Ruthenium(II)-catalyzed synthesis of CF_3-isoquinolinones *via* C−H activation/annulation of benzoic acids and CF_3-imidoyl sulfoxonium ylides

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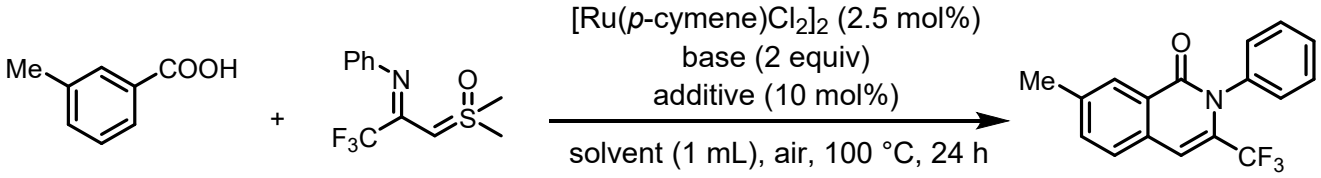
1. General Information

All the solvents were used without further purification. the other commercial chemicals were used without further purification. All reactions were performed under an air of nitrogen in flame-dried glassware, unless otherwise stated. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. Preparative TLC was performed on 1.0 mm silica gel. ^{1}H NMR spectra were recorded on a Bruker Avance III instrument (500 MHz). ^{13}C NMR spectra were recorded on a Bruker Avance III instrument (126 MHz) and were fully decoupled by broad band proton decoupling. High-resolution mass spectra (HRMS) were recorded on an Agilent 1290 mass spectrometer using ESI-TOF (electrospray ionization time-of-flight). IR spectra were recorded on a Nicolet IS 50. IR spectra were recorded in KBr. NMR spectra were recorded in $CDCl_3$. ^{1}H NMR spectra were referenced to residual $CHCl_3$ at 7.26 ppm, and ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.0 ppm. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

2. Experimental Section

2.1 Optimization of the Reaction Conditions

Table S1 Optimization of the Reaction Conditions[a]



1a **2a** **3a**

Entry	Solvent	Base	Additive	Yield (%)[b]
1	DCE	NEt_3	$AgSbF_6$	72
2	DMF	NEt_3	$AgSbF_6$	20
3	MTBE	NEt_3	$AgSbF_6$	26
4	HFIP	NEt_3	$AgSbF_6$	trace
5	toluene	NEt_3	$AgSbF_6$	34
6	^{i}PrOH	NEt_3	$AgSbF_6$	10
7	NMP	NEt_3	$AgSbF_6$	0
8	DMSO	NEt_3	$AgSbF_6$	0
9	THF	NEt_3	$AgSbF_6$	25
10	1,4-dioxane	NEt_3	$AgSbF_6$	10
11	**CH_3CN**	**NEt_3**	**$AgSbF_6$**	**76 (73)[c]**
12	CH_3CN	K_2CO_3	$AgSbF_6$	35
13	CH_3CN	KOAc	$AgSbF_6$	40
14	CH_3CN	$KHCO_3$	$AgSbF_6$	50
15	CH_3CN	KOH	$AgSbF_6$	45
16	CH_3CN	K_2HPO_4	$AgSbF_6$	45
17	CH_3CN	K_3PO_4	$AgSbF_6$	25
18	CH_3CN	KH_2PO_4	$AgSbF_6$	40
19	CH_3CN	NaOH	$AgSbF_6$	0
20	CH_3CN	NaOAc	$AgSbF_6$	57
21	CH_3CN	HCOONa	$AgSbF_6$	25
22	CH_3CN	CH_3ONa	$AgSbF_6$	35
23	CH_3CN	$NaHCO_3$	$AgSbF_6$	54

24	CH_3CN	Na_2CO_3	$AgSbF_6$	35
25	CH_3CN	Na_3PO_4	$AgSbF_6$	62
26	CH_3CN	NaH_2PO_4	$AgSbF_6$	45
27	CH_3CN	^{t}BuOK	$AgSbF_6$	20
28	CH_3CN	^{t}BuONa	$AgSbF_6$	10
27	CH_3CN	Cs_2CO_3	$AgSbF_6$	34
28	CH_3CN	LiOH	$AgSbF_6$	20
29	CH_3CN	CH_3OK	$AgSbF_6$	20
30	CH_3CN	Li_2CO_3	$AgSbF_6$	45
31	CH_3CN	LiOAc	$AgSbF_6$	45
32	CH_3CN	^{t}BuOLi	$AgSbF_6$	0
33	CH_3CN	DBU	$AgSbF_6$	30
34	CH_3CN	Cy_2NH	$AgSbF_6$	48
35	CH_3CN	^{i}Pr$_2$NEt	$AgSbF_6$	47
36	CH_3CN	NEt_3	---	45
37	CH_3CN	---	$AgSbF_6$	48
48	CH_3CN	---	---	46
39[d]	CH_3CN	NEt_3	$AgSbF_6$	65
40[e]	CH_3CN	NEt_3	$AgSbF_6$	74
41[f]	CH_3CN	NEt_3	$AgSbF_6$	44
42[g]	CH_3CN	NEt_3	$AgSbF_6$	0
43[h]	CH_3CN	NEt_3	$AgSbF_6$	58
44[i]	CH_3CN	NEt_3	$AgSbF_6$	66
45[j]	CH_3CN	NEt_3	$AgSbF_6$	50

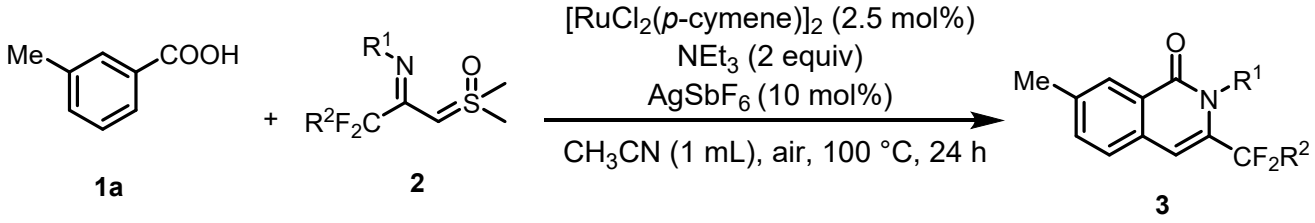
46[k]	CH_3CN	NEt_3	$AgSbF_6$	72
47[l]	CH_3CN	NEt_3	$AgSbF_6$	trace
48	CH_3CN	NEt_3	AgOAc	64
49	CH_3CN	NEt_3	Ag_2CO_3	48
50	CH_3CN	NEt_3	CF_3COAg	54
51	CH_3CN	NEt_3	$AgNO_3$	38
52	CH_3CN	NEt_3	AgOTf	34

[a] **1a** (0.1 mmol), **2a** (0.15 mmol), base (2.0 equiv), additive (10 mol%) and solvent (1 mL) at 100 °C under air for 24 h. [b] The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard. [c] The isolated yield. [d] At 80 °C. [e] At 120 °C. [f] At 60 °C. [g] At 40 °C. [h] **1a** (0.1 mmol), **2a** (0.2 mmol). [i] **1a** (0.15 mmol), **2a** (0.1 mmol). [j] CH_3CN 0.5 mL. [k] CH_3CN 2 mL. [l] Without $[Ru(p\text{-cymene})Cl_2]_2$.

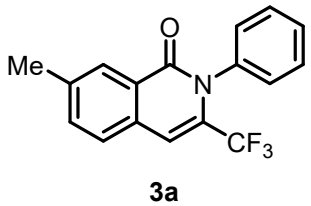
2.2 Procedure for the Synthesis of 2

All compounds **2** are known, which were synthesized following the literature procedures.[1] To a solution of triphenylphosphine (82 mmol, 3 equiv) in CCl_4 (100 mL), triethylamine (32.2 mmol, 1.2 equiv) and fluorinated carboxylic acid (27.4 mmol, 1 equiv) were added dropwise at 0 °C. After stirring for 10 min at 0 °C, the aniline (27.4 mmol, 1 equiv) was added. The mixture was refluxed on an oil bath for 4 h and then cooled at room temperature, and then filtered under reduced pressure. The filtrate was concentrated under vacuum, and the resulting residue was purified by flash chromatography on silica gel with petroleum ether. Then, Trimethylsulfoxonium iodide (30 mmol, 3.0 equiv) was suspended in THF (150 mL) in a 250 mL round bottom flask, ^{t}BuOK (30 mmol, 3.0 equiv) was added and the mixture was stirred at room temperature for 2 hours. After, fluorinated acetimidoyl chloride (10 mmol, 1.0 equiv) was added. The mixture was stirred at room temperature for 3 hours and then filtered through a plug of celite before all volatiles were removed under vacuum. Purification by flash chromatography (DCM/MeOH = 100 : 1) afforded products.

2.3 Procedure for the Synthesis of 3



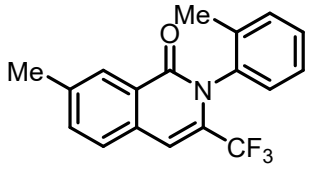
A dried 10 mL Schlenk tube was charged with **3-methylbenzoic acid 1a** (13.6 mg, 0.1 mmol, 1 equiv), **sulfoxonium ylide 2** (0.15 mmol, 1.5 equiv), [Ru(*p*-cymene)Cl_2]$_2$ (1.6 mg, 2.5 mol%), NEt_3 (20.2 mg, 0.2 mmol, 2.0 equiv), $AgSbF_6$ (3.4 mg, 20 mol%) and CH_3CN (1 mL). The reaction mixture was heated to 100 °C on a heating plate for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane to give the corresponding products.



3a

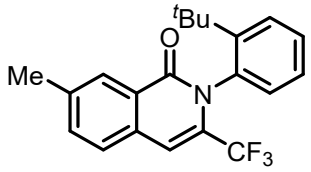
7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3a**) (22.2 mg, 73%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.58 (d, *J* = 1.9 Hz, 2H), 7.50 (dd, *J* = 6.9, 4.6 Hz, 3H), 7.30 (d, *J* = 6.9 Hz, 2H), 7.10 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.7, 140.1, 137.2, 134.7, 131.8, 129.8 (q, *J* =

32.6 Hz), 129.5, 129.2, 129.0, 128.2, 127.4, 127.1, 120.2 (q, J = 273.0 Hz), 107.7 (q, J = 6.1 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{13}F_3NO^+$: 304.0944 $(M + H)^+$, found: 304.0947. m.p. 143-144 °C. IR (KBr): ν = 3093, 3066, 3043, 2926, 1660, 1501, 1490, 1315, 886 cm^{-1}.



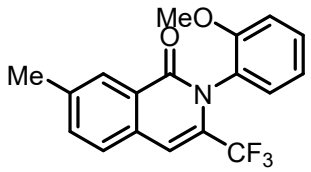
3b

7-methyl-2-(o-tolyl)-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3b**) (19.7 mg, 62%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as Light grey solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.26 (s, 1H), 7.59 (s, 2H), 7.41 – 7.37 (m, 1H), 7.35 (d, J = 6.9 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.21 (d, J = 7.8 Hz, 1H), 7.14 (s, 1H), 2.53 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.9, 140.0, 137.2, 136.2, 134.7, 131.9, 130.6, 129.5 (q, J = 32.4 Hz), 129.45, 129.39, 128.2, 127.4, 127.0, 126.5, 120.1 (q, J = 273.0 Hz), 108.0 (q, J = 6.1 Hz), 21.7, 17.4; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO^+$: 318.1100 $(M + H)^+$, found: 318.1096. m.p. 134-135 °C. IR (KBr): ν = 3093, 3033, 2941, 2925, 1658, 1503, 1492, 1315, 890 cm^{-1}.



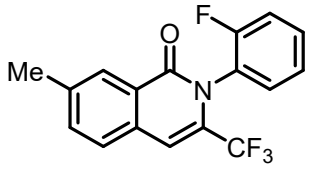
3c

2-(2-(*tert*-butyl)phenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3c**) (13.3 mg, 37%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.26 (s, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.58 (s, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.13 (s, 1H), 7.03 (d, J = 7.8 Hz, 1H), 2.53 (s, 3H), 1.22 (s, 9H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.4, 147.8, 140.1, 134.7, 133.8, 131.8, 131.5, 130.4 (q, J = 31.7 Hz), 130.1, 129.3, 128.3, 127.4, 126.9, 126.3, 120.2 (q, J = 273.3 Hz), 107.8 (q, J = 6.2 Hz), 36.7, 31.7, 21.6; HRMS (ESI-TOF) m/z: calcd for $C_{21}H_{21}F_3NO^+$: 360.1570 $(M + H)^+$, found: 360.1573. m.p. 155-157 °C. IR (KBr): ν = 3090, 2995, 2962, 2919, 2878, 1659, 1501, 1491, 1313, 891 cm^{-1}.



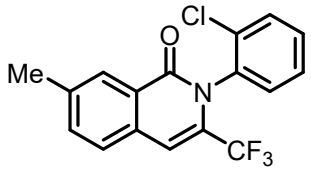
3d

2-(2-methoxyphenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3d**) (15.8 mg, 47%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 6) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.25 (s, 1H), 7.57 (s, 2H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.25 (d, *J* = 5.6 Hz, 1H), 7.09 (s, 1H), 7.09 – 7.05 (m, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 3.75 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.3, 155.9, 139.7, 134.5, 132.0, 130.8, 130.6, 130.1 (q, *J* = 32.6 Hz), 128.2, 127.3, 127.0, 125.9, 120.4, 120.1 (q, *J* = 272.9 Hz), 111.6, 107.6 (q, *J* = 5.9 Hz), 55.7, 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{14}F_3NO_2K^+$: 372.0608 $(M + K)^+$, found: 372.0609. m.p. 112-113 °C. IR (KBr): ν = 3097, 2923, 1671, 1500, 1460, 1315, 1025, 872 cm^{-1}.



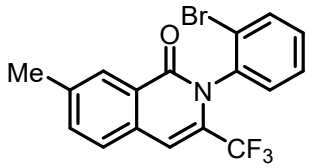
3e

2-(2-fluorophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3e**) (18.8 mg, 59%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 7.61 – 7.56 (m, 2H), 7.52 – 7.47 (m, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.28 (td, *J* = 7.1, 6.4, 1.4 Hz, 1H), 7.28 – 7.21 (m, 1H), 7.12 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.1, 158.9 (d, *J* = 252.0 Hz), 140.2, 134.9, 131.8, 131.4, 131.3, 129.4 (q, *J* = 33.0 Hz), 128.3, 127.5, 126.7, 124.9 (d, *J* = 14.0 Hz), 124.3 (d, *J* = 3.9 Hz), 120.1 (q, *J* = 272.7 Hz), 116.3 (d, *J* = 19.9 Hz), 108.2 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}F_4NO^+$: 322.0850 $(M + H)^+$, found: 322.0846. m.p. 136-137 °C. IR (KBr): ν = 3094, 2927, 1664, 1500, 1316, 1133, 889, 817 cm^{-1}.



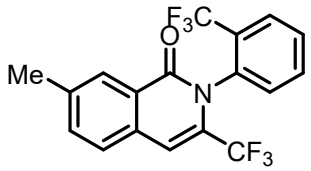
3f

2-(2-chlorophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3f**) (21.3 mg, 63%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as light yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.26 (s, 1H), 7.60 (d, *J* = 10.8 Hz, 2H), 7.58 – 7.55 (m, 1H), 7.49 – 7.44 (m, 1H), 7.44 – 7.40 (m, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.14 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.8, 140.2, 134.9, 134.2, 131.8, 131.23, 131.22, 130.7, 130.0, 129.1 (q, *J* = 33.0 Hz), 128.3, 127.6, 127.4, 126.8, 120.0 (q, *J* = 272.8 Hz), 108.2 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}ClF_3NO^+$: 338.0554 $(M + H)^+$, found: 338.0553. m.p. 123-125 °C. IR (KBr): ν = 3100, 2923, 1670, 1504, 1475, 1314, 884, 736 cm^{-1}.



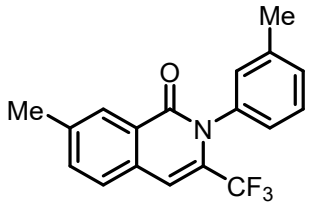
3g

2-(2-bromophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3g**) (18 mg, 47%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.27 (s, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.60 (s, 2H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 1H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.15 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.8, 140.2, 136.6, 134.9, 133.2, 131.8, 131.3, 130.8, 129.0 (q, *J* = 33.2 Hz), 128.3, 128.1, 127.6, 126.9, 124.6, 120.0 (q, *J* = 273.3 Hz), 108.3 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}BrF_3NO^+$: 382.0049 $(M + H)^+$, found: 382.0052. m.p. 140-142 °C. IR (KBr): ν = 3092, 2926, 1668, 1503, 1472, 1314, 861, 651 cm^{-1}.



3h

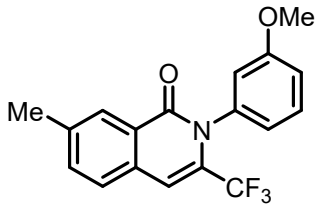
7-methyl-3-(trifluoromethyl)-2-(2-(trifluoromethyl)phenyl)isoquinolin-1(2*H*)-one (**3h**) (18.7 mg, 50%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.12 (s, 1H), 2.52 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.5, 140.3, 134.9, 134.7, 132.6, 132.0, 131.7, 129.9, 129.5 (q, *J* = 20.4 Hz), 129.3 (q, *J* = 18.6 Hz), 128.3, 127.7 (q, *J* = 4.7 Hz), 127.6, 126.6, 123.0 (q, *J* = 273.4 Hz), 120.0 (q, *J* = 272.9 Hz), 108.3 (q, *J* = 6.1 Hz), 21.6; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{12}F_6NO^+$: 372.0818 $(M + H)^+$, found: 372.0816. m.p. 132-133 °C. IR (KBr): ν = 3062, 2918, 1679, 1607, 1497, 1455, 1315, 857 cm^{-1}.



3i

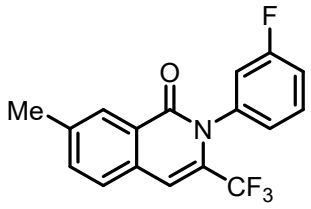
7-methyl-2-(*m*-tolyl)-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3i**) (18.2 mg, 57%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.57 (s, 2H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 3.3 Hz, 3H), 2.53 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.8, 140.0, 138.9, 137.0, 134.7, 131.8, 130.0, 130.0, 129.7 (q, *J* = 32.7 Hz), 128.7, 128.1, 127.4, 127.0, 126.4, 120.2 (q, *J* = 273.1 Hz), 107.6 (q,

J = 6.0 Hz), 21.7, 21.3; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO^+$: 318.1100 $(M + H)^+$, found: 318.1102. m.p. 117-118 °C. IR (KBr): ν = 3095, 3034, 2922, 2865, 1660, 1502, 1488, 1316, 890 cm^{-1}.



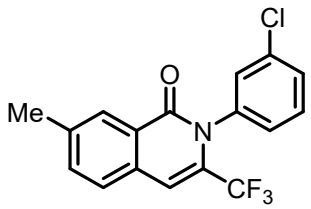
3j

2-(3-methoxyphenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3j**) (21.3 mg, 64%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 6) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 7.60 – 7.55 (m, 2H), 7.40 (t, *J* = 8.1 Hz, 1H), 7.10 (s, 1H), 7.03 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.84 (s, 1H), 3.82 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.6, 160.0, 140.1, 138.1, 134.7, 131.8, 130.0 (q, *J* = 32.7 Hz), 129.6, 128.2, 127.4, 127.0, 121.8, 120.2 (q, *J* = 273.1 Hz), 115.2, 115.2, 107.7 (q, *J* = 6.1 Hz), 55.4, 21.6; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO_2^+$: 334.1049 $(M + H)^+$, found: 334.1046. m.p. 85-86 °C. IR (KBr): ν = 3074, 3006, 2968, 2924, 1664, 1605, 1496, 1313, 1032, 856 cm^{-1}.



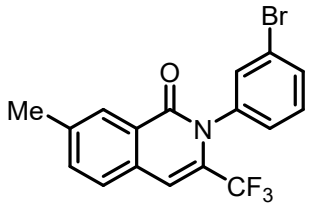
3k

2-(3-fluorophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3k**) (17.1 mg, 53%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as light yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.63 – 7.55 (m, 2H), 7.52 – 7.43 (m, 1H), 7.24 – 7.19 (m, 1H), 7.10 (d, *J* = 6.9 Hz, 2H), 7.06 (d, *J* = 9.0 Hz, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.6 (d, *J* = 248.0 Hz), 162.5, 140.3, 138.4 (d, *J* = 10.0 Hz), 134.9, 131.7, 130.1 (d, *J* = 8.8 Hz), 129.4 (q, *J* = 32.8 Hz), 128.2, 127.5, 126.9, 125.5, 120.1 (q, *J* = 273.0 Hz), 117.4 (d, *J* = 23.2 Hz), 116.5 (d, *J* = 21.0 Hz), 108.0 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}F_4NO^+$: 322.0850 $(M + H)^+$, found: 322.0854. m.p. 113-114 °C. IR (KBr): ν = 3094, 3036, 2924, 1672, 1600, 1503, 1488, 1315, 1131, 871 cm^{-1}.



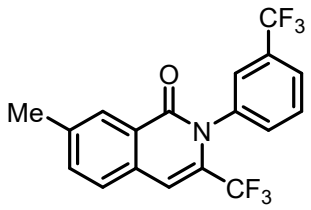
3l

2-(3-chlorophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3l**) (13.4 mg, 40%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.64 – 7.59 (m, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.49 (dt, *J* = 8.2, 1.6 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.33 (s, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.12 (s, 1H), 2.54 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.5, 140.4, 138.1, 134.9, 134.5, 131.7, 130.0, 129.9, 129.6, 129.3 (q, *J* = 32.6 Hz), 128.1, 128.0, 127.5, 126.8, 120.1 (q, *J* = 273.0 Hz), 108.0 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}ClF_3NO^+$: 338.0554 $(M + H)^+$, found: 338.0555. m.p. 150-151 °C. IR (KBr): ν = 3087, 3061, 2922, 1674, 1583, 1504, 1474, 1315, 861, 741 cm^{-1}.



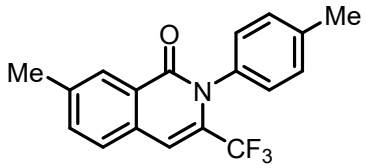
3m

2-(3-bromophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3m**) (26.7 mg, 70%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as brown solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 7.63 – 7.54 (m, 2H), 7.47 (s, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.11 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.5, 140.4, 138.3, 134.9, 132.8, 132.5, 131.7, 130.2, 129.3 (q, *J* = 32.9 Hz), 128.4, 128.2, 127.5, 126.8, 122.2, 120.1 (q, *J* = 273.0 Hz), 108.0 (q, *J* = 6.1 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}BrF_3NO^+$: 382.0049 $(M + H)^+$, found: 382.0054. m.p. 144-146 °C. IR (KBr): ν = 3088, 3060, 2943, 1675, 1506, 1471, 1316, 862, 687 cm^{-1}.



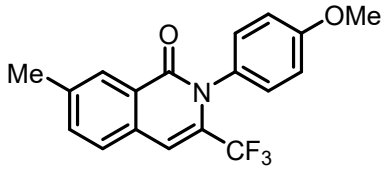
3n

7-methyl-3-(trifluoromethyl)-2-(3-(trifluoromethyl)phenyl)isoquinolin-1(2*H*)-one (**3n**) (27.9 mg, 75%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.61 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.59 (d, *J* = 4.4 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.13 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.6, 140.5, 137.7, 135.0, 133.2, 131.7 (q, *J* = 33.2 Hz), 131.7, 129.6, 129.2 (q, *J* = 32.8 Hz), 128.2, 127.6, 126.9 (q, *J* = 4.1 Hz), 126.8, 126.2 (q, *J* = 3.6 Hz), 123.5 (q, *J* = 272.5 Hz), 120.1 (q, *J* = 272.9 Hz), 108.2 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{11}F_6NOK^+$: 410.0376 $(M + K)^+$, found: 410.0374. m.p. 128-130 °C. IR (KBr): ν = 3095, 3038, 2925, 1660, 1503, 1492, 1317, 891 cm^{-1}.



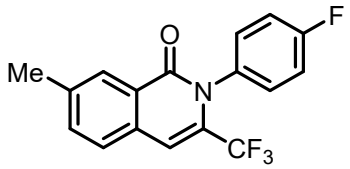
3o

7-methyl-2-(*p*-tolyl)-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3o**) (18.4 mg, 58%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.57 (s, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.09 (s, 1H), 2.52 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.8, 140.0, 139.1, 134.6, 134.4, 131.8, 129.7, 129.2 (q, *J* = 47.5 Hz), 129.1, 128.1, 127.4, 127.0, 120.2 (q, *J* = 272.8 Hz), 107.6 (q, *J* = 6.1 Hz), 21.7, 21.3; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO^+$: 318.1100 $(M + H)^+$, found: 318.1099. m.p. 169-171 °C. IR (KBr): ν = 3095, 3064, 3039, 2950, 2923, 1659, 1510, 1316, 890 cm^{-1}.



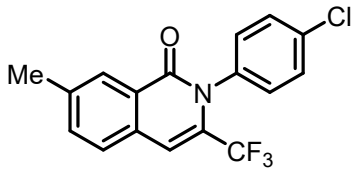
3p

2-(4-methoxyphenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3p**) (14.4 mg, 43%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 6) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 7.61 – 7.53 (m, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.09 (s, 1H), 7.00 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.0, 159.9, 140.0, 134.6, 131.8, 130.5, 130.0 (q, *J* = 32.3 Hz), 129.6, 128.2, 127.4, 127.0, 120.3 (q, *J* = 272.9 Hz), 114.2, 107.6 (q, *J* = 6.1 Hz), 55.4, 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO_2^+$: 334.1049 $(M + H)^+$, found: 334.1050. m.p. 188-189 °C. IR (KBr): ν = 3094, 3007, 2960, 2937, 1659, 1510, 1315, 1035, 896 cm^{-1}.



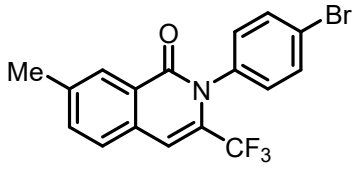
3q

2-(4-fluorophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3q**) (21 mg, 65%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as pale solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.62 – 7.56 (m, 2H), 7.28 (dd, *J* = 8.9, 5.0 Hz, 2H), 7.19 (t, *J* = 8.5 Hz, 2H), 7.11 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.8, 162.8 (d, *J* = 249.0 Hz), 140.3, 134.8, 132.9 (d, *J* = 3.0 Hz), 131.7, 131.3 (d, *J* = 8.9 Hz), 129.6 (q, *J* = 32.6 Hz), 128.1, 127.5, 126.8, 120.1 (q, *J* = 272.8 Hz), 116.1 (d, *J* = 23.0 Hz), 107.9 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}F_4NO^+$: 322.0850 $(M + H)^+$, found: 322.0847. m.p. 197-198 °C. IR (KBr): ν = 3094, 3043, 2927, 1659, 1507, 1316,1131, 892 cm^{-1}.



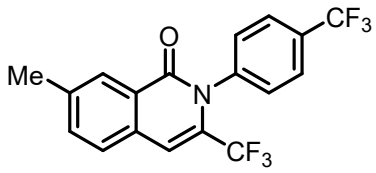
3r

2-(4-chlorophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3r**) (18.7 mg, 55%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.58 (t, *J* = 6.5 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.11 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.6, 140.3, 135.6, 135.3, 134.9, 131.7, 130.9, 129.4 (q, *J* = 32.8 Hz), 129.3, 128.1, 127.5, 126.8, 120.1 (q, *J* = 272.6 Hz), 108.0 (q, *J* = 5.9 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}ClF_3NO^+$: 338.0554 $(M + H)^+$, found: 338.0552. m.p. 198-200 °C. IR (KBr): ν = 3057, 2918, 1676, 1590, 1489, 1315, 858, 738 cm^{-1}.



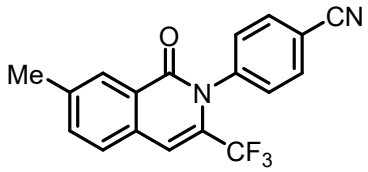
3s

2-(4-bromophenyl)-7-methyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (3s) (24.4 mg, 64%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as Light yellow powder. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.59 (q, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.11 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.6, 140.3, 136.2, 134.9, 132.3, 131.7, 131.2, 129.3 (q, *J* = 32.5 Hz), 128.1, 127.5, 126.8, 123.4, 120.1 (q, *J* = 273.0 Hz), 108.0 (q, *J* = 6.1 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}BrF_3NO^+$: 382.0049 $(M + H)^+$, found: 382.0053. m.p. 119-120 °C. IR (KBr): ν = 3098, 2918, 1663, 1503, 1487, 1315, 879, 654 cm^{-1}.



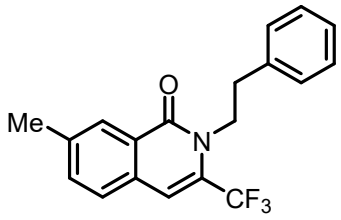
3t

7-methyl-3-(trifluoromethyl)-2-(4-(trifluoromethyl)phenyl)isoquinolin-1(2*H*)-one (**3t**) (15.1 mg, 41%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.63 – 7.57 (m, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.14 (s, 1H), 2.54 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.5, 140.5, 140.4, 135.0, 131.7, 131.5 (q, *J* = 32.8 Hz), 130.3, 129.2 (q, *J* = 32.8 Hz), 128.2, 127.6, 126.8, 126.3 (q, *J* = 3.7 Hz), 123.7 (q, *J* = 272.5 Hz), 120.1 (q, *J* = 272.9 Hz), 108.2 (q, *J* = 6.0 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{12}F_6NO^+$: 372.0818 $(M + H)^+$, found: 372.0816. m.p. 190-192 °C. IR (KBr): ν = 3060, 2925, 1678, 1609, 1505, 1315, 859 cm^{-1}.



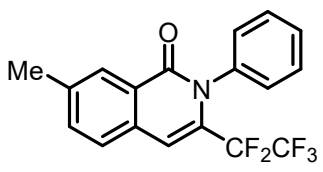
3u

4-(7-methyl-1-oxo-3-(trifluoromethyl)isoquinolin-2(1*H*)-yl)benzonitrile (**3u**) (18.1 mg, 55%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 6) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.21 (s, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.63 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.60 (d, *J* = 8.1 Hz, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 2.54 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.3, 141.4, 140.7, 135.2, 133.0, 131.6, 130.9, 128.9 (q, *J* = 32.8 Hz), 128.1, 127.7, 126.7, 120.0 (q, *J* = 273.0 Hz), 117.9, 113.5, 108.4 (q, *J* = 5.9 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{12}F_3N_2O^+$: 329.0896 $(M + H)^+$, found: 329.0899. m.p. 179-180 °C. IR (KBr): ν = 3099, 3067, 2926, 2231, 1669, 1603, 1504, 1314, 858 cm^{-1}.



3v

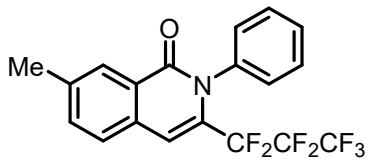
7-methyl-2-phenethyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**3v**) (14.2 mg, 43%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 20) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.29 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.39 – 7.31 (m, 4H), 7.26 (d, *J* = 7.3 Hz, 1H), 7.07 (s, 1H), 4.33 – 4.26 (m, 2H), 3.07 – 3.01 (m, 2H), 2.54 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.2, 139.9, 138.3, 134.4, 131.5, 129.0, 128.9 (q, *J* = 45.0 Hz), 128.6, 127.7, 127.3, 126.9, 126.6, 120.9 (q, *J* = 272.9 Hz), 108.2 (q, *J* = 6.6 Hz), 47.6 (q, *J* = 2.9 Hz), 34.7, 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{16}F_3NOK^+$: 370.0816 $(M + K)^+$, found: 370.0818. m.p. 83-85 °C. IR (KBr): ν = 3056, 3031, 2954, 2941, 1660, 1498, 1461, 1304, 860 cm^{-1}.



3w

7-methyl-3-(perfluoroethyl)-2-phenylisoquinolin-1(2*H*)-one (**3w**) (16.5 mg, 47%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.62 – 7.55 (m, 2H), 7.52 – 7.46 (m, 3H), 7.26 (d, *J* = 7.1 Hz, 2H), 7.02 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.1, 140.4, 137.8, 134.8, 131.7, 129.5, 129.0, 128.8, 128.1, 128.1 (t, *J* = 23.3 Hz), 127.5, 127.0, 119.6 (t, *J* = 37.5 Hz), 117.3 (t, *J* = 37.7 Hz), 110.5 (t, *J* = 6.9 Hz), 21.7;

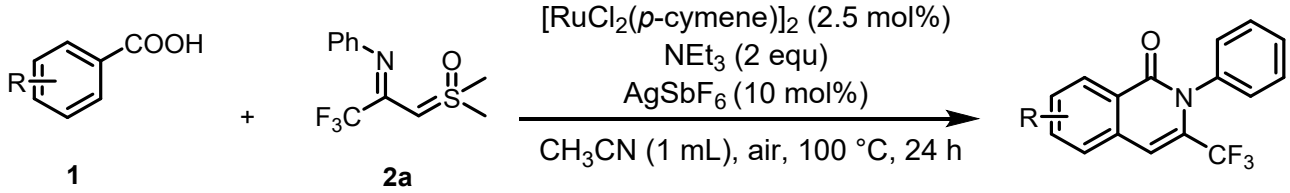
HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{13}F_5NO^+$: 354.0912 $(M + H)^+$, found: 354.0909. m.p. 152-153 °C. IR (KBr): ν = 3087, 3064, 3034, 2962, 1661, 1608, 1501, 1489, 12137, 885 cm^{-1}.



3x

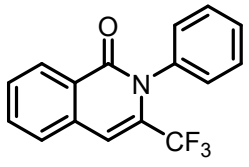
7-methyl-3-(perfluoropropyl)-2-phenylisoquinolin-1(2*H*)-one (**3x**) (16 mg, 40%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.22 (s, 1H), 7.60 (d, *J* = 1.8 Hz, 2H), 7.51 – 7.44 (m, 3H), 7.29 – 7.21 (m, 2H), 7.04 (s, 1H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.1, 140.4, 137.8, 134.8, 131.7, 129.4, 129.0, 128.8, 128.2, 127.5, 127.0, 111.2 (t, *J* = 8.8 Hz), 21.7; HRMS (ESI-TOF) m/z: calcd for $C_{19}H_{13}F_7NO^+$: 404.0880 $(M + H)^+$, found: 404.0881. m.p. 156-157 °C. IR (KBr): ν = 3086, 2928, 1655, 1596, 1502, 1489, 1226, 877 cm^{-1}.

2.4 Procedure for Synthesis of 4



1 **2a** **4**

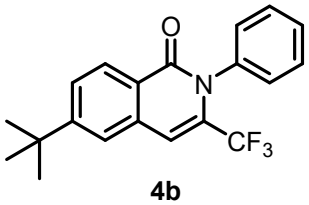
A dried 10 mL Schlenk tube was charged with **benzoic acid 1** (0.1 mmol, 1 equiv), **(*E*)-3-(dimethyl(oxo)-$^{\lambda}$6-sulfanylidene)-1,1,1-trifluoro-*N*-phenylpropan-2-imine 2a** (39.5 mg, 0.15 mmol, 1.5 equiv), [Ru(*p*-cymene)Cl_2]$_2$ (1.6 mg, 2.5 mol%), NEt_3 (20.2 mg, 0.2 mmol, 2.0 equiv), $AgSbF_6$ (3.4 mg, 20 mol%) and CH_3CN (1 mL). The reaction mixture was heated to 100 °C on a heating plate for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane to give the corresponding products.



4a

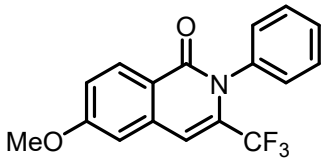
2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4a**) (16.7 mg, 58%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 8.0 Hz, 1H), 7.77 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.65 (ddd, *J* = 8.3, 7.2, 1.3

Hz, 1H), 7.56 – 7.47 (m, 3H), 7.32 – 7.29 (m, 2H), 7.14 (s, 1H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.7, 137.0, 134.2, 133.3, 130.7 (q, *J* = 32.7 Hz), 129.5, 129.3, 129.0, 128.5, 127.5, 127.2, 120.1 (q, *J* = 273.4 Hz), 107.6 (q, *J* = 6.2 Hz); HRMS (ESI-TOF) m/z: calcd for $C_{16}H_{11}F_3NO^+$: 290.0787 $(M + H)^+$, found: 290.0788. m.p. 183-184 °C. IR (KBr): ν = 3097, 1658, 1599, 1488, 1455, 1322, 764, 694 cm^{-1}.



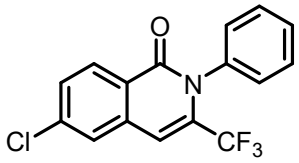
4b

6-(*tert*-butyl)-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4b**) (18.8 mg, 54%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 8.4 Hz, 1H), 7.71 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.64 (s, 1H), 7.50 (d, *J* = 6.9 Hz, 3H), 7.29 (d, *J* = 7.2 Hz, 2H), 7.14 (s, 1H), 1.42 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.6, 157.2, 137.1, 134.2, 130.5 (q, *J* = 32.4 Hz), 129.5, 129.2, 129.0, 128.3, 127.6, 124.8, 123.7, 120.2 (d, *J* = 273.1 Hz), 108.1 (q, *J* = 6.0 Hz), 35.3, 31.1; HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{19}F_3NO^+$: 346.1413 $(M + H)^+$, found: 346.1418. m.p. 103-105 °C. IR (KBr): ν = 3066, 2964, 2869 1675, 1605, 1490, 1304, 889 cm^{-1}.



4c

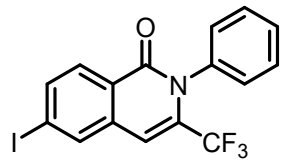
6-methoxy-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4c**) (15.3 mg, 48%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 6) as brown yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 8.8 Hz, 1H), 7.54 – 7.46 (m, 3H), 7.30 (dd, *J* = 7.1, 1.2 Hz, 2H), 7.19 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.05 (s, 1H), 7.03 (d, *J* = 2.5 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.5, 162.4, 137.1, 136.3, 131.3 (q, *J* = 32.6 Hz), 130.6, 129.6, 129.2, 129.0, 120.7, 120.1 (q, *J* = 273.4 Hz), 118.5, 108.7, 107.3 (q, *J* = 6.1 Hz), 55.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{13}F_3NO_2^+$: 320.0893 $(M + H)^+$, found: 320.0898. m.p. 171-172 °C. IR (KBr): ν = 3047, 2928, 1675, 1605, 1488, 1307, 1016, 862 cm^{-1}.



4d

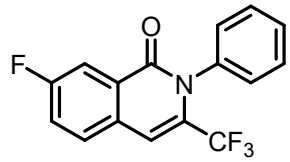
6-chloro-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4d**) (13.5 mg, 42%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as pale solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.37

(d, J = 8.5 Hz, 1H), 7.66 (d, J = 2.0 Hz, 1H), 7.58 (dd, J = 8.6, 2.1 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.31 – 7.28 (m, 2H), 7.04 (s, 1H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.1, 139.9, 136.7, 135.5, 132.1 (q, J = 32.4 Hz), 130.4, 130.0, 129.4, 129.4, 129.1, 126.8, 125.4, 119.9 (q, J = 273.6 Hz), 106.4 (q, J = 6.1 Hz); HRMS (ESI-TOF) m/z: calcd for $C_{16}H_{10}ClF_3NO^+$: 324.0398 $(M + H)^+$, found: 324.0399. m.p. 178-180 °C. IR (KBr): ν = 3092, 3070, 3047, 1663, 1595, 1489, 1294, 857, 732 cm^{-1}.



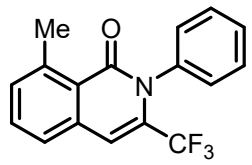
4e

6-iodo-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4e**) (17.3 mg, 42%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as light yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.11 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 1.6 Hz, 1H), 7.94 (dd, J = 8.4, 1.7 Hz, 1H), 7.51 (dd, J = 5.2, 2.0 Hz, 3H), 7.30 – 7.27 (m, 2H), 7.01 (s, 1H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.5, 138.5, 136.7, 136.2, 135.6, 131.8 (q, J = 32.9 Hz), 130.0, 129.4, 129.3, 129.1, 126.3, 119.9 (q, J = 273.7 Hz), 106.1 (q, J = 5.8 Hz), 101.0; HRMS (ESI-TOF) m/z: calcd for $C_{16}H_{10}IF_3NO^+$: 415.9754 $(M + H)^+$, found: 415.9753. m.p. 157-158 °C. IR (KBr): ν = 3082, 3059, 1671, 1585, 1488, 1294, 886, 532 cm^{-1}.



4f

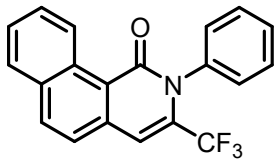
7-fluoro-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4f**) (15.5 mg, 50%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (d, J = 8.0 Hz, 1H), 7.60 (td, J = 8.0, 5.2 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.47 (ddd, J = 9.3, 8.0, 1.1 Hz, 1H), 7.36 (s, 1H), 7.32 – 7.28 (m, 2H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.8, 158.4 (d, J = 254.3 Hz), 136.8, 131.3 (q, J = 32.5 Hz), 130.0 (d, J = 8.0 Hz), 129.4, 129.4, 129.1, 128.6 (d, J = 2.7 Hz), 124.2 (d, J = 3.9 Hz), 123.7 (d, J = 16.0 Hz), 119.9 (q, J = 273.6 Hz), 118.4 (d, J = 19.6 Hz), 100.3 (q, J = 6.1 Hz); HRMS (ESI-TOF) m/z: calcd for $C_{16}H_{10}F_4NO^+$: 308.0693 $(M + H)^+$, found: 308.0690. m.p. 122-124 °C. IR (KBr): ν = 3057, 1676, 1591, 1491, 1481, 1300, 1138, 853 cm^{-1}.



4g

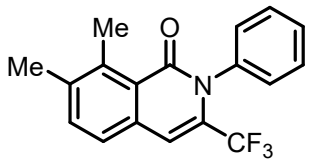
8-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4g**) (18.8 mg, 62%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ

7.59 (t, J = 7.7 Hz, 1H), 7.55 – 7.44 (m, 4H), 7.40 (d, J = 7.4 Hz, 1H), 7.30 (dd, J = 7.2, 1.2 Hz, 2H), 7.04 (s, 1H), 2.87 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.5, 142.9, 137.3, 136.0, 132.7, 132.5, 130.3 (q, J = 32.9 Hz), 129.6, 129.1, 129.1, 125.9, 125.4, 120.0 (q, J = 273.1 Hz), 108.0 (q, J = 6.1 Hz), 23.7; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{13}F_3NO^+$: 304.0944 $(M + H)^+$, found: 304.0943. m.p. 158-159 °C. IR (KBr): ν = 3095, 3067, 3042, 2924, 1665, 1594, 1491, 1474, 1300, 875 cm^{-1}.



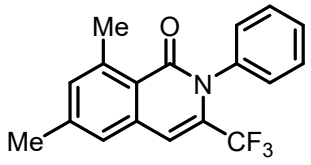
4h

2-phenyl-3-(trifluoromethyl)benzo[h]isoquinolin-1(2*H*)-one (**4h**) (19.9 mg, 59%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as light yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.07 (d, J = 8.1 Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.95 (dd, J = 7.9, 1.6 Hz, 1H), 7.72 (ddd, J = 8.7, 6.9, 1.6 Hz, 1H), 7.67 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.60 – 7.51 (m, 3H), 7.36 (d, J = 6.6 Hz, 2H), 7.24 (s, 1H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.1, 137.4, 136.3, 135.0, 133.6, 131.6, 131.4 (q, J = 33.0 Hz), 129.5, 129.3, 129.1, 129.0, 128.5, 127.6, 127.5, 124.8, 121.4, 120.0 (q, J = 273.4 Hz), 107.7 (q, J = 5.7 Hz); HRMS (ESI-TOF) m/z: calcd for $C_{20}H_{13}F_3NO^+$: 340.0944 $(M + H)^+$, found: 340.0944. m.p. 176-177 °C. IR (KBr): ν = 3067, 1666, 1600, 1488, 1290, 857, 748 cm^{-1}.



4i

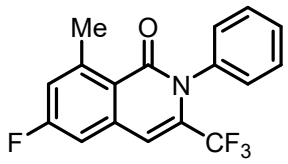
7,8-dimethyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4i**) (22.4 mg, 71%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 15) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 – 7.45 (m, 4H), 7.39 (d, J = 7.9 Hz, 1H), 7.29 (d, J = 7.2 Hz, 2H), 7.01 (s, 1H), 2.83 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.8, 141.0, 139.3, 137.6, 134.9, 134.1, 129.7, 129.5 (q, J = 32.8 Hz), 129.0 (d, J = 2.1 Hz), 125.3, 125.1, 120.1 (q, J = 272.7 Hz), 108.2 (q, J = 6.0 Hz), 21.4, 17.8; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO^+$: 318.1100 $(M + H)^+$, found: 318.1101. m.p. 148-149 °C. IR (KBr): ν = 3073, 2925, 1670, 1593, 1491, 1302, 860 cm^{-1}.



4j

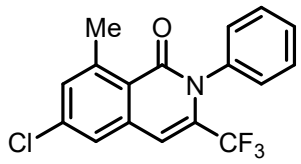
6,8-dimethyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4j**) (23.4 mg, 74%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 15) as light yellow solid. ^{1}H NMR (500 MHz,

Chloroform-*d*) δ 7.54 – 7.45 (m, 3H), 7.31 – 7.26 (m, 33H), 7.22 (s, 1H), 6.98 (s, 1H), 2.83 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 163.4, 143.2, 142.7, 137.4, 136.1, 134.1, 130.3 (q, *J* = 32.5 Hz), 129.7, 129.0, 125.8, 123.1, 120.1 (q, *J* = 272.9 Hz), 107.9 (q, *J* = 5.9 Hz), 23.5, 21.4; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO^+$: 318.1100 $(M + H)^+$, found: 318.1098. m.p. 153-154 °C. IR (KBr): ν = 3100, 3067, 2923, 1669, 1608, 1492, 1301, 862 cm^{-1}.



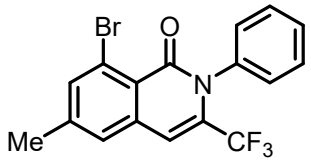
4k

6-fluoro-8-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4k**) (19.3 mg, 60%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 15) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 – 7.47 (m, 3H), 7.29 (d, *J* = 7.1 Hz, 2H), 7.12 (td, *J* = 8.6, 8.2, 2.6 Hz, 2H), 6.98 (s, 1H), 2.86 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.3 (d, *J* = 254.4 Hz), 162.8, 147.1 (d, *J* = 9.6 Hz), 138.4 (d, *J* = 10.7 Hz), 137.0, 131.6 (q, *J* = 32.7 Hz), 129.6, 129.2, 129.1, 122.1 (d, *J* = 1.7 Hz), 120.4 (d, *J* = 22.2 Hz), 119.9 (q, *J* = 273.4 Hz), 110.9 (d, *J* = 21.6 Hz), 107.2 (q, *J* = 5.9, 3.4 Hz), 23.9; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}F_4NO^+$: 322.0850 $(M + H)^+$, found: 322.0853. m.p. 169-170 °C. IR (KBr): ν = 3096, 3072, 2925, 1670, 1601, 1489, 1301, 1129, 758 cm^{-1}.



4l

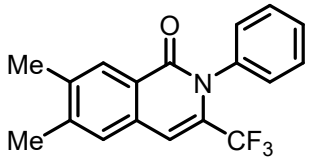
6-chloro-8-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4l**) (19.7 mg, 58%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 15) as yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.56 – 7.47 (m, 3H), 7.47 (d, *J* = 2.1 Hz, 1H), 7.37 (d, *J* = 1.2 Hz, 1H), 7.28 (dd, *J* = 6.9, 1.4 Hz, 2H), 6.95 (s, 1H), 2.83 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.9, 145.2, 138.6, 137.3, 137.0, 132.5, 131.6 (q, *J* = 32.9 Hz), 129.5, 129.3, 129.1, 125.0, 123.8, 119.8 (q, *J* = 273.5 Hz), 106.9 (q, *J* = 5.9 Hz), 23.6; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}ClF_3NO^+$: 338.0554 $(M + H)^+$, found: 338.0550. m.p. 161-162 °C. IR (KBr): ν = 3089, 3069, 2926, 1670, 1583, 1491, 1294, 894, 733 cm^{-1}.



4m

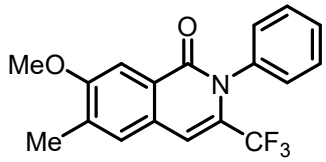
8-bromo-6-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4m**) (16 mg, 42%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 15) as light yellow solid. ^{1}H NMR (500 MHz,

Chloroform-*d*) δ 7.74 (s, 1H), 7.52 – 7.46 (m, 3H), 7.38 (s, 1H), 7.28 (d, *J* = 7.2 Hz, 2H), 6.97 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 160.9, 144.3, 137.8, 137.2, 136.9, 131.3 (q, *J* = 32.8 Hz), 129.6, 129.2, 129.0, 127.5, 123.8, 122.2, 119.8 (q, *J* = 273.4 Hz), 107.0 (q, *J* = 6.0 Hz), 21.1; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}BrF_3NO^+$: 382.0049 $(M + H)^+$, found: 382.0047. m.p. 172-173 °C. IR (KBr): ν = 3067, 2921, 1671, 1604, 1488, 1293, 867, 685 cm^{-1}.



4n

6,7-dimethyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4n**) (22.6 mg, 71%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 15) as Light yellow solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.17 (s, 1H), 7.53 – 7.45 (m, 3H), 7.42 (s, 1H), 7.29 (d, *J* = 7.1 Hz, 2H), 7.04 (s, 1H), 2.43 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.6, 143.4, 139.4, 137.3, 132.3, 129.8 (q, *J* = 32.3 Hz), 129.5, 129.1, 128.9, 128.6, 127.8, 125.1, 120.2 (q, *J* = 273.0 Hz), 107.4 (q, *J* = 6.1 Hz), 20.2, 20.0; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO^+$: 318.1100 $(M + H)^+$, found: 460.1097. m.p. 126-128 °C. IR (KBr): ν = 3058, 2920, 2856, 1672, 1593, 1489, 1300, 881 cm^{-1}.



4o

7-methoxy-6-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**4o**) (25.1 mg, 75%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.76 (s, 1H), 7.55 – 7.46 (m, 3H), 7.43 (s, 1H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.05 (s, 1H), 3.95 (s, 3H), 2.38 (s, 4H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.5, 159.5, 137.4, 134.9, 129.5, 129.1, 129.1, 128.9, 128.3 (q, *J* = 32.6 Hz), 127.8, 126.7, 120.4 (q, *J* = 272.6 Hz), 107.5 (q, *J* = 6.1 Hz), 106.7, 55.8, 16.8; HRMS (ESI-TOF) m/z: calcd for $C_{18}H_{15}F_3NO_2^+$: 334.1049 $(M + H)^+$, found: 334.1049. m.p. 168-169 °C. IR (KBr): ν = 3065, 3045, 2960, 2925, 1663, 1592, 1505, 1490, 1302, 1011, 893 cm^{-1}.

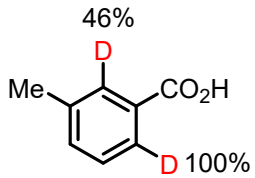
2.5 Procedure for the Gram-Scale Synthesis of 3a

A dried 100 mL Schlenk tube was charged with **3-methylbenzoic acid 1a** (680.8 mg, 5 mmol, 1 equiv), **(*E*)-3-(dimethyl(oxo)-$^{\lambda}$6-sulfanylidene)-1,1,1-trifluoro-*N*-phenylpropan-2-imine 2a** (1.97 g, 7.5 mmol, 1.5 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (76.5 mg, 2.5 mol%), NEt_3 (1.01 g, 10 mmol, 2 equiv), $AgSbF_6$ (171.8 mg, 20 mol%), and CH_3CN (50 mL). The reaction mixture was heated to 100 °C on an oil bath for 24 hours under vigorous stirring. Upon completion, the reaction

mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by flash chromatography on silica gel with ethyl acetate/hexane (1 : 20) to give the corresponding products **7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one** (**3a**) (1.016 g, 67%) as a brown solid.

2.6 Procedure for the Synthesis of D-1a

A dried 10 mL Schlenk tube was charged with **3-methylbenzoic acid 1a** (13.6 mg, 0.1 mmol, 1 equiv), [Ru(*p*-cymene)Cl_2]$_2$ (1.6 mg, 2.5 mol%), NEt_3 (20.2 mg, 0.2 mmol, 2.0 equiv), $AgSbF_6$ (3.4 mg, 20 mol%), CD_3OD (0.1 mL) and CH_3CN (1 mL). The reaction mixture was heated to 100 °C on a heating plate for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane (1:10) to give the corresponding products.

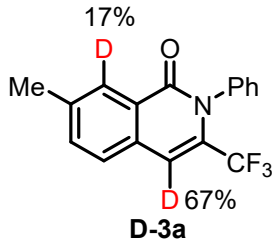


D-1a

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 9.5 Hz, 0.54H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.35 (m, 1H), 2.43 (s, 3H).

2.7 Procedure for the Synthesis of D-3a

A dried 10 mL Schlenk tube was charged with **3-methylbenzoic acid 1a** (13.6 mg, 0.1 mmol, 1 equiv), **(*E*)-3-(dimethyl(oxo)-$^{\lambda}$6-sulfanylidene)-1,1,1-trifluoro-*N*-phenylpropan-2-imine 2a** (39.5 mg, 0.15 mmol, 1.5 equiv), [Ru(*p*-cymene)Cl_2]$_2$ (1.6 mg, 2.5 mol%), NEt_3 (20.2 mg, 0.2 mmol, 2.0 equiv), $AgSbF_6$ (3.4 mg, 20 mol%), CD_3OD (0.1 mL) and CH_3CN (1 mL). The reaction mixture was heated to 100 °C on a heating plate for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane (1:20) to give the corresponding products.

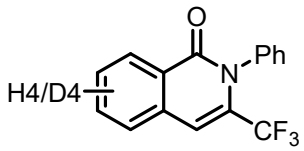


D-3a

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 0.83H), 7.58 (d, *J* = 1.8 Hz, 2H), 7.53 – 7.46 (m, 3H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.11 (s, 0.33H), 2.53 (s, 3H).

2.8 Kinetic Isotope Effect Experiment

A dried 10 mL Schlenk tube was charged with **benzoic acid 1b** (6.1 mg, 0.05 mmol), **D5-benzoic acid** (6.4 mg, 0.05 mmol), **(*E*)-3-(dimethyl(oxo)-λ^6-sulfanylidene)-1,1,1-trifluoro-*N*-phenylpropan-2-imine 2a** (39.5 mg, 0.15 mmol, [Ru(*p*-cymene)Cl_2]$_2$ (1.6 mg, 2.5 mol%), NEt_3 (20.2 mg, 0.2 mmol, 2.0 equiv), $AgSbF_6$ (3.4 mg, 20 mol%), and CH_3CN (1 mL). The reaction mixture was heated to 100 °C on a heating plate for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane (1:20) to give the corresponding products.



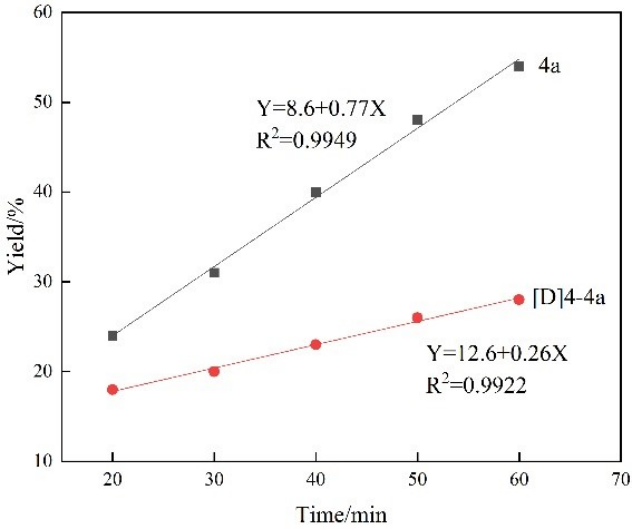
4a/4a-D4

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 7.9 Hz, 0.69H), 7.81 – 7.74 (m, 0.75H), 7.70 – 7.63 (m, 1.5H), 7.55 – 7.48 (m, 3H), 7.31 (d, *J* = 5.5 Hz, 2H), 7.14 (d, *J* = 1.7 Hz, 1H).

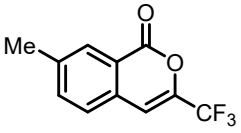
Intermolecular Kinetic Isotope Effect Experiment

Five parallel independent reactions of **1b** or **[D]$_5$-1b** with **2a**, respectively, were performed to determine the corresponding KIE value. **1b** (6.1 mg, 0.05 mmol) or **[D]$_5$-1b** (6.4 mg, 0.05 mmol), **2a** (19.7 mg, 0.15 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (0.8 mg, 2.5 mol%), $AgSbF_6$ (1.7 mg, 10 mol%), NEt_3 (10.1 mg, 2.0 equiv), and CH_3CN (0.5 mL) were placed in a 25 mL Schlenk flask under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, Then ^{1}H NMR conversions were obtained by the use of CH_2Br_2 as the standard.

Time / yield	20 min	30 min	40 min	50 min	60 min
4a	24%	31%	40%	48%	54%
[D]$_4$-4a	18%	20%	23%	26%	28%



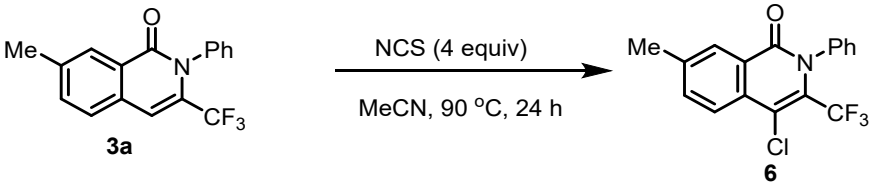
$k_H/k_D = 3$



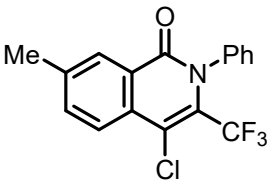
5

Compound **5** was synthesized according to literature.[2] ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 7.63 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 6.97 (s, 1H), 2.52 (s, 3H).

2.9 Synthetic Applications of 3a

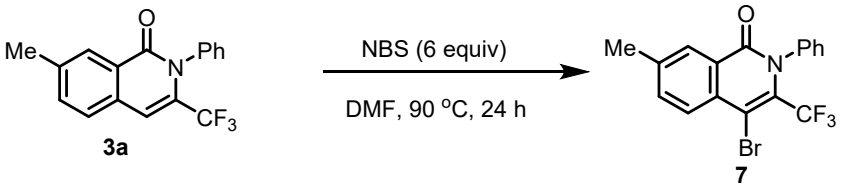


A dried 10 mL Schlenk tube was charged with **7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one 3a** (30.3 mg, 0.1 mmol, 1 equiv), *N*-Chlorosuccinimide (53.4 mg, 0.4 mmol, 4 equiv), and CH_3CN (0.4 mL). The reaction mixture was heated to 90 °C on a heating plate for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane (1:20) to give the corresponding products.

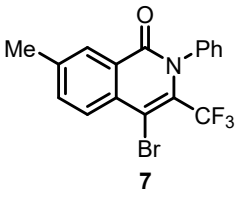


6

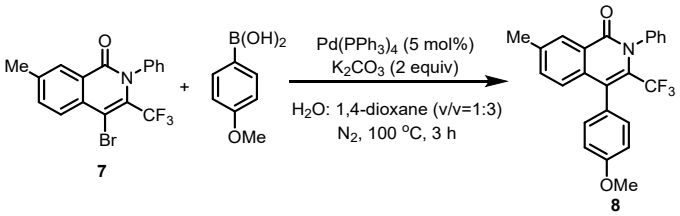
4-chloro-7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**6**) (10.4 mg, 31%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as brown solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 8.11 (d, *J* = 8.3 Hz, 1H), 7.69 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.52 – 7.44 (m, 3H), 7.28 (d, *J* = 7.2 Hz, 2H), 2.54 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.5, 141.3, 138.7, 135.2, 131.4, 128.9, 128.8, 128.7 (d, *J* = 1.8 Hz), 128.4, 127.0 (q, *J* = 31.4 Hz), 126.5, 125.4, 120.5 (q, *J* = 277.2 Hz), 116.5 (q, *J* = 2.3 Hz), 21.5; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}ClF_3NO^+$: 338.0554 (M + H)$^+$, found: 338.0550. m.p. 151-153 °C. IR (KBr): ν = 3083, 3064, 2923, 1672, 1585, 1488, 1295, 843, 739 cm^{-1}.



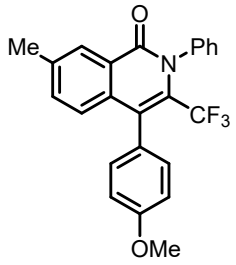
A dried 10 mL Schlenk tube was charged with **7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one 3a** (30.3 mg, 0.1 mmol, 1 equiv), *N*-Bromosuccinimide (106.8 mg, 0.6 mmol, 6 equiv), and DMF (0.5 mL). The reaction mixture was heated to 90 °C on a heating plate for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane (1:20) to give the corresponding products.



4-bromo-7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**7**) (17.4 mg, 46%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 10) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.67 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.52 – 7.43 (m, 3H), 7.28 (d, *J* = 7.4 Hz, 2H), 2.54 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 161.7, 141.2, 139.0, 135.3, 132.4, 128.9, 128.8, 128.6 (q, *J* = 31.4 Hz), 128.5 (d, *J* = 1.7 Hz), 128.4, 128.3, 126.5, 120.4 (q, *J* = 277.6 Hz), 105.8 (q, *J* = 2.8 Hz), 21.4; HRMS (ESI-TOF) m/z: calcd for $C_{17}H_{12}BrF_3NO^+$: 382.0049 (M + H)$^+$, found: 382.0050. m.p. 170-171 °C. IR (KBr): ν = 3067, 3042, 2919, 1676, 1577, 1486, 1290, 818, 672 cm^{-1}.

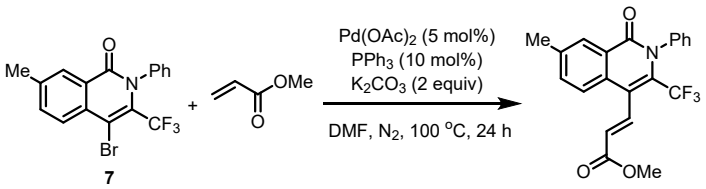


A dried 10 mL Schlenk tube was charged with **4-bromo-7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one** (**7**) (38.2 mg, 0.1 mmol, 1 equiv), (4-methoxyphenyl)boronic acid (22.8 mg, 0.15 mmol, 1.5 equiv), $Pd(PPh_3)_4$ (5.8 mg, 5 mol%), K_2CO_3 (27.6 mg, 0.2 mmol, 2 equiv), and dissolved in 1 mL mixture of water and 1,4-dioxane (1:3). The reaction mixture was heated to 100 °C on a heating plate for 3 hours under N_2. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane (1:4) to give the corresponding products.



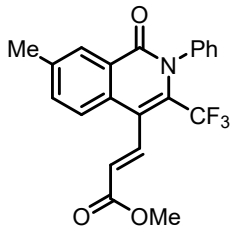
8

4-(4-methoxyphenyl)-7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one (**8**) (23.4 mg, 57%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 4) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.28 (s, 1H), 7.53 – 7.45 (m, 3H), 7.43 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.36 (d, *J* = 7.7 Hz, 2H), 7.25 – 7.21 (m, 2H), 7.08 – 6.98 (m, 3H), 3.89 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 162.4, 159.4, 139.9, 138.6, 134.6, 134.3, 131.0 (d, *J* = 2.2 Hz), 129.4 (d, *J* = 1.8 Hz), 128.7, 128.7, 127.9, 127.4, 127.0, 126.8 (q, *J* = 29.5 Hz), 126.5, 122.5 (q, *J* = 3.1 Hz), 120.9 (q, *J* = 277.0 Hz), 113.8, 55.3, 21.4; HRMS (ESI-TOF) m/z: calcd for $C_{24}H_{19}F_3NO_2^+$: 410.1362 $(M + H)^+$, found: 410.1363. m.p. 184-185 °C. IR (KBr): ν = 3066, 3043, 2962, 2920, 1663, 1591, 1509, 1320,1038, 840 cm^{-1}.



7 **9**

A dried 10 mL Schlenk tube was charged with **4-bromo-7-methyl-2-phenyl-3-(trifluoromethyl)isoquinolin-1(2*H*)-one** (**7**) (38.2 mg, 0.1 mmol, 1 equiv), methyl acrylate (17.2 mg, 0.2 mmol, 2 equiv), $Pd(OAc)_2$ (1.1 mg, 5 mol%), PPh_3 (2.6 mg, 10 mol%), K_2CO_3 (27.6 mg, 0.2 mmol, 2 equiv), and DMF (1 mL). The reaction mixture was heated to 100 °C on a heating plate for 24 hours under N_2. Upon completion, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and filtered through a pad of celite. The filtrate was concentrated under vacuum, and the resulting residue was purified by preparative thin layer chromatography (PTLC) with ethyl acetate : hexane (1:4) to give the corresponding products.



9

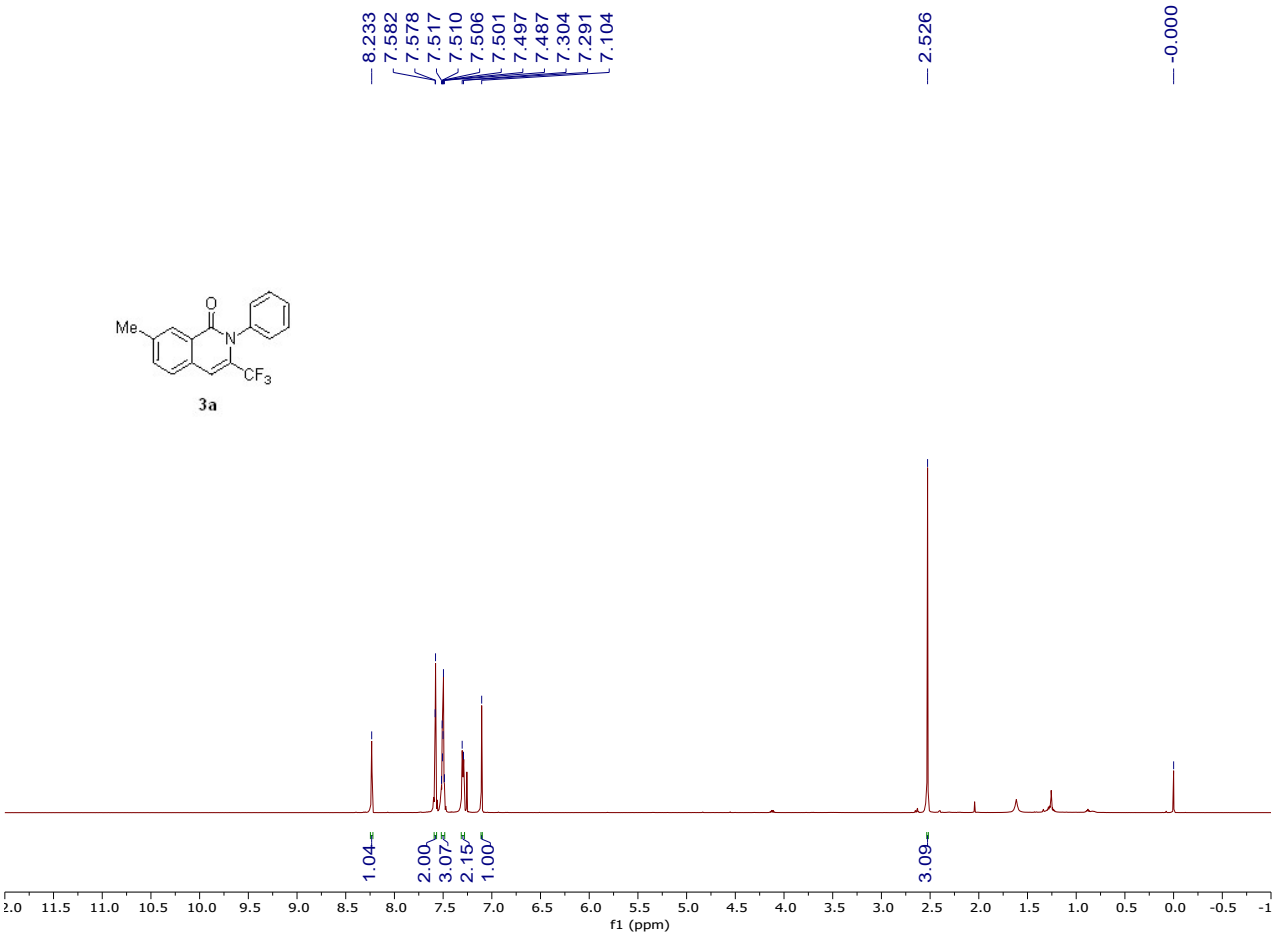
methyl (*E*)-3-(7-methyl-1-oxo-2-phenyl-3-(trifluoromethyl)-1,2-dihydroisoquinolin-4-yl)acrylate (**9**) (33.2 mg, 86%) was prepared from typical procedure (ethyl acetate: hexane = 1 : 4) as white solid. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.28 (s, 1H), 7.88 (dq, *J* = 16.2, 4.4 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.58 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.30 (d, *J* = 7.4 Hz, 2H), 6.17 (d, *J* = 16.2 Hz, 1H), 3.86 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 165.9, 161.9, 140.5, 138.6, 137.9, 134.7, 131.6, 129.2 (d, *J* = 1.8 Hz), 128.9, 128.8, 128.5, 127.0 (q, *J* = 3.3 Hz), 126.6 (q, *J* = 30.7 Hz), 126.5, 125.9, 120.7 (q, *J* = 276.7 Hz), 116.6 (q, *J* = 2.5 Hz), 52.0, 21.5; HRMS (ESI-TOF) m/z: calcd for $C_{21}H_{17}F_3NO_3^+$: 388.1155 $(M + H)^+$, found: 388.1150. m.p. 191-192 °C. IR (KBr): ν = 3052, 2949, 2923, 1720, 1672, 1588, 1500, 1488, 1319, 1078, 879 cm^{-1}.

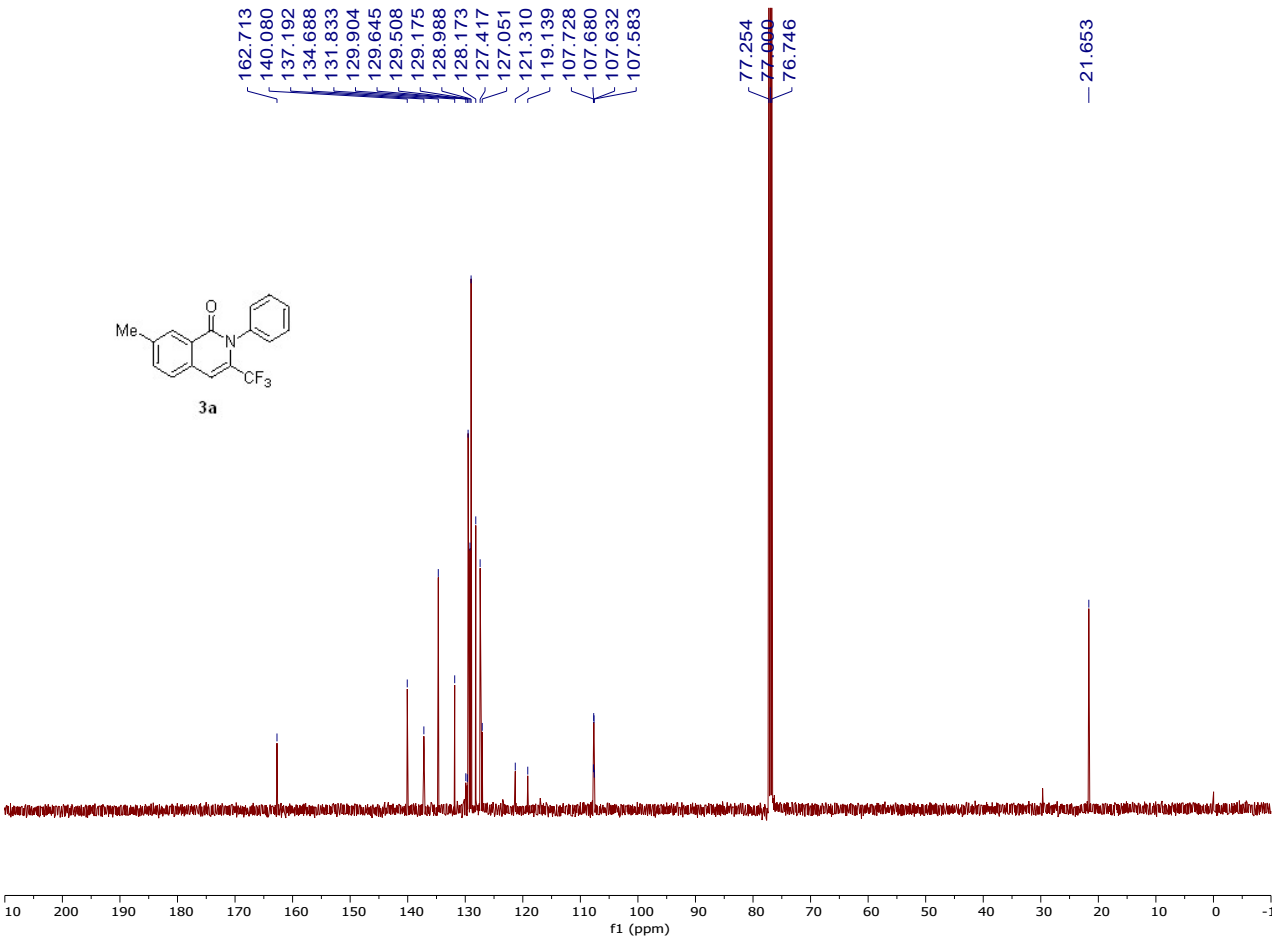
Reference

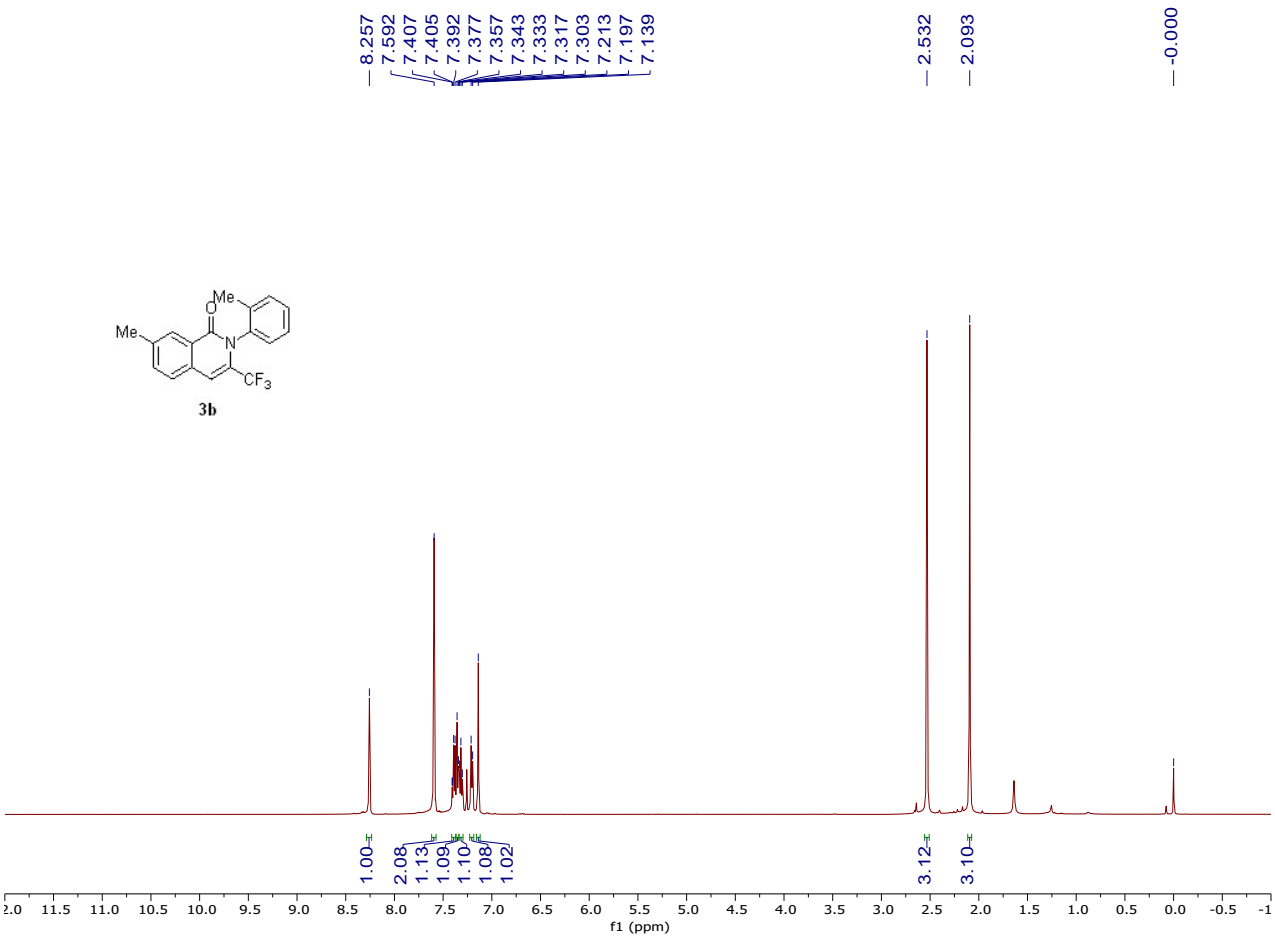
1 (*a*) S. Wen, Q. Tian, Y. Chen, Y. Zhang and G. Cheng, Annulation of CF_3-Imidoyl Sulfoxonium Ylides with 1,3-Dicarbonyl Compounds: Access to 1,2,3-Trisubstituted 5-Trifluoromethylpyrroles. *Org. Lett.*, 2021, **23**, 7407-7411; (*b*) S. Wen, Y. Chen, Q. Tian, Y. Zhang and G. Cheng, Transition-Metal-, Additive-, and Solvent-Free [3+3] Annulation of RCF_2-Imidoyl Sulfoxonium Ylides with Cyclopropenones to Give Multifunctionalized CF_3-Pyridones. *J. Org. Chem.* **2022**, *87*, 1124–1132.

2 K. Zhou, J. Geng, D. Wang, J. Zhang and Y. Zhao, An Indirect Strategy for Trifluoromethylation via an Iridium Catalyst: Approach to Generate Isocoumarin Skeletons in Bioactive Molecules. *Org. Lett.*, 2020, **22**, 5109-5114.

3. ^{1}H and ^{13}C NMR Spectra



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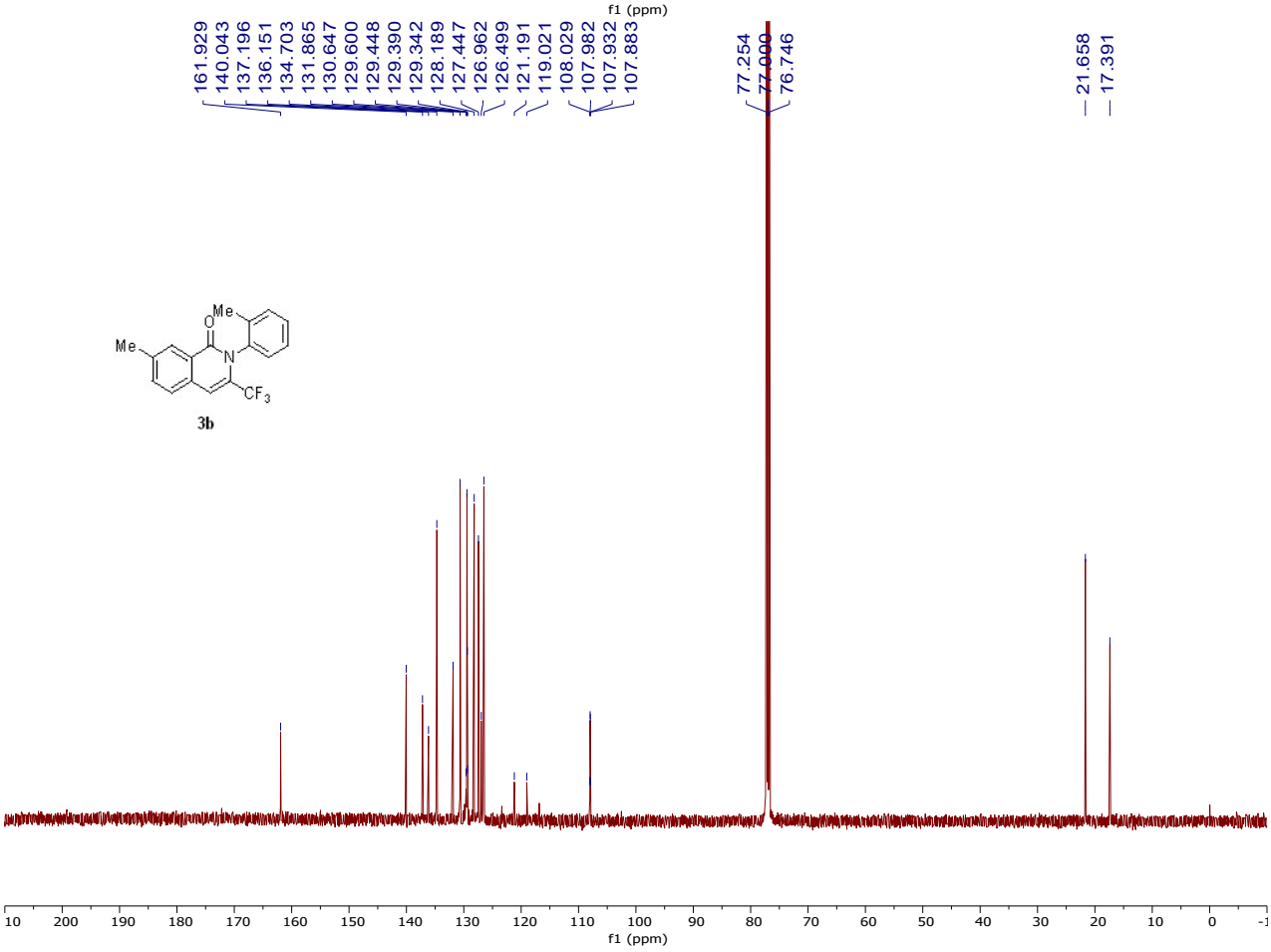
3.12
3.10
f1 (ppm)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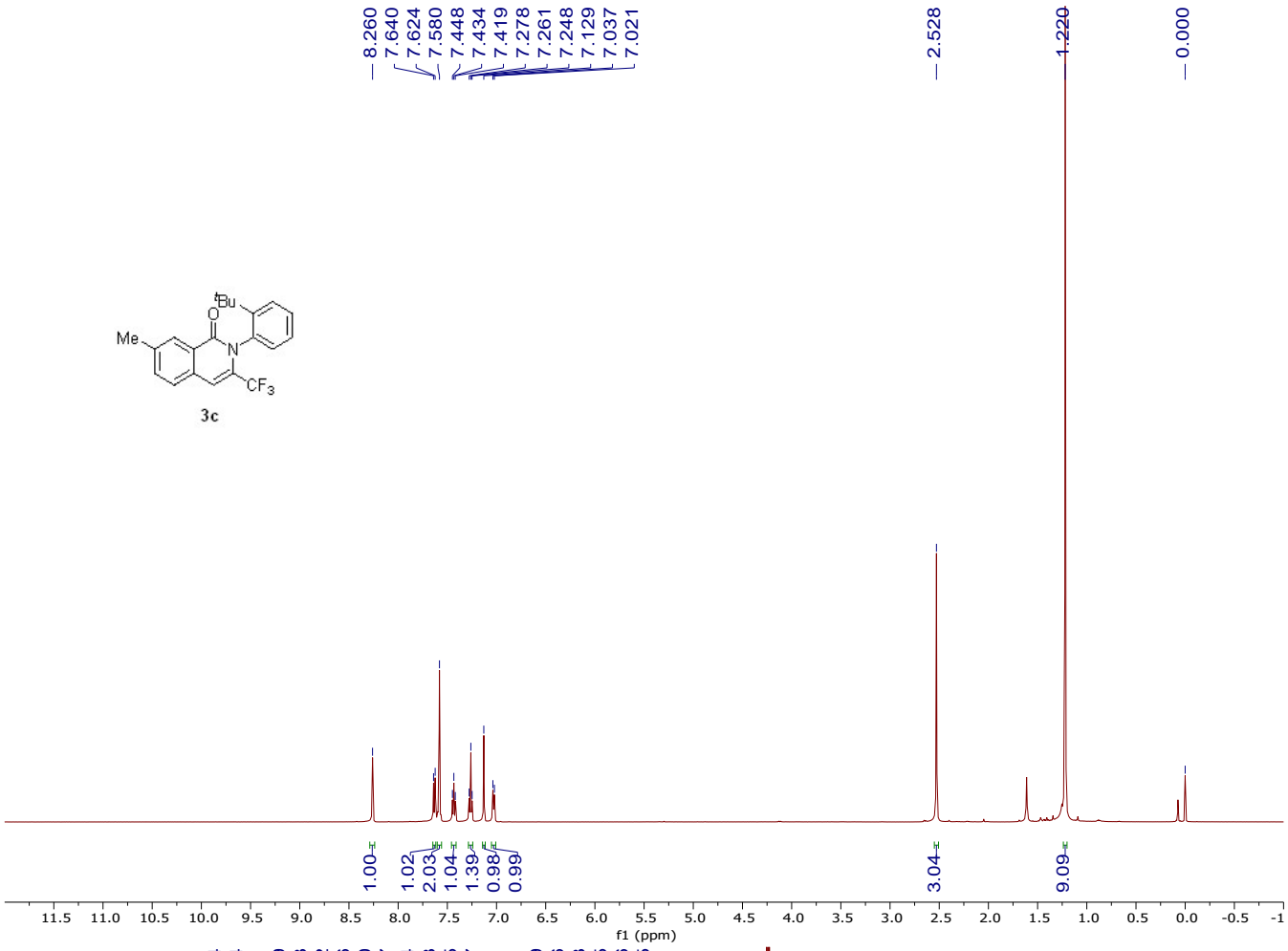
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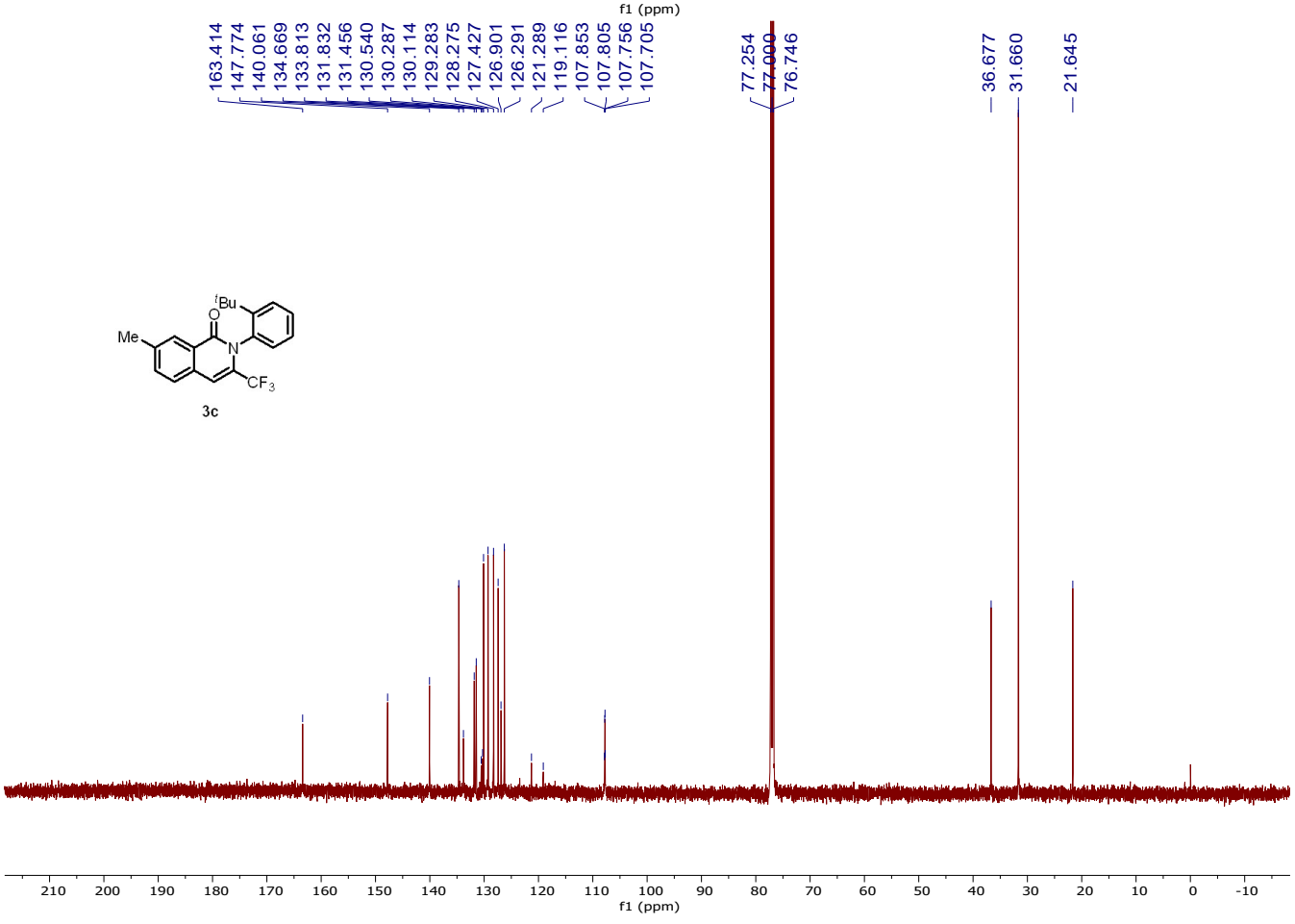
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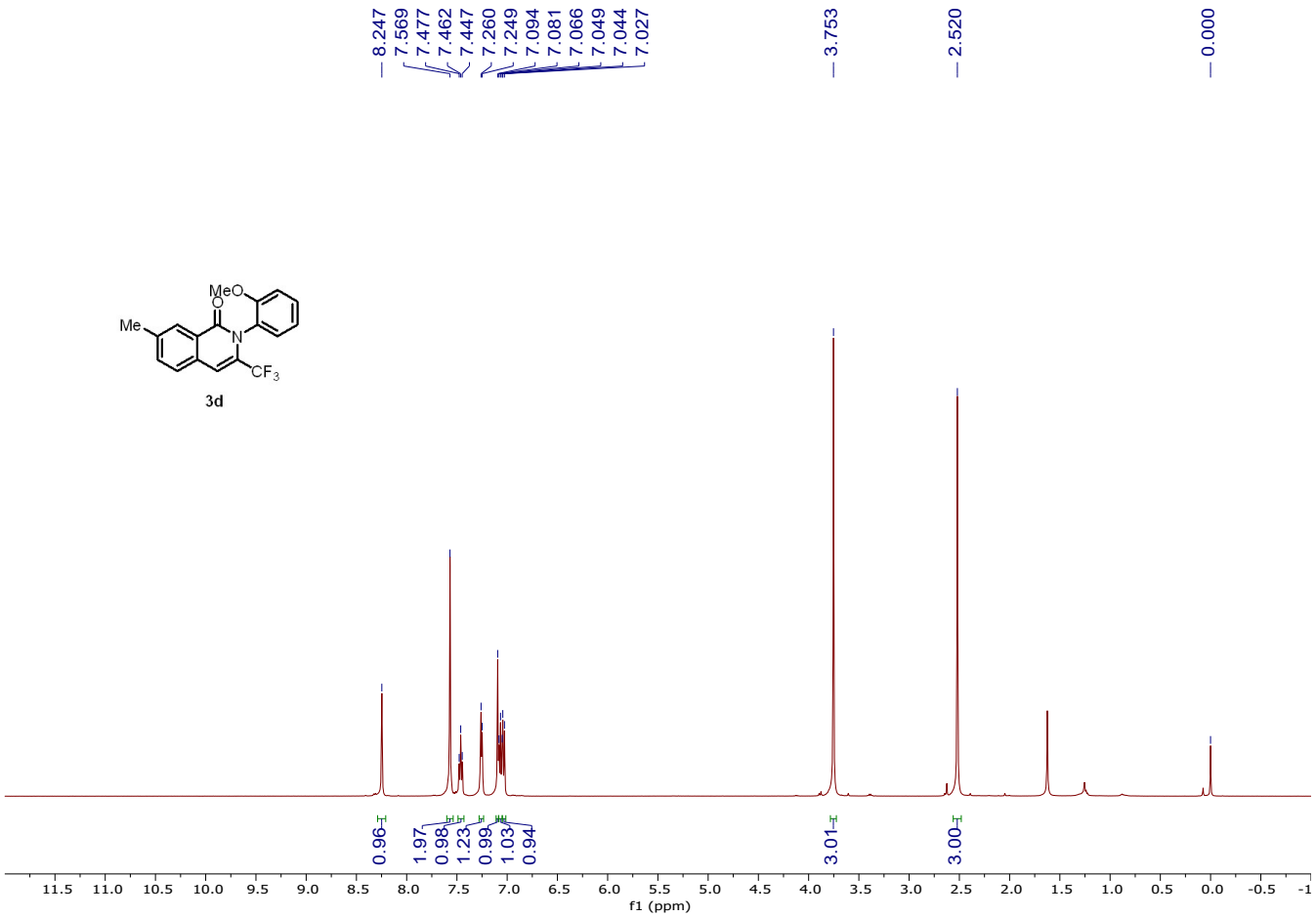
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7.049
7.044
7.027
3.753
2.520
0.000
MeO
O
Me
N
CF3
3d
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0.98
1.23
0.99
1.03
0.94
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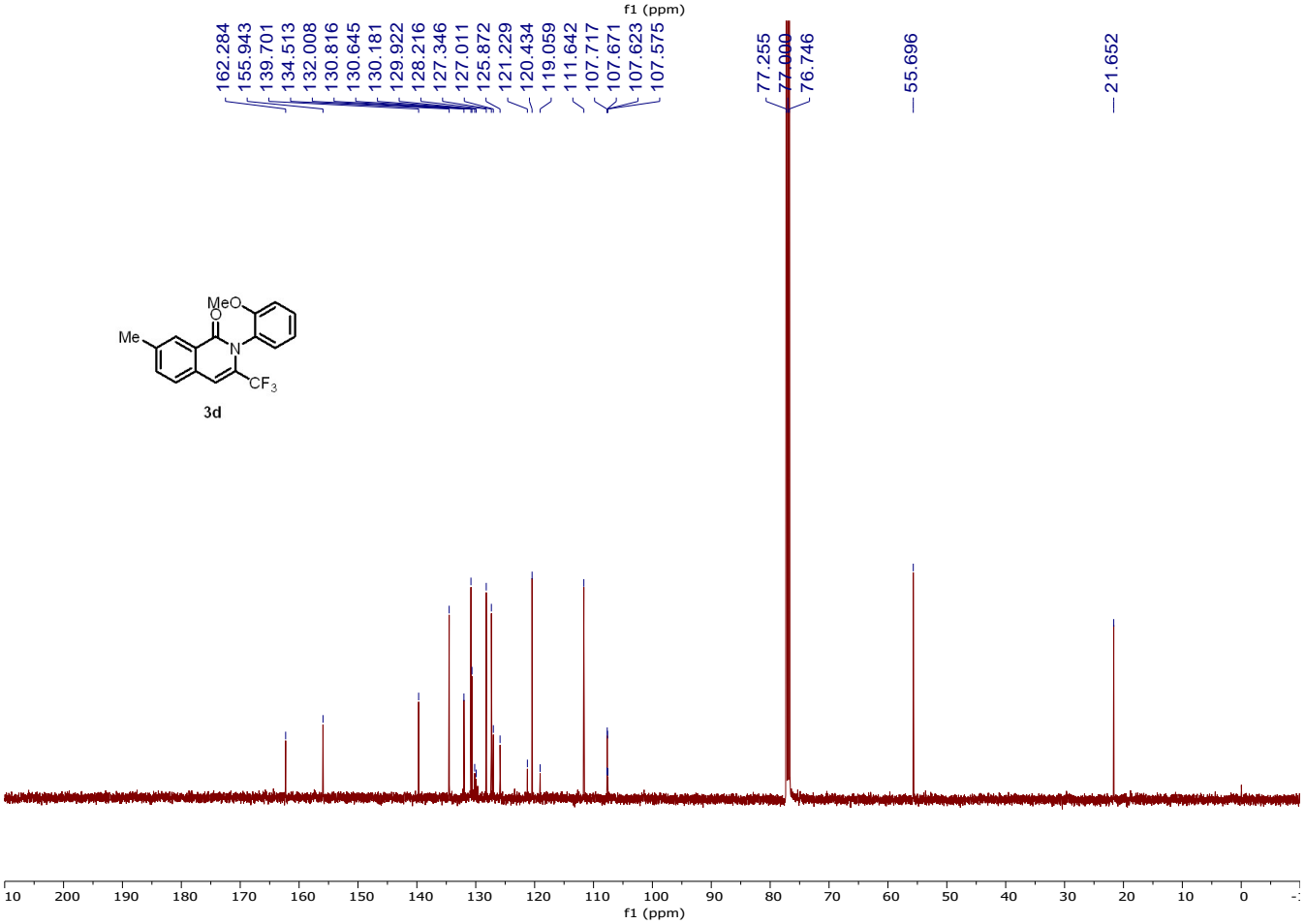
3.00
f1 (ppm)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121.229
120.434
119.059
111.642
107.717
107.671
107.623
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77.000
76.746
55.696
21.652
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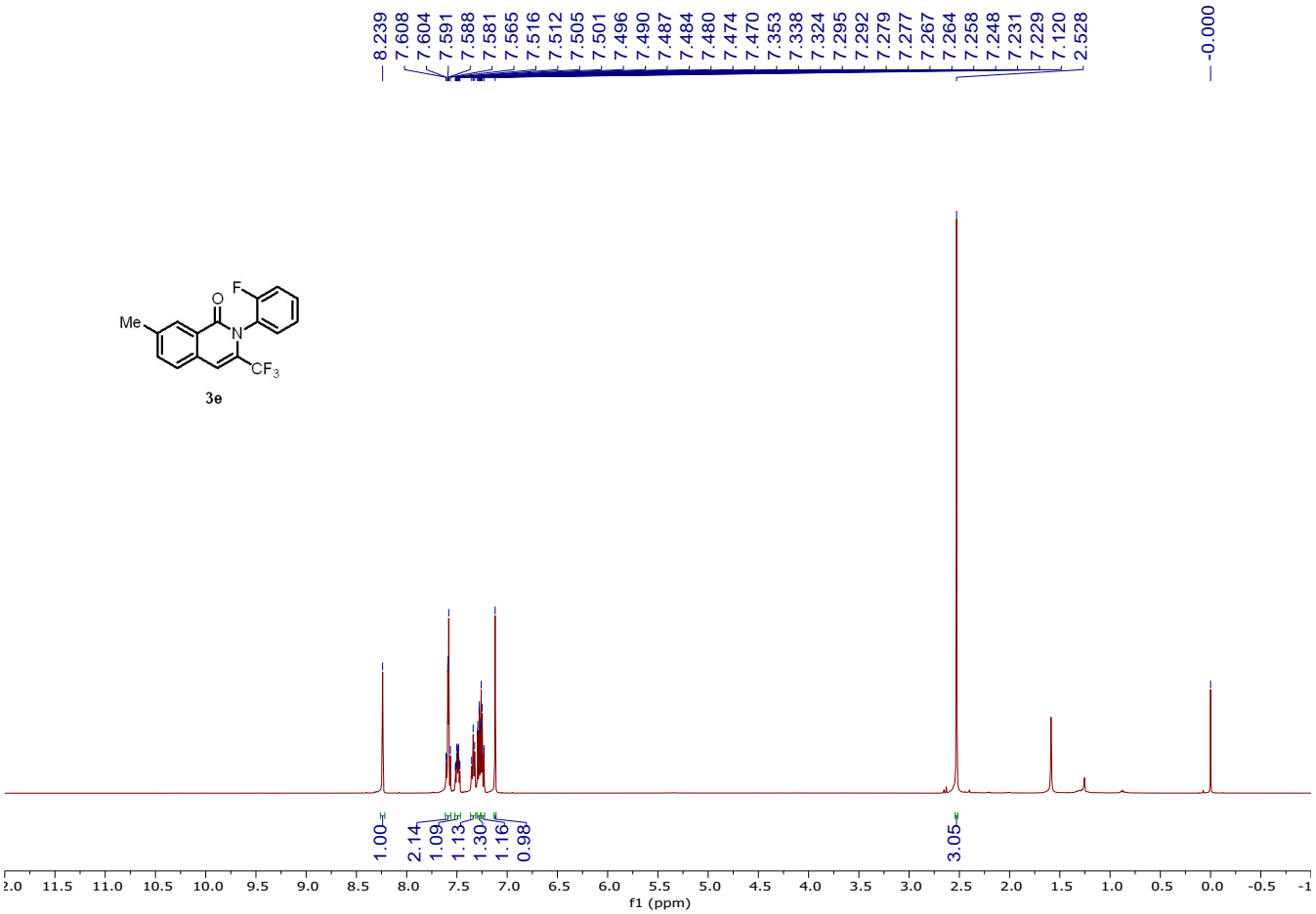
O
Me
N
CF3
3d
f1 (ppm)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7.490
7.487
7.484
7.480
7.474
7.470
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7.295
7.292
7.279
7.277
7.267
7.264
7.258
7.248
7.231
7.229
7.120
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-0.000
Me
O
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1.13
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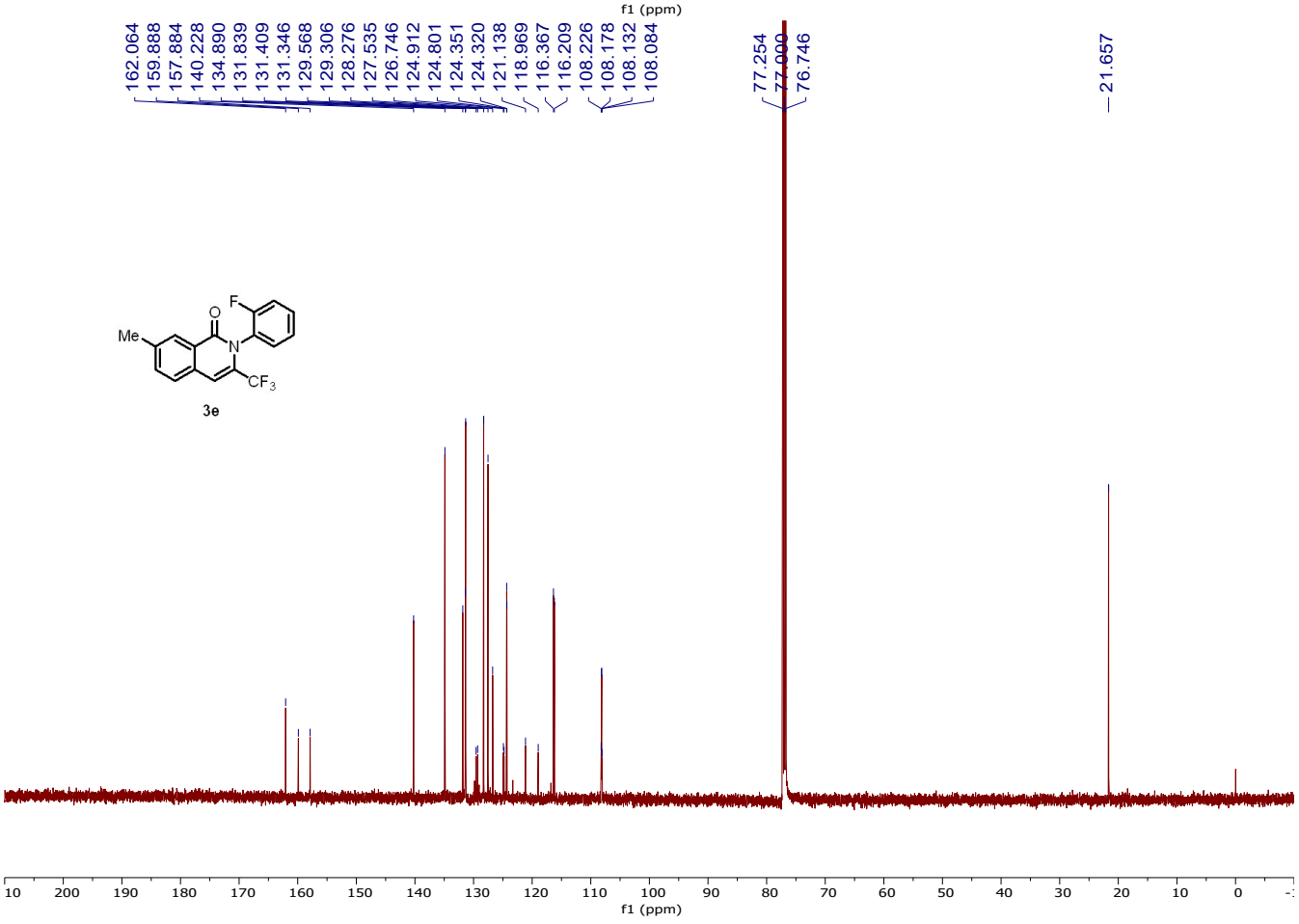
f1 (ppm)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124.801
124.351
124.320
121.138
118.969
116.367
116.209
108.226
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77.000
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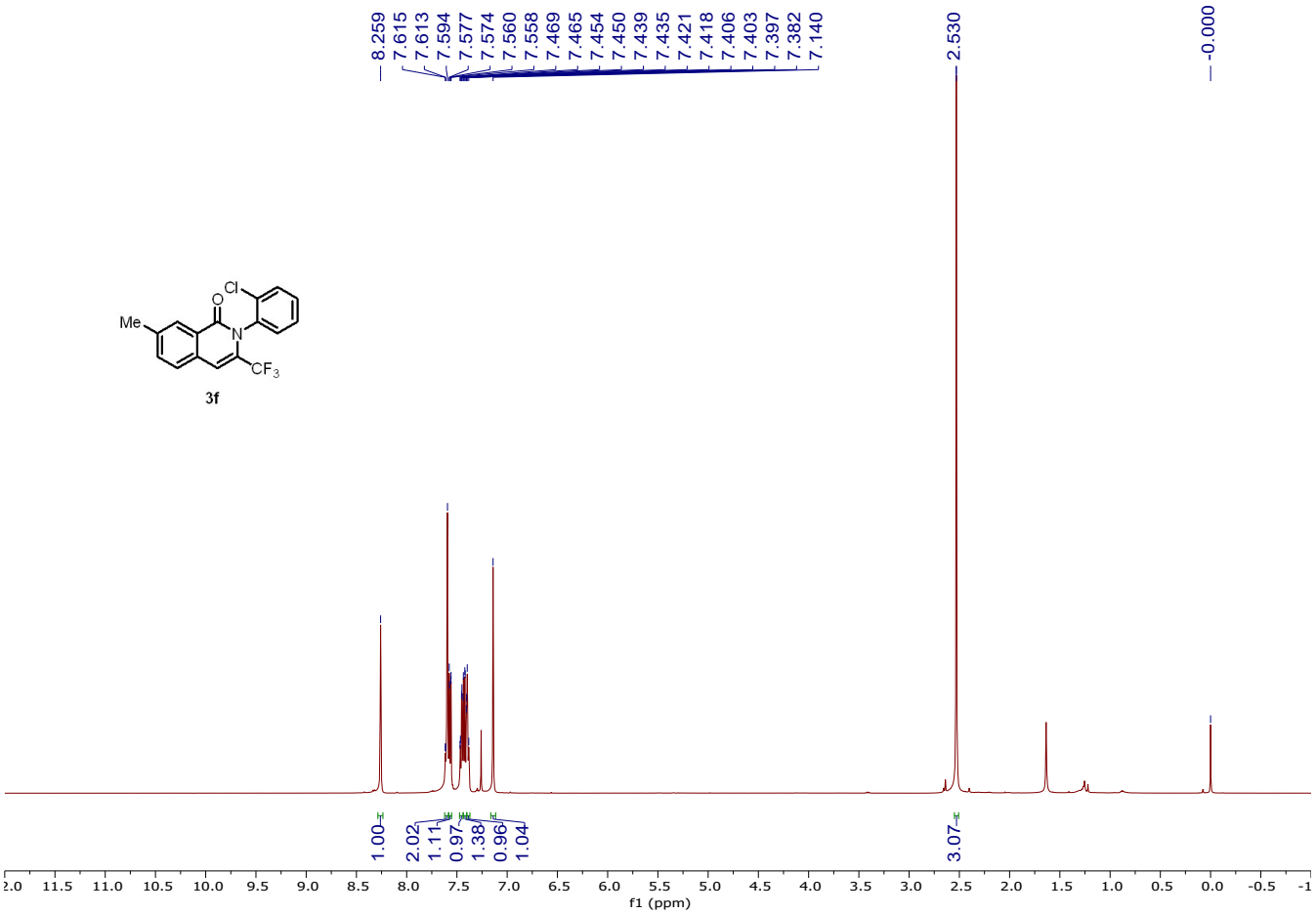
Me
O
N
F
CF3
3e
f1 (ppm)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7.450
7.439
7.435
7.421
7.418
7.406
7.403
7.397
7.382
7.140
2.530
-0.000
Cl
O
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Me
CF3
3f
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2.02
1.11
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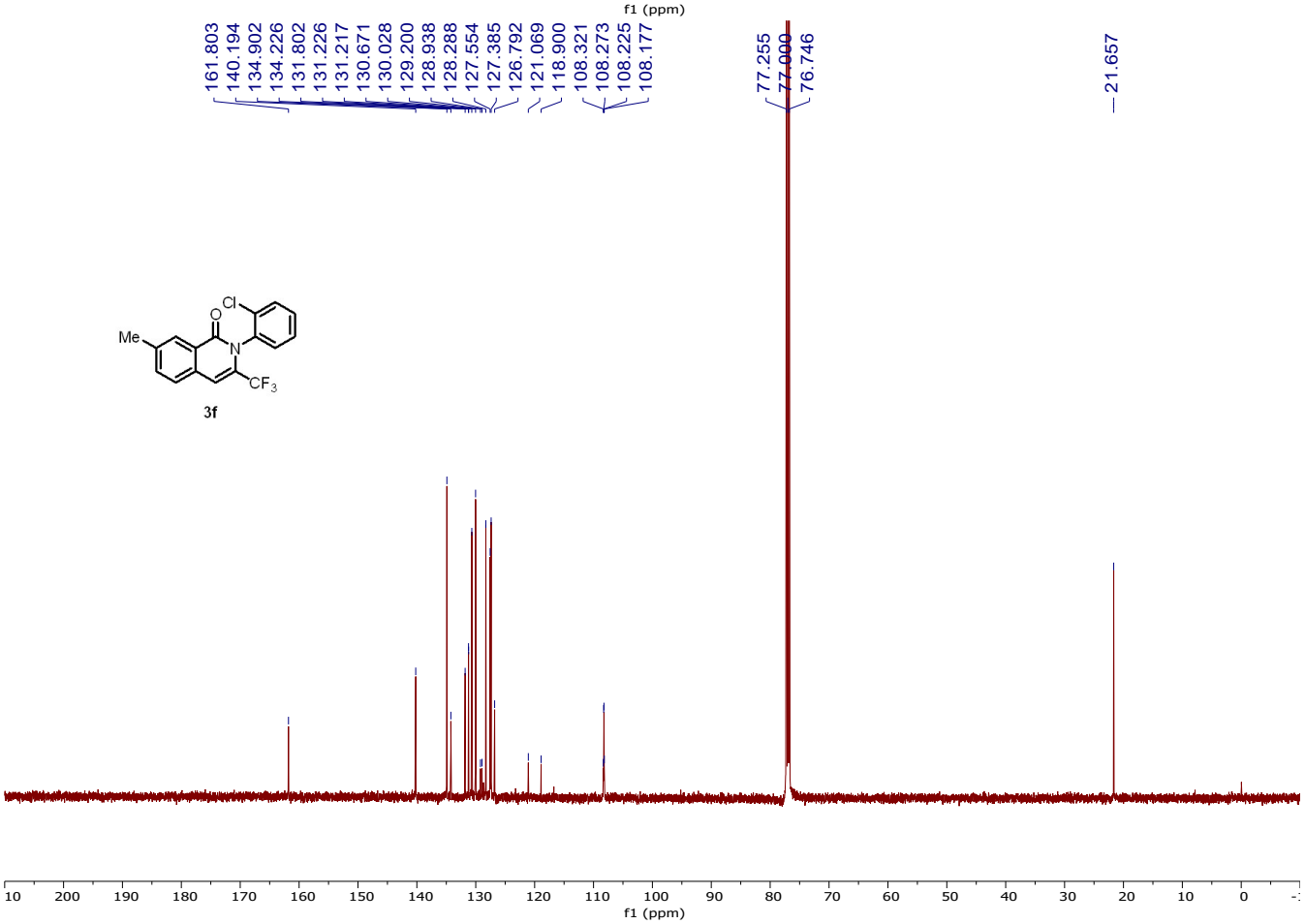
0.96
1.04
3.07
f1 (ppm)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127.554
127.385
126.792
121.069
118.900
108.321
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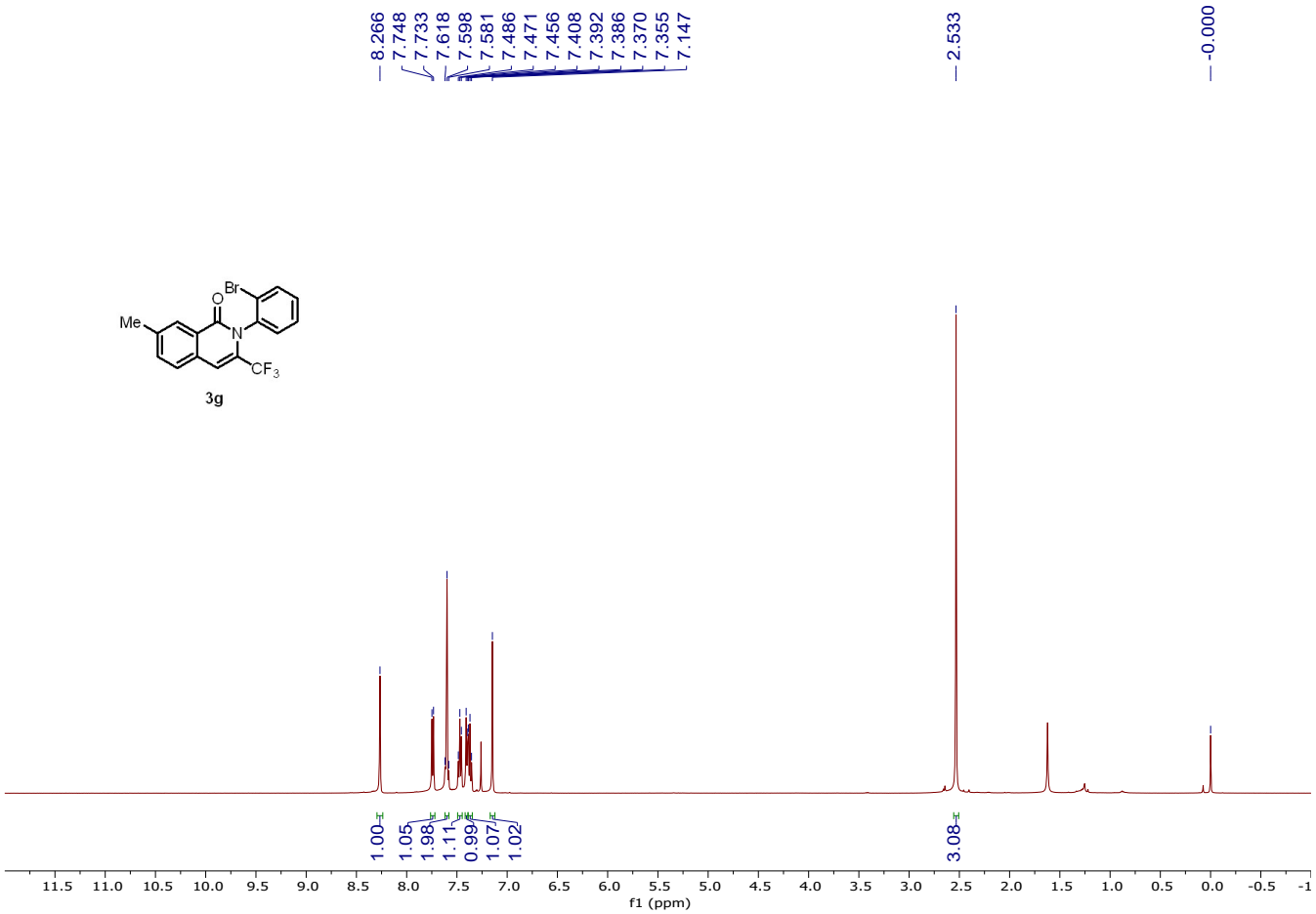
77.000
76.746
21.657
Cl
O
N
Me
CF3
3f
f1 (ppm)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7.370
7.355
7.147
2.533
-0.000
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O
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Me
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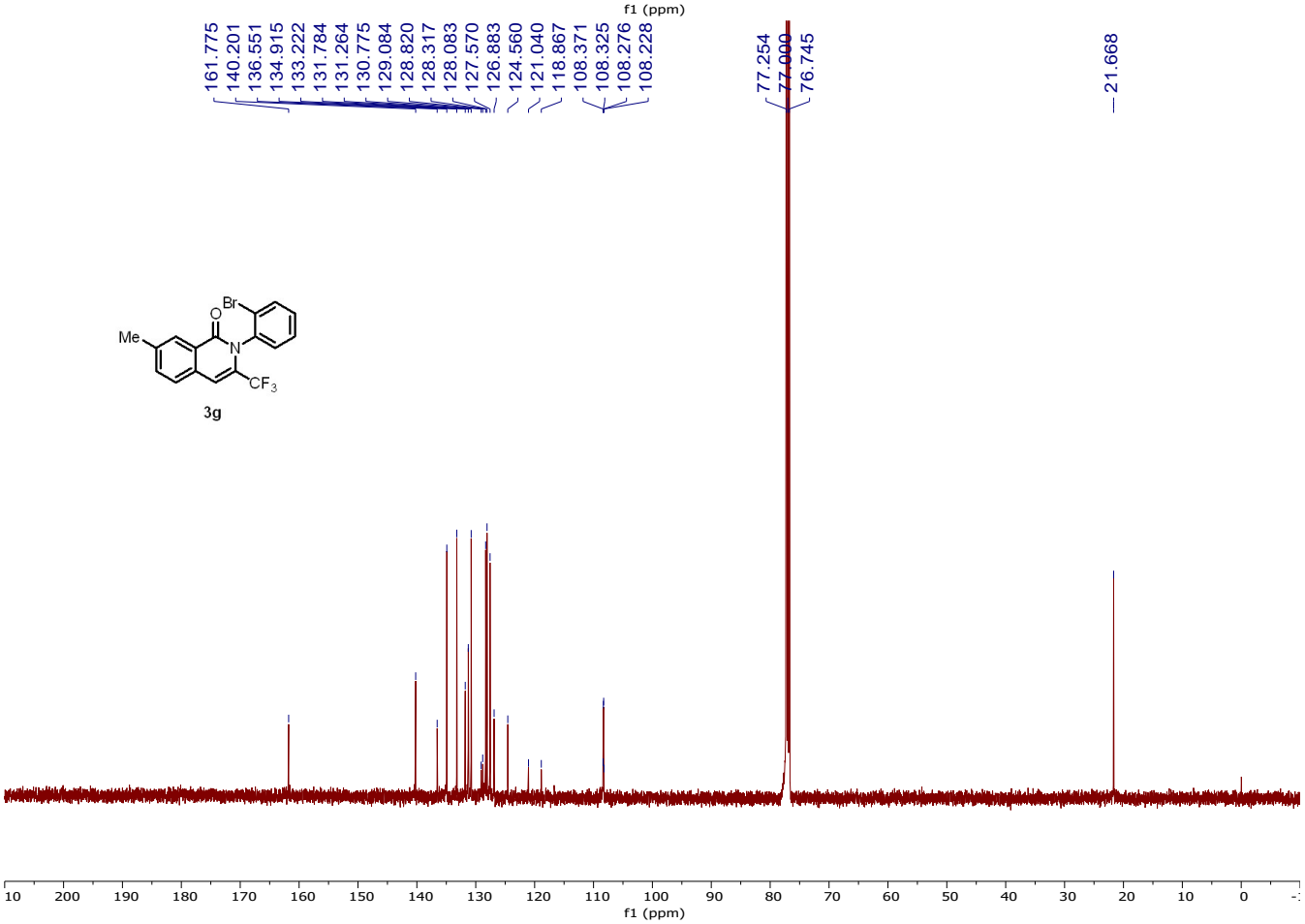
1.00
1.05
1.98
1.11
0.99
1.07
1.02
3.08
f1 (ppm)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130.775
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128.317
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127.570
126.883
124.560
121.040
118.867
108.371
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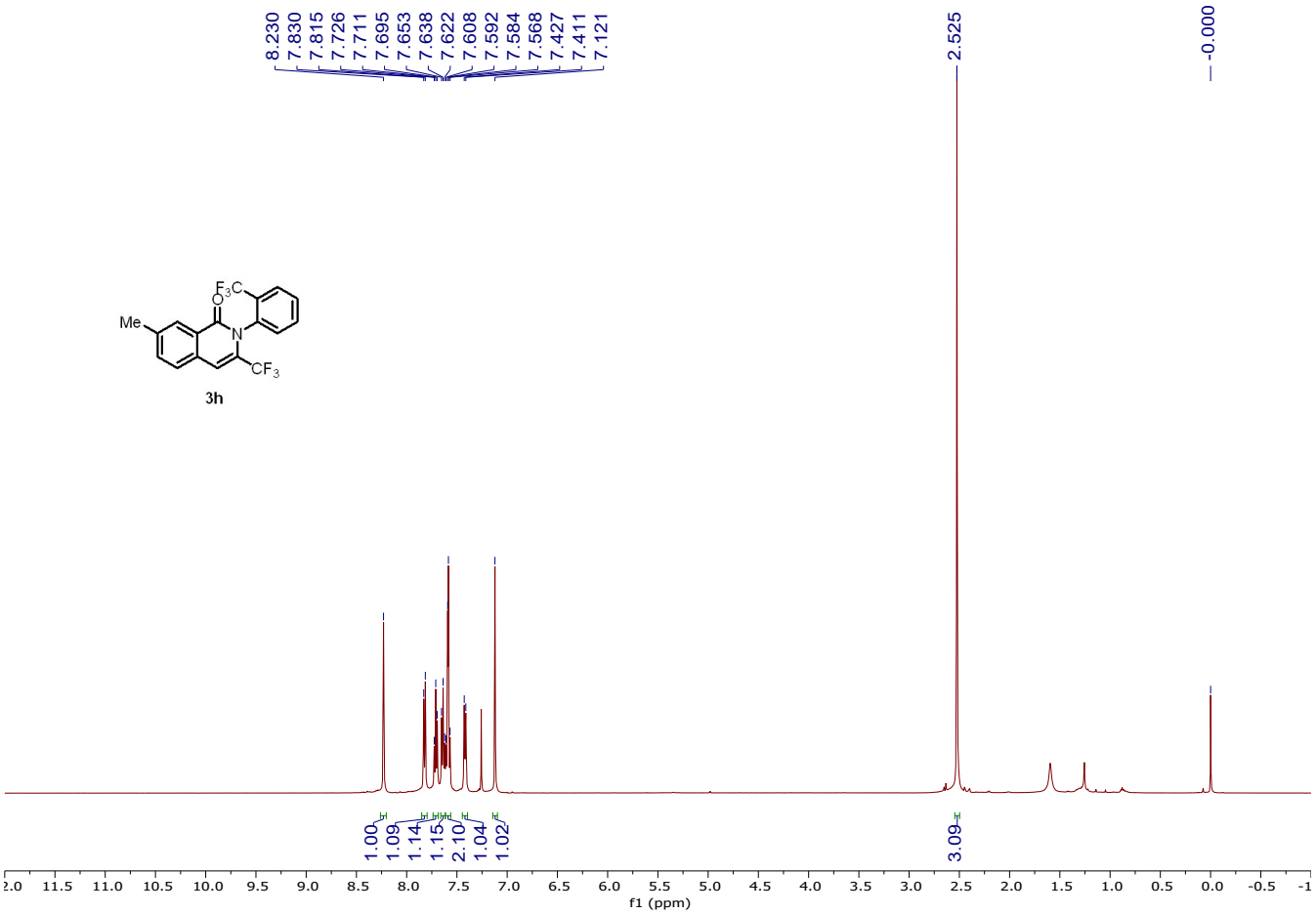
77.254
77.000
76.745
21.668
Br
O
N
Me
CF3
3g
f1 (ppm)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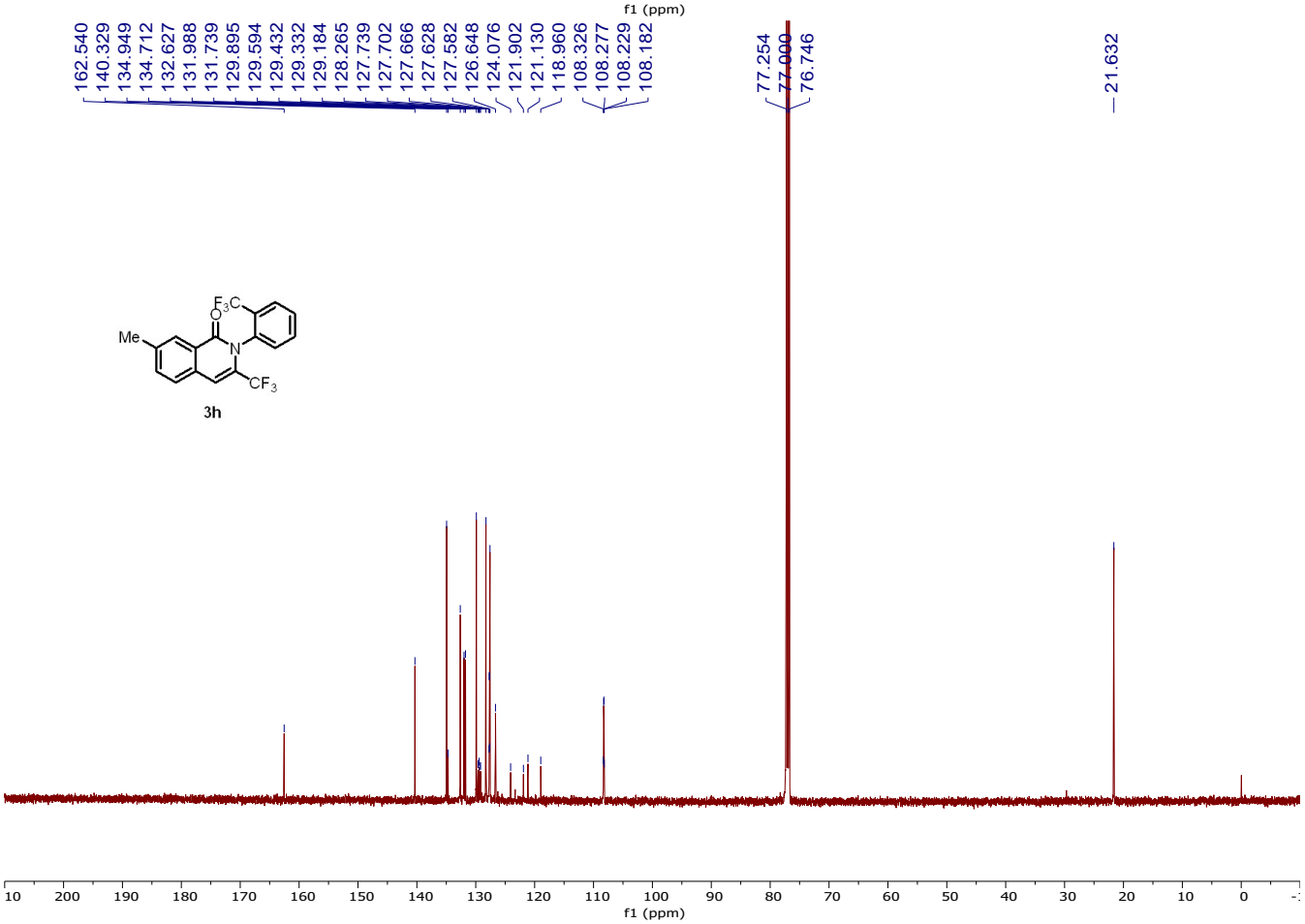
7.695
7.653
7.638
7.622
7.608
7.592
7.584
7.568
7.427
7.411
7.121
2.525
-0.000
1.00
1.09
1.14
1.15
2.10
1.04
1.02
3.09
f1 (ppm)
Me
F3C
O
N
CF3
3h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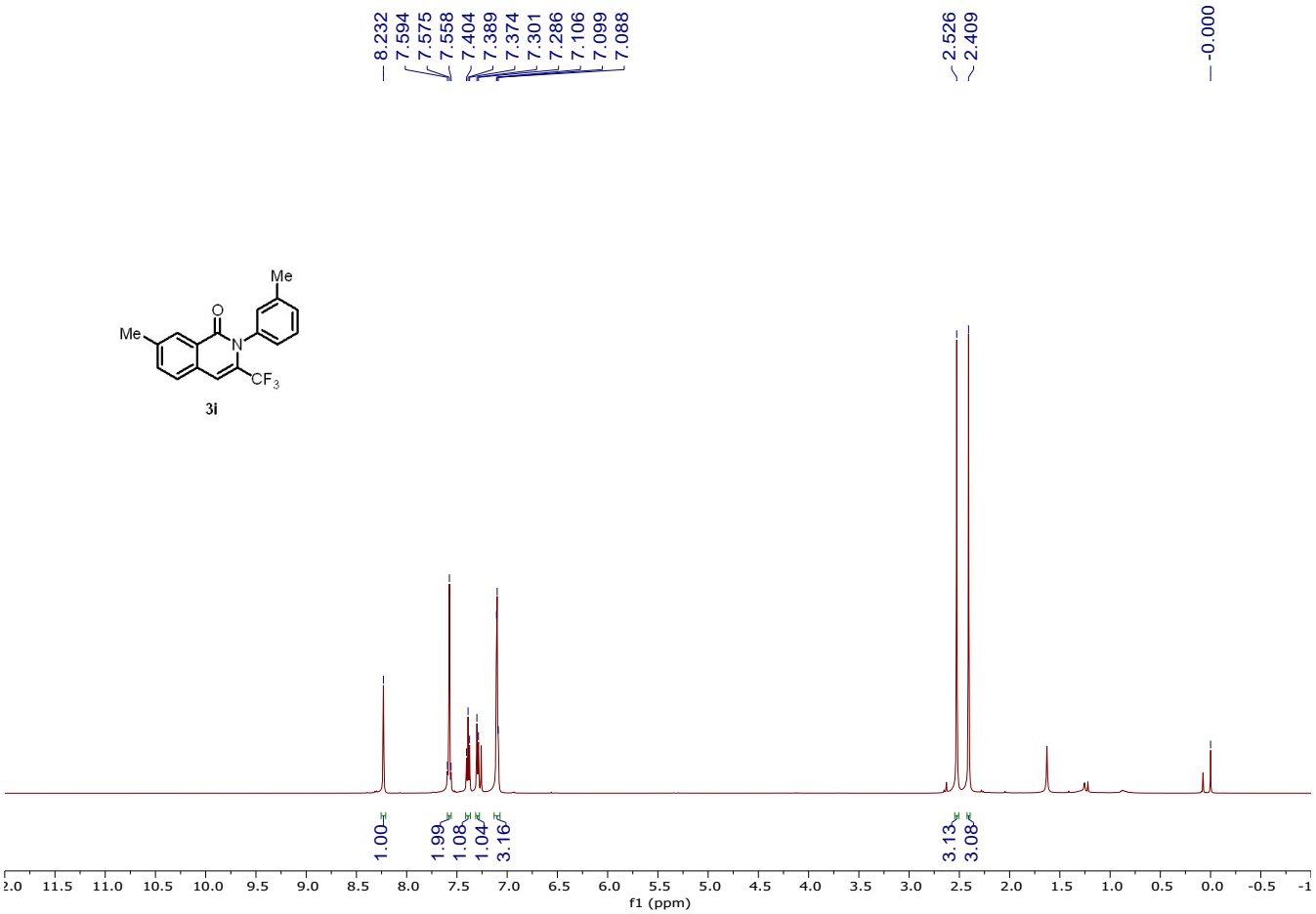
128.265
127.739
127.702
127.666
127.628
127.582
126.648
124.076
121.902
121.130
118.960
108.326
108.277
108.229
108.182
77.254
77.000
76.746
21.632
f1 (ppm)
Me
F3C
O
N
CF3
3h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7.374
7.301
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7.106
7.099
7.088
2.526
2.409
-0.000
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Me
O
N
CF3
3i
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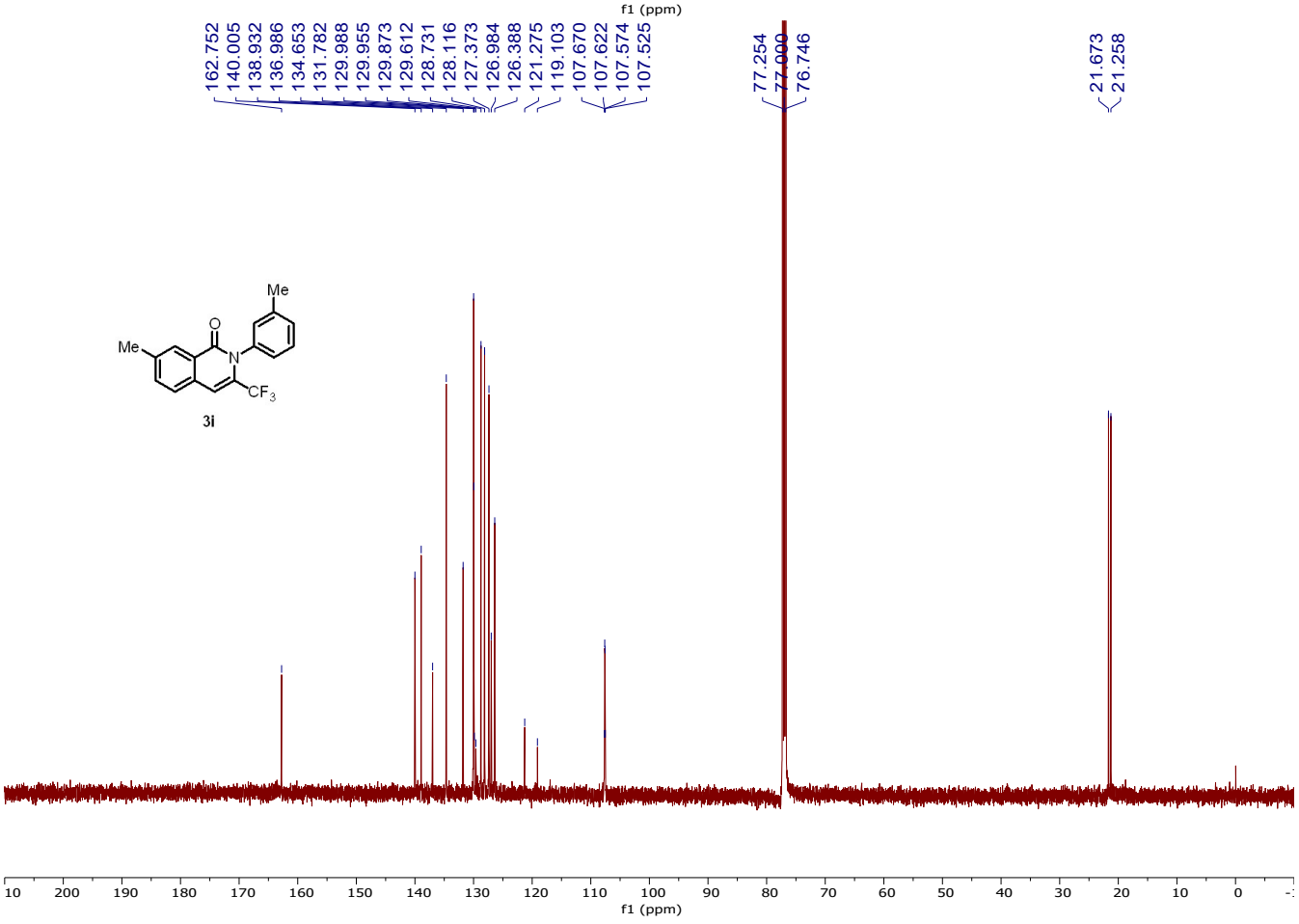
1.99
1.08
1.04
3.16
3.13
3.08
f1 (ppm)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126.388
121.275
119.103
107.670
107.622
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77.000
76.746
21.673
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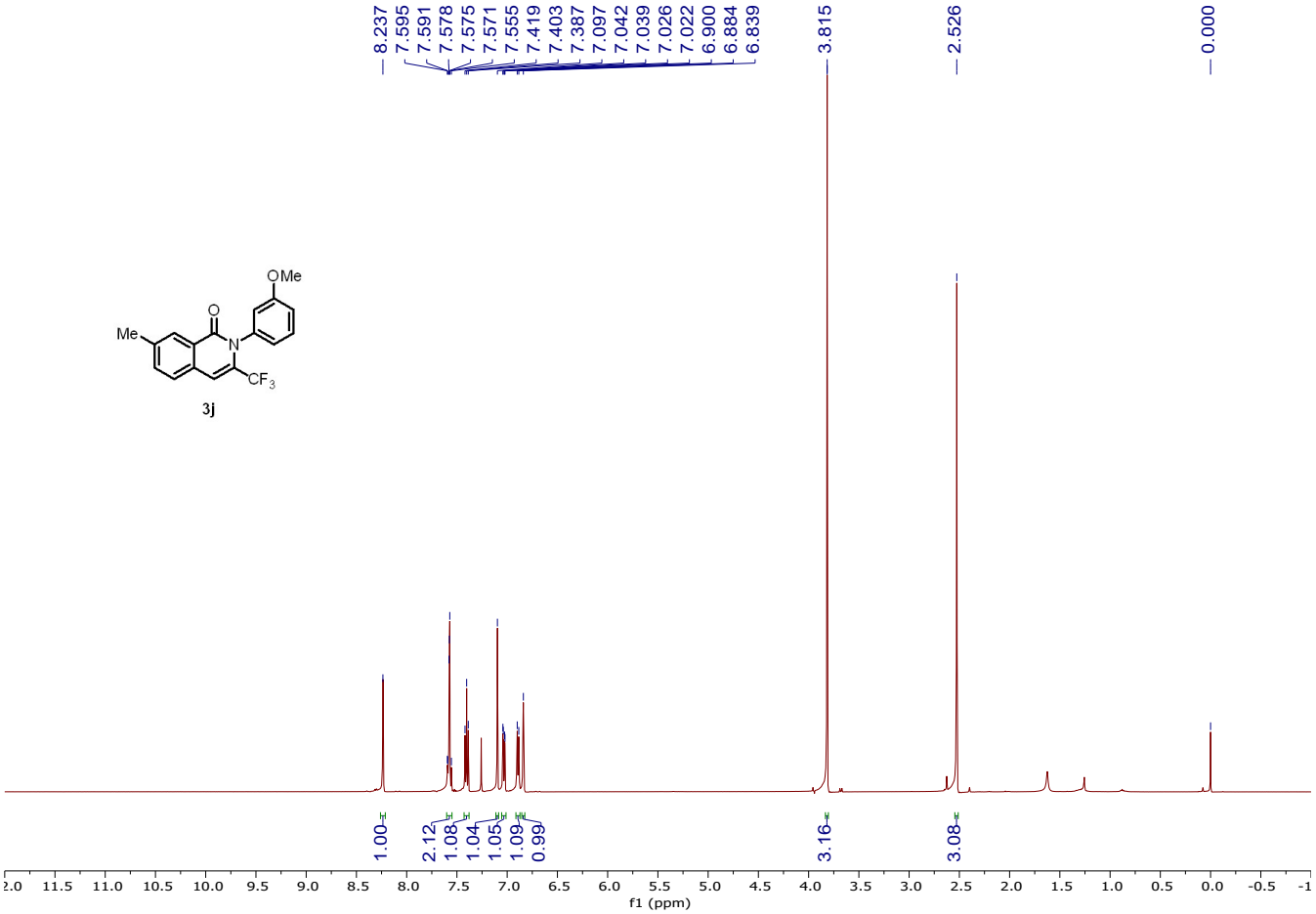
Me
Me
O
N
CF3
3i
f1 (ppm)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7.387
7.097
7.042
7.039
7.026
7.022
6.900
6.884
6.839
3.815
2.526
0.000
OMe
Me
O
N
CF3
3j
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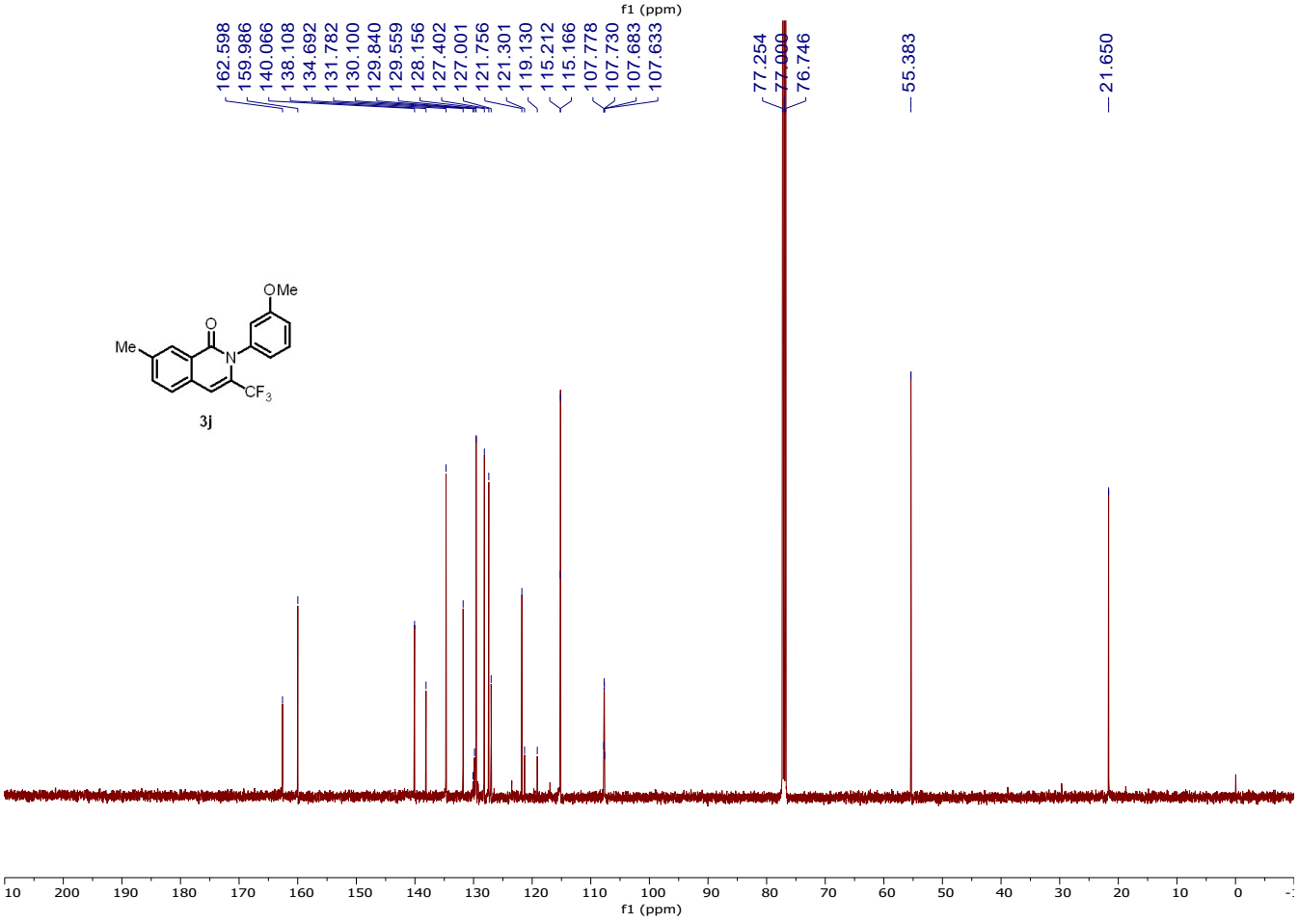
2.12
1.08
1.04
1.05
1.09
0.99
3.16
3.08
f1 (ppm)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127.402
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121.301
119.130
115.212
115.166
107.778
107.730
107.683
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77.000
76.746
55.383
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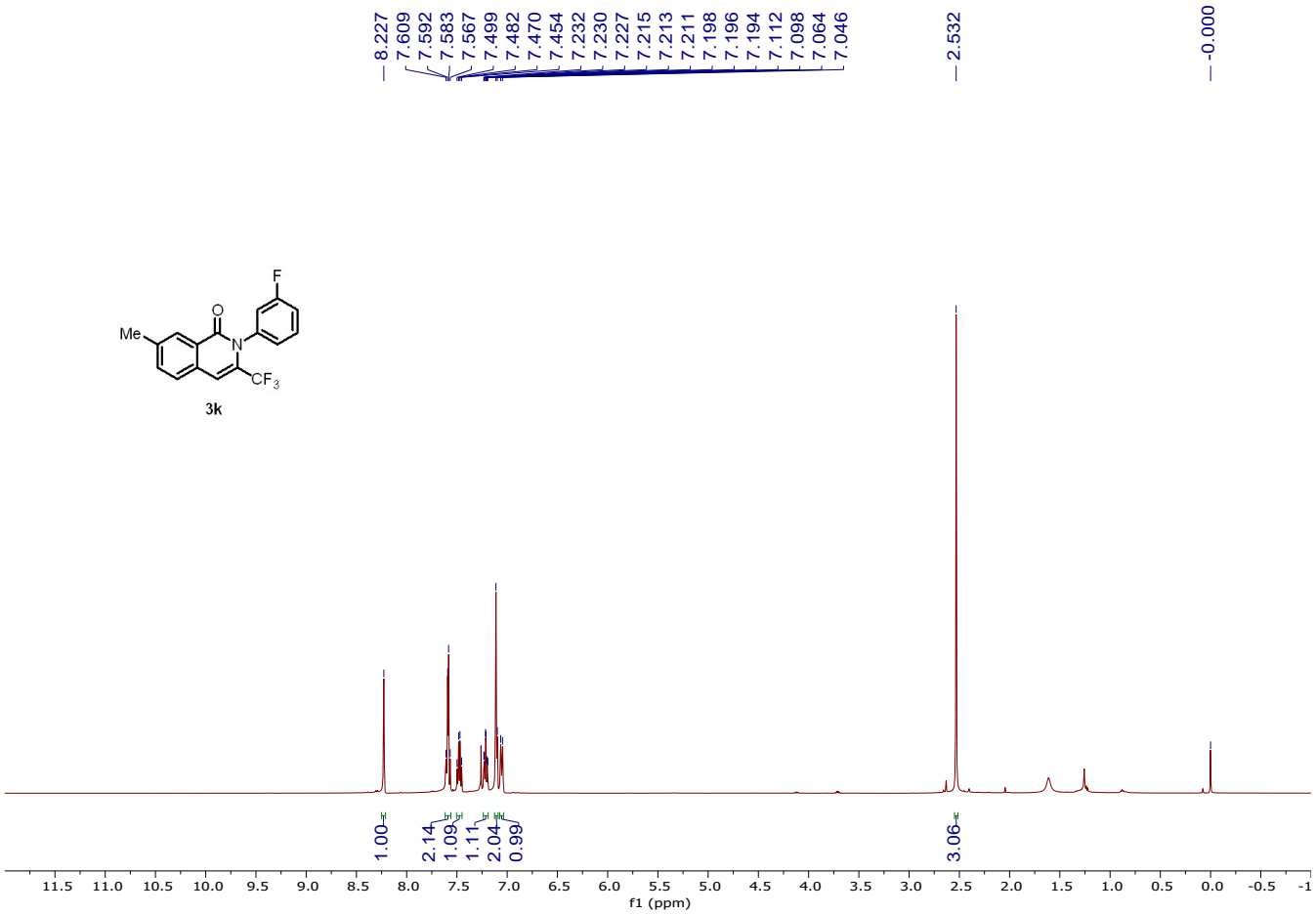
OMe
Me
O
N
CF3
3j
f1 (ppm)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7.470
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7.230
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7.215
7.213
7.211
7.198
7.196
7.194
7.112
7.098
7.064
7.046
2.532
-0.000
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O
N
Me
CF3
3k
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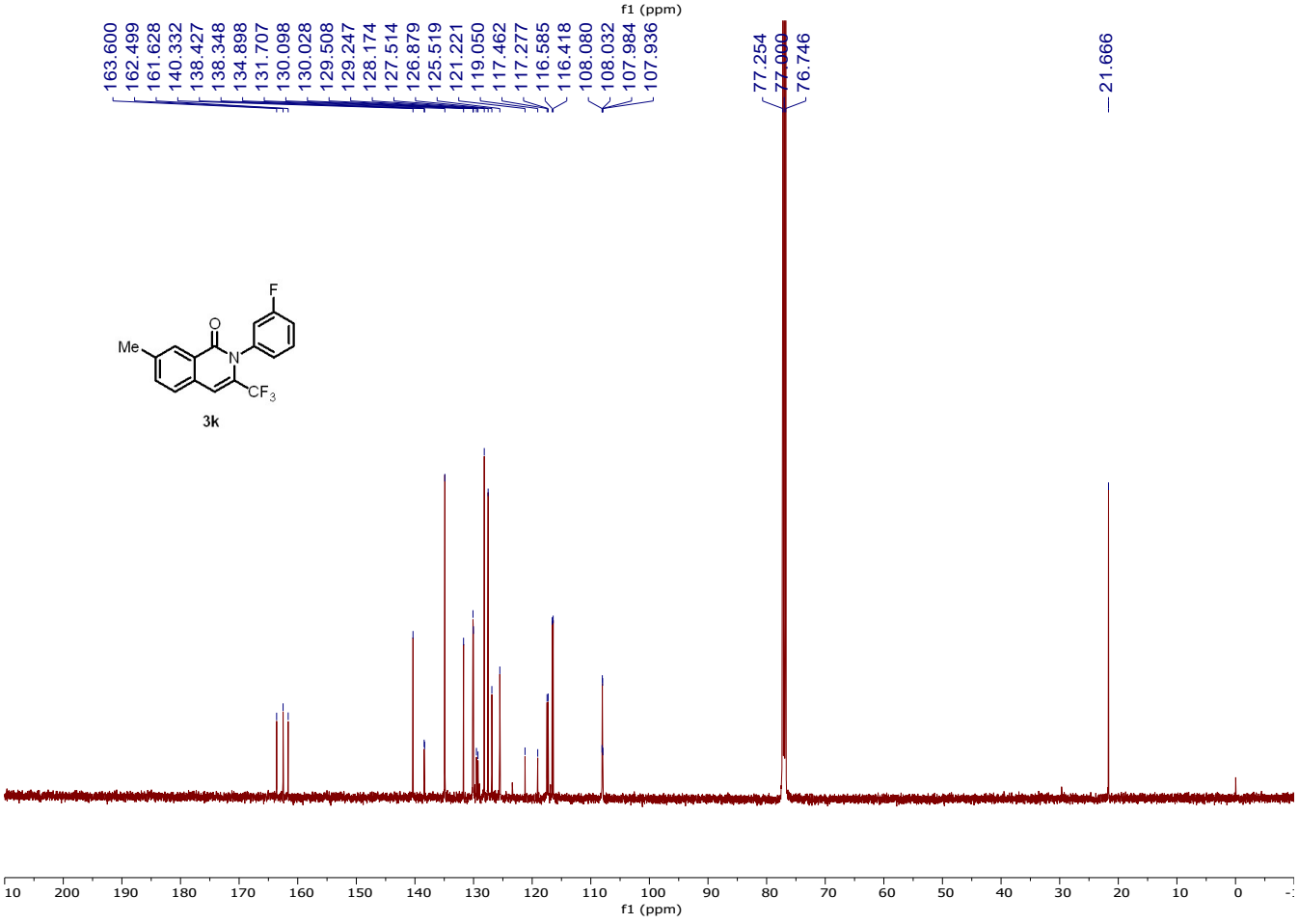
2.14
1.09
1.11
2.04
0.99
3.06
f1 (ppm)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127.514
126.879
125.519
121.221
119.050
117.462
117.277
116.585
116.418
108.080
108.032
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77.000
76.746
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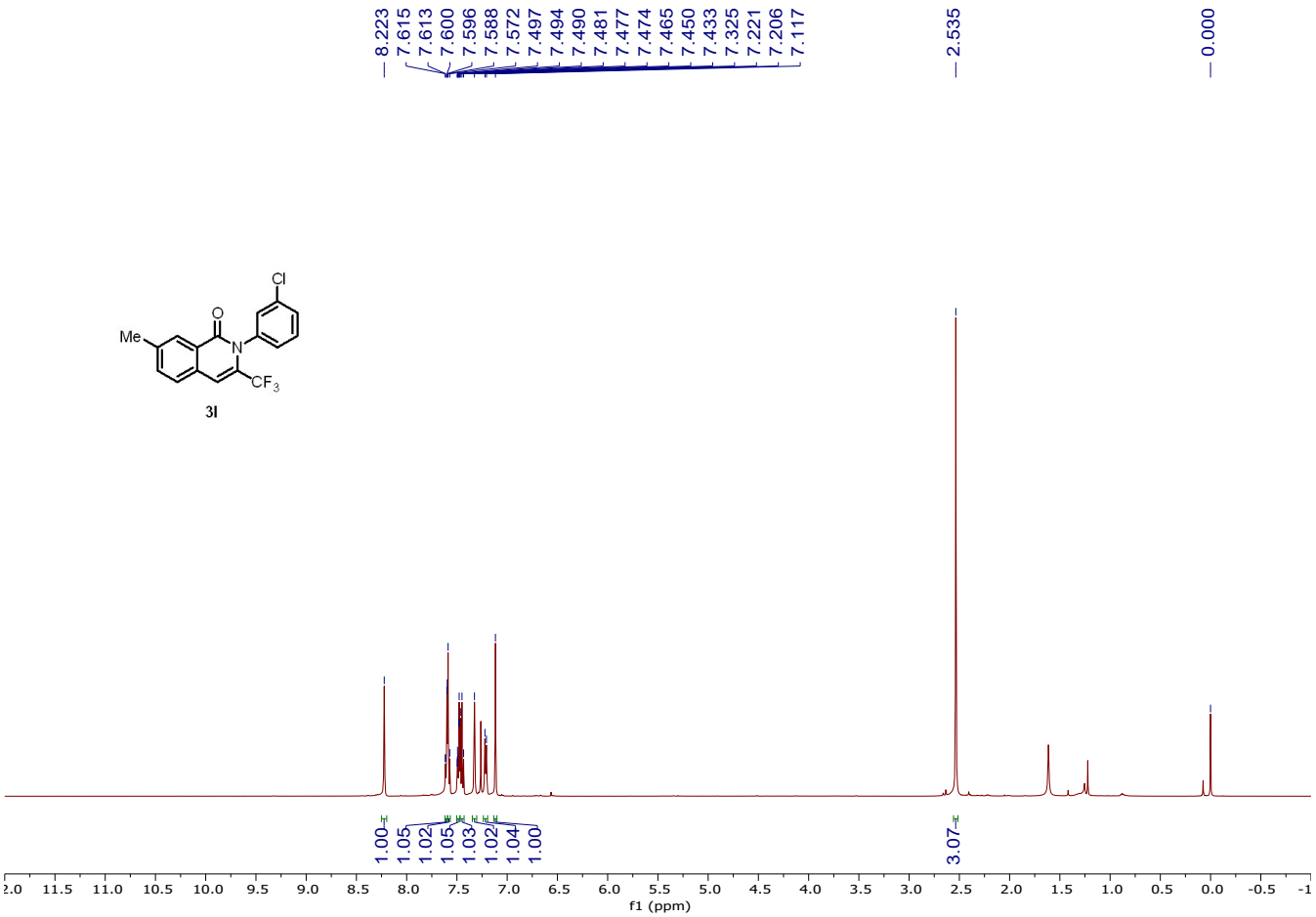
O
N
Me
CF3
3k
f1 (ppm)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7.474
7.465
7.450
7.433
7.325
7.221
7.206
7.117
2.535
0.000
Cl
O
N
Me
CF3
3l
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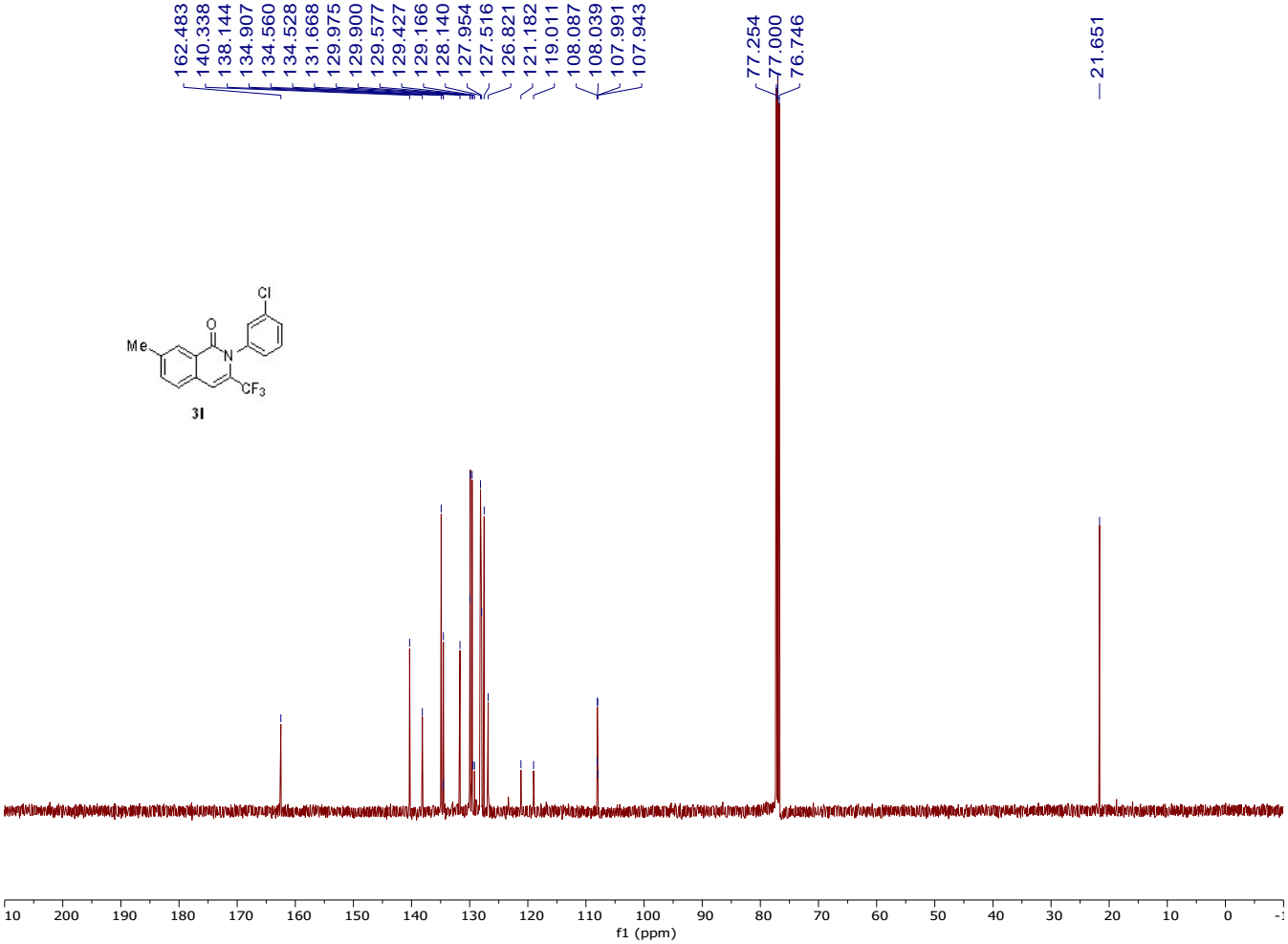
1.05
1.02
1.05
1.03
1.02
1.04
1.00
3.07
f1 (ppm)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128.140
127.954
127.516
126.821
121.182
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108.039
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77.000
76.746
21.651
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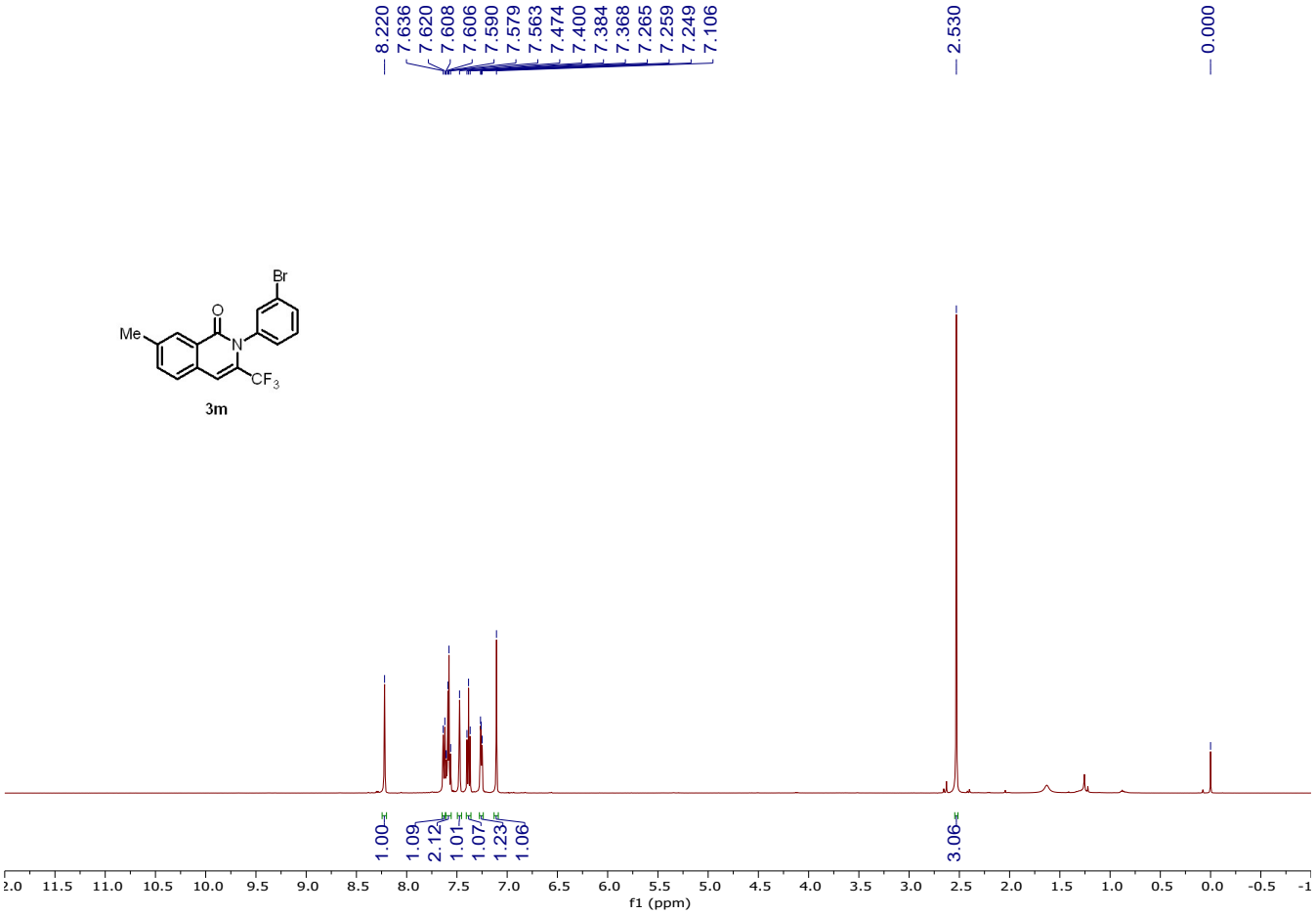
N
Me
CF3
3l
f1 (ppm)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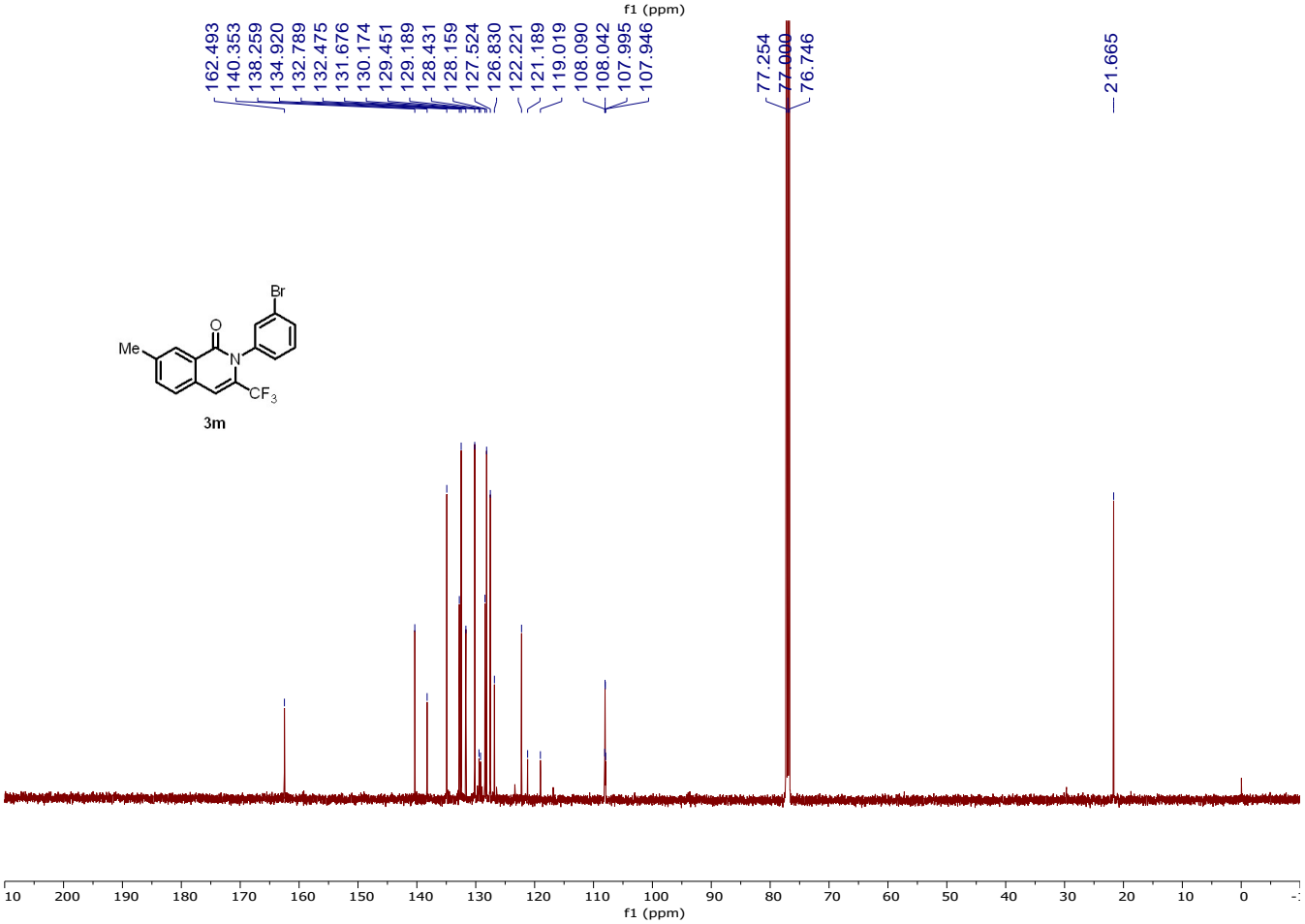
7.265
7.259
7.249
7.106
2.530
0.000
Br
O
N
Me
CF3
3m
1.00
1.09
2.12
1.01
1.07
1.23
1.06
3.06
f1 (ppm)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126.830
122.221
121.189
119.019
108.090
108.042
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77.000
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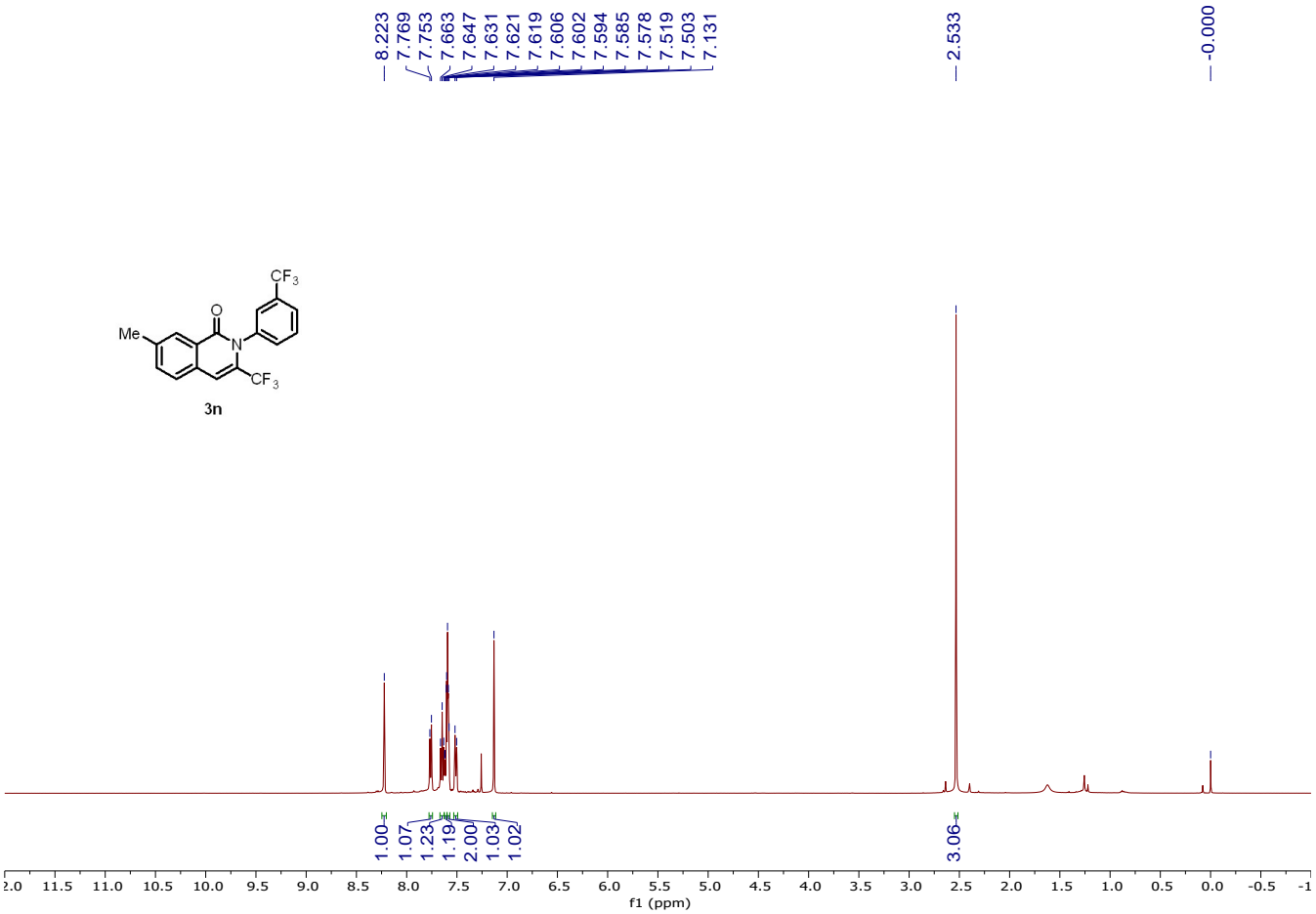
Br
O
N
Me
CF3
3m
f1 (ppm)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7.585
7.578
7.519
7.503
7.131
2.533
-0.000
CF3
O
N
Me
CF3
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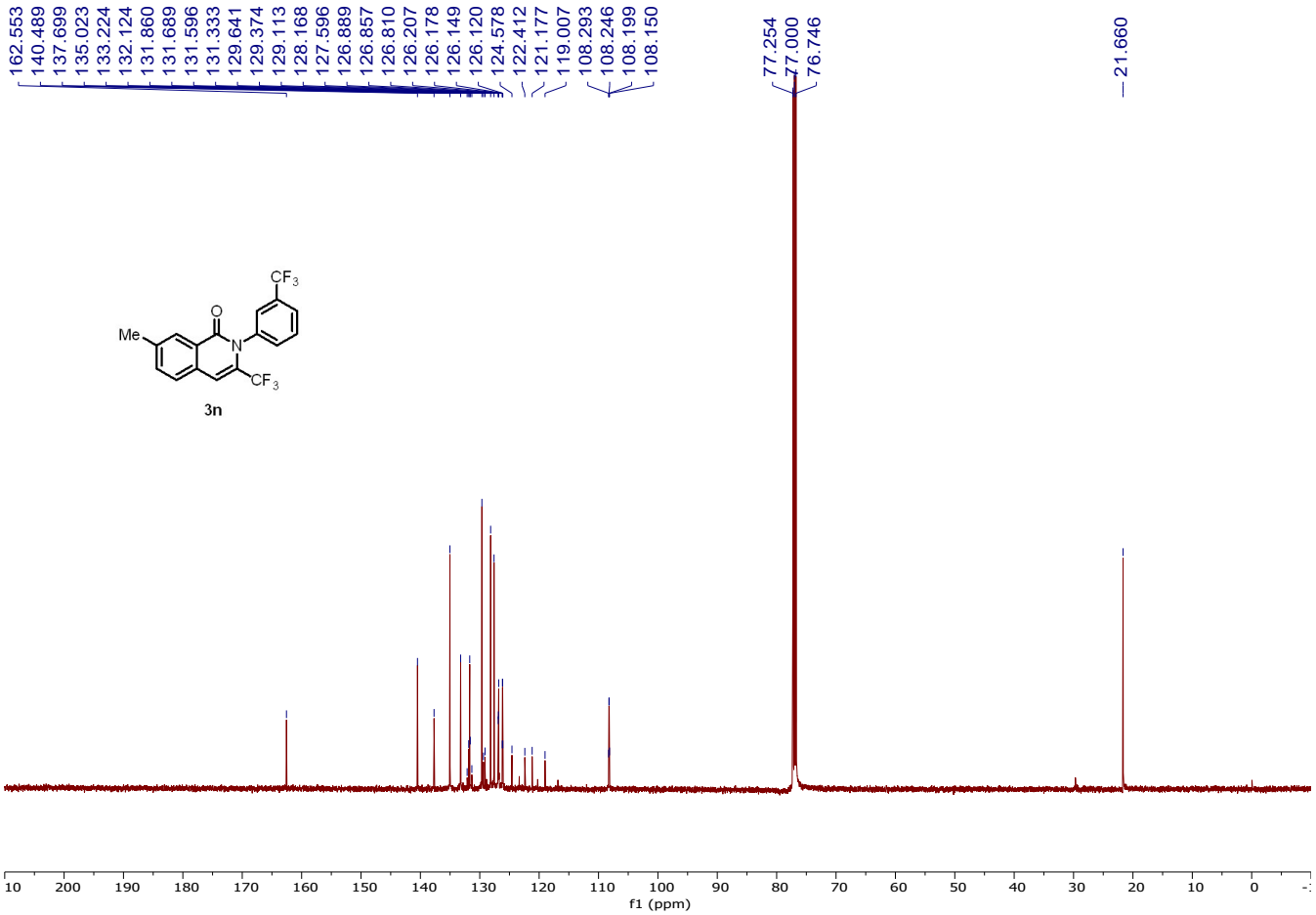
1.07
1.23
1.19
2.00
1.03
1.02
3.06
f1 (ppm)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127.596
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126.149
126.120
124.578
122.412
121.177
119.007
108.293
108.246
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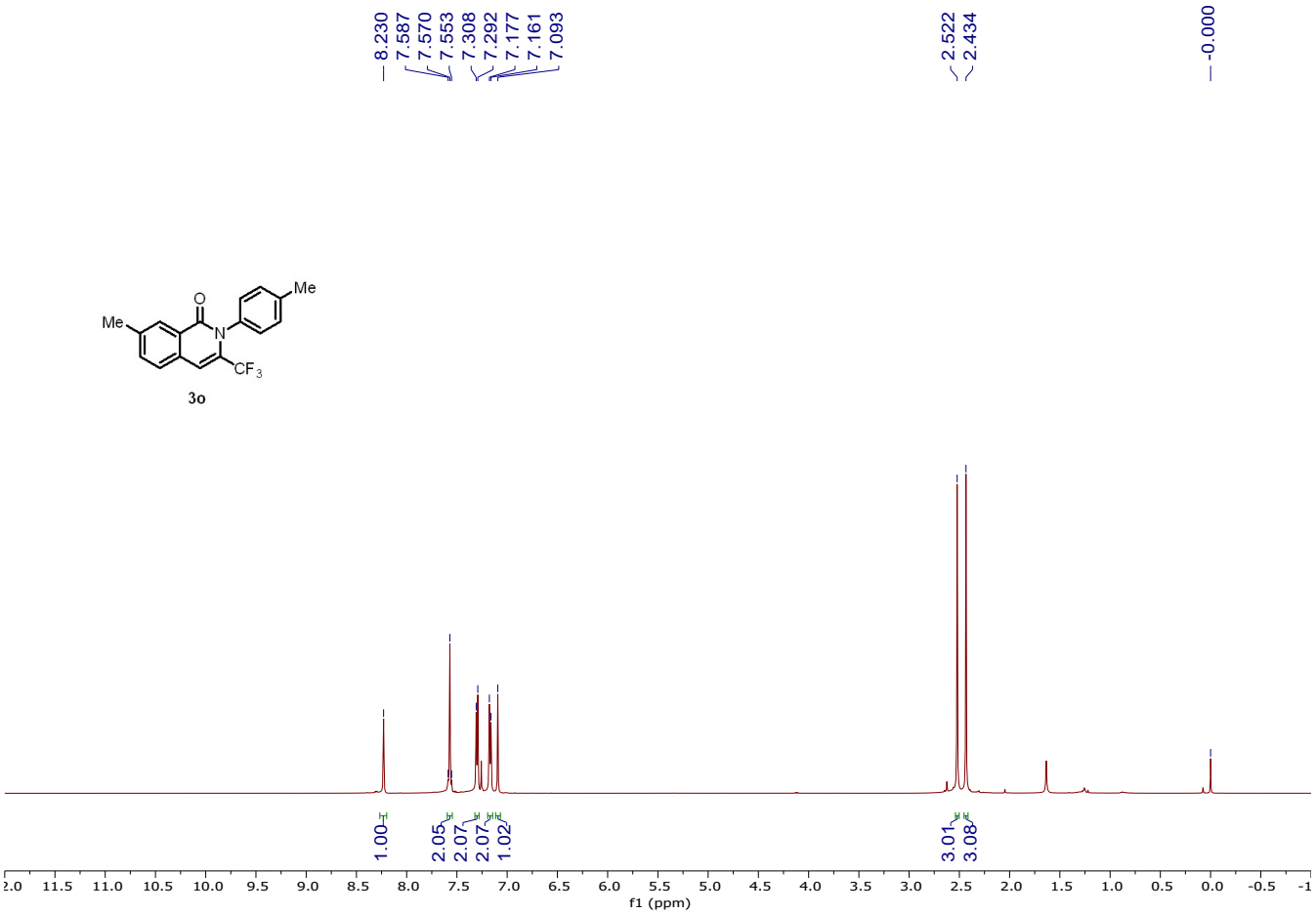
O
N
Me
CF3
3n
f1 (ppm)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7.308
7.292
7.177
7.161
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2.522
2.434
-0.000
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Me
O
N
CF3
3o
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2.07
2.07
1.02
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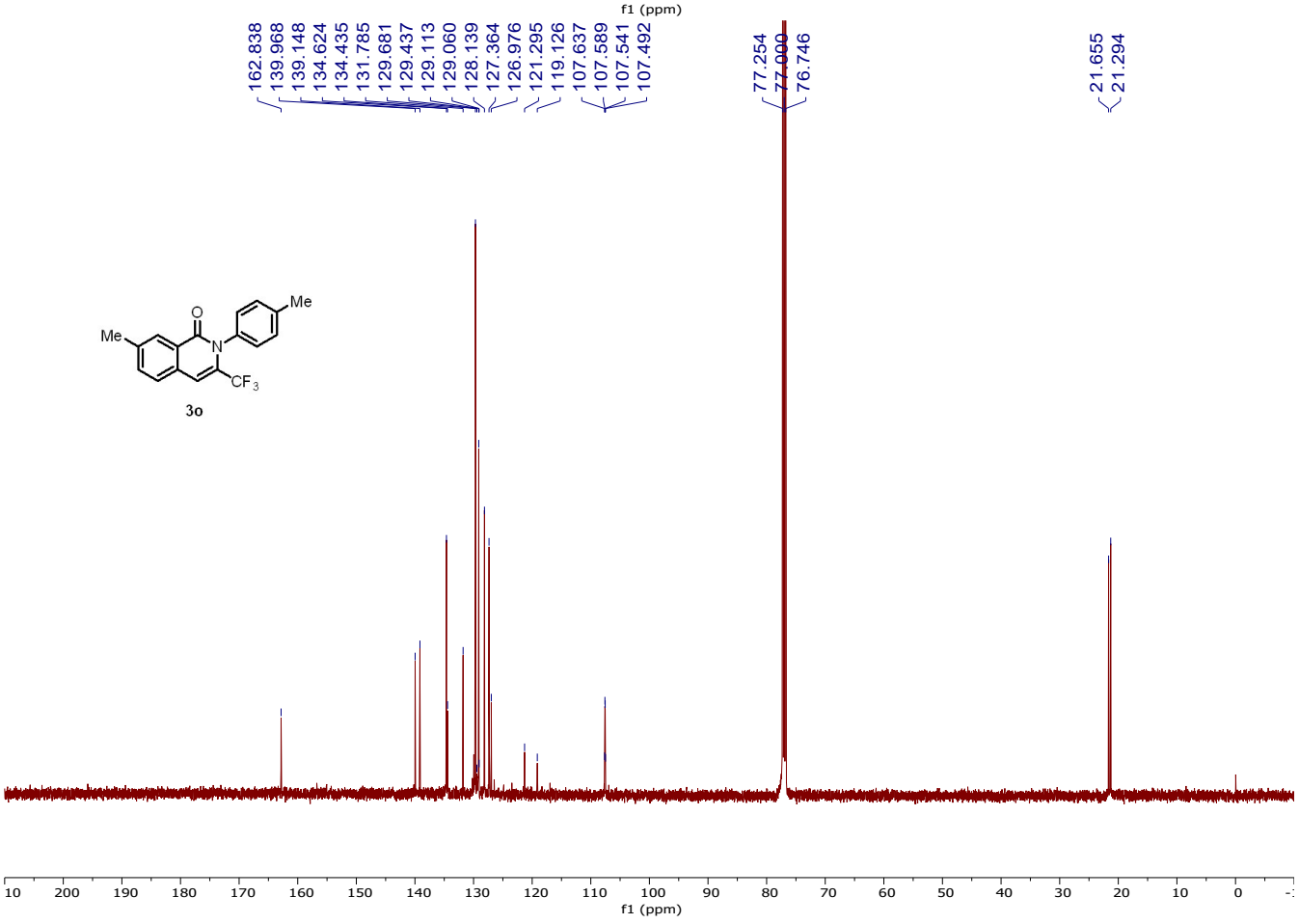
3.08
f1 (ppm)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126.976
121.295
119.126
107.637
107.589
107.541
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77.000
76.746
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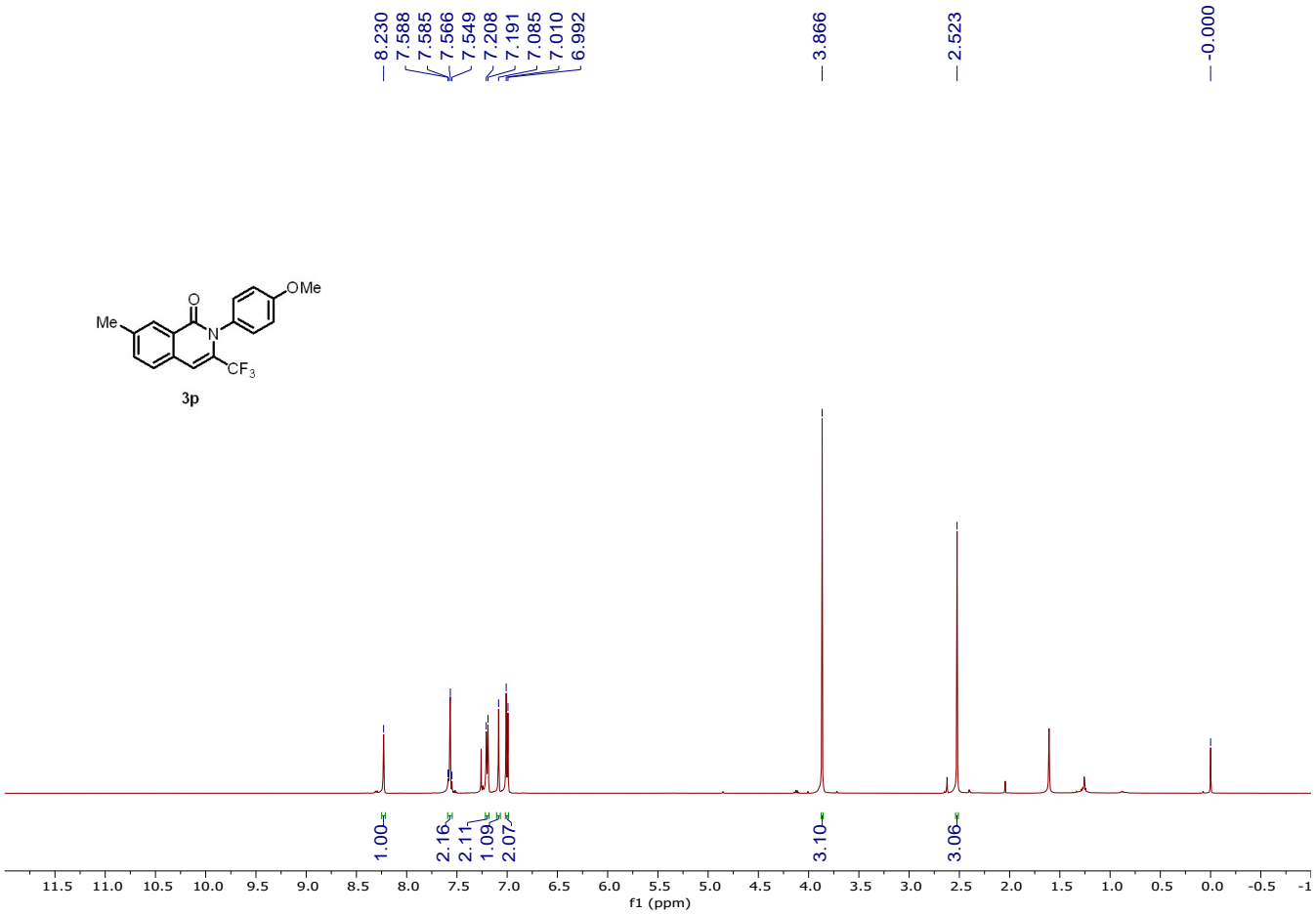
Me
Me
O
N
CF3
3o
f1 (ppm)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7.085
7.010
6.992
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-0.000
OMe
Me
O
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CF3
3p
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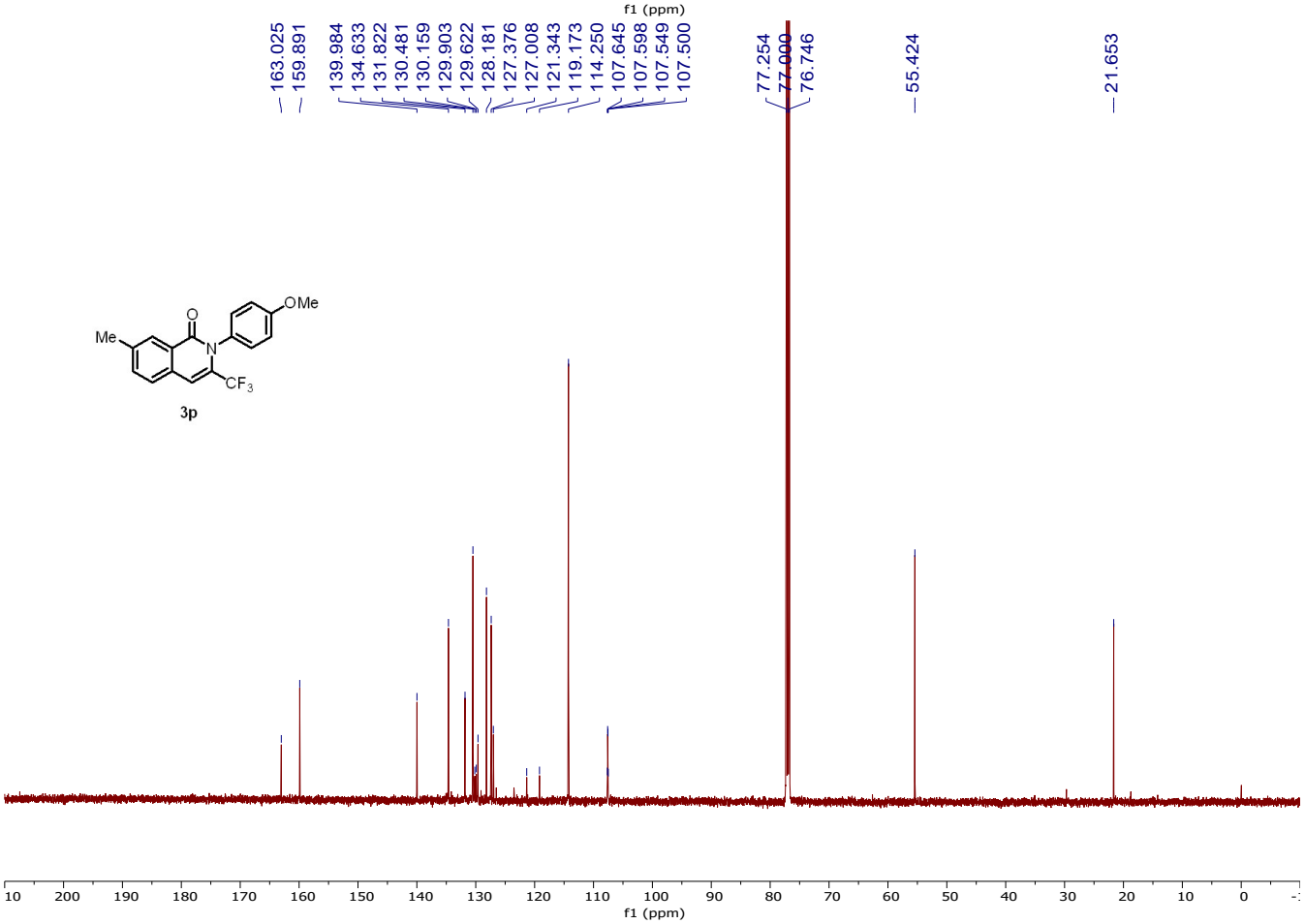
2.11
1.09
2.07
3.10
3.06
f1 (ppm)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119.173
114.250
107.645
107.598
107.549
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77.000
76.746
55.424
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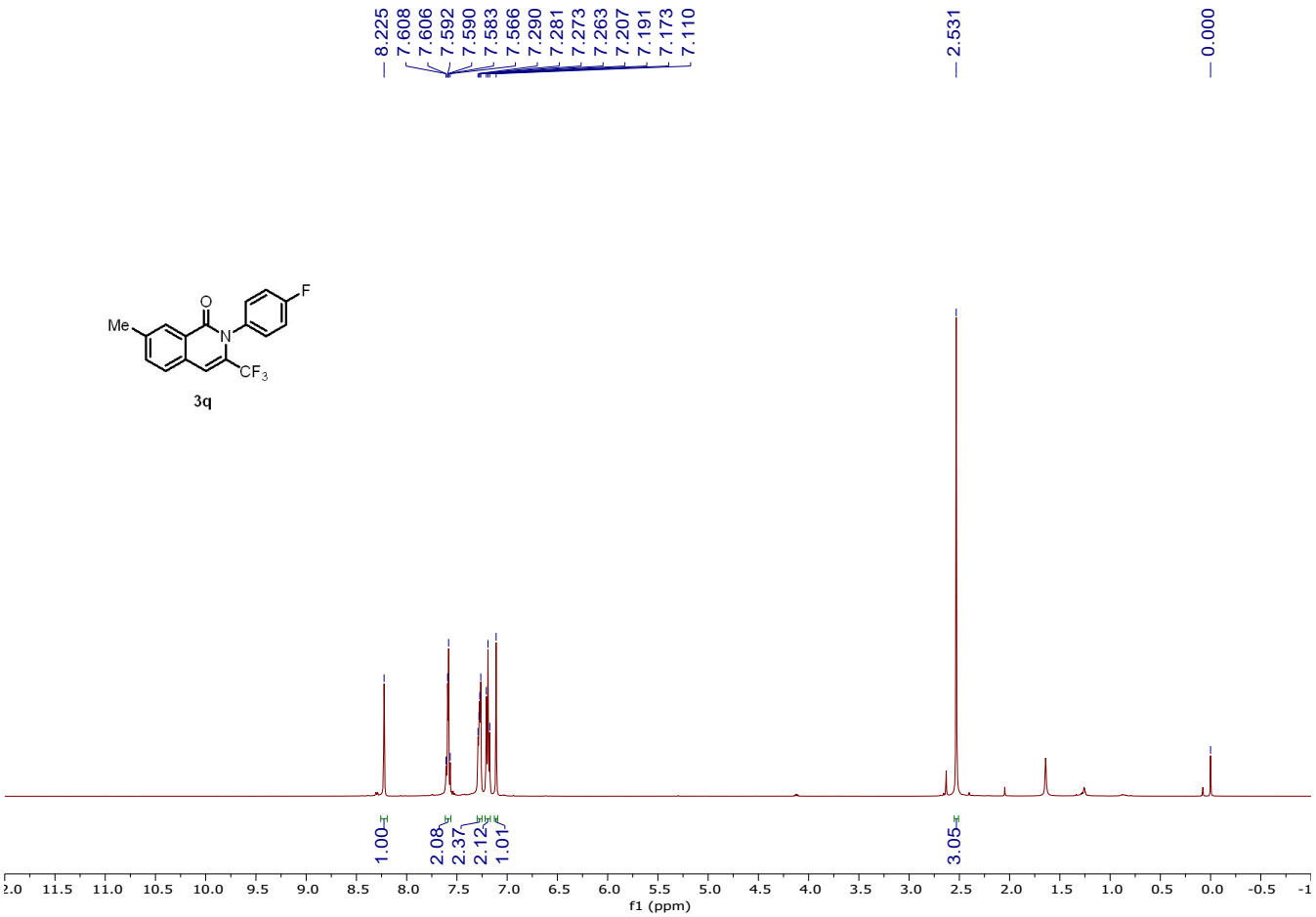
Me
O
N
CF3
3p
f1 (ppm)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7.191
7.173
7.110
2.531
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CF3
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2.12
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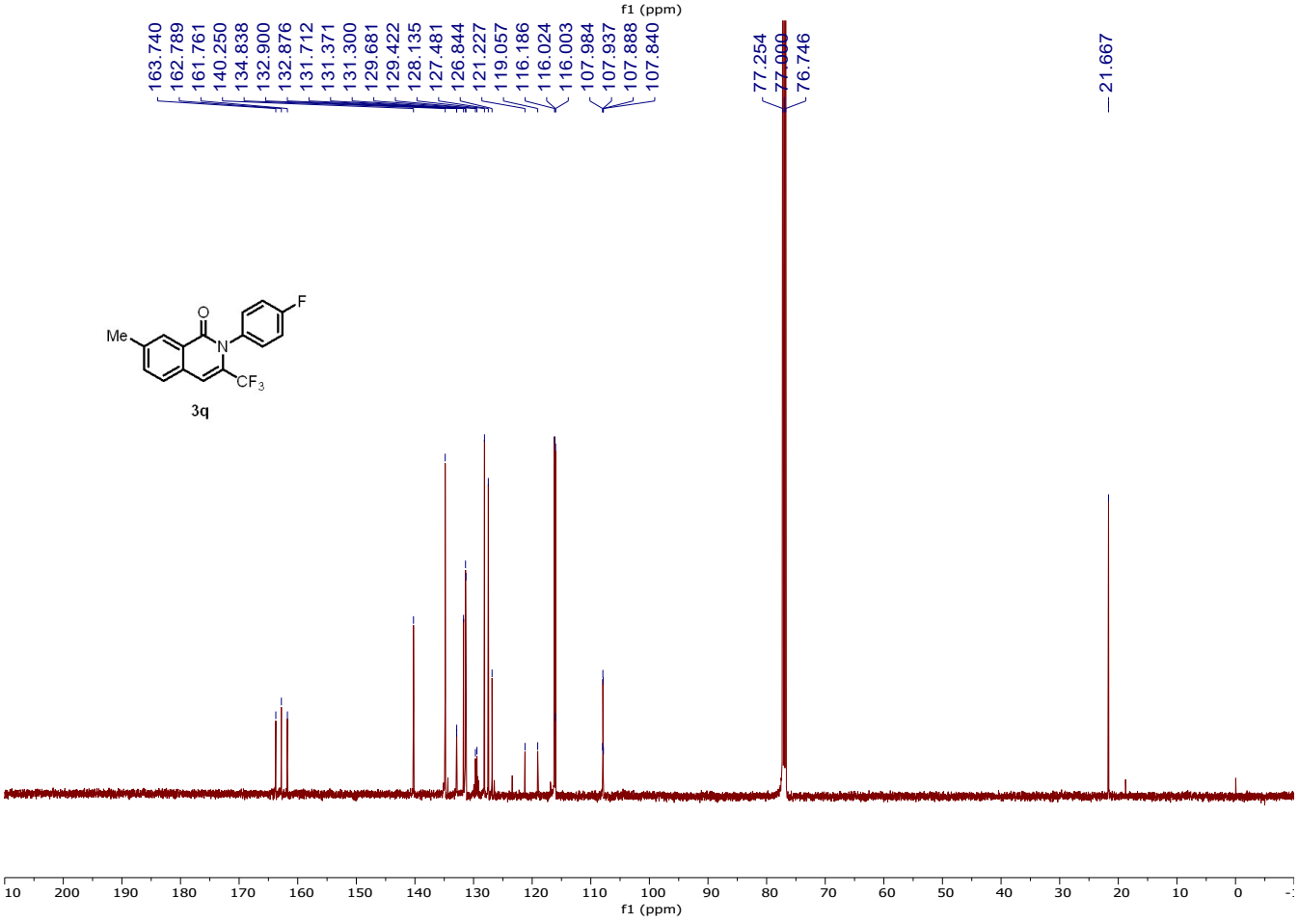
3.05
f1 (ppm)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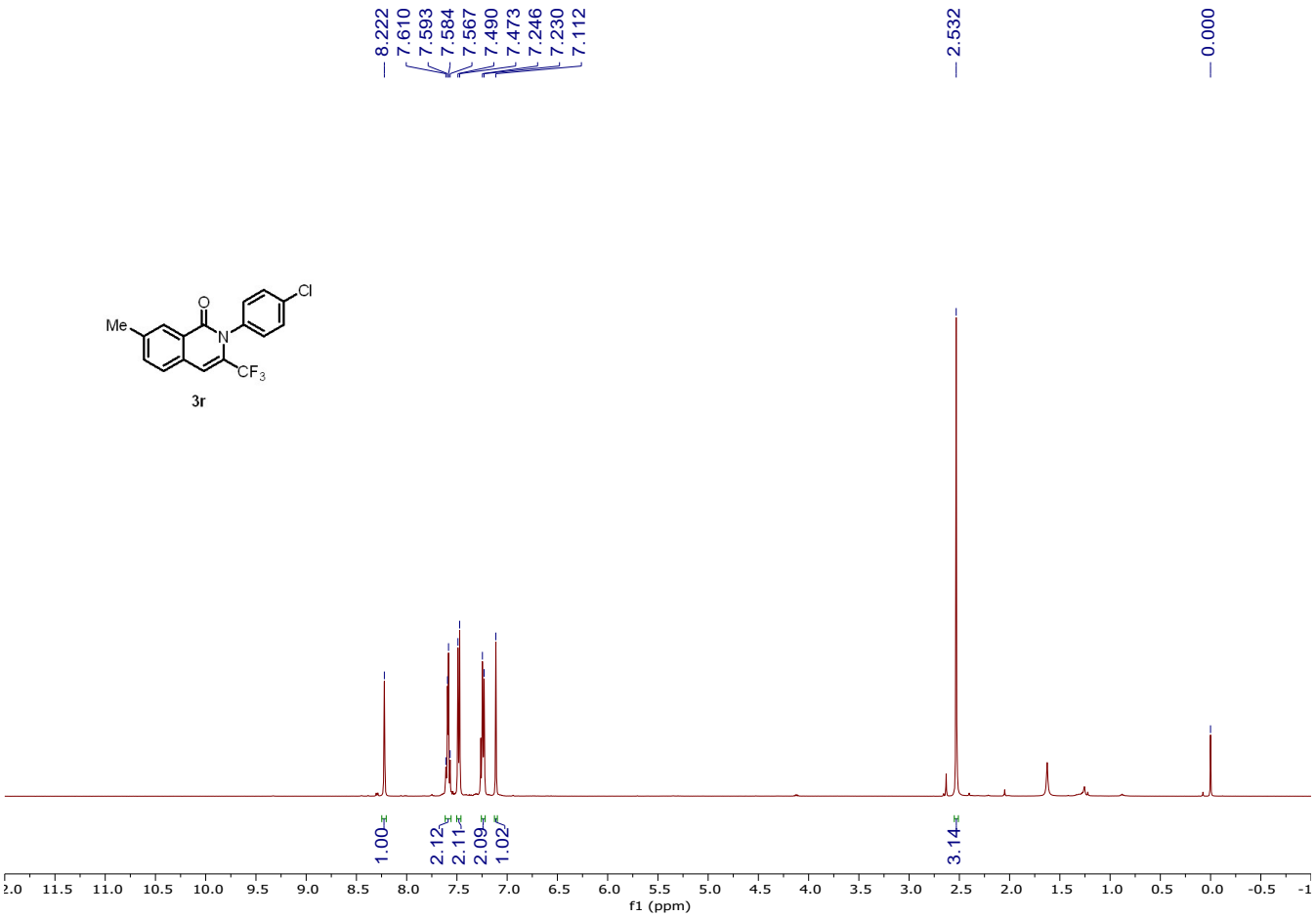
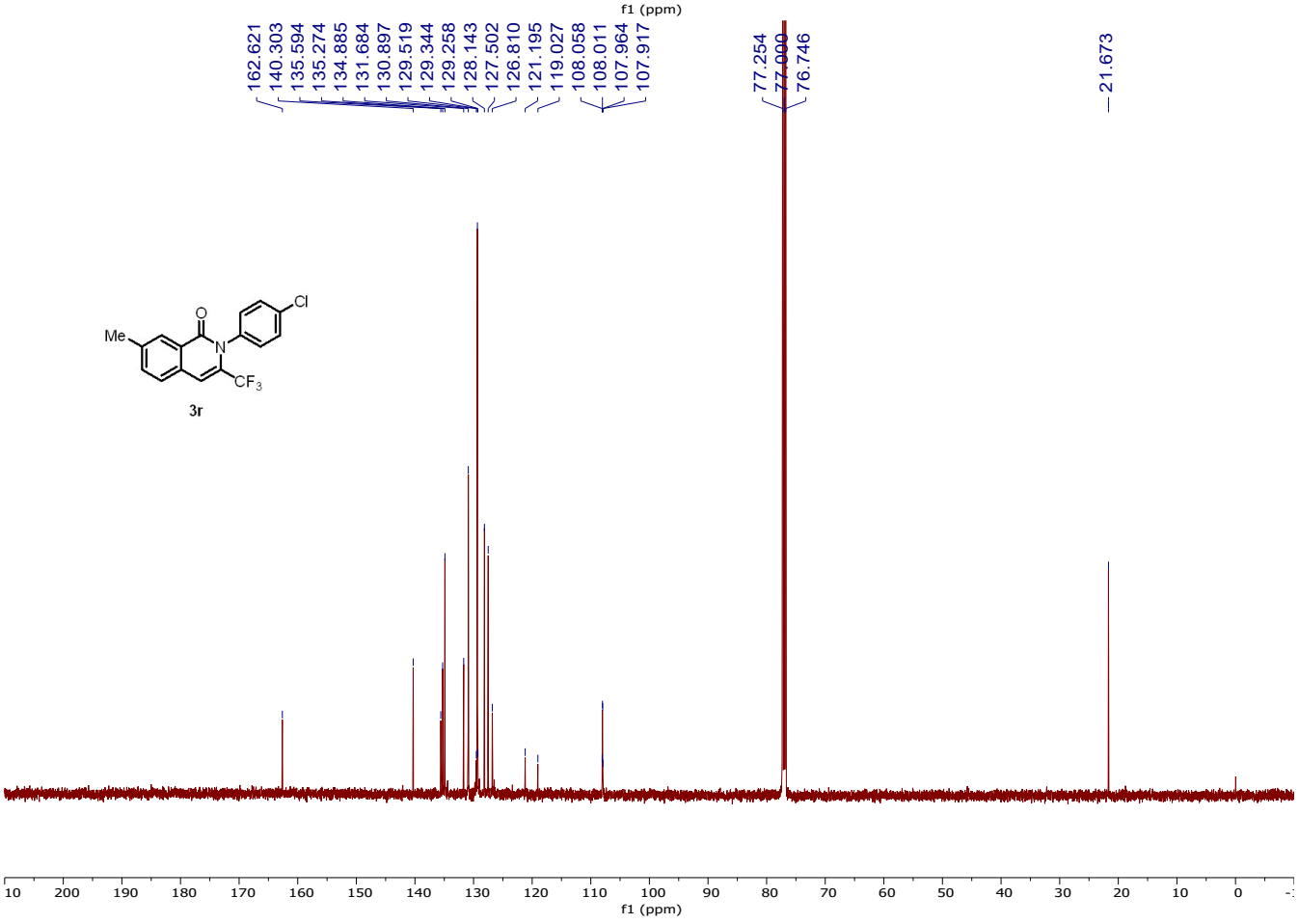
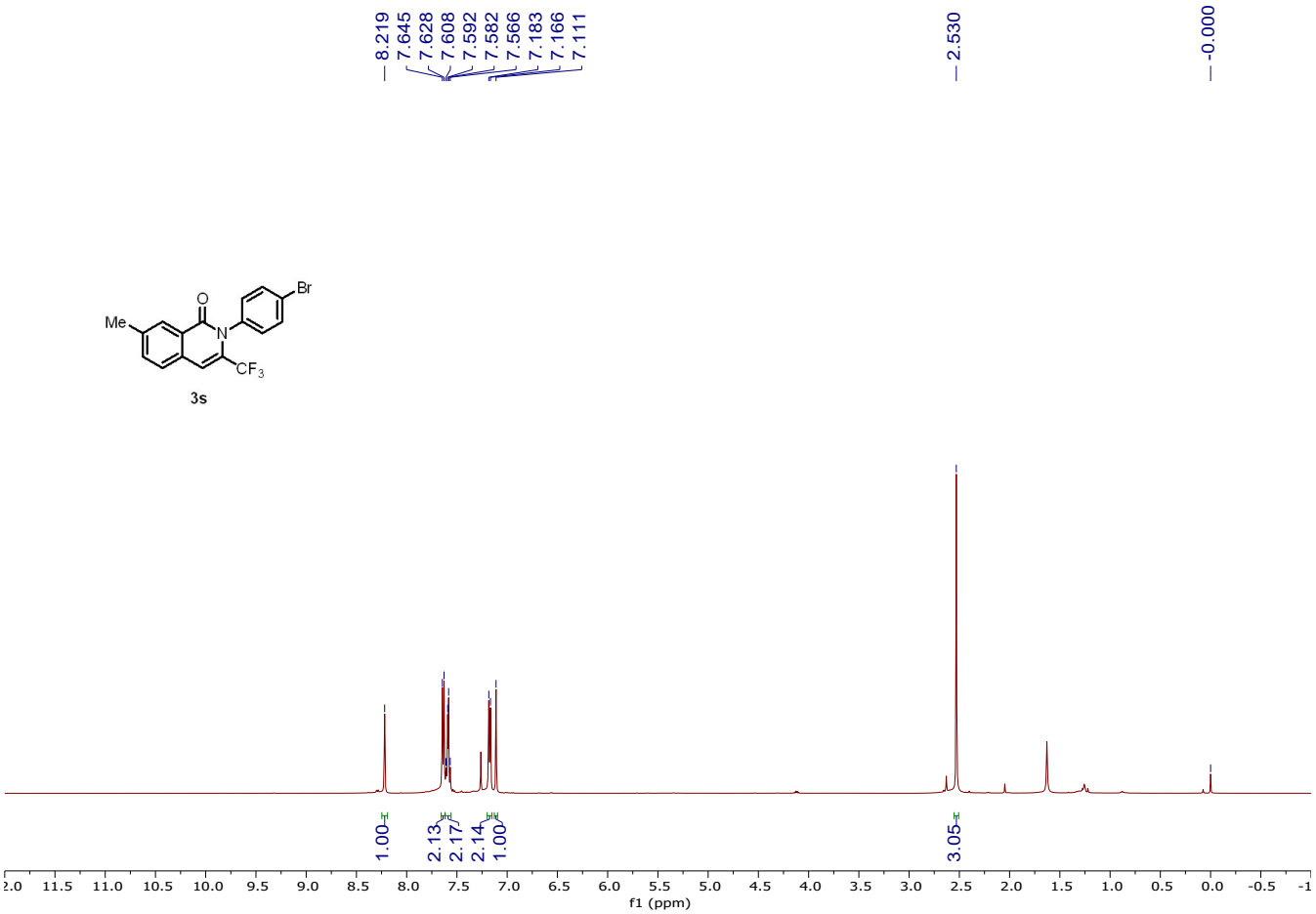
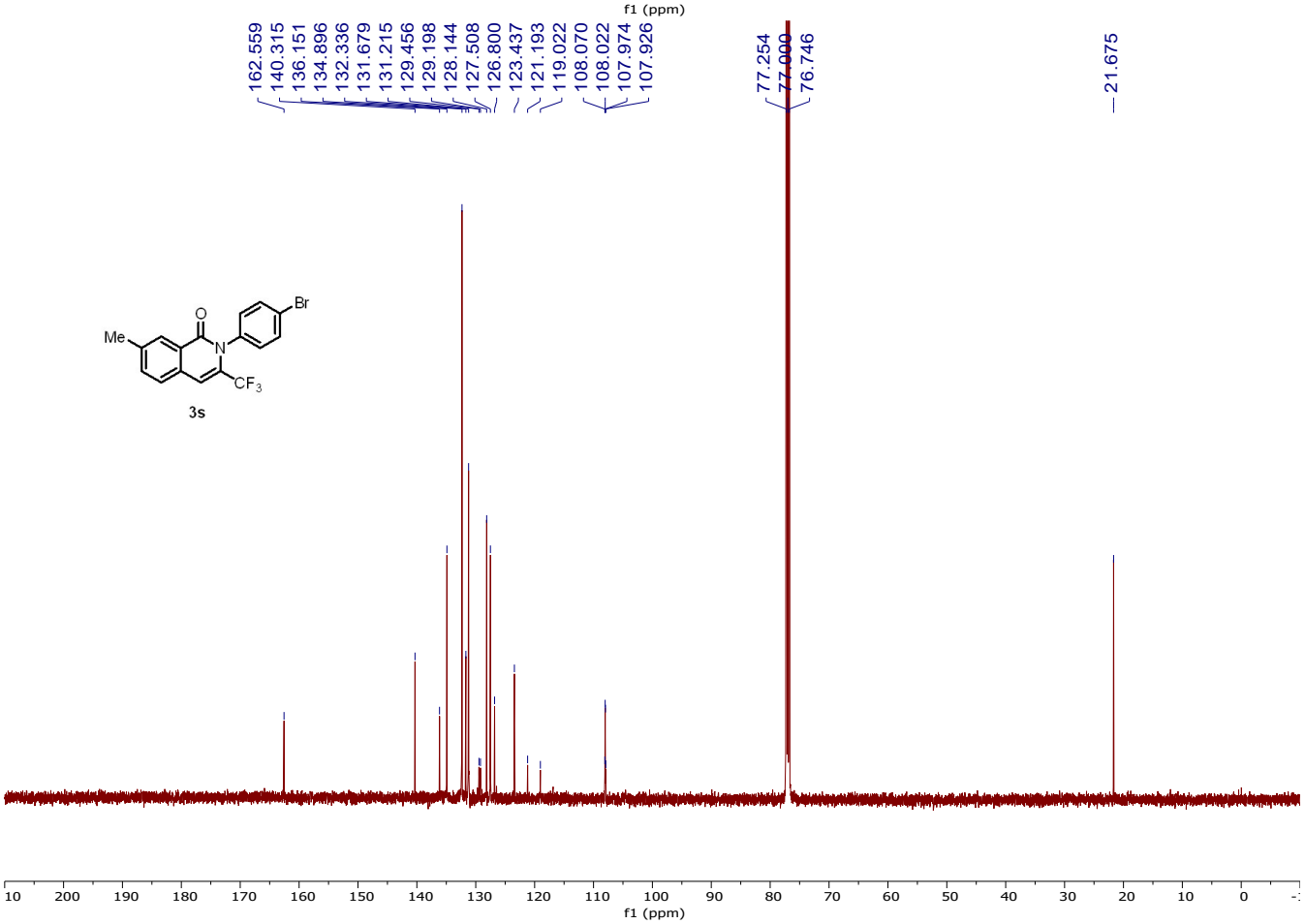
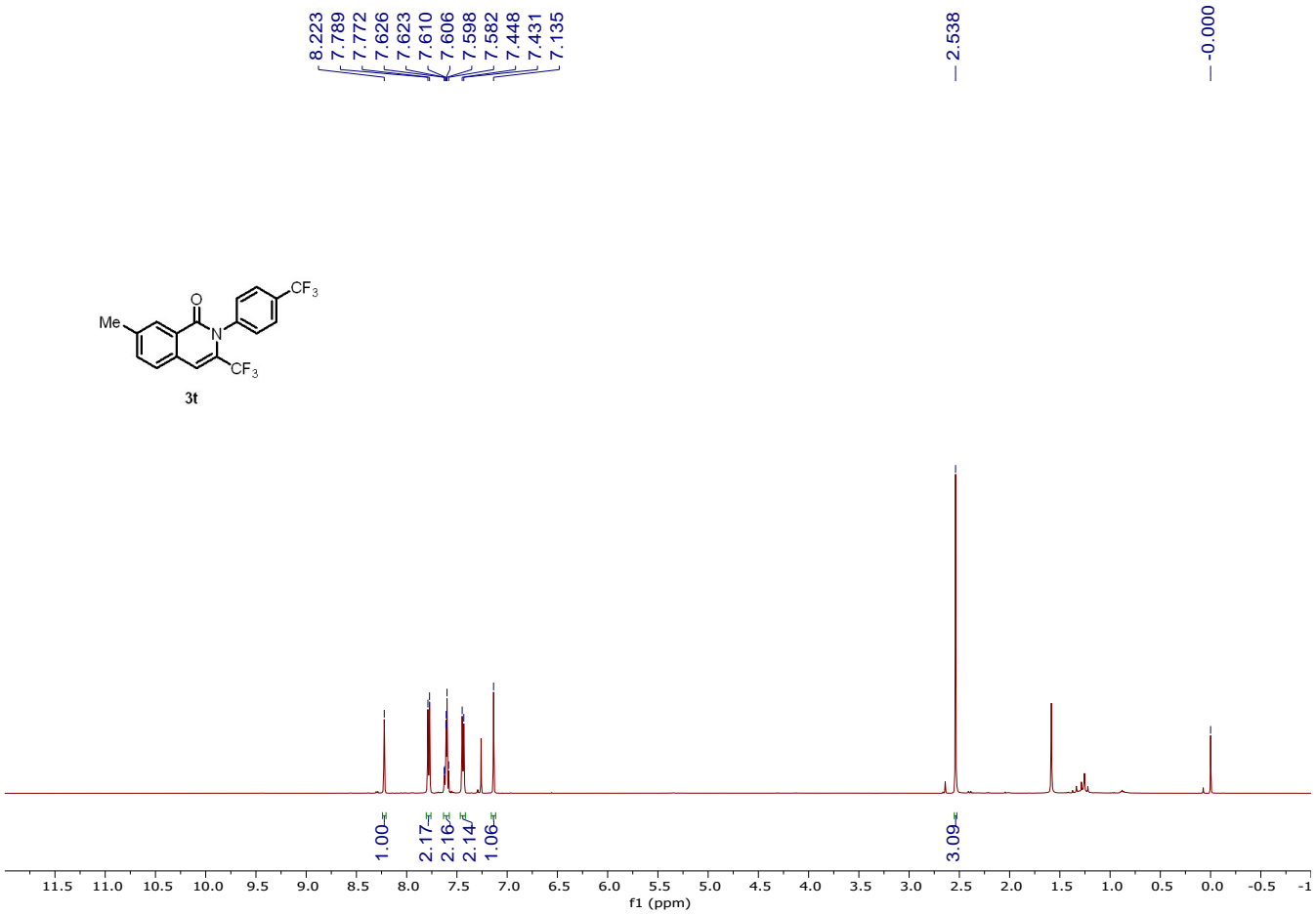
131.712
131.371
131.300
129.681
129.422
128.135
127.481
126.844
121.227
119.057
116.186
116.024
116.003
107.984
107.937
107.888
107.840
77.254
77.000
76.746
21.667
Me
O
N
F
CF3
3q
f1 (ppm)

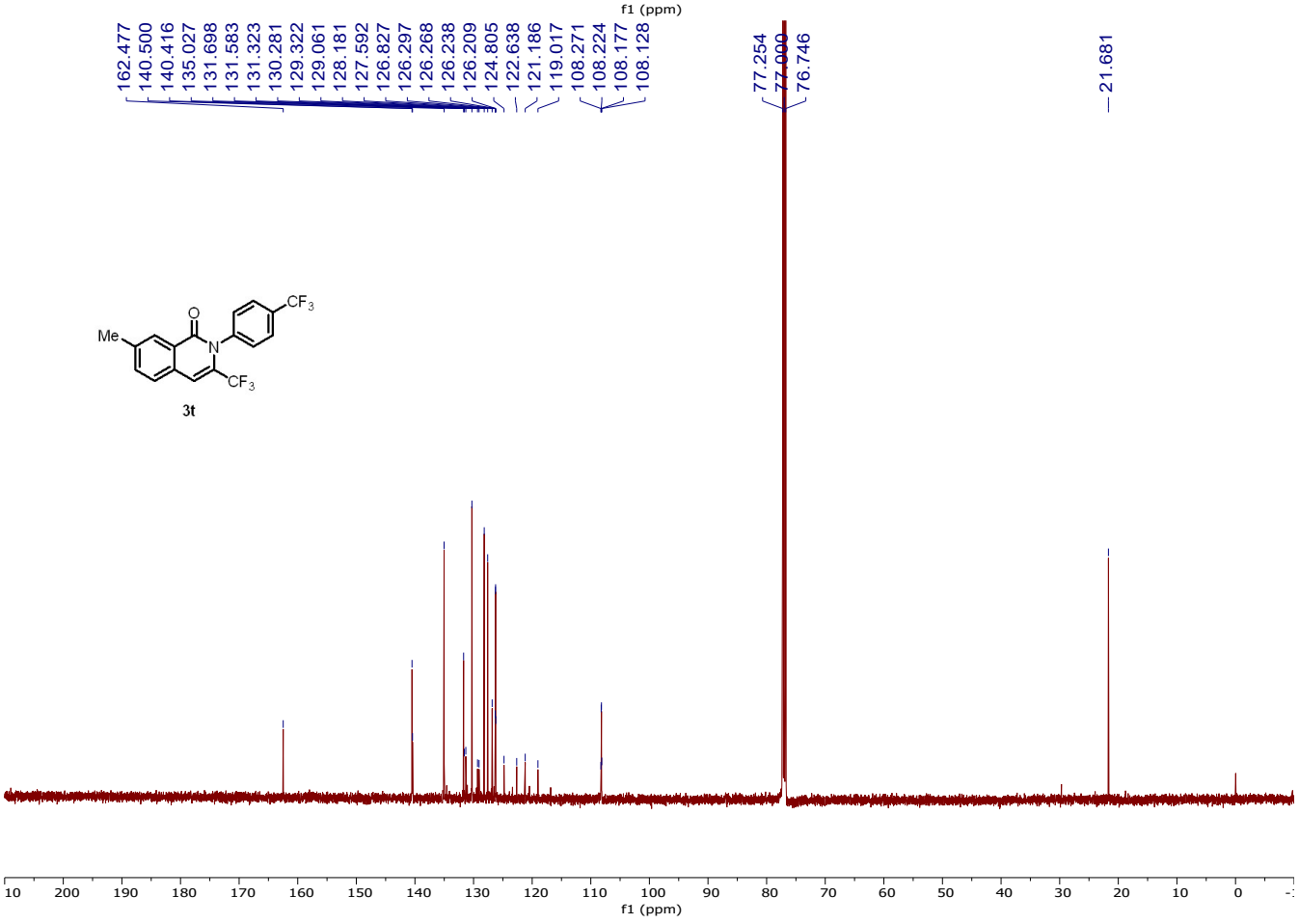

8.222
7.610
7.593
7.584
7.567
7.490
7.473
7.246
7.230
7.112
2.532
0.000
Me
Cl
O
N
CF3
3r
1.00
2.12
2.11
2.09
1.02
3.14
f1 (ppm)

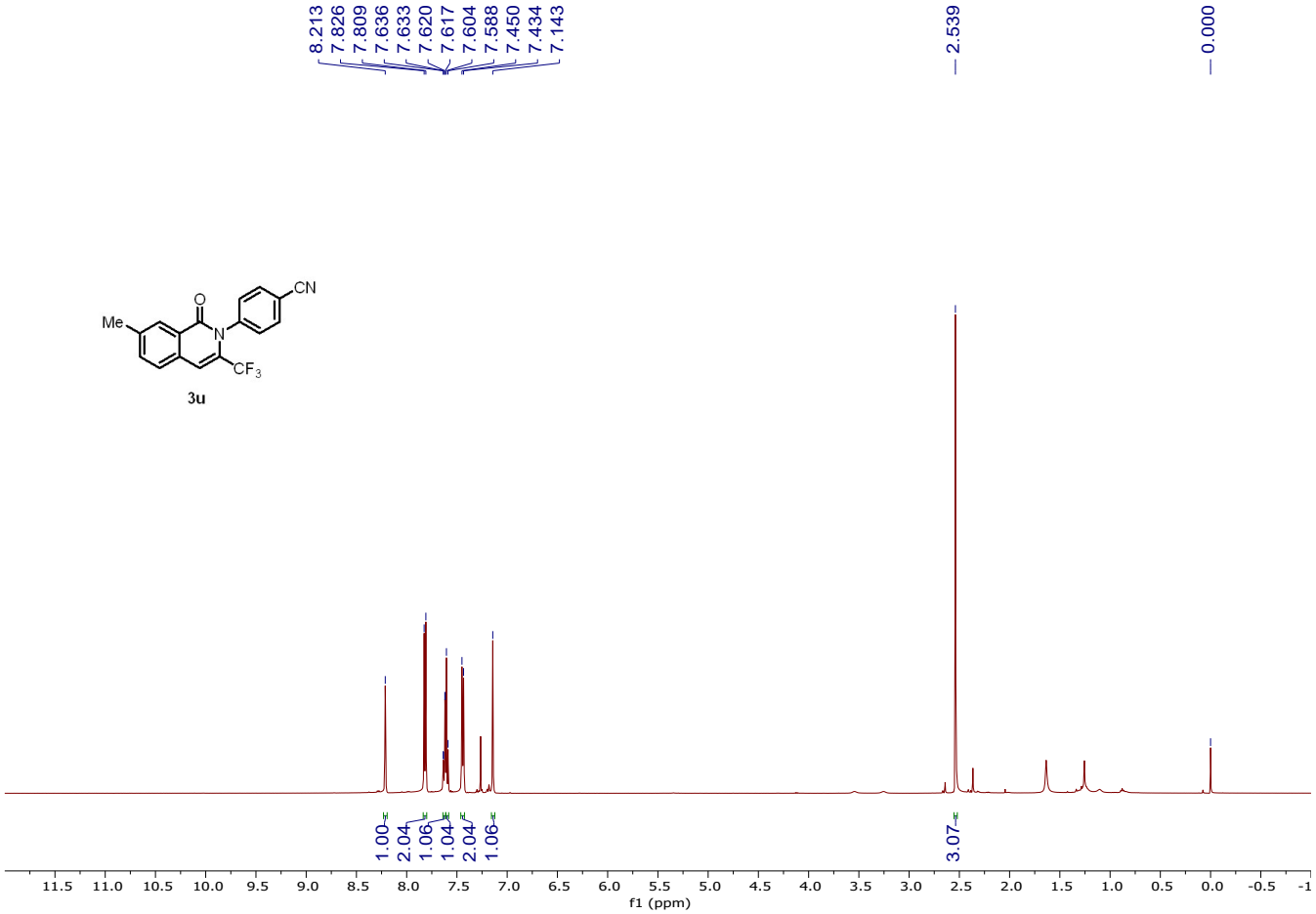

162.621
140.303
135.594
135.274
134.885
131.684
130.897
129.519
129.344
129.258
128.143
127.502
126.810
121.195
119.027
108.058
108.011
107.964
107.917
77.254
77.000
76.746
21.673
Me
Cl
O
N
CF3
3r
f1 (ppm)

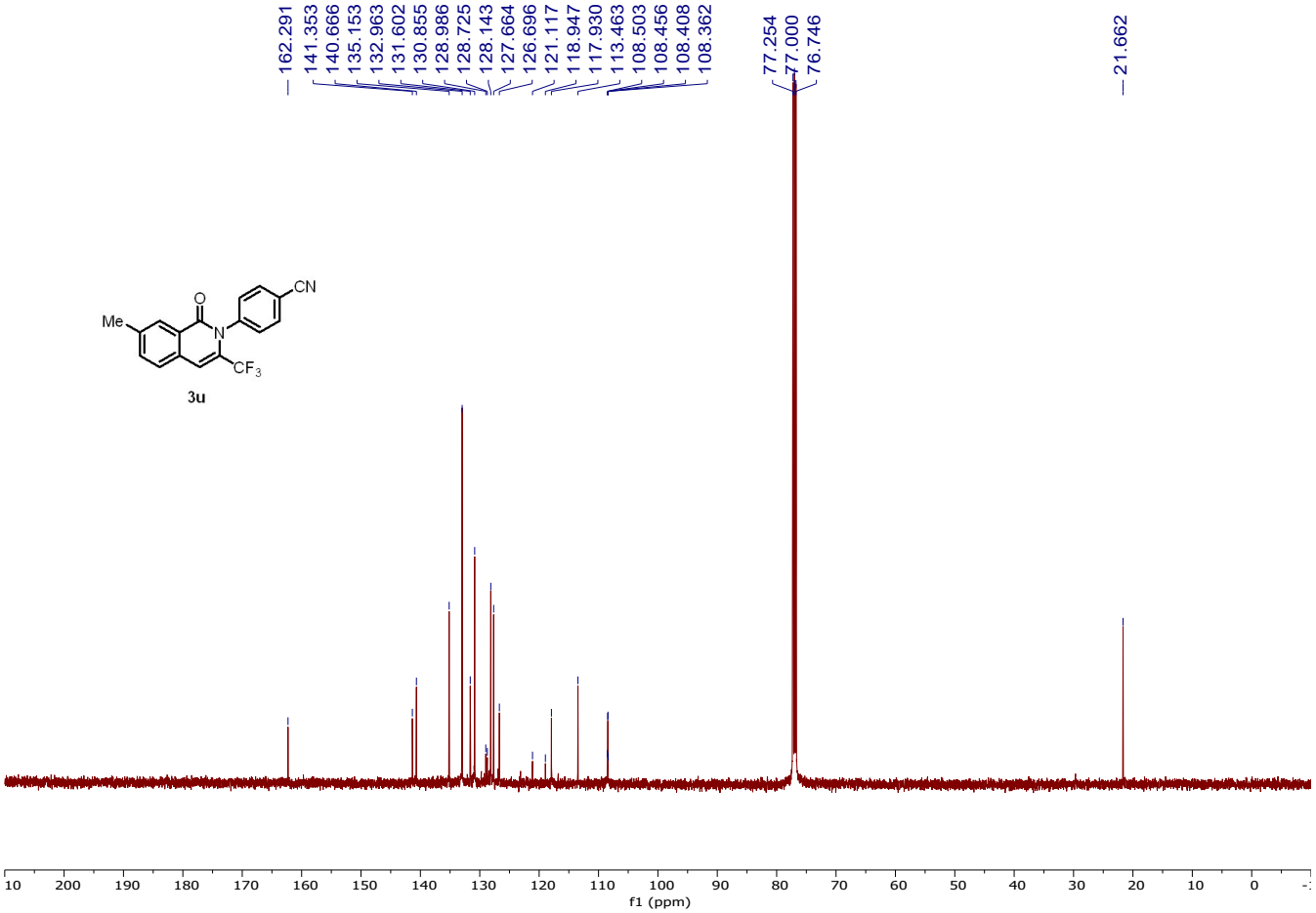

8.219
7.645
7.628
7.608
7.592
7.582
7.566
7.183
7.166
7.111
2.530
-0.000
Me
O
N
Br
CF3
3s
1.00
2.13
2.17
2.14
1.00
3.05
f1 (ppm)


162.559
140.315
136.151
134.896
132.336
131.679
131.215
129.456
129.198
128.144
127.508
126.800
123.437
121.193
119.022
108.070
108.022
107.974
107.926
77.254
77.000
76.746
21.675
Me
O
N
Br
CF3
3s
f1 (ppm)


8.223
7.789
7.772
7.626
7.623
7.610
7.606
7.598
7.582
7.448
7.431
7.135
2.538
-0.000
Me
O
N
CF3
CF3
3t
1.00
2.17
2.16
2.14
1.06
3.09
f1 (ppm)


162.477
140.500
140.416
135.027
131.698
131.583
131.323
130.281
129.322
129.061
128.181
127.592
126.827
126.297
126.268
126.238
126.209
124.805
122.638
121.186
119.017
108.271
108.224
108.177
108.128
77.254
77.000
76.746
21.681
Me
O
N
CF3
CF3
3t
f1 (ppm)


8.213
7.826
7.809
7.636
7.633
7.620
7.617
7.604
7.588
7.450
7.434
7.143
2.539
0.000
CN
Me
O
N
CF3
3u
1.00
2.04
1.06
1.04
2.04
1.06
3.07
f1 (ppm)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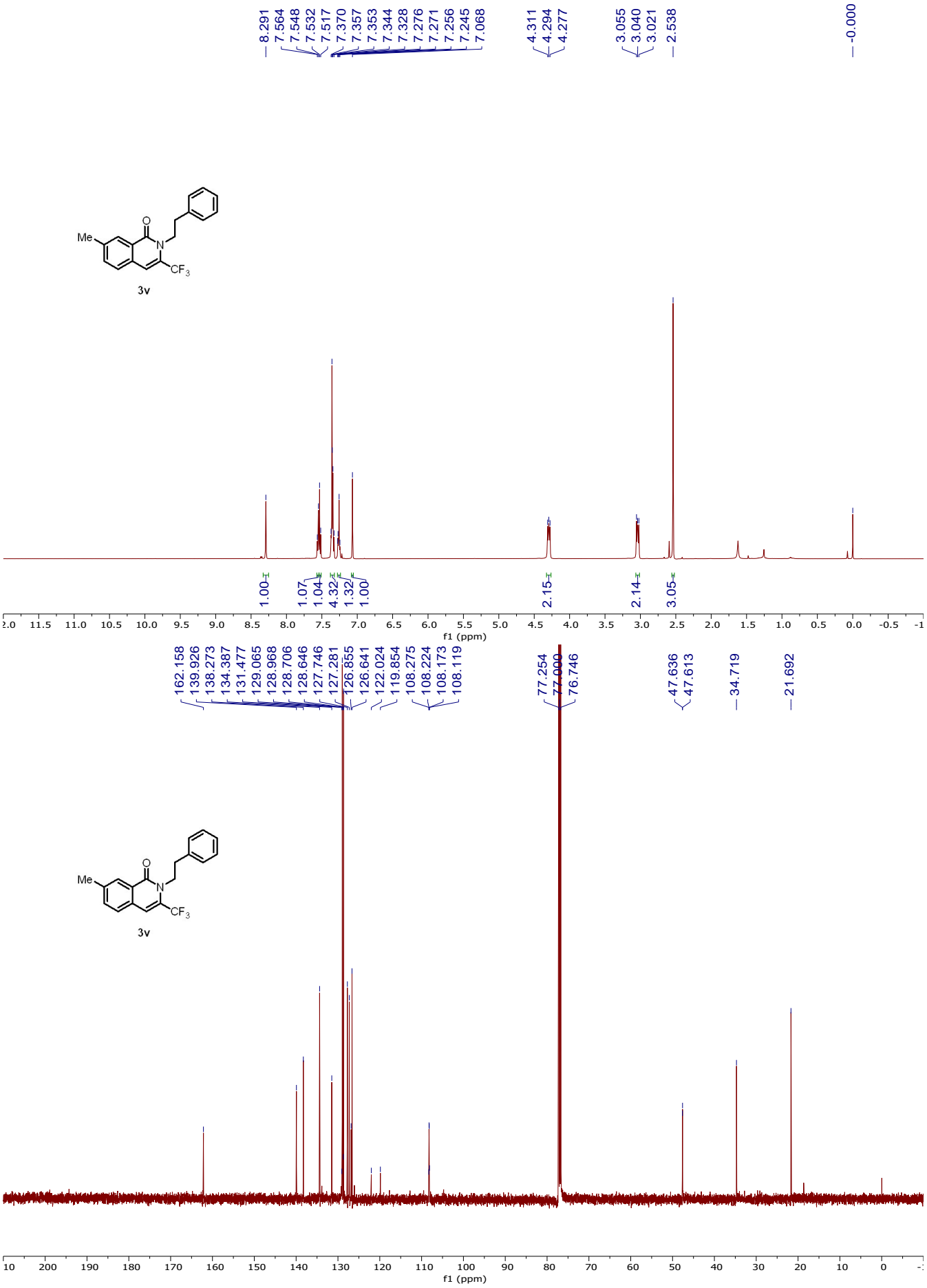
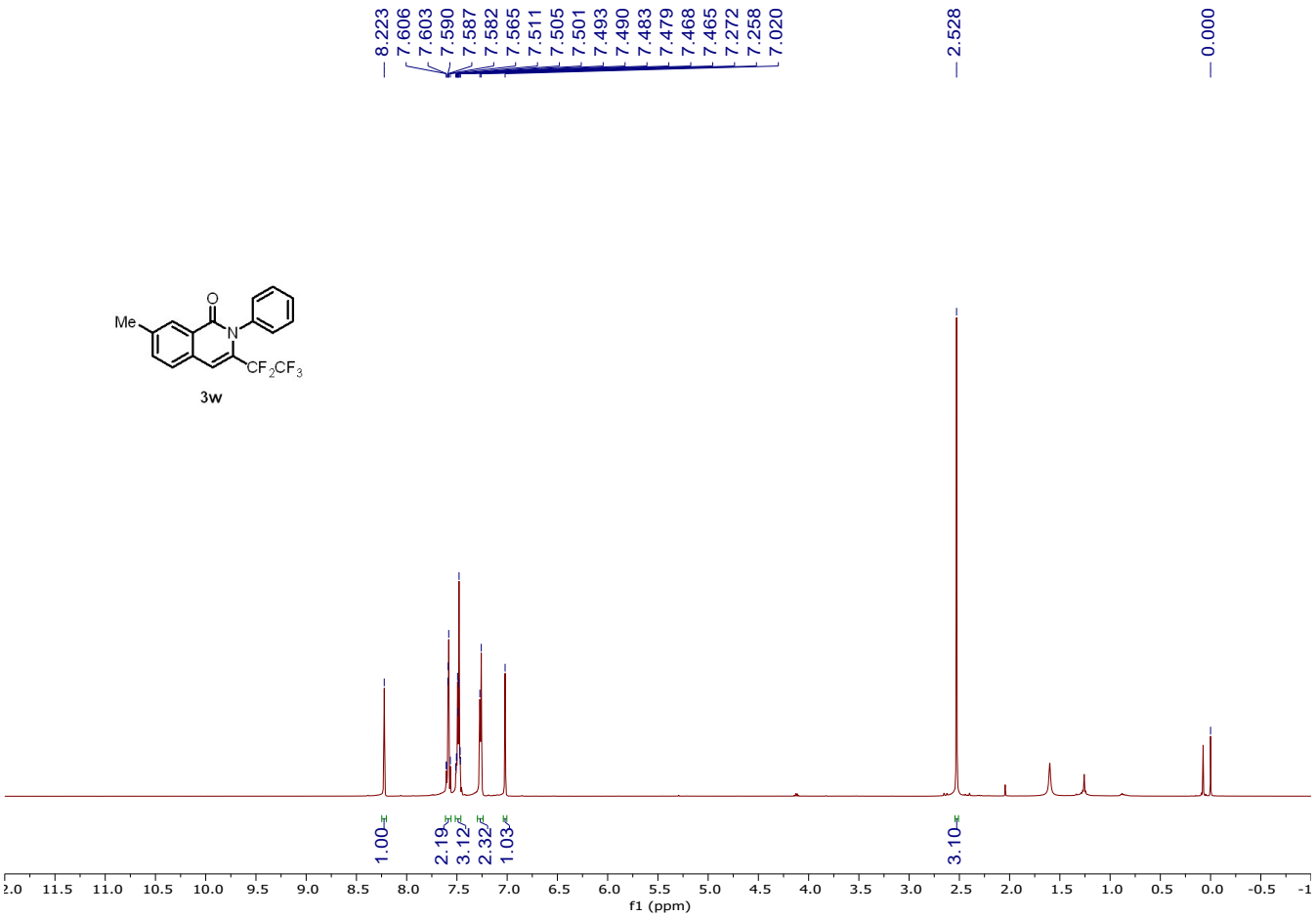
141.353
140.666
135.153
132.963
131.602
130.855
128.986
128.725
128.143
127.664
126.696
121.117
118.947
117.930
113.463
108.503
108.456
108.408
108.362
77.254
77.000
76.746
21.662
CN
Me
O
N
CF3
3u
f1 (ppm)


8.291
7.564
7.548
7.532
7.517
7.370
7.357
7.353
7.344
7.328
7.276
7.271
7.256
7.245
7.068
4.311
4.294
4.277
3.055
3.040
3.021
2.538
-0.000
Me
O
N
CF3
3v
1.00
1.07
1.04
4.32
1.32
1.00
2.15
2.14
3.05
f1 (ppm)
162.158
139.926
138.273
134.387
131.477
129.065
128.968
128.706
128.646
127.746
127.281
126.855
126.641
122.024
119.854
108.275
108.224
108.173
108.119
77.254
77.000
76.746
47.636
47.613
34.719
21.692
Me
O
N
CF3
3v
f1 (ppm)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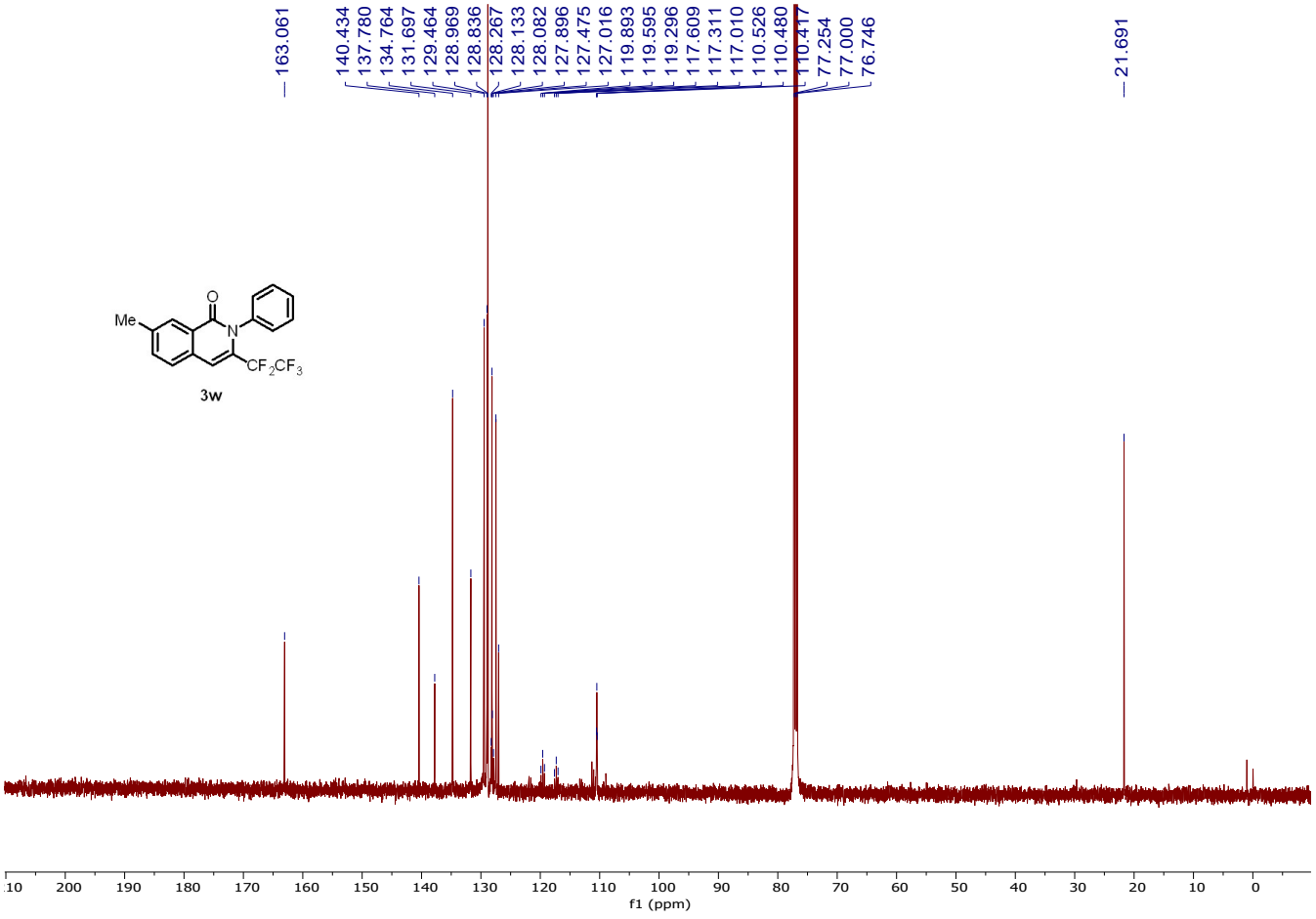
7.606
7.603
7.590
7.587
7.582
7.565
7.511
7.505
7.501
7.493
7.490
7.483
7.479
7.468
7.465
7.272
7.258
7.020
2.528
0.000
Me
O
N
CF2CF3
3w
1.00
2.19
3.12
2.32
1.03
3.10
f1 (ppm)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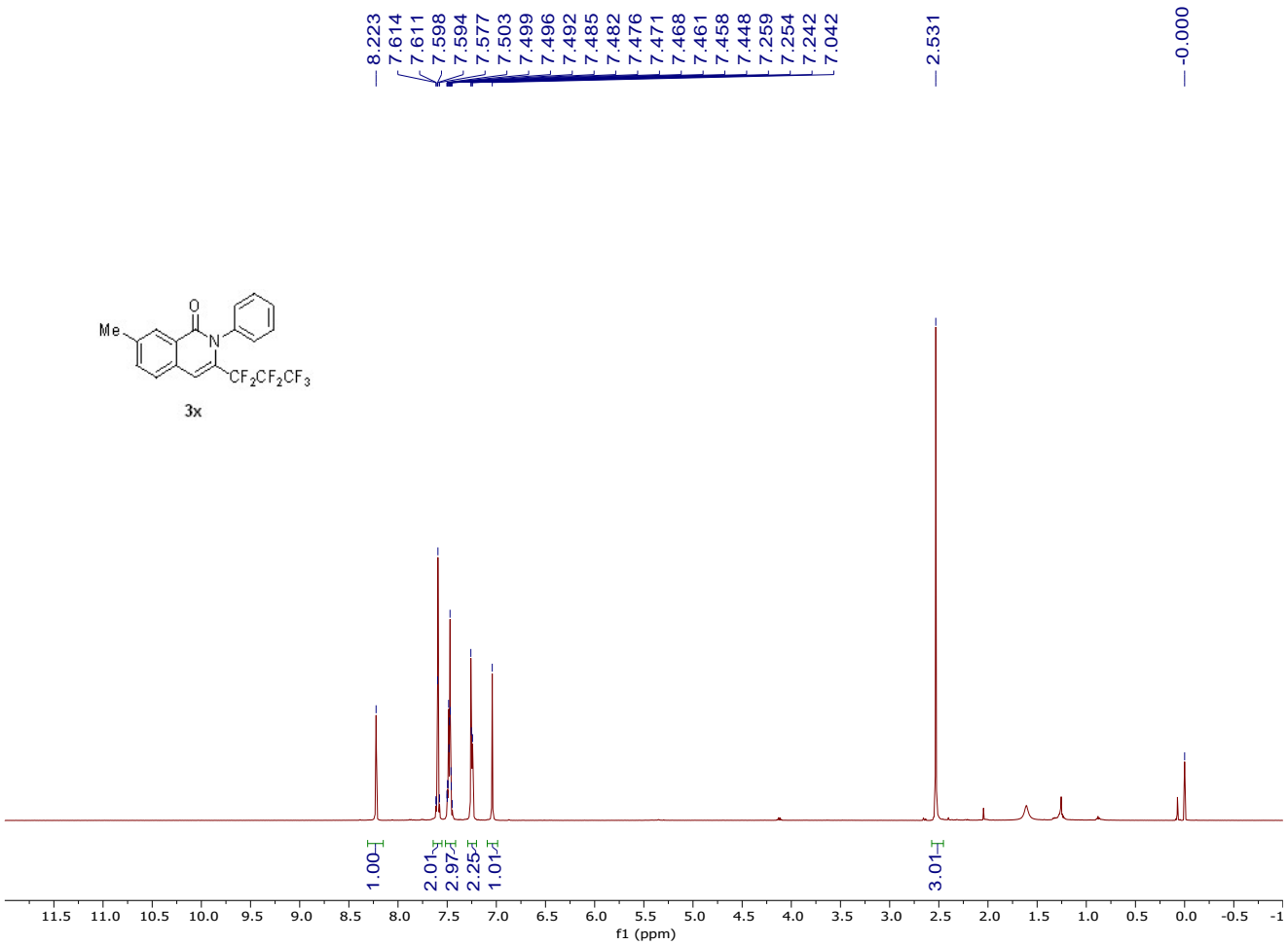
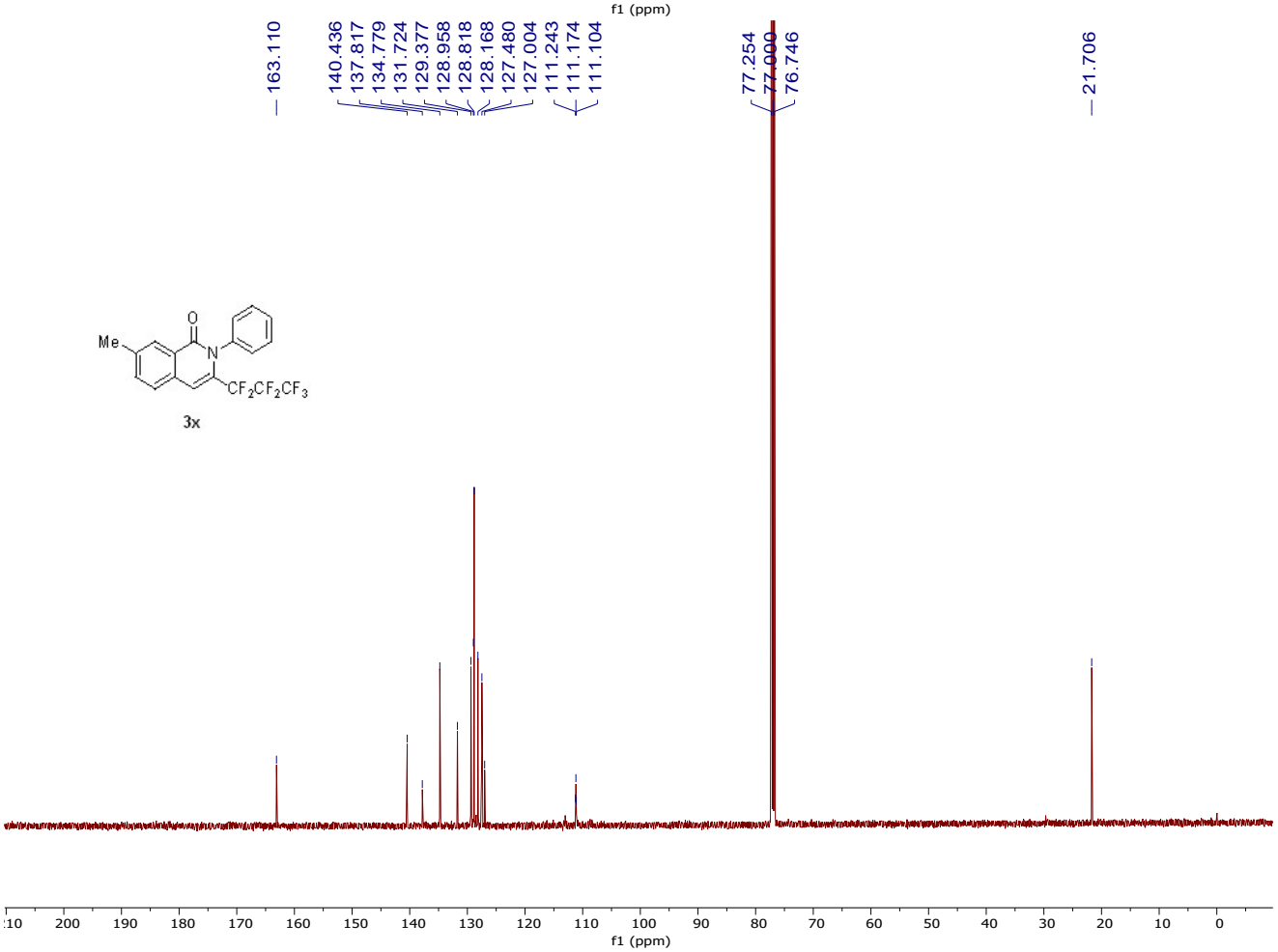
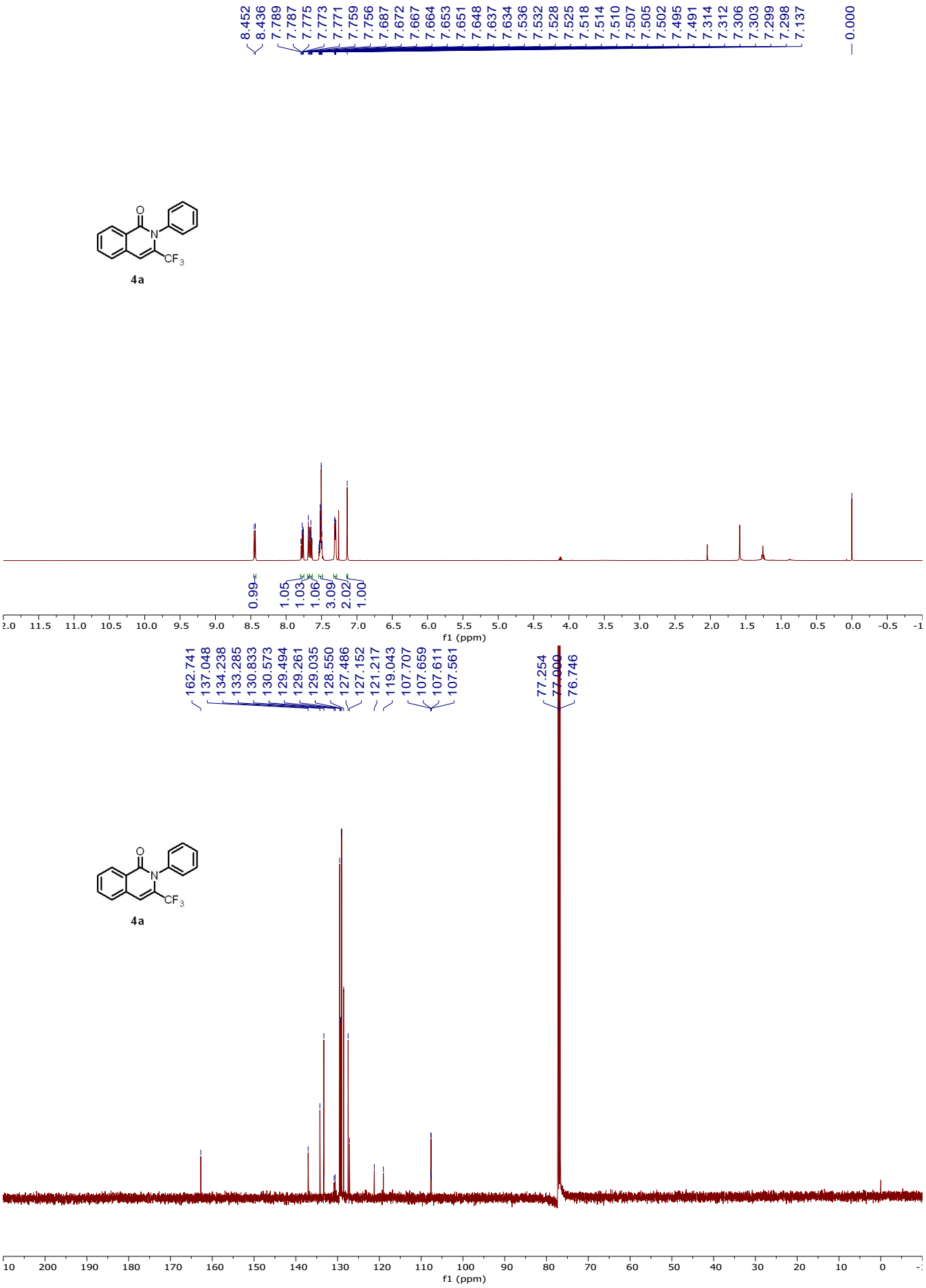
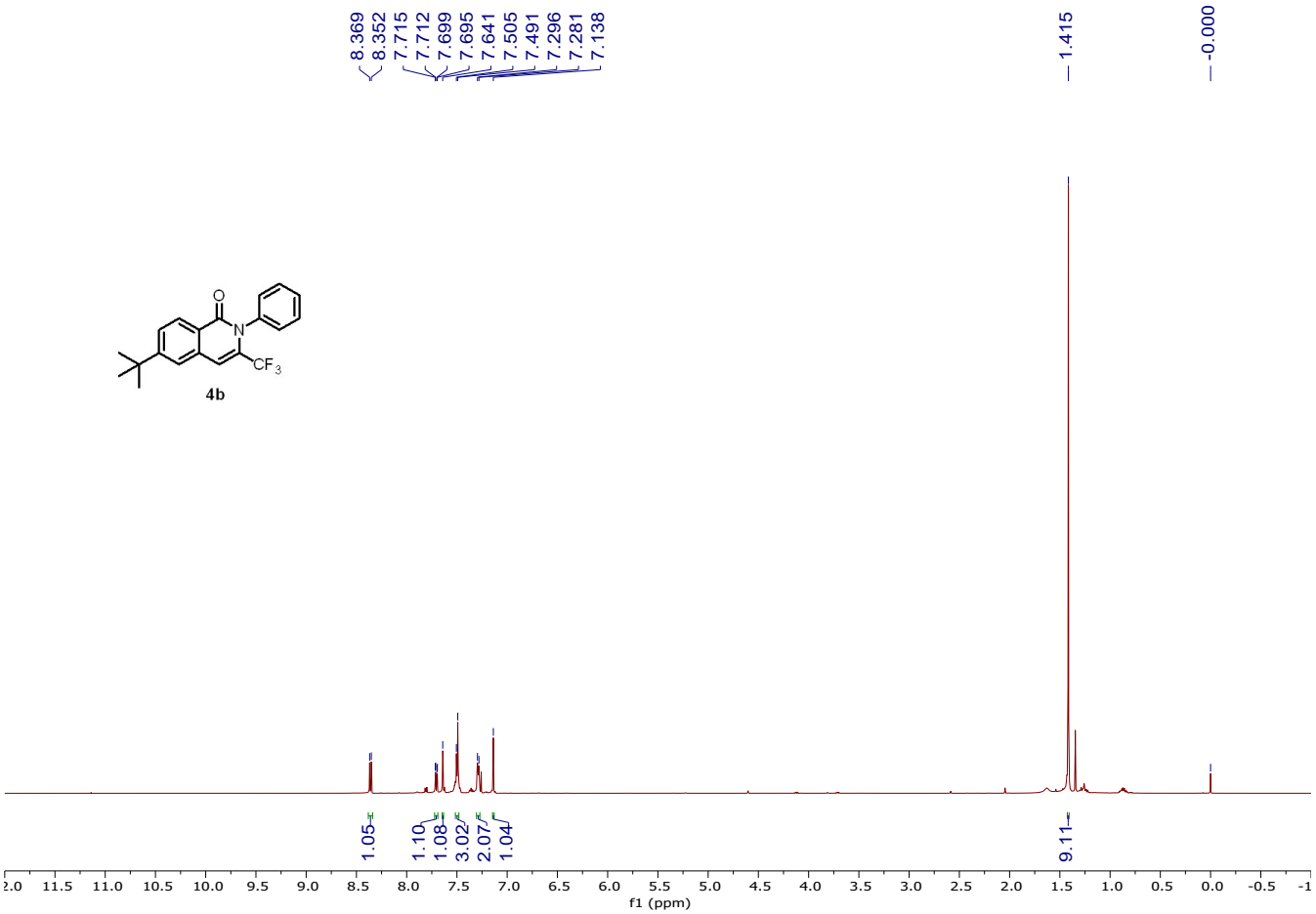
140.434
137.780
134.764
131.697
129.464
128.969
128.836
128.267
128.133
128.082
127.896
127.475
127.016
119.893
119.595
119.296
117.609
117.311
117.010
110.526
110.480
110.417
77.254
77.000
76.746
21.691
Me
O
N
CF2CF3
3w
f1 (ppm)


8.223
7.614
7.611
7.598
7.594
7.577
7.503
7.499
7.496
7.492
7.485
7.482
7.476
7.471
7.468
7.461
7.458
7.448
7.259
7.254
7.242
7.042
2.531
-0.000
Me
O
N
CF2CF2CF3
3x
1.00
2.01
2.97
2.25
1.01
3.01
f1 (ppm)

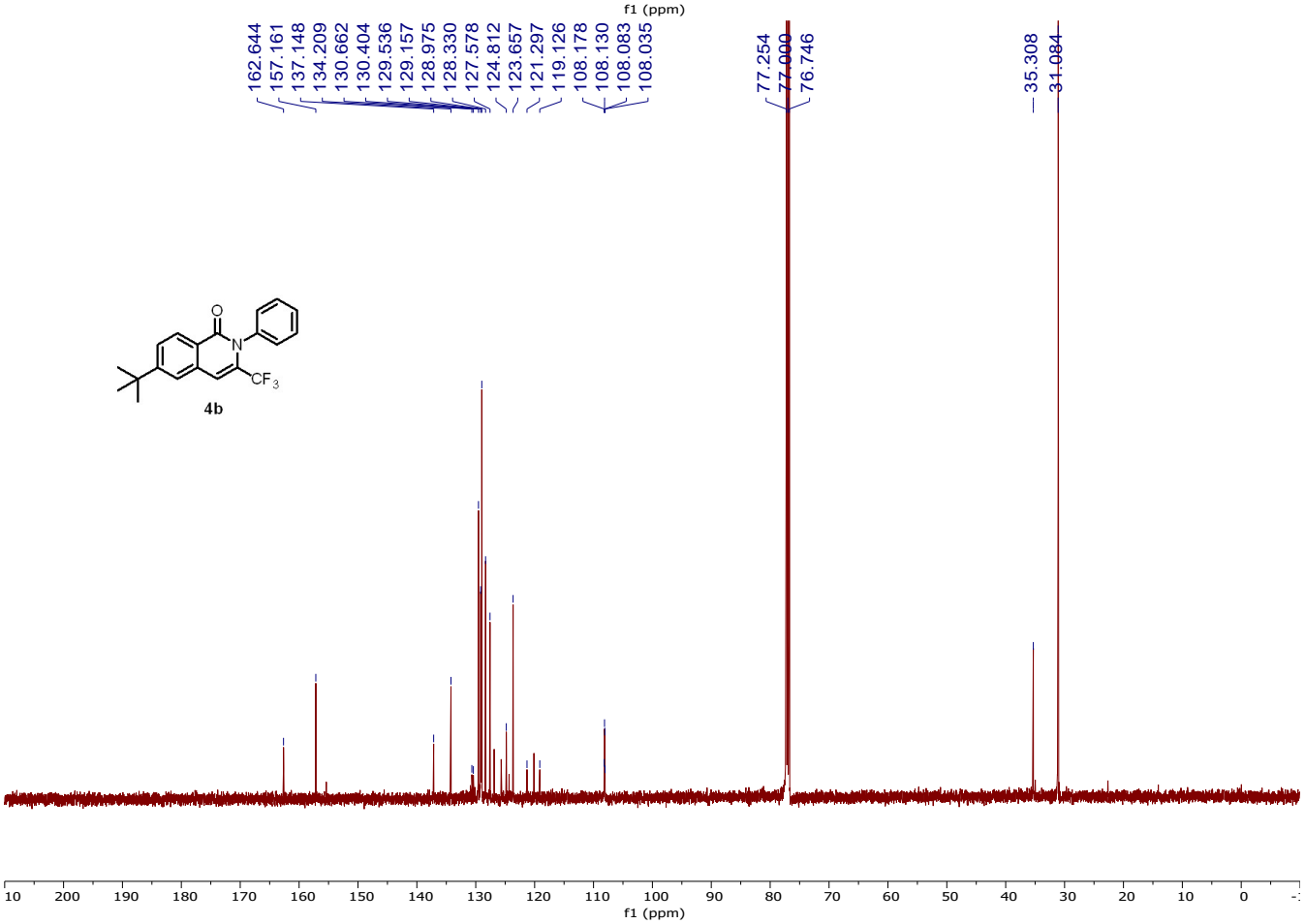

163.110
140.436
137.817
134.779
131.724
129.377
128.958
128.818
128.168
127.480
127.004
111.243
111.174
111.104
77.254
77.000
76.746
21.706
Me
O
N
CF2CF2CF3
3x
f1 (ppm)


8.452
8.436
7.789
7.787
7.775
7.773
7.771
7.759
7.756
7.687
7.672
7.667
7.664
7.653
7.651
7.648
7.637
7.634
7.536
7.532
7.528
7.525
7.518
7.514
7.510
7.507
7.505
7.502
7.495
7.491
7.314
7.312
7.306
7.303
7.299
7.298
7.137
0.000
O
N
CF3
4a
0.99
1.05
1.03
1.06
3.09
2.02
1.00
f1 (ppm)
162.741
137.048
134.238
133.285
130.833
130.573
129.494
129.261
129.035
128.550
127.486
127.152
121.217
119.043
107.707
107.659
107.611
107.561
77.254
77.000
76.746
O
N
CF3
4a
f1 (ppm)


8.369
8.352
7.715
7.712
7.699
7.695
7.641
7.505
7.491
7.296
7.281
7.138
1.415
-0.000
1.05
1.10
1.08
3.02
2.07
1.04
9.11
f1 (ppm)

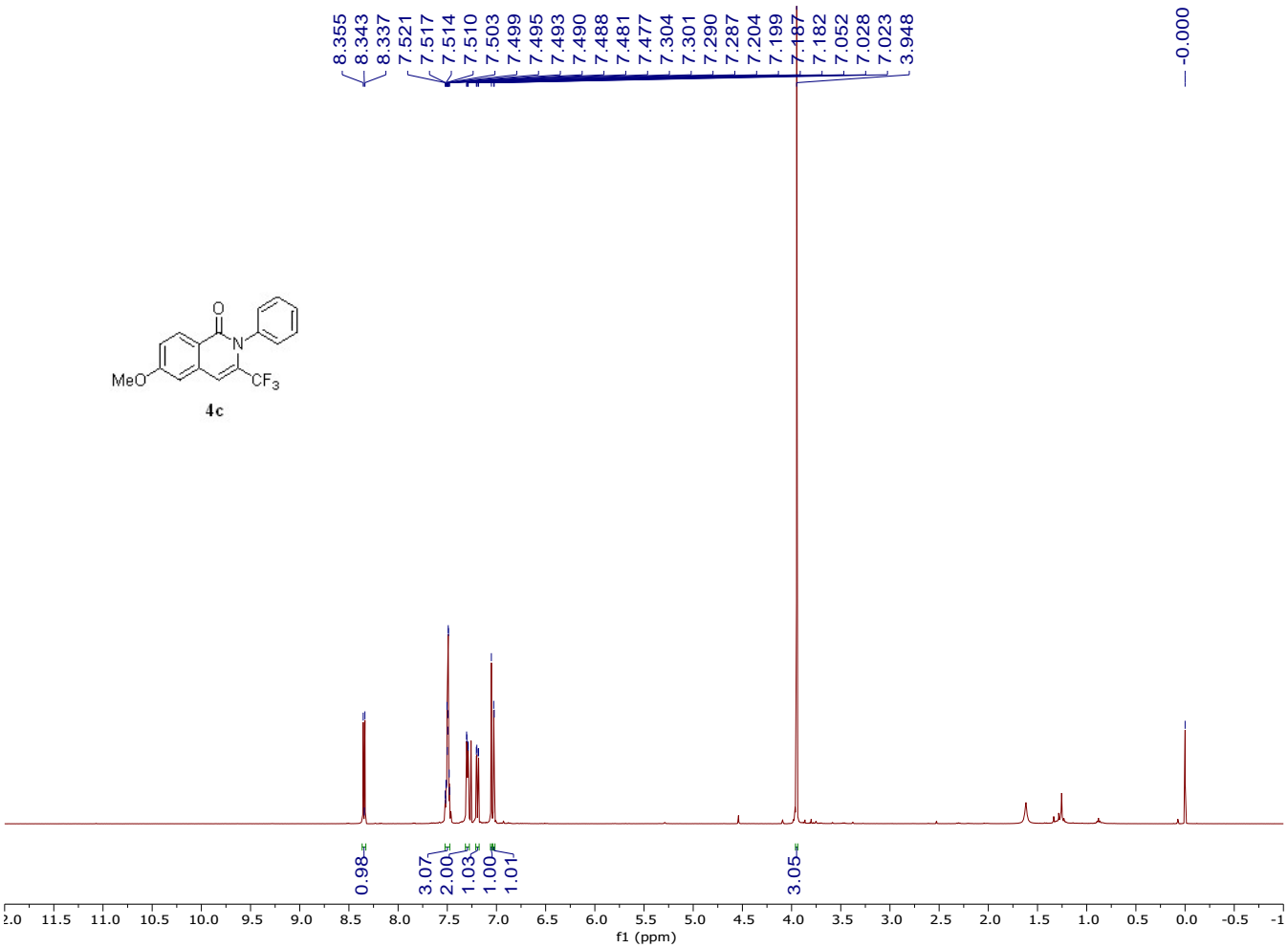
O
N
CF3

4b


162.644
157.161
137.148
134.209
130.662
130.404
129.536
129.157
128.975
128.330
127.578
124.812
123.657
121.297
119.126
108.178
108.130
108.083
108.035
77.254
77.000
76.746
35.308
31.084
f1 (ppm)

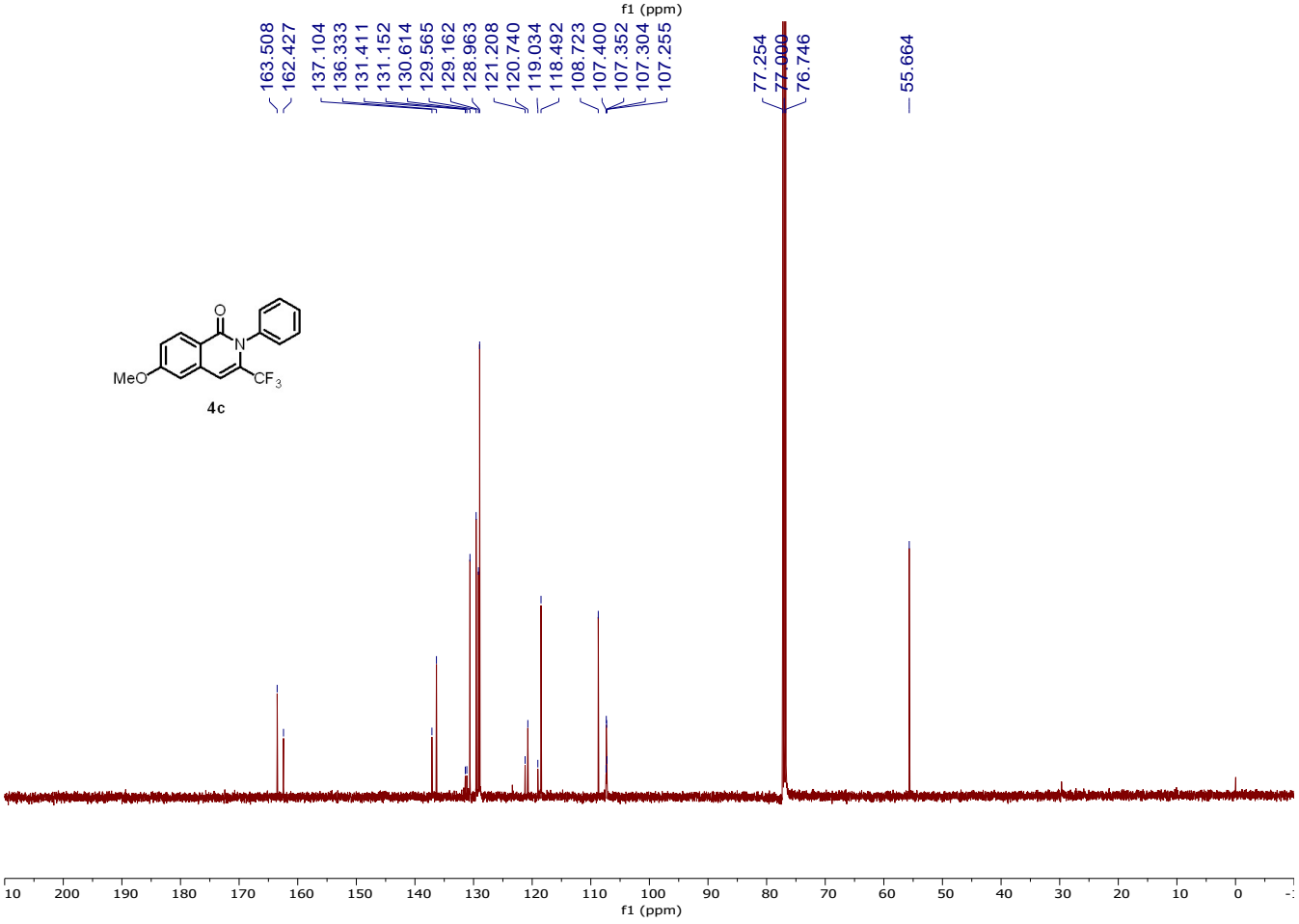
O
N
CF3

4b


8.355
8.343
8.337
7.521
7.517
7.514
7.510
7.503
7.499
7.495
7.493
7.490
7.488
7.481
7.477
7.304
7.301
7.290
7.287
7.204
7.199
7.187
7.182
7.052
7.028
7.023
3.948
-0.000
0.98
3.07
2.00
1.03
1.00
1.01
3.05
f1 (ppm)

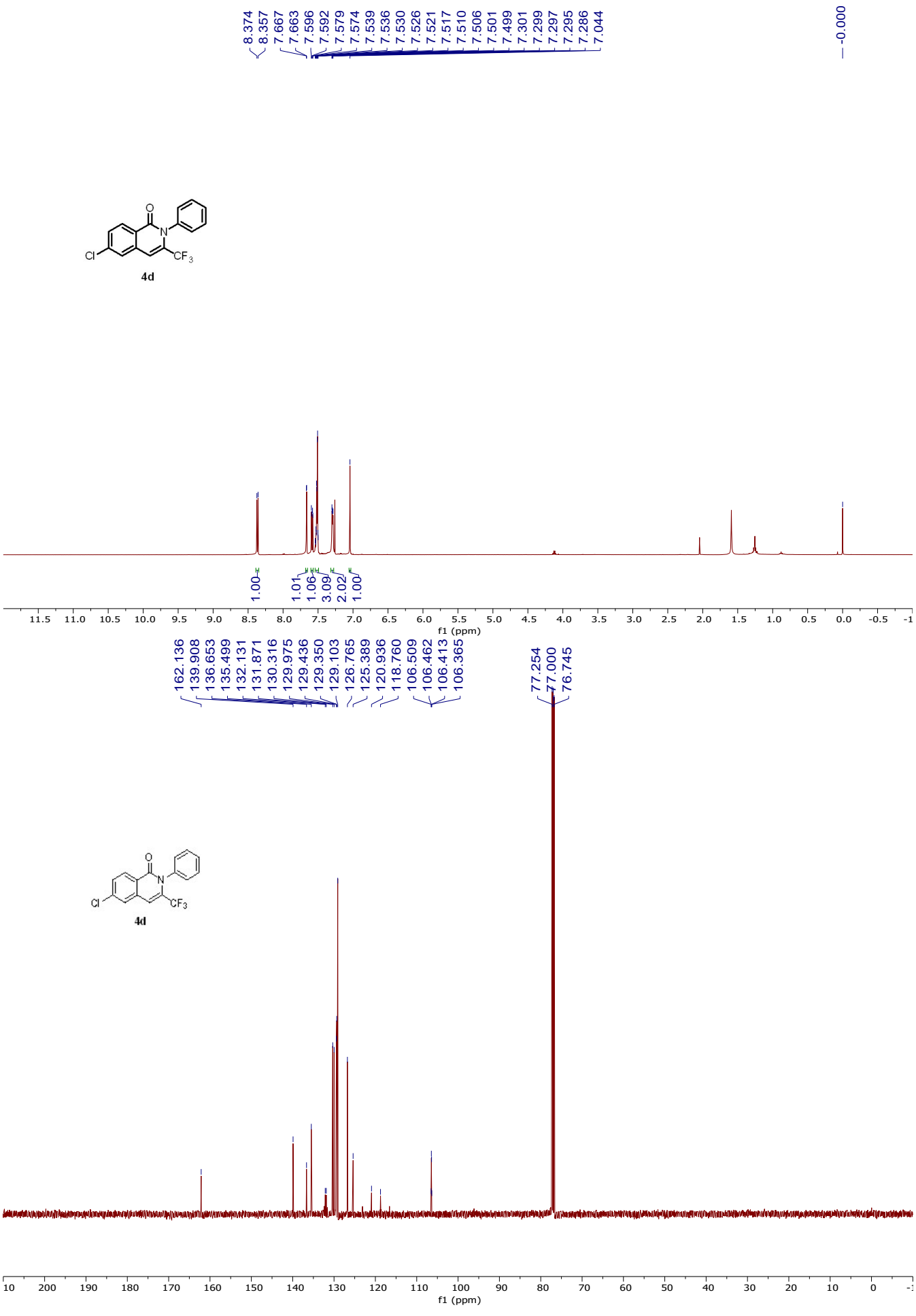
O
N
MeO
CF3

4c


163.508
162.427
137.104
136.333
131.411
131.152
130.614
129.565
129.162
128.963
121.208
120.740
119.034
118.492
108.723
107.400
107.352
107.304
107.255
77.254
77.000
76.746
55.664
f1 (ppm)

O
N
MeO
CF3

4c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8.357
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7.663
7.596
7.592
7.579
7.574
7.539
7.536
7.530
7.526
7.521
7.517
7.510
7.506
7.501
7.499
7.301
7.299
7.297
7.295
7.286
7.044
-0.000
Cl
CF3
4d
1.00
1.01
1.06
3.09
2.02
1.00
f1 (ppm)
162.136
139.908
136.653
135.499
132.131
131.871
130.316
129.975
129.436
129.350
129.103
126.765
125.389
120.936
118.760
106.509
106.462
106.413
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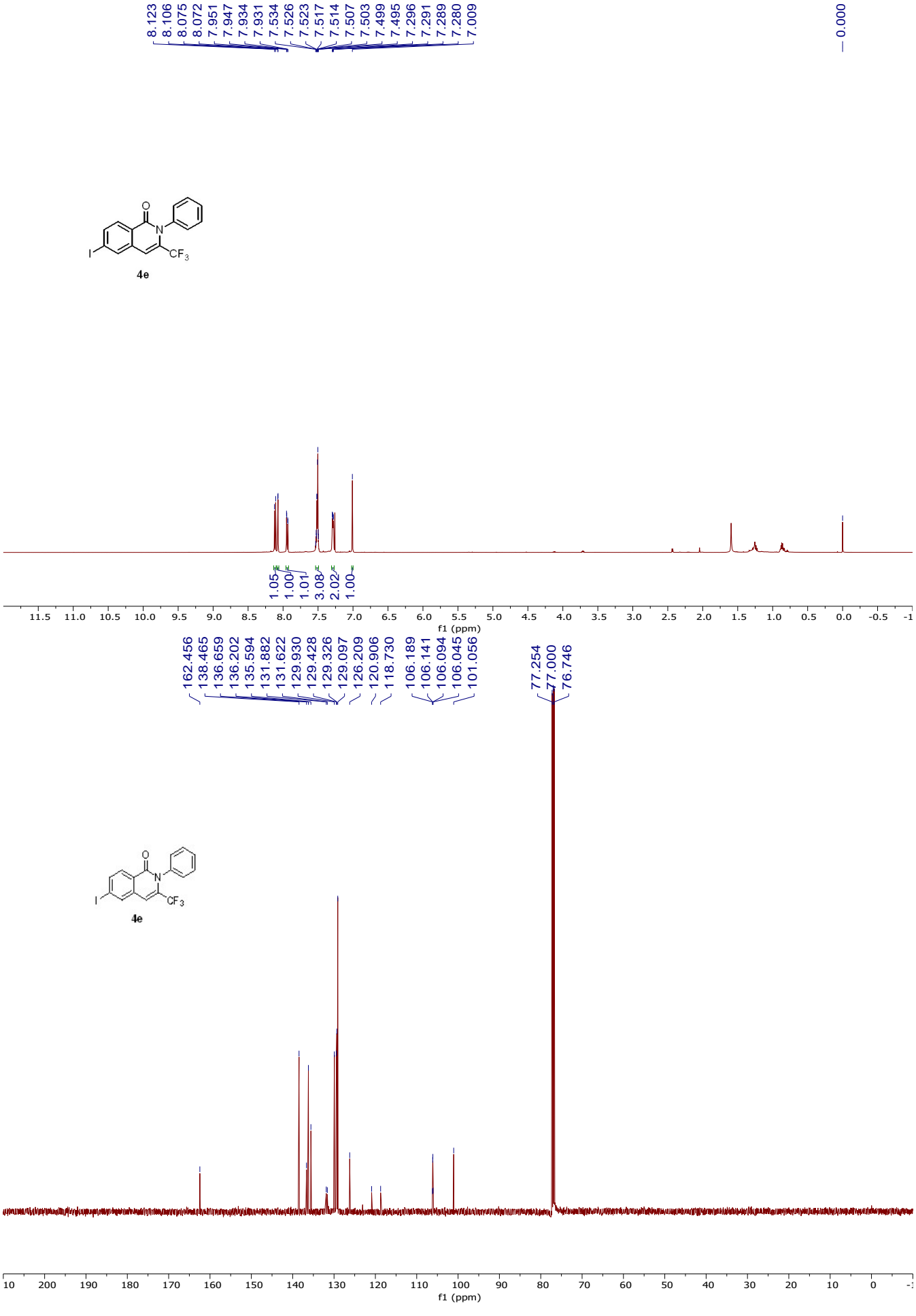
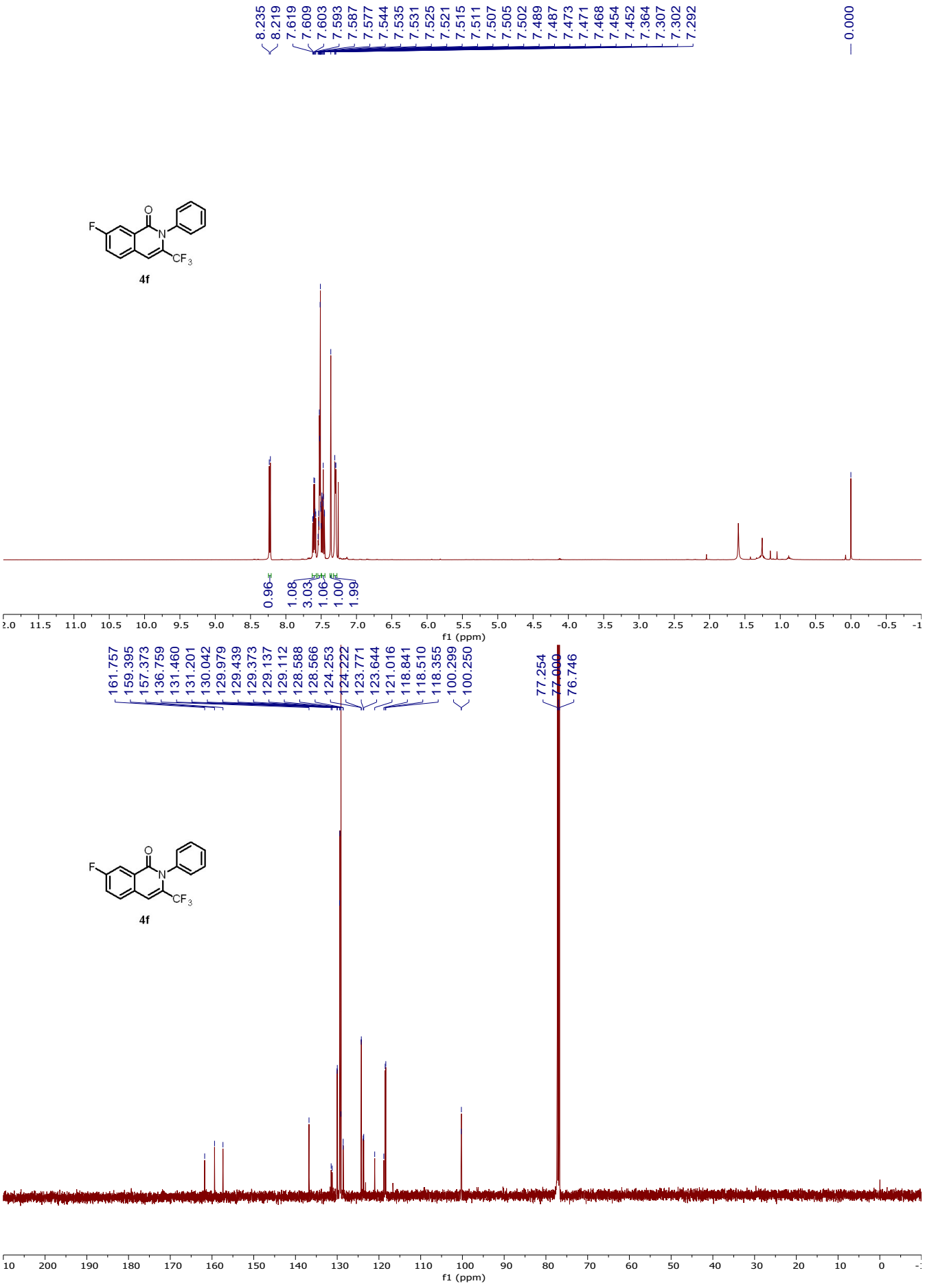
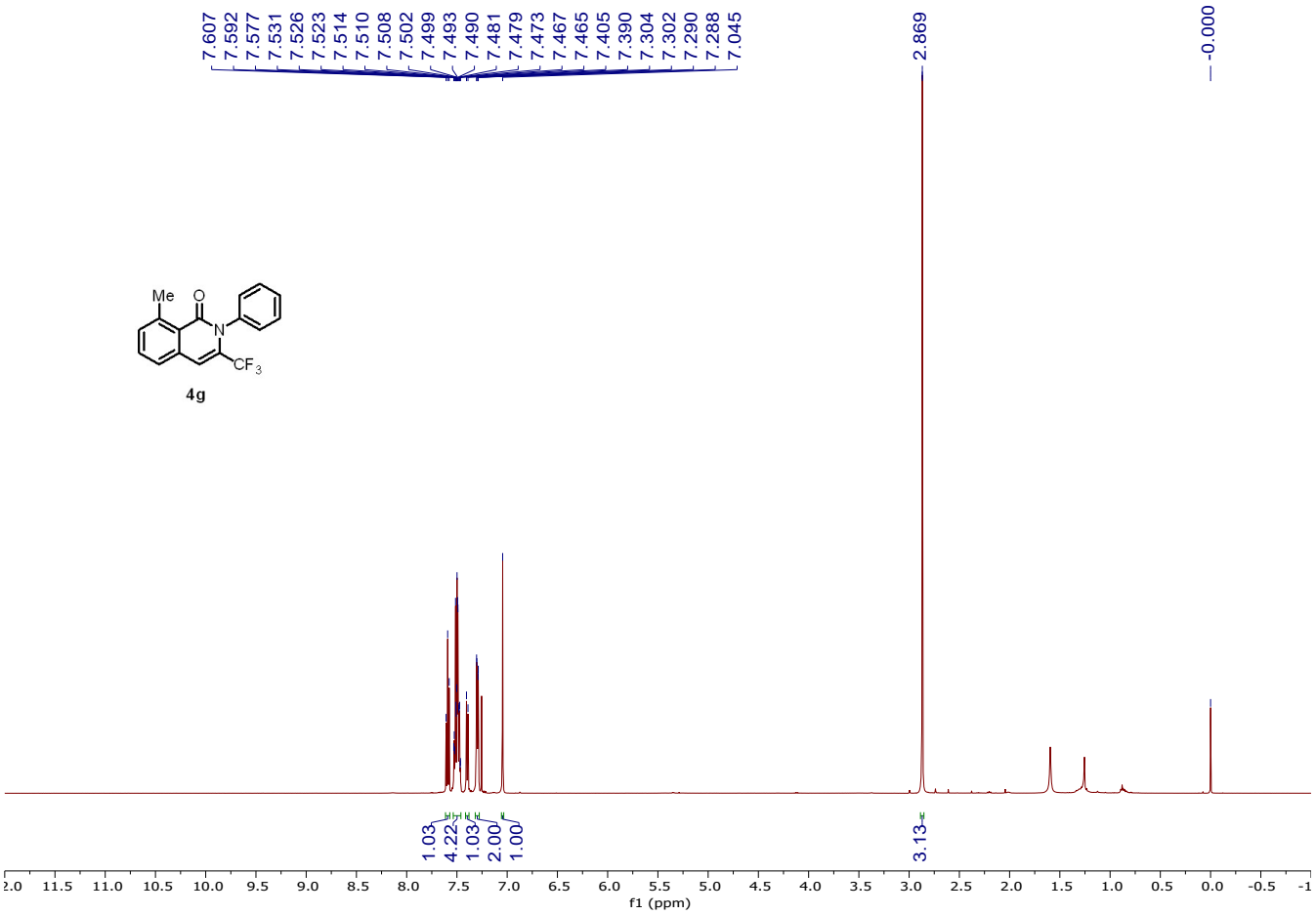
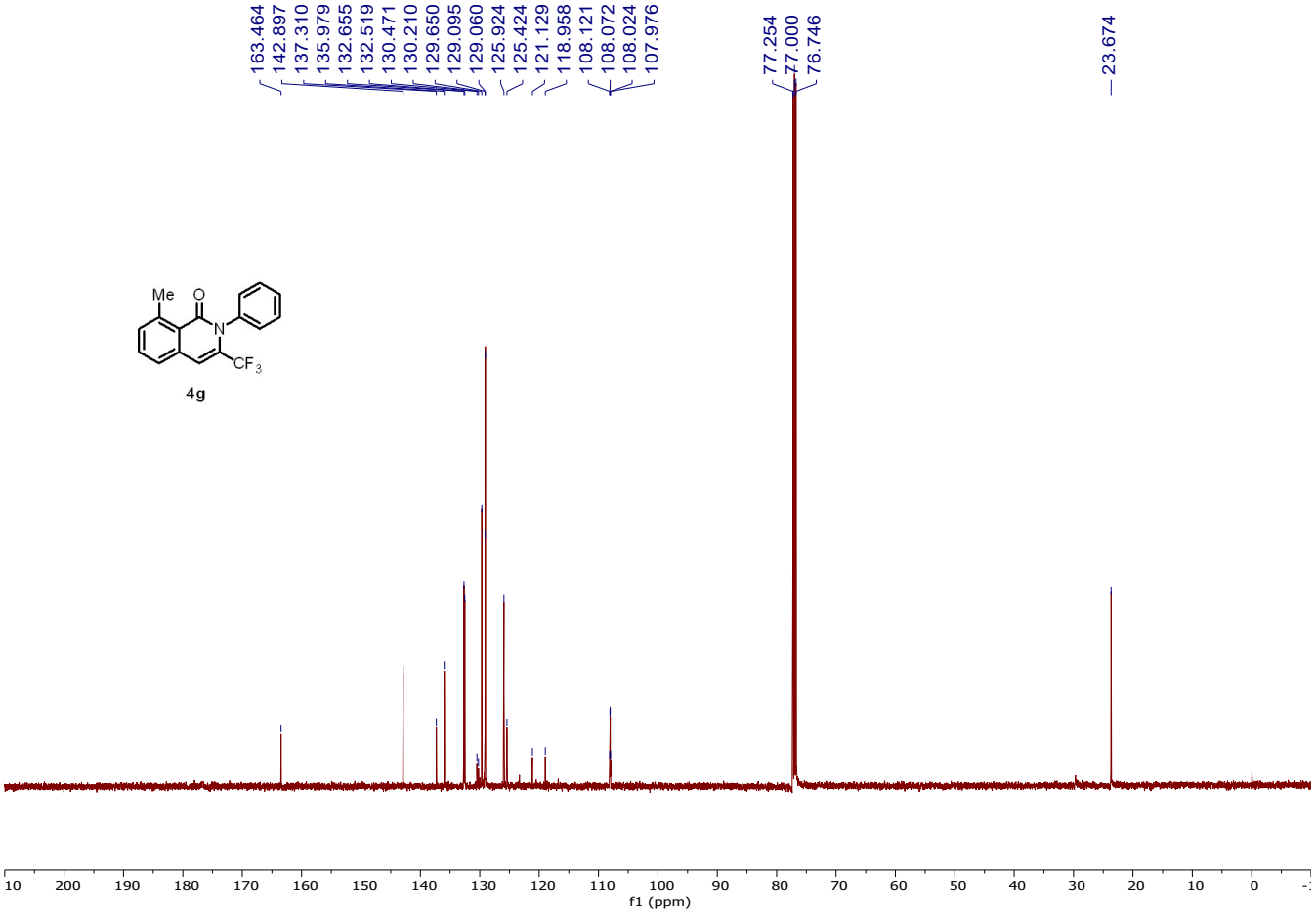
77.000
76.745
Cl
CF3
4d
f1 (ppm)


8.123
8.106
8.075
8.072
7.951
7.947
7.934
7.931
7.534
7.526
7.523
7.517
7.514
7.507
7.503
7.499
7.495
7.296
7.291
7.289
7.280
7.009
0.000
4e
1.05
1.00
1.01
3.08
2.02
1.00
f1 (ppm)
162.456
138.465
136.659
136.202
135.594
131.882
131.622
129.930
129.428
129.326
129.097
126.209
120.906
118.730
106.189
106.141
106.094
106.045
101.056
77.254
77.000
76.746
4e
f1 (ppm)


8.235
8.219
7.619
7.609
7.603
7.593
7.587
7.577
7.544
7.535
7.531
7.525
7.521
7.515
7.511
7.507
7.505
7.502
7.489
7.487
7.473
7.471
7.468
7.454
7.452
7.364
7.307
7.302
7.292
0.000
F
O
N
CF3
4f
0.96
1.08
3.03
1.06
1.00
1.99
f1 (ppm)
161.757
159.395
157.373
136.759
131.460
131.201
130.042
129.979
129.439
129.373
129.137
129.112
128.588
128.566
124.253
124.222
123.771
123.644
121.016
118.841
118.510
118.355
100.299
100.250
77.254
77.000
76.746
F
O
N
CF3
4f
f1 (ppm)


7.607
7.592
7.577
7.531
7.526
7.523
7.514
7.510
7.508
7.502
7.499
7.493
7.490
7.481
7.479
7.473
7.467
7.465
7.405
7.390
7.304
7.302
7.290
7.288
7.045
2.869
-0.000
Me
O
N
CF3
4g
1.03
4.22
1.03
2.00
1.00
3.13
f1 (ppm)


163.464
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135.979
132.655
132.519
130.471
130.210
129.650
129.095
129.060
125.924
125.424
121.129
118.958
108.121
108.072
108.024
107.976
77.254
77.000
76.746
23.674
Me
O
N
CF3
4g
f1 (ppm)


10.082
10.066
8.160
8.143
7.963
7.960
7.947
7.944
7.734
7.731
7.720
7.717
7.713
7.703
7.700
7.682
7.679
7.668
7.666
7.663
7.652
7.649
7.646
7.629
7.578
7.575
7.572
7.569
7.567
7.560
7.557
7.554
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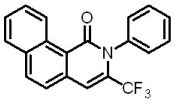
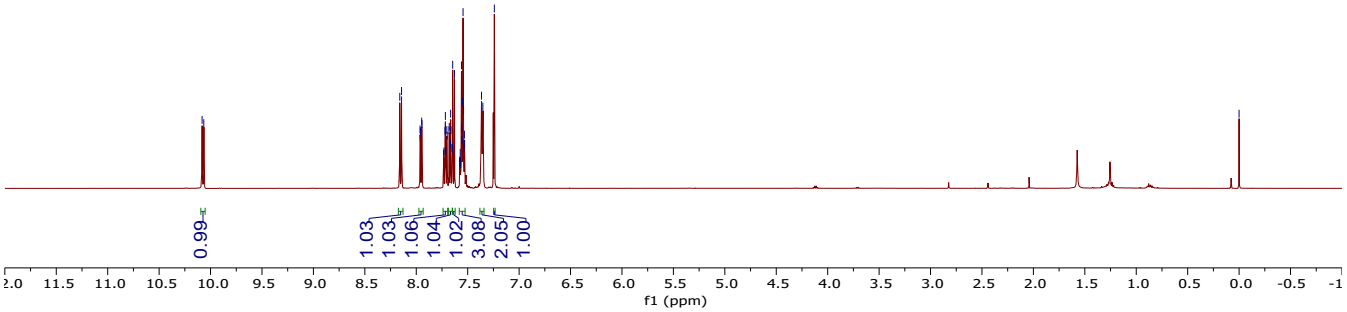
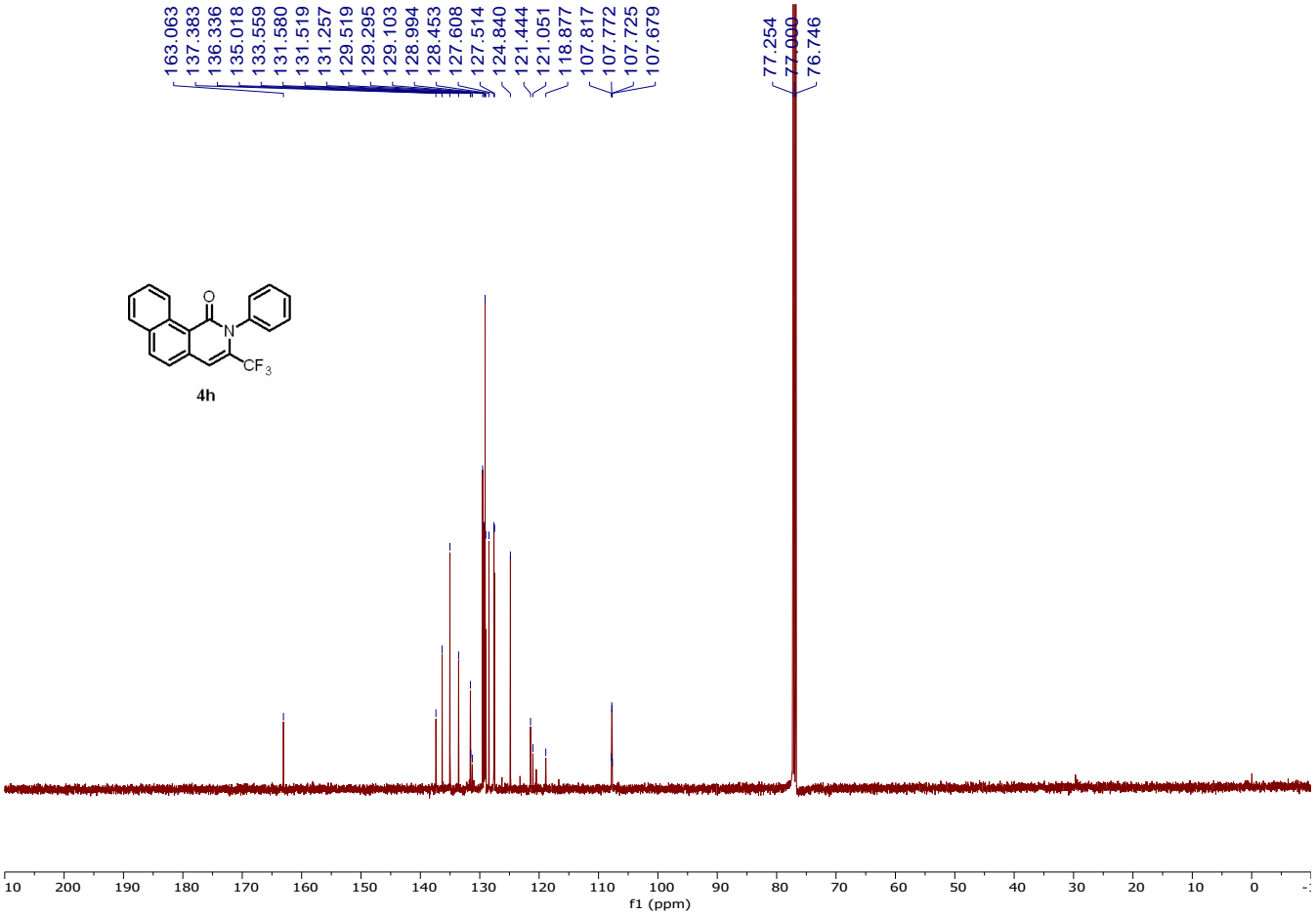
7.545
7.540
7.537
7.532
7.530
7.366
7.353
7.241
0.000


O
N
CF3

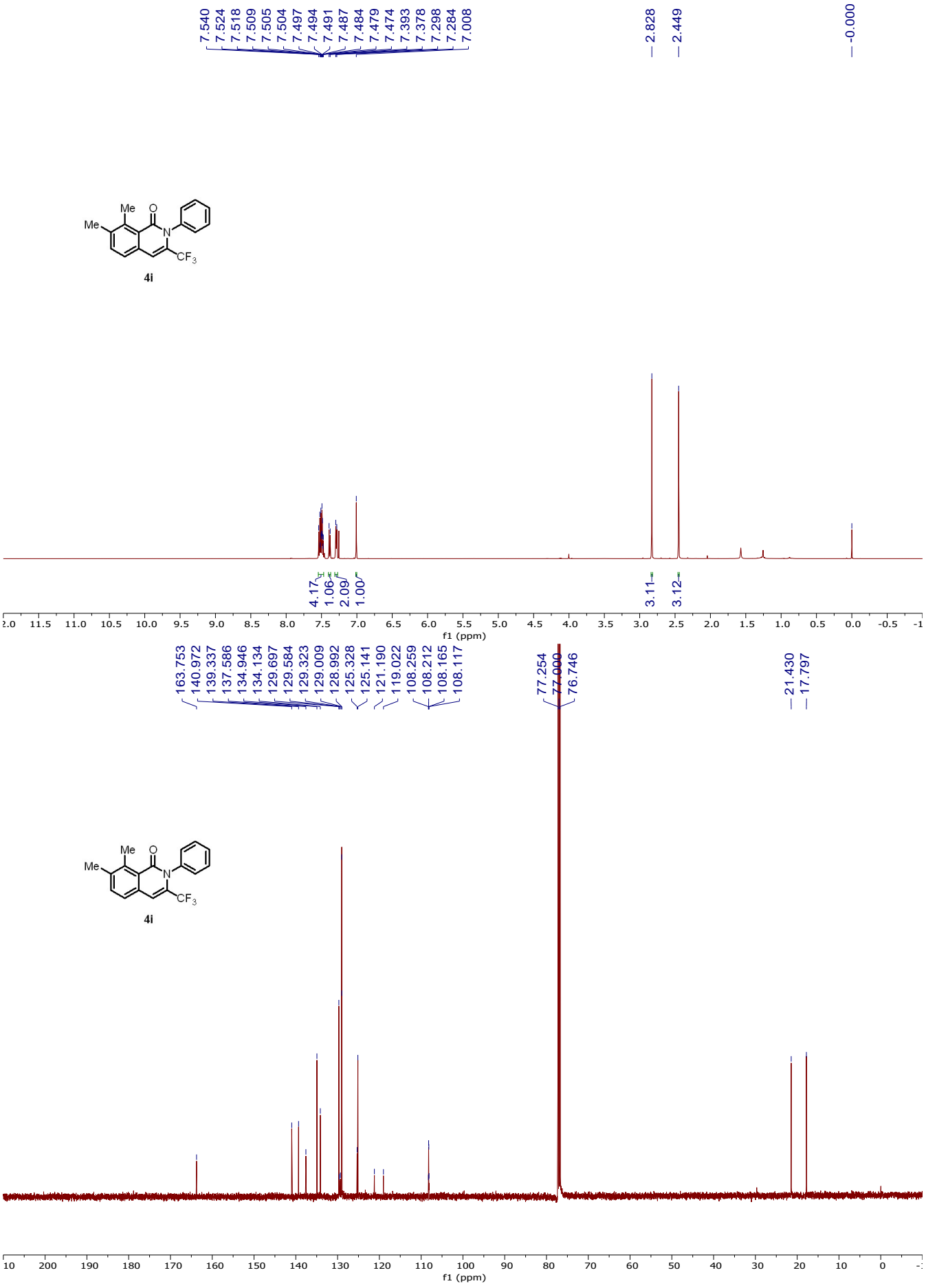
4h

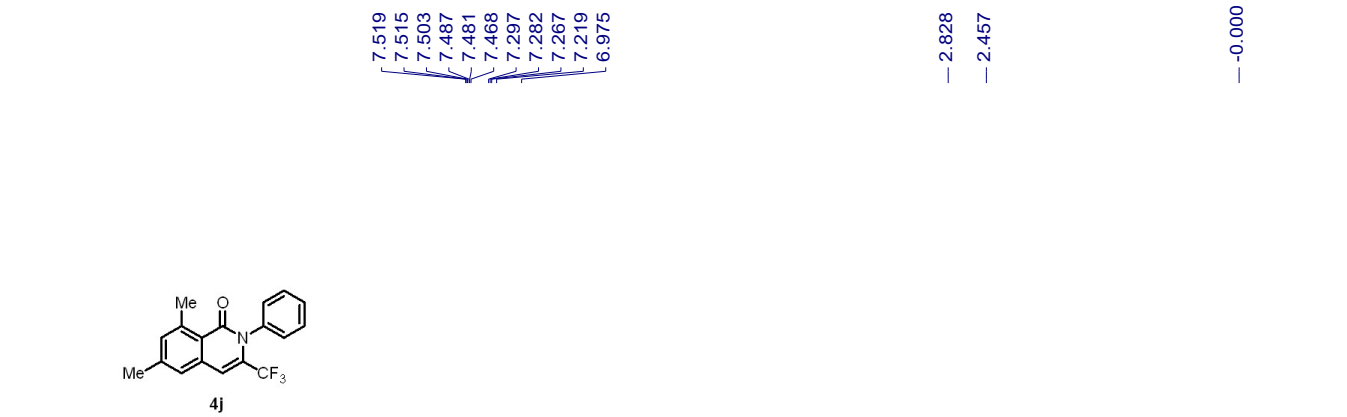

0.99
1.03
1.03
1.06
1.04
1.02
3.08
2.05
1.00
f1 (ppm)

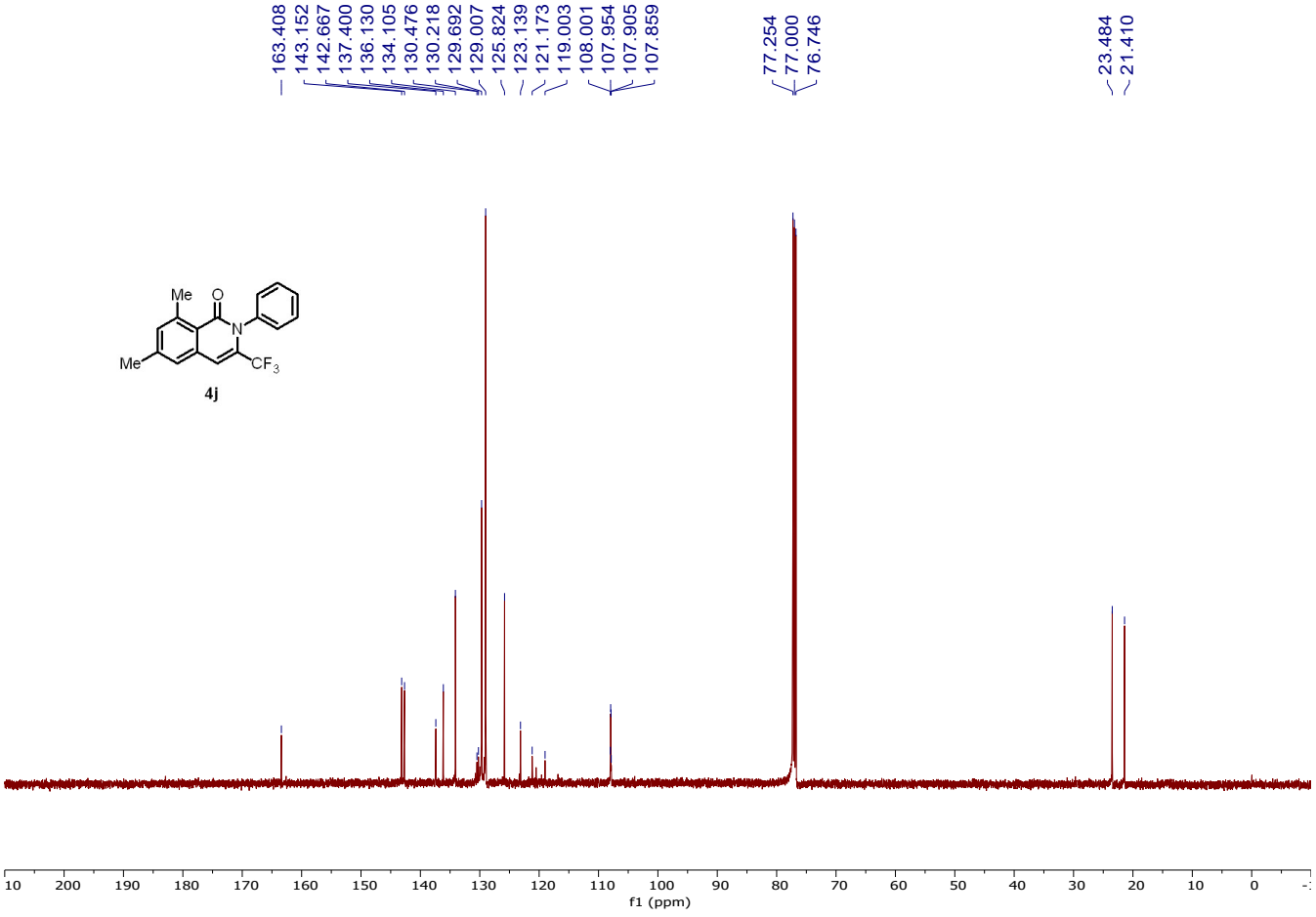

163.063
137.383
136.336
135.018
133.559
131.580
131.519
131.257
129.519
129.295
129.103
128.994
128.453
127.608
127.514
124.840
121.444
121.051
118.877
107.817
107.772
107.725
107.679
77.254
77.000
76.746
f1 (ppm)

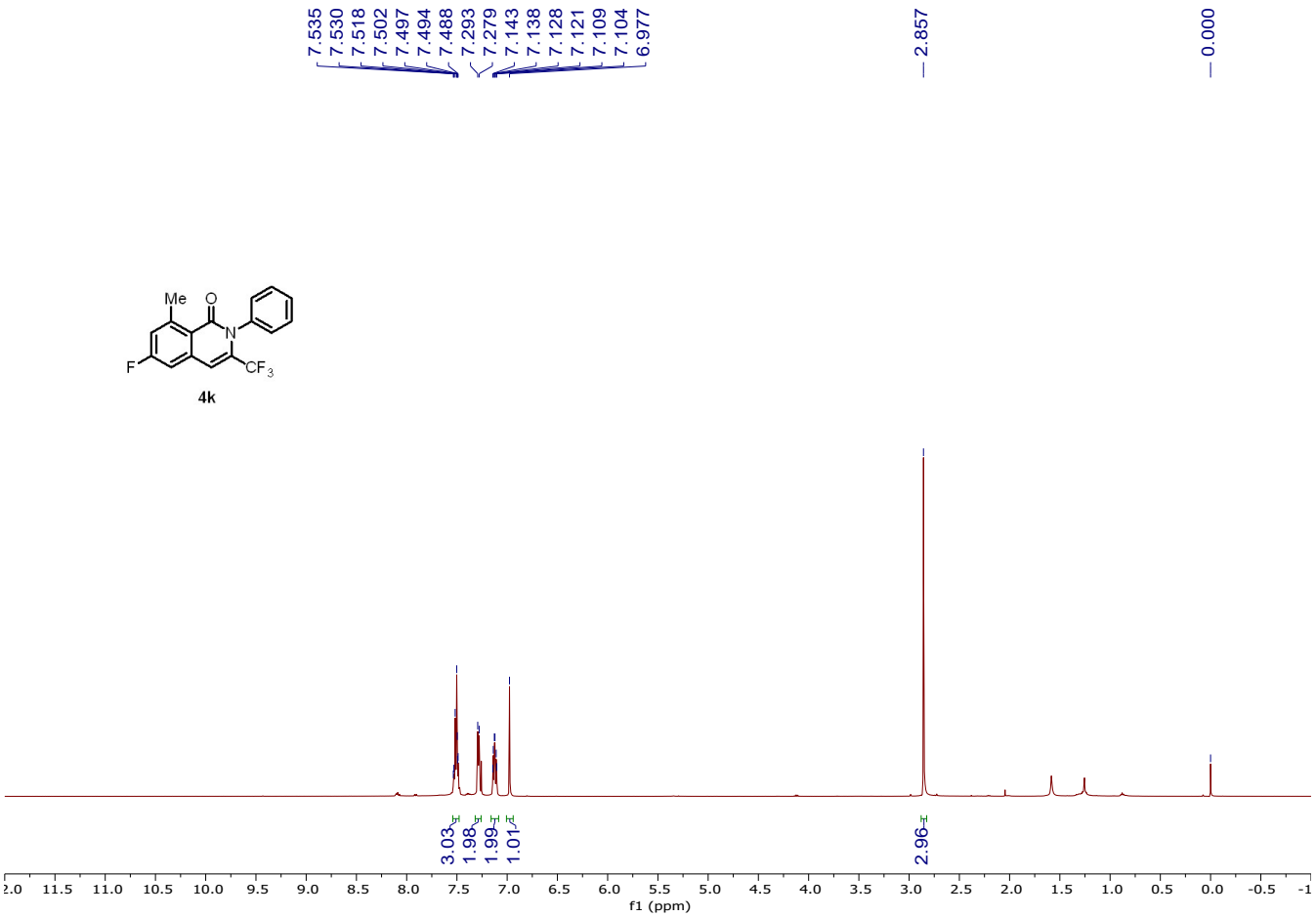
O
N
CF3

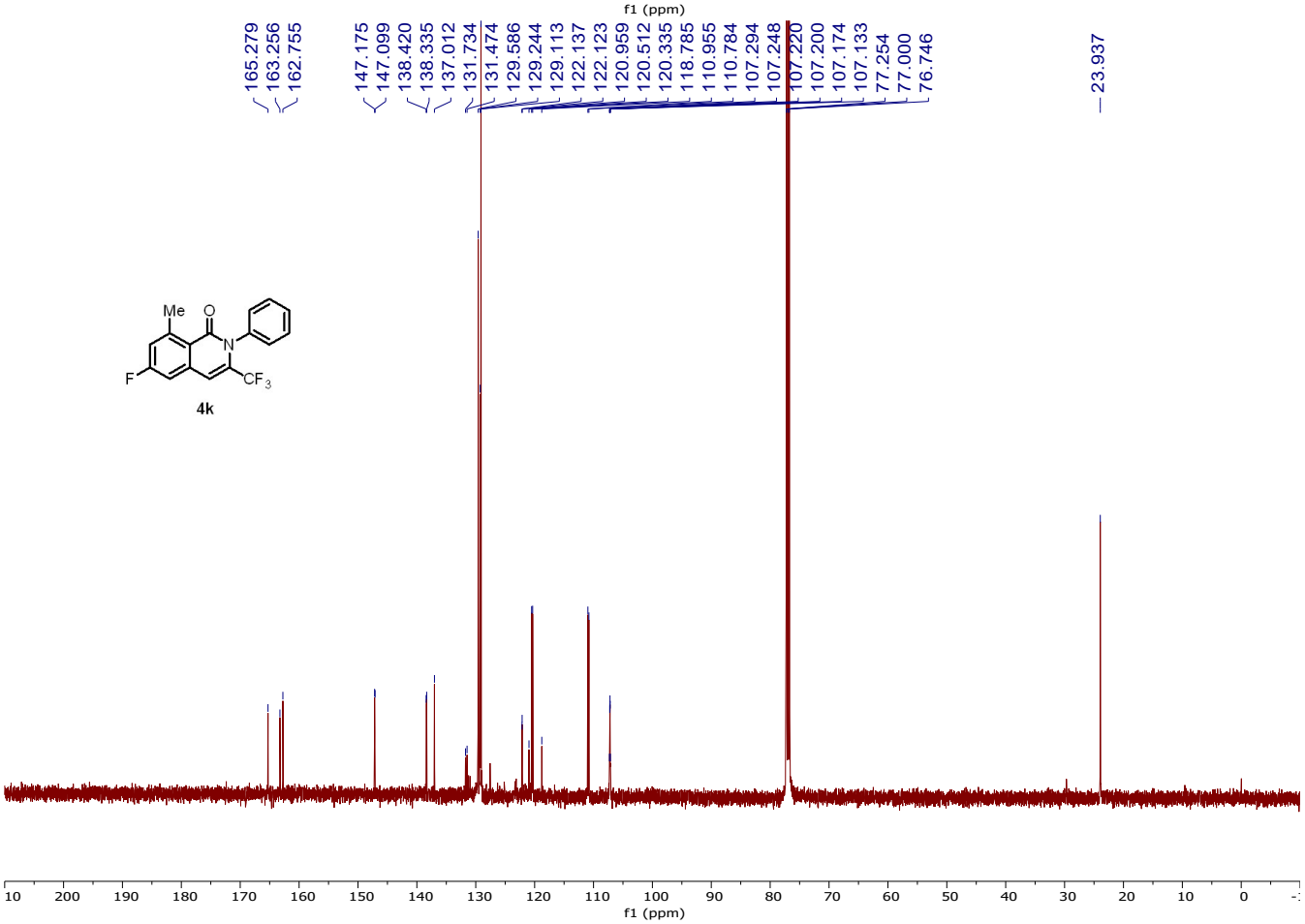
4h

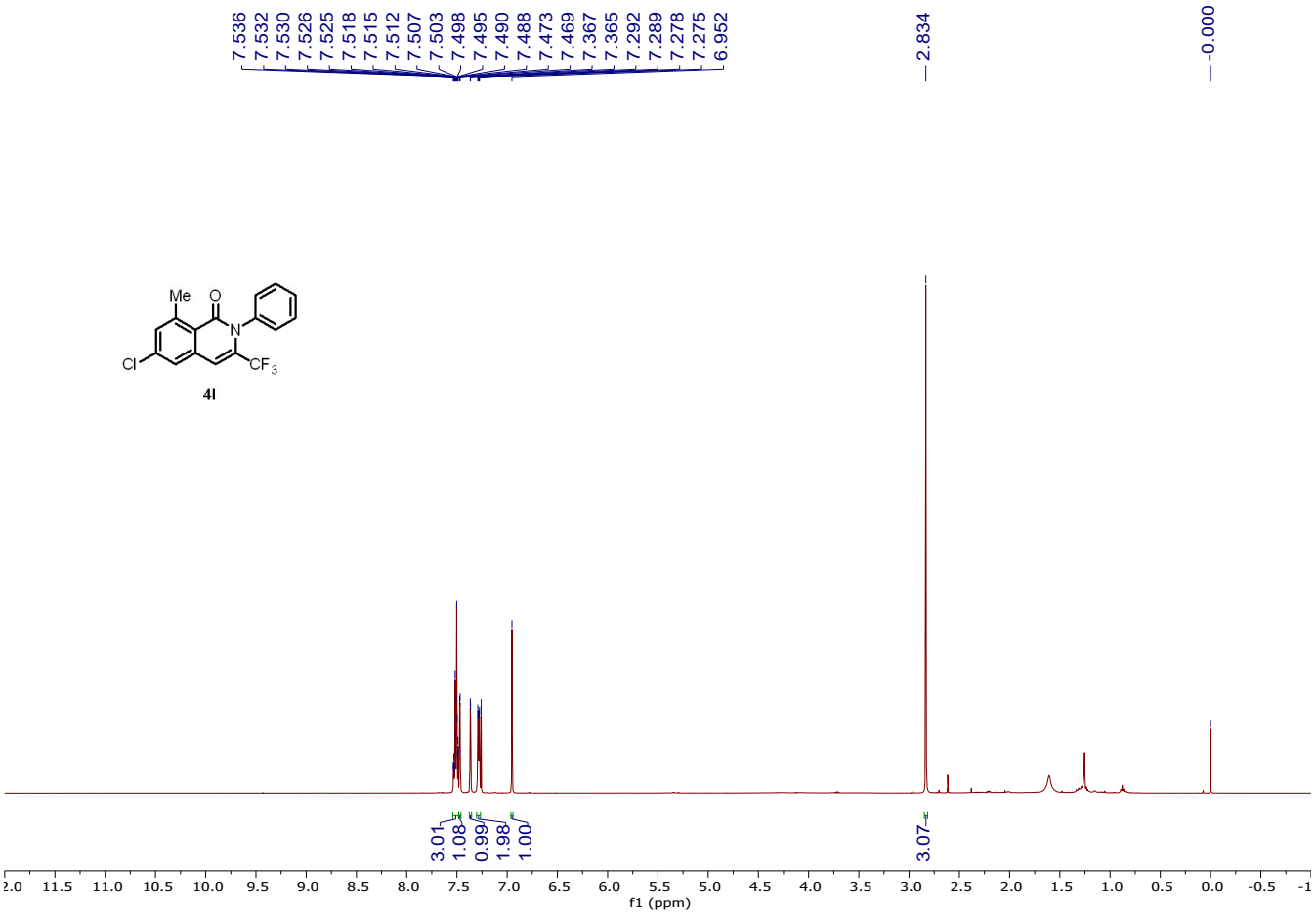

7.540
7.524
7.518
7.509
7.505
7.504
7.497
7.494
7.491
7.487
7.484
7.479
7.474
7.393
7.378
7.298
7.284
7.008
2.828
2.449
-0.000
Me
O
Me
N
CF3
4i
4.17
1.06
2.09
1.00
3.11
3.12
f1 (ppm)
163.753
140.972
139.337
137.586
134.946
134.134
129.697
129.584
129.323
129.009
128.992
125.328
125.141
121.190
119.022
108.259
108.212
108.165
108.117
77.254
77.000
76.746
21.430
17.797
Me
O
Me
N
CF3
4i
f1 (ppm)

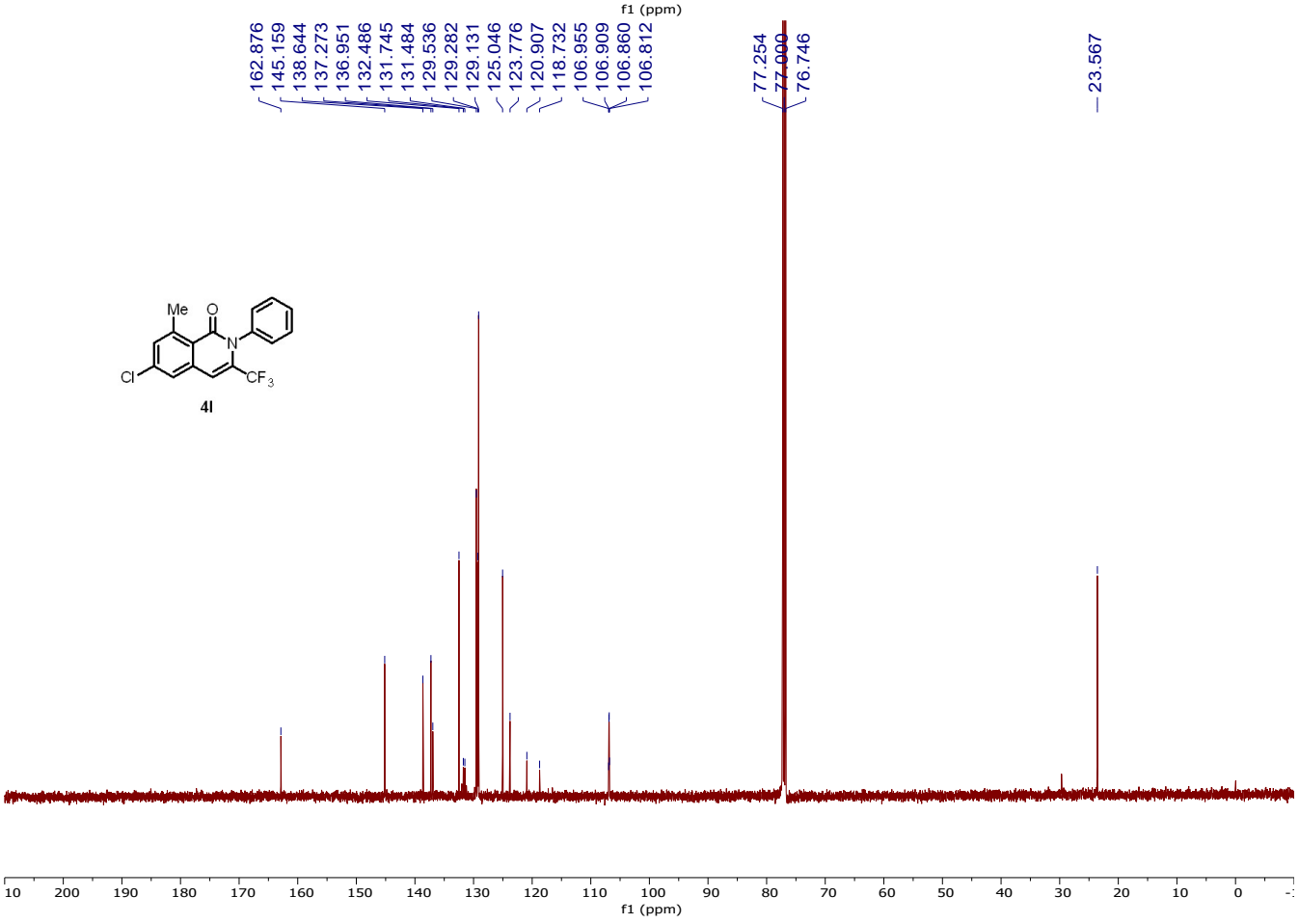

7.519
7.515
7.503
7.487
7.481
7.468
7.297
7.282
7.267
7.219
6.975
2.828
2.457
-0.000
Me
O
N
Me
CF3
4j
3.04
3.03
0.96
0.98
3.00
3.05
f1 (ppm)

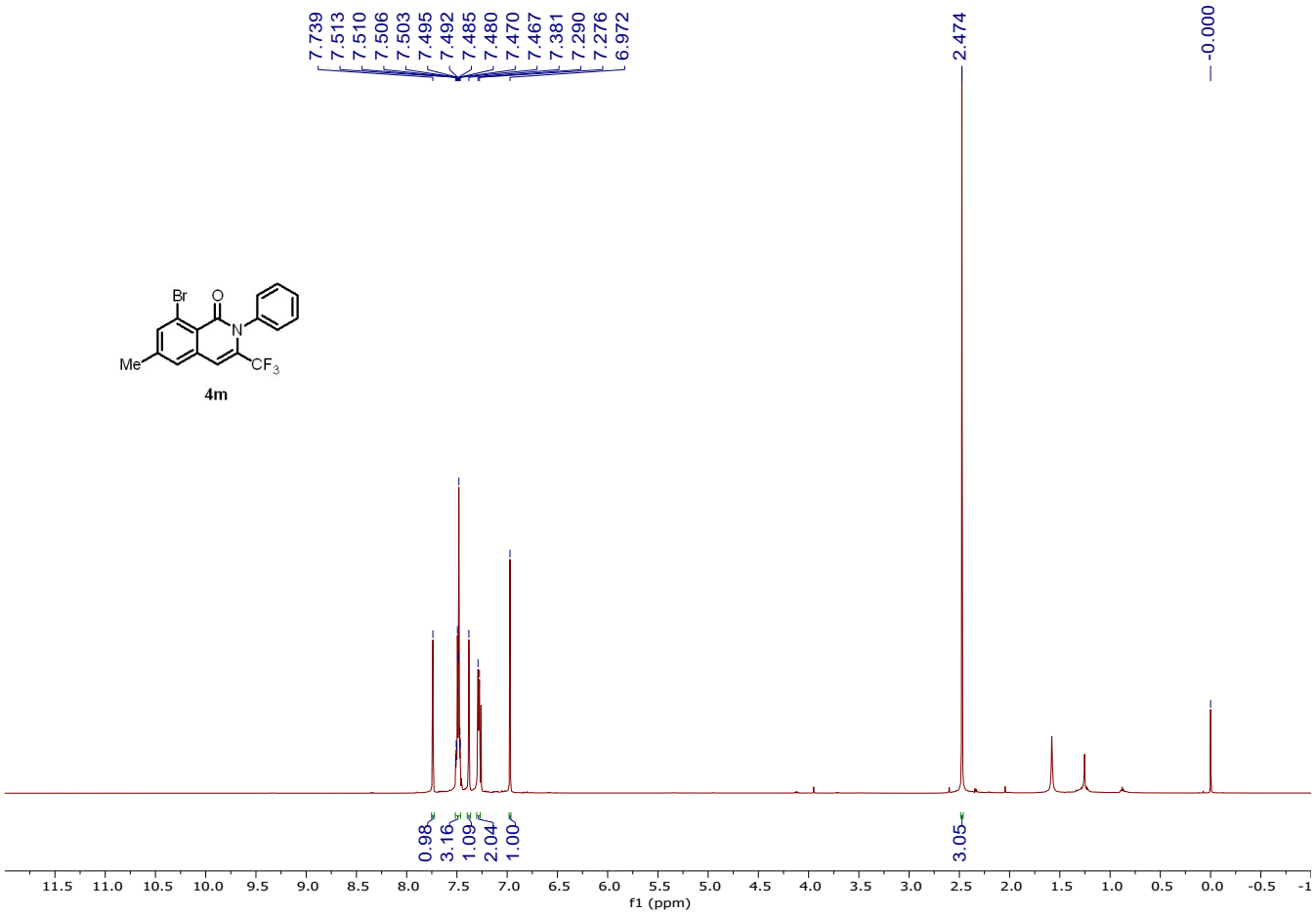

163.408
143.152
142.667
137.400
136.130
134.105
130.476
130.218
129.692
129.007
125.824
123.139
121.173
119.003
108.001
107.954
107.905
107.859
77.254
77.000
76.746
23.484
21.410
Me
O
N
Me
CF3
4j
f1 (ppm)

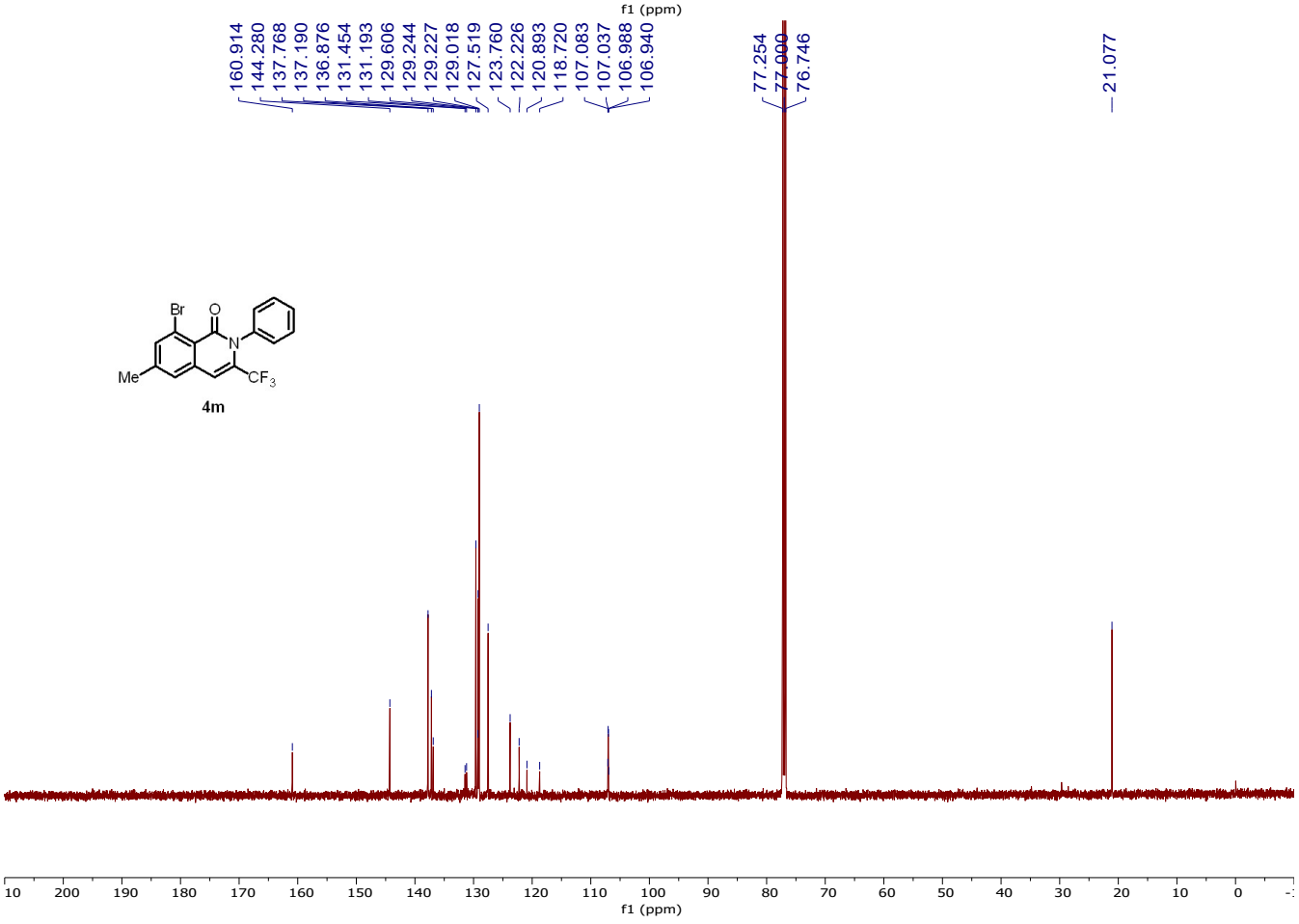

7.535
7.530
7.518
7.502
7.497
7.494
7.488
7.293
7.279
7.143
7.138
7.128
7.121
7.109
7.104
6.977
2.857
0.000
Me
O
N
F
CF3
4k
3.03
1.98
1.99
1.01
2.96
f1 (ppm)

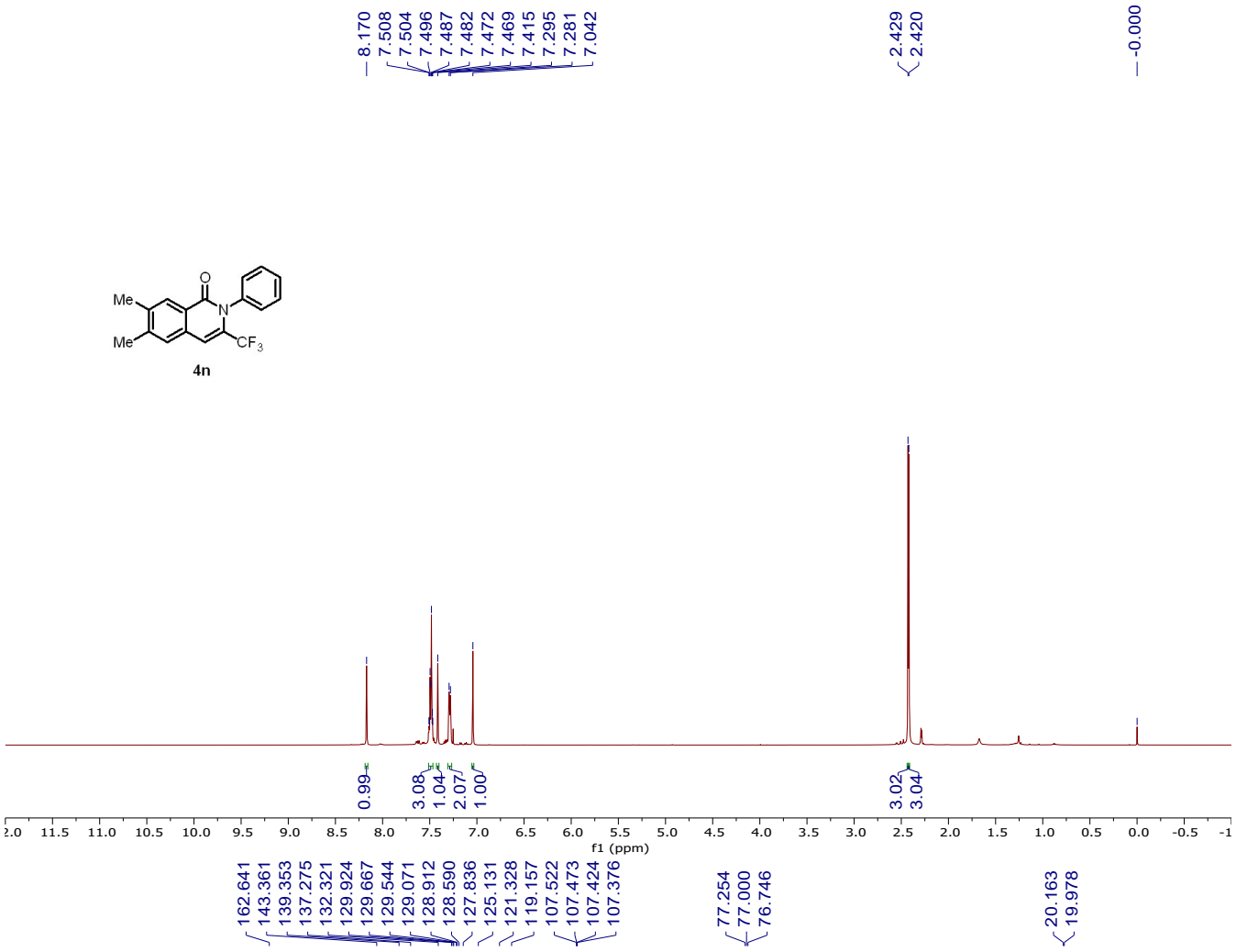

165.279
163.256
162.755
147.175
147.099
138.420
138.335
137.012
131.734
131.474
129.586
129.244
129.113
122.137
122.123
120.959
120.512
120.335
118.785
110.955
110.784
107.294
107.248
107.220
107.200
107.174
107.133
77.254
77.000
76.746
23.937
Me
O
N
F
CF3
4k
f1 (ppm)

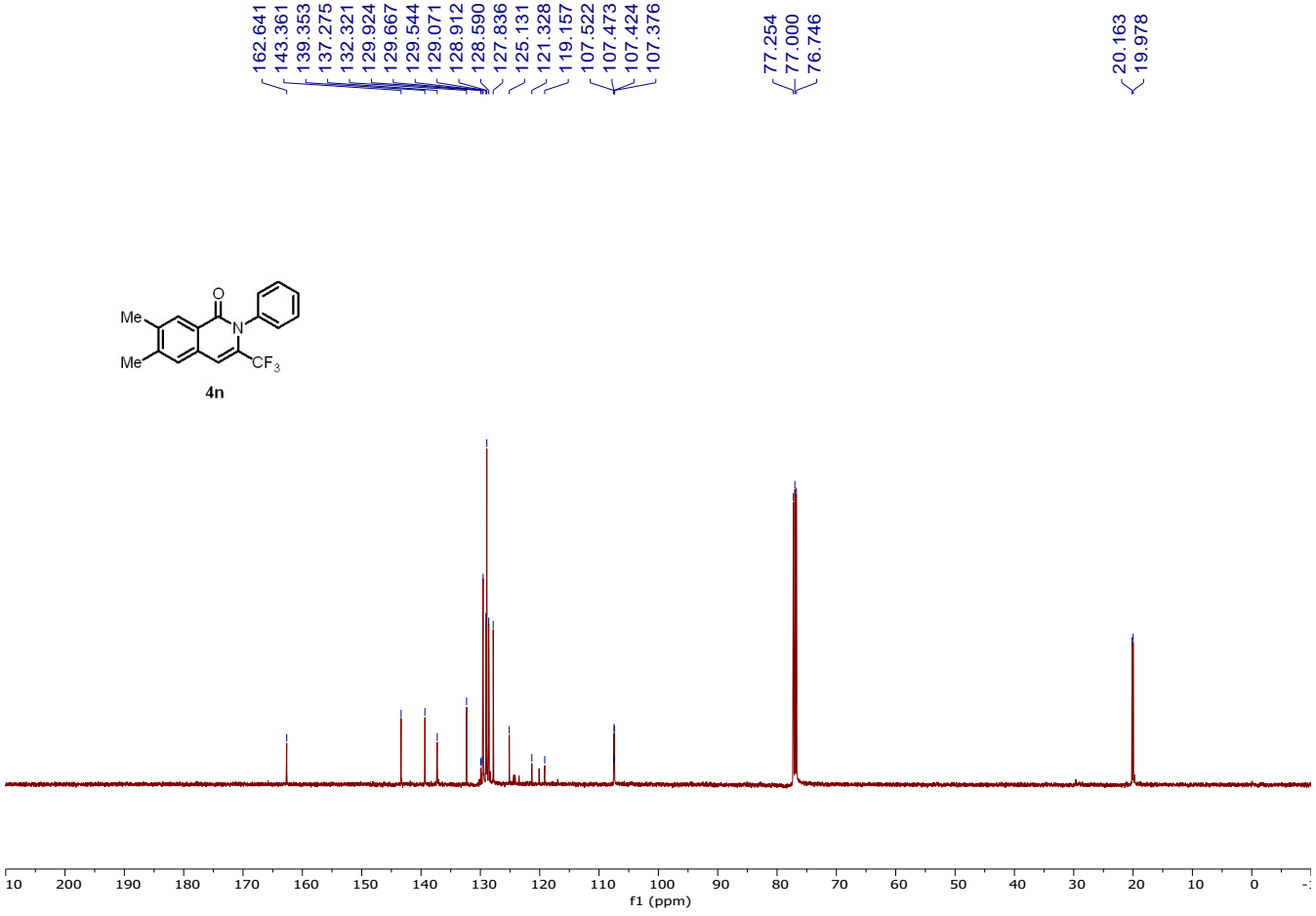

7.536
7.532
7.530
7.526
7.525
7.518
7.515
7.512
7.507
7.503
7.498
7.495
7.490
7.488
7.473
7.469
7.367
7.365
7.292
7.289
7.278
7.275
6.952
2.834
-0.000
Me
O
N
Cl
CF3
4l
3.01
1.08
0.99
1.98
1.00
3.07
f1 (ppm)

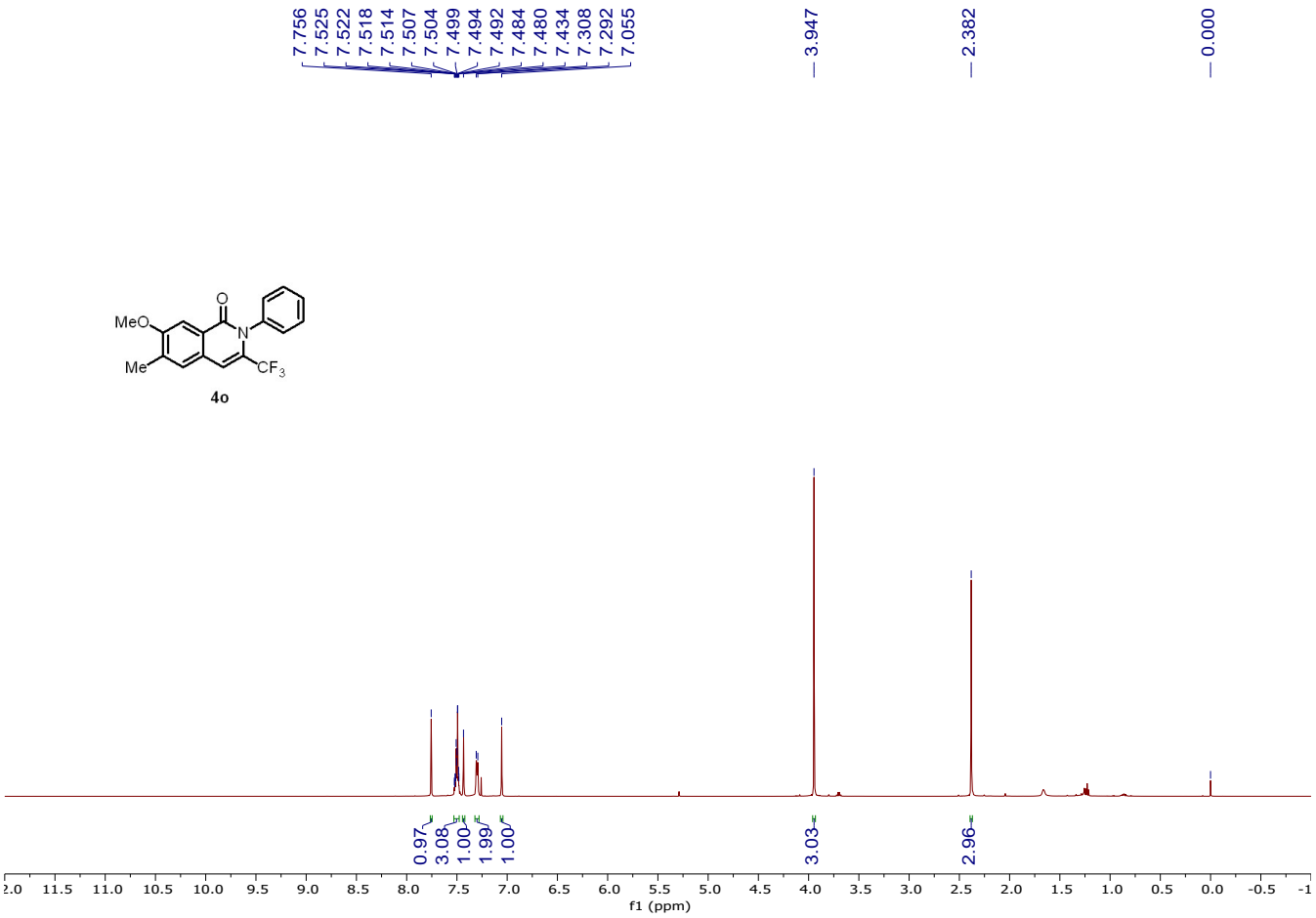

162.876
145.159
138.644
137.273
136.951
132.486
131.745
131.484
129.536
129.282
129.131
125.046
123.776
120.907
118.732
106.955
106.909
106.860
106.812
77.254
77.000
76.746
23.567
Me
O
N
Cl
CF3
4l
f1 (ppm)

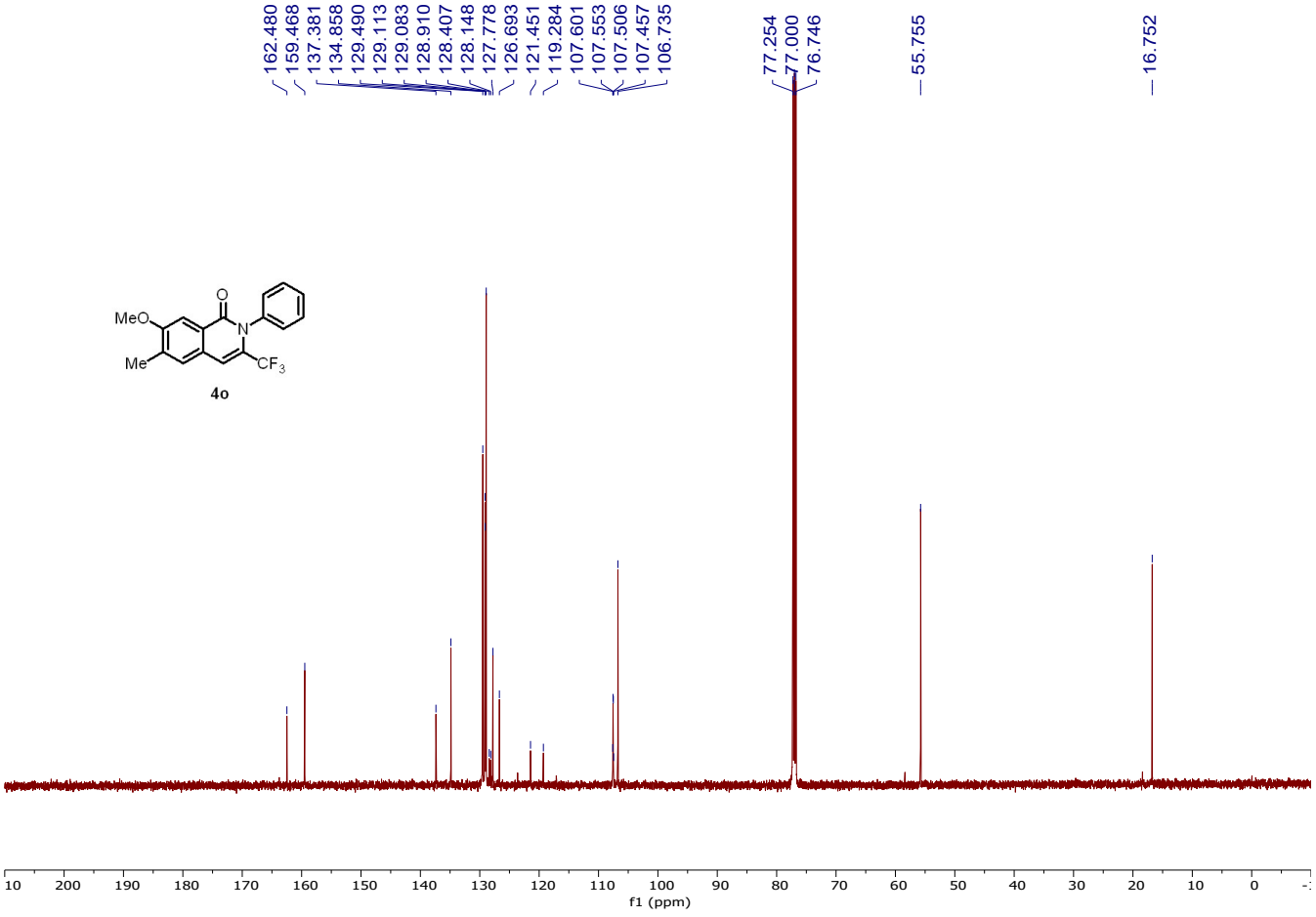

7.739
7.513
7.510
7.506
7.503
7.495
7.492
7.485
7.480
7.470
7.467
7.381
7.290
7.276
6.972
2.474
-0.000
Br
O
N
Me
CF3
4m
0.98
3.16
1.09
2.04
1.00
3.05
f1 (ppm)

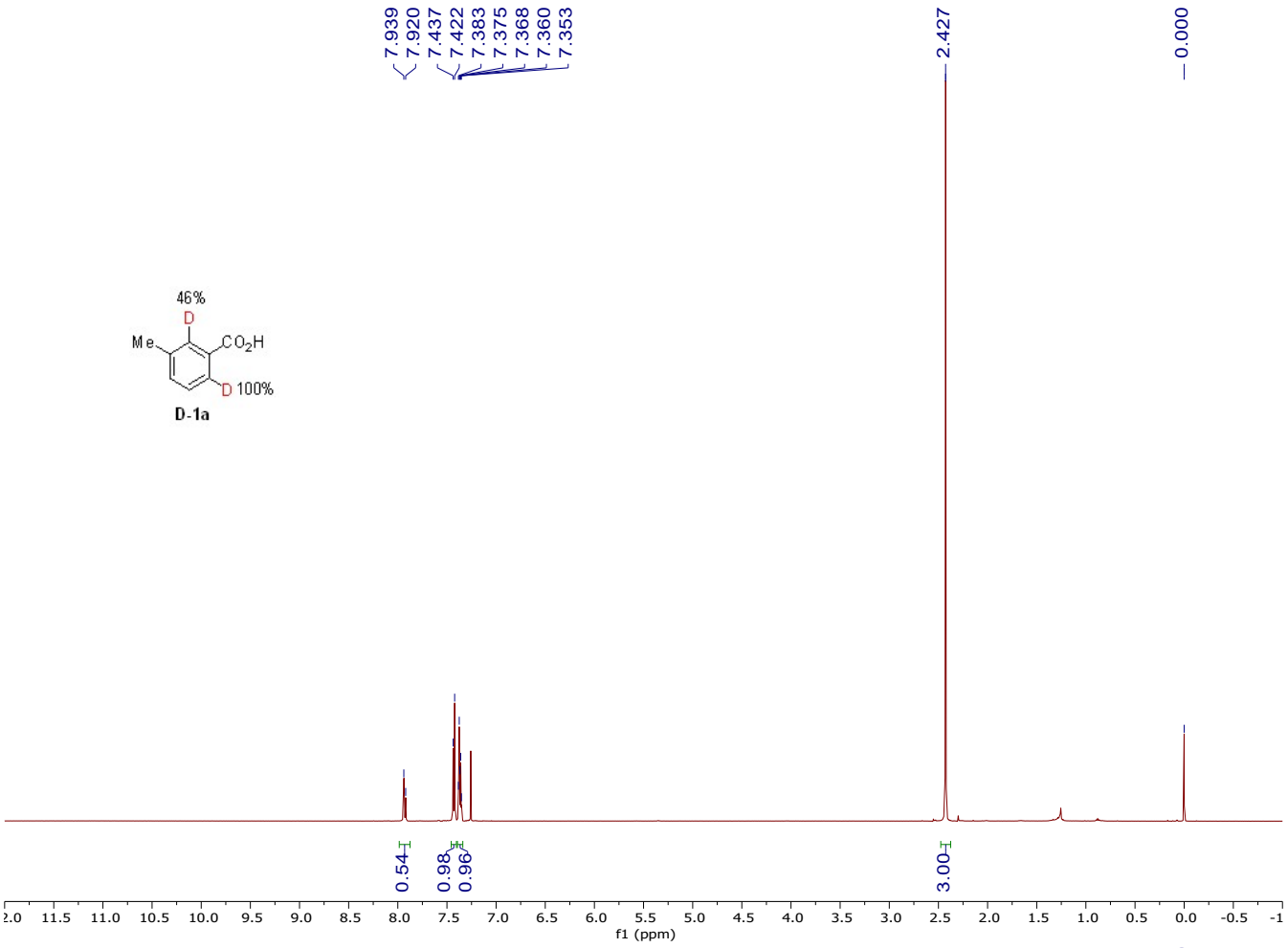

160.914
144.280
137.768
137.190
136.876
131.454
131.193
129.606
129.244
129.227
129.018
127.519
123.760
122.226
120.893
118.720
107.083
107.037
106.988
106.940
77.254
77.000
76.746
21.077
Br
O
N
Me
CF3
4m
f1 (ppm)

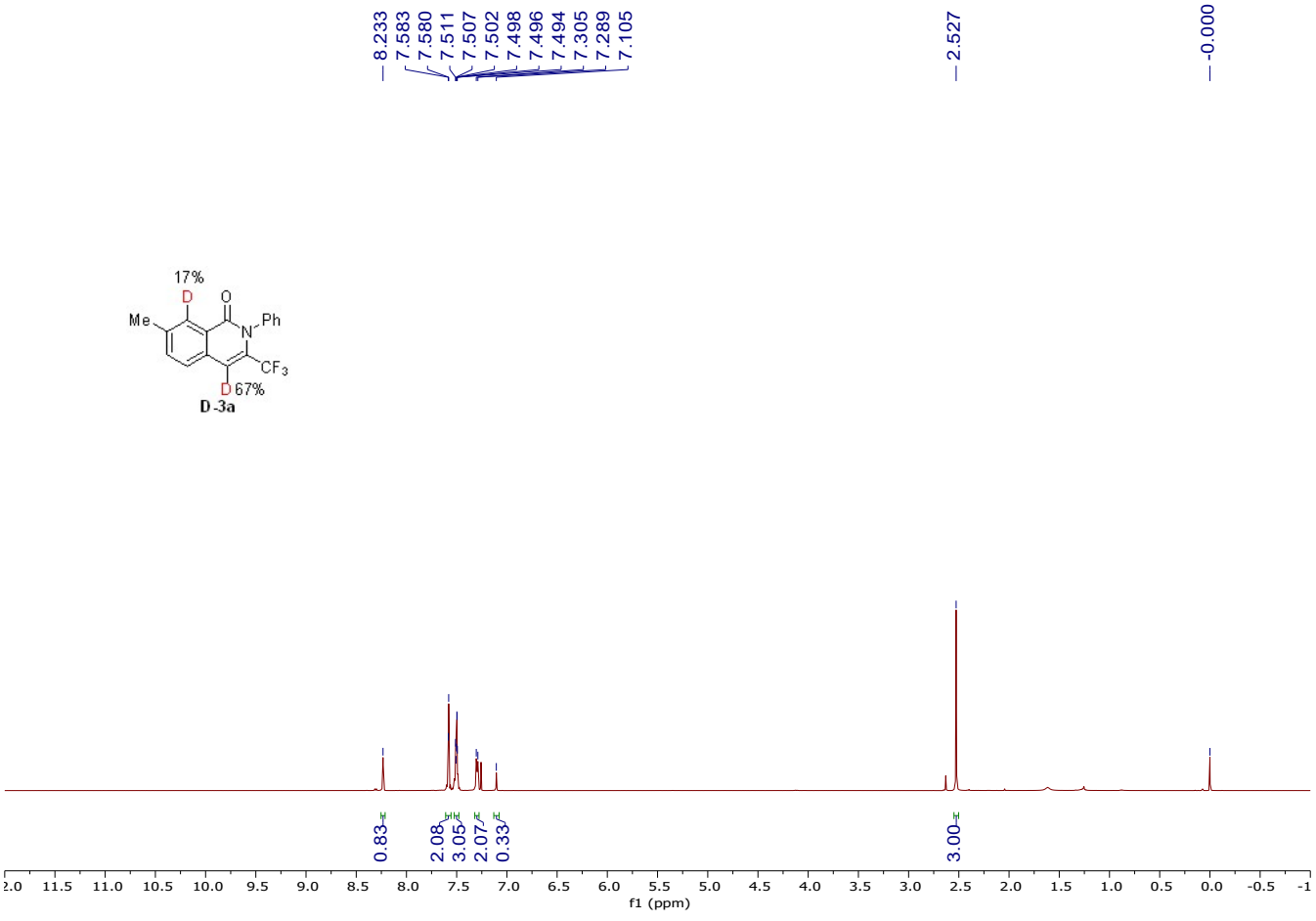

8.170
7.508
7.504
7.496
7.487
7.482
7.472
7.469
7.415
7.295
7.281
7.042
2.429
2.420
-0.000
Me
Me
O
N
CF3
4n
0.99
3.08
1.04
2.07
1.00
3.02
3.04
f1 (ppm)

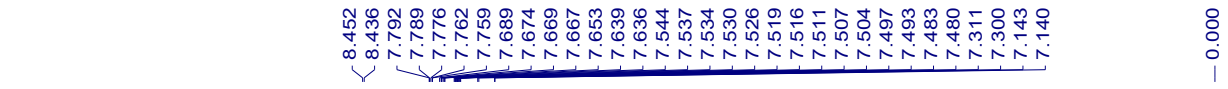

162.641
143.361
139.353
137.275
132.321
129.924
129.667
129.544
129.071
128.912
128.590
127.836
125.131
121.328
119.157
107.522
107.473
107.424
107.376
77.254
77.000
76.746
20.163
19.978
Me
Me
O
N
CF3
4n
f1 (ppm)

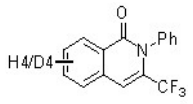

7.756
7.525
7.522
7.518
7.514
7.507
7.504
7.499
7.494
7.492
7.484
7.480
7.434
7.308
7.292
7.055
3.947
2.382
0.000
MeO
Me
CF3
4o
0.97
3.08
1.00
1.99
1.00
3.03
2.96
f1 (ppm)


162.480
159.468
137.381
134.858
129.490
129.113
129.083
128.910
128.407
128.148
127.778
126.693
121.451
119.284
107.601
107.553
107.506
107.457
106.735
77.254
77.000
76.746
55.755
16.752
MeO
Me
CF3
4o
f1 (ppm)

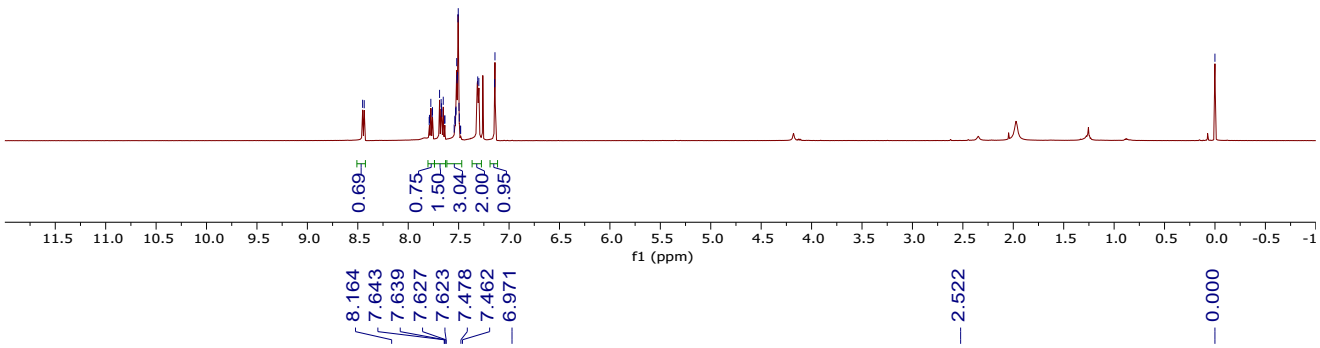

7.939
7.920
7.437
7.422
7.383
7.375
7.368
7.360
7.353
2.427
0.000
46%
D
Me
CO2H
D 100%
D-1a
0.54
0.98
0.96
3.00
f1 (ppm)


8.233
7.583
7.580
7.511
7.507
7.502
7.498
7.496
7.494
7.305
7.289
7.105
2.527
-0.000
17%
D
O
Me
N
Ph
CF3
D 67%
D-3a
0.83
2.08
3.05
2.07
0.33
3.00
f1 (ppm)

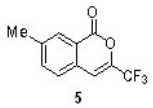

8.452
8.436
7.792
7.789
7.776
7.762
7.759
7.689
7.674
7.669
7.667
7.653
7.639
7.636
7.544
7.537
7.534
7.530
7.526
7.519
7.516
7.511
7.507
7.504
7.497
7.493
7.483
7.480
7.311
7.300
7.143
7.140
0.000


O
Ph
N
H4/D4
CF3

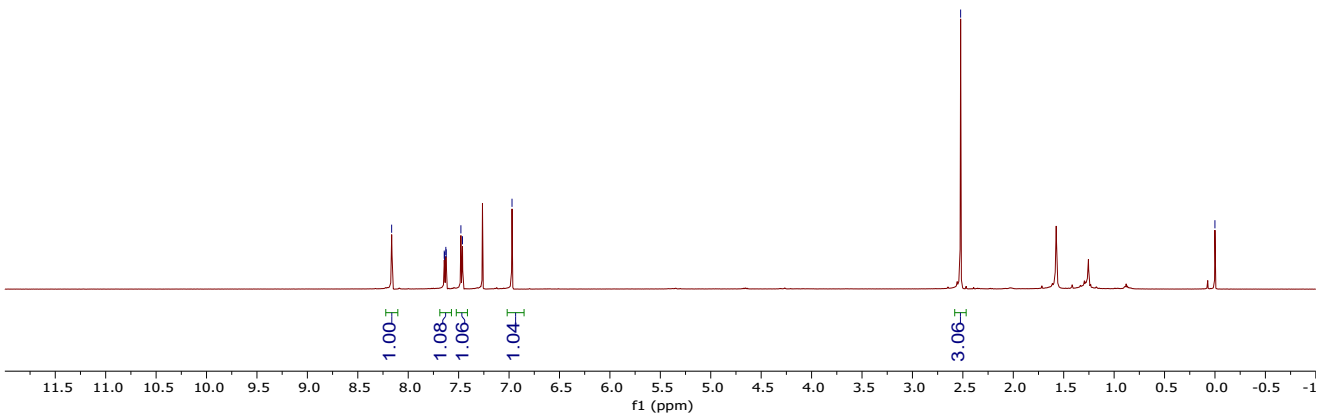
4a/**4a**-D4

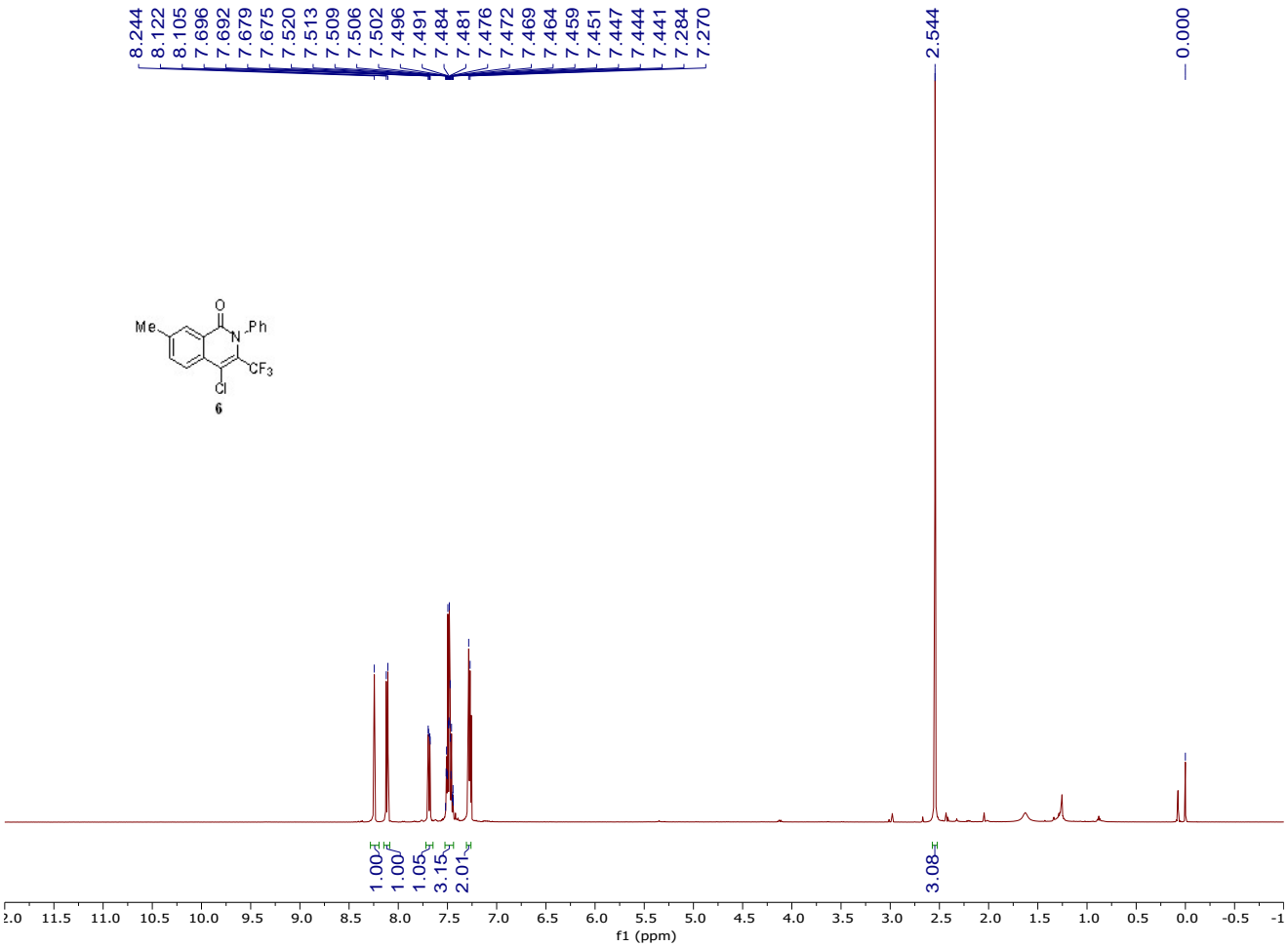

0.69
0.75
1.50
3.04
2.00
0.95
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

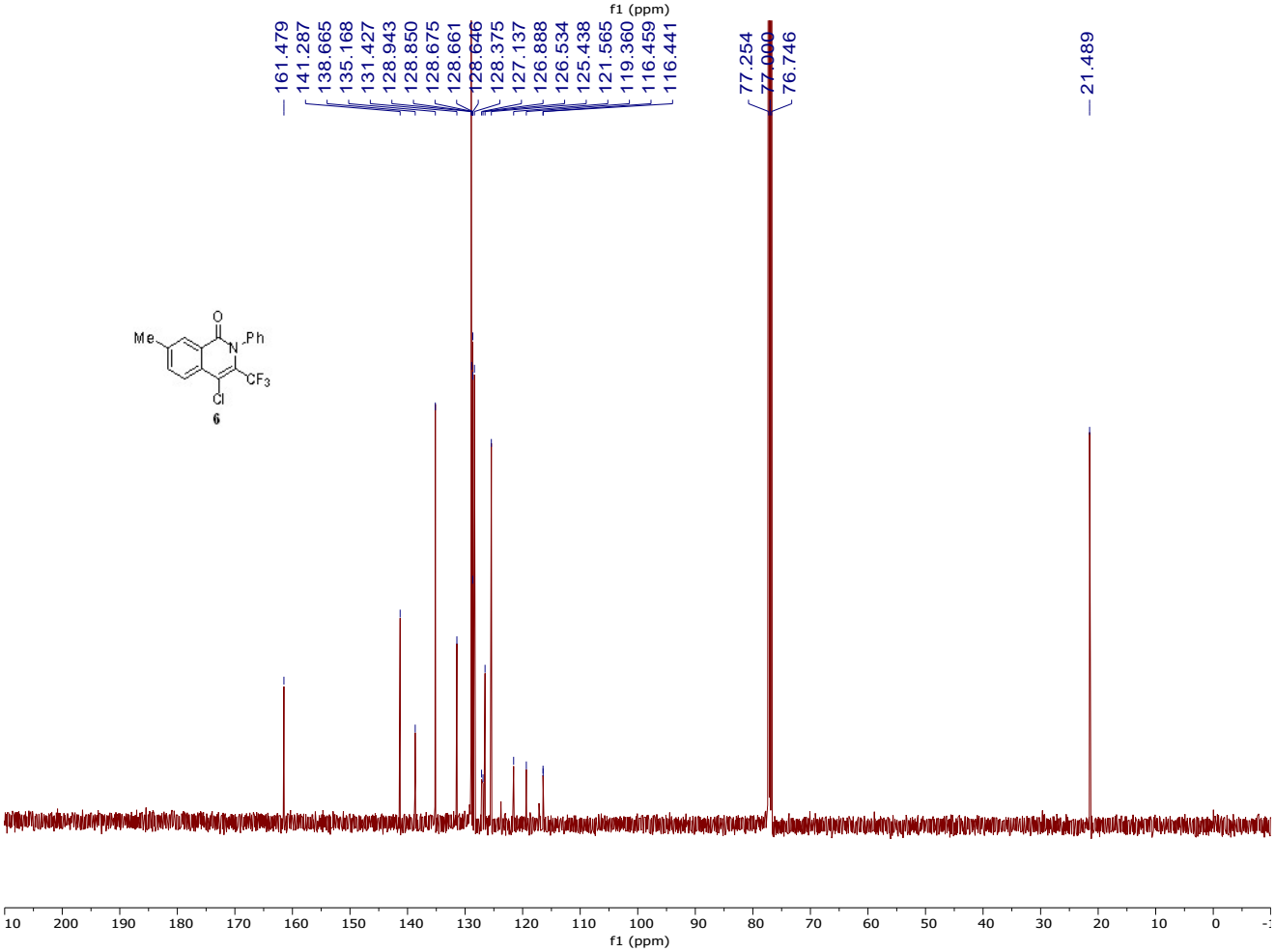
8.164
7.643
7.639
7.627
7.623
7.478
7.462
6.971
2.522
0.000

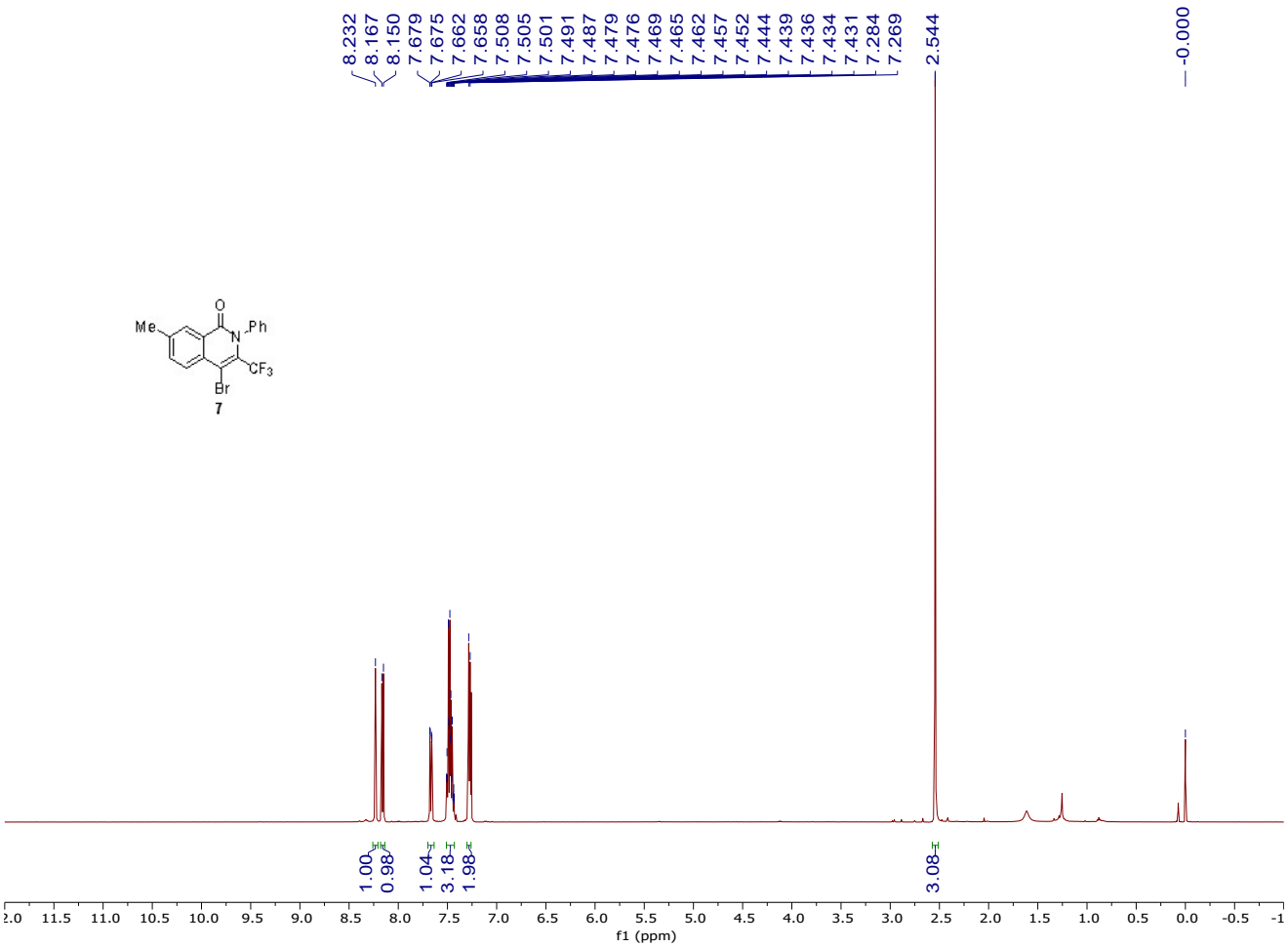

Me
O
O
CF3

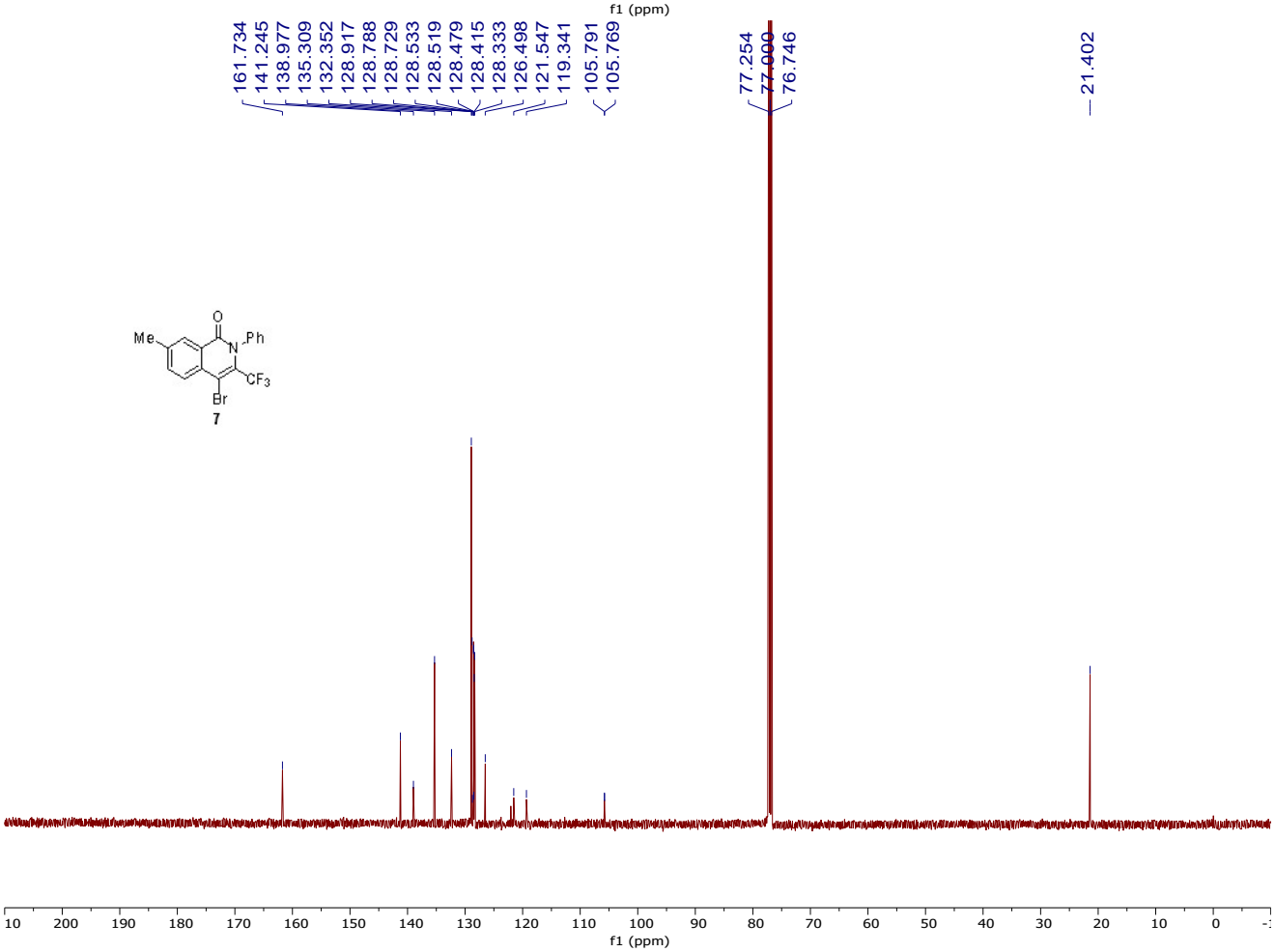
5

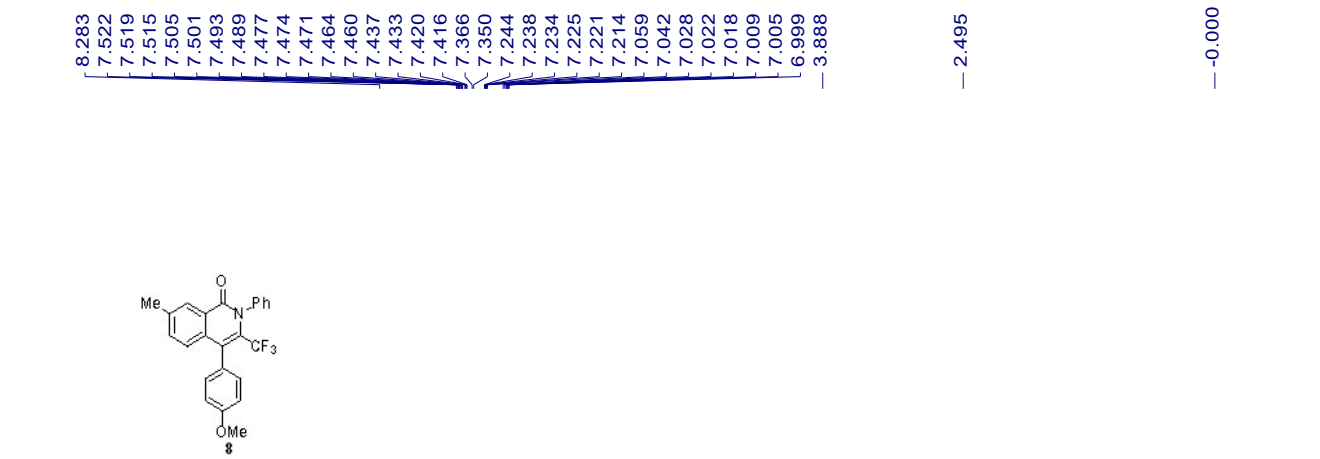

1.00
1.08
1.06
1.04
3.06
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


8.244
8.122
8.105
7.696
7.692
7.679
7.675
7.520
7.513
7.509
7.506
7.502
7.496
7.491
7.484
7.481
7.476
7.472
7.469
7.464
7.459
7.451
7.447
7.444
7.441
7.284
7.270
2.544
0.000
1.00
1.00
1.05
3.15
2.01
3.08
f1 (ppm)
Me
Ph
CF3
Cl
6


161.479
141.287
138.665
135.168
131.427
128.943
128.850
128.675
128.661
128.646
128.375
127.137
126.888
126.534
125.438
121.565
119.360
116.459
116.441
77.254
77.000
76.746
21.489
f1 (ppm)
Me
Ph
CF3
Cl
6

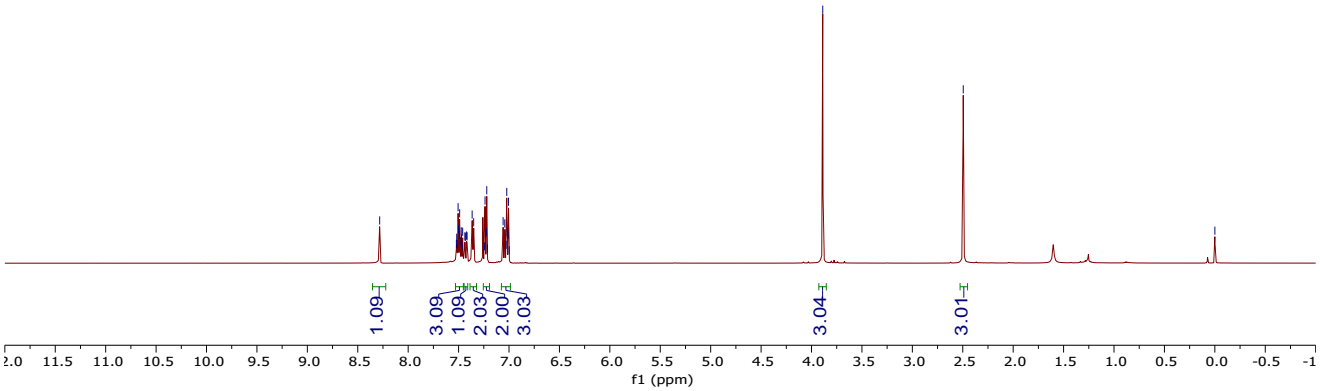

8.232
8.167
8.150
7.679
7.675
7.662
7.658
7.508
7.505
7.501
7.491
7.487
7.479
7.476
7.469
7.465
7.462
7.457
7.452
7.444
7.439
7.436
7.434
7.431
7.284
7.269
2.544
-0.000
1.00
0.98
1.04
3.18
1.98
3.08
f1 (ppm)
Me
Ph
CF3
Br
7

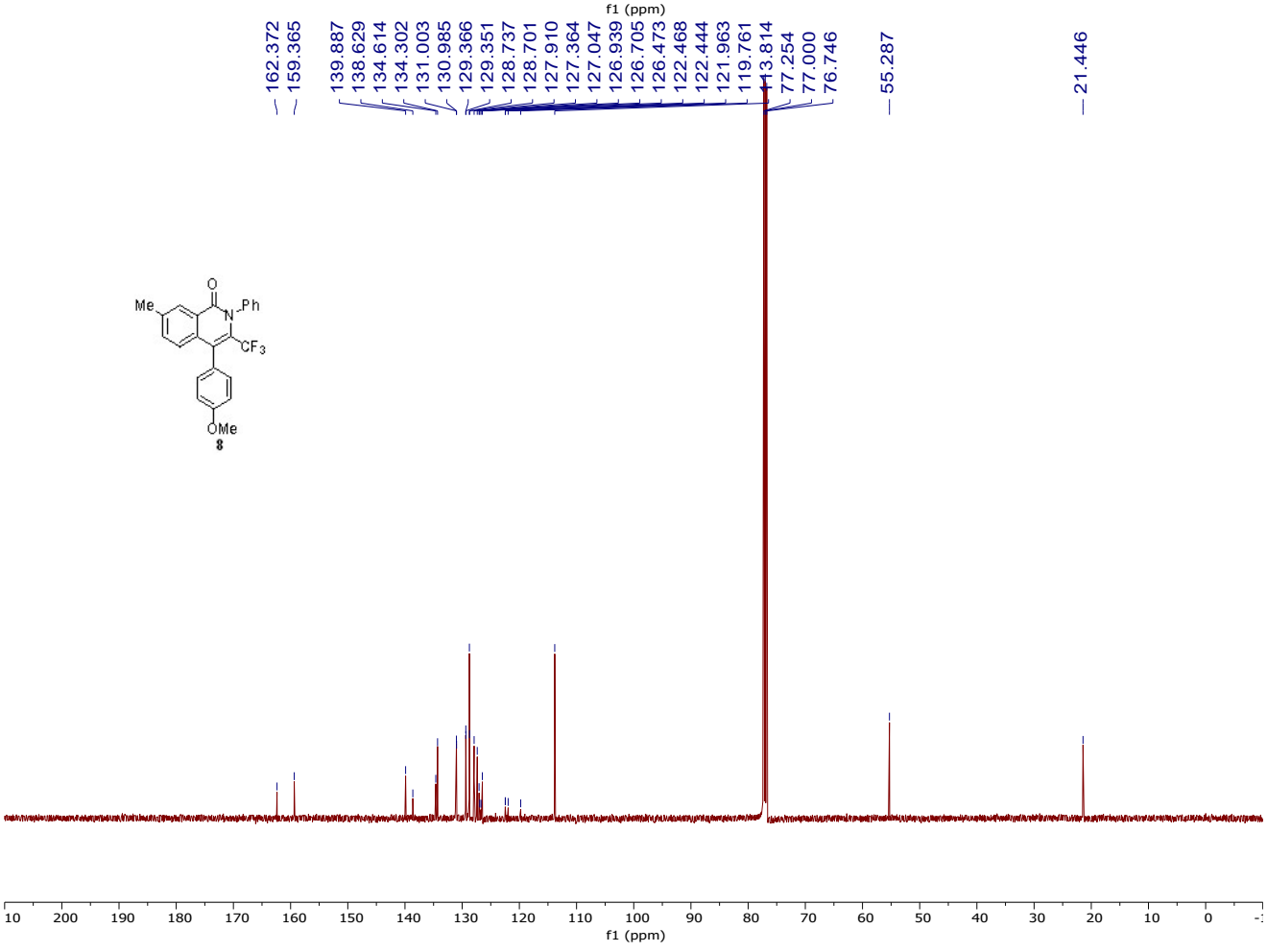

161.734
141.245
138.977
135.309
132.352
128.917
128.788
128.729
128.533
128.519
128.479
128.415
128.333
126.498
121.547
119.341
105.791
105.769
77.254
77.000
76.746
21.402
f1 (ppm)
Me
Ph
CF3
Br
7


8.283
7.522
7.519
7.515
7.505
7.501
7.493
7.489
7.477
7.474
7.471
7.464
7.460
7.437
7.433
7.420
7.416
7.366
7.350
7.244
7.238
7.234
7.225
7.221
7.214
7.059
7.042
7.028
7.022
7.018
7.009
7.005
6.999
3.888
2.495
-0.000

Me
O
N
Ph
CF3
OMe

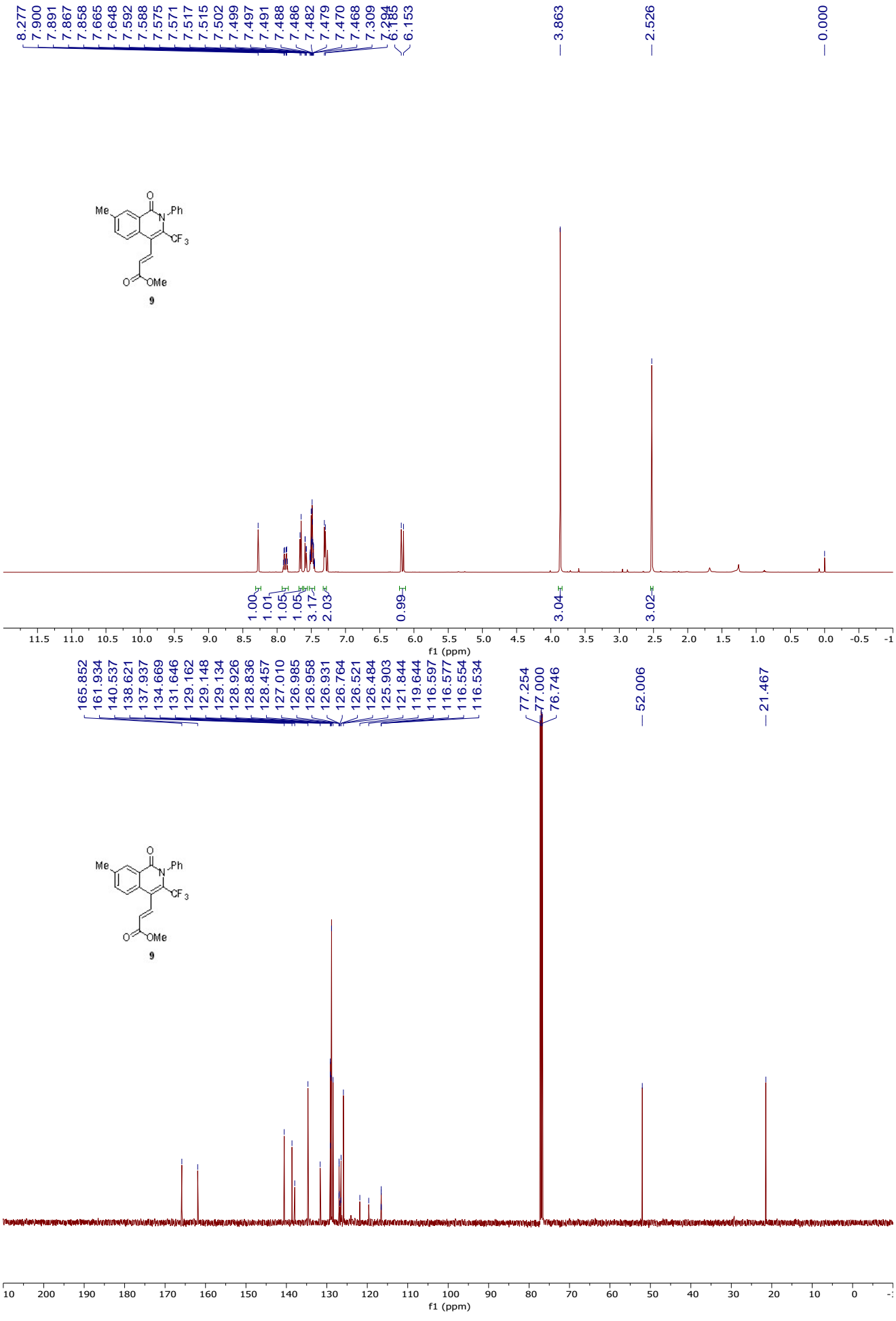
8


1.09
3.09
1.09
2.03
2.00
3.03
3.04
3.01
f1 (ppm)


162.372
159.365
139.887
138.629
134.614
134.302
131.003
130.985
129.366
129.351
128.737
128.701
127.910
127.364
127.047
126.939
126.705
126.473
122.468
122.444
121.963
119.761
113.814
77.254
77.000
76.746
55.287
21.446
f1 (ppm)

Me
O
N
Ph
CF3
OMe

8


8.277
7.900
7.891
7.867
7.858
7.665
7.648
7.592
7.588
7.575
7.571
7.517
7.515
7.502
7.499
7.497
7.491
7.488
7.486
7.482
7.479
7.470
7.468
7.309
7.294
7.185
6.153
3.863
2.526
0.000
Me
Ph
CF3
OMe
9
1.00
1.01
1.05
1.05
3.17
2.03
0.99
3.04
3.02
f1 (ppm)
165.852
161.934
140.537
138.621
137.937
134.669
131.646
129.162
129.148
129.134
128.926
128.836
128.457
127.010
126.985
126.958
126.931
126.764
126.521
126.484
125.903
121.844
119.644
116.597
116.577
116.554
116.534
77.254
77.000
76.746
52.006
21.467
f1 (ppm)