Copper-Catalyzed Synthesis of *β*-Trifluoromethylated Acrylonitriles and Trifluoromethyl-substituted 2*H*-Azirines

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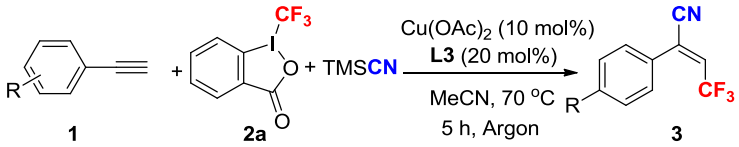
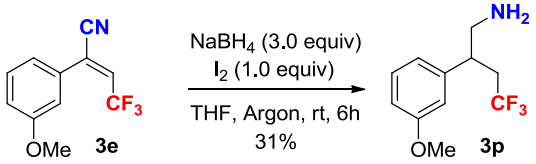
1. General Remarks

For Column chromatography, 200-300 mesh silica gel was employed. Analytical TLC was performed with silica gel GF254 plates. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{19}F NMR (376 MHz) were recorded in $CDCl_3$ using TMS as internal standard. All products were further characterized by high resolution mass spectra (HRMS); copies of their ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra are provided. Unless otherwise noted, reactions were carried out under an argon atmosphere. CH_3CN was distilled from P_2O_5 under reduced pressure before used.

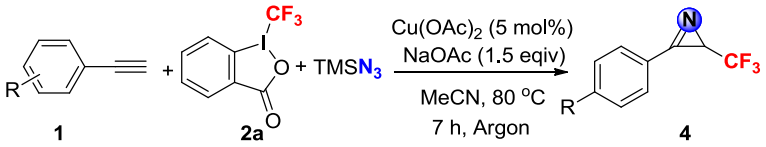
2. General experimental procedure



An oven-dried tube was charged with Togni's reagent **2a** (0.24 mmol) and $Cu(OAc)_2$ (0.02 mmol), 2,2':6',2"-terpyridine **L3** (0.04 mmol). The tube was evacuated and backfilled with argon (repeated three times). Then, TMSCN (0.4 mmol) dissolved in CH_3CN (1.0 mL), and alkynes **1** (0.2 mmol) were added into the tube. The reaction mixture was stirring at 70 ℃ for 5 h and extracted with DCM. The combined organic layers were washed with saturated brine, dried over Na_2SO_4, concentrated in vacuum (Note: the control of temperature and pressure is very important) and purified by flash column chromatography (silica gel) to afford the product **3**.

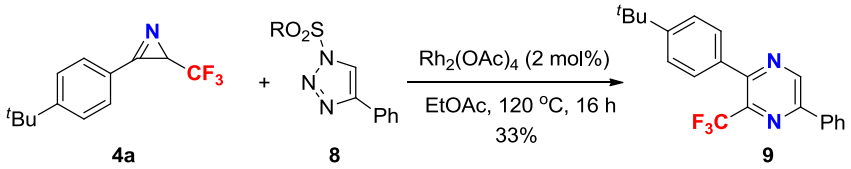


An oven dried Schlenk tube charged with **3e** (1.0 equiv), $NaBH_4$ (3.0 equiv) and I_2 (1.0 equiv) was purged with nitrogen, THF was added. The reaction mixture was then stirring at room temperature for 6 h. The solution was cooled, treated with H_2O and extracted with DCM. The combined organic layers were washed with saturated brine, dried over Na_2SO_4, concentrated in vacuum (Note: the control of temperature and pressure is very important) and purified by flash column chromatography (DCM/MeOH = 200/1) to afford the product **3p**.



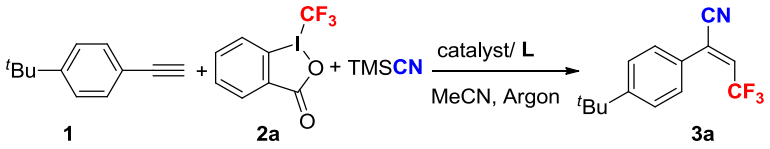
An oven-dried tube was charged with Togni's reagent **2a** (0.26 mmol) and $Cu(OAc)_2$ (0.01 mmol), NaOAc (0.3 mmol). The tube was evacuated and backfilled with argon (repeated three times). Then, $TMSN_3$ (0.36 mmol) dissolved in CH_3CN (1.0 mL), and alkynes **1** (0.2 mmol) were added into the tube. The reaction mixture was stirring at 80 ℃ for 7 h and extracted with DCM. The combined organic layers were washed with saturated brine, dried over Na_2SO_4, concentrated in vacuum (Note: the control of temperature and pressure is very important) and purified by flash column chromatography (silica gel) to afford the product **4**.

An oven dried Schlenk tube charged with $[Rh_2(esp)_2]$ (0.004 mmol) was purged with nitrogen, and a solution of azirine **4** (0.2 mmol) in DCE (0.5 mL) was added. A solution of the freshly prepared diazo compound **6** (0.32 mmol) in DCE (0.5 mL) was added dropwise to the suspension under nitrogen. The reaction mixture was then heated to 90 ℃ for 16 h. The solution was cooled and treated with DDQ (1 equiv). The suspension was stirred at 35 ℃ for 2 h and filtered through a plug of silica gel. The filtrate was concentrated in vacuo, and the residue was purified by flash chromatography using hexanes/ethyl acetate as the eluent to give the desired product **7**.



An oven-dried tube was charged with 2*H*-azirines **4a** (0.2 mmol), N-sulfonyl-4-phenyl-1,2,3-triazole **8**, and $Rh_2(OAc)_4$ (0.004 mmol). Then, EtOAc (1.0 mL) was added into the tube. The reaction mixture was stirring at 120 ℃ for 16 h (monitored by thin-layer chromatography using silica gel precoated glass plates), concentrated in vacuum and purified by flash column chromatography (silica gel) to afford the product **9**.

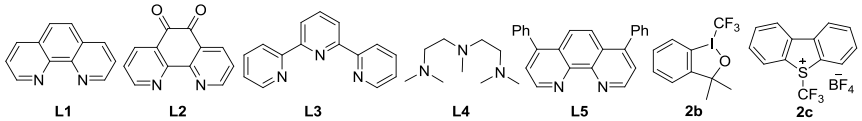
3. Optimization of The Reaction Conditions for *β*-Trifluoromethylated acrylonitriles [a]



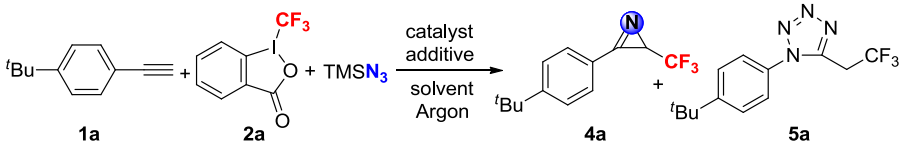
1 2a 3a

Entry	Catalyst (mol %)[b]	Ligand	Solvent	Yield (%)[c]
1	CuBr	—	1,4-dioxane	trace
2	CuBr	—	DCE	trace
3	CuBr	—	DMF	trace
4	CuBr (10)	—	CH_3CN	5 (>20/1)
5	CuBr (10)	L1(20)	CH_3CN	58 (>20/1)
6	$Cu(OTf)_2$	L1(20)	CH_3CN	40 (>20/1)
7	Cu powder	L1(20)	CH_3CN	58 (>20/1)
8	$CuCl_2$ (10)	L1(20)	CH_3CN	56 (>20/1)
9	$Cu(OAc)_2$ (10)	L1(20)	CH_3CN	62 (>20/1)
10	$Cu(OAc)_2$ (10)	L2(20)	CH_3CN	58 (>20/1)
11	$Cu(OAc)_2$ (10)	L3(20)	CH_3CN	71 (>20/1)
12	$Cu(OAc)_2$ (10)	L4(20)	CH_3CN	trace
13	$Cu(OAc)_2$ (10)	L5(20)	CH_3CN	57 (>20/1)
14[d]	—	L3(20)	CH_3CN	0
15[e]	$Cu(OAc)_2$ (10)	L3(20)	CH_3CN	62
16[f]	$Cu(OAc)_2$ (10)	L3(20)	CH_3CN	35

[a]Reaction conditions: **1a** (0.2 mmol), Togni's reagent **2a** (0.24 mmol), TMSCN (0.4 mmol), copper catalyst (10 mol %), ligand (20 mol %), solvent (1.0 mL), 5 h, 70 ℃, under argon. [b]Number given in parenthesis is mol % used. [c]Isolated yield, the ratio of regioisomers was determined by GC-MS. [d]Without copper catalyst. [e]Togni's reagent **2b** was used. [f]Umemoto reagent **2c** was used.



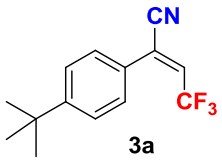
4. Optimization of The Reaction Conditions For Trifluoromethyl-substituted 2*H*-Azirines[a]



Entry	Catalyst (mol %)[b]	Base	Solvent	Temperature (℃)	$TMSN_3$ (equiv)	Yield (**4a**) (%)	Yield (**5a**) (%)
1	$Cu(OAc)_2$/**L3**	—	CH_3CN	70	1.8	trace	—
2	$Cu(OAc)_2$	—	CH_3CN	70	1.8	30	—
3	CuBr	—	CH_3CN	70	1.8	21	—
4	$Cu(MeCN)_4PF_6$	—	CH_3CN	70	1.8	20	—
5	$Cu(OTf)_2$	—	CH_3CN	70	1.8	13	—
6	$Cu(OAc)_2$	K_2CO_3	CH_3CN	70	1.8	41	—
7	$Cu(OAc)_2$	NaO^tBu	CH_3CN	70	1.8	45	—
8	$Cu(OAc)_2$	K_3PO_4	CH_3CN	70	1.8	33	—
9	$Cu(OAc)_2$	$NaHCO_3$	CH_3CN	70	1.8	46	—
10	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	70	1.8	51	—
11	$Cu(OAc)_2$	$NaOA_C$	1,4-dioxane	70	1.8	trace	—
12	$Cu(OAc)_2$	$NaOA_C$	DCE	70	1.8	trace	—
13	$Cu(OAc)_2$	$NaOA_C$	DMF	70	1.8	30	—
14	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	1.8	64	13
15[c]	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	1.8	58	—
16[d]	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	1.8	40	—
17[e]	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	1.8	54	—
18	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	3.0	59	27
19	$Cu(OAc)_2$	$NaOA_C$	DMF	80	3.0	18	0
20	$Cu(OAc)_2$	$NaOA_C$	1,4-dioxane	80	3.0	trace	2
21	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	4.0	30	18
14[f]	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	1.8	61	
14[g]	$Cu(OAc)_2$	$NaOA_C$	CH_3CN	80	1.8	31	
24	$Cu(OAc)_2$	$NaOA_C$/H_2O (1 quiv)	CH_3CN	80	3.0	13	10
25	$Cu(OAc)_2$	$NaOA_C$/*i*PrOH (1 quiv)	CH_3CN	80	3.0	42	27
26	$Cu(OAc)_2$	$NaOA_C$/9-BBN (1 quiv)	CH_3CN	80	3.0	0	0
27	$Cu(OAc)_2$	$NaOA_C$/TFA (1 quiv)	CH_3CN	80	3.0	0	0
28	$Cu(OAc)_2$	$NaOA_C$/1,4-CHD (1 quiv)	CH_3CN	80	3.0	12	20
29	$Cu(OAc)_2$	$NaOA_C$/CF_3CH_2OH (1 quiv)	CH_3CN	80	3.0	13	31
30	$Cu(OAc)_2$	$NaOA_C$/$K_2S_2O_8$ (1 quiv)	CH_3CN	80	3.0	27	21
31[f]	—	$NaOA_C$	CH_3CN	80	1.8	0	0

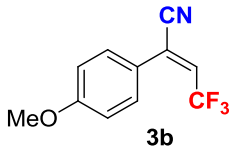
[a]Reaction conditions: **1a** (0.2 mmol), Togni's reagent **2a** (0.26 mmol), $TMSN_3$ (0.36 mmol), copper catalyst (5 mol %), solvent (1.0 mL), 7 h, under argon. [b]Isolated yield. [c]molecular sieves (4Å; 50mg) was added. [d]NaN_3 was used instead of $TMSN_3$. [e]under air condition. [f]Togni's reagent **2b** was used. [g]Umemoto reagent **2c** was used. [h]Without copper catalyst.

5. Characterization Data of 3a-p, 4a-r, 5a, 7a-f and 9



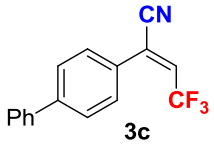
3a

(E)-2-(4-(tert-butyl)phenyl)-4,4,4-trifluorobut-2-enenitrile, 71% yield, E/Z > 20/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.42 (m, 4H), 6.44 (q, *J* = 8.00 Hz, 1H), 1.34 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 129.0 (q, *J* = 37.0 Hz), 128.4 (d, *J* = 2.0 Hz), 126.8, 126.1 (q, *J* = 6.0 Hz), 125.9, 121.0 (q, *J* = 270.0 Hz, CF_3), 117.0, 34.9 , 31.1 .
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (t, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{14}H_{14}F_3N$: [M] + H = 254.1151. Found: 254.1152.



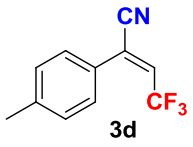
3b

(E)-4,4,4-trifluoro-2-(4-methoxyphenyl)but-2-enenitrile, 65% yield, E/Z = 17/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.44 (q, *J* = 8.4 Hz, 1H), 3.84 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7, 130.4 (q, *J* = 2.0 Hz), 127.7 (q, *J* = 37.0 Hz), 125.7 (q, *J* = 6.0 Hz), 121.9, 121.1 (q, *J* = 270.0 Hz, CF_3), 117.1, 114.3, 55.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (d, *J* =11.3 Hz, 3F).
HRMS (ESI) Calcd for $C_{11}H_8F_3NO$: [M] + H = 228.0631. Found: 228.0630.



3c

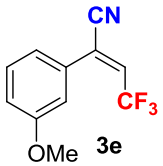
(E)-2-([1,1'-biphenyl]-4-yl)-4,4,4-trifluorobut-2-enenitrile, 62% yield, E/Z = 16/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.40Hz, 2H), 7.61 – 7.55 (m, 4H), 7.46 (t, *J* = 7.42 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 6.49 (q, *J* = 8.00 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 139.5, 129.6 (q, *J* = 37.0 Hz), 129.1, 129.0, 128.9, 128.2, 127.5, 127.1, 125.8 (q, *J* = 6.0 Hz), 121.0 (q, *J* = 270.0 Hz, CF_3), 116.9.
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.8 (d, *J* = 7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{16}H_{10}F_3N$: [M] + H = 274.0838. Found: 274.0839.



3d

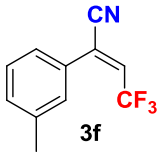
(E)-4,4,4-trifluoro-2-(p-tolyl)but-2-enenitrile, 65% yield, E/Z > 20/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.4 Hz, 2H), 7.27 – 7.25 (m, 2H), 6.44 (q, *J* = 8.0 Hz, 1H), 2.40 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 129.7, 129.2 (q, *J* = 37.0 Hz), 128.5 (d, *J* = 2.0 Hz), 126.9, 126.2 (q, *J* = 6.0 Hz), 121.0 (q, *J* = 270.0 Hz, CF_3), 117.0, 21.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (d, *J* = 7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{11}H_8F_3N$: [M] + H = 212.0682. Found: 212.0683.



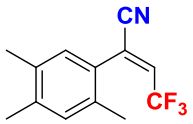
3e

(E)-4,4,4-trifluoro-2-(3-methoxyphenyl)but-2-enenitrile, 60% yield, E/Z = 18/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (t, *J* = 8.00 Hz, 1H), 7.06 – 7.01 (m, 2H), 6.98 (s, 1H), 6.49 (q, *J* = 8.00Hz, 1H), 3.83 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 130.8, 130.2 (q, *J* = 37.0 Hz), 130.0, 126.0 (q, *J* = 6.0 Hz), 120.8 (q, *J* = 272.0 Hz, CF_3), 120.7 (d, *J* = 2.0 Hz), 116.8, 116.7, 113.7 (d, *J* = 2.0 Hz), 55.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.8 (d, *J* =7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{11}H_8F_3NO$: [M] + H = 228.0631. Found: 228.0632.



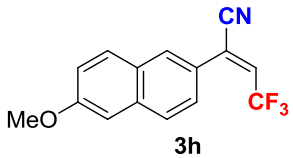
3f

(E)-4,4,4-trifluoro-2-(m-tolyl)but-2-enenitrile, 63% yield, E/Z = 20/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 4H), 6.47 (q, *J* = 8.00 Hz, 1H), 2.40 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 131.8, 129.8 (q, *J* = 37.0 Hz), 129.7, 128.9 (d, *J* = 2.0 Hz), 128.8, 126.3 (q, *J* = 6.0 Hz), 125.6 (d, *J* = 2.0 Hz), 120.9 (q, *J* = 270.0 Hz, CF_3), 116.9, 21.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (s, 3F).
HRMS (ESI) Calcd for $C_{11}H_8F_3N$: [M] + H = 212.0682. Found: 212.0680.



3g

(E)-4,4,4-trifluoro-2-(2,4,5-trimethylphenyl)but-2-enenitrile, 89% yield, E/Z > 20/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (s, 1H), 6.91 (s, 1H), 6.54 (q, *J* = 7.20 Hz, 1H), 2.28 (s, 3H), 2.24 (s, 3H), 2.22 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 134.5, 132.7, 131.9, 131.9 (q, *J* = 34.0 Hz), 129.5 (d, *J* = 2.0 Hz), 126.6, 126.1 (q, *J* = 6.0 Hz), 120.8 (q, *J* = 271.0 Hz, CF_3), 116.0, 19.4, 19.0, 18.8.
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.2 (d, *J* = 7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{13}H_{12}F_3N$: [M] + H = 240.0995. Found: 240.0992.



3h

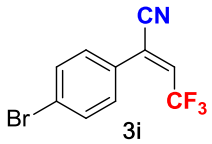
(E)-4,4,4-trifluoro-2-(6-methoxynaphthalen-2-yl)but-2-enenitrile, 67% yield, E/Z > 20/1.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.77 (d, *J* = 8.80 Hz, 2H), 7.49 (d, *J* = 8.00, 1H), 7.24 – 7.19 (m, 1H), 7.13 (d, *J* = 2.00 Hz, 1H), 6.49 (q, *J* = 8.00 Hz, 1H), 3.92 (s, 3H).

^{13}C NMR (100 MHz, CDCl3) δ 159.5, 135.6, 130.2, 129.1 (d, *J* = 2.0 Hz), 128.9 (q, *J* = 37.0 Hz), 128.0 , 127.5 , 126.3 (q, *J* = 6.0 Hz), 125.2 (d, *J* = 2.0 Hz), 124.7, 121.1 (q, *J* = 270.0 Hz, CF_3), 120.2, 117.1, 105.7, 55.4 .

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.7 (d, *J* =6.0 Hz, 3F).

HRMS (ESI) Calcd for $C_{14}H_{10}F_3NO$: [M] + H = 266.0787. Found: 266.0789.



3i

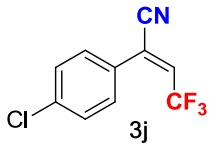
(E)-2-(4-bromophenyl)-4,4,4-trifluorobut-2-enenitrile, 60% yield, E/Z = 16/1.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.80 Hz, 2H), 7.35 (d, *J* = 8.40 Hz, 2H), 6.53 (q, *J* = 7.82 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 132.3, 130.6 (q, *J* = 37.0 Hz), 130.0 (d, *J* = 2.0 Hz), 128.6, 125.8, 125.0 (q, *J* = 6.0 Hz), 120.7 (q, *J* = 270.0 Hz, CF_3), 116.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (d, *J* =7.5 Hz, 3F).

HRMS (ESI) Calcd for $C_9H_5BrF_3N$: [M] + H = 263.9630. Found: 263.9634.



3j

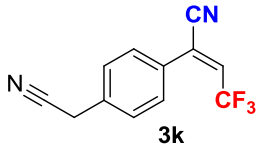
(E)-2-(4-chlorophenyl)-4,4,4-trifluorobut-2-enenitrile, 58% yield, E/Z > 20/1.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46– 7.41 (m, 4H), 6.53 (q, *J* = 7.86 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 130.6 (q, *J* = 37.0 Hz, $CHCF_3$), 129.8 (d, *J* = 2.0 Hz), 129.3, 128.1, 125.0 (q, *J* = 6.0 Hz, $CCHCF_3$), 120.7 (q, *J* = 270.0 Hz, CF_3), 116.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (d, *J* =3.8 Hz, 3F).

HRMS (ESI) Calcd for $C_{10}H_5ClF_3N$: [M] + H = 232.0135. Found: 232.0134.



3k

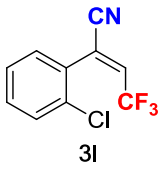
(E)-2-(4-(cyanomethyl)phenyl)-4,4,4-trifluorobut-2-enenitrile, 35% yield, E/Z > 20/1.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 6.55 (q, *J* = 8.0 Hz, 1H), 3.83 (s, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.1, 130.9 (q, *J* = 36.0 Hz, $CHCF_3$), 129.7, 129.3 (d, *J* = 2.0 Hz), 128.5, 125.2 (q, *J* = 5.0 Hz), 120.7 (q, *J* = 270.0 Hz, CF_3), 116.9, 116.5, 23.5.

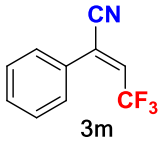
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (d, *J* =3.8 Hz, 3F).

HRMS (ESI) Calcd for $C_{12}H_7F_3N_2$: [M] + H = 237.0634. Found: 237.0638.



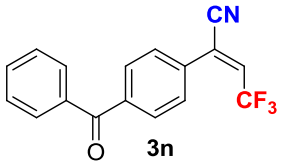
3l

(E)-2-(2-chlorophenyl)-4,4,4-trifluorobut-2-enenitrile, 62% yield, E/Z > 20/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.49 (m, 1H), 7.46 – 7.42(m, 1H), 7.35 (t, *J* = 7.60, 1H), 7.29 – 7.26 (m, 1H), 6.67 (q, *J* = 6.80 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7 (q, *J* = 36.0 Hz), 132.6, 131.9, 130.2 (d, *J* = 2.0 Hz), 130.1, 128.6, 127.2, 123.4 (q, *J* = 6.0 Hz), 120.5 (q, *J* = 270.0 Hz, CF_3), 115.0.
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.5 (d, *J* =3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{10}H_5ClF_3N$: [M] + H = 232.0135. Found: 232.0136.



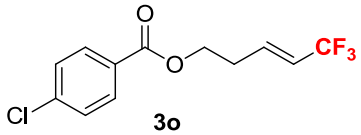
3m

(E)-4,4,4-trifluoro-2-phenylbut-2-enenitrile, 61% yield, E/Z > 20/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50– 7.43 (m, 5H), 6.50 (q, *J* = 8.00Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 131.0, 130.1 (q, J = 37.0 Hz), 129.8, 128.9, 128.4 (d, *J* = 2.0 Hz), 126.1 (q, *J* = 6.0 Hz), 120.9 (q, *J* = 270.0 Hz, CF_3), 116.8.
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.9 (d, *J* = 7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{10}H_6F_3N$: [M] + H = 198.0525. Found: 198.0523.



3n

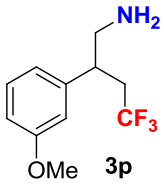
(E)-2-(4-benzoylphenyl)-4,4,4-trifluorobut-2-enenitrile, 29% yield, E/Z = 14/1.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.00 Hz, 2H), 7.81 (d, *J* = 7.20Hz, 2H), 7.61 (t, *J* = 8.40 Hz, 3H), 7.52 (t, *J* = 7.60 Hz, 2H), 6.62 (q, *J* = 7.60 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 139.7, 136.7, 133.2, 133.0, 131.5 (q, *J* = 36.0 Hz), 130.8, 130.3, 130.0, 128.5, 125.1 (q, *J* = 5.0 Hz), 120.7 (q, *J* = 271.0 Hz, CF_3), 116.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.8 (d, *J* = 7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{17}H_{10}F_3NO$: [M] + H = 302.0787. Found: 302.0792.



3o

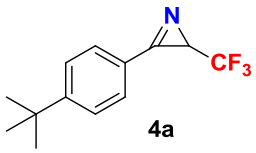
(E)-5,5,5-trifluoropent-3-en-1-yl 4-chlorobenzoate, 30% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.80, 2H), 7.42 (d, *J* = 8.80, 2H), 6.46 – 6.42 (m, 1H), 5.80 – 5.75 (m, 1H), 4.43 (t, *J* = 6.40 Hz, 2H), 2.67– 2.61 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 139.6, 135.9 (q, *J* = 7.0 Hz), 130.9, 128.8,

128.3, 122.6 (q, J = 267.0 Hz, CF_3), 121.0 (q, J = 34.0 Hz), 62.7, 30.9.
^{19}F NMR (376 MHz, $CDCl_3$) δ -64.4 (t, J = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{12}H_{10}ClF_3NO_2$: [M] + H = 279.0394. Found: 279.0391.



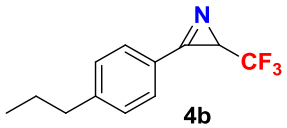
3p

4,4,4-trifluoro-2-(3-methoxyphenyl)butan-1-amine, 31% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, J = 8.0 Hz, 1H), 6.87 (dd, J = 8.4 Hz, J = 2.0 Hz, 1H), 6.79 (d, J = 7.6 Hz, 1H), 6.74 (d, J = 1.6 Hz, 1H), 3.81 (s, 3H), 3.47 (d, J = 32.8 Hz, 2H), 3.29–3.23 (m, 1H), 3.20–3.14 (m, 1H), 3.00–2.92 (m, 1H), 2.47–2.38 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 139.4, 131.0, 125.8 (q, J = 276.0 Hz), 119.3, 113.6, 113.5, 55.3, 52.6, 39.0 (q, J = 3.0 Hz), 38.4 (d, J = 28.0 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -63.8.8 (s, 3F).
HRMS (ESI) Calcd for $C_{11}H_{14}F_3NO$: [M] + H = 234.1100. Found: 234.1103.



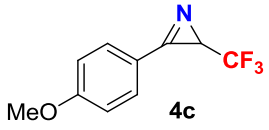
4a

3-(4-(tert-butyl)phenyl)-2-(trifluoromethyl)-2H-azirine, 64% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.40 Hz, 2H), 7.63 (d, J = 8.40 Hz, 2H), 2.68 (q, J = 4.40 Hz, 1H), 1.37 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 158.5, 130.3, 126.5, 124.3 (q, J = 272.0Hz, CF_3), 119.2, 35.4 , 31.0, 29.2 (q, J = 42.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (s, 3F).
HRMS (ESI) Calcd for $C_{13}H_{14}F_3N$: [M] + H = 242.1157. Found: 242.1154.



4b

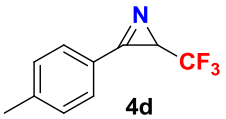
3-(4-propylphenyl)-2-(trifluoromethyl)-2H-azirine, 52% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 2.72 - 2.67 (m, 3H), 1.74-1.65(m, 2H), 0.97 (t, J = 7.3 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2 (d, J = 1.0 Hz), 150.3, 130.4, 129.6, 124.3 (q, J = 272.0 Hz, CF_3), 119.5, 38.3, 29.3 (q, J = 42.0 Hz, $CHCF_3$), 24.2, 13.7.
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (d, J = 3.8Hz, 3F).
HRMS (ESI) Calcd for $C_{12}H_{12}F_3N$: [M] + H = 228.0995. Found: 228.0997.



4c

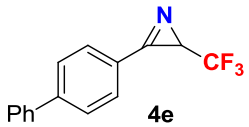
3-(4-methoxyphenyl)-2-(trifluoromethyl)-2H-azirine, 62% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.85 (m, 2H), 7.09 (d, *J* = 8.8 Hz, 2H), 3.92 (s, 3H), 2.66 (q, *J* = 4.6 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 159.1, 132.5, 124.4 (q, *J* = 272.0 Hz, CF_3), 115.0, 114.4, 55.6, 29.2 (q, *J* = 42.0 Hz , $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (d, J = 4.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{10}H_8F_3NO$: [M] + H = 216.0631. Found: 216.0633.



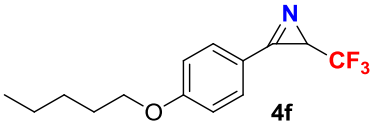
4d

3-(p-tolyl)-2-(trifluoromethyl)-2H-azirine, 54% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.1 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 2.68 (q, *J* = 4.6 Hz, 1H), 2.48 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 145.6, 130.4, 130.2, 124.3 (q, *J* = 272.0 Hz, CF_3), 119.3, 29.3 (q, *J* = 42.0 Hz, $CHCF_3$), 21.9.
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (d, J = 4.7 Hz, 3F).
HRMS (ESI) Calcd for $C_{10}H_8F_3N$: [M] + H = 200.0682. Found: 200.0683.



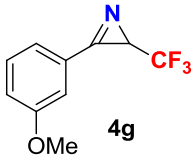
4e

3-([1,1'-biphenyl]-4-yl)-2-(trifluoromethyl)-2H-azirine, 55% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.97 (m, 2H), 7.82 – 7.80 (m, 2H), 7.65 – 7.63(m, 2H), 7.51 – 7.47 (m, 2H), 7.45 – 7.41 (m, 1H), 2.74 (q, *J* = 4.80 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3 (d, J = 1.0Hz), 147.2, 139.3, 130.9, 129.1, 128.7, 128.1, 127.3, 124.3 (q, *J* = 272.0 Hz, CF_3), 120.7, 29.5 (q, *J* = 32.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.6 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{15}H_{10}F_3N$: [M] + H = 262.0838. Found: 262.0840.



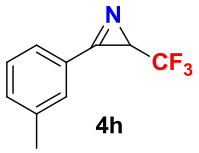
4f

3-(4-(pentyloxy)phenyl)-2-(trifluoromethyl)-2H-azirine, 40% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.80 Hz, 2H), 7.07 (d, *J* = 8.80Hz, 2H), 4.06 (t, *J* = 6.40 Hz, 2H), 2.65 (q, *J* = 4.40 Hz, 1H), 1.87 – 1.80 (m, 2H), 1.50 – 1.37(m, 4H), 0.95 (t, *J* = 7.20 Hz, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 159.1, 132.5, 124.4 (q, *J* = 272.0 Hz, CF_3), 115.4 , 114.1, 68.5, 29.2 (q, *J* = 42.0 Hz, $CHCF_3$), 28.7, 28.1, 22.4, 14.0.
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{14}H_{16}F_3NO$: [M] + H = 272.1257. Found: 272.1259.



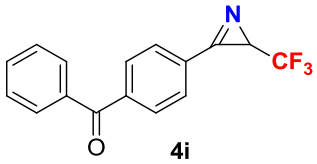
4g

3-(3-methoxyphenyl)-2-(trifluoromethyl)-2H-azirine, 54% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.48 (m, 2H), 7.44 – 7.43 (m, 1H), 7.23 – 7.20 (m, 1H), 3.90 (s, 3H), 2.73 (q, *J* = 4.40 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9 (d, J = 1.0 Hz), 160.2, 130.6, 124.2 (q, *J* = 271.9 Hz, CF_3), 123.2, 123.1, 121.0, 114.1, 55.6, 29.8 (q, *J* = 43.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.5 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{10}H_8F_3NO$: [M] + H = 216.0637. Found: 216.0632.



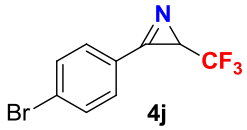
4h

3-(m-tolyl)-2-(trifluoromethyl)-2H-azirine, 53% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 4.40 Hz, 2H), 7.50 – 7.48 (m, 2H), 2.70 (q, *J* = 4.80 Hz, 1H), 2.47 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (d, *J* = 2.0 Hz), 139.5, 135.2, 130.8, 129.3, 127.6, 124.3 (d, *J* = 272.0 Hz, CF_3), 122.0, 29.5 (q, *J* = 42.0 Hz, $CHCF_3$), 21.2.
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{10}H_8F_3N$: [M] + H = 200.0682. Found: 200.0684.



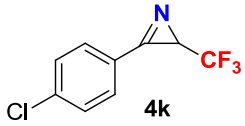
4i

phenyl(4-(2-(trifluoromethyl)-2H-azirin-3-yl)phenyl)methanone, 55% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.40 Hz, 2H), 7.99 (d, *J* = 8.40 Hz, 2H), 7.83 (d, *J* = 7.20 Hz, 2H), 7.65 (t, *J* = 7.20 Hz, 1H), 7.53 (t, *J* = 7.60 Hz, 2H), 2.82 (q, *J* = 4.80Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 160.7 (d, *J* = 1.0 Hz), 142.5, 136.4, 133.2, 130.5, 130.1, 130.0, 128.5, 124.9, 124.0 (d, *J* = 272.0 Hz, CF_3), 29.8 (q, *J* = 43.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.6 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{16}H_{10}F_3NO$: [M] + H = 290.0787. Found: 290.0788.



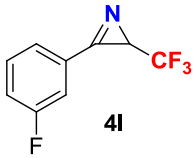
4j

3-(4-bromophenyl)-2-(trifluoromethyl)-2H-azirine, 61% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 4H), 2.75 (q, *J* = 4.80 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3 (d, *J* = 1.8 Hz), 133.0, 131.5, 129.7, 124.0 (q, *J* = 272.0 Hz, CF_3), 121.0, 29.7 (q, *J* = 43.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_9H_5BrF_3N$: [M] + H = 263.30. Found: 263.9634.



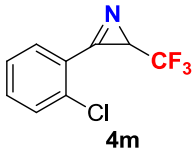
4k

3-(4-chlorophenyl)-2-(trifluoromethyl)-2H-azirine, 53% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 2.75 (q, J = 4.5 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 141.0, 131.5, 130.0, 124.1 (q, *J* = 272.0 Hz, CF_3), 120.6 , 29.7 (q, *J* = 42.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (s, 3F).
HRMS (ESI) Calcd for $C_9H_5ClF_3N$: [M] + H = 220.0141. Found: 220.0139.



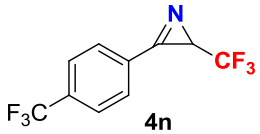
4l

3-(3-fluorophenyl)-2-(trifluoromethyl)-2H-azirine, 48% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.72 (m, 1H), 7.64 – 7.52 (m, 2H), 7.42 –7.37 (m, 1H), 2.77 (q, *J* = 4.80 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8 (d, *J* = 248.0 Hz), 160.6 (d, *J* = 1.0 Hz), 131.4 (d, *J* = 8.0 Hz), 126.2 (d, *J* = 3.0 Hz), 124.0 (q, *J* = 272.0 Hz, CF_3), 124.0 (d, *J* = 8.0 Hz), 121.6 (d, *J* = 21.0 Hz), 116.8 (d, *J* = 23.0 Hz), 30.0 (q, *J* = 43.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.8 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_9H_5F_4N$: [M] + H = 204.0431. Found: 204.0434.



4m

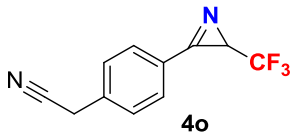
3-(2-chlorophenyl)-2-(trifluoromethyl)-2H-azirine, 48% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.87 (m, 1H), 7.62 – 7.61 (m, 2H), 7.53 – 7.49 (m, 1H), 2.76 (q, *J* = 4.40 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 136.9, 135.0, 133.0, 131.0, 127.5, 124.0 (d, *J* = 272.0 Hz, CF_3), 121.0, 29.6 (q, *J* = 42.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -68.0 (s, 3F).
HRMS (ESI) Calcd for $C_9H_5ClF_3N$: [M] + H = 220.0135. Found: 220.0137.



4n

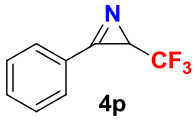
2-(trifluoromethyl)-3-(4-(trifluoromethyl)phenyl)-2H-azirine, 62% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 2.82 (q, *J* = 4.8 Hz, 1H),
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 135.8 (q, *J* = 33.0 Hz), 130.6, 126.5 (q, *J* = 4.0 Hz), 125.4, 124.6, 123.9 (q, *J* = 272.0 Hz, CF_3), 30.1 (q, *J* = 43.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -63.4 (s, 3F), -67.8 (s, 3F) .

HRMS (ESI) Calcd for $C_{10}H_5F_6N$: [M] + H = 254.0399. Found: 254.0404.



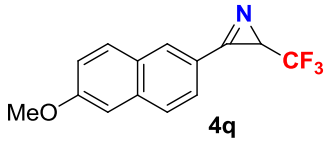
4o

2-(4-(2-(trifluoromethyl)-2H-azirin-3-yl)phenyl)acetonitrile, 39% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 3.90 (s, 2H), 2.76 (q, *J* = 4.4 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 136.6, 131.1, 129.1, 124.1 (q, *J* = 272.0 Hz, CF_3), 122.1, 116.6, 29.7 (q, *J* = 42.0 Hz, $CHCF_3$), 23.9.
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7 (s, 3F).
HRMS (ESI) Calcd for $C_{11}H_7F_3N_2$: [M] + H = 225.0634. Found: 225.0638.



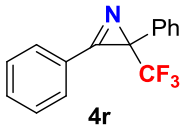
4p

3-phenyl-2-(trifluoromethyl)-2H-azirine, 60% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.91 (m, 2H), 7.91 – 7.68 (m, 1H), 7.62-7.59 (m, 2H), 2.73 (q, J = 4.6 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (d, *J* = 1.0 Hz), 134.4, 130.3, 129.4 (s), 124.3 (q, *J* = 272.0 Hz, CF_3), 122.1, 29.5 (q, *J* = 42.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.7(d, *J* =3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_9H_6F_3N$: [M] + H = 186.0525. Found: 186.0527.



4q

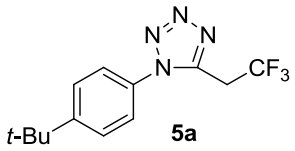
3-(6-methoxynaphthalen-2-yl)-2-(trifluoromethyl)-2H-azirine, 54% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.94 (dd, *J* = 6.80, 1.60 Hz, 1H), 7.90 – 7.87 (m, 2H), 7.28 – 7.25 (m, 1H), 7.20 (d, *J* = 2.40 Hz, 1H), 3.97 (s, 3H), 2.77 (q, J = 4.40 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 160.3 , 137.9 , 132.8 , 130.9 , 128.2 , 128.0 , 125.2 , 124.4 (q, *J* = 272.0 Hz, CF_3), 120.4 , 117.0 , 106.1 , 55.5 , 29.5 (q, *J* = 42.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -67.5 (d, *J* = 3.8 Hz, 3F).
HRMS (ESI) Calcd for $C_{14}H_{10}F_3NO$: [M] + H = 266.0787. Found: 266.0789.



4r

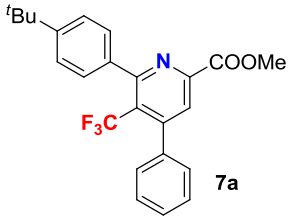
2,3-diphenyl-2-(trifluoromethyl)-2H-azirine, 19% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.67 – 7.64 (m, 1H), 7.60 – 7.56 (m, 2H), 7.46 (d, *J* = 6.8 Hz, 2H), 7.36 – 7.32 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 134.4, 133.7, 130.4, 129.6, 128.6, 128.5, 127.4,

124.8 (d, J = 274.0Hz, CF_3), 121.7, 40.3 (q, J = 38.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -65.3 (s, 3F).
HRMS (ESI) Calcd for $C_{15}H_{10}F_3N$: [M] + H = 262.0838. Found: 262.0835.



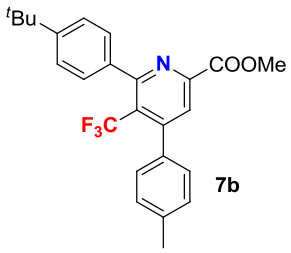
5a

1-(4-(tert-butyl)phenyl)-5-(2,2,2-trifluoroethyl)-1H-tetrazole.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.80 Hz, 2H), 7.37 (d, J = 8.80 Hz, 2H), 3.81 (q, J = 9.60 Hz, 2H), 1.40 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 146.5 (d, J = 3.0 Hz), 130.1, 127.1, 125.0, 123.3 (q, J = 276.0 Hz, CF_3), 35.0, 31.1, 29.4 (q, J = 33.0 Hz, $CHCF_3$).
^{19}F NMR (376 MHz, $CDCl_3$) δ -68.3 (t, J = 7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{13}H_{15}F_3N_4$: [M] + H = 285.1322. Found: 285.1318.



7a

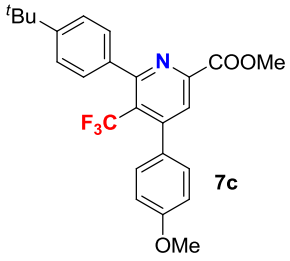
methyl 6-(4-(tert-butyl)phenyl)-4-phenyl-5-(trifluoromethyl)picolinate,54% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.57 (d, J = 8.00 Hz, 2H), 7.48 (d, J = 7.60 Hz, 5H), 7.45 – 7.43 (m, 2H), 4.00 (s, 3H), 1.36 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 160.1, 152.8 (d, J = 2.0 Hz), 152.1, 148.5, 138.5, 137.1, 128.9, 128.6 (d, J = 2.0 Hz), 128.4 , 128.1, 125.6 , 125.1 , 125.1 (q, J = 29.0 Hz, CCF_3), 123.6 (q, J = 274.0 Hz, CF_3), 53.2, 34.7, 31.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -49.0 (s, 3F).
HRMS (ESI) Calcd for $C_{24}H_{22}F_3NO_2$: [M] + H = 414.1675. Found: 414.1672.



7b

methyl 6-(4-(tert-butyl)phenyl)-4-(p-tolyl)-5-(trifluoromethyl)picolinate, 67% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.56 (d, J = 8.40 Hz, 2H), 7.48 (d, J = 8.40Hz, 2H), 7.34 (d, J = 8.00 Hz, 2H), 7.29 (d, J = 8.00 Hz, 2H), 4.00 (s, 3H), 2.43 (s, 3H), 1.36 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 160.1, 152.9 (d, J = 2.0 Hz), 152.1, 148.4, 138.9, 137.2, 135.6, 129.1, 128.6, 128.1 (d, J = 1.0 Hz), 125.7, 125.1, 125.1 (q, J = 29.0 Hz, CCF_3), 123.6 (q, J = 274.0 Hz, CF_3), 53.1, 34.7, 31.2, 21.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -49.0 (s, 3F).

HRMS (ESI) Calcd for $C_{25}H_{24}F_3NO_2$: [M] + H = 428.1832. Found: 428.1827.



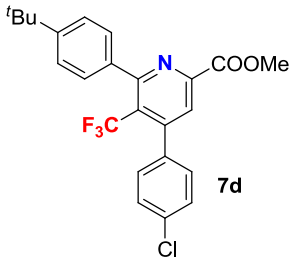
Methyl 6-(4-(tert-butyl)phenyl)-4-(4-methoxyphenyl)-5-(trifluoromethyl)picolinate, 63% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.57 (d, *J* = 8.40 Hz, 2H), 7.48 (d, *J* = 8.40 Hz, 2H), 7.40 (d, *J* = 8.40 Hz, 2H), 7.01 (d, *J* = 8.80 Hz, 2H), 4.00 (s, 3H), 3.87 (s, 3H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 160.2, 160.1, 152.5 (d, *J* = 2.0 Hz), 152.0, 148.3, 137.3, 130.8, 129.6, 128.5 (d, *J* = 2.0 Hz), 125.6, 125.1, 125.0 (q, *J* = 29.0 Hz, CCF_3), 123.7 (q, *J* = 274.0 Hz, CF_3), 113.8, 55.3, 53.1, 34.6, 31.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -49.1 (s, 3F).

HRMS (ESI) Calcd for $C_{25}H_{24}F_3NO_3$: [M] + H = 444.1781. Found: 444.1773.



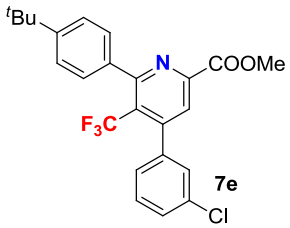
methyl 6-(4-(tert-butyl)phenyl)-4-(4-chlorophenyl)-5-(trifluoromethyl)picolinate, 60% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02(s, 1H), 7.55 (d, *J* = 8.40 Hz, 2H), 7.50 – 7.46 (m, 4H), 7.38 (d, *J* = 8.80 Hz, 2H), 4.01 (s, 3H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8 , 160.2 (d, *J* = 1.0 Hz), 152.3, 151.5 (d, *J* = 2.0 Hz), 148.6, 136.9, 136.8, 135.3, 129.5 (d, *J* = 1.0 Hz), 128.7, 128.5 (d, *J* = 1.0 Hz), 125.3, 125.1, 125.0 (q, *J* = 29.0 Hz, CCF_3), 123.5 (q, *J* = 274.0 Hz, CF_3), 53.2, 34.7, 31.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -49.0 (s, 3F).

HRMS (ESI) Calcd for $C_{24}H_{21}ClF_3NO_2$: [M] + H = 448.1286. Found: 448.1282.



methyl 6-(4-(tert-butyl)phenyl)-4-(3-chlorophenyl)-5-(trifluoromethyl)picolinate, 56% yield.

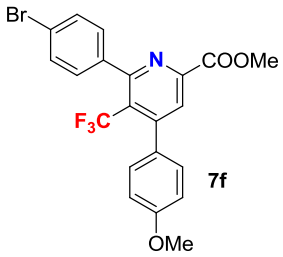
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.56 (d, *J* = 8.40Hz, 2H), 7.49 (d, *J* =

8.40 Hz, 2H), 7.45 (s, 2H), 7.42 (t, *J* = 7.60 Hz, 1H), 7.32 (d, *J* = 7.60Hz, 1H), 4.01 (s, 3H), 1.36 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 160.2, 152.3, 151.1 (d, *J* = 2.0 Hz), 148.7, 140.0, 136.9, 134.4, 129.7, 129.1, 128.6 (d, *J* = 1.0 Hz), 128.2, 126.4, 125.3, 125.1, 124.9 (q, *J* = 29.0 Hz, CCF_3), 123.4 (q, *J* = 274.0 Hz, CF_3), 53.3, 34.7, 31.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -49.0 (s, 3F).

HRMS (ESI) Calcd for $C_{24}H_{21}ClF_3NO_2$: [M] + H = 448.1286. Found: 448.1280.



7f

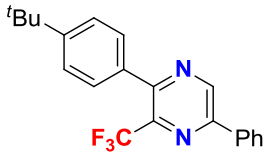
methyl 6-(4-bromophenyl)-4-(4-methoxyphenyl)-5-(trifluoromethyl)picolinate, 50% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.61 (d, *J* = 8.40 Hz, 2H), 7.50 (d, *J* = 8.40 Hz, 2H), 7.38 (d, *J* = 8.80 Hz, 2H), 7.02 (d, *J* = 8.80 Hz, 2H), 4.01 (s, 3H), 3.88 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 160.4, 158.8, 152.8 (d, *J* = 2.0 Hz), 148.5, 139.0, 131.4, 130.5 (d, *J* = 2.0 Hz), 130.4, 129.6, 126.3, 125.1 (q, *J* = 29.0 Hz, CCF_3), 123.6, 123.5 (q, *J* = 275.0Hz, CF_3), 114.0, 55.3, 53.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -49.0 (s, 3F).

HRMS (ESI) Calcd for $C_{21}H_{15}BrF_3NO_3$: [M] + H = 466.0260. Found: 466.0256.



9

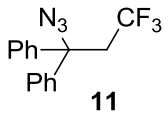
2-(4-(tert-butyl)phenyl)-5-phenyl-3-(trifluoromethyl)pyrazine, 33% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.16 – 8.14 (m, 2H), 7.59 – 7.51 (m, 7H), 1.38 (d, *J* = 0.70 Hz, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 151.4, 149.2, 142.6, 140.0 (q, *J* = 34.0 Hz, CCF_3), 134.7, 133.7, 130.6, 129.2, 128.6 (d, *J* = 2.0 Hz), 127.1, 125.3, 121.7 (q, *J* = 273.0 Hz, CF_3), 34.8, 31.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.9 (s, 3F).

HRMS (ESI) Calcd for $C_{21}H_{19}F_3N_2$: [M] + H = 357.1573. Found: 357.1569.



11

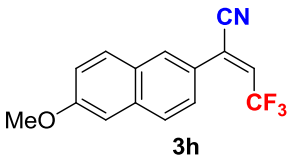
(1-azido-3,3,3-trifluoropropane-1,1-diyl)dibenzene

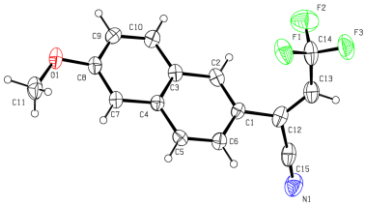
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.19 (m, 10H), 3.26 (q, *J* = 10.00 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 128.6, 128.1, 126.6, 125.1 (q, *J* = 277.0Hz, CF_3), 68.3 (d, *J* = 1.0 Hz), 42.3 (q, *J* = 27.0 Hz, CH_2CF_3).

^{19}F NMR (376 MHz, $CDCl_3$) δ -59.4 (t, *J* =7.5 Hz, 3F).
HRMS (ESI) Calcd for $C_{15}H_{12}F_3N_3$: [M-N_2] + H = 264.0995. Found: 264.0996.

6. Crystallographic data of 3h





Datablock:

Bond precision: C-C = 0.0085 A Wavelength=0.71073

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alpha=90 beta=92.84(2) gamma=90

Temperature: 293 K

	Calculated	Reported
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Hall group	-P 2ybc	-P 2ybc
Moiety formula	C15 H10 F3 N O	C15 H10 F3 N O
Sum formula	C15 H10 F3 N O	C15 H10 F3 N O
Mr	277.24	277.24
Dx,g cm-3	1.409	1.409
Z	4	4
Mu (mm-1)	0.118	0.118
F000	568.0	568.0
F000'	568.39	
h,k,lmax	16,16,8	16,16,8
Nref	2566	2566
Tmin,Tmax	0.968,0.976	0.386,1.000
Tmin'	0.962	

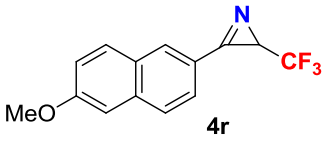
Correction method= MULTI-SCAN

Data completeness= 0.997 Theta(max)= 26.020

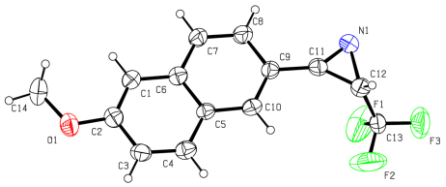
R(reflections)= 0.1085(887) wR2(reflections)= 0.3752(2559)

S = 0.917 Npar= 182

Crystallographic data of 4r



4r



Datablock:

Bond precision: C-C = 0.0059 A Wavelength=0.71000

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alpha=90 beta=104.113(7) gamma=90

Temperature: 293 K

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Volume	619.24(8)	619.25(8)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C14 H10 F3 N O	C14 H10 F3 N O
Sum formula	C14 H10 F3 N O	C14 H10 F3 N O
Mr	265.23	265.23
Dx,g cm-3	1.423	1.422
Z	2	2
Mu (mm-1)	0.121	0.121
F000	272.0	272.0
F000'	272.19	
h,k,lmax	11,6,15	11,6,15
Nref	2461[1369]	1934
Tmin,Tmax	0.959,0.970	0.758,1.000
Tmin'	0.959	

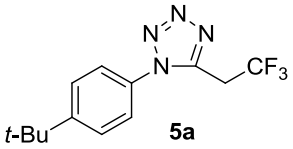
Correction method= MULTI-SCAN

Data completeness= 1.41/0.79 Theta(max)= 25.990

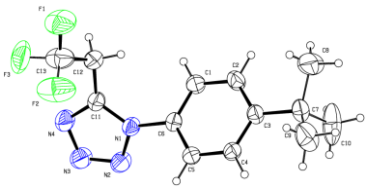
R(reflections)= 0.0591(1339) wR2(reflections)= 0.1470(1934)

S = 1.076 Npar= 173

Crystallographic data of 5a



5a



Datablock:

Bond precision: C-C = 0.0044 A Wavelength=0.71073

Cell: a=11.3589(5) b=8.1467(4) c=15.8924(7)
alpha=90 beta=99.885(5) gamma=90

Temperature: 293 K

	Calculated	Reported
Volume	1448.81(12)	1448.80(11)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C13 H15 F3 N4	C13 H15 F3 N4
Sum formula	C13 H15 F3 N4	C13 H15 F3 N4
Mr	284.29	284.29
Dx,g cm-3	1.303	1.303
Z	4	4
Mu (mm-1)	0.108	0.108
F000	592.0	592.0
F000'	592.33	
h,k,lmax	14,10,19	14,10,19
Nref	2841	2830
Tmin,Tmax	0.967,0.973	0.822,1.000
Tmin'	0.966	

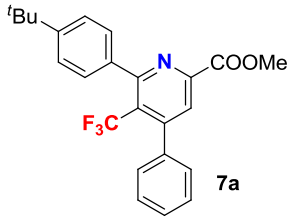
Correction method= MULTI-SCAN

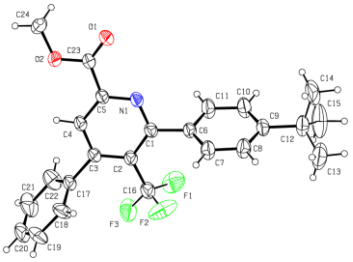
Data completeness= 0.996 Theta(max)= 26.020

R(reflections)= 0.0637(1506) wR2(reflections)= 0.1959(2830)

S = 1.036 Npar= 233

Crystallographic data of 7a





Datablock:

Bond precision: C-C = 0.0049 A Wavelength=0.71073

Cell: a=33.4249(17) b=6.2204(3) c=20.9937(9)
alpha=90 beta=96.885(4) gamma=90

Temperature:294 K

	Calculated	Reported
Volume	4333.5(4)	4333.5(3)
Space group	C 2/c	C 1 2/c 1
Hall group	-C 2yc	-C 2yc
Moiety formula	C24 H22 F3 N O2	C24 H22 F3 N O2
Sum formula	C24 H22 F3 N O2	C24 H22 F3 N O2
Mr	413.43	413.43
Dx,g cm-3	1.267	1.267
Z	8	8
Mu (mm-1)	0.098	0.098
F000	1728.0	1728.0
F000'	1729.03	
h,k,lmax	40,7,25	40,7,25
Nref	4265	4254
Tmin,Tmax	0.964,0.973	0.703,1.000
Tmin'	0.964	

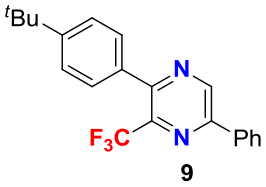
Correction method= MULTI-SCAN

Data completeness= 0.997 Theta(max)= 26.020

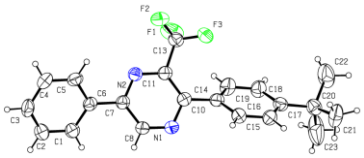
R(reflections)= 0.0635(2053) wR2(reflections)= 0.1951(4254)

S = 1.046 Npar= 333

Crystallographic data of 9



9



Datablock:

Bond precision: C-C = 0.0078 A Wavelength=0.71073

Cell: a=9.987(3) b=10.061(3) c=10.1680(16)
alpha=71.21(2) beta=75.39(2) gamma=79.84(2)

Temperature: 295 K

	Calculated	Reported
Volume	930.9(4)	930.8(4)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C21 H19 F3 N2	C21 H19 F3 N2
Sum formula	C21 H19 F3 N2	C21 H19 F3 N2
Mr	356.38	356.38
Dx,g cm-3	1.271	1.272
Z	2	2
Mu (mm-1)	0.096	0.096
F000	372.0	372.0
F000'	372.20	
h,k,lmax	12,12,12	12,12,12
Nref	3682	3647
Tmin,Tmax	0.967,0.976	0.374,1.000
Tmin'	0.967	

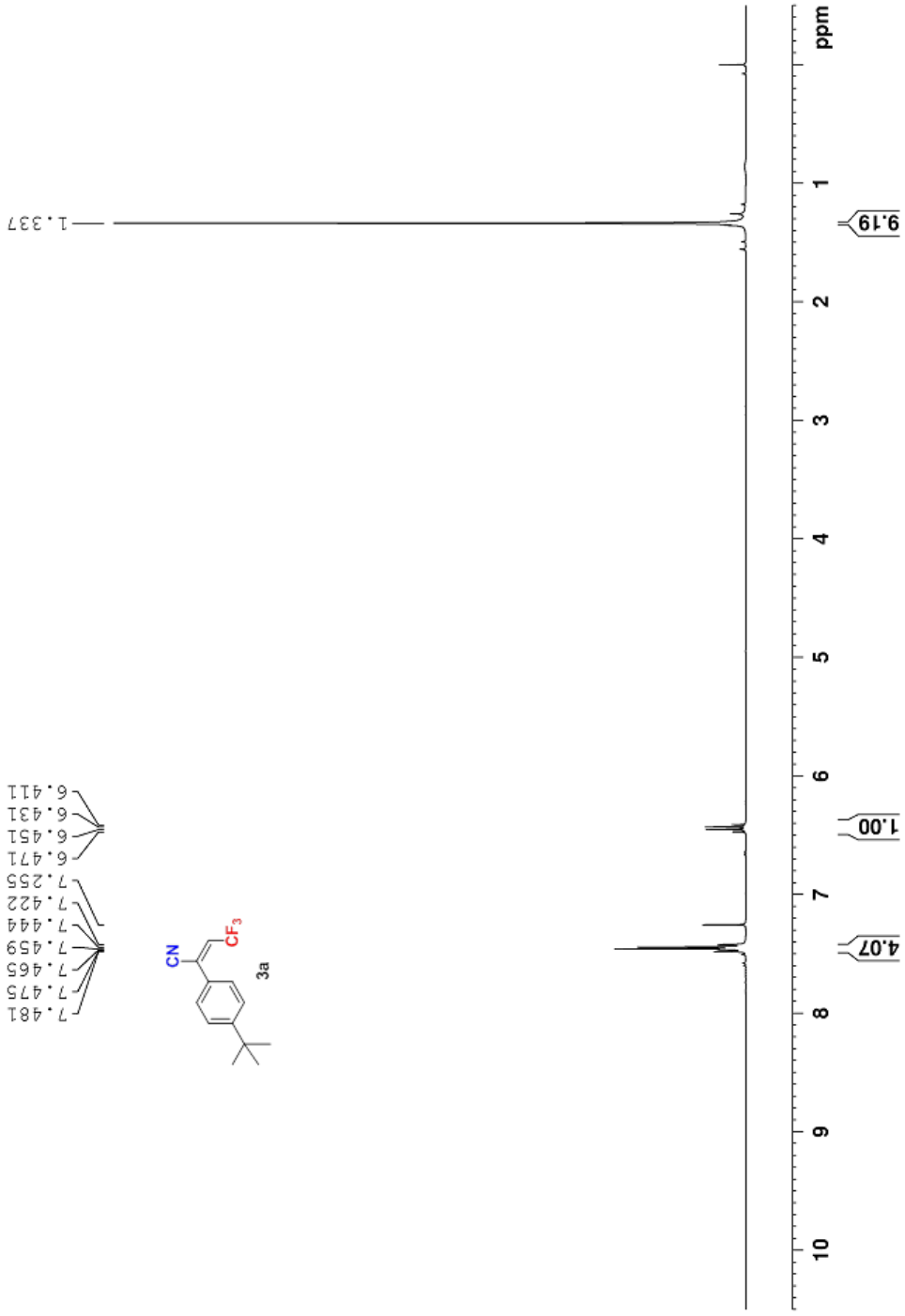
Correction method= MULTI-SCAN

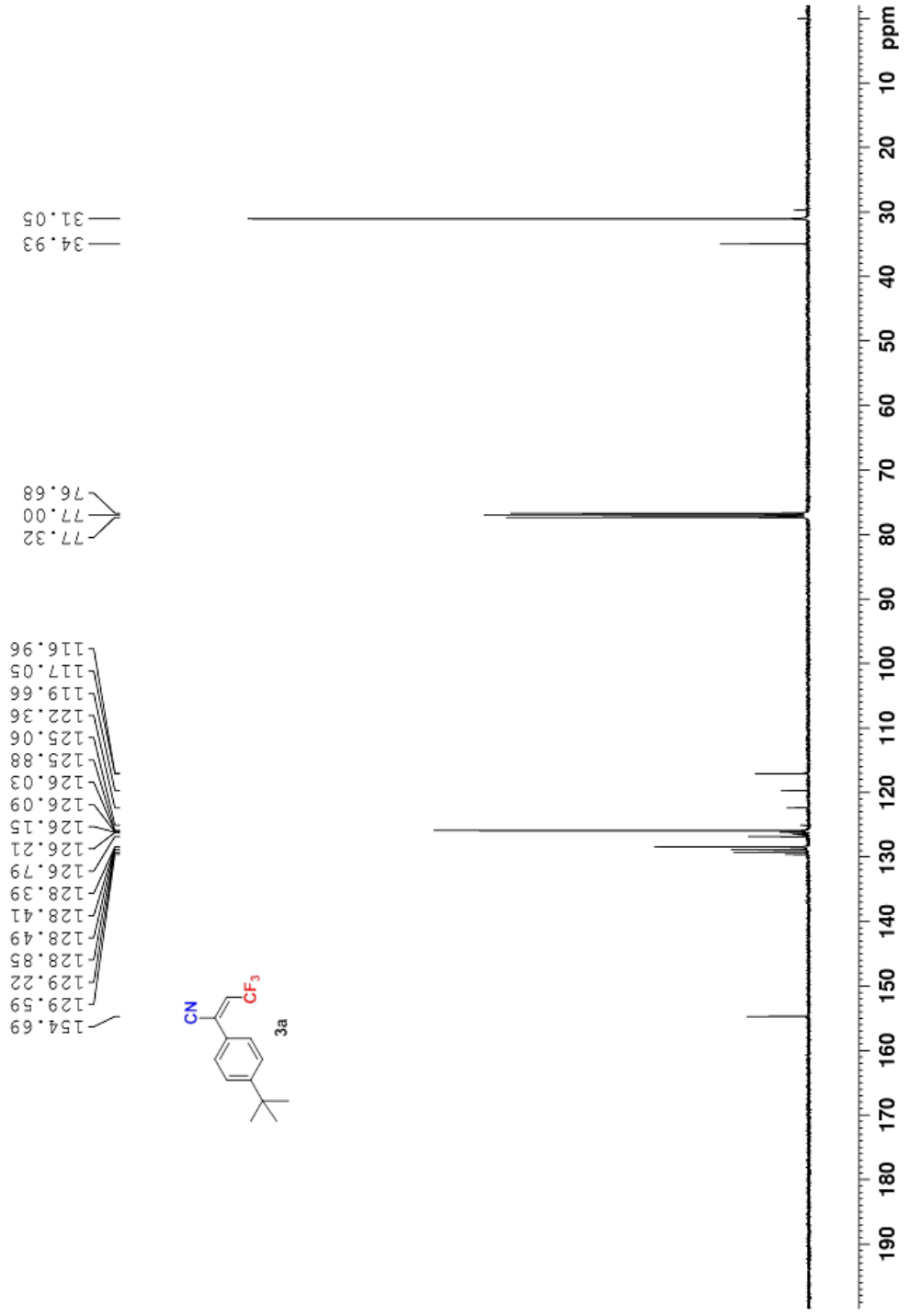
Data completeness= 0.990 Theta(max)= 26.020

R(reflections)= 0.0880(1222) wR2(reflections)= 0.3307(3647)

S = 0.950 Npar= 239

7、^{1}H NMR、^{13}C NMR、^{19}F NMR Spectra for Substrates 3a-p, 4a-r, 5a, 7a-f and 9

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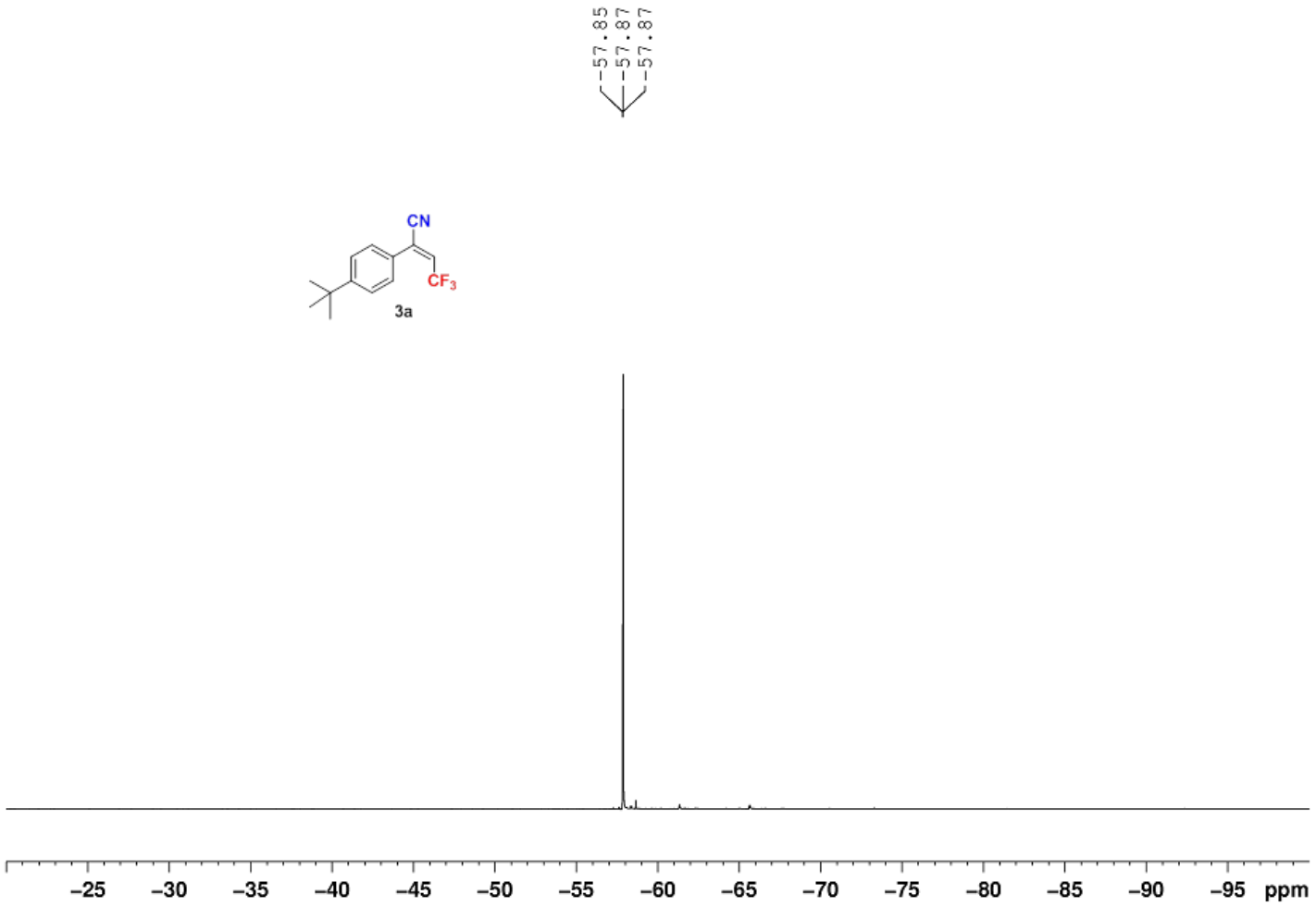
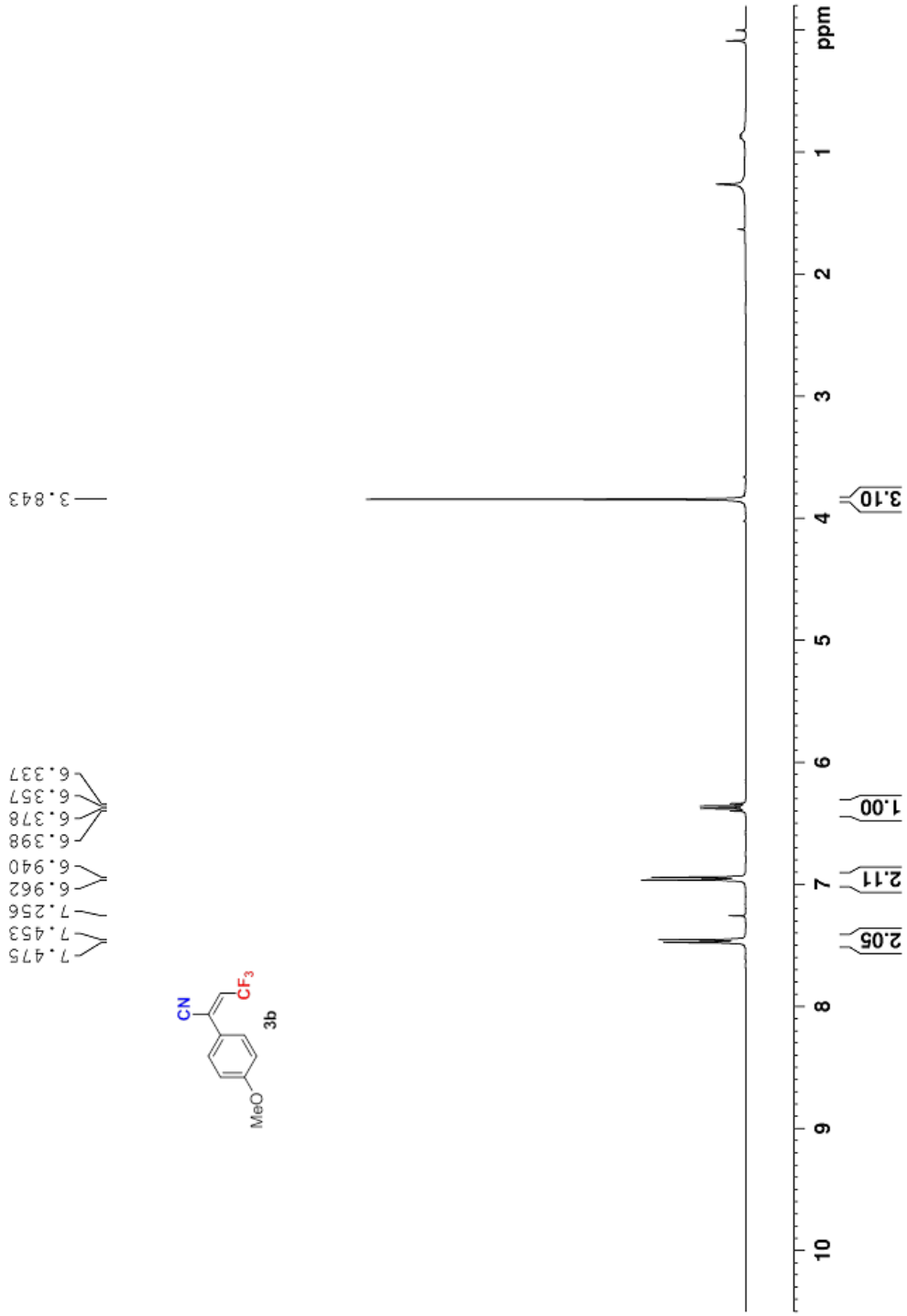
76.68
77.00
77.32
116.96
117.05
119.66
122.36
125.06
125.88
126.03
126.09
126.15
126.21
126.79
128.39
128.41
128.49
128.85
129.22
129.59
154.69
CN
CF3
3a
ppm


-57.85
-57.87
-57.87
CN
CF3
3a
−25
−30
−35
−40
−45
−50
−55
−60
−65
−70
−75
−80
−85
−90
−95
ppm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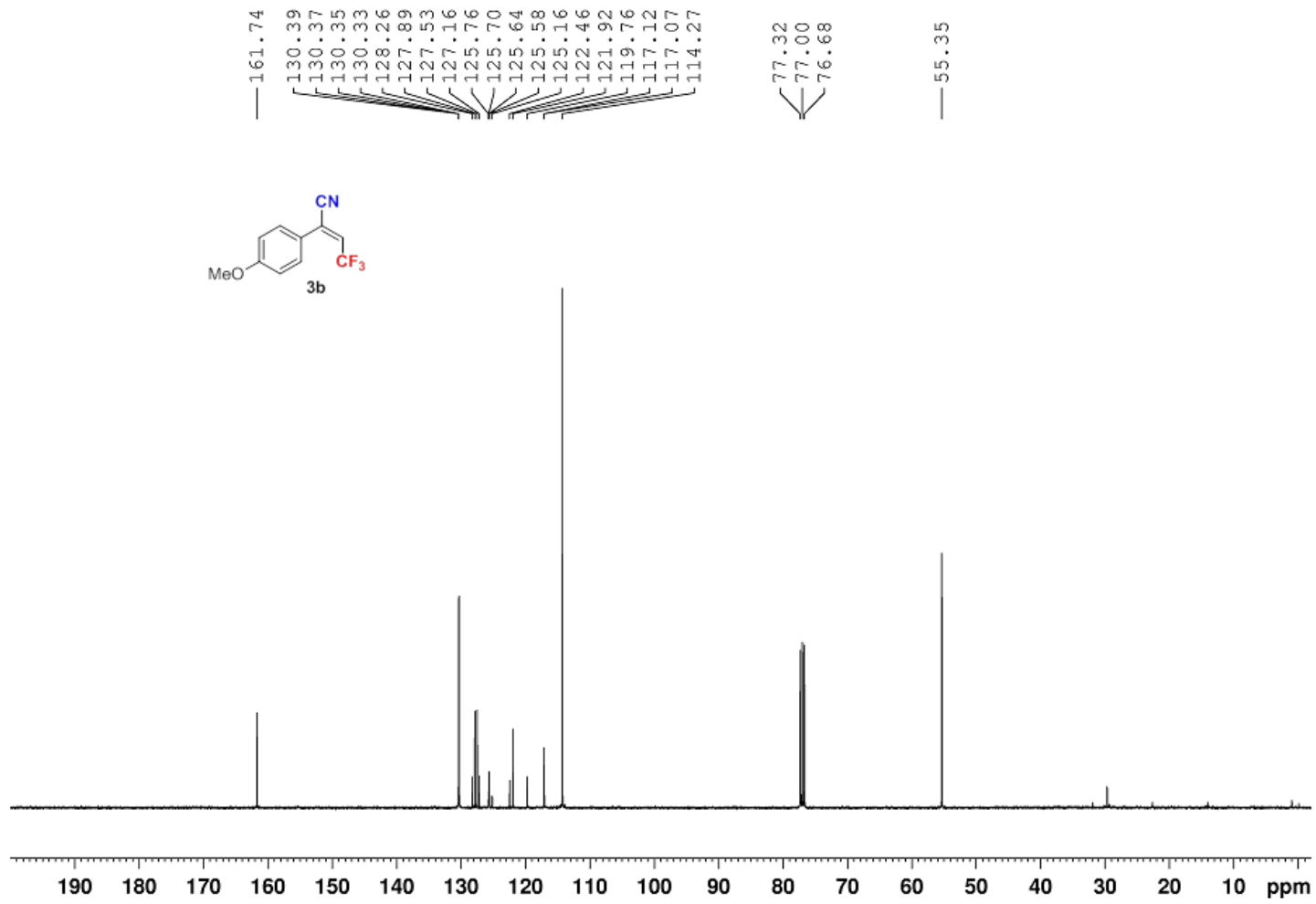
6.337
6.357
6.378
6.398
6.940
6.962
7.256
7.453
7.475
CN
CF3
3b
MeO
3.10
1.00
2.11
2.05
ppm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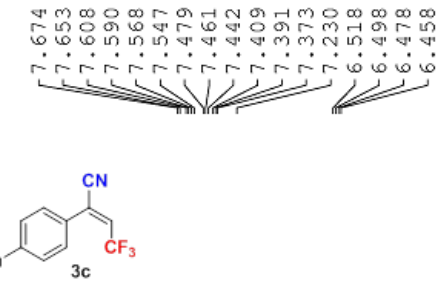
130.39
130.37
130.35
130.33
128.26
127.89
127.53
127.16
125.76
125.70
125.64
125.58
125.16
122.46
121.92
119.76
117.12
117.07
114.27
77.32
77.00
76.68
55.35
CN
CF3
MeO
3b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-57.92
-57.95
CN
CF3
MeO
3b
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm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7.547
7.479
7.461
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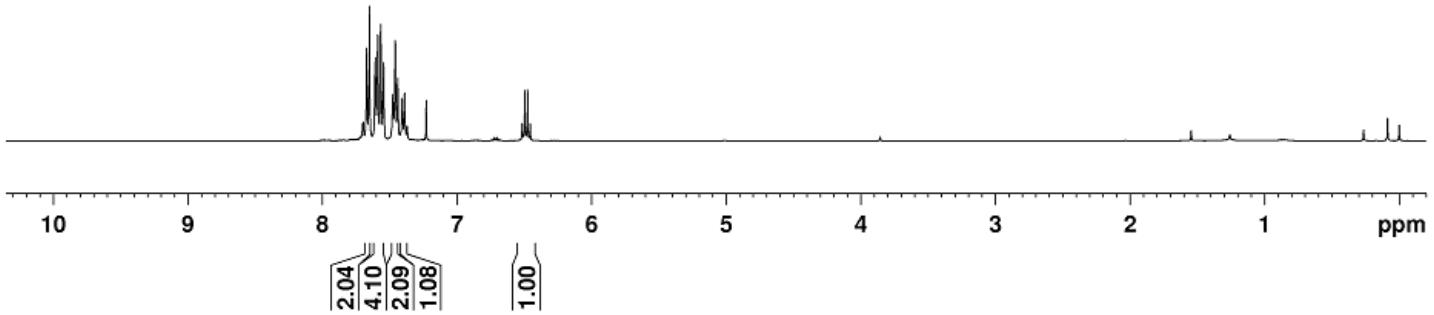
7.391
7.373
7.230
6.518
6.498
6.478
6.458
CN
CF3
Ph
3c


10
9
8
7
6
5
4
3
2
1
ppm
2.04
4.10
2.09
1.08
1.00

77.32
77.00
76.68
116.86
116.91
119.61
122.31
125.01
125.74
125.79
125.85
125.91
127.14
127.47
128.24
128.97
129.04
129.06
129.47
129.83
130.20
139.46
143.93
CN
CF3
Ph
3c
ppm

-57.77
-57.79
CN
CF3
Ph
3c
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.393
7.372
7.265
7.255
7.245
6.467
6.447
6.427
6.407
2.402
CN
CF3
3d
ppm
1
2
3
4
5
6
7
8
9
10
3.02
1.00
2.10
2.04

21.40
77.32
77.00
76.68
117.01
119.65
122.35
125.05
126.08
126.14
126.20
126.26
126.91
128.47
128.49
128.62
128.98
129.35
129.58
129.71
141.64
CN
CF3
3d
ppm

-57.88
-57.90
CN
CF3
3d
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

3.830
7.380
7.360
7.340
7.255
7.060
7.040
7.028
7.007
6.981
6.521
6.502
6.482
6.463
CN
CF3
OMe
3e
3.01
1.00
1.03
2.13
1.10
ppm

55.36
77.32
77.00
76.68
113.72
113.74
116.73
116.82
117.35
119.49
120.74
120.76
122.20
124.90
125.91
125.97
126.03
129.70
130.02
130.07
130.43
130.80
130.83
159.68
CN
CF3
OMe
3e
ppm

-57.83
-57.85
CN
CF3
OMe
3e
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

2.395
7.336
7.317
7.299
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6.500
6.480
6.460
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CF3
3f
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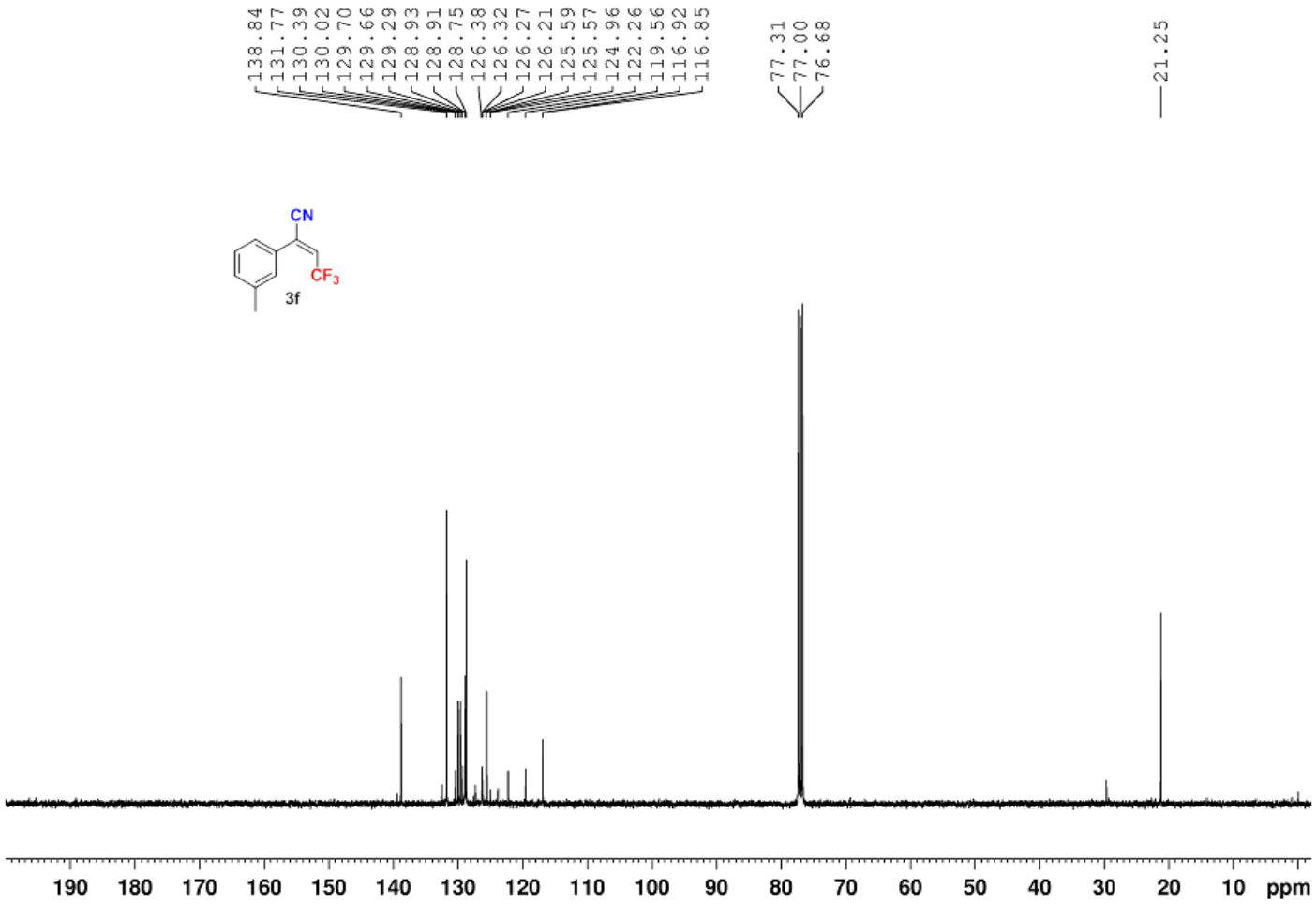
1.00
4.15
ppm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128.93
128.91
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126.38
126.32
126.27
126.21
125.59
125.57
124.96
122.26
119.56
116.92
116.85
77.31
77.00
76.68
21.25
CN
CF3
3f
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-57.87
CN
CF3
3f
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.234
7.021
6.913
6.570
6.552
6.534
6.515
2.283
2.236
2.218
CN
CF3
3g
ppm
1
2
3
4
5
6
7
8
9
10
0.95
1.00
0.96
3.10
3.02
2.94

139.17
134.49
132.75
132.57
132.22
131.88
131.51
129.49
129.47
126.61
126.14
126.09
126.03
125.98
124.85
122.15
119.44
116.74
116.00
77.32
77.00
76.68
19.44
19.01
18.75
CN
CF3
3g
ppm

-59.22
-59.24
CN
CF3
3g
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

3.923
7.923
7.778
7.756
7.503
7.483
7.241
7.223
7.217
7.201
7.194
7.135
7.130
6.518
6.498
6.478
6.458
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CF3
MeO
3h
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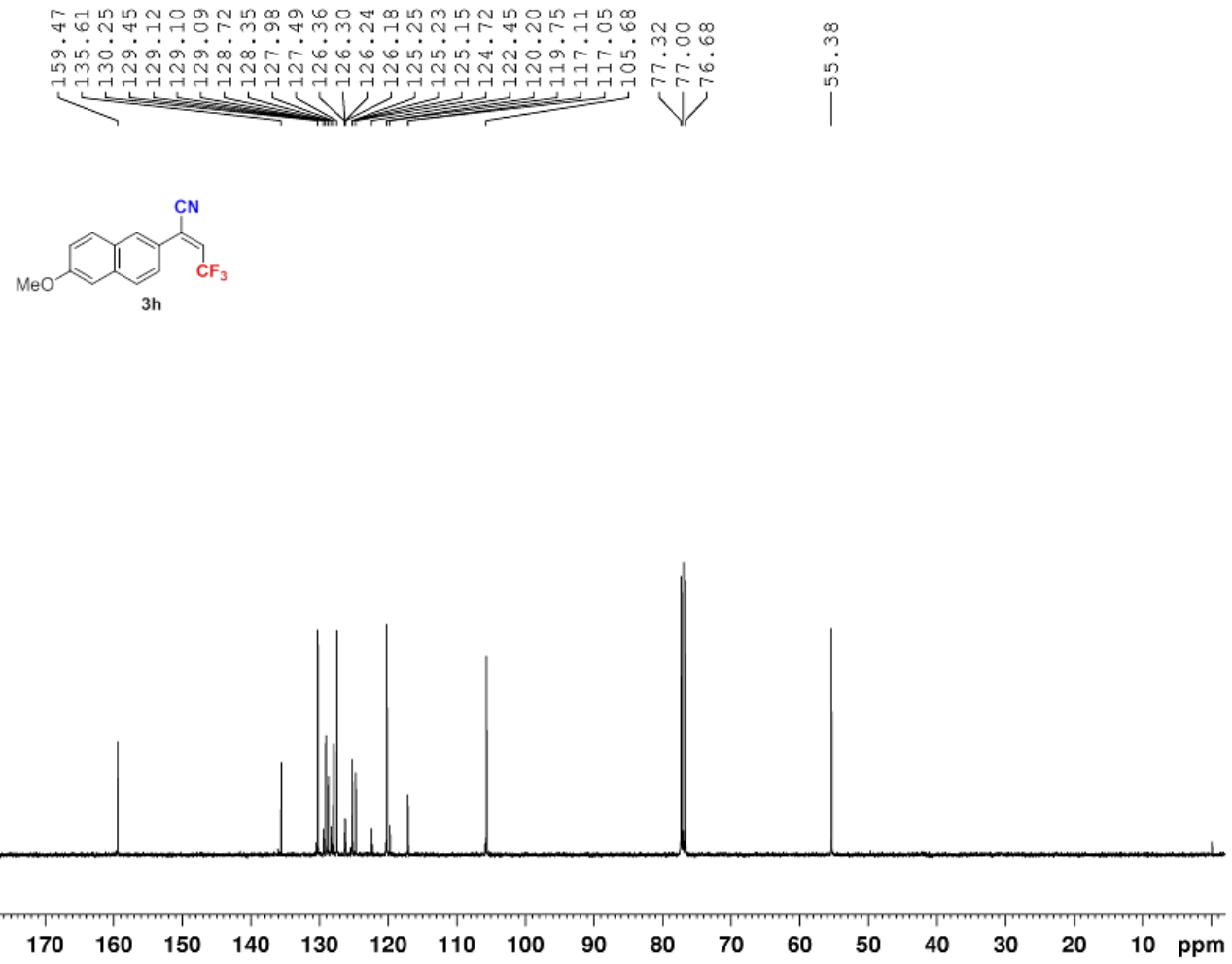
1.04
1.06
1.06
1.00
3.11
ppm


159.47
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129.10
129.09
128.72
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127.98
127.49
126.36
126.30
126.24
126.18
125.25
125.23
125.15
124.72
122.45
120.20
119.75
117.11
117.05
105.68
77.32
77.00
76.68
55.38
CN
CF3
MeO
3h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-57.698
-57.714
CN
CF3
MeO
3h
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.617
7.595
7.356
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6.538
6.519
6.499
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3i
Br
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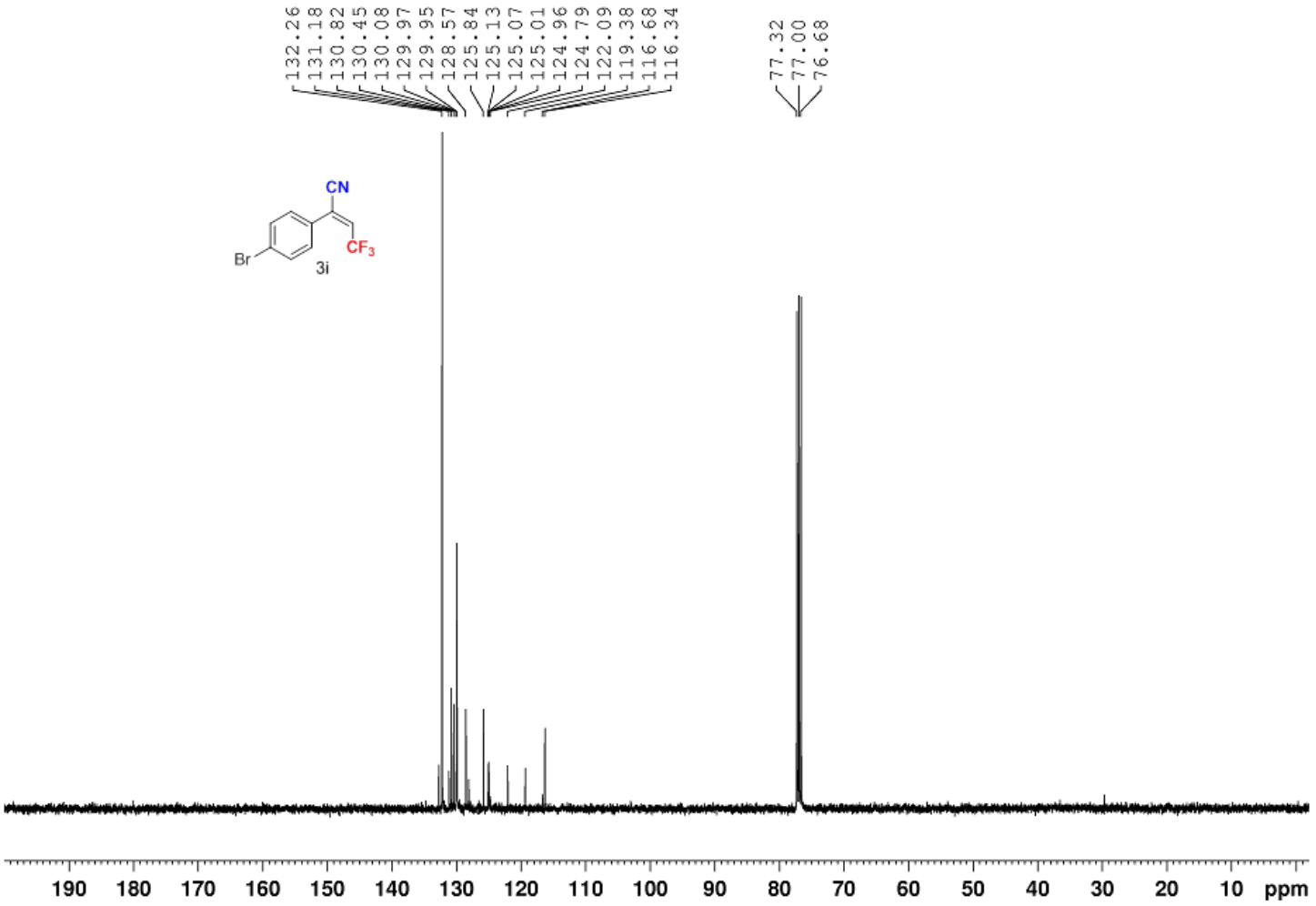
2.07
ppm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129.95
128.57
125.84
125.13
125.07
125.01
124.96
124.79
122.09
119.38
116.68
116.34
77.32
77.00
76.68
CN
CF3
Br
3i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-57.89
-57.91
CN
CF3
Br
3i
-25
-30
-35
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-45
-50
-55
-60
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-75
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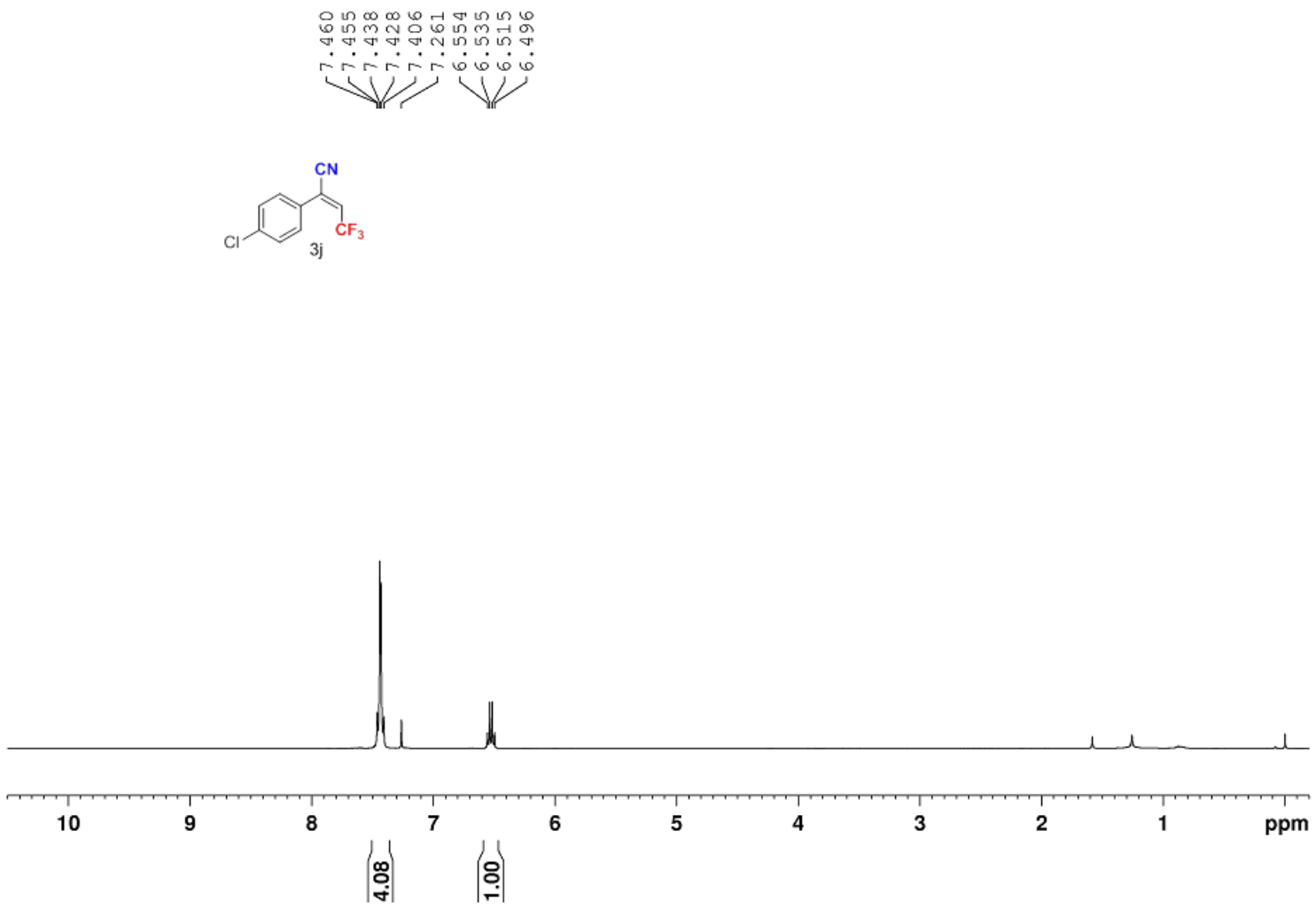
-85
-90
-95
ppm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7.261
6.554
6.535
6.515
6.496
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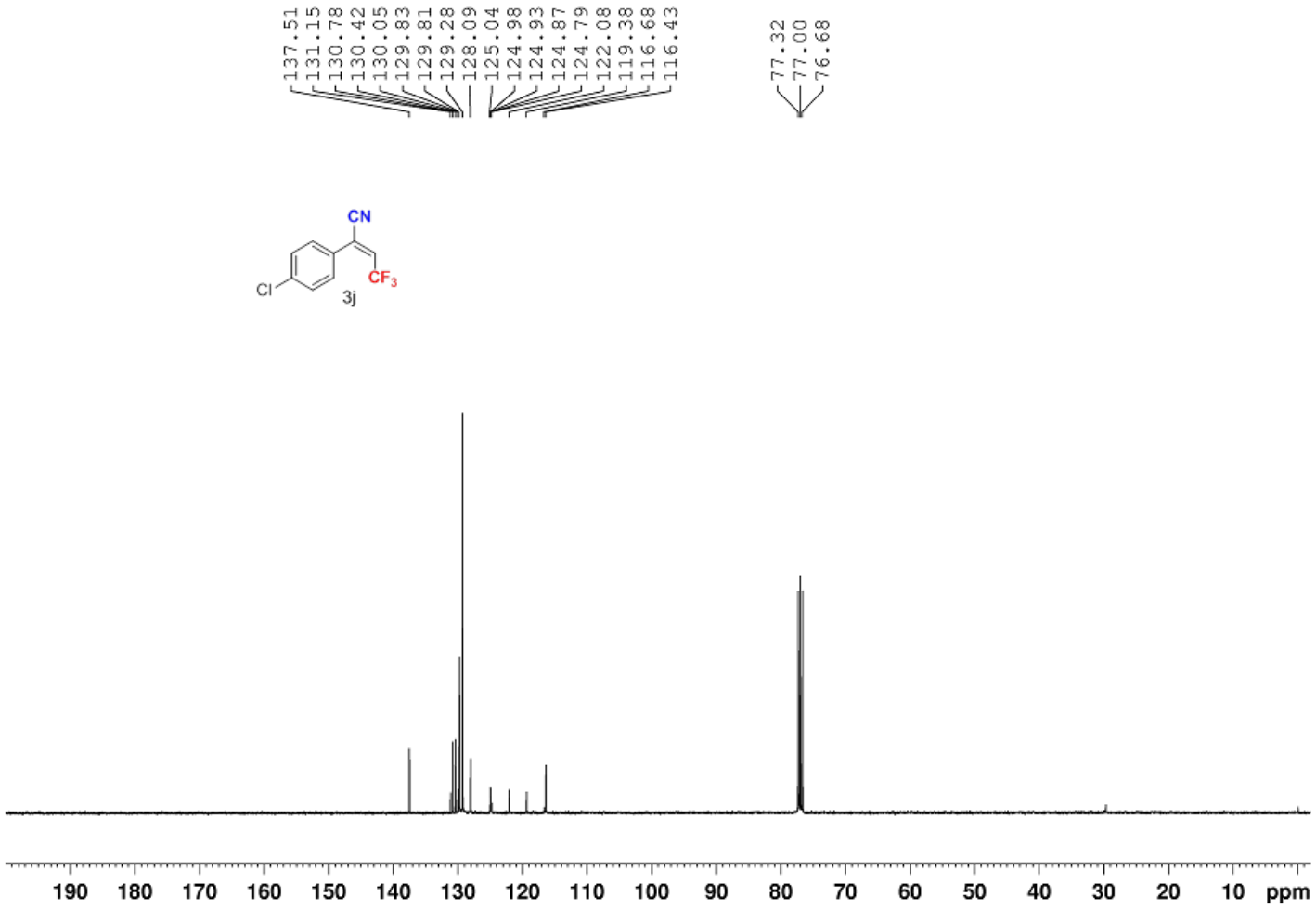
CF3
Cl
3j
10
9
8
7
6
5
4
3
2
1
ppm
4.08
1.00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125.04
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124.93
124.87
124.79
122.08
119.38
116.68
116.43
77.32
77.00
76.68
CN
CF3
Cl
3j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-57.92
-57.93
CN
CF3
Cl
3j
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

3.825
6.523
6.542
6.562
6.581
7.264
7.444
7.465
7.499
7.519
CN
CF3
3k
N
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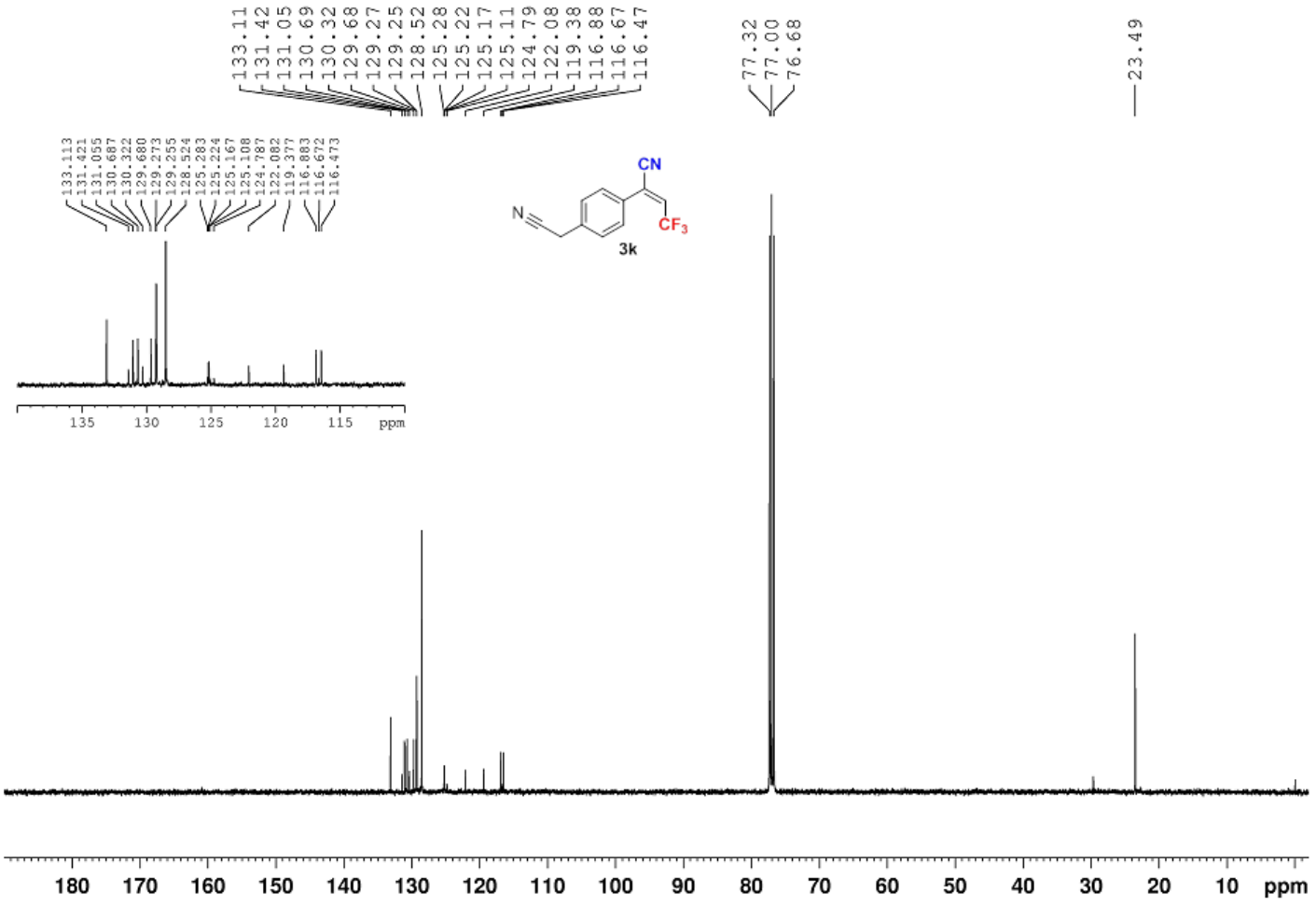
1.00
2.03
2.04
ppm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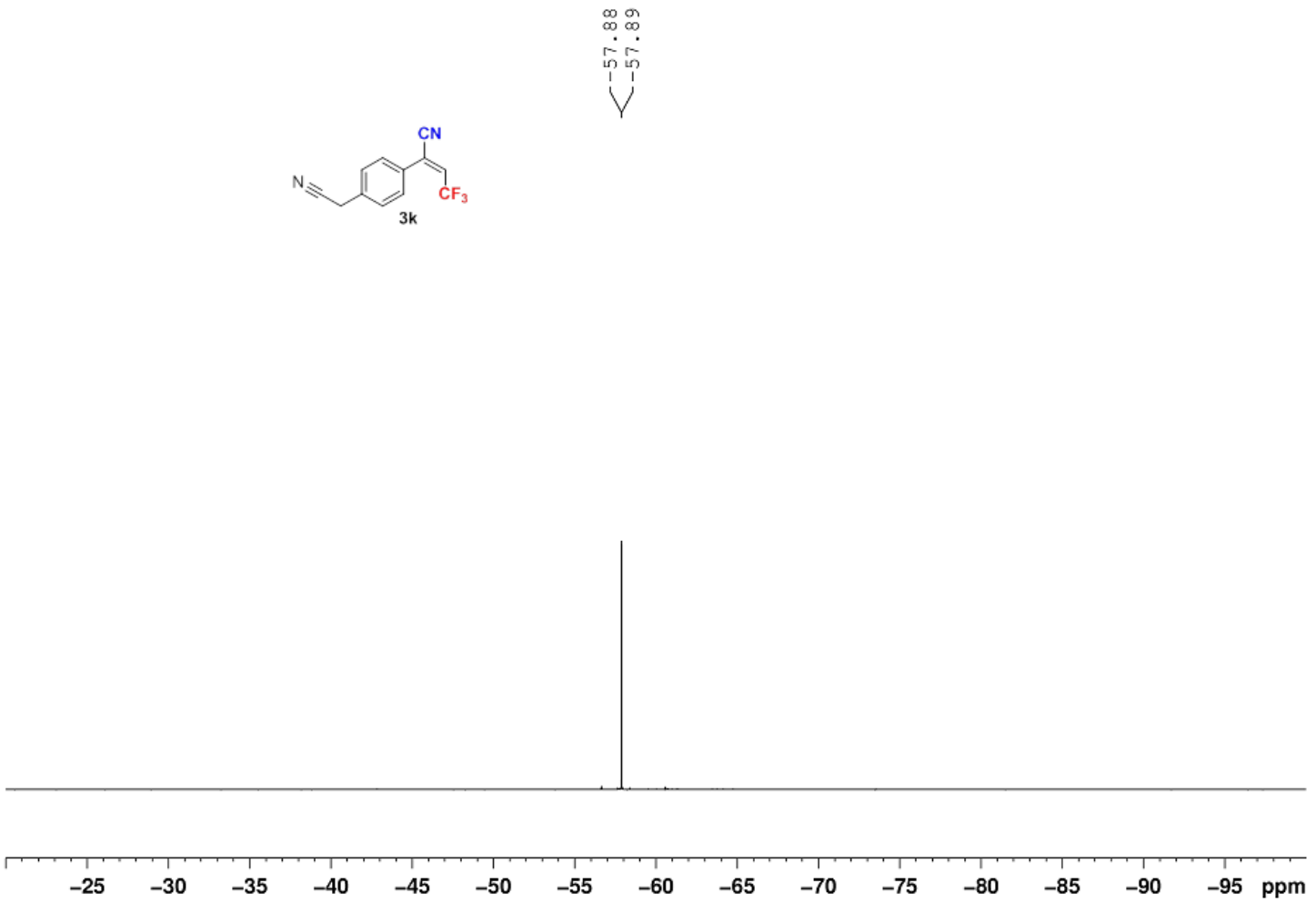
130.32
129.68
129.27
129.25
128.52
125.28
125.22
125.17
125.11
124.79
122.08
119.38
116.88
116.67
116.47
77.32
77.00
76.68
23.49
CN
N
CF3
3k
135
130
125
120
115
ppm
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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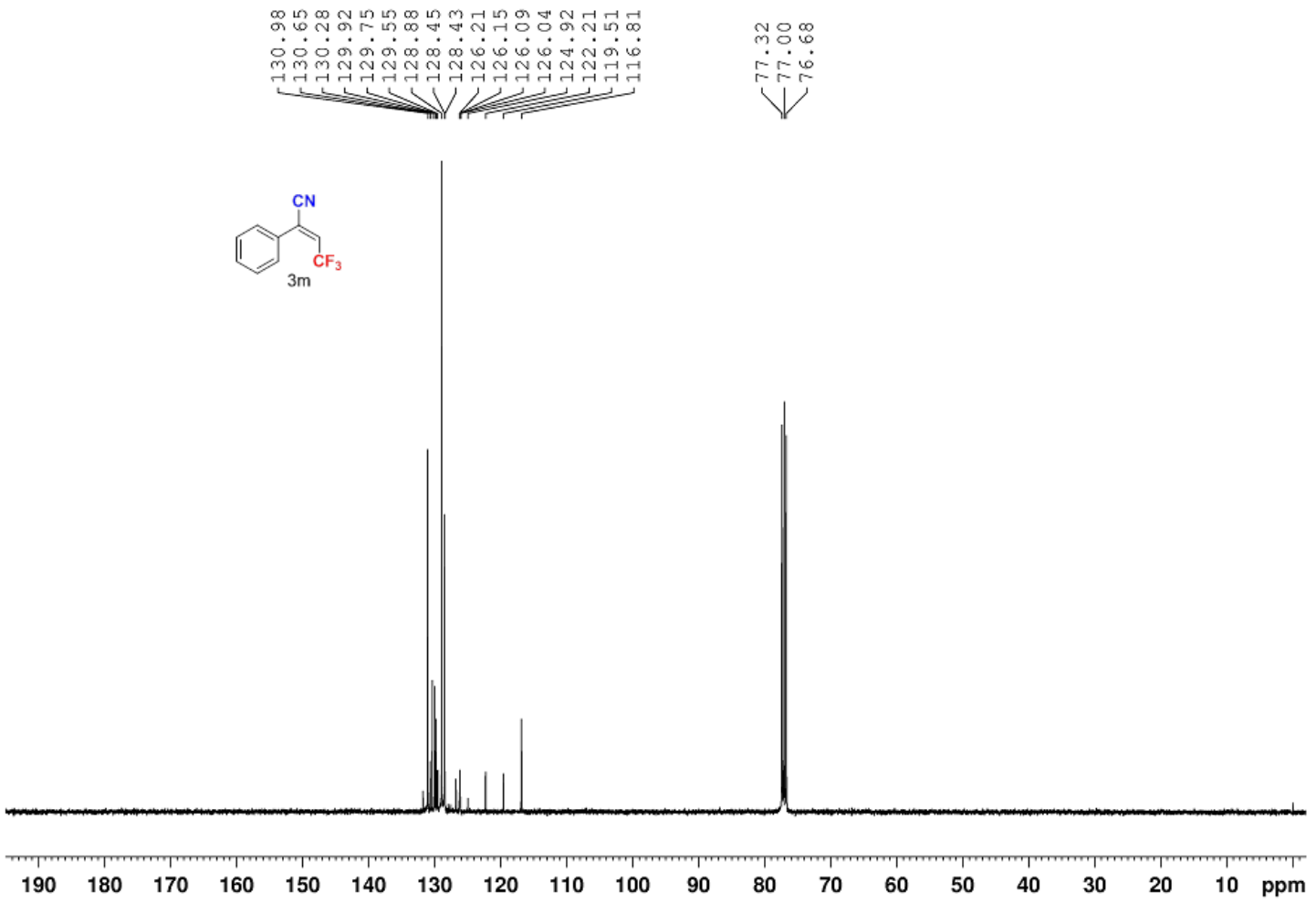
CN
N
CF3
3k
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.507
7.487
7.456
7.453
7.437
7.435
7.418
7.415
7.373
7.354
7.335
7.294
7.275
7.259
6.699
6.681
6.664
6.646
CN
CF3
Cl
3l
ppm
1.00
1.02
1.04
1.05
1.07

77.32
77.00
76.68
115.00
116.42
119.12
121.83
123.31
123.37
123.42
123.48
124.54
127.15
128.63
130.06
130.14
130.16
131.85
132.63
133.16
133.52
133.87
134.23
CN
CF3
Cl
3I
ppm

-59.47
-59.48
CN
CF3
Cl
3l
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.500
7.490
7.481
7.468
7.455
7.431
7.252
6.527
6.508
6.488
6.468
CN
CF3
3m
5.01
1.00
ppm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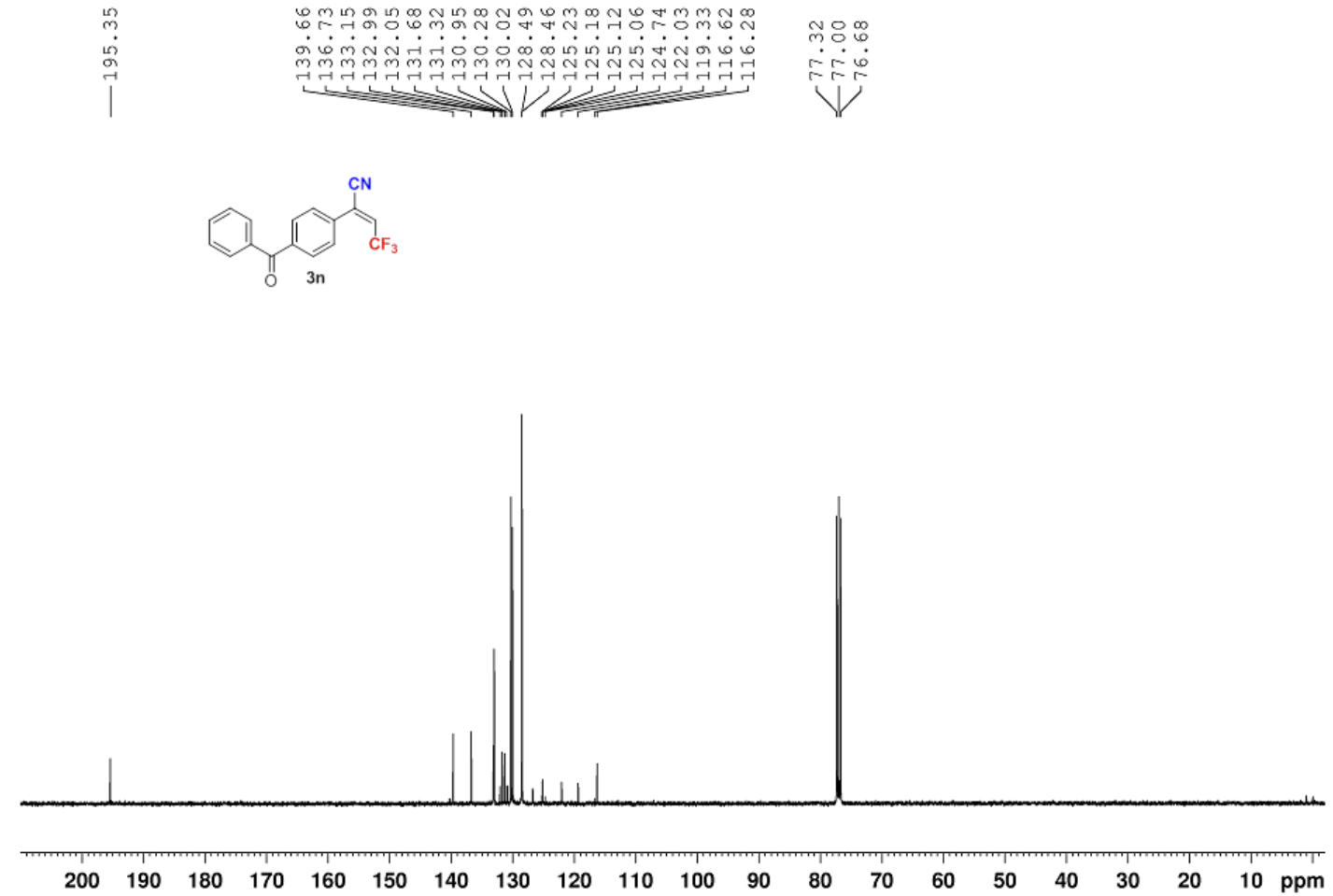
130.65
130.28
129.92
129.75
129.55
128.88
128.45
128.43
126.21
126.15
126.09
126.04
124.92
122.21
119.51
116.81
77.32
77.00
76.68
CN
CF3
3m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-57.88
-57.90
CN
CF3
3m
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.894
7.874
7.821
7.803
7.633
7.611
7.590
7.535
7.516
7.497
7.264
6.652
6.633
6.613
6.594
CN
CF3
O
3n
ppm
1
2
3
4
5
6
7
8
9
10
1.00
2.10
3.01
2.08
2.04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132.99
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131.68
131.32
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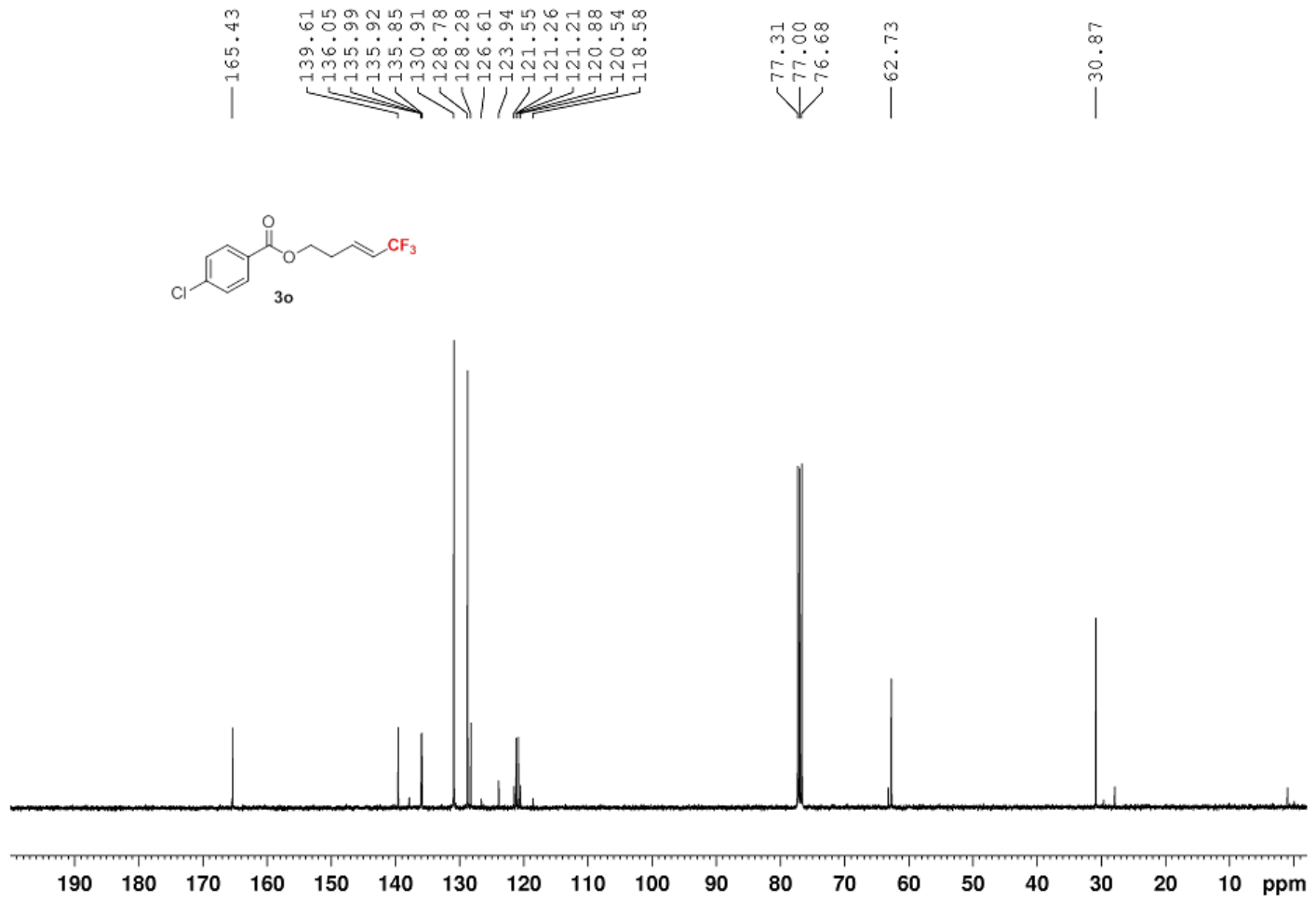
130.28
130.02
128.49
128.46
125.23
125.18
125.12
125.06
124.74
122.03
119.33
116.62
116.28
77.32
77.00
76.68
CN
CF3
O
3n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-57.82
-57.84
CN
CF3
3n
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.963
7.941
7.432
7.410
7.265
6.463
6.458
6.446
6.441
6.436
6.429
6.424
6.418
5.803
5.787
5.784
5.767
5.764
5.748
4.443
4.427
4.411
2.668
2.663
2.658
2.652
2.647
2.642
2.636
2.631
2.626
2.620
2.615
2.610
CF3
O
O
Cl
3o
ppm
1
2
3
4
5
6
7
8
9
10
1.89
2.03
1.00
0.89
2.06
2.06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139.61
136.05
135.99
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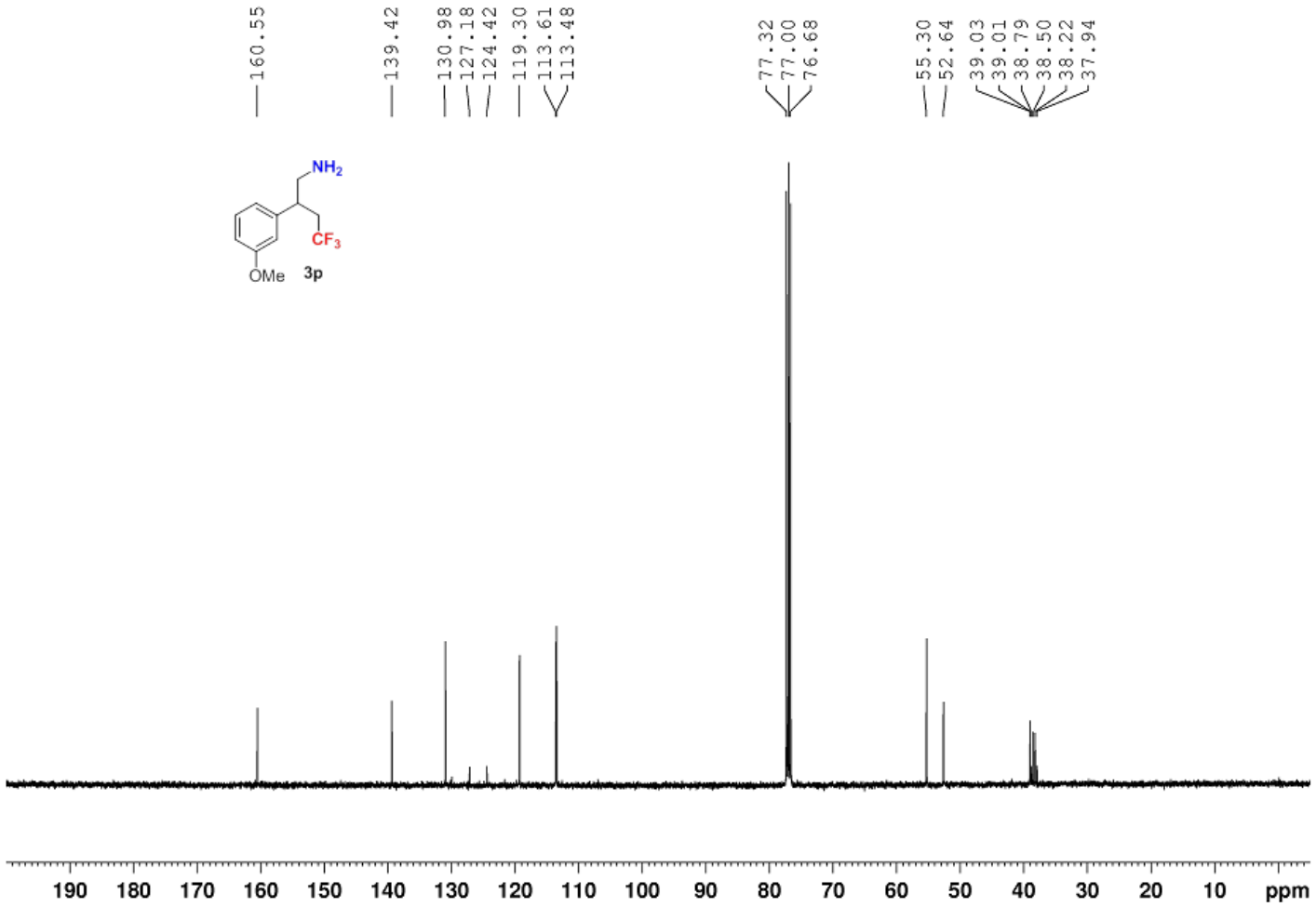
135.85
130.91
128.78
128.28
126.61
123.94
121.55
121.26
121.21
120.88
120.54
118.58
77.31
77.00
76.68
62.73
30.87
O
O
CF3
Cl
3o
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

-64.40
-64.41
-64.42
CF3
O
O
Cl
3o
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm

7.337
7.317
7.297
7.263
6.878
6.872
6.857
6.852
6.799
6.780
6.742
6.737
3.812
3.515
3.433
3.285
3.274
3.257
3.245
3.228
3.198
3.187
3.177
3.165
3.155
3.143
3.003
2.994
2.971
2.942
2.918
2.475
2.465
2.447
2.438
2.424
2.420
2.408
2.398
2.381
NH2
CF3
OMe
3p
ppm
1.03
1.02
1.02
0.97
3.09
1.93
1.00
1.02
1.00
2.09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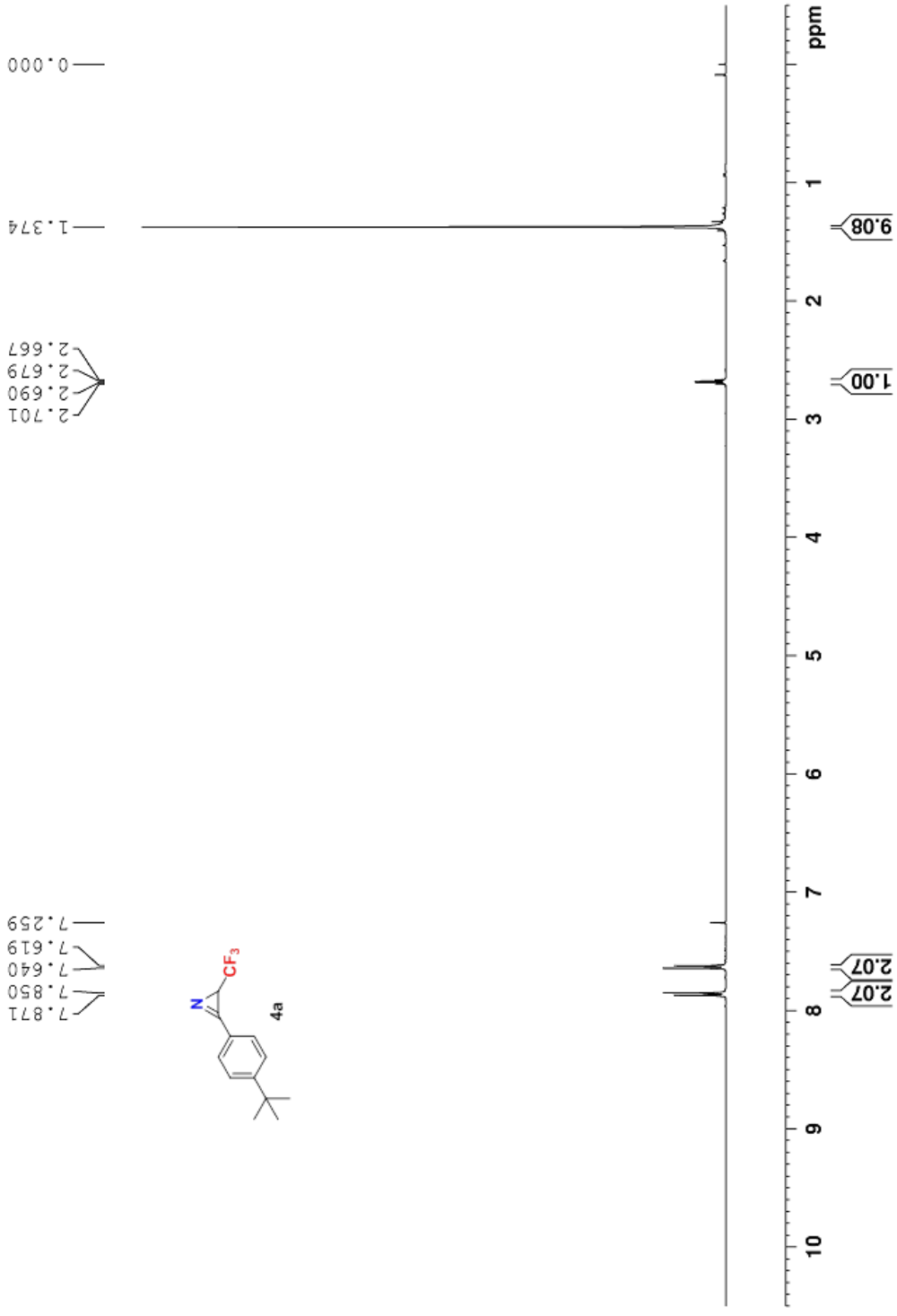
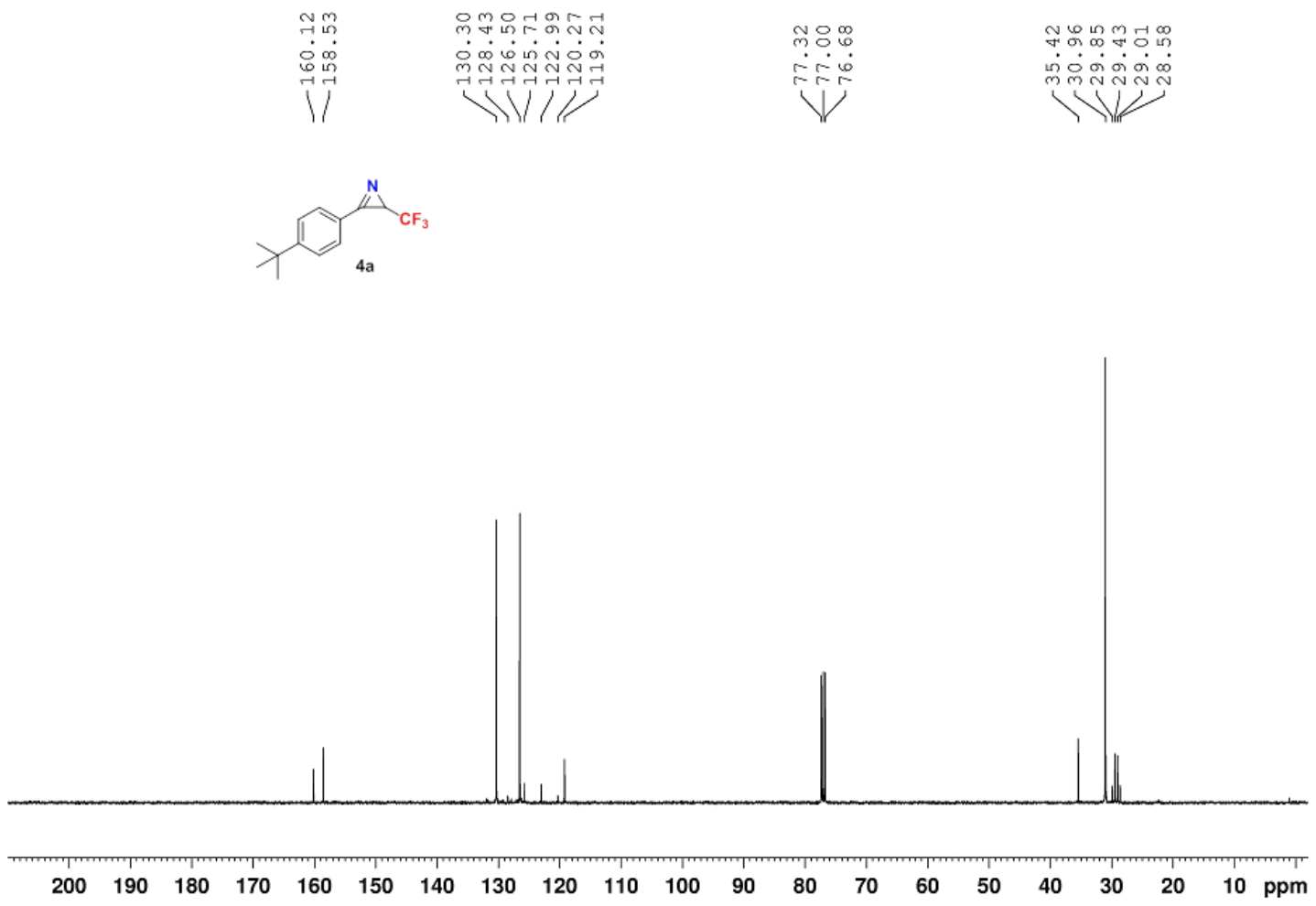
113.48
77.32
77.00
76.68
55.30
52.64
39.03
39.01
38.79
38.50
38.22
37.94
NH2
CF3
OMe
3p
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

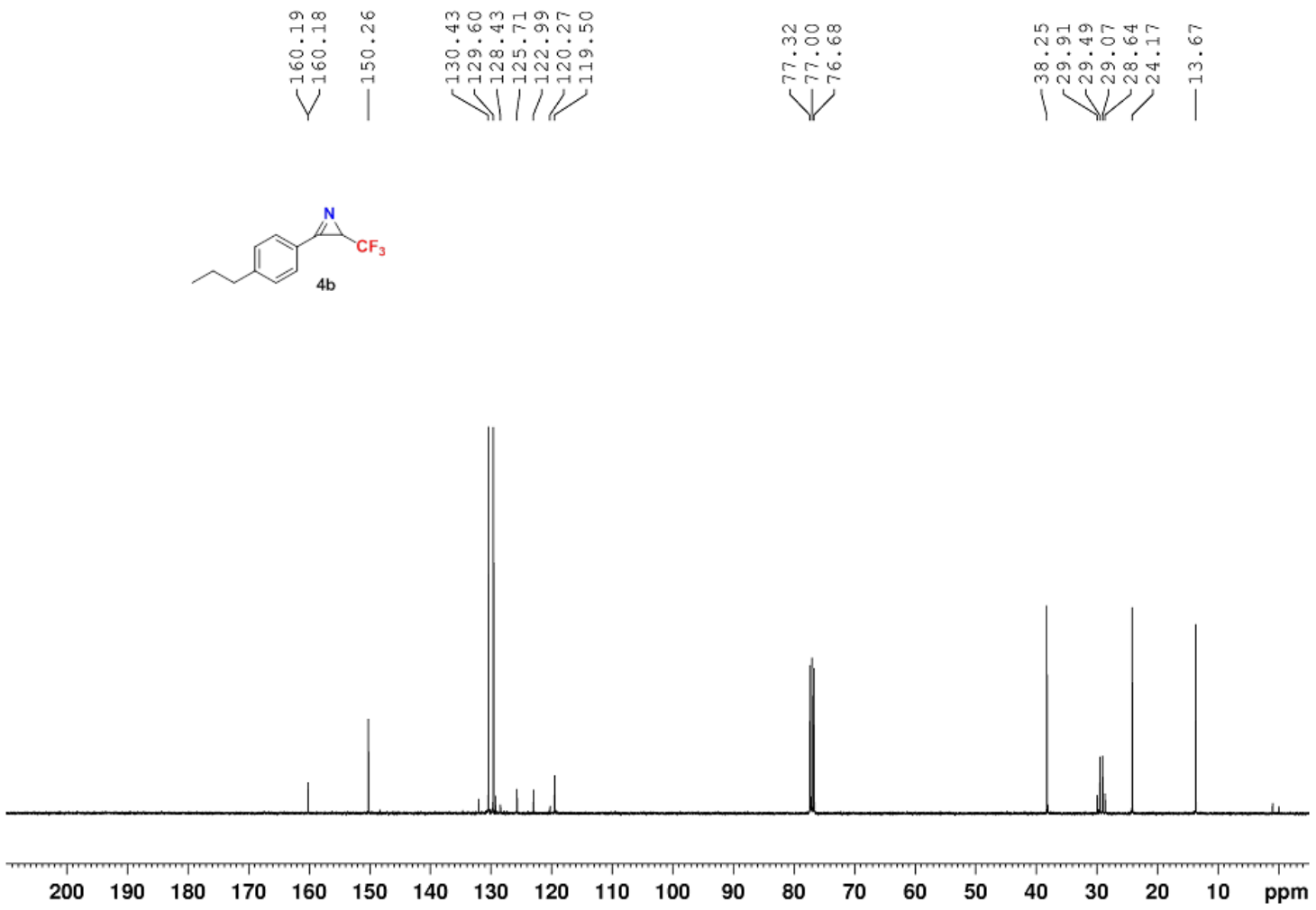
-63.76
NH2
CF3
OMe
3p
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm


0.000
1.374
2.667
2.679
2.690
2.701
7.259
7.619
7.640
7.850
7.871
4a
ppm
9.08
1.00
2.07
2.07


160.12
158.53
130.30
128.43
126.50
125.71
122.99
120.27
119.21
77.32
77.00
76.68
35.42
30.96
29.85
29.43
29.01
28.58
N
CF3
4a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

-67.65
N
CF3
4a
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

7.843
7.823
7.423
7.402
7.261
2.720
2.701
2.690
2.682
2.678
2.667
1.744
1.725
1.706
1.687
1.669
1.650
0.988
0.970
0.952
N
CF3
4b
ppm
3.04
2.00
3.03
2.00
1.97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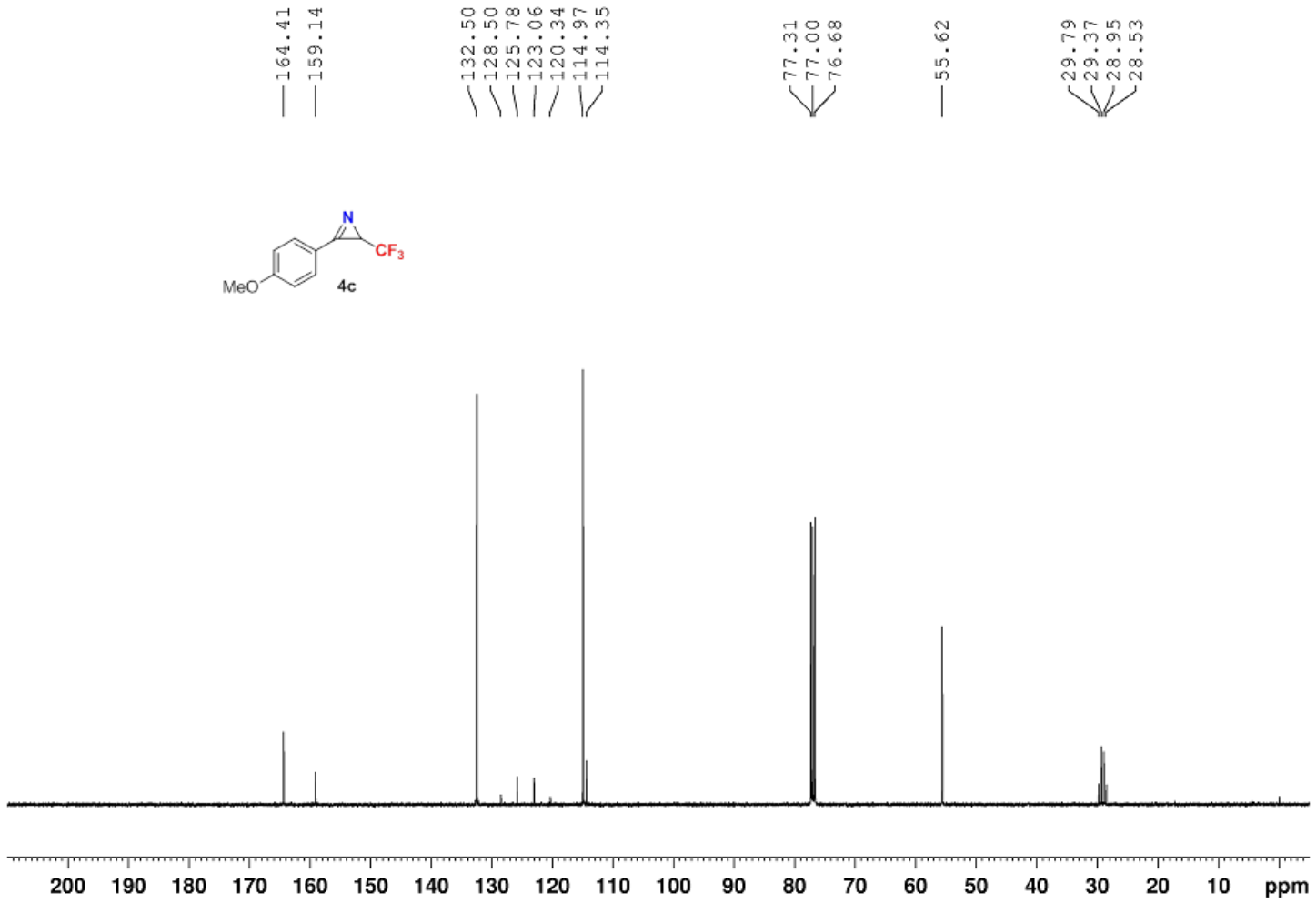
160.18
150.26
130.43
129.60
128.43
125.71
122.99
120.27
119.50
77.32
77.00
76.68
38.25
29.91
29.49
29.07
28.64
24.17
13.67
N
CF3
4b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

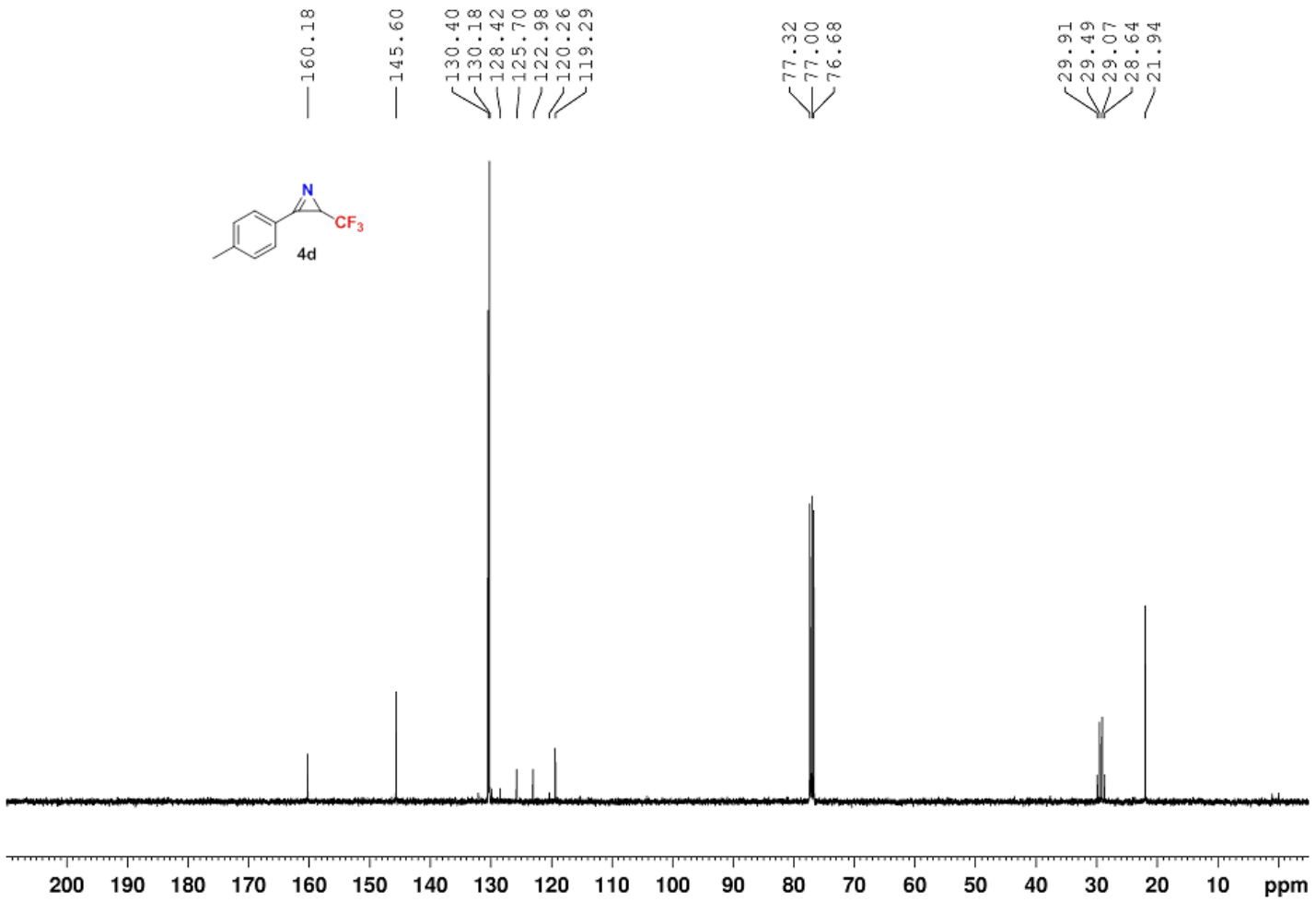
-67.65
-67.66
N
CF3
4b
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

7.882
7.876
7.871
7.858
7.854
7.847
7.268
7.102
7.085
7.080
3.915
2.682
2.670
2.659
2.647
N
CF3
MeO
4c
ppm
0.98
3.00
2.05
2.00


164.41
159.14
132.50
128.50
125.78
123.06
120.34
114.97
114.35
77.31
77.00
76.68
55.62
29.79
29.37
28.95
28.53
N
CF3
MeO
4c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-67.65
-67.66
N
CF3
MeO
4c
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

7.819
7.799
7.417
7.397
7.260
2.700
2.688
2.677
2.665
2.478
4d
2.02
2.05
1.00
3.07
ppm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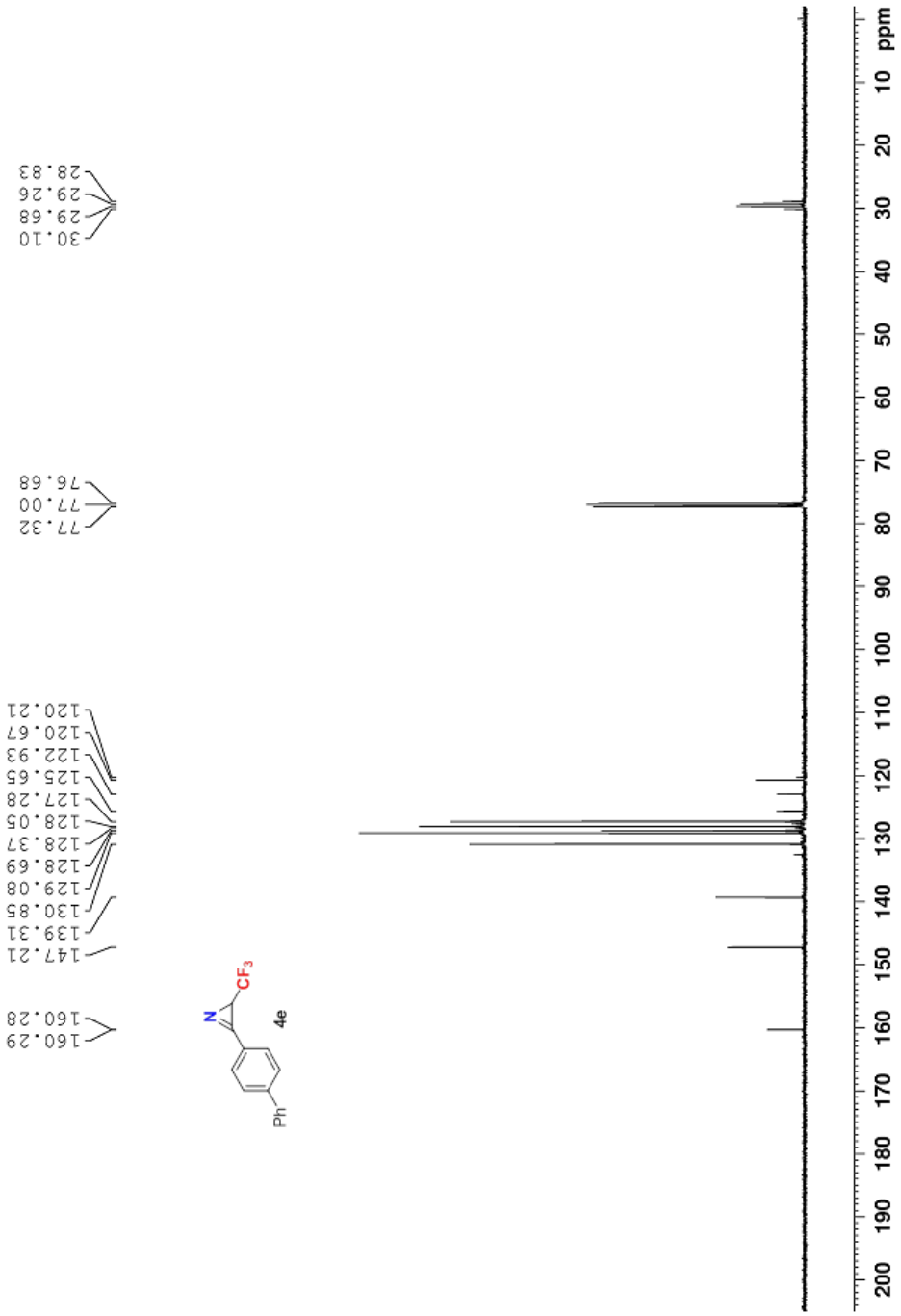
145.60
130.40
130.18
128.42
125.70
122.98
120.26
119.29
77.32
77.00
76.68
29.91
29.49
29.07
28.64
21.94
N
CF3
4d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

-67.68
-67.69
CF3
N
4d
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

2.756
2.745
2.733
2.722
7.988
7.967
7.816
7.795
7.651
7.647
7.630
7.513
7.509
7.505
7.492
7.488
7.473
7.452
7.449
7.445
7.436
7.431
7.424
7.412
7.235
CF3
N
Ph
4e
ppm
1.00
2.05
2.07
2.08
2.11
1.03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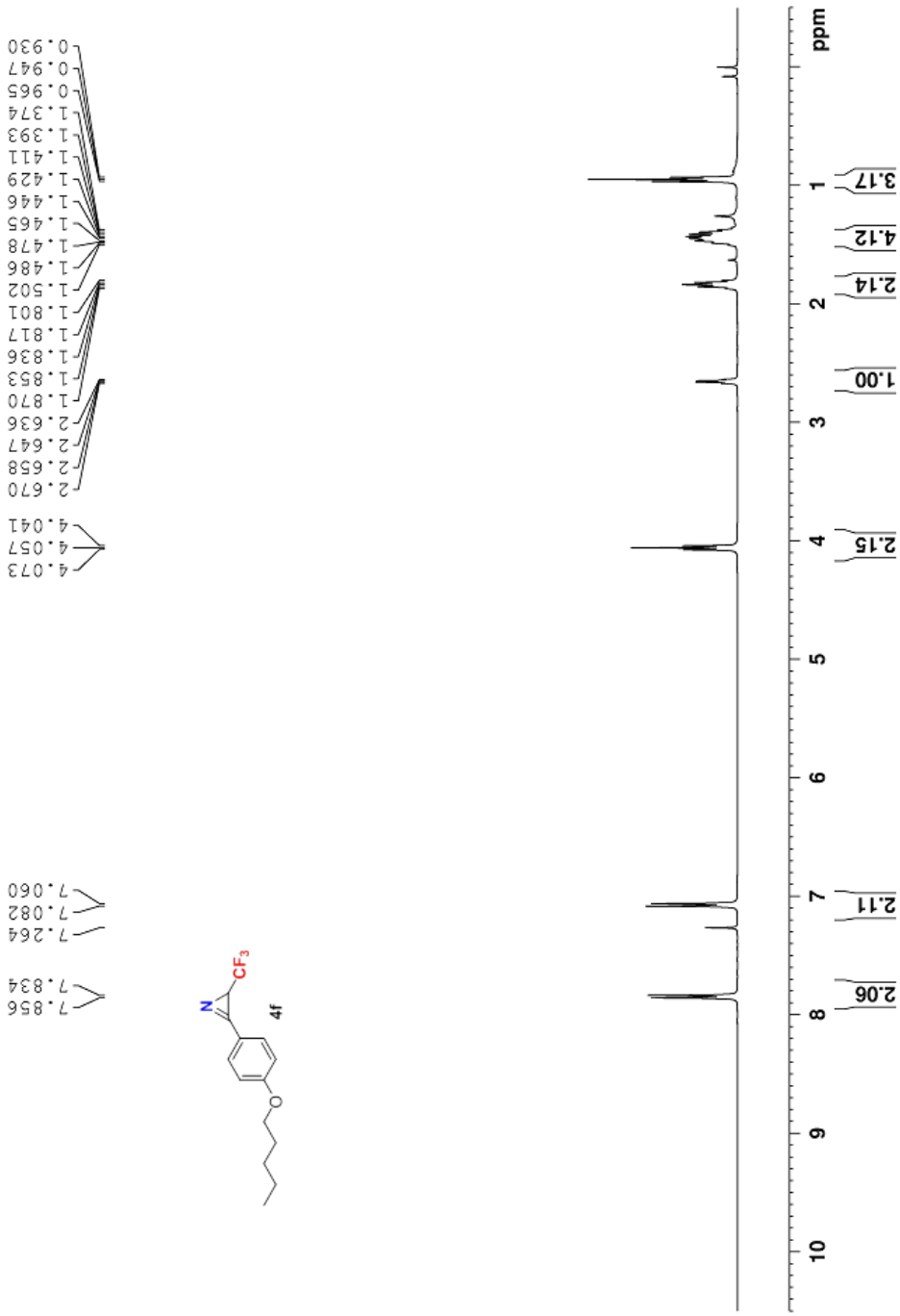
29.26
29.68
30.10
76.68
77.00
77.32
120.21
120.67
122.93
125.65
127.28
128.05
128.37
128.69
129.08
130.85
139.31
147.21
160.28
160.29
N
CF3
4e
Ph
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-67.56
-67.58
CF3
N
Ph
4e
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm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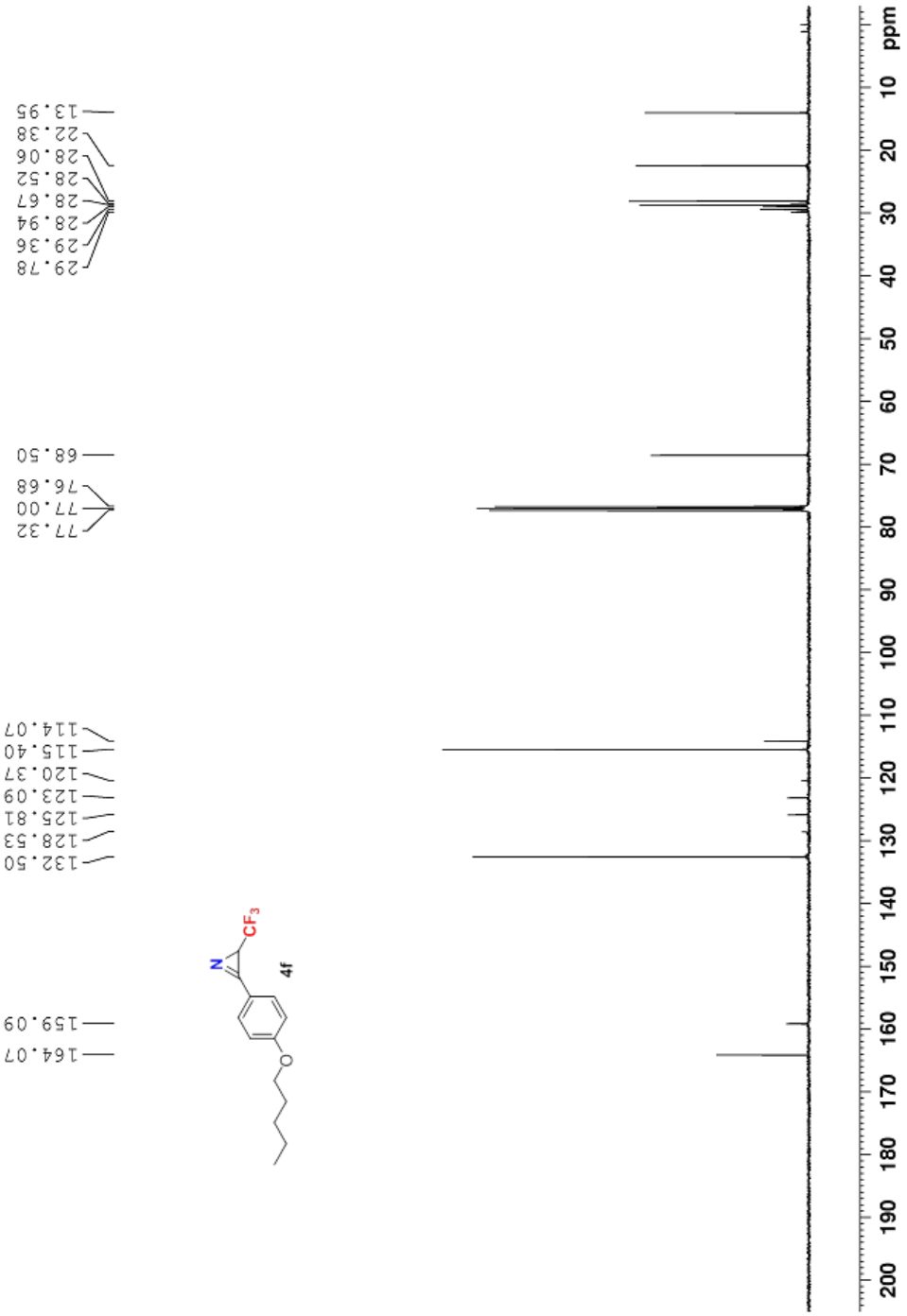
0.947
0.965
1.374
1.393
1.411
1.429
1.446
1.465
1.478
1.486
1.502
1.801
1.817
1.836
1.853
1.870
2.636
2.647
2.658
2.670
4.041
4.057
4.073
7.060
7.082
7.264
7.834
7.856
CF3
N
O
4f
ppm
1
2
3
4
5
6
7
8
9
10
3.17
4.12
2.14
1.00
2.15
2.11
2.06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22.38
28.06
28.52
28.67
28.94
29.36
29.78
68.50
76.68
77.00
77.32
114.07
115.40
120.37
123.09
125.81
128.53
132.50
159.09
164.07
4f
CF3
N
O
ppm

-67.65
-67.66
CF3
N
O
4f
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

7.536
7.517
7.497
7.492
7.481
7.478
7.437
7.434
7.430
7.262
7.234
7.228
7.223
7.215
7.210
7.204
3.895
2.744
2.732
2.721
2.709
N
CF3
4g
OMe
ppm
1.00
3.07
1.08
1.03
2.08

160.90
160.89
160.16
130.55
128.29
125.57
123.18
123.10
122.85
121.04
120.13
114.09
77.32
77.00
76.69
55.57
30.40
29.98
29.55
29.13
CF3
N
OMe
4g
ppm

-67.70
-67.71
CF3
N
OMe
4g
ppm
-30
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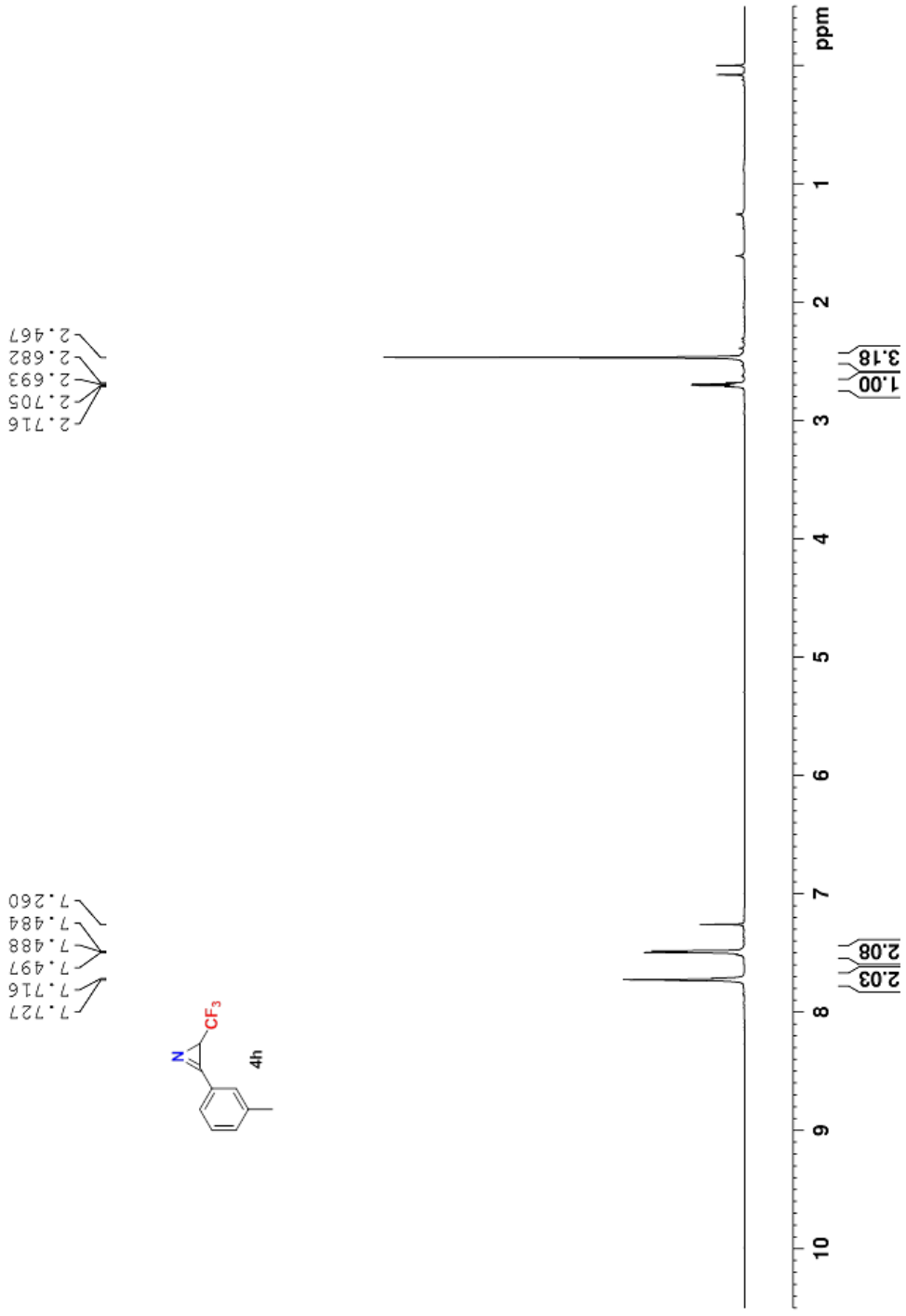
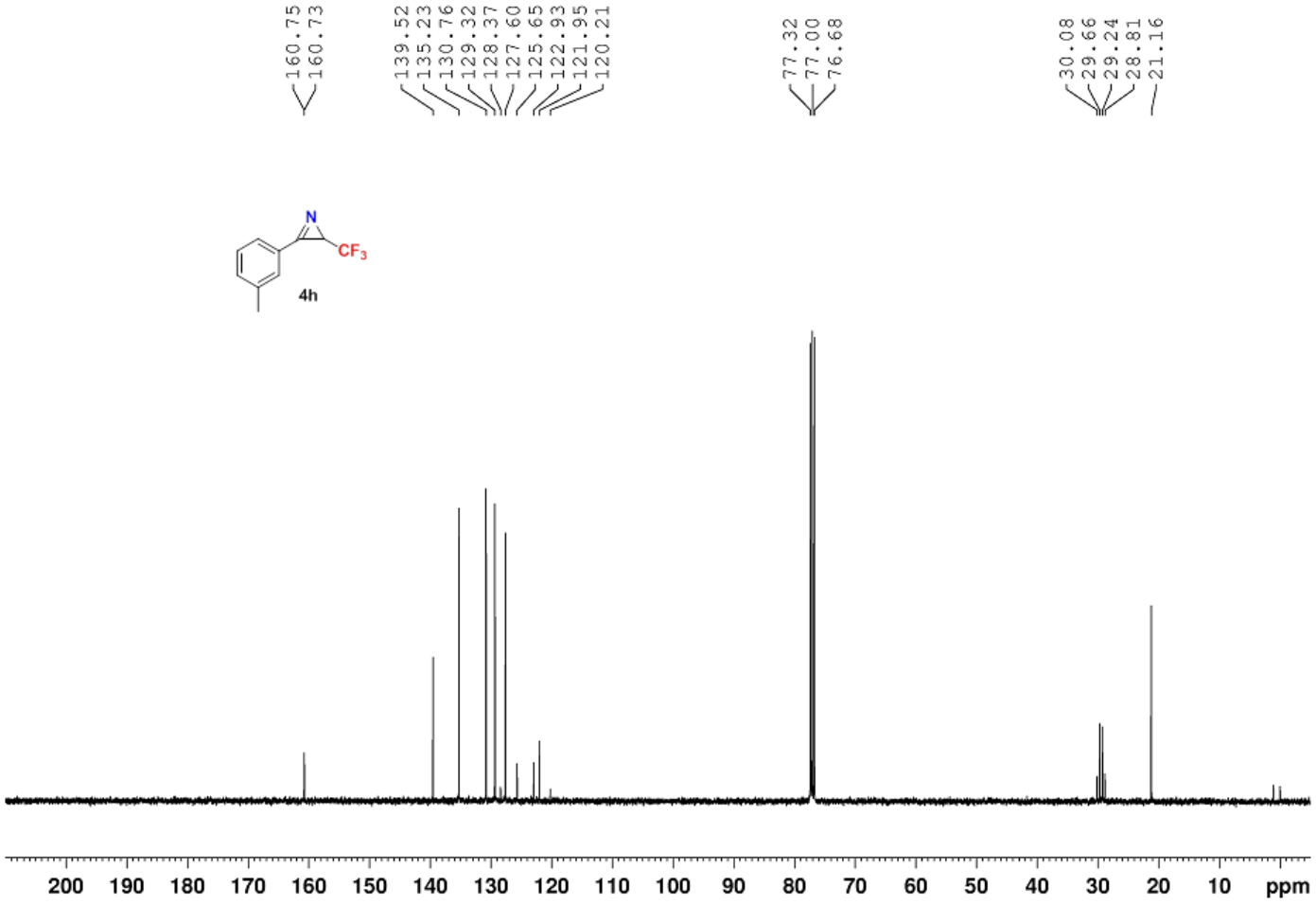
-50
-60
-70
-80
-90
-100
-110


7.727
7.716
7.497
7.488
7.484
7.260
2.716
2.705
2.693
2.682
2.467
CF3
N
4h
2.03
2.08
1.00
3.18
ppm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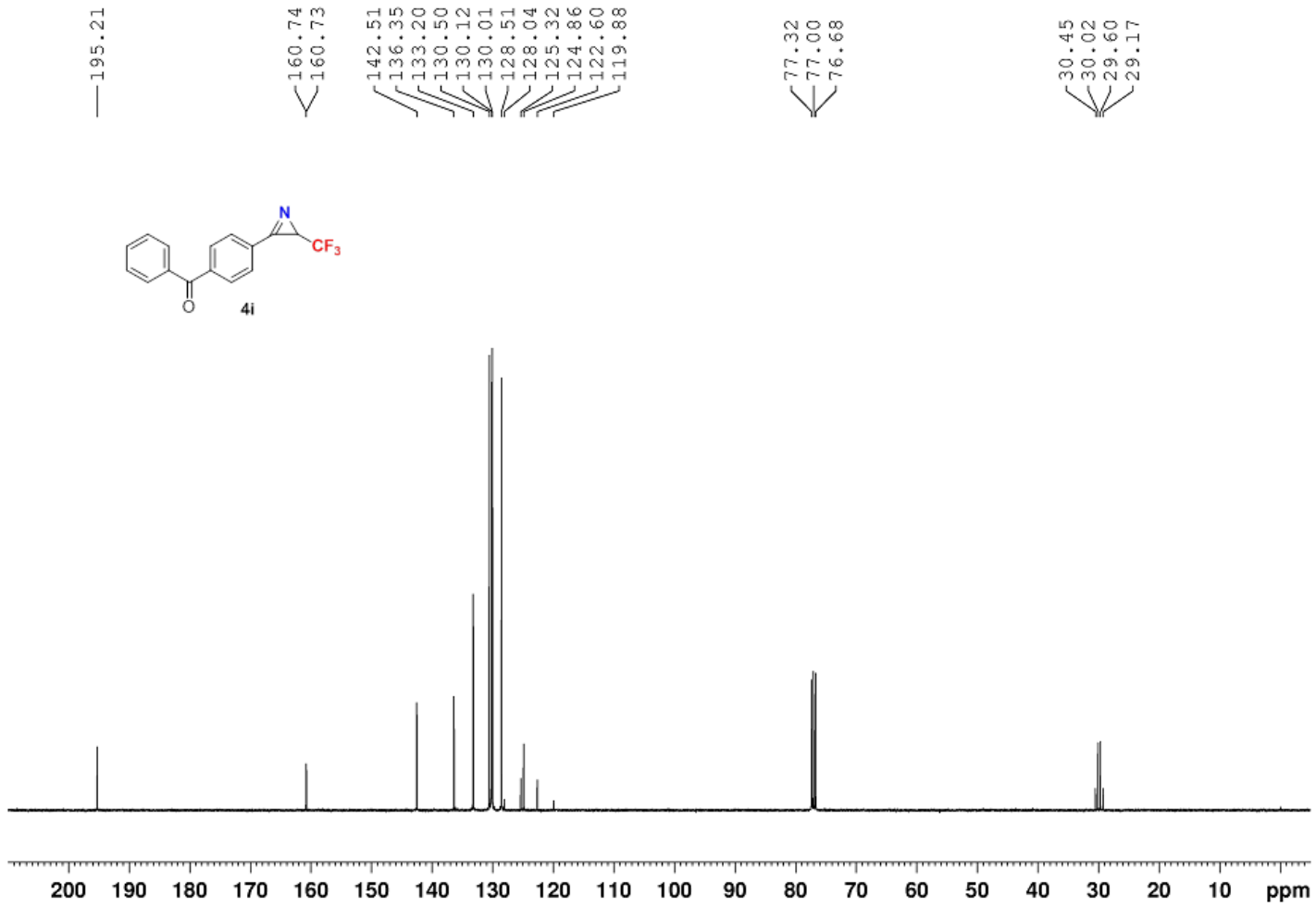
135.23
130.76
129.32
128.37
127.60
125.65
122.93
121.95
120.21
77.32
77.00
76.68
30.08
29.66
29.24
28.81
21.16
N
CF3
4h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-67.67
-67.68
CF3
N
4h
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

8.065
8.044
8.005
7.985
7.839
7.821
7.670
7.652
7.633
7.546
7.527
7.508
7.283
2.841
2.830
2.818
2.807
N
CF3
O
4i
ppm
1.00
2.07
2.11
2.09
1.05
2.08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160.74
160.73
142.51
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130.50
130.12
130.01
128.51
128.04
125.32
124.86
122.60
119.88
77.32
77.00
76.68
30.45
30.02
29.60
29.17
N
CF3
O
4i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

-67.64
-67.65
CF3
N
O
4i
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

7.265
7.752
7.758
7.774
7.781
7.797
7.803
2.730
2.741
2.753
2.764
4j
Br
N
CF3
4.15
1.00
ppm

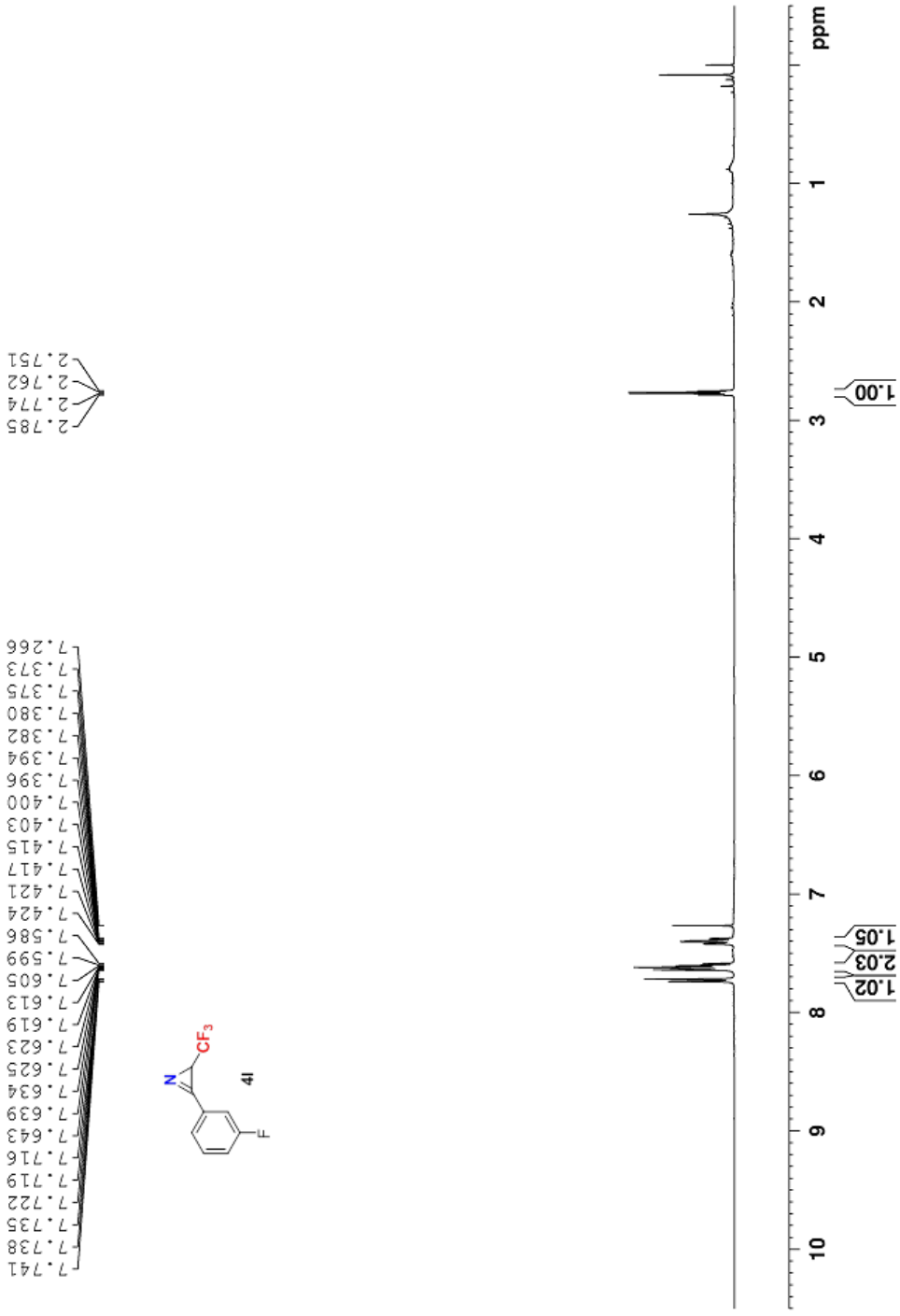
160.32
132.97
131.53
129.66
128.12
125.40
122.68
120.95
119.96
77.31
77.00
76.68
30.34
29.92
29.49
29.07
4j
Br
N
CF3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

-67.70
-67.71
CF3
N
Br
4j
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

7.879
7.858
7.612
7.591
7.265
2.762
2.751
2.740
2.728
N
CF3
Cl
4k
2.07
2.07
1.00
ppm

160.13
141.02
131.51
130.00
128.14
125.42
122.70
120.55
119.98
77.32
77.00
76.69
30.36
29.93
29.51
29.08
N
CF3
Cl
4k
ppm

-67.72
CF3
N
Cl
4k
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm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7.375
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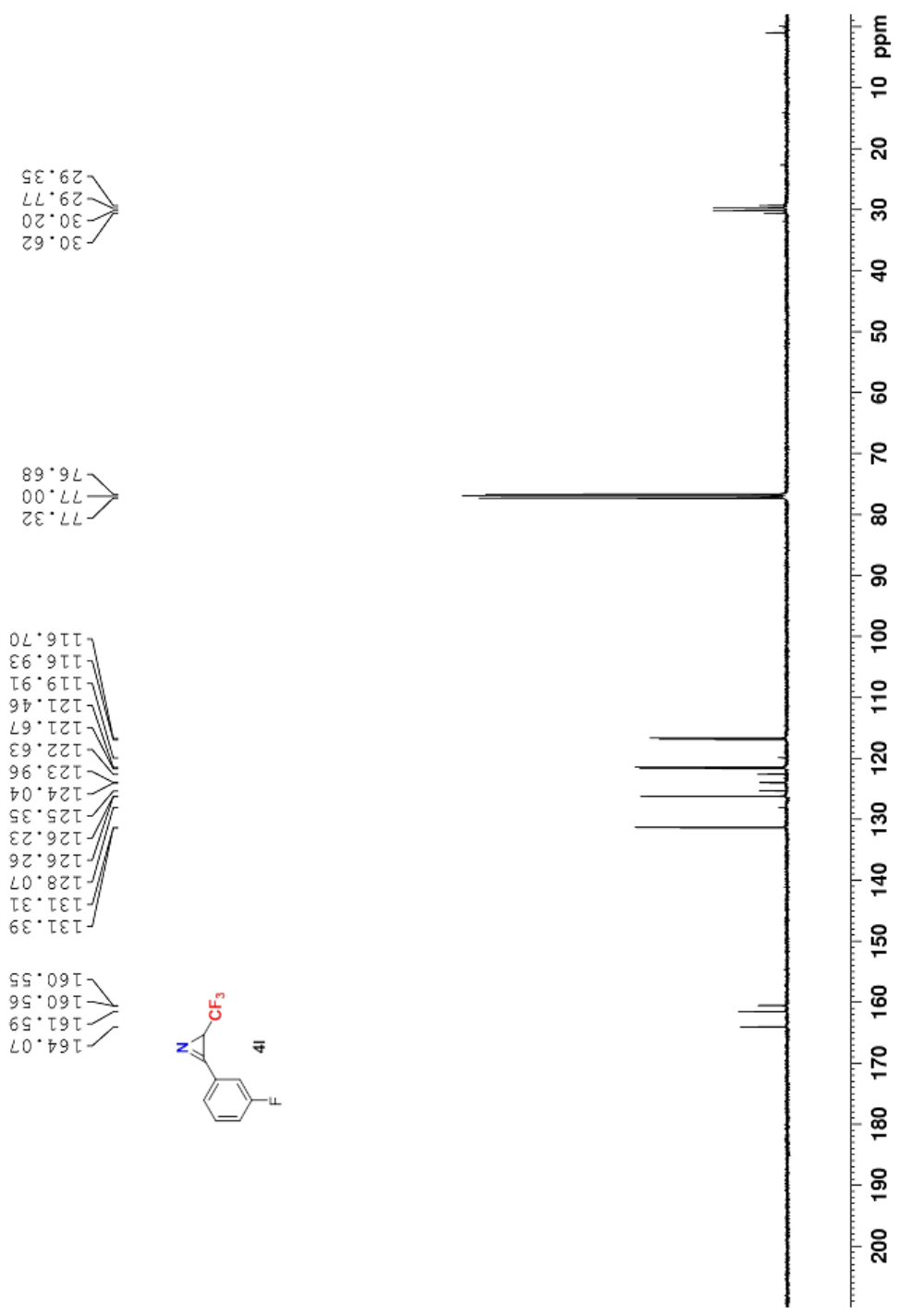
7.400
7.403
7.415
7.417
7.421
7.424
7.586
7.599
7.605
7.613
7.619
7.623
7.625
7.634
7.639
7.643
7.716
7.719
7.722
7.735
7.738
7.741
2.751
2.762
2.774
2.785
CF3
N
F
4l
ppm
1.00
1.02
2.03
1.05


164.07
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160.56
160.55
131.39
131.31
128.07
126.26
126.23
125.35
124.04
123.96
122.63
121.67
121.46
119.91
116.93
116.70
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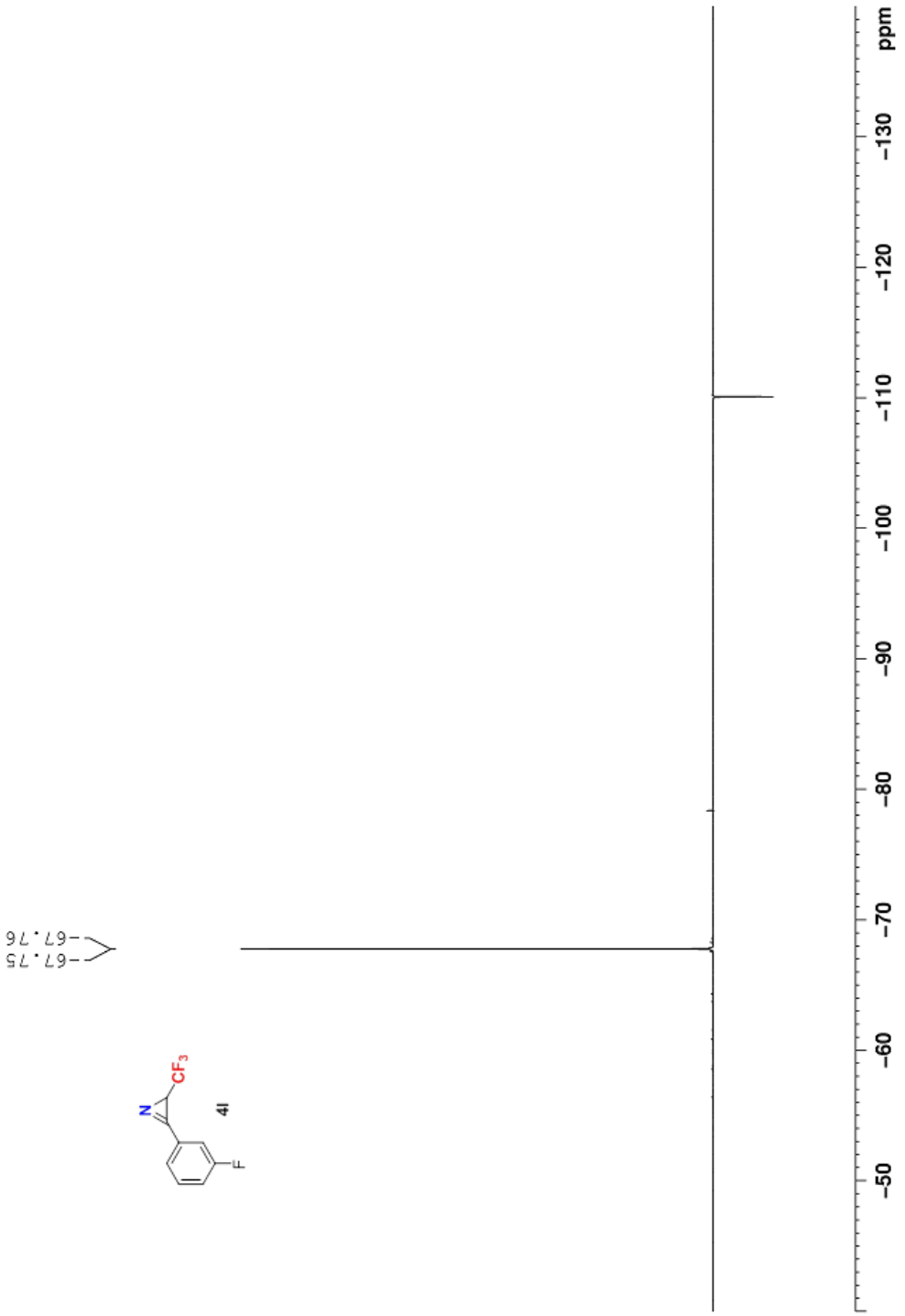
F
4l
ppm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-67.76
CF3
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F
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-100
-110
-120
-130
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2.750
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7.505
7.512
7.514
7.520
7.525
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7.609
7.617
7.622
7.866
7.869
7.871
7.887
7.889
N
CF3
Cl
4m
ppm
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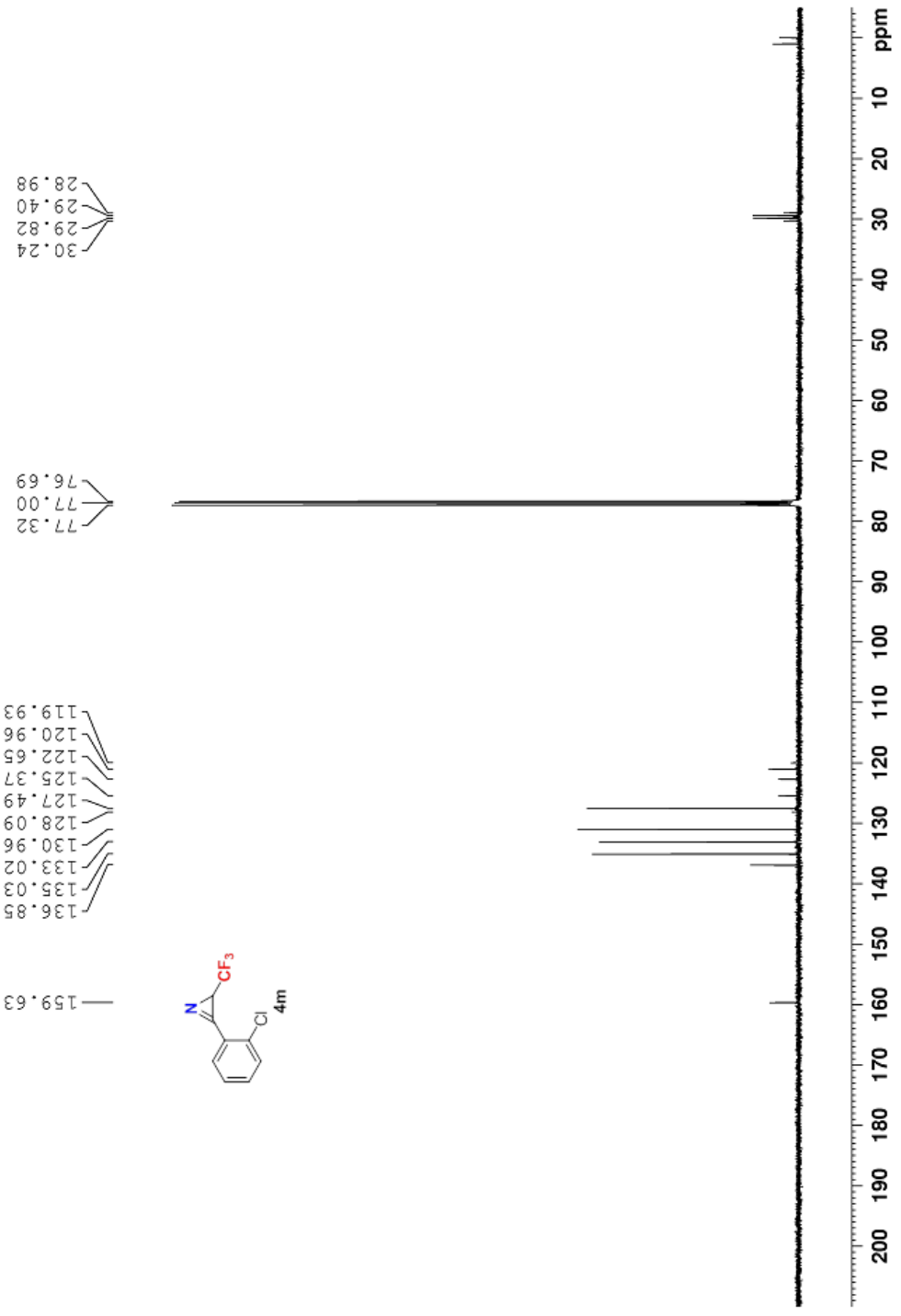
1.03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128.09
130.96
133.02
135.03
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159.63
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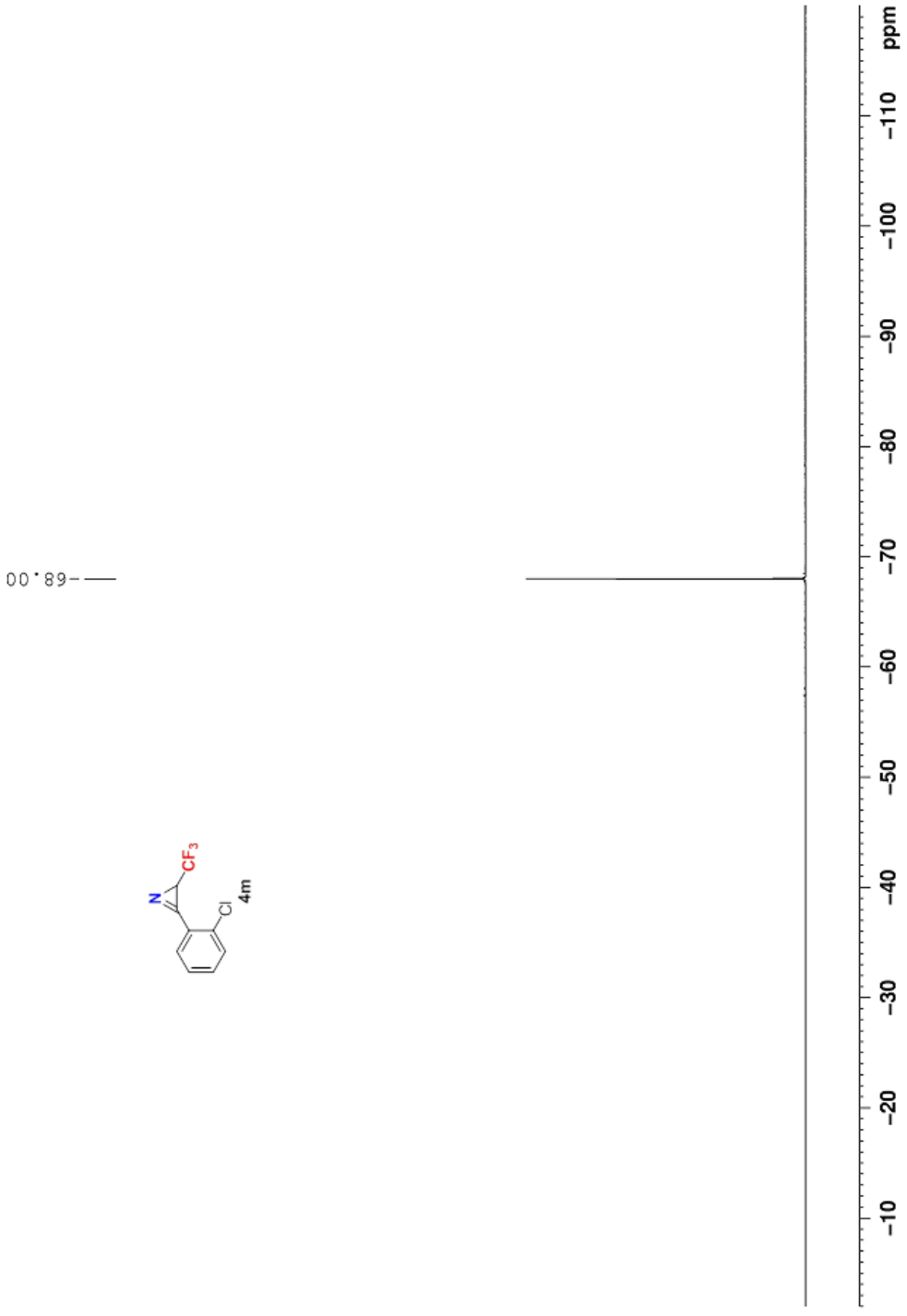
CF3
Cl
4m
ppm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CF3
Cl
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-40
-50
-60
-70
-80
-90
-100
-110
ppm

8.076
8.056
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7.263
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2.821
2.809
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4n
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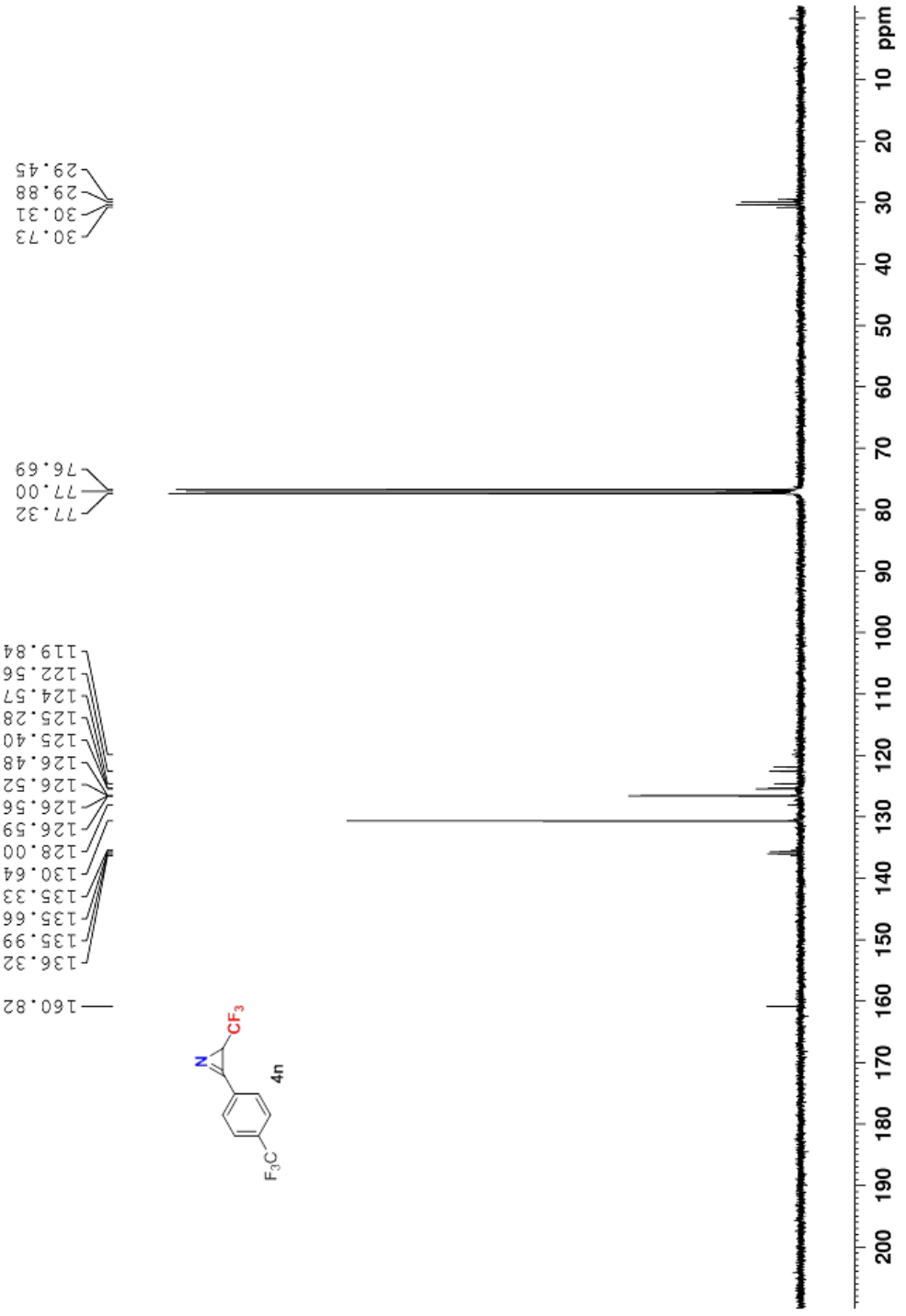
2.06
2.07
ppm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77.32
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125.28
125.40
126.48
126.52
126.56
126.59
128.00
130.64
135.33
135.66
135.99
136.32
160.82
CF3
N
4n
F3C
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200

-67.81
-63.43
4n
ppm
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110

7.970
7.950
7.624
7.604
7.267
3.901
2.778
2.766
2.755
2.744
4o
N
CF3
N
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3
4
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8
9
10
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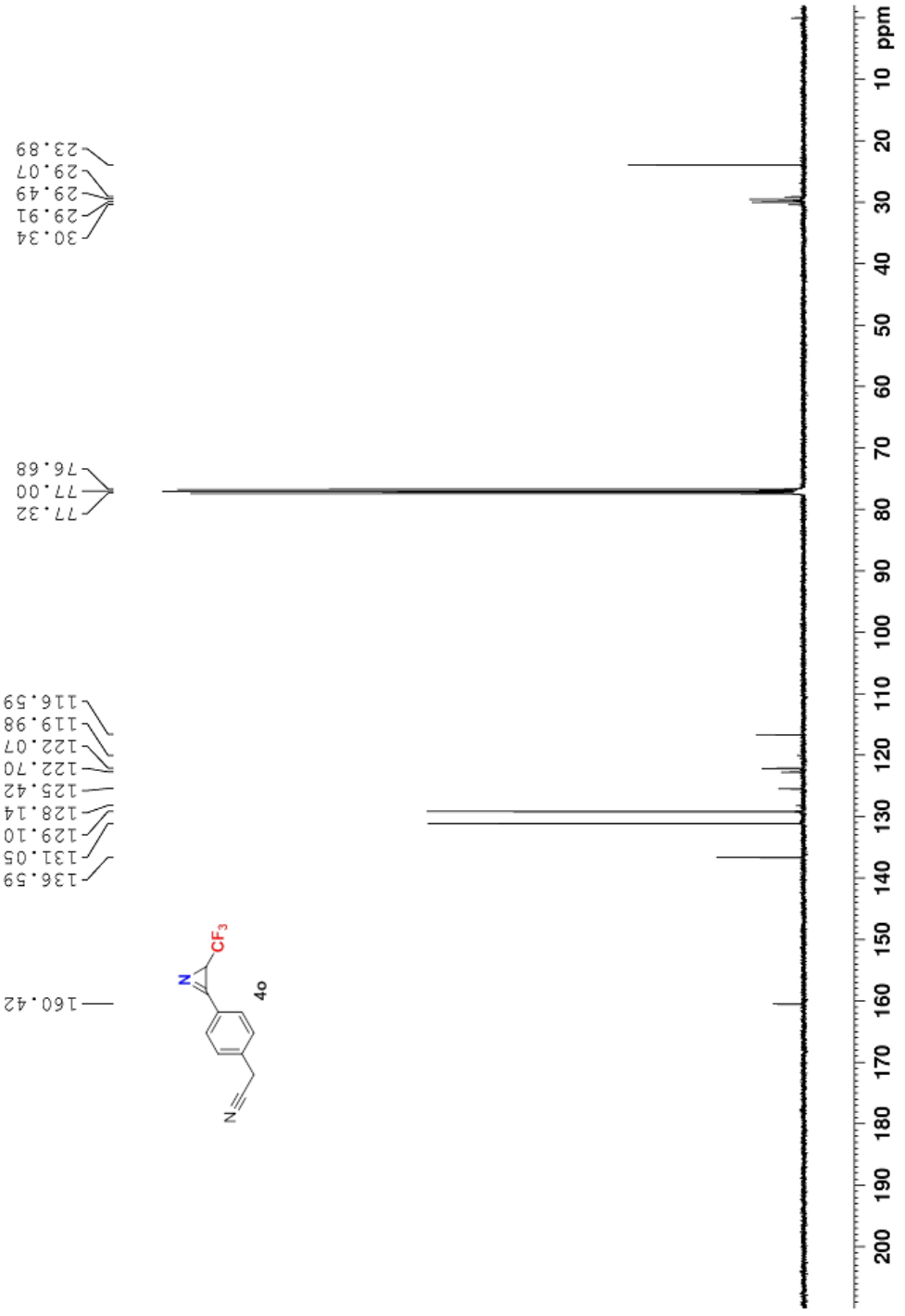
2.08
2.05
2.04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76.68
77.00
77.32
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122.07
122.70
125.42
128.14
129.10
131.05
136.59
160.42
4o
CF3
N
N
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200

-67.71
CF3
N
4o
N
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

2.738
2.727
2.715
2.704
7.583
7.601
7.604
7.620
7.658
7.662
7.665
7.675
7.680
7.686
7.696
7.699
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7.916
7.929
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CF3
4p
ppm
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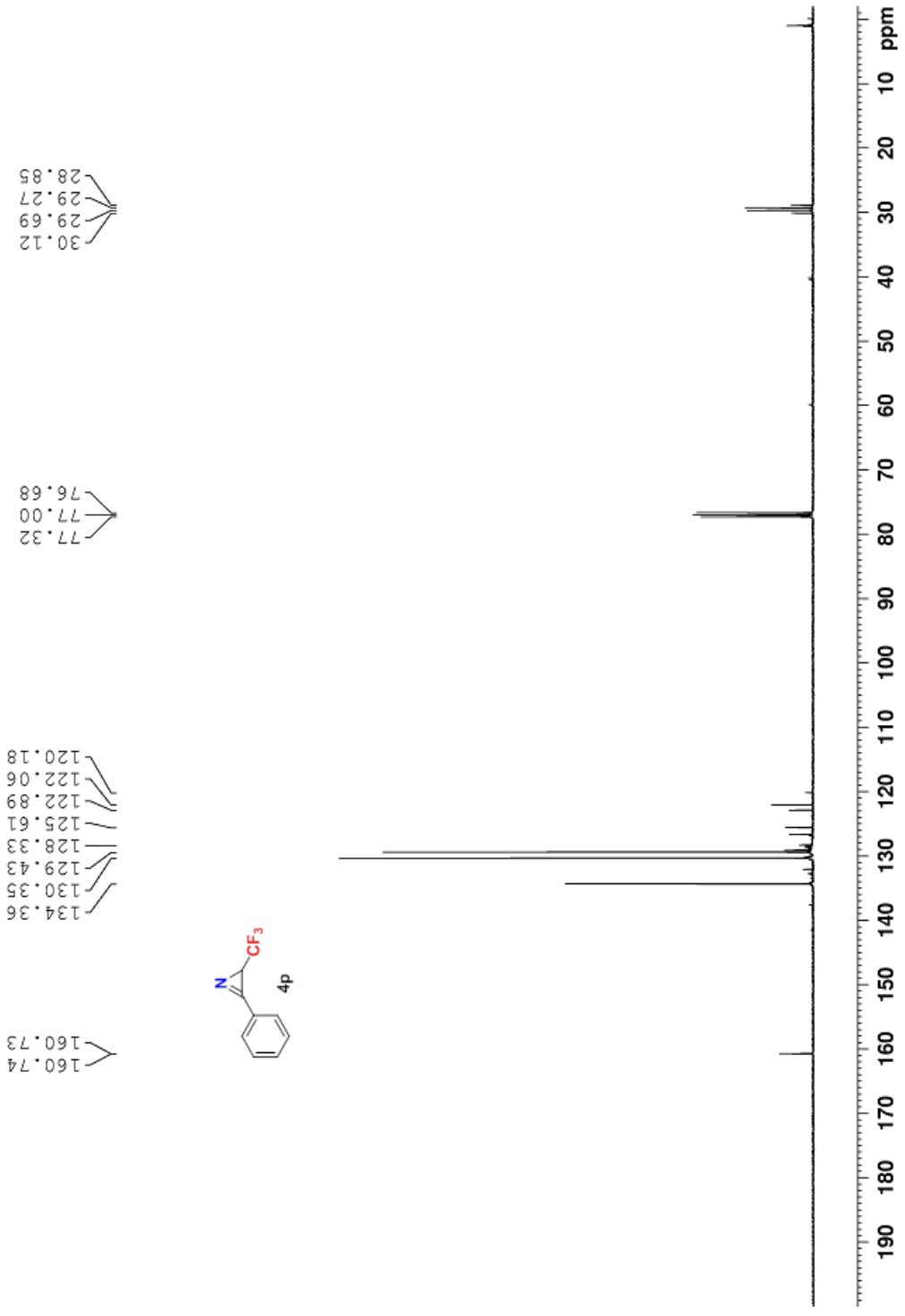
1.08
2.05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120.18
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122.89
125.61
128.33
129.43
130.35
134.36
160.73
160.74
4p
CF3
N
ppm

-67.66
-67.67
CF3
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4p
-10
-20
-30
-40
-50
-60
-70
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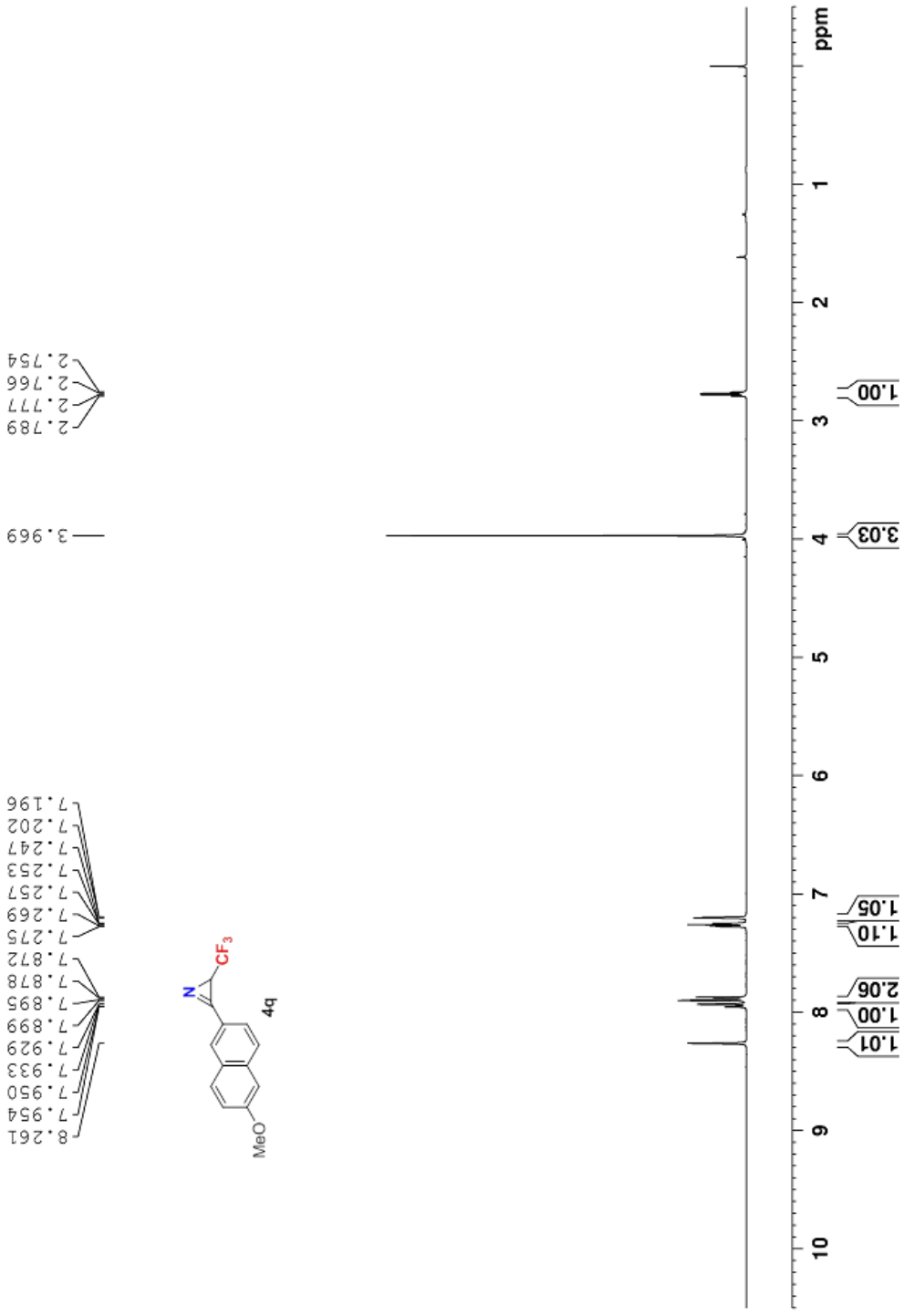
-90
-100
-110
ppm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2.777
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3.969
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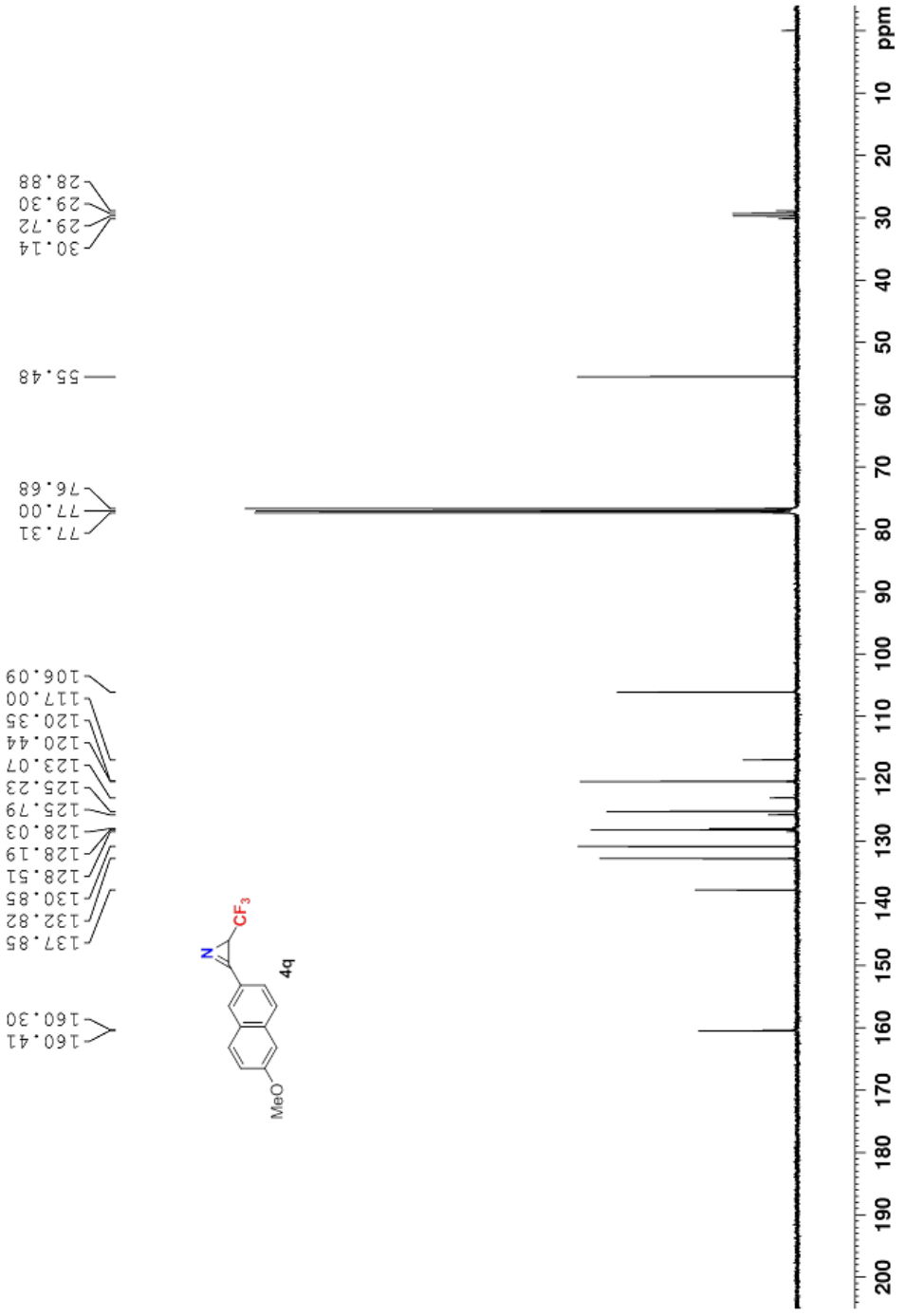
7.202
7.247
7.253
7.257
7.269
7.275
7.872
7.878
7.895
7.899
7.929
7.933
7.950
7.954
8.261
CF3
N
MeO
4q
1.00
3.03
1.05
1.10
2.06
1.00
1.01
ppm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76.68
77.00
77.31
106.09
117.00
120.35
120.44
123.07
125.23
125.79
128.03
128.19
128.51
130.85
132.82
137.85
160.30
160.41
N
CF3
MeO
4q
ppm

-67.50
-67.51
CF3
N
MeO
4q
ppm
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
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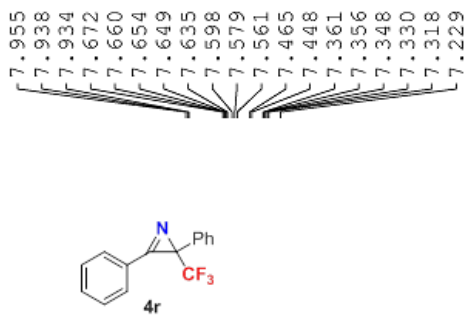
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7.649
7.635
7.598
7.579
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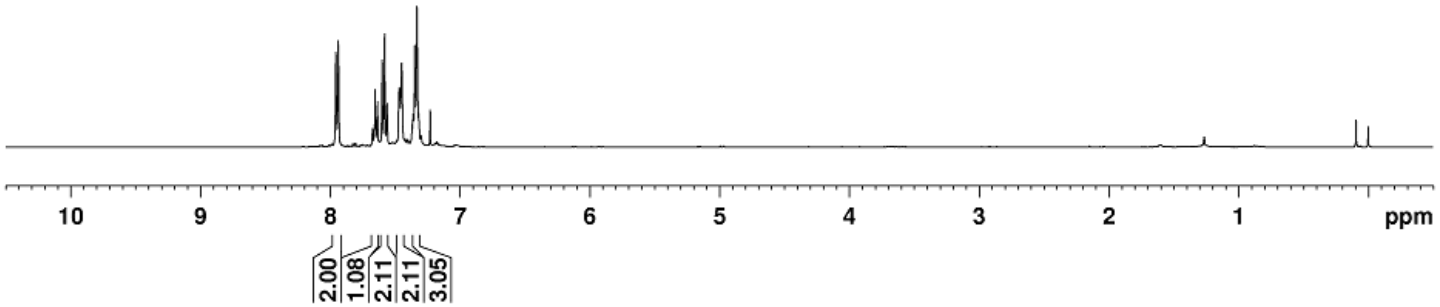
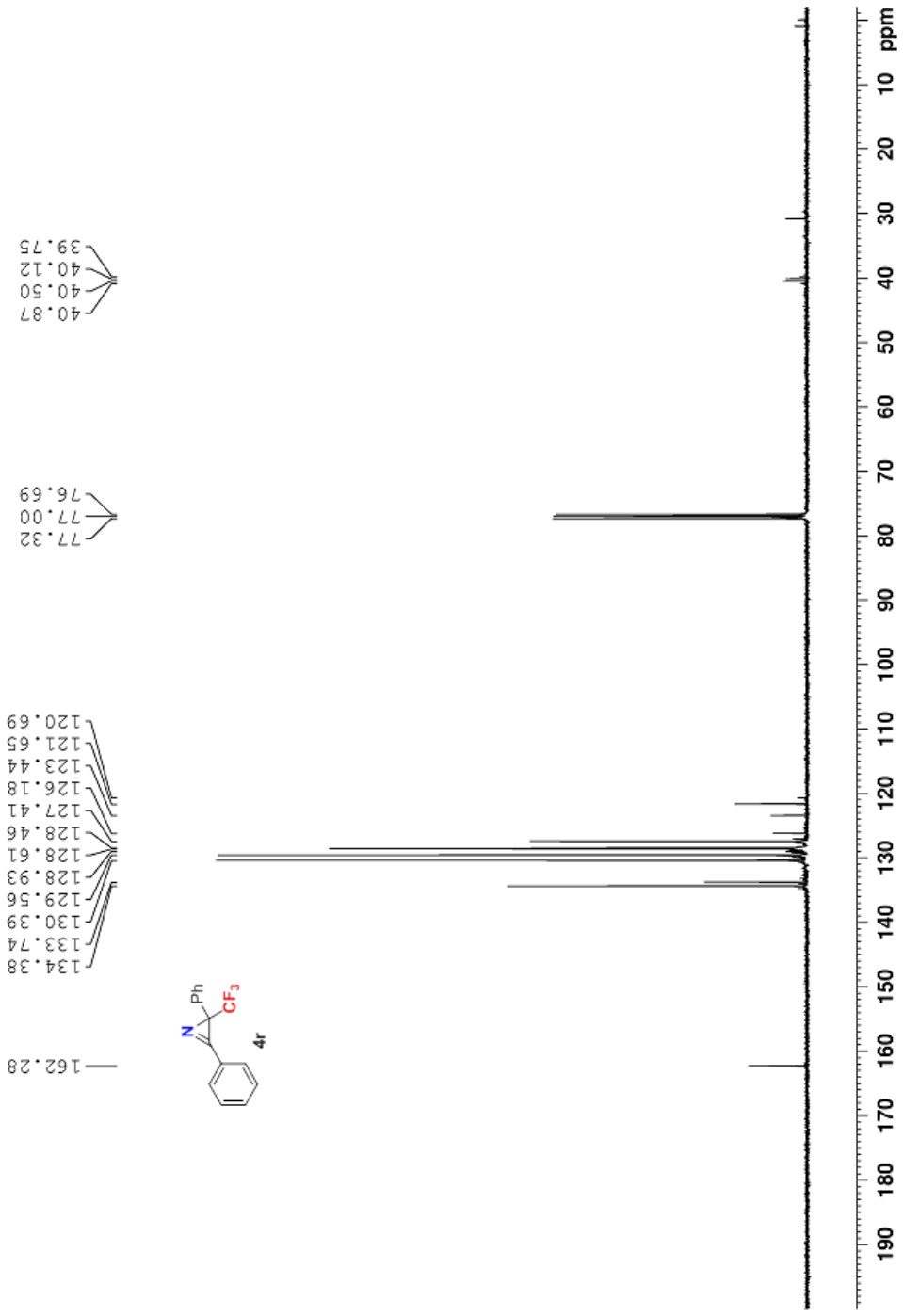
7.448
7.361
7.356
7.348
7.330
7.318
7.229
N
Ph
CF3
4r


10
9
8
7
6
5
4
3
2
1
ppm
2.00
1.08
2.11
2.11
3.05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129.56
128.93
128.61
128.46
127.41
126.18
123.44
121.65
120.69
77.32
77.00
76.69
40.87
40.50
40.12
39.75
Ph
CF3
N
4r
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

-65.28
Ph
CF3
N
4r
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

1.396
3.849
3.825
3.801
3.778
7.647
7.625
7.377
7.355
7.285
5a
t-Bu
CF3
9.04
2.00
1.96
2.00
ppm

154.83
146.53
146.50
130.11
127.40
127.14
124.98
124.64
121.88
119.11
77.32
77.00
76.68
35.02
31.09
29.91
29.57
29.24
28.90
5a
t-Bu
ppm

-68.25
-68.28
-68.30
5a
t-Bu
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm

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7.555
7.494
7.475
7.451
7.442
7.432
7.427
7.256
4.002
1.360
COOMe
N
F3C
tBu
7a
ppm
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2
3
4
5
6
7
8
9
10
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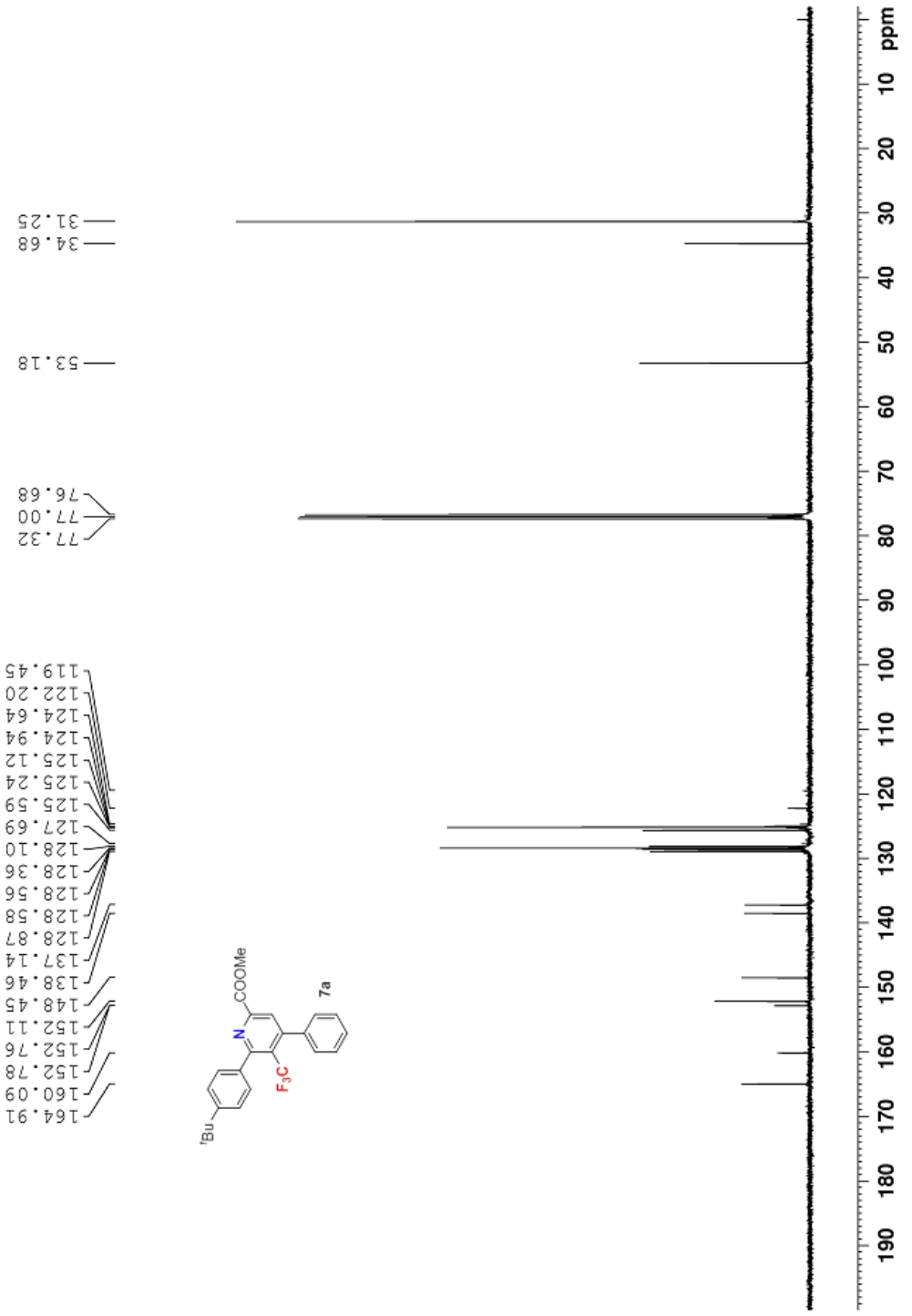
3.00
1.00
2.08
5.18
2.00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125.24
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128.58
128.87
137.14
138.46
148.45
152.11
152.76
152.78
160.09
164.91
tBu
F3C
N
COOMe
7a
ppm

-49.00
COOMe
N
F3C
tBu
7a
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
ppm

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7.573
7.552
7.490
7.469
7.354
7.334
7.301
7.281
7.254
3.998
2.433
1.358
COOMe
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F3C
tBu
9.15
3.03
3.00
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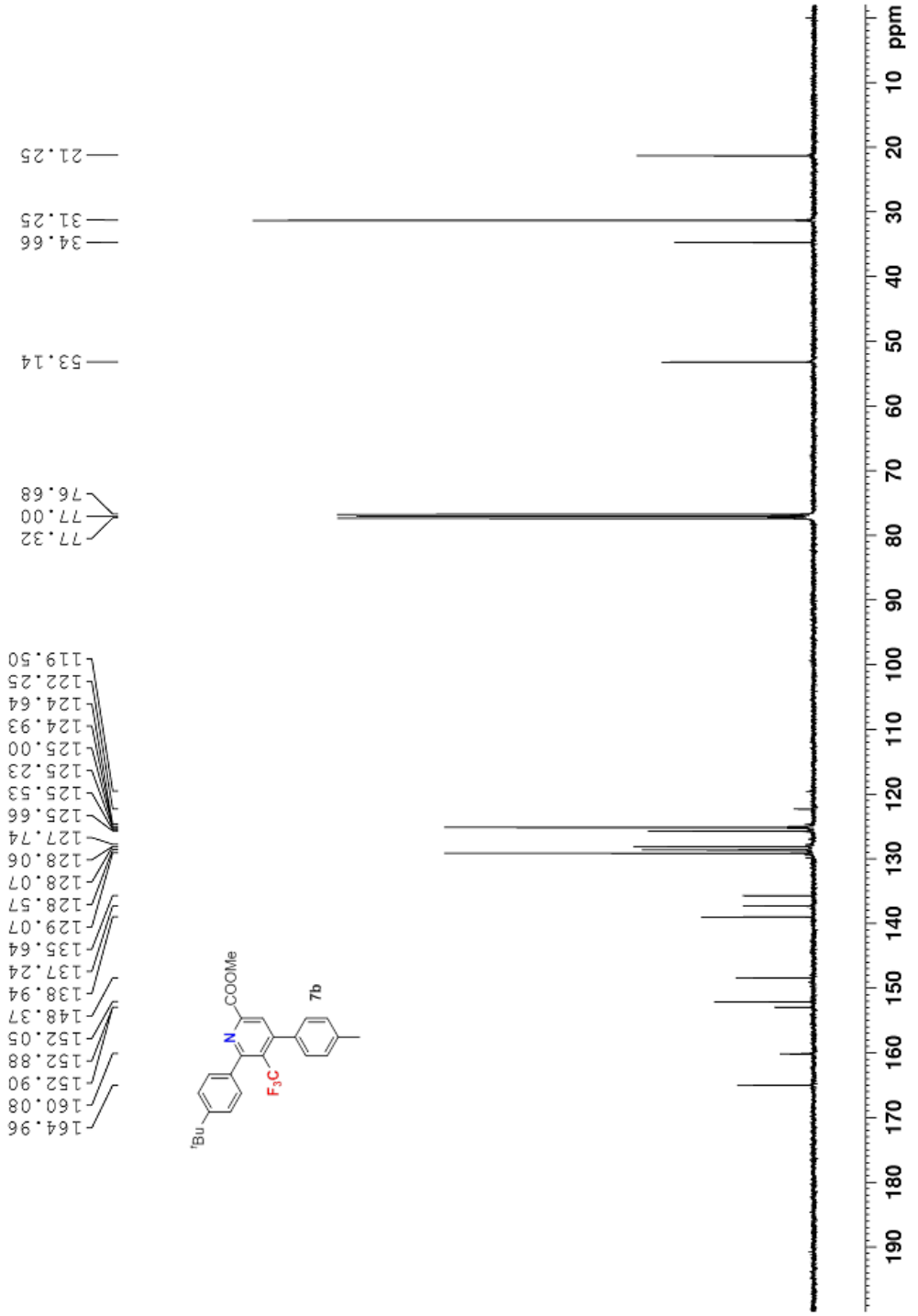
2.09
2.01
2.08
0.97
ppm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124.93
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125.53
125.66
127.74
128.06
128.07
128.57
129.07
135.64
137.24
138.94
148.37
152.05
152.88
152.90
160.08
164.96
COOMe
7b
F3C
tBu
ppm

-48.99
COOMe
N
F3C
tBu
7b
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
ppm

1.359
3.869
3.999
8.048
7.577
7.556
7.492
7.471
7.409
7.388
7.259
7.023
7.001
COOMe
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tBu
OMe
7c
9.18
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2.10
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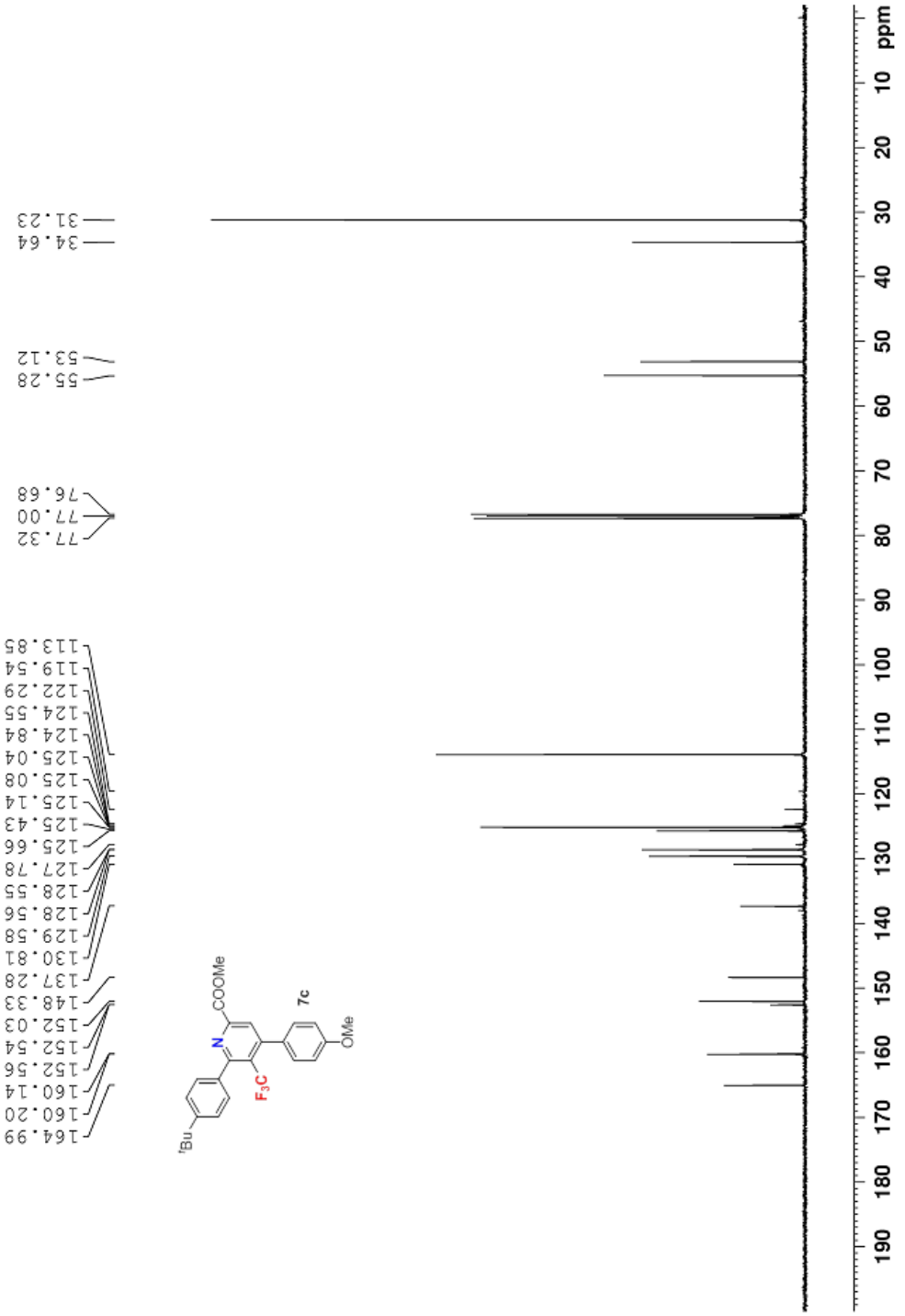
ppm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125.14
125.43
125.66
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128.56
129.58
130.81
137.28
148.33
152.03
152.54
152.56
160.14
160.20
164.99
COOMe
N
F3C
tBu
7c
OMe
ppm

-49.05
COOMe
7c
N
OMe
F3C
tBu
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
ppm


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7.542
7.495
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7.478
7.474
7.462
7.394
7.372
7.262
COOMe
N
F3C
tBu
Cl
7d
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4.13
2.07
1.00
ppm
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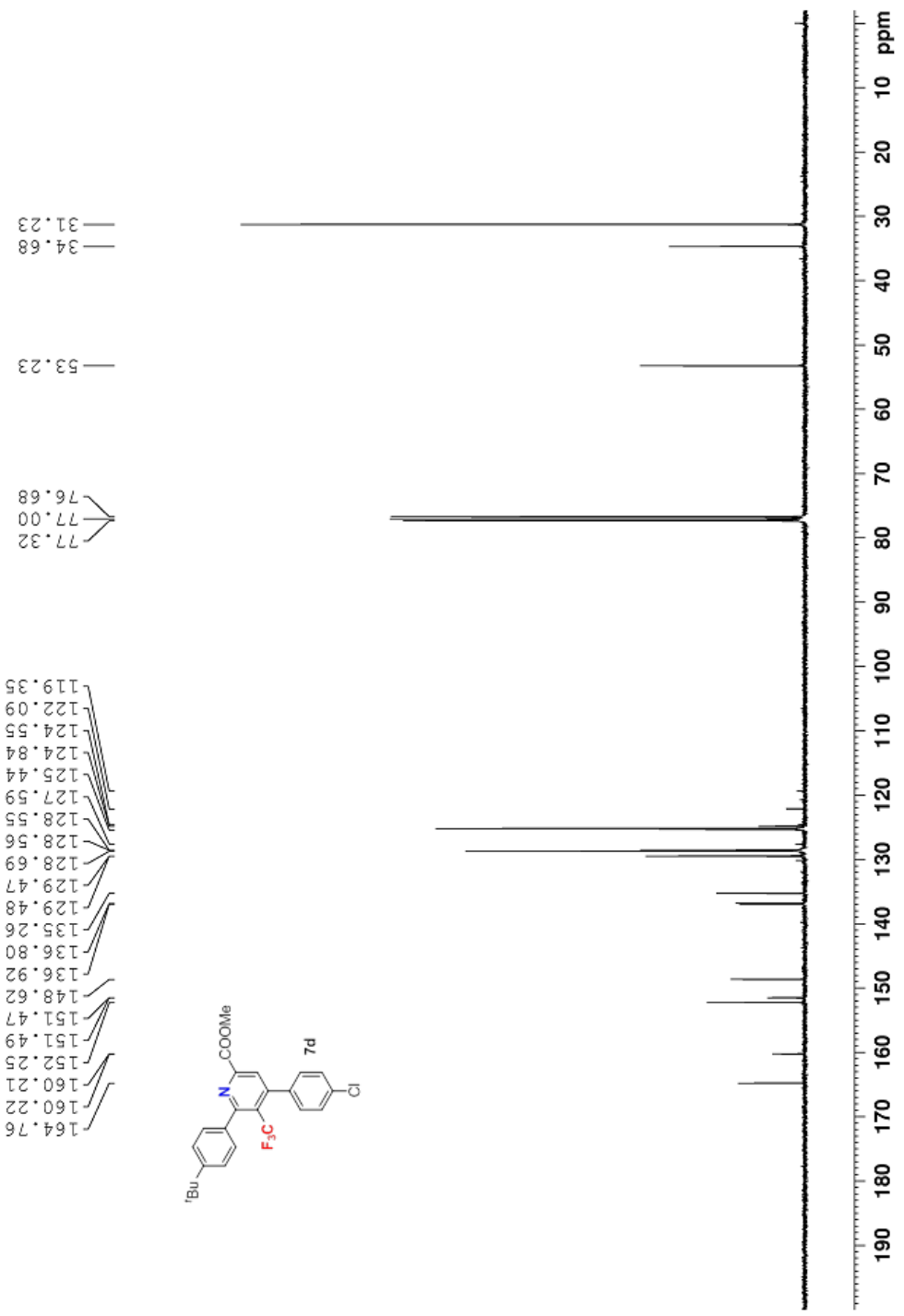
3
4
5
6
7
8
9
10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128.56
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129.47
129.48
135.26
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151.49
152.25
160.21
160.22
164.76
COOMe
7d
N
F3C
Cl
tBu
ppm
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40
50
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80
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120
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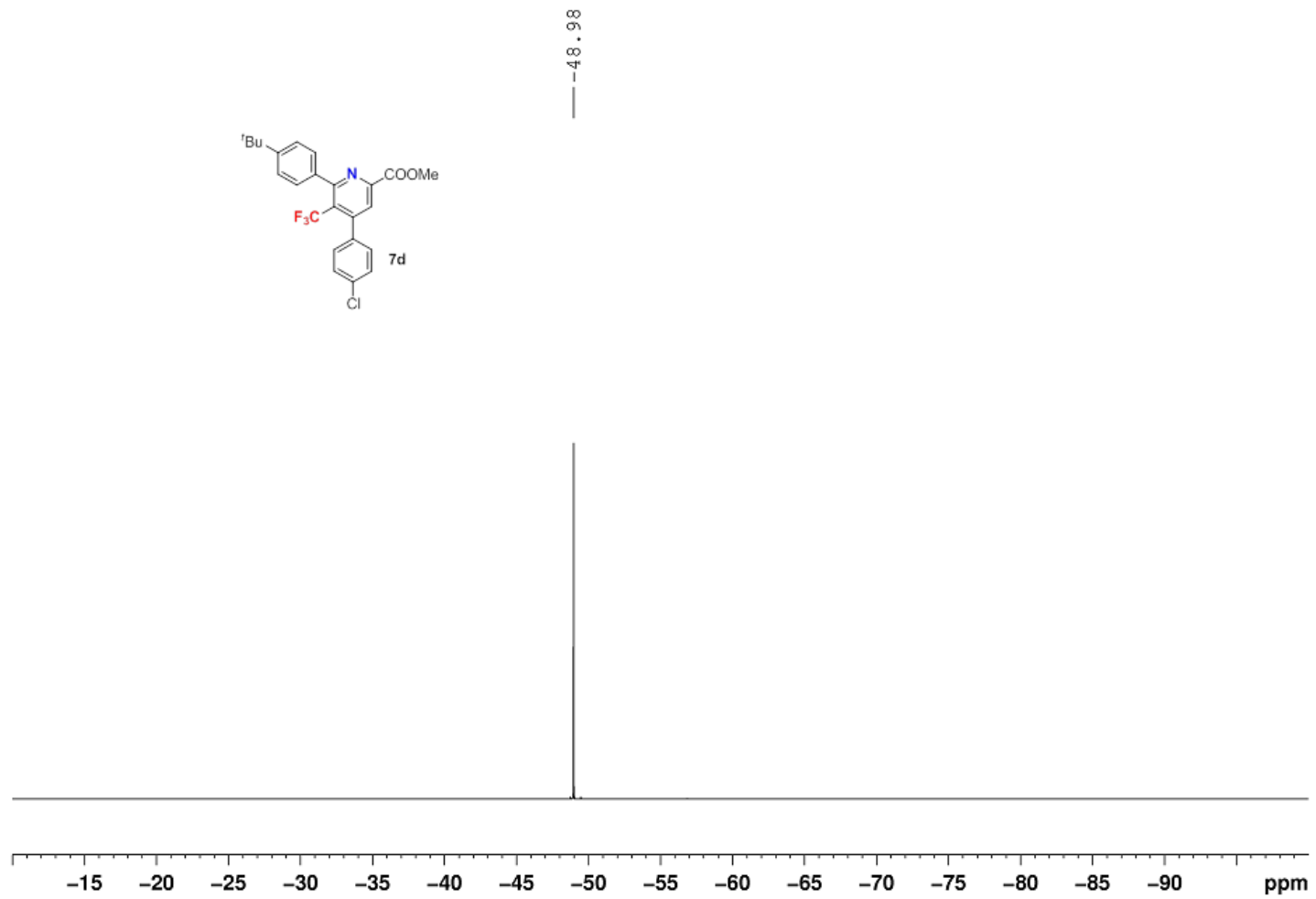
180
190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COOMe
F3C
7d
Cl
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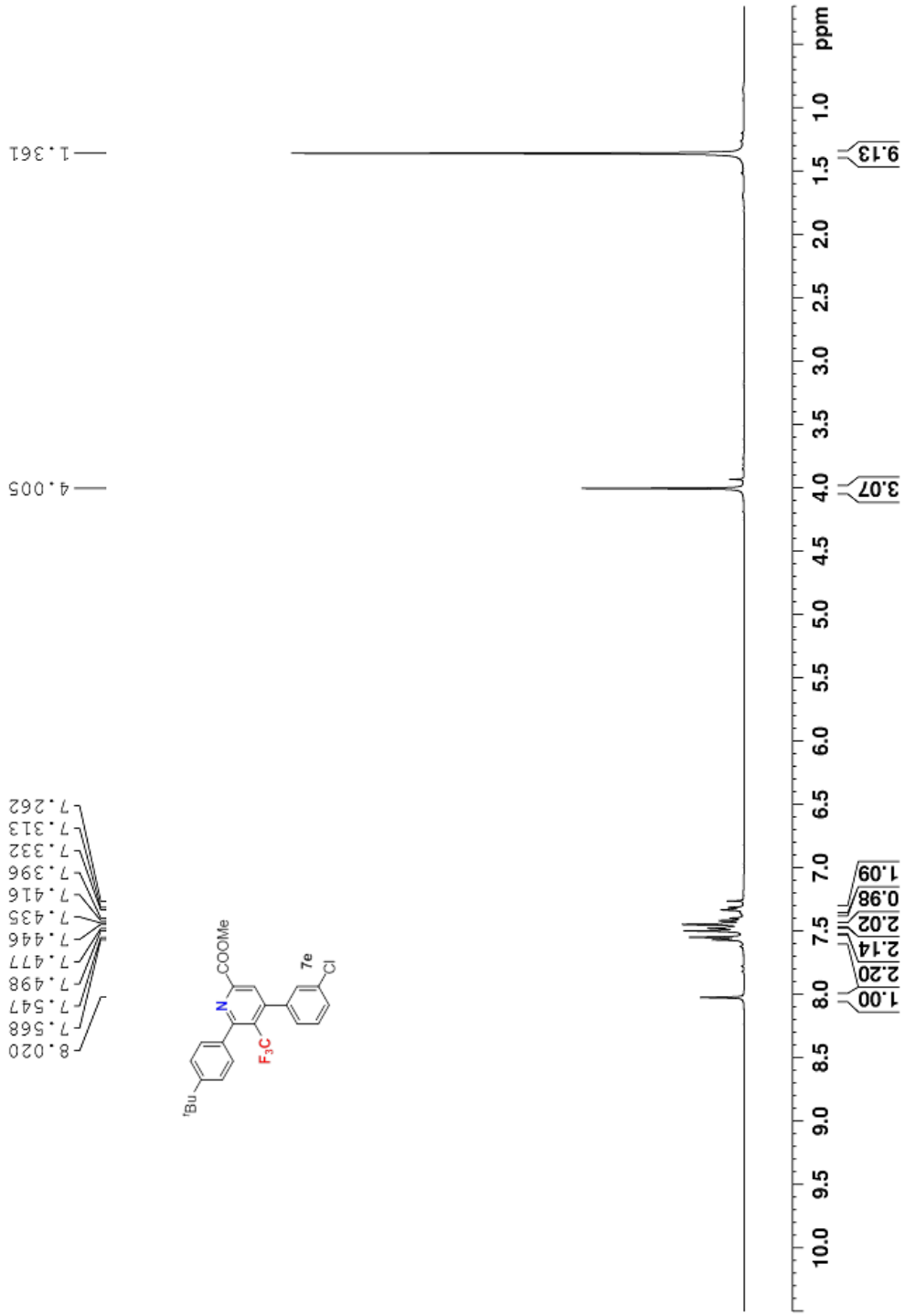
-90
ppm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7.332
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7.262
COOMe
N
F3C
7e
Cl
tBu
9.13
3.07
1.00
2.20
2.14
2.02
0.98
1.09
ppm
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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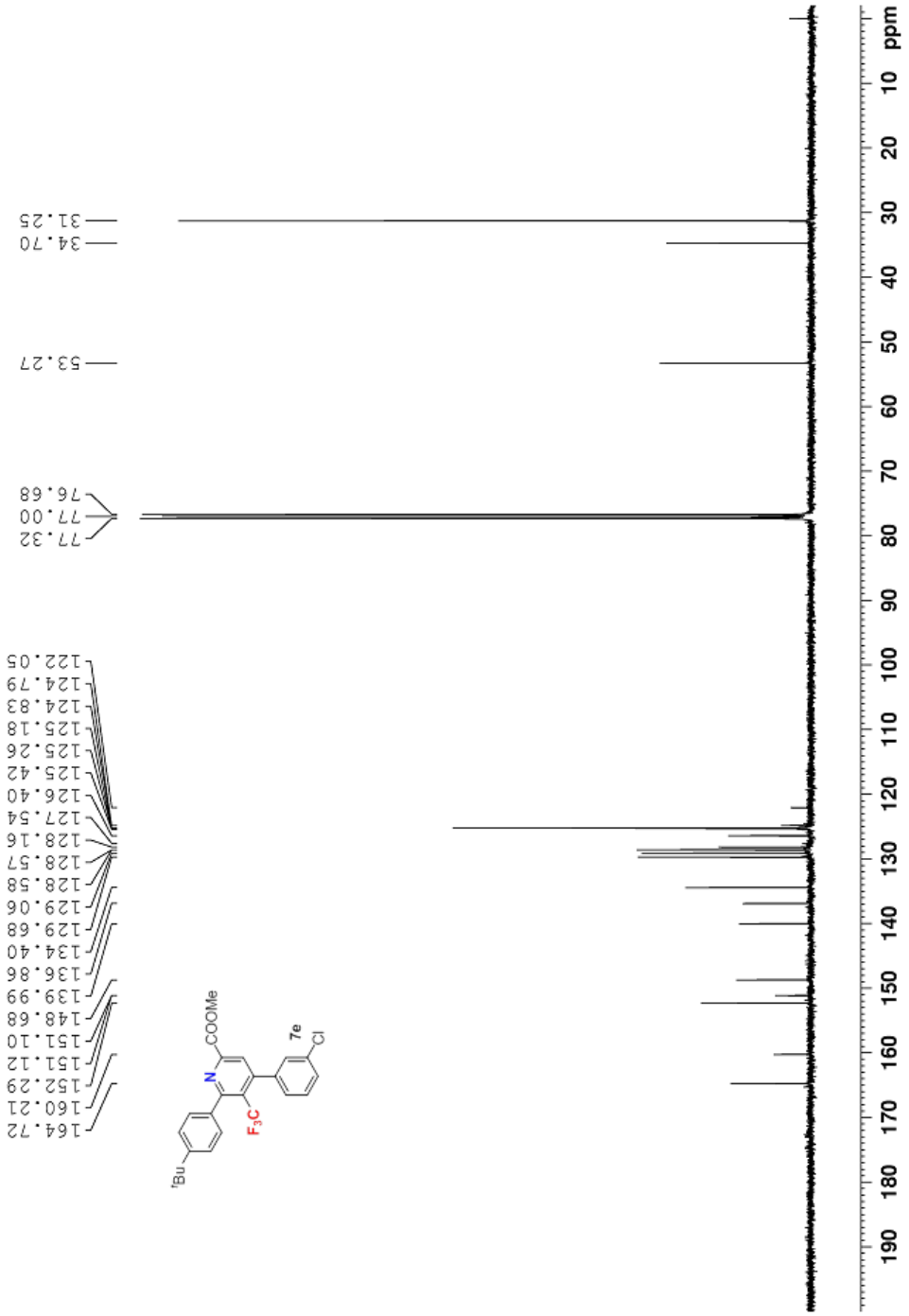
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0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125.26
125.42
126.40
127.54
128.16
128.57
128.58
129.06
129.68
134.40
136.86
139.99
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151.10
151.12
152.29
160.21
164.72
COOMe
N
F3C
7e
Cl
tBu
ppm
10
20
30
40
50
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80
90
100
110
120
130
140
150
160
170
180
190

-49.00
COOMe
N
7e
Cl
F3C
tBu
ppm
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90

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7.489
7.393
7.371
7.264
7.026
7.004
4.010
3.880
COOMe
N
F3C
Br
OMe
7f
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2.08
2.15
2.09
3.11
3.10
ppm

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77.32
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126.25
127.62
129.59
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130.50
130.52
131.36
139.00
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152.84
158.83
160.35
164.73
COOMe
N
F3C
Br
OMe
7f
ppm

-49.04
COOMe
N
7f
OMe
F3C
Br
ppm
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-20
-25
-30
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8.135
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tBu
F3C
Ph
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ppm
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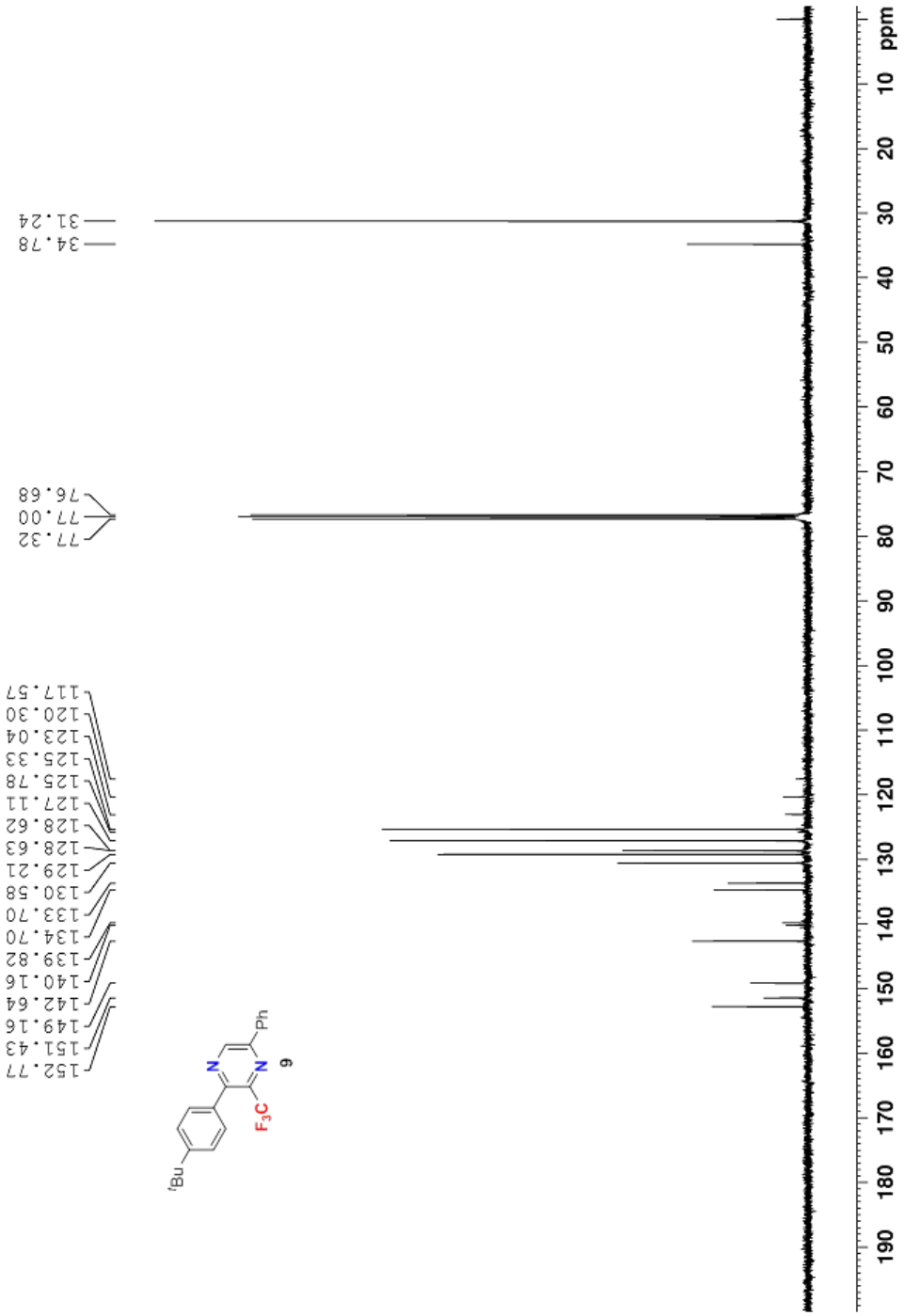
9.24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128.63
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139.82
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149.16
151.43
152.77
tBu
F3C
Ph
N
N
6
ppm
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20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190

-61.85
Ph
N
N
F3C
tBu
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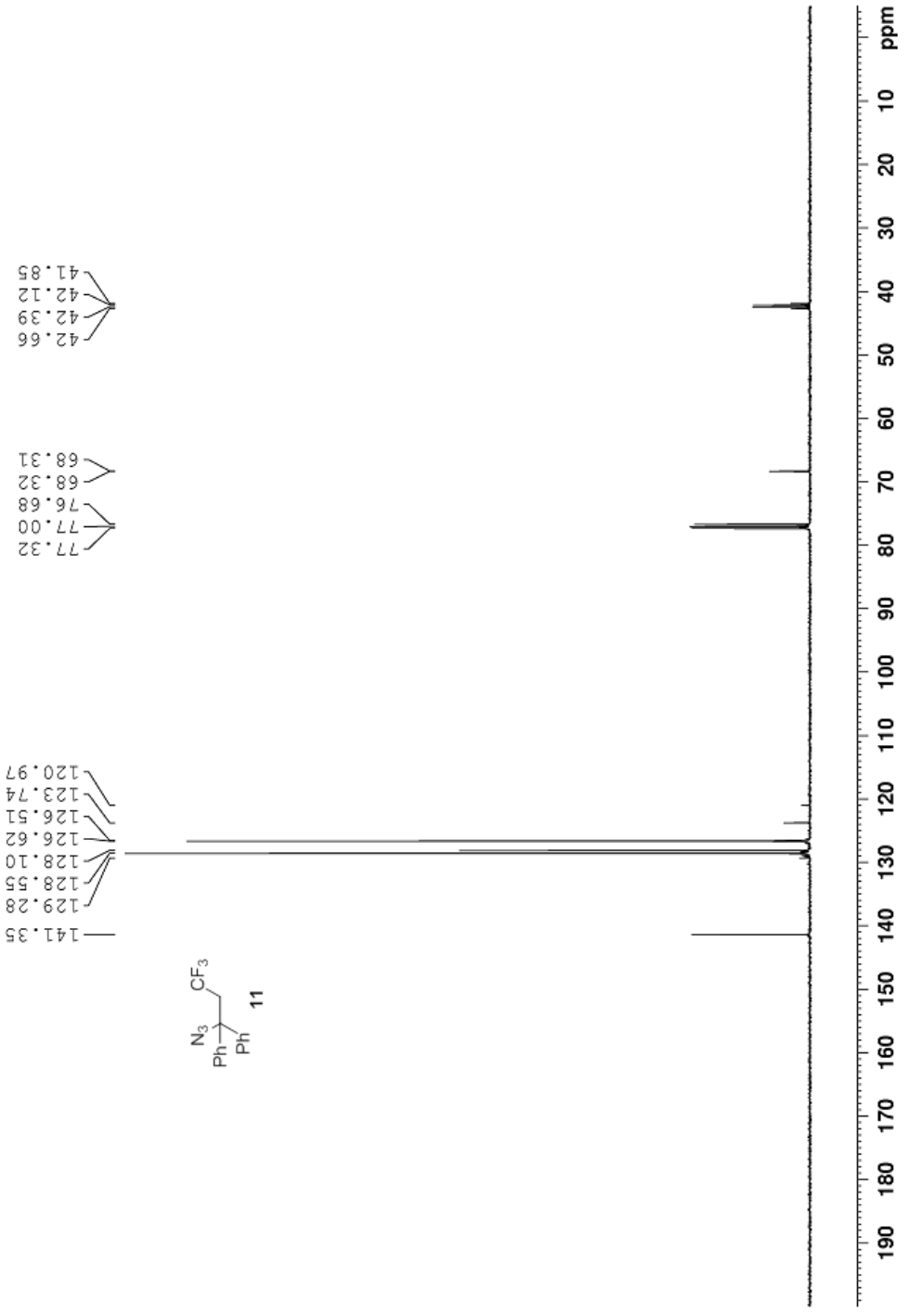
7.295
7.300
7.308
7.318
7.326
7.332
7.336
7.350
7.354
7.357
N3
CF3
Ph
Ph
11
2.00
9.95
ppm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129.28
128.55
128.10
126.62
126.51
123.74
120.97
77.32
77.00
76.68
68.32
68.31
42.66
42.39
42.12
41.85
CF3
N3
Ph
Ph
11
ppm

-59.38
-59.41
-59.43
N3
CF3
Ph
Ph
11
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
ppm