Supporting Information

For

Palladium-Catalyzed Intramolecular Aminofluorination of Unactivated Alkenes

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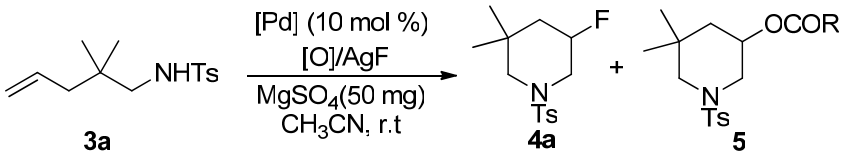
General Considerations.

All commercially available compounds were used as received, and all were purchased from Aldrich and Alfa Aesar. NMR spectra were obtained on a Varian Inova 400 (400 MHz for ^{1}H; 376 MHz for ^{19}F; 100 MHz for ^{13}C) spectrometer. The chemical shifts (δ) are given in parts per million relative to internal standard TMS (0 ppm for ^{1}H) and $CDCl_3$ (77.0 ppm for ^{13}C). Flash column chromatography was performed on silica gel 60 (particle size 200-400 mesh ASTM, purchased from Yantai, China) and eluted with petroleum ether/ethyl acetate. Acetonitrile was dried by refluxing over CaH_2 for 6h followed by fractional distillation. Compounds **3a-3m**[S1] were synthesized according to the reported procedure.

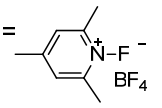
General procedure for screening of intramolecular aminofluorination of Unactivated alkene 3a: In a dry glass tube, Pd catalyst (0.01 mmol), AgF (0.5 mmol), Oxidant (0.2 mmol), $MgSO_4$ (0.2 mmol) and N-tosylamine alkene **3a** (0.1 mmol) were dissolved in 0.5 mL dry CH_3CN. The reaction mixture was stirred at room temperature for 24 h, then the mixture was filtered and the solid was washed by CH_2Cl_2. Filtrates were combined and concentrated under vacuum and the residue was analyzed by ^{1}H NMR with 1,3,5-trimethoxybenezene as internal standard. The results were summarized in Table S1.

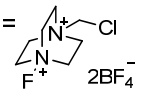
Table S1. Palladium-catalyzed intramolecular aminofluorination of alkene **1a**.[a]

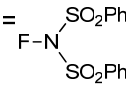


3a **4a** **5**

Entry	[Pd]	[O] (2 eq)/ MF (2.5 eq)	Solvent	Yield (%)[b]	
				4a	**5**[c]
1	$Pd(OAc)_2$	**1**	CH_3CN	0	--
2	$Pd(OAc)_2$	**2**	CH_3CN	0	--
3	$Pd(OAc)_2$	NFSi[f]	CH_3CN	0	--
4	$Pd(OAc)_2$	$PhIF_2$	CH_3CN	0	--
5	$Pd(OAc)_2$	$PhI(OAc)_2$ /AgF	CH_3CN	38%	24% (**5a**)
6	$Pd(OAc)_2$	$PhI(OCO^tBu)_2$ /AgF	CH_3CN	77%	17% (**5b**)
7	$Pd(OAc)_2$	$PhI(OCOCF_3)_2$ /AgF	CH_3CN	0	40% (**5c**)
8	$Pd(OAc)_2$	$PhI(OCOPh)_2$ /AgF	CH_3CN	34%	40% (**5d**)
9[d]	$Pd(OAc)_2$	-- /AgF	CH_3CN	0	--
10	$Pd(OAc)_2$	Oxone /AgF	CH_3CN	0	--
11	$Pd(OAc)_2$	NCS /AgF	CH_3CN	0	--
12	$Pd(OAc)_2$	H_2O_2 /AgF	CH_3CN	0	--
13[e]	$Pd(OAc)_2$	$PhI(OCO^tBu)_2$ /AgF	CH_3CN	69%	25% (**5b**)
14	--	$PhI(OCO^tBu)_2$ /AgF	CH_3CN	0	0 (**5b**)
15	$PdCl_2$	$PhI(OCO^tBu)_2$ /AgF	CH_3CN	65%	20% (**5b**)
16	$Pd(OCOCF_3)_2$	$PhI(OCO^tBu)_2$ /AgF	CH_3CN	33%	9% (**5b**)
17	$PdCl_2(CH_3CN)_2$	$PhI(OCO^tBu)_2$ /AgF	CH_3CN	45%	20% (**5b**)
18	$Pd(OAc)_2$	$PhI(OCO^tBu)_2$ /Bu_4NF	CH_3CN	0	0 (**5b**)
19[d]	**$Pd(OAc)_2$**	**$PhI(OCO^tBu)_2$ /AgF**	**CH_3CN**	**86%**	**10%** (**5b**)
20	$Pd(OAc)_2$	$PhI(OCO^tBu)_2$ /AgF	$(CH_2Cl)_2$	13	25 (**5b**)
21	$Pd(OAc)_2$	$PhI(OCO^tBu)_2$ /AgF	TBME	15	46 (**5b**)
22	$Pd(OAc)_2$	$PhI(OCO^tBu)_2$ /AgF	Dioxane	0	30 (**5b**)
23	$Pd(OAc)_2$	$PhI(OCO^tBu)_2$ /AgF	DMF	0	55 (**5b**)

1 = 

2 = 

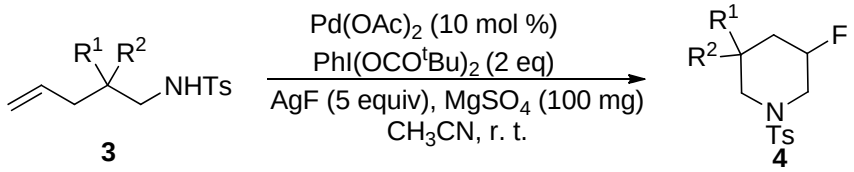
NFSi = 

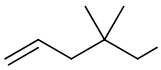
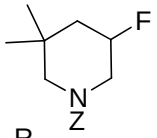
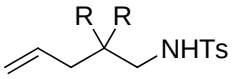
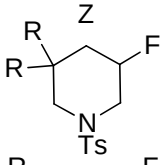
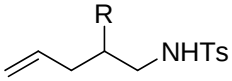
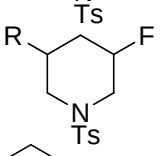
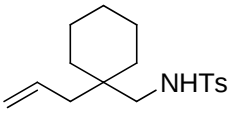
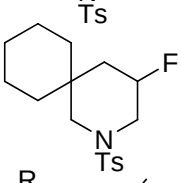
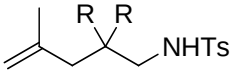
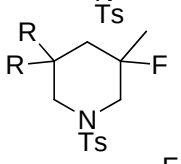
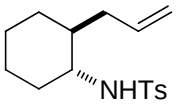
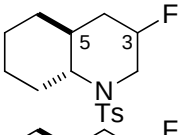
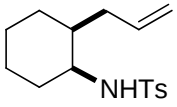
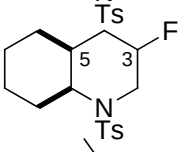
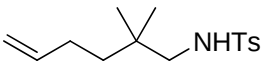
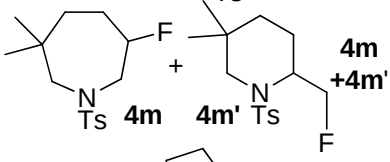
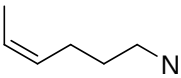
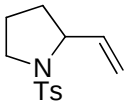
[a]Reaction condition: **3a** (0.1 mmol), [Pd] (0.01 mmol), AgF (0.25 mmol), [O] (0.2 mmol), $MgSO_4$ (50 mg) in 0.5 mL CH_3CN at room temperature. [b]^1H NMR yield with 1,3,5-trimethoxybenzene as internal standard. [c]**5a**: R= Me, **5b**: R = ^{t}Bu, **5c**: R = CF_3, **5d**: R= Ph. [d]AgF (5 eq). [e]without $MgSO_4$. [f]NFSi = *N*-fluorodibenzene-sulfonimide

General procedure for aminofluorination of unactivated alkenes:

In a dry glass tube, $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), AgF (125.9 mg, 1.0 mmol), $PhI(OCO^tBu)_2$ (162.5 mg, 0.4 mmol), $MgSO_4$ (0.4 mmol) and alkenes **3** (0.2 mmol) were dissolved in dry CH_3CN (1.0 mL). The reaction mixture was stirred at room temperature for 24 h, then the mixture was filtered and the solid was washed by CH_2Cl_2. Filtrates were combined and concentrated under vacuum. The residue purified by column chromatography on silica gel with a gradient eluant of petroleum ether and ethyl acetate, afforded the products **4**. The results were summarized in Table S2.

Table S2. Palladium-catalyzed intramolecular aminofluorination of alkenes.[a]



Entry	Alkene		Product		Yield[b]
1		**3a** Z = Ts		**4a**	84%
2		**3b** Ns		**4b**	74%
3		**3c** Boc		**4c**	0
4		**3d** R = H		**4d**	80%
5		**3e** R = Ph		**4e**	83%
6		**3f** R = Me		**4f**	89% (1.3:1)[c]
7		**3g** R = Ph		**4g**	55% (2:1)[c]
8		**3h**		**4h**	79%
9		**3i** R = Me		**4i**	83%
10		**3j** R = Ph		**4j**	80%
11		*trans*-**3k**		**4k**	87% (4:1)[d]
12		*cis*-**3k**		**4l**	82% (1:5)[d]
13	 **3m**		 **4m** **4m'**	**4m +4m'**	58% (5:1)[e]
14		**3n**		**4n**	75%

[a]Reactions were conducted at 0.2 mmol scale. [b]Isolated yield (the ratio of diastereoselectivity which determined by ^{19}F NMR). [c]The ratio of *trans* and *cis* isomers. [d]The ratio of 3,5-*trans* and 3,5-*cis* isomers. [e]The ratio of **4m**:**4m'**.

For the products **4f, 4g, 4k, and 4l**, the isomers were separated by column chromatography. The relative stereochemistry of these compounds was verified by the analysis of ^{1}H NMR and

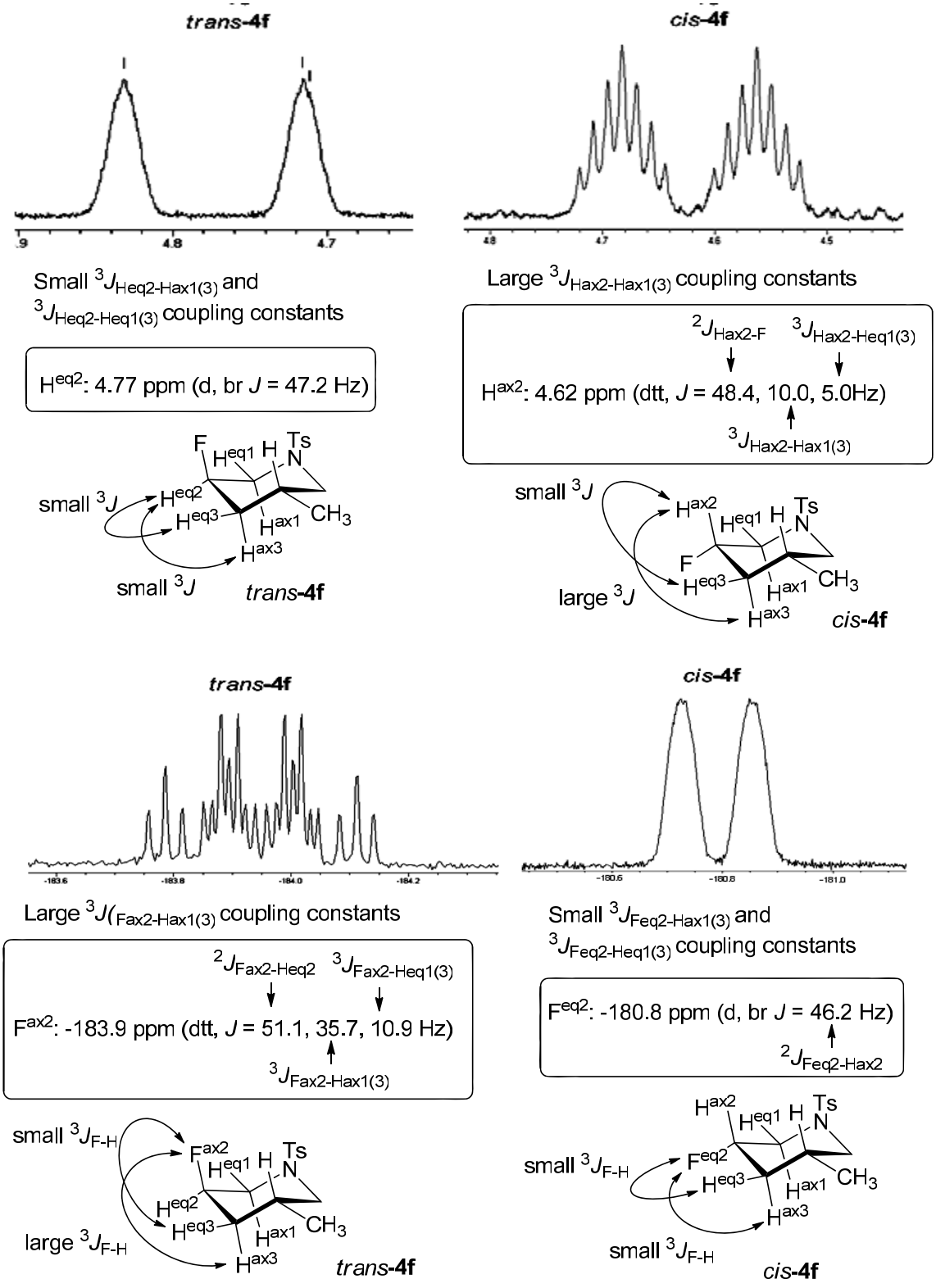


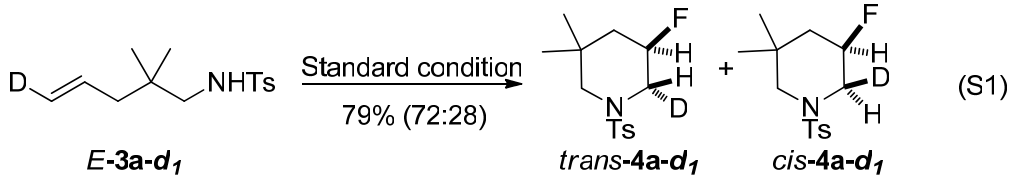
Figure S1: The NMR spectroscopy of *trans*-**4f** and *cis*-**4f**: top, the ^{1}H NMR of proton at 3 position; bottom, the ^{19}F NMR. (Hax2 is the proton at carbon 2 in the axial position, Fax2 is the fluorine at carbon 2 in the axial position).

^{19}F NMR coupling constants. The assignment of structure of *trans*-**4f** and *cis*-**4f** were shown in Figure S1. Based on the assumption that the large coupling observes between two vicinal protons at axial position (such as, H^{ax2} and H^{ax3} of *cis*-**4f** in Figure S1), and small coupling between both protons in the equatorial position or between two protons in the axial and equatorial position,[S2] the signal at 4.62 ppm (dtt, J = 48.4, 10.0, 5.0 Hz) should belongs (belong) to *cis*-**4f** due to the larger coupling (10.0 Hz), which occurs between H^{ax2} and $H^{ax1(3)}$ (meaning H^{ax1} and H^{ax3}, see Figure S1, right on the top). In contrast, the signal at 4.77 ppm (d, br) should belong to *trans*-**4f,** which the small coupling occurs between H^{eq2} and $H^{eq1(3)}$ or $H^{ax1(3)}$ (Figure S1, left on the top).

On the other hand, the similar coupling of ^{19}F NMR was observed. For the corresponding ^{19}F NMR spectroscopy of *cis*-**4f**, the chemical shift of F^{eq2} is -180.8 (d, br, J = 46.2 Hz). The possible reason for the broad d is resulted by the small coupling between F^{eq2} and $H^{eq1(3)}$ or $H^{ax1(3)}$ (Figure S1, right on the bottom). The *trans*-**4f** have a ^{19}F signal at -183.9ppm (dtt, J = 51.1, 35.7, 10.9 Hz). Those coupling constants are existence in F^{ax2}-H^{eq2} (51.1), F^{ax2}-$H^{ax1(3)}$ (35.7) and F^{ax2}-$H^{eq1(3)}$ (10.9) (Figure S1, left on the bottom). For the ^{19}F NMR, above analysis indicates that the large coupling is also observed between both fluorine and proton in the axial position, which is the same as ^{1}H NMR.

Mechanistic Studies:

In order to gain some mechanistic insight of the aminofluorination process, we synthesized deuterated substrates *E*-**3a-*d*$_1$** according to the literature procedure.[S3] And then *E*-**3a-*d*$_1$** was applied to the standard reaction condition. The result was listed in eq S1, and the crude HNMR spectrum was given in Figure S2.



E-**3a-*d*$_1$** *trans*-**4a-*d*$_1$** *cis*-**4a-*d*$_1$** (S1)

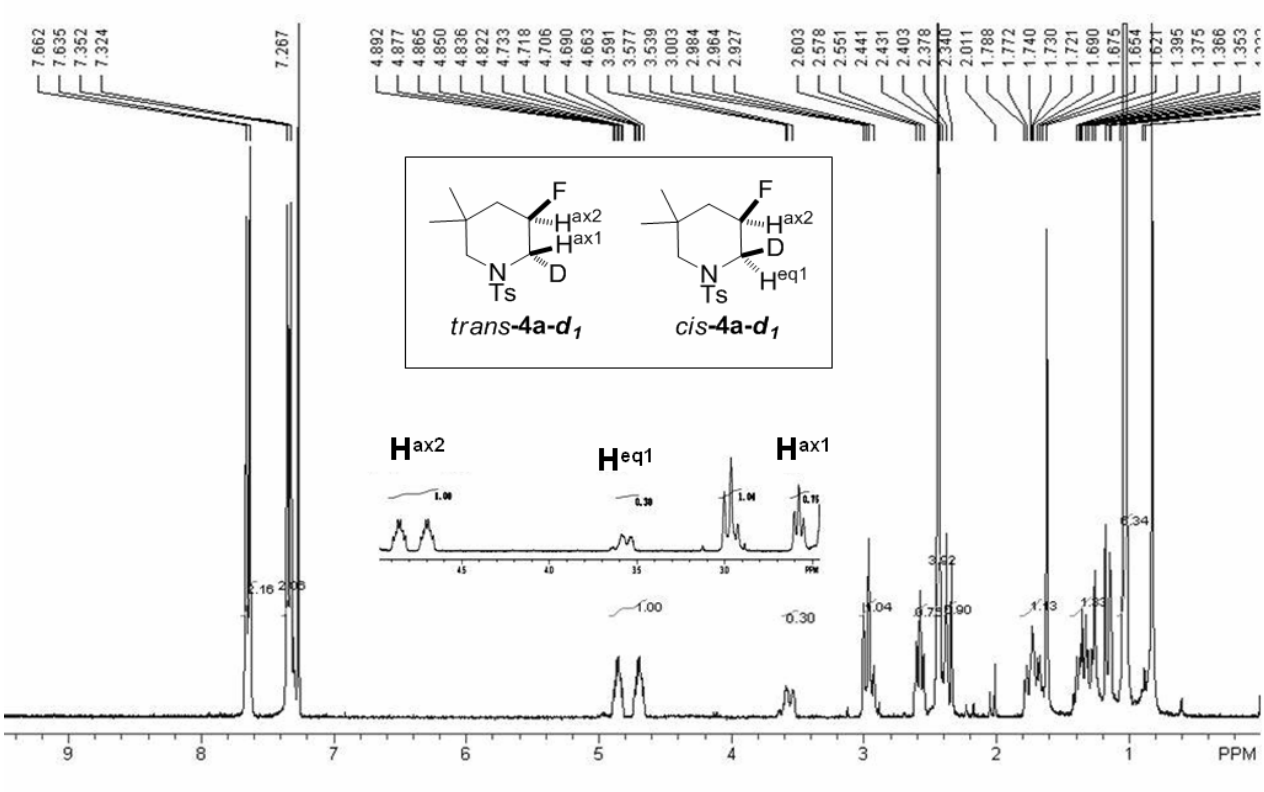
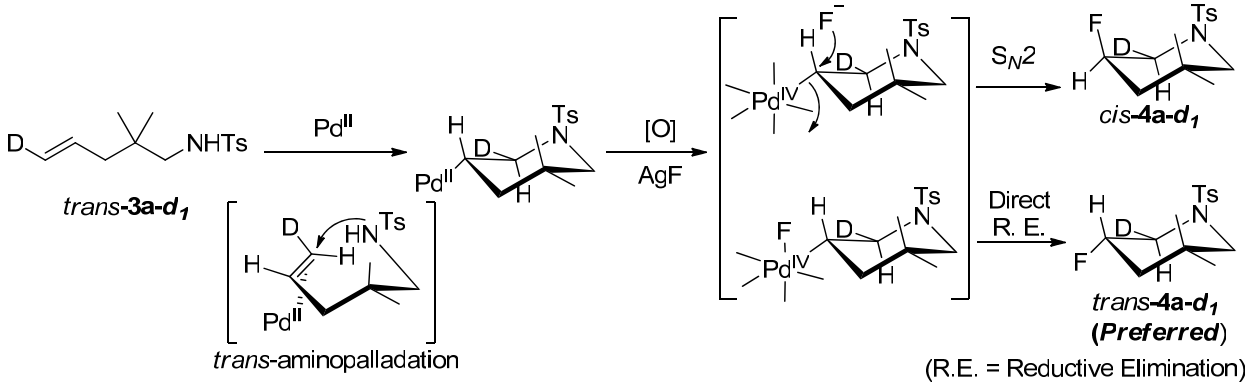


Figure S2. The HNMR spectrum of reaction of *E*-**3a-*d*$_1$.**

A possible catalytic cycle based on our findings is shown in Scheme S1: Pd(II)-mediated *trans*-amino-palladation of the alkene with attack at the terminal carbon (*6-endo*) generates a Pd(II) intermediate that undergoes an oxidation step by $PhI(OPiv)_2$/AgF. Reductive elimination from the Pd(IV) intermediate generates the C—F bond, where direct reductive elimination is favored, albeit competing with S_N2 nucleophilic attack by fluorine.

Scheme S1. The possible mechanism for aminofluorination of alkenes.



The characterization of compounds 4a, *cis*-4a-*d*$_1$ and *trans*-4a-*d*$_1$:

The identification of structures of ***cis*-4a-*d*$_1$** and ***trans*-4a-*d*$_1$** were compared with the structure of compound **4a**, including ^{1}H-^{1}H COSY (Figure S3), coupling constant of ^{1}H NMR

(Figure S4) and NOESY-1D (Figure S5).

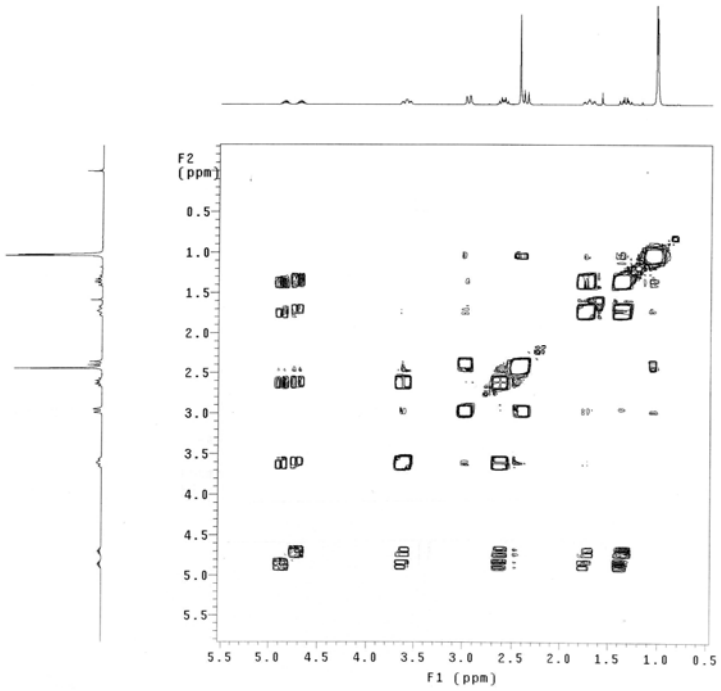
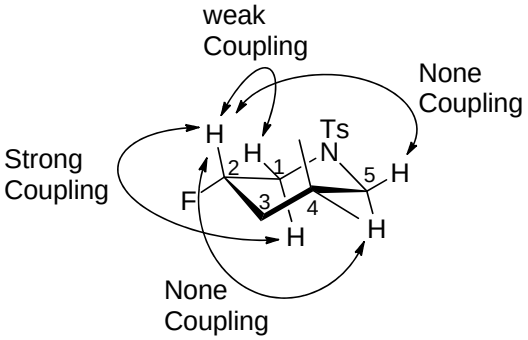


Figure S3. The ^{1}H-^{1}H COSEY spectroscopy of **4a**



Scheme S2. H-H COSY Spectrum of Compound **4a**

For the structure of **4a,** the H-H COSY spectroscopy shows that a strong coupling occurs between the proton at the 4.77 ppm and 3.61ppm, and weak coupling at 4.77ppm and 2.62ppm. However, there are no coupling between 4.77ppm and 2.96 (and 2.38 ppm). The big coupling constant 47.6Hz of signal at 4.77ppm (dtt, J = 47.6, 8.4, 4 Hz) is coupled by fluorine atom at the same carbon C2. Thus, the signal at 4.77ppm is proton at C2. The signal at 3.61ppm and 2.62 ppm are the proton at C1, and 2.96 and 2.38 ppm are the proton at C5 (see Figure S3 and Scheme S2).

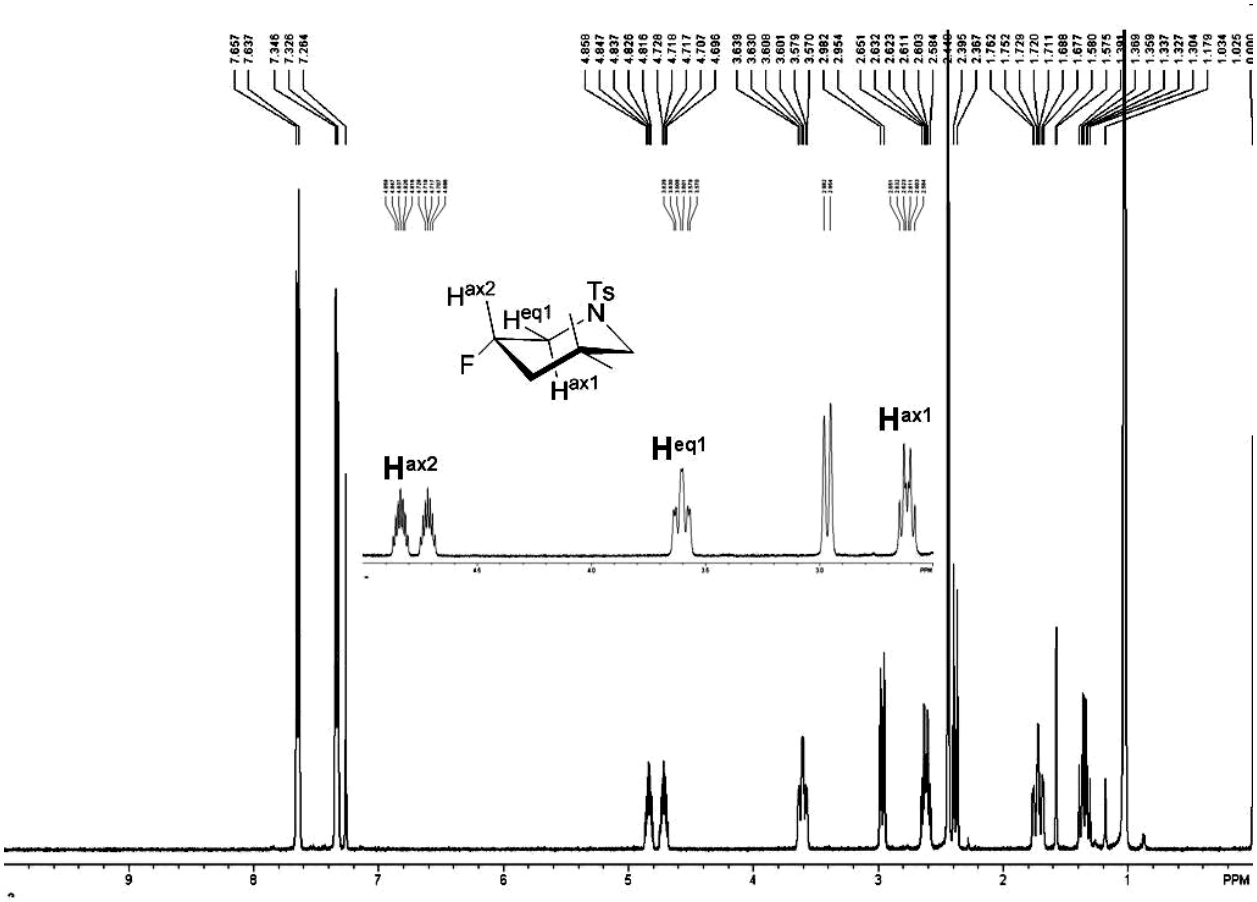
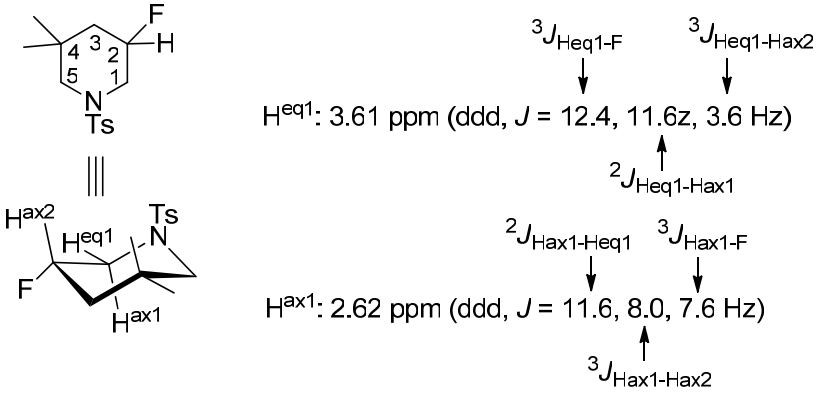


Figure S4. The ^{1}H NMR spectroscopy of compound **4a**.



Scheme S3. The ^{1}H NMR spectrum and assignment of compound **4a**

For compound **4a**, the signal at 3.61ppm is a ddd (J = 12.4, 11.6, 3.6Hz), and the coupling constants should belong to $J_{\text{Heq1-Hax2}}$ (3.6Hz), $J_{\text{Heq1-Hax1}}$ (11.6Hz) and $J_{\text{Heq1-F}}$ (12.4Hz), respectively. While, the signal at 2.62ppm is also a ddd (J = 11.6, 8.0, 7.6Hz). The coupling constants should also belong to $J_{\text{Hax1-Hax2}}$ (8.0Hz), $J_{\text{Hax1-Heq1}}$ (11.6Hz) and $J_{\text{Heq1-F}}$ (7.6Hz). Based on above analysis, the signal at 3.61 should belong to H^{eq1}, and 2.62 should be H^{ax1} (see Scheme S3).

Furthermore, the NOESY spectroscopy shows that there are stronger NOE between H^{ax2} and H^{eq1}, and weak NOE with H^{ax2} and H^{ax1}, which means H^{ax2} and H^{eq1} in one side of ring, and H^{ax2} and H^{ax1} in cross sides of ring (Scheme S4 and Figure S5). This result also supports the assignment of compound **4a**.

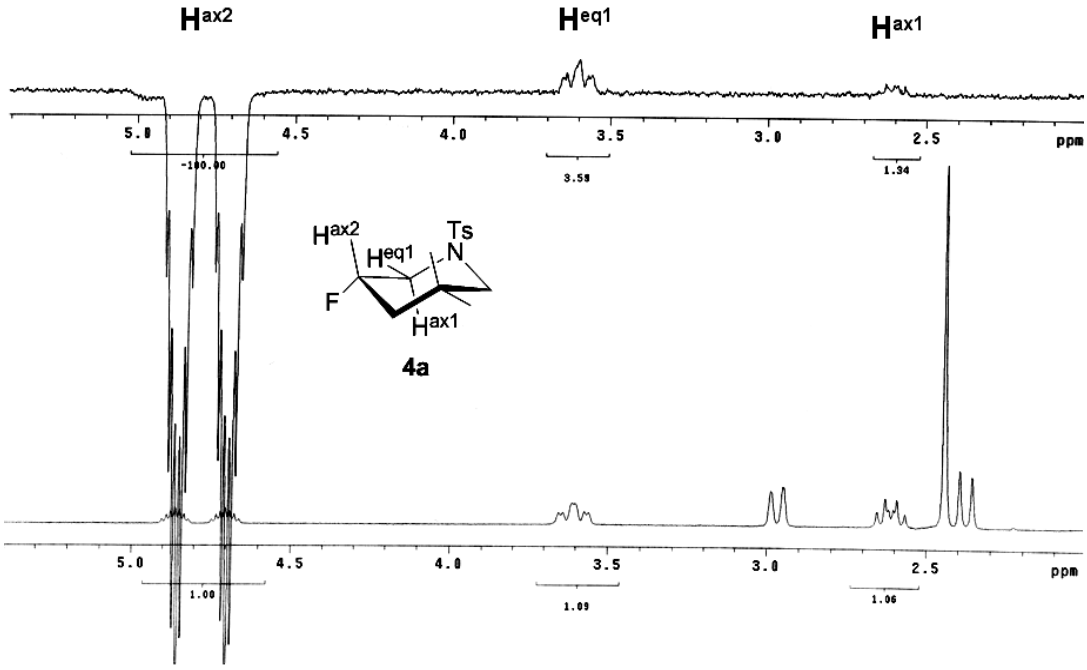
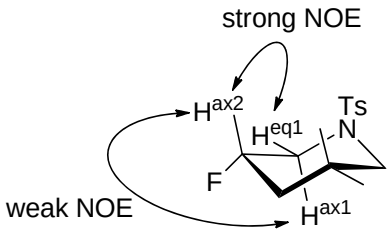
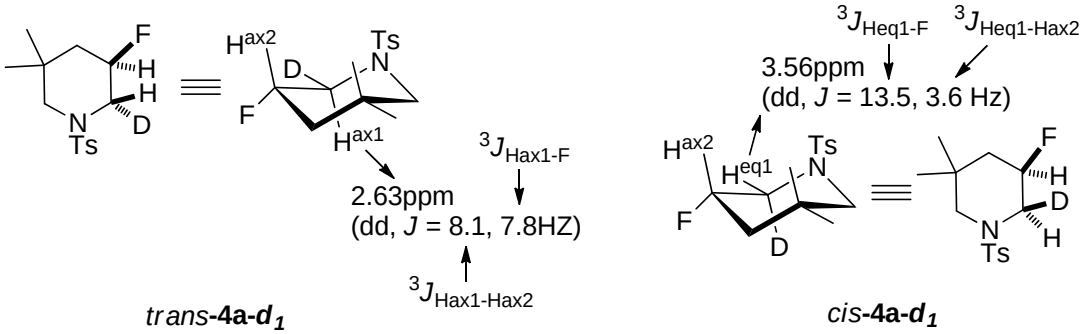


Figure S5. The NOESY-1D spectroscopy of compound **4a**: top, NOSEY-1D spectroscopy; bottom, ^{1}H NMR spectrum.



Scheme S4. NOESY 1D Spectrum of Compound **4a**

Finally, according to the structure of compound **4a**, the identification of deuterium labeled products *cis*-**4a**-d_1 and *trans*-**4a**-d_1 was listed in Scheme S5. Thus the ratio of *trans*-**4a**-d_1 and *cis*-**4a**-d_1 is 72:28 (see Figure S2).



Scheme S5. The ^{1}H NMR spectrum and assignment of compounds *trans*-**4a-*d*$_1$** and *cis*-**4a-*d*$_1$**

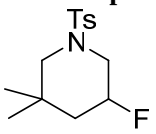
Reference:

[S1] Michael, F. E.; Cochran, B. M.; *J. Am. Chem. Soc.*, **2006**, *128*, 4246–4247

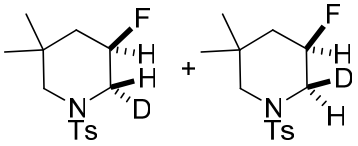
[S2] Kemp, W. *Organic Spectroscopy*, MacMillian Press Ltd, London, 3rd edn., 1991.

[S3] Sherman, E. S.; Fuller, P. H.; Kasi, D.; Chemler, S. R. *J. Org. Chem.* **2007**, *72*, 3896 – 3905.

New compounds characterization:

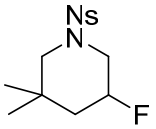


4a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.77 (dtt, *J* = 47.6, 8.4, 4.0 Hz, 1H), 3.61 (ddd, *J* = 12.4, 11.6, 3.6 Hz, 1H), 2.97 (d, *J* = 11.2 Hz, 1H), 2.62 (ddd, *J* = 11.6, 8.0, 7.6 Hz, 1H), 2.44 (s, 3H), 2.38 (d, *J* = 11.2 Hz, 1H), 1.72 (ddd, *J* = 16.8, 13.2, 4.0 Hz, 1H), 1.35 (ddd, *J* = 12.8, 12.8, 8.8 Hz, 1H), 1.03 (s, 3H), 1.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 133.5, 129.7, 127.5, 85.6 (d, *J* = 231.9 Hz), 56.6 (d, *J* = 1.5 Hz), 49.9 (d, *J* = 38.0 Hz), 42.6 (d, *J* = 23.6 Hz), 31.8 (d, *J* = 9.9 Hz), 27.8 (d, *J* = 2.4 Hz), 25.9, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -183.16 (d, *J* = 45.5 Hz). HRMS: m/z (EI) calculated $[M+H]^+$: 286.1272, measured: 286.1276.



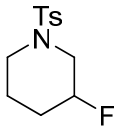
trans-**4a-*d*$_1$** *cis*-**4a-*d*$_1$**

cis-**4a-*d*$_1$**: ^{1}H NMR (300M, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.77 (dm, *J* = 47.7 Hz, 1H), 3.61 (dd, *J* = 13.5, 3.6 Hz, 1H), 2.97 (m, 1H), 2.44 (s, 3H), 2.38 (d, *J* = 11.2 Hz, 1H), 1.72 (ddd, *J* = 16.8, 13.2, 4.0 Hz, 1H), 1.35 (ddd, *J* = 12.8, 12.8, 8.8 Hz, 1H), 1.03 (s, 3H), 1.02 (s, 3H). *trans*-**4a-*d*$_1$** ^{1}H NMR (300M, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.77 (dm, *J* = 47.7 Hz, 1H), 2.97 (m, 1H), 2.63 (dd, *J* = 8.1, 7.8 Hz, 1H), 2.44 (s, 3H), 2.38 (d, *J* = 11.2 Hz, 1H), 1.72 (ddd, *J* = 16.8, 13.2, 4.0 Hz, 1H), 1.35 (ddd, *J* = 12.8, 12.8, 8.8 Hz, 1H), 1.03 (s, 3H), 1.02 (s, 3H). HRMS: m/z (ESI) calculated $[M+Na]^+$: 309.1154, measured: 309.1145.

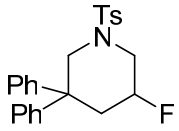


4b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 8.8 Hz, 2H), 4.80 (dm, *J* = 47.2 Hz, 1H), 3.56 (ddd, *J* = 16.0, 11.6, 4.0 Hz, 1H), 2.97 (d, *J* = 11.6 Hz, 1H), 2.89 (dt, *J* = 11.6, 7.6 Hz, 1H), 2.61 (d, *J* = 12.0 Hz, 1H), 1.71 (ddd, *J* = 20.4, 13.6, 4.0 Hz, 1H), 1.46 (dt, *J* = 12.8, 8.0 Hz, 1H), 1.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 142.9, 128.6, 124.4, 85.4 (d, *J* = 175.5 Hz), 56.6, 49.5 (d, *J* = 28.3 Hz), 42.2 (d, *J* = 17.8 Hz), 31.8 (d, *J* = 6.9 Hz), 27.4 (d,

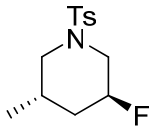
J = 2.2 Hz), 26.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -182.60 (dm, J = 42.9 Hz). HRMS: m/z (ESI) calculated $[M+Na]^+$: 339.0785, measured: 339.0793.



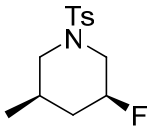
4d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 4.67 (dm, J = 46.8 Hz, 1H), 3.38 (dd, J = 18.4, 11.6 Hz, 1H), 3.12(m, 1H), 3.00 (dt, J = 11.2, 7.2 Hz, 1H), 2.89 (m, 1H), 2.44 (s, 3H), 1.85 (m, 2H), 1.63 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 133.3, 129.7, 127.6, 85.7 (d, J = 175.5 Hz), 49.6 (d, J = 27 Hz), 45.7, 29.2 (d, J = 20.1 Hz), 21.5, 21.1 (d, J = 6.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -182.72 (m). HRMS: m/z (ESI) calculated $[M+H]^+$: 258. 0959, measured: 258.0962.



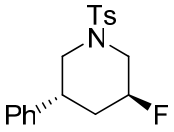
4e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.36-7.12 (m, 10H), 4.55 (dm, J = 47.2 Hz, 1H), 4.50 (d, J = 12.4 Hz, 1H), 4.03 (m, 1H), 2.96 (m, 1H), 2.42 (s, 3H), 2.40 (d, J = 13.2 Hz, 1H), 2.29 (dt, J = 10.0, 5.6 Hz, 1H), 2.15 (q, J = 11.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 144.1, 143.1, 132.1, 129.9, 128.7, 128.6, 127.8, 127.7, 126.9, 126.5, 126.4, 85.6 (d, J = 172.4 Hz), 53.8, 49.8 (d, J = 30.7 Hz), 46.4 (d, J = 10.8 Hz), 41.1 (d, J = 19.0 Hz), 21.5. ^{19}FNMR (376 MHz,$CDCl_3$) δ -185.52 (d, J = 47.0 Hz). HRMS: m/z (ESI) calculated $[M+Na]^+$: 432.1404, measured: 432.1418.



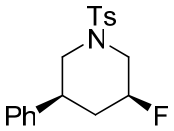
trans-**4f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 4.77 (br d, J = 47.2 Hz, 1H), 3.89 (dt, J = 11.6, 3.2 Hz, 1H), 3.65 (d, J = 8.0 Hz, 1H), 2.58 (dd, J = 35.6, 13.2 Hz, 1H), 2.43 (s, 3H), 2.15-1.95 (m, 3H), 1.2-1.0 (m, 1H), 0.89 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 133.8, 129.6, 127.6, 85.2 (d, J = 175.5 Hz), 52.1, 49.0 (d, J = 21.5 Hz), 36.5 (d, J = 20.8 Hz), 25.4, 21.5, 18.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -183.95 (dtt, J = 51.1, 35.7, 10.9 Hz). HRMS: m/z (ESI) calculated $[M+H]^+$: 272.1115, measured: 272.1121.



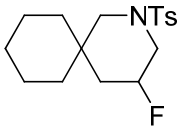
cis-**4f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.62 (dtt, *J* = 48.4, 10.0, 5.0 Hz, 1H), 4.03 (m, 1H), 3.64 (m, 1H), 2.45 (s, 3H), 2.20-2.12 (m, 2H), 1.88-1.78 (m, 2H), 1.00 (m, 1H), 0.94 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 133.1, 129.8, 127.6, 86.9 (d, *J* = 174.5 Hz), 52.2 (d, *J* = 1.5 Hz), 49.4 (d, *J* = 31.1 Hz), 38.8 (d, *J* = 17.4 Hz), 29.1 (d, *J* = 10.6 Hz), 21.5, 18.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -180.8 (br d, *J* = 46.2 Hz). HRMS: m/z (ESI) calculated $[M+H]^+$: 272.1115, measured: 272.1125.



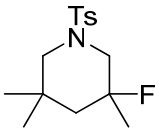
trans-**4g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.35-7.25 (m, 5H), 7.16 (d, *J* = 7.2 Hz, 2H), 4.90 (br d, *J* = 46.8 Hz, 1H), 4.13 (m, 1H), 3.92 (m, 1H), 3.25 (m, 1H), 2.62 (dd, *J* = 37.6, 13.2 Hz, 1H), 2.43 (s, 3H), 2.42 (m, 1H), 2.24 (m, 1H), 1.70 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 141.2, 133.8, 129.7, 128.8, 127.6, 127.3, 127.1, 85.0 (d, *J* = 166.9 Hz), 51.6, 48.9 (d, *J* = 21.5 Hz), 36.1, 35.0 (d, *J* = 21.6 Hz), 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -184.50 (ddt, *J* = 47.0, 35.6, 10.9 Hz). HRMS: m/z (ESI) calculated $[M+H]^+$: 334.1272, measured: 334.1274.



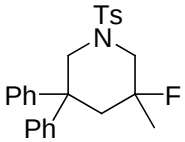
cis-**4g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.36-7.25 (m, 5H), 7.17 (d, *J* = 6.4 Hz, 2H), 4.78 (dm, *J* = 48.4 Hz, 1H), 4.20 (m, 1H), 3.87 (m, 1H), 2.96 (m, 1H), 2.44 (s, 3H), 2.40 (m, 1H), 2.25 (dt, *J* = 10.4, 4.0 Hz, 1H), 2.15 (t, *J* = 10.4 Hz, 1H), 1.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 140.1, 133.19, 129.9, 128.8, 127.6, 127.5, 127.1, 86.9 (d, *J* = 175.5 Hz), 52.0, 49.5 (d, *J* = 31.5 Hz), 40.1 (d, *J* = 10.4 Hz), 37.0 (d, *J* = 18.6 Hz), 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -181.2 (br d, *J* = 47.4 Hz). HRMS: m/z (ESI) calculated $[M+H]^+$: 334.1272, measured: 334.1275.



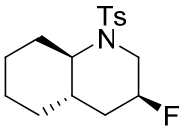
4h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.77 (dm, *J* = 47.6 Hz, 1H), 3.61 (ddd, *J* = 13.6, 11.2, 3.6 Hz, 1H), 3.19 (d, *J* = 12.0 Hz, 1H), 2.66 (dt, *J* = 11.2, 7.6 Hz, 1H), 2.44 (s, 3H), 2.42 (d, *J* = 12.0 Hz, 1H), 1.81 (ddd, *J* = 17.6, 13.2, 4.4 Hz, 1H), 1.58-1.22 (m, 11H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6, 133.5, 129.7, 127.4, 85.4 (d, *J* = 173.3 Hz), 54.0, 50.2 (d, *J* = 28.2 Hz), 36.2, 34.5 (d, *J* = 16.7 Hz), 33.9, 26.1, 21.5, 21.4, 21.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -185.52 (d, *J* = 47.8 Hz). HRMS: m/z (ESI) calculated $[M+H]^+$: 326.1585, measured: 326.1589.



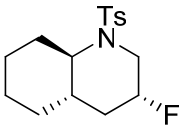
4i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 3.73 (dt, *J* = 12.8, 11.6 Hz, 1H), 3.31 (d, *J* = 11.6 Hz, 1H), 2.43 (s, 3H), 2.31 (dd, *J* = 31.6, 12.4 Hz, 1H), 2.11 (d, *J* = 11.2 Hz, 1H), 1.74 (m, 1H), 1.30 (d, *J* = 20.4 Hz, 3H), 1.22 (dd, *J* = 10, 10 Hz, 1H), 1.13 (d, *J* = 1.2 Hz, 3H), 0.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 133.9, 129.6, 127.4, 91.1 (d, *J* = 176.2 Hz), 56.5, 53.9 (d, *J* = 24.8 Hz), 46.7 (d, *J* = 20.8 Hz), 31.0, 29.0, 25.7 (d, *J* = 10.4 Hz), 25.5 (d, *J* = 8.2 Hz), 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -145.05 (m). HRMS: m/z (ESI) calculated $[M+Na]^+$: 322.1248, measured: 322.1260.



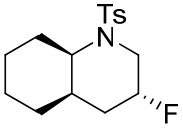
4j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 2H), 7.43-7.23 (m, 10H), 7.16 (q, *J* = 7.2 Hz, 2H), 3.65 (d, *J* = 12.4 Hz, 1H), 3.39 (d, *J* = 12.4 Hz, 1H), 3.07 (dd, *J* = 11.6, 14.4 Hz, 1H), 2.98 (t, *J* = 10.0 Hz, 1H), 2.65 (t, *J* = 13.2 Hz, 1H), 2.49 (dd, *J* = 18.0, 13.2 Hz, 1H), 2.39 (s, 3H), 1.12 (d, *J* = 22.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 145.1, 143.9, 132.3, 129.8, 128.4, 128.3, 127.7, 127.1, 126.8, 126.4, 126.2, 91.4 (d, *J* = 173.2 Hz), 54.5 (d, *J* = 28.3 Hz), 53.8, 45.6 (d, *J* = 6.7 Hz), 44.8 (d, *J* = 10.8 Hz), 25.1 (d, *J* = 23.0 Hz), 21.5 .^{19}F NMR (376 MHz, $CDCl_3$) δ -138.06 (m). HRMS: m/z (ESI) calculated $[M+Na]^+$: 446.1561, measured: 446.1572.



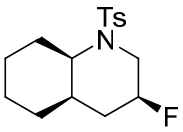
3,5-*trans*-4k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 4.75 (dm, *J* = 49.2 Hz, 1H), 4.03 (m, 1H), 3.28 (ddd, *J* = 24.4, 14.4, 3.6 Hz, 1H), 2.75 (dt, *J* = 10.8, 3.6 Hz, 1H), 2.43 (s, 3H), 2.25 (m, 1H), 1.86 (m, 1H), 1.80-1.62(m, 4H) 1.43 (m, 1H), 1.30-1.10 (m, 3H), 0.96 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 138.2, 129.6, 127.0, 85.7 (d, *J* = 174.9 Hz), 63.6, 48.5 (d, *J* = 25.3 Hz), 36.0 (d, *J* = 21.5 Hz), 35.5, 32.6, 31.4, 25.6, 25.2, 21.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -180.90 (m). HRMS: m/z (ESI) calculated $[M+Na]^+$: 334.1248, measured: 334.1261.



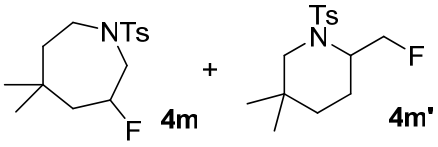
3,5-*cis*-4k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 4.68 (dm, *J* = 44.4 Hz, 1H), 4.28 (m, 1H), 2.86 (ddd, *J* = 12.4, 8.4, 6.8 Hz, 1H), 2.45 (m, 1H), 2.43 (s, 3H), 2.20 (m, 1H), 2.10 (m, 1H), 1.84-1.36 (m, 5H), 1.22-1.00 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 137.2, 129.6, 127.2, 87.3 (d, *J* = 176.0 Hz), 64.2, 51.5 (d, *J* = 29.6 Hz), 39.1 (d, *J* = 9.1 Hz), 38.1 (d, *J* = 17.5 Hz), 33.0, 31.1, 25.7, 25.1, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -175.15 (dm, *J* = 47.0 Hz). HRMS: m/z (ESI) calculated $[M+H]^+$: 312.1428, measured: 312.1430.



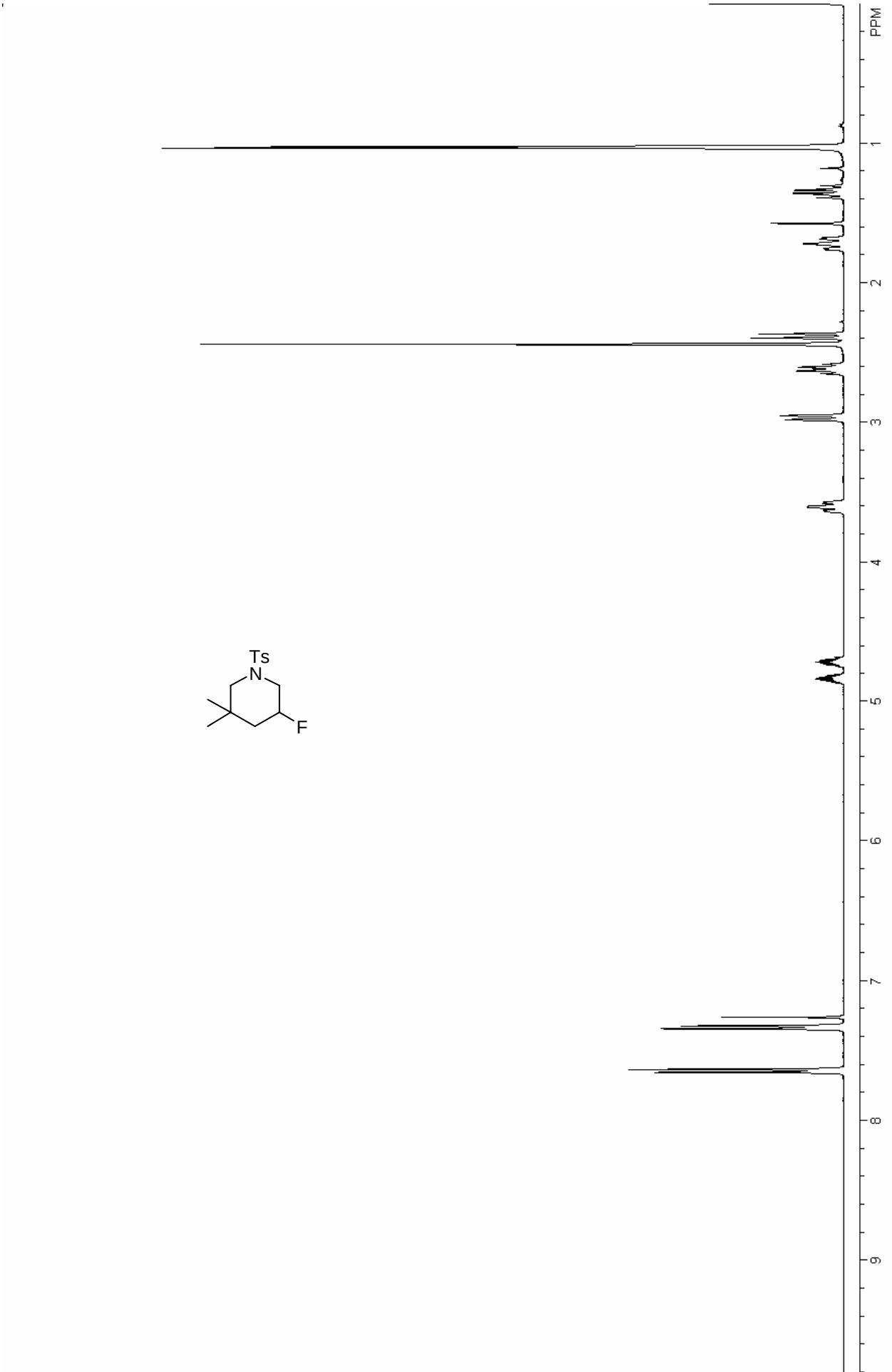
3,5-*trans*-4l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 4.75 (dm, *J* = 47.2 Hz, 1H), 4.06 (m, 1H), 3.85 (dt, *J* = 12.0, 4.8 Hz, 1H), 3.13 (dd, *J* = 42.0, 14.4 Hz, 1H), 2.41 (s, 3H), 2.05 (m, 1H), 1.98-1.20 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 138.0, 129.4, 127.3, 86.1 (d, *J* = 175.2 Hz), 54.5, 43.6 (d, *J* = 21.3 Hz), 30.1, 28.2 (d, *J* = 21.2 Hz), 27.9, 25.3, 23.7, 21.5, 19.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -182.80 (m). HRMS: m/z (ESI) calculated $[M+H]^+$: 312.1428, measured: 312.1433.



3,5-*cis*-4l: ^{1}H NMR (400 MHz, $CDCl_3$, TMS), δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 4.42 (dm, *J* = 48.4 Hz, 1H), 4.00 (dd, *J* =12.4, 5.2 Hz, 1H), 3.93 (ddd, *J* = 12.4, 8.0, 4.0 Hz, 1H), 2.85 (ddd, *J* = 14.4, 10.8, 4.4 Hz, 1H), 2.42 (s, 3H), 1.92-1.20 (m, 11H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 138.1, 129.8, 126.8, 85.5 (d, *J* = 175.50 Hz), 54.1 (d, *J* = 1.5 Hz), 43.2 (d, *J* = 31.3 Hz), 33.4 (d, *J* = 10.7 Hz), 30.7 (d, *J* = 6.0 Hz), 30.5, 25.3, 23.3, 21.5, 19.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -179.57 (d, *J* = 46.6 Hz). HRMS: m/z (ESI) calculated $[M+H]^+$: 312.1428, measured: 312.1436.



Products **4m** and **4m'** can not be separated column chromatography on silica gel. **4m**-major：^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.85 (dm, *J* = 46.8 Hz, 1H), 3.62 (ddd, *J* = 18.4, 14.4, 6.4 Hz, 1H), 3.10 (d, *J* = 14.4 Hz, 1H), 3.03 (ddd, *J* = 19.6, 14.0, 6.4 Hz, 1H), 2.72 (d, *J* = 14.4 Hz, 1H), 2.43 (s, 3H), 2.05-1.82 (m, 2H), 1.40-1.20 (m, 2H), 1.03 (s, 3H), 0.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 133.6, 129.7, 127.2, 90.8 (d, *J* = 170.6 Hz), 61.6, 54.5 (d, *J* = 31.1 Hz), 34.4, 33.7 (d, *J* = 6.8 Hz), 27.8, 27.5 (d, *J* = 20.4 Hz), 26.4, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -174.22 (m). **4m'**-minor: ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 4.40 (dm, *J* = 46.4 Hz, 1H), 4.33 (m, 1H), 4.26 (m, 1H), 3.35 (m, 1H), 3.23 (m, 1H), 2.42 (s, 3H), 1.45-1.30 (m, 2H), 1.23-1.10 (m, 2H), 0.90 (s, 3H), 0.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 135.5, 129.5, 127.0, 81.4 (d, *J* = 173.7 Hz), 52.2, 50.8 (d, *J* = 21.3 Hz), 42.0, 32.5, 30.2, 28.8, 23.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -223.52 (dt, *J* = 19.2, 48.5 Hz). HRMS: m/z (EI) calculated $[M+H]^+$: 300.1428, measured: 300.1419.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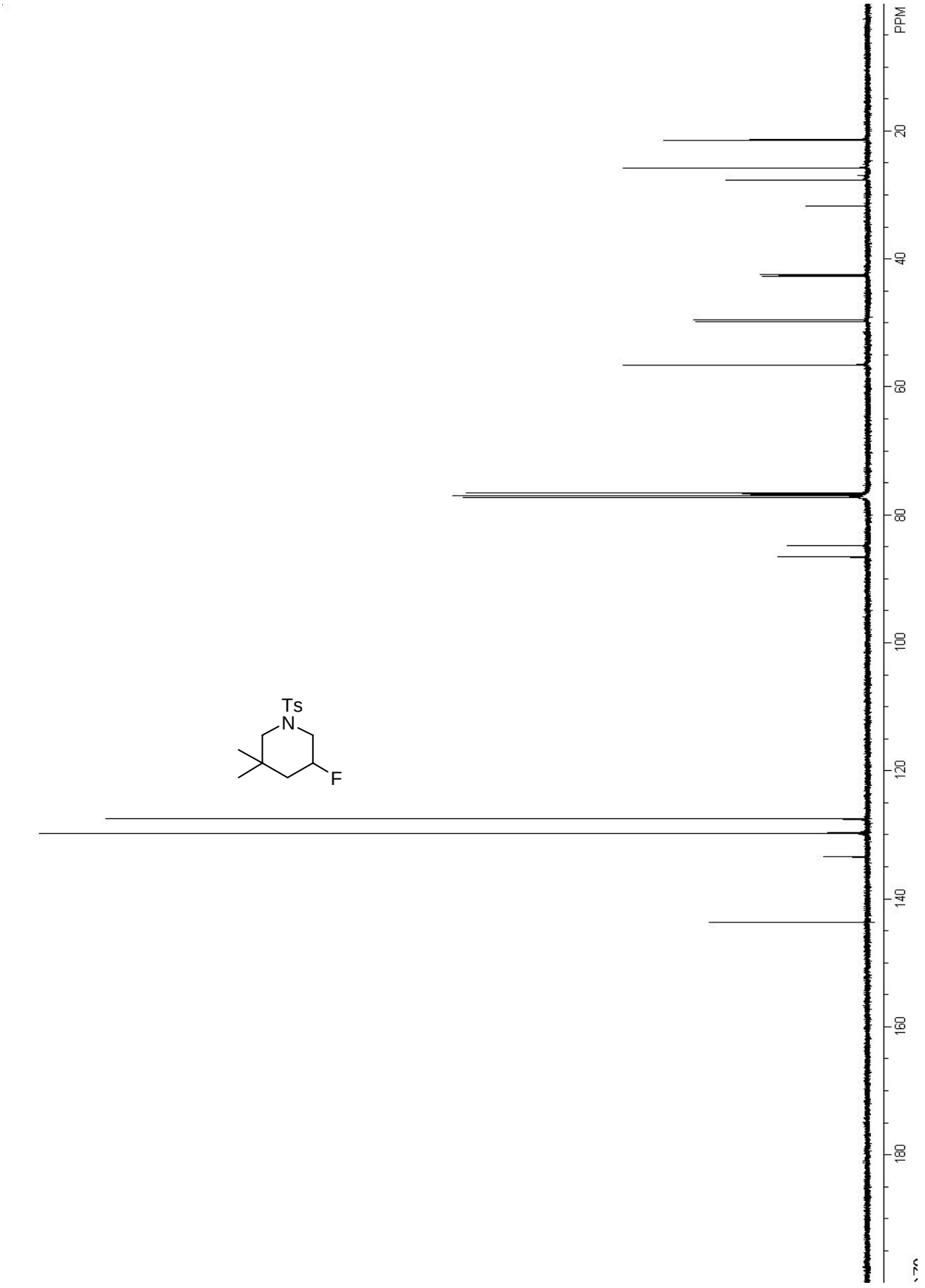
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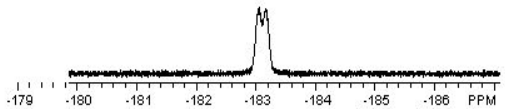
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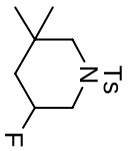
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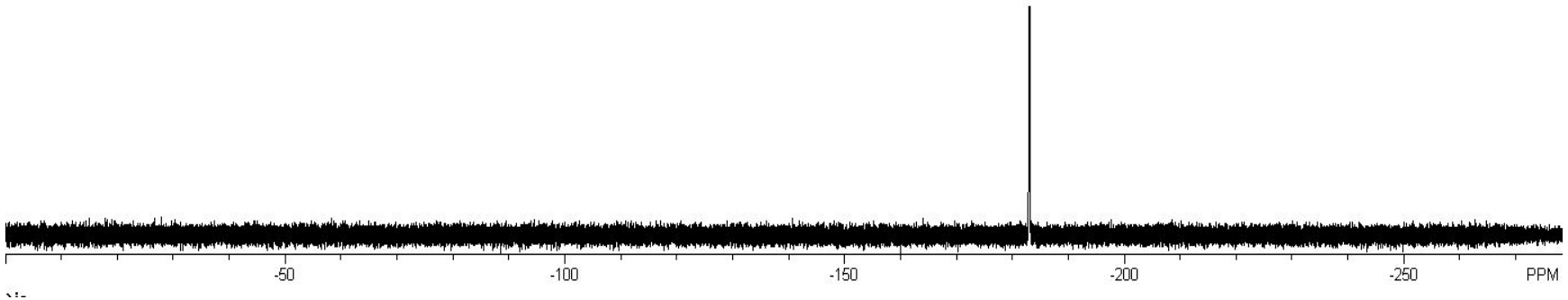
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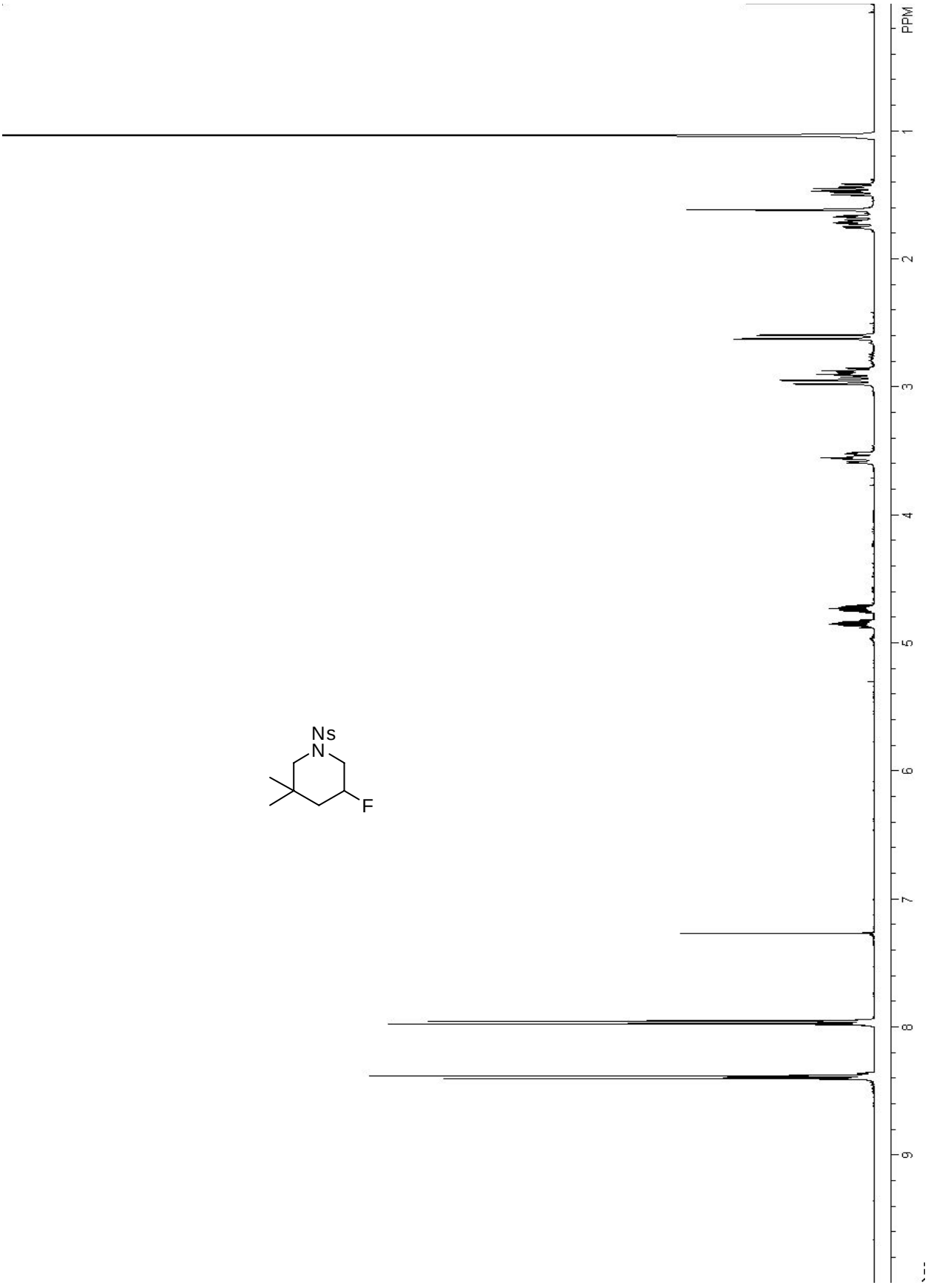
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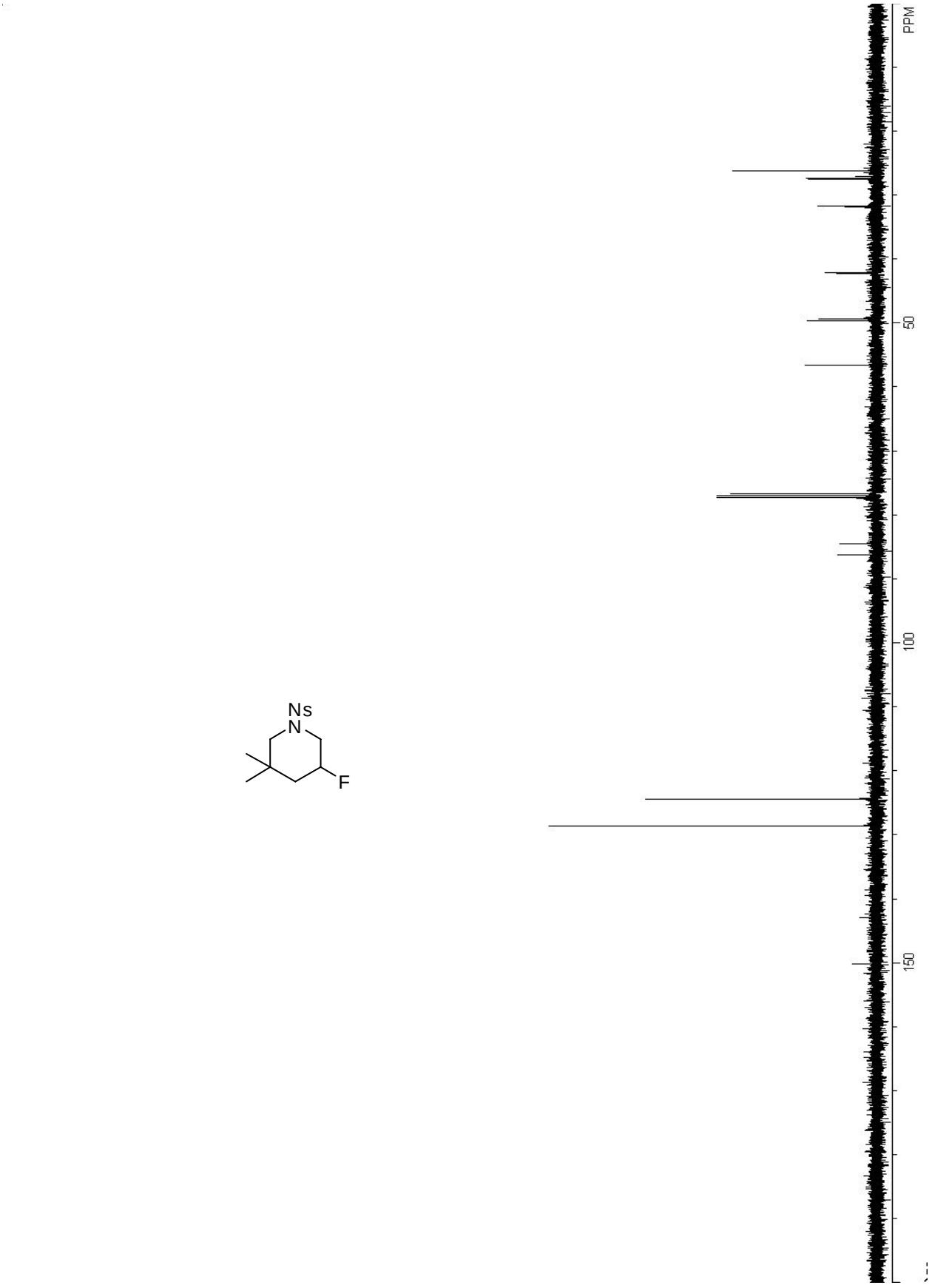
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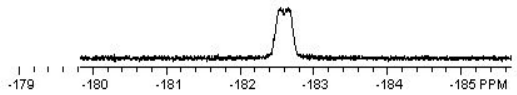
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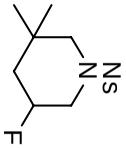
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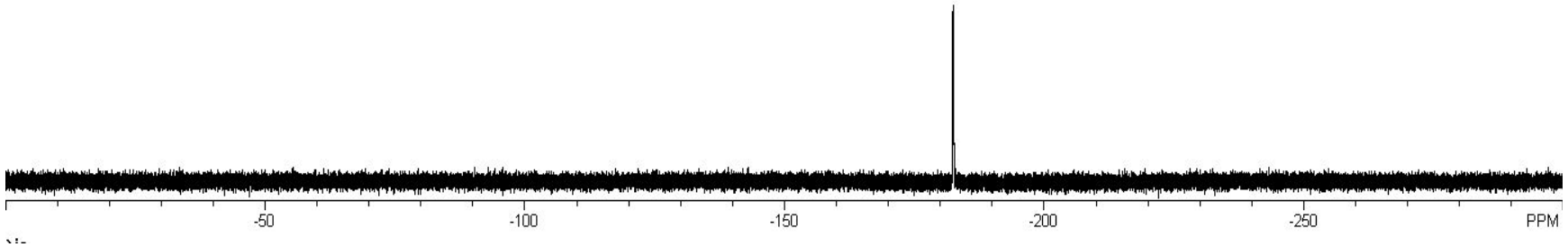
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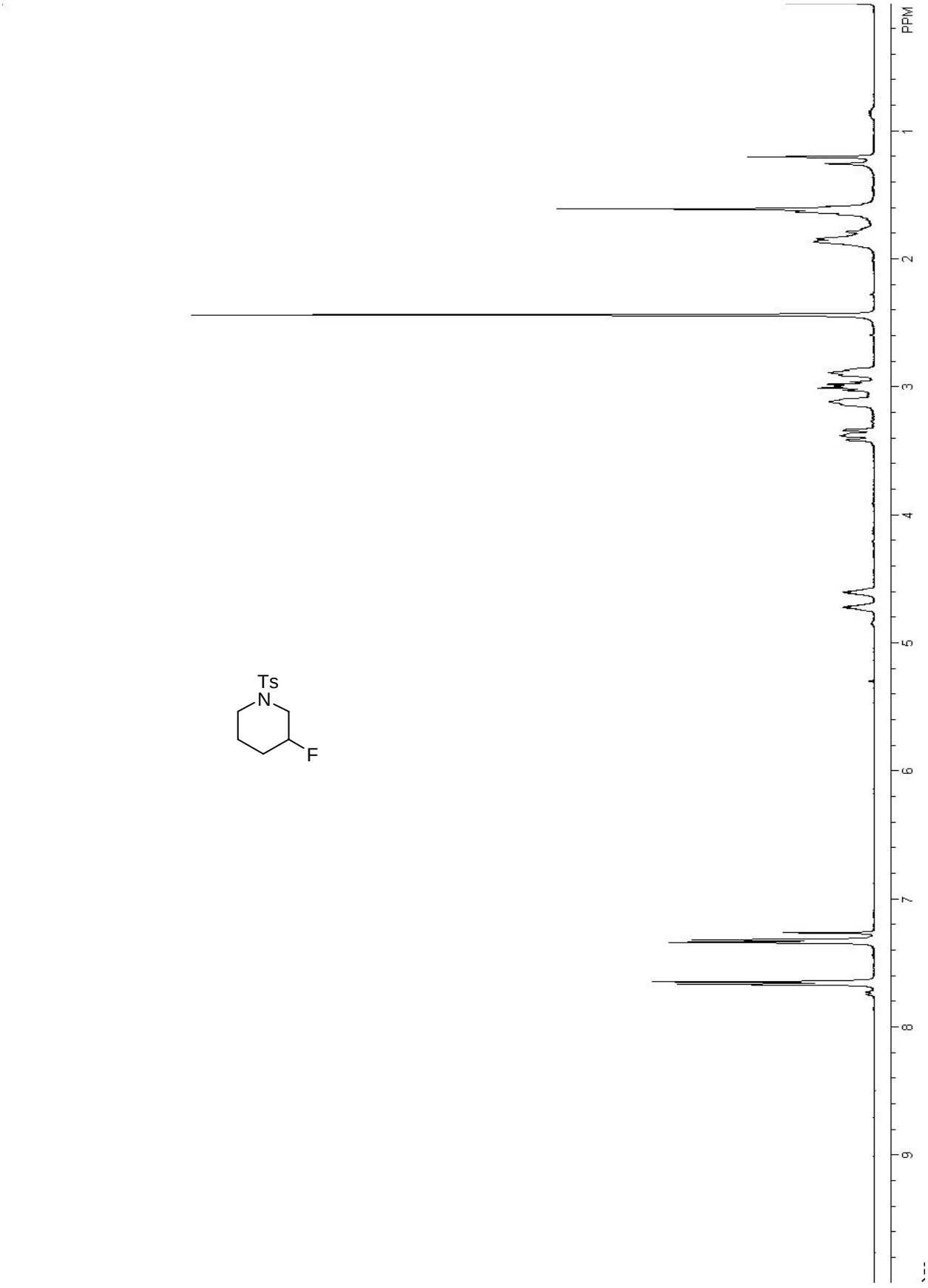
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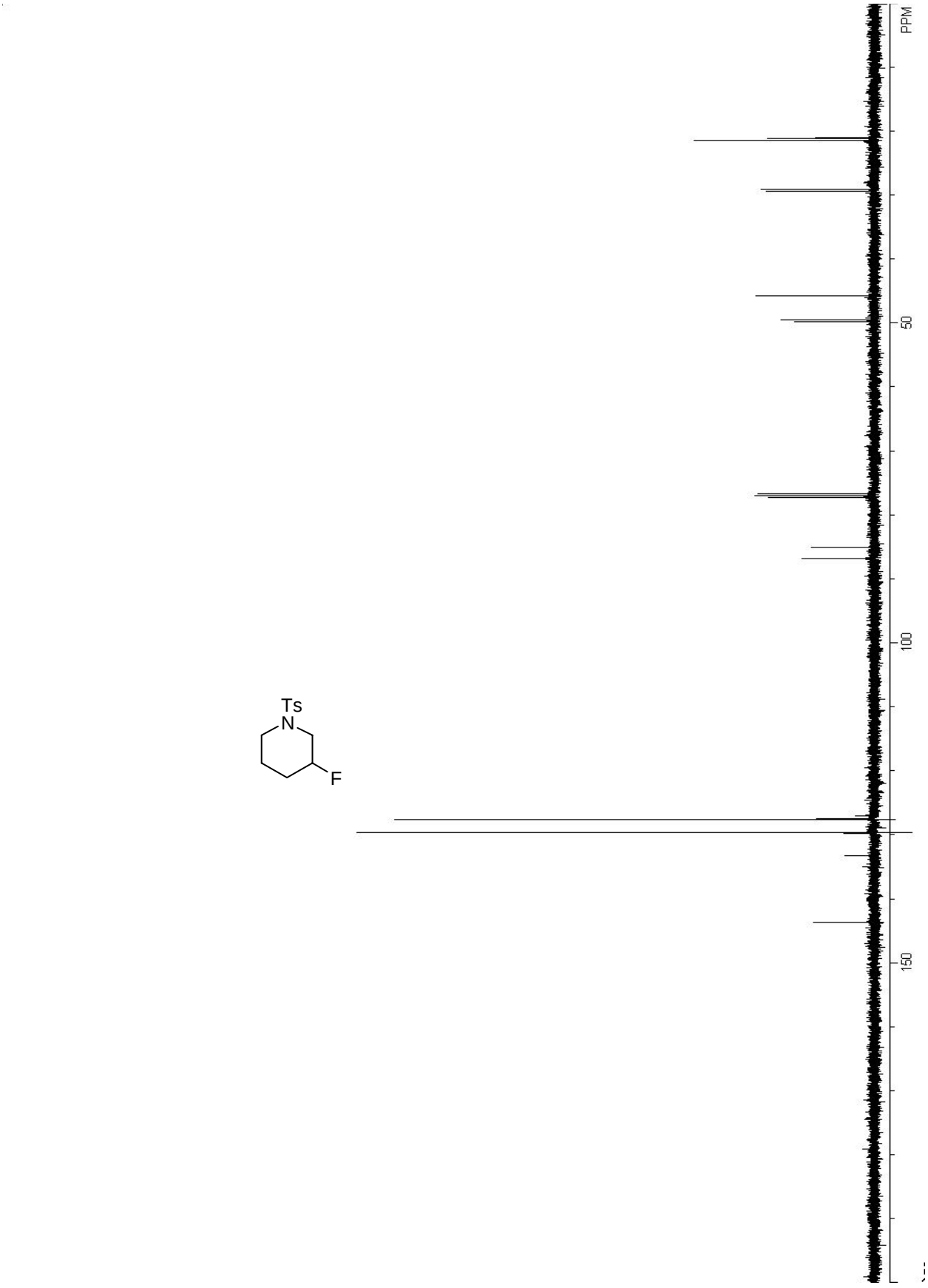
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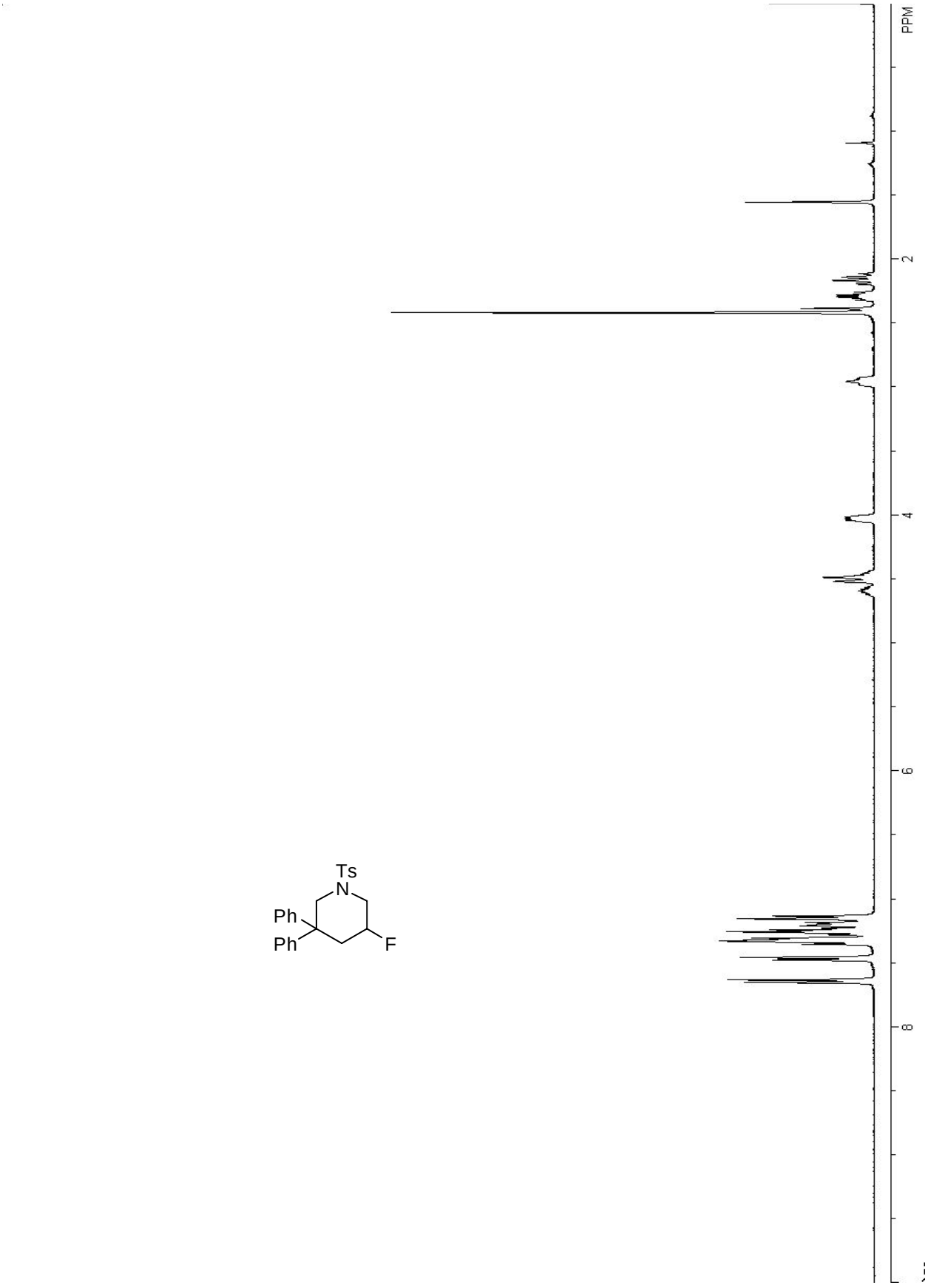
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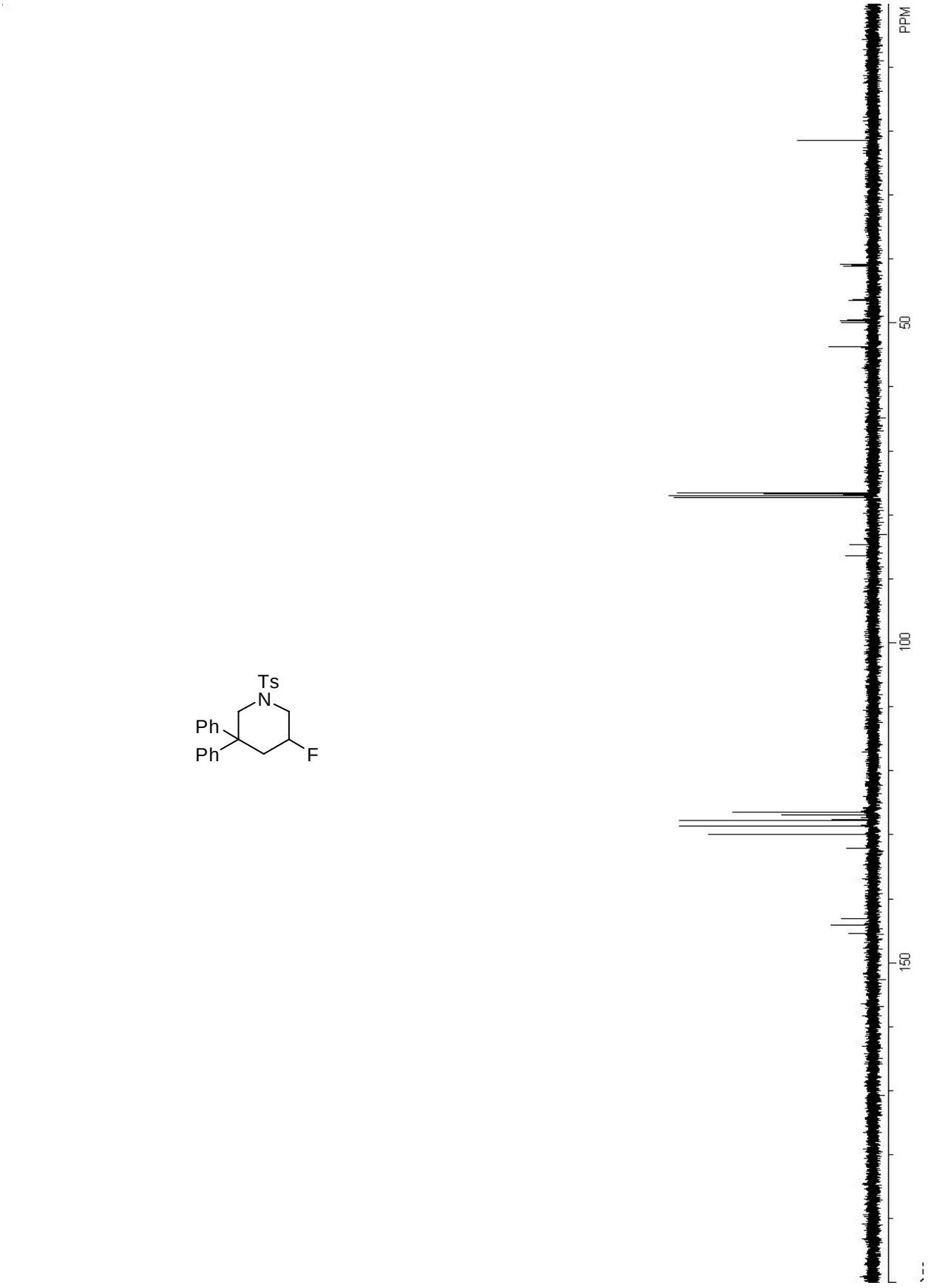
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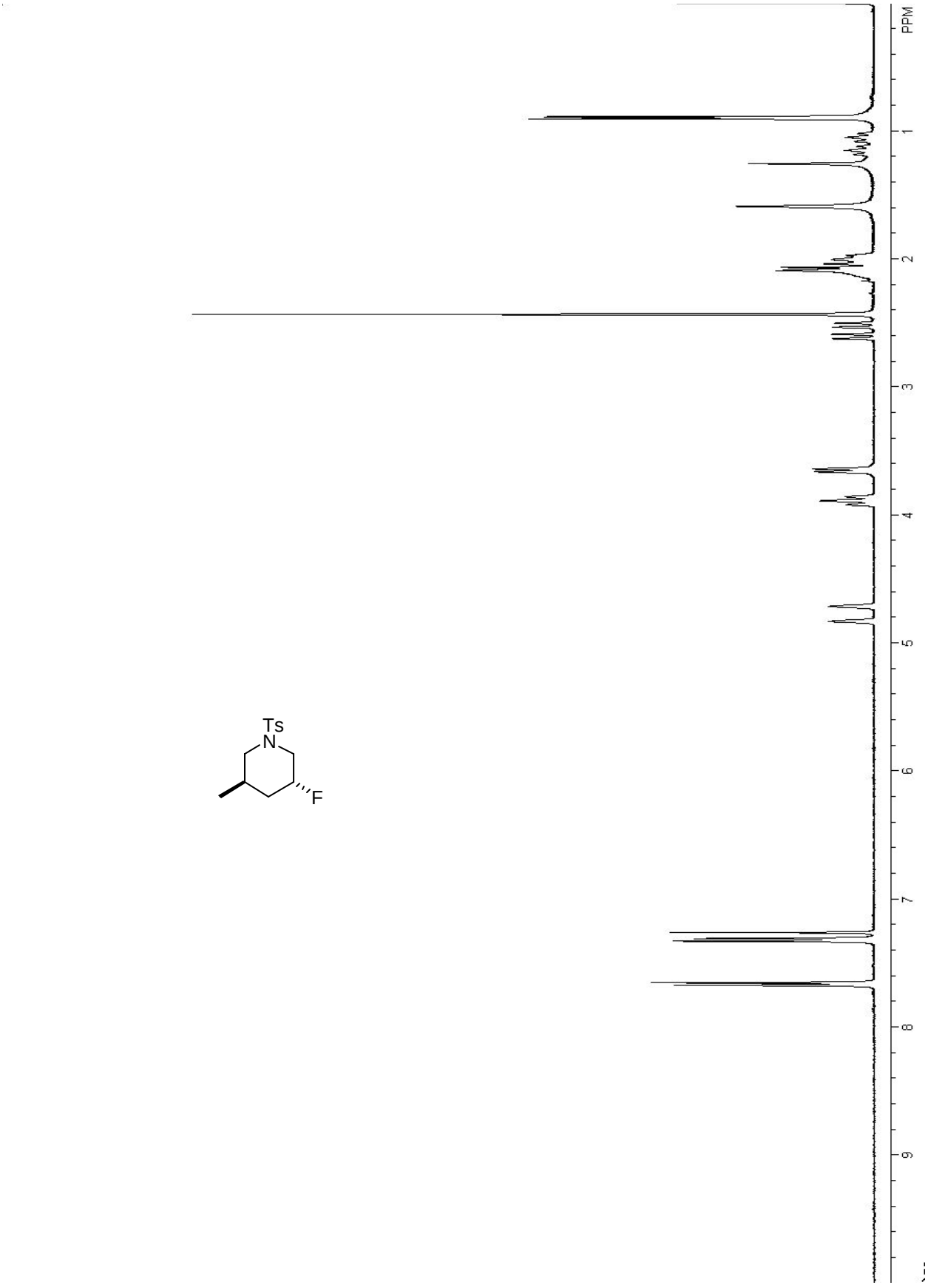
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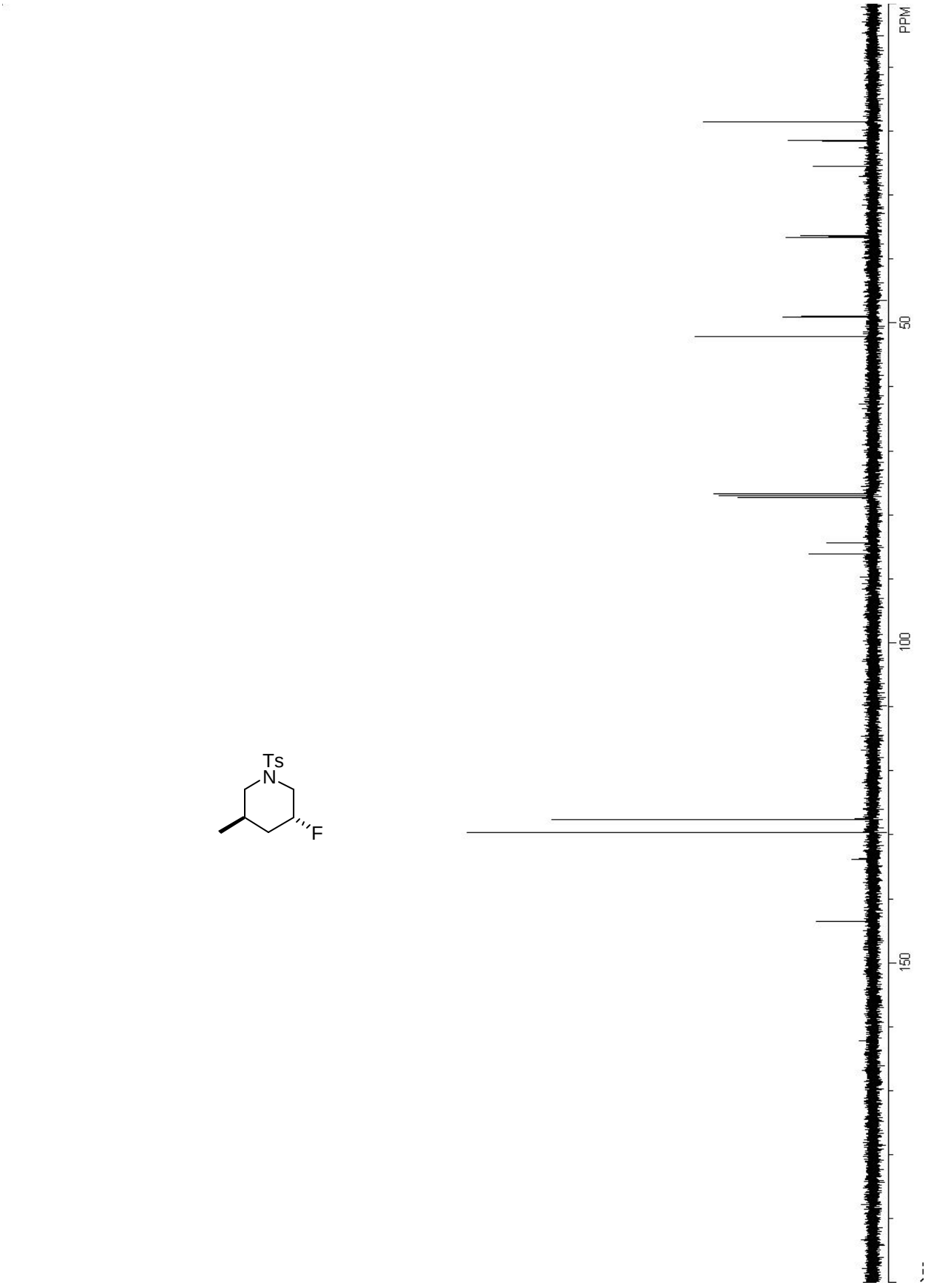
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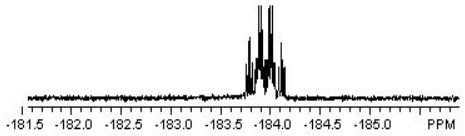
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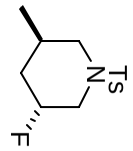
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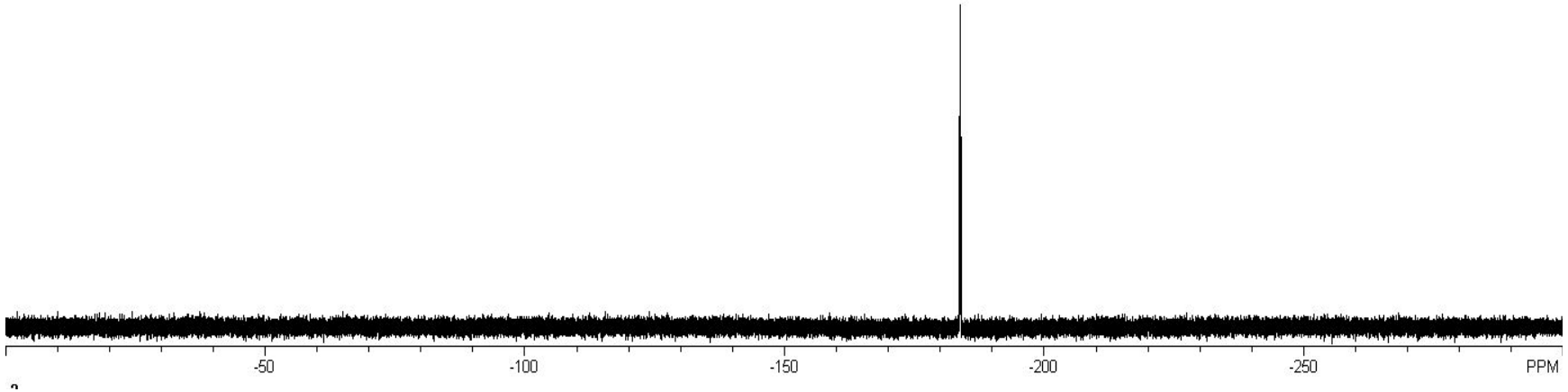
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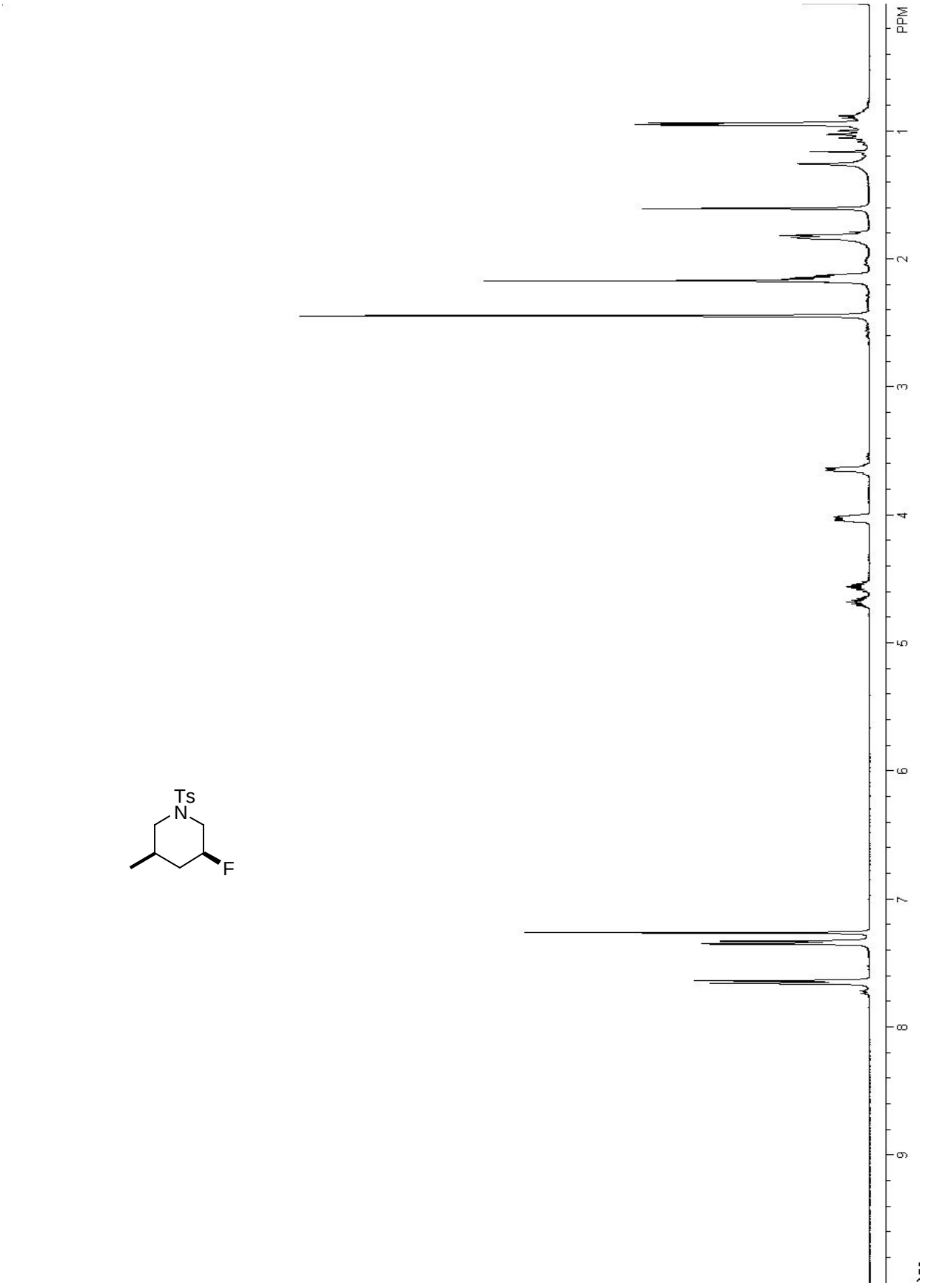
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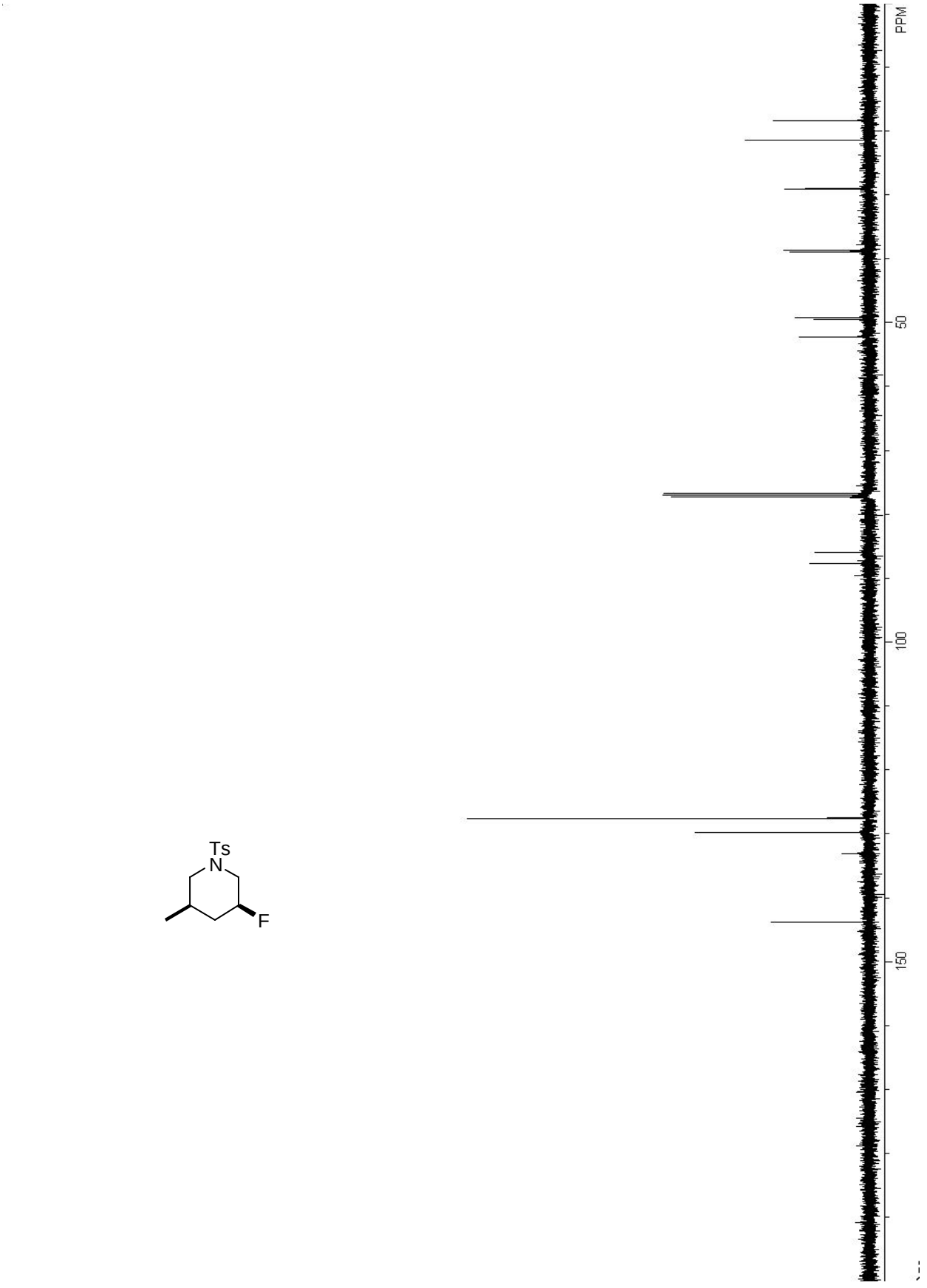
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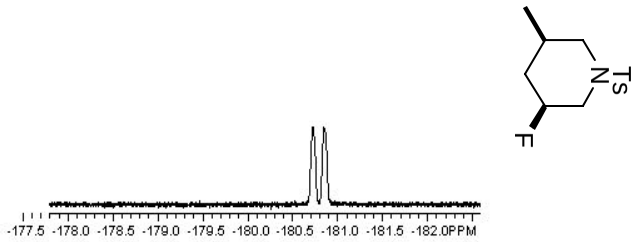
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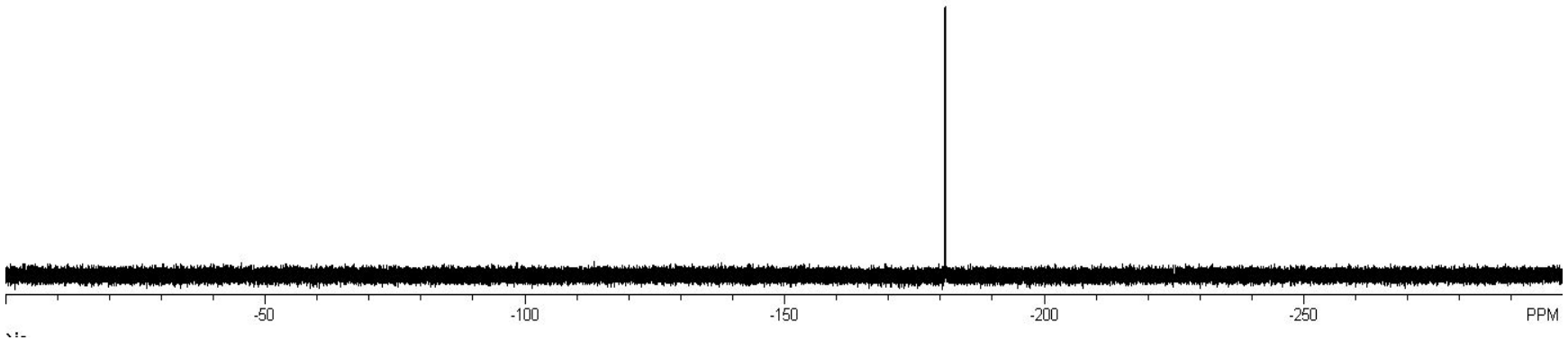
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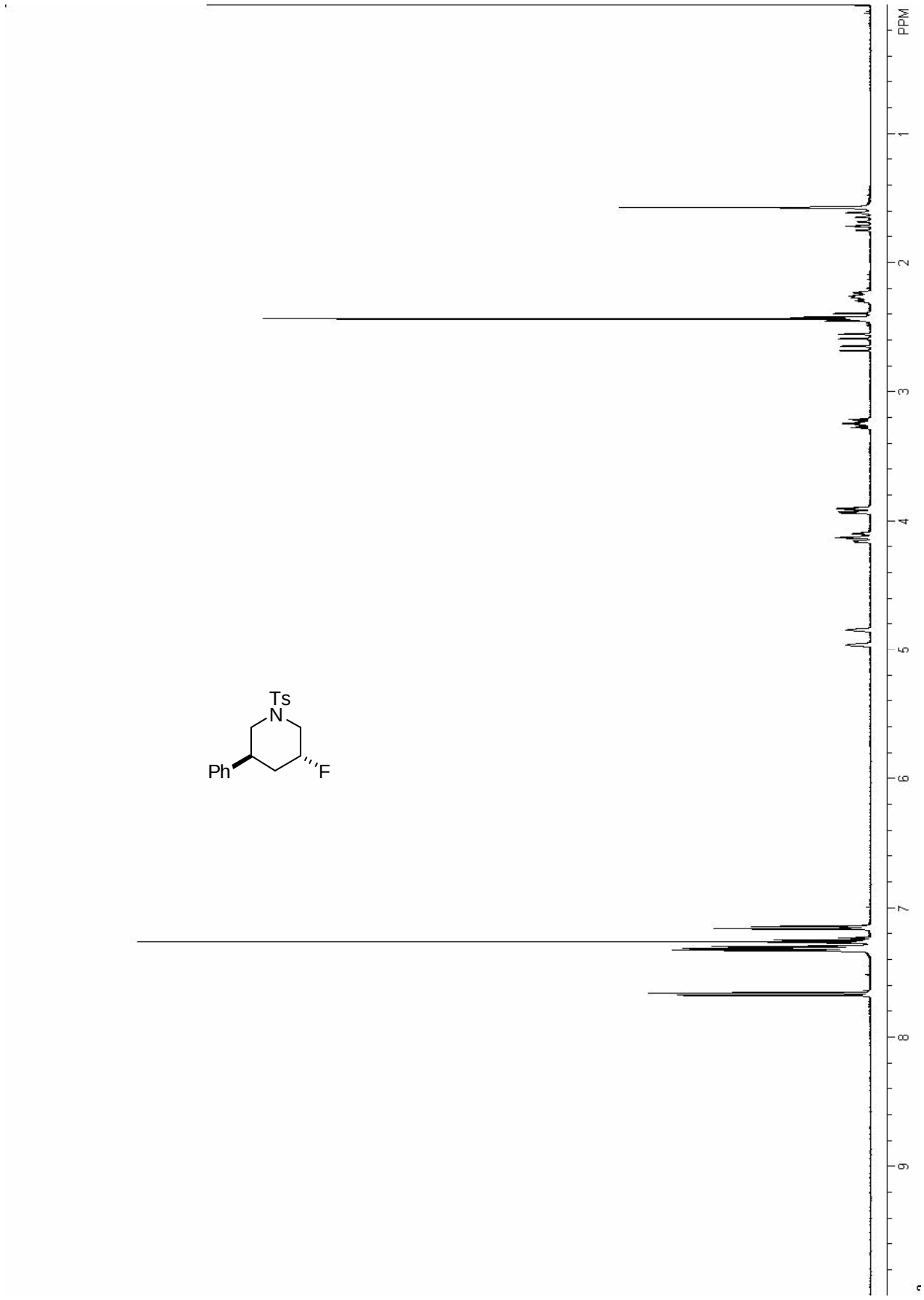
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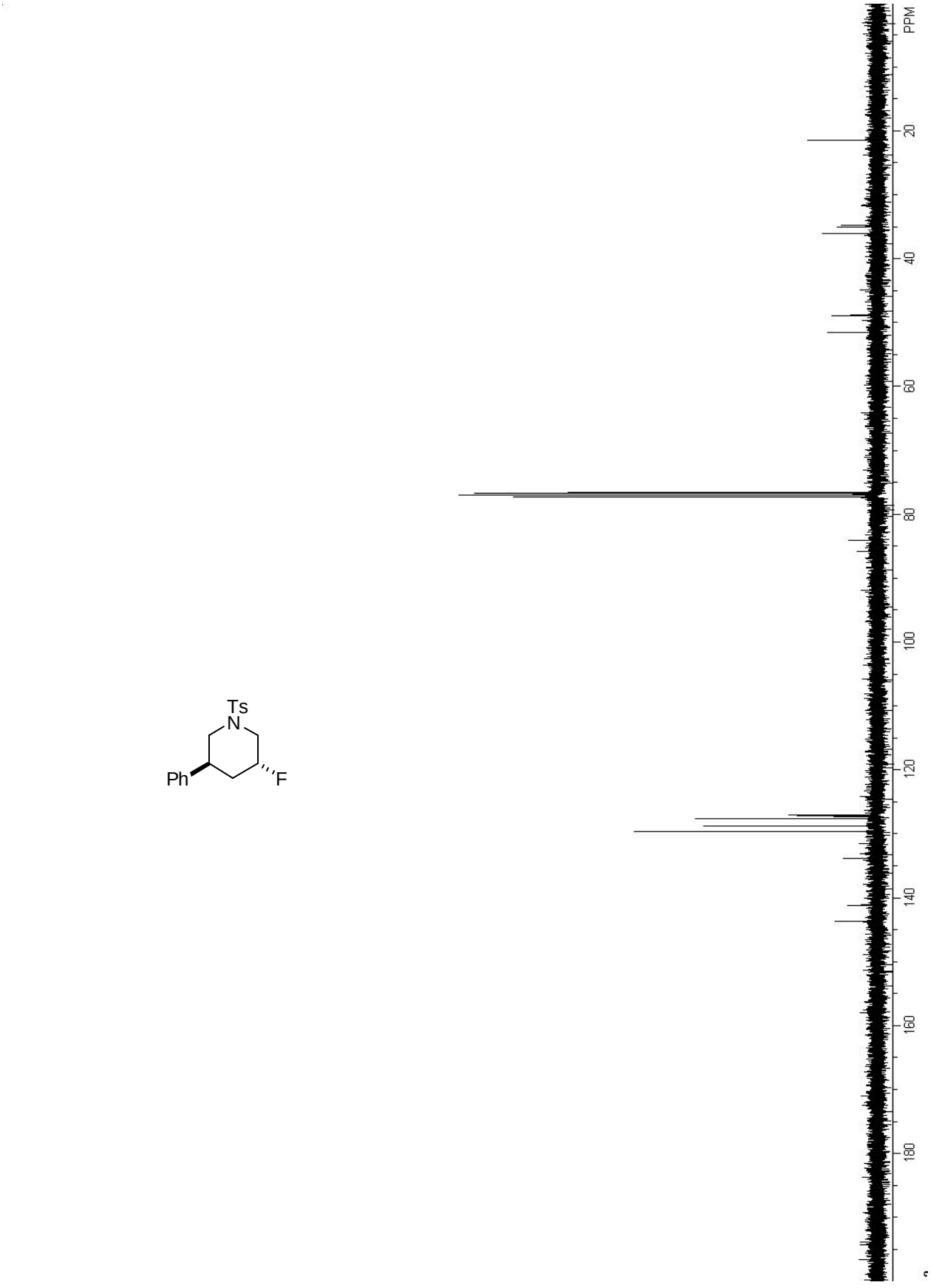
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Ph
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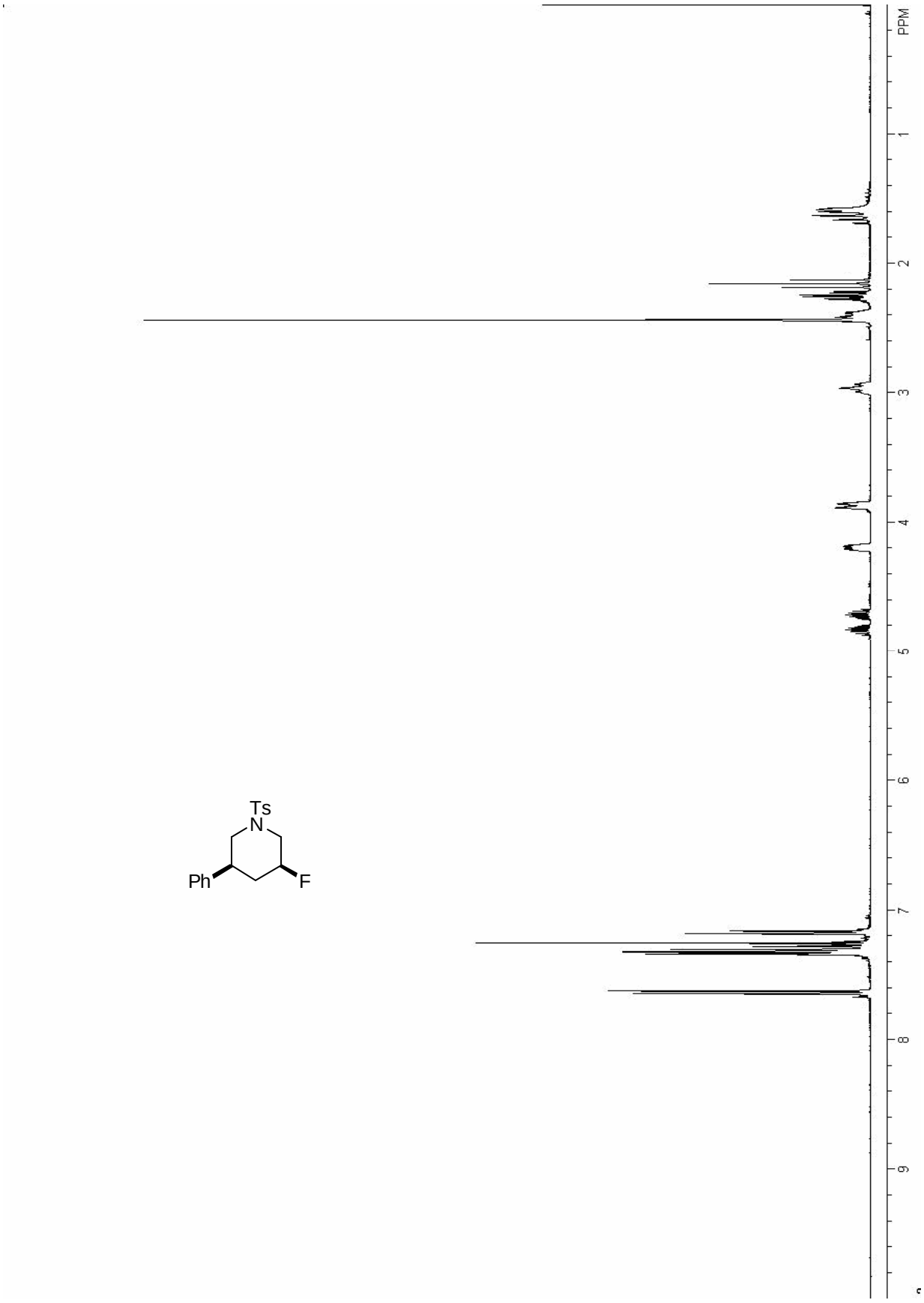
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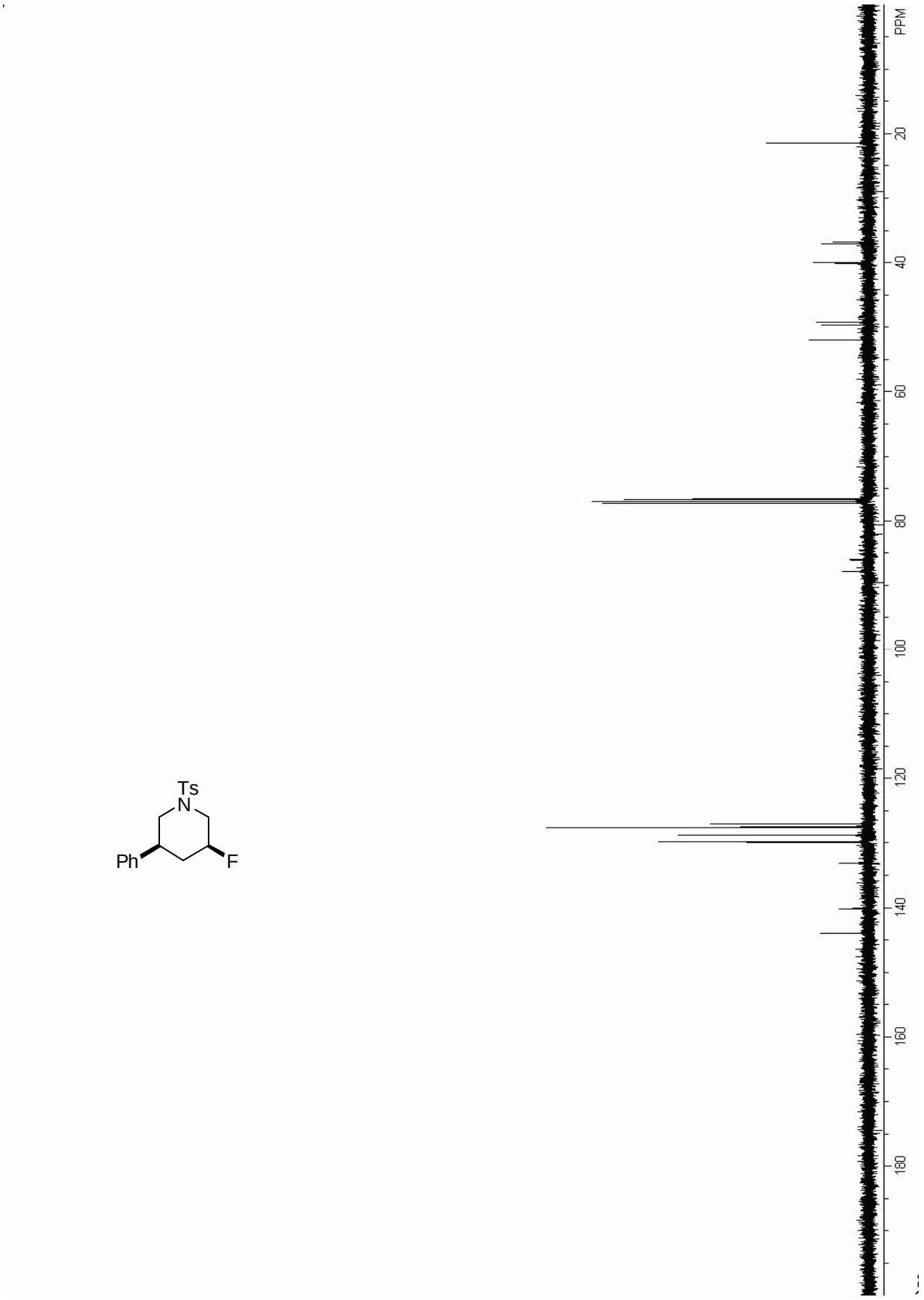
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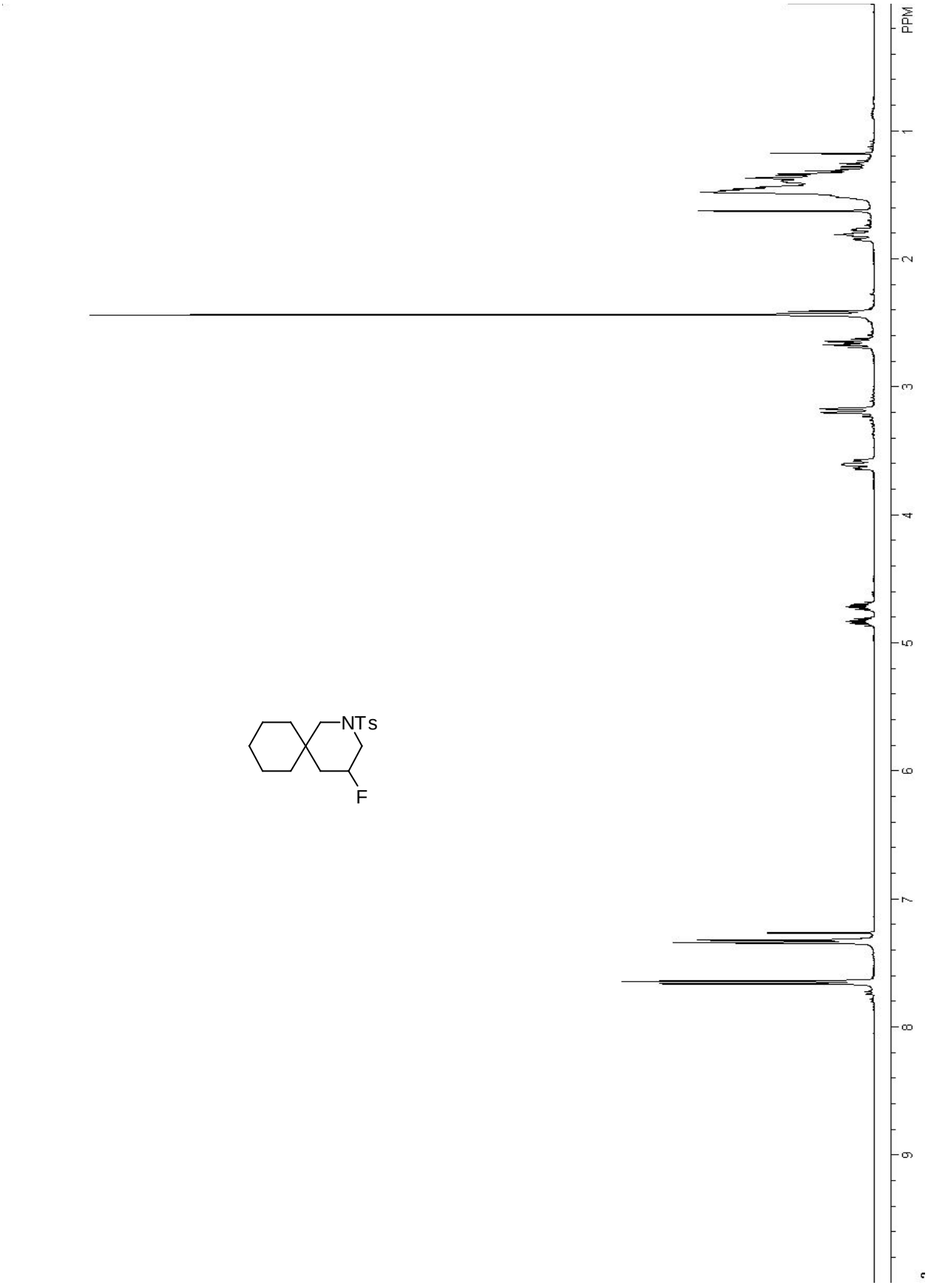
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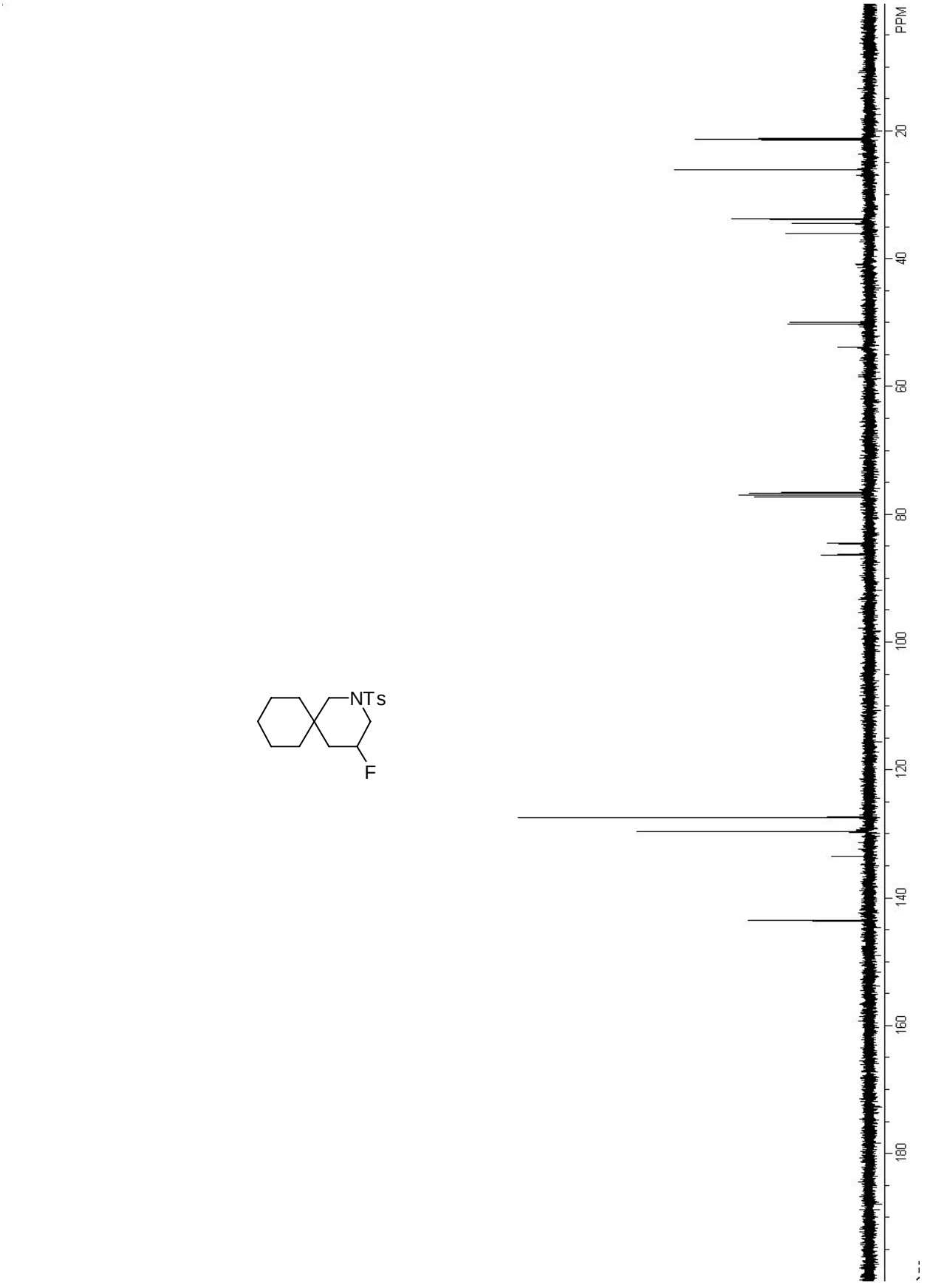
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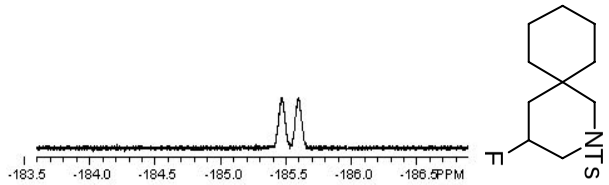
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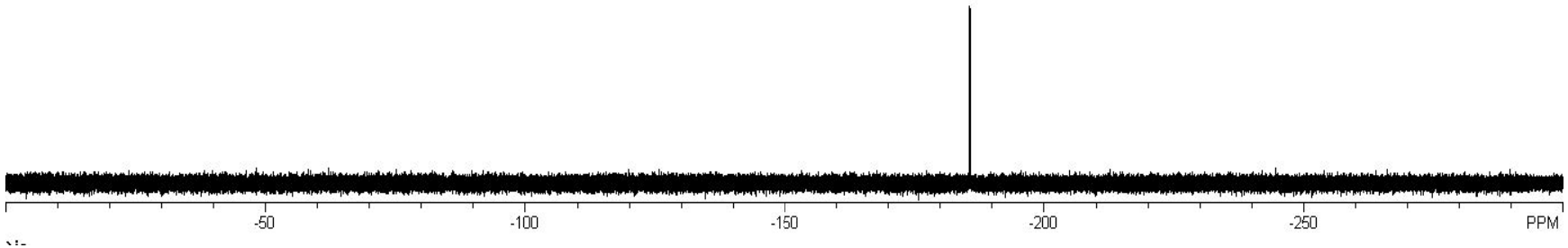
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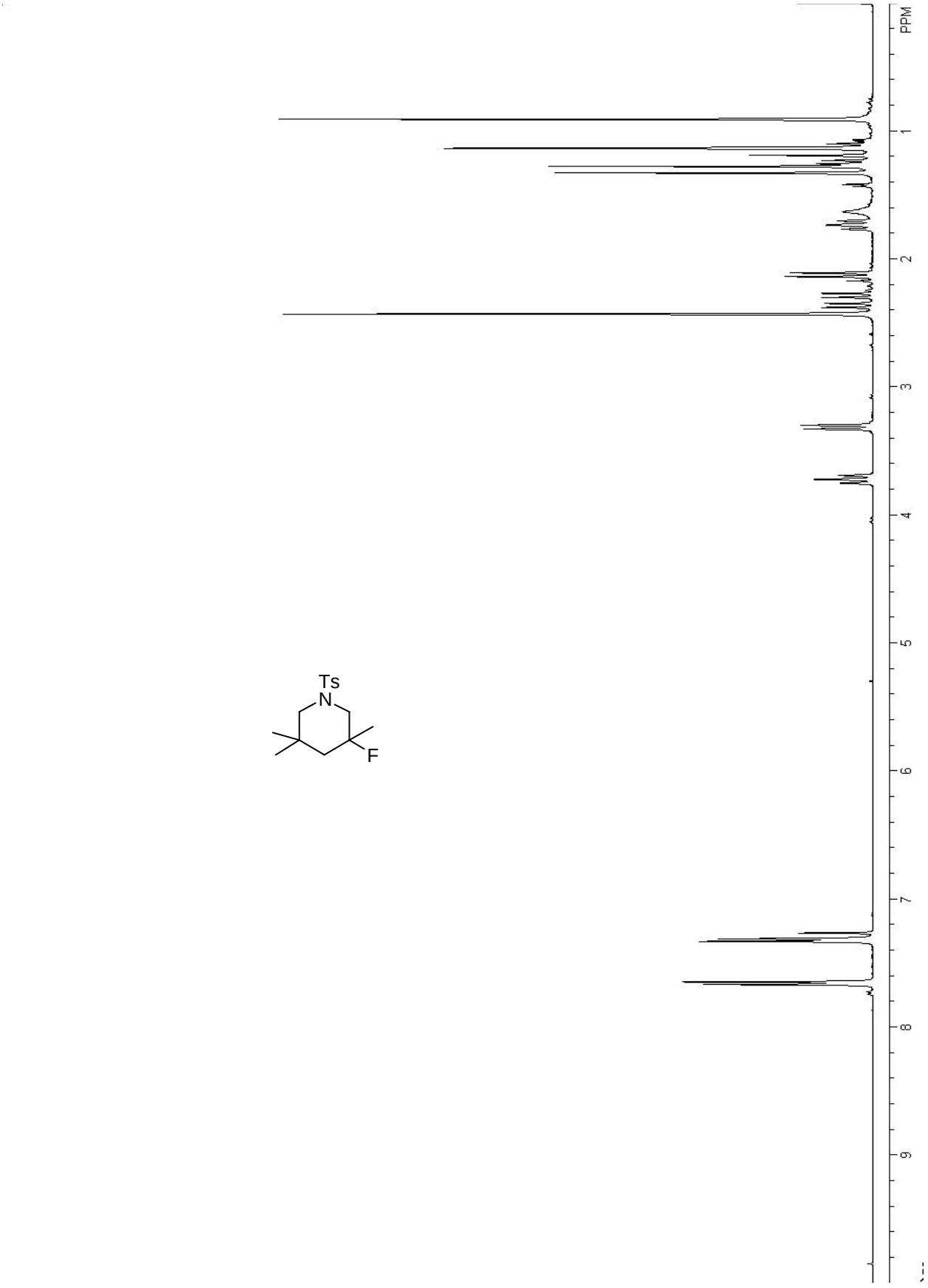
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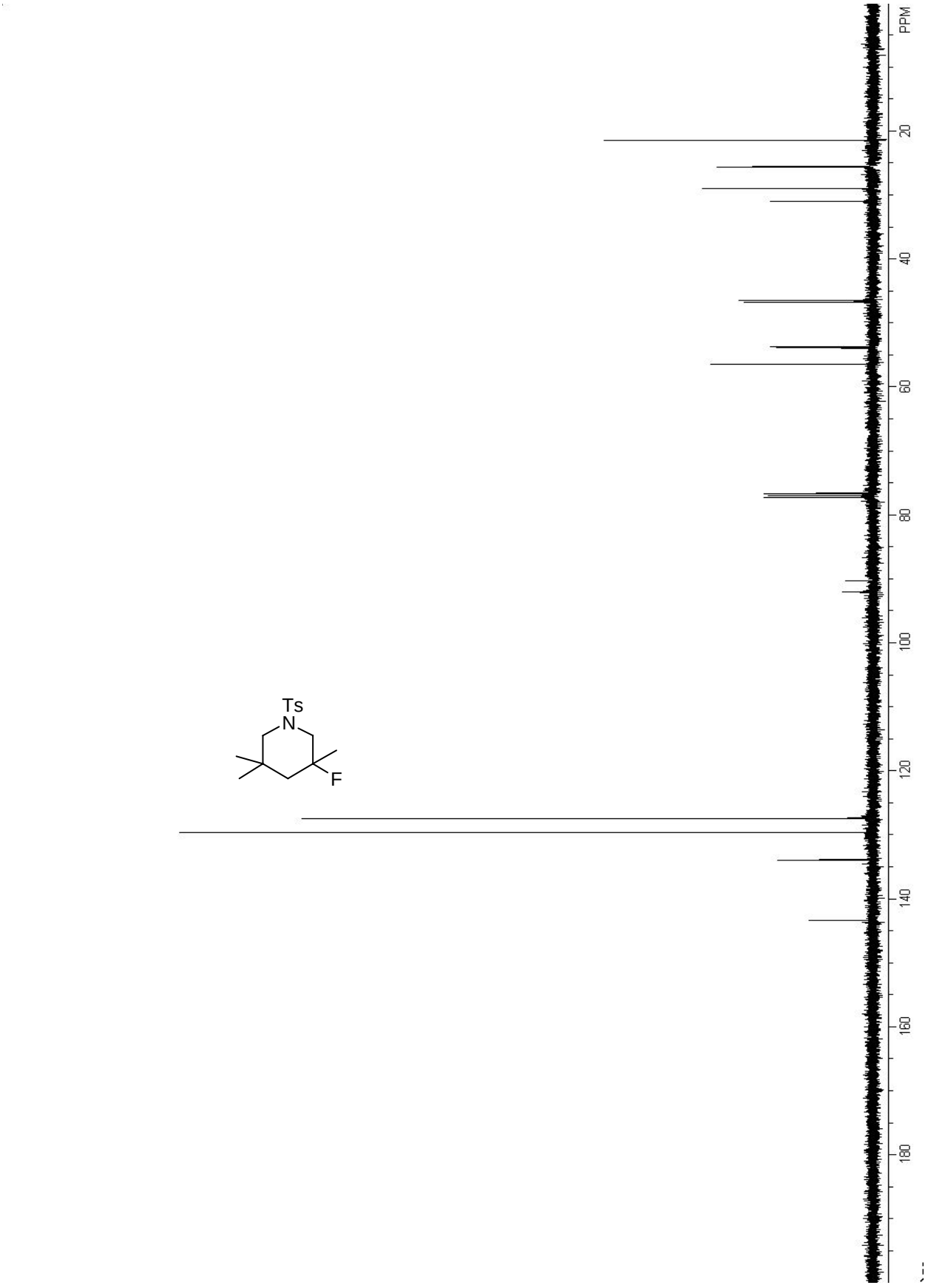
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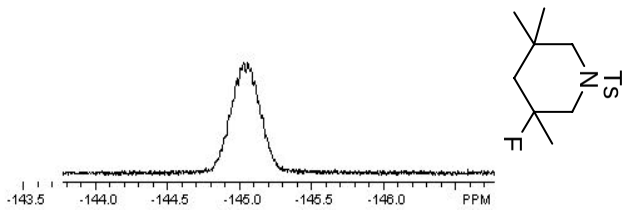
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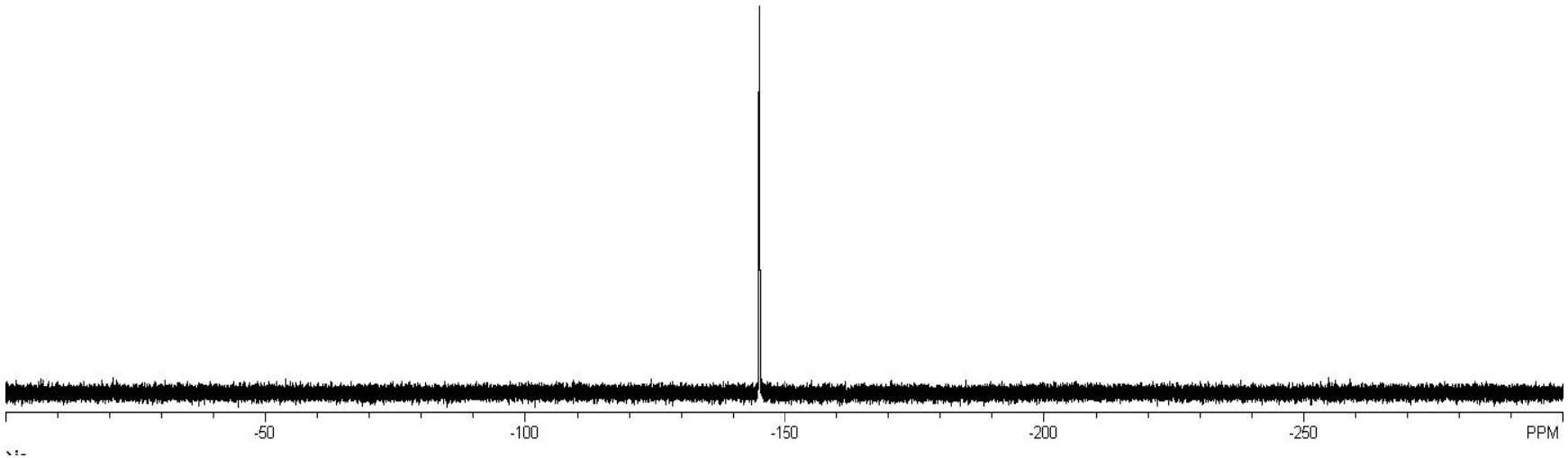
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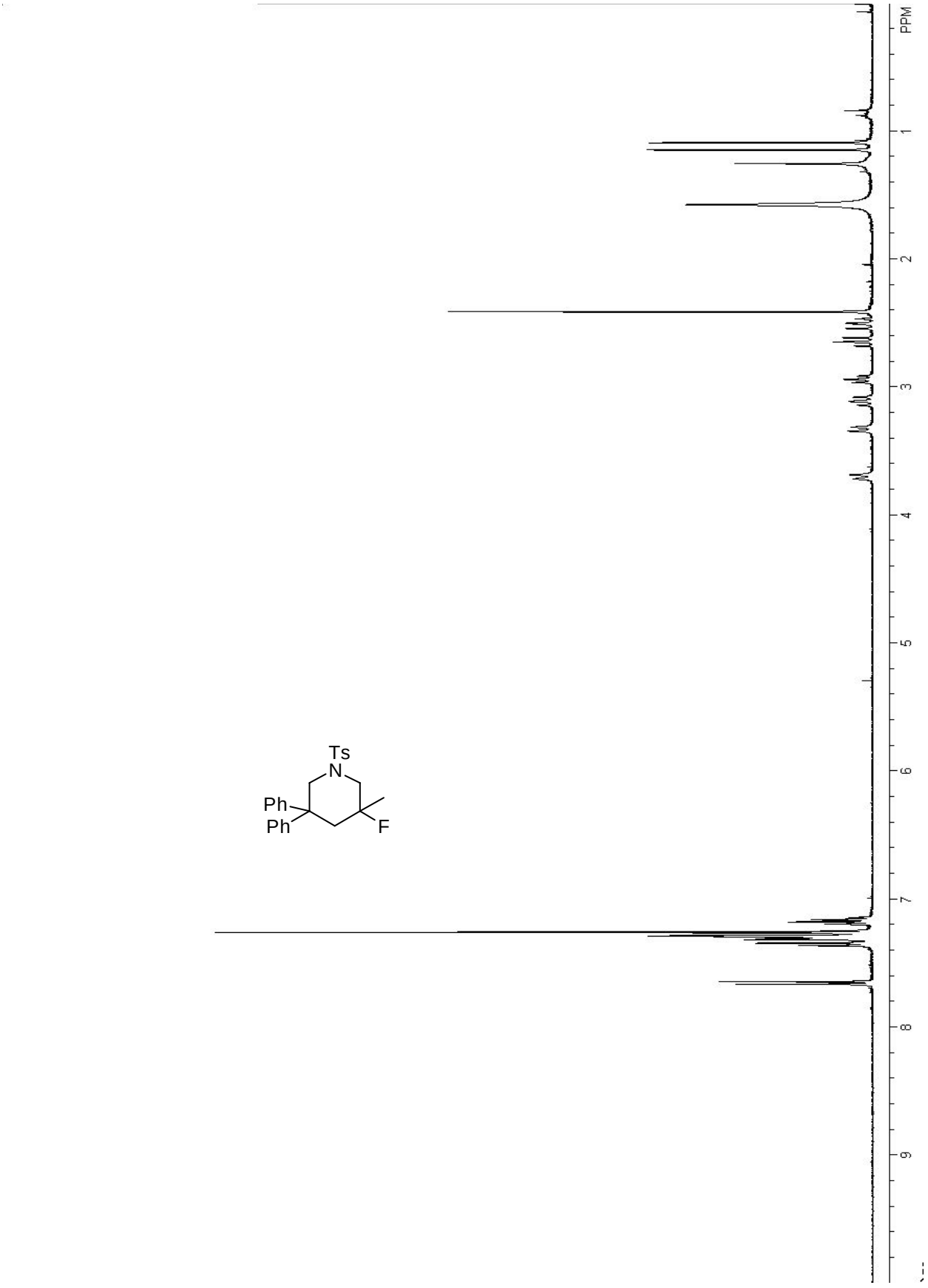
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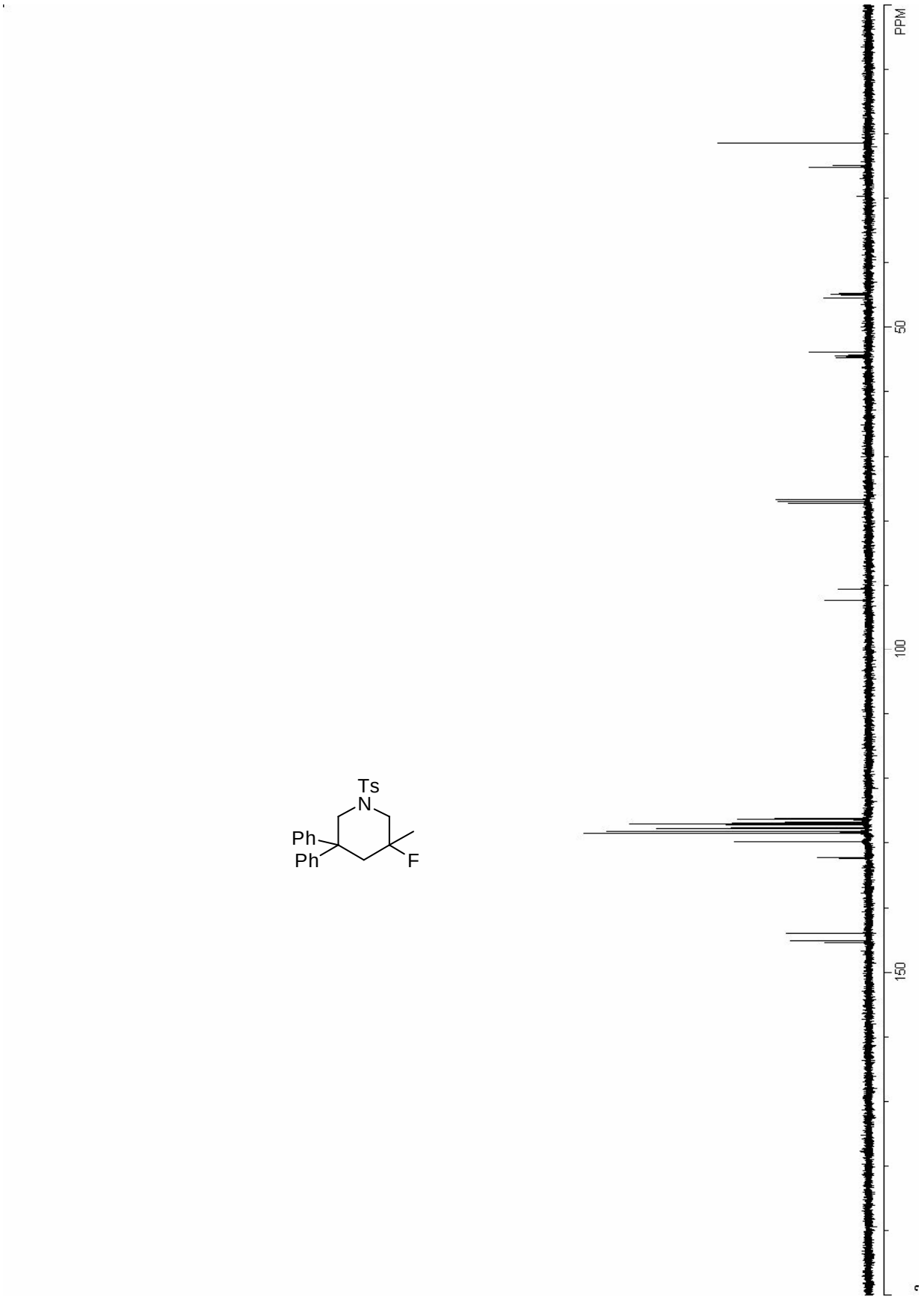
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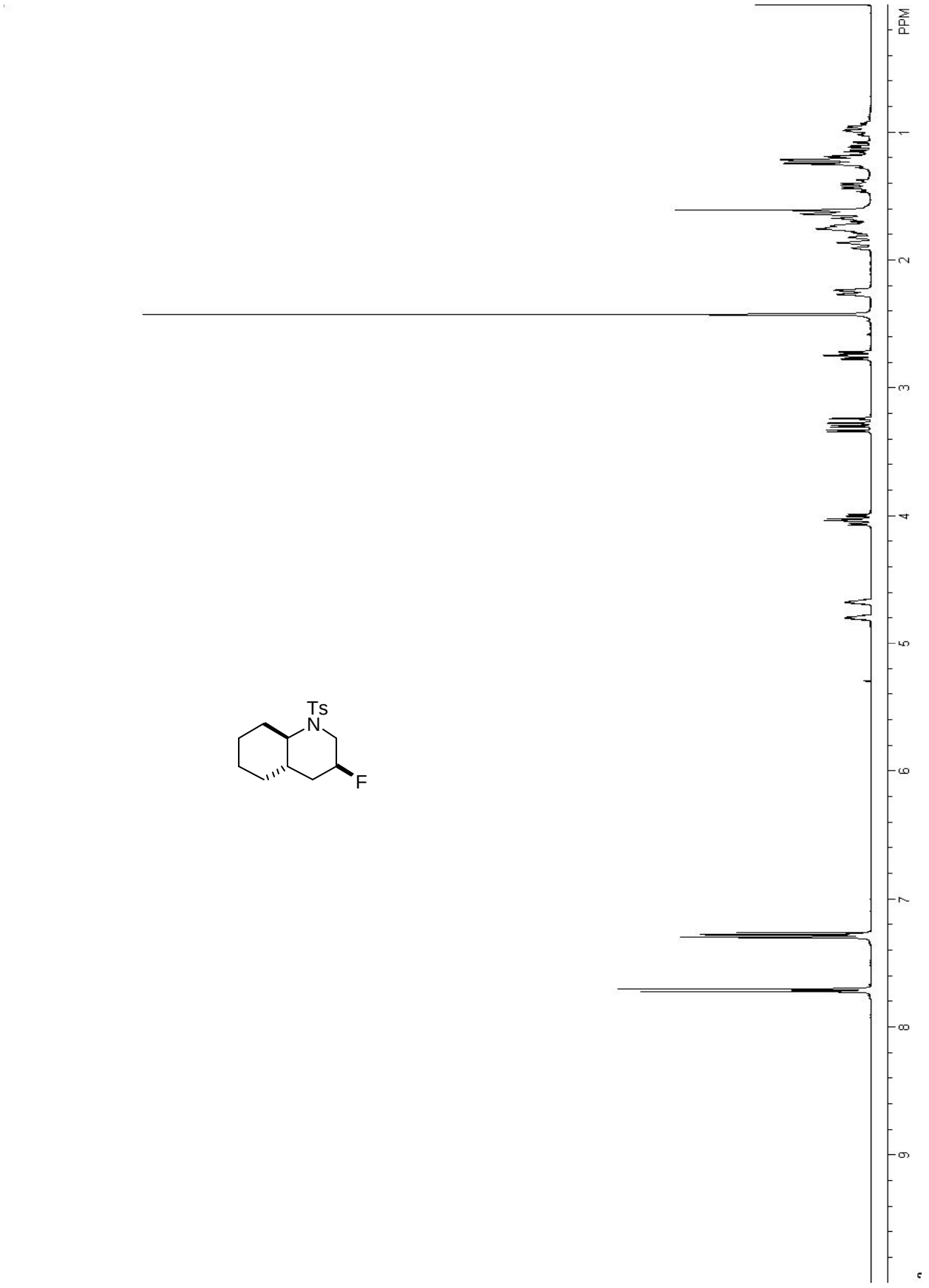
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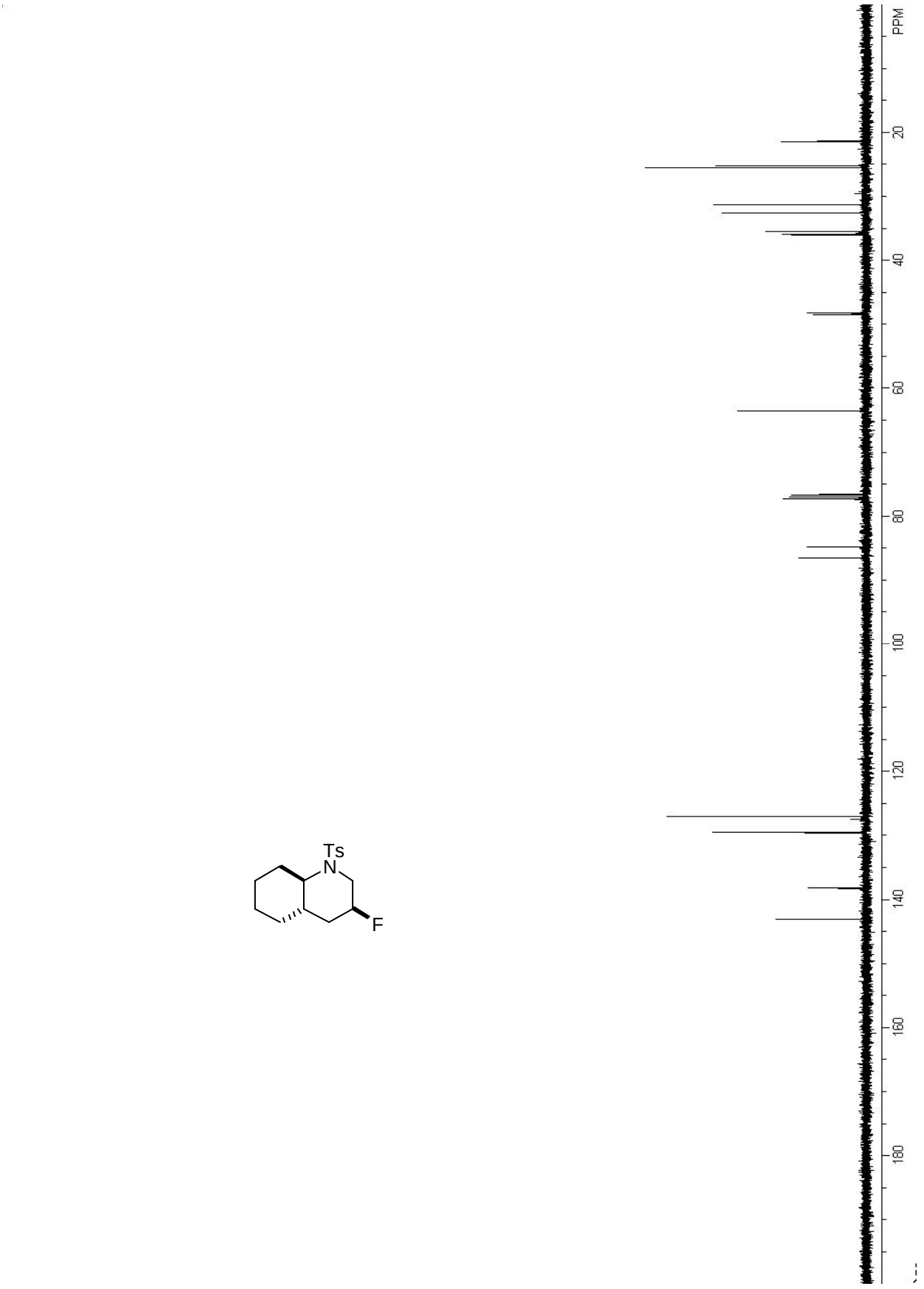
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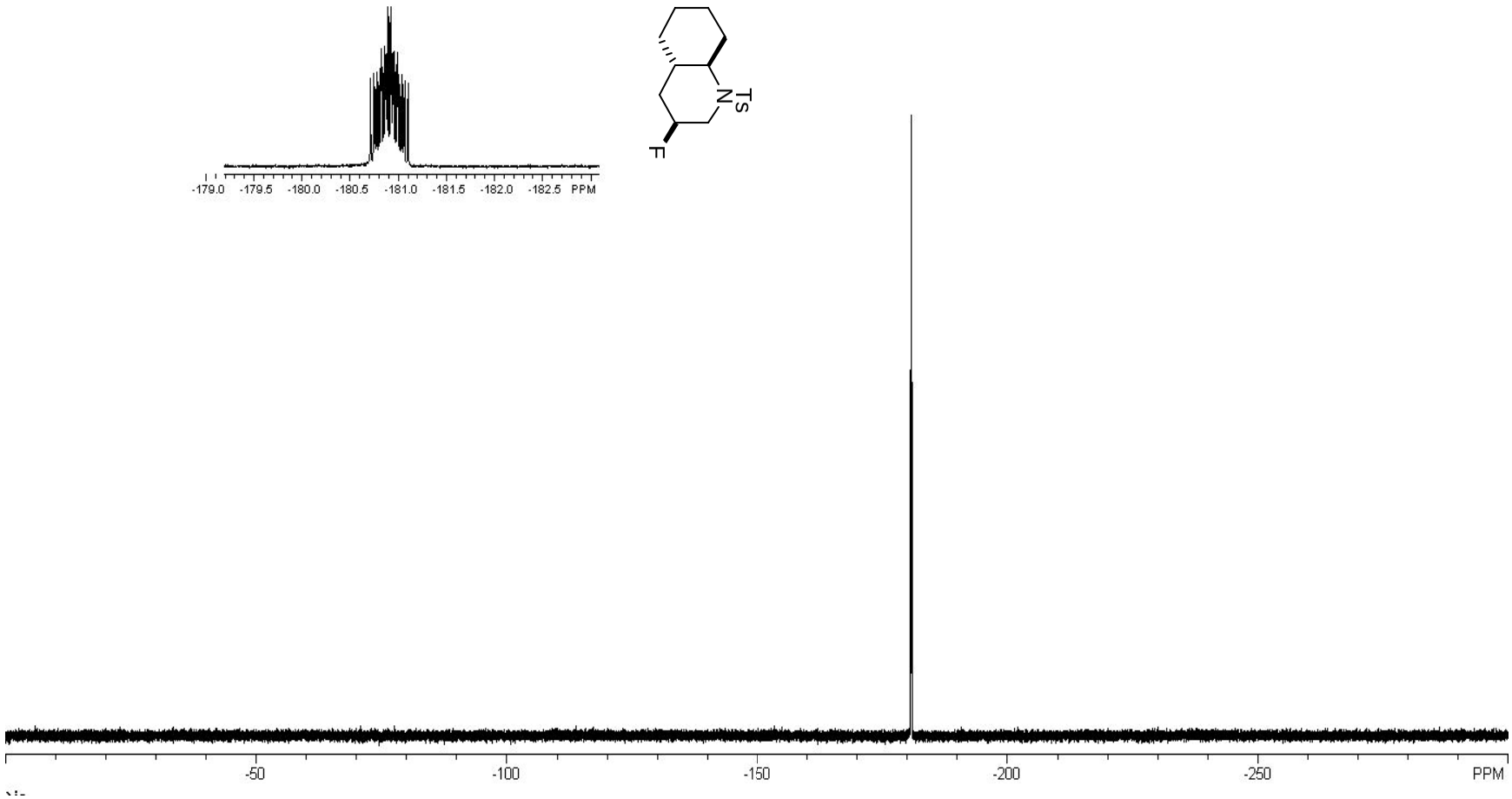
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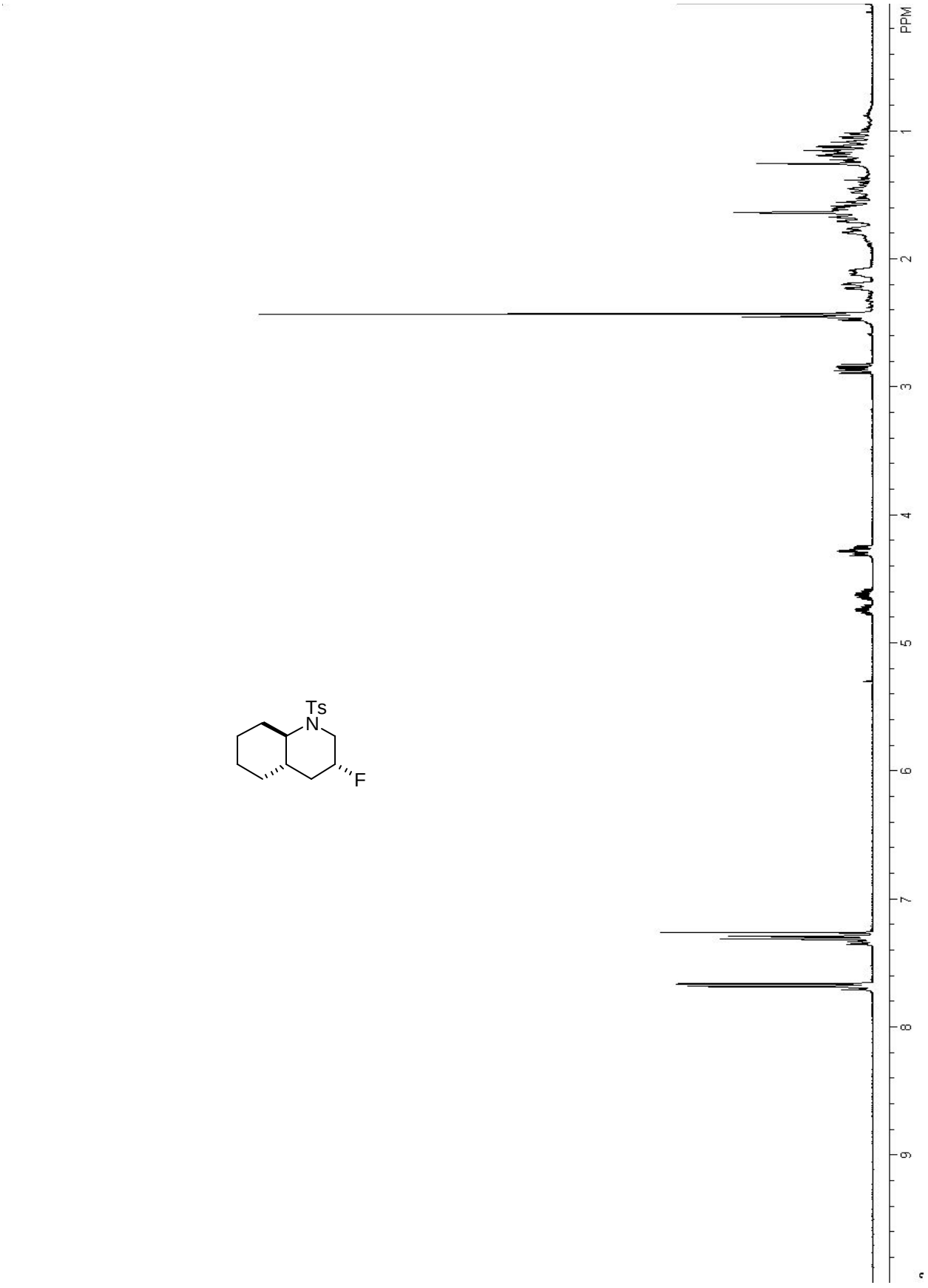
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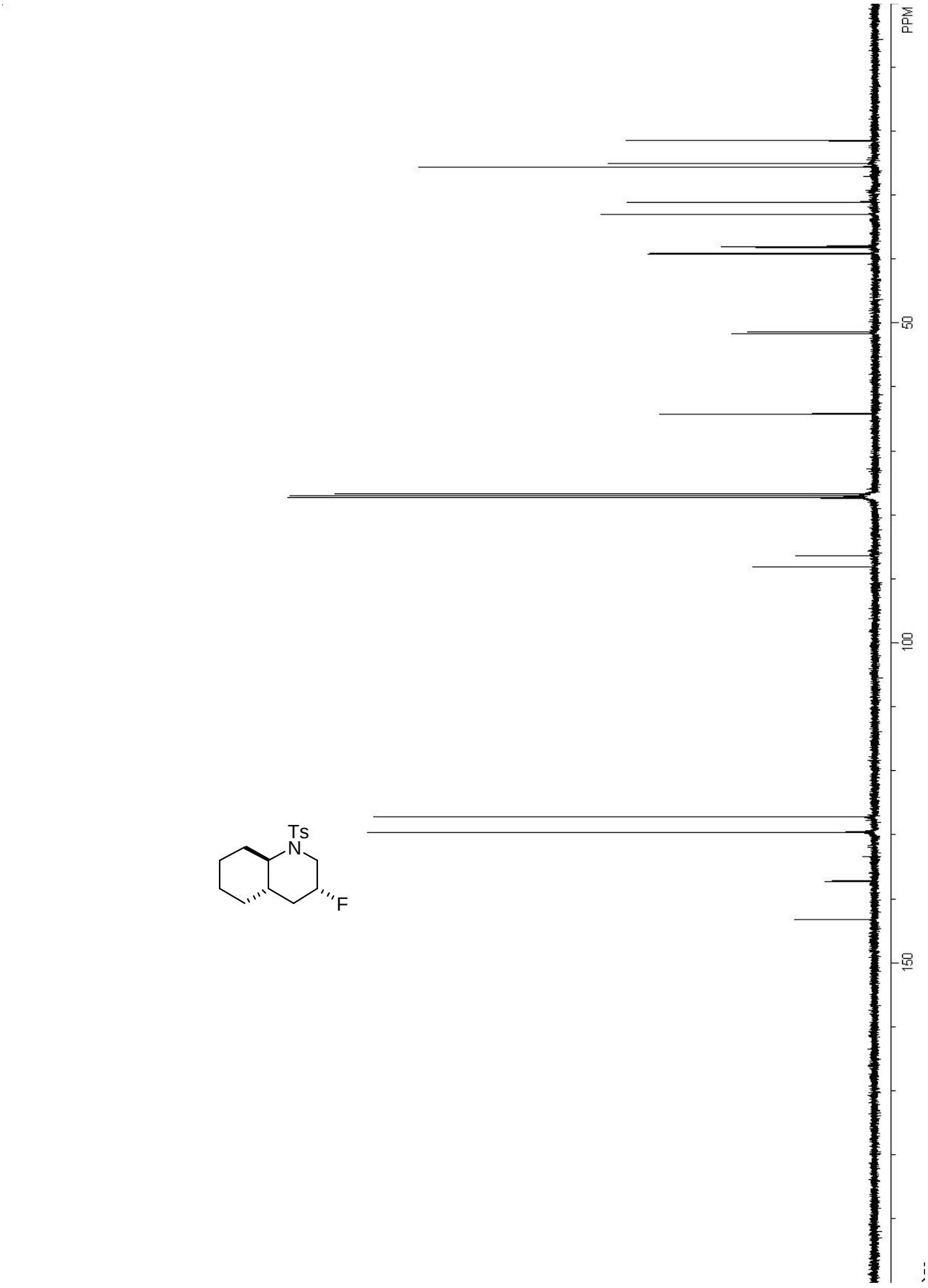
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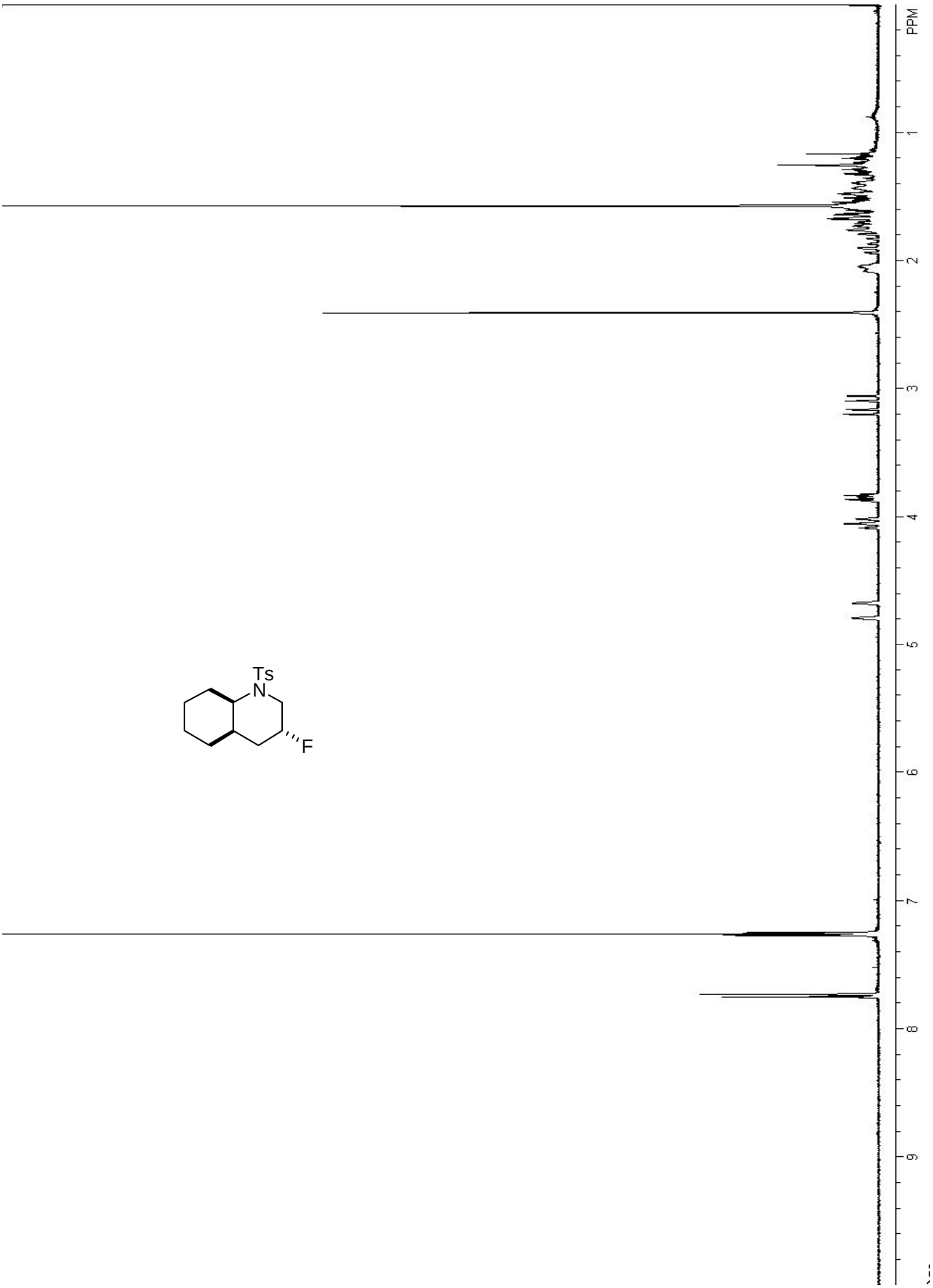
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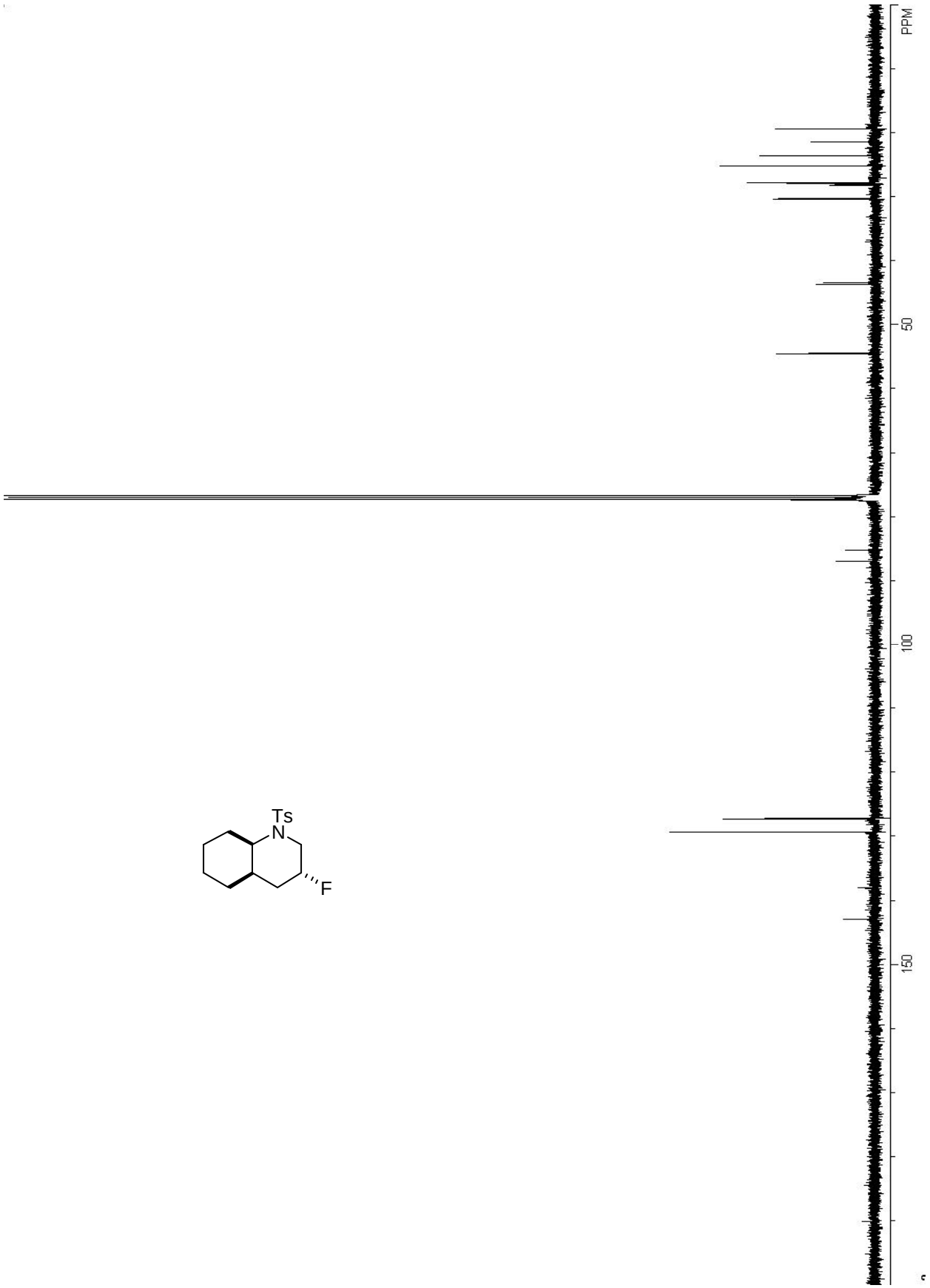
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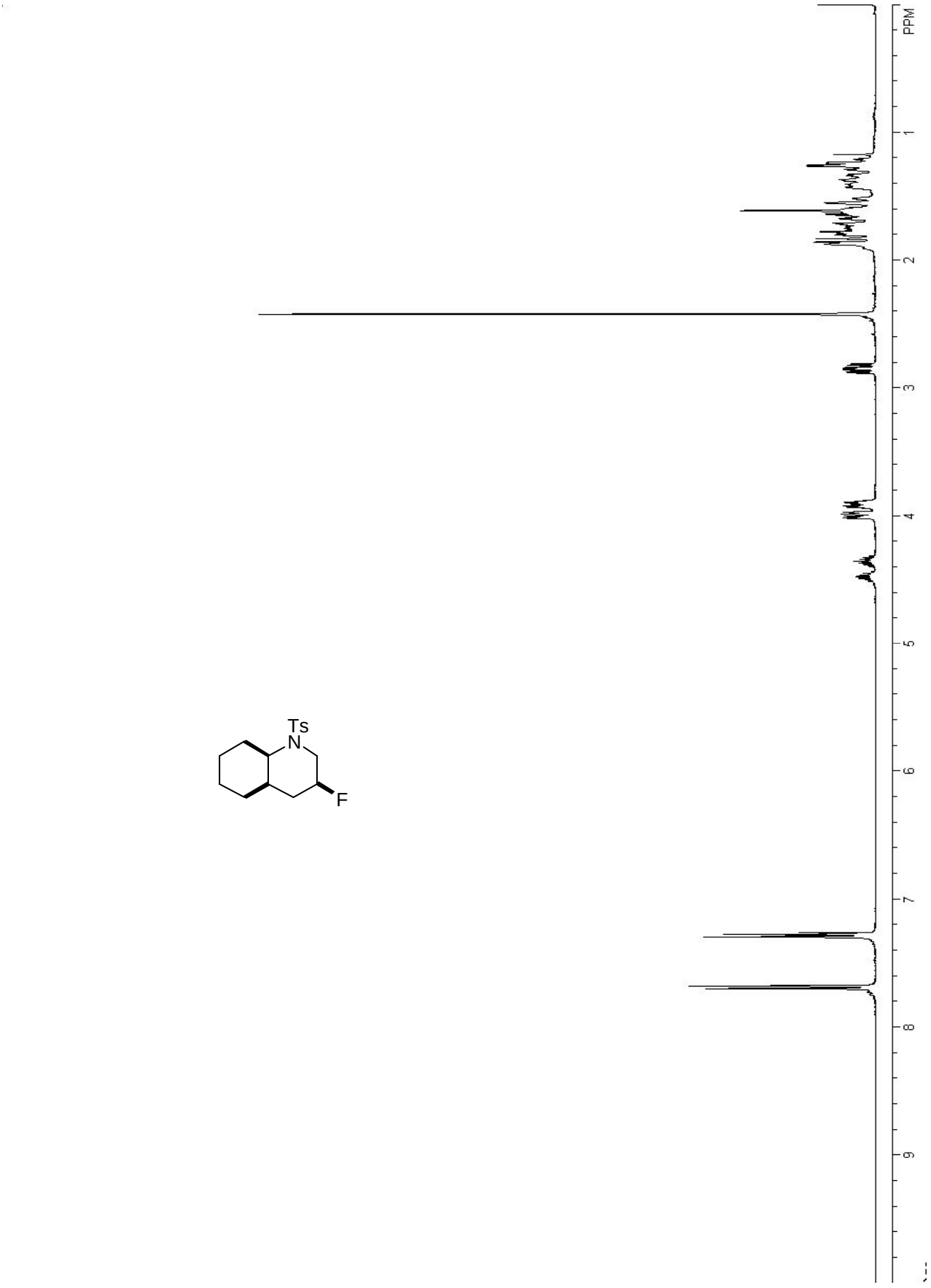
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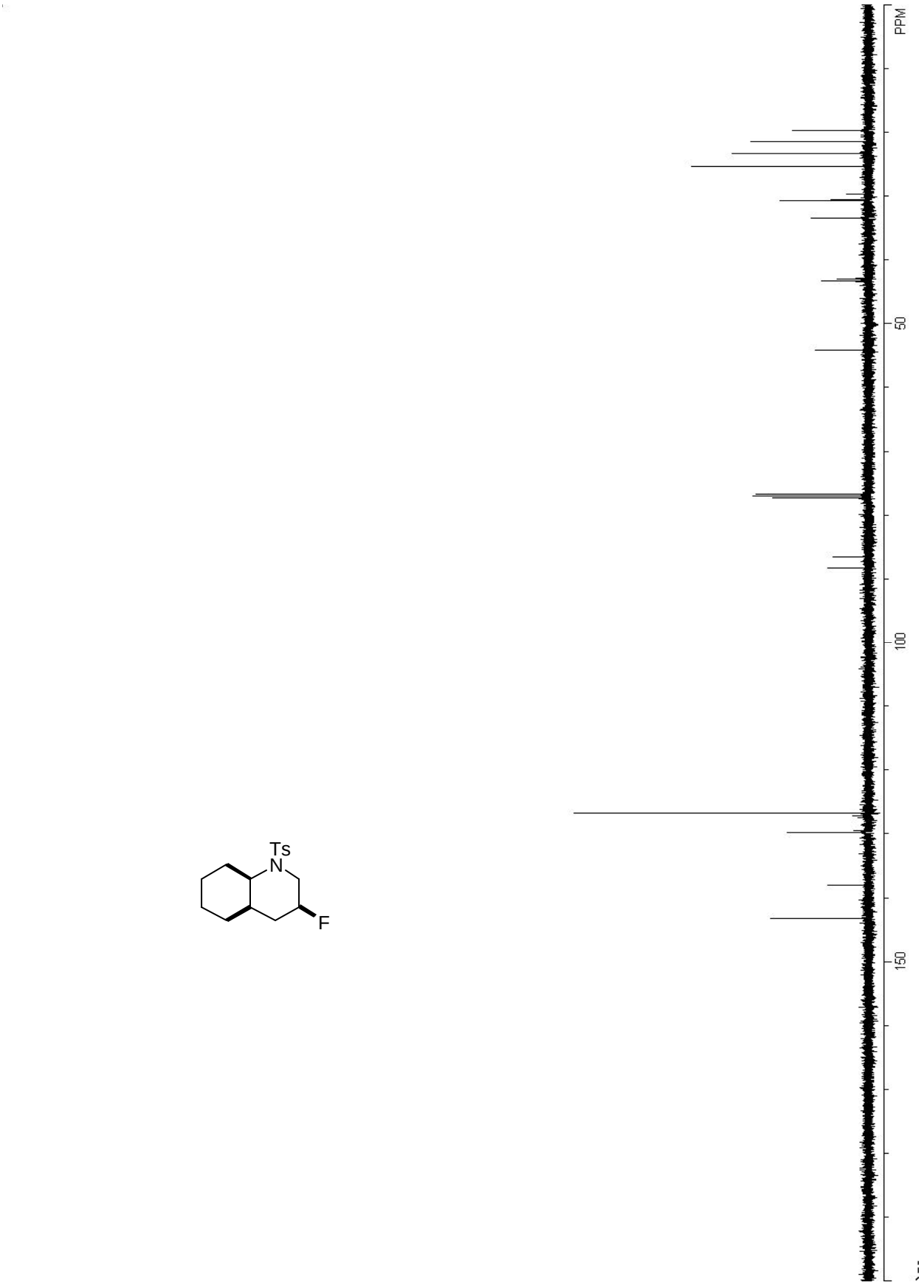
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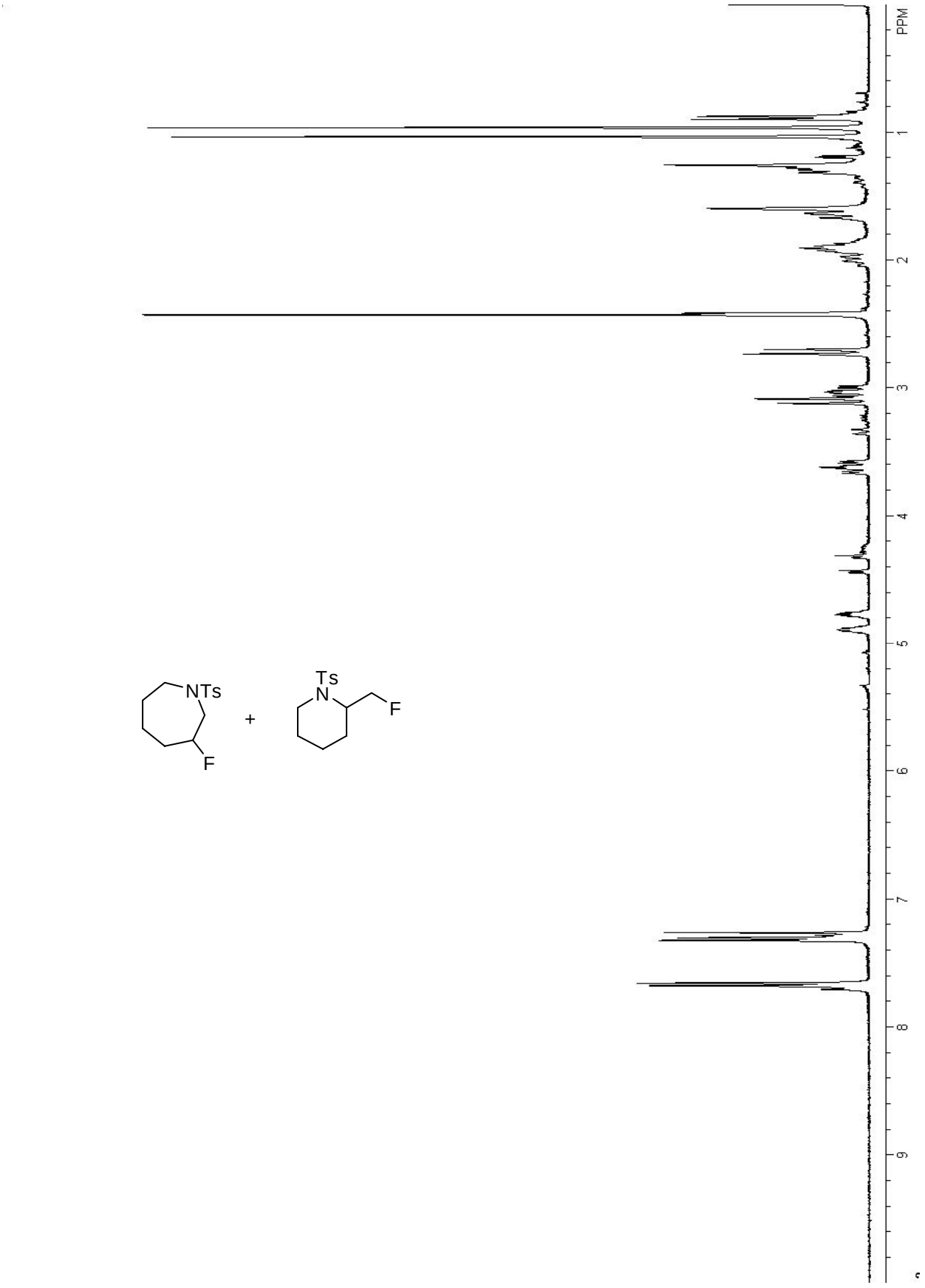
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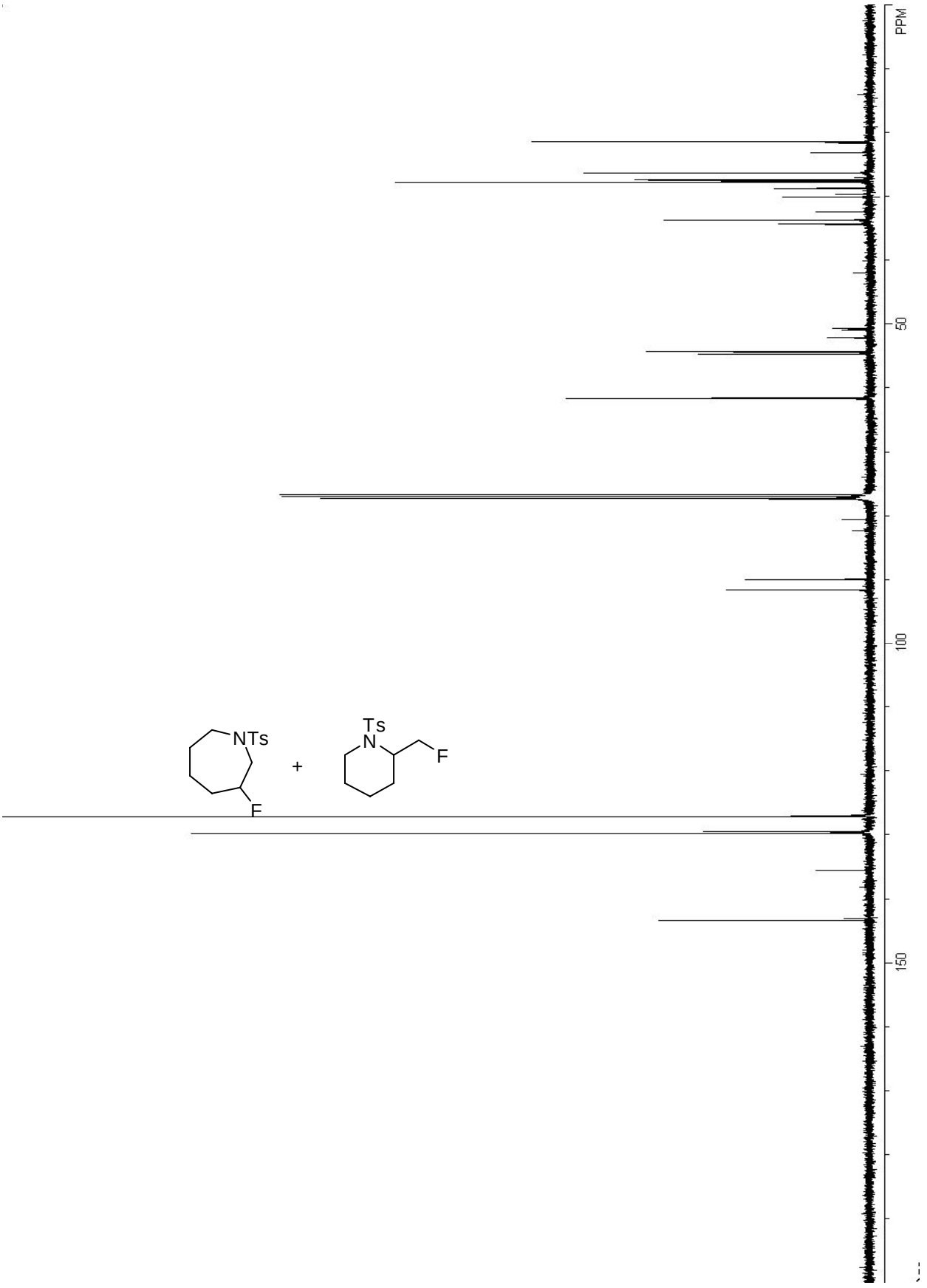
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PPM
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