Supporting information

1-Trifluoromethylated Isoquinolines *via* Radical Trifluoromethylation of Isonitriles

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General

All manipulations were conducted with a standard *Schlenk* tube under Ar. All solvents and chemicals were used as received from the suppliers (*Alfa, Acros, Aldrich, ABCR, Fluka*).

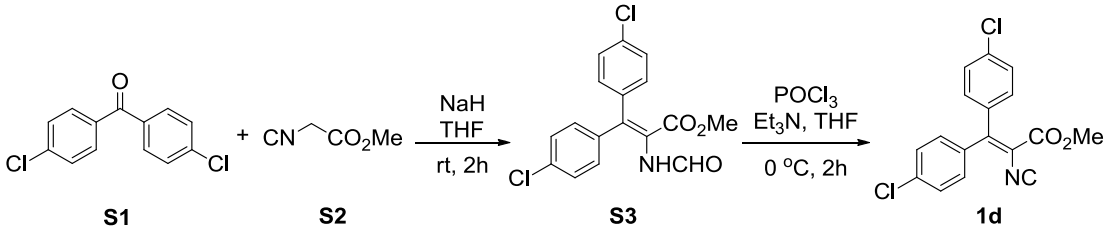
Solvents for flash column chromatography (FC) and extractions have been distilled once. FC was performed using silica gel 60 (40-63µm, *Merck*). Thin layer chromatography (TLC) was performed using silica gel 60 F_{254} plates from *Merck*.

^{1}H NMR spectra were recorded on a *Bruker DPX-300* spectrometer or *AV-400* spectrometer at room temperature. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in $CDCl_3$ as an internal standard. ^{13}C NMR spectra were obtained by the same NMR spectrometer and were calibrated with $CDCl_3$ (δ = 77.00 ppm). ^{19}F NMR spectra were obtained by the same NMR spectrometer and using $CFCl_3$ as external standard. Data for ^{1}H NMR are reported as follows: chemical shifts (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration and assignment. Data for ^{13}C NMR are reported in terms of chemical shift and multiplicity where appropriate. IR-spectra were recorded on a *Digilab Excalibur FTS 4000* device equipped with a *MKII Golden Gate Single Reflection ATR System*. Mass spectra were performed on a *Bruker Daltronics MicroTof*, a *Waters-Micromass Quatro LCZ* or an *Orbitrap LTQ XL* for ESI-MS and HRMS.

Synthesis of vinyl isonitriles:

All β-aryl-α-isocyano-acrylates were prepared according to reported methods.[1,2]

A typical procedure (synthesis of **1d**) is shown below:



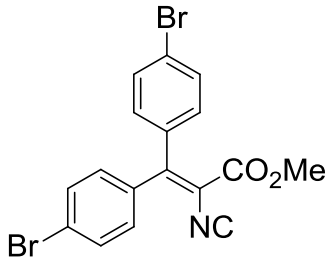
Methyl 3,3-bis(4-chlorophenyl)-2-isocyanoacrylate (1d)

A mixture of bis(4-chlorophenyl)methanone **S1** (2.51 g, 10.0 mmol) and methyl isocyanoacetate **S2** (0.99 g, 10.0 mmol) in THF (10.0 mL) was added dropwise to a suspension of NaH (60% in oil) (0.48 g, 12.0 mmol) in THF (10.0 mL) at room temperature and the mixture was stirred for 2 h at room temperature. 10% AcOH was added to the mixture at 0 °C until there is no hydrogen release. The solvent was removed under reduced pressure and the residue was extracted with CH_2Cl_2 three times. The combined organic layer was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel by using a 1:1 mixture of pentane/EtOAc as an eluent to provide analytical pure product **S3** as a white solid (2.44 g, 70%);

A THF solution (10.0 mL) of **S3** (1.75 g, 5.0 mmol) and NEt_3 (5.6 mL, 40 mmol) was cooled to 0 ℃. Then, $POCl_3$ (0.93 mL, 10.0 mmol) was added dropwise and the mixture was stirred at 0 ℃ for 2 h. After the reaction was completed, the mixture was quenched by aqueous saturated Na_2CO_3 solution and stirred for 1 h. The mixture was extracted with CH_2Cl_2 three times. The combined organic layer was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel by using a 10:1 mixture of pentane/EtO_2 as an eluent to provide analytical pure product **1d** as yellow solid (1.49 g, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49-7.46 (m, 2H, Ar-*H*), 7.44-7.41 (m, 2H, Ar-*H*), 7.15-7.12 (m, 2H, Ar-*H*), 6.93-6.90 (m, 2H, Ar-*H*), 3.64 (s, 3H, C*H*$_3$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.0 (*C*), 161.2 (*C*), 152.1 (*C*), 136.0 (*C*), 135.7 (*C*), 131.9 (2×*C*H), 131.6 (2×*C*H), 131.4 (2×*C*H), 130.6 (2×*C*H), 125.2 (*C*), 124.4 (*C*), 114.0 (*C*), 53.1 (*C*H$_3$); **IR** (neat)**:** 2952, 2113, 1731, 1585, 1468, 1435, 1396, 1324, 1255, 1117, 1072, 1011, 914, 823, 731; **HRMS** (ESI) calculated for

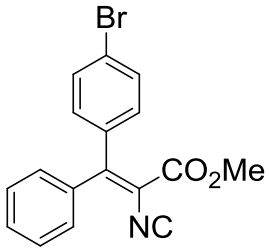
$C_{17}H_{11}Cl_2NO_2Na$ $[M+Na]^+$ m/z 354.0059, found 354.0060.

Methyl 3,3-bis(4-bromophenyl)-2-isocyanoacrylate (1e)



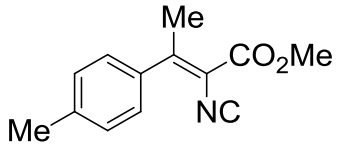
This compound was prepared via the same procedure described for **1d**, except that bis(4-bromophenyl)methanone was used in place of bis(4-chlorophenyl)methanone. **1e** was obtained in 60% yield over two steps as yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33-7.30 (m, 2H, Ar-*H*), 7.29-7.25 (m, 2H, Ar-*H*), 7.22-7.19 (m, 2H, Ar-*H*), 7.00-6.97 (m, 2H, Ar-*H*), 3.64 (s, 3H, C*H*$_3$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.9 (*C*), 161.7 (*C*), 152.0 (*C*), 136.7 (*C*), 136.1 (*C*), 135.6 (*C*), 135.3 (*C*), 131.2 (2×*C*H), 130.5 (2×*C*H), 128.9 (2×*C*H), 128.7 (2×*C*H), 114.1 (*C*), 53.1 (*C*H$_3$); **IR** (neat)**:** 2952, 2113, 1730, 1589, 1489, 1435, 1400, 1324, 1253, 1116, 1090, 1014, 913, 826, 731; **HRMS** (ESI) calculated for $C_{17}H_{11}Br_2NO_2Na$ $[M+Na]^+$ m/z 441.9049, found 441.9037.

(*E*)-Methyl 3-(4-bromophenyl)-2-isocyano-3-phenylacrylate (1g)



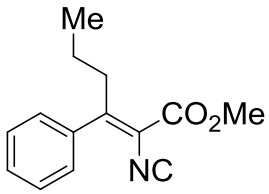
This compound was prepared via the same procedure described for **1d**, except that (4-bromophenyl)(phenyl)methanone was used in place of bis(4-chlorophenyl)methanone. **1g** was obtained in 43% yield over two steps as yellow solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.43-7.39 (m, 2H, Ar-*H*), 7.34-7.30 (m, 3H, Ar-*H*), 7.26-7.23 (m, 2H, Ar-*H*), 6.95-6.90 (m, 2H, Ar-*H*), 3.63 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.6 (*C*), 161.8 (*C*), 153.4 (*C*), 136.9 (*C*), 136.6 (*C*), 131.5 (2×*C*H), 130.6 (2×*C*H), 130.4 (*C*H), 129.7 (2×*C*H), 128.5 (2×*C*H), 124.0 (*C*), 114.0 (*C*), 52.9 (*C*H$_3$); **IR** (neat)**:** 2952, 2112, 1729, 1585, 1484, 1435, 1327, 1252, 1115, 1071, 1010, 909, 822, 731, 698; **HRMS** (ESI) calculated for $C_{17}H_{12}NO_2BrNa$ $[M+Na]^+$ m/z 363.9944, found 363.9951.

(*Z*)-Methyl 2-isocyano-3-(p-tolyl)but-2-enoate (1i)



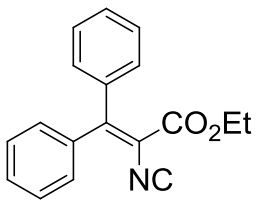
This compound was prepared via the same procedure described for **1d**, except that 1-(p-tolyl)ethanone was used in place of bis(4-chlorophenyl)methanone. **1i** was obtained in 47% yield over two steps as yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.2 Hz, 2H, Ar-*H*), 7.15 (d, *J* = 8.2 Hz, 2H, Ar-*H*), 3.79 (s, 3H, C*H*$_3$), 2.46 (s, 3H, C*H*$_3$), 2.29 (s, 3H, C*H*$_3$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.9 (*C*), 161.8 (*C*), 156.1 (*C*), 139.6 (*C*), 136.3 (*C*), 129.1 (2×*C*H), 127.0 (2×*C*H), 114.0 (*C*), 52.7 (*C*H$_3$), 21.5 (*C*H$_3$), 21.2 (*C*H$_3$); **IR** (neat)**:** 2954, 2114, 1727, 1602, 1511, 1435, 1254, 1122, 1072, 1052, 817; **HRMS** (ESI) calculated for $C_{13}H_{13}NO_2Na$ $[M+Na]^+$ m/z 238.0838, found 238.0853.

(*Z*)-Methyl 2-isocyano-3-phenylhex-2-enoate (1j)



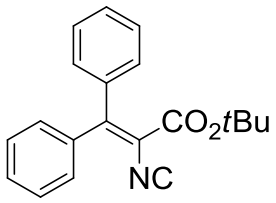
This compound was prepared via the same procedure described for **1d**, except that 1-phenylbutan-1-one was used in place of bis(4-chlorophenyl)methanone. **1j** was obtained in 45% yield over two steps as yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.38-7.30 (m, 3H, Ar-*H*), 7.23-7.17 (m, 2H, Ar-*H*), 3.79 (s, 3H, C*H*$_3$), 2.89-2.84 (m, 2H, C*H*$_2$), 1.38-1.26 (m, 2H, C*H*$_2$), 0.82 (t, *J* = 7.4 Hz, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.1 (*C*), 161.5 (*C*), 160.5 (*C*), 138.2 (*C*), 129.1 (*C*H), 128.5 (2×*C*H), 127.0 (2×*C*H), 114.7 (*C*), 52.7 (*C*H$_3$), 35.9 (*C*H$_2$), 21.4 (*C*H$_2$), 13.7 (*C*H$_3$); **IR** (neat)**:** 2960, 2115, 1729, 1597, 1436, 1255, 1130, 1090, 770, 701; **HRMS** (ESI) calculated for $C_{14}H_{15}NO_2Na$ $[M+Na]^+$ m/z 252.0995, found 252.0991.

Ethyl 2-isocyano-3,3-diphenylacrylate (1n)



This compound was prepared via the same procedure described for **1d**, except that ethyl 2-cyanoacetate was used in place of isocyanoacetate. **1n** was obtained in 68% yield over two steps as yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.21-7.11 (m, 8H, Ar-*H*), 6.95-6.91 (m, 2H, Ar-*H*), 3.90 (q, *J* = 7.1 Hz, 2H, Ar-*H*), 0.85 (t, *J* = 7.1 Hz, 3H, Ar-*H*); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.7 (*C*), 161.9 (*C*), 153.7 (*C*), 138.0 (*C*), 137.3 (*C*), 130.1 (*C*H), 129.8 (2×*C*H), 129.4 (*C*H), 129.0 (2×*C*H), 128.4 (2×*C*H), 128.1 (2×*C*H), 114.3 (*C*), 62.1 (CH_2), 13.5 (CH_3); **IR** (neat)**:** 3058, 2983, 2111, 1724, 1590, 1491, 1445, 1368, 1251, 1111, 1016, 763, 698; **HRMS** (ESI) calculated for $C_{18}H_{15}NO_2Na$ $[M+Na]^+$ m/z 300.0995, found 300.0991.

***tert*-Butyl 2-isocyano-3,3-diphenylacrylate (1o)**



This compound was prepared via the same procedure described for **1d**, except that *tert*-butyl 2-cyanoacetate was used in place of isocyanoacetate. **1o** was obtained in 70% yield over two steps as yellow solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42-7.32 (m, 8H, Ar-*H*), 7.16-7.13 (m, 2H, Ar-*H*), 1.28 (s, 9H, 3×CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.3 (*C*), 160.9 (*C*), 152.0 (*C*), 138.4 (*C*), 137.5 (*C*), 129.9 (*C*H), 129.8 (2×*C*H), 129.2 (3×*C*H), 128.3 (2×*C*H), 128.2 (2×*C*H), 116.0 (*C*), 83.4 (*C*), 27.4 (3×CH_3); **IR** (neat)**:** 3059, 2981, 2112, 1721, 1590, 1491, 1332, 1277, 1163, 1118, 842, 753, 698; **HRMS** (ESI) calculated for $C_{20}H_{19}NO_2Na$ $[M+Na]^+$ m/z 328.1308, found 328.1305.

General procedure for the preparation of 1-trifluoromethylated isoquinolines:

Method A:

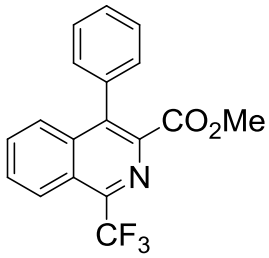
β-Aryl-α-isocyano-acrylate **1** (0.2 mmol, 1.0 equiv), *Togni*-reagent **2**[3] (0.3 mmol, 1.5 equiv), and Bu_4NI (0.01 mmol, 0.05 equiv) were placed in a dry *Schlenk* tube under argon. Dry 1,4-dioxane (1.0 mL) was added and the reaction mixture was stirred at 80 ^oC for 3 h and the reaction was monitored by TLC. The crude reaction mixture was purified by flash column chromatography on silica gel to afford the product.

Method B:

β-Aryl-α-isocyano-acrylate **1** (0.2 mmol, 1.0 equiv), *Togni*-reagent **2** (0.4 mmol, 2.0 equiv), and Bu_4NI (0.01 mmol, 0.05 equiv) were placed in a dry *Schlenk* tube under argon. Dry 1,4-dioxane (1.0 mL) was added and the reaction mixture was stirred at 80 ^oC for 6 h and the reaction was monitored by TLC. The crude reaction mixture was purified by flash column chromatography on silica gel to afford the product.

Physical data of the compounds

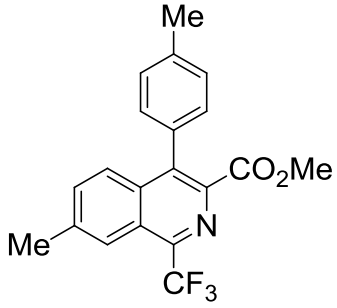
Methyl 4-phenyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3a)



According to **method A** with methyl 2-isocyano-3,3-diphenylacrylate **1a** (53.4 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.6 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.8 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3a** as white solid (52.5 mg, 80%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34-8.31 (m, 1H, Ar-*H*), 7.75-7.70 (m, 1H, Ar-*H*), 7.67-7.66 (m, 2H, Ar-*H*), 7.46-7.42 (m, 3H, Ar-*H*), 7.27-7.25 (m, 2H, Ar-*H*), 3.63 (s, 3H, C*H*$_3$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.4 (*C*), 145.6 (q, *J* = 33.8 Hz, *C*), 140.0 (*C*), 137.5 (*C*), 137.1 (*C*), 134.9 (*C*), 131.4

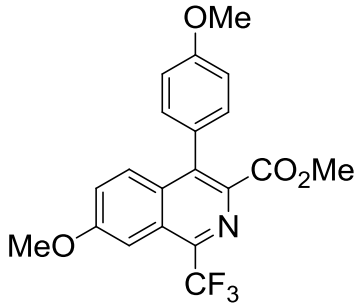
(*C*H), 129.9 (*C*H), 129.4 (*C*H), 128.5 (*C*H), 128.4 (*C*H), 127.4 (*C*H), 125.0 (*C*), 124.7 (q, *J* = 3.1 Hz, *C*H), 121.8 (q, *J* = 275.0 Hz, *C*F_3), 52.6 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.77 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2953, 1738, 1440, 1401, 1240, 1179, 1126, 1003, 771, 701 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{12}NO_2F_3Na$ $[M+Na]^+$ m/z 354.0712, found 354.0708.

Methyl 7-methyl-4-(*p*-tolyl)-1-(trifluoromethyl)isoquinoline-3-carboxylate (3b)



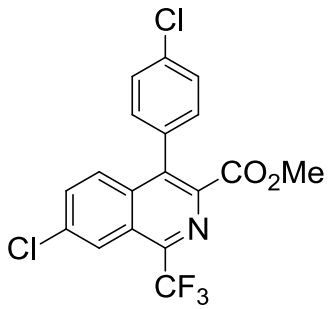
According to **method A** with methyl 2-isocyano-3,3-di-*p*-tolylacrylate **1b** (58.9 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.7 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.7 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3b** as pale yellow solid (52.1 mg, 73%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.05 (s, 1H, Ar-*H*), 7.58 (d, *J* = 9.0 Hz, 1H, Ar-*H*), 7.47 (dd, *J* = 8.9, 1.4 Hz, 1H, Ar-*H*), 7.24 (d, *J* = 7.8 Hz, 2H, Ar-*H*), 7.13 (d, *J* = 8.1 Hz, 2H, Ar-*H*), 3.66 (s, 3H, C*H*$_3$), 2.53 (s, 3H, C*H*$_3$), 2.38 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.6 (*C*), 144.6 (q, *J* = 33.7 Hz, *C*), 140.5 (*C*), 139.2 (*C*), 138.2 (*C*), 137.7 (*C*), 135.5 (*C*), 133.6 (*C*H), 132.1 (*C*), 129.2 (*C*H), 129.1 (*C*H), 127.3 (*C*H), 125.3 (*C*), 123.4 (q, *J* = 3.0 Hz, *C*H), 121.9 (q, *J* = 274.9 Hz, *C*F_3), 52.6 (*C*H_3), 22.2 (*C*H_3), 21.4 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.83 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2952, 1737, 1439, 1397, 1236, 1176, 1118, 1010, 976, 818, 757, 696 cm^{-1}; **HRMS** (ESI) calculated for $C_{20}H_{16}NO_2F_3Na$ $[M+Na]^+$ m/z 382.1025, found 382.1029.

Methyl 7-methoxy-4-(4-methoxyphenyl)-1-(trifluoromethyl)isoquinoline-3-carboxylate (3c)



According to **method A** with methyl 2-isocyano-3,3-bis(4-methoxyphenyl)acrylate **1c** (65.5 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.5 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.8 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 5/1) to afford the desired product **3c** as white solid (52.1 mg, 67%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 9.6 Hz, 1H, Ar-*H*), 7.52-7.48 (m, 1H, Ar-*H*), 7.29 (dd, *J* = 9.6, 2.4 Hz, 1H, Ar-*H*), 7.19-7.15 (m, 2H, Ar-*H*), 6.98-6.95 (m, 2H, Ar-*H*), 3.93 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 3.67 (s, 3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.7 (*C*), 160.2 (*C*), 159.7 (*C*), 143.4 (q, *J* = 33.5 Hz, *C*), 138.4 (*C*), 137.6 (*C*), 132.9 (*C*), 130.6 (*C*H), 129.1 (*C*H), 127.2 (*C*), 126.9 (*C*), 124.3 (*C*H), 122.0 (q, *J* = 274.7 Hz, *C*F_3), 113.8 (*C*H), 102.3 (q, *J* = 3.1 Hz, *C*H), 55.6 (*C*H_3), 55.3 (*C*H_3), 52.6 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.59 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2952, 1734, 1613, 1517, 1418, 1290, 1229, 1173, 1119, 1030, 837 cm^{-1}; **HRMS** (ESI) calculated for $C_{20}H_{16}NO_4F_3Na$ $[M+Na]^+$ m/z 414.0924, found 414.0918.

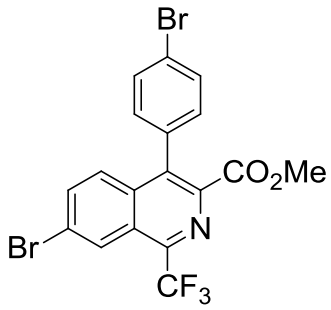
Methyl 7-chloro-4-(4-chlorophenyl)-1-(trifluoromethyl)isoquinoline-3-carboxylate (3d)



According to **method A** with methyl 3,3-bis(4-chlorophenyl)-2-isocyanoacrylate **1d** (66.9 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.6 mg, 0.30 mmol, 1.5 equiv)

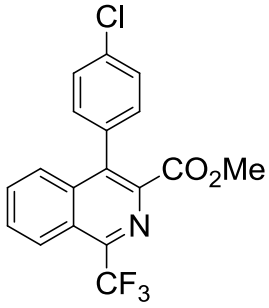
and Bu_4NI (3.8 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3d** as pale yellow solid (57.5 mg, 72%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.29-8.28 (m, 1H, Ar-*H*), 7.63 (dd, *J* = 9.2, 2.0 Hz, 1H, Ar-*H*), 7.57 (d, *J* = 9.0 Hz, 1H, Ar-*H*), 7.46-7.42 (m, 2H, Ar-*H*), 7.21-7.17 (m, 2H, Ar-*H*), 3.69 (s, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.8 (*C*), 145.0 (q, *J* = 34.3 Hz, *C*), 140.1 (*C*), 136.7 (*C*), 136.4 (*C*), 135.4 (*C*), 135.0 (*C*), 132.9 (*C*), 132.8 (*C*H), 130.7 (*C*H), 128.9 (*C*H), 128.8 (*C*H), 125.5 (*C*), 123.8 (q, *J* = 3.4 Hz, *C*H), 121.4 (q, *J* = 275.0 Hz, *C*F_3), 52.8 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.00 (s, 3F, C*F_3*); **IR** (neat)**:** 2954, 1737, 1497, 1440, 1393, 1238, 1178, 1127, 1009, 978, 838 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{10}NO_2Cl_2F_3Na$ $[M+Na]^+$ m/z 421.9933, found 421.9935.

Methyl 7-bromo-4-(4-bromophenyl)-1-(trifluoromethyl)isoquinoline-3-carboxylate (3e)



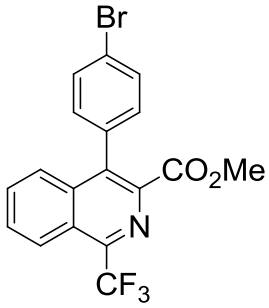
According to **method A** with methyl 3,3-bis(4-bromophenyl)-2-isocyanoacrylate **1e** (84.8 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.5 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.7 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3e** as pale yellow solid (72.1 mg, 74%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47-8.46 (m, 1H, Ar-*H*), 7.76 (dd, *J* = 9.0, 1.8 Hz, 1H, Ar-*H*), 7.62-7.58 (m, 2H, Ar-*H*), 7.49 (d, *J* = 9.3 Hz, 1H, Ar-*H*), 7.15-7.10 (m, 2H, Ar-*H*), 3.70 (s, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.8 (*C*), 144.9 (q, *J* = 34.3 Hz, *C*), 140.0 (*C*), 136.5 (*C*), 135.5 (*C*), 135.3 (*C*H), 133.3 (*C*), 131.8 (*C*H), 130.9 (*C*H), 128.7 (*C*H), 127.1 (q, *J* = 3.3 Hz, *C*H), 125.8 (*C*), 125.2 (*C*), 123.2 (*C*), 121.4 (q, *J* = 275.3 Hz, *C*F_3), 52.9 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.90 (s, 3F, C*F_3*); **IR** (neat)**:** 2952, 1735, 1492, 1440, 1389, 1236, 1177, 1123, 1079, 1006, 976, 826 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{10}NO_2Br_2F_3Na$ $[M+Na]^+$ m/z 511.8903, found 511.8904.

Methyl 4-(4-chlorophenyl)-1-(trifluoromethyl)isoquinoline-3-carboxylate (3f)



According to **method A** with (*E*)-methyl 3-(4-chlorophenyl)-2-isocyano-3-phenylacrylate **1f** (60.1 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.4 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.8 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3f** as white solid (47.3 mg, 65%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.36-8.33 (m, 1H, Ar-*H*), 7.78-7.60 (m, 3H, Ar-*H*), 7.44 (dt, *J* = 8.9, 2.2 Hz, 2H, Ar-*H*), 7.21 (dt, *J* = 8.9, 2.2 Hz, 2H, Ar-*H*), 3.69 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.2 (*C*), 146.0 (q, *J* = 34.2 Hz, *C*), 139.9 (*C*), 137.0 (*C*), 136.4 (*C*), 134.8 (*C*), 133.5 (*C*), 131.7 (*C*H), 130.8 (*C*H), 130.1 (*C*H), 128.7 (*C*H), 127.1 (*C*H), 125.0 (*C*), 124.8 (q, *J* = 3.2 Hz, *C*H), 121.7 (q, *J* = 275.0 Hz, *C*F$_3$), 52.7 (*C*H$_3$); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.83 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2954, 1734, 1491, 1438, 1400, 1239, 1178, 1125, 1002, 830, 772, 681 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{11}NO_2ClF_3Na$ $[M+Na]^+$ m/z 388.0323, found 388.0329.

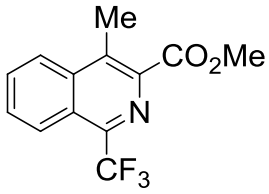
Methyl 4-(4-bromophenyl)-1-(trifluoromethyl)isoquinoline-3-carboxylate (3g)



According to **method A** with (*E*)-methyl 3-(4-bromophenyl)-2-isocyano-3-phenylacrylate **1g** (68.9 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.6 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3g** as

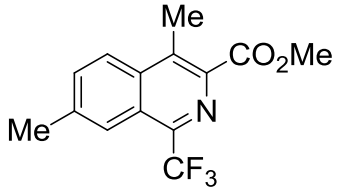
white solid (62.9 mg, 77%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.77-7.63 (m, 3H, Ar-*H*), 7.58 (dt, *J* = 8.3 Hz, 2H, Ar-*H*), 7.14 (d, *J* = 8.3 Hz, 2H, Ar-*H*), 3.68 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.1 (*C*), 146.0 (q, *J* = 33.8 Hz, *C*), 139.8 (*C*), 136.9 (*C*), 136.4 (*C*), 134.0 (*C*), 131.7 (*C*H), 131.1 (*C*H), 130.1 (*C*H), 127.1 (*C*H), 125.0 (*C*), 124.8 (q, *J* = 3.1 Hz, *C*H), 122.9 (*C*), 121.7 (q, *J* = 275.0 Hz, *C*F_3), 52.7 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.82 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2954, 1731, 1487, 1439, 1389, 1240, 1179, 1130, 1071, 1002, 733 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{11}NO_2BrF_3Na$ $[M+Na]^+$ m/z 431.9817, found 431.9811.

Methyl 4-methyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3h)



According to **method A** with (*Z*)-methyl 2-isocyano-3-phenylbut-2-enoate **1h** (40.7 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.3 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.8 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3h** as white solid (37.6 mg, 70%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.28-8.25 (m, 1H, Ar-*H*), 8.17 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.83-7.77 (m, 1H, Ar-*H*), 7.75-7.70 (m, 1H, Ar-*H*), 3.97 (s, 3H, C*H*$_3$), 2.85 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.9 (*C*), 144.2 (q, *J* = 33.6 Hz, *C*), 139.7 (*C*), 137.2 (*C*), 133.9 (*C*), 131.3 (*C*H), 129.7 (*C*H), 125.1 (q, *J* = 3.1 Hz, *C*H), 125.0 (*C*H), 124.6 (*C*), 121.8 (q, *J* = 274.8 Hz, *C*F_3), 52.9 (*C*H_3), 14.7 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.69 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2956, 1726, 1440, 1376, 1297, 1231, 1194, 1122, 1062, 969, 764 cm^{-1}; **HRMS** (ESI) calculated for $C_{13}H_{10}NO_2F_3Na$ $[M+Na]^+$ m/z 292.0556, found 292.0557.

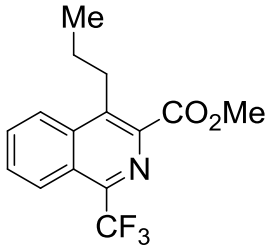
Methyl 4,7-dimethyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3i)



According to **method A** with (*Z*)-methyl 2-isocyano-3-(p-tolyl)but-2-enoate **1i** (43.8

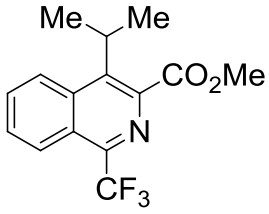
mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.2 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.8 mg, 10 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3i** as white solid (39.6 mg, 70%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 8.00 (brs, 1H, Ar-*H*), 7.62 (dd, *J* = 8.8, 1.6 Hz, 1H, Ar-*H*), 3.96 (s, 3H, C*H*$_3$), 2.84 (s, 3H, C*H*$_3$), 2.54 (s, 3H, C*H*$_3$); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.0 (*C*), 143.4 (q, *J* = 33.4 Hz, *C*), 140.4 (*C*), 138.8 (*C*), 135.5 (*C*), 134.0 (*C*), 133.5 (*C*H), 124.9 (*C*), 124.8 (*C*H), 124.0 (q, *J* = 3.0 Hz, *C*H), 121.9 (q, *J* = 274.7 Hz, *C*F$_3$), 52.8 (*C*H$_3$), 22.1 (*C*H$_3$), 14.7 (*C*H$_3$); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.75 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2956, 1715, 1443, 1371, 1300, 1232, 1171, 1111, 1076, 980, 819 cm^{-1}; **HRMS** (ESI) calculated for $C_{14}H_{12}NO_2F_3Na$ $[M+Na]^+$ m/z 306.0712, found 306.0720.

Methyl 4-propyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3j)



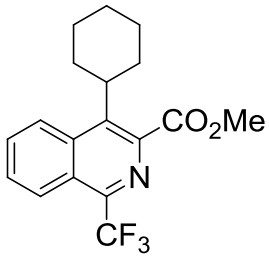
According to **method A** with (*Z*)-methyl 2-isocyano-3-phenylhex-2-enoate **1j** (49.1 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.3 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3j** as white solid (45.8 mg, 77%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.28 (d, *J* = 8.7 Hz, 1H, Ar-*H*), 8.18 (d, *J* = 8.7 Hz, 1H, Ar-*H*), 7.82-7.77 (m, 1H, Ar-*H*), 7.74-7.69 (m, 1H, Ar-*H*), 3.96 (s, 3H, C*H*$_3$), 3.28-3.22 (m, 2H, C*H*$_2$), 1.75-1.67 (m, 2H, C*H*$_2$), 1.03 (d, *J* = 7.4 Hz, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz , $CDCl_3$) δ 166.9 (*C*), 144.3 (q, *J* = 33.4 Hz, *C*), 139.7 (*C*), 138.1 (*C*), 136.7 (*C*), 131.2 (*C*H), 129.6 (*C*H), 125.3 (q, *J* = 3.2 Hz, *C*H), 125.1 (*C*), 125.0 (*C*H), 121.9 (q, *J* = 274.8 Hz, *C*F$_3$), 52.8 (*C*H$_3$), 30.3 (*C*H$_2$), 24.5 (*C*H$_2$), 14.4 (*C*H$_3$); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.72 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2960, 2874, 1733 1440, 1401, 1303, 1239, 1215, 1165, 1121, 1072, 968, 774, 685 cm^{-1}; **HRMS** (ESI) calculated for $C_{15}H_{14}NO_2F_3Na$ $[M+Na]^+$ m/z 320.0869, found 320.0864.

Methyl 4-isopropyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3k)



According to **method A** with (*Z*)-methyl 2-isocyano-4-methyl-3-phenylpent-2-enoate **1k** (46.6 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.4 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (4.0 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3k** as white solid (35.8 mg, 60%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.28 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.78-7.73 (m, 1H, Ar-*H*), 7.70-7.65 (m, 1H, Ar-*H*), 3.96 (s, 3H, CH_3), 3.81-3.67 (m, 1H, C*H*), 1.51 (d, *J* = 7.5 Hz, 6H, 2×CH_3); **^{13}C NMR** (75 MHz , $CDCl_3$) δ 168.3 (*C*), 144.5 (q, *J* = 33.1 Hz, *C*), 141.6 (*C*), 139.7 (*C*), 136.1 (*C*), 130.6 (*C*H), 128.9 (*C*H), 125.6 (q, *J* = 3.2 Hz, *C*H), 125.4 (*C*H), 125.2 (*C*), 121.9 (q, *J* = 274.8 Hz, *C*F_3), 52.9 (*C*H_3), 29.7 (*C*H), 21.9 (2×*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.61 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2968, 1737, 1450, 1402, 1355, 1290, 1227, 1176 1127, 1031, 970, 770, 687 cm^{-1}; **HRMS** (ESI) calculated for $C_{15}H_{14}NO_2F_3Na$ $[M+Na]^+$ m/z 320.0869, found 320.0867.

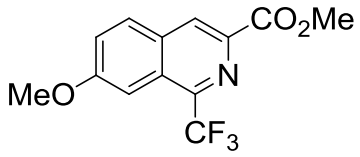
Methyl 4-cyclohexyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3l)



According to **method B** with (*Z*)-methyl 3-cyclohexyl-2-isocyano-3-phenylacrylate **1l** (54.6 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.7 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3l** as white solid (37.1 mg, 55%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (brs, 1H, Ar-*H*), 8.25 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 7.76-7.72 (m, 1H, Ar-*H*), 7.68-7.63 (m, 1H, Ar-*H*), 3.95 (s, 3H, CH_3), 3.31-3.26 (m, 1H, C*H*), 1.97-1.75 (m, 7H, CH_2), 1.44-1.28 (m, 3H, CH_2); **^{13}C NMR** (100 MHz , $CDCl_3$) δ 168.5 (*C*), 144.3 (q, *J* = 33.6

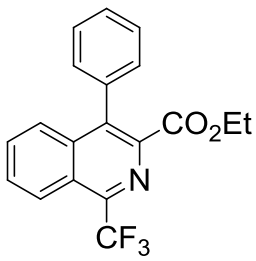
Hz, *C*), 141.8 (*C*), 138.4 (*C*), 136.3 (*C*), 130.6 (*C*H), 128.8 (*C*H), 125.4 (q, *J* = 3.1 Hz, *C*H), 125.1 (*C*H), 125.0 (*C*), 121.8 (q, *J* = 274.8 Hz, *C*F_3), 52.8 (*C*H_3), 41.2 (*C*), 31.5 (2×*C*H_2), 27.3 (2×*C*H_2), 25.9 (*C*H_2); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.60 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2931, 2856, 1736, 1449, 1401, 1370, 1218, 1121, 1078, 999, 972, 768, 685 cm^{-1}; **HRMS** (ESI) calculated for $C_{18}H_{18}NO_2F_3Na$ $[M+Na]^+$ m/z 360.1182, found 360.1181.

Methyl 7-methoxy-1-(trifluoromethyl)isoquinoline-3-carboxylate (3m)



According to **method A** with (*Z*)-methyl 2-isocyano-3-(4-methoxyphenyl)acrylate **1m** (44.0 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.6 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/DCM = 3/1-DCM) to afford the desired product **3m** as white solid (31.4 mg, 55%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.59 (s, 1H, Ar-*H*), 7.89 (d, *J* = 9.0 Hz, 1H, Ar-*H*), 7.48 (s, 1H, Ar-*H*), 7.42 (dd, *J* = 9.0, 2.4 Hz, 1H, Ar-*H*), 3.98 (s, 3H, C*H*$_3$), 3.93 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz , $CDCl_3$) δ 165.4 (*C*), 161.3 (*C*), 144.7 (q, *J* = 33.7 Hz, *C*), 138.0 (*C*), 132.7 (*C*), 130.5 (*C*H), 127.8 (*C*), 127.2 (*C*H), 124.9 (*C*H), 122.0 (q, *J* = 274.8 Hz, *C*F_3), 102.7 (q, *J* = 3.3 Hz, *C*H), 55.7 (*C*H_3), 52.9 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.82 (s, 3F, C*F*$_3$); **IR** (neat)**:** 3008, 2957, 1710, 1623, 1502, 1454, 1416, 1320, 1262, 1226, 1179, 1120, 1019, 825 cm^{-1}; **HRMS** (ESI) calculated for $C_{13}H_{10}NO_3F_3Na$ $[M+Na]^+$ m/z 308.0505, found 308.0499.

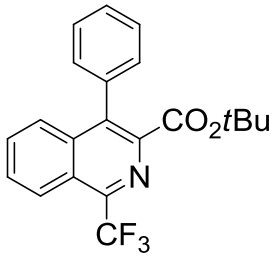
Ethyl 4-phenyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3n)



According to **method A** with ethyl 2-isocyano-3,3-diphenylacrylate **1n** (56.1 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.5 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel

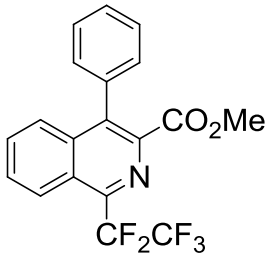
column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3n** as white solid (48.1 mg, 70%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.74-7.66 (m, 3H, Ar-*H*), 7.44-7.42 (m, 3H, Ar-*H*), 7.29-7.26 (m, 2H, Ar-*H*), 4.06 (q, *J* = 7.1 Hz, 2H, CH_2), 0.91 (t, *J* = 7.1 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.3 (*C*), 145.7 (q, *J* = 33.7 Hz, *C*), 140.9 (*C*), 137.0 (*C*), 136.7 (*C*), 135.1 (*C*), 131.4 (*C*H), 129.7 (*C*H), 129.6 (*C*H), 128.5 (*C*H), 128.3 (*C*H), 127.3 (*C*H), 124.9 (*C*), 124.7 (q, *J* = 3.1 Hz, *C*H), 121.9 (q, *J* = 275.0 Hz, *C*F_3), 61.6 (*C*H_2), 13.6 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.74 (s, 3F, C*F*$_3$); **IR** (neat)**:** 2983, 1733, 1406, 1236, 1179, 1123, 995, 771, 700 cm^{-1}; **HRMS** (ESI) calculated for $C_{19}H_{14}NO_2F_3Na$ $[M+Na]^+$ m/z 368.0869, found 368.0866.

***tert*-Butyl 4-phenyl-1-(trifluoromethyl)isoquinoline-3-carboxylate (3o)**



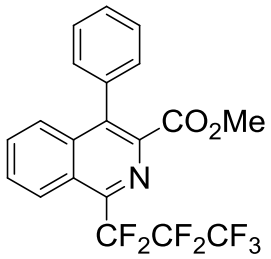
According to **method A** with *tert*-butyl 2-isocyano-3,3-diphenylacrylate **1o** (61.7 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.6 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3o** as white solid (59.6 mg, 80%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.31-8.28 (m, 1H, Ar-*H*), 7.70-7.61 (m, 3H, Ar-*H*), 7.46-7.41 (m, 3H, Ar-*H*), 7.31-7.26 (m, 2H, Ar-*H*), 1.14 (s, 9H, 3×CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.5 (*C*), 145.7 (q, *J* = 33.7 Hz, *C*), 142.1 (*C*), 137.0 (*C*), 135.6 (*C*), 135.4 (*C*), 131.2 (*C*H), 129.9 (*C*H), 129.4 (*C*H), 128.39 (*C*H), 128.36 (*C*H), 127.1 (*C*H), 124.7 (*C*), 124.6 (q, *J* = 3.2 Hz, *C*H), 121.9 (q, *J* = 275.0 Hz, *C*F_3), 82.5 (*C*), 27.5 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.63 (s, 3F, C*F*$_3$); **IR** (neat)**:** 3056, 2987, 1723, 1407, 1249, 1119, 996, 935, 848, 767, 699 cm^{-1}; **HRMS** (ESI) calculated for $C_{21}H_{18}NO_2F_3Na$ $[M+Na]^+$ m/z 396.1182, found 396.1180.

Methyl 1-(perfluoroethyl)-4-phenylisoquinoline-3-carboxylate (5a)



According to **method A** with methyl 2-isocyano-3,3-diphenylacrylate **1a** (53.3 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **4a**[5] (111.6 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **5a** as pale yellow solid (40.2 mg, 53%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.74-7.65 (m, 3H, Ar-*H*), 7.47-7.43 (m, 3H, Ar-*H*), 7.28-7.25 (m, 2H, Ar-*H*), 3.62 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.5 (*C*), 145.5 (t, *J* = 26.2 Hz, *C*), 140.4 (*C*), 137.1 (*C*), 137.0 (*C*), 134.9 (*C*), 131.2 (*C*H), 129.7 (*C*H), 129.5 (*C*H), 128.6 (*C*H), 128.4 (*C*H), 127.5 (*C*H), 126.1 (*C*), 124.8 (t, *J* = 6.0 Hz, *C*H), 120-100 (m, *C*), 52.5 (*C*H$_3$); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -80.76 (t, *J* = 1.4, 3F, CF_2CF_3), -107.22 (brs, 2F, CF_2CF_3); **IR** (neat)**:** 2954, 1737, 1445, 1403, 1326, 1227, 1170, 1104, 1069, 1049, 993, 959, 877, 770, 701 cm^{-1}; **HRMS** (ESI) calculated for $C_{19}H_{12}NO_2F_5Na$ $[M+Na]^+$ m/z 404.0680, found 404.0680.

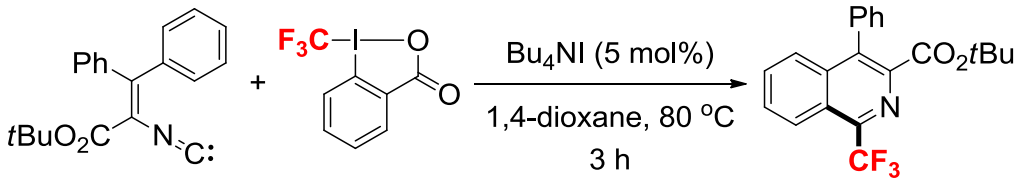
Methyl 1-(perfluoropropyl)-4-phenylisoquinoline-3-carboxylate (5b)



According to **method A** with methyl 2-isocyano-3,3-diphenylacrylate **1a** (53.5 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **4b**[6] (126.3 mg, 0.30 mmol, 1.5 equiv) and Bu_4NI (4.0 mg, 11 μmol, 0.05 equiv). The crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **5b** as pale yellow solid (46.4 mg, 54%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.40-8.37 (m, 1H, Ar-*H*), 7.72-7.61 (m, 3H, Ar-*H*), 7.46-7.43 (m, 3H, Ar-*H*), 7.29-7.26 (m, 2H, Ar-*H*), 3.62 (s, 3H, C*H*$_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.5 (*C*),

145.3 (t, *J* = 24.5 Hz, *C*), 140.7 (*C*), 137.2 (*C*), 136.9 (*C*), 134.9 (*C*), 131.1 (*C*H), 129.7 (*C*H), 129.5 (*C*H), 128.6 (*C*H), 128.4 (*C*H), 127.5 (*C*H), 126.5 (*C*), 125.1-124.9 (m, *C*), 120-100 (m, *C*), 52.5 (*C*H_3); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -79.41 (t, *J* = 9.6 Hz, 3F, $CF_2CF_2CF_3$), -106.15 – -106.25 (m, 2F, $CF_2CF_2CF_3$), -124.03 (t, *J* = 9.6 Hz, 2F, $CF_2CF_2CF_3$); **IR** (neat)**:** 2955, 1738, 1445, 1341, 1203, 1114, 987, 946, 854, 769, 700 cm^{-1}; **HRMS** (ESI) calculated for $C_{20}H_{12}NO_2F_7Na$ $[M+Na]^+$ m/z 454.0648, found 454.0651.

Lager scale experiment

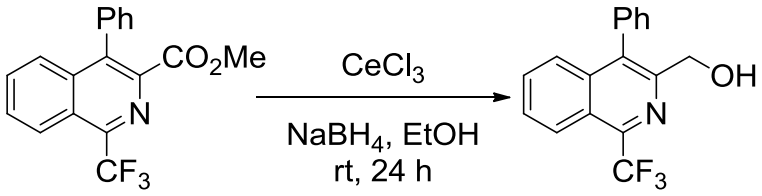


1o (1.0 eq.) **2** (1.5 eq.) 71% yield **3o**

2.0 mmol 0.53 g

tert-Butyl 2-isocyano-3,3-diphenylacrylate **1o** (0.556 g, 0.002 mol, 1.0 equiv), *Togni*-reagent **2** (0.953 g, 0.003 mol, 1.5 equiv) and Bu_4NI (37.6 mg, 0.10 mmol, 0.05 equiv) were placed in a dry *Schlenk* tube under argon. Dry 1,4-dioxane (10.0 mL) was added and the reaction mixture was stirred at 80 ^oC for 3 h as monitored by TLC. The solvent was removed and the crude reaction mixture was purified by flash silica gel column chromatography (pentane/diethyl ether = 10/1) to afford the desired product **3o** (0.530 g, 71%).

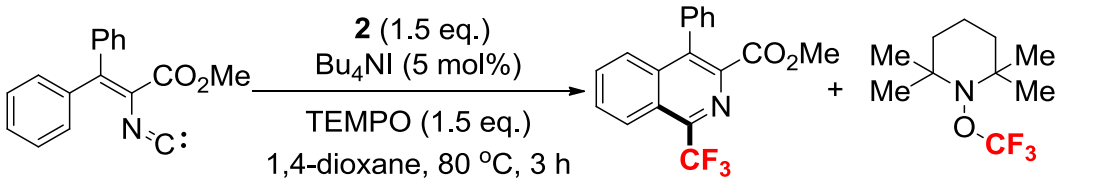
The reduction of 3a



3a 65%

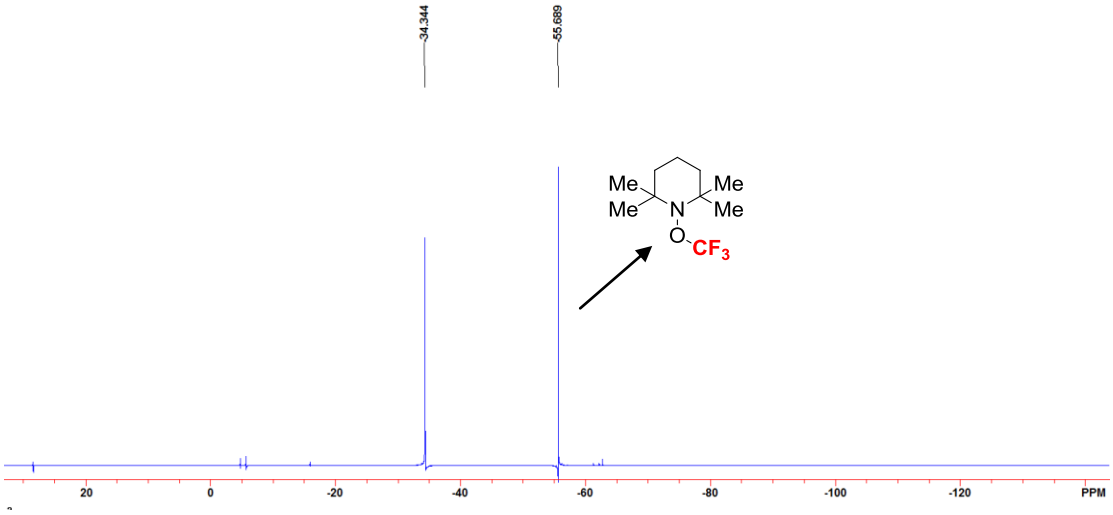
$NaBH_4$ (39.7 mg, 1.00 mmol, 5.0 equiv) was added to a stirred solution of methyl 4-phenyl-1-(trifluoromethyl)isoquinoline-3-carboxylate **3a** (66.8 mg, 0.20 mmol, 1.0 equiv) and $CeCl_3 \cdot 7H_2O$ (4.2 mg, 10 μmol, 0.05 equiv) in EtOH (2.0 mL) at room temperature. The resulting suspension was stirred for 24 h. The solvent was removed in vacuo and the residue was purified by silica gel column chromatography (PE/Et_2O = 3/1) to afford 39.3 mg (65%) of product as pale yellow solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.29-8.26 (m, 1H, Ar-*H*), 7.64-7.56 (m, 2H, Ar-*H*), 7.53-7.43 (m, 4H, Ar-*H*), 7.22-7.19 (m, 2H, Ar-*H*), 4.53 (s, 2H, C*H*$_2$), 3.59 (brs, 1H, O*H*); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 147.4 (*C*), 144.8 (q, *J* = 33.4 Hz, *C*), 137.2 (*C*), 134.3 (*C*), 133.7 (*C*), 131.0 (*C*H), 129.5 (*C*H), 129.0 (*C*H), 128.7 (*C*H), 128.3 (*C*H), 126.1 (*C*H), 124.6 (q, *J* = 3.0 Hz, *C*H), 123.8 (*C*), 122.1 (q, *J* = 274.5 Hz, *C*F_3), 62.0 (*C*H_2); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.69 (s, 3F, C*F*$_3$); **IR** (neat)**:** 3443, 3062, 2924, 2884, 1573, 1407, 1348, 1291, 1174, 1126, 1070, 997, 771, 702 cm^{-1}; **HRMS** (ESI) calculated for $C_{17}H_{12}NOF_3Na$ $[M+Na]^+$ m/z 326.0763, found 326.0756.

Mechanistic study



1a (1.0 eq.) **3a** (0%) detected by ^{19}F NMR

β-Aryl-α-isocyano-acrylates **1a** (53.2 mg, 0.20 mmol, 1.0 equiv), *Togni*-reagent **2** (95.8 mg, 0.30 mmol, 1.5 equiv), Bu_4NI (3.9 mg, 11 μmol, 0.05 equiv) and TEMPO (47.5 mg, 0.30 mmol, 1.5 equiv) were placed in a dry *Schlenk* tube under argon. Dry 1,4-dioxane (1.0 mL) was added and the reaction mixture was stirred at 80 °C for 3 h. ^{19}F NMR analysis of this reaction mixture showed that TEMPO-CF_3 was formed. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -55.7. **^{19}F NMR** spectrum was matching with literature data.[4]



References:

(1) Jiang, H.; Cheng, Y.; Wang, R.; Zhang, Y.; Yu, S. *Chem. Commun.* **2014**, *50*, 6164.

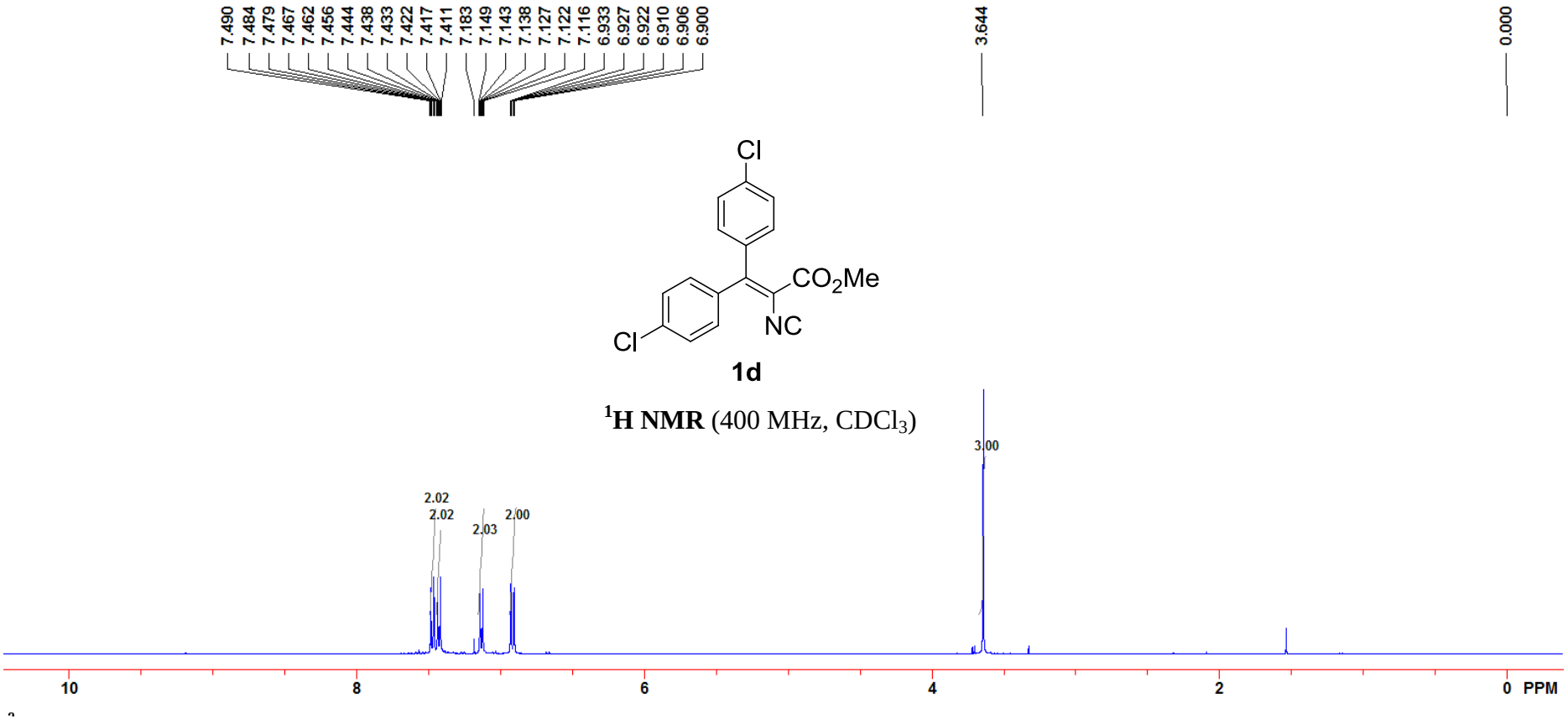
(2) Suzuki, M.; Nunami, K.-I.; Matsumoto, K.; Yoneda, N.; Kasuga, O.; Yoshida, H.; Yamaguchi, T. *Chem. Pharm. Bull.* **1980**, *28*, 2374.

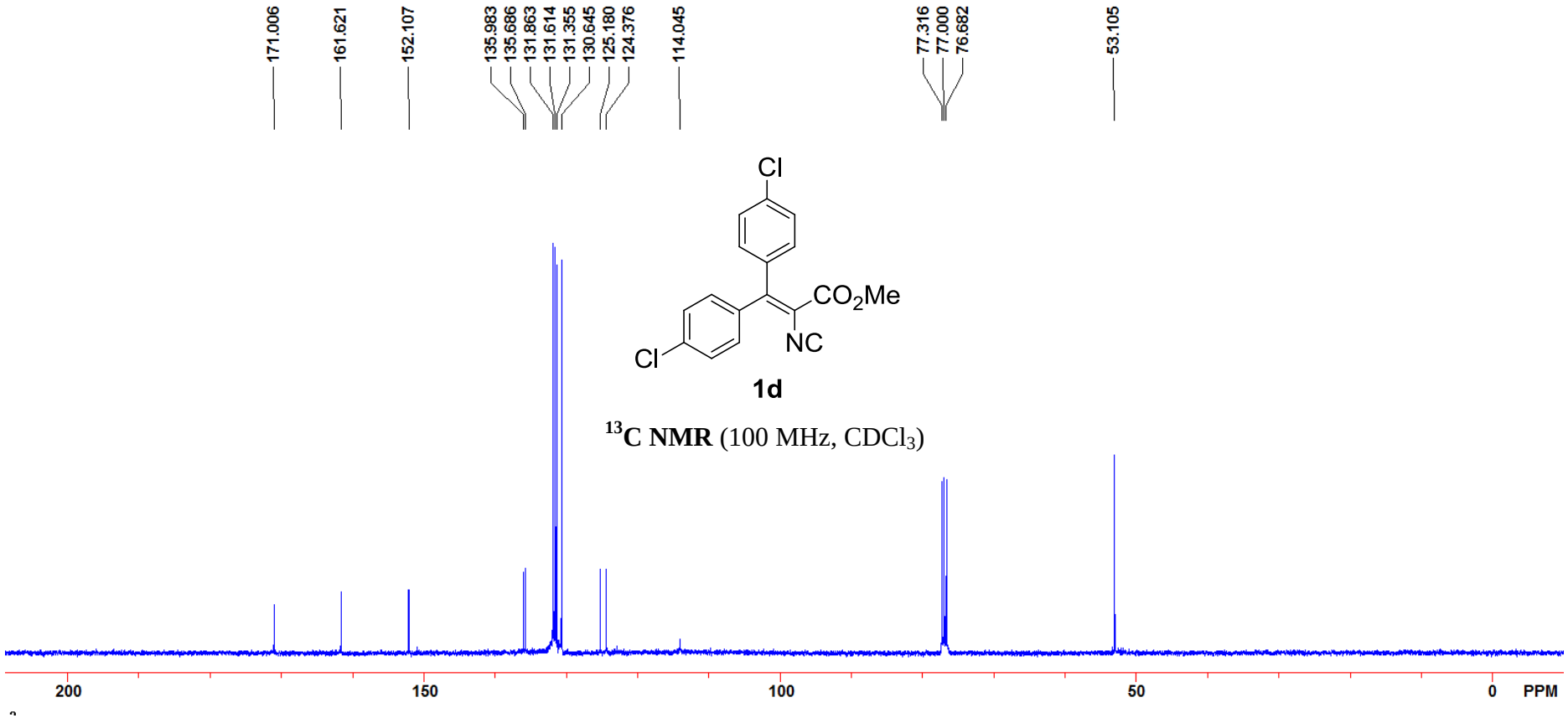
(3) Eisenberger, P.; Gischig, S.; Togni, A. *Chem.-Eur. J.* **2006**, *12*, 2579.

(4) Wang, X.; Ye, Y.; Zhang, S.; Feng, J.; Xu, Y.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2011**, *133*, 16410.

(5) Li, Y.; Studer, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 8221.

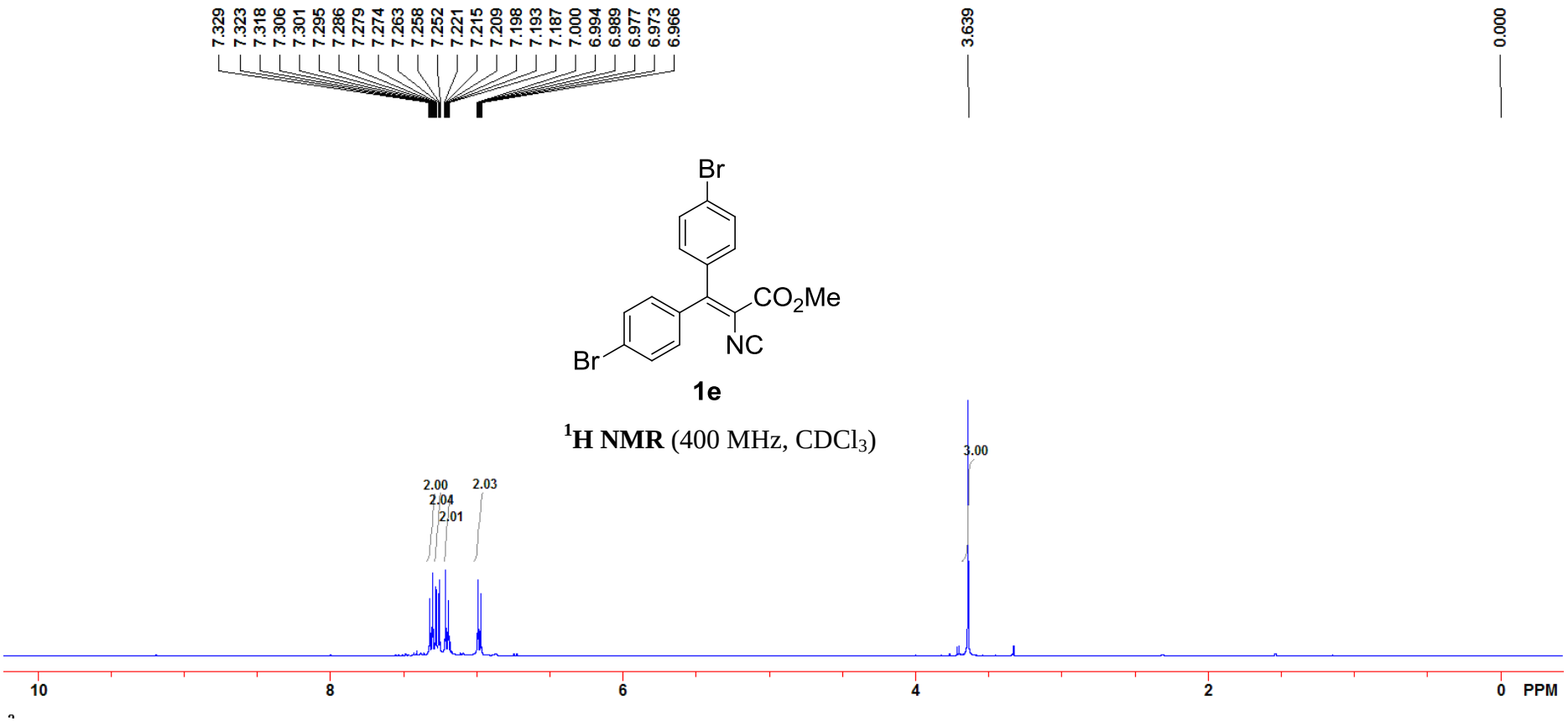
(6) Zhang, B.; Mück-Lichtenfeld, C.; Daniliuc, C. G.; Studer, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 10792.

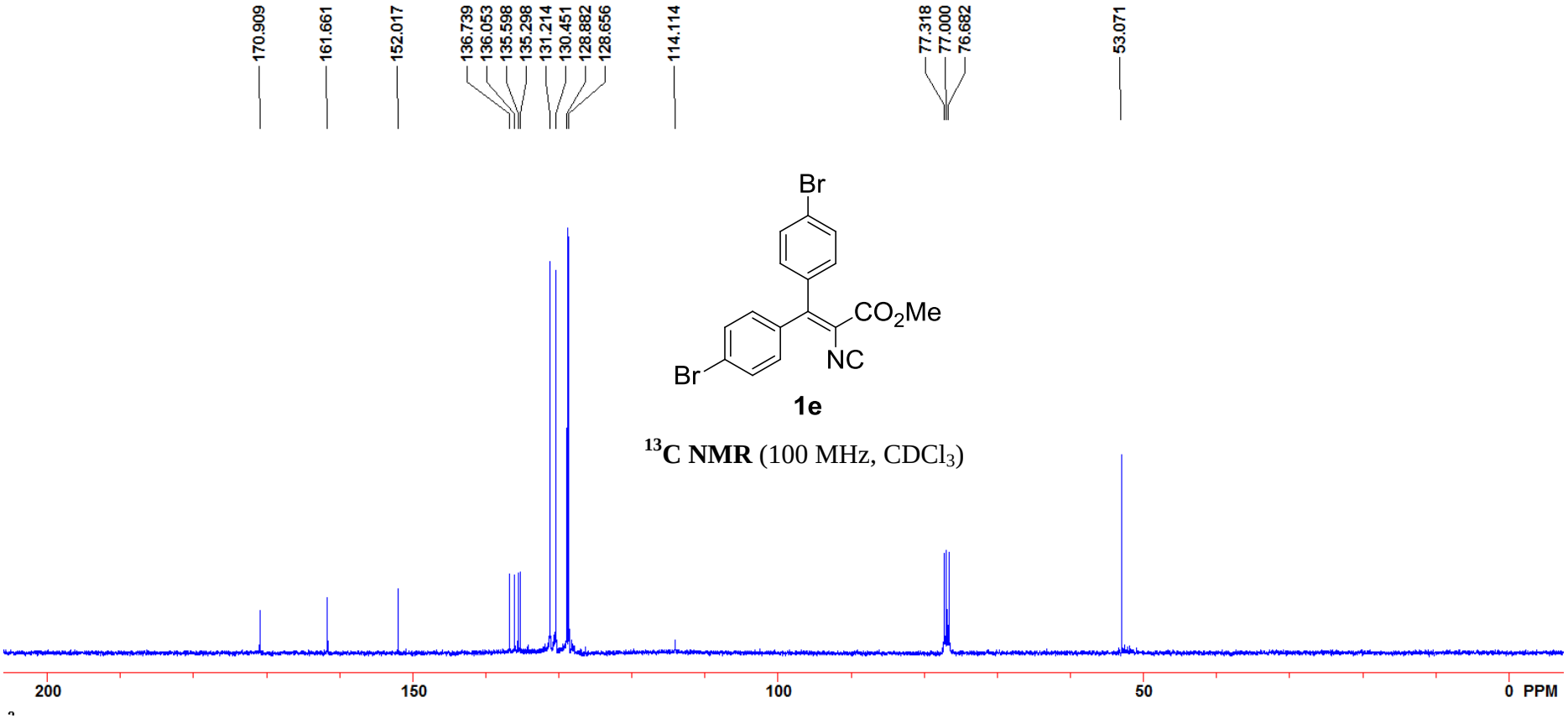

7.490
7.484
7.479
7.467
7.462
7.456
7.444
7.438
7.433
7.422
7.417
7.411
7.183
7.149
7.143
7.138
7.127
7.122
7.116
6.933
6.927
6.922
6.910
6.906
6.900
3.644
0.000
Cl
CO2Me
NC
Cl
1d
1H NMR (400 MHz, CDCl3)
3.00
2.02
2.02
2.03
2.00
10
8
6
4
2
0 PPM



1d

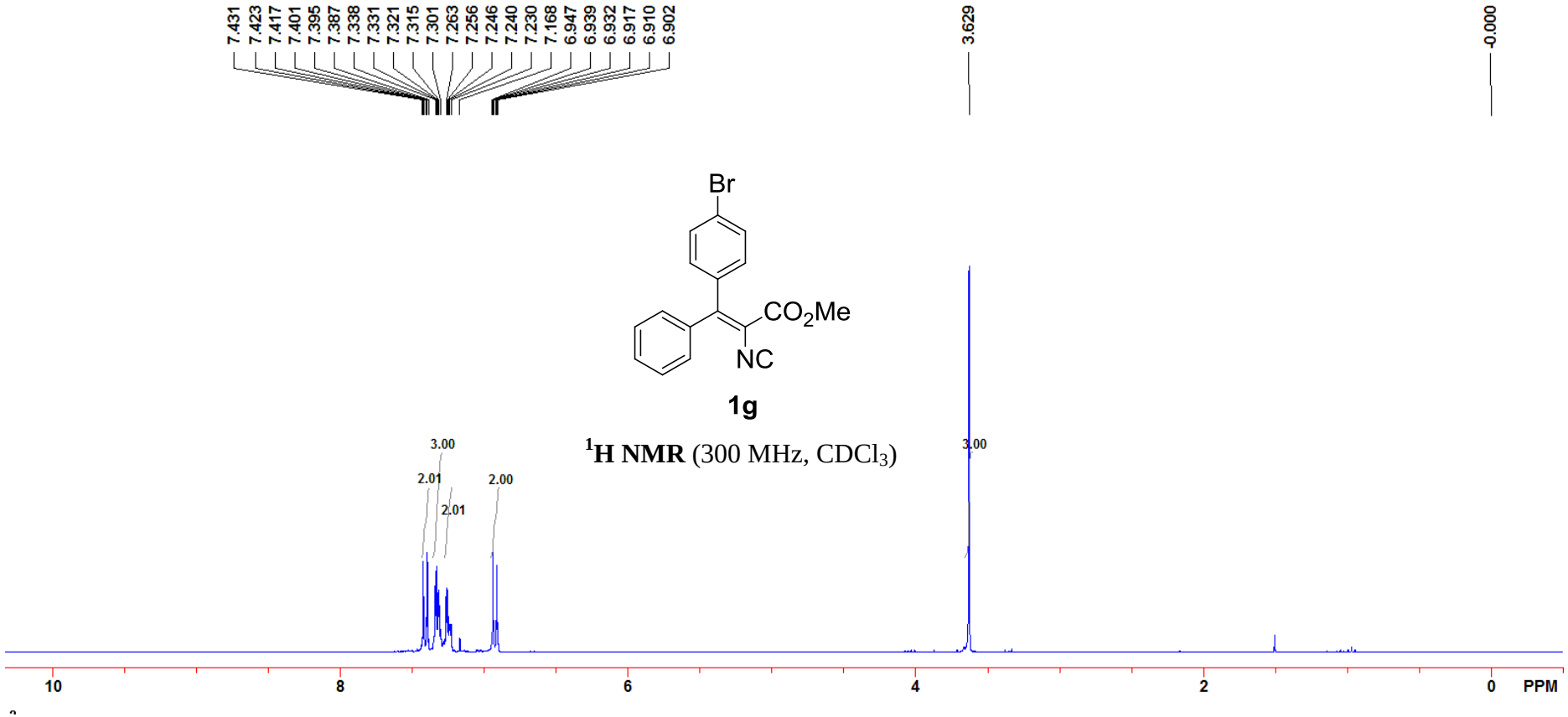
^{13}**C NMR** (100 MHz, $CDCl_3$)

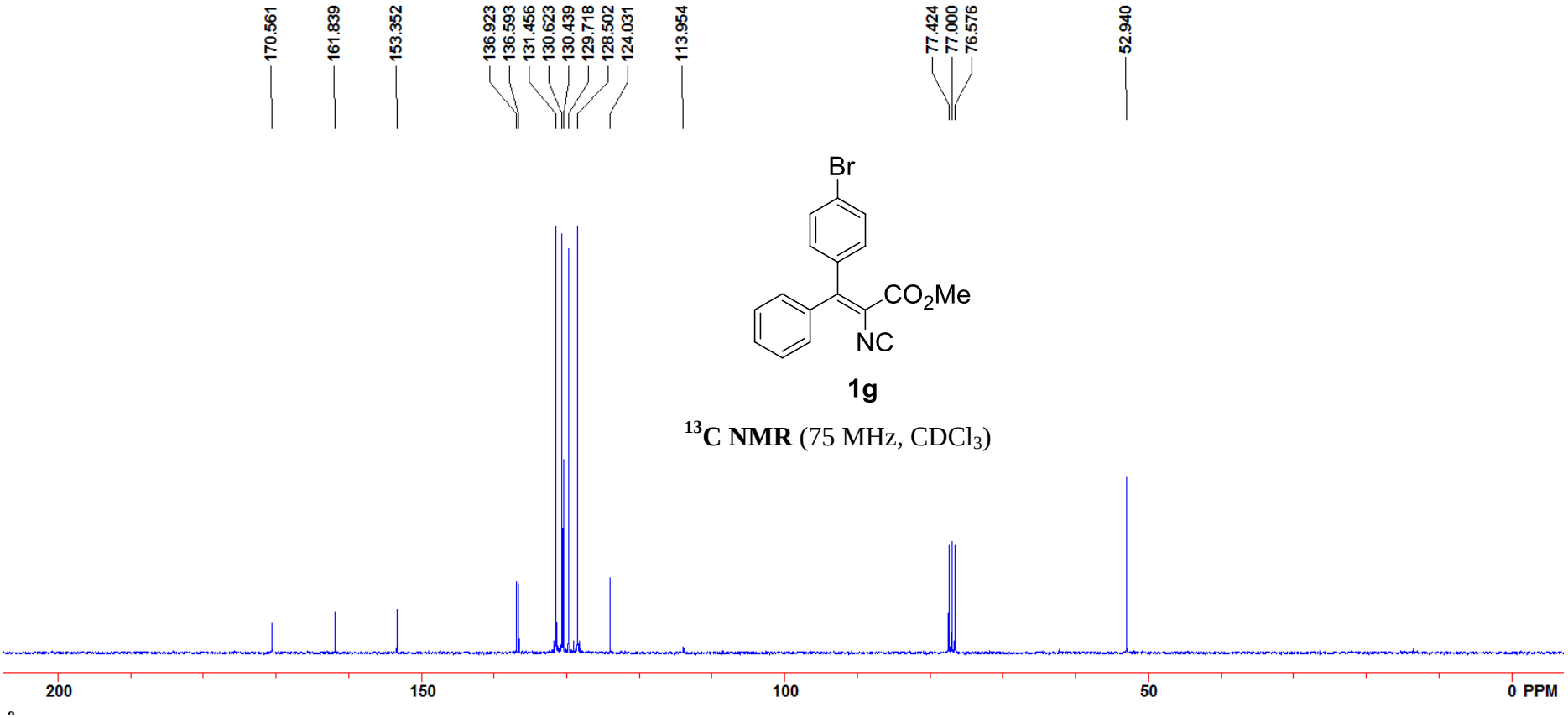

7.329
7.323
7.318
7.306
7.301
7.295
7.286
7.279
7.274
7.263
7.258
7.252
7.221
7.215
7.209
7.198
7.193
7.187
7.000
6.994
6.989
6.977
6.973
6.966
3.639
0.000
Br
CO2Me
NC
Br
1e
1H NMR (400 MHz, CDCl3)
2.00
2.04
2.01
2.03
3.00
10
8
6
4
2
0
PPM



1e

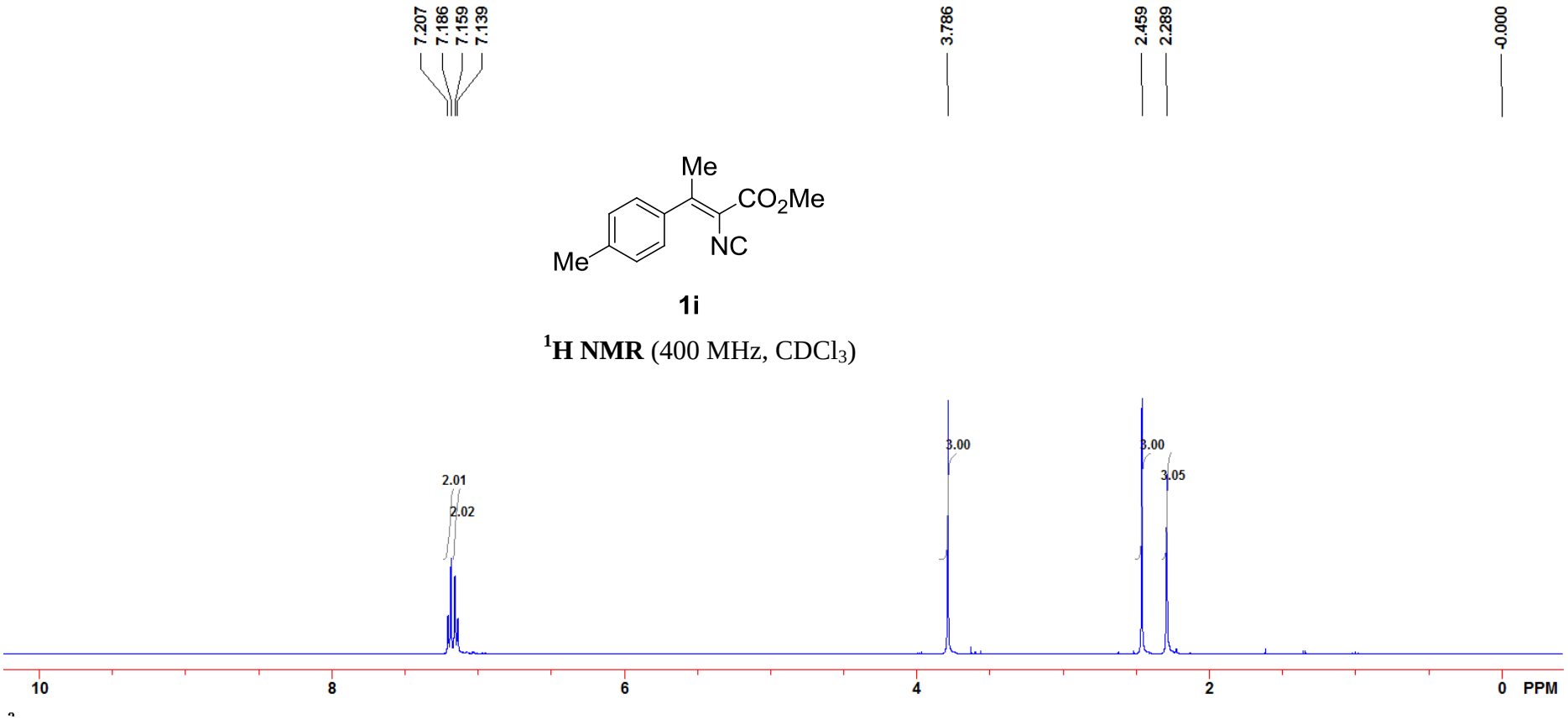
^{13}C NMR (100 MHz, $CDCl_3$)


7.431
7.423
7.417
7.401
7.395
7.387
7.338
7.331
7.321
7.315
7.301
7.263
7.256
7.246
7.240
7.230
7.168
6.947
6.939
6.932
6.917
6.910
6.902
3.629
-0.000
Br
CO2Me
NC
1g
1H NMR (300 MHz, CDCl3)
3.00
2.01
2.01
2.00
3.00
10
8
6
4
2
0
PPM



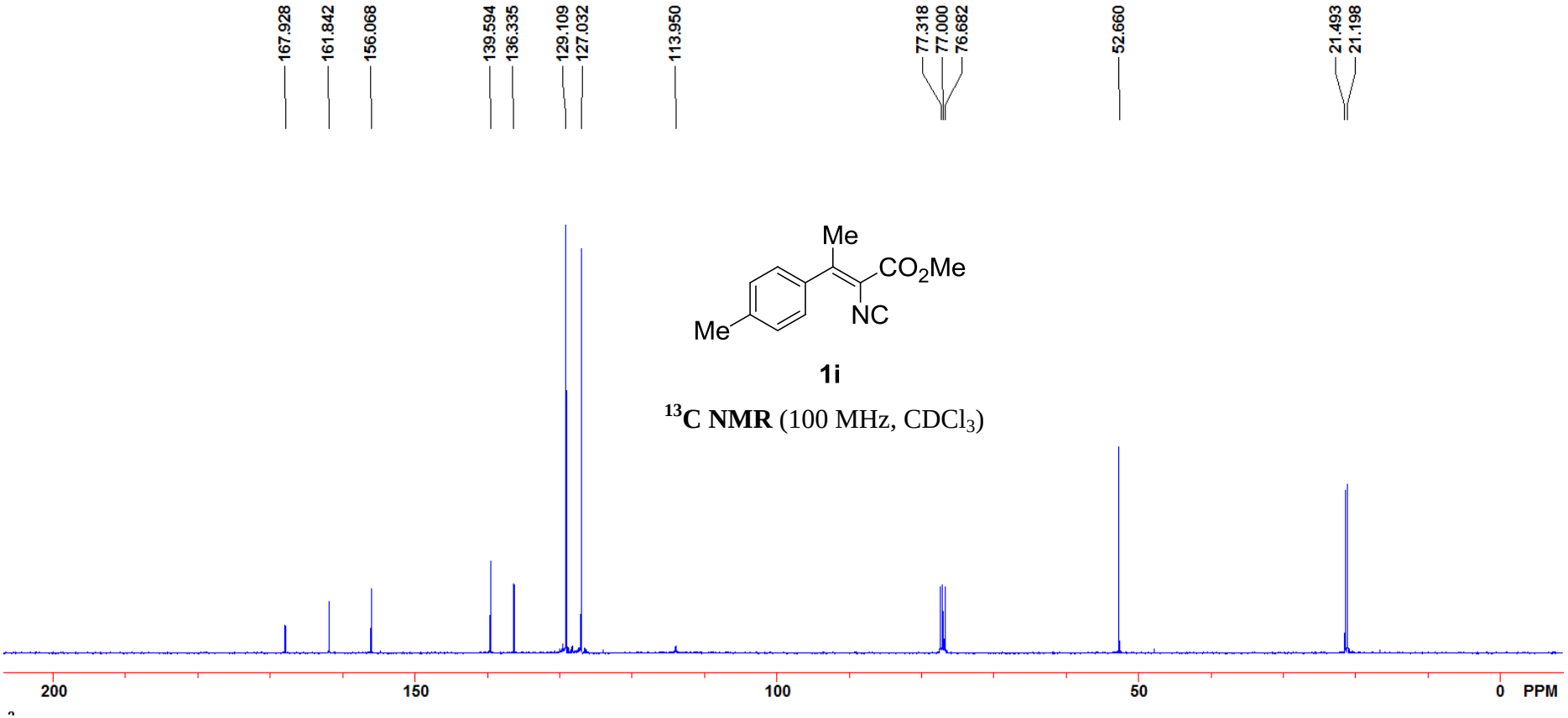
1g

^{13}C NMR (75 MHz, $CDCl_3$)



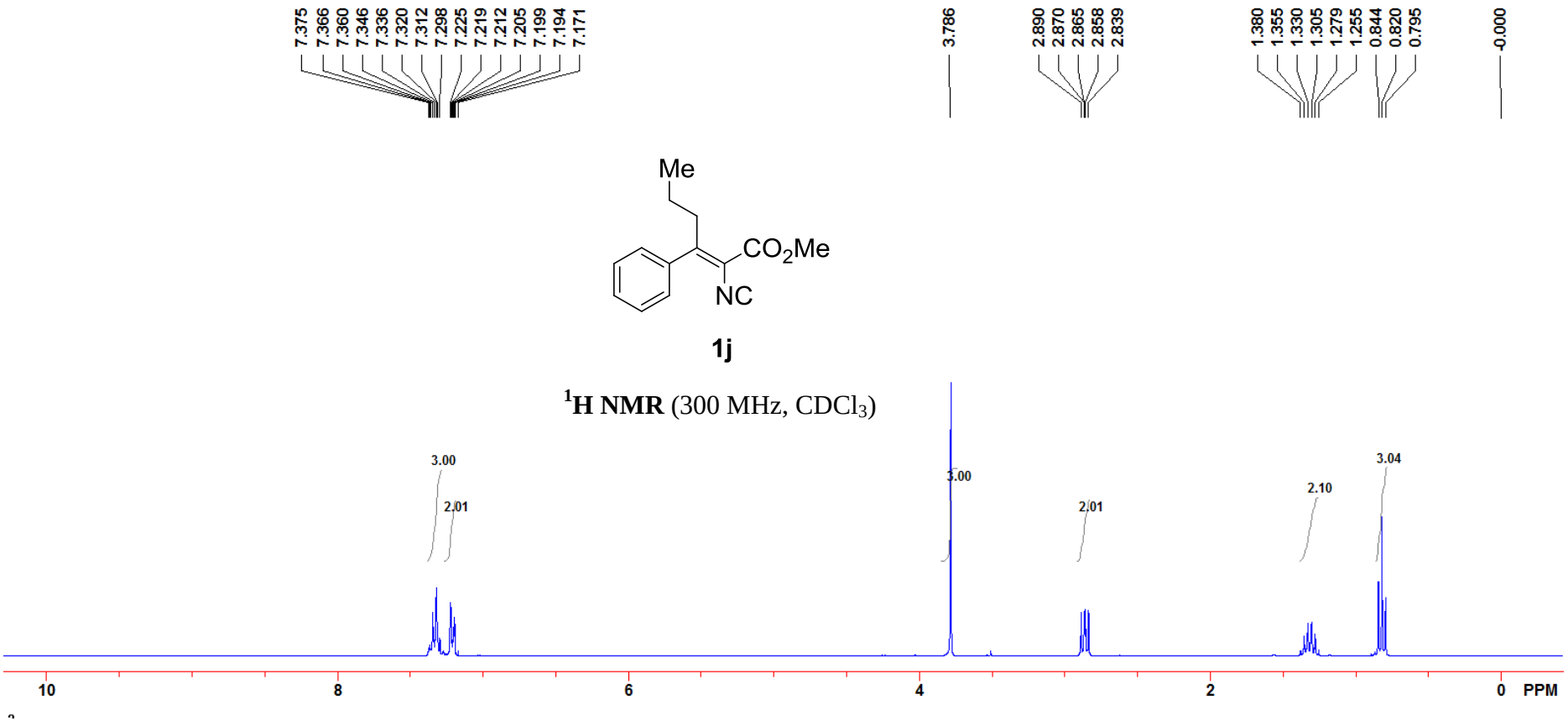
1i

^{1}H NMR (400 MHz, $CDCl_3$)



1i

^{13}C NMR (100 MHz, $CDCl_3$)


7.375
7.366
7.360
7.346
7.336
7.320
7.312
7.298
7.225
7.219
7.212
7.205
7.199
7.194
7.171
3.786
2.890
2.870
2.865
2.858
2.839
1.380
1.355
1.330
1.305
1.279
1.255
0.844
0.820
0.795
-0.000
Me
CO2Me
NC
1j
1H NMR (300 MHz, CDCl3)
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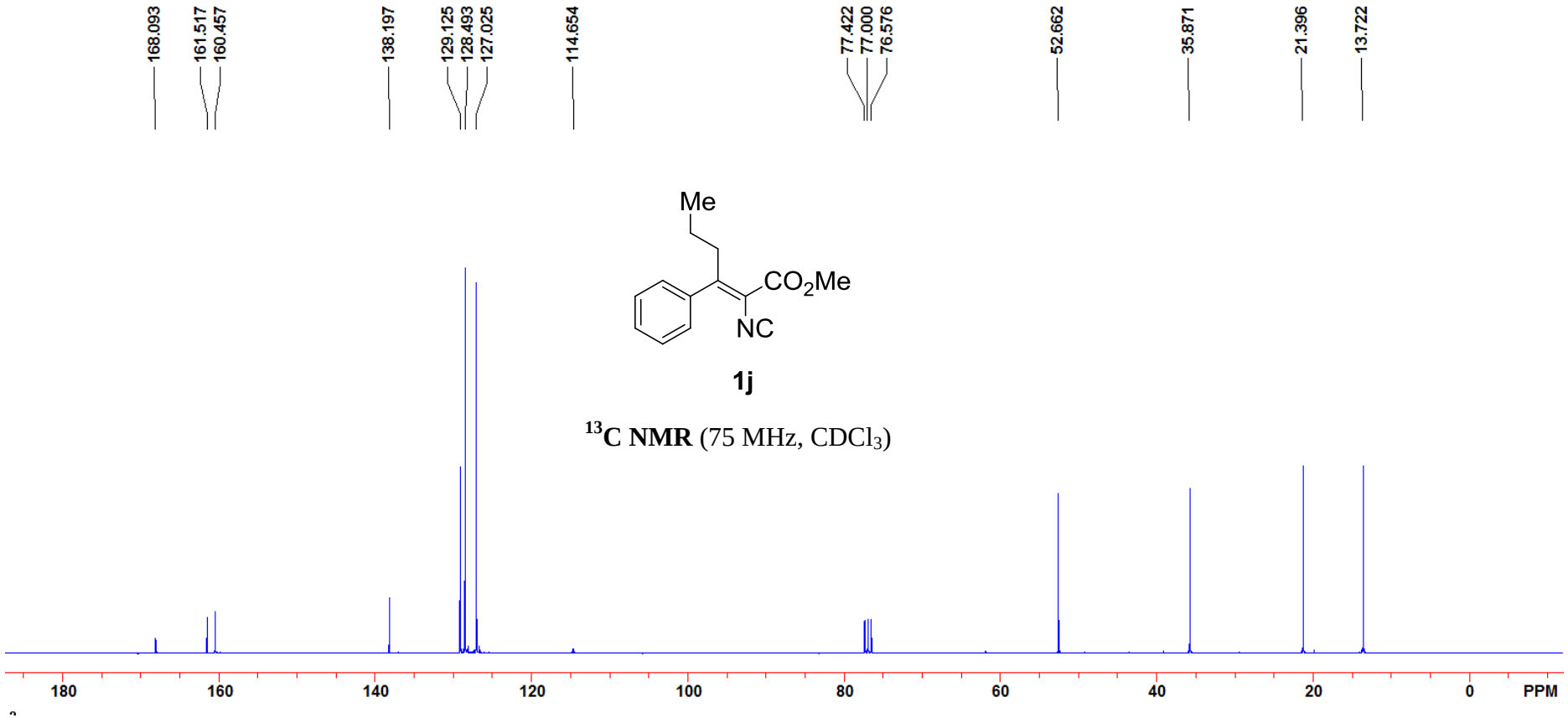
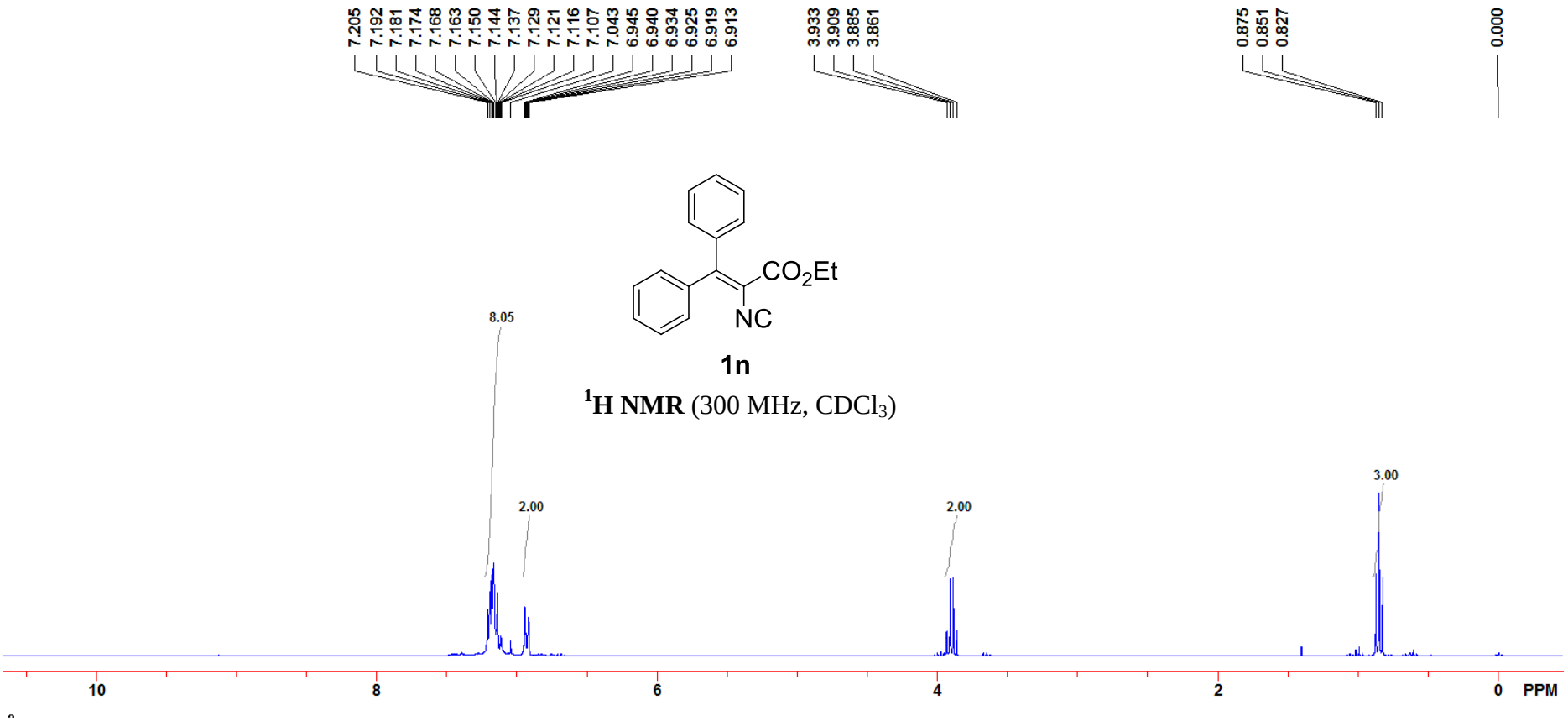
2.01
3.00
2.01
2.10
3.04
10
8
6
4
2
0
PPM



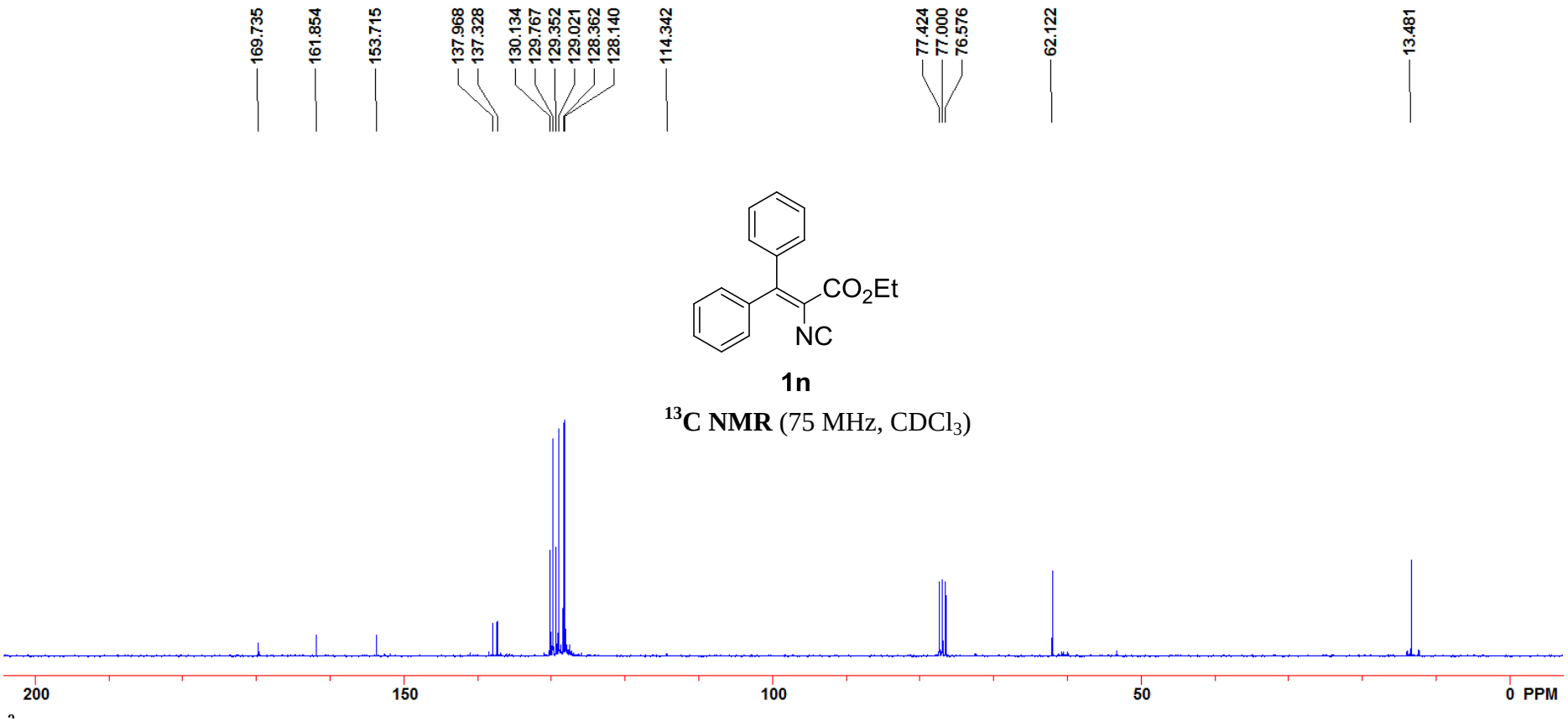
1j

^{13}C NMR (75 MHz, $CDCl_3$)



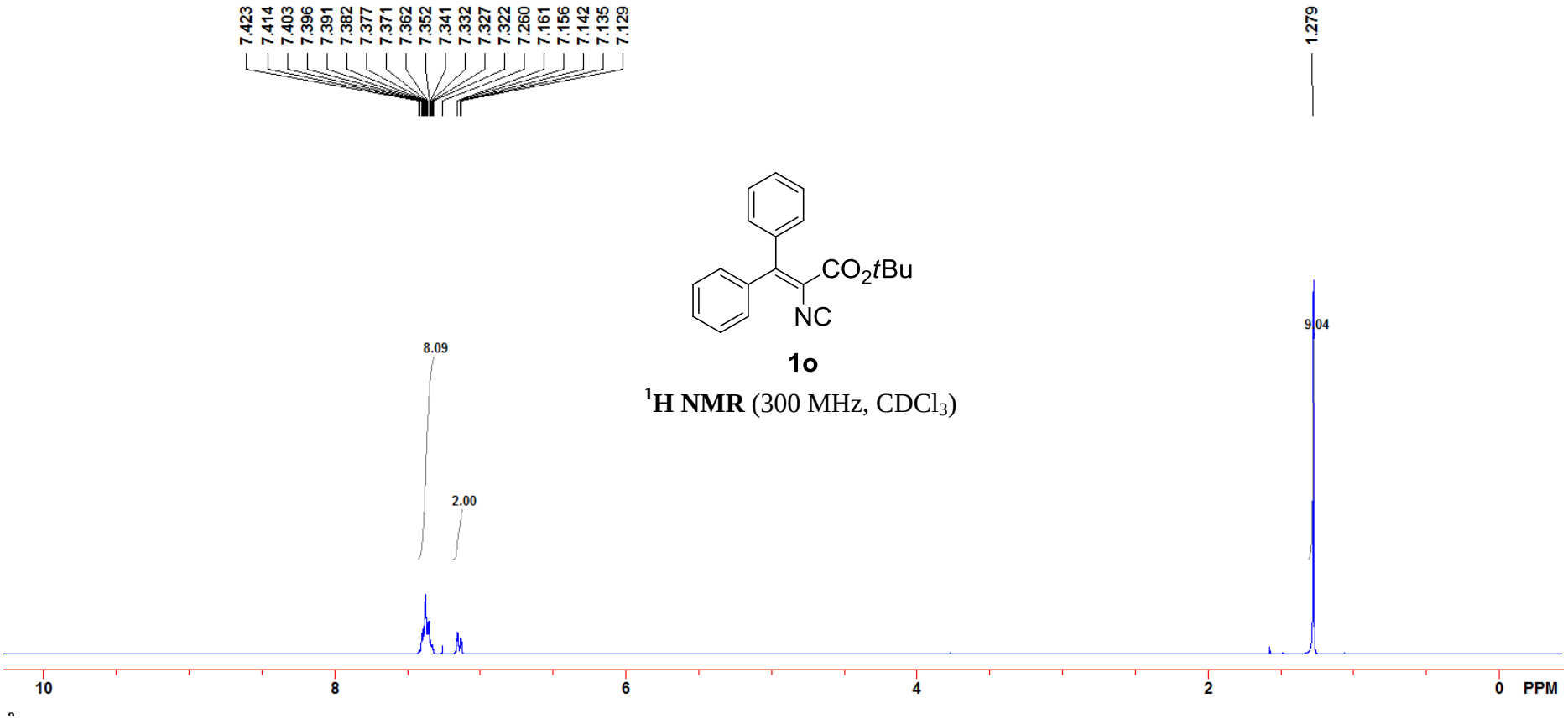
1n

^{1}H NMR (300 MHz, $CDCl_3$)



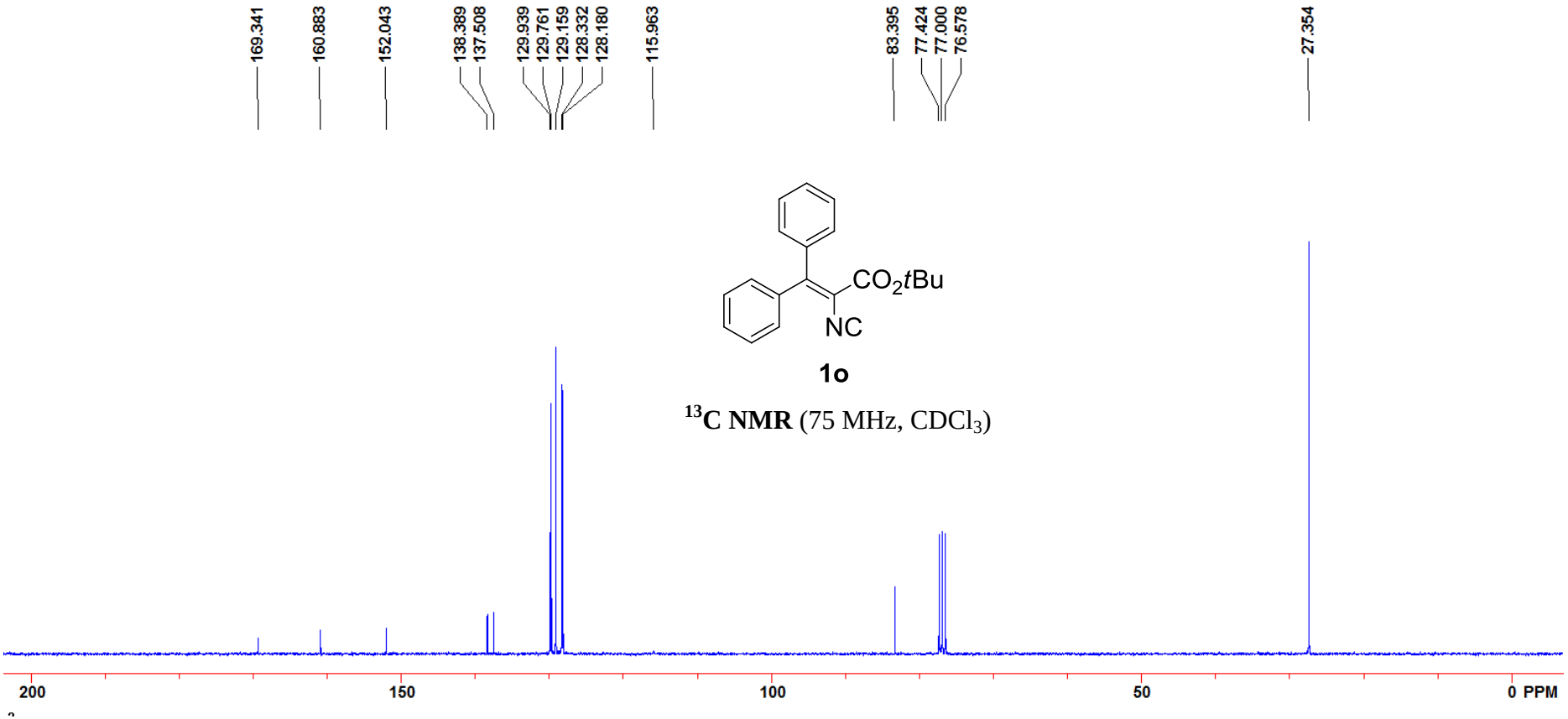
1n

^{13}C NMR (75 MHz, $CDCl_3$)



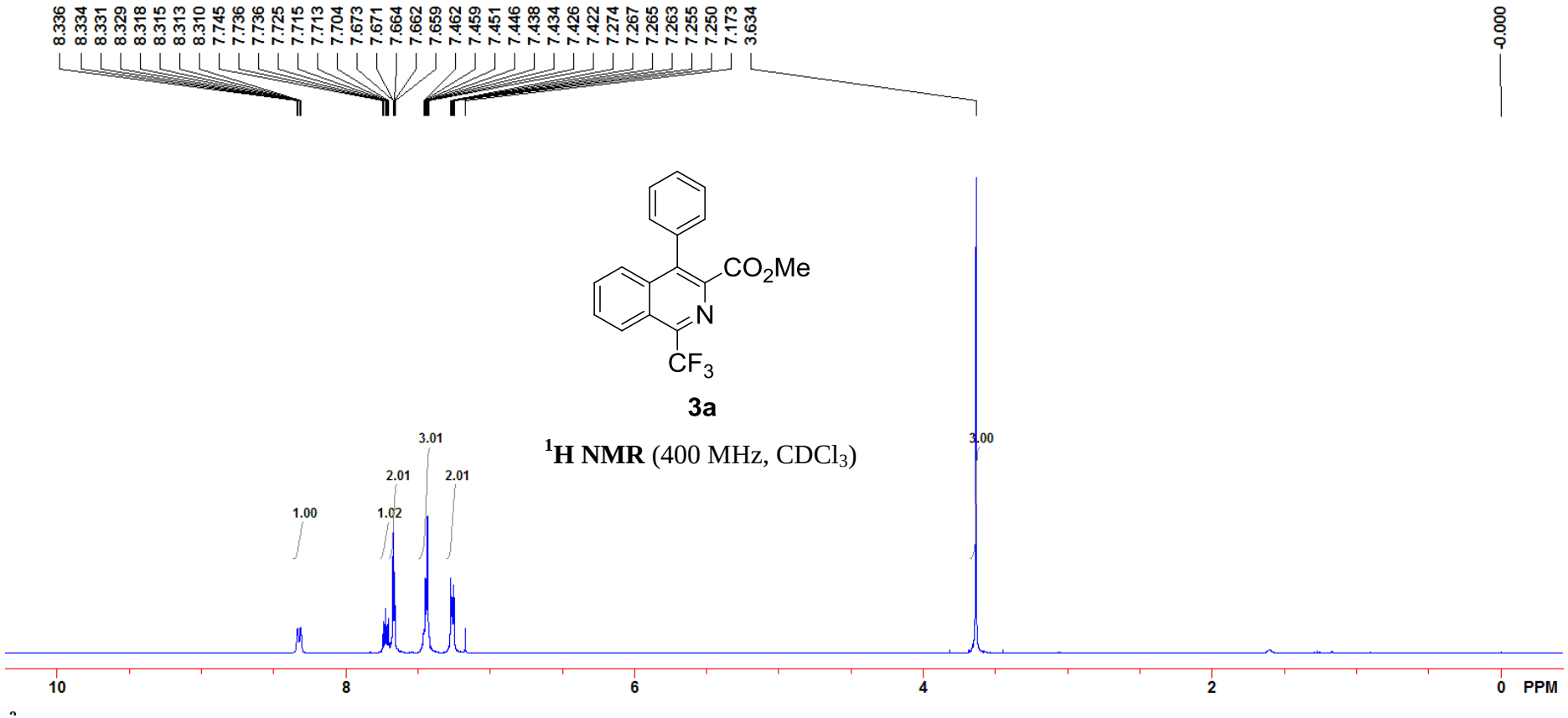
1o

^{1}H NMR (300 MHz, $CDCl_3$)



1o

^{13}C NMR (75 MHz, $CDCl_3$)


8.336
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8.315
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8.310
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7.713
7.704
7.673
7.671
7.664
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7.659
7.462
7.459
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7.446
7.438
7.434
7.426
7.422
7.274
7.267
7.265
7.263
7.255
7.250
7.173
3.634
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CO2Me
N
CF3
3a
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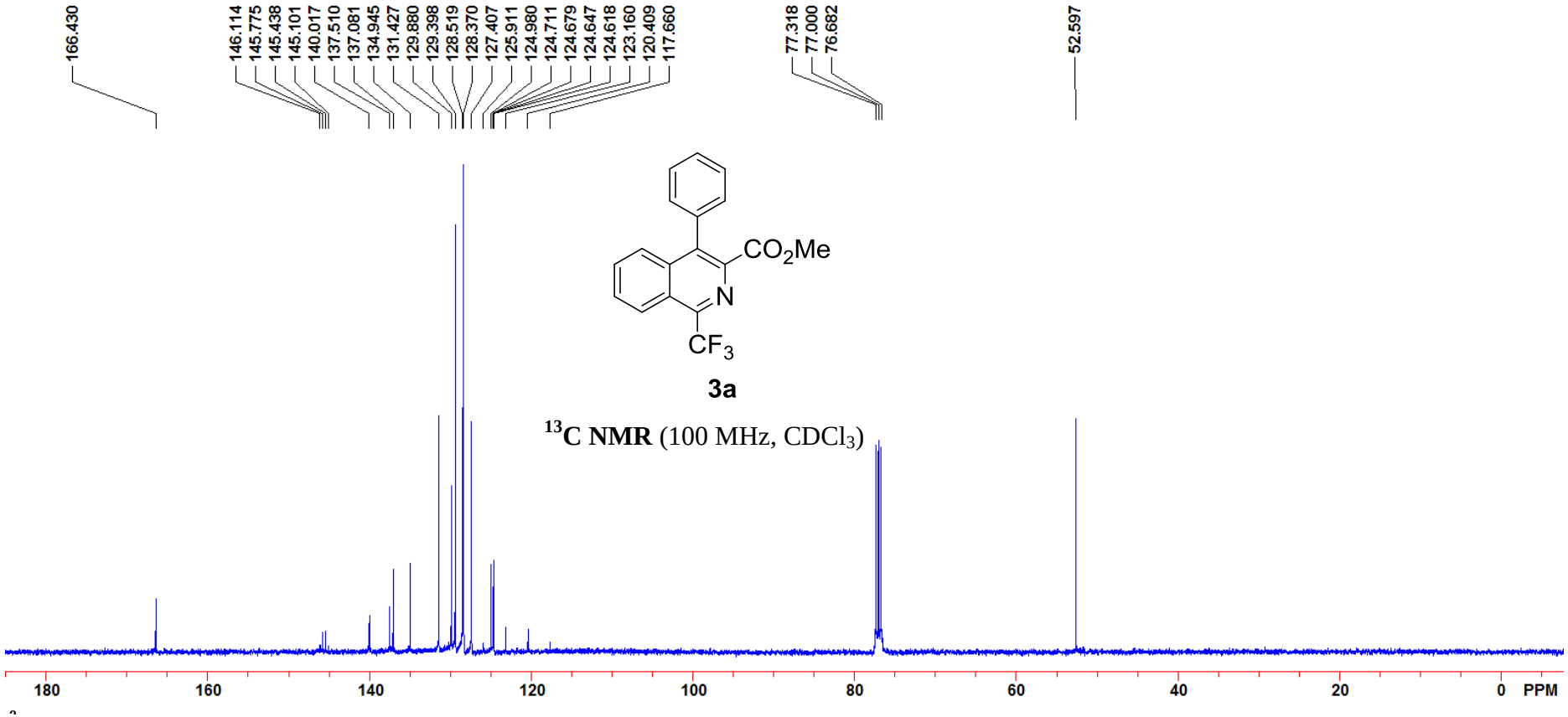
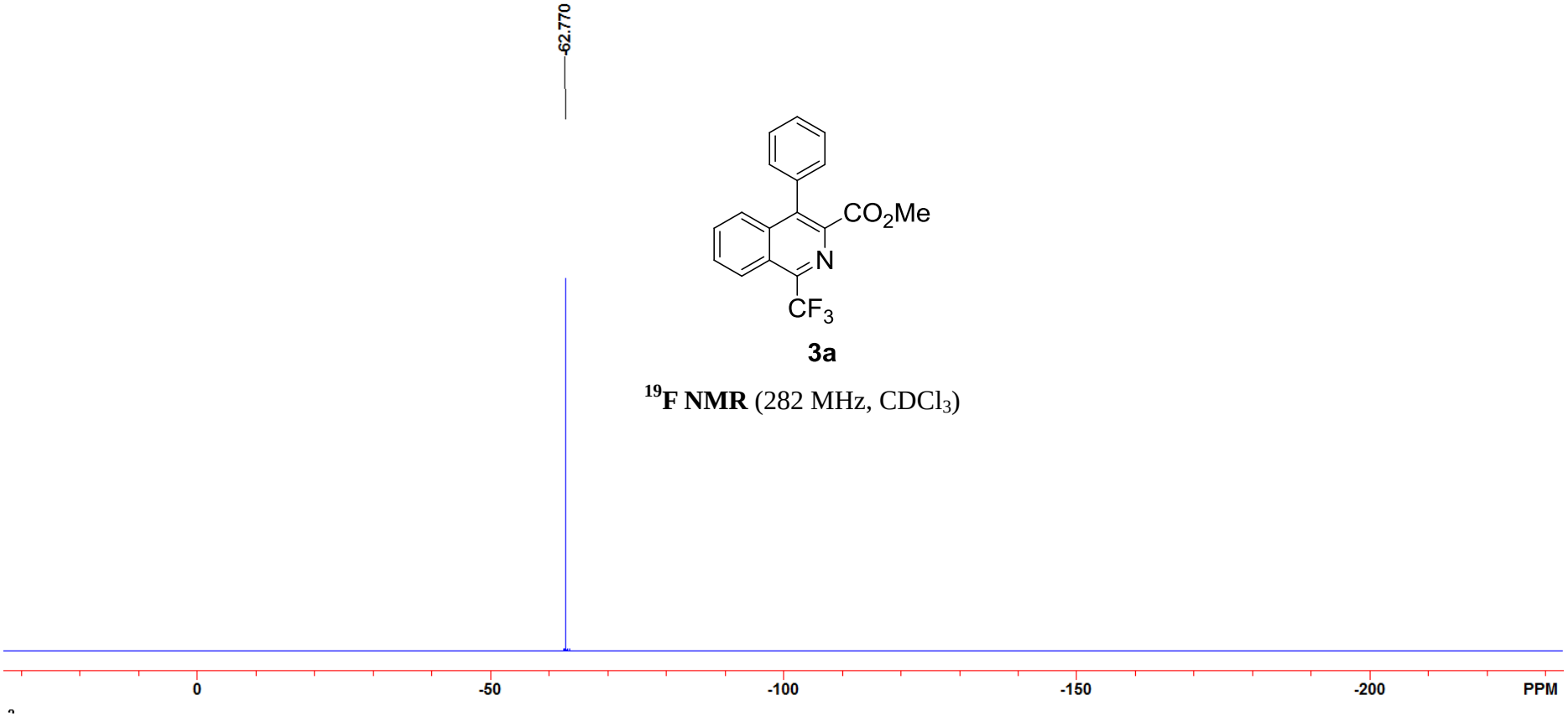
2.01
3.01
2.01
3.00
10
8
6
4
2
0
PPM



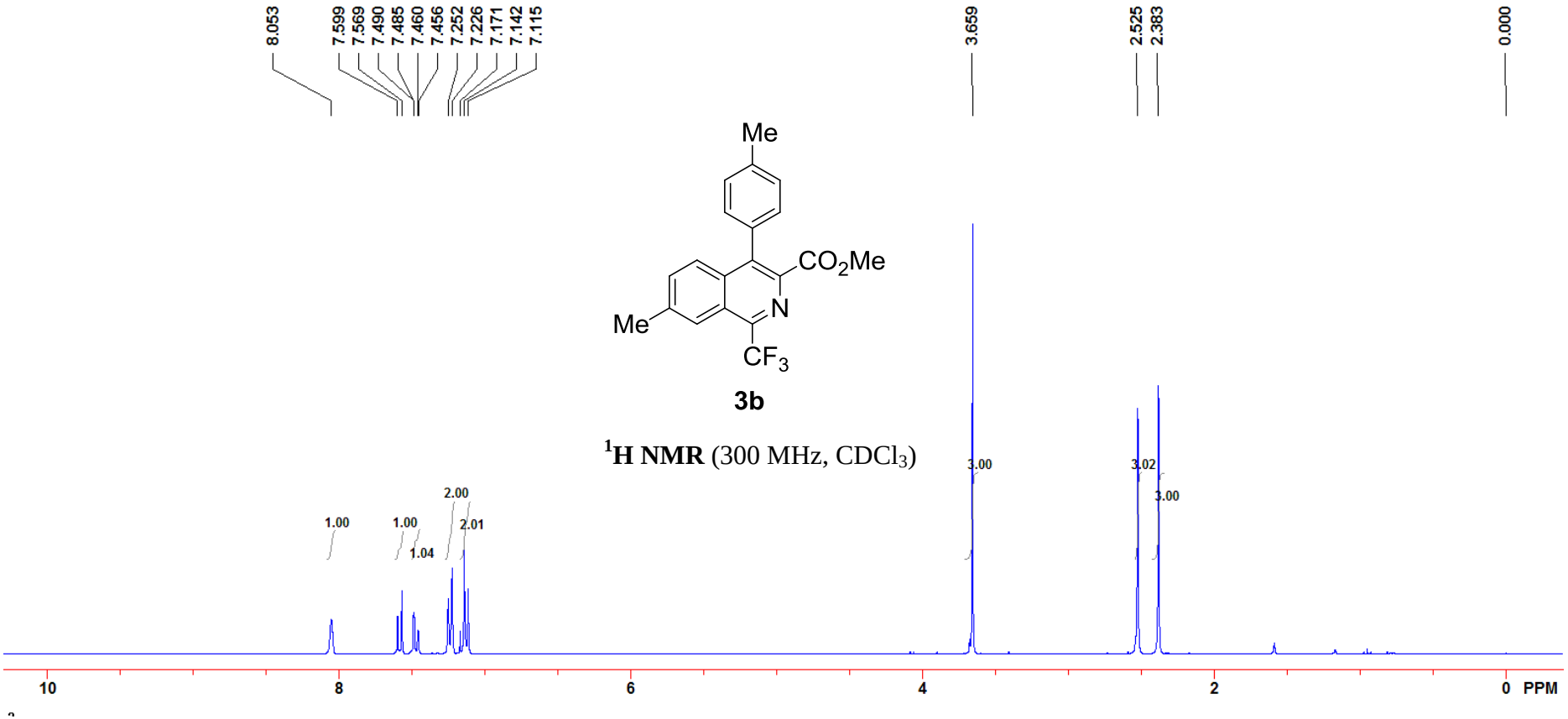
3a

^{13}C NMR (100 MHz, $CDCl_3$)



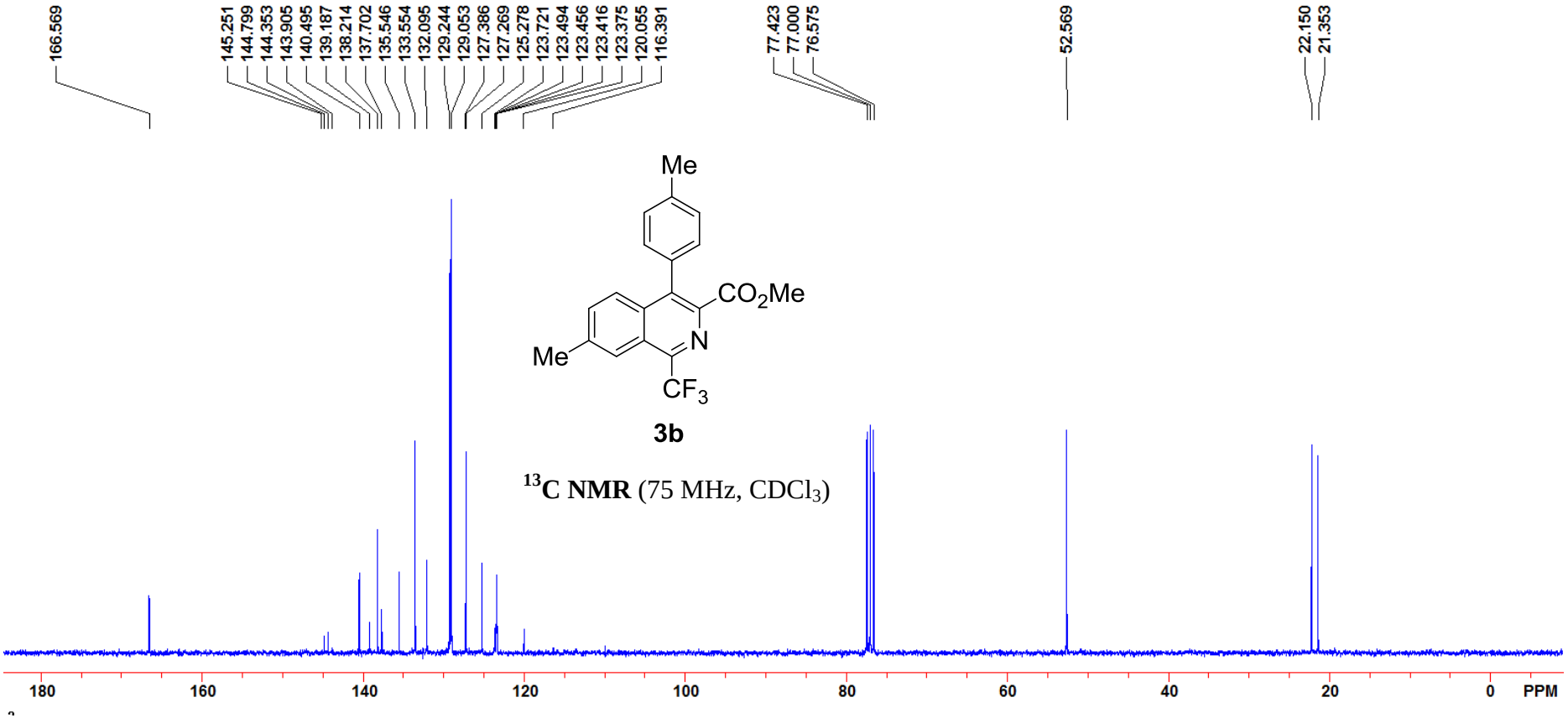
3a

^{19}F NMR (282 MHz, $CDCl_3$)



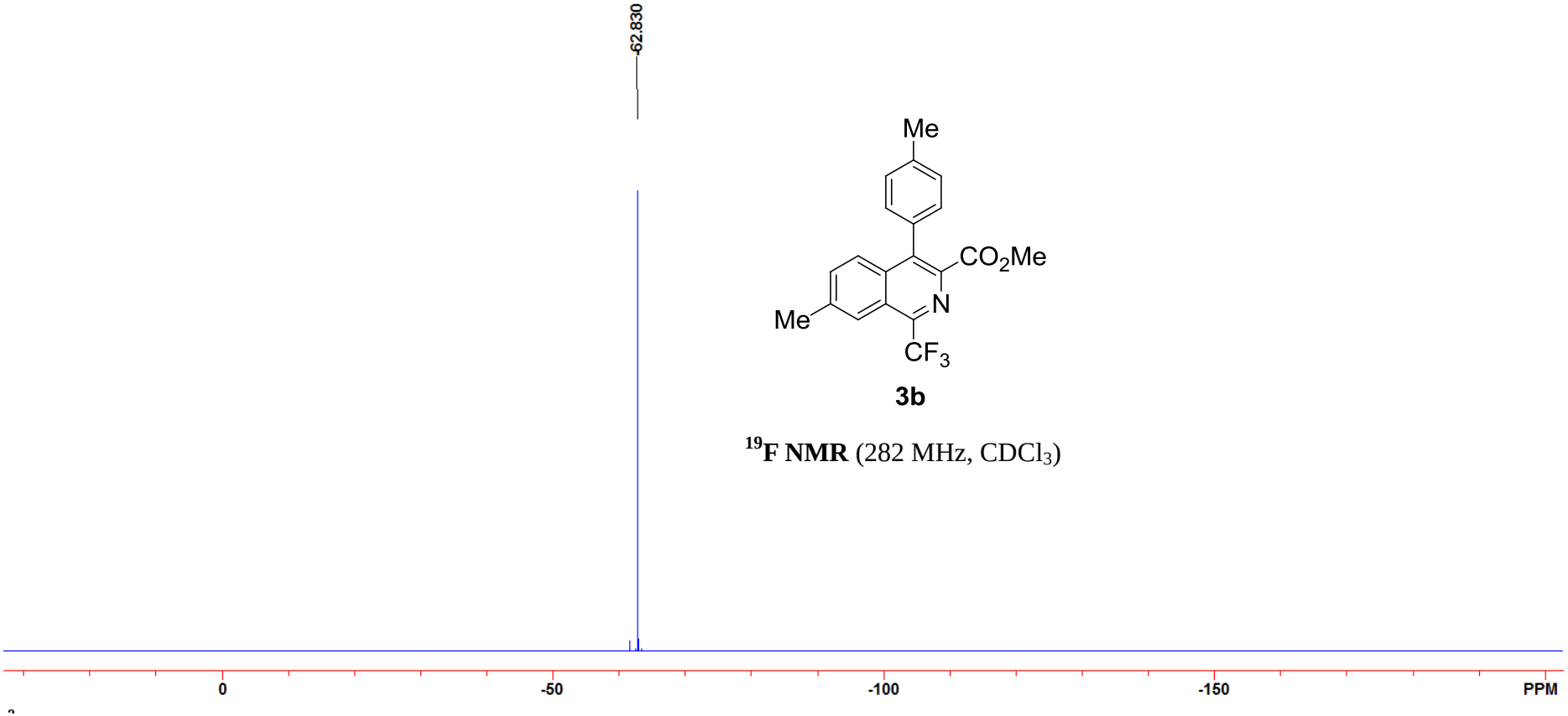
3b

^{1}H NMR (300 MHz, $CDCl_3$)



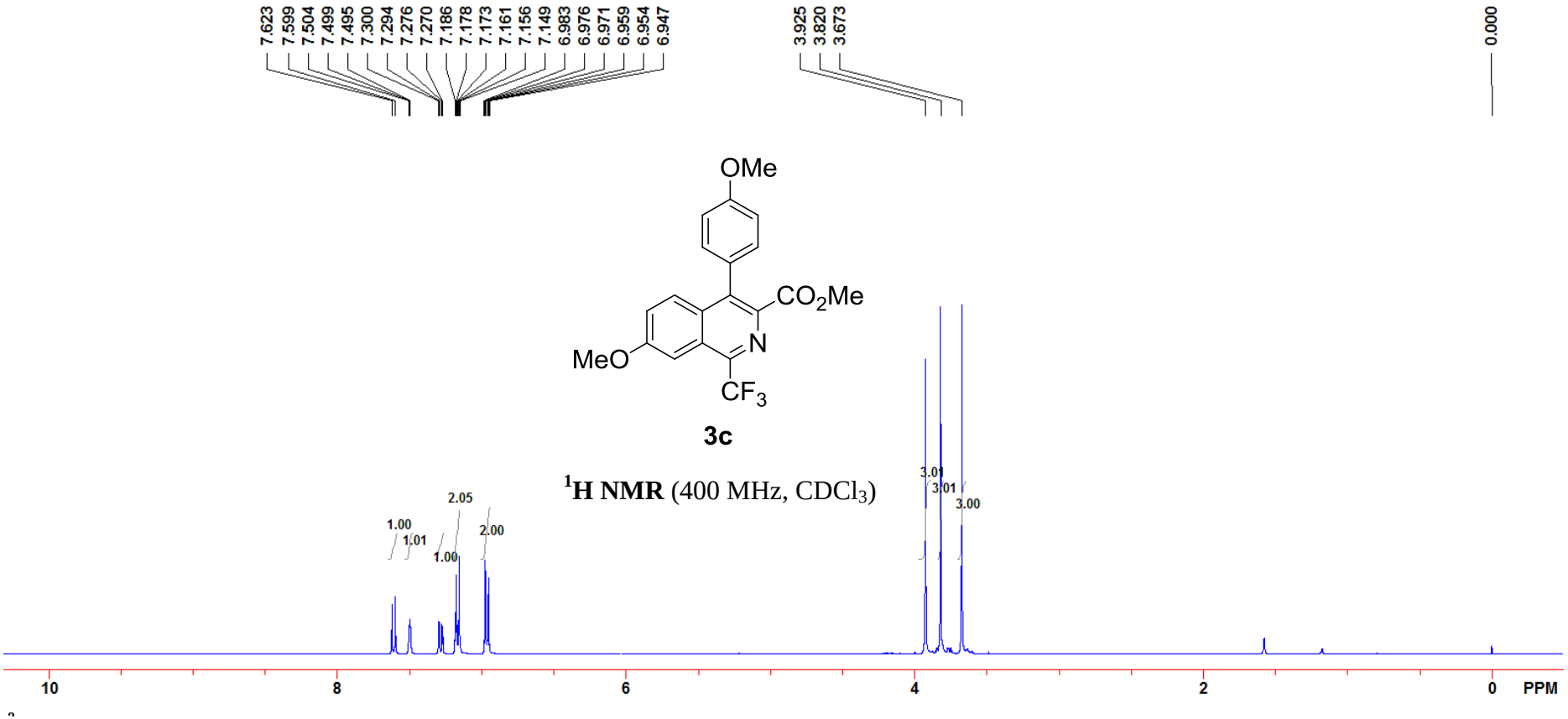
3b

^{13}C NMR (75 MHz, $CDCl_3$)



3b

^{19}F NMR (282 MHz, $CDCl_3$)


7.623
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7.276
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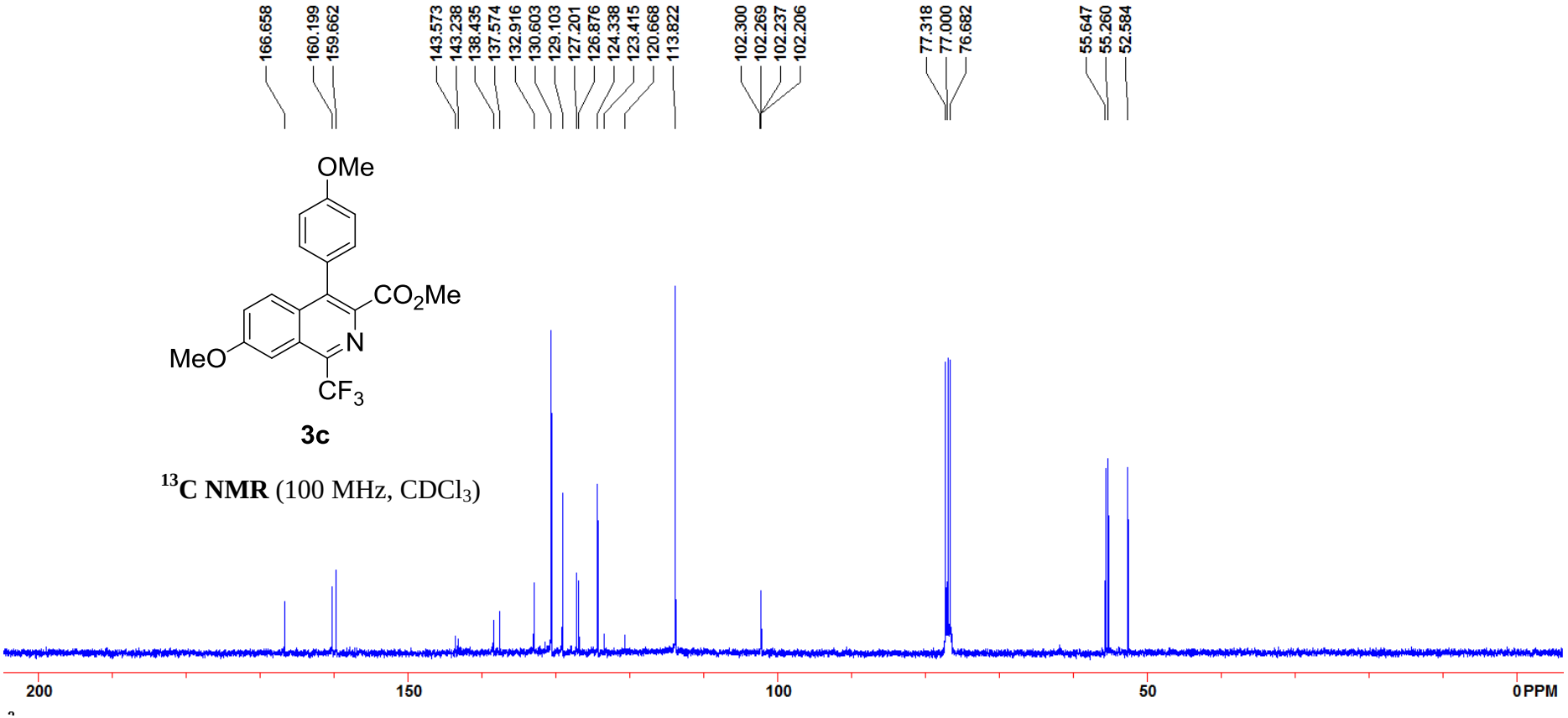
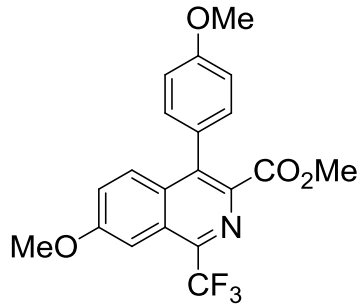
7.178
7.173
7.161
7.156
7.149
6.983
6.976
6.971
6.959
6.954
6.947
3.925
3.820
3.673
0.000
OMe
CO2Me
N
MeO
CF3
3c
1H NMR (400 MHz, CDCl3)
1.00
1.01
1.00
2.05
2.00
3.01
3.01
3.00
10
8
6
4
2
0
PPM



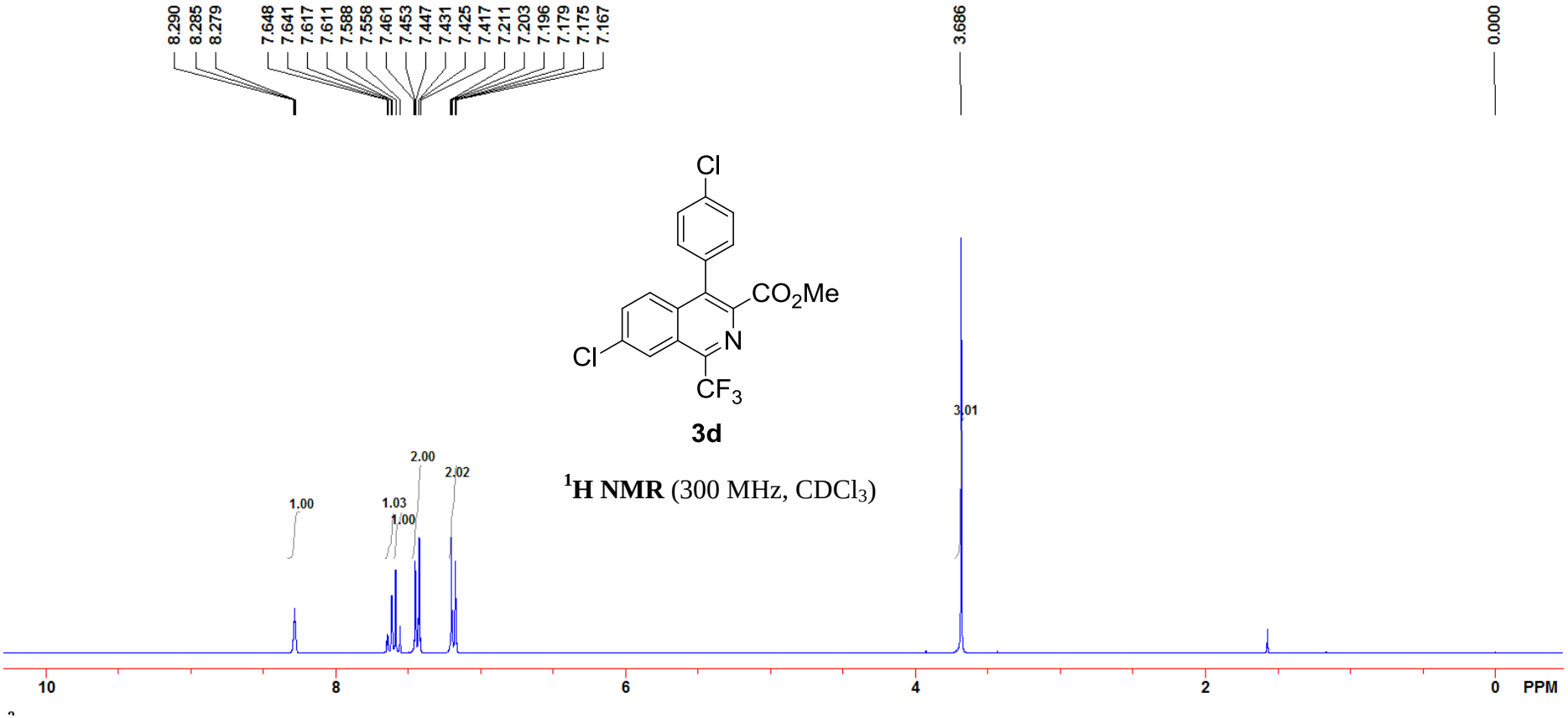
3c

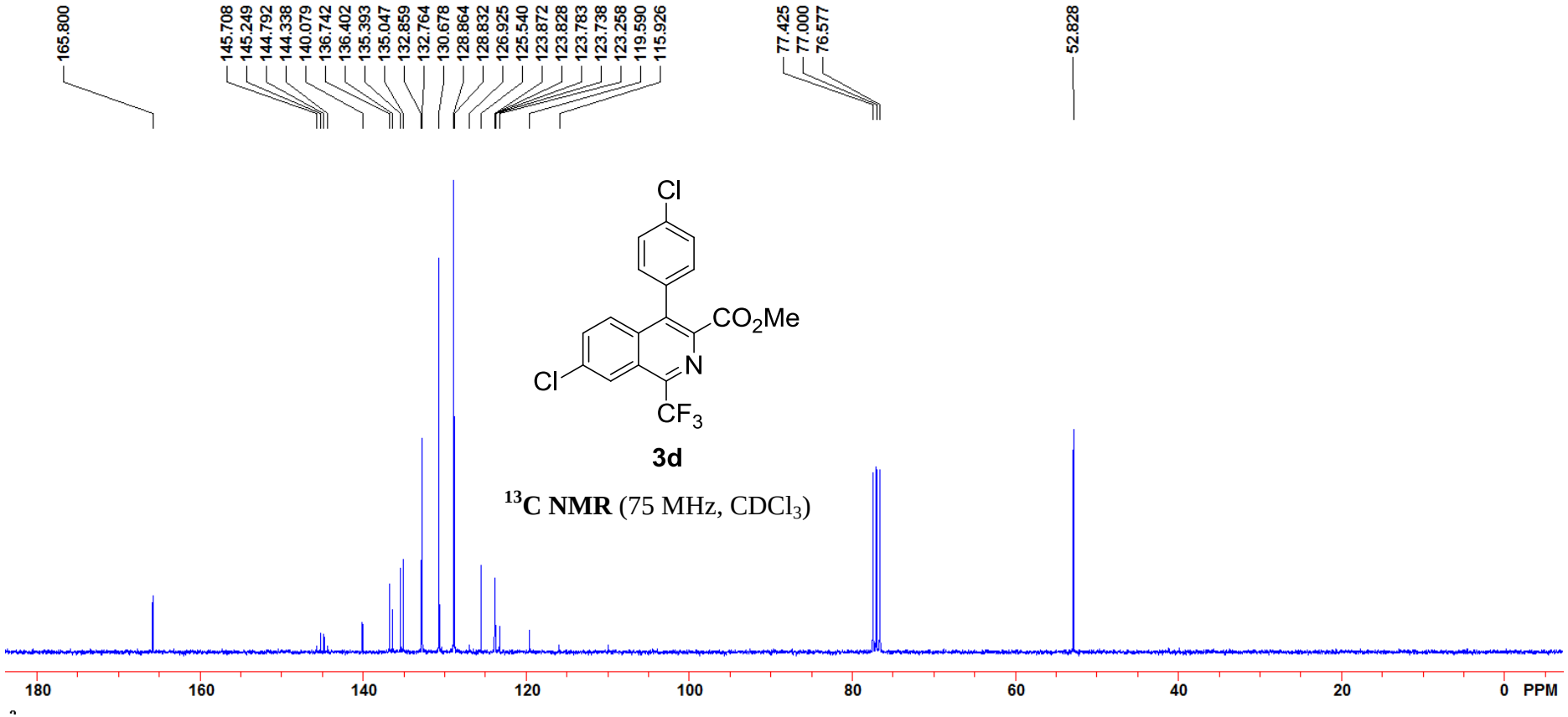
^{13}C NMR (100 MHz, $CDCl_3$)



3c

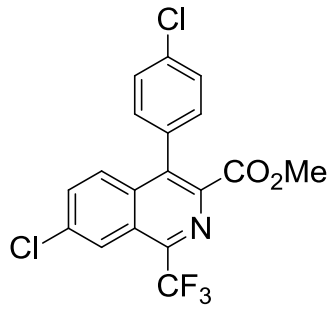
^{19}F NMR (282 MHz, $CDCl_3$)


8.290
8.285
8.279
7.648
7.641
7.617
7.611
7.588
7.558
7.461
7.453
7.447
7.431
7.425
7.417
7.211
7.203
7.196
7.179
7.175
7.167
3.686
0.000
Cl
CO2Me
N
Cl
CF3
3d
1H NMR (300 MHz, CDCl3)
1.00
1.03
1.00
2.00
2.02
3.01
10
8
6
4
2
0
PPM



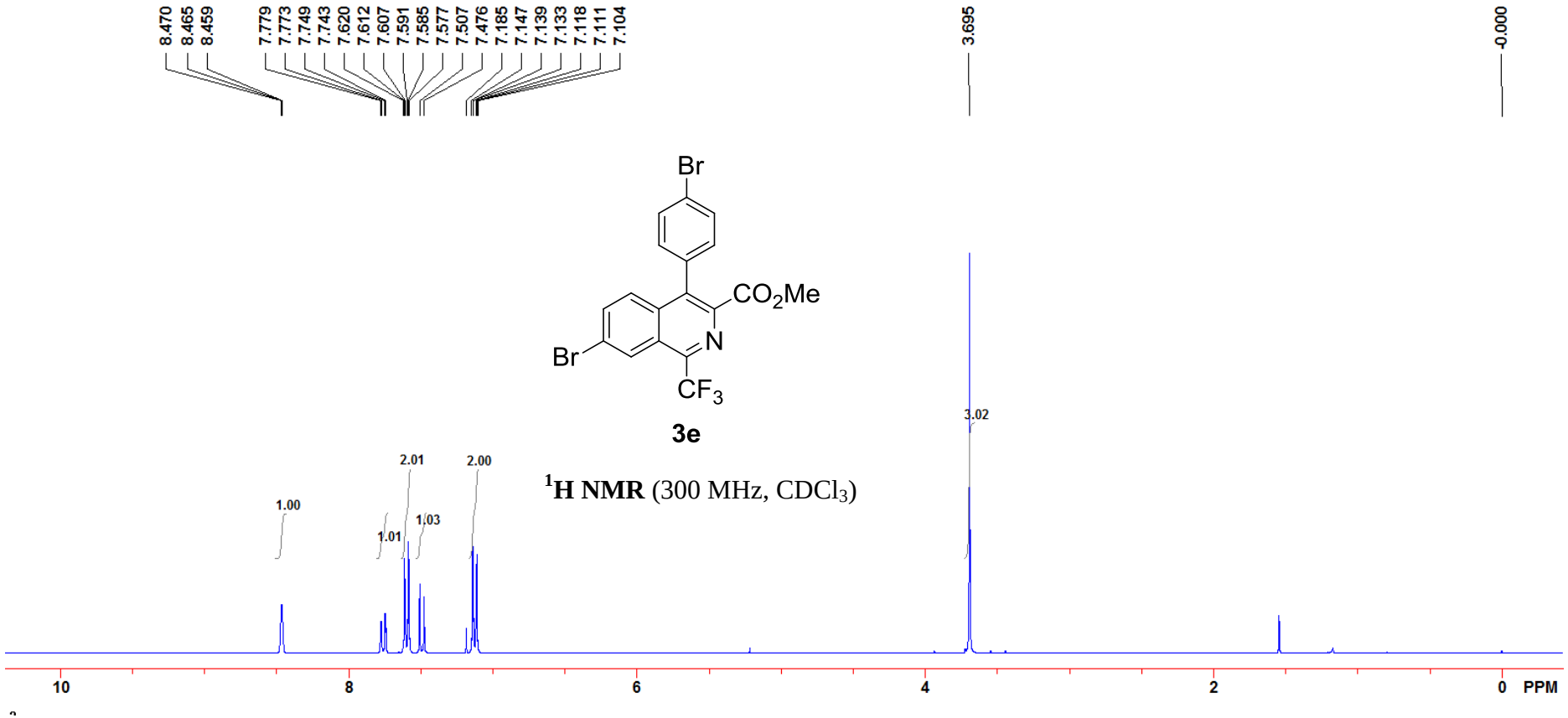
3d

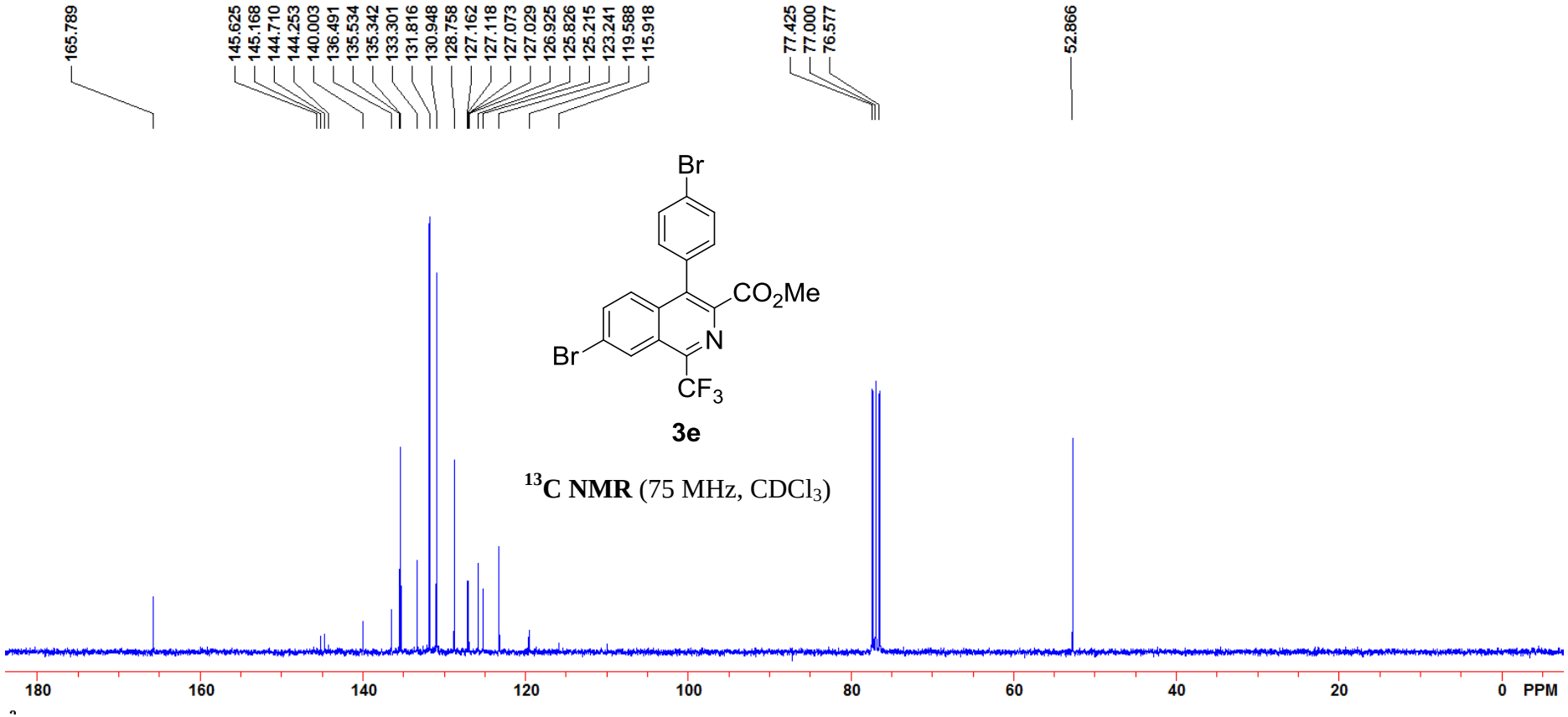
^{13}C NMR (75 MHz, $CDCl_3$)



3d

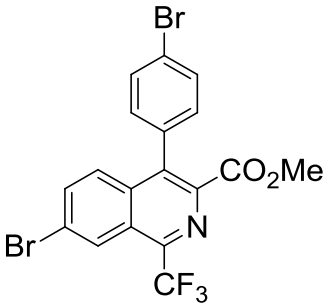
^{19}F NMR (282 MHz, $CDCl_3$)


8.470
8.465
8.459
7.779
7.773
7.749
7.743
7.620
7.612
7.607
7.591
7.585
7.577
7.507
7.476
7.185
7.147
7.139
7.133
7.118
7.111
7.104
3.695
-0.000
Br
CO2Me
N
Br
CF3
3e
1H NMR (300 MHz, CDCl3)
1.00
1.01
2.01
1.03
2.00
3.02
10
8
6
4
2
0
PPM



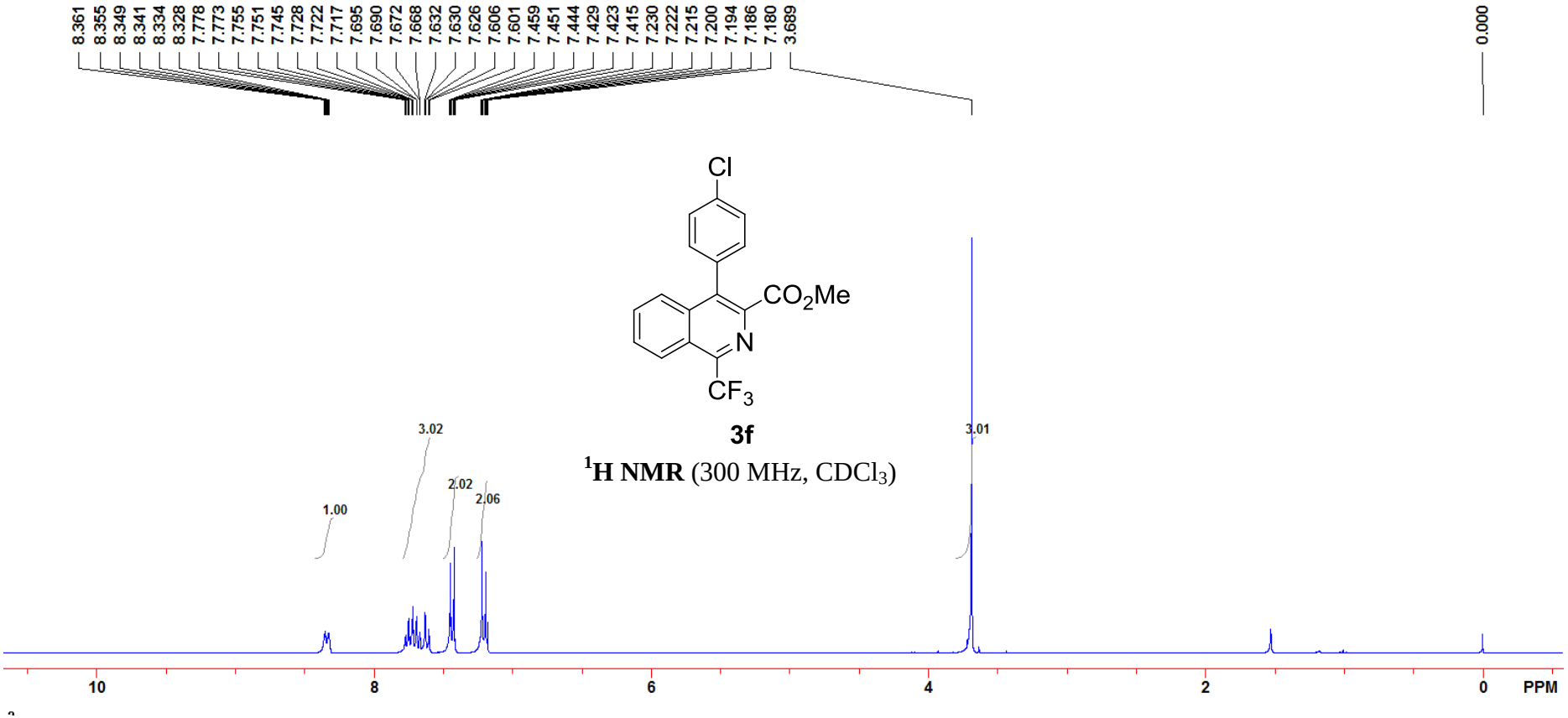
3e

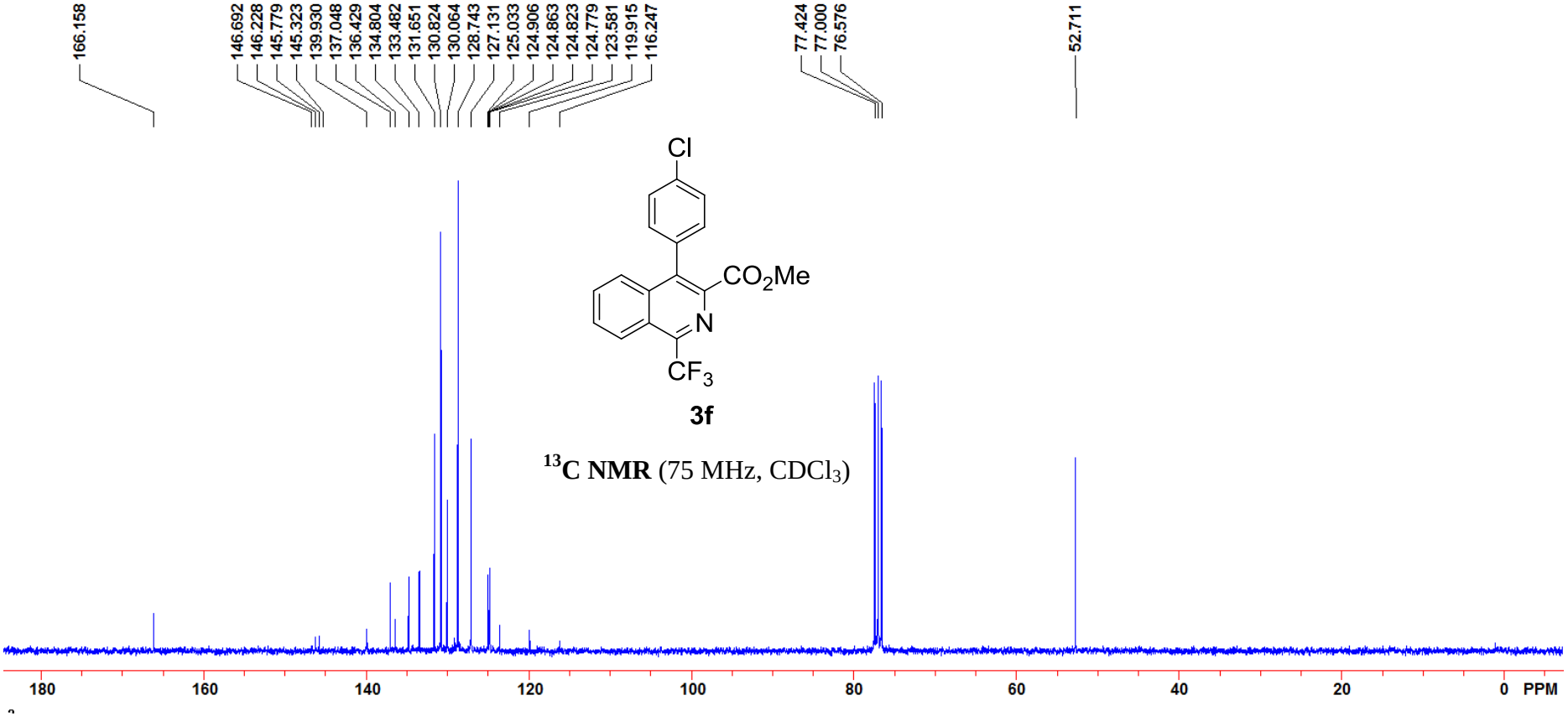
^{13}C NMR (75 MHz, $CDCl_3$)



3e

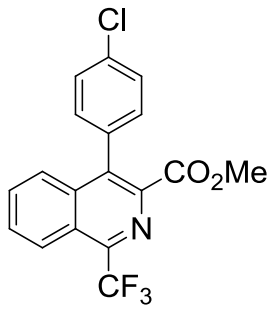
^{19}F NMR (282 MHz, $CDCl_3$)


8.361
8.355
8.349
8.341
8.334
8.328
7.778
7.773
7.755
7.751
7.745
7.728
7.722
7.717
7.695
7.690
7.672
7.668
7.632
7.630
7.626
7.606
7.601
7.459
7.451
7.444
7.429
7.423
7.415
7.230
7.222
7.215
7.200
7.194
7.186
7.180
3.689
0.000
Cl
CO2Me
N
CF3
3f
1H NMR (300 MHz, CDCl3)
3.02
2.02
2.06
1.00
3.01
10
8
6
4
2
0
PPM



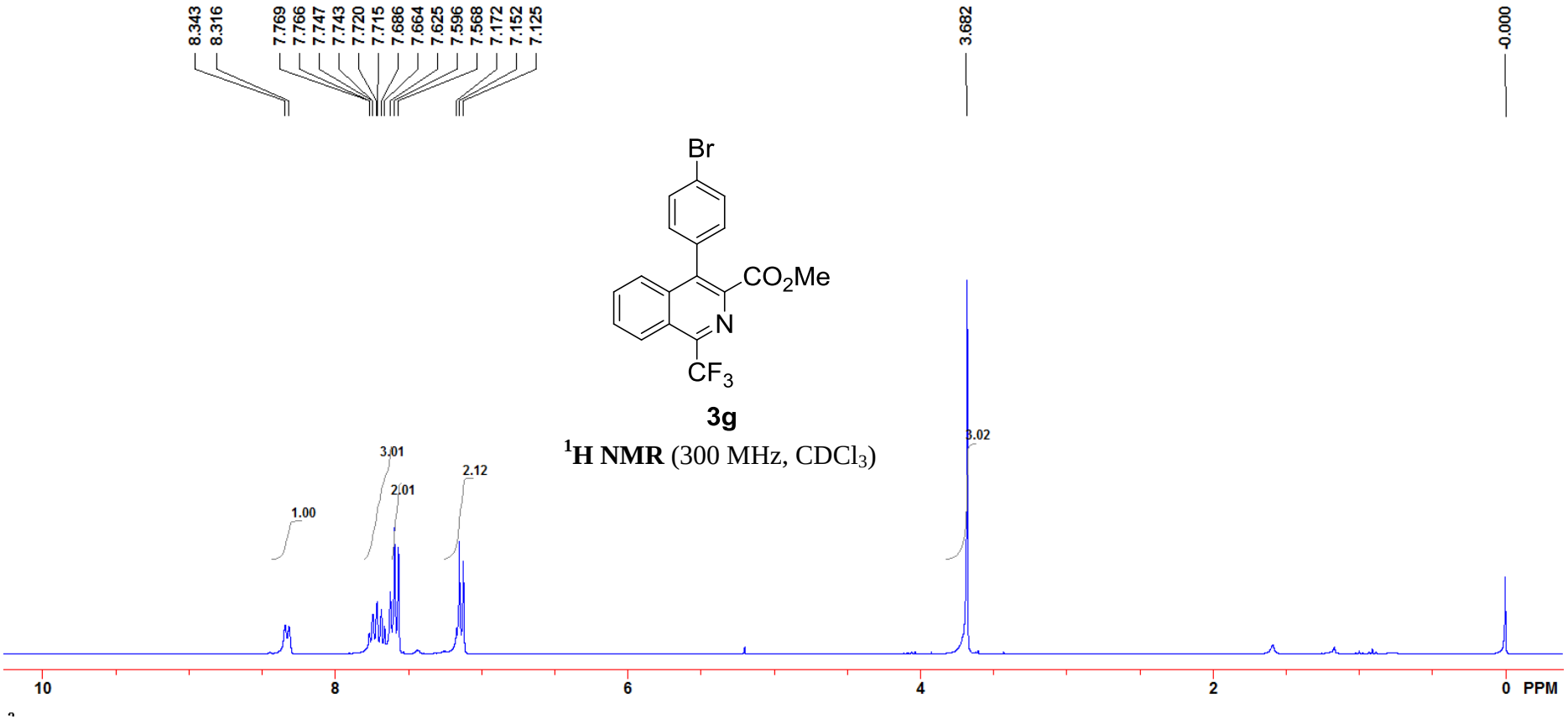
3f

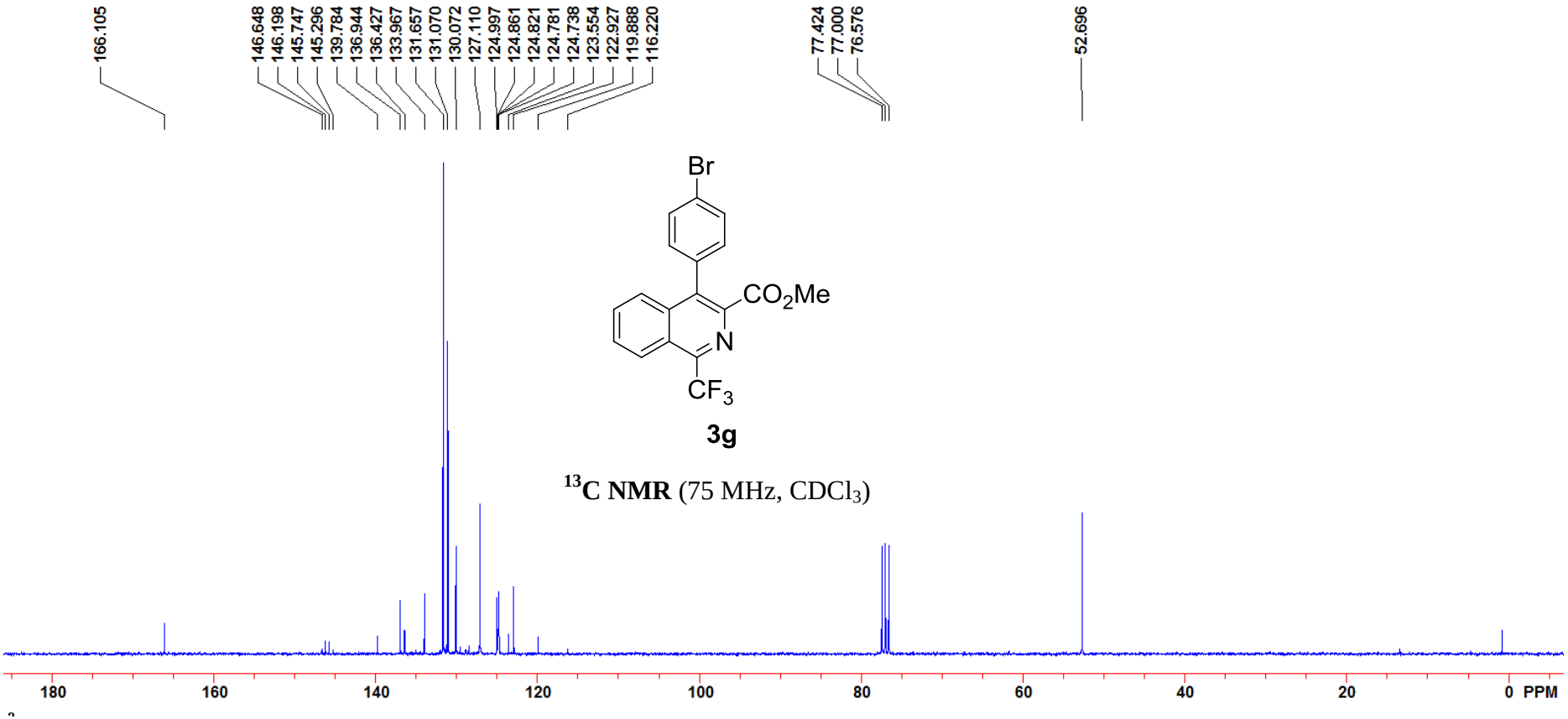
^{13}C NMR (75 MHz, $CDCl_3$)



3f

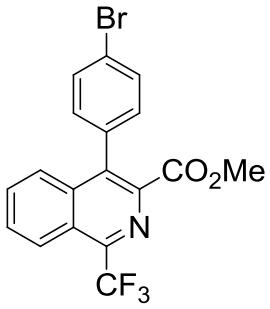
^{19}F NMR (282 MHz, $CDCl_3$)


8.343
8.316
7.769
7.766
7.747
7.743
7.720
7.715
7.686
7.664
7.625
7.596
7.568
7.172
7.152
7.125
3.682
-0.000
Br
CO2Me
N
CF3
3g
1H NMR (300 MHz, CDCl3)
1.00
3.01
2.01
2.12
3.02
10
8
6
4
2
0
PPM



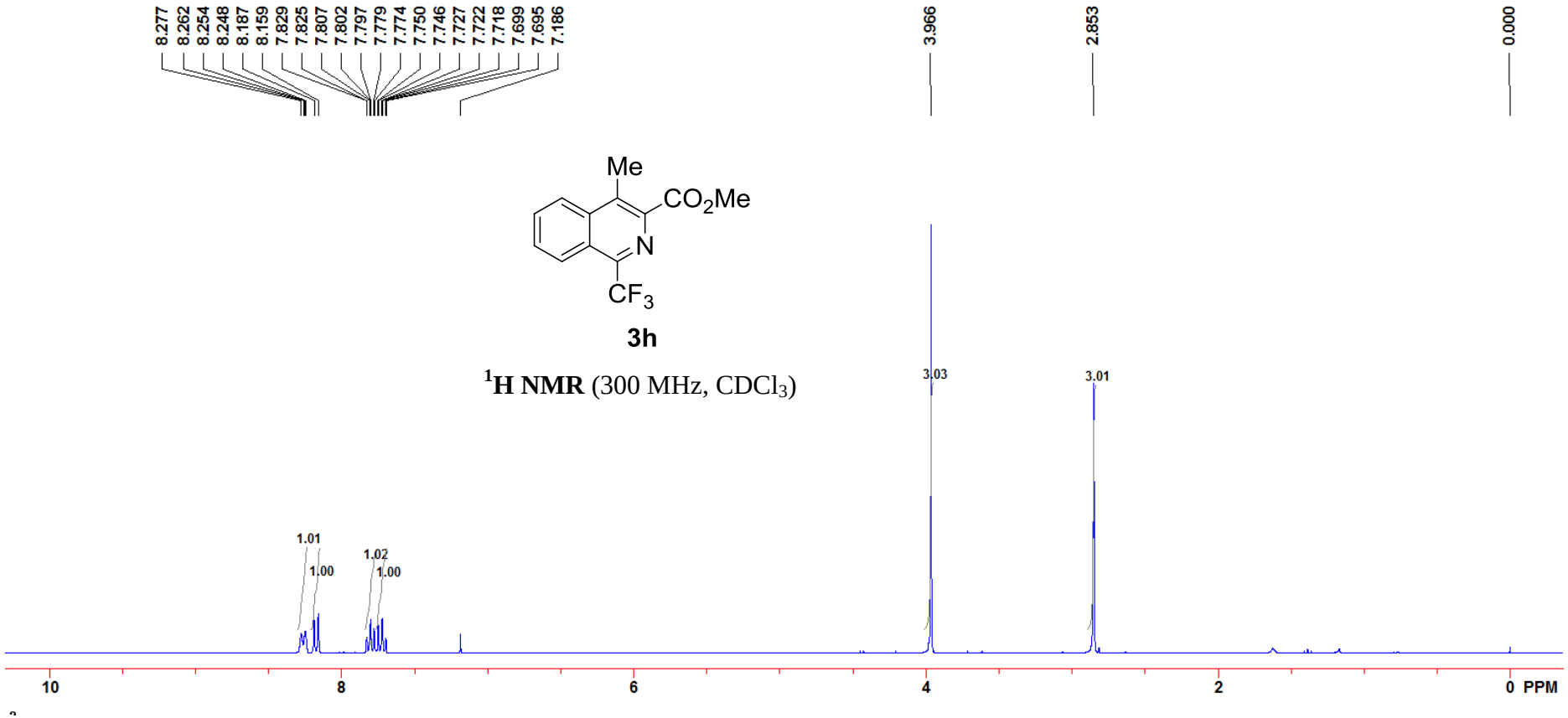
3g

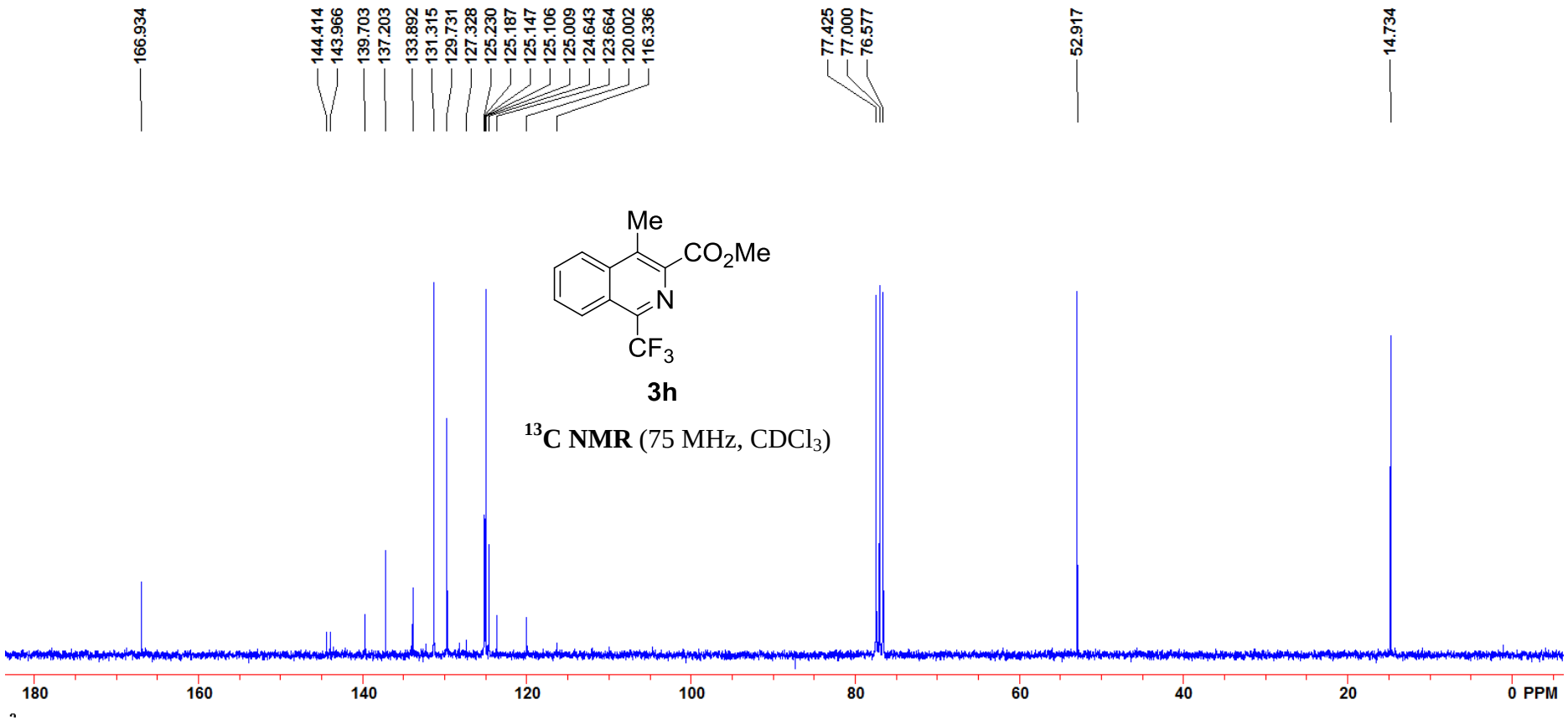
^{13}C NMR (75 MHz, $CDCl_3$)



3g

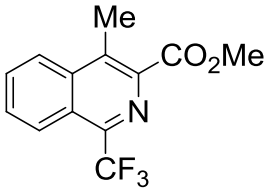
^{19}F NMR (282 MHz, $CDCl_3$)


8.277
8.262
8.254
8.248
8.187
8.159
7.829
7.825
7.807
7.802
7.797
7.779
7.774
7.750
7.746
7.727
7.722
7.718
7.699
7.695
7.186
3.966
2.853
0.000
Me
CO2Me
N
CF3
3h
1H NMR (300 MHz, CDCl3)
3.03
3.01
1.01
1.00
1.02
1.00
10
8
6
4
2
0 PPM



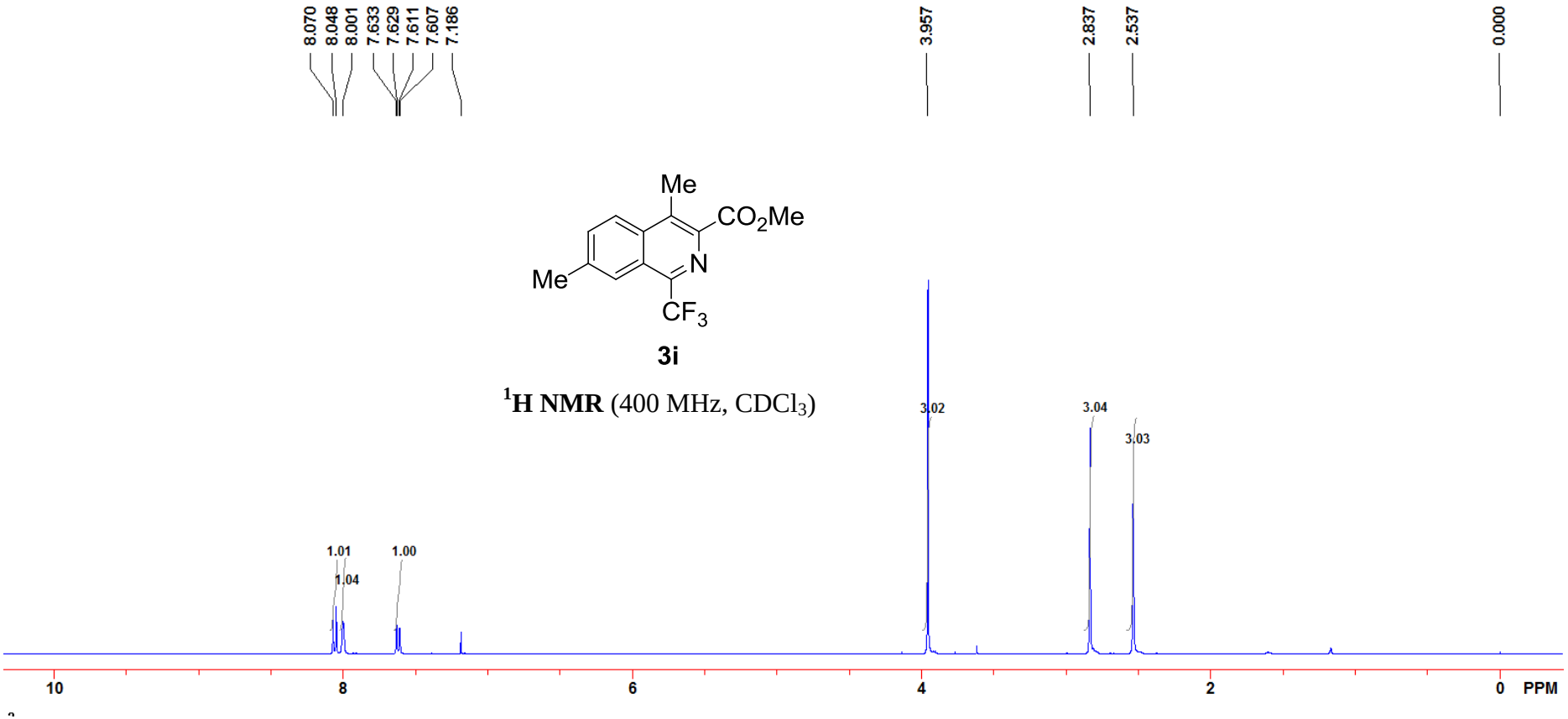
3h

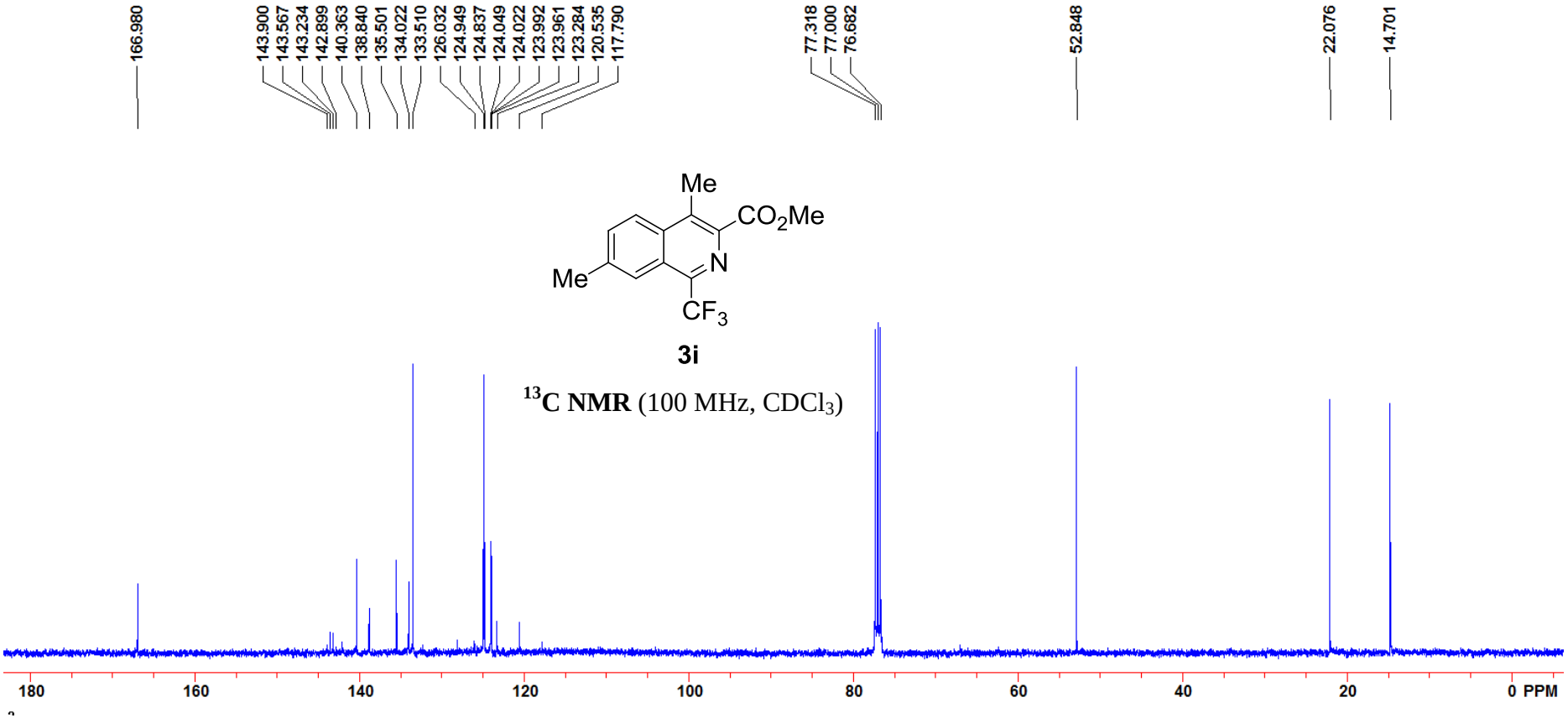
^{13}C NMR (75 MHz, $CDCl_3$)



3h

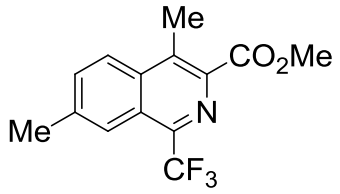
^{19}F NMR (282 MHz, $CDCl_3$)


8.070
8.048
8.001
7.633
7.629
7.611
7.607
7.186
3.957
2.837
2.537
0.000
Me
CO2Me
N
Me
CF3
3i
1H NMR (400 MHz, CDCl3)
1.01
1.04
1.00
3.02
3.04
3.03
10
8
6
4
2
0
PPM



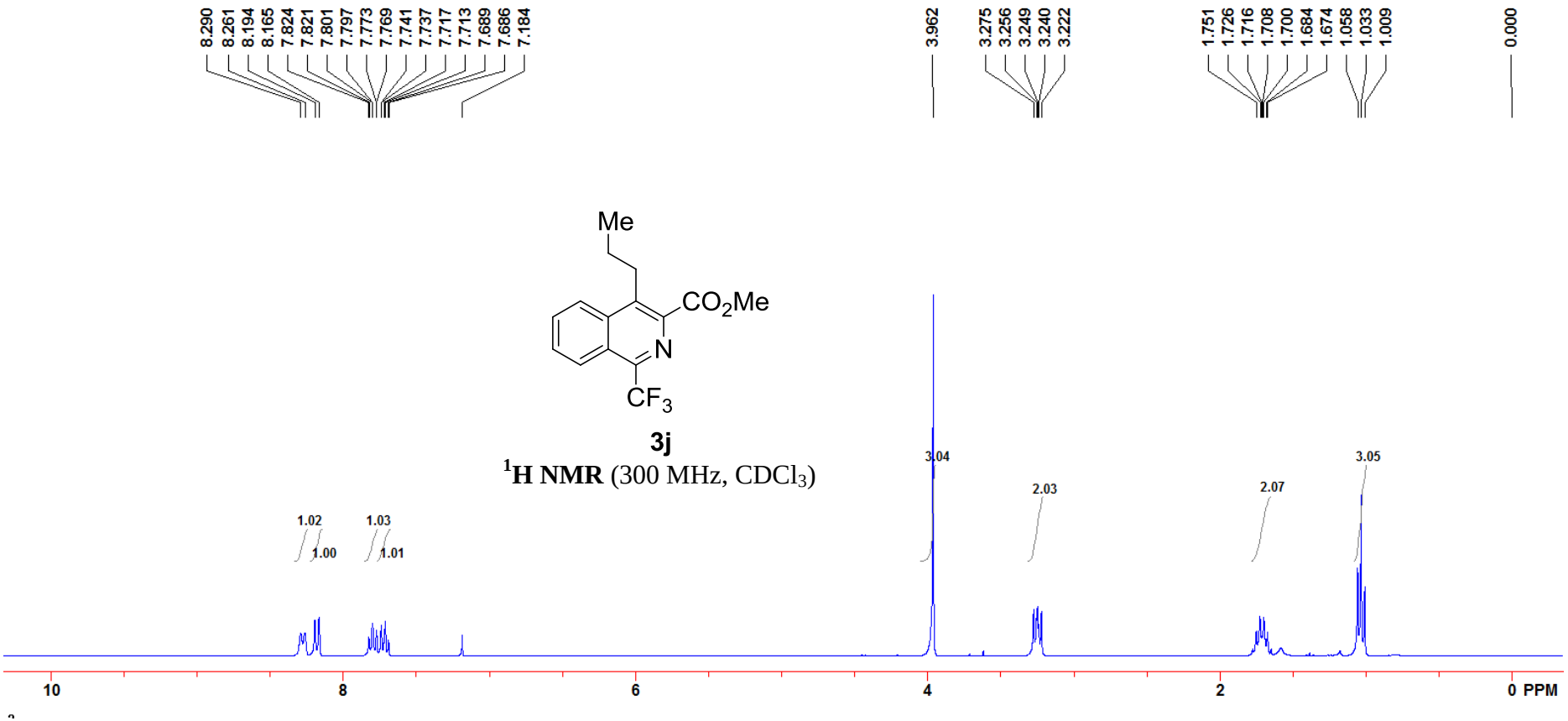
3i

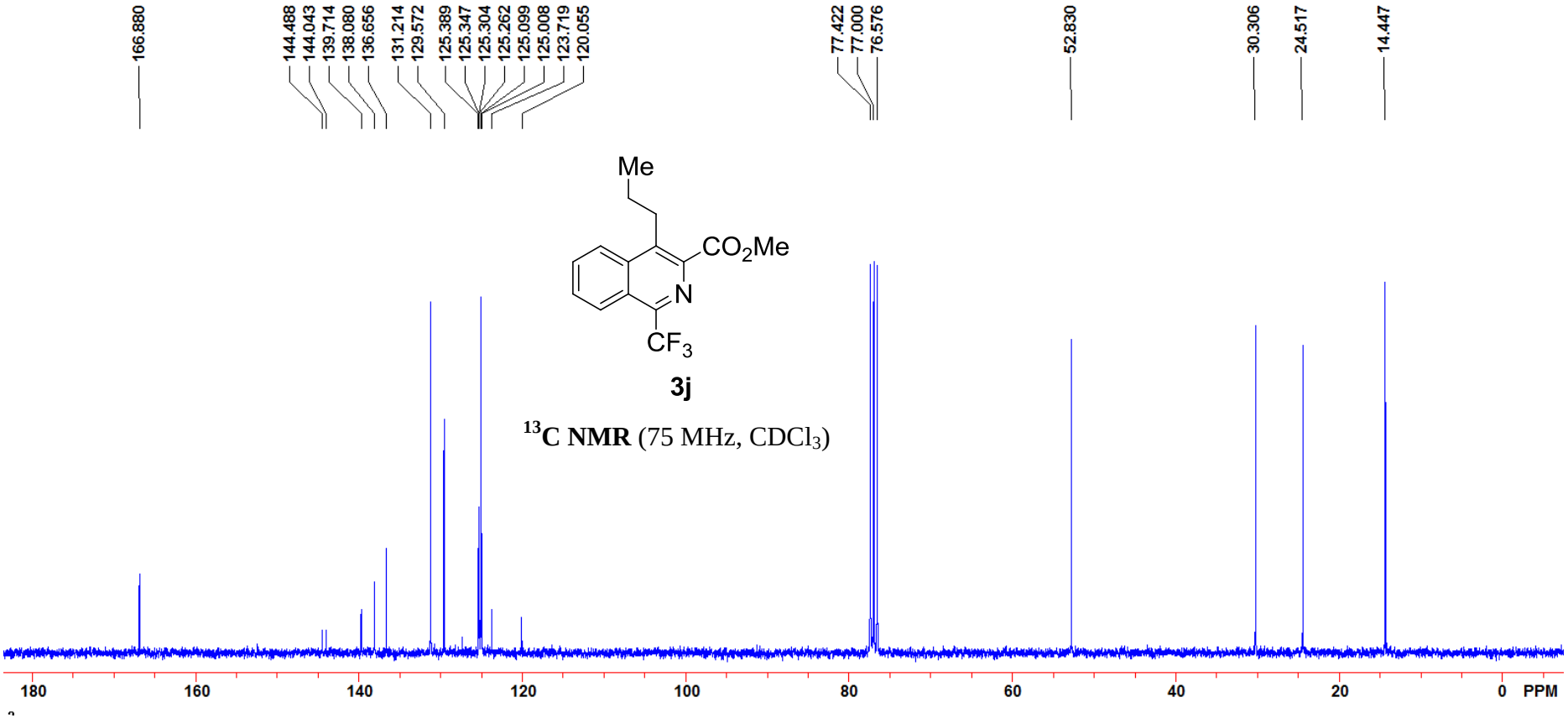
^{13}C NMR (100 MHz, $CDCl_3$)



3i

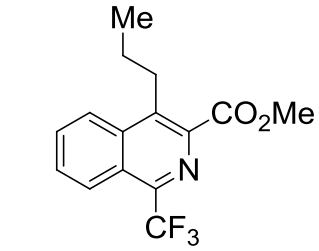
^{19}F NMR (282 MHz, $CDCl_3$)


8.290
8.261
8.194
8.165
7.824
7.821
7.801
7.797
7.773
7.769
7.741
7.737
7.717
7.713
7.689
7.686
7.184
3.962
3.275
3.256
3.249
3.240
3.222
1.751
1.726
1.716
1.708
1.700
1.684
1.674
1.058
1.033
1.009
0.000
Me
CO2Me
N
CF3
3j
1H NMR (300 MHz, CDCl3)
1.02
1.00
1.03
1.01
3.04
2.03
2.07
3.05
10
8
6
4
2
0 PPM



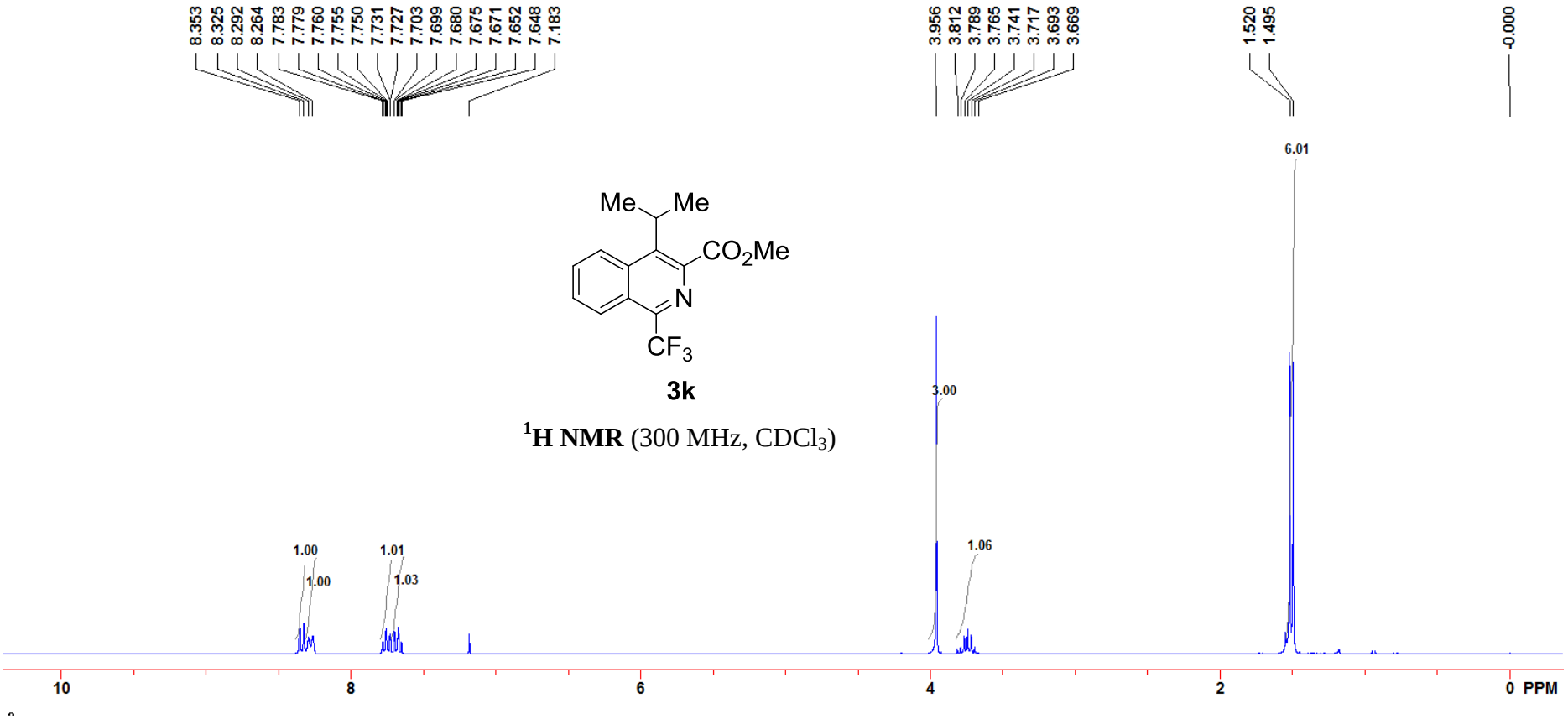
3j

^{13}C NMR (75 MHz, $CDCl_3$)



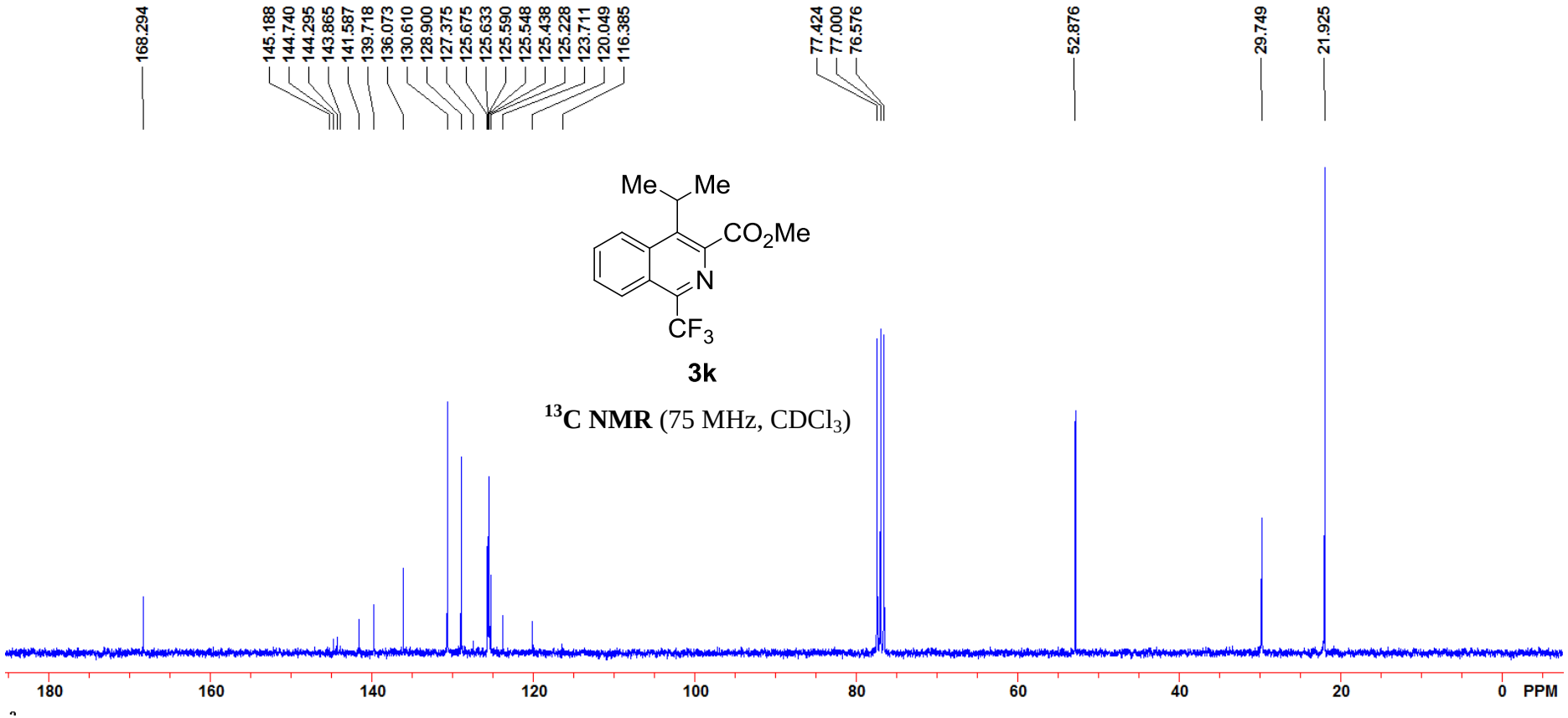
3j

^{19}F NMR (282 MHz, $CDCl_3$)



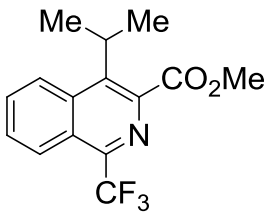
3k

^{1}H NMR (300 MHz, $CDCl_3$)



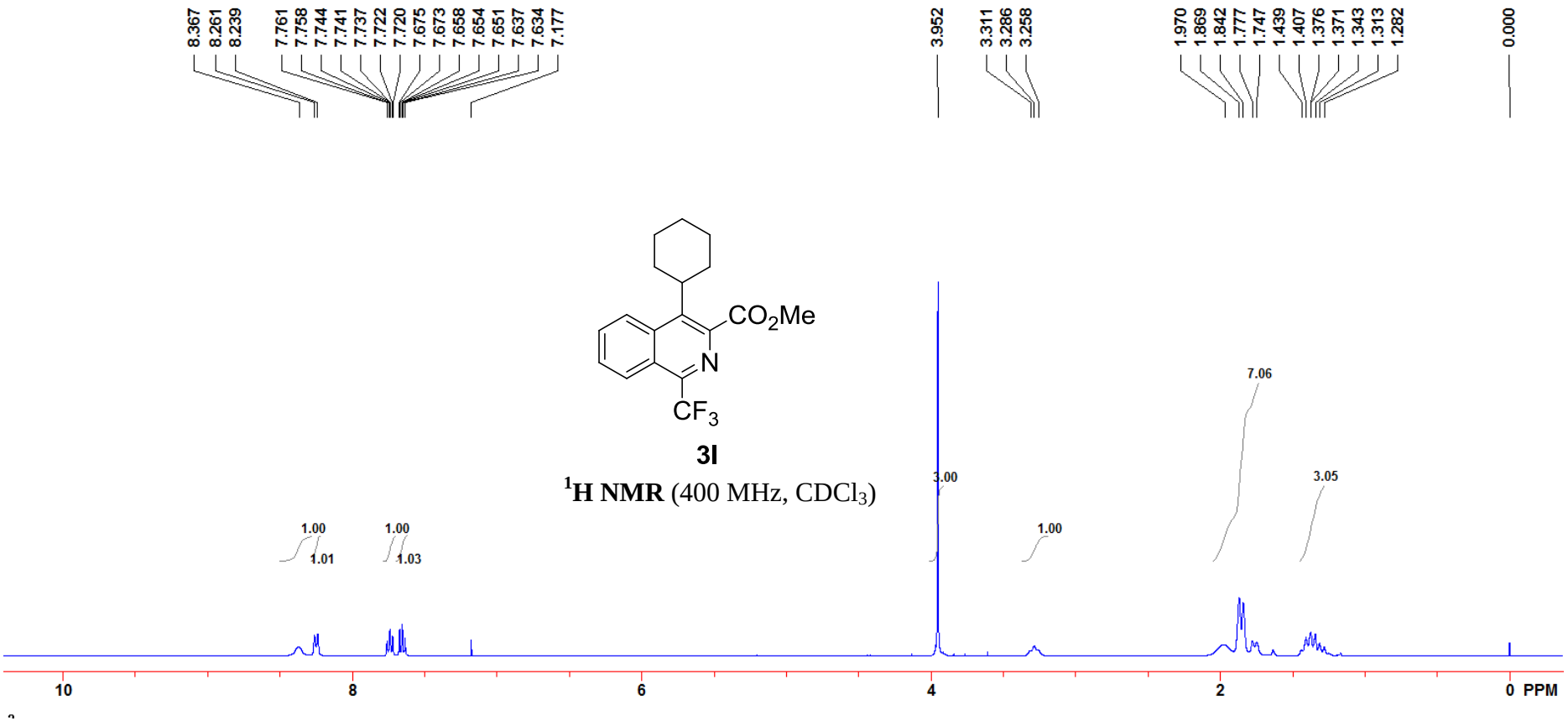
3k

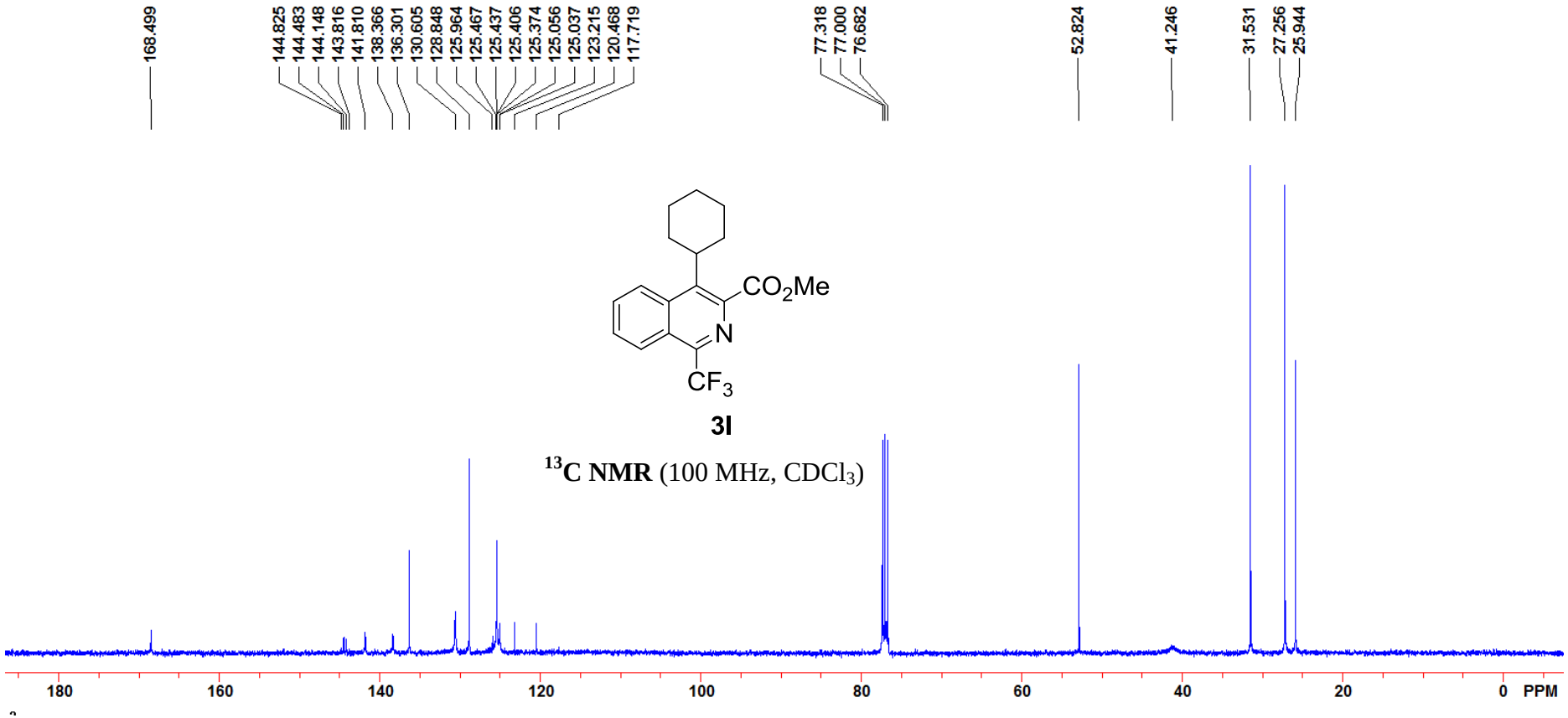
^{13}C NMR (75 MHz, $CDCl_3$)



3k

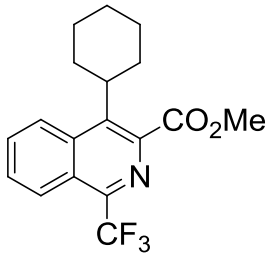
^{19}F NMR (282 MHz, $CDCl_3$)


8.367
8.261
8.239
7.761
7.758
7.744
7.741
7.737
7.722
7.720
7.675
7.673
7.658
7.654
7.651
7.637
7.634
7.177
3.952
3.311
3.286
3.258
1.970
1.869
1.842
1.777
1.747
1.439
1.407
1.376
1.371
1.343
1.313
1.282
0.000
CO2Me
N
CF3
3l
1H NMR (400 MHz, CDCl3)
1.00
1.01
1.00
1.03
3.00
1.00
7.06
3.05
10
8
6
4
2
0 PPM



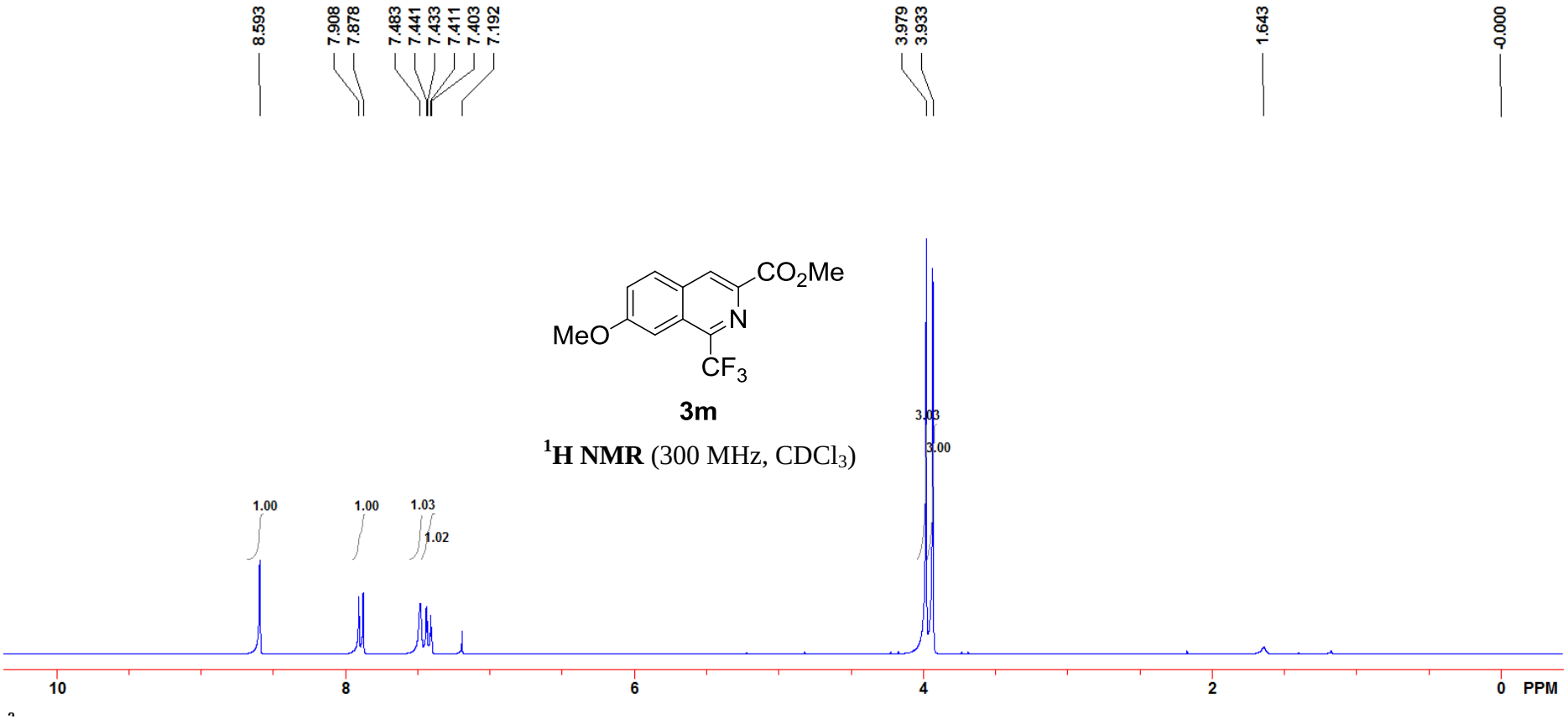
3l

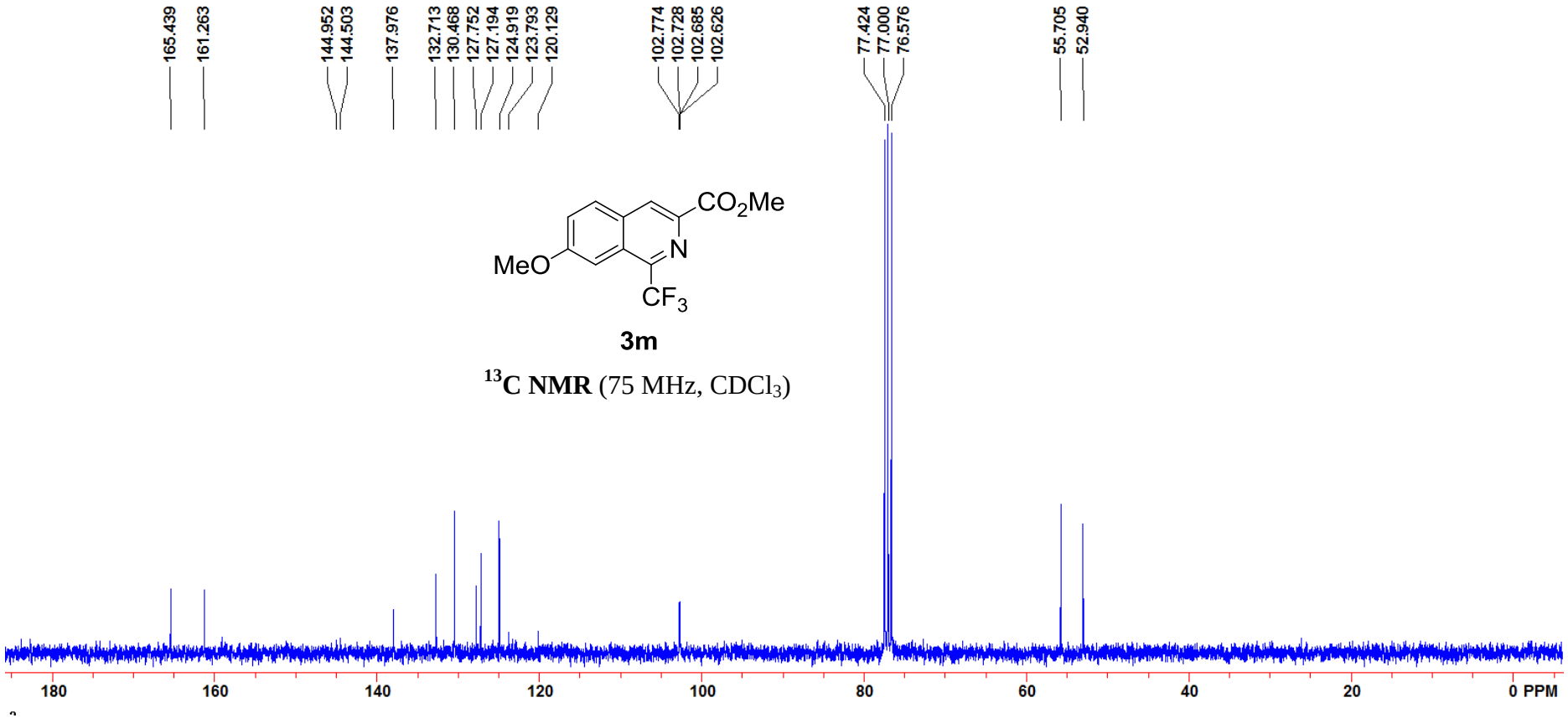
^{13}C NMR (100 MHz, $CDCl_3$)



3l

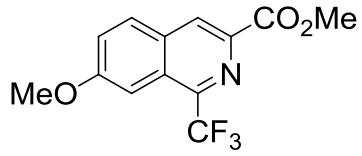
^{19}F NMR (282 MHz, $CDCl_3$)


8.593
7.908
7.878
7.483
7.441
7.433
7.411
7.403
7.192
3.979
3.933
1.643
0.000
CO2Me
N
MeO
CF3
3m
1H NMR (300 MHz, CDCl3)
1.00
1.00
1.03
1.02
3.03
3.00
10
8
6
4
2
0
PPM



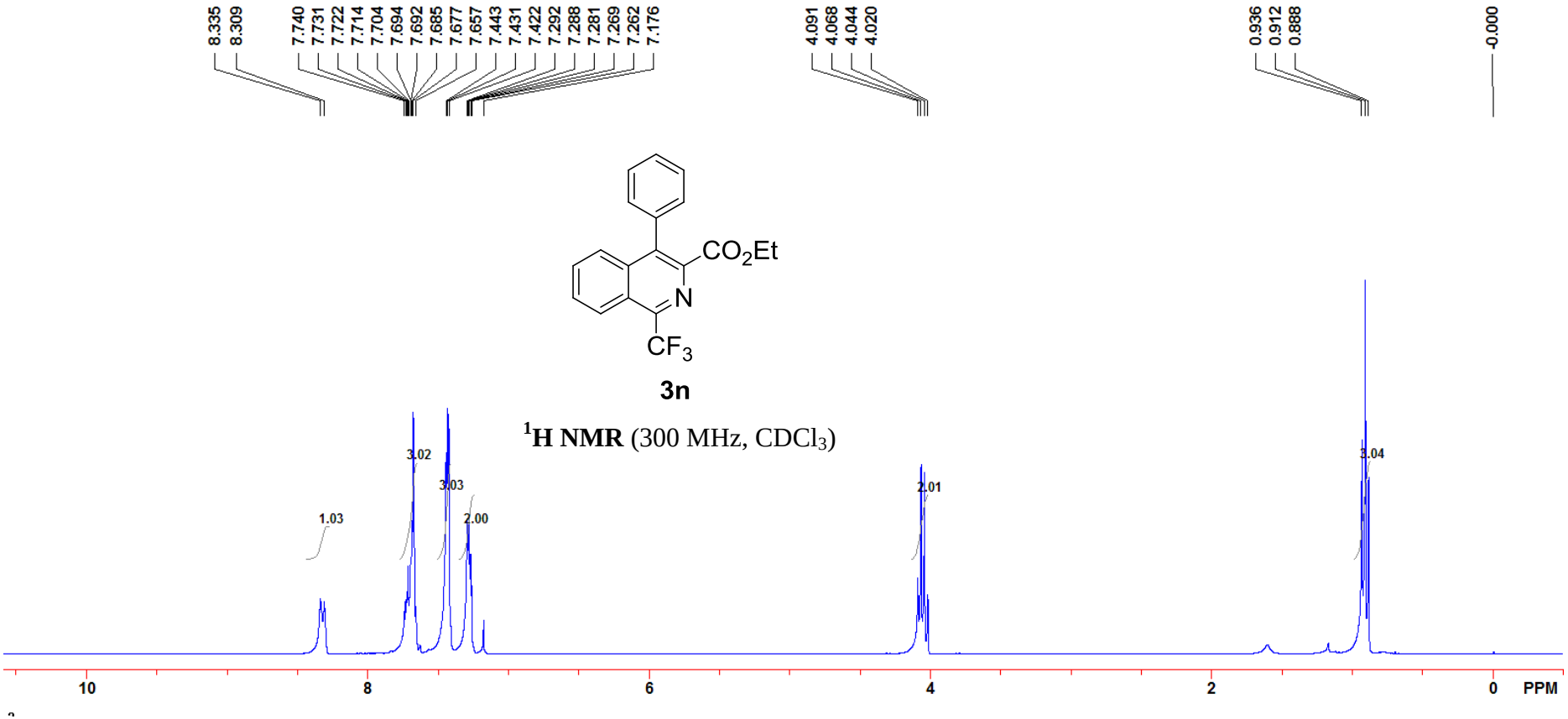
3m

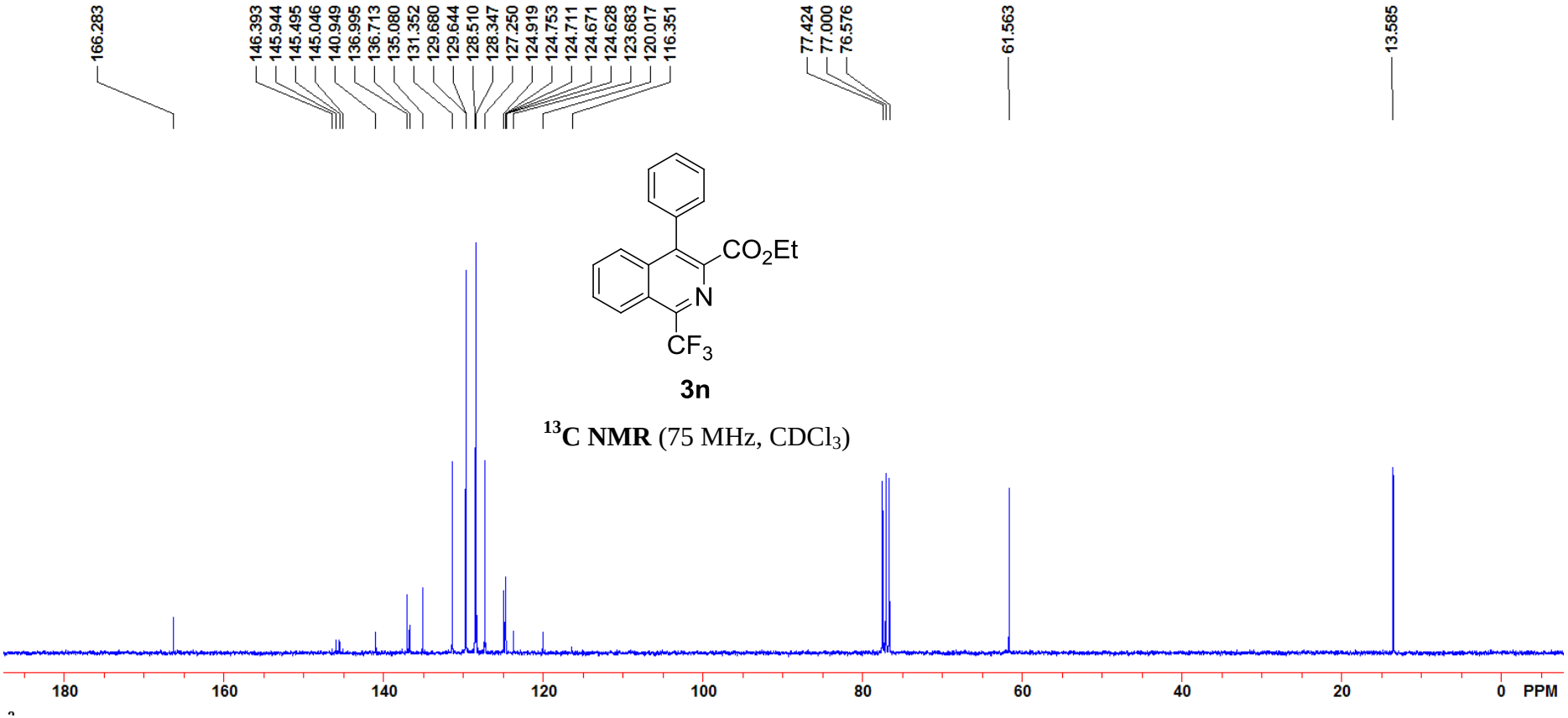
^{13}C NMR (75 MHz, $CDCl_3$)



3m

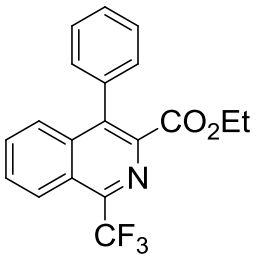
^{19}F NMR (282 MHz, $CDCl_3$)


8.335
8.309
7.740
7.731
7.722
7.714
7.704
7.694
7.692
7.685
7.677
7.657
7.443
7.431
7.422
7.292
7.288
7.281
7.269
7.262
7.176
4.091
4.068
4.044
4.020
0.936
0.912
0.888
-0.000
CO2Et
N
CF3
3n
1H NMR (300 MHz, CDCl3)
1.03
3.02
3.03
2.00
2.01
3.04
10
8
6
4
2
0
PPM



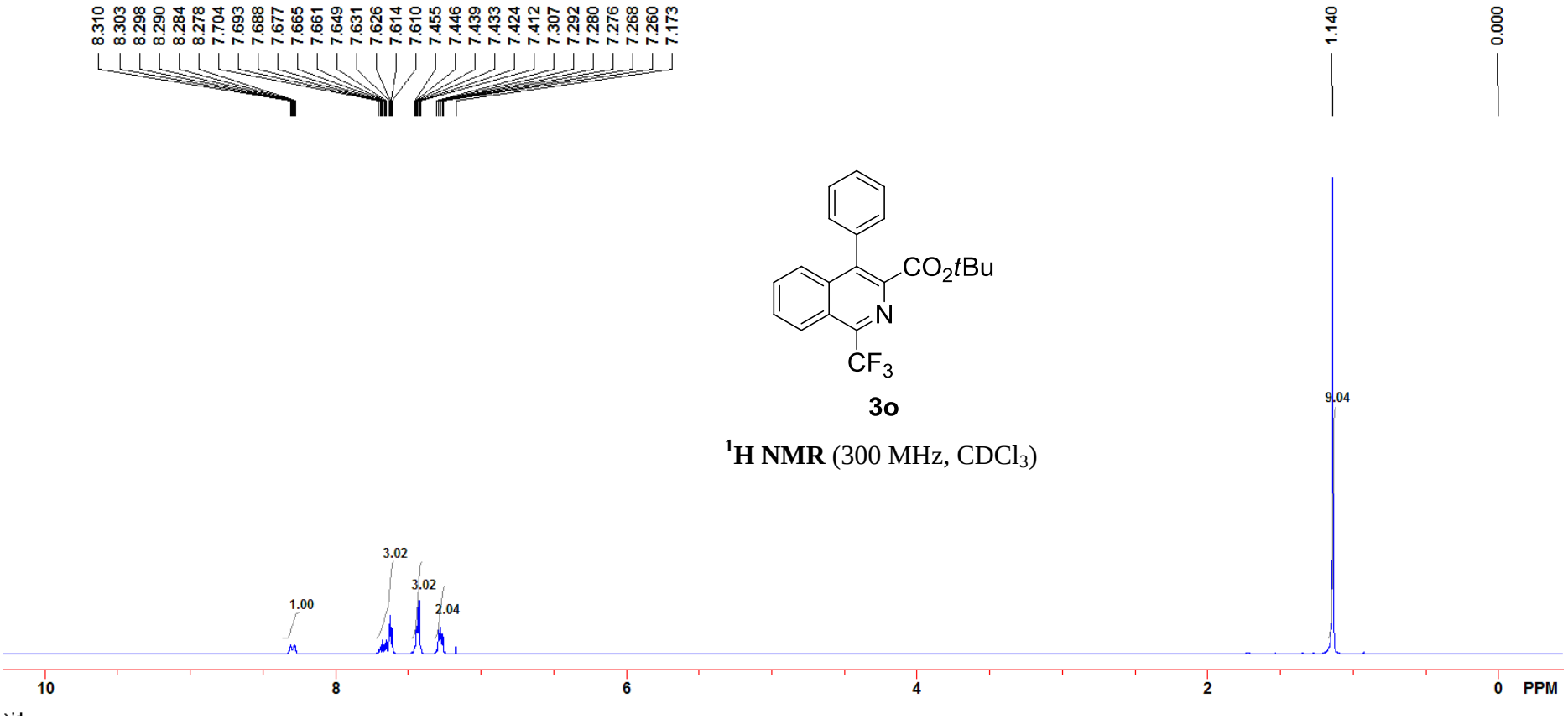
3n

^{13}C NMR (75 MHz, $CDCl_3$)



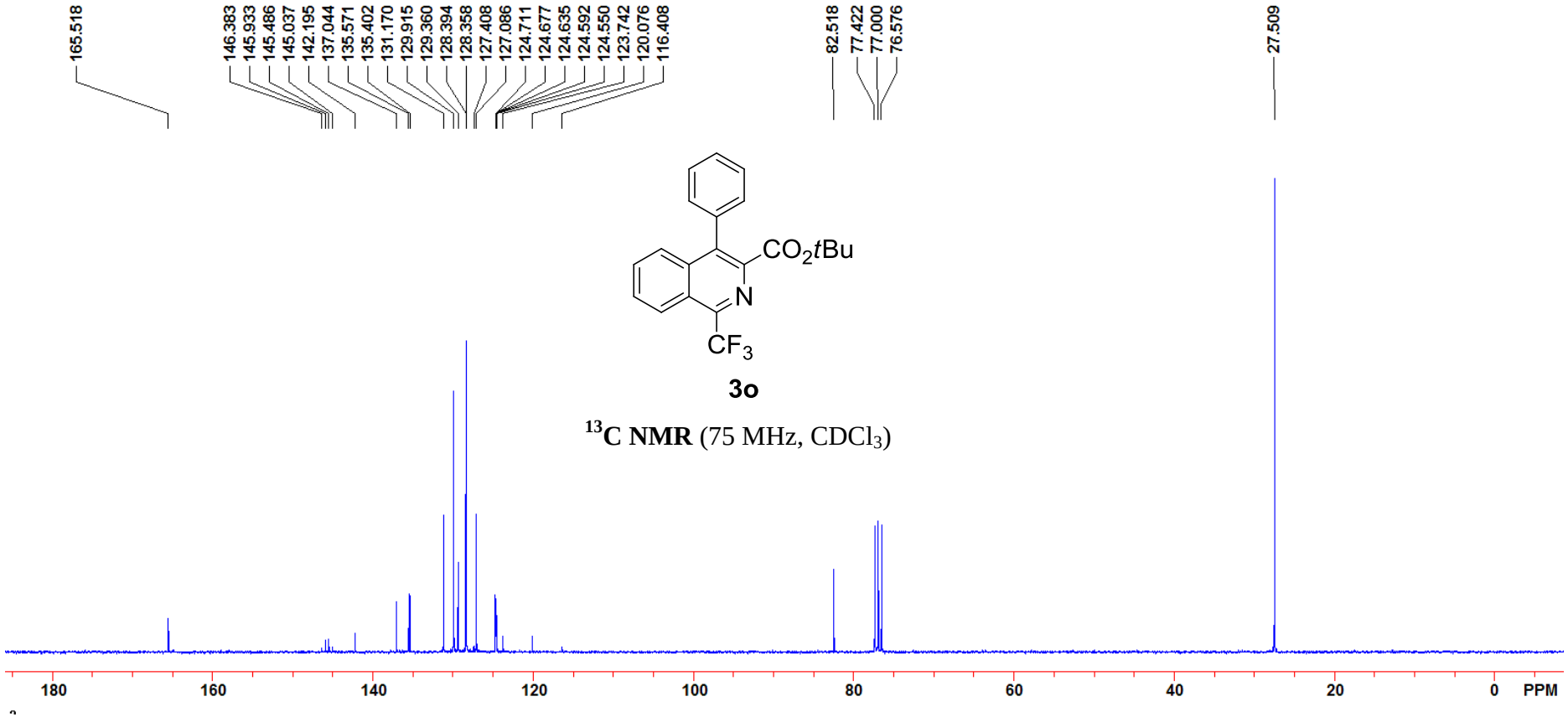
3n

^{19}F NMR (282 MHz, $CDCl_3$)



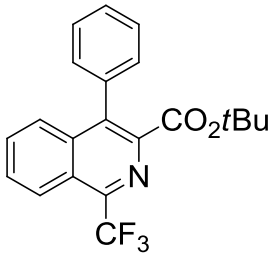
3o

^{1}H NMR (300 MHz, $CDCl_3$)



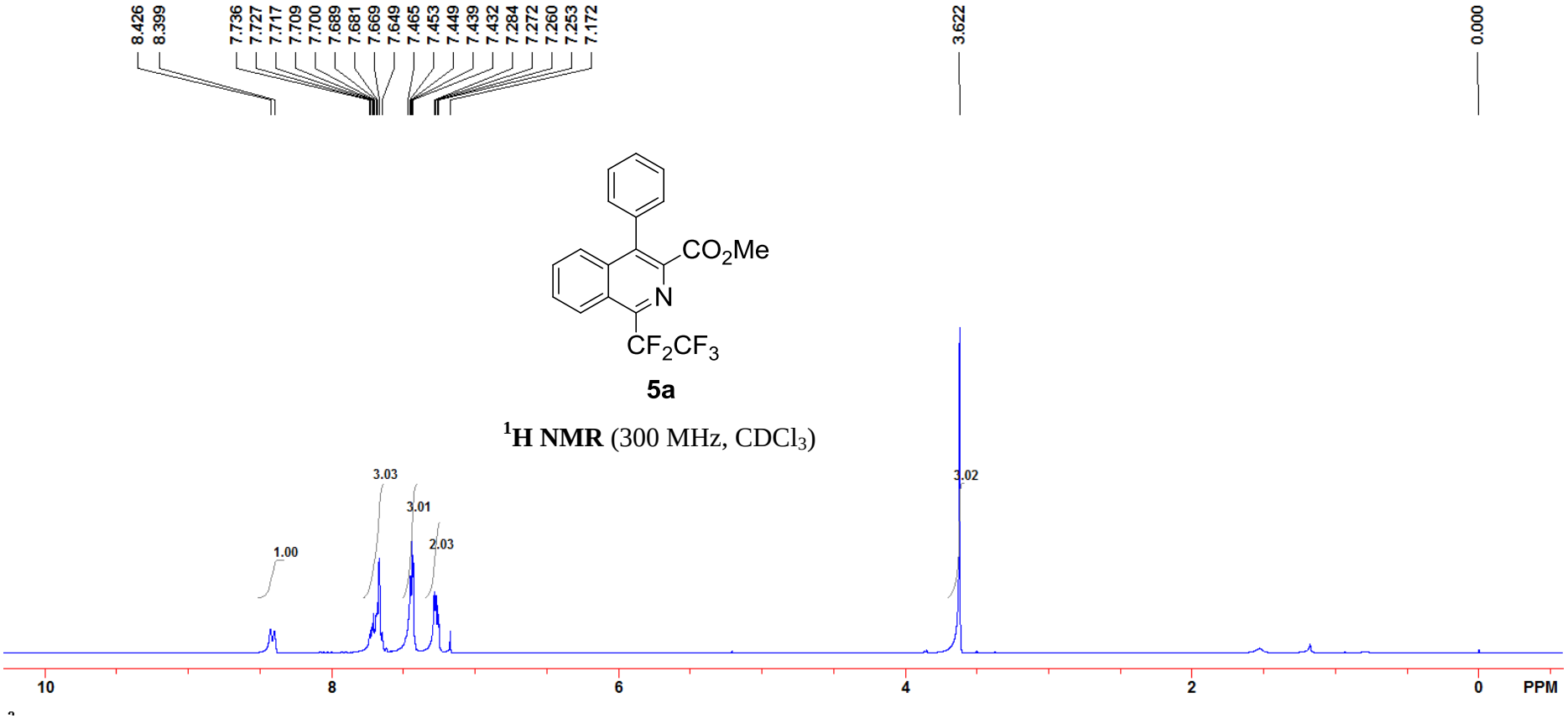
3o

^{13}C NMR (75 MHz, $CDCl_3$)



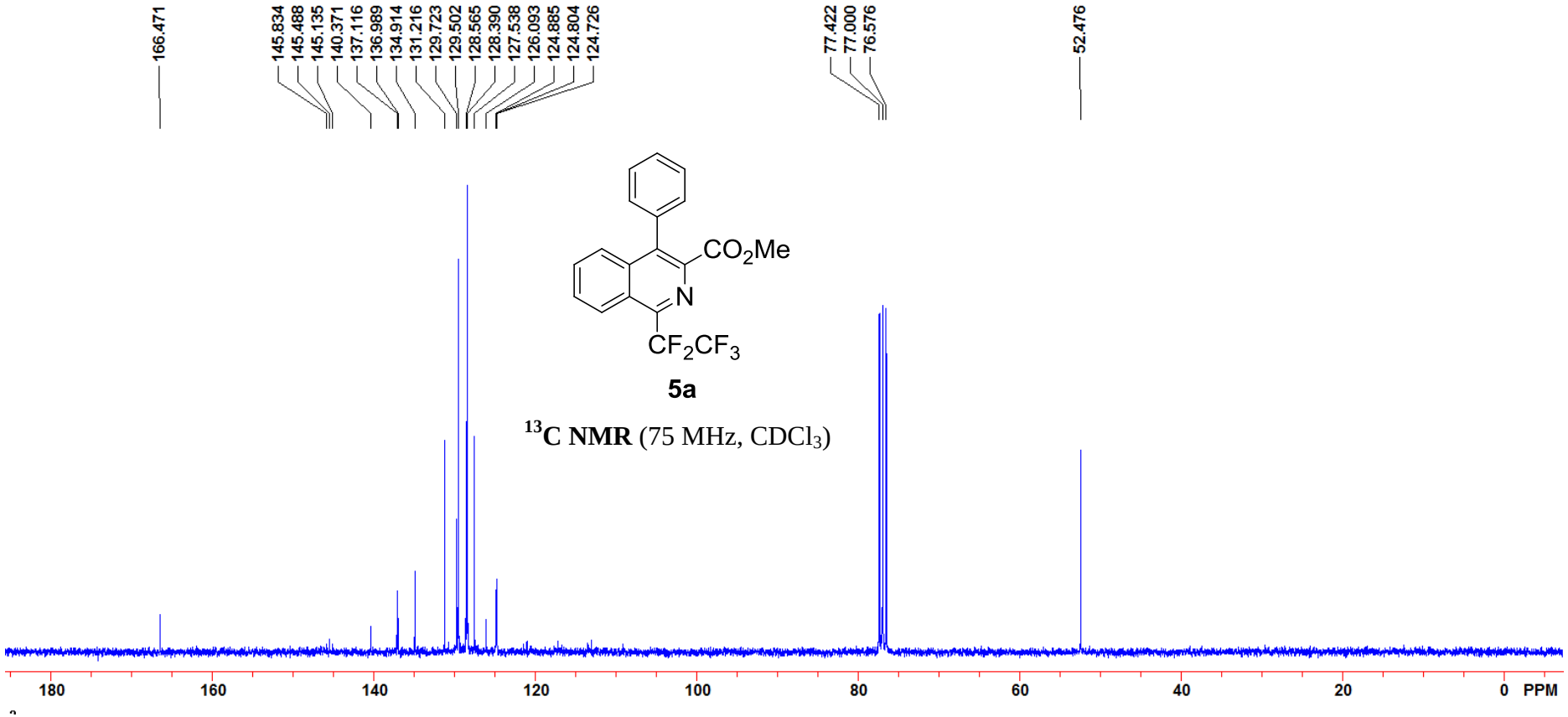
3o

^{19}F NMR (282 MHz, $CDCl_3$)



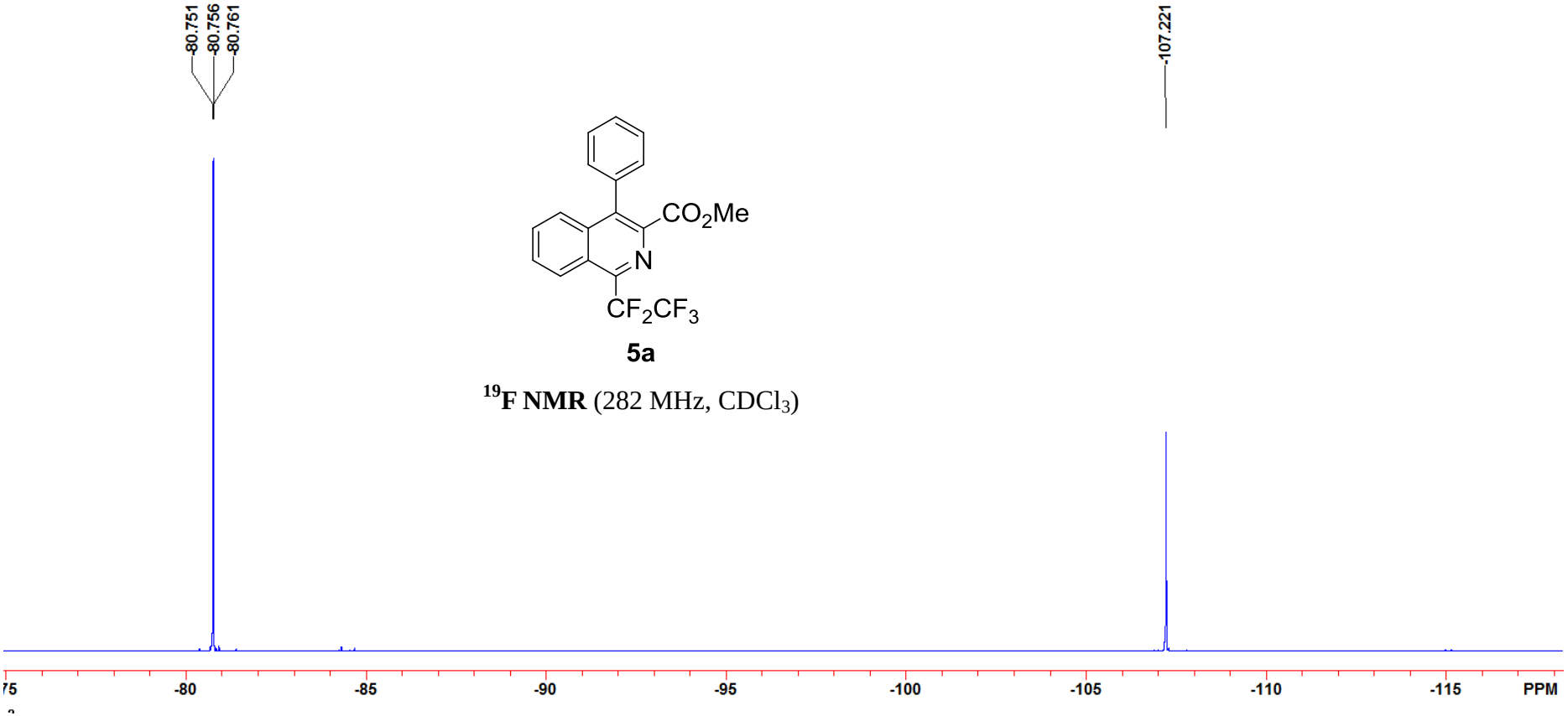
5a

^{1}H NMR (300 MHz, $CDCl_3$)



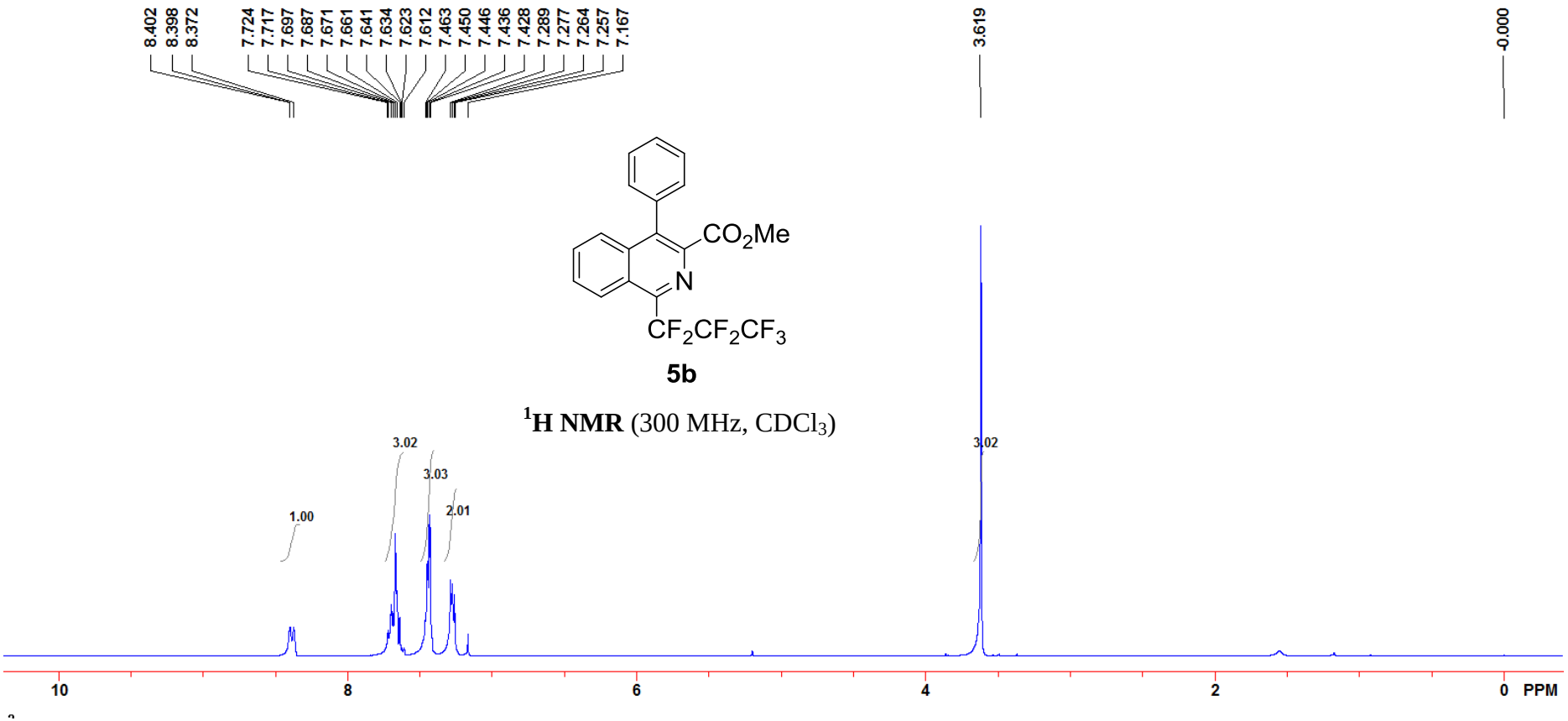
5a

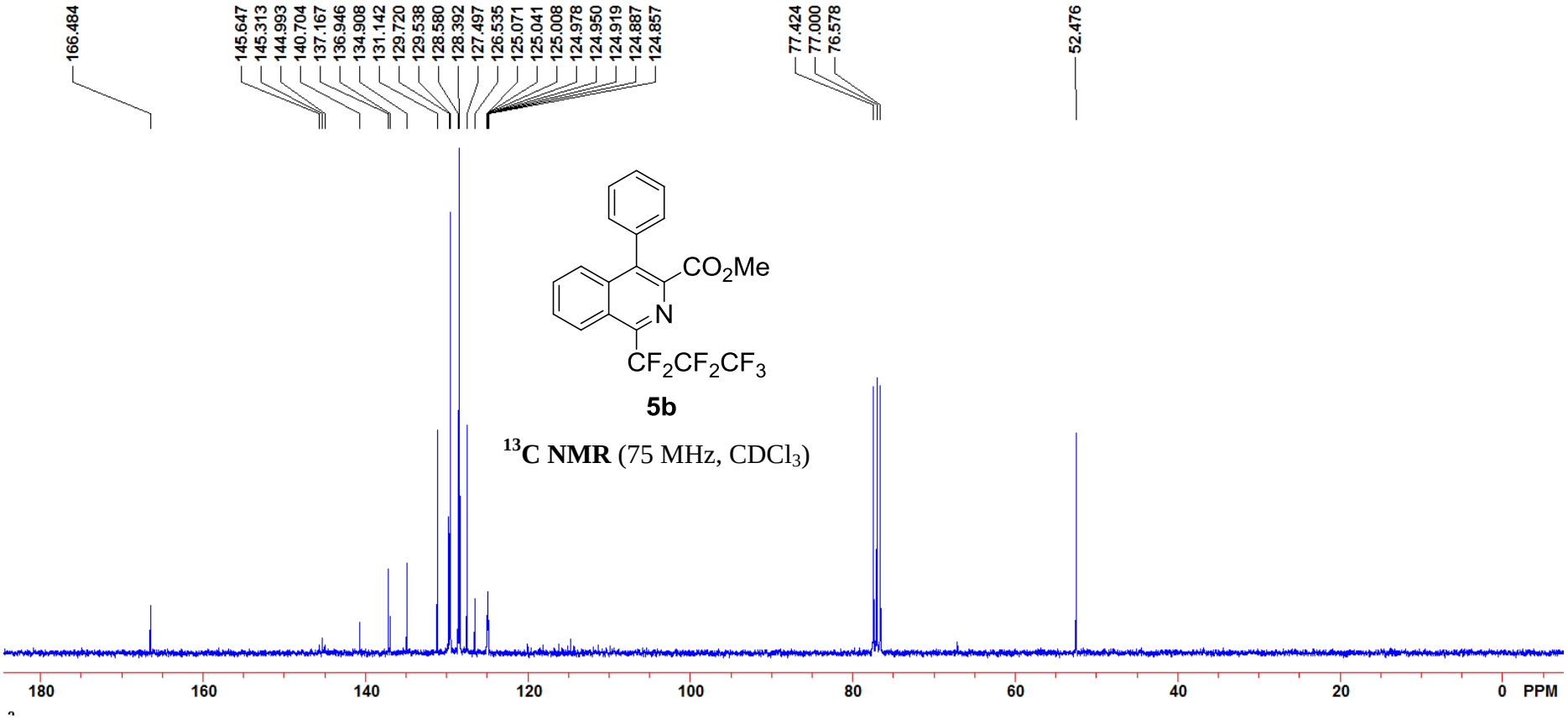
^{13}C NMR (75 MHz, $CDCl_3$)



5a

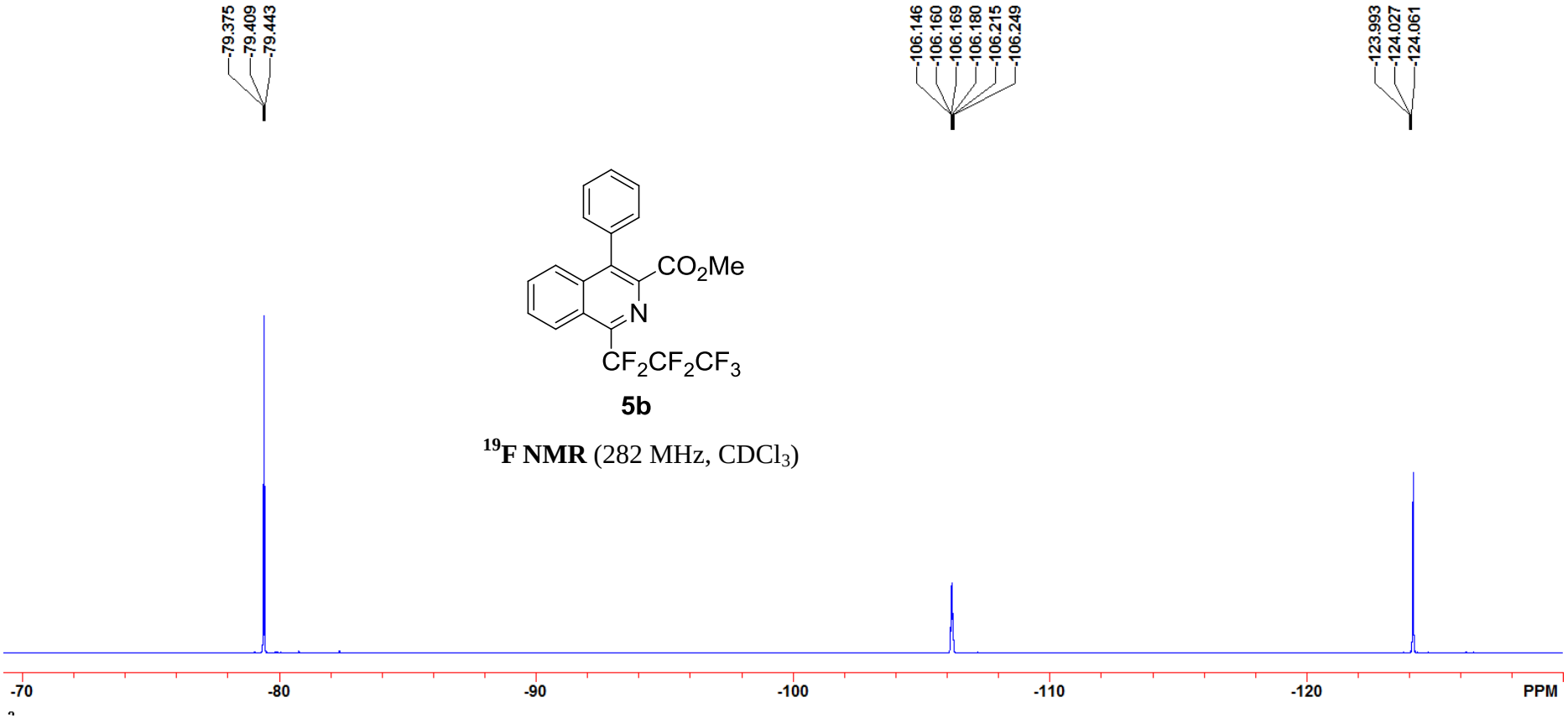
^{19}F NMR (282 MHz, $CDCl_3$)


8.402
8.398
8.372
7.724
7.717
7.697
7.687
7.671
7.661
7.641
7.634
7.623
7.612
7.463
7.450
7.446
7.436
7.428
7.289
7.277
7.264
7.257
7.167
3.619
-0.000
CO2Me
N
CF2CF2CF3
5b
1H NMR (300 MHz, CDCl3)
1.00
3.02
3.03
2.01
3.02
10
8
6
4
2
0
PPM



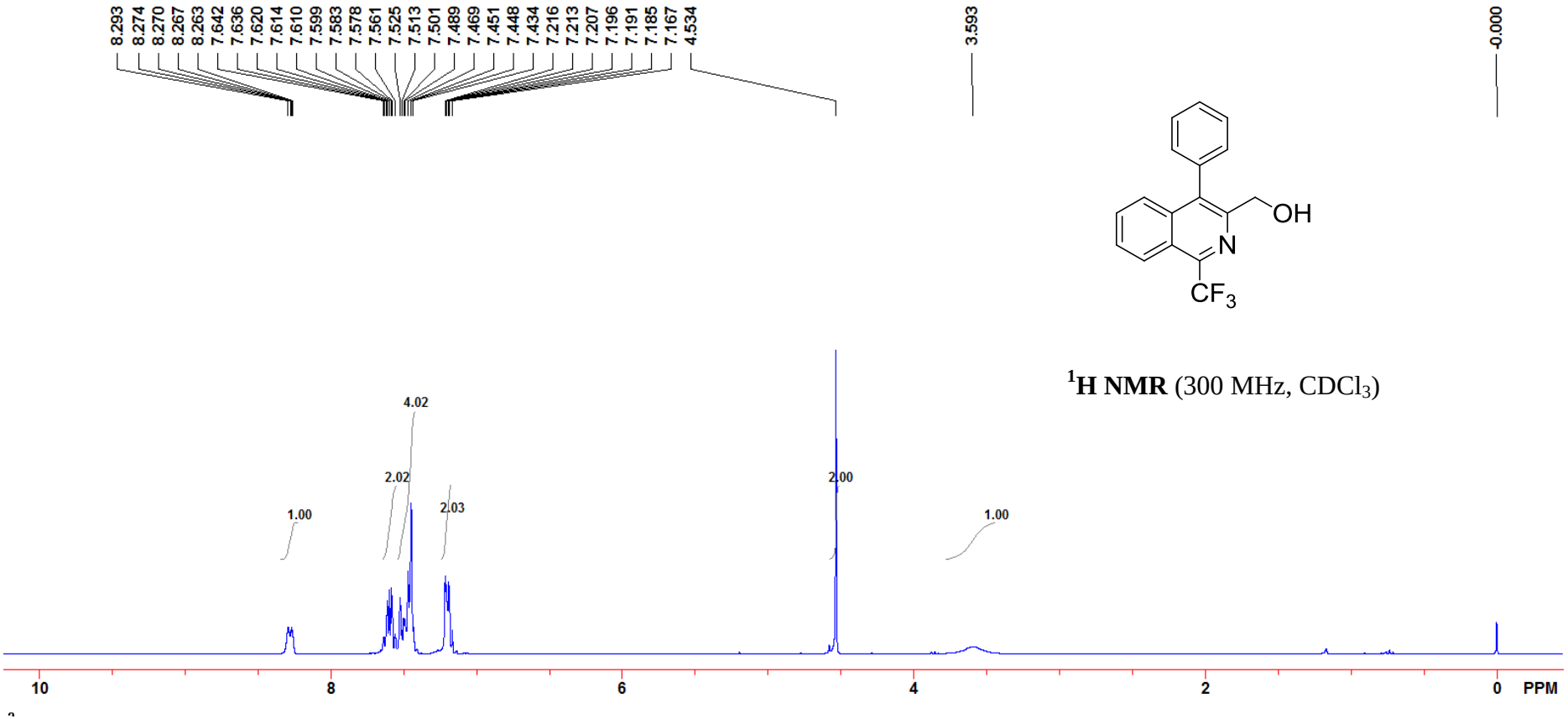
5b

^{13}C NMR (75 MHz, $CDCl_3$)

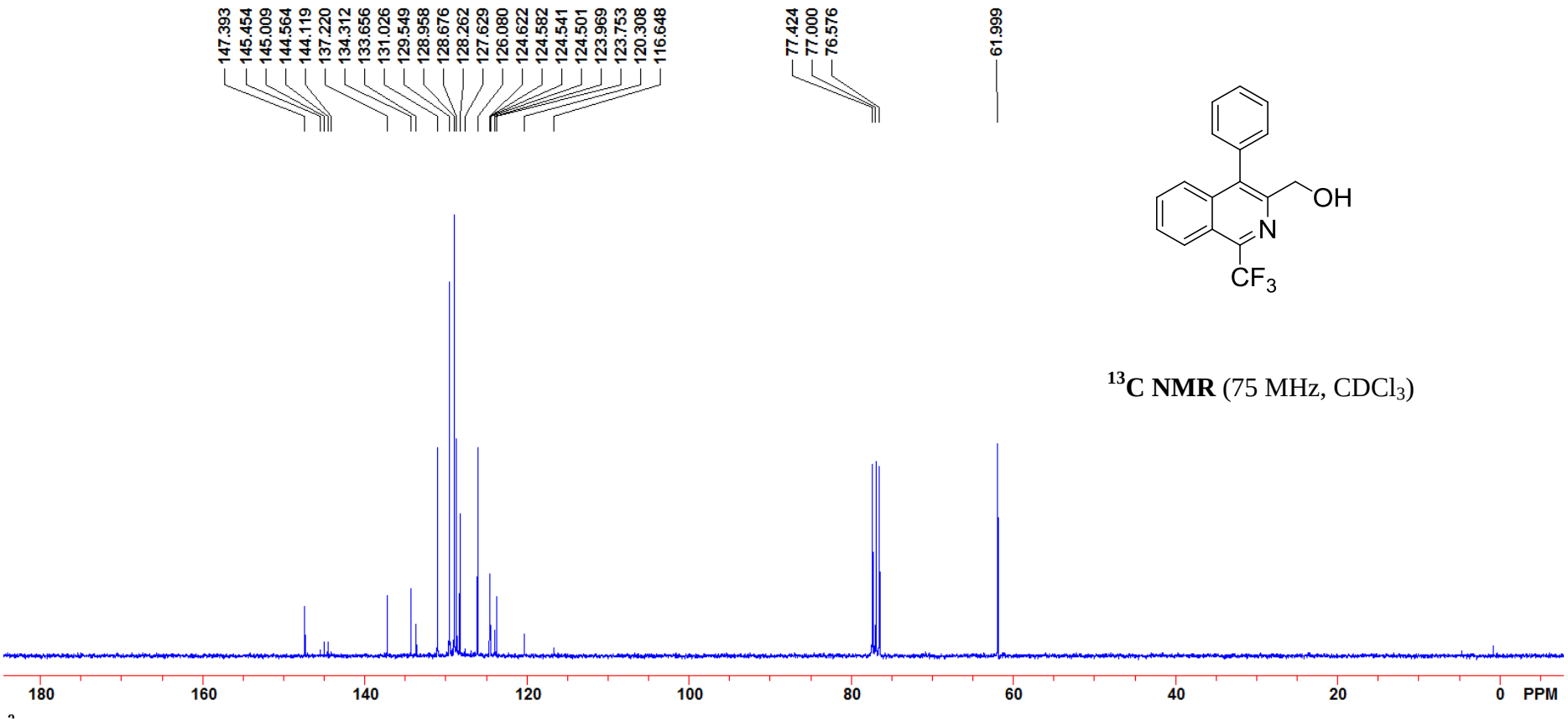


5b

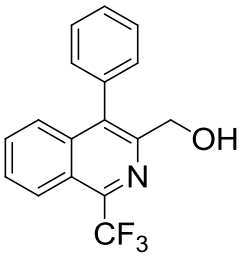
^{19}F NMR (282 MHz, $CDCl_3$)



^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



^{19}F NMR (282 MHz, $CDCl_3$)