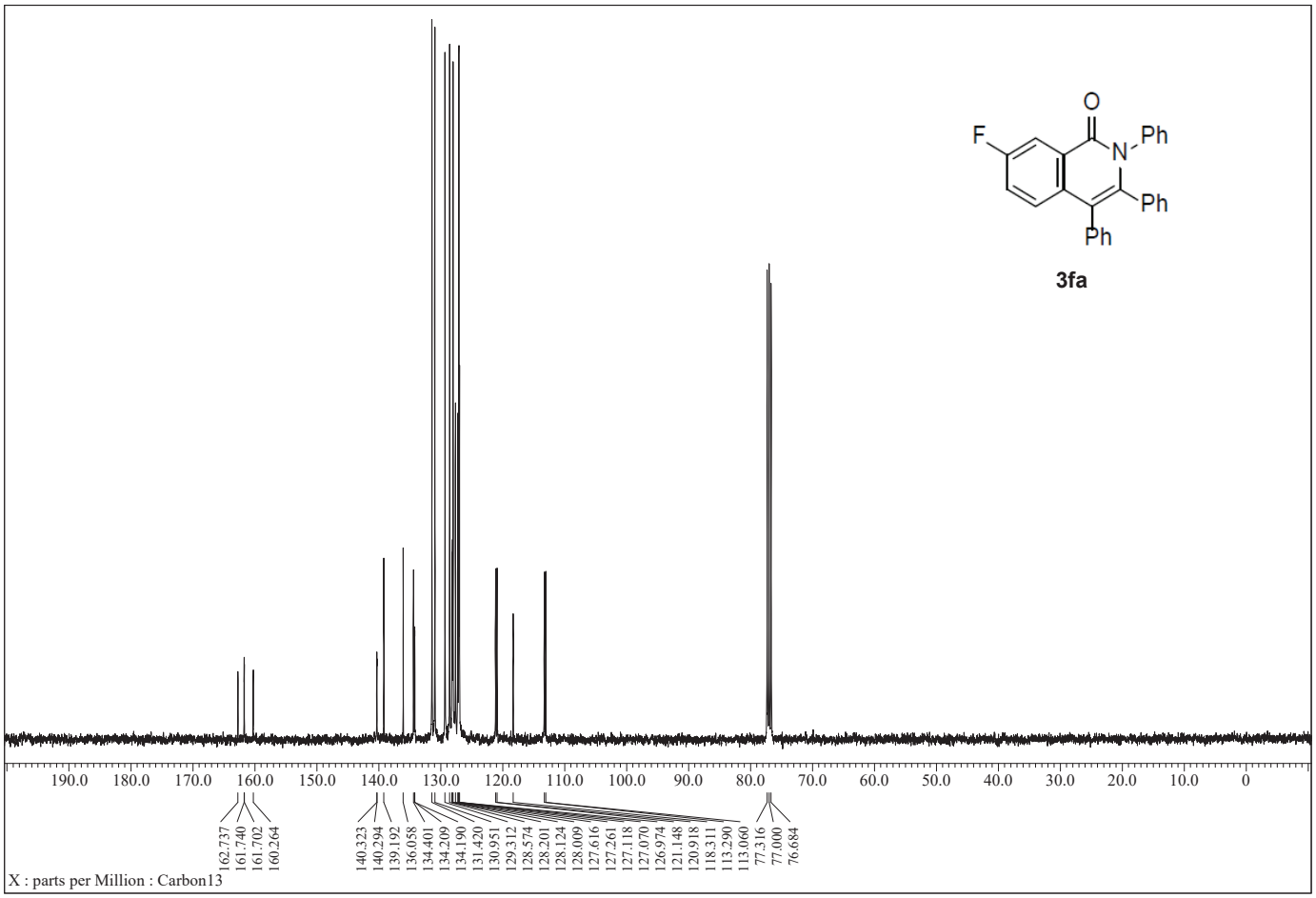

MeO
O
N
Ph
Ph
Ph
3da from 5f
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.267
158.789
139.604
138.732
136.499
134.765
131.622
131.526
131.200
129.437
128.507
127.894
127.472
127.357
127.079
127.022
126.782
126.667
122.796
118.762
108.067
77.316
77.000
76.684
55.640
X : parts per Million : Carbon13

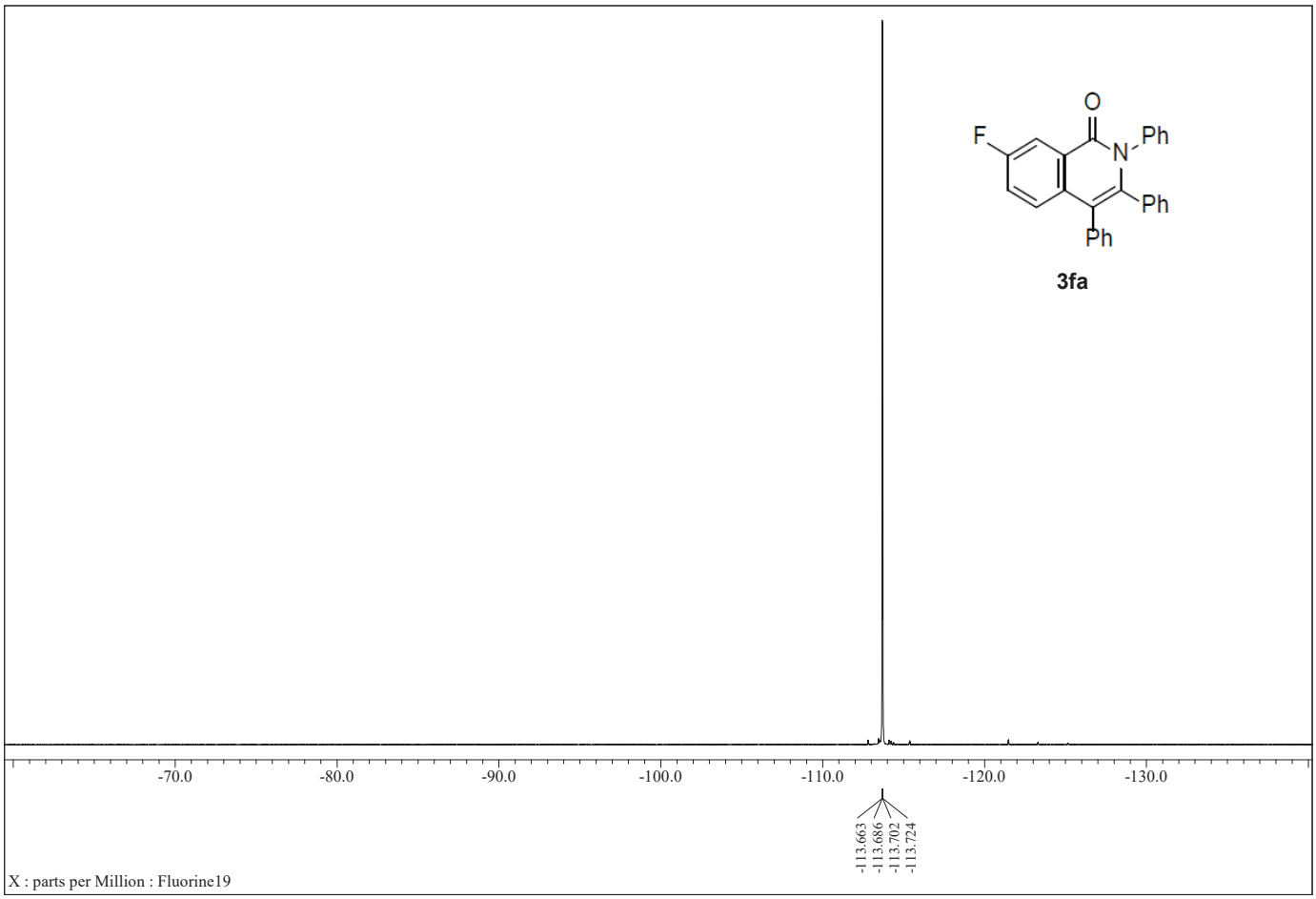

F3C
O
N
Ph
Ph
Ph
3ea
10.19
5.07
0.94
1.00
1.89
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.845
8.843
8.842
8.840
7.776
7.772
7.754
7.750
7.389
7.368
7.258
7.254
7.248
7.241
7.237
7.234
7.222
7.218
7.216
7.213
7.208
7.204
7.198
7.191
7.184
7.180
7.177
7.172
7.167
7.162
7.156
7.147
7.143
7.140
7.135
7.130
7.124
7.117
7.114
7.111
7.104
7.100
7.096
7.095
7.093
7.087
7.076
6.933
6.932
6.927
6.922
6.917
6.913
6.910
6.905
6.896
6.893
6.888
6.886
6.878
6.876
6.870
6.864
6.858
6.840
0.000
X : parts per Million : Proton


O
F3C
N
Ph
Ph
Ph
3ea
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
161.989
143.394
140.052
138.926
135.589
134.187
131.437
130.714
129.283
129.195
128.864
128.728
128.526
128.490
128.457
128.193
127.985
127.870
127.547
127.216
126.516
126.011
125.970
125.929
125.886
125.297
125.280
122.571
119.864
118.254
77.319
77.000
76.684
X : parts per Million : Carbon13

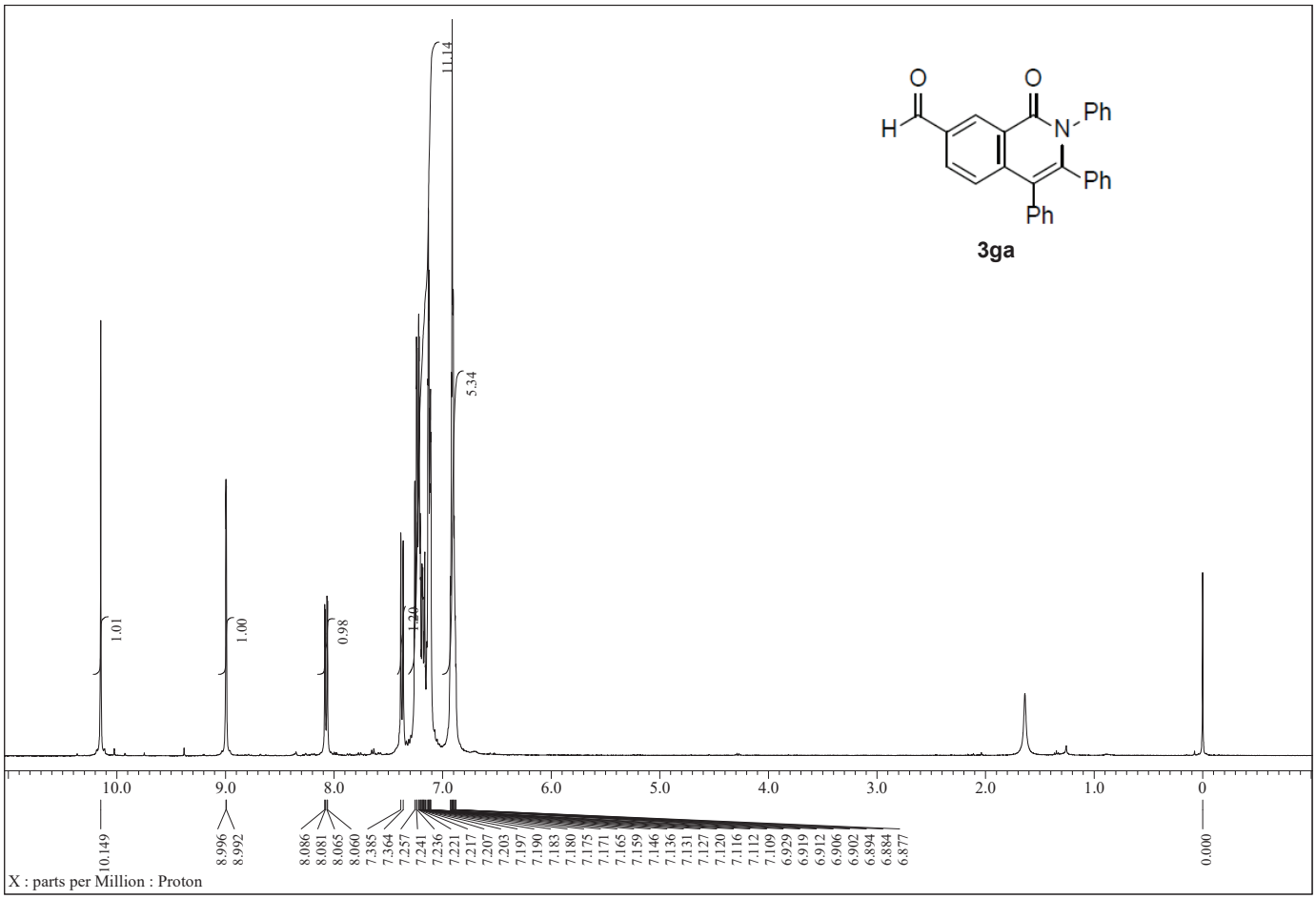

O
F3C
N
Ph
Ph
Ph
3ea
-70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0
-62.837
X : parts per Million : Fluorine19


12.57
5.33
1.00
O
F
N
Ph
Ph
Ph
3fa
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.215
8.209
8.191
8.187
7.313
7.306
7.290
7.283
7.273
7.265
7.261
7.253
7.238
7.237
7.233
7.223
7.219
7.206
7.187
7.176
7.172
7.168
7.162
7.155
7.140
7.134
7.130
7.123
7.112
7.108
7.091
6.882
0.000
X : parts per Million : Proton

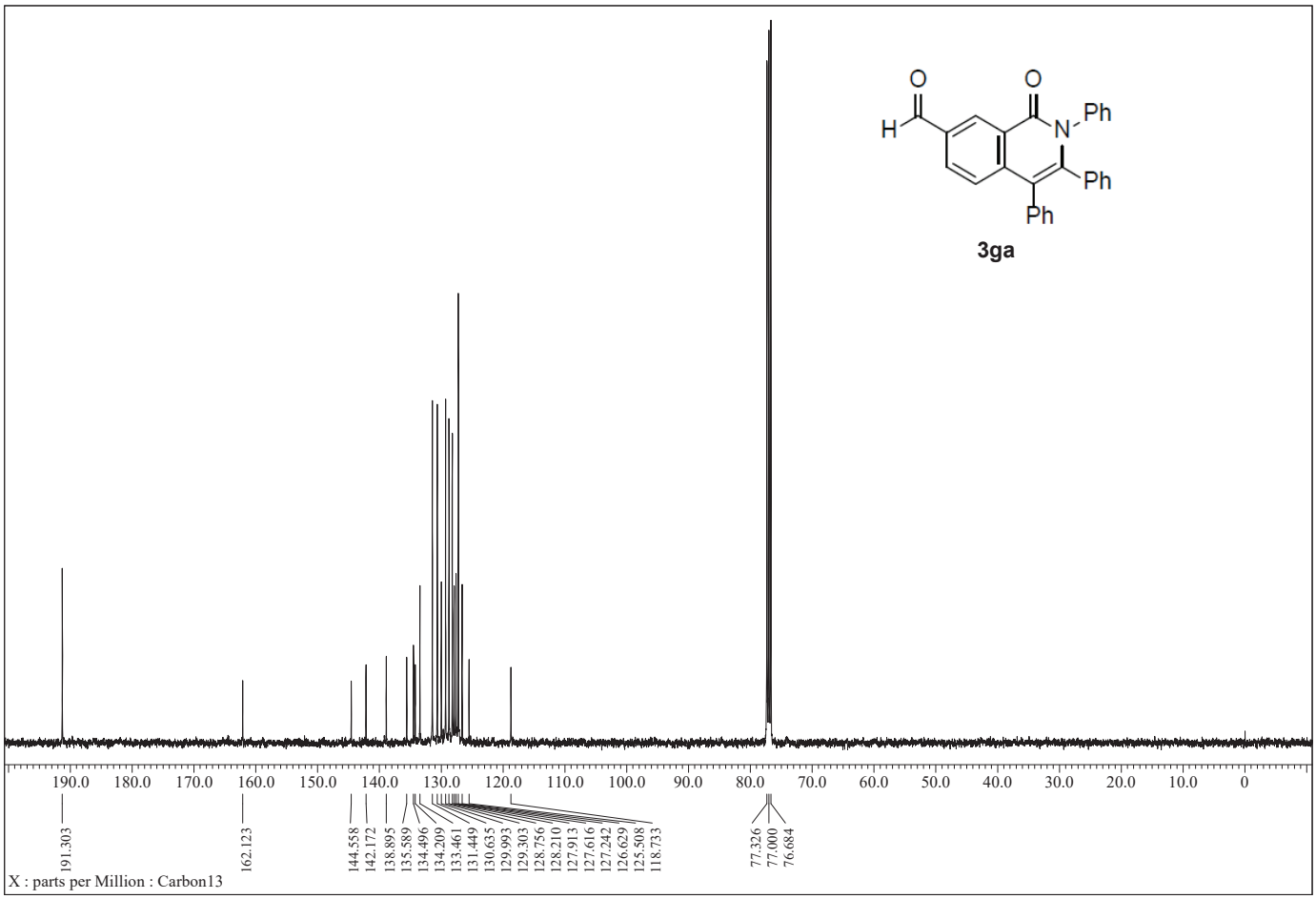

O
F
N
Ph
Ph
Ph
3fa
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.737
161.740
161.702
160.264
140.323
140.294
139.192
136.058
134.401
134.209
134.190
131.420
130.951
129.312
128.574
128.201
128.124
128.009
127.616
127.261
127.118
127.070
126.974
121.148
120.918
118.311
113.290
113.060
77.316
77.000
76.684
X : parts per Million : Carbon13

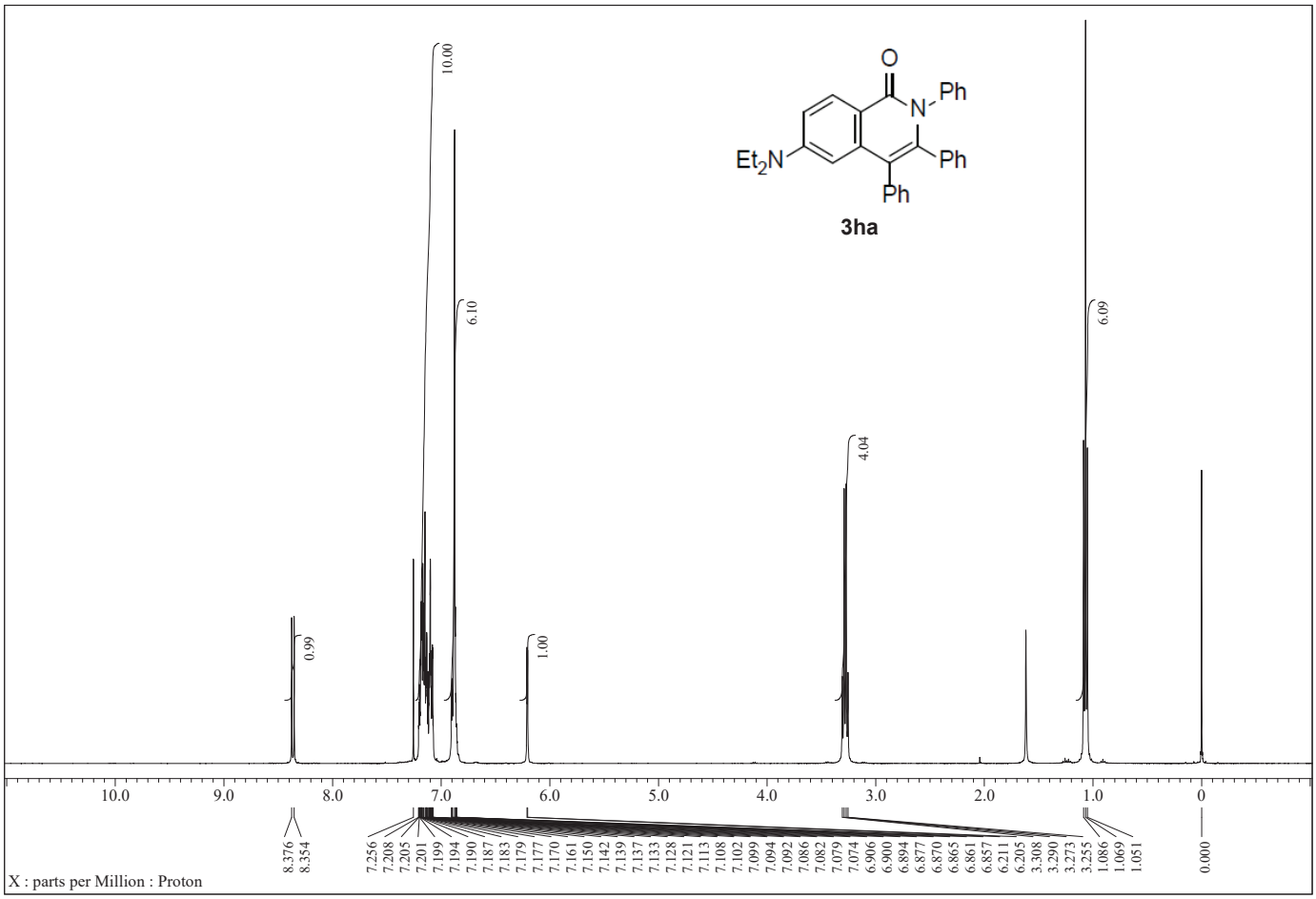

F
O
N
Ph
Ph
Ph
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-113.663
-113.686
-113.702
-113.724
X : parts per Million : Fluorine19

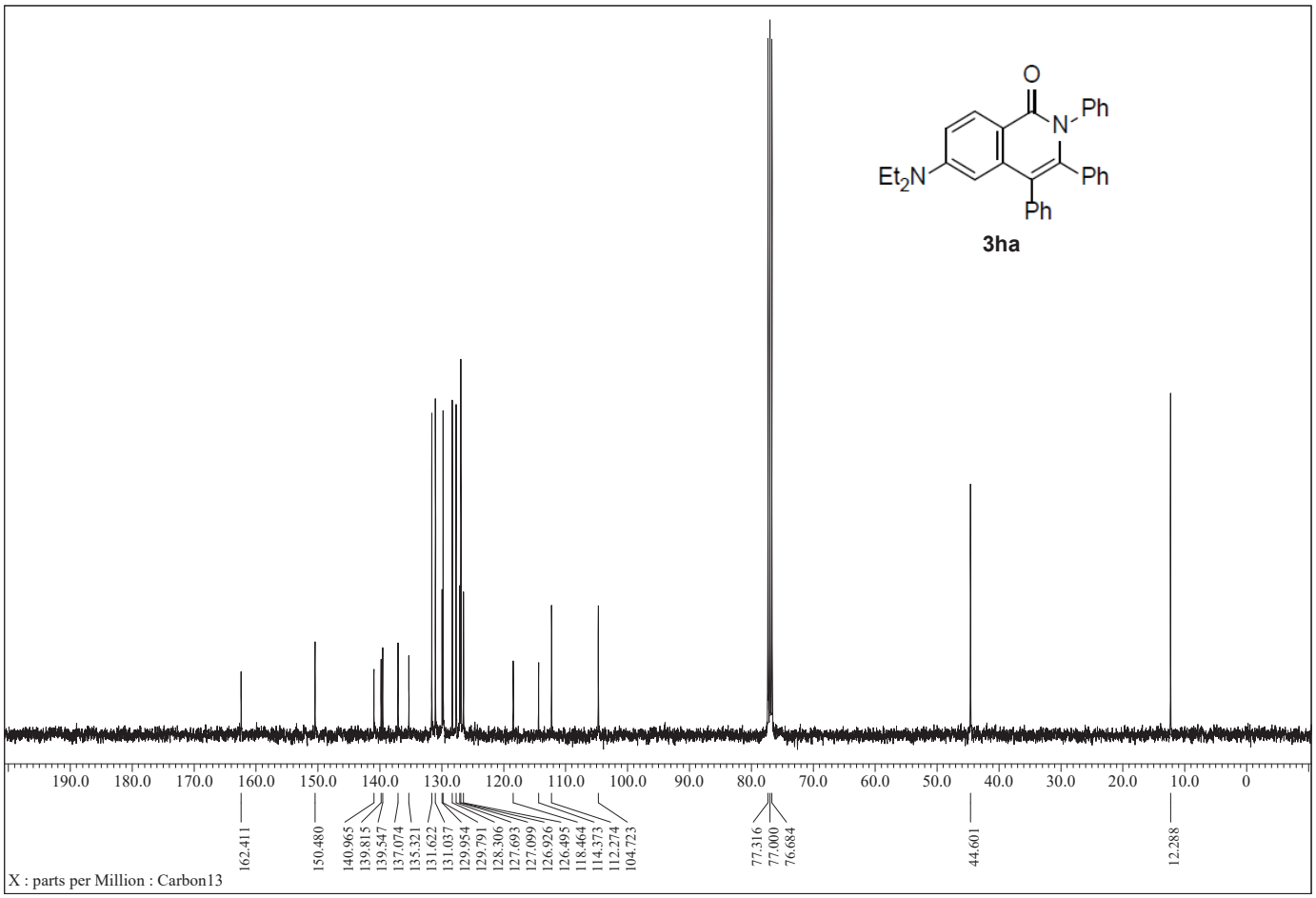
3fa

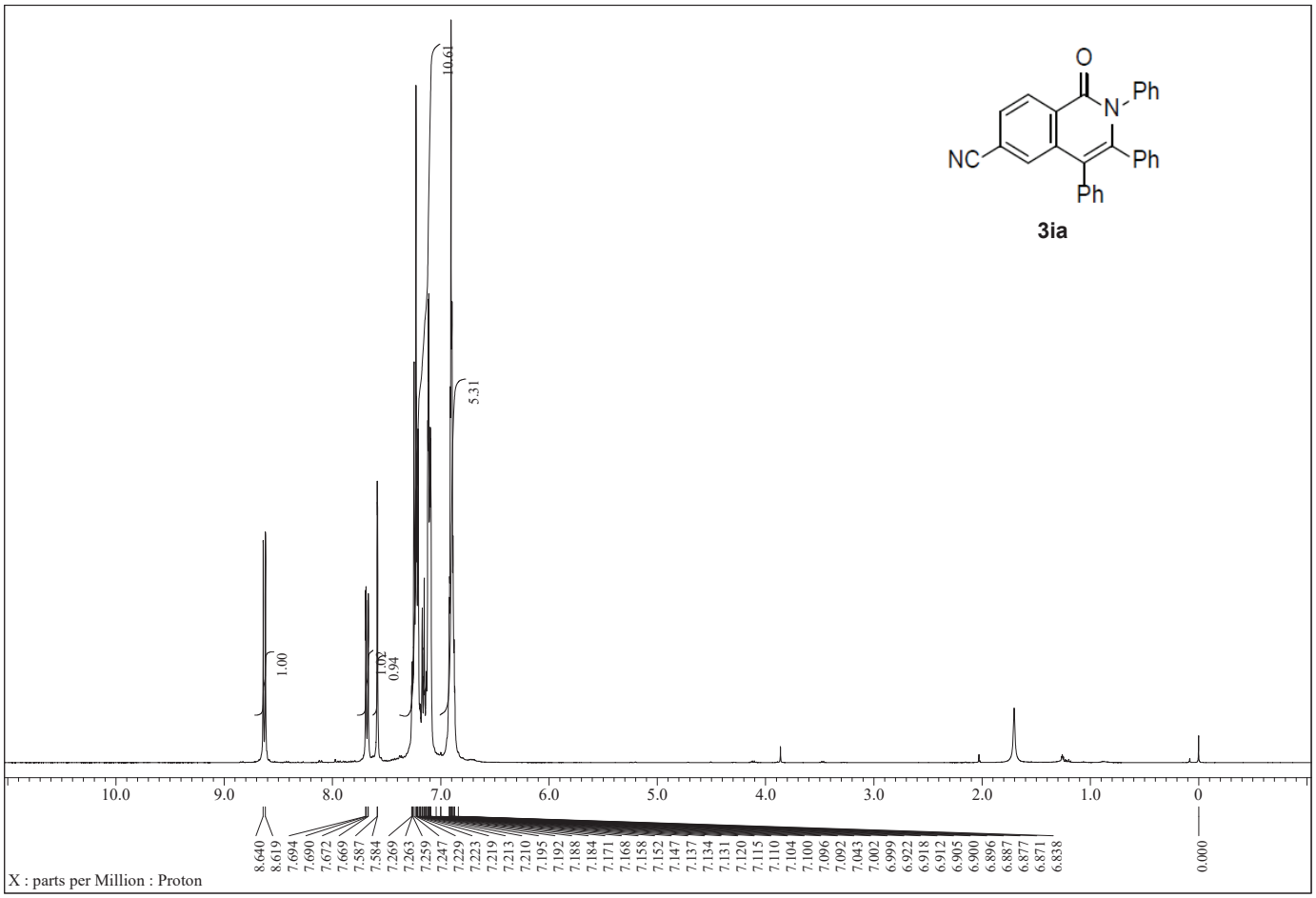

H
O
O
N
Ph
Ph
Ph
11.14
5.34
1.01
1.00
0.98
1.20
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.149
8.996
8.992
8.086
8.081
8.065
8.060
7.385
7.364
7.257
7.241
7.236
7.221
7.217
7.207
7.203
7.197
7.190
7.183
7.180
7.175
7.171
7.165
7.159
7.146
7.136
7.131
7.127
7.120
7.116
7.112
7.109
6.929
6.919
6.912
6.906
6.902
6.894
6.884
6.877
0.000
X : parts per Million : Proton

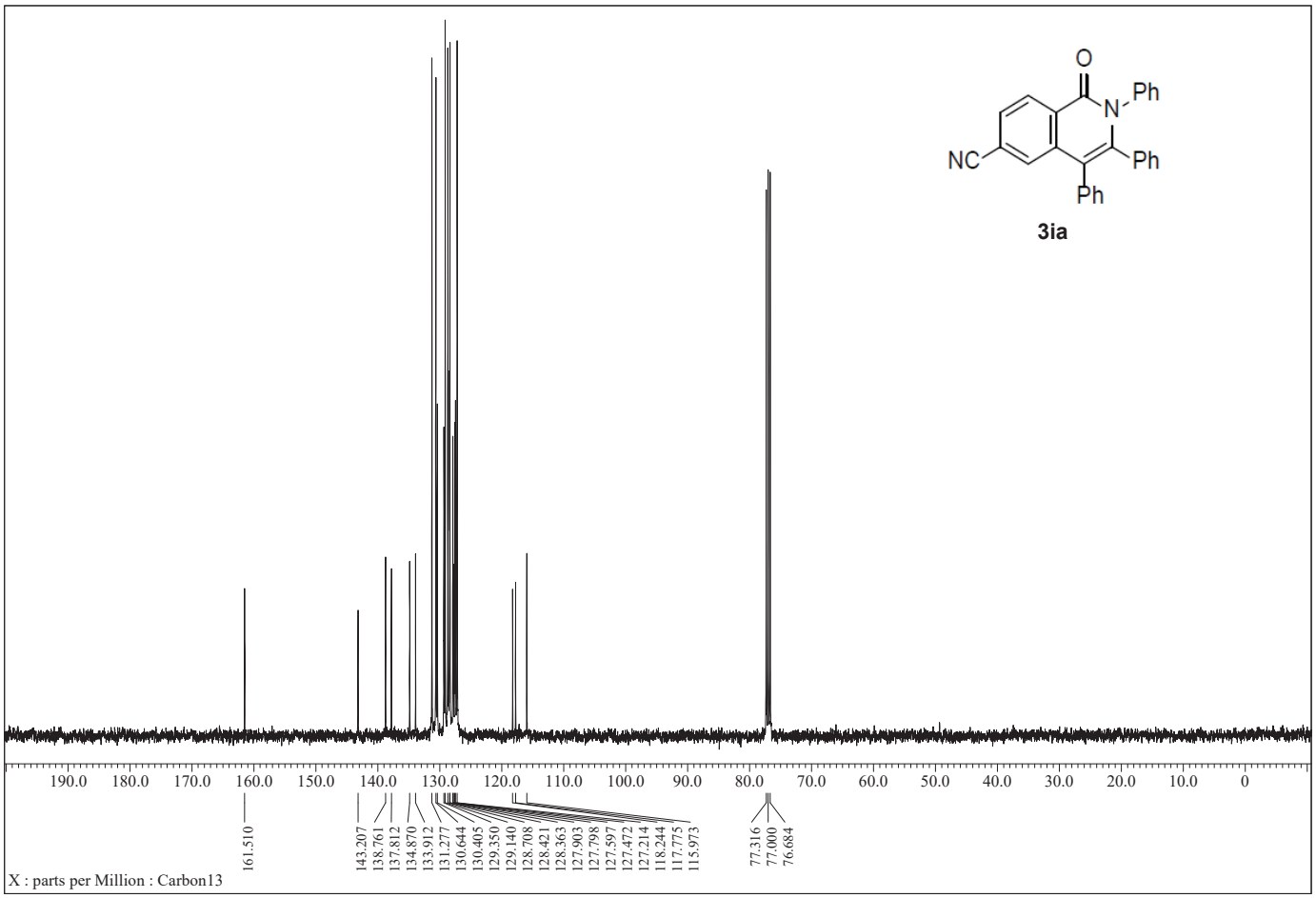
3ga

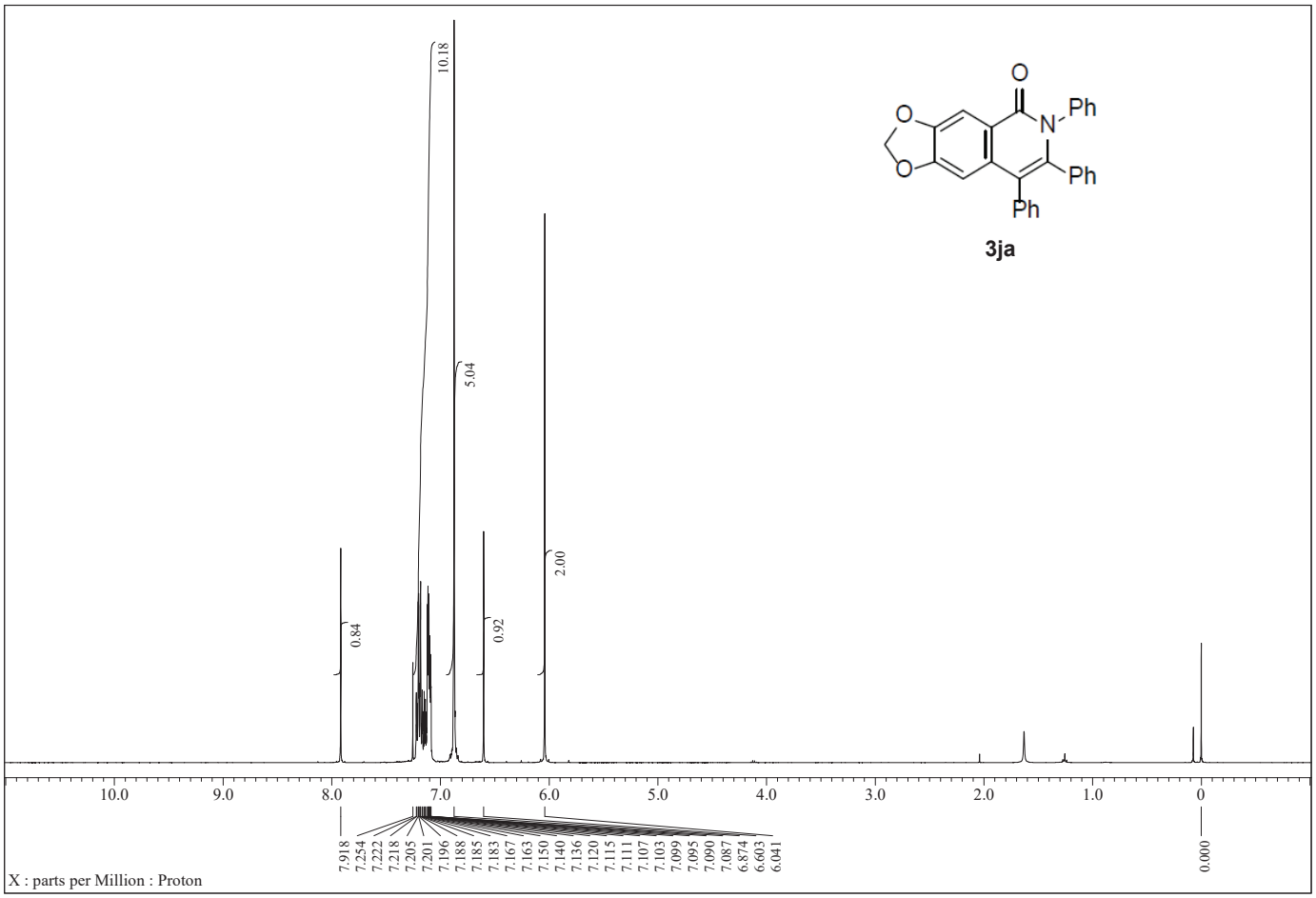

O
O
H
N
Ph
Ph
Ph
3ga
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
191.303
162.123
144.558
142.172
138.895
135.589
134.496
134.209
133.461
131.449
130.635
129.993
129.303
128.756
128.210
127.913
127.616
127.242
126.629
125.508
118.733
77.326
77.000
76.684
X : parts per Million : Carbon13

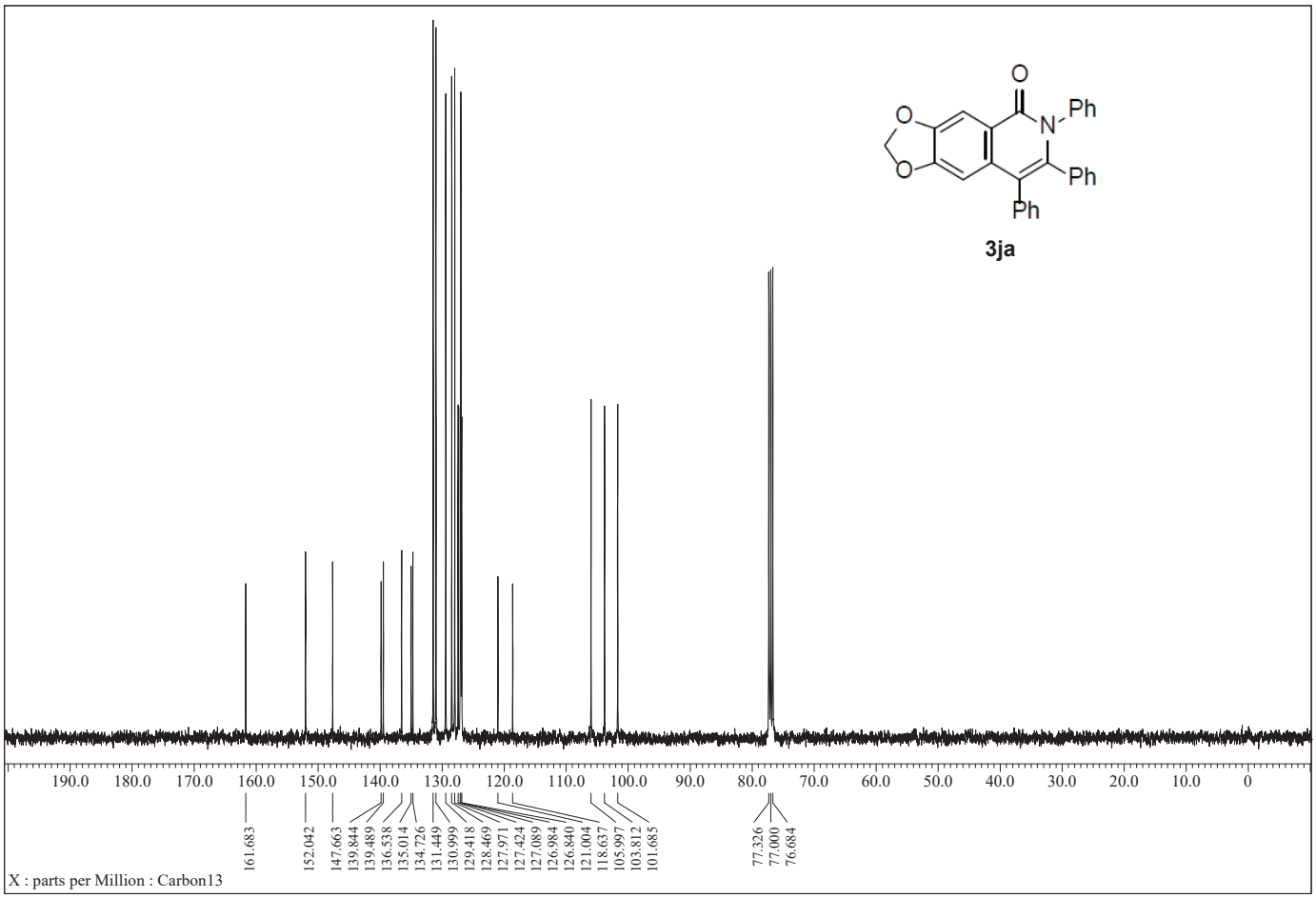

O
N
Ph
Ph
Ph
Et2N
3ha
10.00
6.10
6.09
4.04
0.99
1.00
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.376
8.354
7.256
7.208
7.205
7.201
7.199
7.194
7.190
7.187
7.183
7.179
7.177
7.170
7.161
7.150
7.142
7.139
7.137
7.133
7.128
7.121
7.113
7.108
7.102
7.099
7.094
7.092
7.086
7.082
7.079
7.074
6.906
6.900
6.894
6.877
6.870
6.865
6.861
6.857
6.211
6.205
3.308
3.290
3.273
3.255
1.086
1.069
1.051
0.000
X : parts per Million : Proton

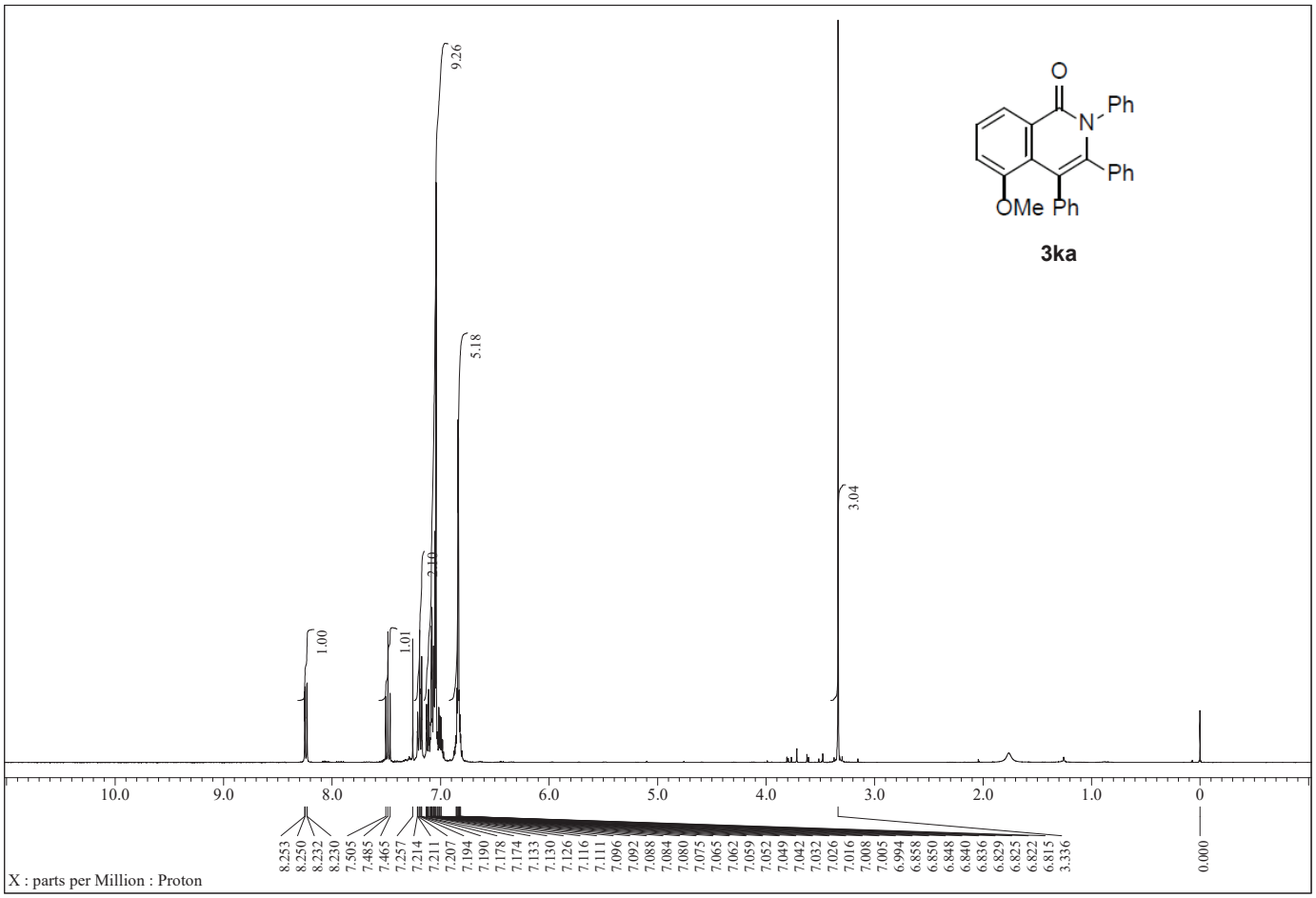

O
N
Ph
Ph
Ph
Et2N
3ha
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.411
150.480
140.965
139.815
139.547
137.074
135.321
131.622
131.037
129.954
129.791
128.306
127.693
127.099
126.926
126.495
118.464
114.373
112.274
104.723
77.316
77.000
76.684
44.601
12.288
X : parts per Million : Carbon13

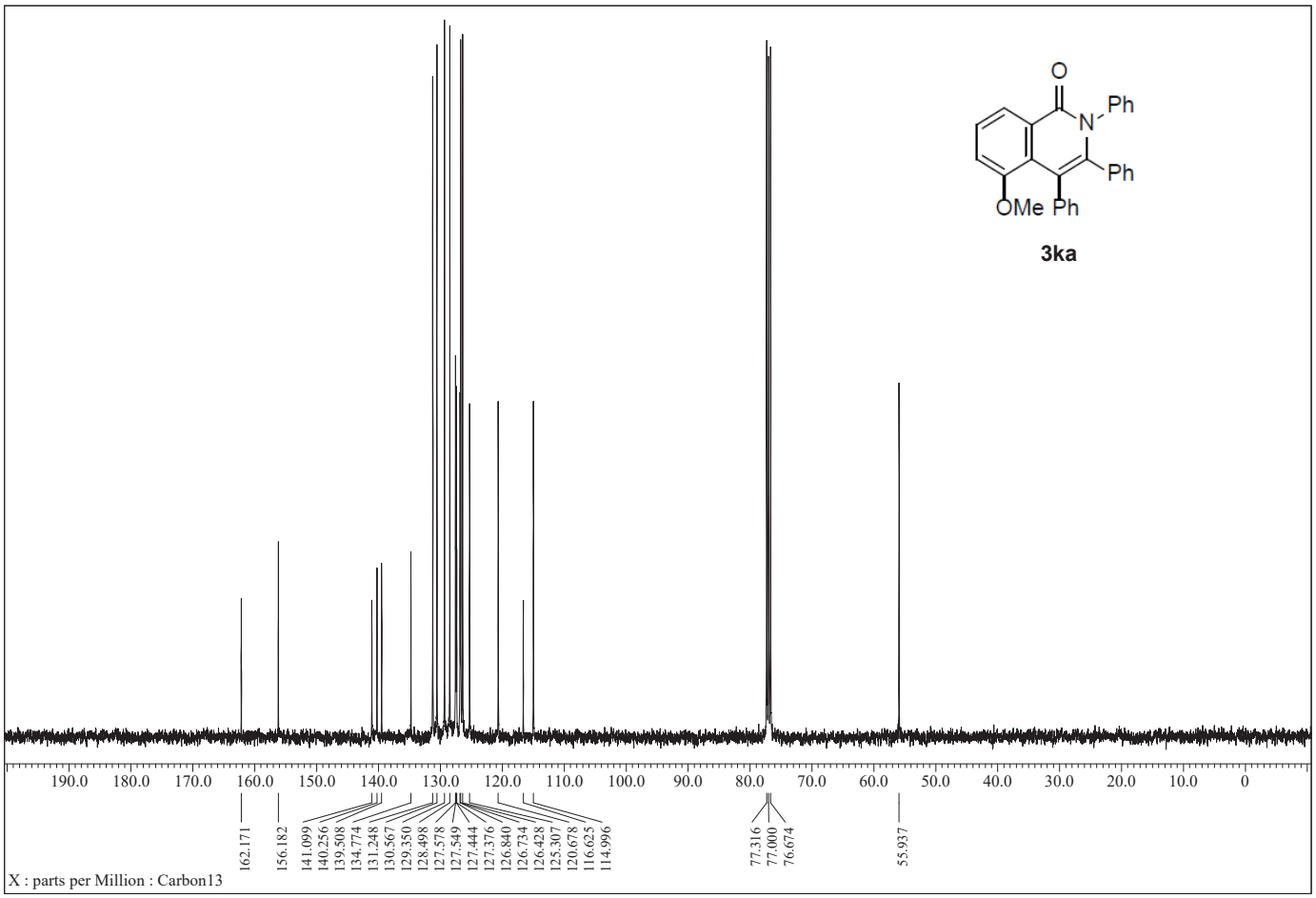

O
N
Ph
Ph
Ph
NC
3ia
10.61
5.31
1.00
1.02
0.94
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.640
8.619
7.694
7.690
7.672
7.669
7.587
7.584
7.269
7.263
7.259
7.247
7.229
7.223
7.219
7.213
7.210
7.195
7.192
7.188
7.184
7.171
7.168
7.158
7.152
7.147
7.137
7.134
7.131
7.120
7.115
7.110
7.104
7.100
7.096
7.092
7.043
7.002
6.999
6.922
6.918
6.912
6.905
6.900
6.896
6.887
6.877
6.871
6.838
0.000
X : parts per Million : Proton

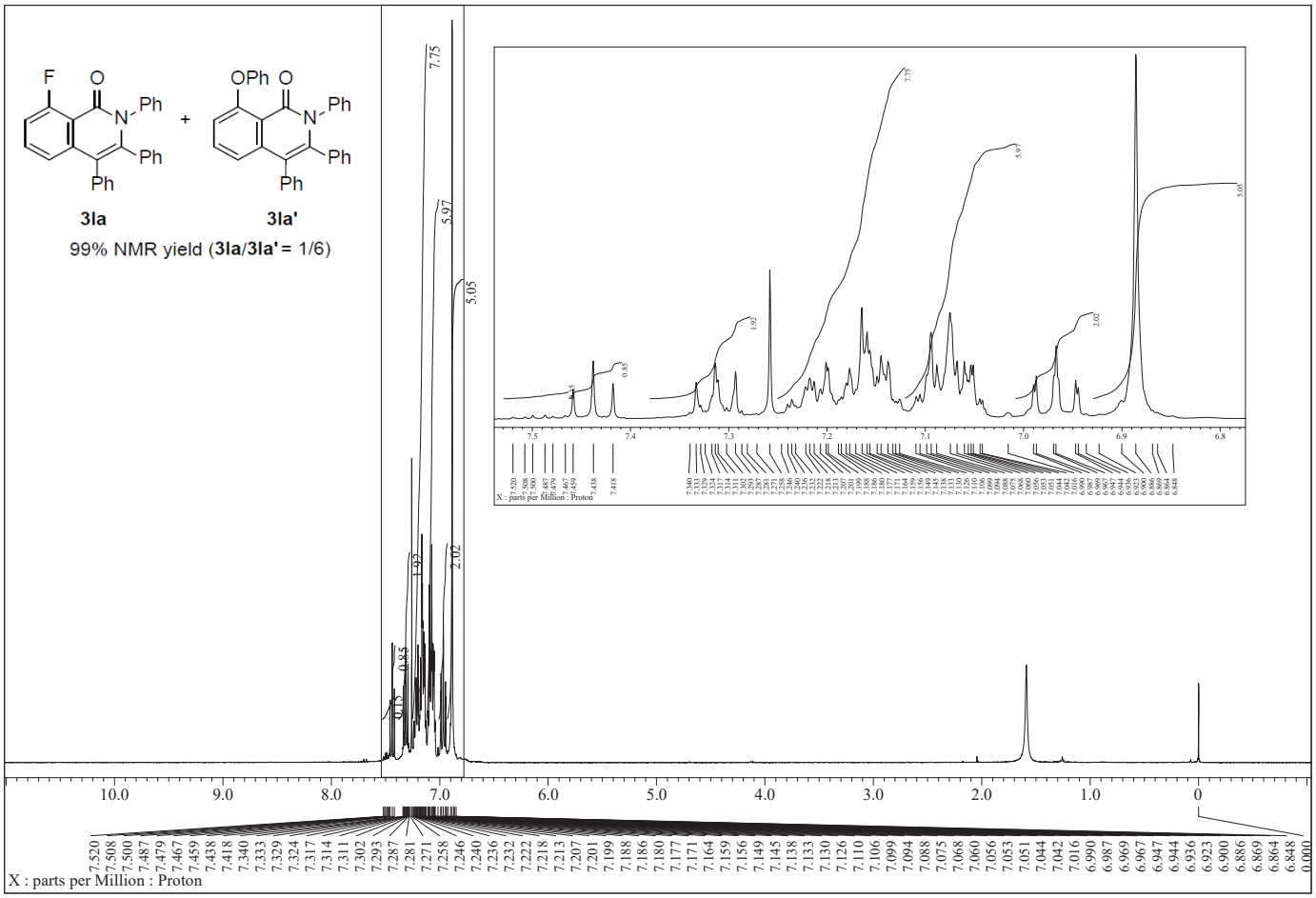

O
N
Ph
Ph
Ph
NC
3ia
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
161.510
143.207
138.761
137.812
134.870
133.912
131.277
130.644
130.405
129.350
129.140
128.708
128.421
128.363
127.903
127.798
127.597
127.472
127.214
118.244
117.775
115.973
77.316
77.000
76.684
X : parts per Million : Carbon13

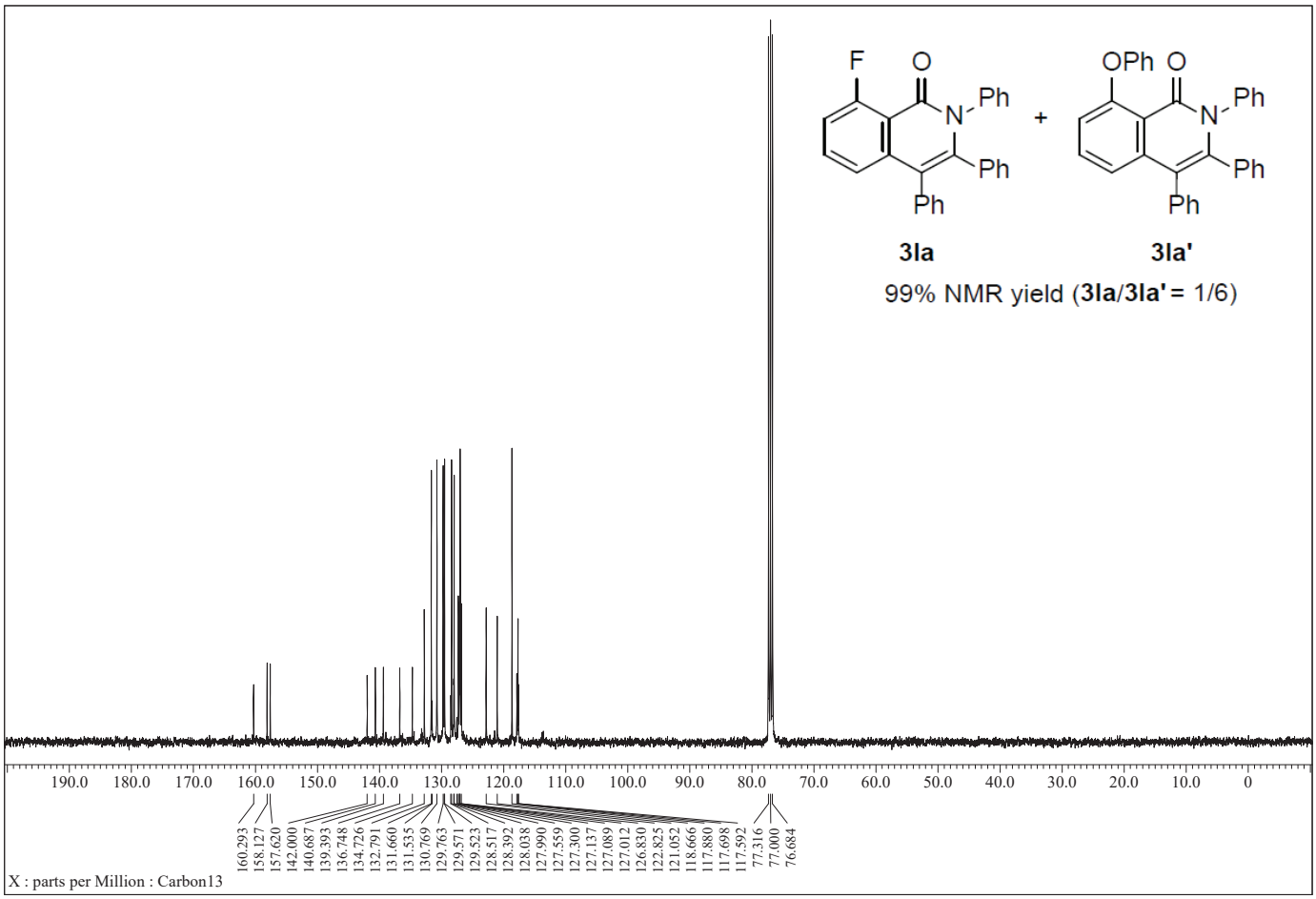

10.18
5.04
2.00
0.92
0.84
O
O
O
N
Ph
Ph
Ph
3ja
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.918
7.254
7.222
7.218
7.205
7.201
7.196
7.188
7.185
7.183
7.167
7.163
7.150
7.140
7.136
7.120
7.115
7.111
7.107
7.103
7.099
7.095
7.090
7.087
6.874
6.603
6.041
0.000
X : parts per Million : Proton

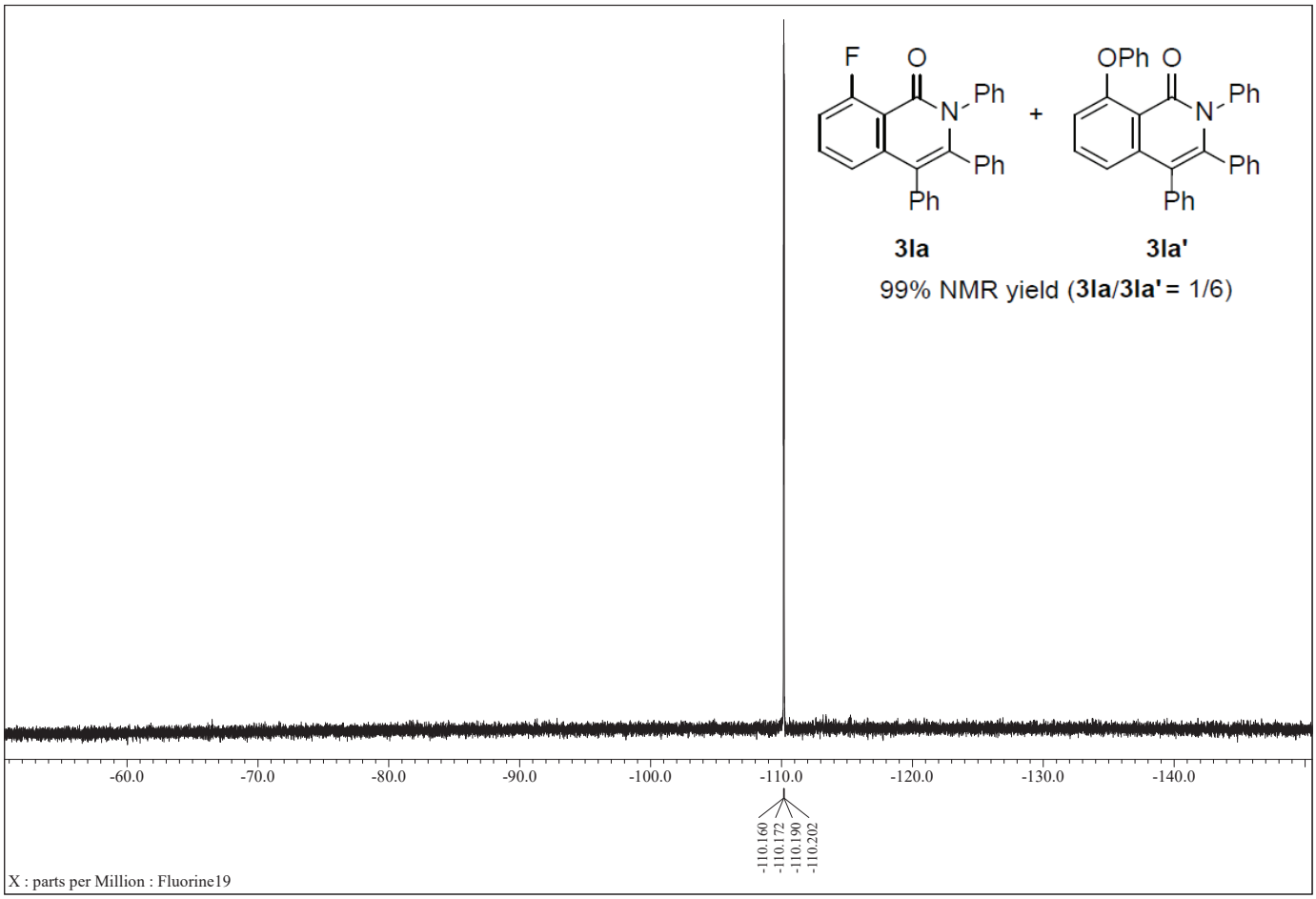

O
O
O
N
Ph
Ph
Ph
3ja
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
161.683
152.042
147.663
139.844
139.489
136.538
135.014
134.726
131.449
130.999
129.418
128.469
127.971
127.424
127.089
126.984
126.840
121.004
118.637
105.997
103.812
101.685
77.326
77.000
76.684
X : parts per Million : Carbon13

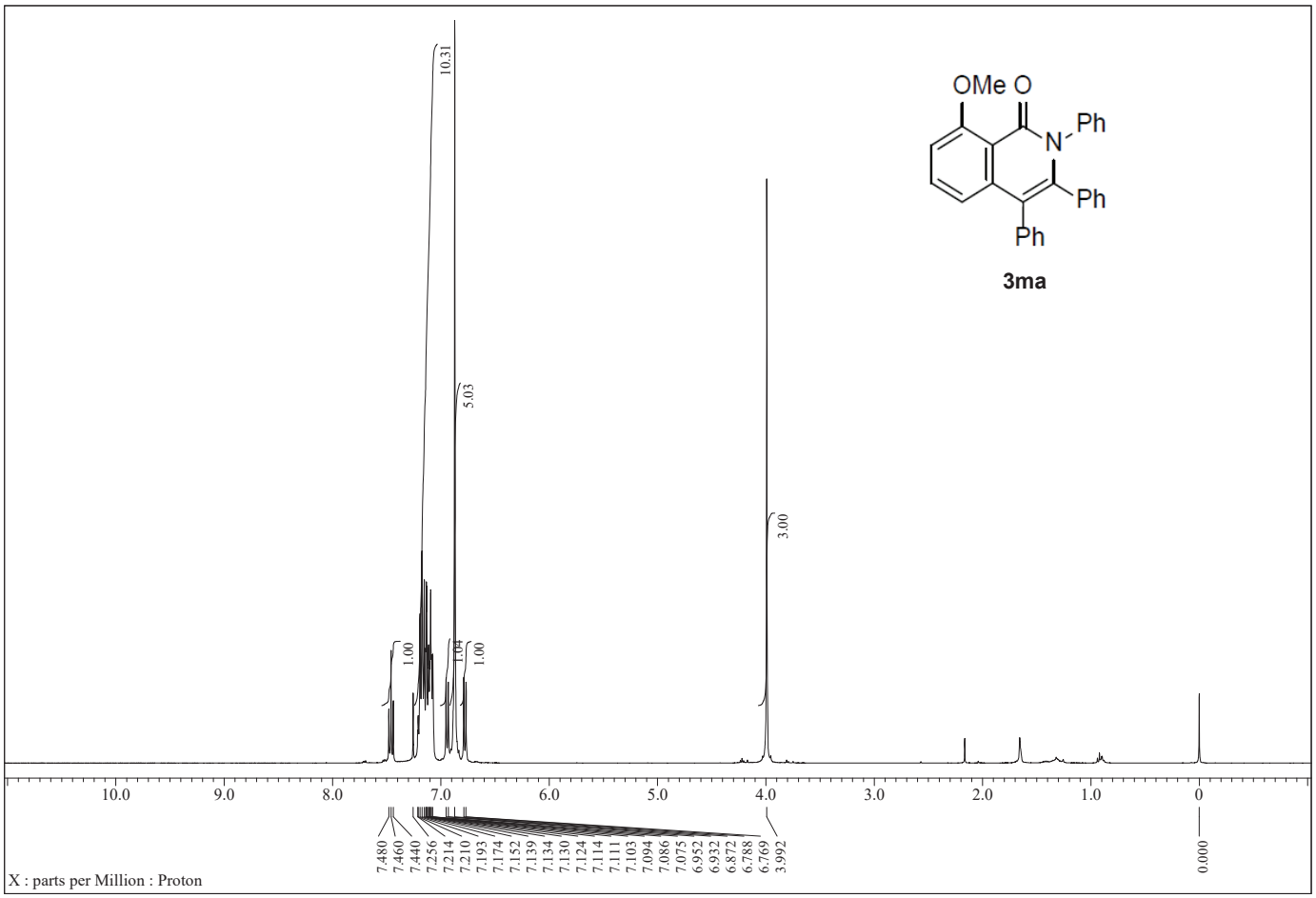

O
N
Ph
Ph
OMe Ph
3ka
9.26
5.18
3.04
2.10
1.00
1.01
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.253
8.250
8.232
8.230
7.505
7.485
7.465
7.257
7.214
7.211
7.207
7.194
7.190
7.178
7.174
7.133
7.130
7.126
7.116
7.111
7.096
7.092
7.088
7.084
7.080
7.075
7.065
7.062
7.059
7.052
7.049
7.042
7.032
7.026
7.016
7.008
7.005
6.994
6.858
6.850
6.848
6.840
6.836
6.829
6.825
6.822
6.815
3.336
0.000
X : parts per Million : Proton

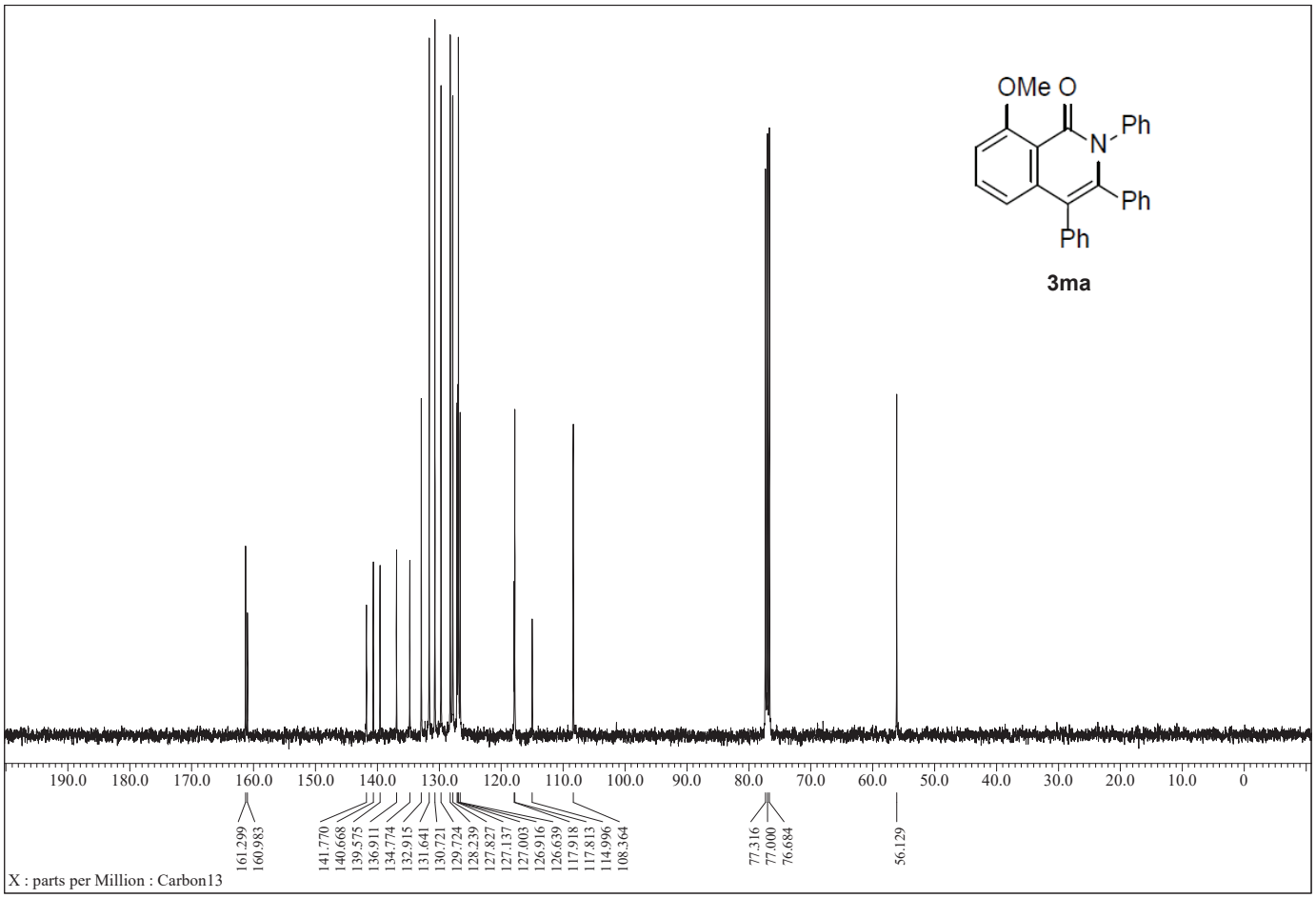

O
N
Ph
Ph
OMe Ph
3ka
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.171
156.182
141.099
140.256
139.508
134.774
131.248
130.567
129.350
128.498
127.578
127.549
127.444
127.376
126.840
126.734
126.428
125.307
120.678
116.625
114.996
77.316
77.000
76.674
55.937
X : parts per Million : Carbon13

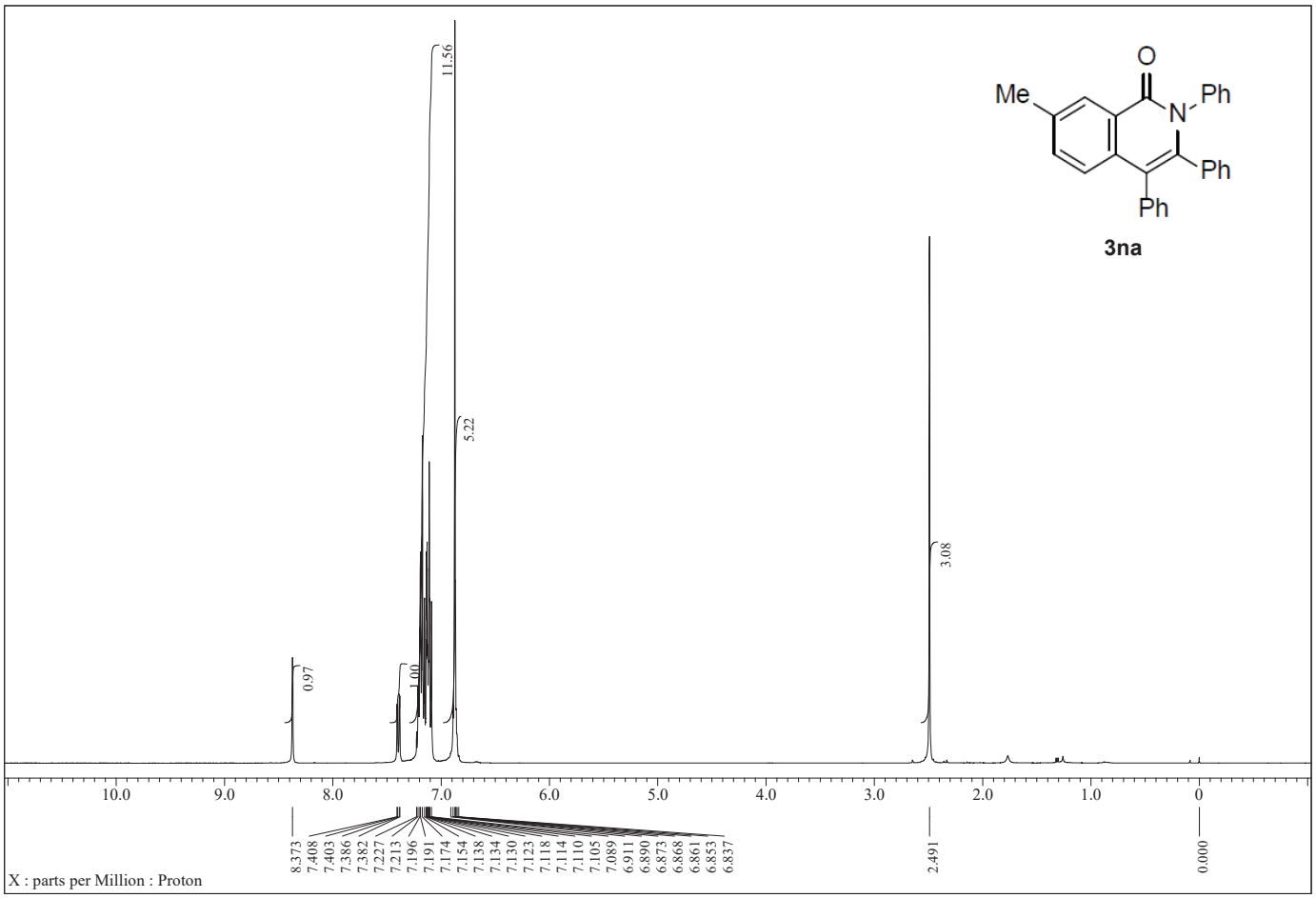

F
O
Ph
N
Ph
Ph
+
OPh
O
Ph
N
Ph
Ph
3la
3la'
99% NMR yield (3la/3la' = 1/6)
7.75
5.97
5.05
2.02
1.93
0.85
0.85
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
X : parts per Million : Proton

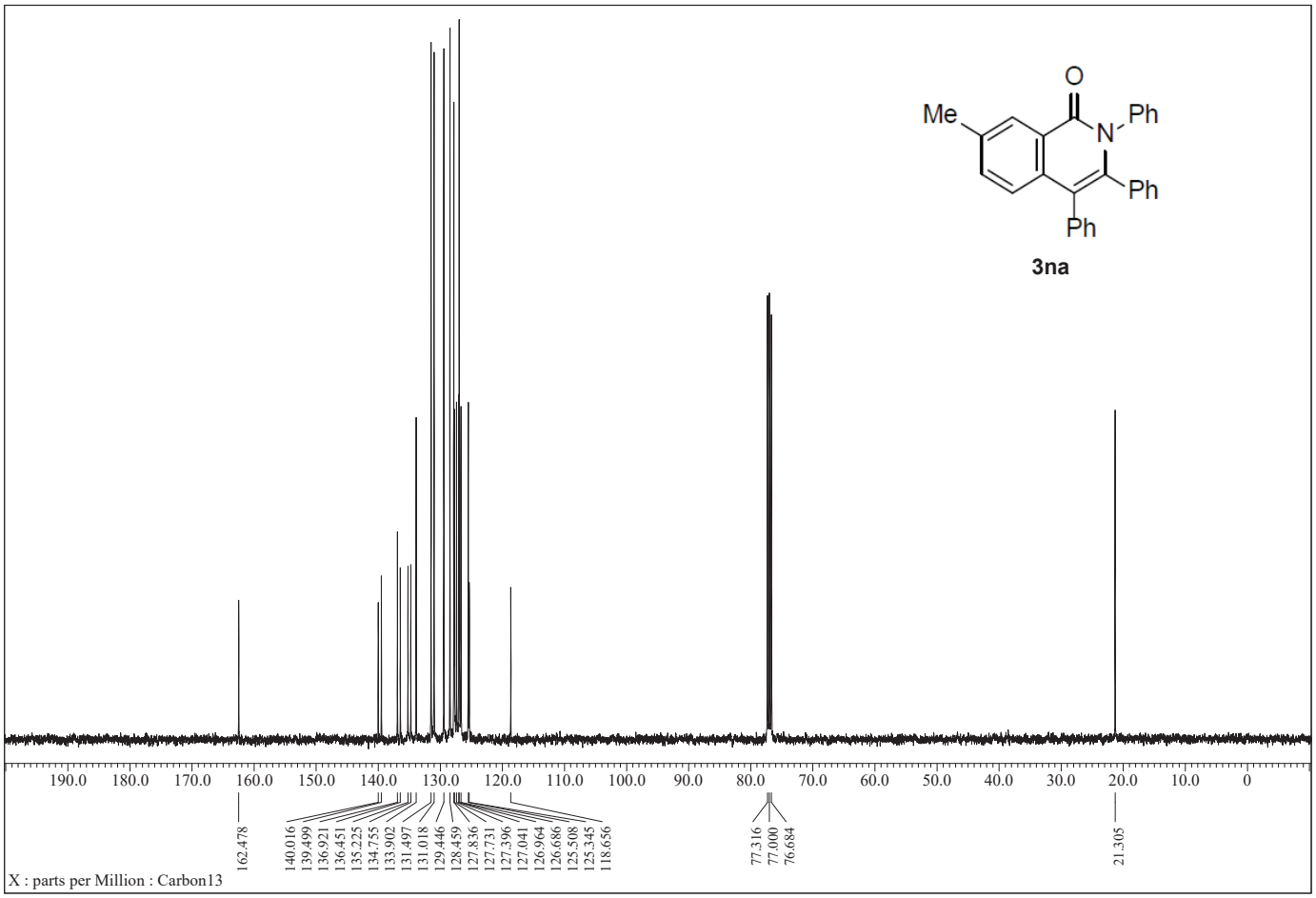

F
O
Ph
N
Ph
Ph
+
OPh
O
Ph
N
Ph
Ph
3la
3la'
99% NMR yield (3la/3la' = 1/6)
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
160.293
158.127
157.620
142.000
140.687
139.393
136.748
134.726
132.791
131.660
131.535
130.769
129.763
129.571
129.523
128.517
128.392
128.038
127.990
127.559
127.300
127.137
127.089
127.012
126.830
122.825
121.052
118.666
117.880
117.698
117.592
77.316
77.000
76.684
X : parts per Million : Carbon13

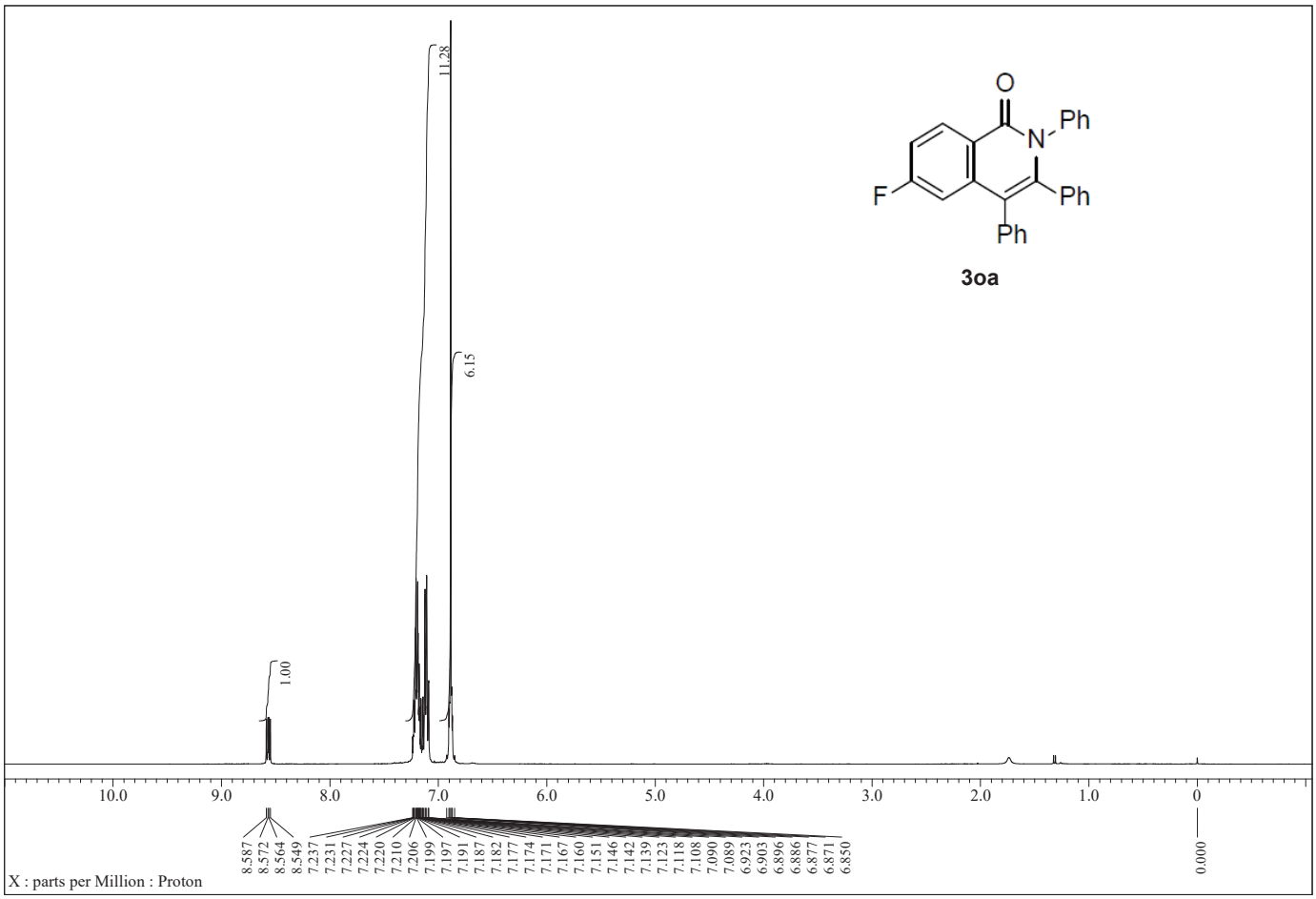

F
O
Ph
N
Ph
Ph
+
OPh
O
Ph
N
Ph
Ph
3la
3la'
99% NMR yield (3la/3la' = 1/6)
-60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0
-110.160
-110.172
-110.190
-110.202
X : parts per Million : Fluorine19

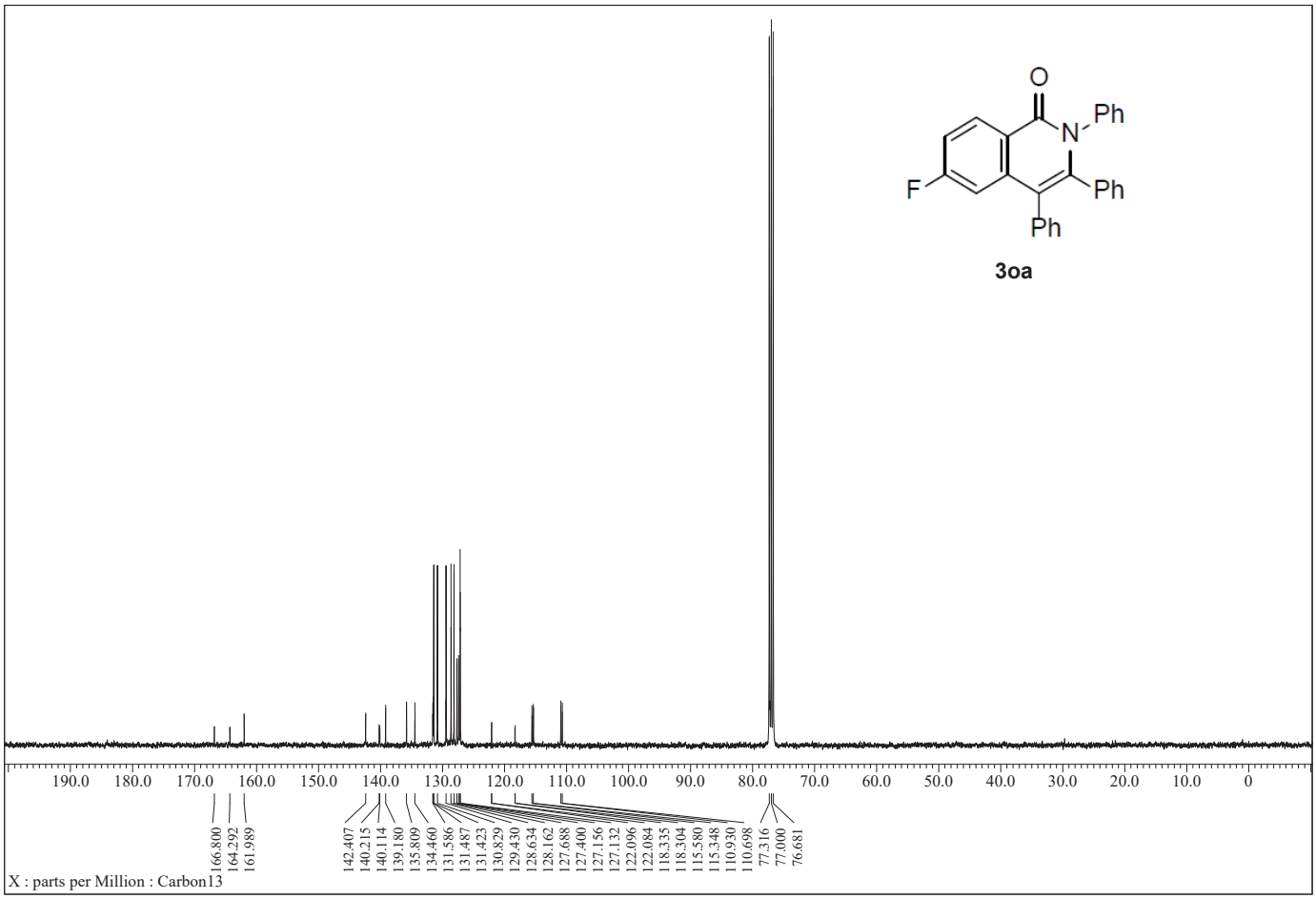

OMe O
Ph
N
Ph
Ph
3ma
10.31
5.03
3.00
1.00
1.04
1.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.480
7.460
7.440
7.256
7.214
7.210
7.193
7.174
7.152
7.139
7.134
7.130
7.124
7.114
7.111
7.103
7.094
7.086
7.075
6.952
6.932
6.872
6.788
6.769
3.992
0.000
X : parts per Million : Proton

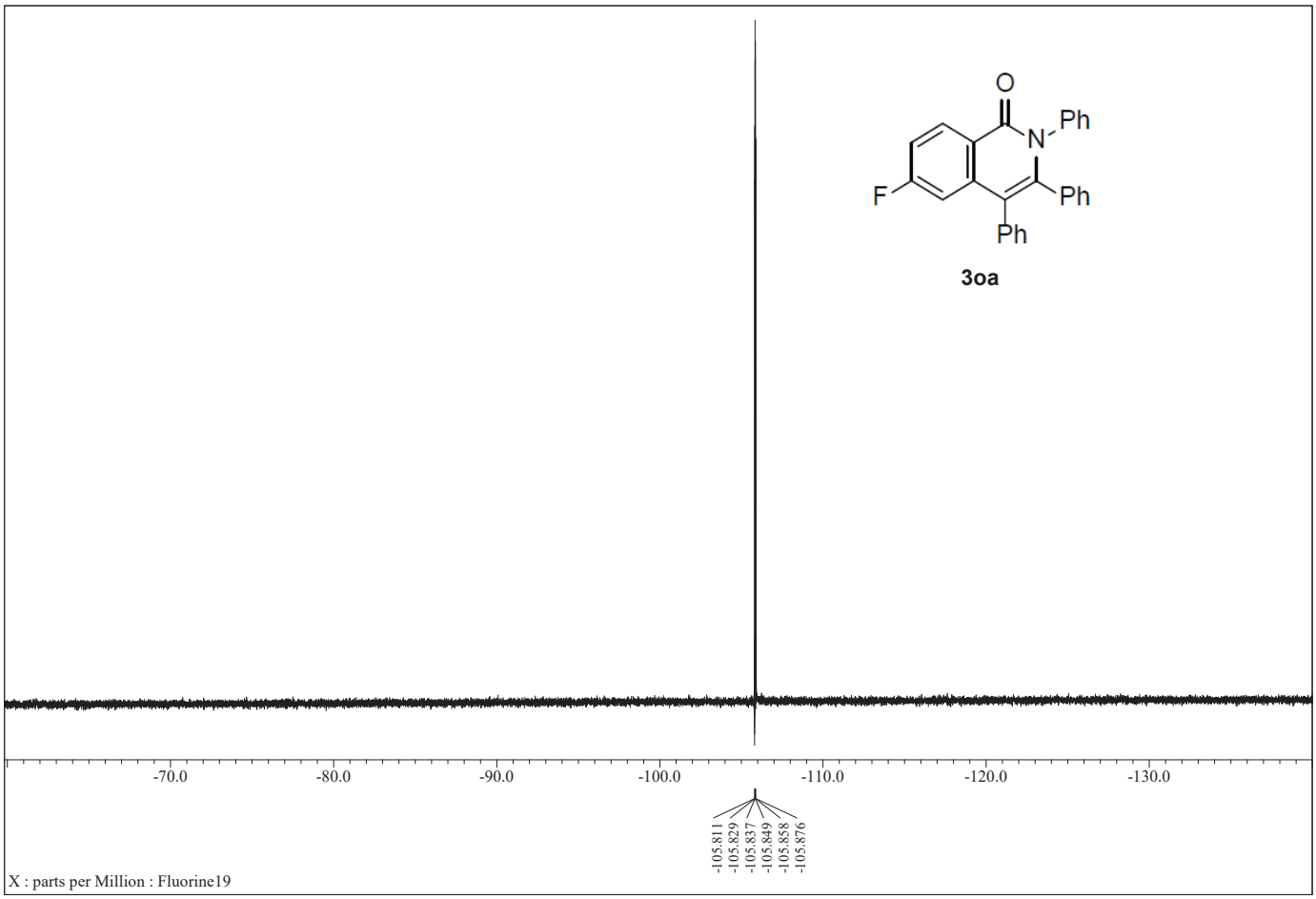

OMe O
Ph
N
Ph
Ph
3ma
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
161.299
160.983
141.770
140.668
139.575
136.911
134.774
132.915
131.641
130.721
129.724
128.239
127.827
127.137
127.003
126.916
126.639
117.918
117.813
114.996
108.364
77.316
77.000
76.684
56.129
X : parts per Million : Carbon13


O
Me
N
Ph
Ph
Ph
3na
11.56
5.22
3.08
1.00
0.97
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.373
7.408
7.403
7.386
7.382
7.227
7.213
7.196
7.191
7.174
7.154
7.138
7.134
7.130
7.123
7.118
7.114
7.110
7.105
7.089
6.911
6.890
6.873
6.868
6.861
6.853
6.837
2.491
0.000
X : parts per Million : Proton

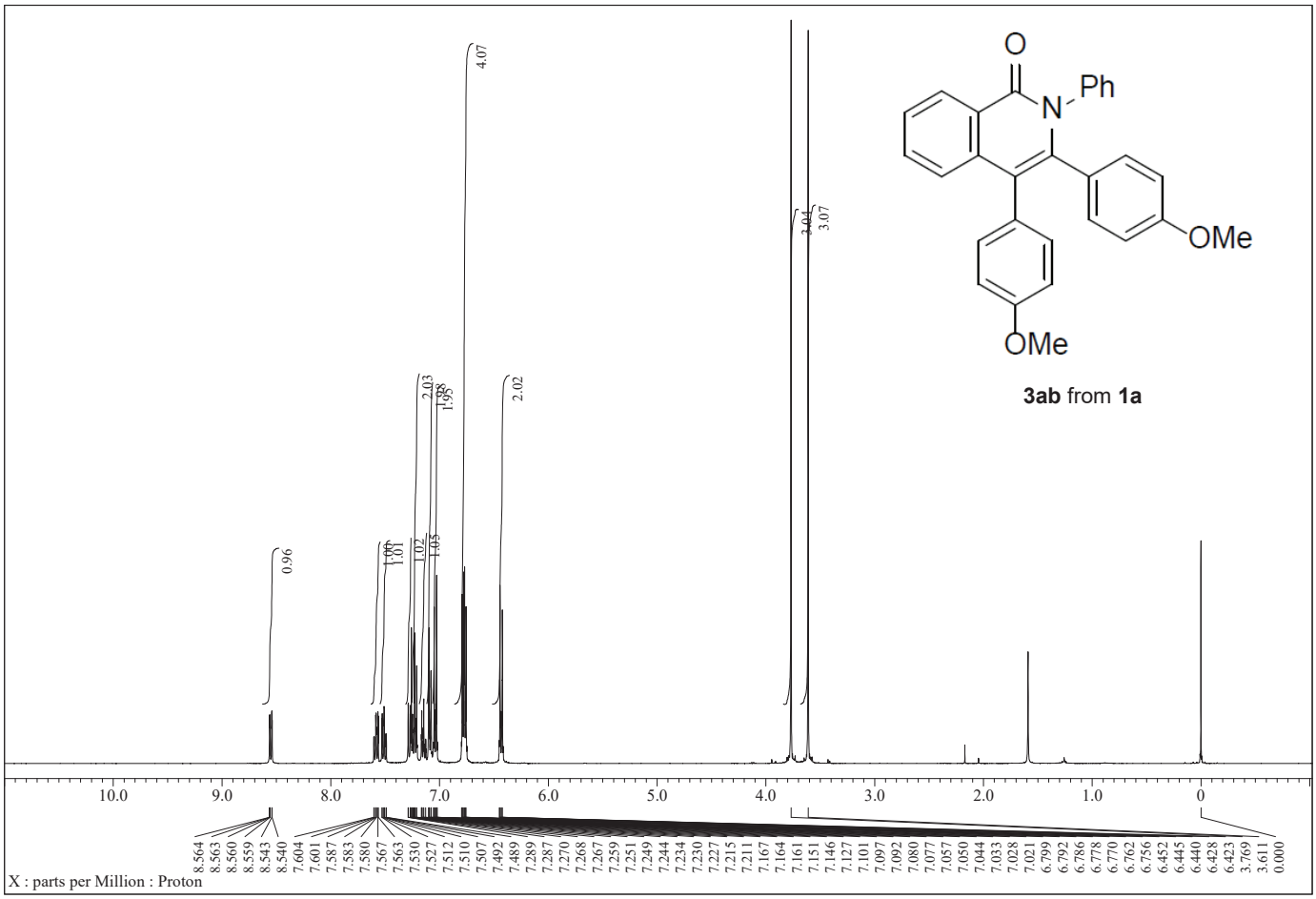

O
Me
N
Ph
Ph
Ph
3na
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.478
140.016
139.499
136.921
136.451
135.225
134.755
133.902
131.497
131.018
129.446
128.459
127.836
127.731
127.396
127.041
126.964
126.686
125.508
125.345
118.656
77.316
77.000
76.684
21.305
X : parts per Million : Carbon13


11.28
6.15
1.00
O
N
Ph
Ph
Ph
F
3oa
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.587
8.572
8.564
8.549
7.237
7.231
7.227
7.224
7.220
7.210
7.206
7.199
7.197
7.191
7.187
7.182
7.177
7.174
7.171
7.167
7.160
7.151
7.146
7.142
7.139
7.123
7.118
7.108
7.090
7.089
6.923
6.903
6.896
6.886
6.877
6.871
6.850
0.000
X : parts per Million : Proton

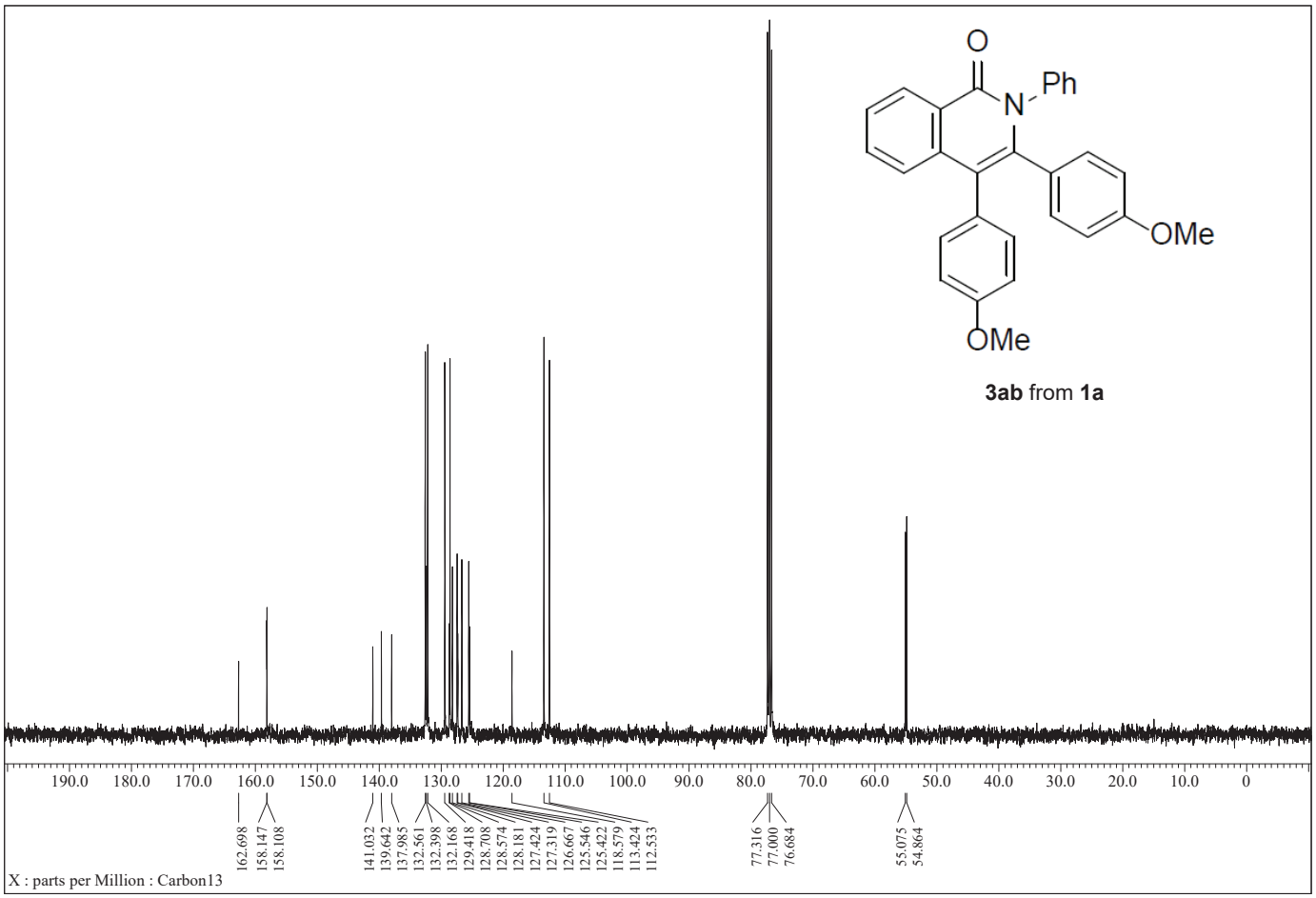

O
N
Ph
Ph
Ph
F
3oa
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
166.800
164.292
161.989
142.407
140.215
140.114
139.180
135.809
134.460
131.586
131.487
131.423
130.829
129.430
128.634
128.162
127.688
127.400
127.156
127.132
122.096
122.084
118.335
118.304
115.580
115.348
110.930
110.698
77.316
77.000
76.681
X : parts per Million : Carbon13

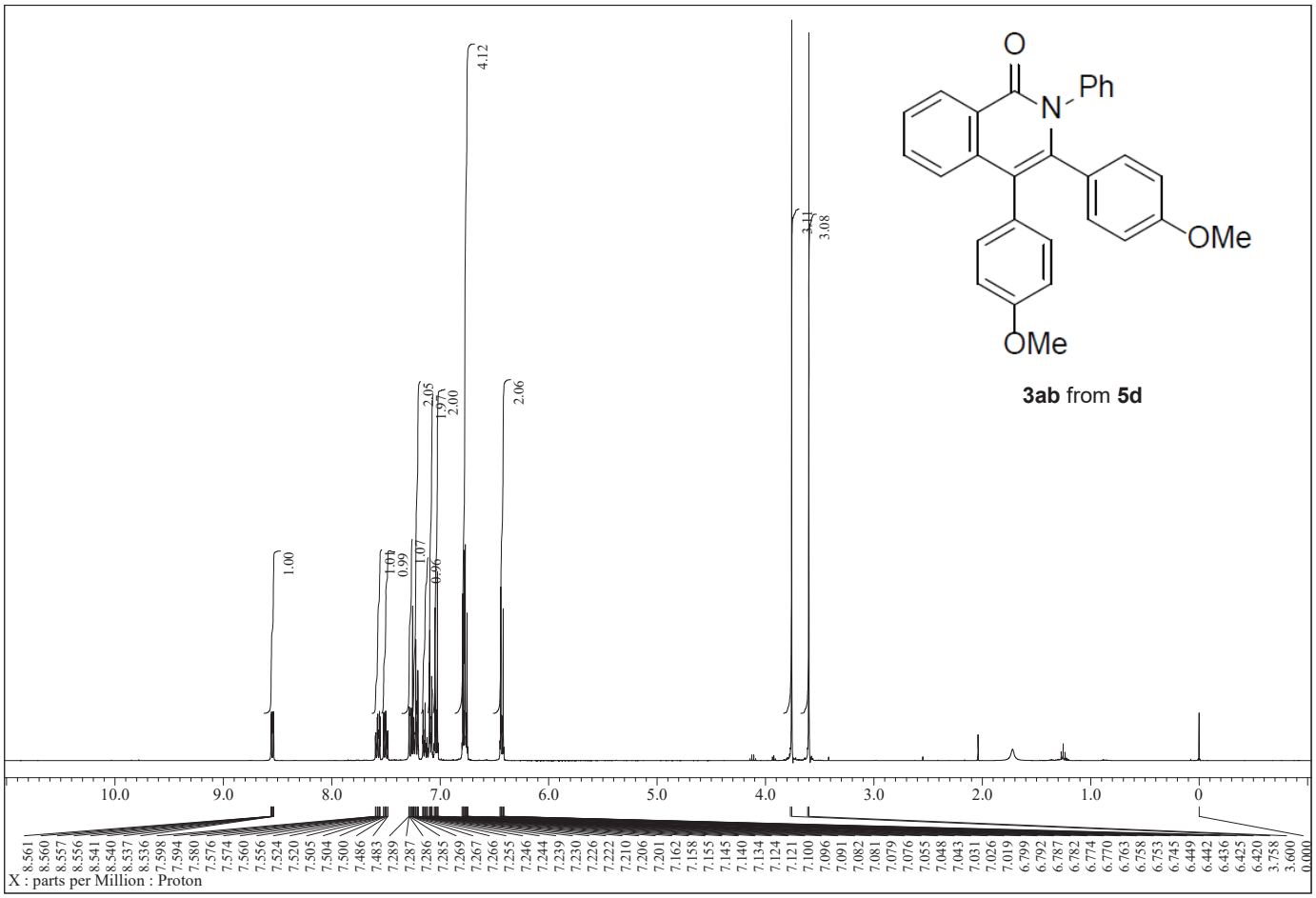


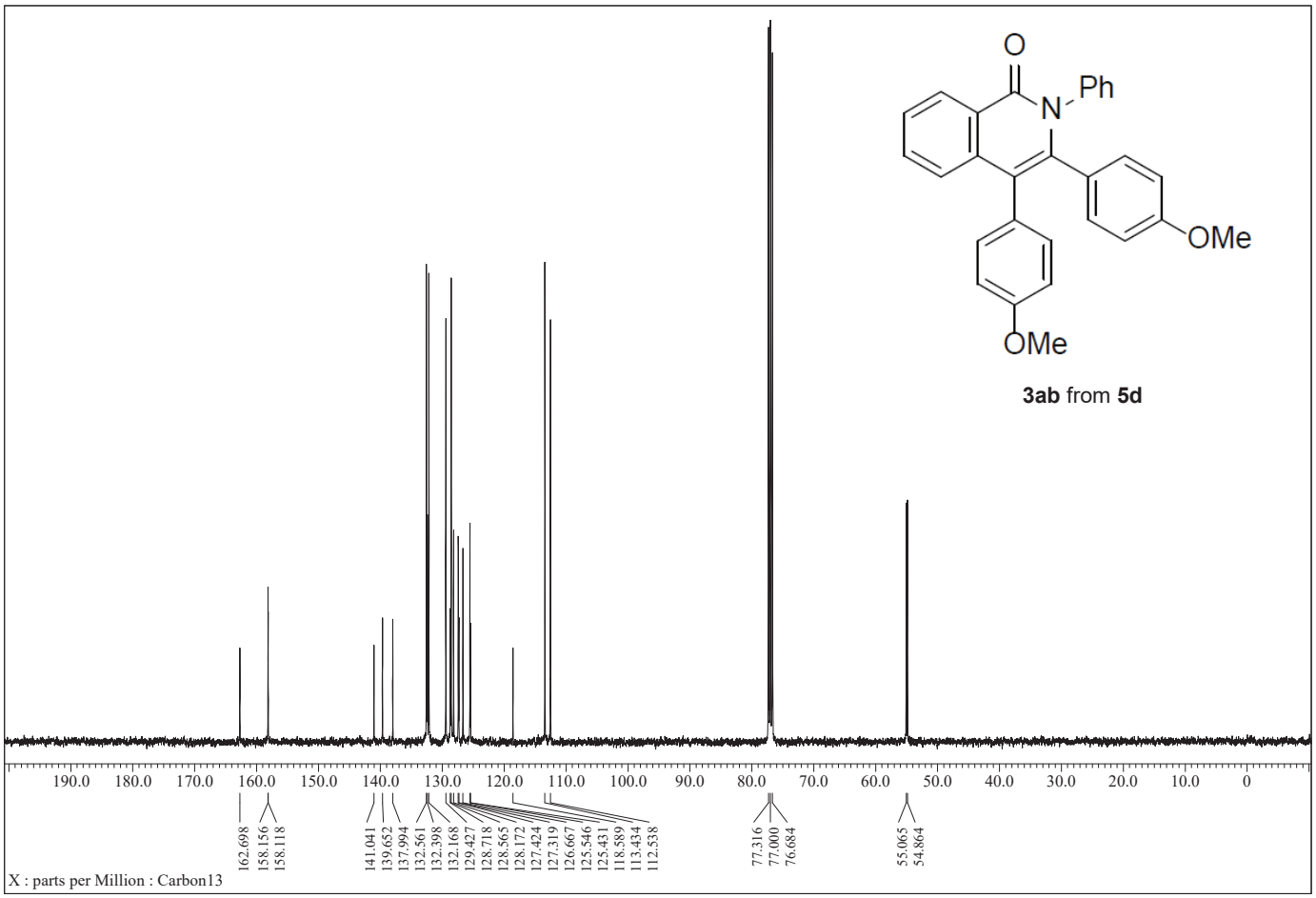
3oa



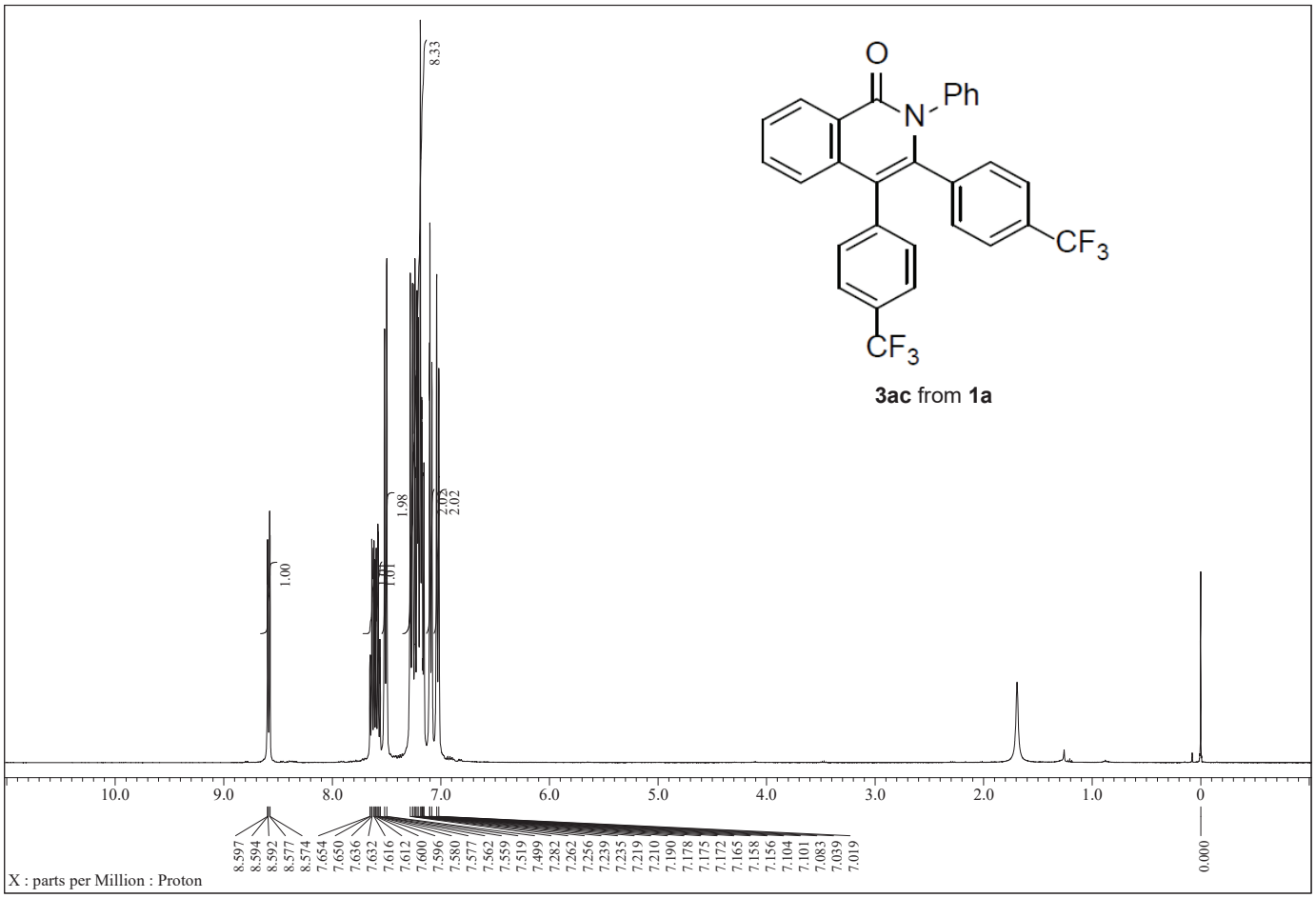
3ab from **1a**


O
N
Ph
OMe
OMe
3ab from 1a
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.698
158.147
158.108
141.032
139.642
137.985
132.561
132.398
132.168
129.418
128.708
128.574
128.181
127.424
127.319
126.667
125.546
125.422
118.579
113.424
112.533
77.316
77.000
76.684
55.075
54.864
X : parts per Million : Carbon13

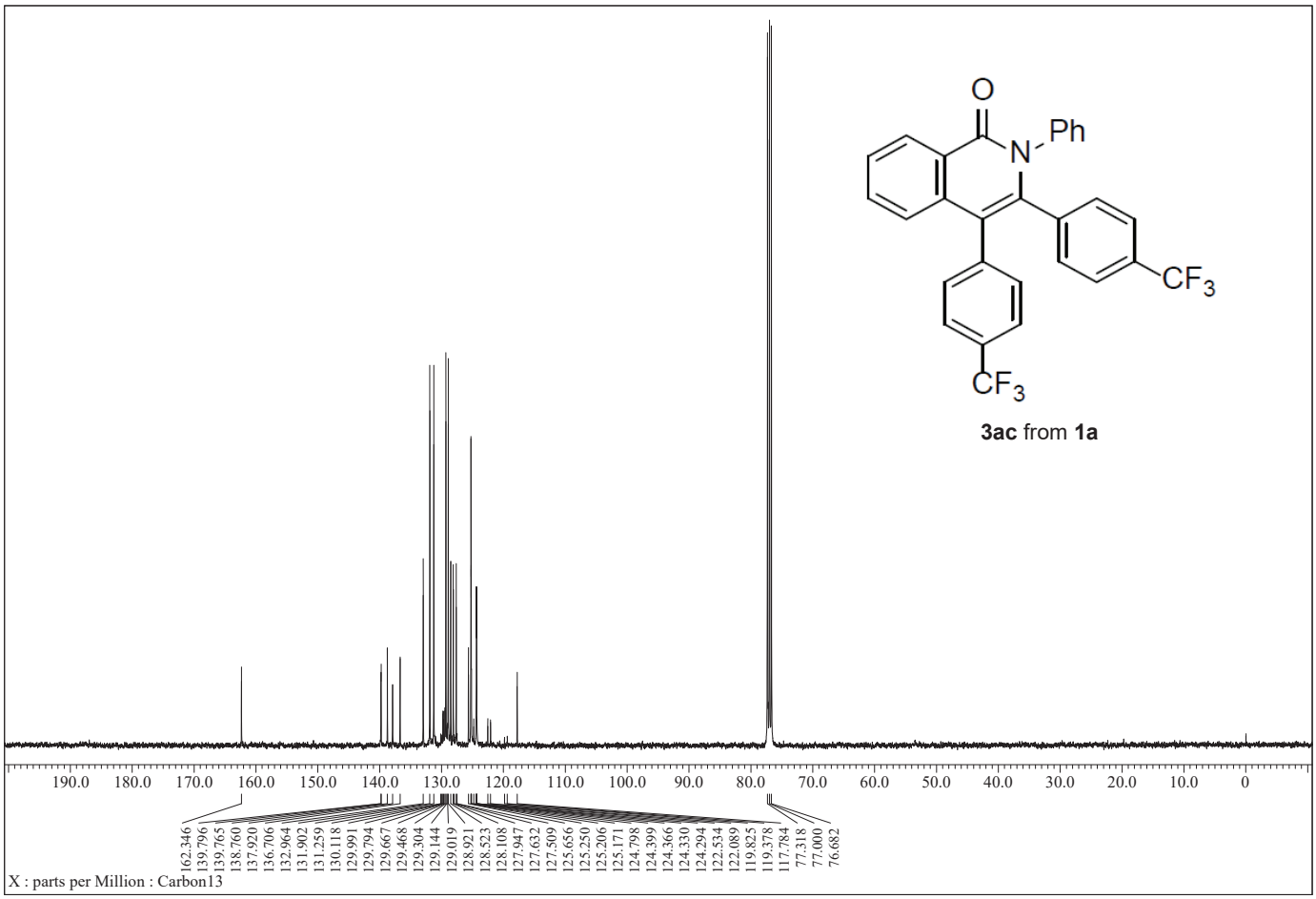

O
N
Ph
OMe
OMe
3ab from 5d
4.12
3.11
3.08
2.06
2.05
1.97
2.00
1.00
1.07
0.99
1.07
0.96
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
X : parts per Million : Proton



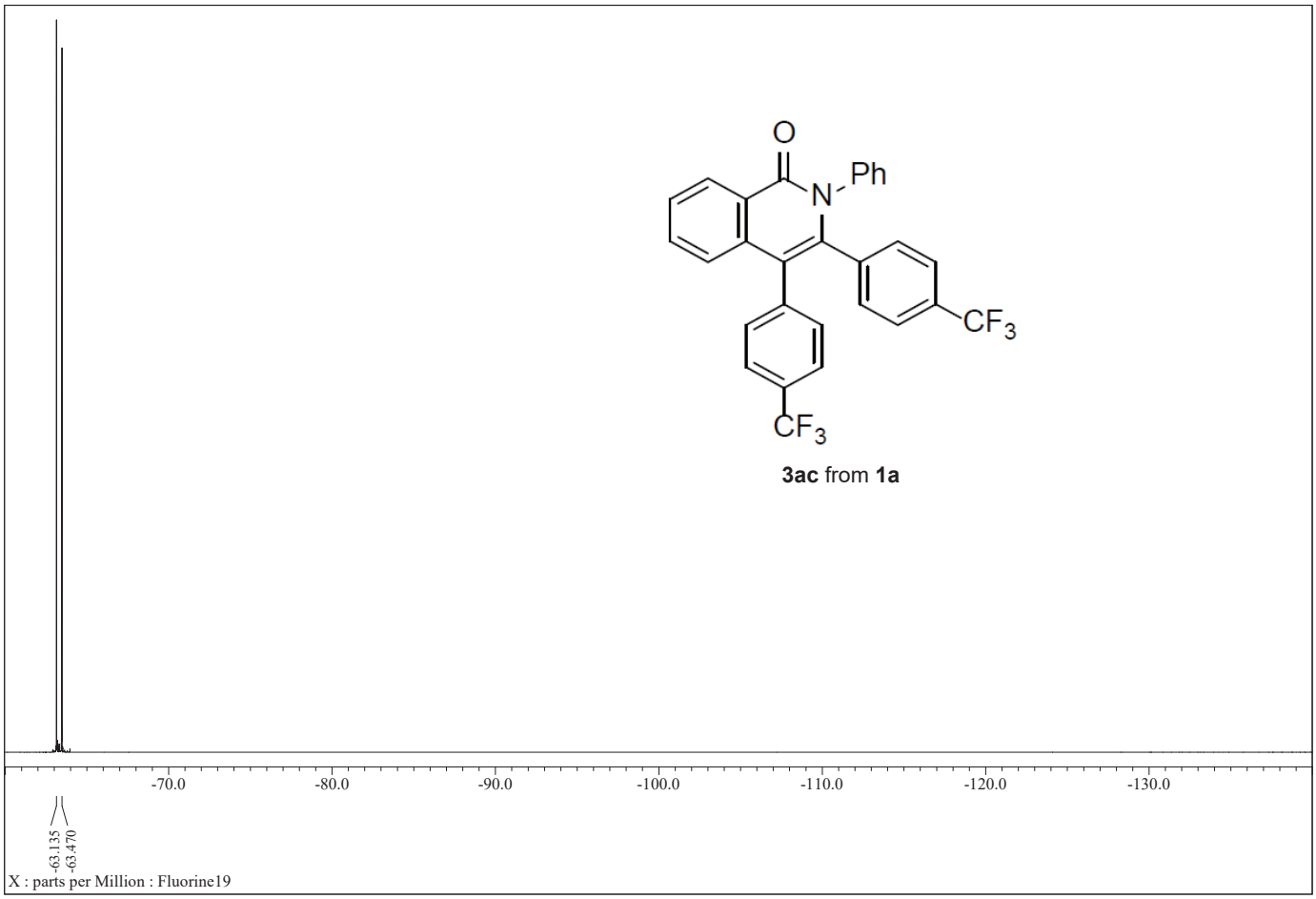
3ab from **5d**



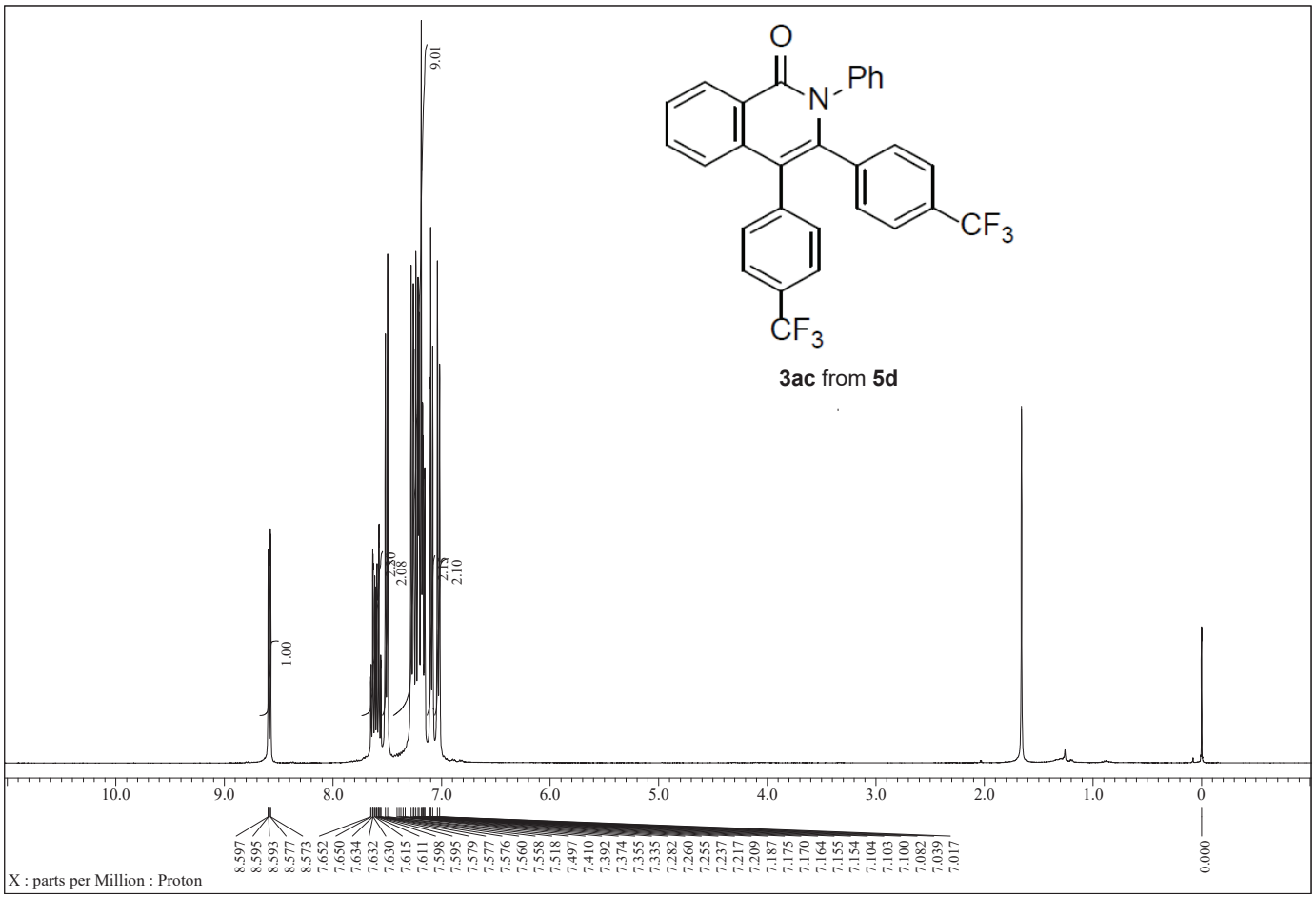
3ac from **1a**

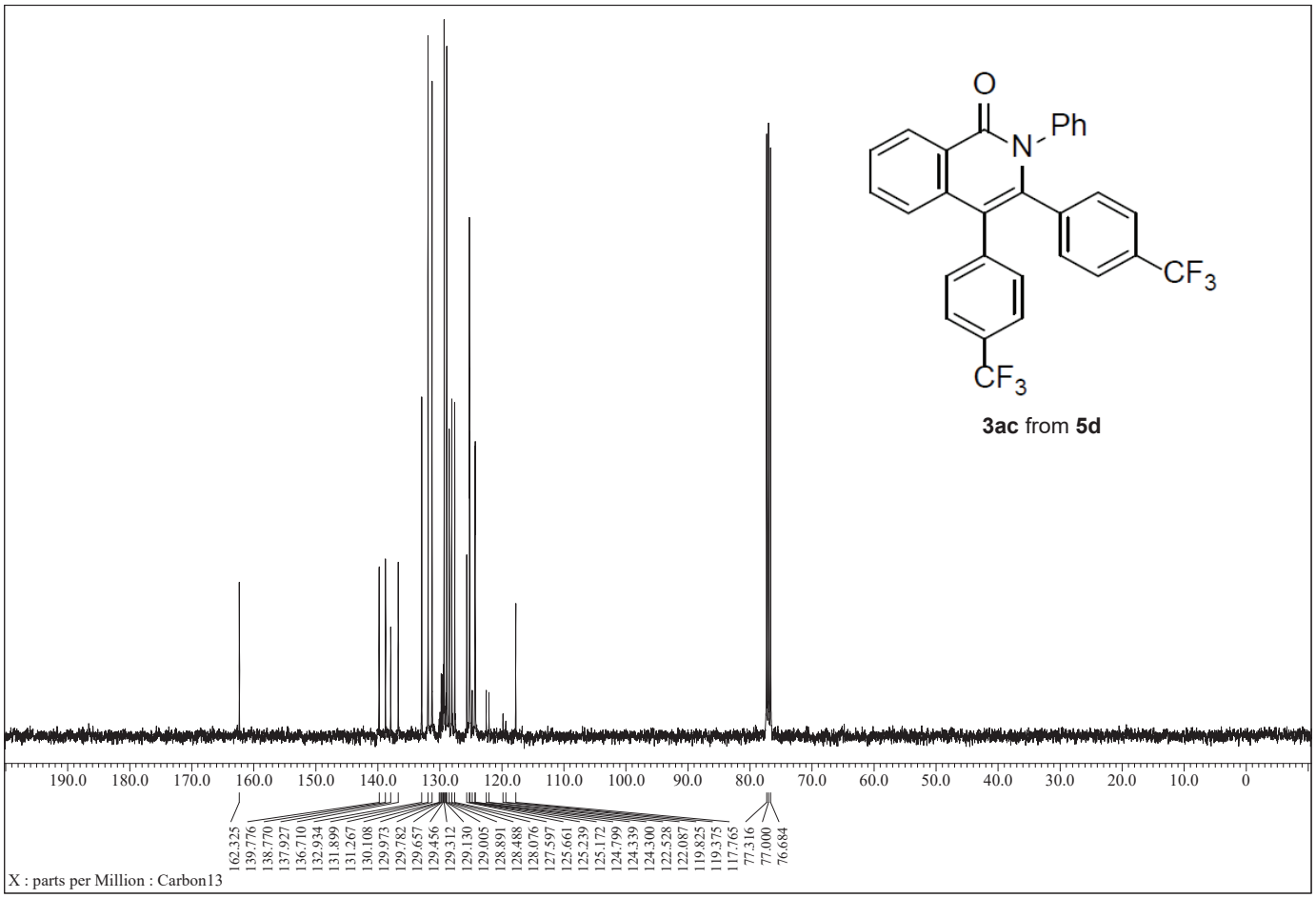


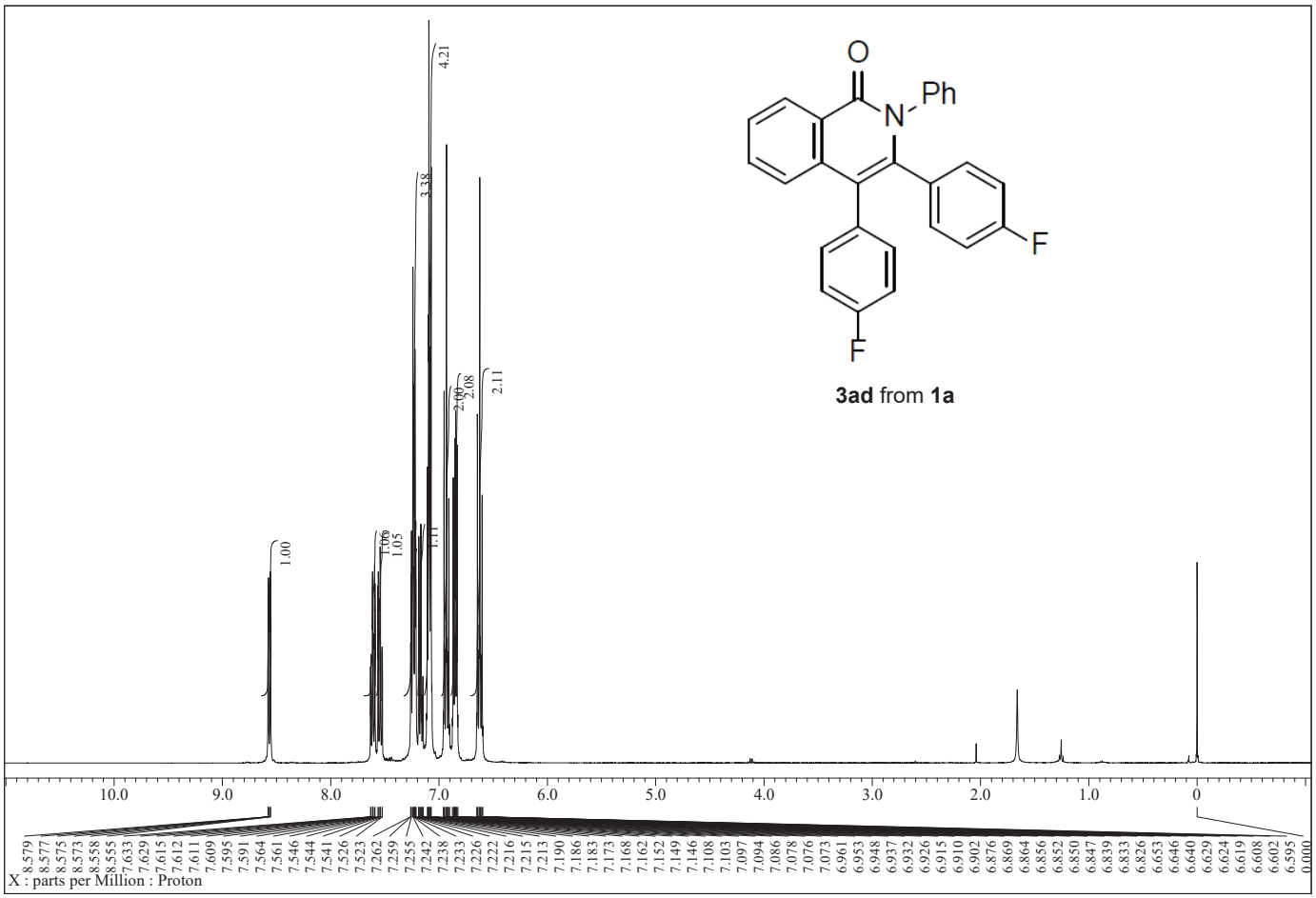
3ac from **1a**

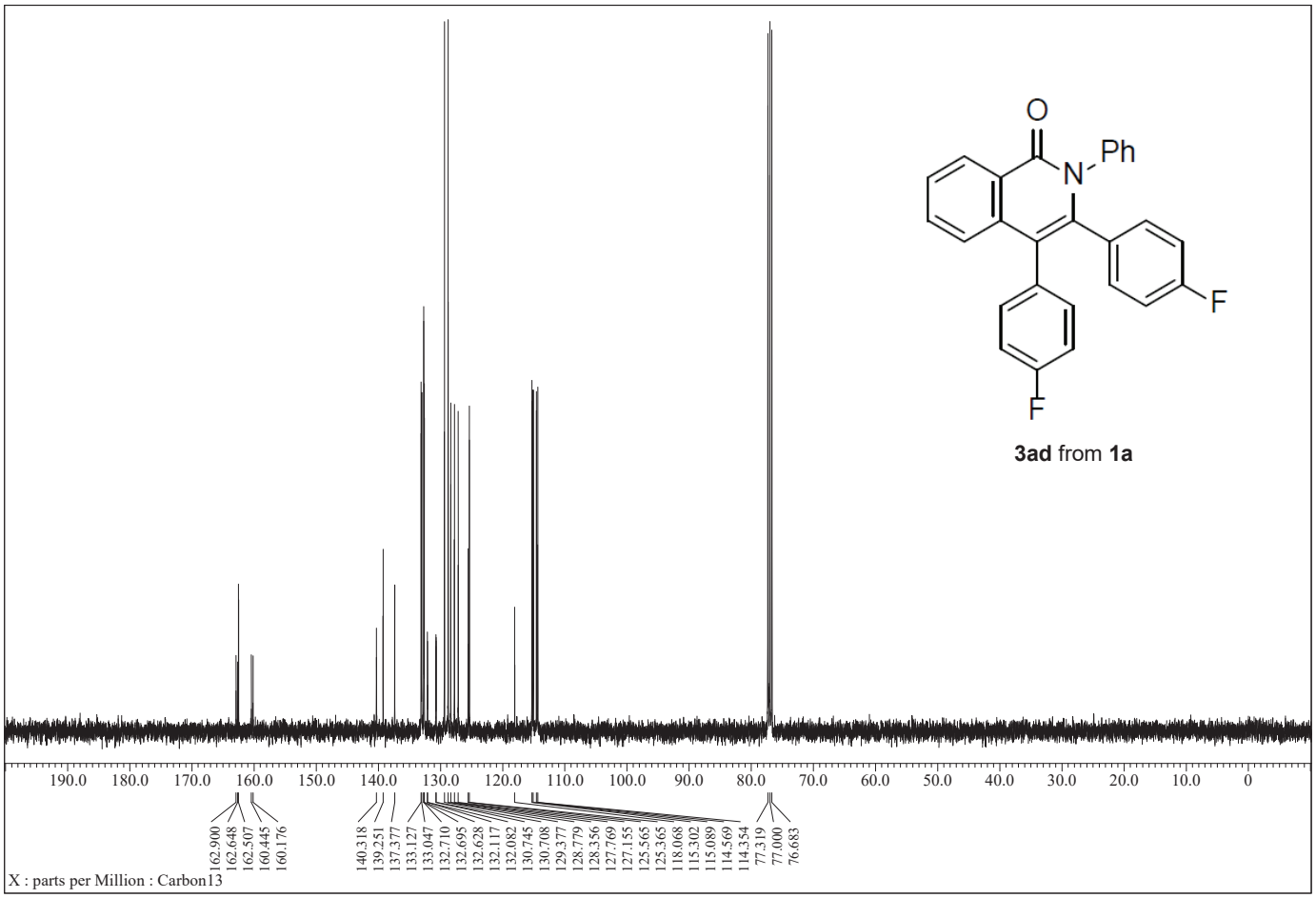


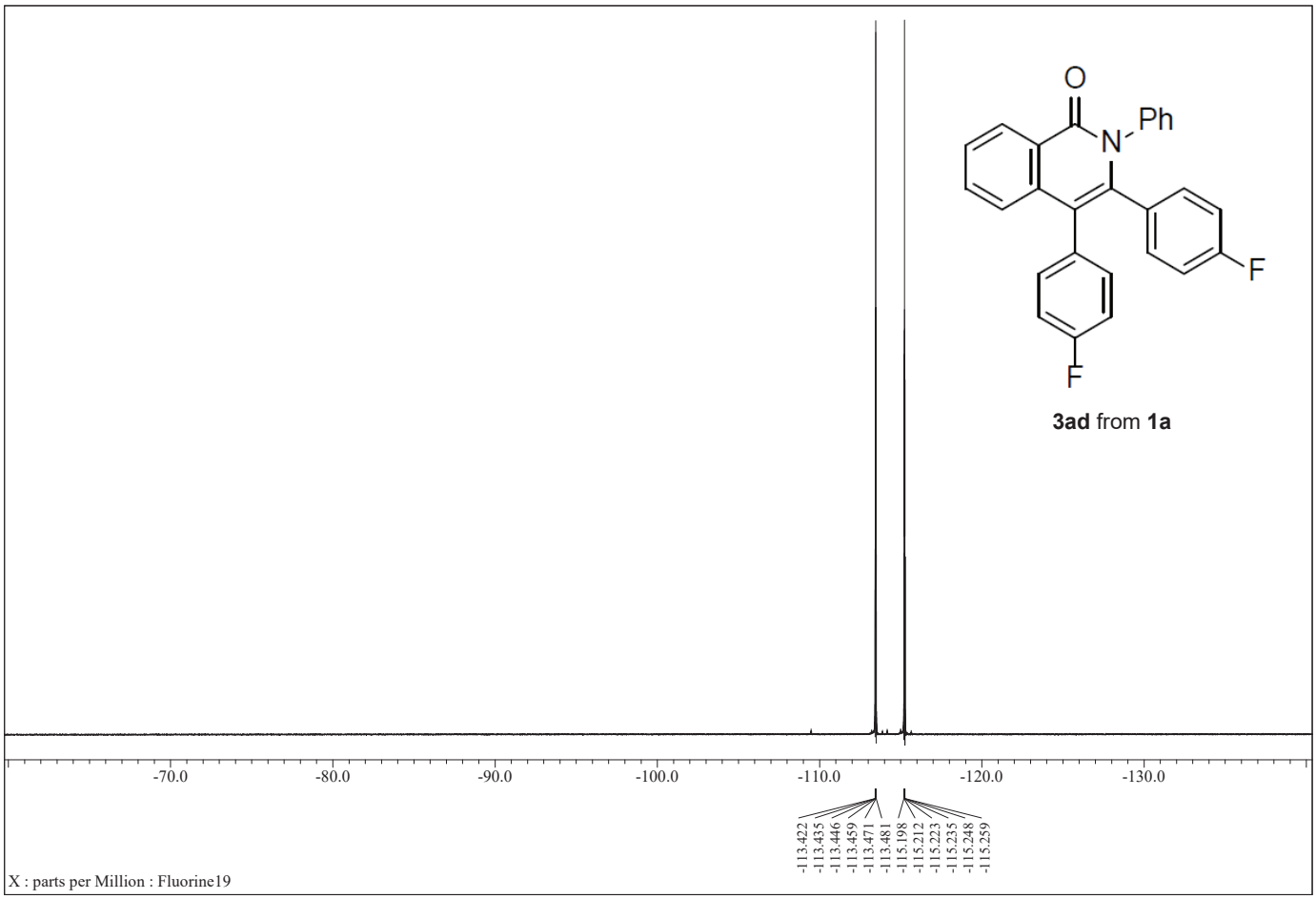
3ac from **1a**


O
N
Ph
CF3
CF3
3ac from 5d
9.01
2.30
2.08
2.15
2.10
1.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
0.000
8.597
8.595
8.593
8.577
8.573
7.652
7.650
7.634
7.632
7.630
7.615
7.611
7.598
7.595
7.579
7.577
7.576
7.560
7.558
7.518
7.497
7.410
7.392
7.374
7.355
7.335
7.282
7.260
7.255
7.237
7.217
7.209
7.187
7.175
7.170
7.164
7.155
7.154
7.104
7.103
7.100
7.082
7.039
7.017
X : parts per Million : Proton

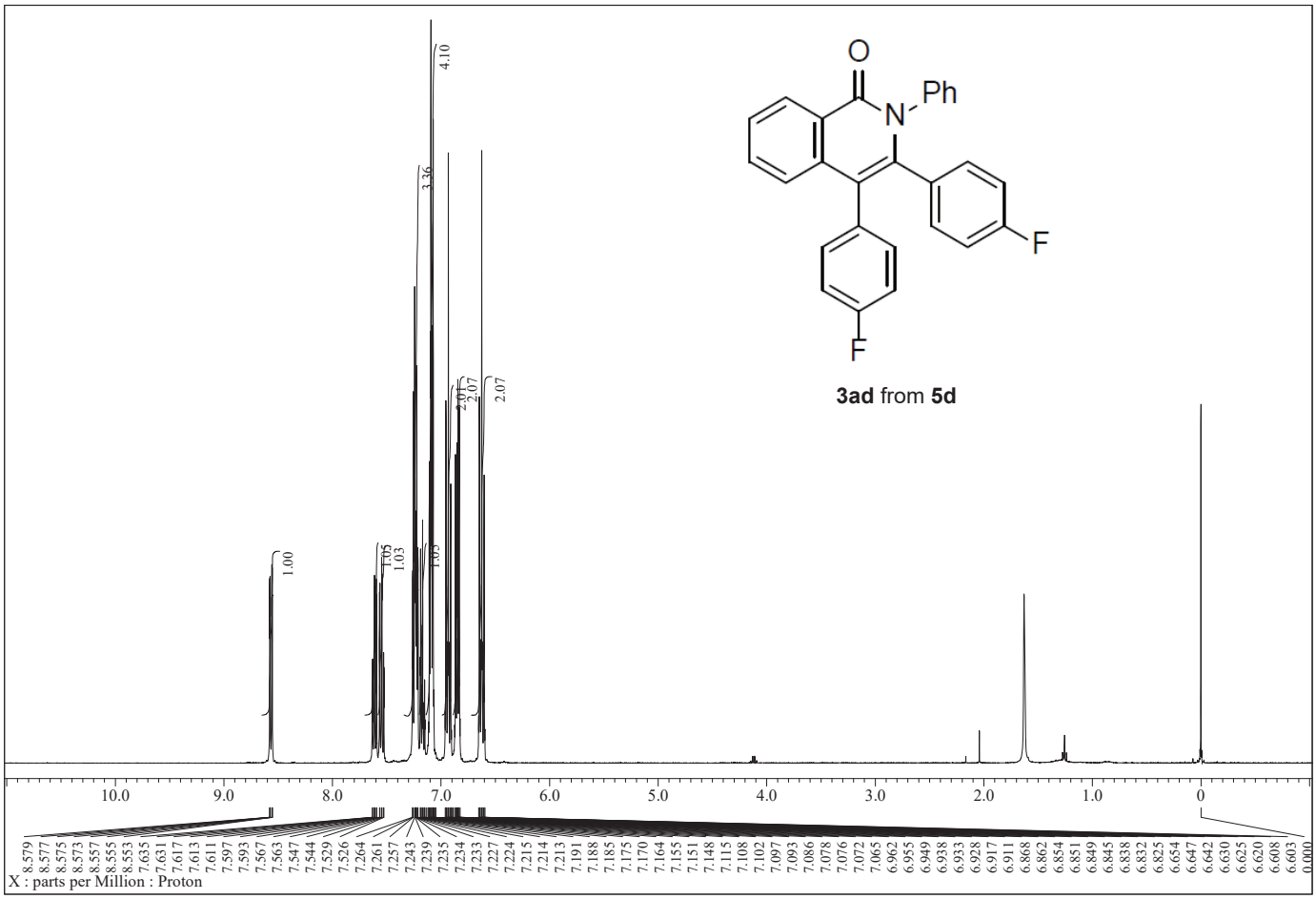

O
N
Ph
CF3
CF3
3ac from 5d
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
162.325
139.776
138.770
137.927
136.710
132.934
131.899
131.267
130.108
129.973
129.782
129.657
129.456
129.312
129.130
129.005
128.891
128.488
128.076
127.597
125.661
125.239
125.172
124.799
124.339
124.300
122.528
122.087
119.825
119.375
117.765
77.316
77.000
76.684
X : parts per Million : Carbon13


O
N
Ph
F
F
3ad from 1a
4.21
3.38
2.11
2.08
2.00
1.11
1.06
1.05
1.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

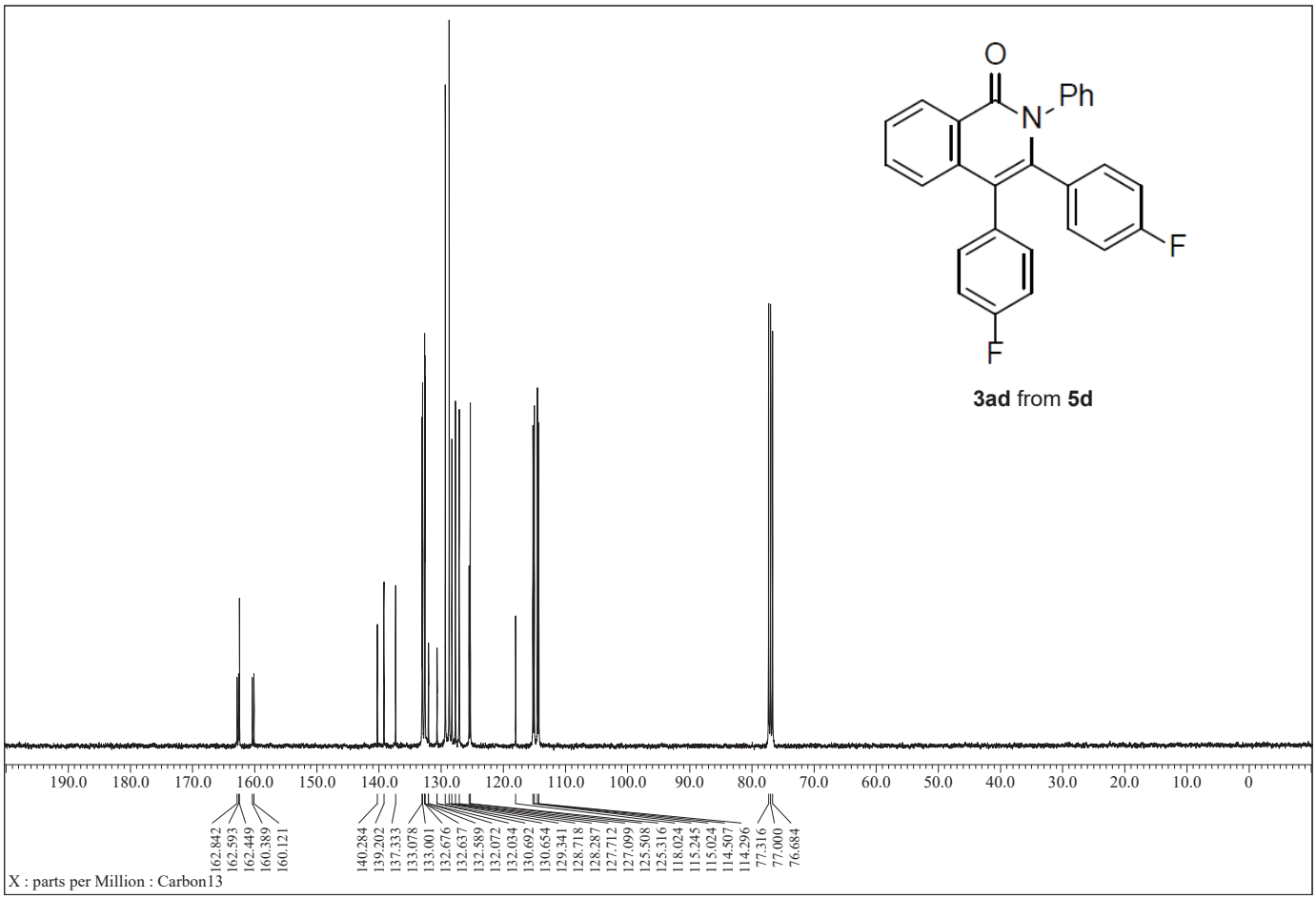

O
N
Ph
F
F
3ad from 1a
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13

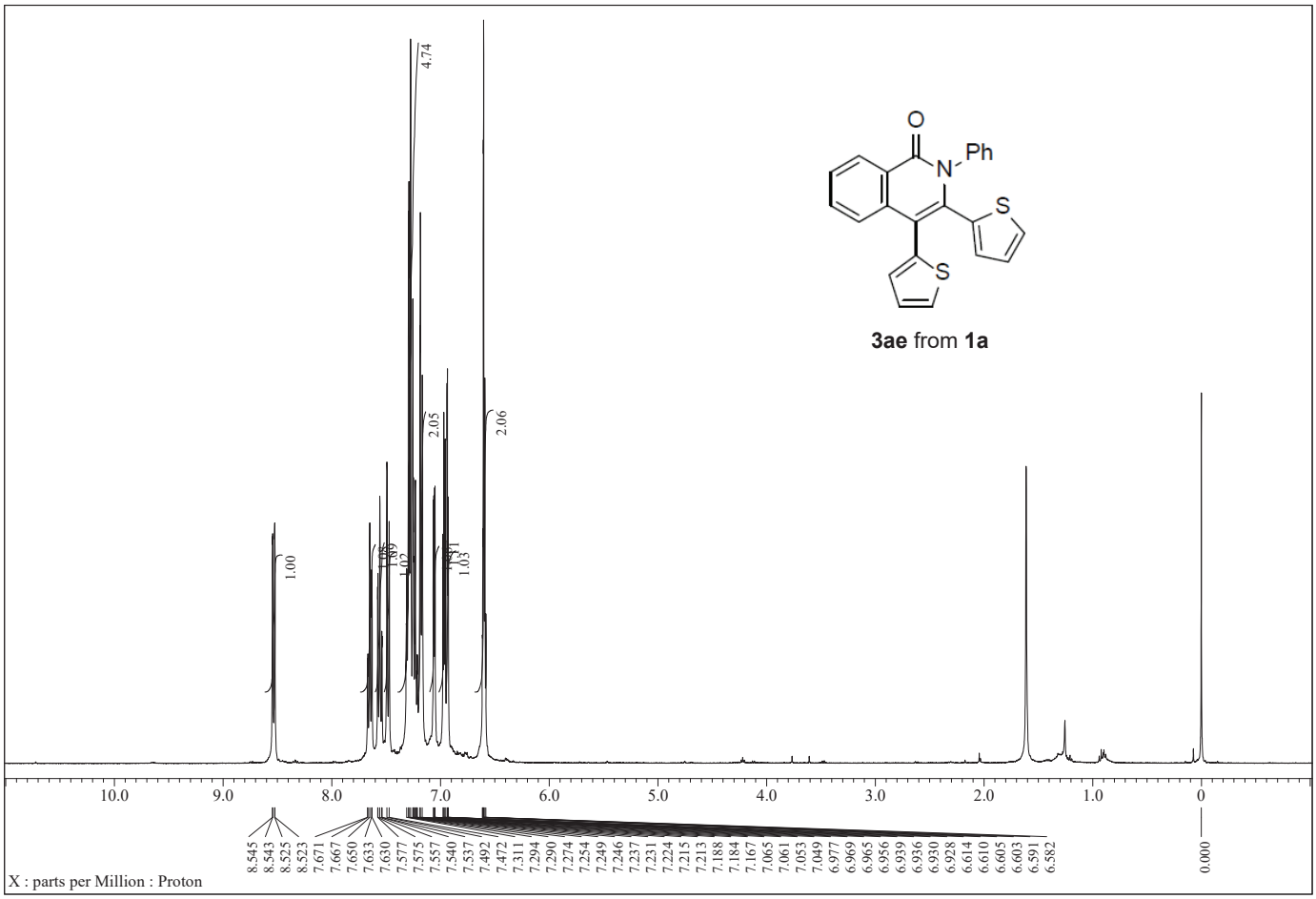


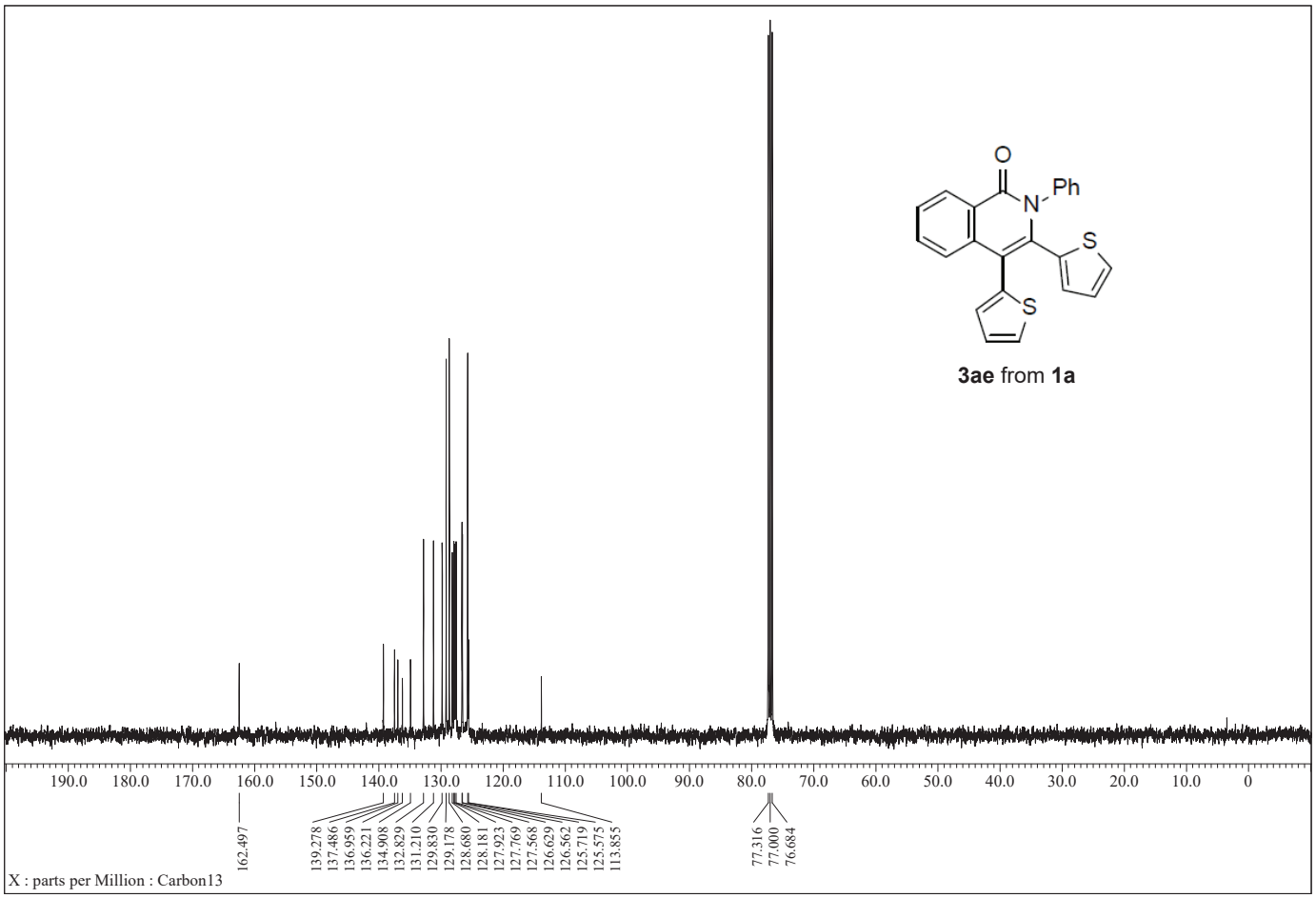
3ad from **1a**

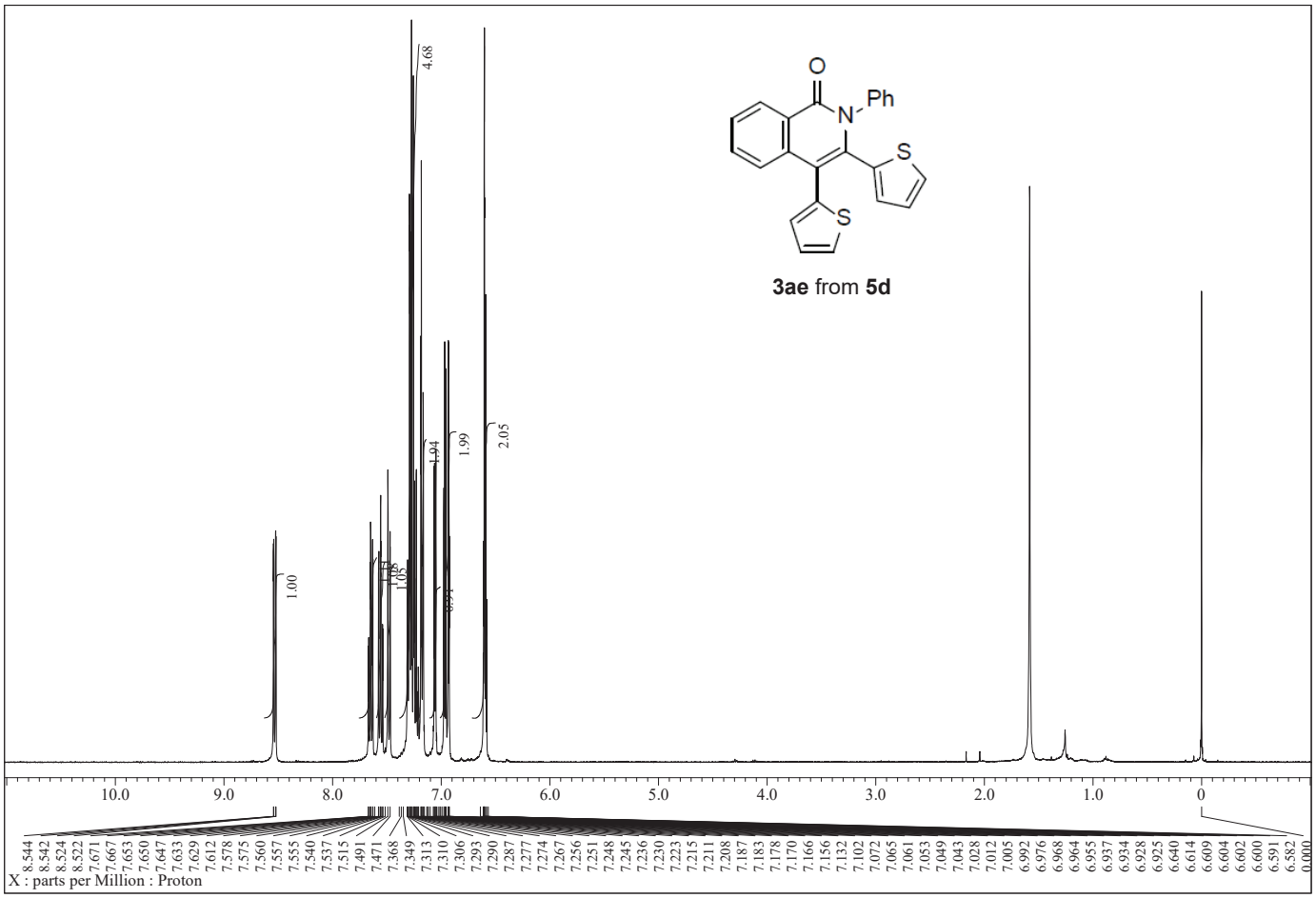


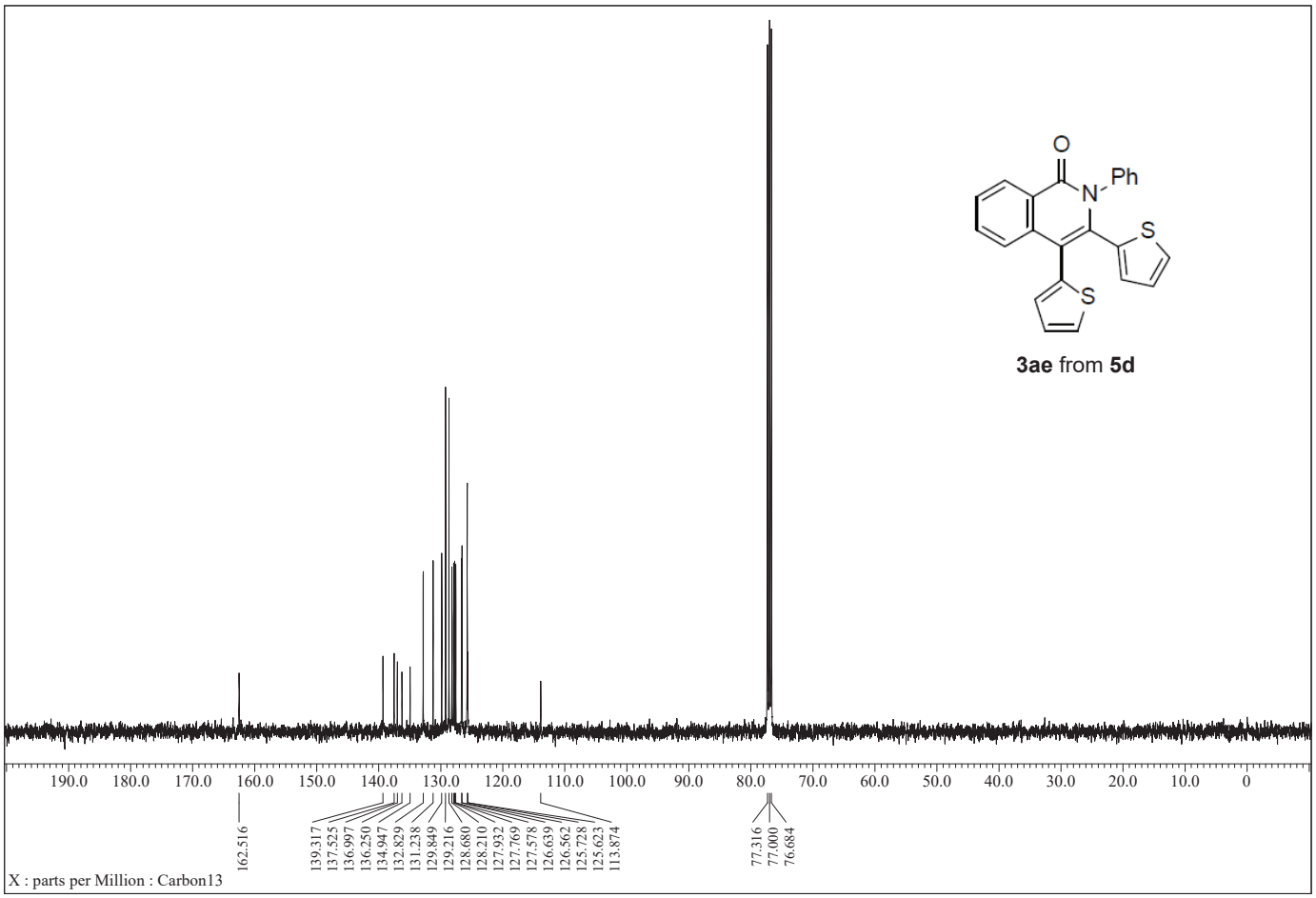
3ad from **5d**

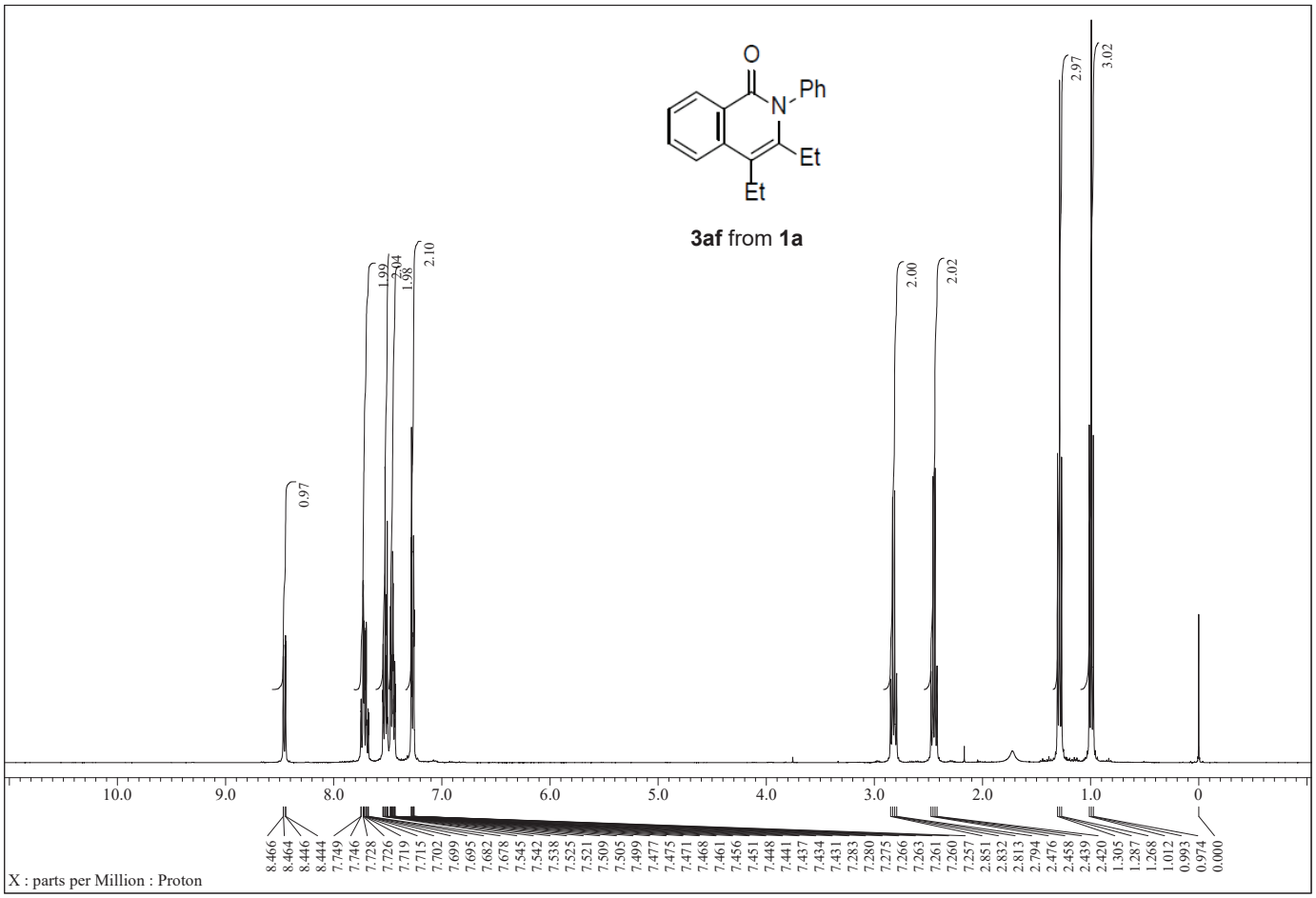

O
N
Ph
F
F
3ad from 5d
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.842 162.593 162.449 160.389 160.121 140.284 139.202 137.333 133.078 133.001 132.676 132.637 132.589 132.072 132.034 130.692 130.654 129.341 128.718 128.287 127.712 127.099 125.508 125.316 118.024 115.245 115.024 114.507 114.296 77.316 77.000 76.684
X : parts per Million : Carbon13

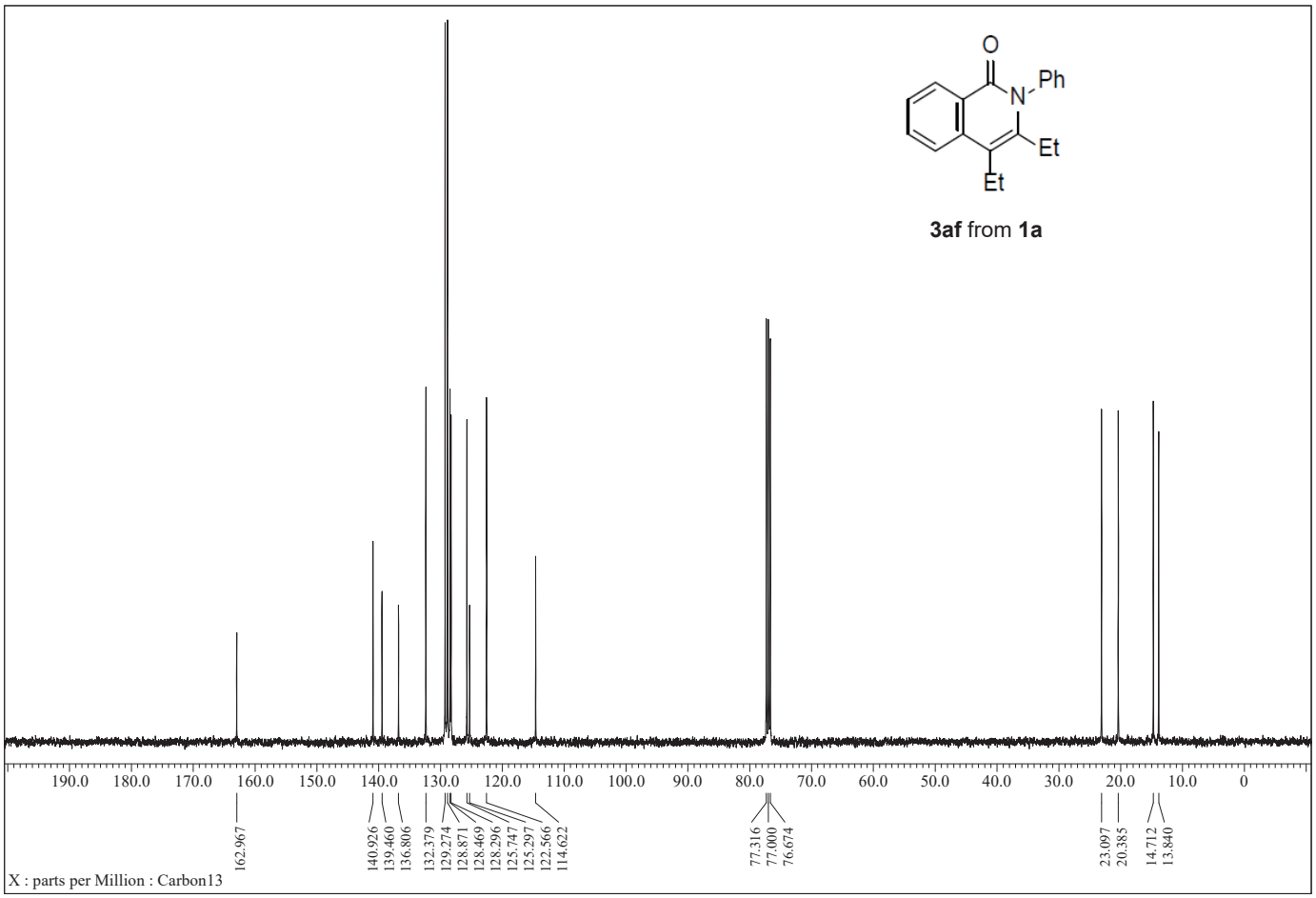

4.74
2.05
2.06
1.00
1.02
1.03
O
N
Ph
S
S
3ae from 1a
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.545 8.543 8.525 8.523 7.671 7.667 7.650 7.633 7.630 7.577 7.575 7.557 7.540 7.537 7.492 7.472 7.311 7.294 7.290 7.274 7.254 7.249 7.246 7.237 7.231 7.224 7.215 7.213 7.188 7.184 7.167 7.065 7.061 7.053 7.049 6.977 6.969 6.965 6.956 6.939 6.936 6.930 6.928 6.614 6.610 6.605 6.603 6.591 6.582 0.000
X : parts per Million : Proton

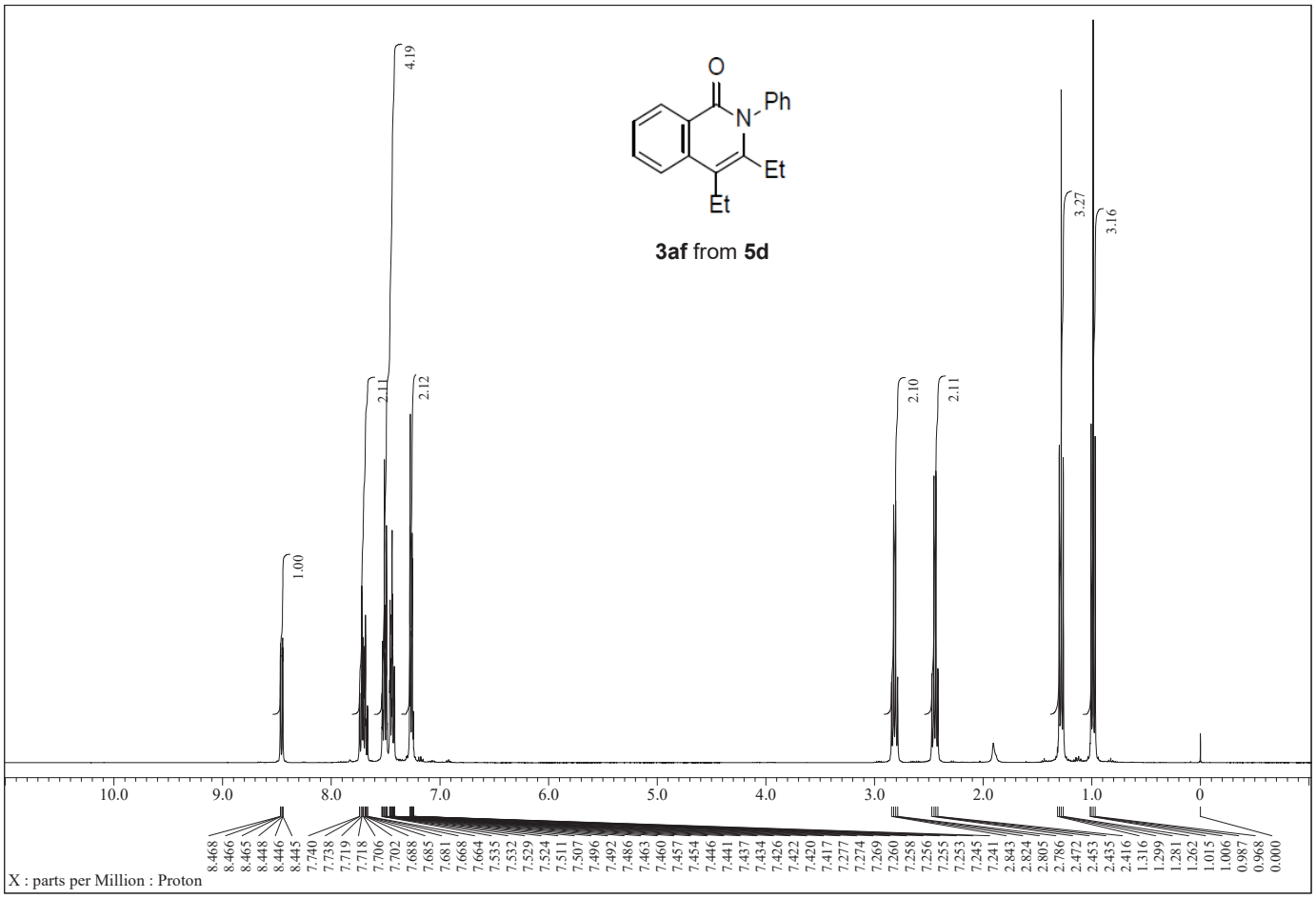

O
N
Ph
S
S
3ae from 1a
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.497
139.278 137.486 136.959 136.221 134.908 132.829 131.210 129.830 129.178 128.680 128.181 127.923 127.769 127.568 126.629 126.562 125.719 125.575 113.855
77.316 77.000 76.684
X : parts per Million : Carbon13

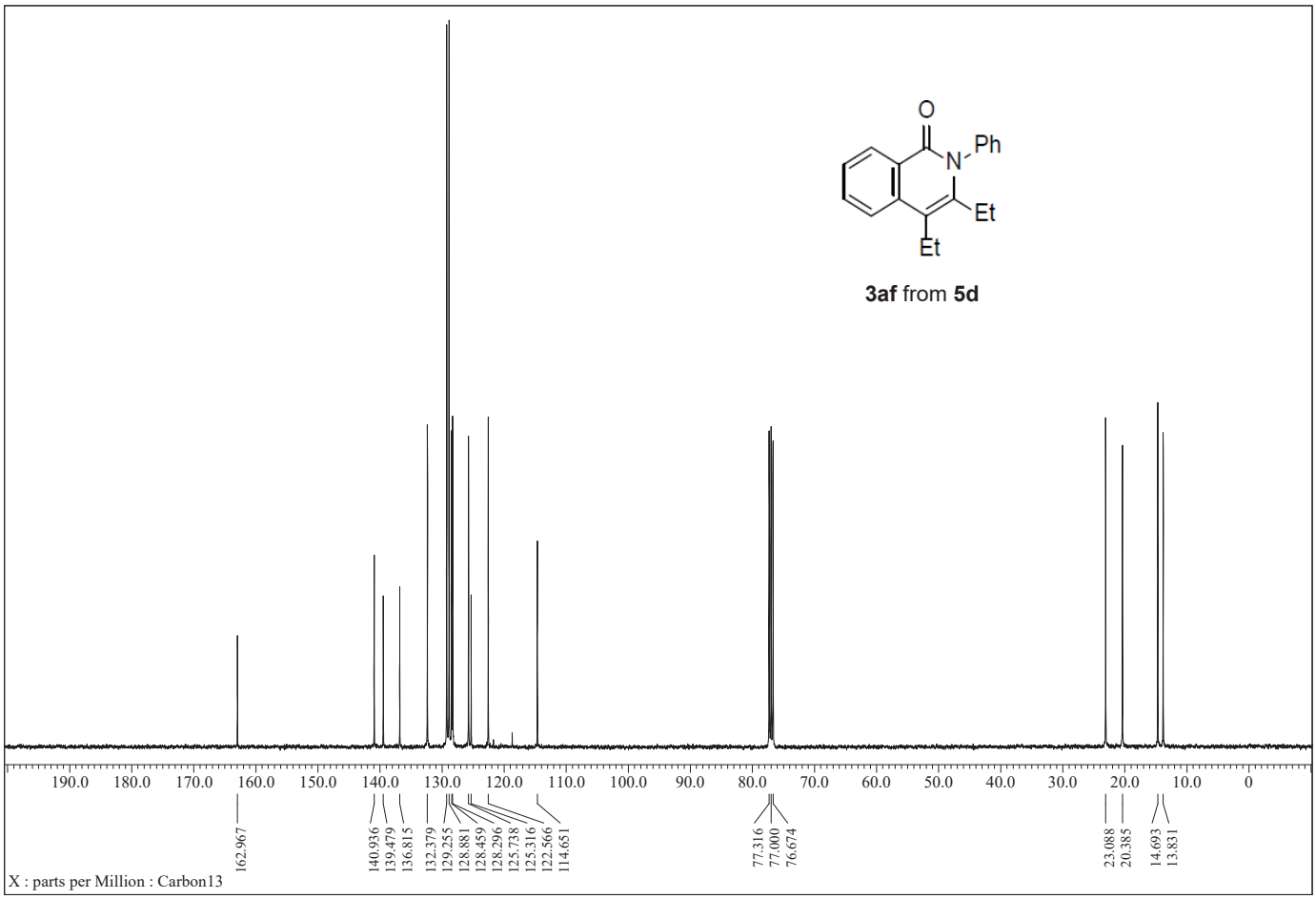

O
N
Ph
S
S
3ae from 5d
4.68
1.94
1.99
2.05
1.00
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
X : parts per Million : Proton

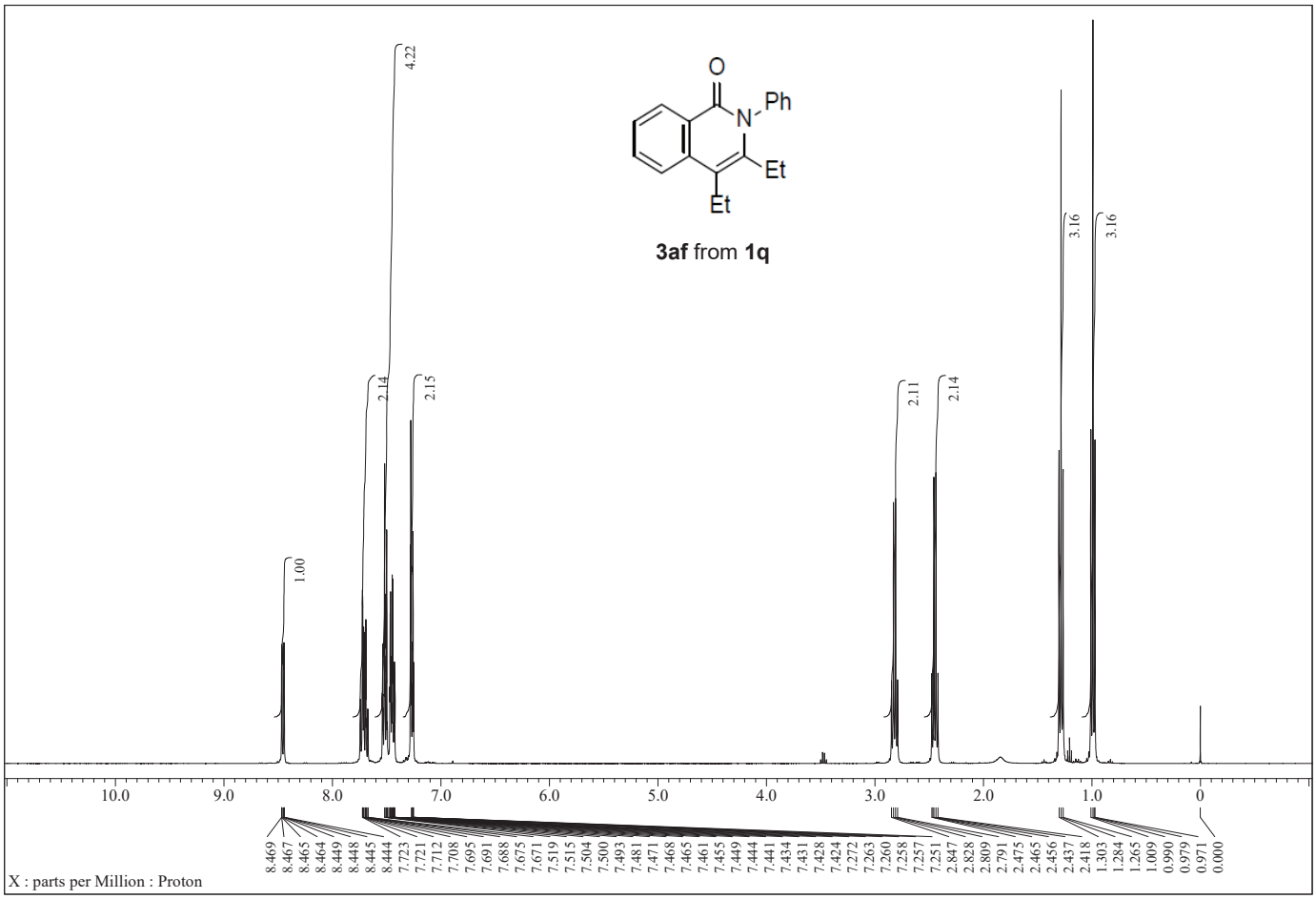

O
N
Ph
S
S
3ae from 5d
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.516
139.317
137.525
136.997
136.250
134.947
132.829
131.238
129.849
129.216
128.680
128.210
127.932
127.769
127.578
126.639
126.562
125.728
125.623
113.874
77.316
77.000
76.684
X : parts per Million : Carbon13

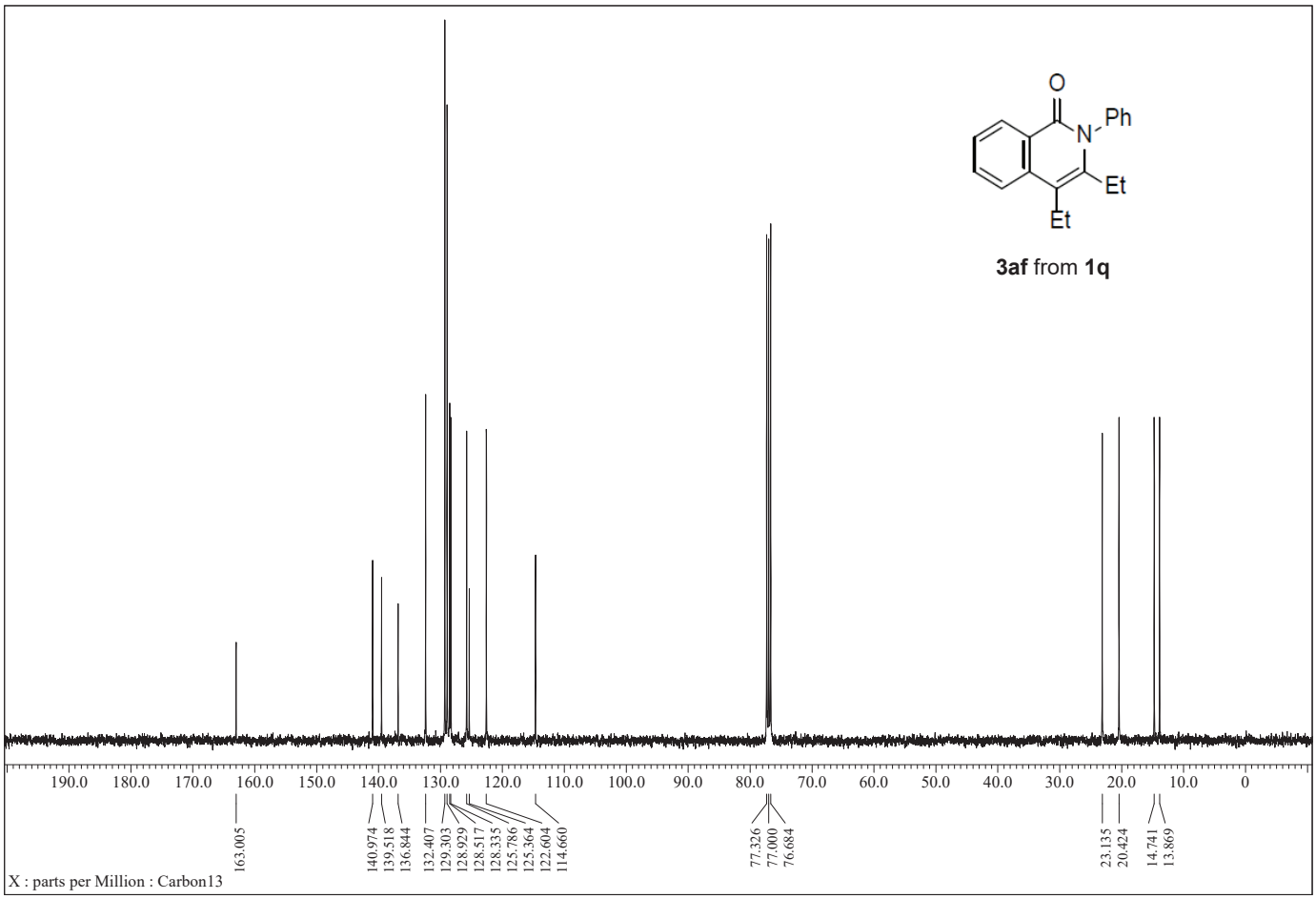

O
N
Ph
Et
Et
3af from 1a
0.97
1.99
2.04
1.98
2.10
2.00
2.02
2.97
3.02
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.466
8.464
8.446
8.444
7.749
7.746
7.728
7.726
7.719
7.715
7.702
7.699
7.695
7.682
7.678
7.545
7.542
7.538
7.525
7.521
7.509
7.505
7.499
7.477
7.475
7.471
7.468
7.461
7.456
7.451
7.448
7.441
7.437
7.434
7.431
7.283
7.280
7.275
7.266
7.263
7.261
7.260
7.257
2.851
2.832
2.813
2.794
2.476
2.458
2.439
2.420
1.305
1.287
1.268
1.012
0.993
0.974
0.000
X : parts per Million : Proton

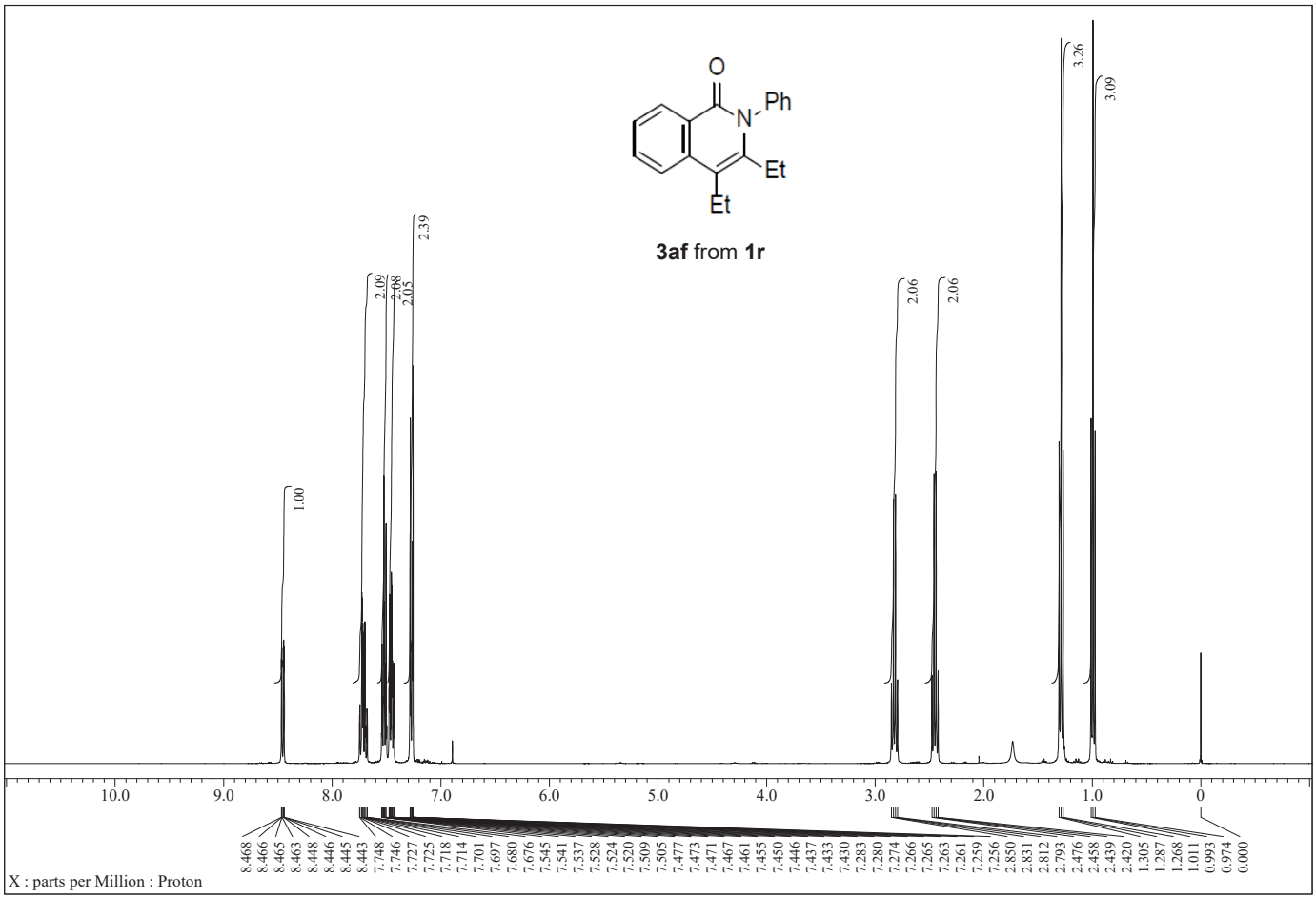

O
N
Ph
Et
Et
3af from 1a
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.967
140.926
139.460
136.806
132.379
129.274
128.871
128.469
128.296
125.747
125.297
122.566
114.622
77.316
77.000
76.674
23.097
20.385
14.712
13.840
X : parts per Million : Carbon13

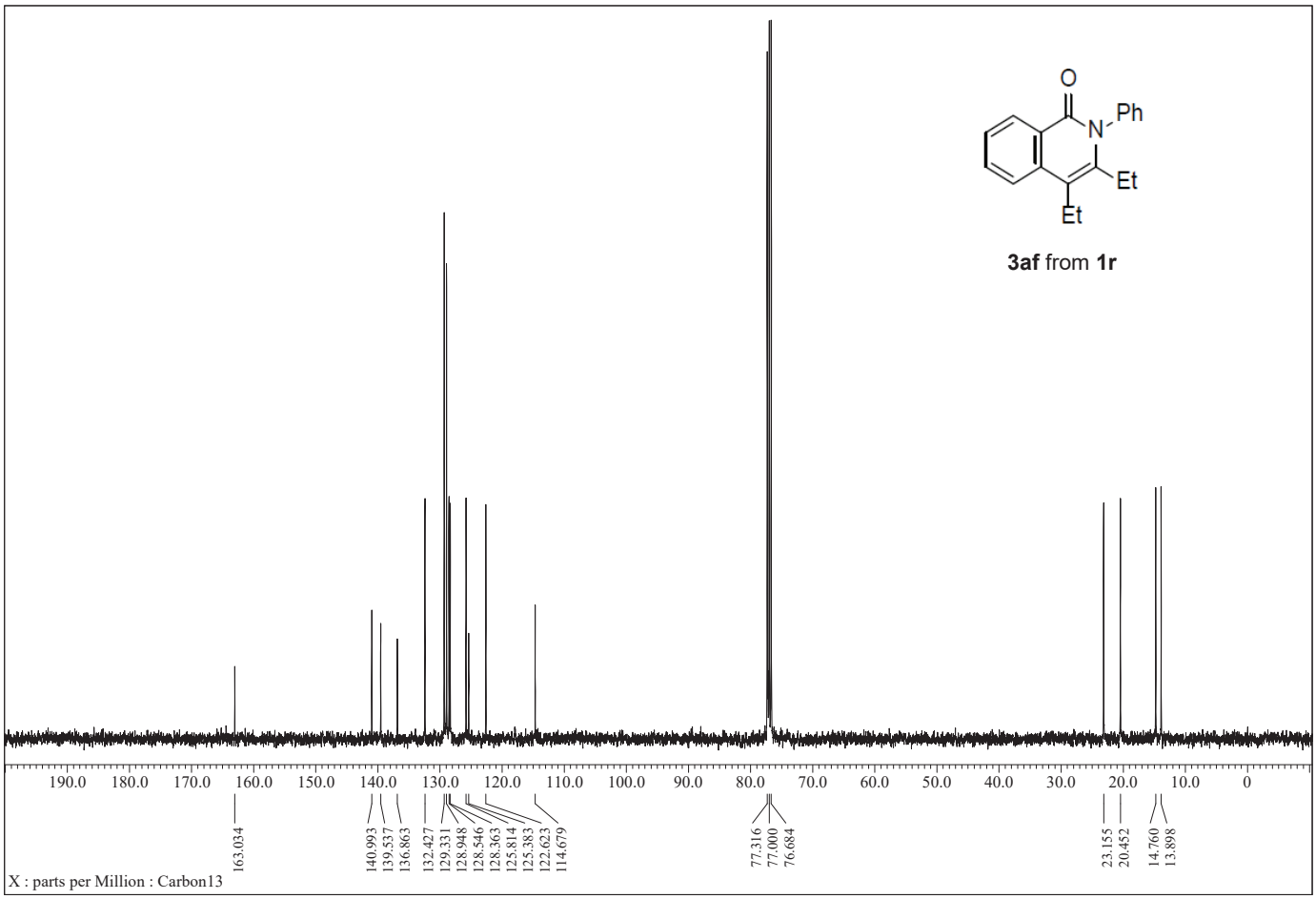

O
N
Ph
Et
Et
3af from 5d
4.19
2.11
2.12
1.00
2.10
2.11
3.27
3.16
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.468 8.466 8.465 8.448 8.446 8.445
7.740 7.738 7.719 7.718 7.706 7.702 7.688 7.685 7.681 7.668 7.664 7.535 7.532 7.529 7.524 7.511 7.507 7.496 7.492 7.486 7.463 7.460 7.457 7.454 7.446 7.441 7.437 7.434 7.426 7.422 7.420 7.417 7.277 7.274 7.269 7.260 7.258 7.256 7.255 7.253 7.245 7.241
2.843 2.824 2.805 2.786 2.472 2.453 2.435 2.416 1.316 1.299 1.281 1.262 1.015 1.006 0.987 0.968 0.000
X : parts per Million : Proton

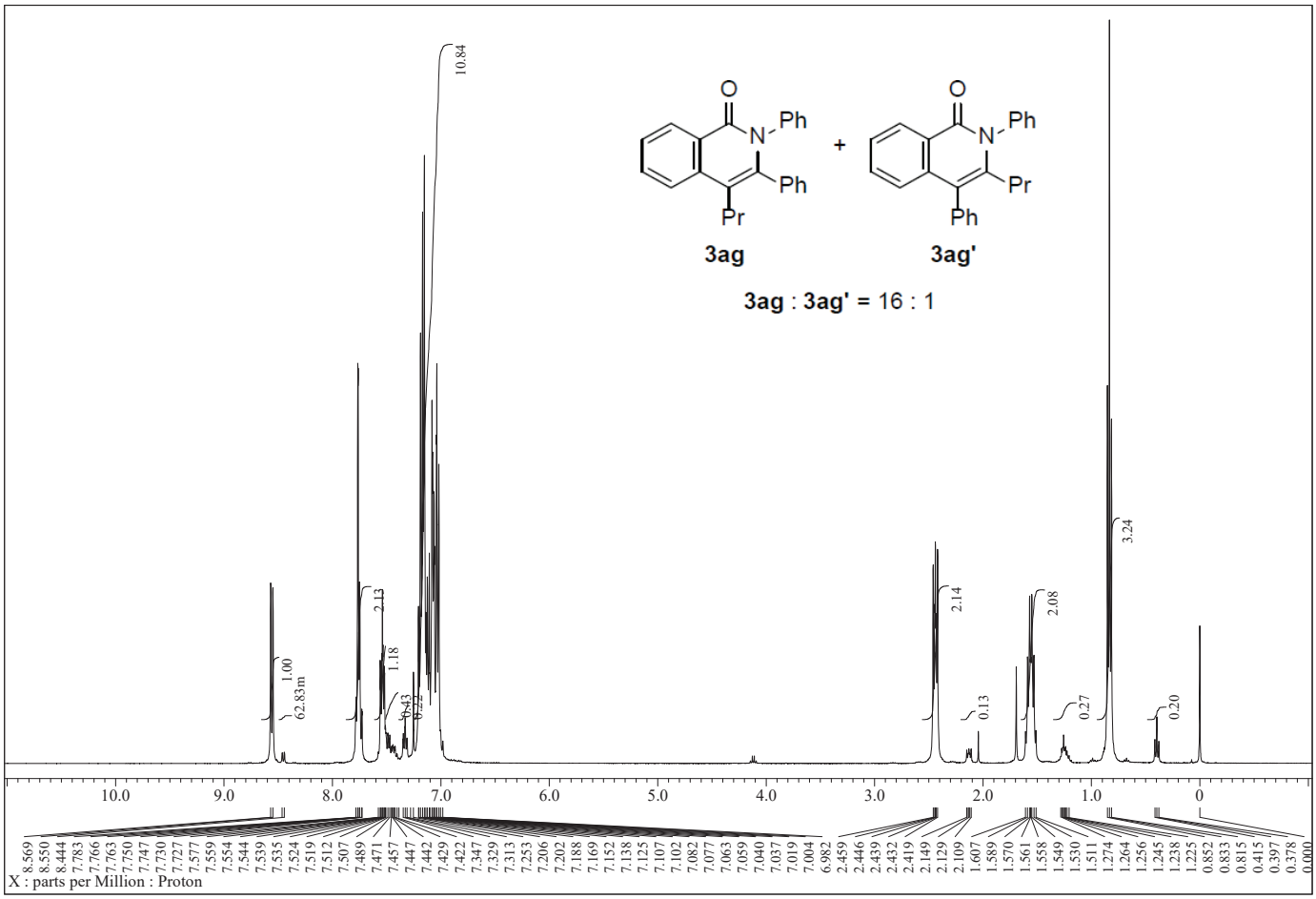

O
N
Ph
Et
Et
3af from 5d
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
162.967
140.936
139.479
136.815
132.379
129.255
128.881
128.459
128.296
125.738
125.316
122.566
114.651
77.316
77.000
76.674
23.088
20.385
14.693
13.831
X : parts per Million : Carbon13

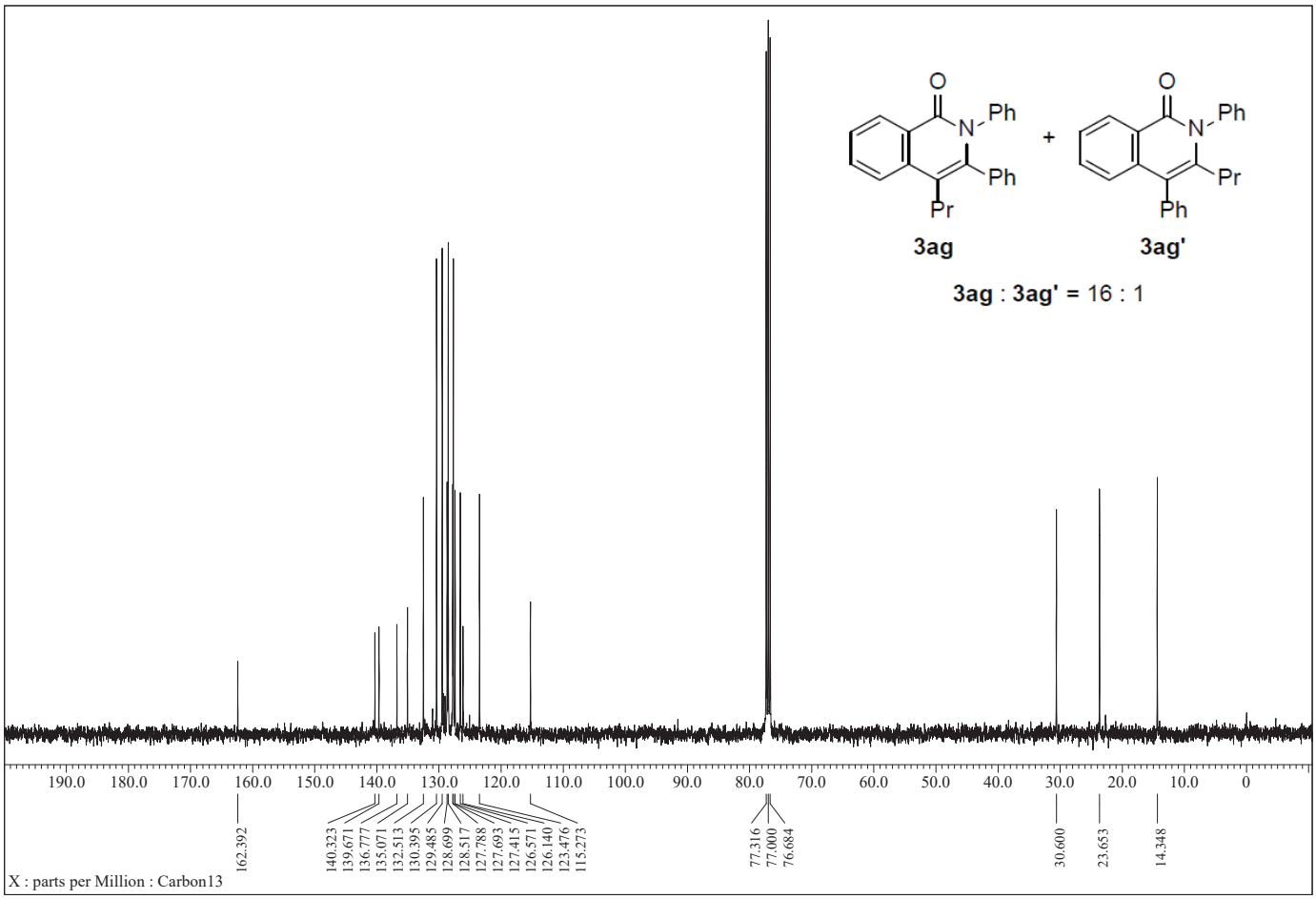

O
N
Ph
Et
Et
3af from 1q
4.22
2.14
2.15
1.00
2.11
2.14
3.16
3.16
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.469 8.467 8.465 8.464 8.449 8.448 8.445 8.444 7.723 7.721 7.712 7.708 7.695 7.691 7.688 7.675 7.671 7.519 7.515 7.504 7.500 7.493 7.481 7.471 7.468 7.465 7.461 7.455 7.449 7.444 7.441 7.434 7.431 7.428 7.424 7.272 7.263 7.260 7.258 7.257 7.251 2.847 2.828 2.809 2.791 2.475 2.465 2.456 2.437 2.418 1.303 1.284 1.265 1.009 0.990 0.979 0.971 0.000
X : parts per Million : Proton

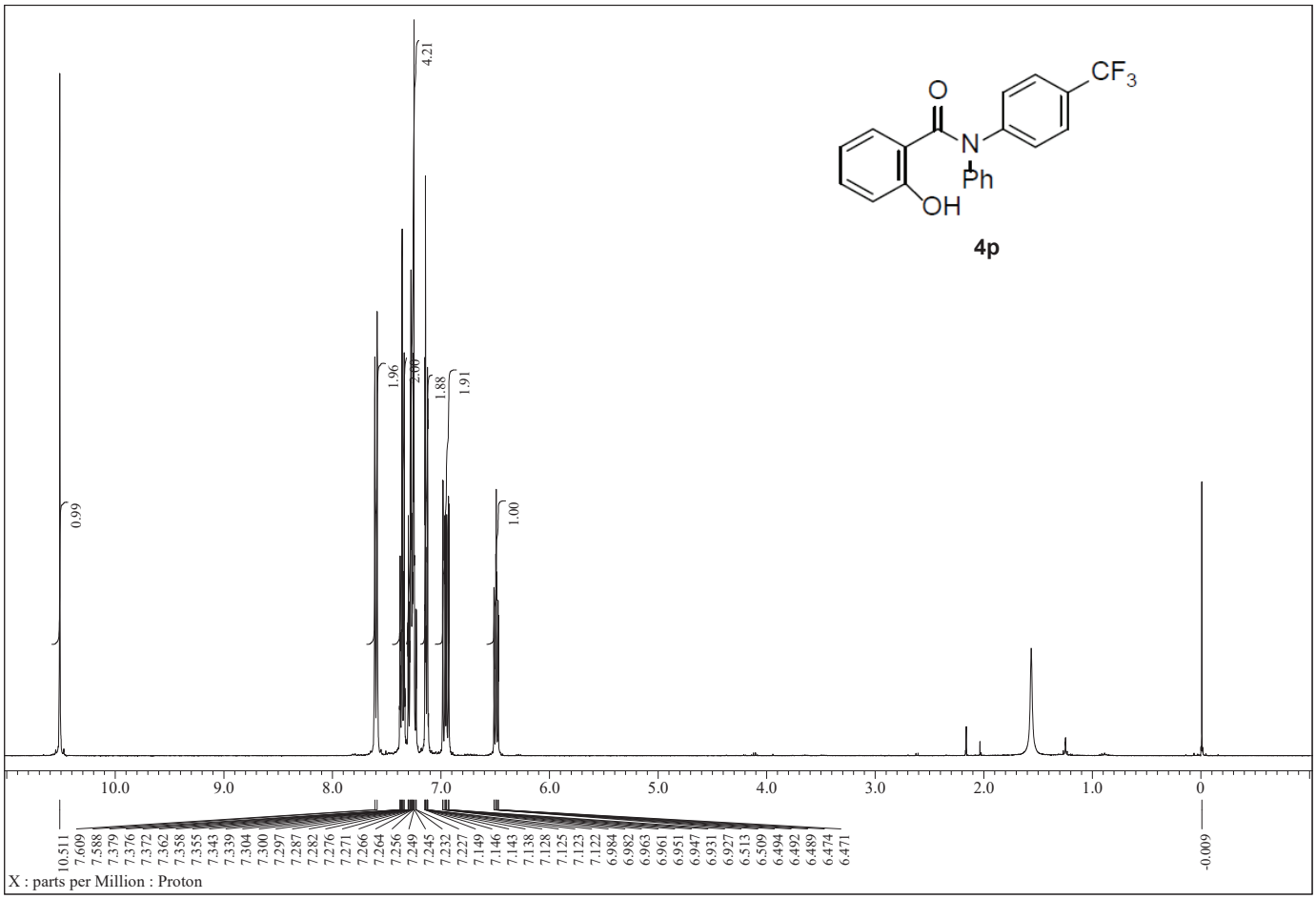

O
N
Ph
Et
Et
3af from 1q
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
163.005
140.974
139.518
136.844
132.407
129.303
128.929
128.517
128.335
125.786
125.364
122.604
114.660
77.326
77.000
76.684
23.135
20.424
14.741
13.869
X : parts per Million : Carbon13

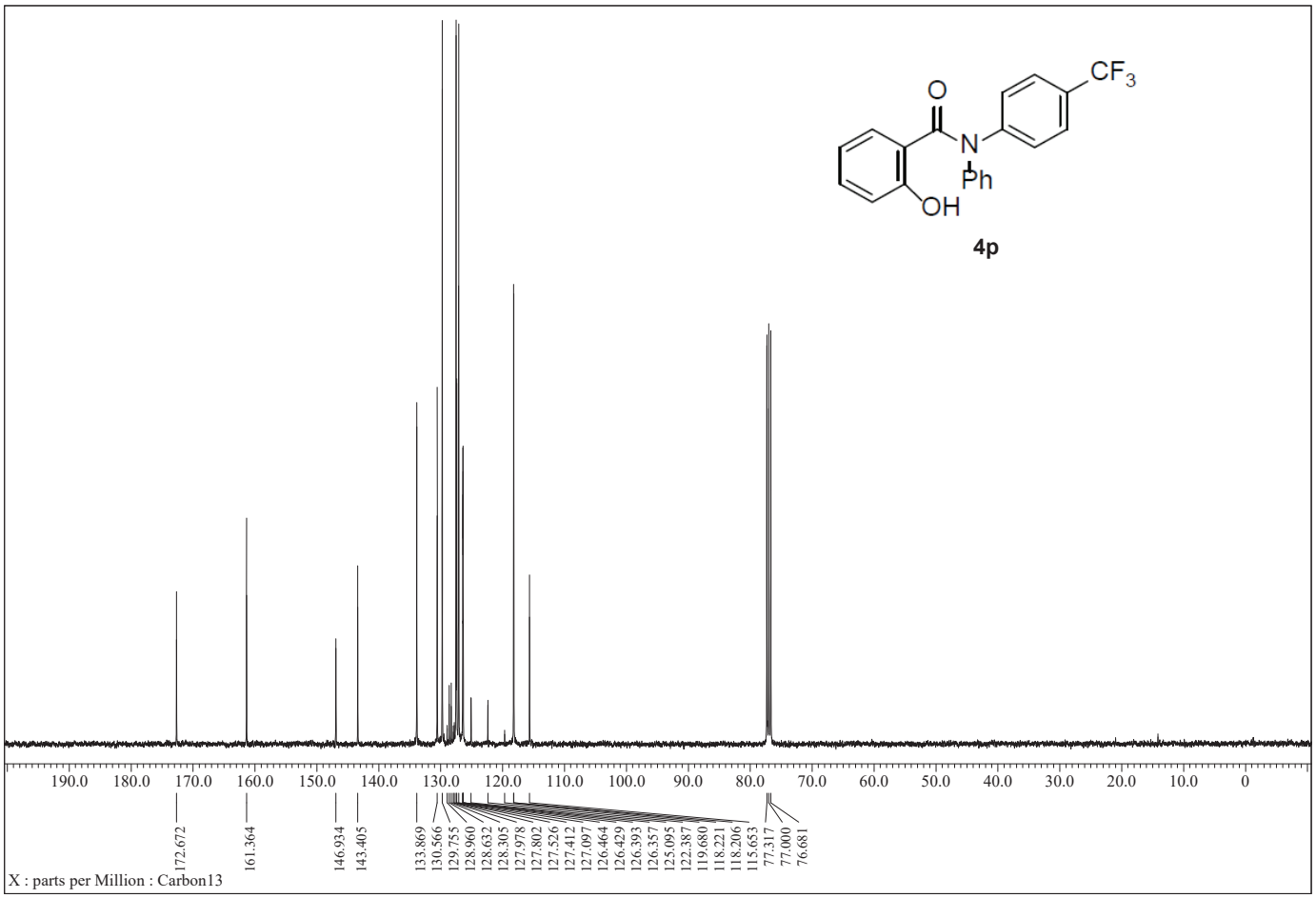

O
N
Ph
Et
Et
3af from 1r
1.00
2.09
2.08
2.05
2.39
2.06
2.06
3.26
3.09
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.468 8.466 8.465 8.463 8.448 8.446 8.445 8.443 7.748 7.746 7.727 7.725 7.718 7.714 7.701 7.697 7.680 7.676 7.545 7.541 7.537 7.528 7.524 7.520 7.509 7.505 7.477 7.473 7.471 7.467 7.461 7.455 7.450 7.446 7.437 7.433 7.430 7.283 7.280 7.274 7.266 7.265 7.263 7.261 7.259 7.256 2.850 2.831 2.812 2.793 2.476 2.458 2.439 2.420 1.305 1.287 1.268 1.011 0.993 0.974 0.000
X : parts per Million : Proton

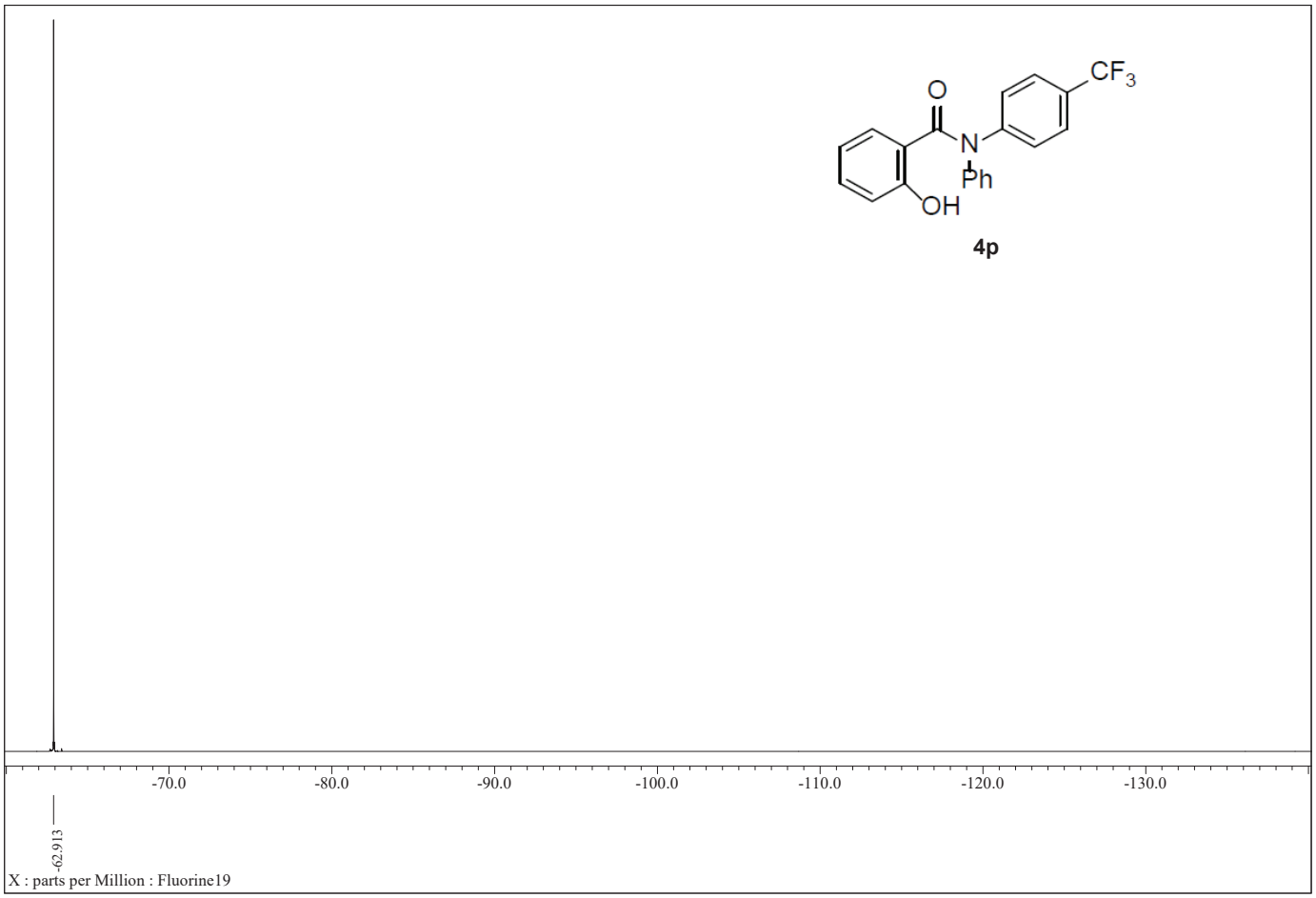

O
N
Ph
Et
Et
3af from 1r
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
163.034
140.993
139.537
136.863
132.427
129.331
128.948
128.546
128.363
125.814
125.383
122.623
114.679
77.316
77.000
76.684
23.155
20.452
14.760
13.898
X : parts per Million : Carbon13

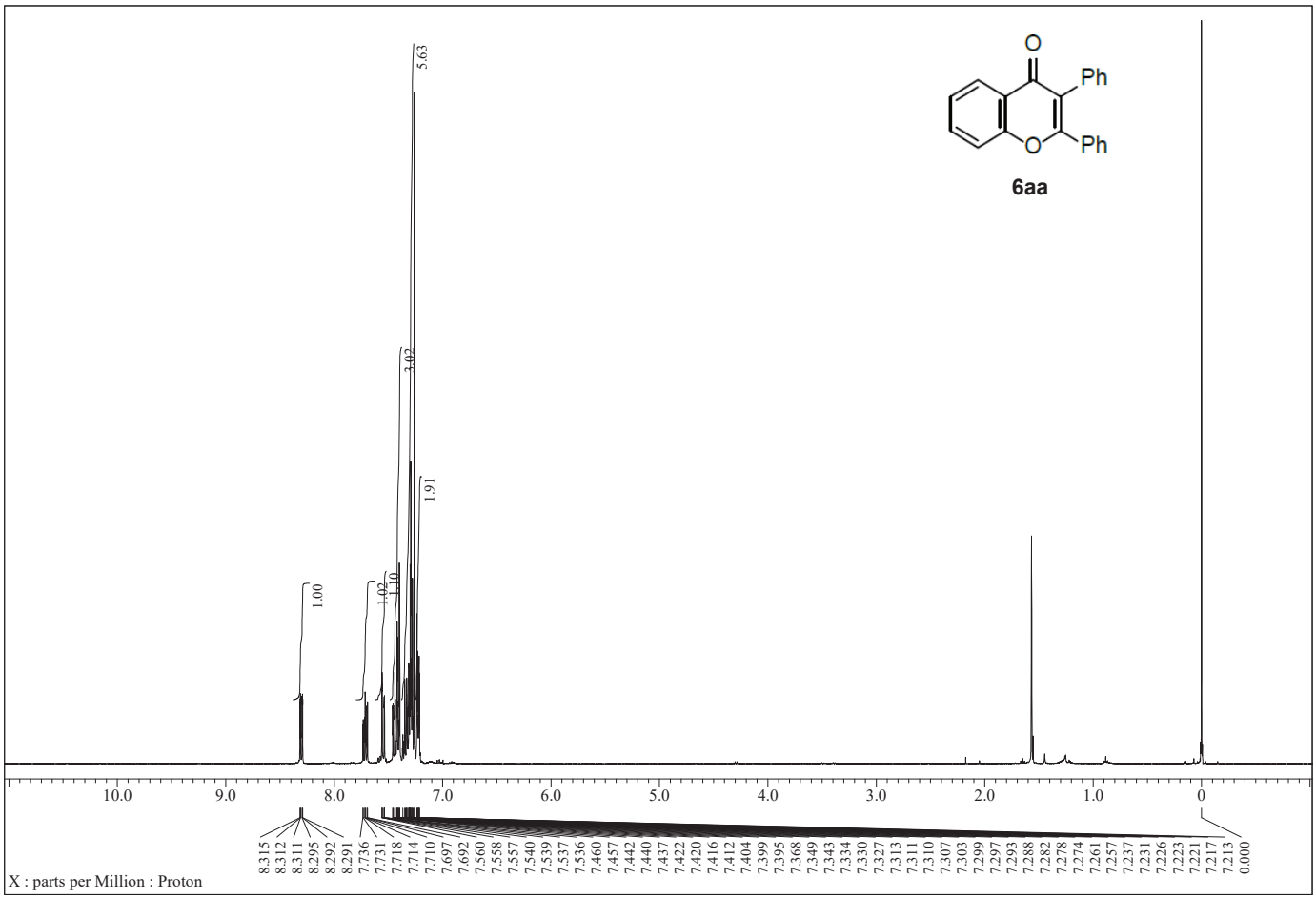

O
N
Ph
Ph
Pr
+
O
N
Ph
Pr
Ph
3ag
3ag'
3ag : 3ag' = 16 : 1
10.84
2.13
1.18
1.00
62.83m
2.14
0.13
2.08
0.27
3.24
0.20
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
X : parts per Million : Proton


3ag
3ag'
3ag : 3ag' = 16 : 1
X : parts per Million : Carbon13


4p
X : parts per Million : Proton


O
N
Ph
OH
CF3
4p
190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
172.672
161.364
146.934
143.405
133.869
130.566
129.755
128.960
128.632
128.305
127.978
127.802
127.526
127.412
127.097
126.464
126.429
126.393
126.357
125.095
122.387
119.680
118.221
118.206
115.653
77.317
77.000
76.681
X : parts per Million : Carbon13


O
N
Ph
OH
CF3
4p
-70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0
-62.913
X : parts per Million : Fluorine19


O
Ph
O
Ph
6aa
5.63
3.02
1.91
1.00
1.02
1.10
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.315
8.312
8.311
8.295
8.292
8.291
7.736
7.731
7.718
7.714
7.710
7.697
7.692
7.560
7.558
7.557
7.540
7.539
7.537
7.536
7.460
7.457
7.442
7.440
7.437
7.422
7.420
7.416
7.412
7.404
7.399
7.395
7.368
7.349
7.343
7.334
7.330
7.327
7.313
7.311
7.310
7.307
7.303
7.299
7.297
7.293
7.288
7.282
7.278
7.274
7.261
7.257
7.237
7.231
7.226
7.223
7.221
7.217
7.213
0.000
X : parts per Million : Proton