Electronic Supplementary Material (ESI) for ChemComm.
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The Asymmetric Synthesis of CF_3- Containing Spiro[pyrrolidin-3,2'-oxindole] through the Organocatalytic 1, 3-dipolar Cycloaddition Reaction

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A. General Information

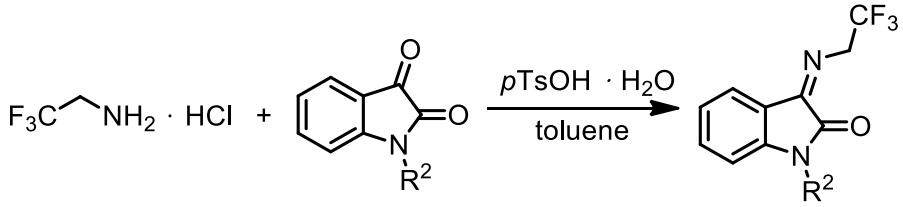
Reactions were monitored by thin layer chromatography (TLC), and compounds were visualized with a UV light at 254 nm. Column chromatography purifications were carried out using silica gel. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker (300 MHz) spectrometer in $CDCl_3$, unless otherwise stated, using tetramethylsilane (TMS) as internal standard. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in $He^{20}z$ (Hz). Mass peaks are identified by the corresponding *m/z* values. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column, Chiracel OD-H column and Chiracel IA column. Optical rotations were measured on a digital polarimeter and are reported as follows: $[\alpha]_D^T$ (concentration (g/100 mL), solvent).

All solvents were obtained from commercial sources and were purified according to standard procedures. The catalyst was prepared according to literature procedure. [1]

Reference:

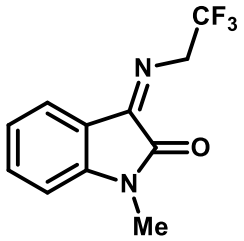
[1] a) M. Marigo, T. C. Wabnitz, D. Fielenbach, K. A. Jørgensen, *Angew. Chem.* 2005, 117, 804; *Angew. Chem. Int. Ed.* 2005, **44**, 794; b) Y. Hayashi, H. Gotoh, T. Hayashi, M. Shoji, *Angew. Chem.* 2005, **117**, 4284; *Angew. Chem. Int. Ed.* 2005, **44**, 4212.

B. General Procedure for Syntheses of the *N*-(2,2,2-Trifluoroethyl) Isatin-derived Imines (GP1) and Their Analytical Data



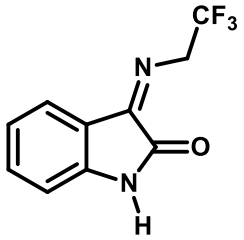
Isatin (10 mmol), 2,2,2-trifluoroethylamine hydrochloride (15 mmol) and *p*-toluenesulfonic acid (0.5 mmol) were suspended in toluene (10 mL) in a two-neck flask with a water separator and a condenser. The mixture was then heated to separate the water until complete disappearance of the starting materials, after which it was cooled to room temperature, washed with a small quantity of saturated $NaHCO_3$ solution and dried by Na_2SO_4. After an evaporation of the organic solvent, the crude residue was purified by flash chromatography (silica gel, hexane/ethyl acetate) and afforded the resulting ketimine as described below.

1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1a)



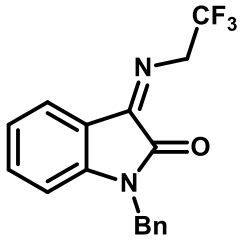
Ketimine **1a** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 1.89 g of **1a** in 78.1% yield as a yellow solid, mp = 104 – 105 ℃. ^{1}H NMR (300 MHz, CDCl3) δ 7.69 (d, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 4.83 (q, *J* = 9.6 Hz, 2H), 3.23(s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 158.6, 155.7, 146.2, 133.8, 125.1 (q, J_{CF} = 276.2 Hz), 123.4, 122.9, 120.5, 108.8, 53.5 (q, J_{CF} = 32.0 Hz), 25.8. ^{19}F NMR (282 MHz, CDCl3) δ −71.9, −71.1. HRMS (ESI) *m/z* calcd for $C_{11}H_9F_3N_2NaO$ $[M+Na]^+$: 265.0559, found 265.0560.

3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1b)



Ketimine **1b** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 1.69 g of **1b** in 74.1% yield as a yellow solid, mp = 205 – 206 ℃. ^{1}H NMR (300 MHz, DMSO-d6) δ 8.39 (s, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.8, 1H), 7.12 (t, *J* = 7.5, 1H), 6.89 (d, *J* = 8.1 Hz, 1H), 4.82 (q, *J* = 9.7 Hz, 2H). ^{13}C NMR (75MHz, DMSO-d6) δ 159.7, 156.4, 145.3, 134.0, 122.4, 122.3, 120.6, 125.5 (q, J_{CF} = 276.0 Hz), 110.9, 52.3 (q, J_{CF} = 31.0 Hz). ^{19}F NMR (282 MHz, DMSO-d6) δ -70.0, -70.5. HRMS (ESI) *m/z* calcd for $C_{10}H_7F_3N_2NaO$ $[M+Na]^+$: 251.0403, found 251.0404.

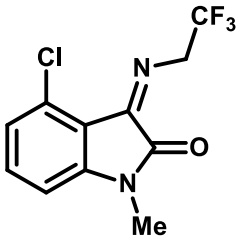
1-benzyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1c)



Ketimine **1c** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 2.39 g of **1c** in 75.2% yield as a yellow solid, mp = 154 – 155 ℃. ^{1}H NMR (300 MHz, CDCl3) δ 7.73 (d, *J* = 7.5 Hz, 1H), 7.06 – 7.38 (m, 6H),

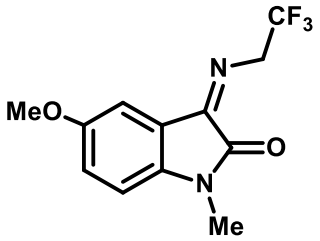
7.09 (t, J = 7.5 Hz, 1H), 6.74 (d, J = 8.1 Hz, 1H), 4.83 – 4.93 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 155.6, 145.5, 134.9, 133.7, 129.0, 128.0, 127.4, 125.1 (q, J_{CF} = 274.5 Hz), 123.5, 123.1, 120.7, 109.8, 53.6 (q, J_{CF} = 32.3 Hz), 43.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -71.1, -71.9. HRMS (ESI) *m/z* calcd for $C_{17}H_{13}F_3N_2NaO$ $[M+Na]^+$: 341.0872, found 341.0874.

4-chloro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1d)



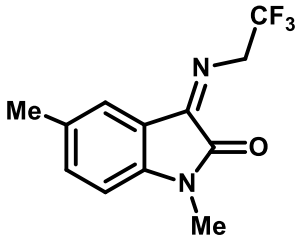
Ketimine **1d** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 1.88 g of **1d** in 68.1% yield as a yellow solid, mp = 187 – 188 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (t, J = 8.1 Hz, 1H), 7.10 (d, J = 8.1 Hz, 1H), 6.76 (d, J = 7.8 Hz, 1H), 4.87 (q, J = 9.6 Hz, 2H), 3.24 (s, 3H). ^{13}C NMR (75 MHz, C_3D_6O) δ 158.4, 155.2, 149.3, 135.1, 131.3, 126.4 (q, J_{CF} = 273.5 Hz), 125.6, 117.5, 108.8, 54.3 (q, J_{CF} = 32.0 Hz), 26.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ −72.1. HRMS (ESI) *m/z* calcd for $C_{11}H_9ClF_3N_2O$ $[M+H]^+$: 277.0350, found 233.0351.

5-methoxy-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1e)



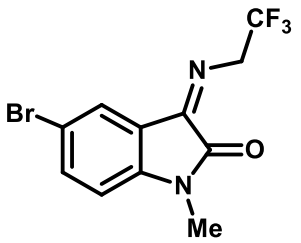
Ketimine **1e** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 1.99 g of **1e** in 73.2% yield as a yellow solid, mp = 133 – 134℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, J = 1.8 Hz, 1H), 7.01 (dd, J = 8.4, 2.7 Hz, 1H), 6.75 (d, J = 8.4 Hz, 1H), 4.84 (q, J = 9.7 Hz, 2H), 3.83 (s, 3H), 3.20 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 156.5, 156.0, 139.9, 125.0 (q, J_{CF} = 274.0 Hz), 121.1, 120.0, 109.6, 107.8, 55.9, 53.4 (q, J_{CF} = 32.0 Hz), 25.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -71.9. HRMS (ESI) *m/z* calcd for $C_{12}H_{11}F_3N_2NaO_2$ $[M+Na]^+$: 295.0665, found 295.0670.

1,5-dimethyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1f)



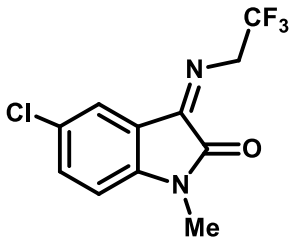
Ketimine **1f** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 1.92 g of **1f** in 75.0% yield as a yellow solid, mp = 145 – 146 ℃. ^{1}H NMR (300 MHz, CDCl3) δ 7.54 (s, 1H), 7.25 (d, *J* = 7.2 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 4.83 (q, *J* = 9.7 Hz, 2H), 3.21 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 158.7, 155.9, 144.0, 134.1, 133.2, 125.1 (q, J_{CF} = 274.5 Hz), 123.4, 120.4, 108.5, 53.4 (q, J_{CF} = 32.0 Hz), 25.8, 20.8. ^{19}F NMR (282 MHz, CDCl3) δ -71.9. HRMS (ESI) *m/z* calcd for $C_{12}H_{11}F_3N_2NaO$ $[M+Na]^+$: 279.0716, found 279.0720.

5-bromo-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1g)



Ketimine **1g** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 2.30 g of **1g** in 71.9% yield as a yellow solid, mp = 147 – 148 ℃. ^{1}H NMR (300 MHz, CDCl3) δ 7.84 (d, *J* = 1.8 Hz, 1H), 7.59 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 4.83 (q, *J* = 9.7 Hz, 2H), 3.23 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 158.0, 154.7, 145.0, 136.2, 125.9, 124.8 (q, J_{CF} = 274.7 Hz), 121.9, 116.3, 110.3, 53.7 (q, J_{CF} = 32.3 Hz), 25.9. ^{19}F NMR (282 MHz, CDCl3) δ −71.9. HRMS (ESI) *m/z* calcd for $C_{11}H_8BrF_3N_2NaO$ $[M+Na]^+$: 342.9664, found 342.9670.

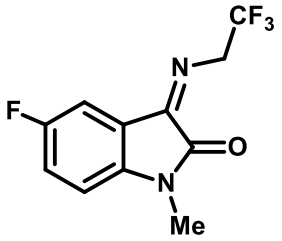
5-chloro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1h)



Ketimine **1h** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 2.01 g of **1h** in 72.8% yield as a yellow solid, mp = 119 –120 ℃. ^{1}H NMR (300MHz, CDCl3) δ 7.68 (d, *J* = 1.8 Hz, 1H), 7.43 (dd, *J* =8.4, 1.8

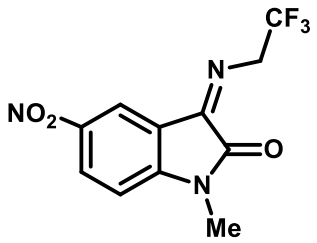
Hz, 1H), 6.78 (d, J = 8.4 Hz, 1H), 4.82 (q, J = 9.7 Hz, 2H), 3.23 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.1, 154.9, 144.6, 133.3, 129.2, 124.9 (q, J_{CF} = 274.5 Hz), 123.1, 121.6, 109.9, 53.7 (q, J_{CF} = 32.3 Hz), 26.0. ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.9. HRMS (ESI) *m/z* calcd for $C_{11}H_8ClF_3N_2NaO$ $[M+Na]^+$: 299.0169, found 299.0176.

5-fluoro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1i)



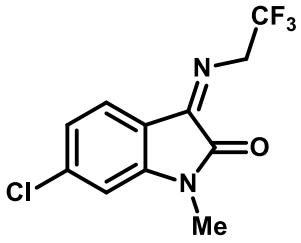
Ketimine **1i** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 1.82 g of **1i** in 70.0% yield as a yellow solid, mp = 110 –111 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (dd, J = 7.5, 2.7 Hz, 1H), 7.18 (td, J = 8.7, 2.7 Hz, 1H), 6.79 (dd, J = 8.4, 3.6 Hz, 1H), 4.83 (q, J = 9.6 Hz, 2H), 3.23 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.1, 158.4, 157.9, 155.3, 142.2, 124.9 (q, J_{CF} = 274.2 Hz), 121.6 (d, J_{CF} = 7.5 Hz), 115.1(dd, J_{CF} = 712.5, 24 Hz), 109.7 (d, J_{CF} = 7.5 Hz), 53.6 (q, J_{CF} = 32.3 Hz), 25.9. ^{19}F NMR (282 MHz, $CDCl_3$): δ −71.9, −119.0. HRMS (ESI) *m/z* calcd for $C_{11}H_5F_4N_2NaO$ $[M+Na]^+$: 283.0465, found 283.0468.

1-methyl-5-nitro-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1j)



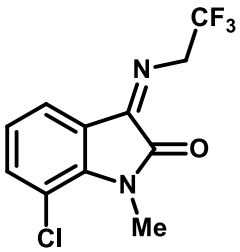
Ketimine **1j** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 1.72 g of **1j** in 59.9% yield as a yellow solid, mp = 207 – 208 ℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, J = 2.3 Hz, 1H), 8.43 (dd, J = 8.7, 2.3 Hz, 1H), 7.01 (d, J = 8.7 Hz, 1H), 4.85 (q, J = 9.6 Hz, 2H), 3.35 (s, 3H). ^{13}C NMR (75 MHz, C_3D_6O) δ 159.5, 155.3, 152.5, 144.6, 130.5, 126.2 (q, J_{CF} =273.5 Hz), 121.7, 118.0, 110.6, 54.2 (q, J_{CF} = 32.0 Hz), 26.6. ^{19}F NMR (282 MHz, $CDCl_3$) δ -71.8. HRMS (ESI) *m/z* calcd for $C_{11}H_8BrF_3N_3NaO_3$ $[M+Na]^+$: 310.0410, found 310.0416.

6-chloro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1k)



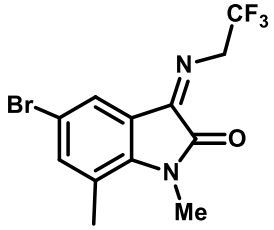
Ketimine **1k** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 2.01 g of **1k** in 72.8% yield as a yellow solid, mp = 129 – 130 ℃. ^{1}H NMR (300 MHz, CDCl3) δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 6.85 (s, 1H) 4.81 (q, *J* = 9.6 Hz, 2H), 3.22 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 158.4, 154.5, 147.2, 139.8, 124.9 (q, J_{CF} = 274.5 Hz), 123.9, 123.5, 118.8, 109.6, 53.6 (q, J_{CF} = 32.3 Hz), 25.9. ^{19}F NMR (282 MHz, CDCl3) δ −71.9. HRMS (ESI) *m/z* calcd for $C_{11}H_8ClF_3N_2NaO$ $[M+Na]^+$: 299.0169, found 299.0175.

7-chloro-1-methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1l)



Ketimine **1l** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 2.04 g of **1l** in 73.9% yield as a yellow solid, mp = 150 – 151℃. ^{1}H NMR (300 MHz, CDCl3) δ 7.64 (dd, *J* = 7.5, 0.6 Hz, 1H), 7.38 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.04 (t, *J* = 7.8 Hz, 1H), 4.81 (q, *J* = 9.7 Hz, 2H), 3.60 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 158.6, 154.6, 141.7, 135.8, 124.2, 123.1, 124.9 (q, J_{CF} = 274.7 Hz), 121.5, 116.2, 53.8 (q, J_{CF} = 32.3 Hz), 29.1. ^{19}F NMR (282 MHz, CDCl3) δ −71.9. HRMS (ESI) *m/z* calcd for $C_{11}H_8ClF_3N_2NaO$ $[M+Na]^+$: 299.0169, found299.0172.

omo-1,5-dimethyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one(1m)

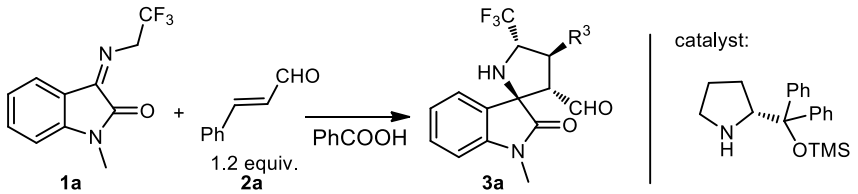


Ketimine **1m** was obtained according to **GP1**. Chromatography on a silica gel using hexane/AcOEt as an eluent afforded 2.30 g of **1m** in 68.9% yield as a yellow solid, mp = 178 –179 ℃. ^{1}H NMR (300 MHz, CDCl3) δ 7.67 (s, 1H), 7.32 (s, 1H), 4.80 (q, *J* = 9.7

Hz, 2H), 3.47 (s, 3H), 2.53 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 154.7, 142.9, 139.4, 125.1(q, J_{CF} = 274.2 Hz), 123.7, 122.6, 116.0, 53.8 (q, J_{CF} = 32.0 Hz), 29.1, 18.5. ^{19}F NMR (282 MHz, $CDCl_3$) δ −71.9. HRMS (ESI) *m/z* calcd for $C_{12}H_{10}BrF_3N_2NaO$ $[M+Na]^+$: 356.9821, found 356.9826.

C. Reaction Condition Optimization

Table 1: Optimization reaction conditions.[a]

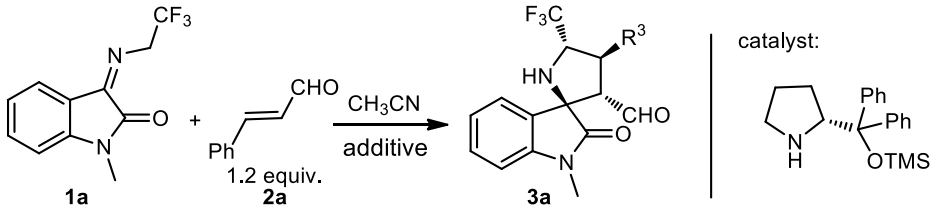


1a 2a 3a

entry	solvent	time [h]	yield [%][b]	dr[c]	ee [%][d]
1	DCM	40	98%	> 20:1	97%
2	THF	36	96%	> 20:1	99%
3	MTBE	44	94%	8:1	94%/55%
4	Tol	51	98%	> 20:1	93%
5	Et_2O	50	98%	> 20:1	92%
6	**CH_3CN**	**28**	**98%**	**> 20:1**	**99%**
7	DCE	28	98%	> 20:1	95%
8	MeOH	70	98%	> 20:1	88%

[a] Reactions were carried out with **1a** (0.2 mmol), **2a** (0.24 mmol), PhCOOH (0.02 mmol) and catalyst (0.02 mmol) in different solvents (0.1 M) at RT. [b] Yield of isolated **3a**. [c] Determined by crude ^{1}H and ^{19}F NMR or chiral phase HPLC analysis. [d] Determined by chiral phase HPLC analysis.

Table 2: Screening of different additives. [a].

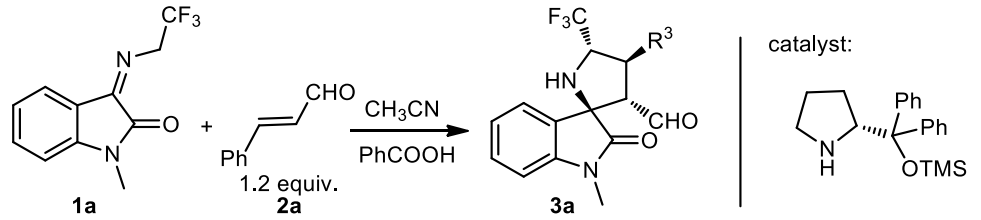


1a 2a 3a

entry	additive	time [h]	yield[%][b]	dr[c]	ee[%][d]
1	-	48	98%	> 20:1	98%
2	**PhCOOH**	**28**	**98%**	**> 20:1**	**99%**
3	AcOH	30	98%	> 20:1	93%
4[e]	pTsOH	-	-	-	-
5	Et_3N	-	-	-	-

[a] Reactions were carried out with **1a** (0.2 mmol), **2a** (0.24 mmol), corresponding additive (0.02 mmol) and catalyst (0.02 mmol) in CH_3CN (0.1 M) at RT. [b] Yield of isolated **3a**. [c] Determined by crude ^{1}H and ^{19}F NMR or chiral phase HPLC analysis. [d] Determined by chiral phase HPLC analysis. [e] Did not react.

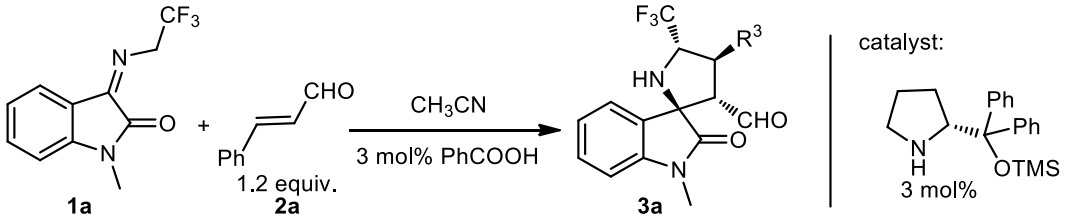
Table 3: Catalyst loading screening.[a]



entry	catalyst loading (eq.)	time [h]	yield[%][b]	dr[c]	ee[%][d]
1	0.1	28	99%	> 20:1	99%
2	0.06	32	98%	> 20:1	99%
3	**0.03**	**36**	**98%**	**> 20:1**	**99%**
4[e]	0.01	-	-	-	-

[a] Reactions were carried out with **1a** (0.2 mmol), **2a** (0.24 mmol), corresponding additive and catalyst in CH_3CN (0.1 M) at RT. [b] Yield of isolated **3a**. [c] Determined by crude ^1H and ^{19}F NMR or chiral phase HPLC analysis. [d] Determined by chiral phase HPLC analysis. [e] Did not react.

Table 4: Screening for reaction concentration.[a]



entry	reaction concentration[b]	time [h]	yield[%][c]	dr[d]	ee[%][e]
1	**0.2 M**	**24**	**98%**	> 20:1	**99%**
2	0.1 M	36	98%	> 20:1	99%
3	0.07 M	40	98%	-	97%
4	0.05 M	48	99%	-	97%

[a] Reactions were carried out with **1a** (0.2 mmol), **2a** (0.24 mmol), PhCOOH (3 mol%) and catalyst (3 mol%) in CH_3CN at RT. [b] Yield of isolated **3a**. [c] Controled by addition of different quantity of solvent. [d] Determined by crude ^1H and ^{19}F NMR or chiral phase HPLC analysis. [e] Determined by chiral phase HPLC analysis.

D. Representative Procedure

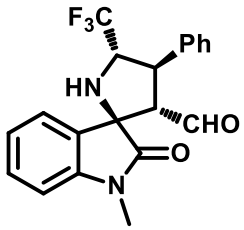
A vial equipped with a magnetic stir bar was charged with appropriate ketimine (0.2 mmol), the catalyst (0.006 mmol), benzoic acid (3 mol%) and anhydrous acetonitrile (1 mL) at room temperature. Corresponding aldehyde (0.24 mmol) was added in one portion and the reaction was stirred for the designated time, after which it was concentrated and purified by column chromatography. Enantiomeric ratios of the pure products were determined using chiral HPLC.

Racemates were prepared following the general procedure by combination of equivalent (*R*)-

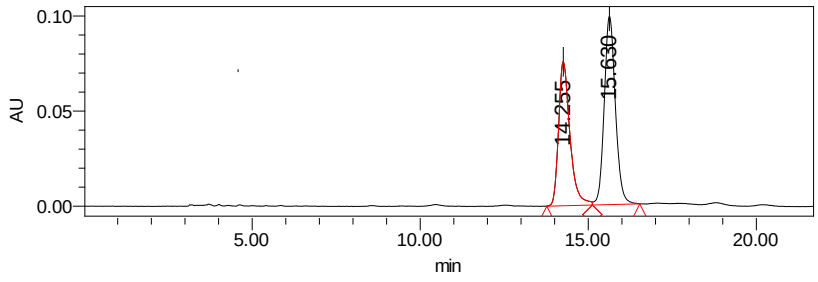
and (*S*)-catalysts.

E. Analytical Data and HPLC Chromatogram of the Addition Products

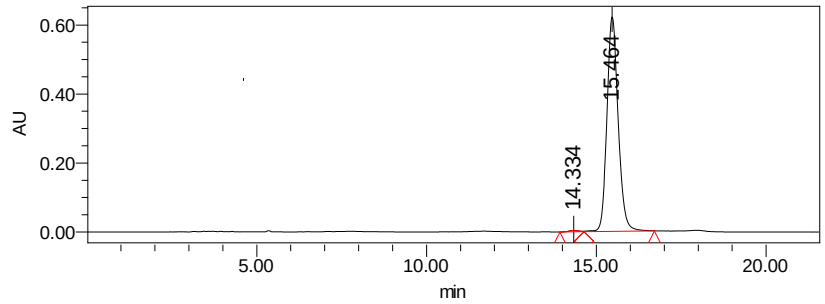
(2'*R*,3'*S*,4'*R*,5'*S*)-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3a)



From 48.4 mg (0.2 mmol) ketimine **1a** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 71.8 mg (96.0% yield) compound **3a** was obtained as a colorless solid, mp = 168 - 169 ℃. $[\alpha]_D^{20}$ = +35 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2-propanol 90:10, 1.0 mL/min). Retention time: *t*major = 15.5 and *t*minor = 14.3 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.08 (d, *J* = 1.6 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.38 – 7.26 (m, 5H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 7.7 Hz, 1H), 4.59 – 4.73 (m, 1H), 4.23 (t, *J* = 10.2 Hz, 1H), 3.64 (dd, *J* = 10.6, 1.6 Hz, 1H), 3.26 (s, 3H), 2.76 (d, *J* = 5.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.9, 176.8, 141.2, 135.7, 128.4, 127.3, 126.5, 126.3, 126.2, 123.8 (q, J_{CF} = 277.7 Hz), 123.7, 122.0, 107.2, 66.0, 64.4, 63.6 (q, J_{CF} = 29.3 Hz), 43.8, 25.0. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{20}H_{18}F_3N_2O_2$ $[M+H]^+$: 375.1315, found 375.1311.

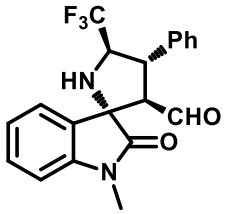


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		14.255	1784665	43.80	75808	BV	Unknown
2		15.630	2289820	56.20	99196	VB	Unknown

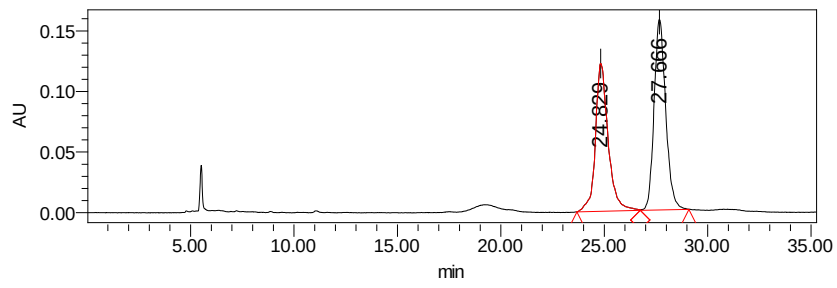


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		14.334	83584	0.58	3849	Bv	Unknown
2		15.464	14283336	99.42	621619	vB	Unknown

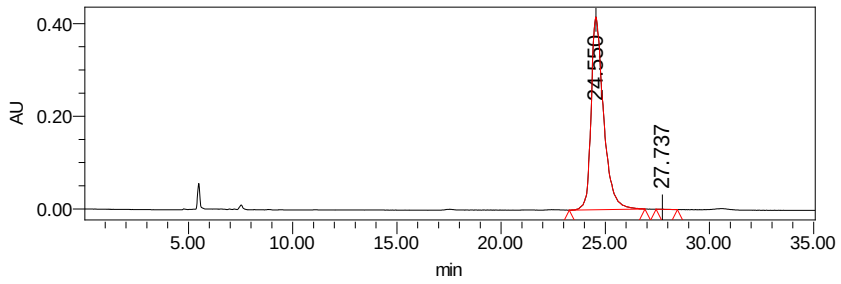
(2'*S*,3'*R*,4'*S*,5'*R*)-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3a')



From 48.4 mg (0.2 mmol) ketimine **1a** and cinnamaldehyde 30 µl (0.24 mmol, 1.2 equiv) using (*S*)-diphenylprolinol silyl ether as catalyst, 73.3 mg (98.0 % yield) compound **3a'** was obtained as a colorless solid, mp = 166 - 167 ℃. $[\alpha]_D^{20}$ = -48 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 95: 5, 1.0 mL/min). Retention time: t_{major} = 24.6 and t_{minor} = 27.7 min. 1H NMR (300 MHz, CDCl3) δ 9.08 (d, *J* = 1.6 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.38 – 7.25 (m, 5H), 7.13 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 7.7 Hz, 1H), 4.59 – 4.47 (m, 1H), 4.23 (t, *J* = 10.2 Hz, 1H), 3.63 (dd, *J* = 10.6, 1.5 Hz, 1H), 3.26 (s, 3H), 2.76 (d, *J* = 6.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.9, 176.8, 141.2, 135.7, 128.4, 127.3, 126.5, 126.3, 126.2, 123.8 (q, J_{CF} = 277.7 Hz), 123.7, 122.0, 107.2, 66.0, 64.4, 63.6 (q, J_{CF} = 29.3 Hz), 43.8, 25.0. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{20}H_{18}F_3N_2O_2$ $[M+H]^+$: 375.1315, found 375.1318.

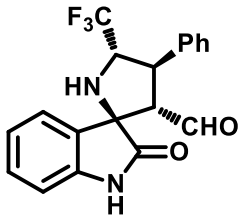


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		24.829	5219205	45.90	121979	BV	Unknown
2		27.666	6151015	54.10	157195	VB	Unknown

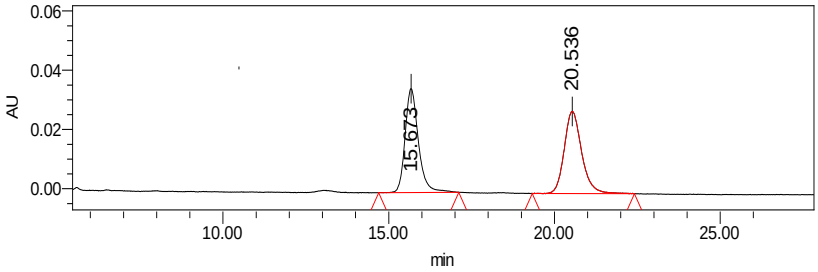


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		24.550	17242410	99.96	416113	bb	Unknown
2		27.737	7610	0.04	307	bb	Unknown

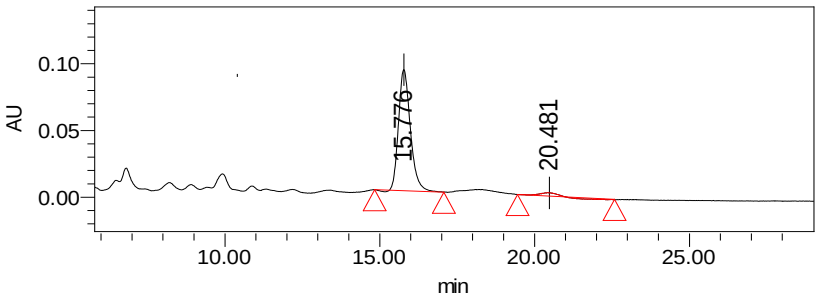
(2'*R*,3'*S*,4'*R*,5'*S*)-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3b)



From 45.6 mg (0.2 mmol) ketimine **1b** and cinnamaldehyde 30 µl (0.24 mmol, 1.2 equiv), 64.8 mg (90.0% yield) compound **3b** was obtained as a white solid , mp = 71 - 72 ℃. $[\alpha]_D^{20}$ = +46 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 88% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane /2–propanol / dichloromethane 95:5:5, 1.0 mL/min). Retention time: t_{major} = 15.8 and t_{minor} = 20.5 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.11 (d, *J* = 1.5 Hz, 1H), 8.55 (s, 1H), 7.48 – 7.45 (m, 2H), 7.38 – 7.27 (m, 5H), 7.12 (td, *J* = 7.7, 0.9 Hz, 1H), 6.92 (d, *J* = 7.7 Hz, 1H), 4.55 – 4.46 (m, 1H), 4.23 (t, *J* = 10.3 Hz, 1H), 3.66 (dd, *J* = 10.8, 1.4 Hz, 1H), 2.59 (s, 1H). 13C NMR (75 MHz, CDCl3) δ 194.9, 179.4, 138.2, 135.4, 128.4, 127.4, 126.9, 126.5, 126.3, 124.0, 123.7 (q, J_{CF} = 277.8 Hz), 122.1, 109.1, 66.5, 64.4, 63.7 (q, J_{CF} = 29.3 Hz), 43.78. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9. HRMS (ESI) *m/z* calcd for $C_{19}H_{16}F_3N_2O_2$ $[M+H]^+$: 361.1158, found 361.1157.



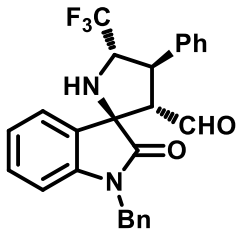
	名称	保留时间	面积	% 面积	高度	积分类型	峰类型
1		15.673	981065	49.21	35082	bb	未知
2		20.536	1012633	50.79	27719	bb	未知



	名称	保留时间	面积	% 面积	高度	积分类型	峰类型
1		15.776	2446957	93.97	90613	bb	未知
2		20.481	156884	6.03	2456	bb	未知

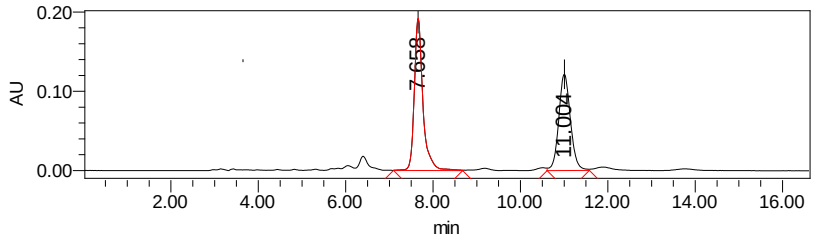
hexane /2–propanol / dichloromethane 95:5:5, 1.0 mL/min)

(2'*R*,3'*S*,4'*R*,5'*S*)-1-benzyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3c)

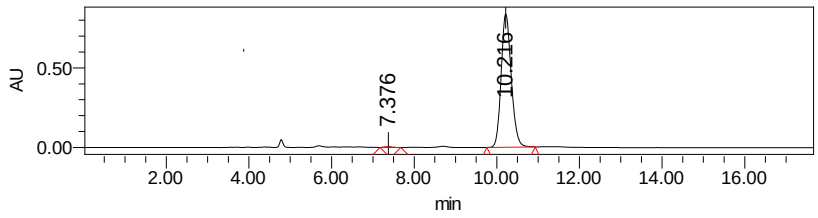


From 63.6 mg (0.2 mmol) ketimine **1c** and cinnamaldehyde 30 µl (0.24 mmol, 1.2 equiv), 80.1 mg (89.0% yield) compound **3c** was obtained as a white solid, mp = 70 - 71 ℃. $[\alpha]_D^{20}$ = +25 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 70:30, 1.0

mL/min). Retention time: t_{major} = 10.2 and t_{minor} = 7.4 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (d, *J* = 1.6, 1H), 7.50 – 7.47 (m, 2H), 7.39 – 7.26 (m, 8H), 7.25 – 7.18 (m, 2H), 7.08 (td, *J* = 7.6, 0.8, 1H), 6.75 (d, *J* = 7.7, 1H), 4.93 (dd, *J* = 68.4, 15.6, 2H), 4.58 – 4.48 (m, 1H), 4.26 (t, *J* = 10.4, 1H), 3.72 (dd, *J* = 10.9, 1.5, 1H), 2.86 (d, *J* = 7.0, 1H). 13C NMR (75 MHz, CDCl3) δ 196.4, 178.7, 142.0, 137.2, 135.1, 130.0, 129.1, 129.0, 128.3, 128.2, 128.0, 128.0, 127.2, 125.5 (q, J_{CF} = 277.8 Hz), 125.4, 123.8, 109.9, 67.9, 66.6, 65.5 (q, J_{CF} = 29.3 Hz), 45.7, 44.3. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{26}H_{22}F_3N_2O_2$ $[M+H]^+$: 451.1628, found 451.1627.

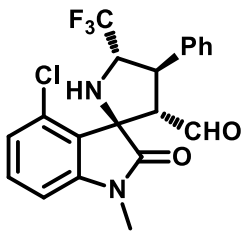


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		7.658	2631784	53.78	191849	VV	Unknown
2		11.004	2261456	46.22	121575	VV	Unknown

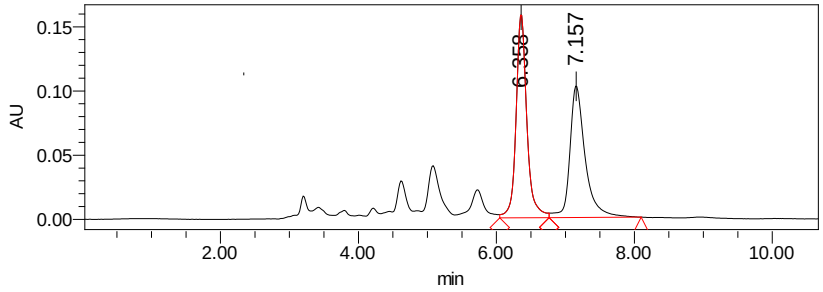


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		7.376	54418	0.38	3871	VV	Unknown
2		10.216	14189778	99.62	838884	bb	Unknown

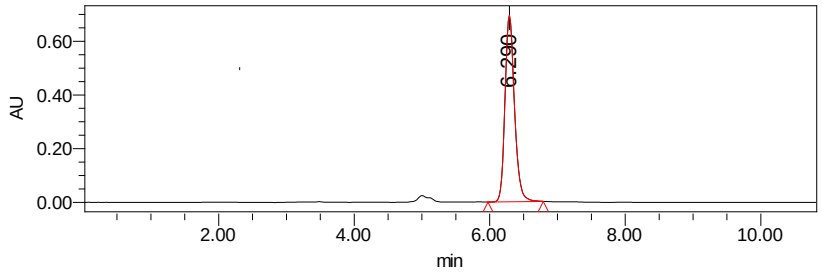
(2'*R*,3'*S*,4'*R*,5'*S*)-4-chloro-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3, 2'-pyrrolidine]-3'-carbaldehyde(3d)



From 55.2 mg (0.2 mmol) ketimine **1d** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 75.9 mg (93.0% yield) compound **3d** was obtained as a white solid, mp = 76 - 77 ℃. $[\alpha]_D^{20}$ = -11 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 70:30, 1.0 mL/min). Retention time: t_{major} = 6.3 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.48 (d, *J* = 1.0 Hz, 1H), 7.53 – 7.50 (m, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.05 (d, *J* = 8.2 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 4.59 (d, *J* = 3.8 Hz, 1H), 4.30 (t, *J* = 10.4 Hz, 1H), 3.60 (d, *J* = 10.6 Hz, 1H), 3.26 (s, 3H), 2.59 (s, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 197.0, 179.2, 145.2, 137.6, 131.7, 131.5, 129.1, 128.3, 127.9, 125.2 (q, J_{CF} = 277.8 Hz), 124.8, 123.9, 107.5, 67.8, 66.4, 65.6 (q, J_{CF} = 19.7 Hz), 46.9, 26.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.1. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O_2$ $[M+H]^+$: 409.0925, found 409.0926.

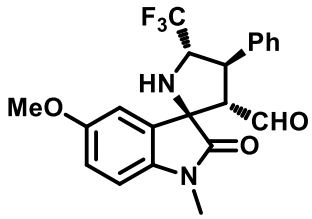


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		6.358	1714801	51.99	158926	VV	Unknown
2		7.157	1583651	48.01	102798	VB	Unknown

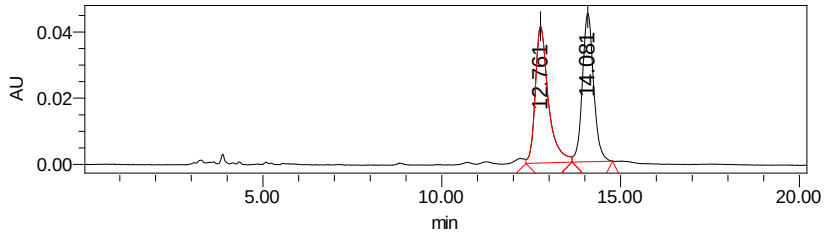


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		6.290	6751790	100.00	694476	bb	Unknown

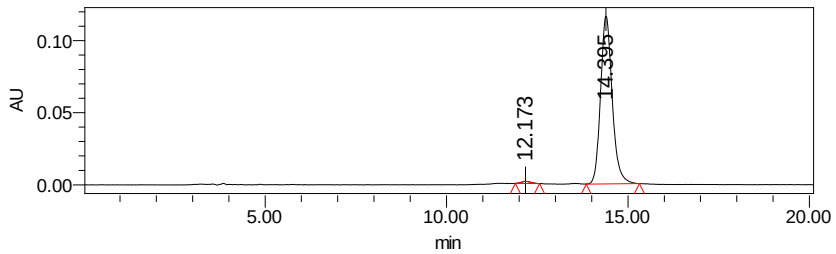
(2'*R*,3'*S*,4'*R*,5'*S*)-5-methoxy-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3e)



From 54.4 mg (0.2 mmol) ketimine **1e** and cinnamaldehyde 30 µl (0.24 mmol, 1.2 equiv), 74.5 mg (95.0% yield) compound **3e** was obtained as a white solid, mp = 69 - 70 ℃. $[\alpha]_D^{20}$ = -21 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 98% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane /2–propanol/ dichloromethane 95:5:0.5, 1.0 mL/min). Retention time: t_{major} = 14.4 and t_{minor} = 12.2 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.08 (d, *J* = 1.5 Hz, 1H), 7.49 – 7.47 (m, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.27 (m, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 6.85 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 1H), 4.58 – 4.46(m, 1H), 4.21 (t, *J* = 10.3 Hz, 1H), 3.79 (s, 3H), 3.64 (dd, *J* = 10.7, 1.4 Hz, 1H), 3.23 (s, 3H), 2.80 (d, *J* = 6.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.8, 176.5, 155.0, 135.6, 134.4, 127.8, 127.3, 126.5, 126.2, 123.8 (q, J_{CF} = 277.8 Hz), 112.6, 110.9, 107.6, 66.4, 64.5, 63.7 (q, J_{CF} = 29.3 Hz), 54.1, 43.7, 25.1. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}F_3N_2O_3$ $[M+H]^+$: 405.1421, found 405.1419.



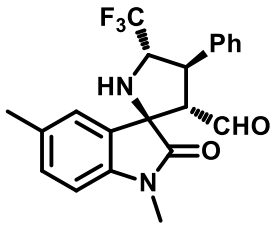
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		12.761	1046461	51.66	41338	VV	Unknown
2		14.081	979395	48.34	44872	VB	Unknown



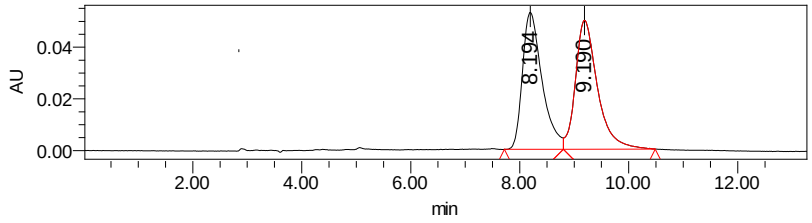
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		12.173	26743	1.02	1501	BB	Unknown

2		14.395	2595321	98.98	116405	BB	Unknown

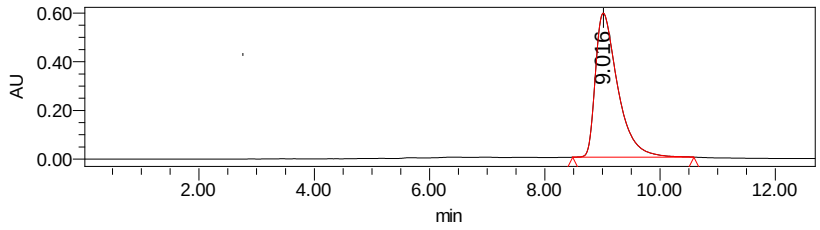
(2'*R*,3'*S*,4'*R*,5'*S*)-1,5-dimethyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3f)



From 51.2 mg (0.2 mmol) ketimine **1f** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 71.4 mg (92.0% yield) compound **3f** was obtained as a white solid, mp = 148 - 149 ℃. $[\alpha]_D^{20}$ = +9 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel OD-H column, hexane/2–propanol 85:15, 1.0 mL/min). Retention time: t_{major} = 9.0 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.08 (d, *J* = 1.3 Hz, 1H), 7.49 (d, *J* = 7.3 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.75 (d, *J* = 8.0 Hz, 1H), 4.59 – 4.48 (m, 1H), 4.21 (t, *J* = 10.2 Hz, 1H), 3.63 (dd, *J* = 10.5, 1.1 Hz, 1H), 3.24 (s, 3H), 2.73 (d, *J* = 6.8 Hz, 1H), 2.35 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 195.6, 177.5, 139.5, 136.4, 132.5, 129.3, 127.9, 127.2, 126.9, 126.8, 125.0, 124.4 (q, J_{CF} = 277.8 Hz), 107.6, 66.7, 65.0, 64.3 (q, J_{CF} = 29.3 Hz), 44.3, 25.7, 20.1. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}F_3N_2O_2$ $[M+H]^+$: 389.1471, found 389.1468.

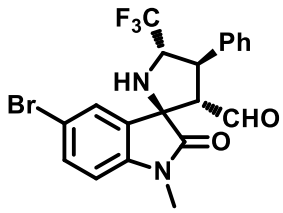


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		8.194	1326441	48.70	53019	BV	Unknown
2		9.190	1397519	51.30	49900	Vb	Unknown

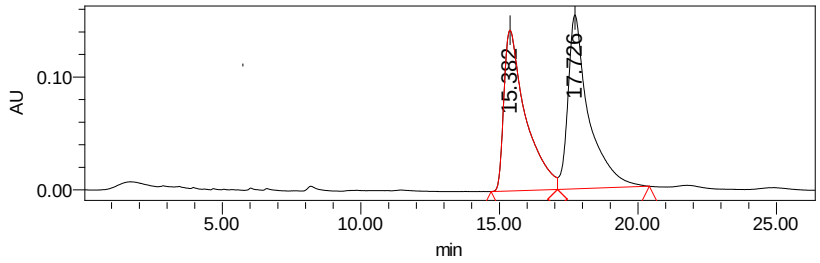


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		9.016	15922096	100.00	592000	bb	Unknown

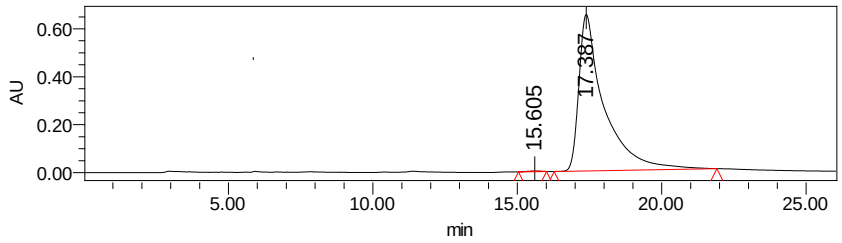
(2'*R*,3'*S*,4'*R*,5'*S*)-5-bromo-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3g)



From 64.0 mg (0.2 mmol) ketimine **1g** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 85.9 mg (95.0% yield) compound **3g** was obtained as a white solid, mp = 77 - 78 ℃. $[\alpha]_D^{20}$ = -55 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel AD-H column, hexane/2–propanol 90:10, 1.0 mL/min). Retention time: t_{major} = 17.4 and t_{minor} = 15.6 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.14 (d, *J* = 1.6 Hz, 1H), 7.49 – 7.46 (m, 4H), 7.39 – 7.37 (m, 2H), 7.35 – 7.29 (m, 1H), 6.77 – 6.74 (m, 1H), 4.57 – 4.45 (m, 1H), 4.18 (t, *J* = 10.4 Hz, 1H), 3.63 (dd, *J* = 10.9, 1.6 Hz, 1H), 3.26 (s, 3H), 2.75 (d, *J* = 6.7 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 195.3, 176.9, 140.9, 135.8, 131.9, 129.3, 128.1, 127.4, 127.1, 127.0, 124.3 (q, J_{CF} = 276.8 Hz), 115.4, 109.3, 66.6, 65.1, 64.3 (q, J_{CF} = 29.3 Hz), 44.5, 25.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}BrF_3N_2O_2$ $[M+H]^+$: 453.0420, found 453.0420. 25.75

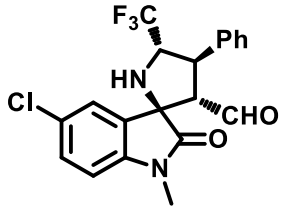


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		15.382	7755847	49.19	142479	BV	Unknown
2		17.726	8012813	50.81	154048	VB	Unknown

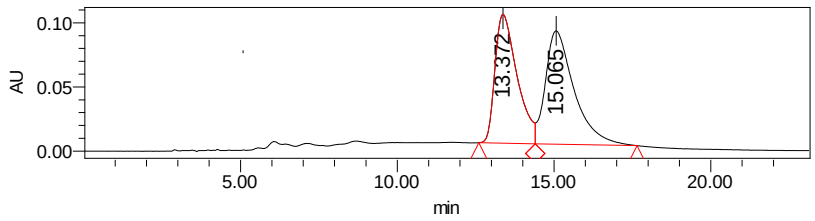


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		15.605	74059	0.19	2261	bb	Unknown
2		17.387	39583860	99.81	652846	BB	Unknown

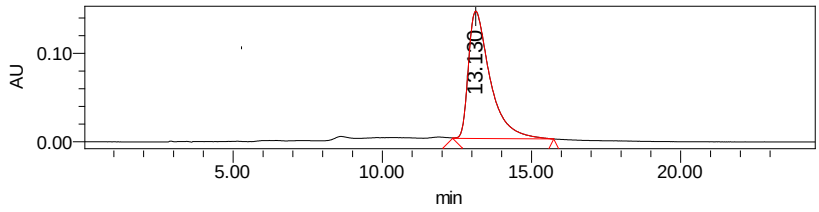
(2'*R*,3'*S*,4'*R*,5'*S*)-5-chloro-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3, 2'-pyrrolidine]-3'-carbaldehyde(3h)



From 55.2 mg (0.2 mmol) ketimine **1h** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 76.7 mg (94.0% yield) compound **3h** was obtained as a white solid, mp = 69 - 70 ℃. $[\alpha]_D^{20}$ = -35 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel OD-H column, hexane/2–propanol 85:15, 1.0 mL/min). Retention time: t_{major} = 13.1 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.13 (d, *J* = 1.6 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.40 – 7.29 (m, 5H), 6.80 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.54 – 4.47 (m, 1H), 4.18 (t, *J* = 10.4 Hz, 1H), 3.64 (dd, *J* = 10.9, 1.6 Hz, 1H), 3.26 (s, 3H), 2.76 (d, *J* = 6.7 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 196.2, 178.1, 141.4, 136.8, 130.0, 130.0, 129.3, 129.1, 128.2, 128.0, 125.7, 125.3 (q, J_{CF} = 277.8 Hz), 109.8, 67.7, 66.2, 65.4 (q, J_{CF} =29.5 Hz), 45.5, 26.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O_2$ $[M+H]^+$: 409.0925, found 409.0923.

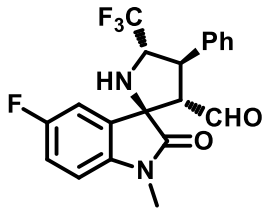


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		13.372	4928357	46.73	100450	BV	Unknown
2		15.065	5616980	53.27	88334	VB	Unknown



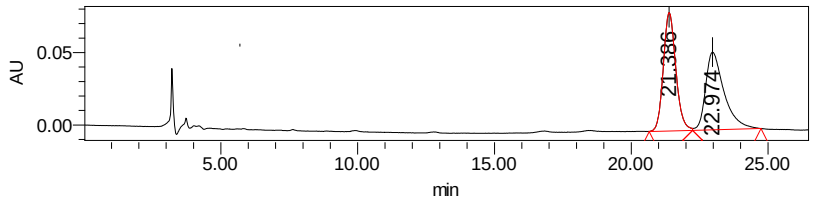
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		13.130	7287904	100.00	144129	VB	Unknown

(2'*R*,3'*S*,4'*R*,5'*S*)-5-fluoro-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3, 2'-pyrrolidine]-3'-carbaldehyde(3i)

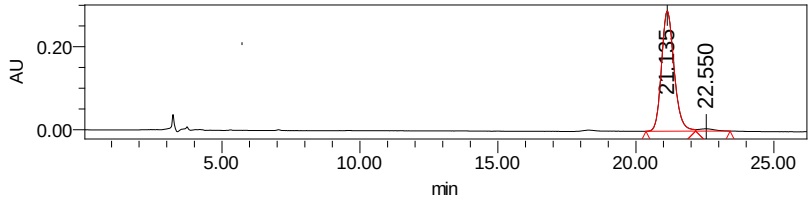


From 52.0 mg (0.2 mmol) ketimine **1i** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 72.1 mg (92.0% yield) compound **3i** was obtained as a white solid, mp = 67 - 68 ℃. $[\alpha]_D^{20}$ = +20 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 95% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane /2–propanol / dichloromethane 95:5:5, 1.0 mL/min). Retention time: t_{major} = and t_{minor} = min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.11 (d, *J* = 1.6 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.39 – 7.34 (m, 2H), 7.32 – 7.28 (m, 1H), 7.13 (dd, *J* = 7.6, 2.5 Hz, 1H), 7.05 (td, *J* = 8.7, 2.6 Hz, 1H), 6.81 (dd, *J* = 8.5, 4.0 Hz, 1H), 4.56 – 4.44 (m, 1H), 4.18 (t, *J* = 10.4 Hz, 1H), 3.66 (dd, *J* = 11.0, 1.5 Hz, 1H), 3.26 (s, 3H), 2.80 (d, *J* = 6.9 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 196.4, 178.1, 159.6 (d, J_{CF} =240 Hz), 138.8 (d, J_{CF} =2.25 Hz), 137.0, 130.1 (d, J_{CF} =7.5 Hz), 129.1, 128.2, 128.0, 125.5 (q, J_{CF} = 277.8 Hz), 116.4 (d, J_{CF} =22.5 Hz), 113.5 (d, J_{CF} =22.5 Hz), 109.6 (d,

J_{CF} =7.5 Hz), 68.0 (d, J_{CF} =1.5 Hz), 66.3, 65.4 (q, J_{CF} = 29.3 Hz), 45.5, 26.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -75.0, -118.2. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}F_4N_2O_2$ $[M+H]^+$: 393.1221, found 393.1221.

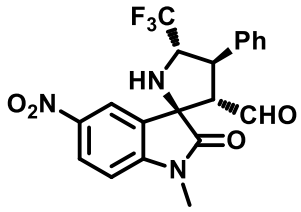


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		21.386	2596341	50.78	81656	BV	Unknown
2		22.974	2516779	49.22	53611	VB	Unknown



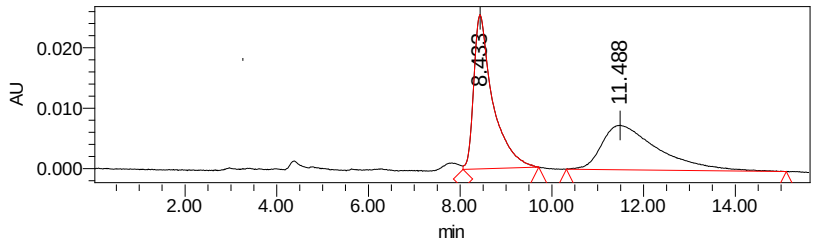
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		21.135	9195383	97.61	289391	BV	Unknown
2		22.550	225590	2.39	5531	VB	Unknown

(2'*R*,3'*S*,4'*R*,5'*S*)-1-methyl-5-nitro-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3j)

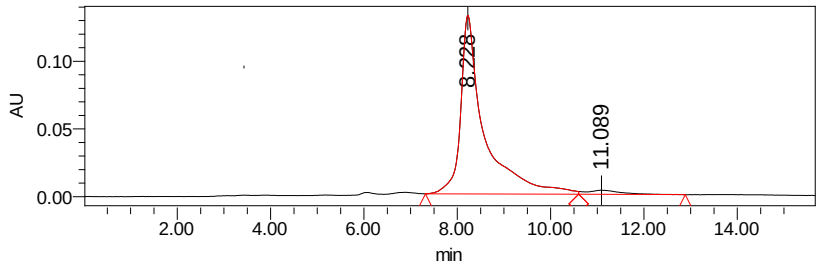


From 57.4 mg (0.2 mmol) ketimine **1j** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 78.6 mg (58.0% yield) compound **3j** was obtained as a yellow solid, mp = 117 - 118 ℃. $[\alpha]_D^{20}$ = -73 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^{1}H and ^{19}F NMR analysis. 94% ee was determined by HPLC analysis (Daicel Chiralcel AD-H column, hexane/2–propanol 70:30, 1.0 mL/min). Retention time: t_{major} = 8.2 and t_{minor} = 11.1 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.19 (d, *J* = 1.5 Hz, 1H), 8.32 (dd, *J* = 8.6, 2.2 Hz, 1H), 8.24

(d, *J* = 2.2 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.34 – 7.30 (m, 1H), 6.98 (d, *J* = 8.6 Hz, 1H), 4.55 – 4.48 (m, 1H), 4.23 (t, *J* = 10.5 Hz, 1H), 3.68 (dd, *J* = 11.4, 1.4 Hz, 1H), 3.35 (s, 3H), 2.83 (d, *J* = 6.5 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ196.2, 178.6, 148.3, 144.1, 136.1, 129.7, 129.3, 128.3, 128.09, 127.0, 120.9, 125.1 (q, J_{CF} = 277.3 Hz), 108.6, 67.3, 66.4, 65.4 (q, J_{CF} = 29.5 Hz), 45.9, 27.3.^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}F_3N_3O_4$ $[M+H]^+$: 420.1166, found 420.1160.

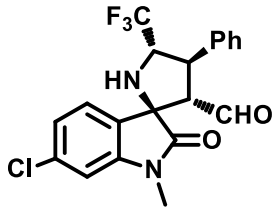


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		8.433	728558	53.66	25480	VB	Unknown
2		11.488	629218	46.34	7346	bb	Unknown



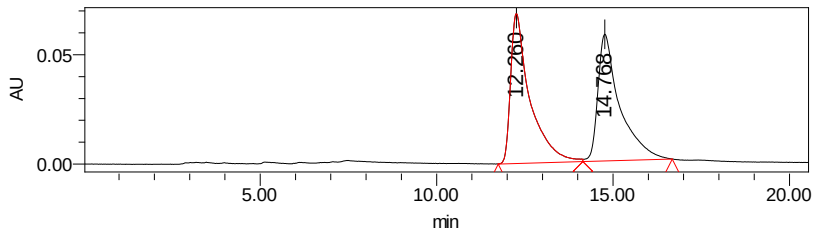
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		8.228	4621787	96.84	131920	bv	Unknown
2		11.089	150870	3.16	2997	vb	Unknown

(2'*R*,3'*S*,4'*R*,5'*S*)-6-chloro-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3, 2'-pyrrolidine]-3'-carbaldehyde(3k)

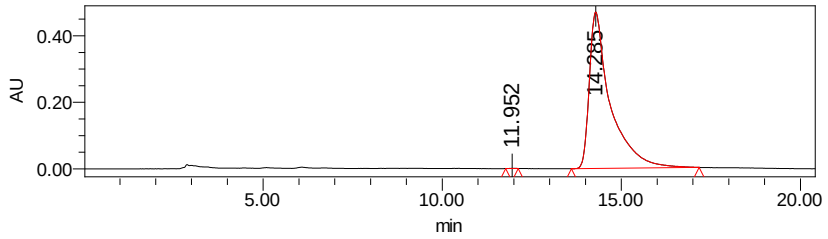


From 55.2 mg (0.2 mmol) ketimine **1k** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 75.9 mg (93.0% yield) compound **3k** was obtained as a colorless solid, mp = 171 - 172 ℃. $[\alpha]_D^{20}$ = +26 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^{1}H and ^{19}F NMR

analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel AD-H column, hexane/2–propanol 90:10, 1.0 mL/min). Retention time: t_{major} = 14.3 and t_{minor} = 12.0 min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (s, 1H), 7.46 (d, *J* = 7.4 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.30 – 7.26 (m, 2H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.87 (s, 1H), 4.57 – 4.45 (m, 1H), 4.19 (t, *J* = 10.3 Hz, 1H), 3.63 (d, *J* = 10.7 Hz, 1H), 3.25 (s, 3H), 2.74 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 196.2, 178.5, 144.0, 137.0, 136.0, 129.1, 128.2, 128.0, 126.5, 126.4, 125.3 (q, J_{CF} = 277.8 Hz), 123.6, 109.7, 67.4, 66.1, 65.3 (q, J_{CF} = 29.5 Hz), 45.5, 26.9. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O_2$ $[M+H]^+$: 409.0925, found 409.0925.

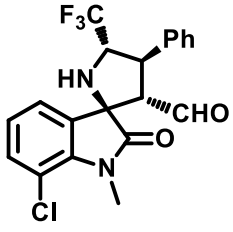


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		12.260	2606480	51.07	68604	BV	Unknown
2		14.768	2497015	48.93	57985	VB	Unknown

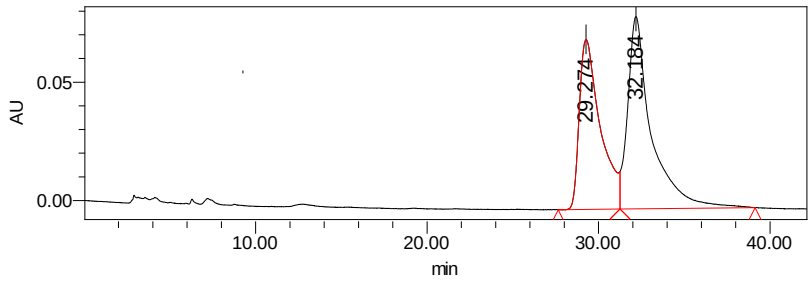


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		11.952	7014	0.04	577	BB	Unknown
2		14.285	19179254	99.96	470292	BB	Unknown

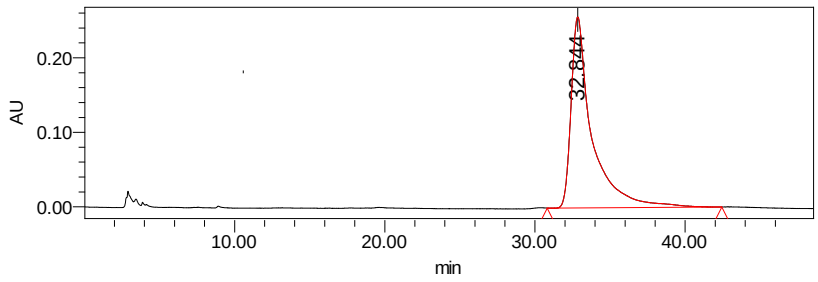
(2'*R*,3'*S*,4'*R*,5'*S*)-7-chloro-1-methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3, 2'-pyrrolidine]-3'-carbaldehyde(3l)



From 55.2 mg (0.2 mmol) ketimine **1l** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 76.7 mg (94.0% yield) compound **3l** was obtained as a white solid, mp = 57 - 58 ℃. $[\alpha]_D^{20}$ = +25 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel AD-H column, hexane/2–propanol 95:5, 1.0 mL/min). Retention time: t_{major} = 32.8 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.08 (d, *J* = 1.4 Hz, 1H), 7.48 – 7.45 (m, 2H), 7.39 – 7.33 (m, 2H), 7.31 – 7.23 (m, 3H), 7.05 (t, *J* = 7.5 Hz, 1H), 4.58 – 4.47 (m, 1H), 4.19 (t, *J* = 10.3 Hz, 1H), 3.65 – 3.61 (m, 4H), 2.73 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 195.2, 178.1, 137.7, 136.0, 131.2, 130.1, 128.0, 127.1, 126.9, 123.5, 123.0, 124.3 (q, J_{CF} = 278.0 Hz), 115.3, 66.1, 65.3, 64.2 (q, J_{CF} = 29.3 Hz), 44.2, 29.2. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O_2$ $[M+H]^+$: 409.0925, found 409.0925.

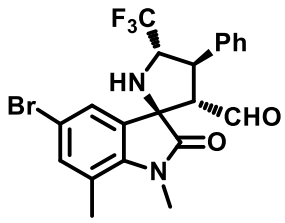


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		29.274	6124504	44.09	71775	bv	Unknown
2		32.184	7765161	55.91	81219	vb	Unknown

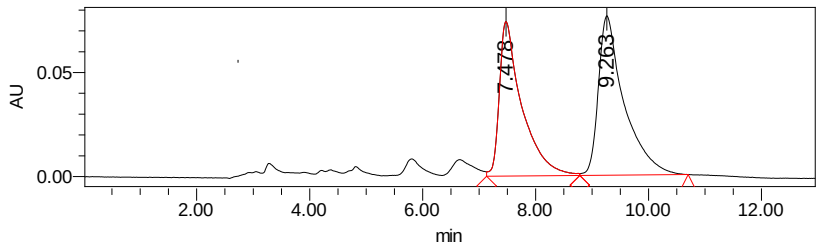


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		32.844	24694299	100.00	256172	bb	Unknown

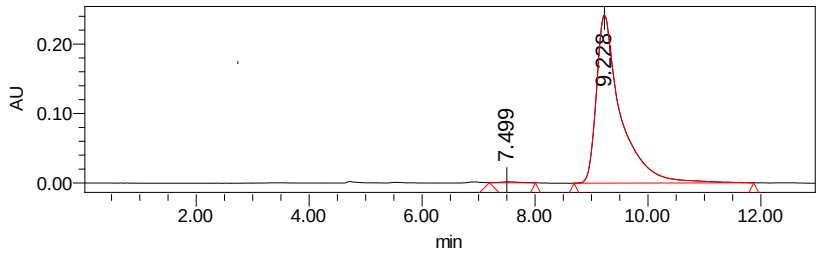
(2'*R*,3'*S*,4'*R*,5'*S*)-5-bromo-1,7-dimethyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3m)



From 66.8 mg (0.2 mmol) ketimine **1m** and cinnamaldehyde 30 μl (0.24 mmol, 1.2 equiv), 85.8 mg (92.0% yield) compound **3m** was obtained as a white solid, mp = 78 - 79 ℃. $[\alpha]_D^{20}$ = -32 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 99% ee was determined by HPLC analysis (Daicel Chiralcel AD-H column, hexane/2–propanol 70:30, 1.0 mL/min). Retention time: t_{major} = 9.2 and t_{minor} = 7.5 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.10 (d, *J* = 1.5 Hz, 1H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.30 – 7.28 (m, 2H), 7.22 (s, 1H), 4.55 – 4.74 (m, 1H), 4.16 (t, *J* = 10.3 Hz, 1H), 3.58 (dd, *J* = 10.8, 1.4 Hz, 1H), 3.51 (s, 3H), 2.72 (d, *J* = 6.0 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (75 MHz, CDCl3) δ 196.4, 179.1, 139.7, 136.9, 136.2, 130.9, 129.1, 128.2, 128.0, 126.3, 125.3 (q, J_{CF} = 277.8 Hz), 122.5, 116.2, 67.0, 66.3, 65.3 (q, J_{CF} = 29.5 Hz), 45.4, 30.2, 18.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{21}H_{19}BrF_3N_2O_2$ $[M+H]^+$: 467.0577, found 467.0556.



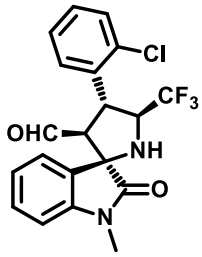
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		7.478	2051319	45.92	74196	VV	Unknown
2		9.263	2416081	54.08	76623	VB	Unknown



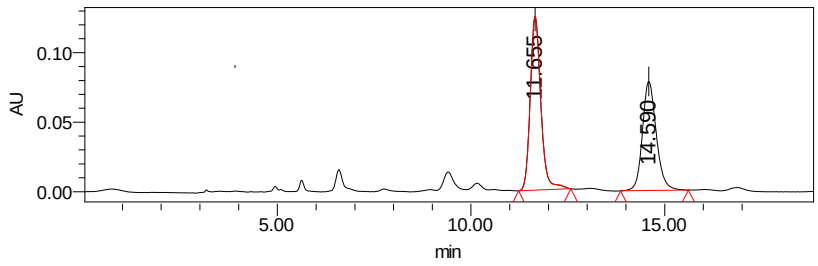
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		7.499	35634	0.49	1379	VB	Unknown

2		9.228	7209609	99.51	242243	Bb	Unknown

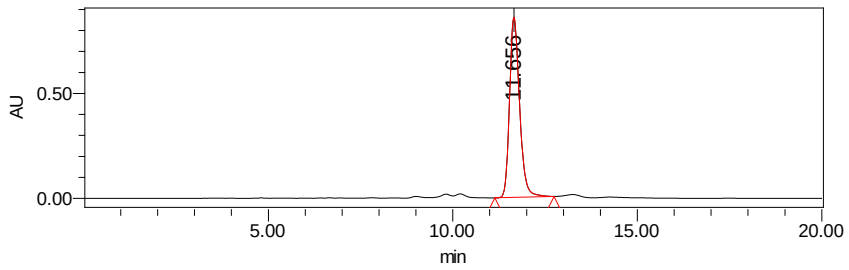
(2'*R*,3'*S*,4'*R*,5'*S*)-4'-(2-chlorophenyl)-1-methyl-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3n)



From 48.4 mg (0.2 mmol) ketimine **1a** and 2-chlorocinnamaldehyde 40.0 mg (0.24 mmol, 1.2 equiv), 72.6 mg (89.0% yield) compound **3n** was obtained as a white solid, mp = 178 - 179 ℃. $[\alpha]_D^{20}$ = +44 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 11.7 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.16 (d, *J* = 2.1Hz, 1H), 7.64 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.45 – 7.29 (m, 4H), 7.25 – 7.13 (m, 2H), 6.87 (d, *J* = 7.8 Hz, 1H), 4.93 (t, *J* = 10.3 Hz, 1H), 4.60 – 4.48 (m, 1H), 3.65 (d, *J* = 10.3 Hz, 1H), 3.26 (s, 3H), 2.82 (d, *J* = 7.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 178.2, 142.9, 134.7, 134.4, 130.1, 129.0, 128.0, 127.7, 125.3, 125.3 (q, J_{CF} = 277.0 Hz), 123.8, 108.9, 68.0, 66.1, 65.0 (q, J_{CF} = 29.0 Hz), 41.6, 26.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -75.3. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O_2$ $[M+H]^+$: 409.0925, found 409.0916.

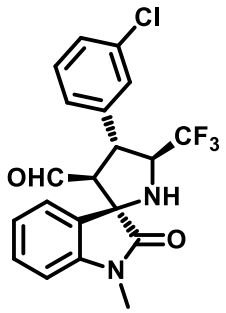


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		11.655	2377841	54.90	125052	bb	Unknown
2		14.590	1953458	45.10	78406	Bb	Unknown

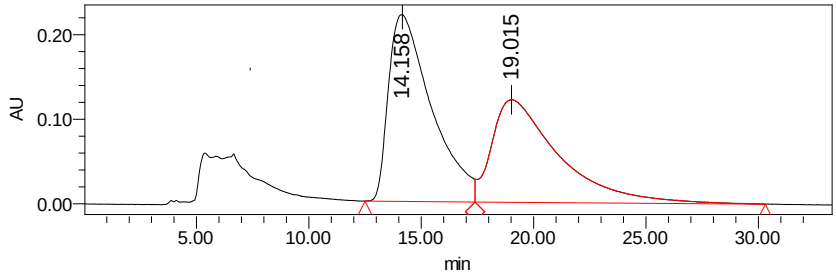


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		11.656	16201373	100.00	858770	bb	Unknown

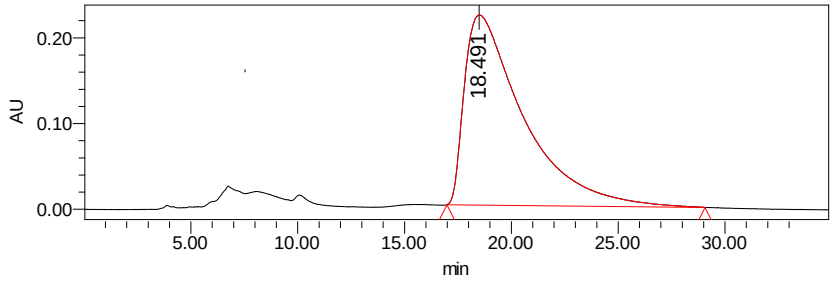
(2'*R*,3'*S*,4'*R*,5'*S*)-4'-(3-chlorophenyl)-1-methyl-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3o)



From 48.4 mg (0.2 mmol) ketimine **1a** and 3-chlorocinnamaldehyde 40.0 mg (0.24 mmol, 1.2 equiv), 75.1 mg (92.0% yield) compound **3o** was obtained as a white solid, mp = 67 - 68 ℃. $[\alpha]_D^{20}$ = +15 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel OB-H column, hexane/2–propanol 80: 20, 1.0 mL/min). Retention time: t_{major} = 18.5 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.07 (d, *J* = 1.2 Hz, 1H), 7.50 (d, *J* = 1.8 Hz, 1H), 7.41 – 7.24 (m, 5H), 7.14 (td, *J* = 7.7, 0.5 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 4.59 – 4.47 (m, 1H), 4.19 (t, *J* = 10.1 Hz, 1H), 3.60 (dd, *J* = 10.3, 1.1 Hz, 1H), 3.28 (s, 3H), 2.72 (d, *J* = 6.6 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 196.1, 178.6, 142.9, 139.8, 134.7, 130.3, 130.2, 128.4, 128.1, 127.6, 126.6, 125.4, 125.3 (q, J_{CF} = 278.0 Hz), 123.8, 108.9, 67.6, 65.8, 65.0 (q, J_{CF} = 29.5 Hz), 44.8, 26.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}ClF_3N_2O_2$ $[M+H]^+$: 409.0925, found 409.0915.

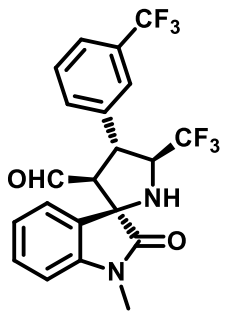


	名称	保留时间	面积	% 面积	高度	积分类型	峰类型
1		14.158	29343010	53.97	220684	bv	未知
2		19.015	25021867	46.03	121348	vb	未知



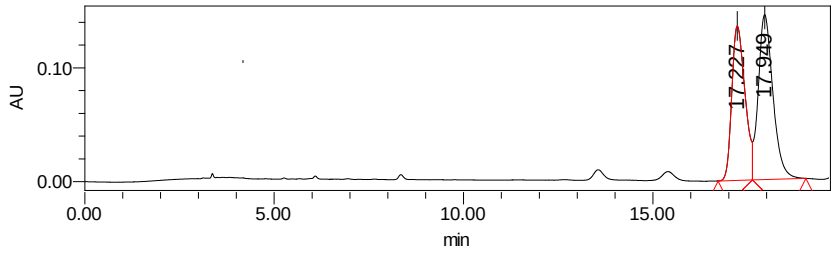
	名称	保留时间	面积	% 面积	高度	积分类型	峰类型
1		18.491	42601494	100.00	221802	bb	未知

(2'*R*,3'*S*,4'*R*,5'*S*)-1-methyl-2-oxo-5'-(trifluoromethyl)-4'-(3-(trifluoromethyl)phenyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3p)

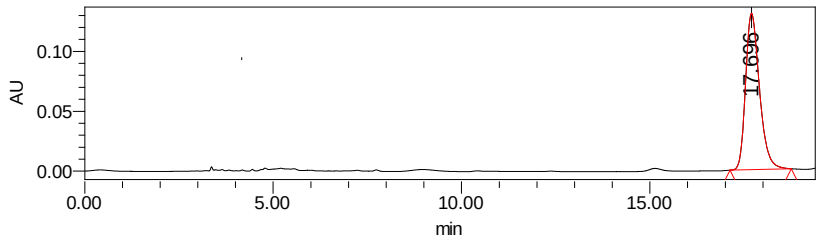


From 48.4 mg (0.2 mmol) ketimine **1a** and 3-trifluorocinnamaldehyde 48.0 mg (0.24 mmol, 1.2 equiv), 80.5 mg (91.0% yield) compound **3p** was obtained as a white solid, mp = 57 - 58 ℃. $[\alpha]_D^{20}$ = +21 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 95:5, 1.0 mL/min). Retention time: t_{major} = 17.7 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.08 (d, *J* = 1.1 Hz, 1H), 7.73 (d, *J* = 9.2 Hz, 2H), 7.56 – 7.47 (m, 2H), 7.39

– 7.26 (m, 2H), 7.14 (td, J = 7.6, 0.8 Hz, 1H), 6.89 (d, J = 7.8 Hz, 1H), 4.63 – 4.51 (m, 1H), 4.29 (t, J = 10.0 Hz, 1H), 3.63 (dd, J = 10.2, 0.9 Hz, 1H), 3.28 (s, 3H), 2.74 (d, J = 6.5 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ 196.0, 178.6, 142.9, 138.9, 131.8, 131.3 (q, J_{CF} = 32.3Hz), 130.3, 129.6, 127.4, 125.5, 125.2 (q, J_{CF} = 278.0 Hz), 125.1(q, J_{CF} = 3.8 Hz), 124.8 (q, J_{CF} = 3.5 Hz), 123.9 (q, J_{CF} = 271.0 Hz), 123.8, 108.9, 67.5, 65.7, 65.1 (q, J_{CF} = 30.2 Hz), 44.8, 26.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.5, -74.9. HRMS (ESI) *m/z* calcd for $C_{21}H_{17}F_6N_2O_2$ $[M+H]^+$: 443.1189, found 443.1175.

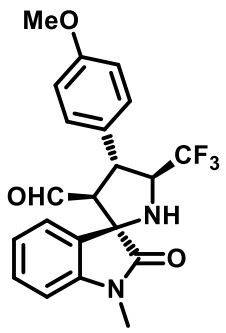


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		17.227	3284685	45.64	135590	BV	Unknown
2		17.949	3912169	54.36	145067	VB	Unknown

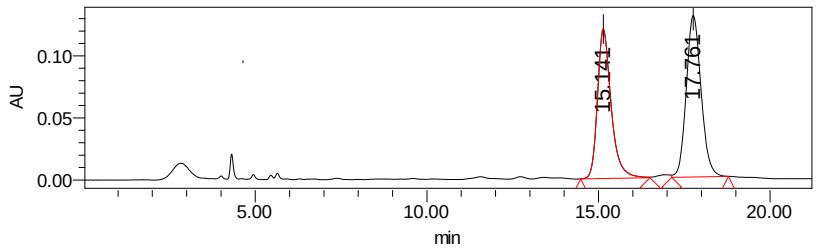


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		17.696	3341270	100.00	130586	BB	Unknown

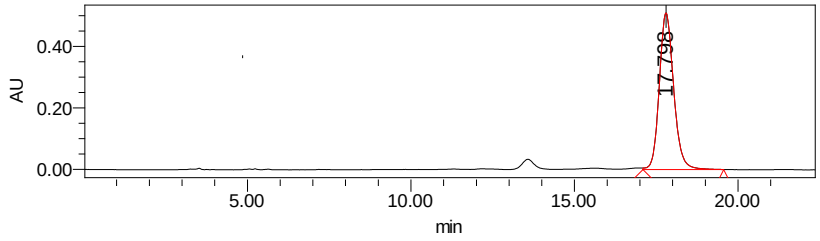
(2'*R*,3'*S*,4'*R*,5'*S*)-4'-(4-methoxyphenyl)-1-methyl-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3q)



From 48.4 mg (0.2 mmol) ketimine **1a** and 4-methoxy cinnamaldehyde 38.8 mg (0.24 mmol, 1.2 equiv), 66.3 mg (82.0% yield) compound **3q** was obtained as a white solid, mp = 69 - 70 ℃. $[\alpha]_D^{20}$ = -5 (c = 1.0, $CHCl_3$). Dr (10:1) determined by ^1H and ^{19}F and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 17.8 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.19 (d, *J* = 2.2 Hz, 0.09H), 9.09 (d, *J* = 1.6 Hz, 0.90H), 7.41 – 7.32 (m, 4H), 7.16 –7.11 (m, 1H), 6.90 – 6.86 (m, 3H), 4.50 – 4.43 (m, 1H), 4.19 (t, *J* = 10.3 Hz, 1H), 3.80 (s, 0.27H), 3.79 (s, 2.61H), 3.59 (dd, *J* = 10.7, 1.5 Hz, 1H), 3.27 (s, 2.72H), 3.25 (s, 0.27H), 2.73 (d, *J* = 6.8 Hz, 1H).^{13}C NMR (75 MHz, CDCl3) δ 196.8, 178.6, 159.1, 142.8, 130.0, 129.2, 129.1, 128.1, 125.5 (q, J_{CF} = 277.8 Hz), 125.3, 123.7, 114.4, 108.8, 67.7, 66.1, 65.3 (q, J_{CF} = 29.0 Hz), 55.2, 44.8, 26.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.7, -74.8. HRMS (ESI) *m/z* calcd for $C_{21}H_{20}F_3N_2O_3$ $[M+H]^+$: 405.1412, found 405.1412.

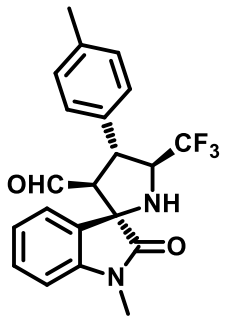


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		15.141	3339819	46.24	120491	BV	Unknown
2		17.761	3883094	53.76	129989	VB	Unknown

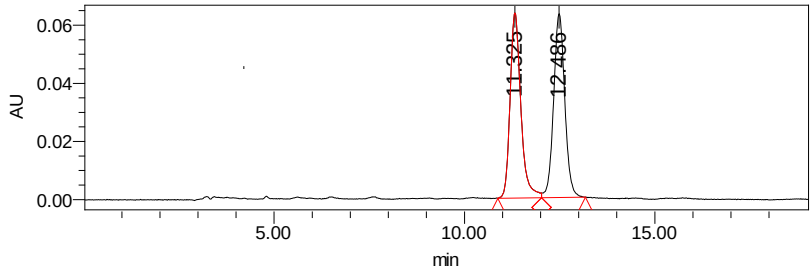


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		17.798	15526610	100.00	508942	VB	Unknown

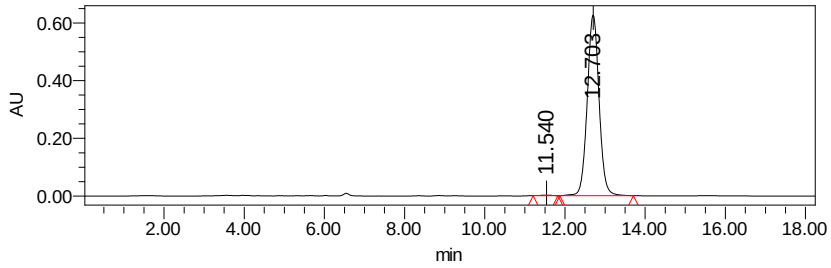
(2'*R*,3'*S*,4'*R*,5'*S*)-1-methyl-2-oxo-4'-(p-tolyl)-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3r)



From 48.4 mg (0.2 mmol) ketimine **1a** and 4-methylcinnamaldehyde 35.0 mg (0.24 mmol, 1.2 equiv), 69.9 mg (90.0% yield) compound **3r** was obtained as a yellow solid, mp = 173 – 174 ℃. $[\alpha]_D^{20}$ = +20 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 12.7 and t_{minor} = 11.5 min. ^1H NMR (300 MHz, $CDCl_3$) δ9.08 (s, 1H), 7.37 – 7.31 (m, 4H), 7.18 – 7.11 (m, 3H), 6.87 (d, *J* = 7.8 Hz, 1H), 4.52 – 4.45 (m, 1H), 4.20 (t, *J* = 10.3 Hz, 1H), 3.62 (d, *J* = 10.8 Hz, 1H), 3.27 (s, 3H), 2.75 (d, *J* = 6.9 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ196.8, 178.5, 142.9, 137.6, 134.2, 130.1, 129.8, 128.3, 128.1, 125.6 (q, J_{CF} = 278.0 Hz), 125.4, 123.7, 108.9, 67.8, 66.2, 65.4 (q, J_{CF} = 65.4 Hz), 45.3, 26.7, 21.1. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.8. HRMS (ESI) *m/z* calcd for $C_{21}H_{19}F_3N_2NaO_2$ $[M+Na]^+$: 411.1291, found 411.1297.



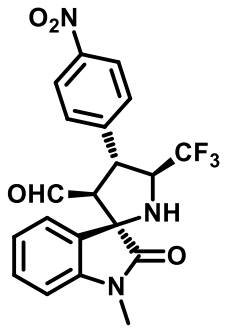
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		11.325	1249218	49.21	63732	BV	Unknown
2		12.486	1289261	50.79	63266	VB	Unknown



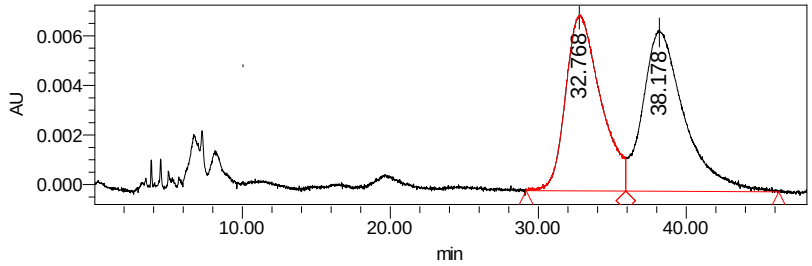
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		11.540	26453	0.21	1347	bb	Unknown

2		12.703	12816926	99.79	627331	bb	Unknown

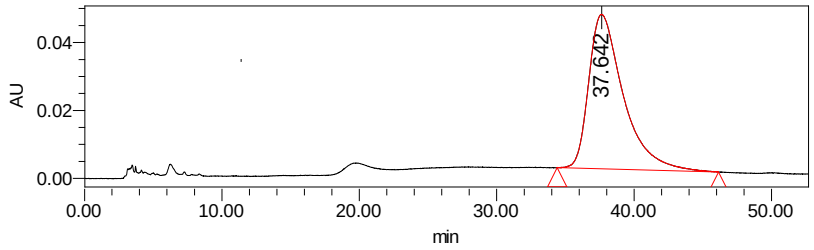
(2'*R*,3'*S*,4'*R*,5'*S*)-1-methyl-4'-(4-nitrophenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3, 2'-pyrrolidine]-3'-carbaldehyde(3s)



From 48.4 mg (0.2 mmol) ketimine **1a** and 4-nitro cinnamaldehyde 41.2 mg (0.24 mmol, 1.2 equiv), 80.5 mg (96.0% yield) compound **3s** was obtained as a pale brown solid, mp = 233 - 234 ℃. $[\alpha]_D^{20}$ = +14 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel OD-H column, hexane/2–propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 37.6 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.21 (d, *J* = 8.7 Hz, 2H), 7.72 (d, *J* = 8.7 Hz, 2H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.28 (d, *J* = 7.0 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 4.69 – 4.58 (m, 1H), 4.33 (t, *J* = 9.7 Hz, 1H), 3.59 (d, *J* = 9.7 Hz, 1H), 3.29 (s, 3H), 2.73 (d, *J* = 6.1 Hz, 1H). ^{13}C NMR (75 MHz, CDCl3) δ195.8, 178.8, 147.4, 145.6, 143.0, 130.5, 129.5, 128.4 (q, J_{CF} = 257.3Hz), 126.8, 125.6, 124.2, 124.0, 109.1, 67.4, 65.4, 64.8 (q, J_{CF} = 29.8Hz), 44.4, 26.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ -74.9. HRMS (ESI) *m/z* calcd for $C_{20}H_{17}F_3N_3O_4$ $[M+H]^+$: 420.1166, found 420.1155.

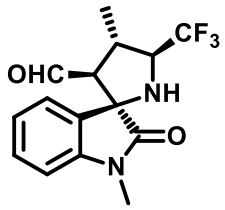


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		32.768	1164459	47.94	7086	bv	Unknown
2		38.178	1264781	52.06	6466	vb	Unknown

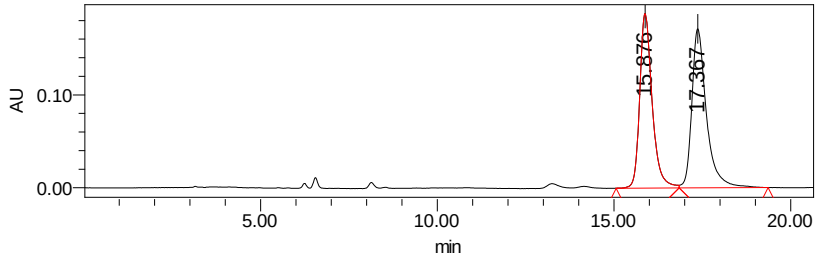


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		37.642	7967590	100.00	45503	bb	Unknown

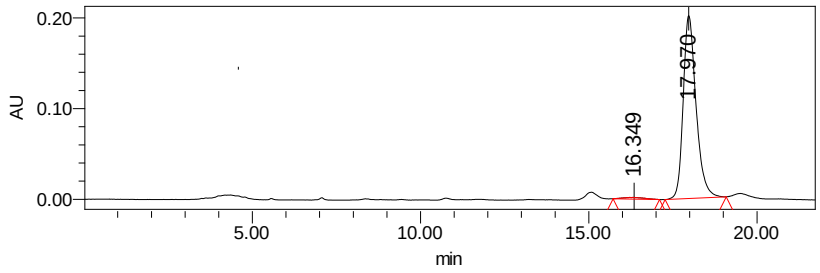
(2'*R*,3'*S*,4'*S*,5'*S*)-1,4'-dimethyl-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine] -3'-carbaldehyde(3t)



From 48.4 mg (0.2 mmol) ketimine **1a** and crotonaldehyde 19.8 µl (0.24 mmol, 1.2 equiv), 48.7 mg (78% yield) compound **3t** was obtained as colorless oil. $[\alpha]_D^{20}$ = +49 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. 97% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 95:5, 1.0 mL/min). Retention time: t_{major} = 18.0 and t_{minor} = 16.3 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.09 (s, 1H), 7.34 – 7.27 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 3.95 – 3.88 (m, 1H), 3.24 (s, 3H), 3.17 – 3.02 (m, 2H), 2.67 (d, *J* = 6.5 Hz, 1H), 1.33 (d, *J* = 5.8 Hz, 3H). ^{13}C NMR (75 MHz, CDCl3) δ197.3, 178.2, 142.6, 129.8, 129.0, 125.0, 123.7, 125.9 (q, J_{CF} = 277.3 Hz), 108.7, 68.0, 65.7, 65.1(q, J_{CF} = 28.7 Hz), 35.0, 35.0, 26.7, 16.8. ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.2, -75.2. HRMS (ESI) *m/z* calcd for $C_{15}H_{16}F_3N_2O_2$ $[M+H]^+$: 313.1158, found 313.1146.

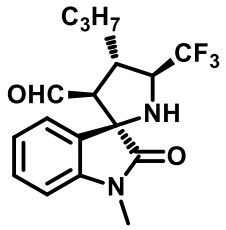


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		15.876	4594264	48.29	187900	bv	Unknown
2		17.367	4920108	51.71	171310	vb	Unknown

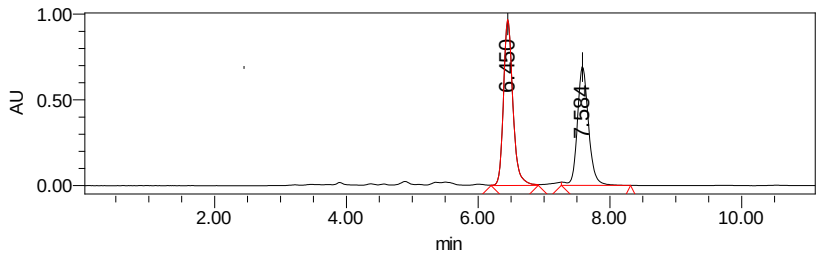


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		16.349	77713	1.43	1779	bb	Unknown
2		17.970	5357092	98.57	201752	bb	Unknown

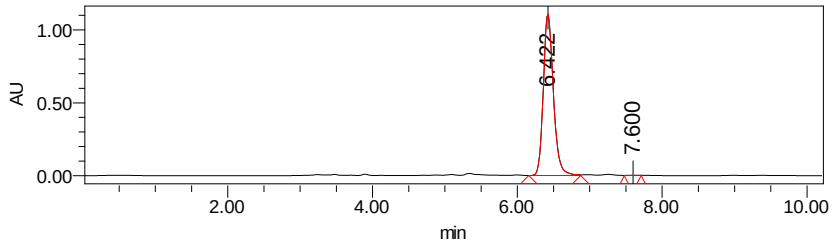
(2'*R*,3'*S*,4'*S*,5'*S*)-1-methyl-2-oxo-4'-propyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carbaldehyde(3u)



From 48.4 mg (0.2 mmol) ketimine **1a** and trans-2-hexenal 27.8 μl (0.24 mmol, 1.2 equiv), 59.9 mg (88.0% yield) compound **3u** was obtained as a amorphous solid. $[\alpha]_D^{20}$ = +68 (c = 1.0, $CHCl_3$). Dr (>20:1) determined by ^1H and ^{19}F NMR analysis. >99% ee was determined by HPLC analysis (Daicel Chiralcel IA column, hexane/2–propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 6.4 and t_{minor} = 7.6 min. ^1H NMR (300 MHz, $CDCl_3$) δ 9.28 (d, *J* = 2.8 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 4.13 (q, *J* = 6.8 Hz, 1H), 3.20 (s, 3H), 3.10 – 2.98 (m, 2H), 2.55 (d, *J* = 6.4 Hz, 1H), 1.86 – 1.77 (m, 1H), 1.73 – 1.61 (m, 1H), 1.35 – 1.23 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ198.3, 178.7, 143.0, 130.0, 127.5, 125.8 (q, J_{CF} = 277.0 Hz), 125.6, 123.4, 108.7, 68.7, 63.9 (q, J_{CF} = 29.3 Hz), 63.0, 39.5, 34.8, 26.5, 20.6, 14.0. ^{19}F NMR (282 MHz, $CDCl_3$) δ -75.1, -76.6. HRMS (ESI) *m/z* calcd for $C_{17}H_{20}F_3N_2O_2$ $[M+H]^+$: 341.1471, found 341.1467.

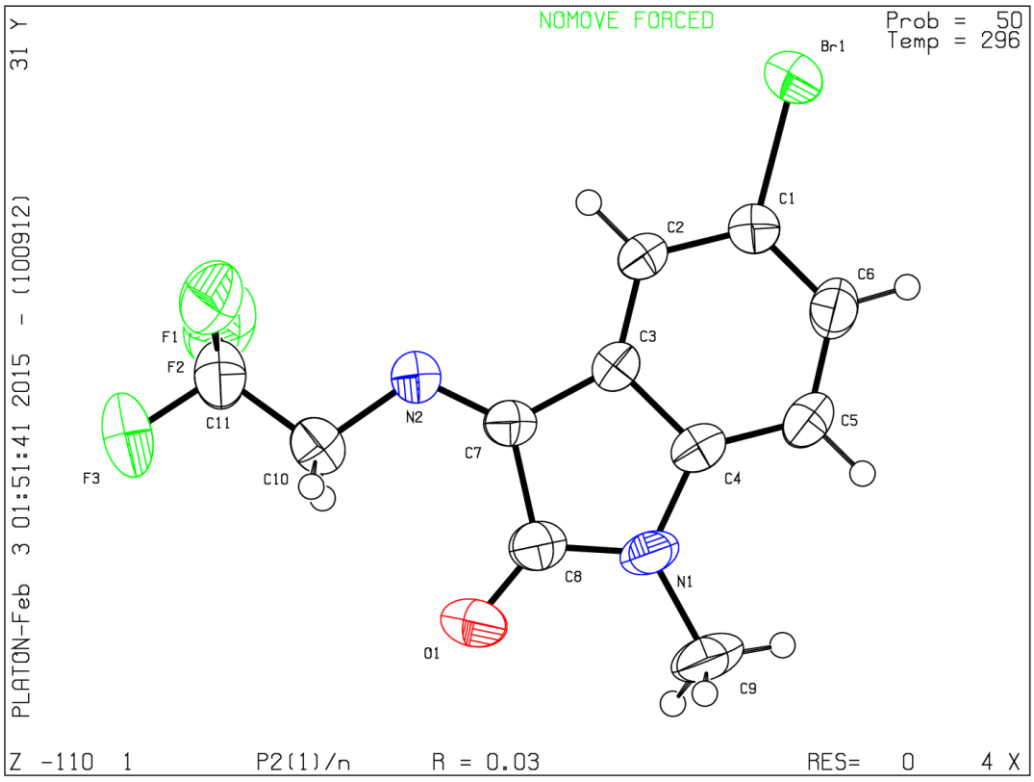


	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		6.450	9560826	53.96	968333	Vv	Unknown
2		7.584	8158691	46.04	692927	vb	Unknown

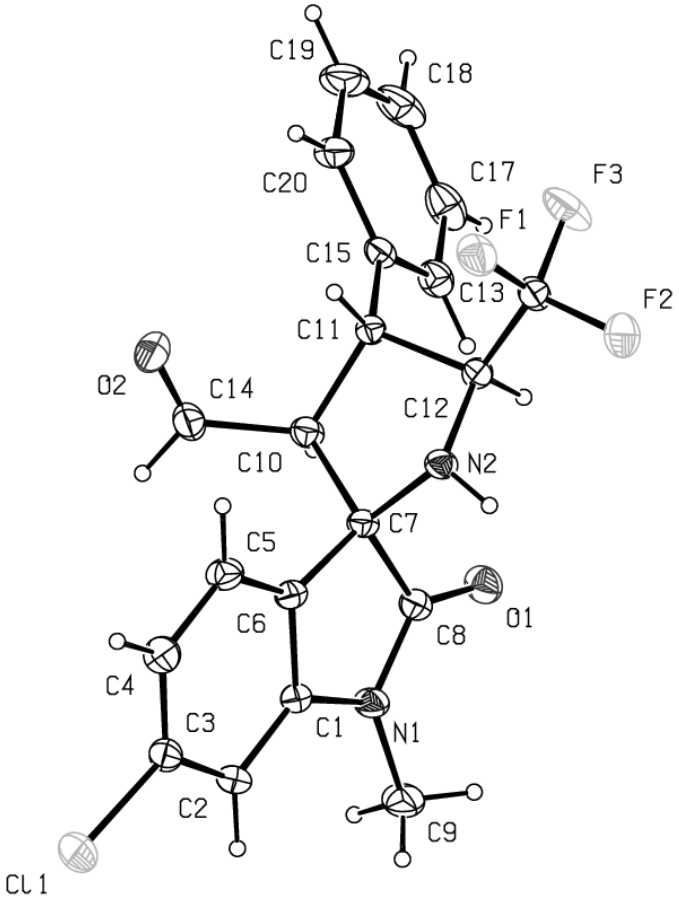


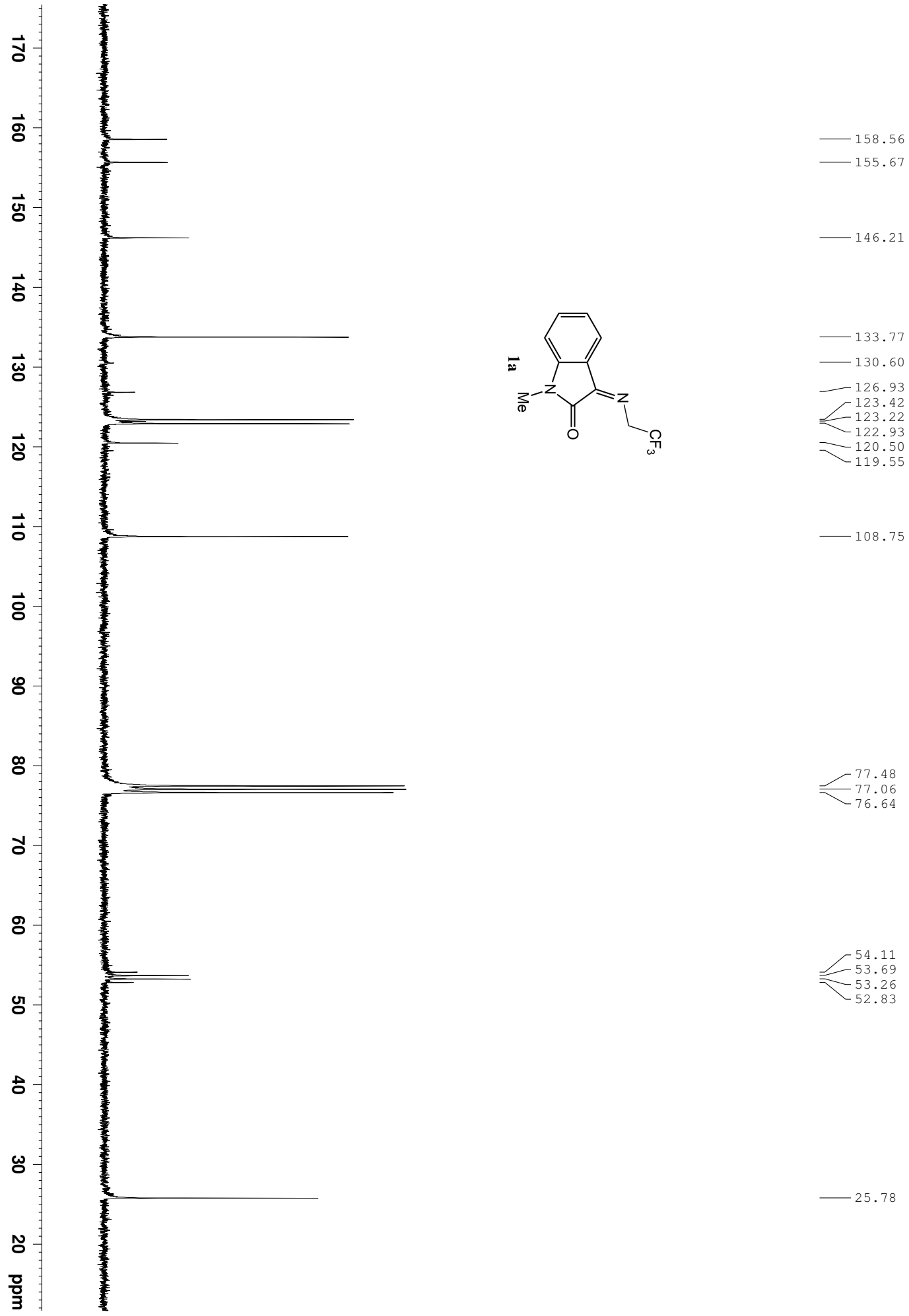
	Name	Retention Time	Area	% Area	Height	Int Type	Peak Type
1		6.422	10705018	99.95	1106876	VV	Unknown
2		7.600	5611	0.05	779	BB	Unknown

F. Crystal Structure of 1g



G. Crystal *S*tructure of 3k

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123.22
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120.50
119.55
108.75
77.48
77.06
76.64
54.11
53.69
53.26
52.83
25.78
1a
Me
N
O
N
CF3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

0
-10
-20
-30
-40
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-70
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-120
-130
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ppm
1a
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N
N
O
CF3
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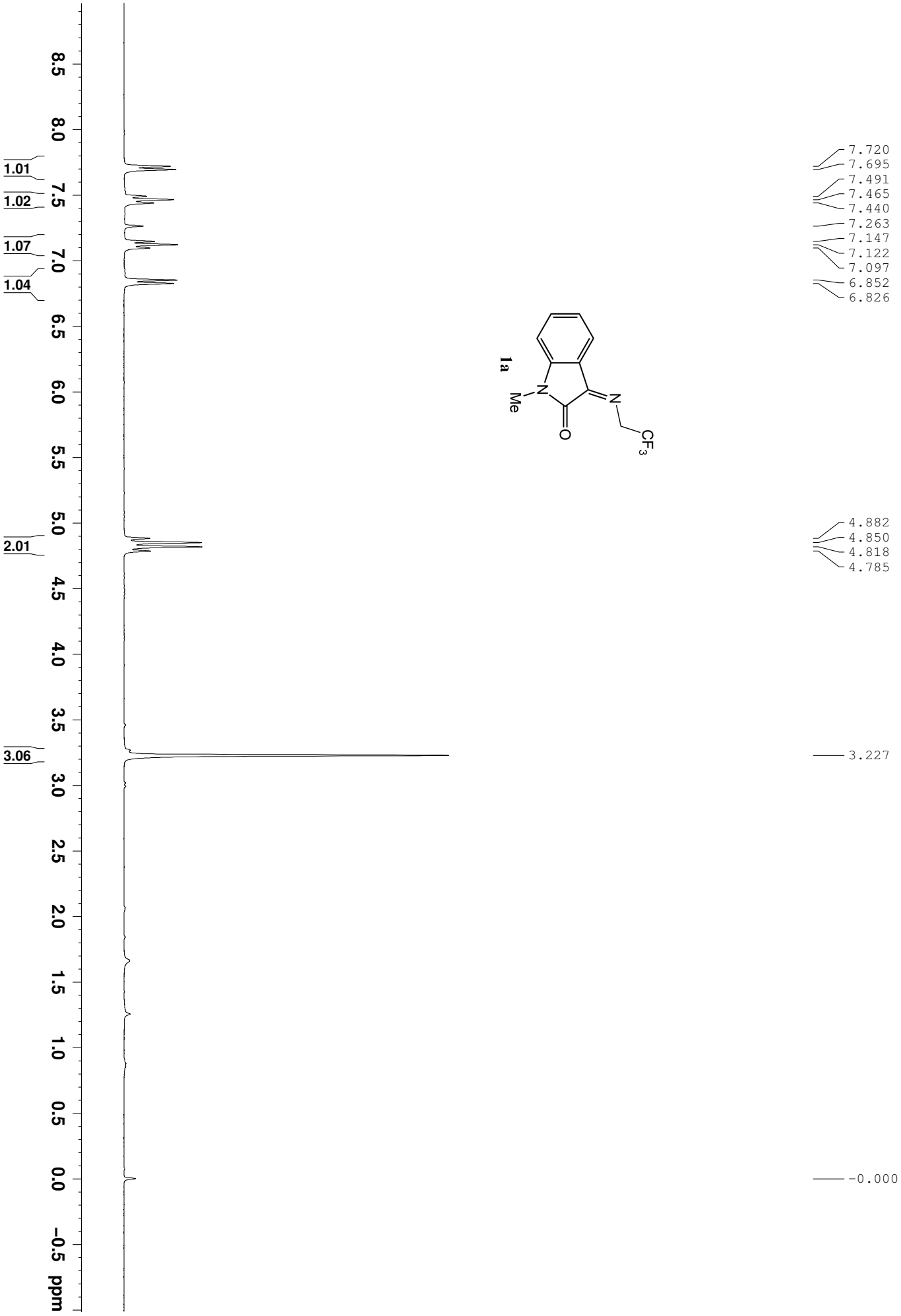
-71.889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1.04
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
ppm
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7.491
7.465
7.440
7.263
7.147
7.122
7.097
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6.826
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4.818
4.785
3.227
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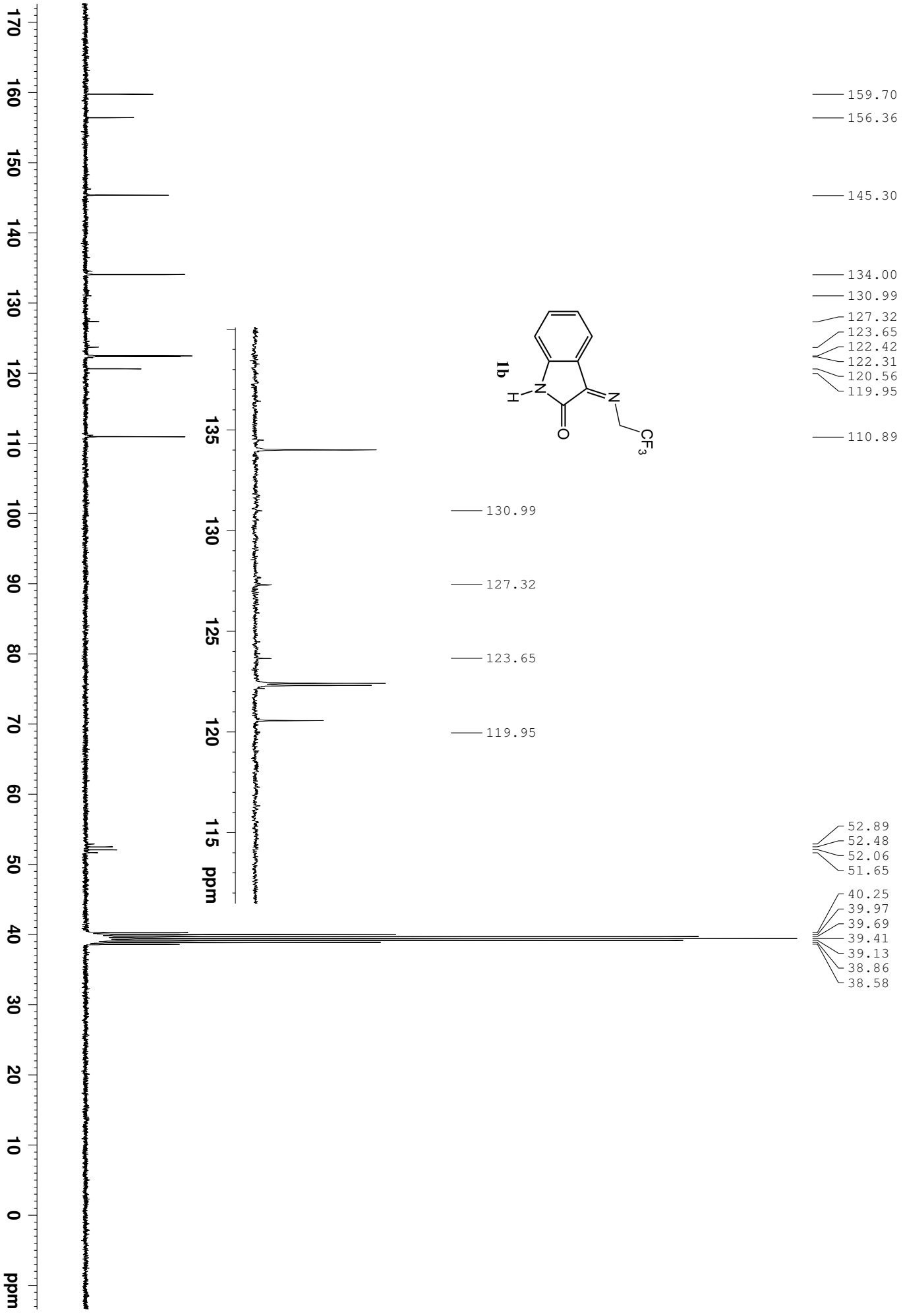
O
N
CF3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120.56
119.95
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51.65
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39.97
39.69
39.41
39.13
38.86
38.58
130.99
127.32
123.65
119.95
ppm

-10
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-40
-50
-60
-70
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-110
-120
-130
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1b
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N
O
N
CF3
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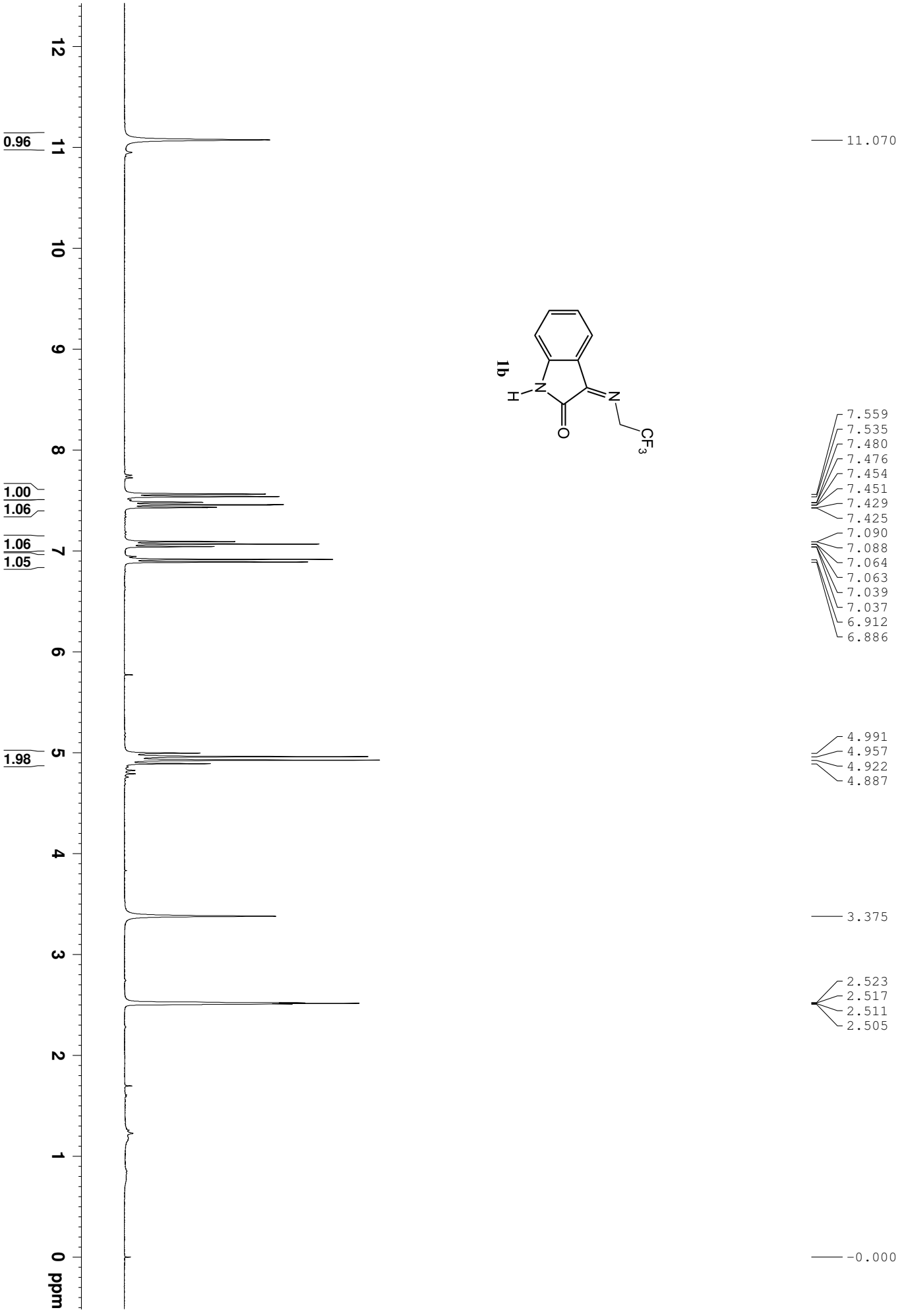
-70.460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4
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2
1
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1.05
1.98
11.070
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7.535
7.480
7.476
7.454
7.451
7.429
7.425
7.090
7.088
7.064
7.063
7.039
7.037
6.912
6.886
4.991
4.957
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2.517
2.511
2.505
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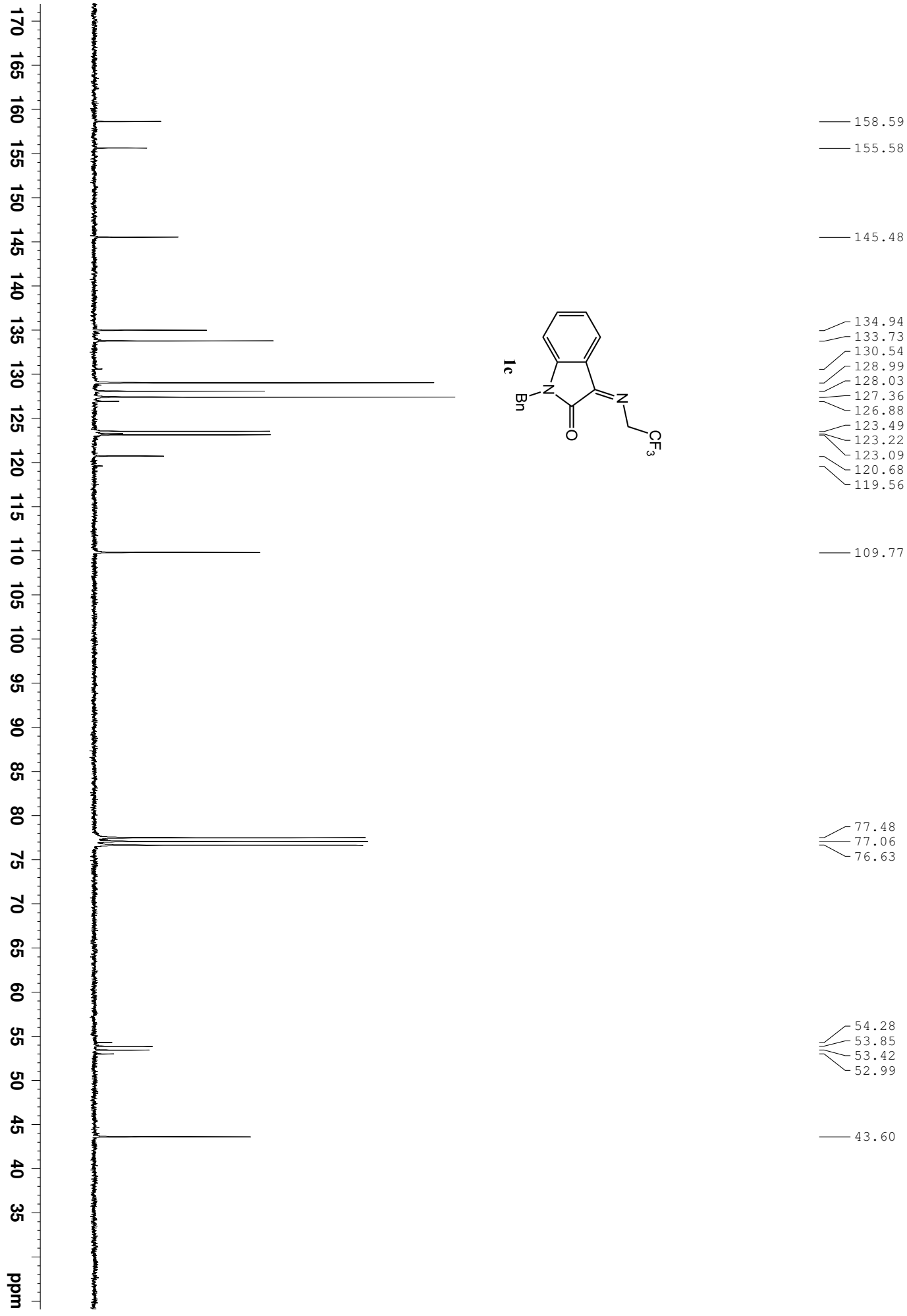
N
O
N
CF3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120.68
119.56
109.77
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77.06
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54.28
53.85
53.42
52.99
43.60
1c
Bn
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O
N
CF3
170
165
160
155
150
145
140
135
130
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120
115
110
105
100
95
90
85
80
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65
60
55
50
45
40
35
ppm

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Bn
N
O
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CF3
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-71.87
10
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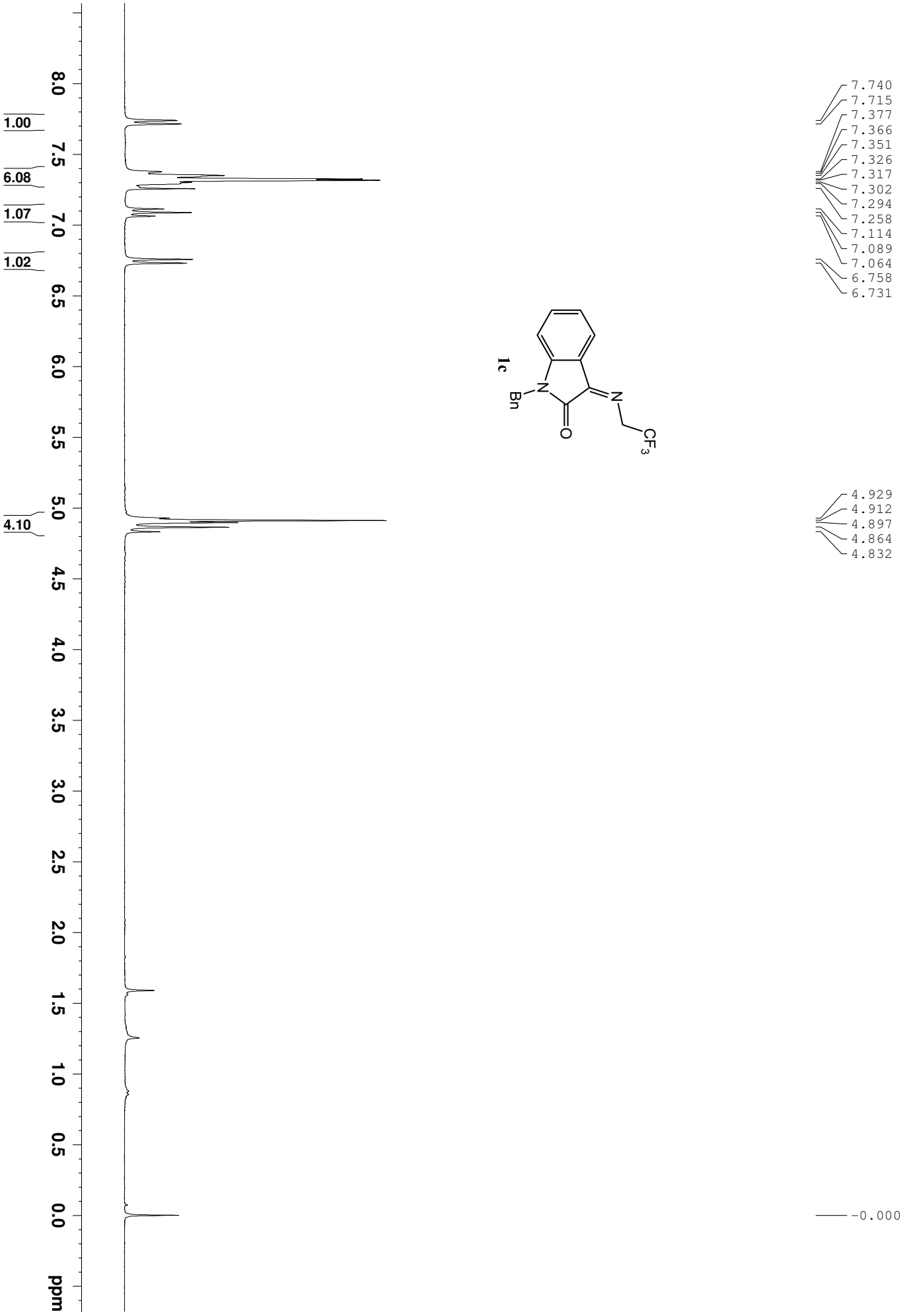
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7.114
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6.731
4.929
4.912
4.897
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4.832
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6.08
1.07
1.02
4.10
8.0
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6.0
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4.5
4.0
3.5
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ppm
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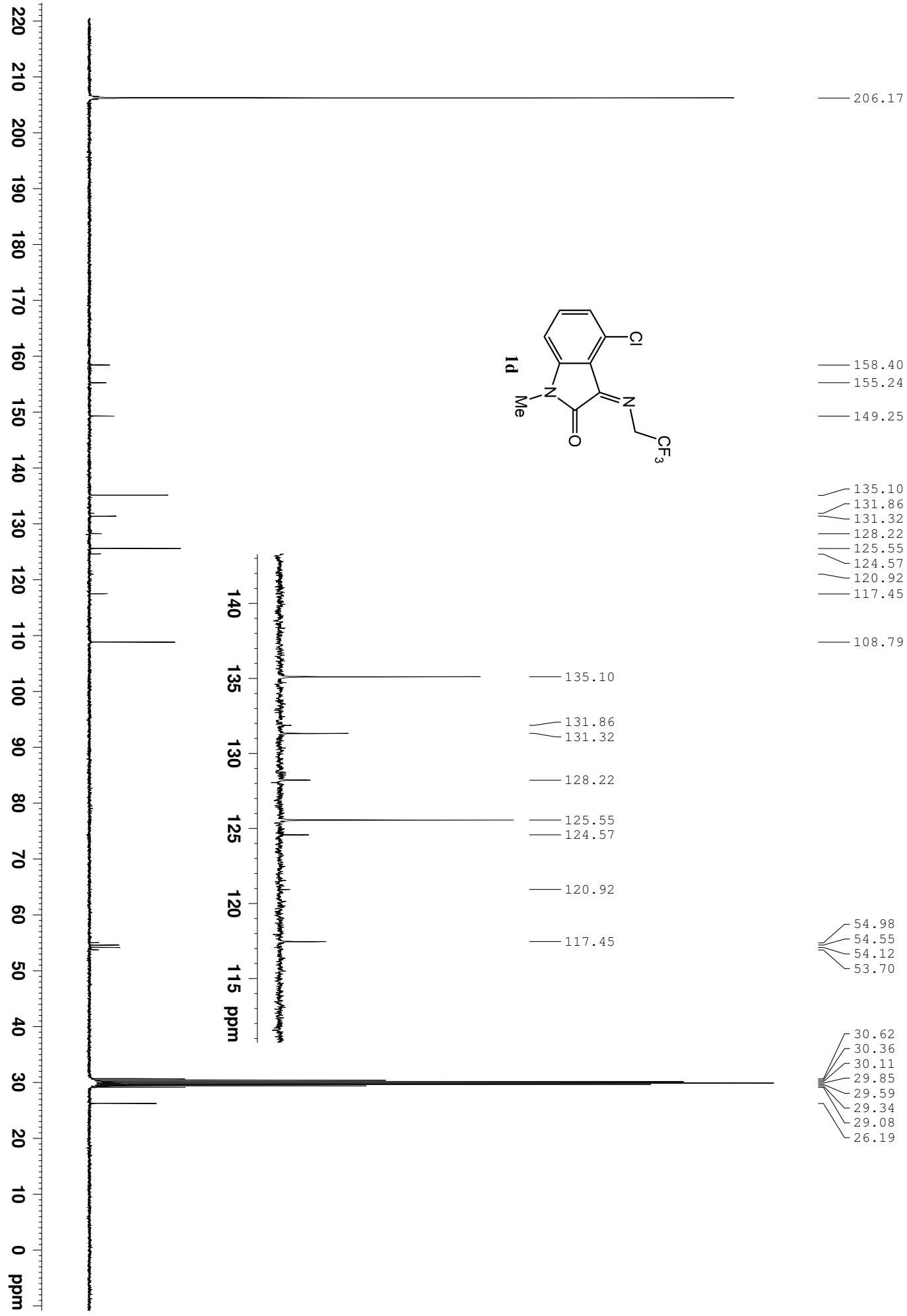
O
N
CF3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O
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125.55
124.57
120.92
117.45
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54.98
54.55
54.12
53.70
30.62
30.36
30.11
29.85
29.59
29.34
29.08
26.19
140
135
130
125
120
115 ppm
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

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1d
Cl
N
Me
O
N
CF3


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3.0
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2.0
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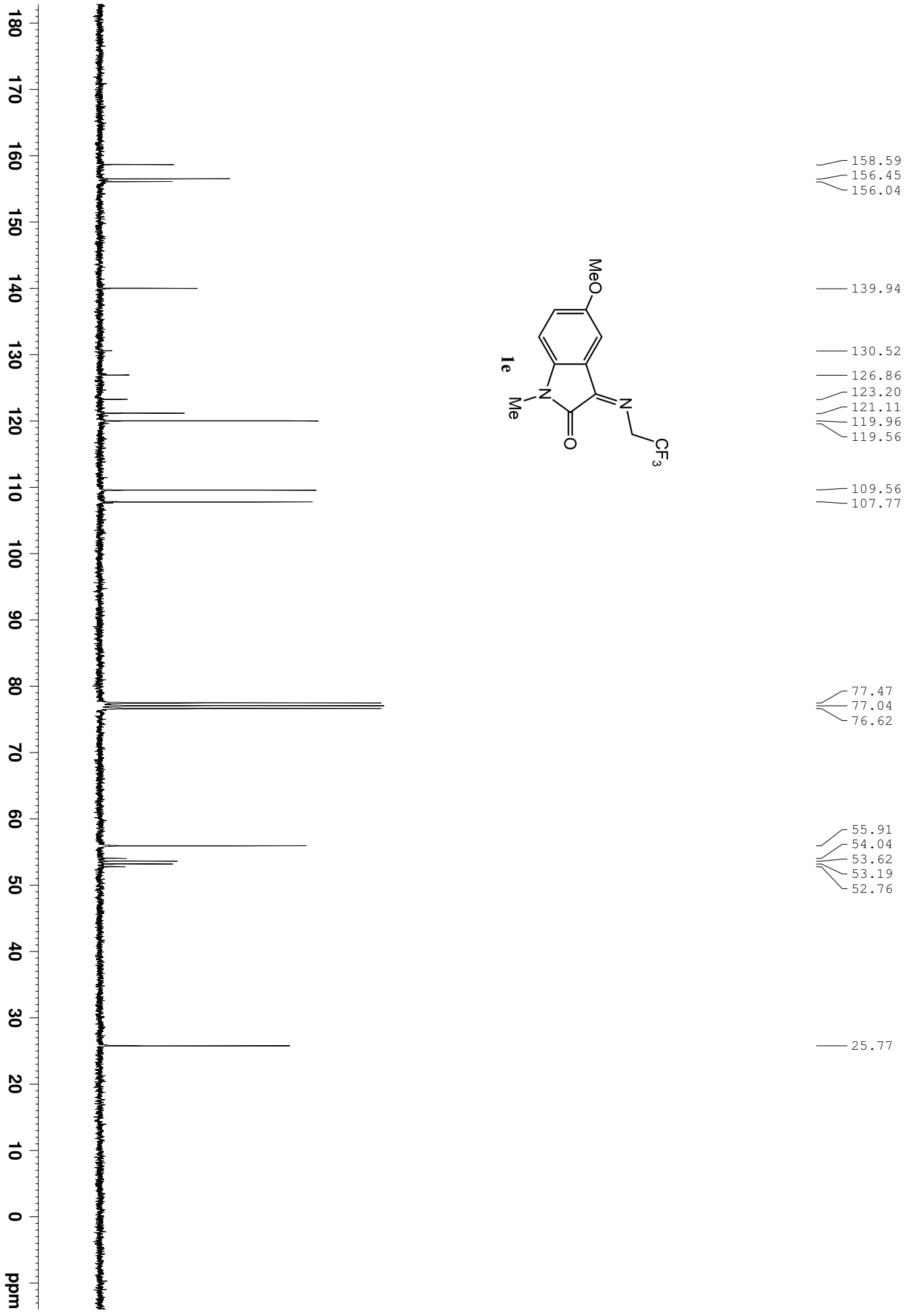
O
N
CF3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53.19
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Me
O
CF3
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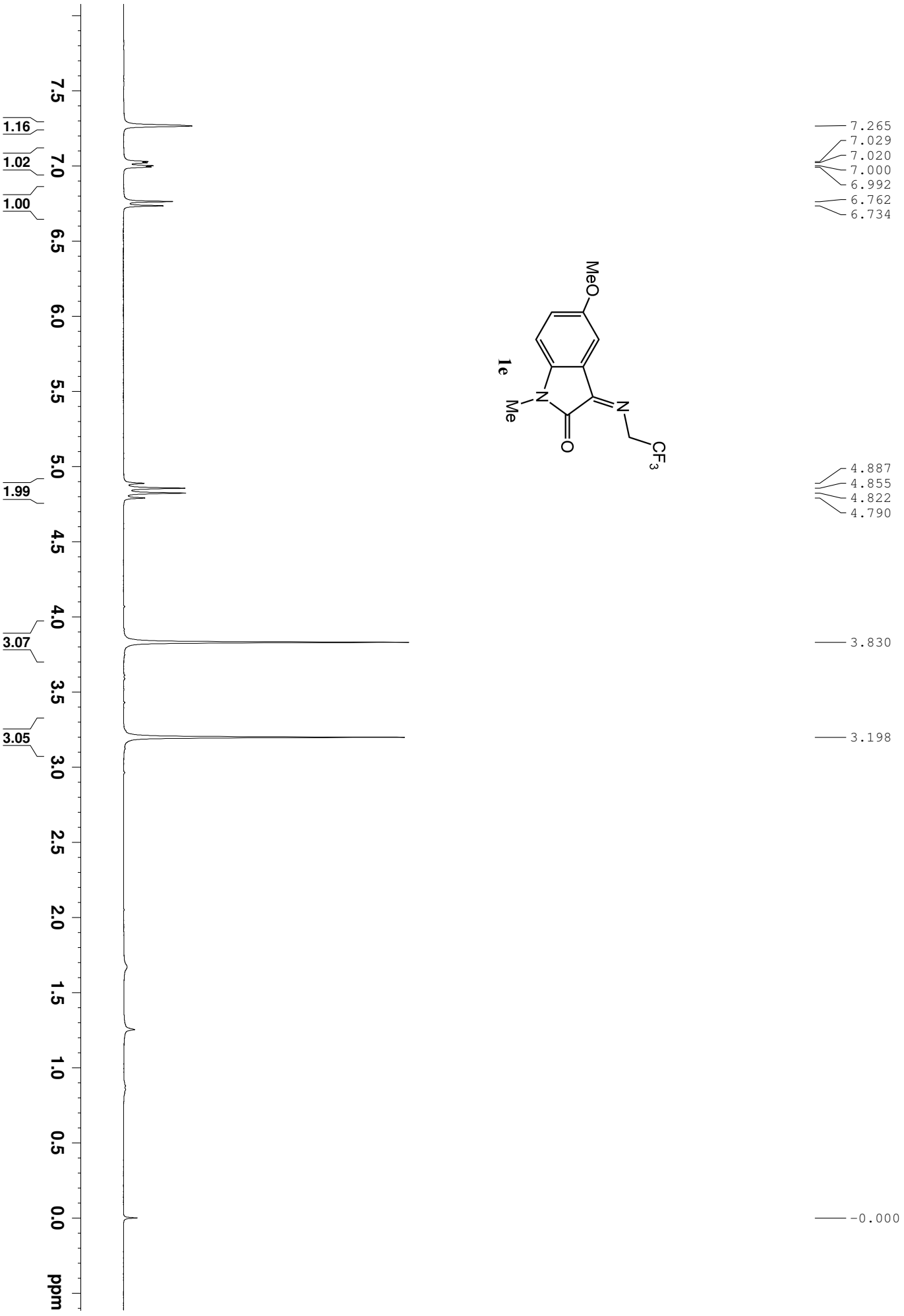
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ppm
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N
Me
O
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CF3
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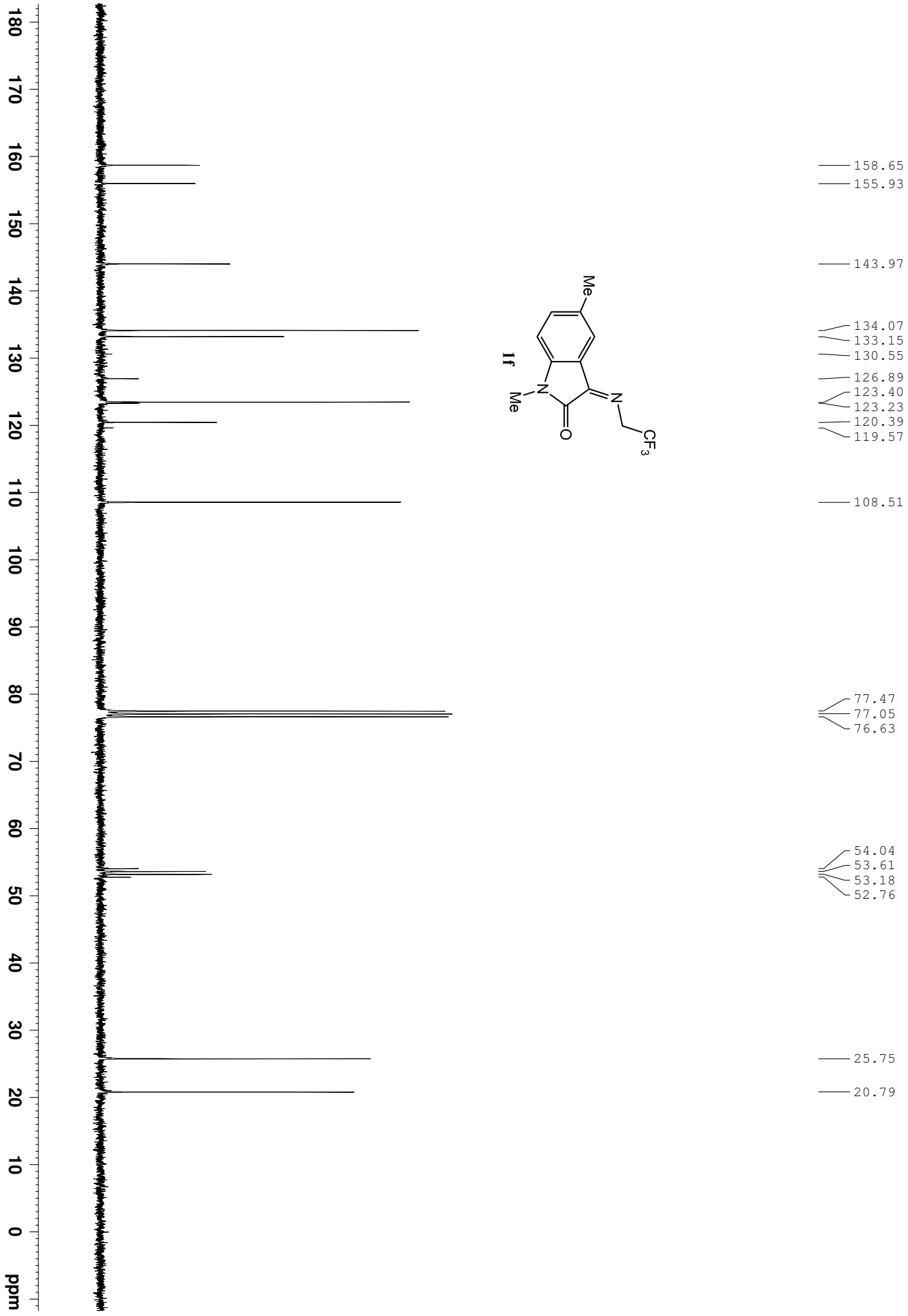
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N
Me
O
N
CF3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

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-50
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Me
O
N
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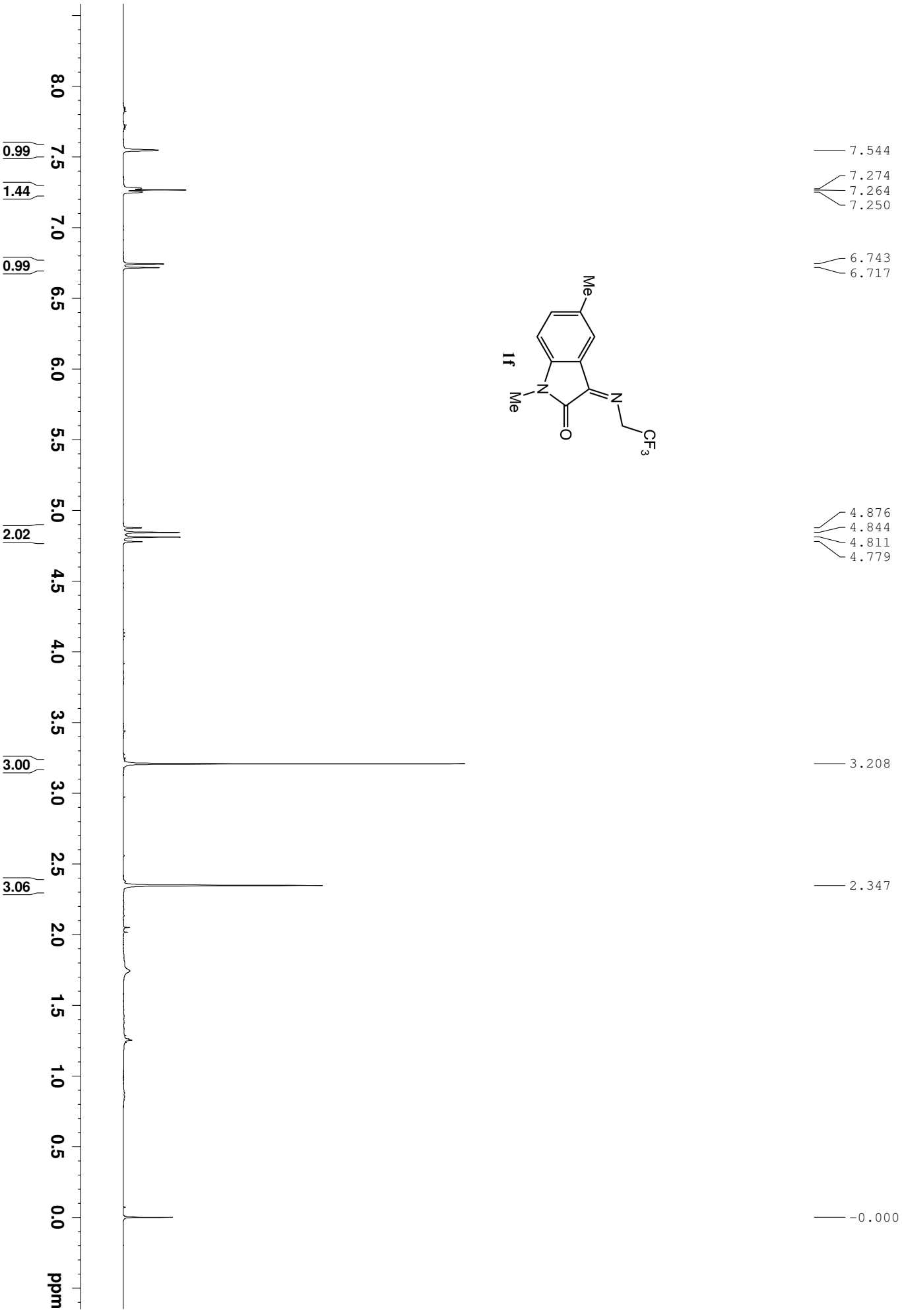
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
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6.717
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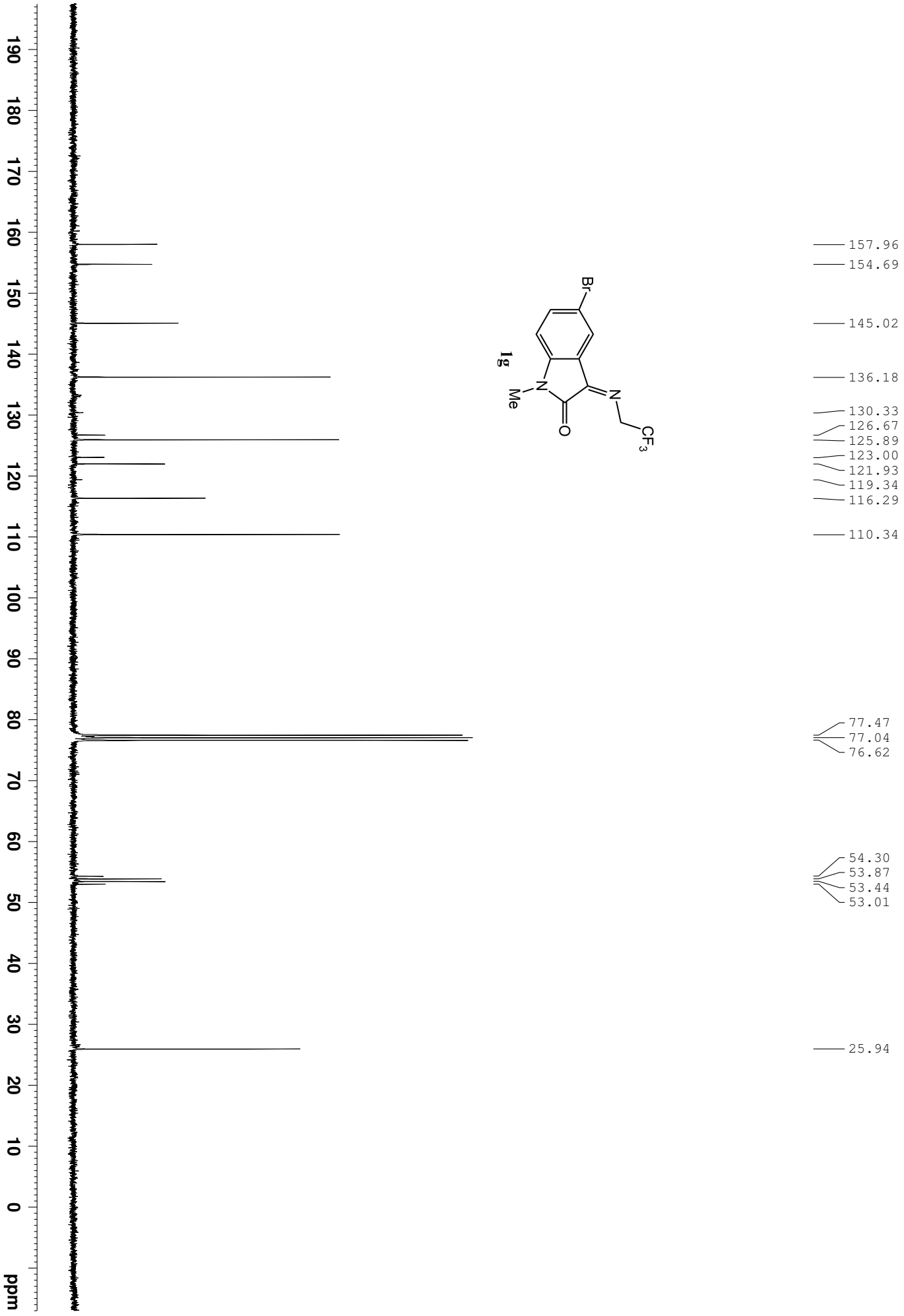
CF3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123.00
121.93
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77.47
77.04
76.62
54.30
53.87
53.44
53.01
25.94
1g
Br
N
Me
O
N
CF3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

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ppm
-71.884
1g
Br
N
Me
O
N
CF3


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7.605
7.598
7.577
7.571
7.264
6.760
6.732
4.875
4.842
4.810
4.778
3.228
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2.02
3.08
ppm
1g
Br
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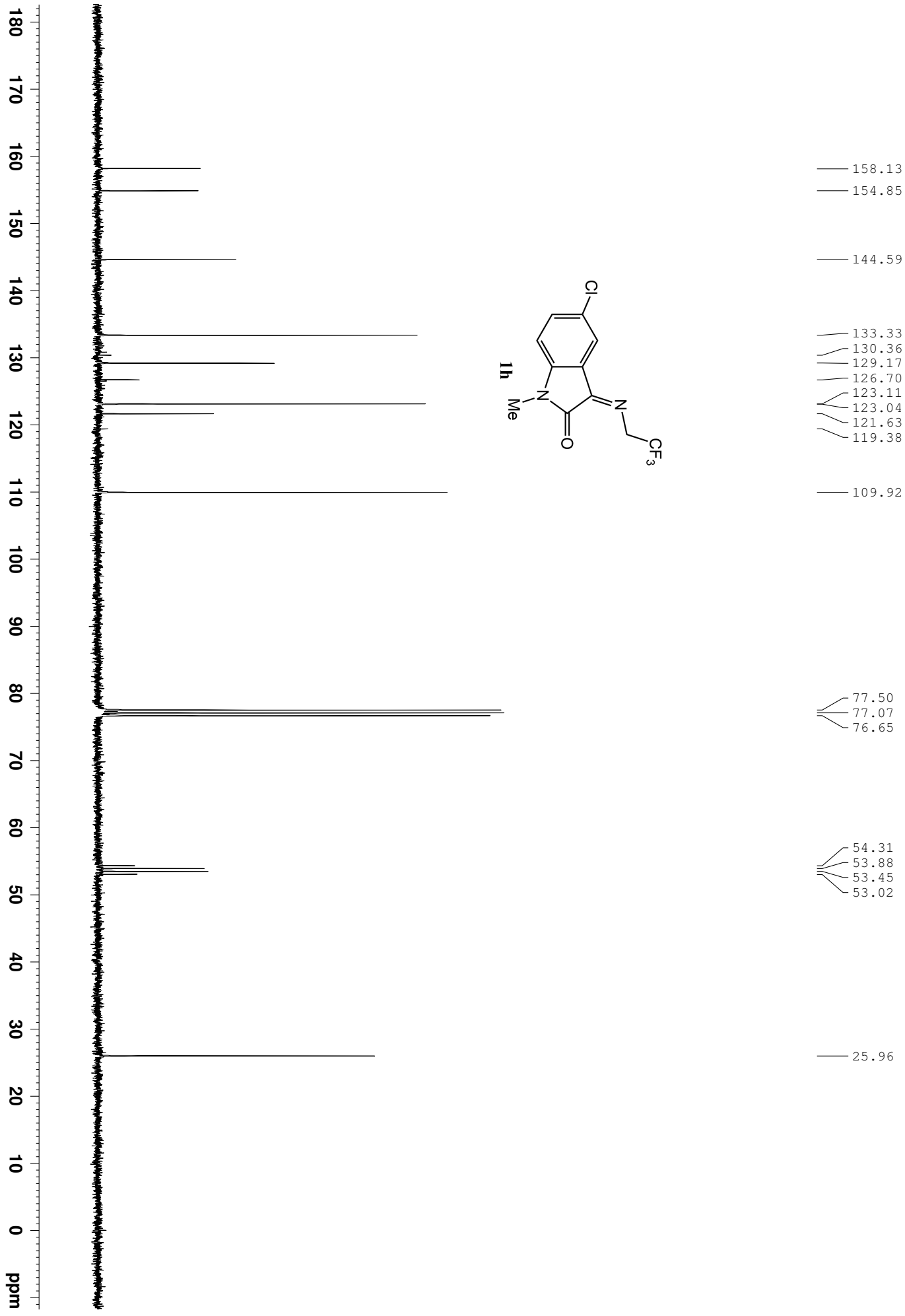
Me
O
N
CF3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77.07
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54.31
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53.02
25.96
1h
Cl
Me
N
O
N
CF3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
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ppm

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ppm
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Cl
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Me
O
N
CF3


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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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0.0
ppm
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1.06
1.07
2.05
3.29
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7.267
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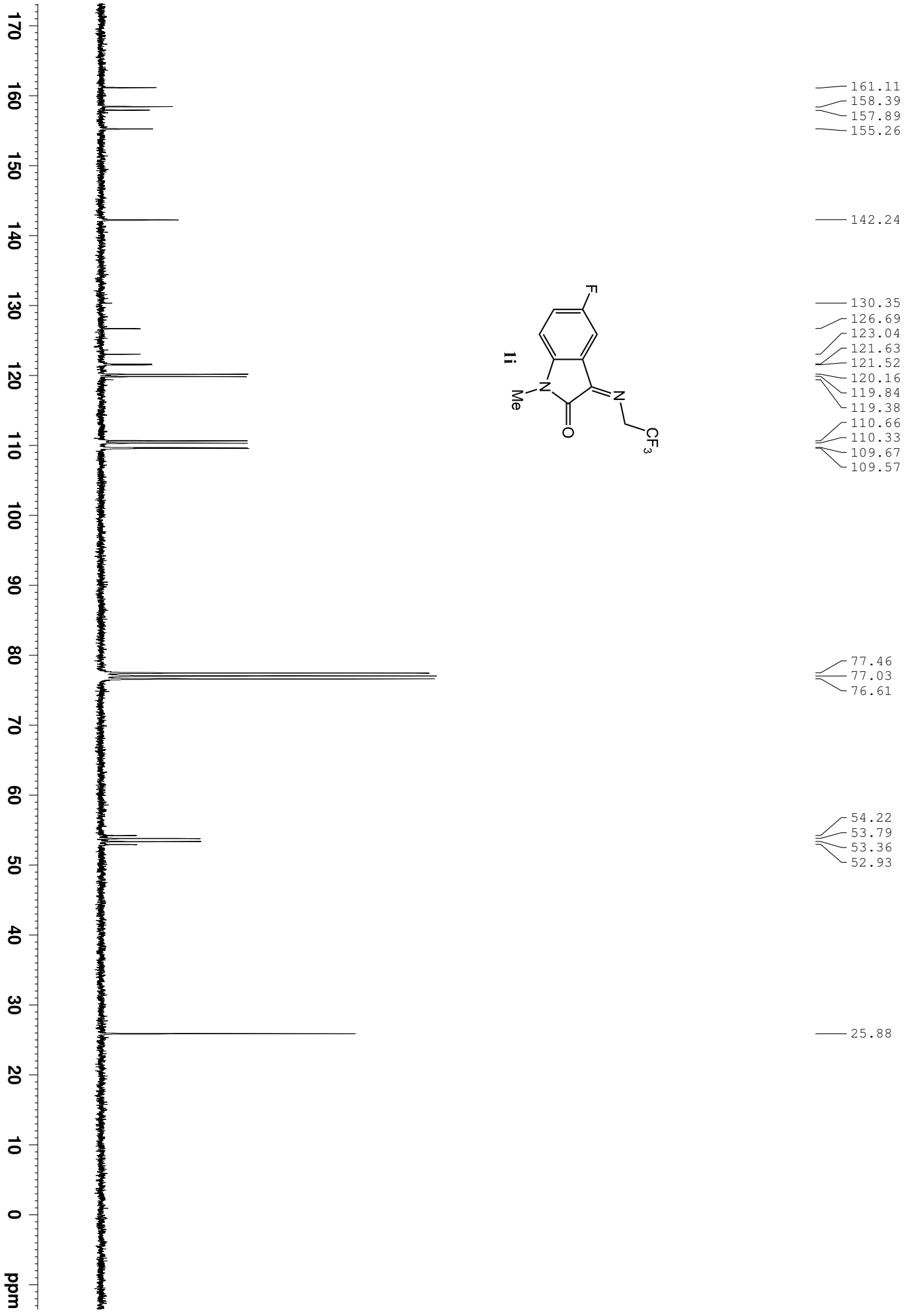
Cl
N
Me
O
N
CF3

1h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110.66
110.33
109.67
109.57
77.46
77.03
76.61
54.22
53.79
53.36
52.93
25.88
1i
F
N
Me
O
N
CF3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

-20
-30
-40
-50
-60
-70
-80
-90
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-120
-130
-140
ppm
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F
N
Me
O
N
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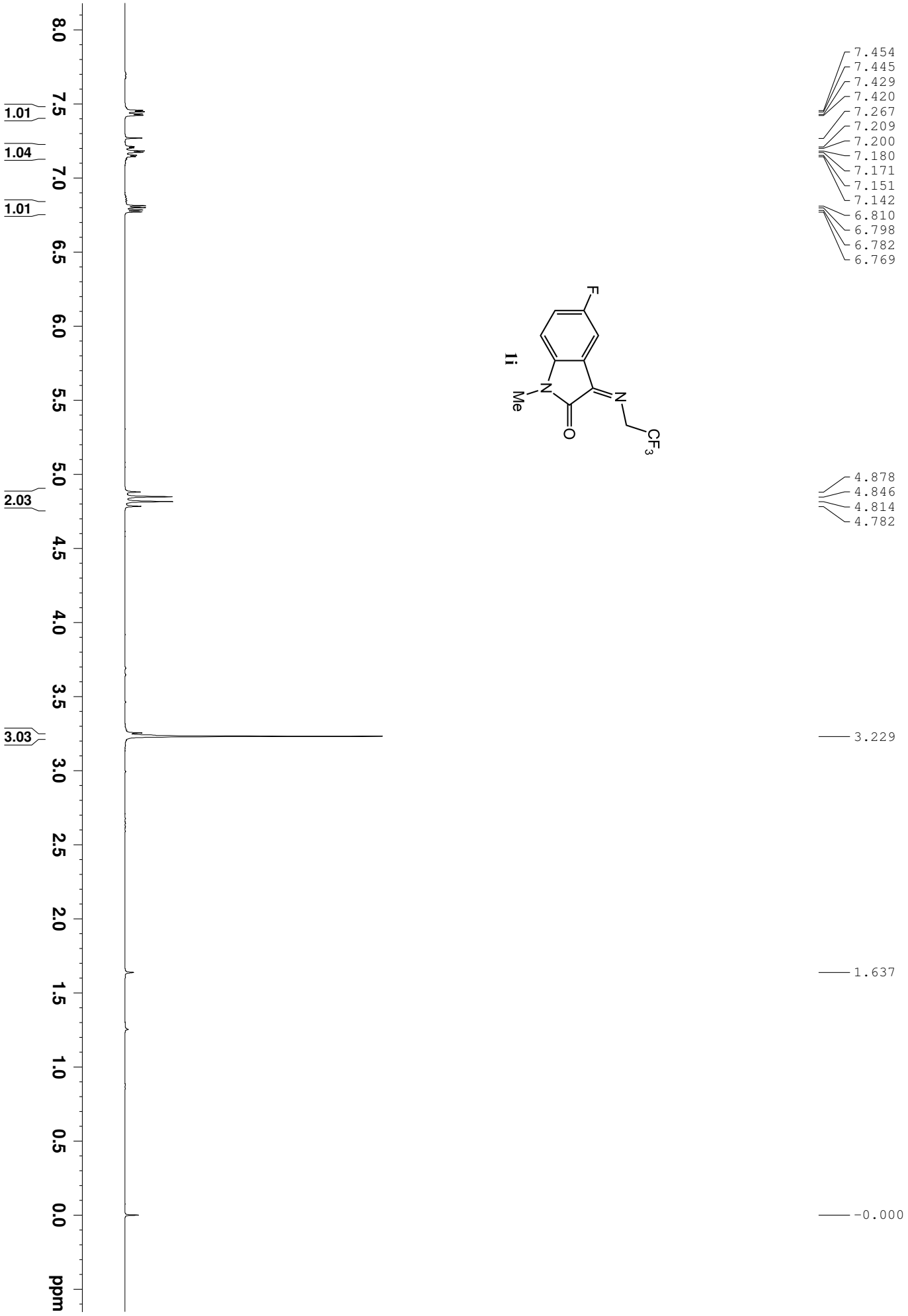
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7.142
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6.798
6.782
6.769
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4.846
4.814
4.782
3.229
1.637
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1.04
1.01
2.03
3.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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0.5
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ppm
1i
F
N
Me
O
N
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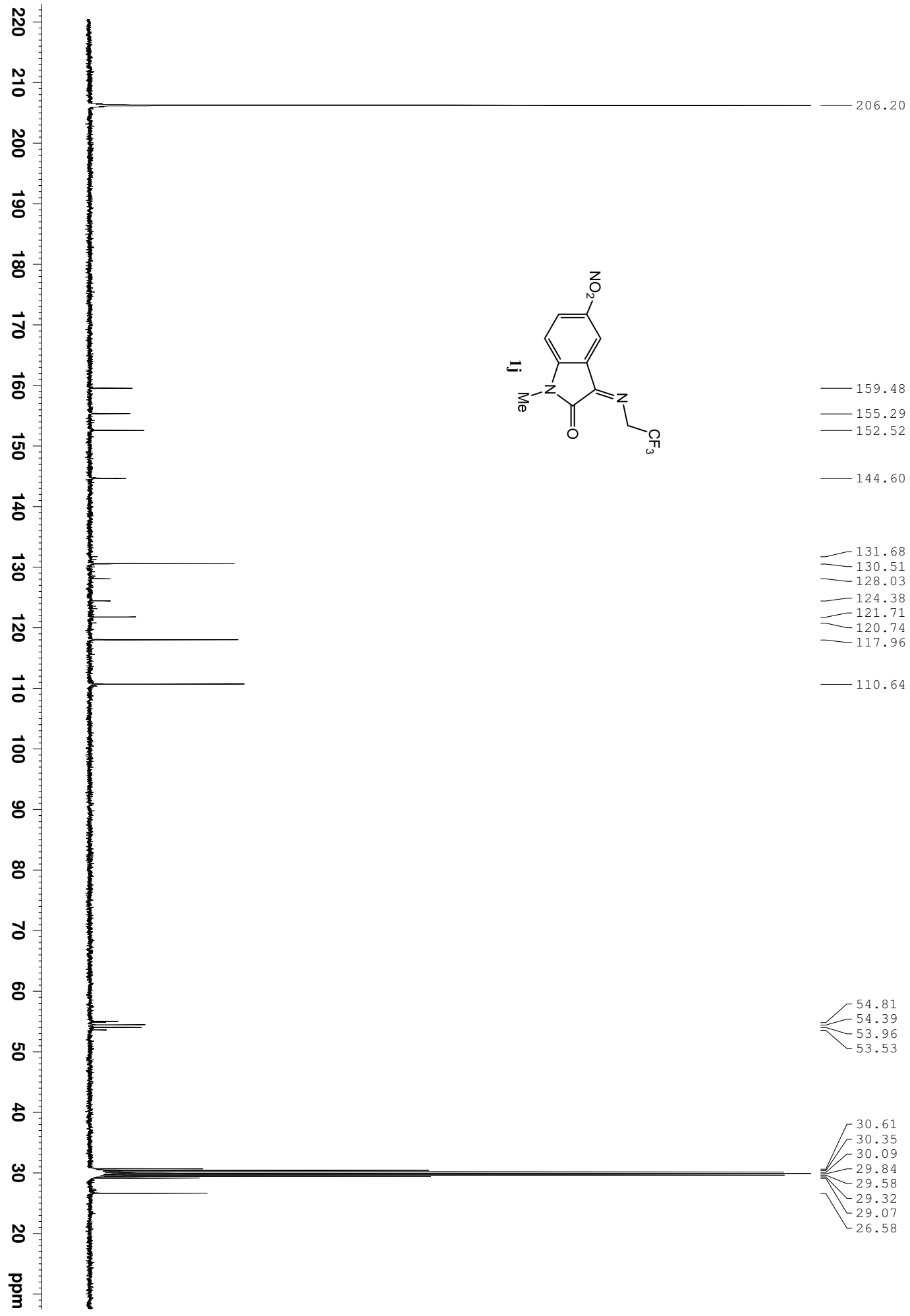
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120.74
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110.64
54.81
54.39
53.96
53.53
30.61
30.35
30.09
29.84
29.58
29.32
29.07
26.58
1j
Me
O
N
N
CF3
NO2
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

-10
-20
-30
-40
-50
-60
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-100
-110
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ppm
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Me
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CF3
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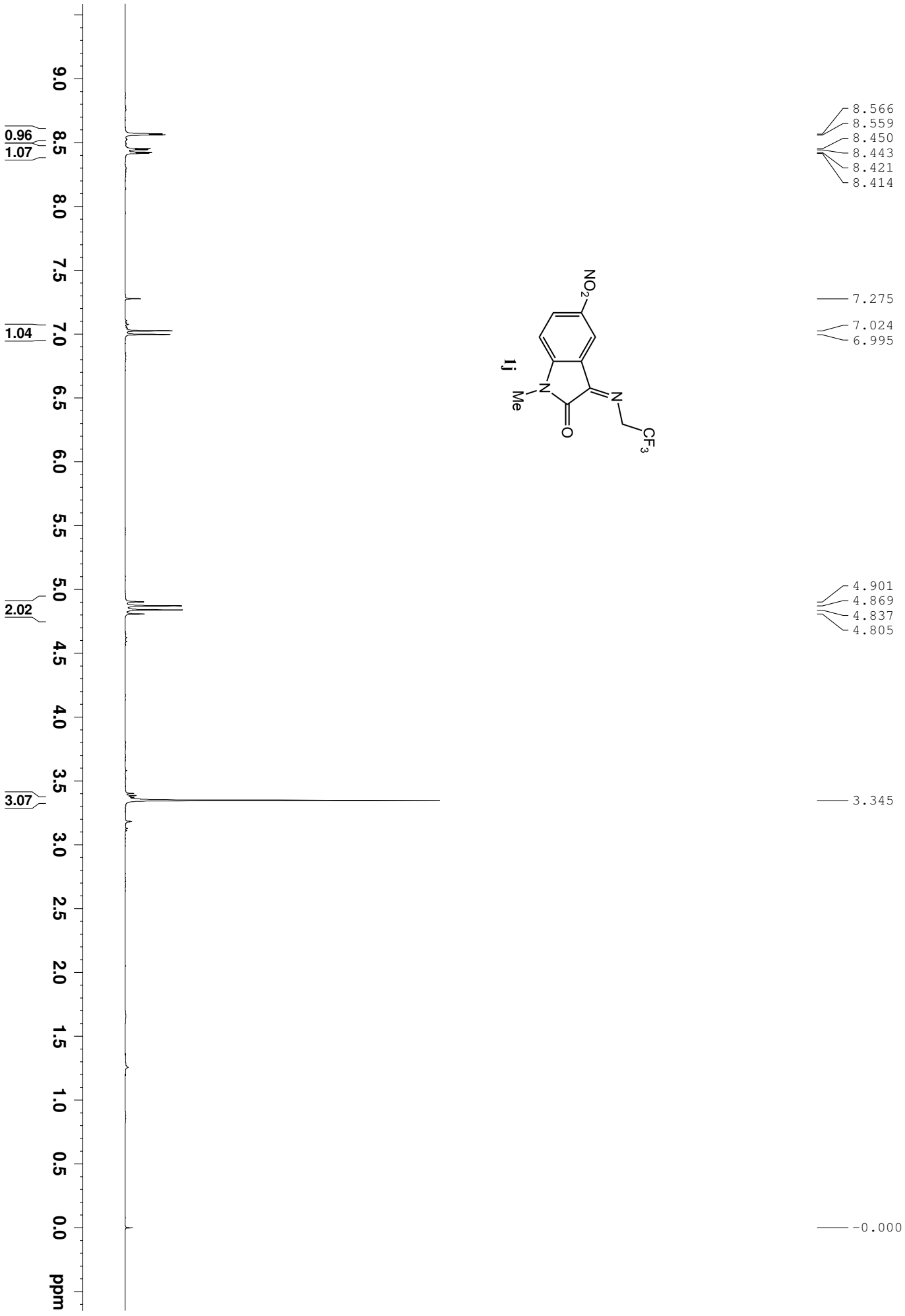
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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8.450
8.443
8.421
8.414
7.275
7.024
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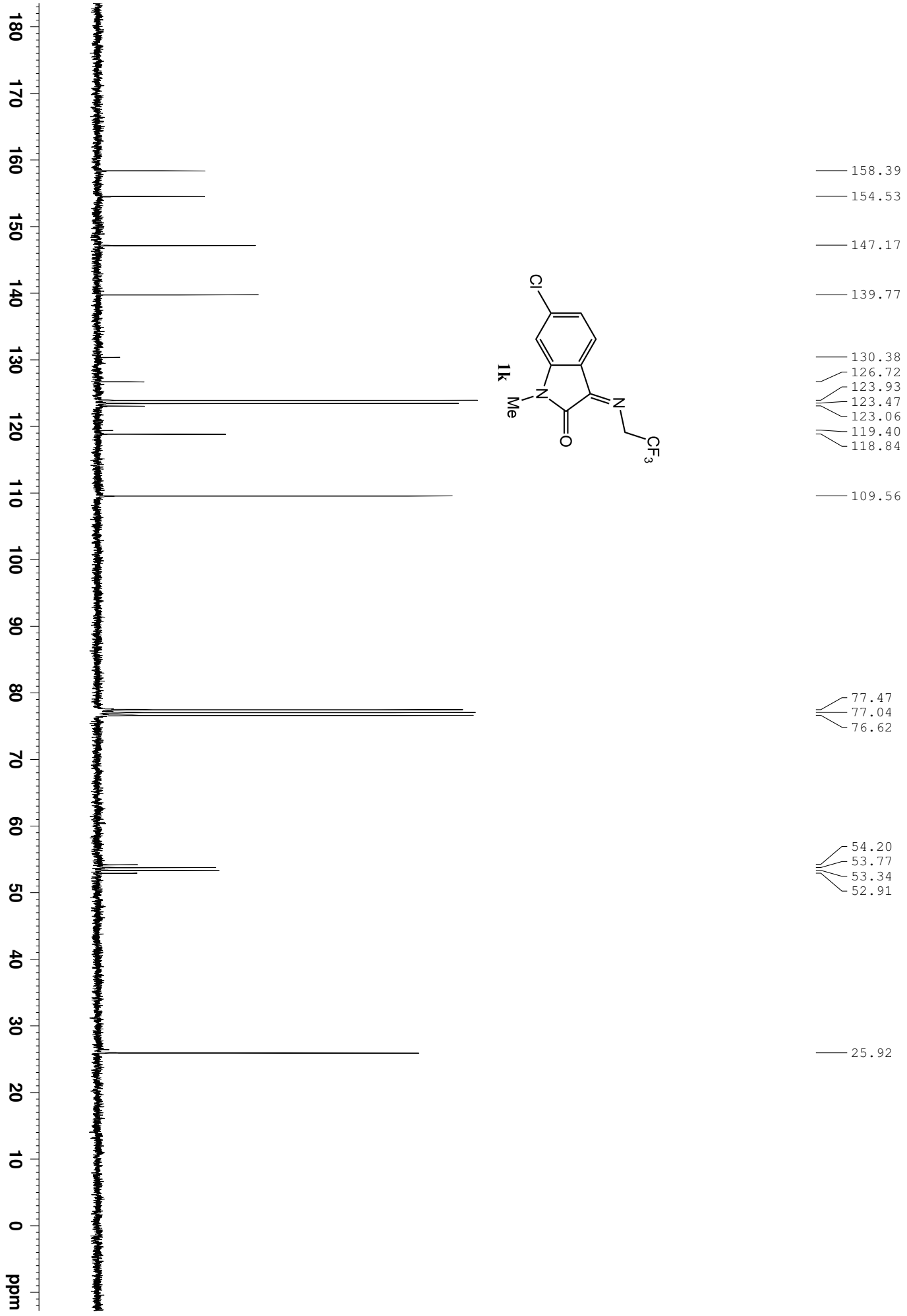
NO2
N
Me
O
N
CF3
1j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123.47
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77.47
77.04
76.62
54.20
53.77
53.34
52.91
25.92
1k
Cl
N
Me
O
N
CF3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
ppm
Cl
1k
N
Me
O
N
CF3
-71.891


1.03
1.07
1.05
2.09
3.04
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
ppm
7.651
7.625
7.265
7.117
7.091
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4.793
4.761
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1k
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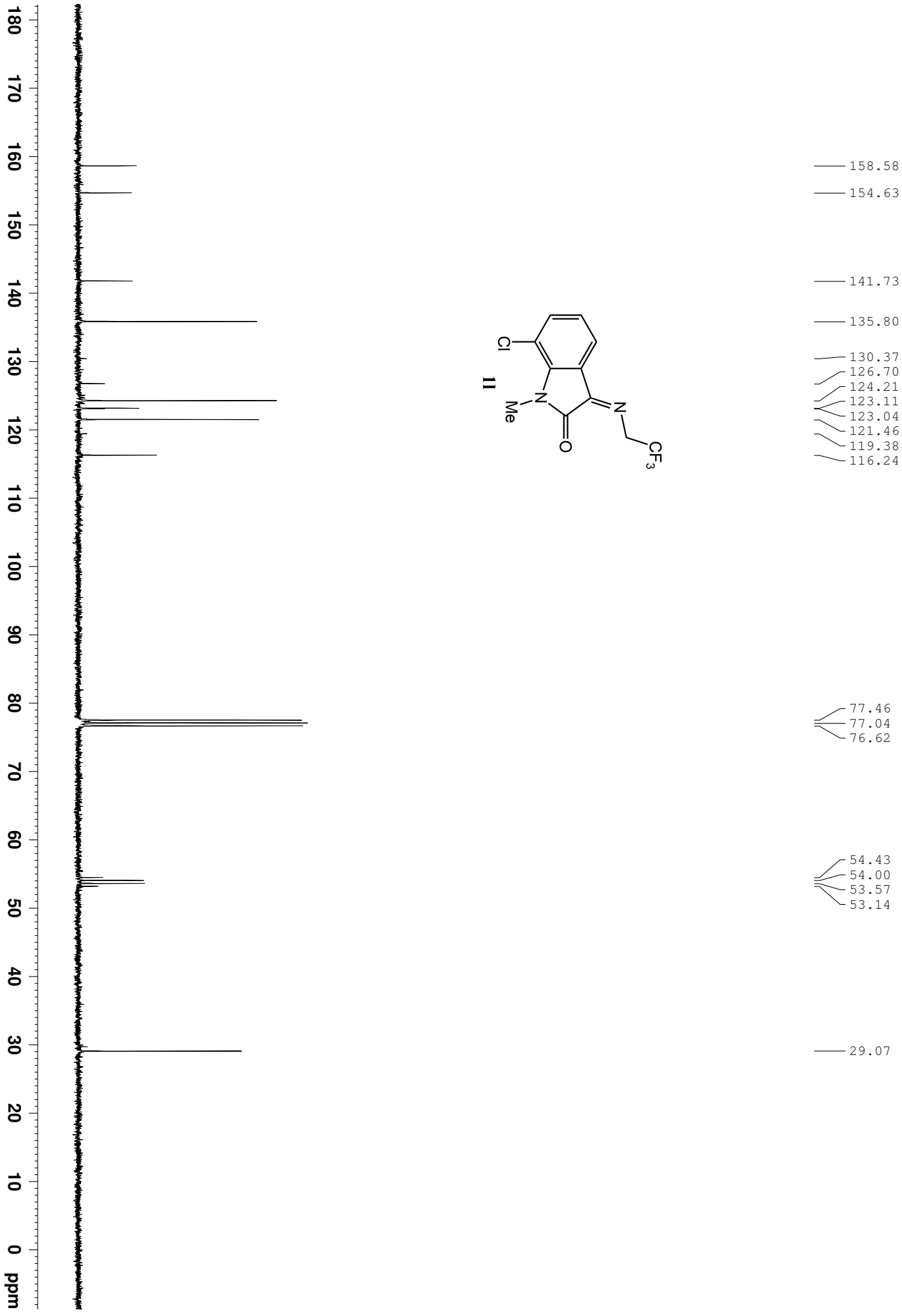
Me
O
N
CF3


180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
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154.63
141.73
135.80
130.37
126.70
124.21
123.11
123.04
121.46
119.38
116.24
77.46
77.04
76.62
54.43
54.00
53.57
53.14
29.07
Cl
N
Me
O
N
CF3

11

-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm
-71.902
11
Cl
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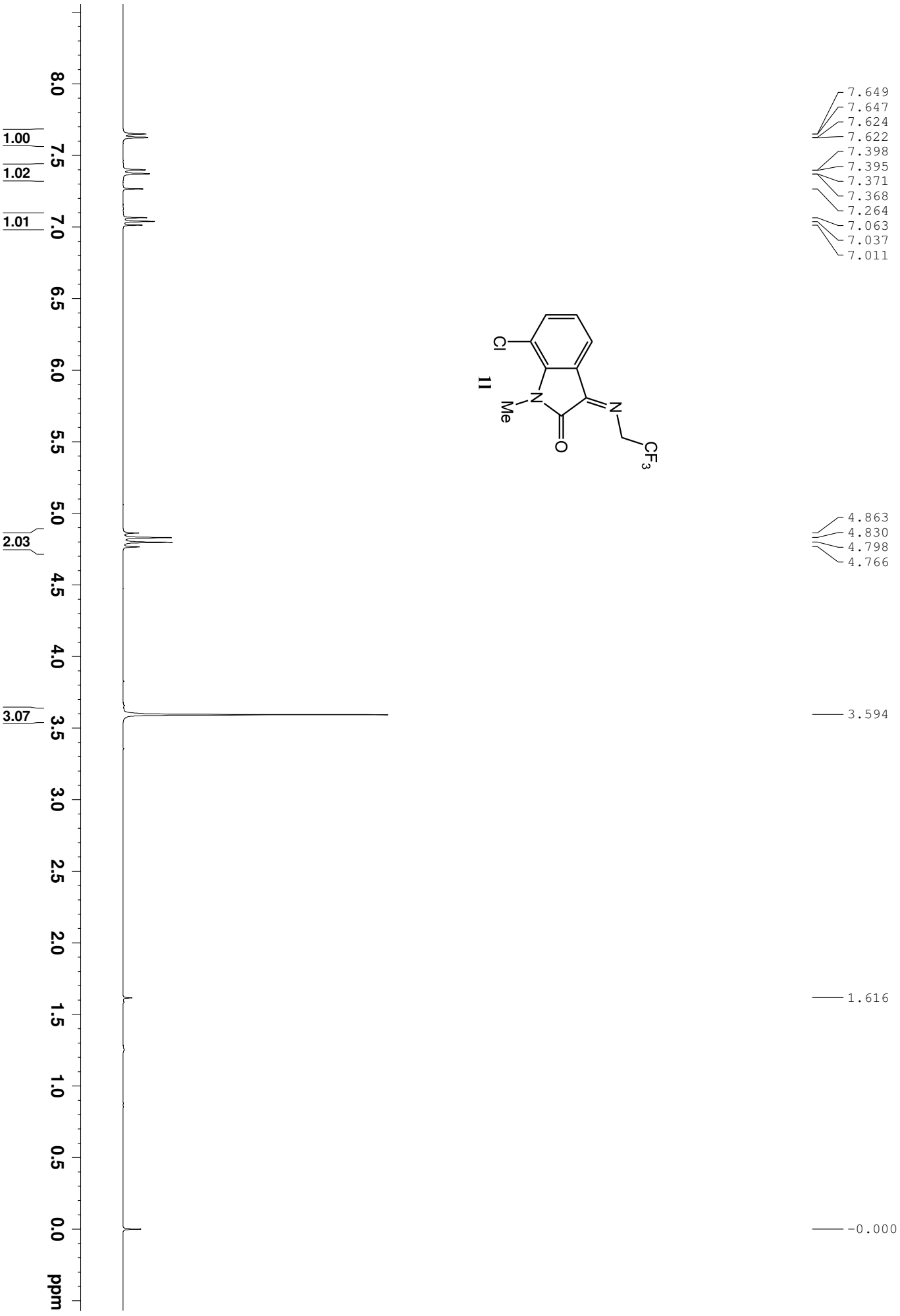
Me
O
N
CF3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7.624
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7.368
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7.063
7.037
7.011
4.863
4.830
4.798
4.766
3.594
1.616
-0.000
1.00
1.02
1.01
2.03
3.07
Cl
N
Me
O
N
CF3
11
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
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2.0
1.5
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0.5
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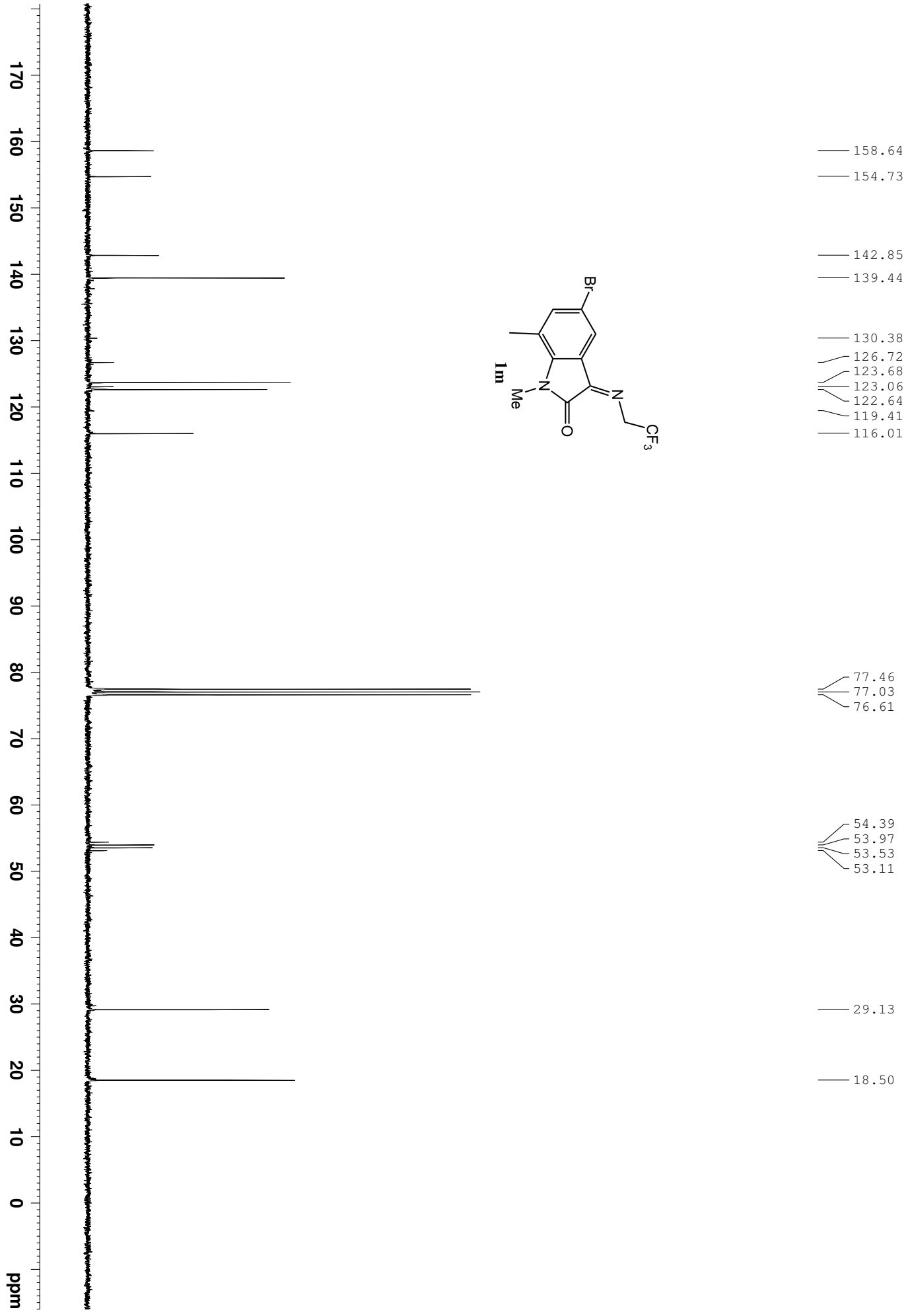
ppm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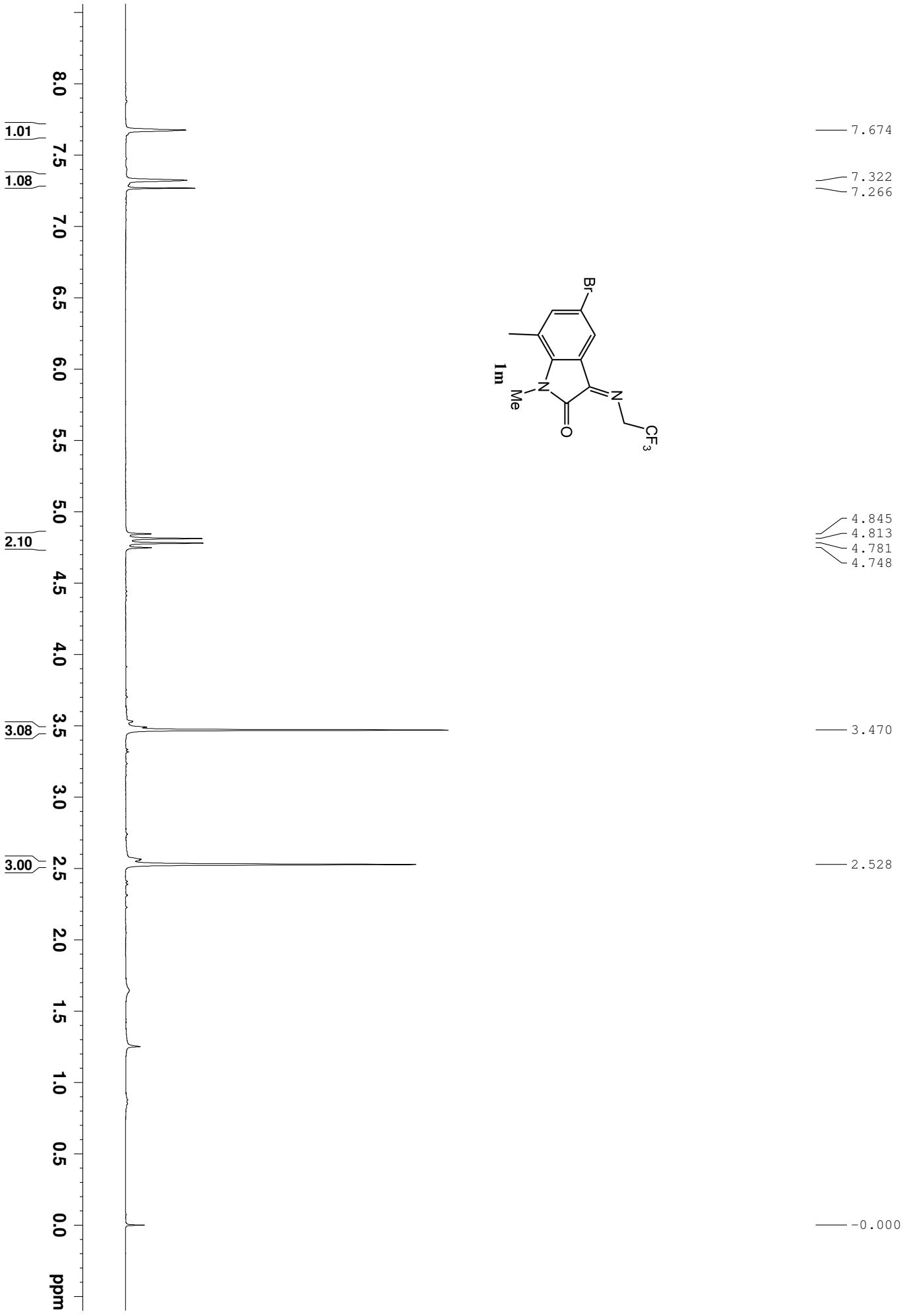
139.44
130.38
126.72
123.68
123.06
122.64
119.41
116.01
77.46
77.03
76.61
54.39
53.97
53.53
53.11
29.13
18.50
1m
Br
Me
N
O
CF3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm
Br
Im
Me
N
O
N
CF3
-71.902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1.08
2.10
3.08
3.00
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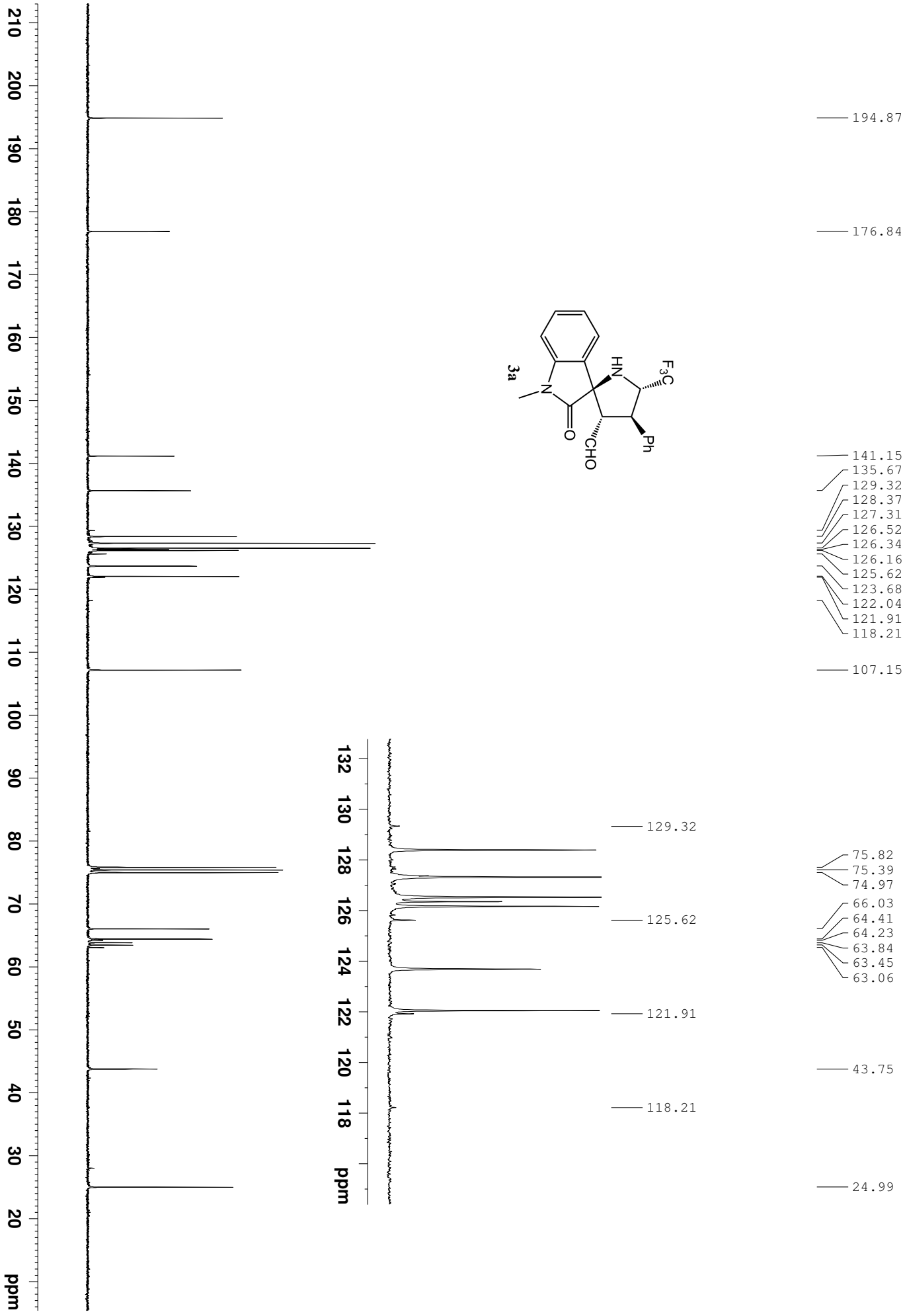
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
7.674
7.322
7.266
4.845
4.813
4.781
4.748
3.470
2.528
-0.000
Br
1m
Me
N
O
N
CF3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176.84
141.15
135.67
129.32
128.37
127.31
126.52
126.34
126.16
125.62
123.68
122.04
121.91
118.21
107.15
75.82
75.39
74.97
66.03
64.41
64.23
63.84
63.45
63.06
43.75
24.99
3a
HN
N
O
CHO
Ph
F3C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm
132 130 128 126 124 122 120 118 ppm
129.32
125.62
121.91
118.21

-64
-65
-66
-67
-68
-69
-70
-71
-72
-73
-74
-75
-76
-77
-78
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-80
-81
-82
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ppm
3a
HN
N
O
CHO
Ph
F3C
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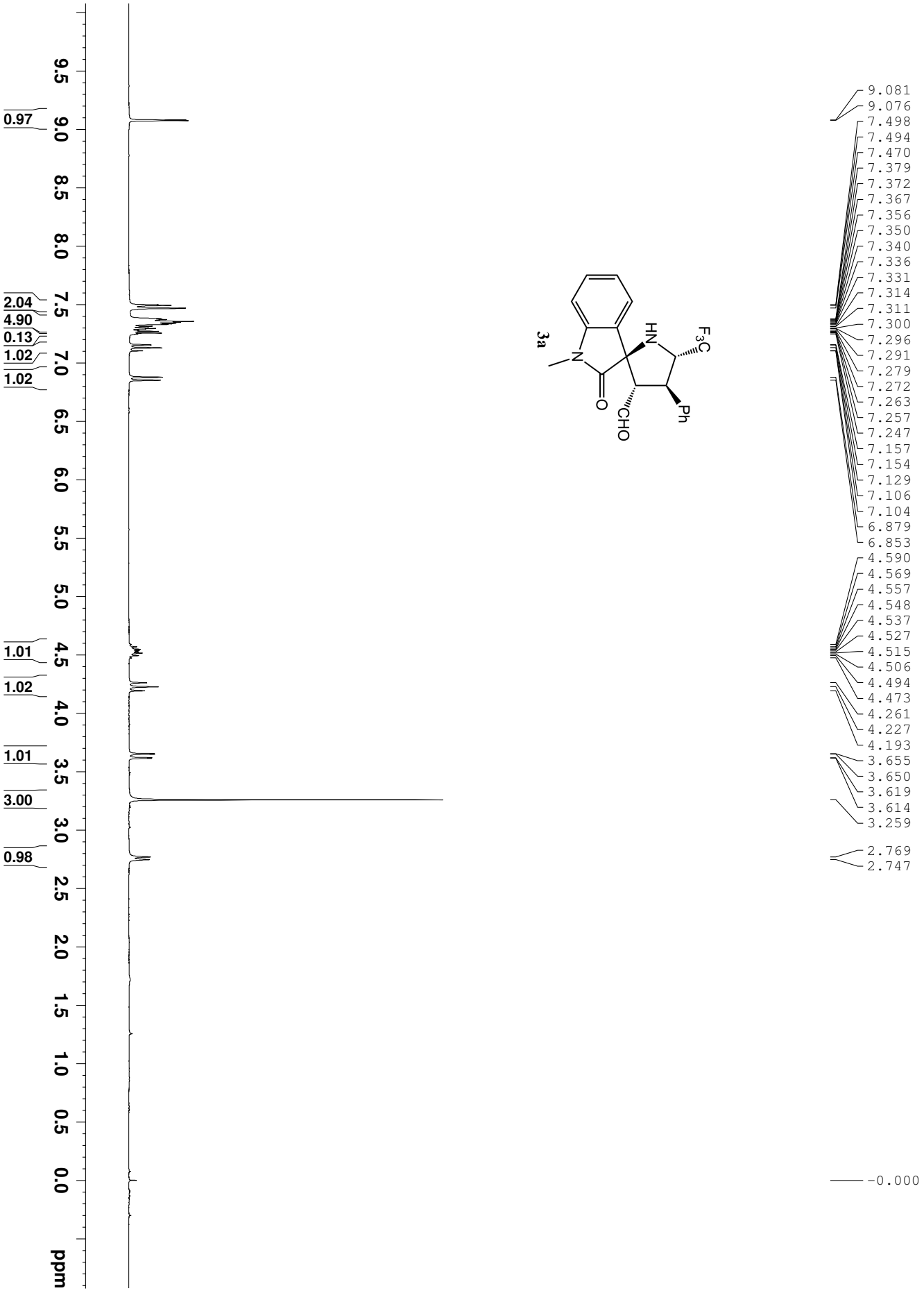
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1.01
1.02
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3.00
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3a
HN
F3C
N
O
CHO
Ph
9.081
9.076
7.498
7.494
7.470
7.379
7.372
7.367
7.356
7.350
7.340
7.336
7.331
7.314
7.311
7.300
7.296
7.291
7.279
7.272
7.263
7.257
7.247
7.157
7.154
7.129
7.106
7.104
6.879
6.853
4.590
4.569
4.557
4.548
4.537
4.527
4.515
4.506
4.494
4.473
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4.193
3.655
3.650
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3.259
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2.747
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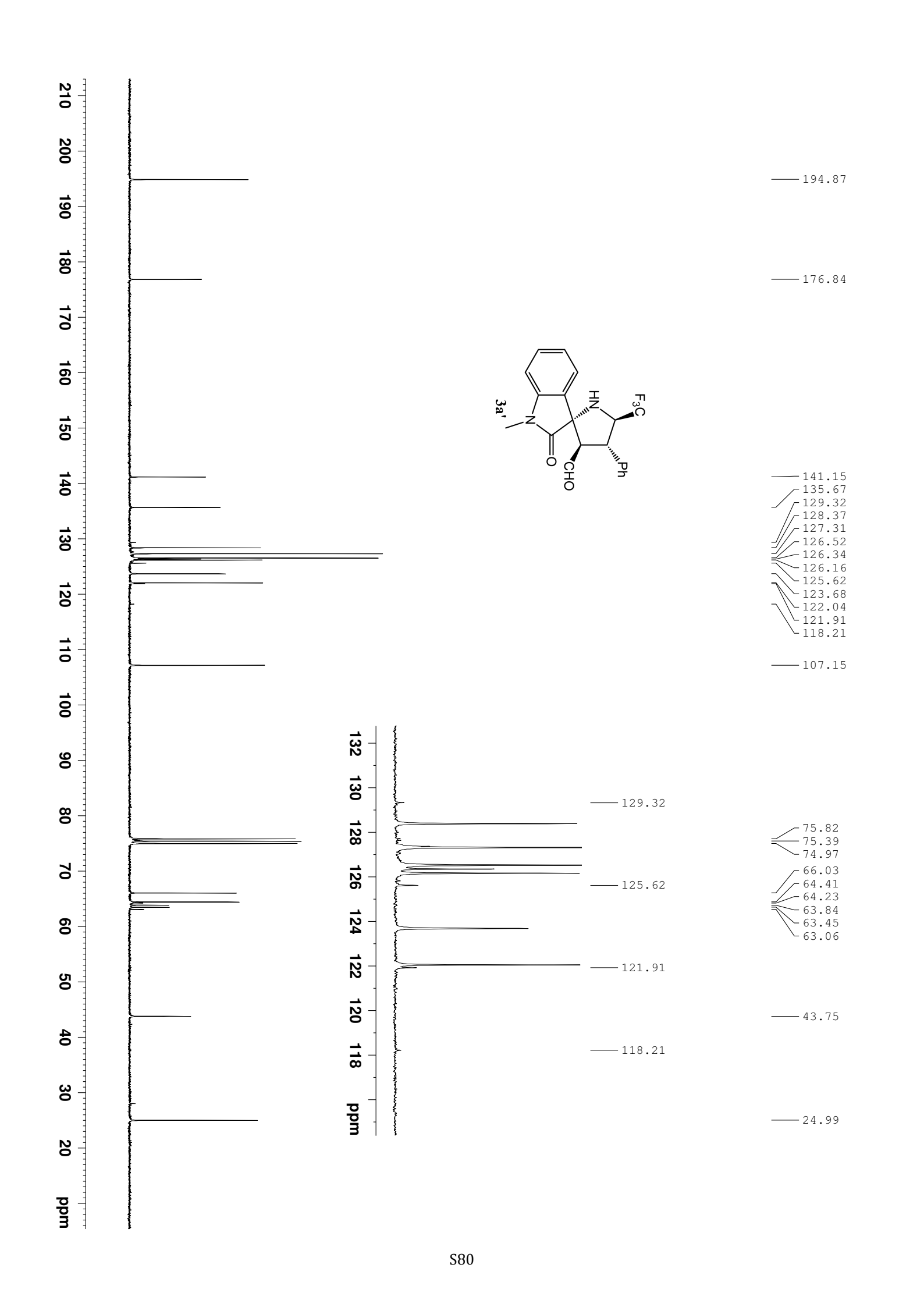
194.87
176.84
141.15
135.67
129.32
128.37
127.31
126.52
126.34
126.16
125.62
123.68
122.04
121.91
118.21
107.15
75.82
75.39
74.97
66.03
64.41
64.23
63.84
63.45
63.06
43.75
24.99
3a'
HN
N
O
CHO
Ph
F3C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm
132 130 128 126 124 122 120 118 ppm
129.32
125.62
121.91
118.21

-74.823
3a'
HN
N
O
CHO
Ph
F3C
-66
-67
-68
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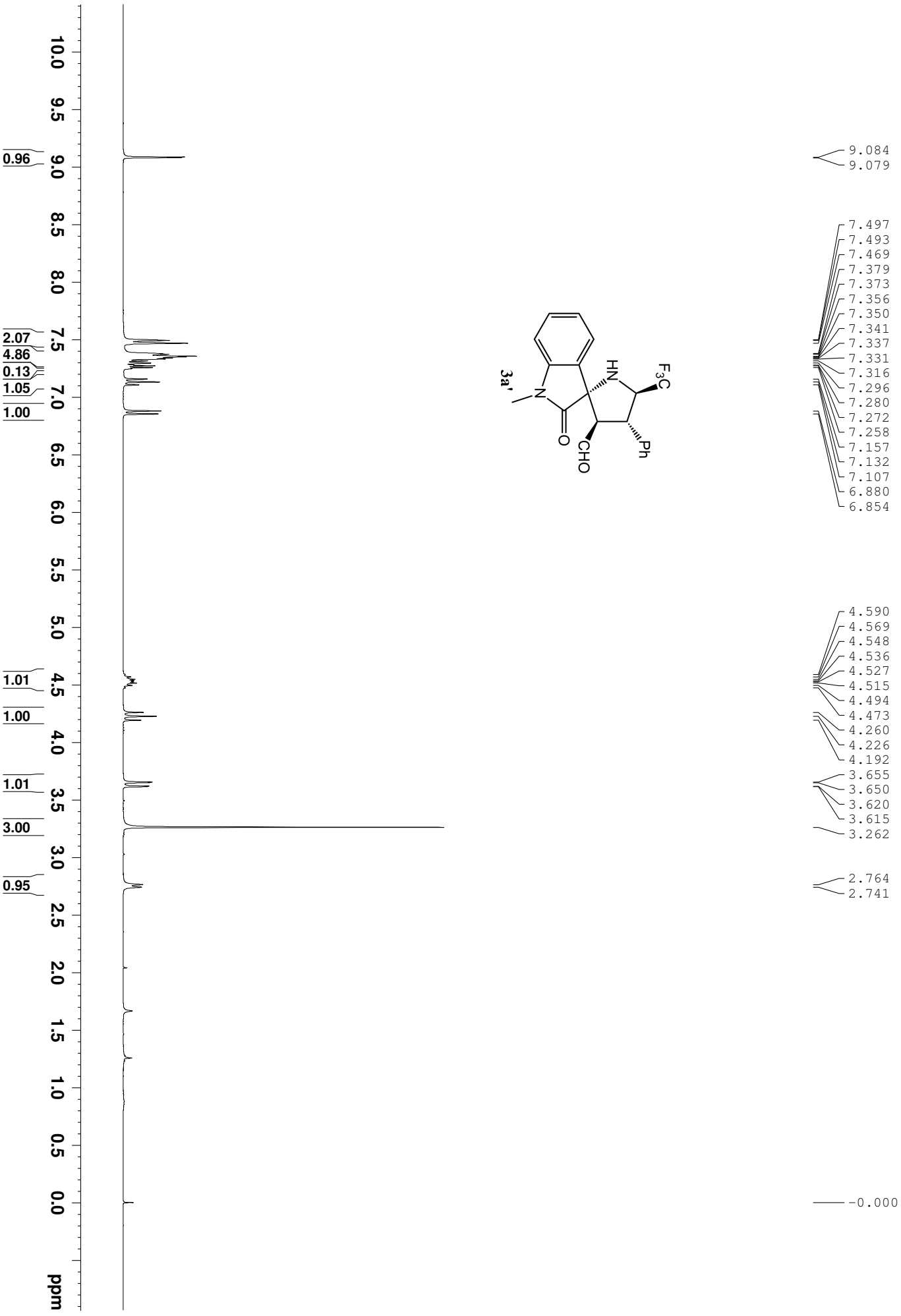
-70
-71
-72
-73
-74
-75
-76
-77
-78
-79
-80
-81
-82
ppm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7.337
7.331
7.316
7.296
7.280
7.272
7.258
7.157
7.132
7.107
6.880
6.854
4.590
4.569
4.548
4.536
4.527
4.515
4.494
4.473
4.260
4.226
4.192
3.655
3.650
3.620
3.615
3.262
2.764
2.741
-0.000
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2.07
4.86
0.13
1.05
1.00
1.01
1.00
1.01
3.00
0.95
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
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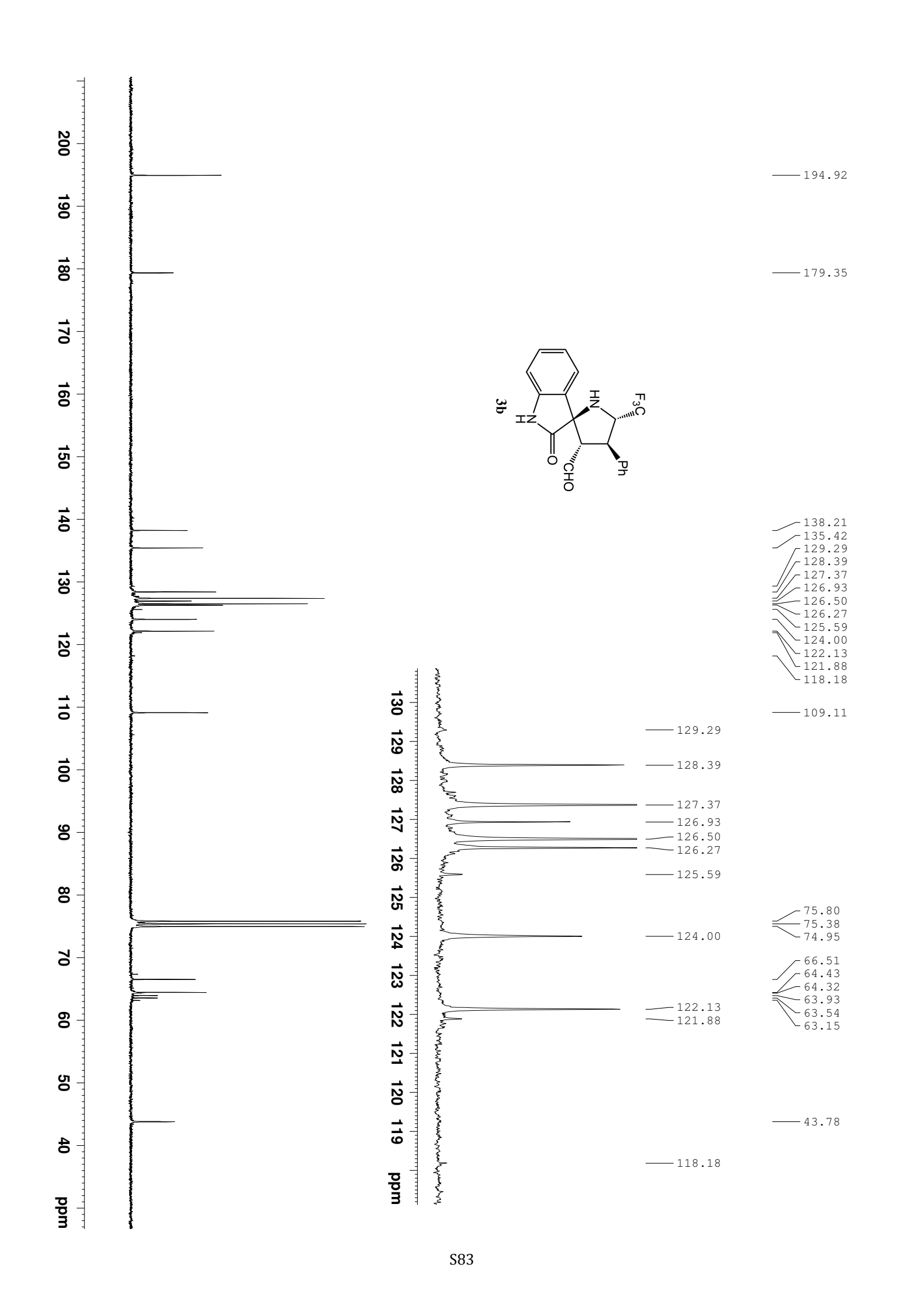
ppm
3a'
N
O
HN
CHO
Ph
F3C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3b
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126.50
126.27
125.59
124.00
122.13
121.88
118.18
109.11
75.80
75.38
74.95
66.51
64.43
64.32
63.93
63.54
63.15
43.78
ppm

-55
-60
-65
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-75
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-85
-90
-95
ppm
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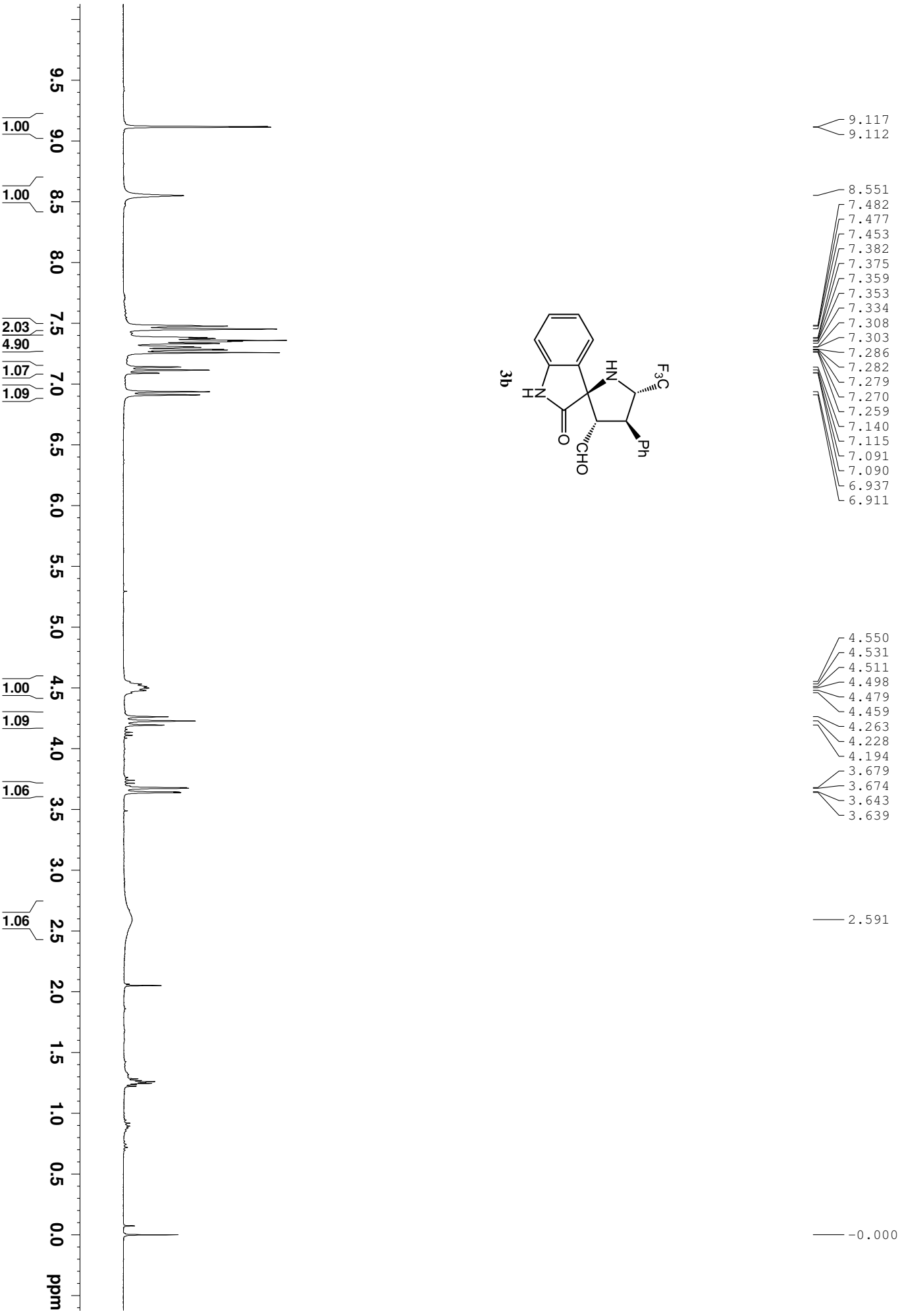
HN
H
N
O
CHO
Ph
F3C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1.09
1.00
1.09
1.06
1.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3b
HN
F3C
N
H
O
CHO
Ph
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9.112
8.551
7.482
7.477
7.453
7.382
7.375
7.359
7.353
7.334
7.308
7.303
7.286
7.282
7.279
7.270
7.259
7.140
7.115
7.091
7.090
6.937
6.911
4.550
4.531
4.511
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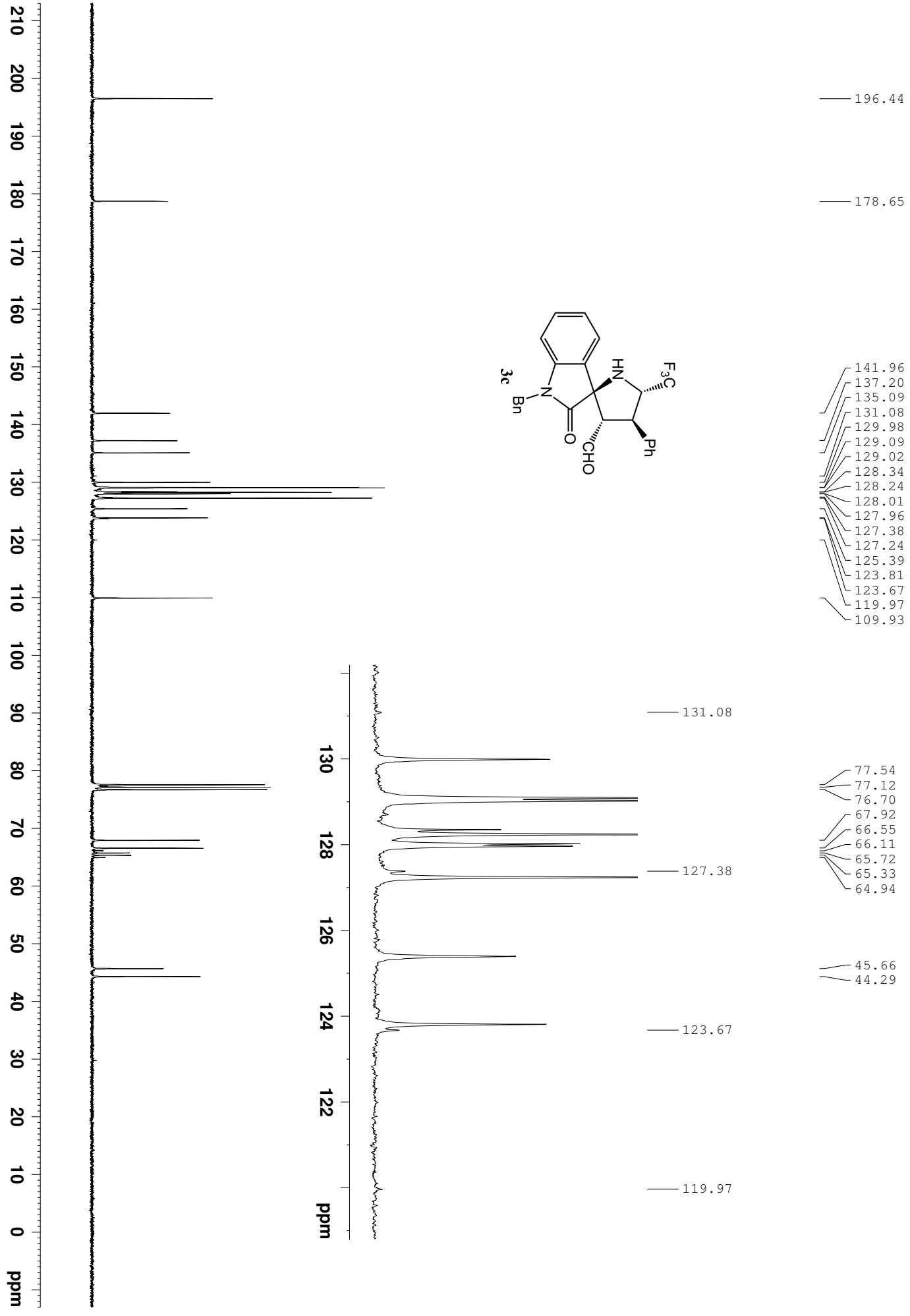
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Bn
N
O
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CHO
Ph
F3C
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135.09
131.08
129.98
129.09
129.02
128.34
128.24
128.01
127.96
127.38
127.24
125.39
123.81
123.67
119.97
109.93
77.54
77.12
76.70
67.92
66.55
66.11
65.72
65.33
64.94
45.66
44.29
ppm

-66
-67
-68
-69
-70
-71
-72
-73
-74
-75
-76
-77
-78
-79
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ppm
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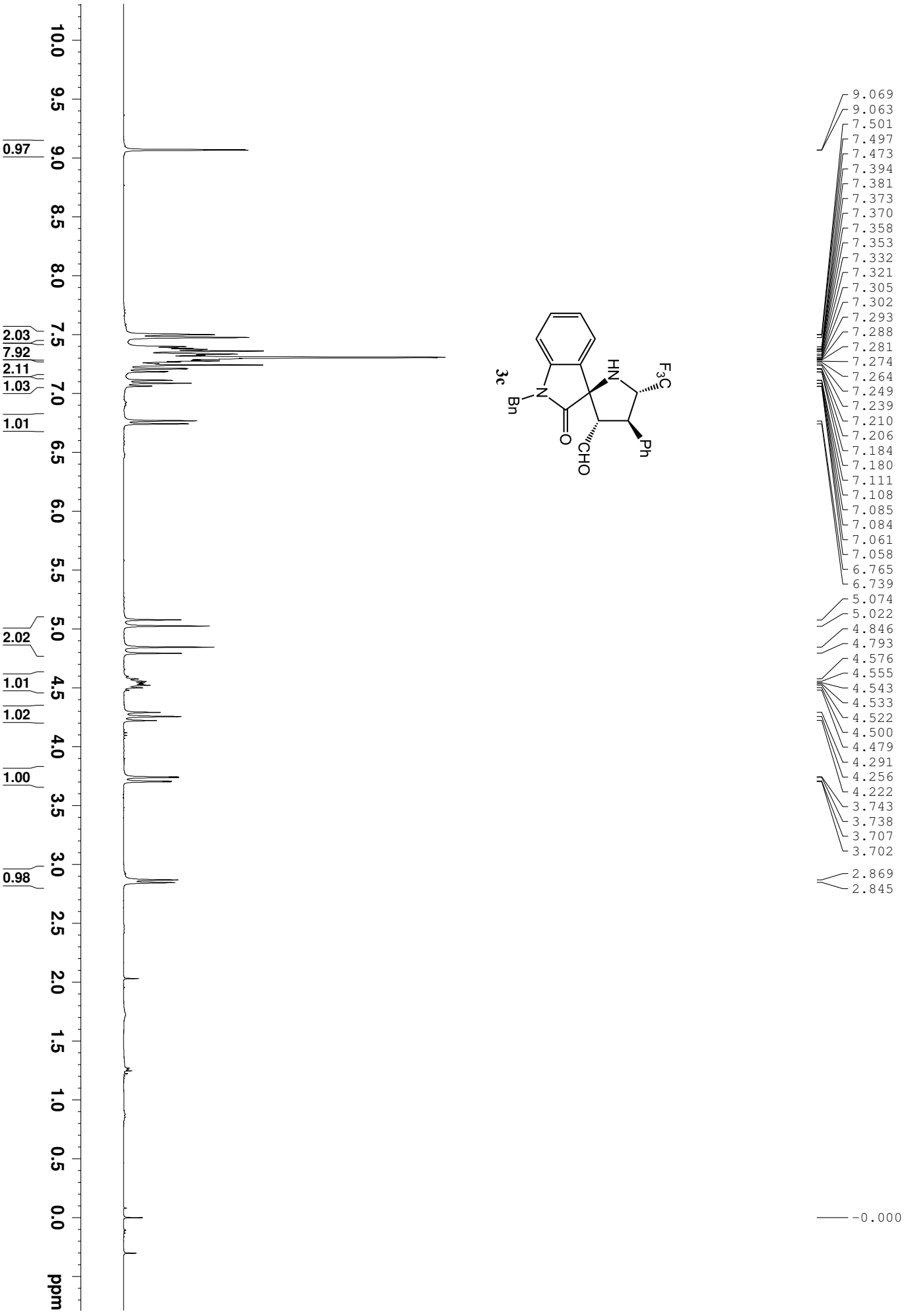
N
O
CHO
HN
F3C
Ph
-74.767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Bn
N
O
HN
CHO
Ph
F3C
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8.0
7.5
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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7.92
2.11
1.03
1.01
2.02
1.01
1.02
1.00
0.98
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9.063
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7.381
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7.370
7.358
7.353
7.332
7.321
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7.302
7.293
7.288
7.281
7.274
7.264
7.249
7.239
7.210
7.206
7.184
7.180
7.111
7.108
7.085
7.084
7.061
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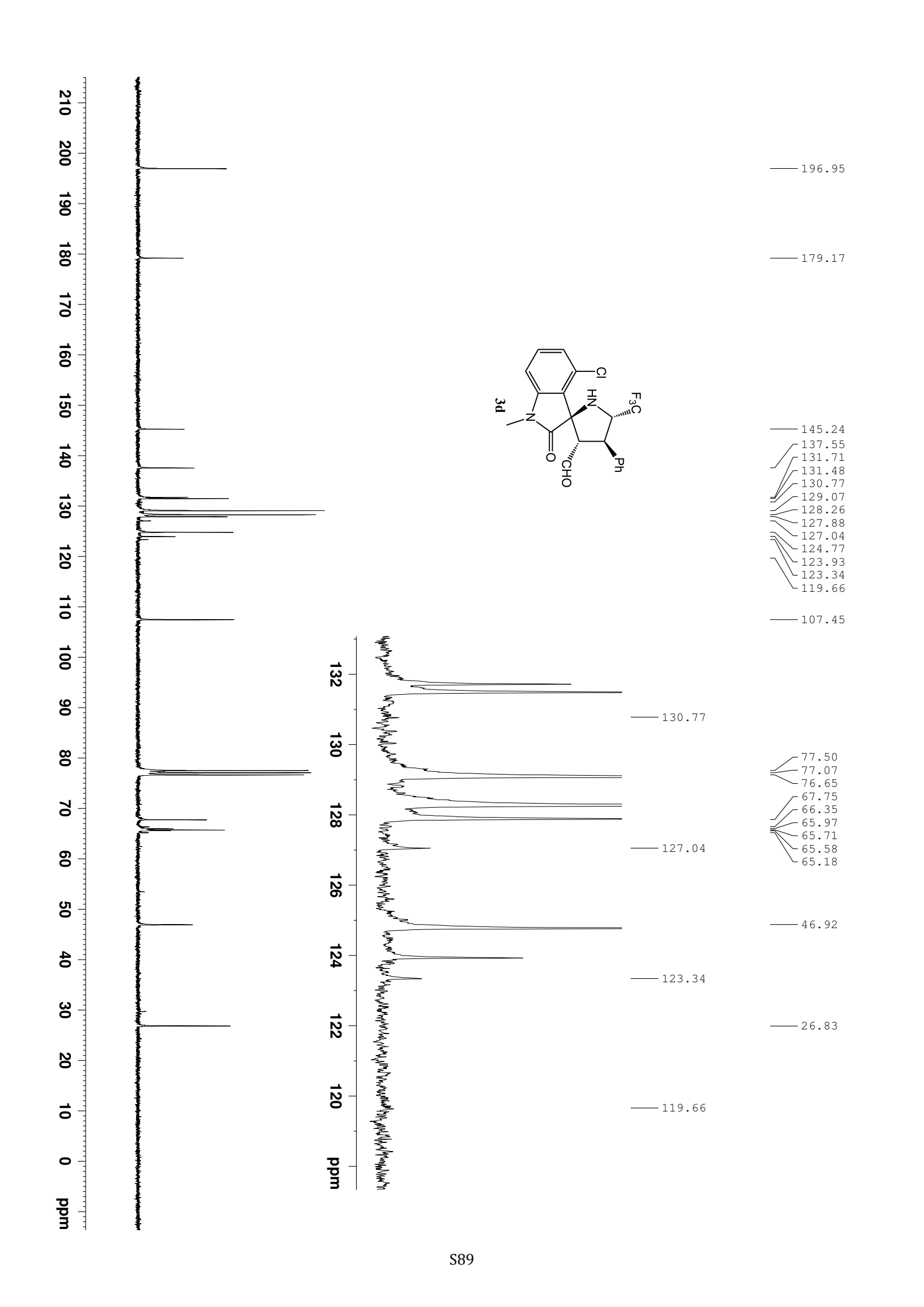
3d
Cl
HN
F3C
N
O
CHO
Ph
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130.77
129.07
128.26
127.88
127.04
124.77
123.93
123.34
119.66
107.45
77.50
77.07
76.65
67.75
66.35
65.97
65.71
65.58
65.18
46.92
26.83
ppm

-74.051
3d
Cl
HN
F3C
N
O
CHO
Ph
ppm
-68
-69
-70
-71
-72
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-74
-75
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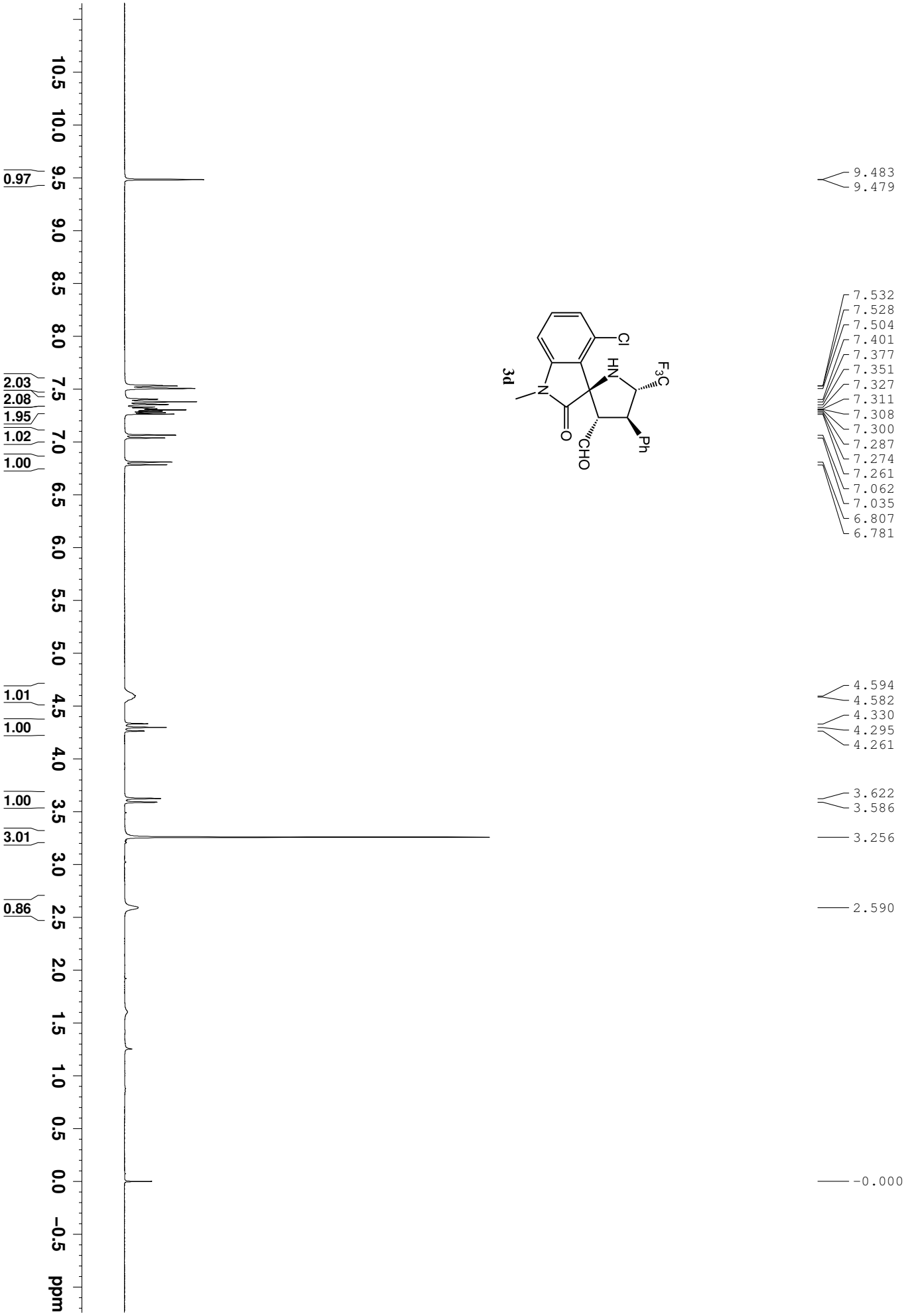
-77
-78
-79


3d
Cl
HN
F3C
N
O
CHO
Ph
9.483
9.479
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7.528
7.504
7.401
7.377
7.351
7.327
7.311
7.308
7.300
7.287
7.274
7.261
7.062
7.035
6.807
6.781
4.594
4.582
4.330
4.295
4.261
3.622
3.586
3.256
2.590
-0.000
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2.08
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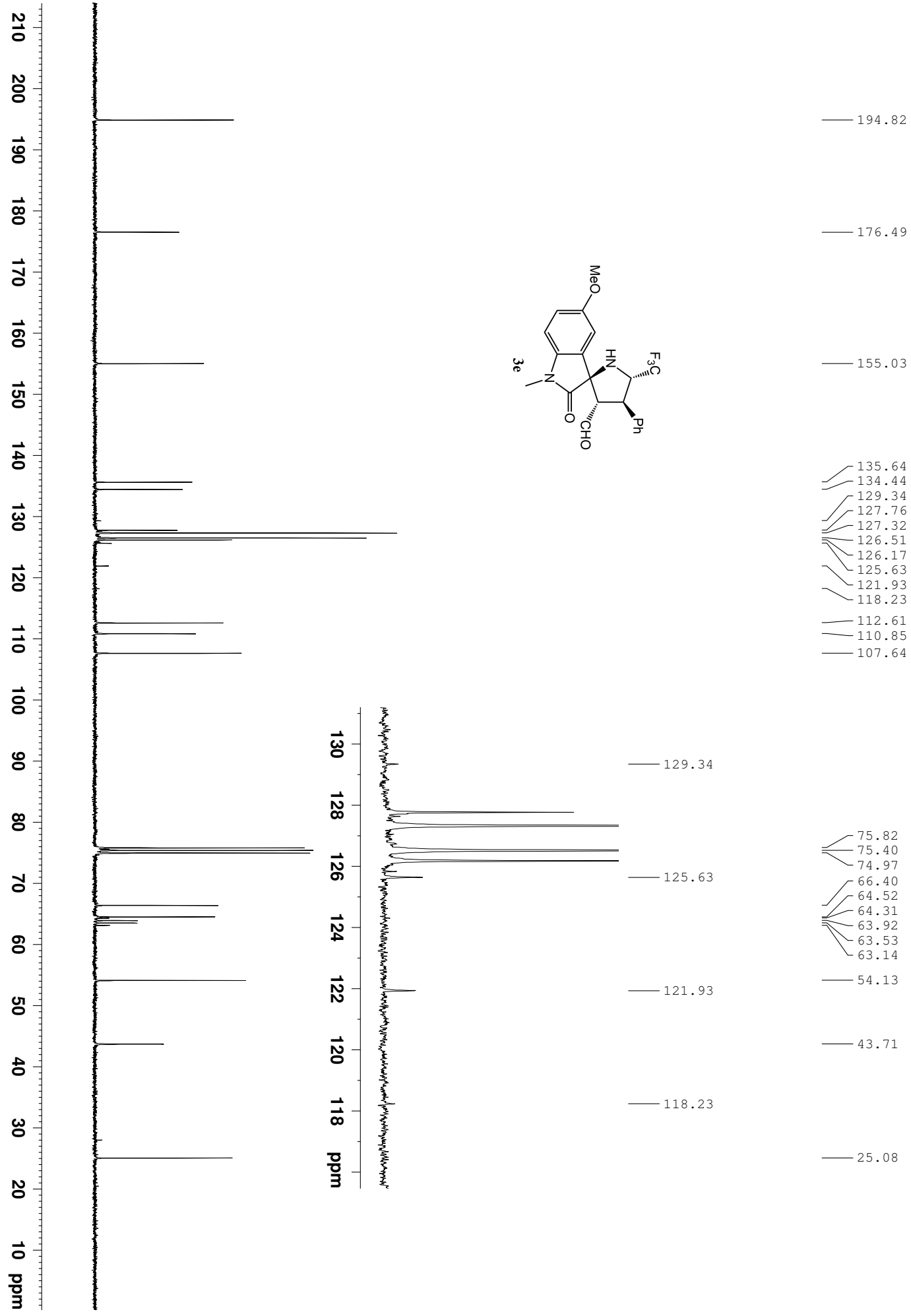
1.00
1.00
3.01
0.86
ppm


MeO
HN
F3C
3e
N
O
CHO
Ph
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127.76
127.32
126.51
126.17
125.63
121.93
118.23
112.61
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74.97
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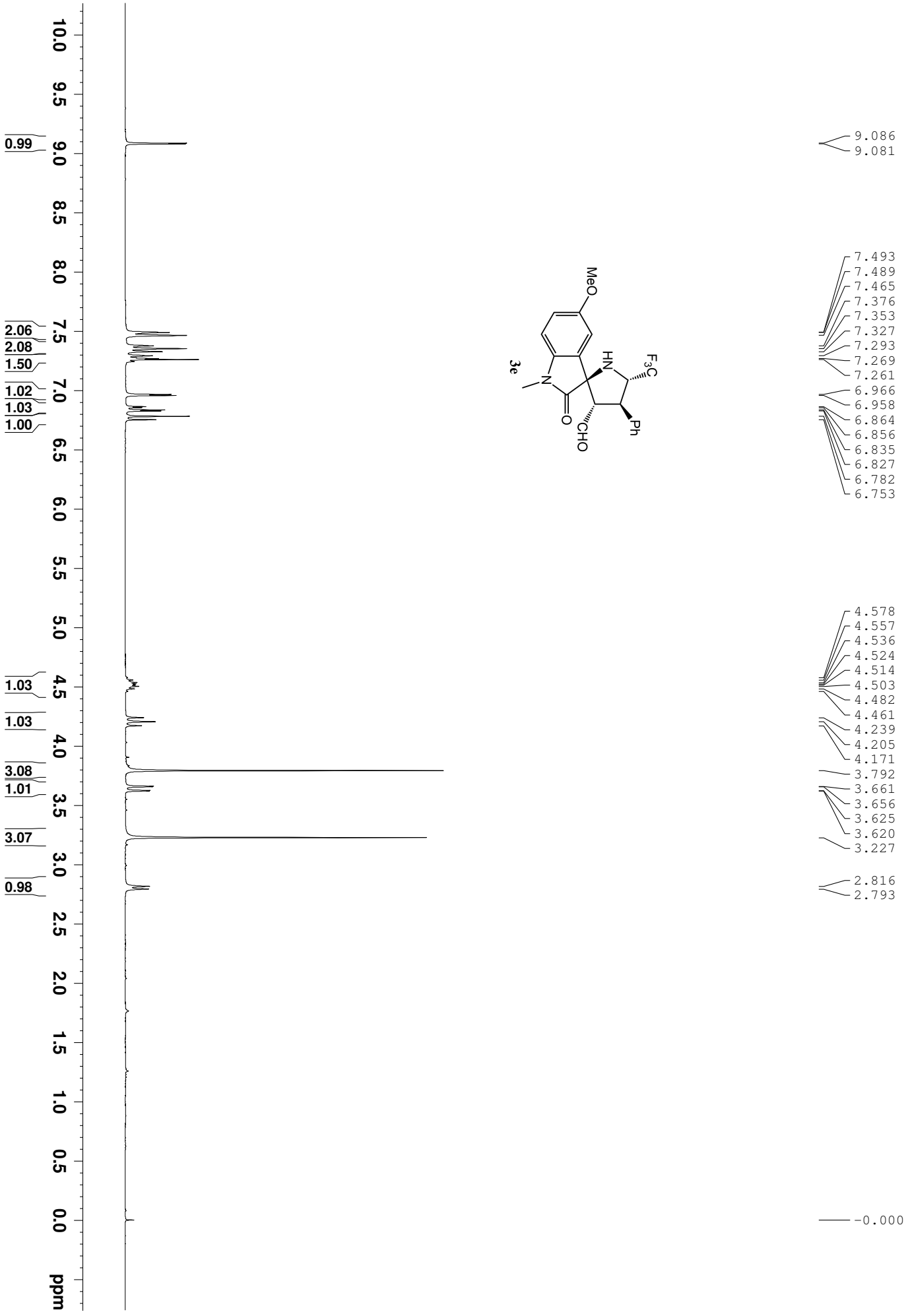
63.53
63.14
54.13
43.71
25.08
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
130 128 126 124 122 120 118 ppm

MeO
HN
F3C
3e
N
O
CHO
Ph

-74.83
-66
-67
-68
-69
-70
-71
-72
-73
-74
-75
-76
-77
-78
-79
-80
-81
-82
-83
-84
ppm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HN
F3C
3e
N
O
CHO
Ph
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7.353
7.327
7.293
7.269
7.261
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6.958
6.864
6.856
6.835
6.827
6.782
6.753
4.578
4.557
4.536
4.524
4.514
4.503
4.482
4.461
4.239
4.205
4.171
3.792
3.661
3.656
3.625
3.620
3.227
2.816
2.793
-0.000
0.99
2.06
2.08
1.50
1.02
1.03
1.00
1.03
1.03
3.08
1.01
3.07
0.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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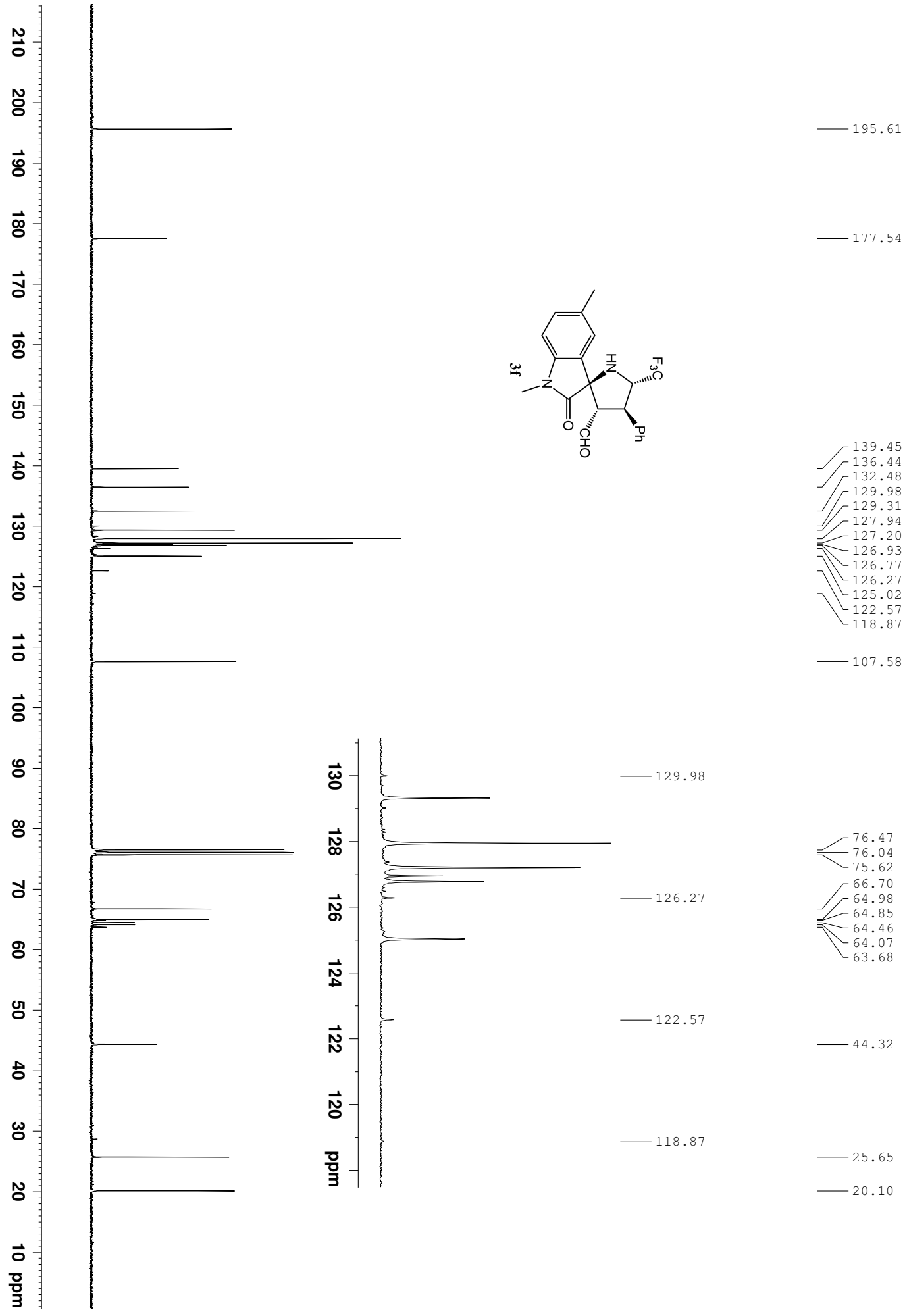
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm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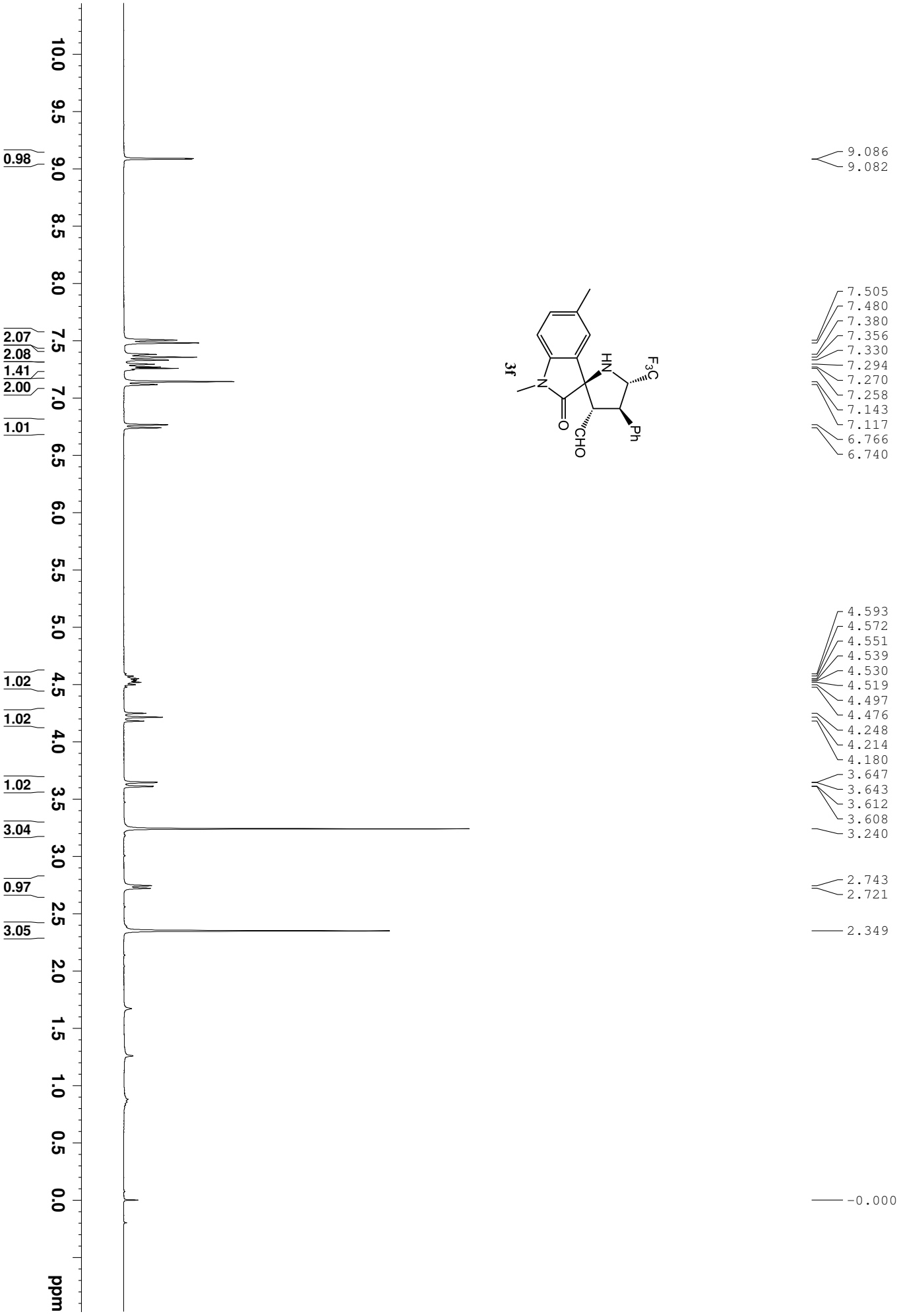
125.02
122.57
118.87
107.58
76.47
76.04
75.62
66.70
64.98
64.85
64.46
64.07
63.68
44.32
25.65
20.10
3f
HN
N
O
CHO
Ph
F3C
ppm

-74.775
3f
HN
F3C
N
O
CHO
Ph
-65
-66
-67
-68
-69
-70
-71
-72
-73
-74
-75
-76
-77
-78
-79
-80
-81
-82
-83
-84
ppm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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.98
2.07
2.08
1.41
2.00
1.01
1.02
1.02
1.02
3.04
0.97
3.05
3f
HN
F3C
N
O
CHO
Ph
9.086
9.082
7.505
7.480
7.380
7.356
7.330
7.294
7.270
7.258
7.143
7.117
6.766
6.740
4.593
4.572
4.551
4.539
4.530
4.519
4.497
4.476
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3.647
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3.612
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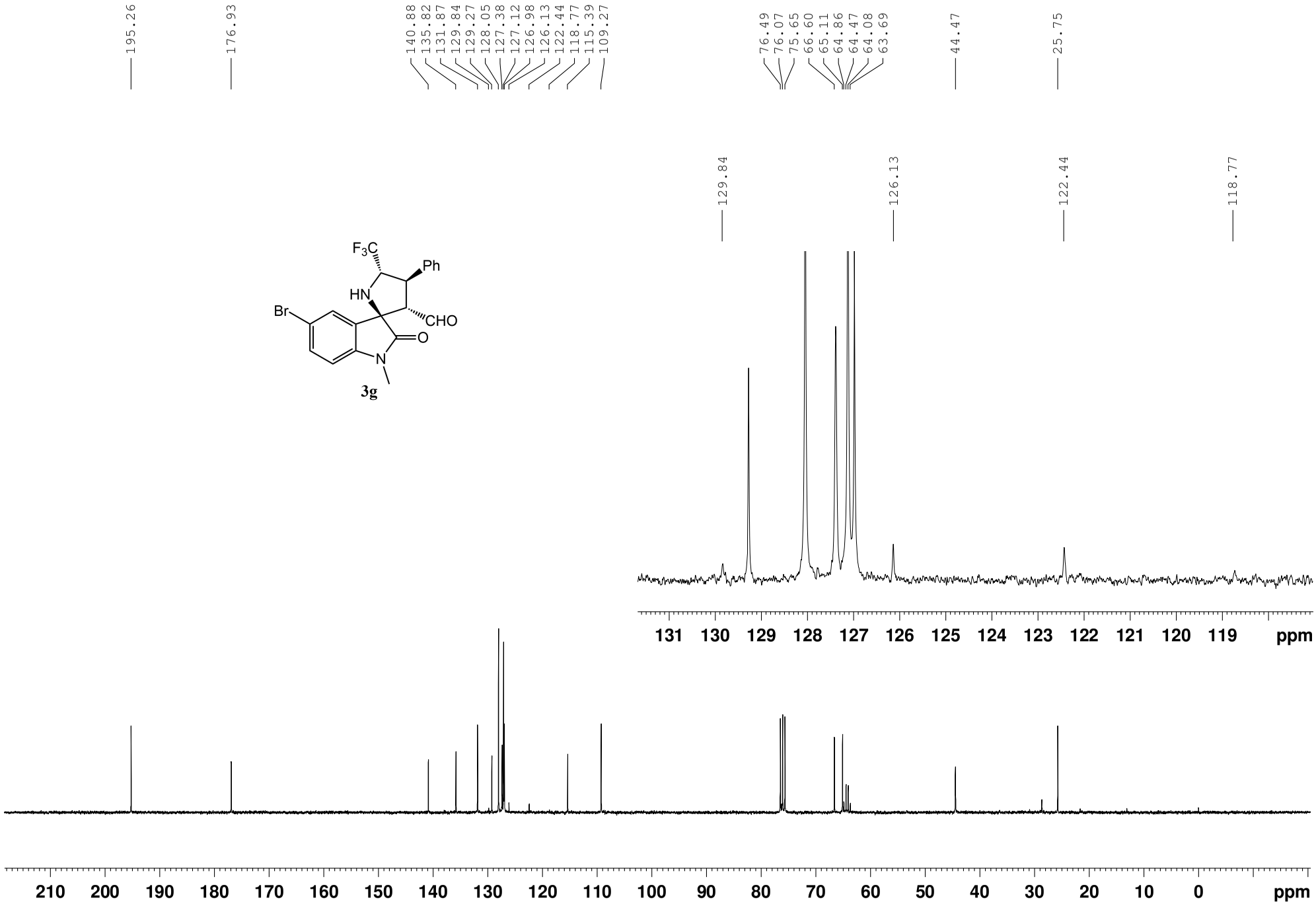
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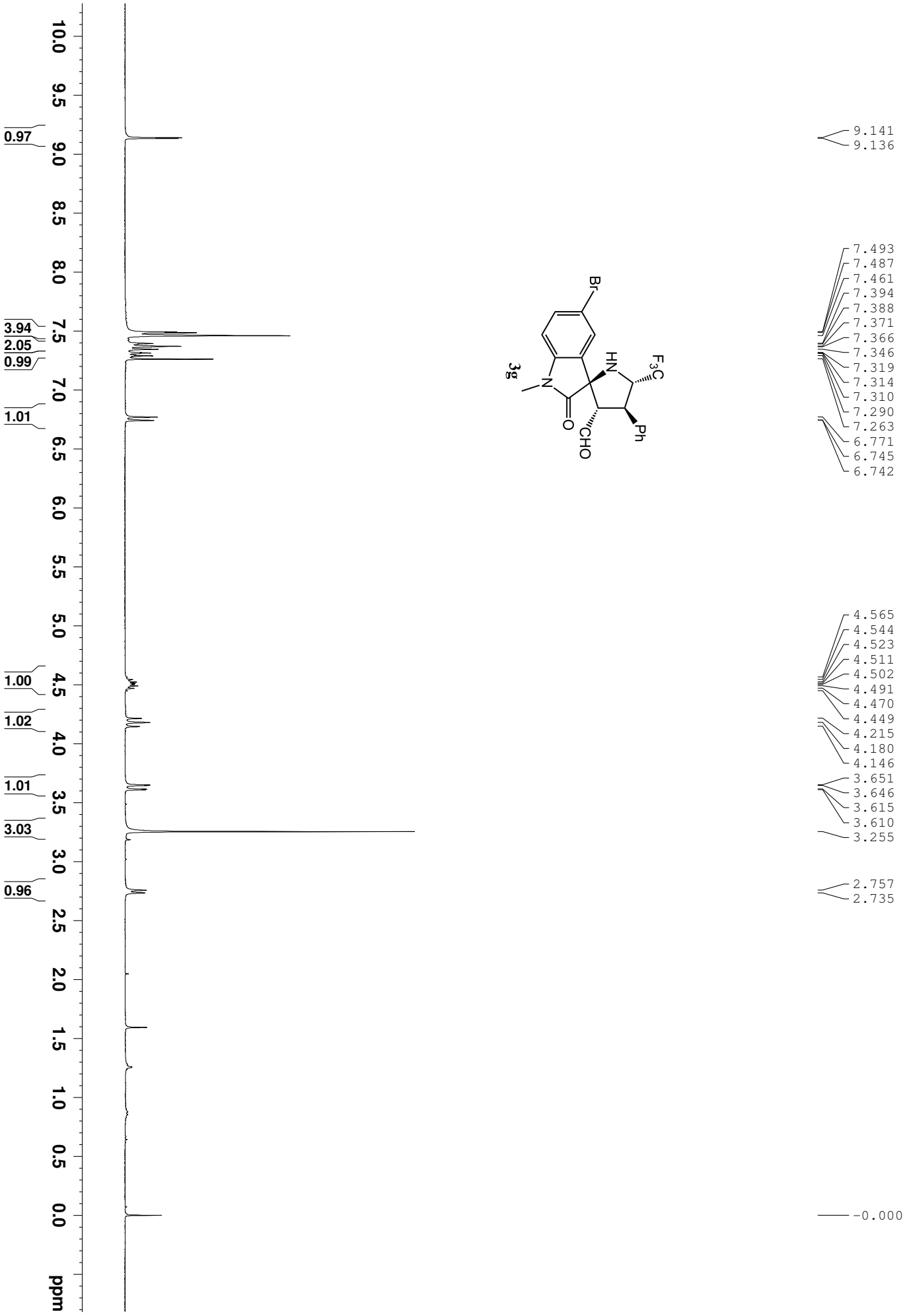
126.13
122.44
118.77
115.39
109.27
76.49
76.07
75.65
66.60
65.11
64.86
64.47
64.08
63.69
44.47
25.75
129.84
126.13
122.44
118.77
F3C
Ph
HN
Br
CHO
O
N
3g
131 130 129 128 127 126 125 124 123 122 121 120 119 ppm
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

-74.867
3g
Br
HN
F3C
N
O
CHO
Ph
-67
-68
-69
-70
-71
-72
-73
-74
-75
-76
-77
-78
-79
-80
-81
-82
-83
ppm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6.5
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5.5
5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.97
3.94
2.05
0.99
1.01
1.00
1.02
1.01
3.03
0.96
Br
HN
F3C
3g
N
O
CHO
Ph
9.141
9.136
7.493
7.487
7.461
7.394
7.388
7.371
7.366
7.346
7.319
7.314
7.310
7.290
7.263
6.771
6.745
6.742
4.565
4.544
4.523
4.511
4.502
4.491
4.470
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4.146
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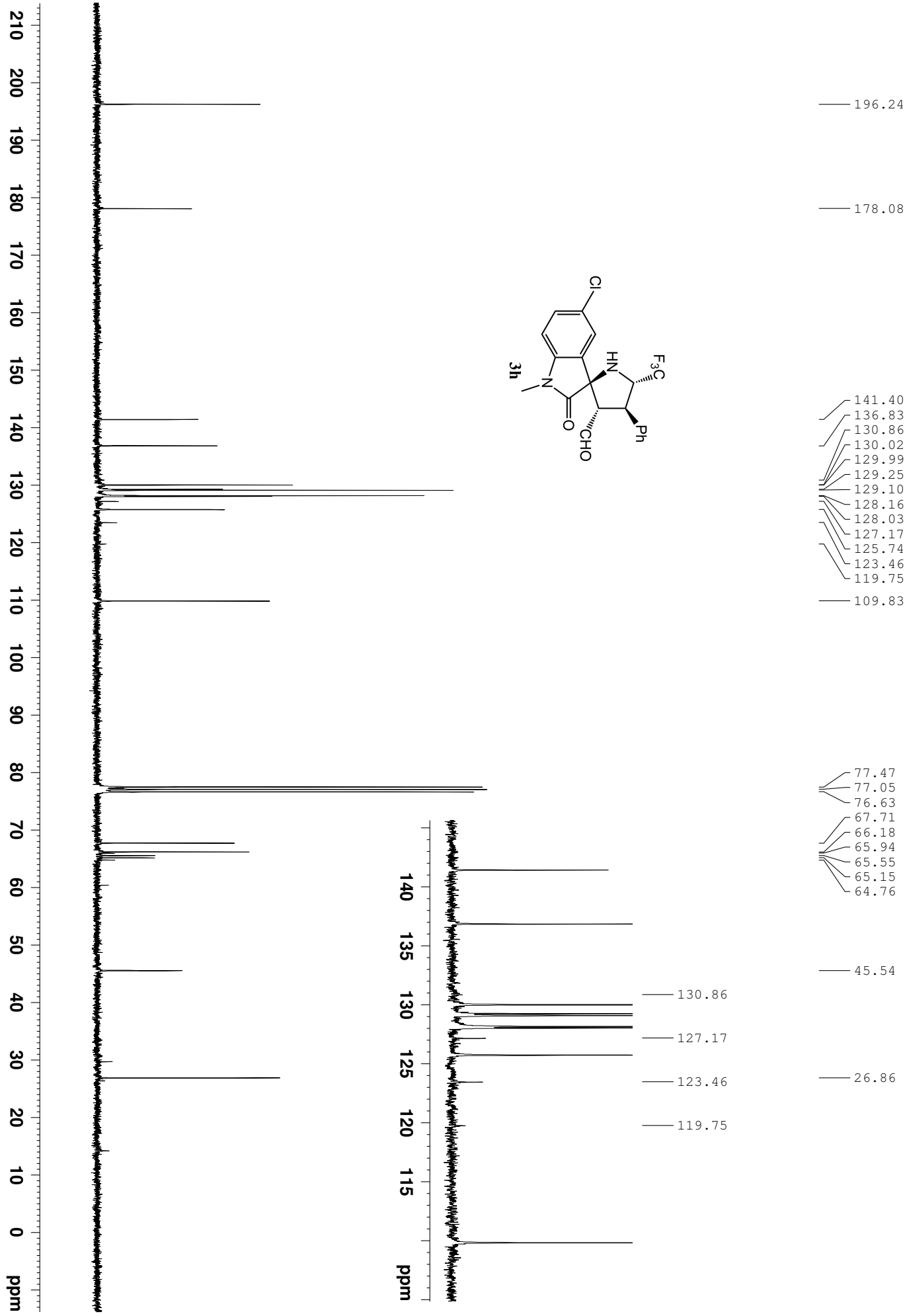
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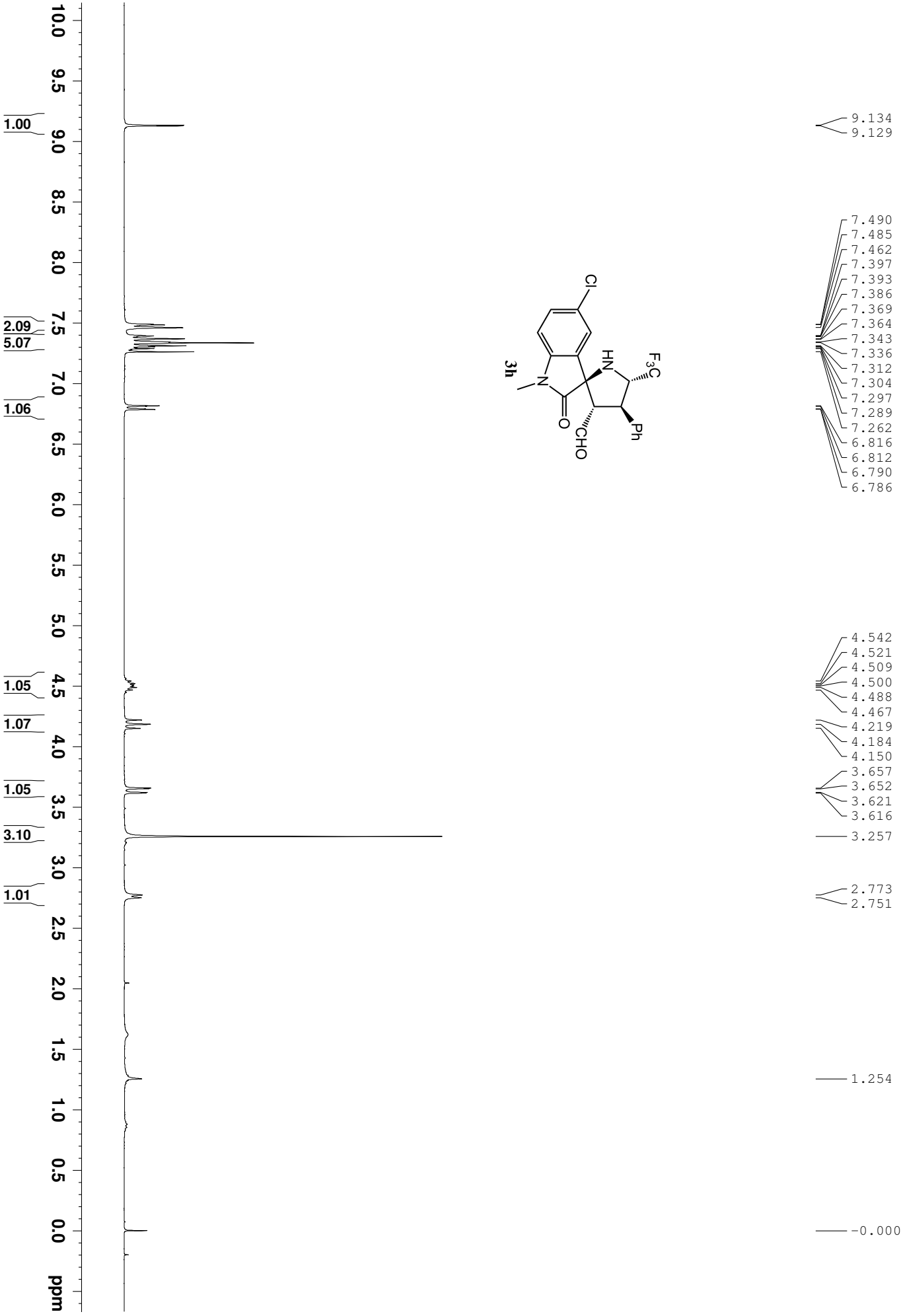
129.10
128.16
128.03
127.17
125.74
123.46
119.75
109.83
77.47
77.05
76.63
67.71
66.18
65.94
65.55
65.15
64.76
45.54
26.86
130.86
127.17
123.46
119.75
3h
Cl
HN
F3C
N
O
CHO
Ph
ppm
ppm

-74.894
3h
Cl
HN
F3C
N
O
CHO
Ph
-65
-66
-67
-68
-69
-70
-71
-72
-73
-74
-75
-76
-77
-78
-79
-80
-81
-82
-83
-84
ppm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5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
2.09
5.07
1.06
1.05
1.07
1.05
3.10
1.01
Cl
HN
F3C
3h
N
O
CHO
Ph
9.134
9.129
7.490
7.485
7.462
7.397
7.393
7.386
7.369
7.364
7.343
7.336
7.312
7.304
7.297
7.289
7.262
6.816
6.812
6.790
6.786
4.542
4.521
4.509
4.500
4.488
4.467
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3.652
3.621
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1.254
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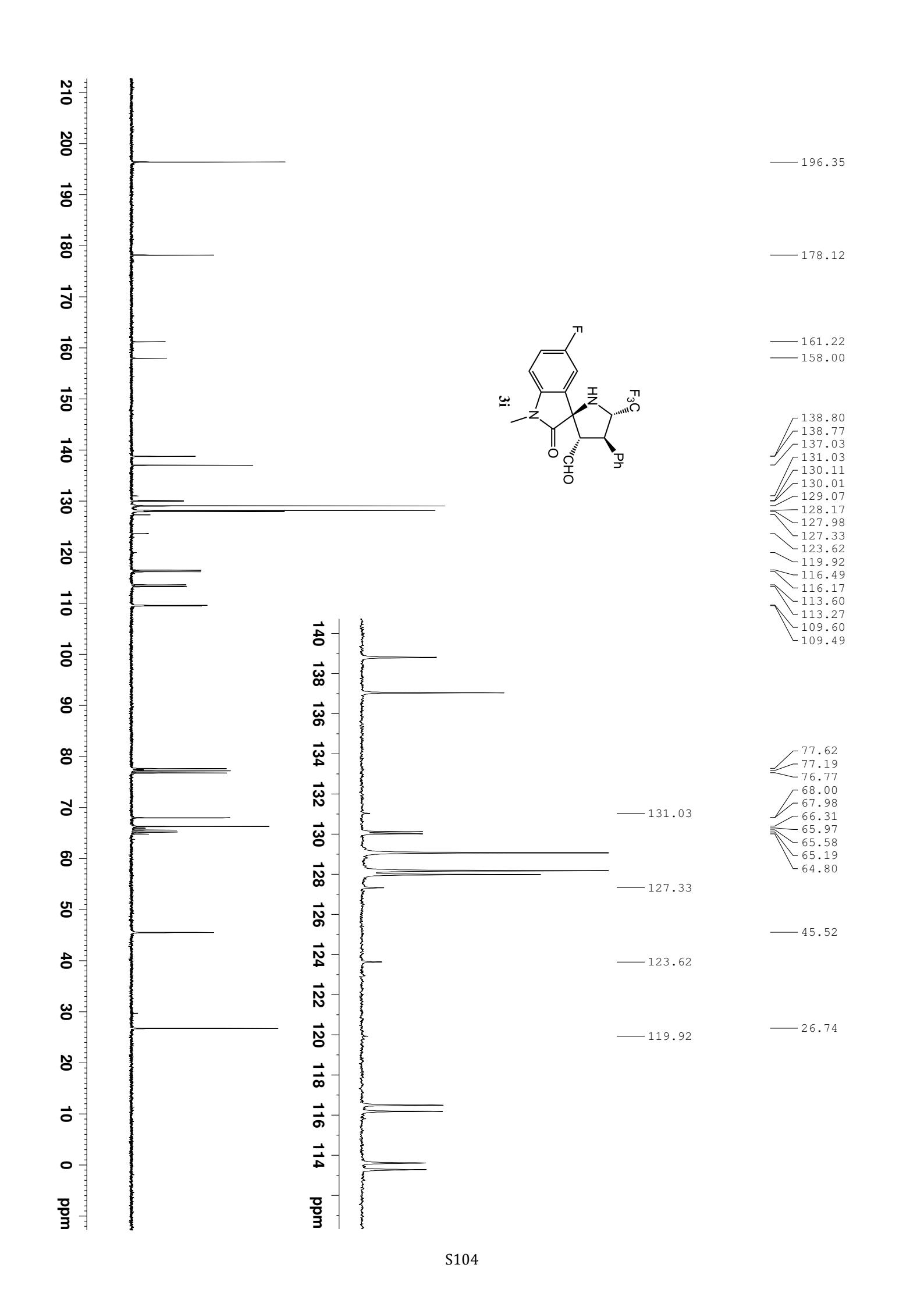
3i
F
HN
F3C
N
O
CHO
Ph
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131.03
130.11
130.01
129.07
128.17
127.98
127.33
123.62
119.92
116.49
116.17
113.60
113.27
109.60
109.49
77.62
77.19
76.77
68.00
67.98
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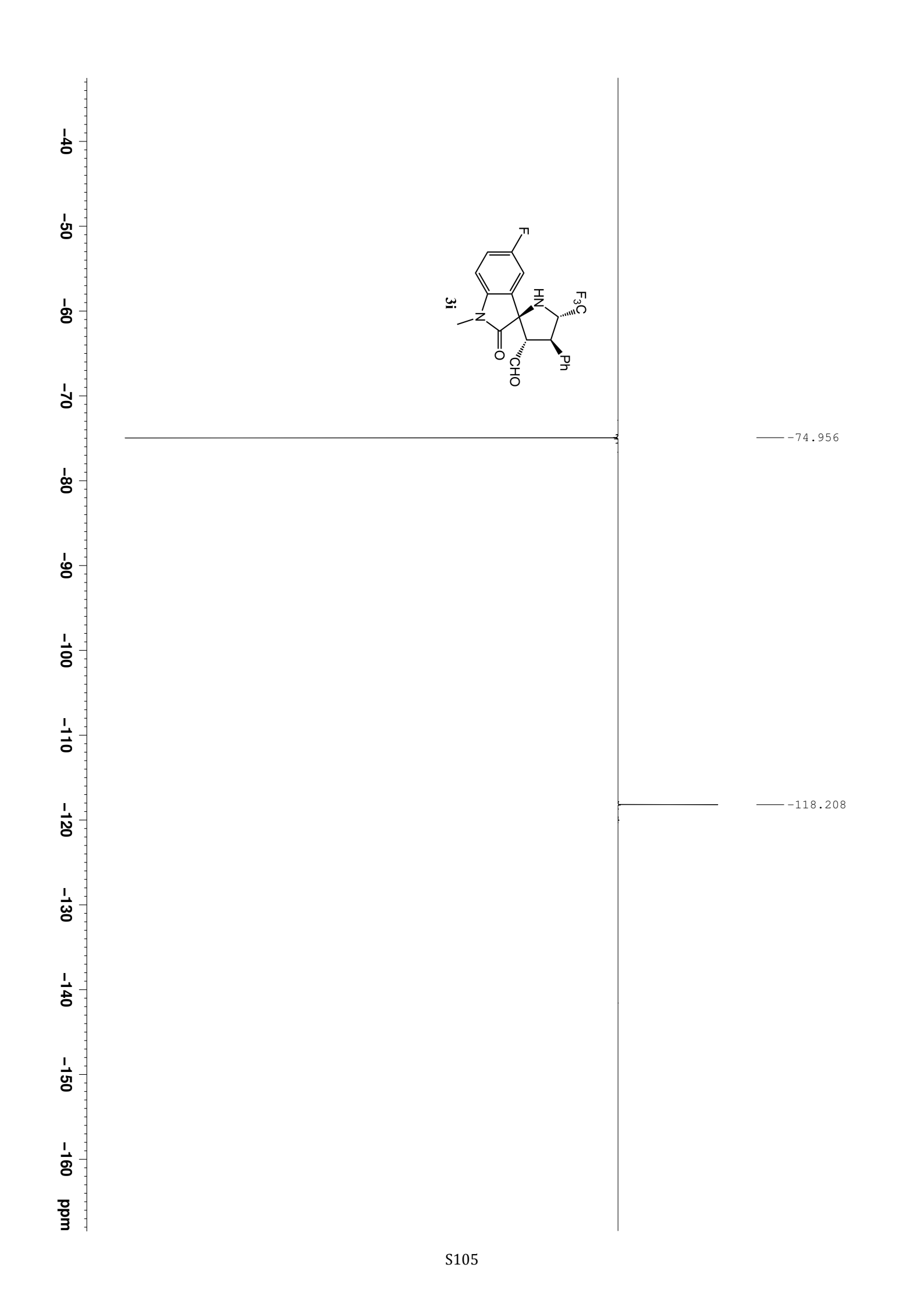
65.19
64.80
45.52
26.74
131.03
127.33
123.62
119.92
ppm
ppm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-100
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-150
-160
ppm
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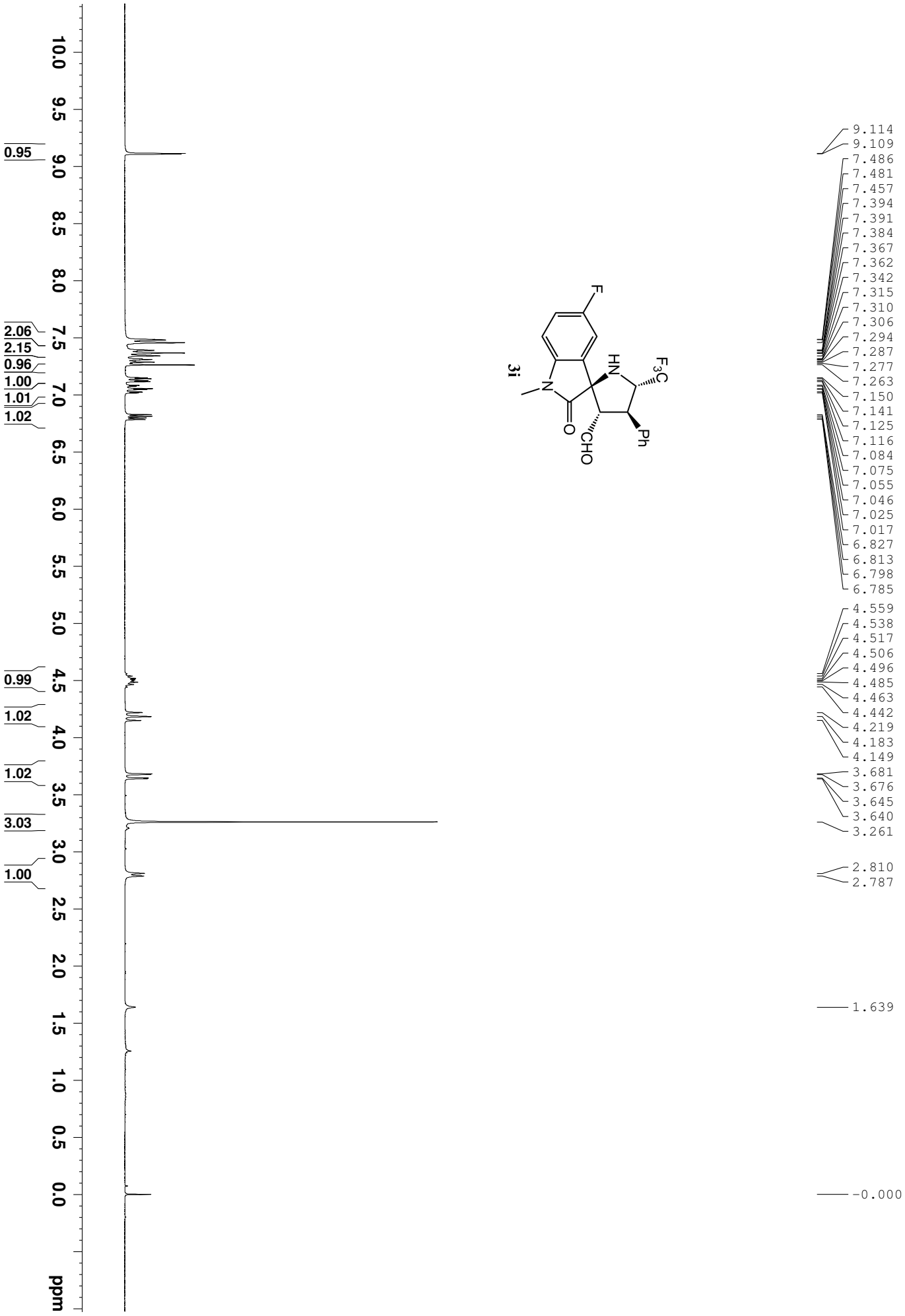
F3C
N
O
CHO
Ph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1.02
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9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3i
F
HN
F3C
N
O
CHO
Ph
9.114
9.109
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7.481
7.457
7.394
7.391
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7.367
7.362
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7.310
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7.294
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7.277
7.263
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7.141
7.125
7.116
7.084
7.075
7.055
7.046
7.025
7.017
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6.798
6.785
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4.538
4.517
4.506
4.496
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4.442
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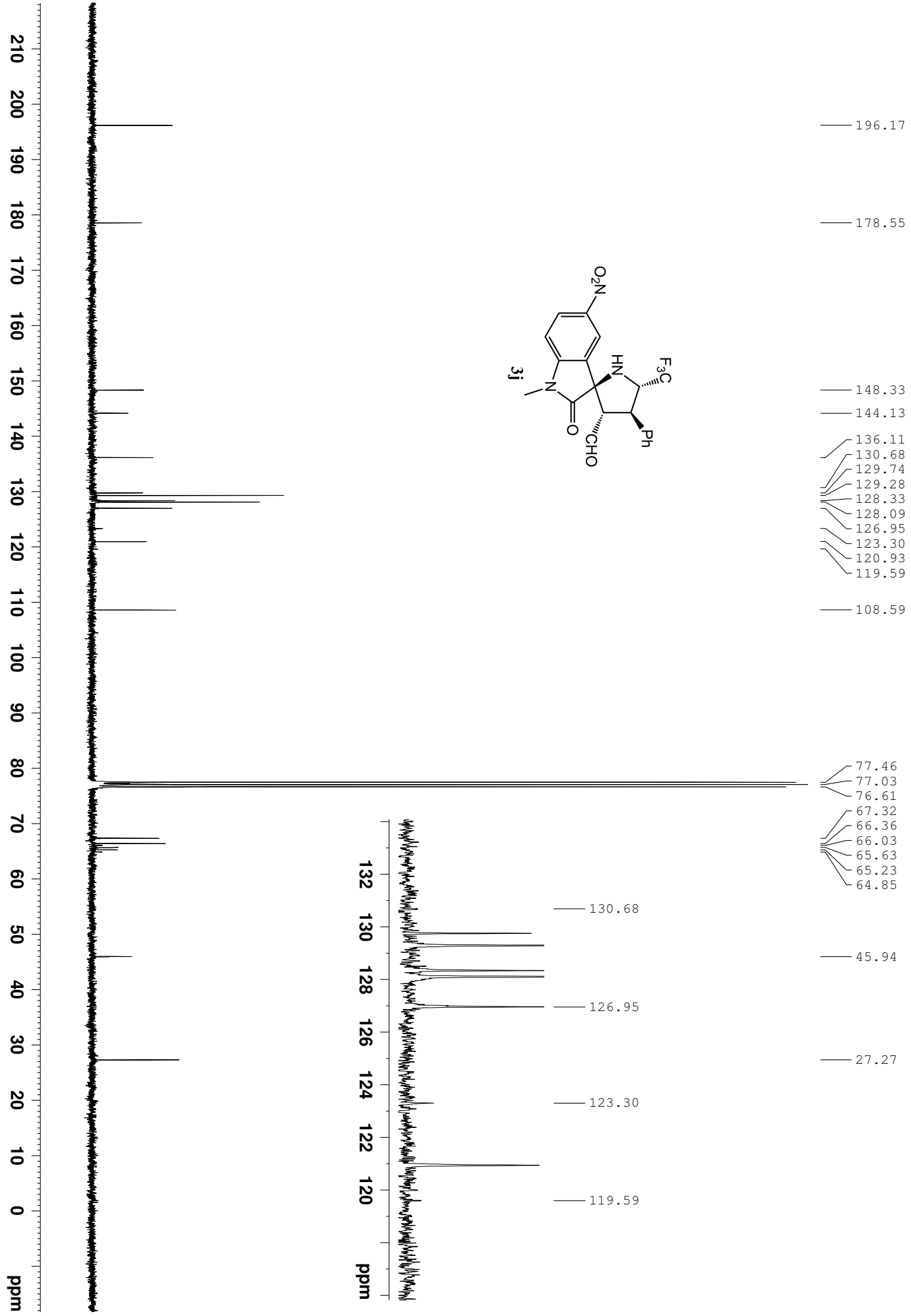
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HN
F3C
N
O
CHO
Ph
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129.74
129.28
128.33
128.09
126.95
123.30
120.93
119.59
108.59
77.46
77.03
76.61
67.32
66.36
66.03
65.63
65.23
64.85
45.94
27.27
130.68
126.95
123.30
119.59
ppm

-74.88
3j
O2N
HN
F3C
N
O
CHO
Ph
-66
-67
-68
-69
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-74
-75
-76
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-79
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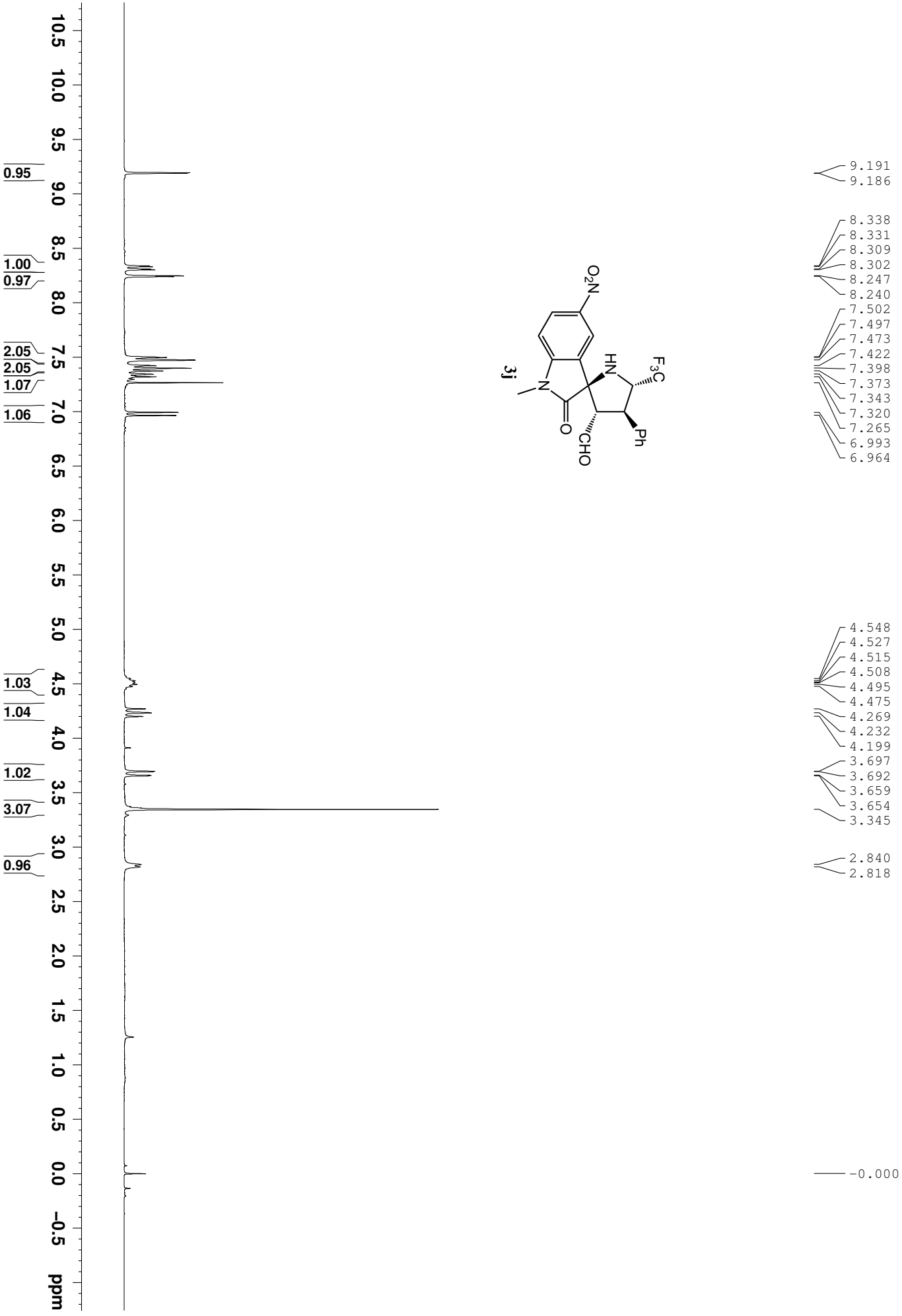
-81
-82
-83
ppm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7.398
7.373
7.343
7.320
7.265
6.993
6.964
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4.527
4.515
4.508
4.495
4.475
4.269
4.232
4.199
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3.692
3.659
3.654
3.345
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1.00
0.97
2.05
2.05
1.07
1.06
1.03
1.04
1.02
3.07
0.96
10.5
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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
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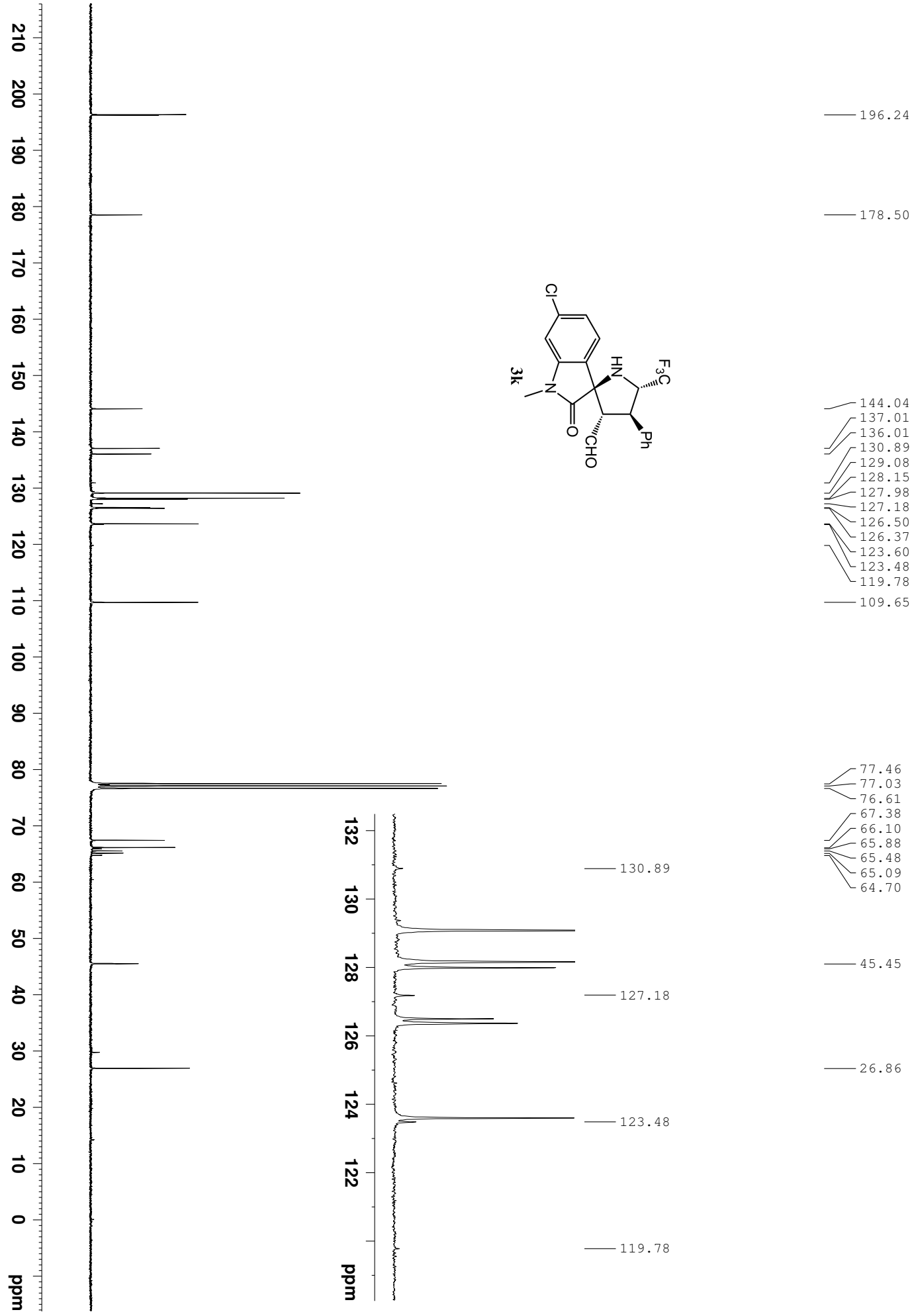
0.0
-0.5
ppm
3j
O2N
HN
F3C
N
O
CHO
Ph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123.48
119.78
109.65
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77.03
76.61
67.38
66.10
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Cl
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F3C
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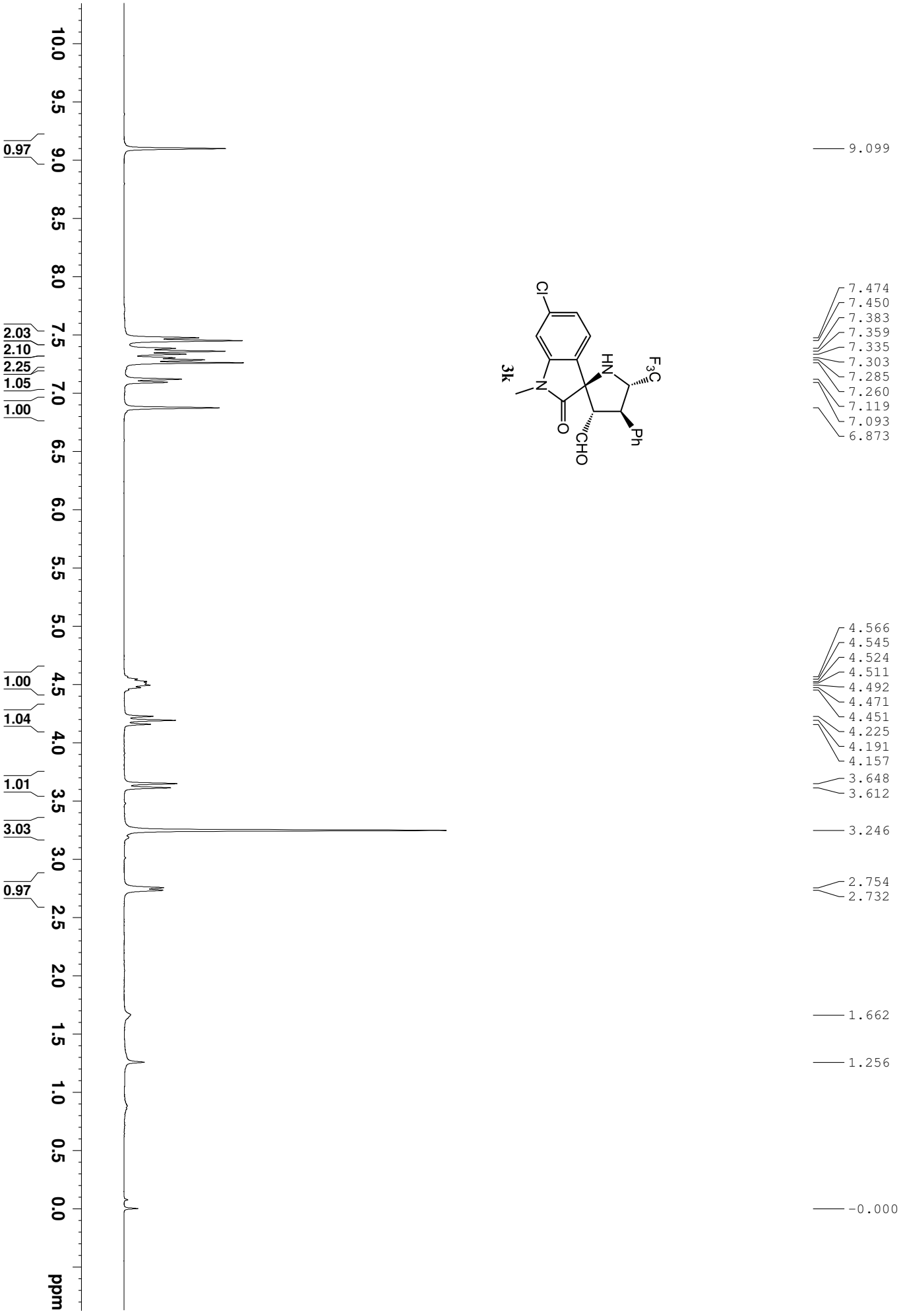
N
O
CHO
Ph
ppm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6.5
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.97
2.03
2.10
2.25
1.05
1.00
1.00
1.04
1.01
3.03
0.97
Cl
3k
N
O
HN
F3C
Ph
CHO
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7.450
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7.359
7.335
7.303
7.285
7.260
7.119
7.093
6.873
4.566
4.545
4.524
4.511
4.492
4.471
4.451
4.225
4.191
4.157
3.648
3.612
3.246
2.754
2.732
1.662
1.256
-0.000

-66
-67
-68
-69
-70
-71
-72
-73
-74
-75
-76
-77
-78
-79
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-81
-82
-83
ppm
Cl
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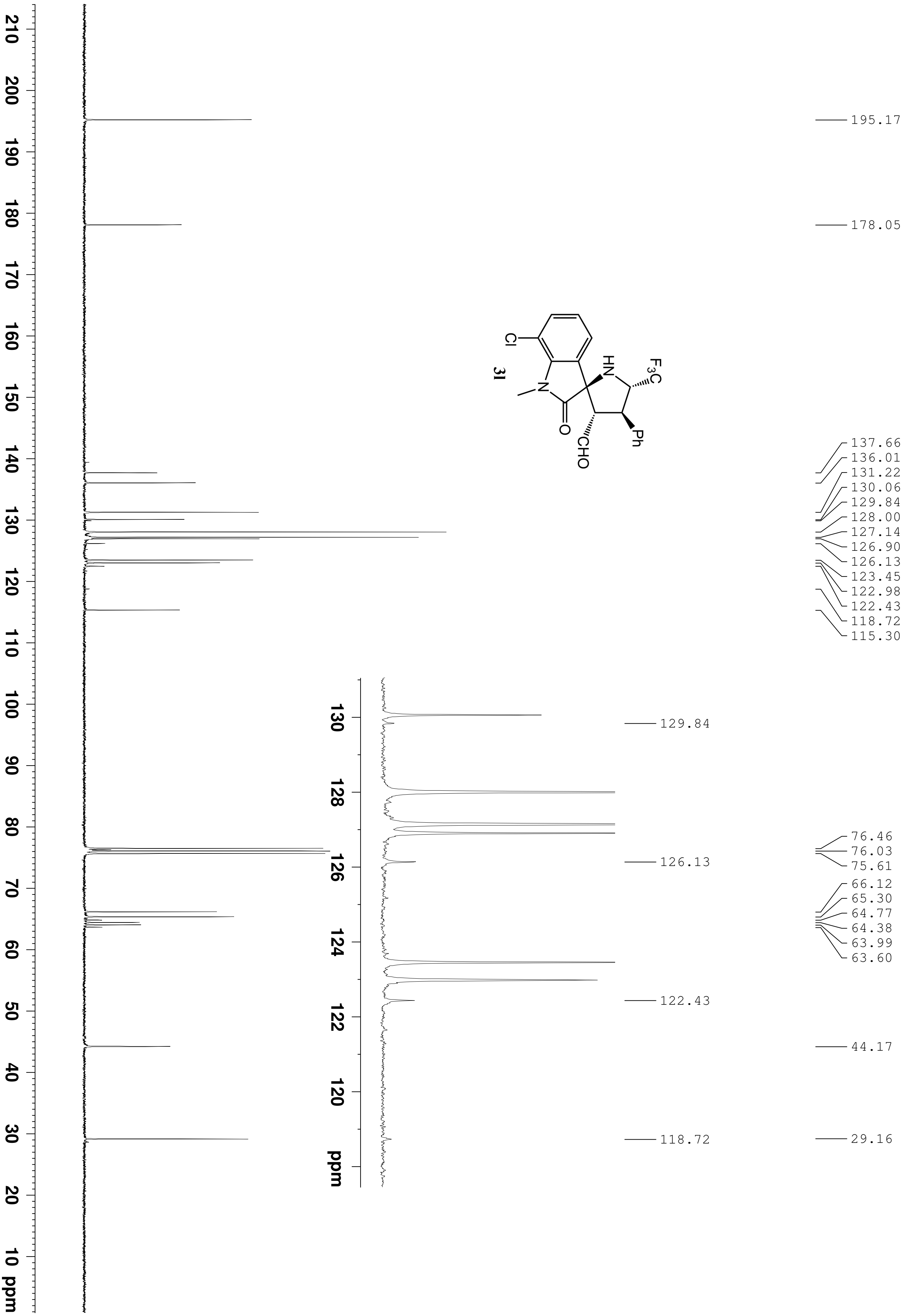
F3C
3k
N
O
CHO
Ph
-74.897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126.13
123.45
122.98
122.43
118.72
115.30
76.46
76.03
75.61
66.12
65.30
64.77
64.38
63.99
63.60
44.17
29.16
129.84
126.13
122.43
118.72
Cl
N
O
HN
F_3C
Ph
CHO
3l
ppm

-66
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-68
-69
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-72
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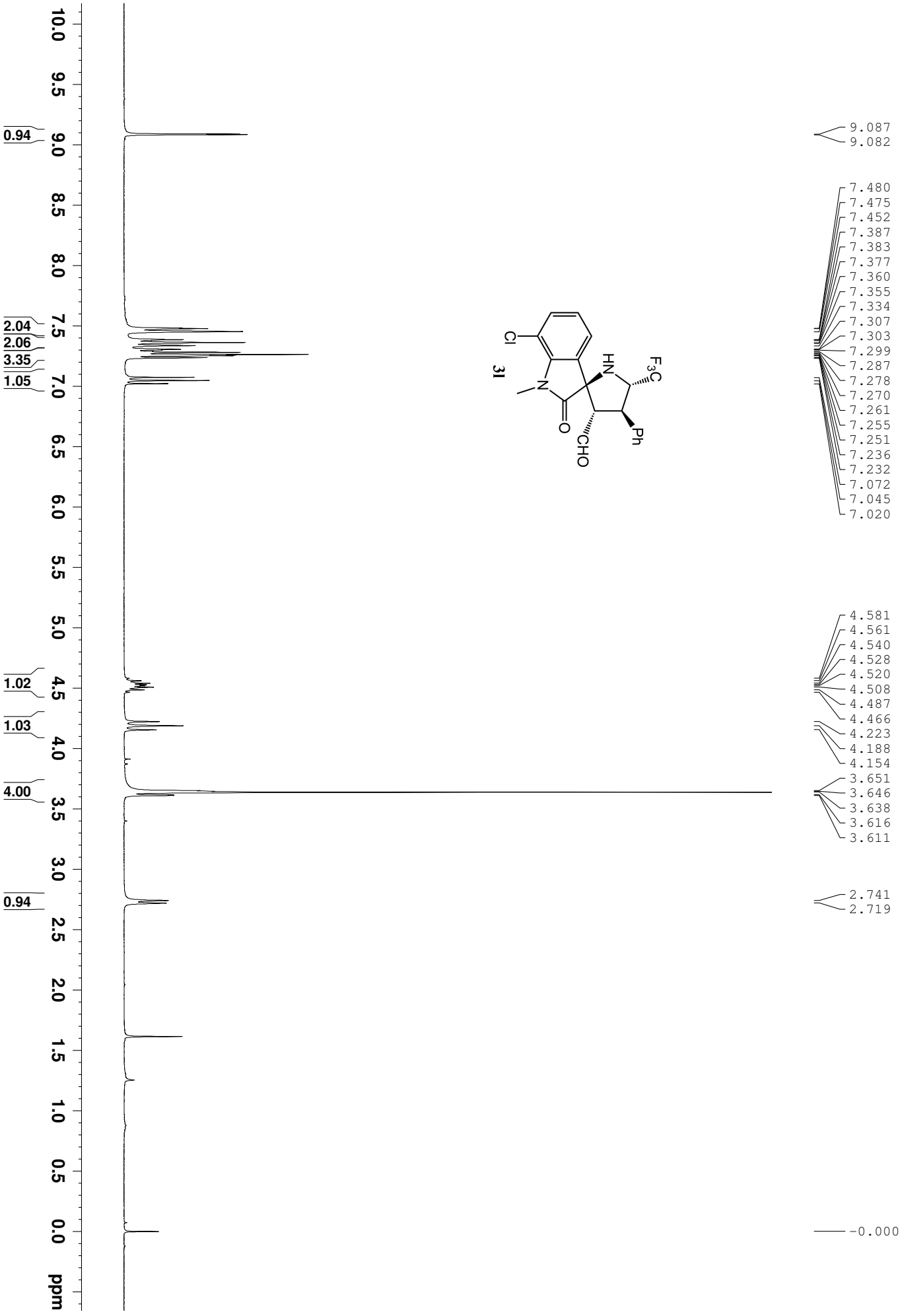
Ph
F3C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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Cl
HN
F3C
N
O
CHO
Ph
3l
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7.383
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7.360
7.355
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7.307
7.303
7.299
7.287
7.278
7.270
7.261
7.255
7.251
7.236
7.232
7.072
7.045
7.020
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4.540
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4.520
4.508
4.487
4.466
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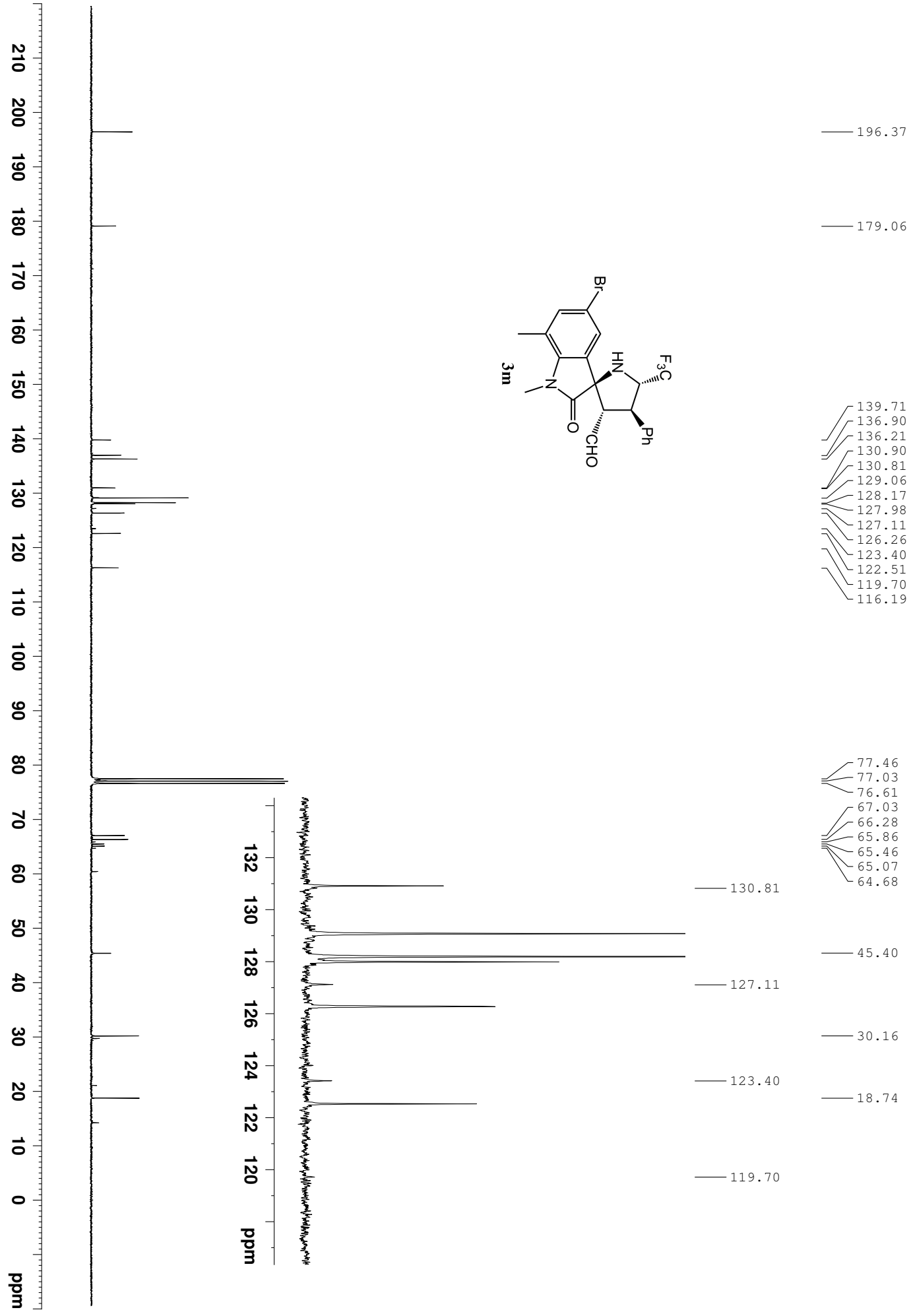
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123.40
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77.03
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67.03
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65.46
65.07
64.68
45.40
30.16
18.74
Br
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F3C
N
O
CHO
Ph
3m
ppm
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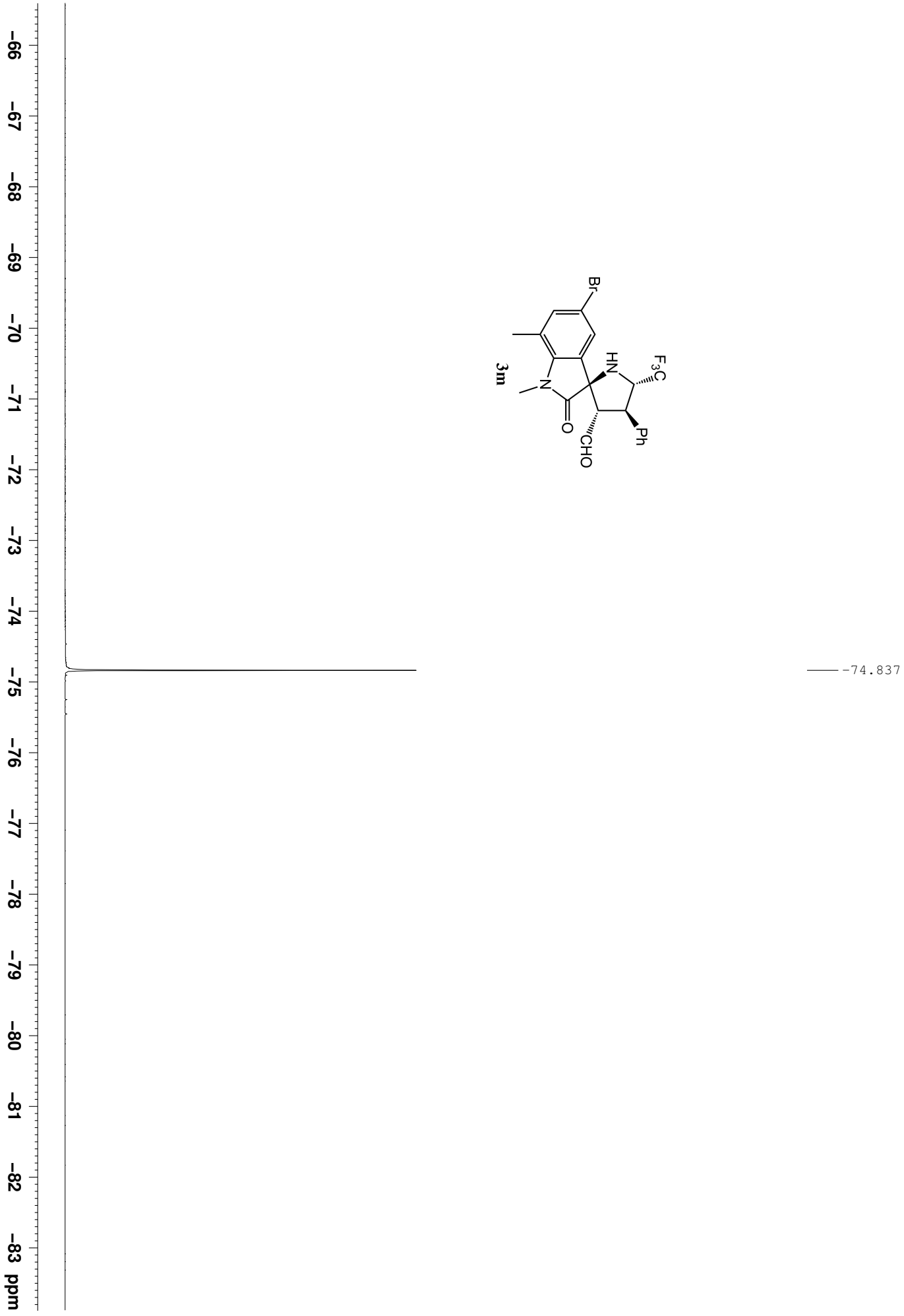
132 130 128 126 124 122 120


-66
-67
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-69
-70
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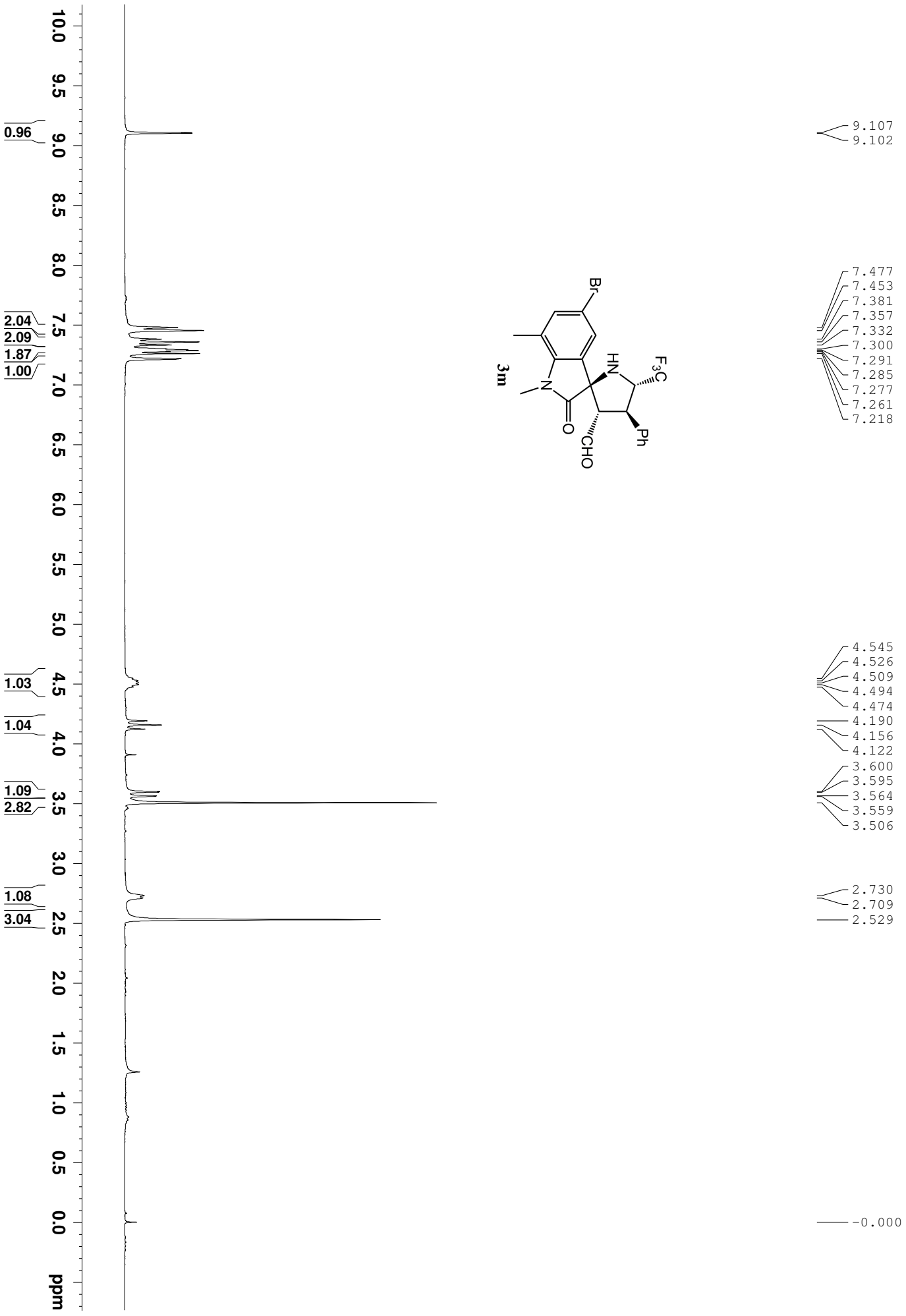
-72
-73
-74
-75
-76
-77
-78
-79
-80
-81
-82
-83 ppm
Br
HN
F3C
N
O
CHO
Ph
3m
-74.837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4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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2.09
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1.00
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1.04
1.09
2.82
1.08
3.04
Br
HN
F3C
N
O
CHO
Ph
3m
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7.332
7.300
7.291
7.285
7.277
7.261
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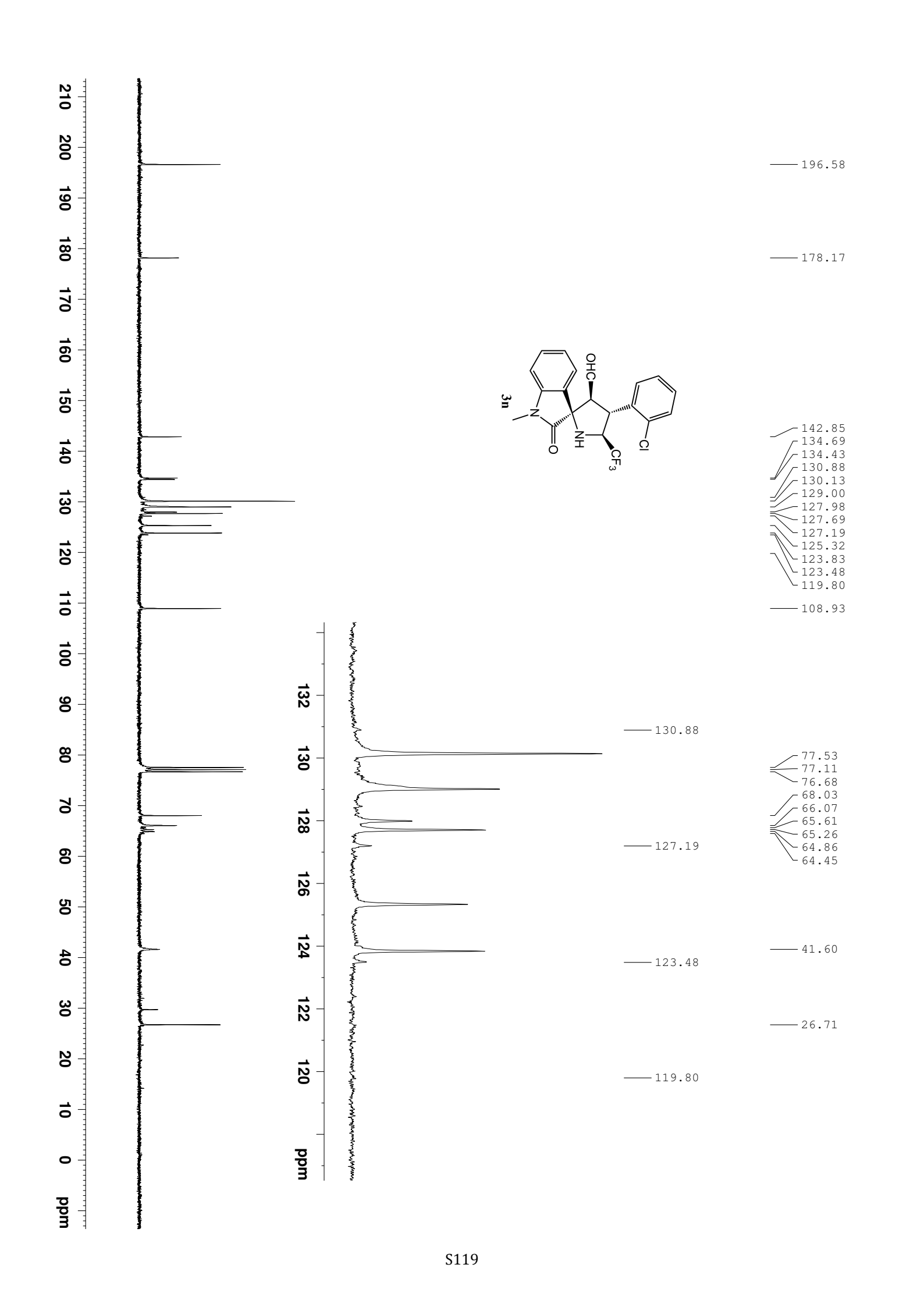
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125.32
123.83
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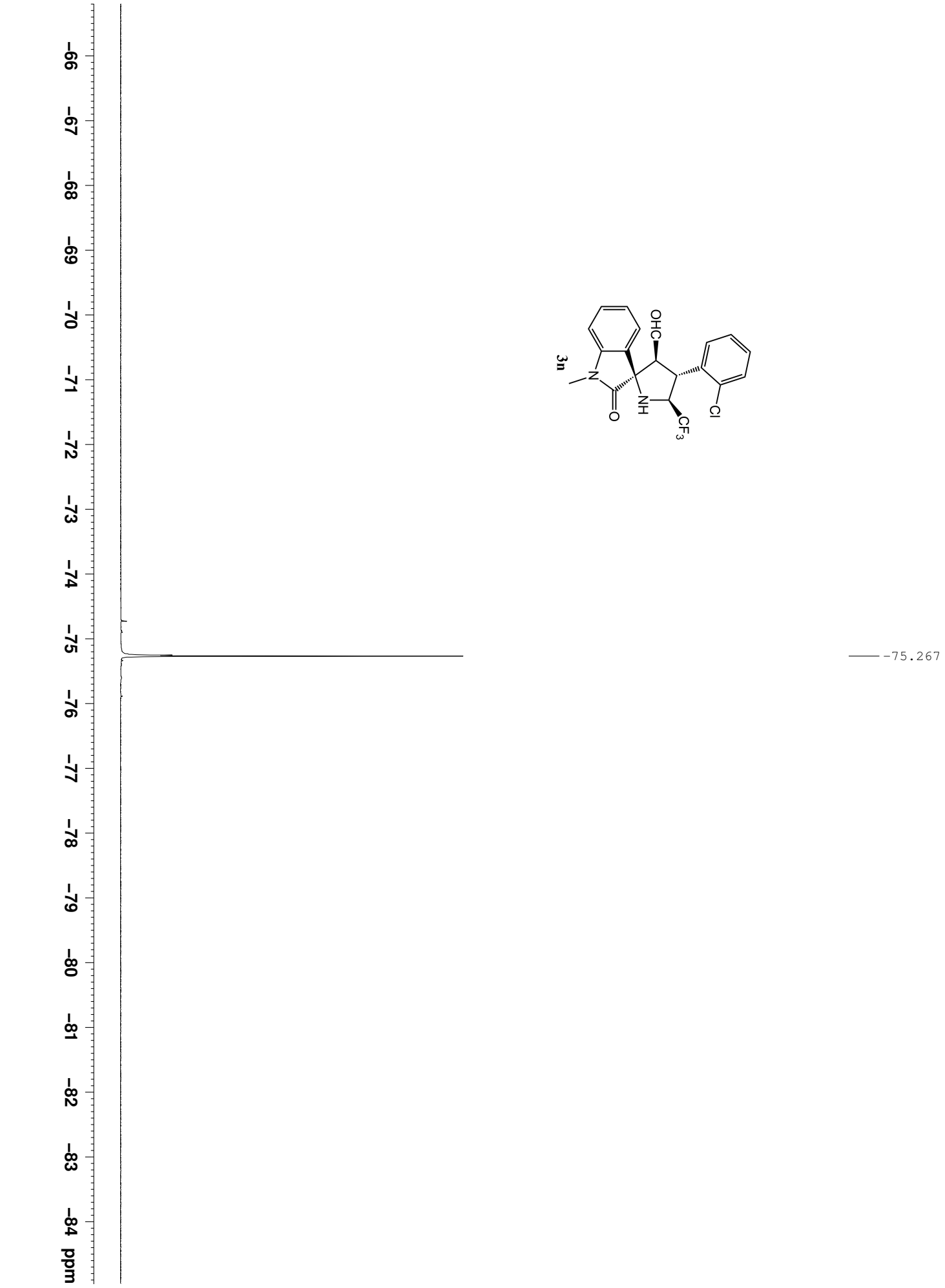
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Cl
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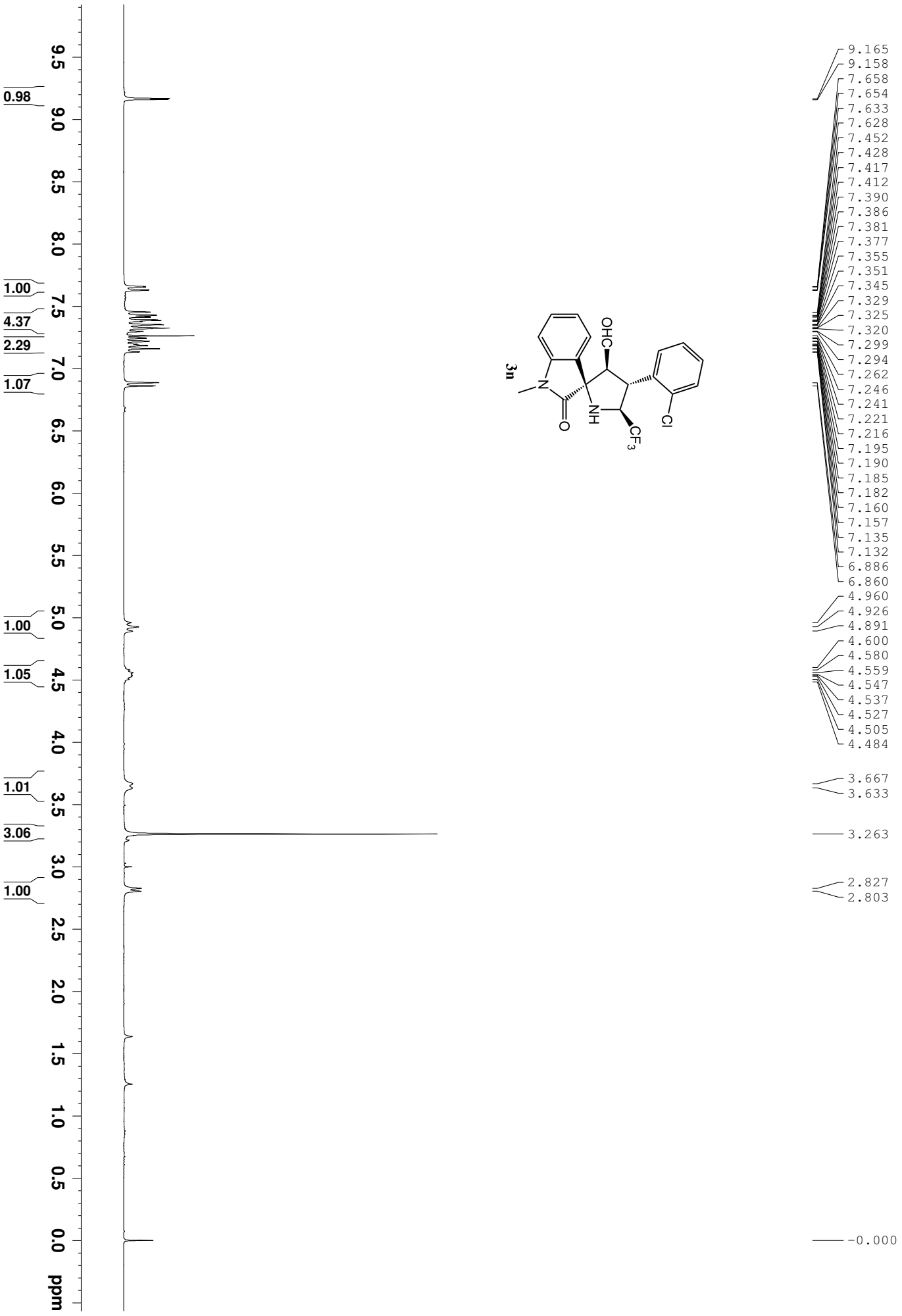
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7.351
7.345
7.329
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7.294
7.262
7.246
7.241
7.221
7.216
7.195
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7.185
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7.160
7.157
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6.860
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3.06
1.00
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7.0
6.5
6.0
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5.0
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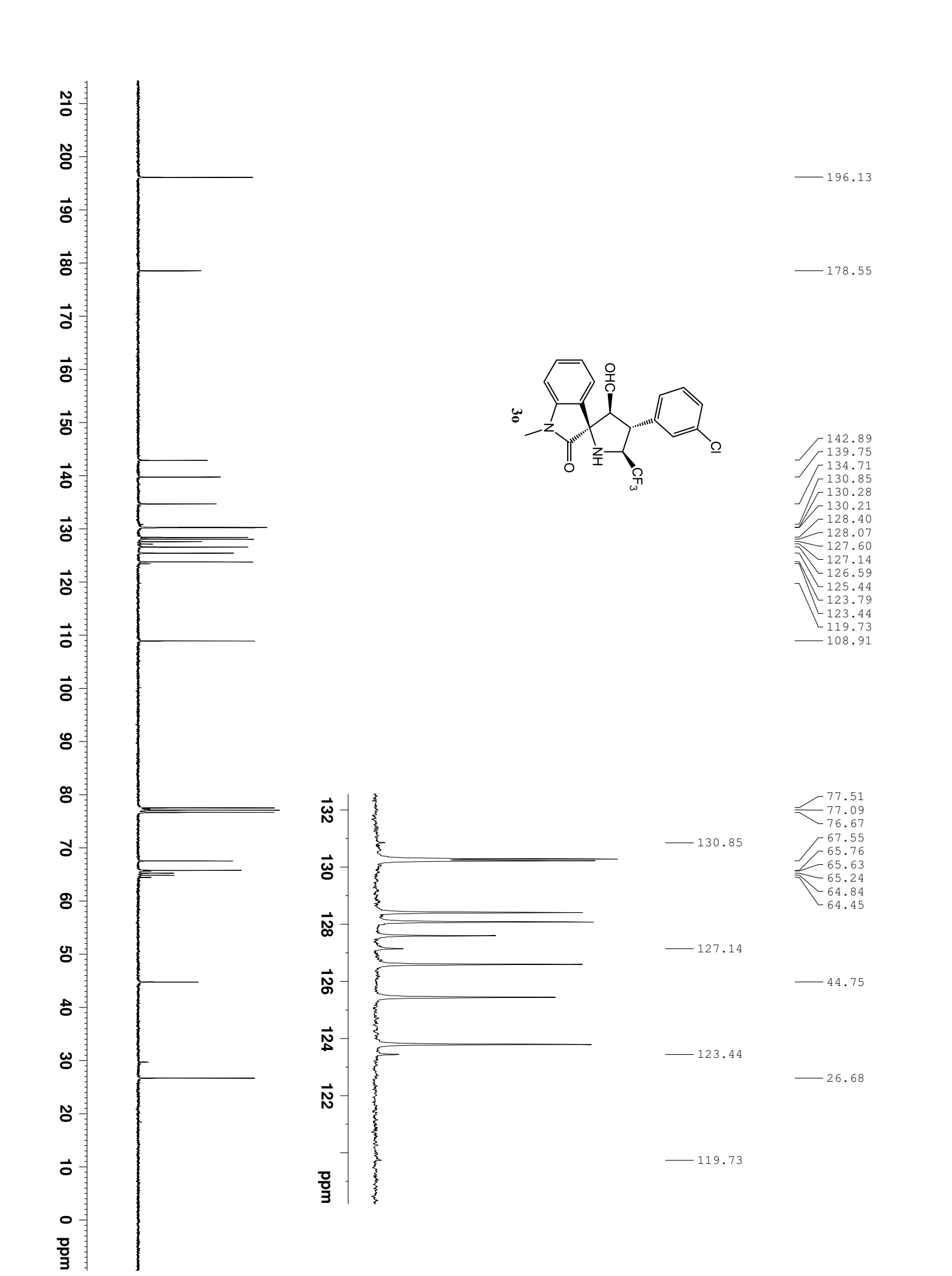
CF3
Cl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128.07
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123.44
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77.51
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76.67
67.55
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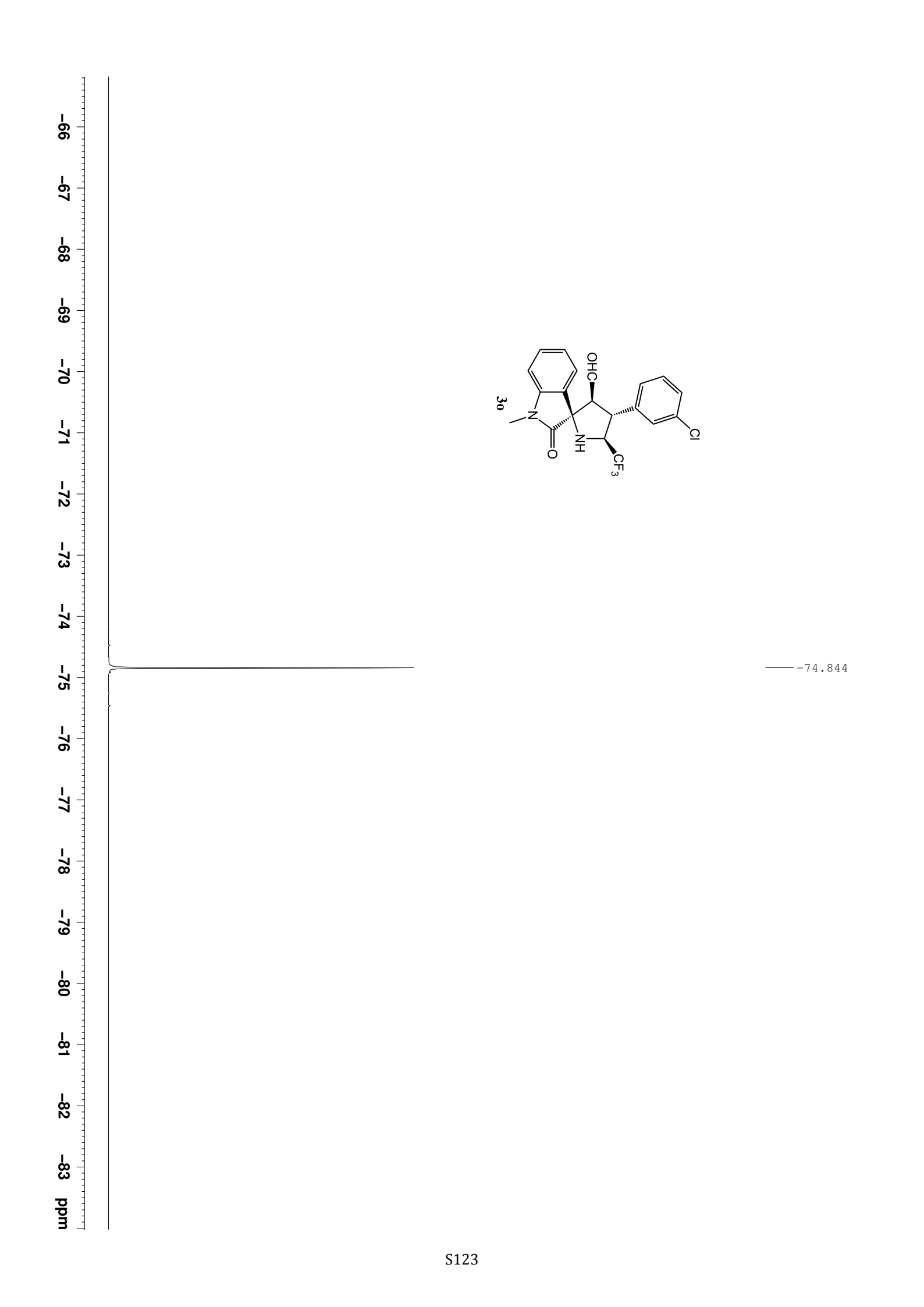
ppm
ppm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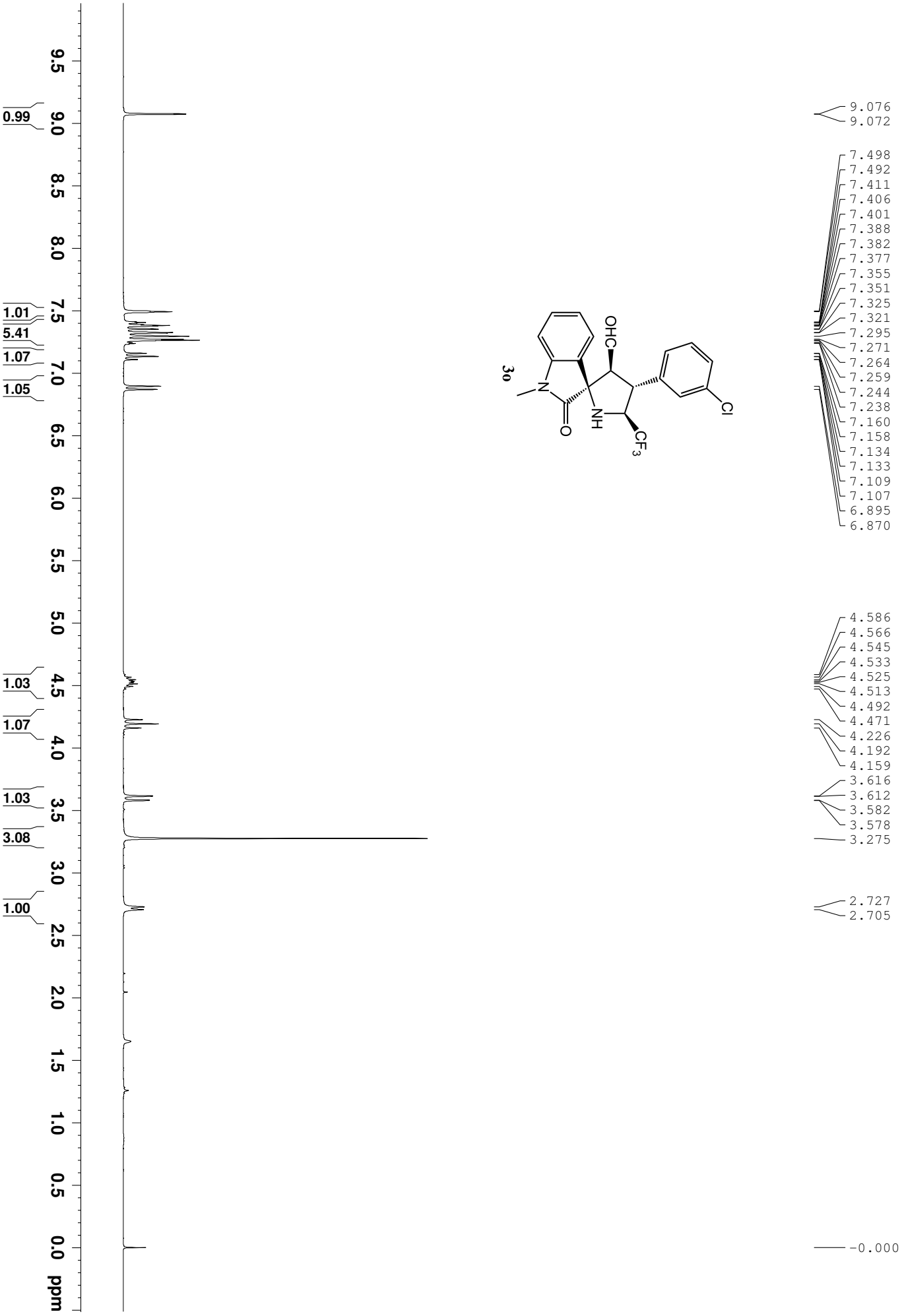
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1.07
1.05
1.03
1.07
1.03
3.08
1.00
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O
NH
CF3
Cl
3o
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7.382
7.377
7.355
7.351
7.325
7.321
7.295
7.271
7.264
7.259
7.244
7.238
7.160
7.158
7.134
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4.566
4.545
4.533
4.525
4.513
4.492
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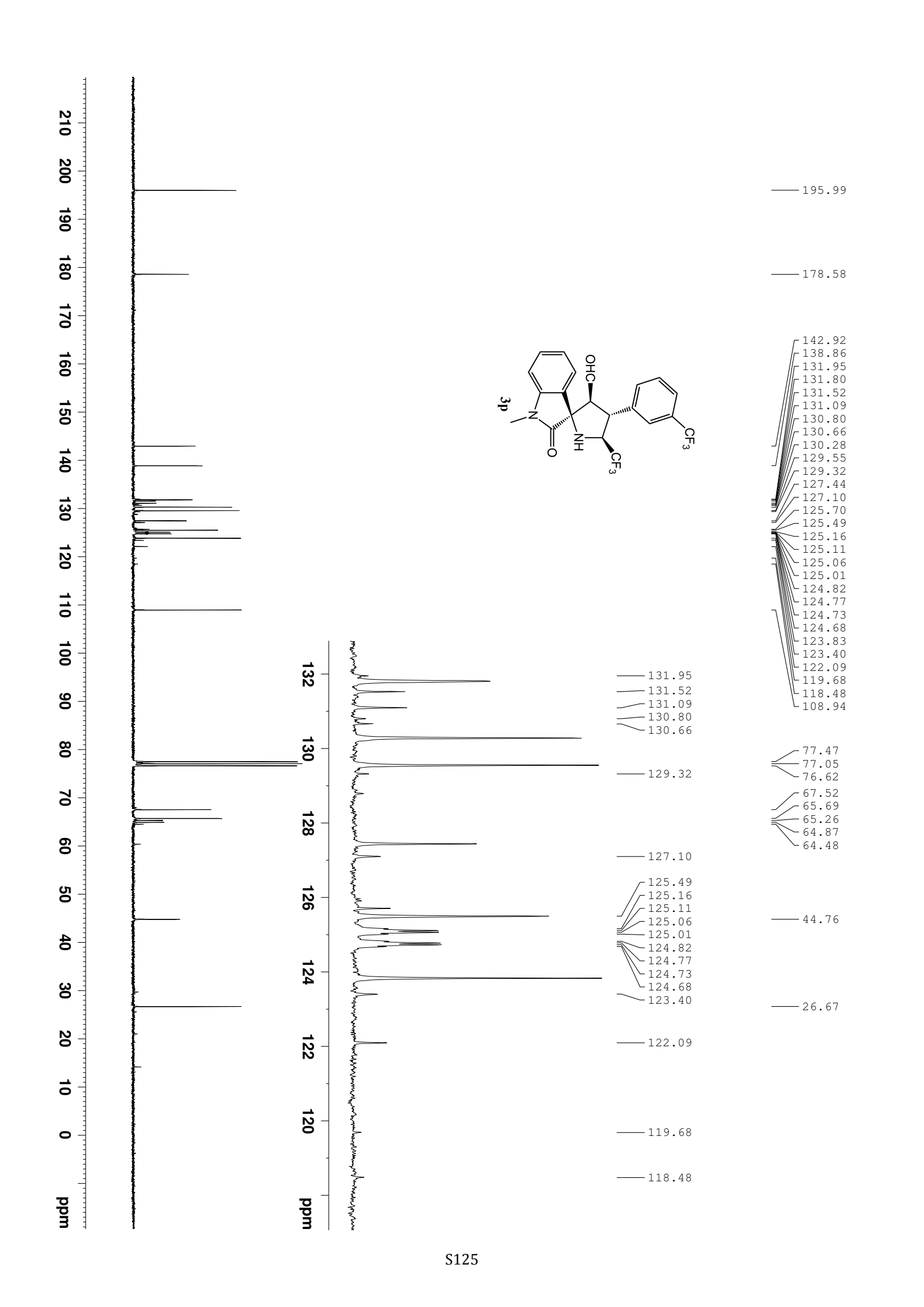
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129.32
127.44
127.10
125.70
125.49
125.16
125.11
125.06
125.01
124.82
124.77
124.73
124.68
123.83
123.40
122.09
119.68
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77.47
77.05
76.62
67.52
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65.26
64.87
64.48
44.76
26.67
OHC
3p
N
O
NH
CF3
CF3
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131.52
131.09
130.80
130.66
129.32
127.10
125.49
125.16
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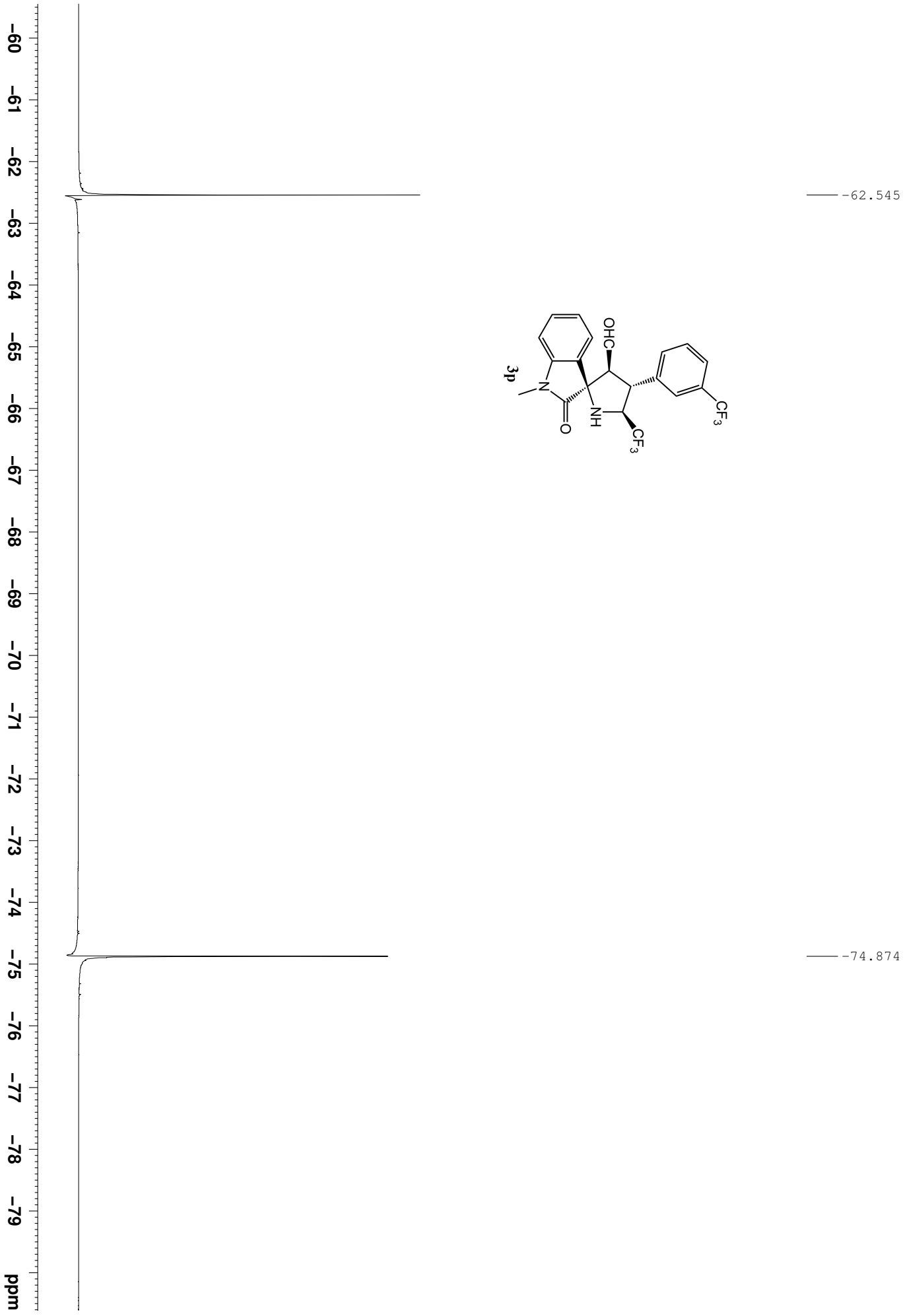
124.73
124.68
123.40
122.09
119.68
118.48
ppm
ppm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-69
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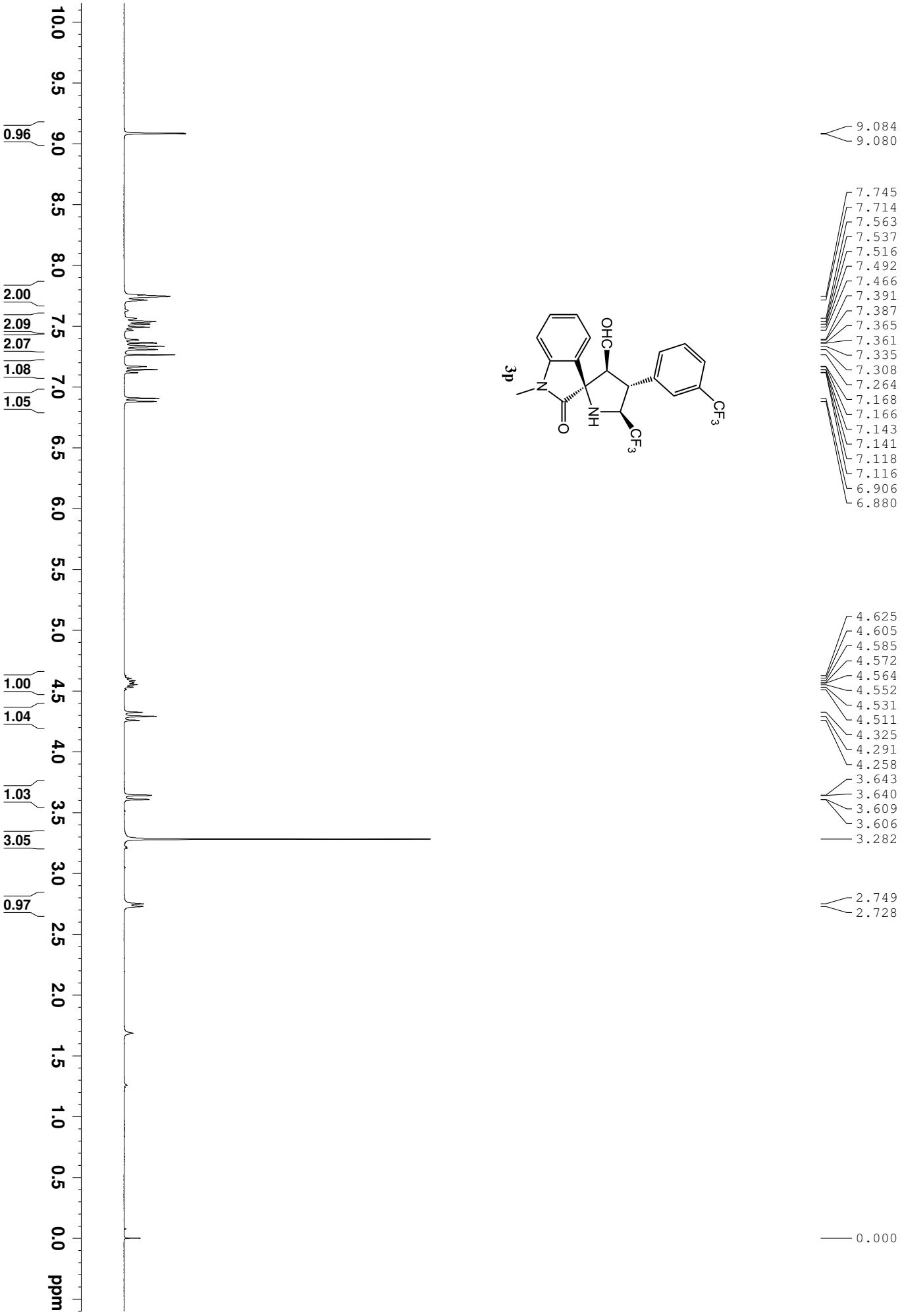
N
O
NH
CF3
CF3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6.5
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5.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.96
2.00
2.09
2.07
1.08
1.05
1.00
1.04
1.03
3.05
0.97
3p
OHC
N
O
NH
CF3
CF3
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9.080
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7.714
7.563
7.537
7.516
7.492
7.466
7.391
7.387
7.365
7.361
7.335
7.308
7.264
7.168
7.166
7.143
7.141
7.118
7.116
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6.880
4.625
4.605
4.585
4.572
4.564
4.552
4.531
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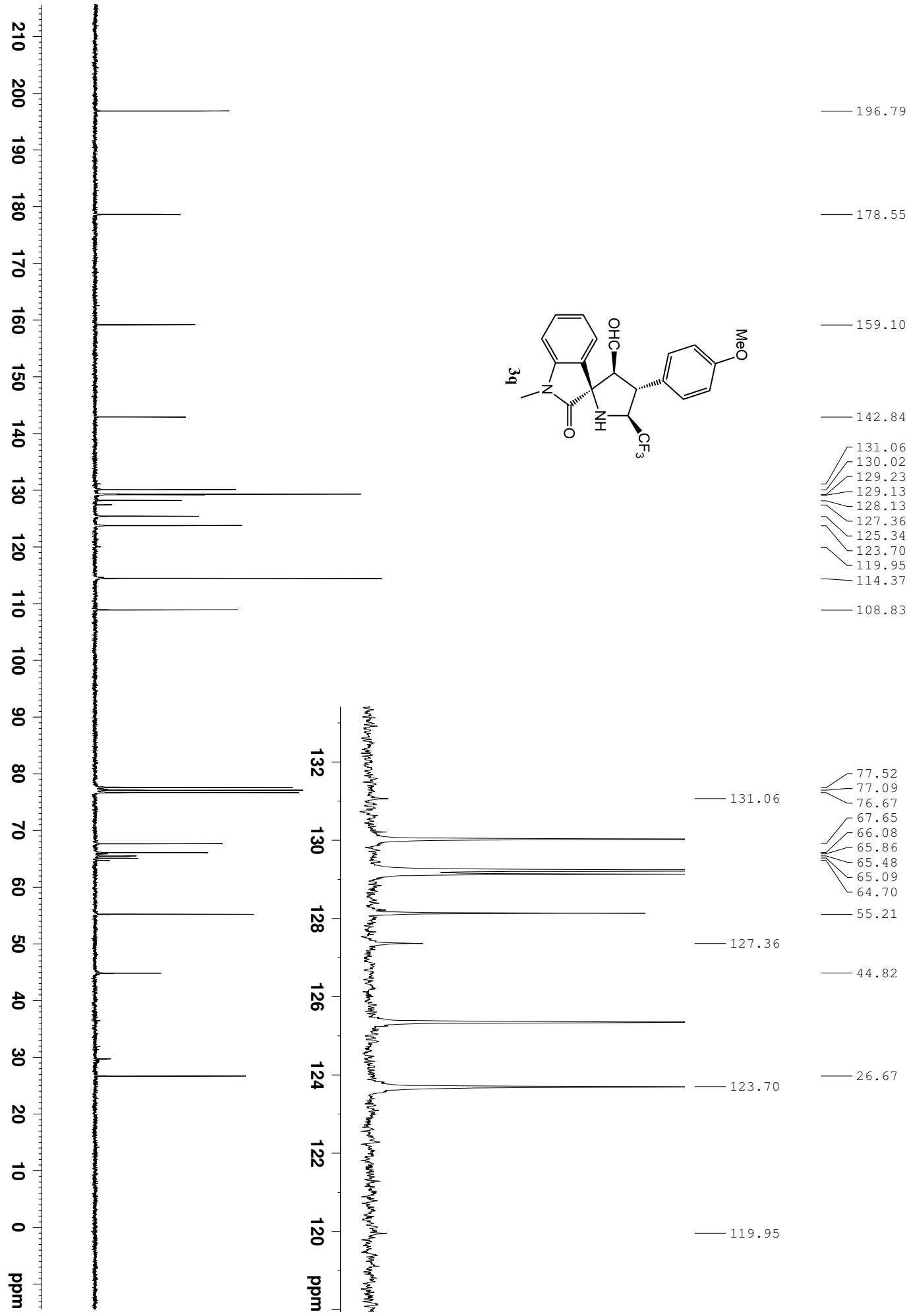
0.000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OHC
MeO
N
NH
O
CF3
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159.10
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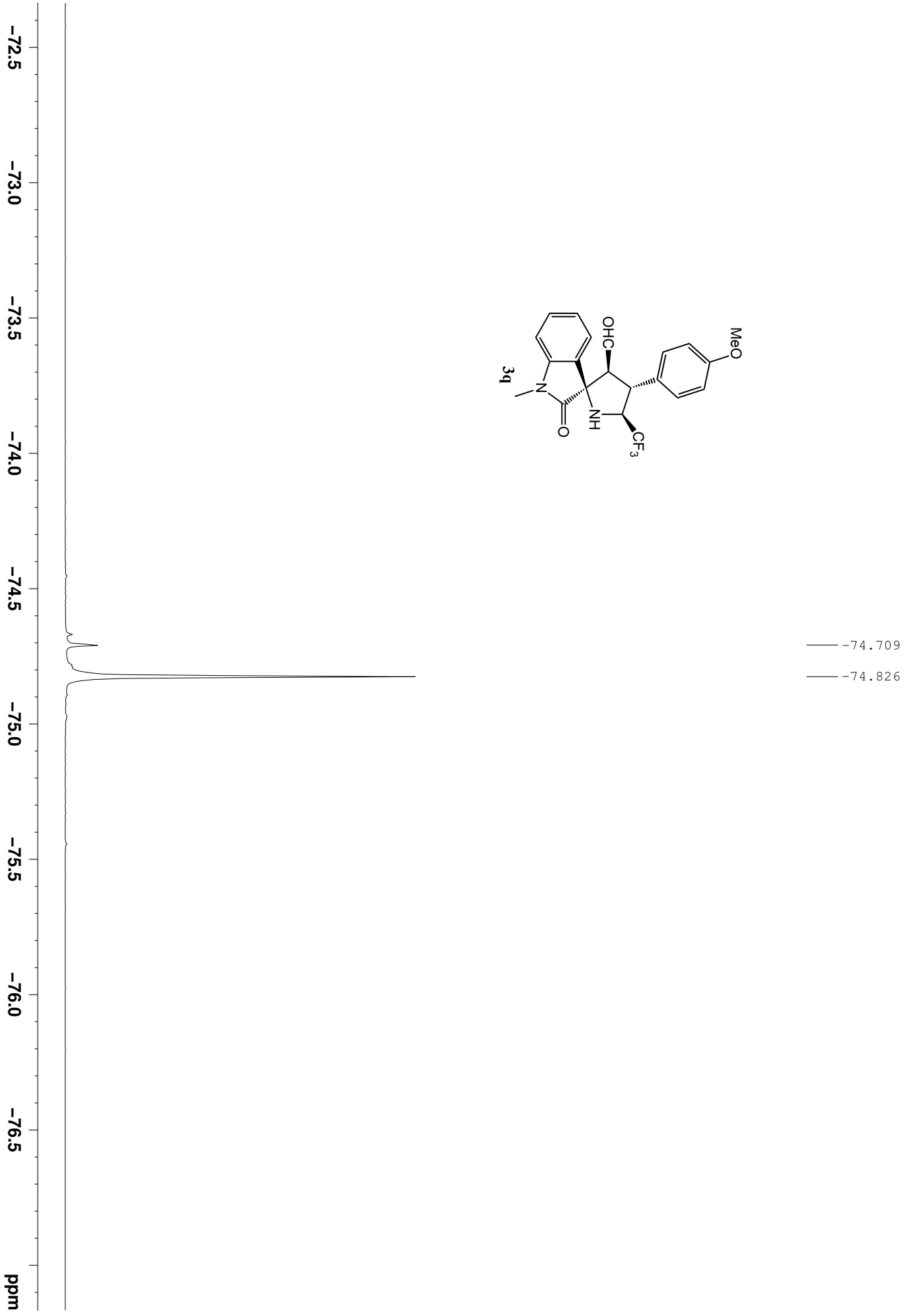
130.02
129.23
129.13
128.13
127.36
125.34
123.70
119.95
114.37
108.83
77.52
77.09
76.67
67.65
66.08
65.86
65.48
65.09
64.70
55.21
44.82
26.67
ppm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-73.5
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ppm
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MeO
N
NH
O
CF3
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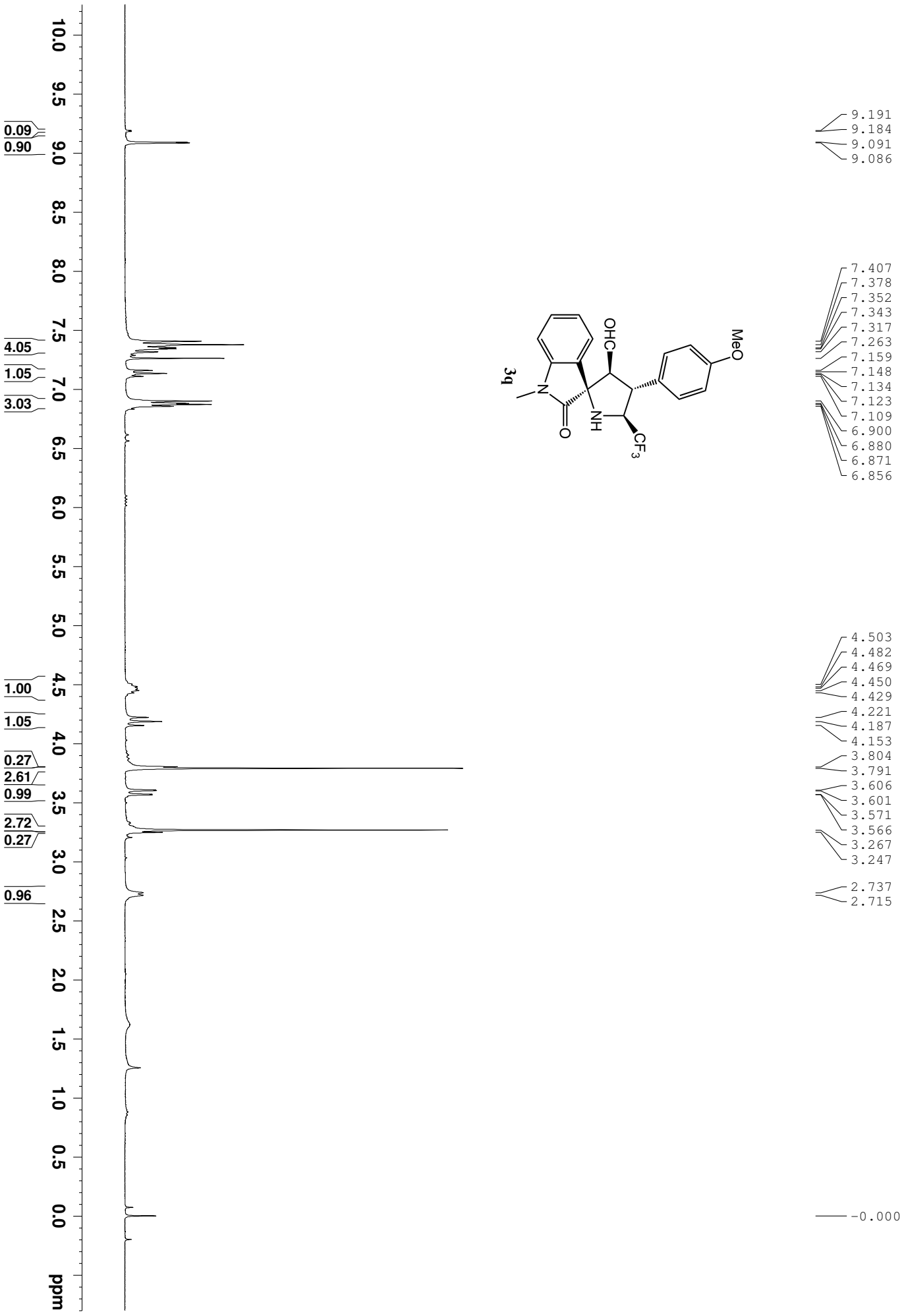
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7.352
7.343
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7.263
7.159
7.148
7.134
7.123
7.109
6.900
6.880
6.871
6.856
4.503
4.482
4.469
4.450
4.429
4.221
4.187
4.153
3.804
3.791
3.606
3.601
3.571
3.566
3.267
3.247
2.737
2.715
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0.09
0.90
4.05
1.05
3.03
1.00
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ppm
3q
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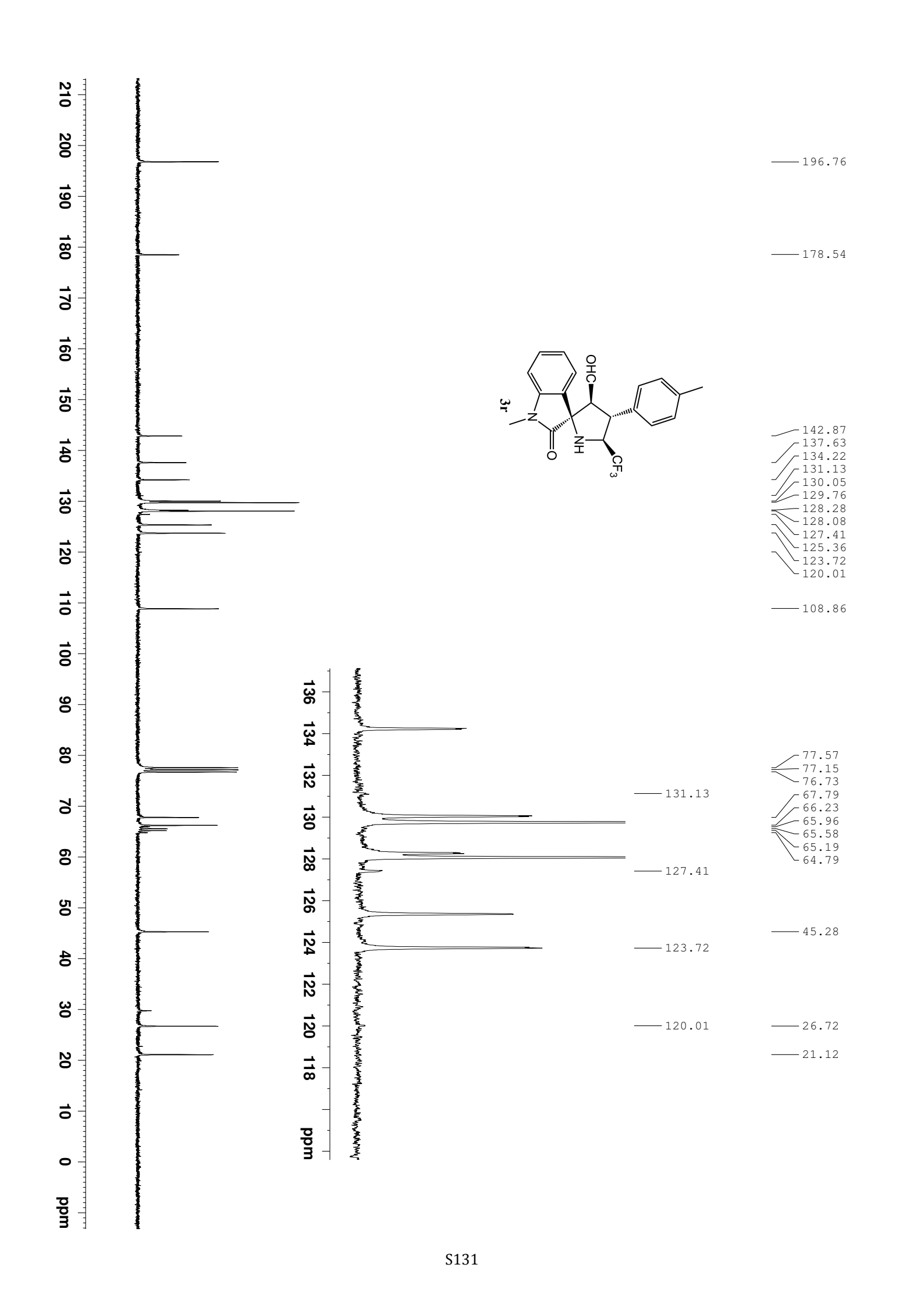
MeO
NH
CF3
O
N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O
NH
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131.13
130.05
129.76
128.28
128.08
127.41
125.36
123.72
120.01
108.86
77.57
77.15
76.73
67.79
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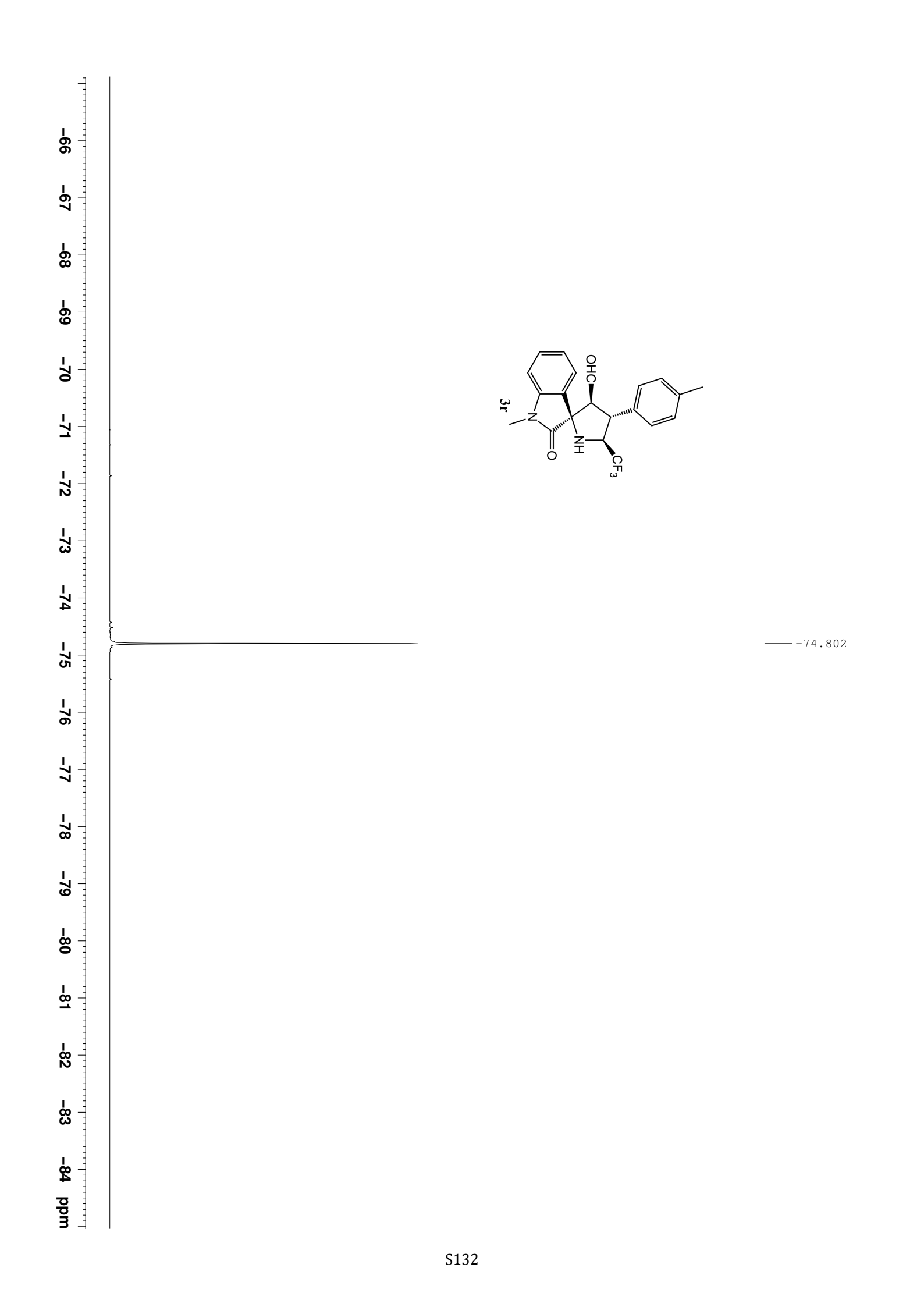
ppm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-75
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-83
-84
ppm
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O
NH
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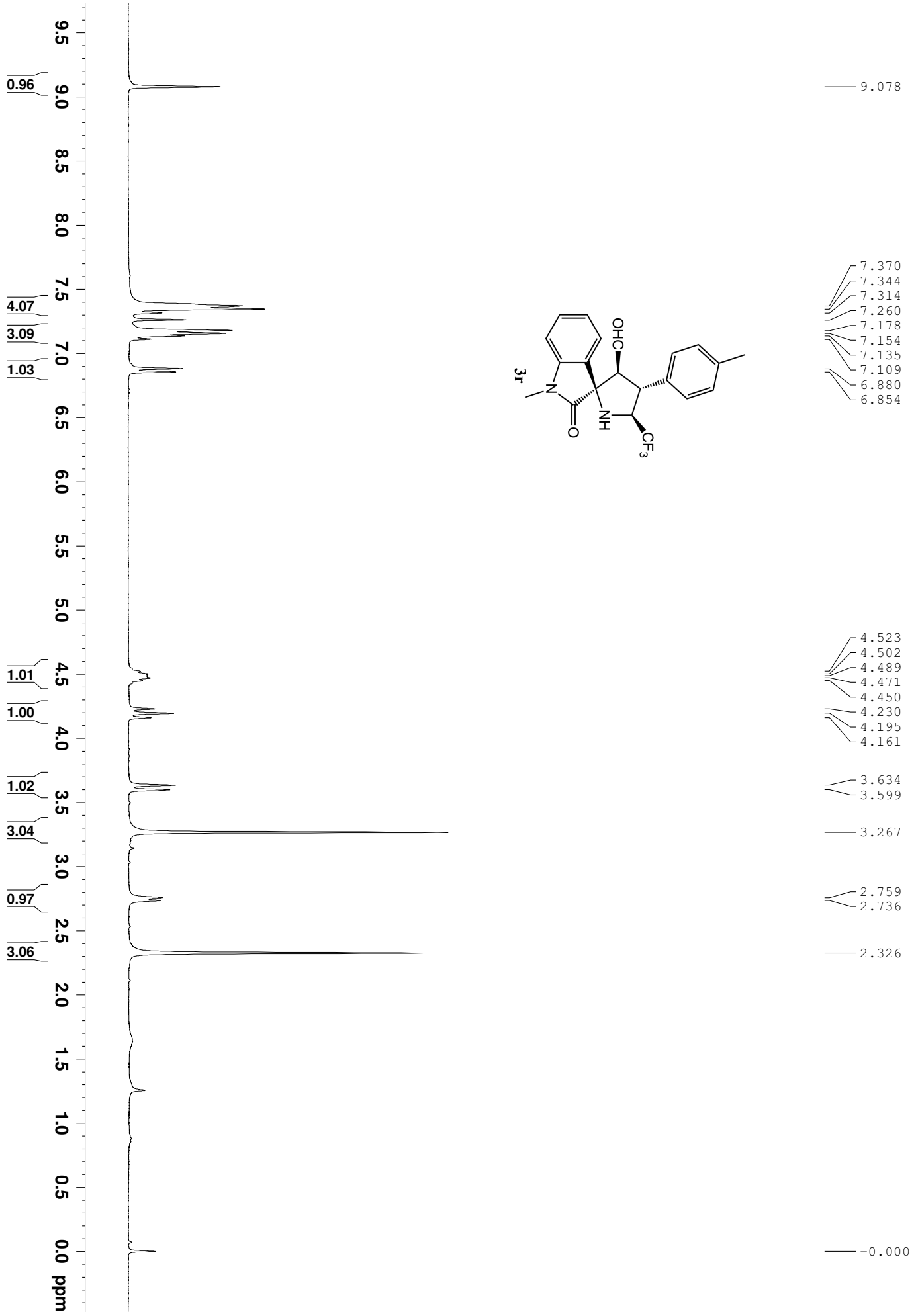
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7.135
7.109
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6.854
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4.502
4.489
4.471
4.450
4.230
4.195
4.161
3.634
3.599
3.267
2.759
2.736
2.326
-0.000
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4.07
3.09
1.03
1.01
1.00
1.02
3.04
0.97
3.06
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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ppm
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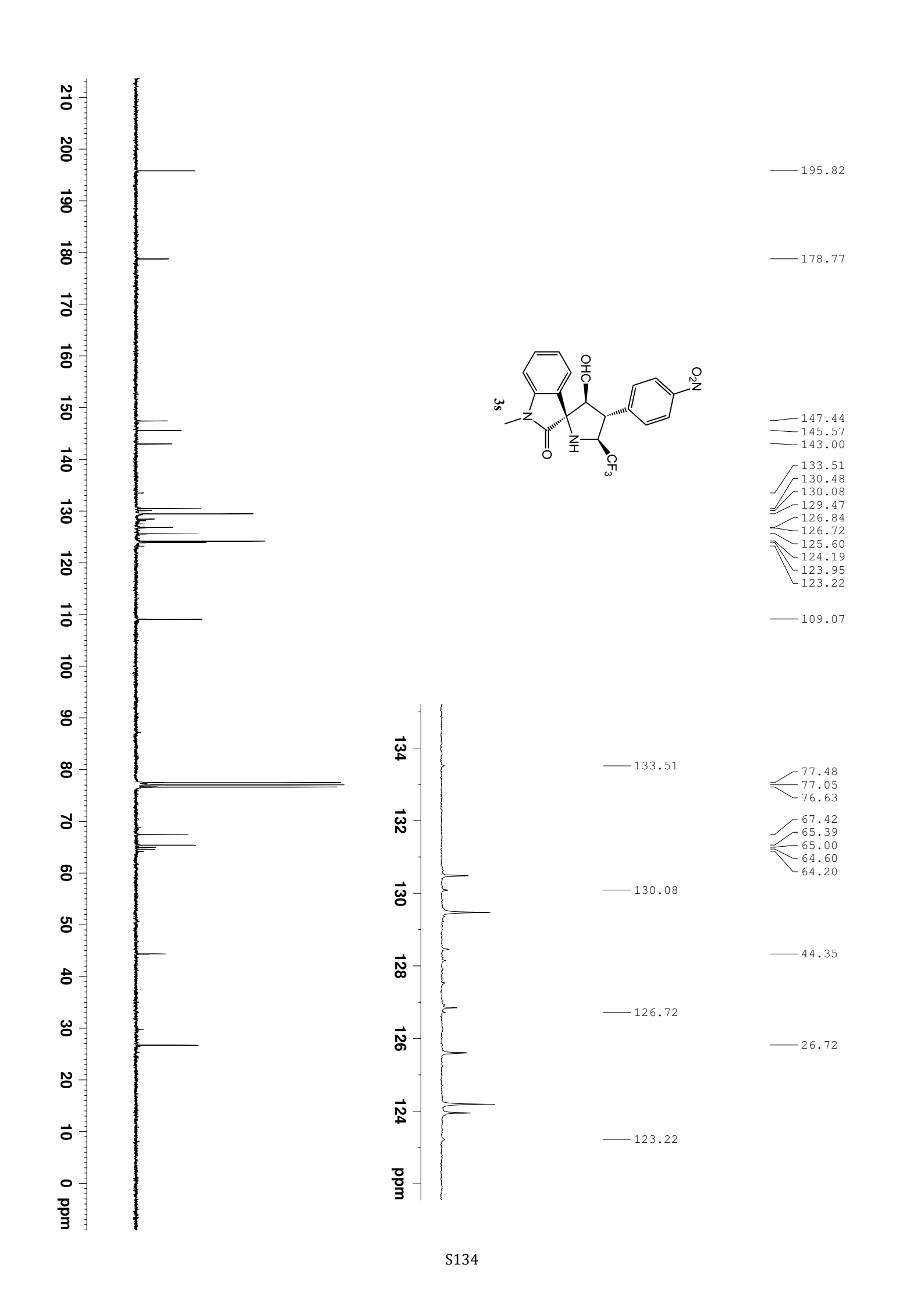
OHC
N
O
NH
CF3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126.84
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125.60
124.19
123.95
123.22
109.07
77.48
77.05
76.63
67.42
65.39
65.00
64.60
64.20
44.35
26.72
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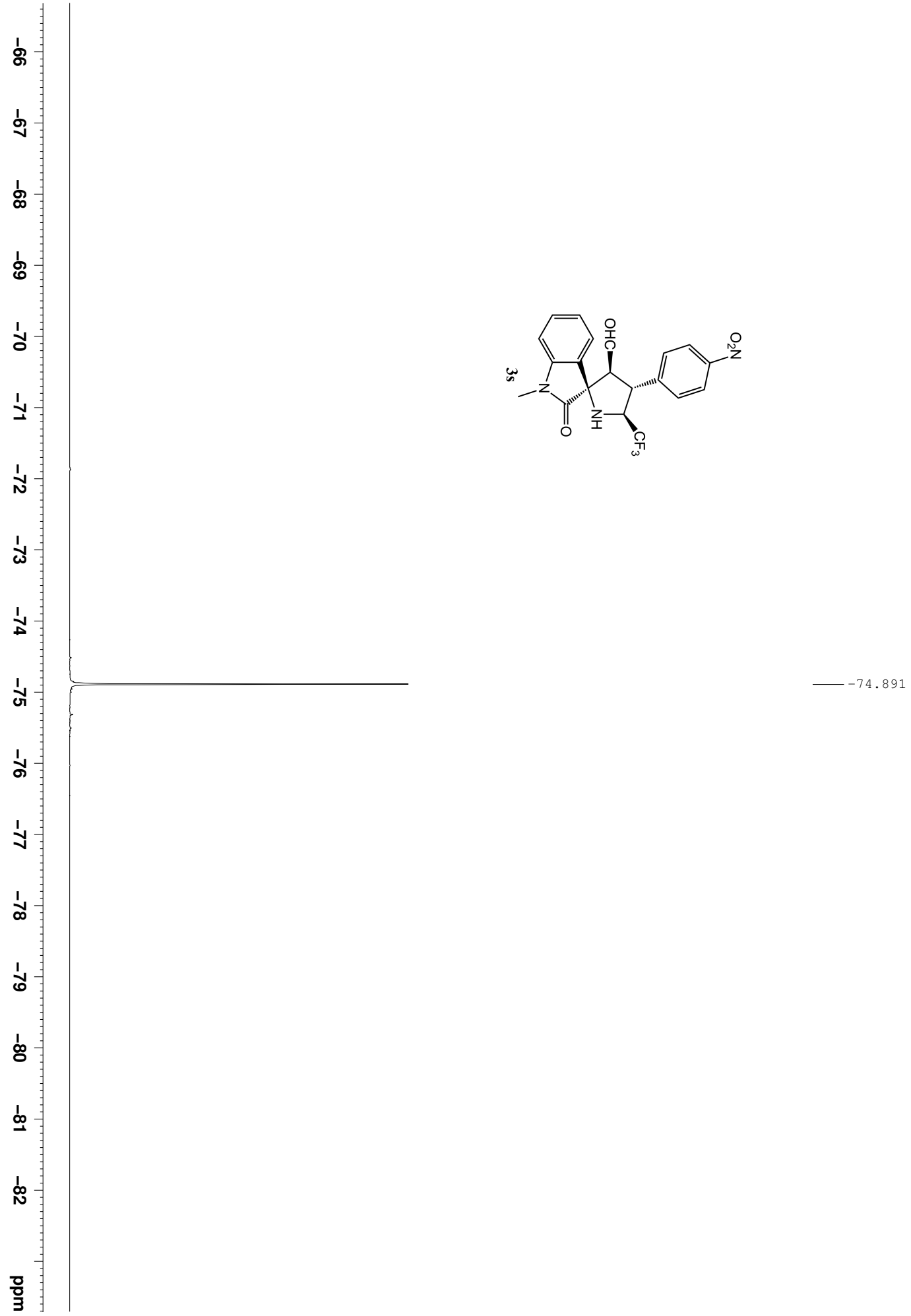
O2N
3s
N
NH
O
CF3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
134 132 130 128 126 124 ppm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-68
-69
-70
-71
-72
-73
-74
-75
-76
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-78
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-80
-81
-82
ppm
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O
NH
OHC
CF3
O2N
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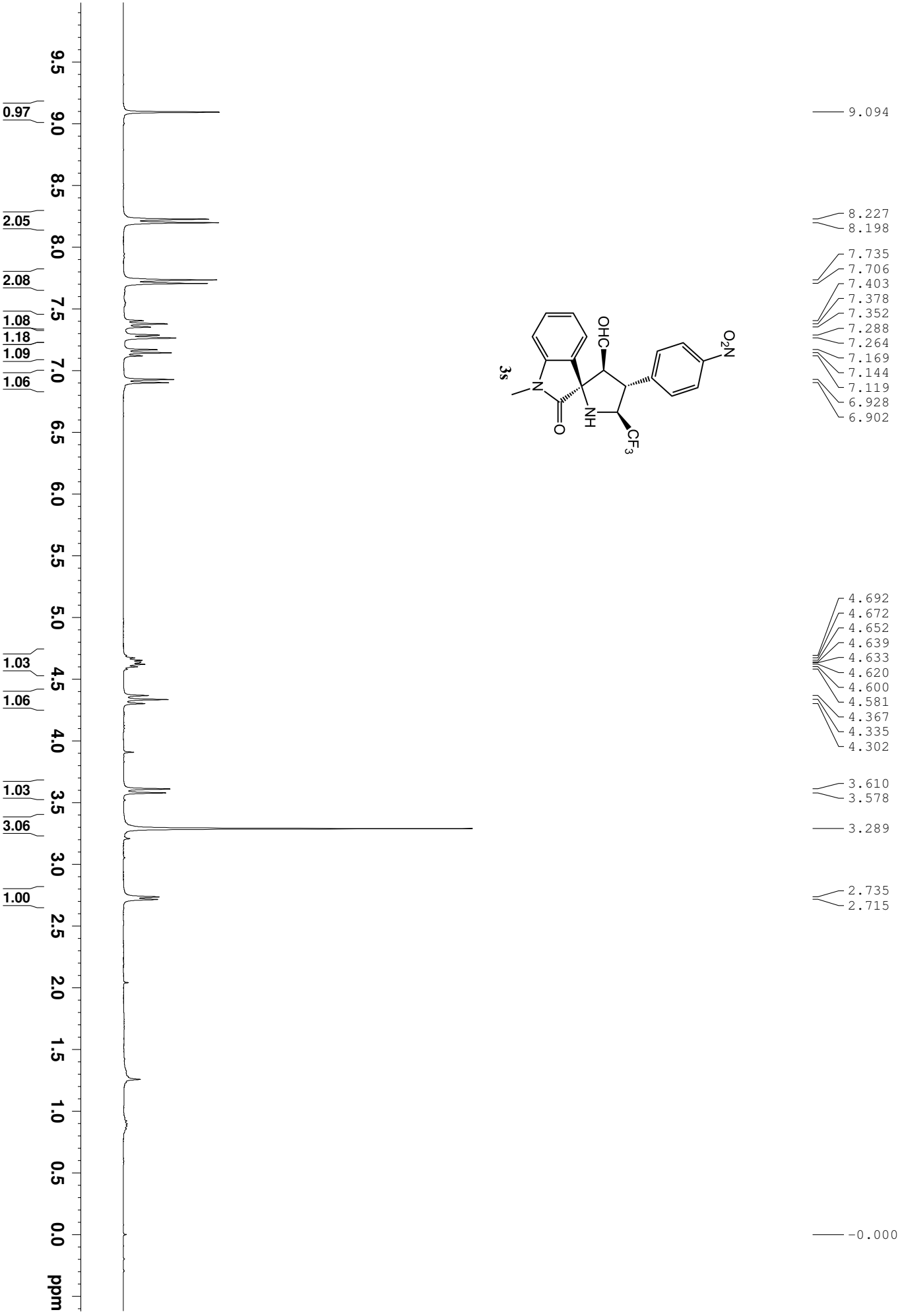
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7.144
7.119
6.928
6.902
4.692
4.672
4.652
4.639
4.633
4.620
4.600
4.581
4.367
4.335
4.302
3.610
3.578
3.289
2.735
2.715
-0.000
0.97
2.05
2.08
1.08
1.18
1.09
1.06
1.03
1.06
1.03
3.06
1.00
OHC
O2N
3s
N
NH
O
CF3
9.5
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8.5
8.0
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7.0
6.5
6.0
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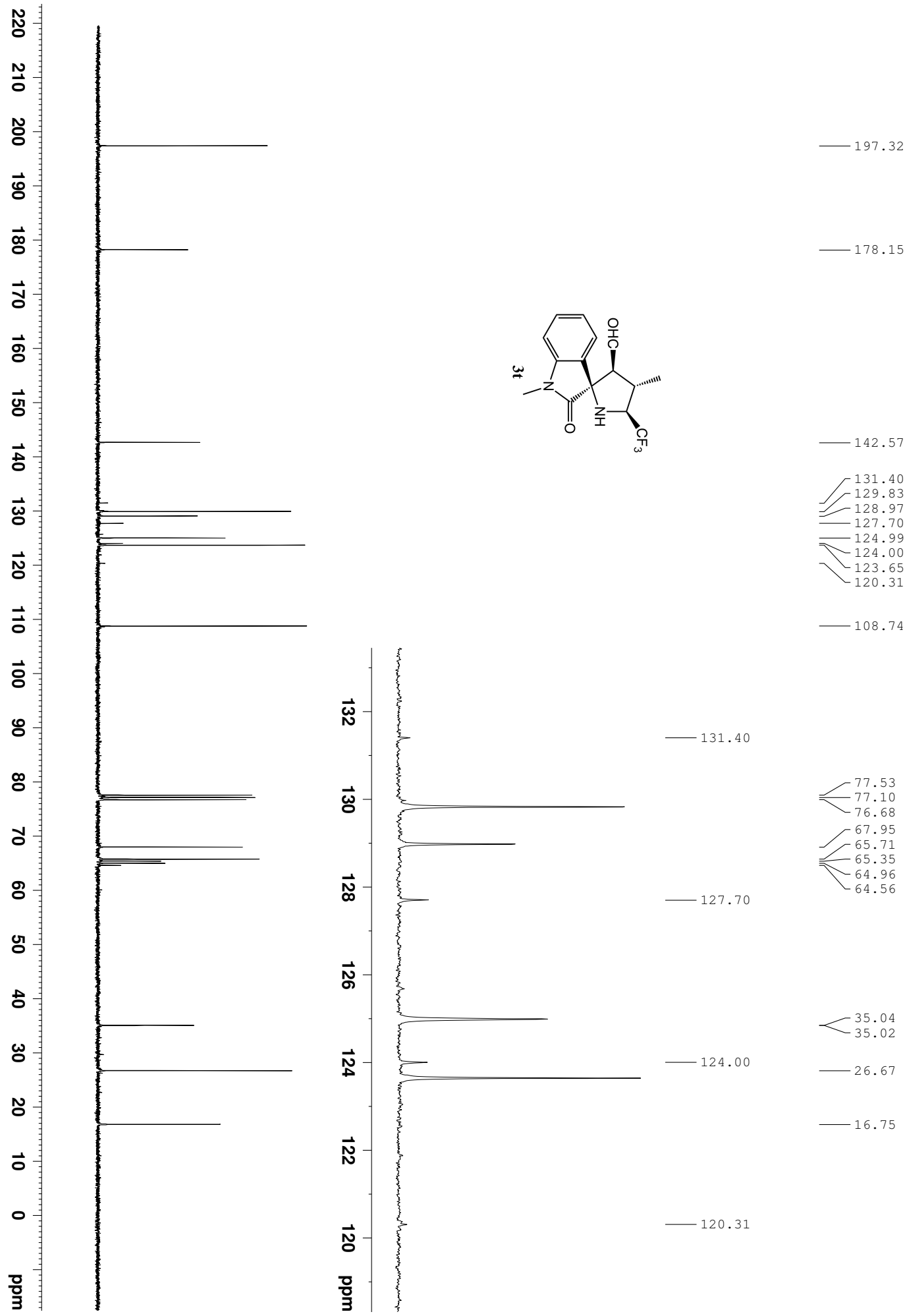
ppm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O
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128.97
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124.99
124.00
123.65
120.31
108.74
77.53
77.10
76.68
67.95
65.71
65.35
64.96
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26.67
16.75
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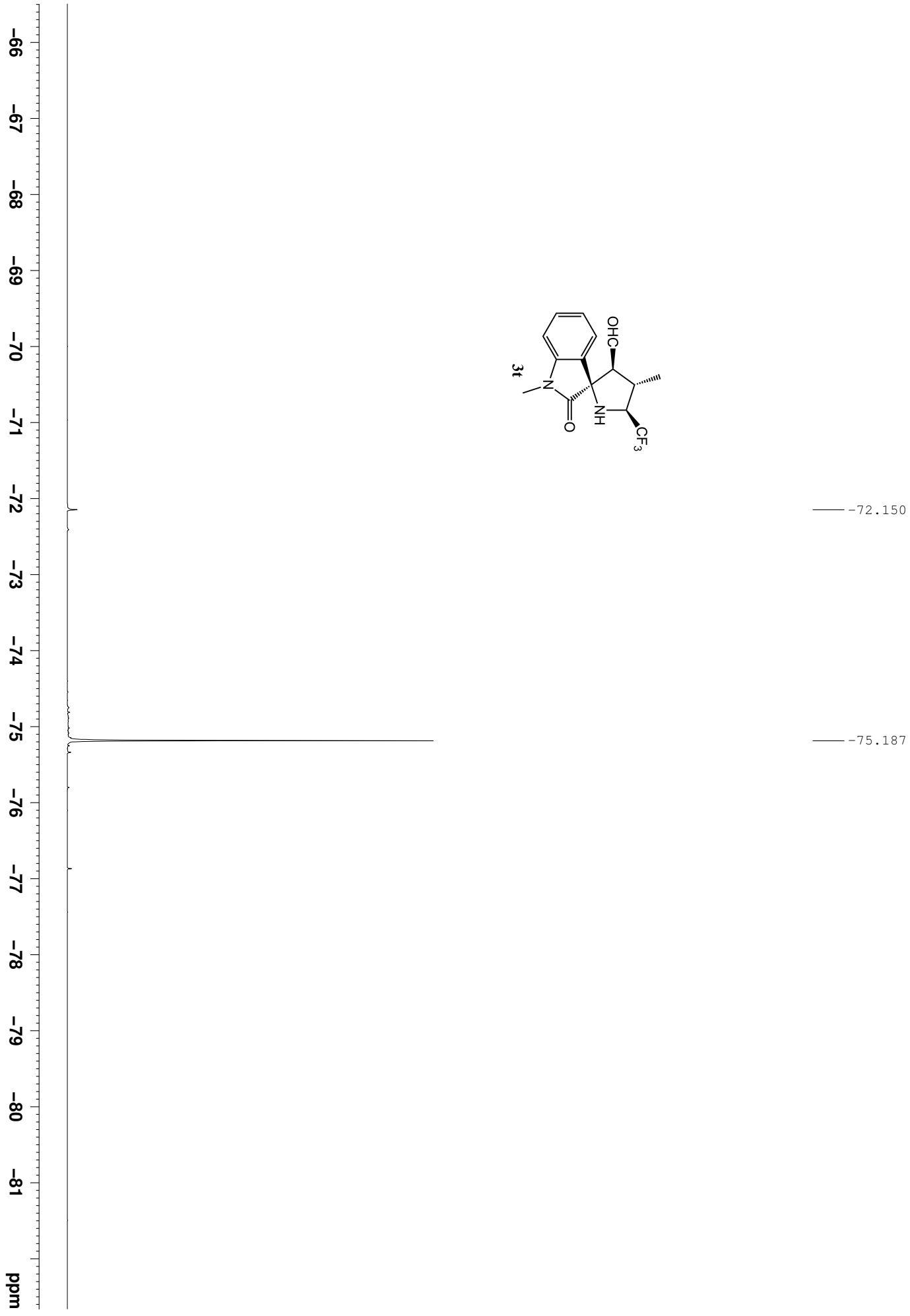
132 130 128 126 124 122 120 ppm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-70
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ppm
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N
NH
O
CF3
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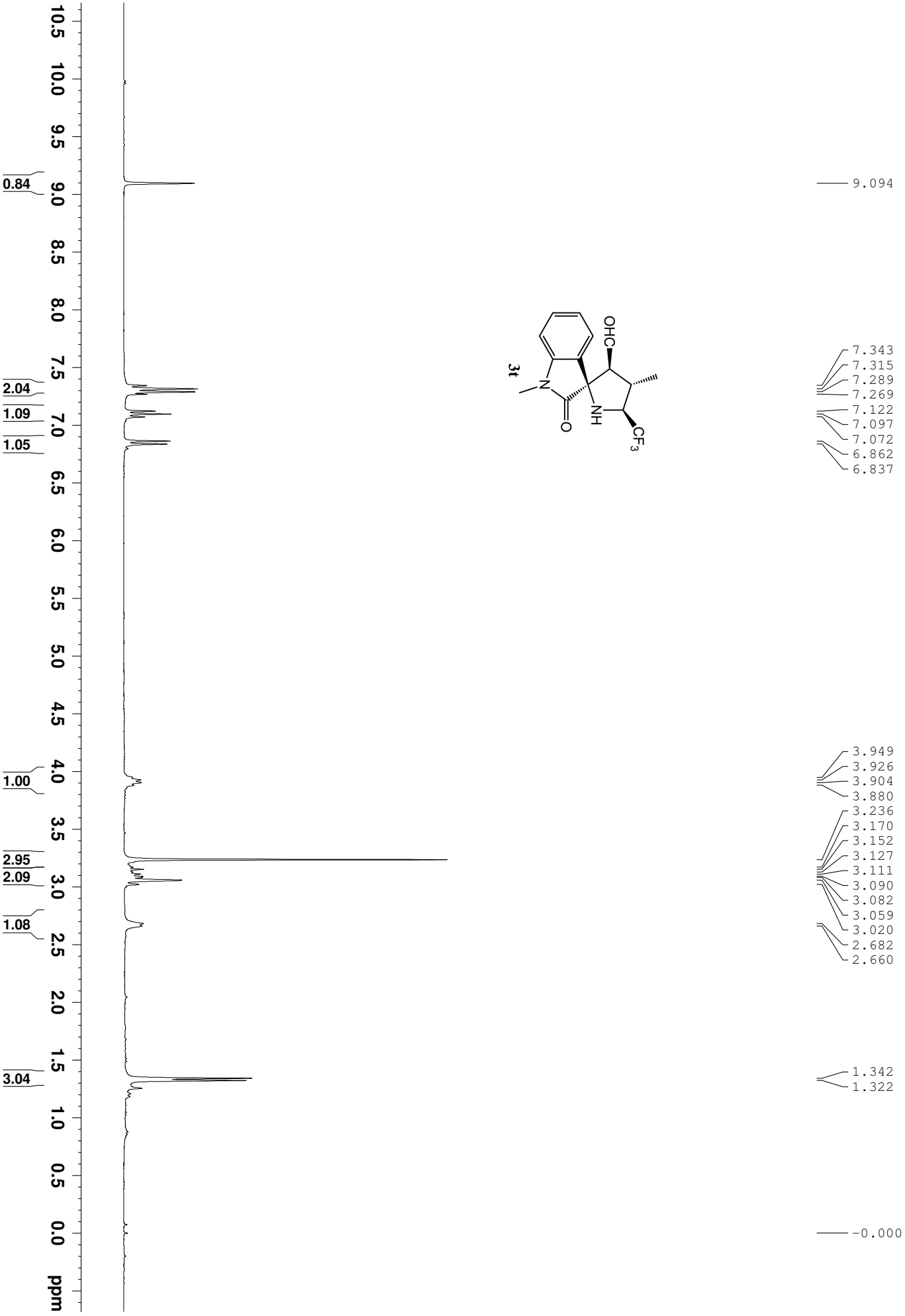
-75.187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3.0
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2.0
1.5
1.0
0.5
0.0
ppm
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1.09
1.05
1.00
2.95
2.09
1.08
3.04
3t
OHC
N
NH
O
CF3
9.094
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7.315
7.289
7.269
7.122
7.097
7.072
6.862
6.837
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3.926
3.904
3.880
3.236
3.170
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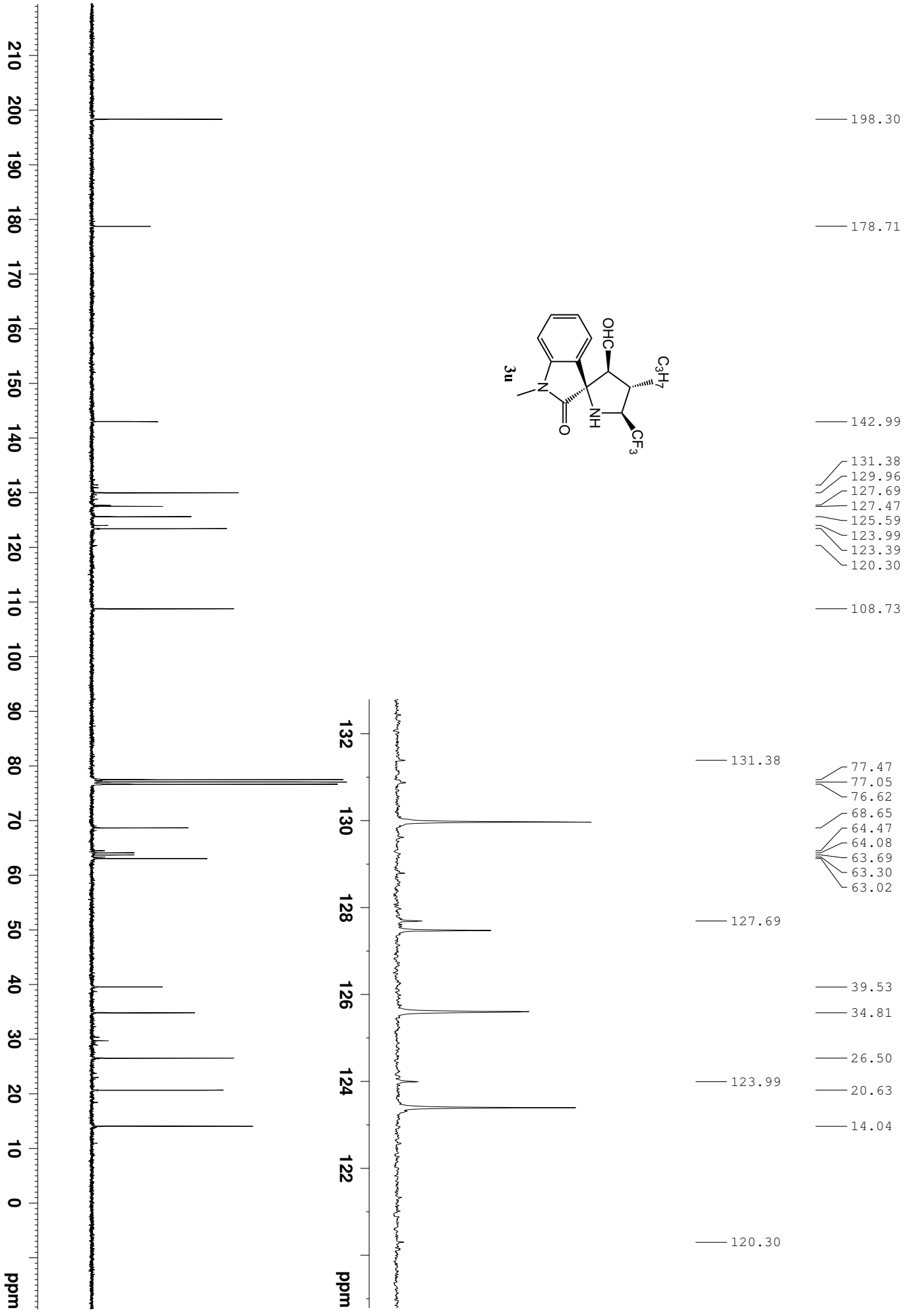
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C3H7
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O
CF3
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125.59
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123.39
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108.73
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68.65
64.47
64.08
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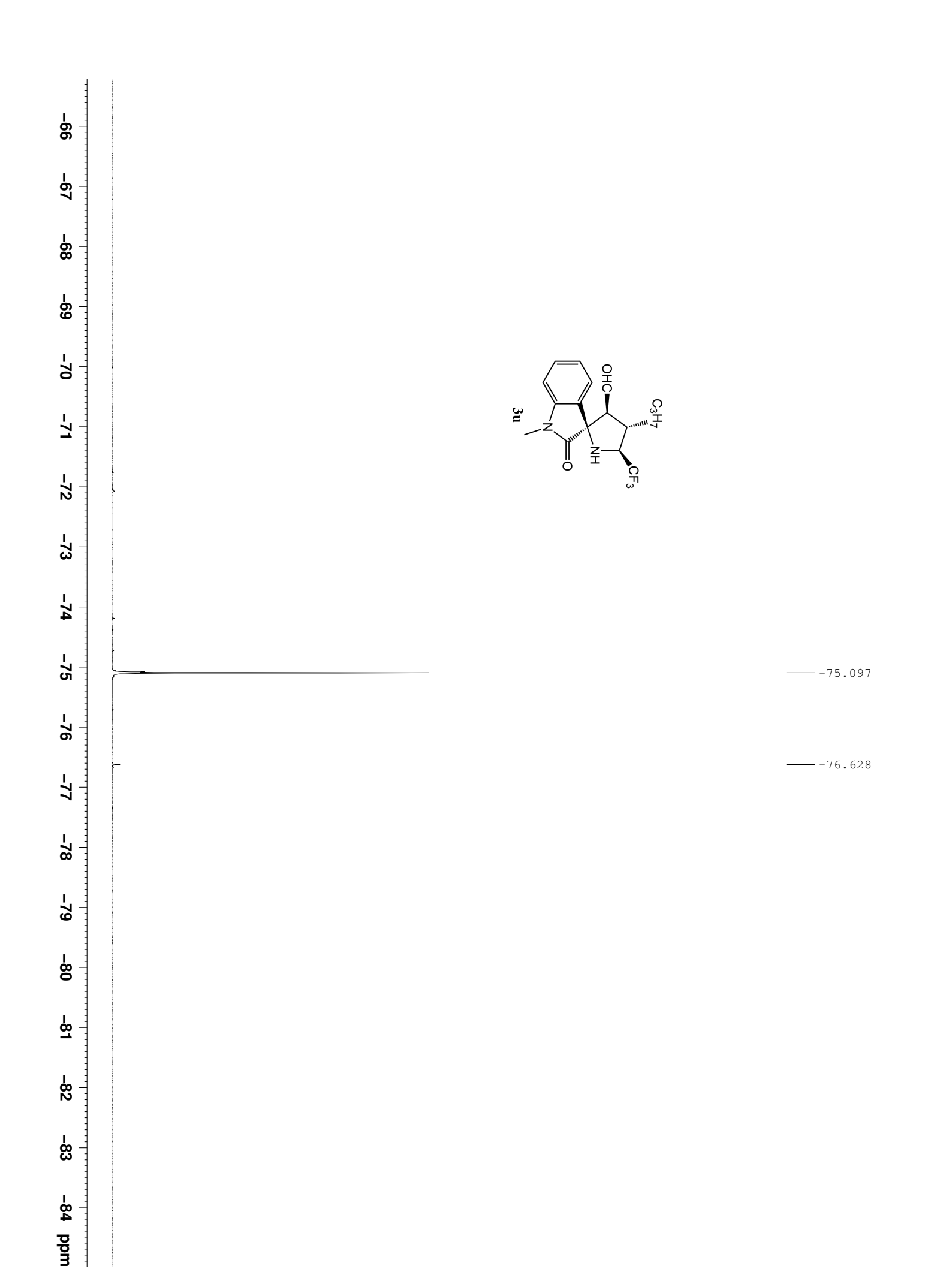
ppm
ppm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-78
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NH
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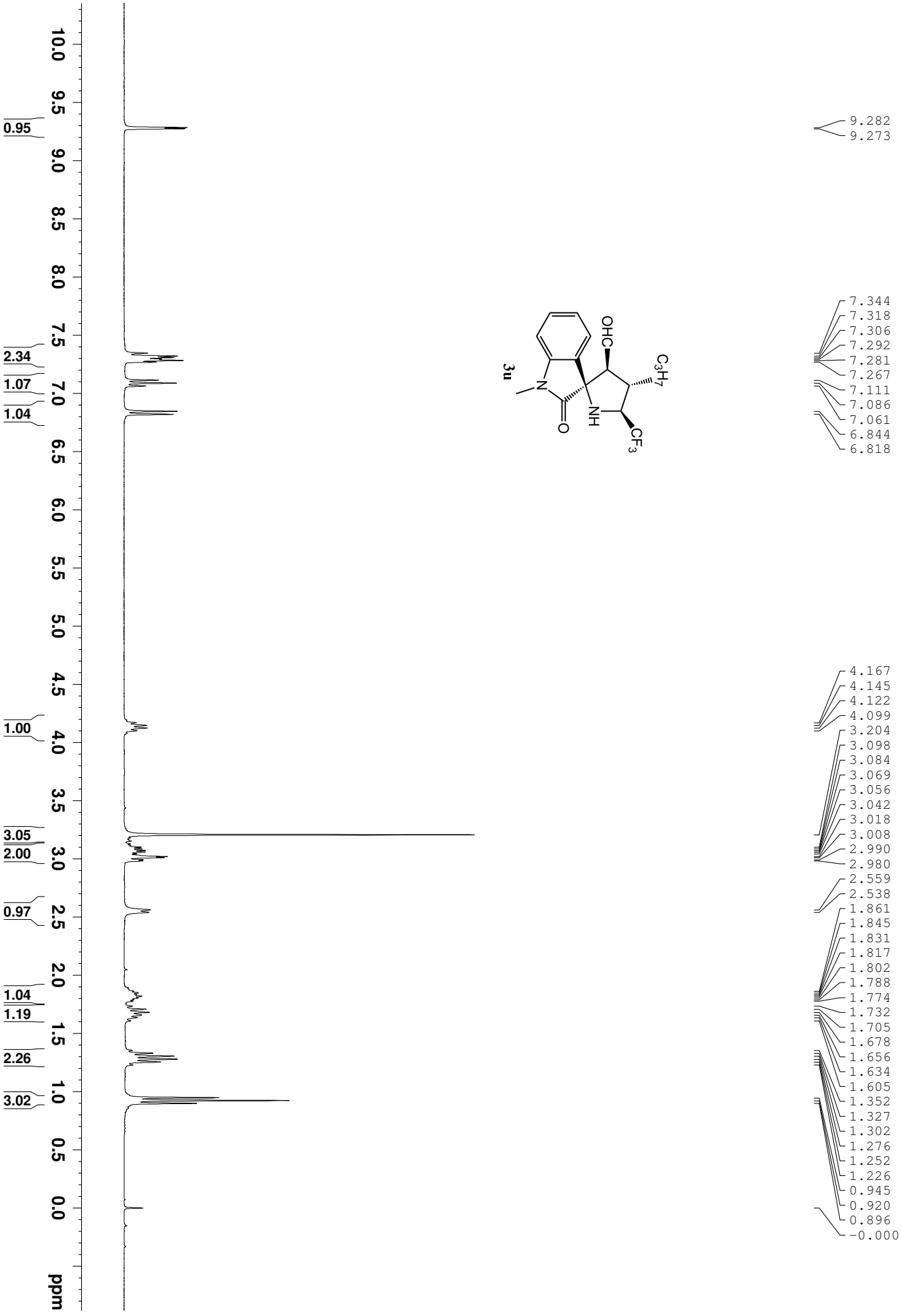
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7.061
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6.818
4.167
4.145
4.122
4.099
3.204
3.098
3.084
3.069
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3.042
3.018
3.008
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2.980
2.559
2.538
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1.802
1.788
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1.732
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1.226
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0.920
0.896
-0.000
0.95
2.34
1.07
1.04
1.00
3.05
2.00
0.97
1.04
1.19
2.26
3.02
ppm
3u
OHC
C3H7
CF3
NH
N
O