Brønsted Base-Modulated Regioselective Palladium-Catalyzed Intramolecular Aerobic Oxidative Amination of Alkenes: Formation of Seven-Membered Amides and Evidence for Allylic C—H Activation

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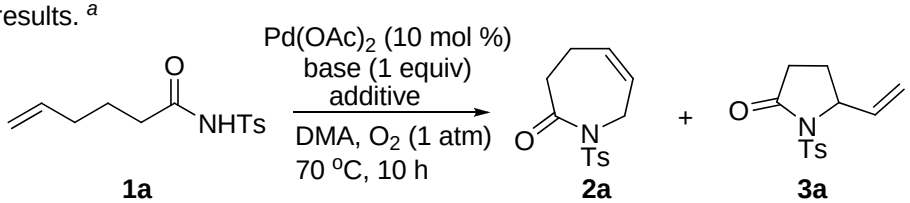
General Considerations.

All commercially available compounds were used as received, and all were purchased from Aldrich, Alfa Aesar and Acros. ^{1}H and ^{13}C spectra were recorded on a Varian Mercury-300 MHz or Varian Unity-400 MHz spectrometers, and $CDCl_3$ was purchased from Aldrich. The chemical shifts (δ) are given in parts per million relative to internal TMS (0 ppm for ^{1}H), CDCl3 (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) with hexanes/ethyl acetate. Solvents (DMF, DMA and NMP) were dried with BaO at around 100 ^{0}C for 5hrs and distallatized under vacuum, kept with 4Å Molecular Seives.

General procedure for the optimized reaction condition.

In a glass tube, substrate **1a** (0.1 mmol), catalyst (0.01 mmol), and additives (see Table S1) were combined in 1.0 mL solvent. The reaction tubes were placed into a custom 12-well parallel reactor mounted in a 300 ML Parr bomb and sealed. The whole system was purged with molecular oxygen for ca. 10 times. Then the oxygen pressure was increased to 1.0 atm and the reactor was warmed to 70° C. The reactions were stirred for 8-10 hours. After the reactions were stopped they were fast flashed by a short silic gel with ethyl acetate, then the solution was concentrated *in vacuo*. After concentrating, 1,3,5-trimethoxybenzene (1mL of a known concentration solution in $CDCl_3$) was added to the reaction mixture. The oxidative amination product was evaluated by ^{1}H NMR spectroscopy relative to an internal standard. The results were summarized in Table S1.

Table S1. Palladium-catalyzed aerobic oxidative allylic C-H amination:Screen results. [a]

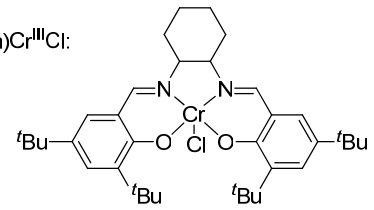


1a **2a** **3a**

Entry	Base	additive	Yield%[b](**2a:3a**)[c]
1	NaOAc	--	44 (3.9:1)
2	NaOAc	Pyridine (40%)	27 (1.0:1)
3	NaOAc	MA[g] (40%)	58 (5.6:1)
4	NaOAc	BQ[h] (40%)	39 (5.5:1)
5	NaOAc	nbd[i] (20%)	35 (3.7:1)
6	NaOAc	Ethyl Acryate (1 eq)	44 (2.8:1)
7	NaOAc	MA (40%), 4Å MS (15mg)	72 (5.7:1)
8	**NaOBz**	**MA (40%), 4Å MS (15mg)**	**90 (5.6:1)**
9	NaOBz	MA (40%), 4Å MS (15mg)	69 (4.0:1)
10[d]	NaOBz	MA (40%), 4Å MS (15mg)	60 (3.2:1)
11[e]	**--**	**--**	20 (0:100)
12	Amberlite IRA-400 (OH) (10 mg)	MA (40%), 4Å MS (15mg)	45 (0:100)
13[f]	Amberlite IRA-400 (OH) (10 mg)	(salen)Cr(III)Cl (10 mol %)	**58 (0:100)**
14[f]	--	**(salen)Cr(III)Cl (10 mol %)**	**65 (0:100)**
15[f]	NaOBz (25 %)	--	35 (85:15)
16[f]	NaOBz (25 %)	(salen)Cr(III)Cl (10 mol %)	46 (84:16)
17[f]	NaOBz (100 %)	--	43 (82:18)
18[f]	NaOBz (100 %)	(salen)Cr(III)Cl (10 mol %)	54 (80:20)

[a]The reaction was conducted on a 0.1 mol scale in 1 mL DMA; [b]Yiled determined by ^{1}HNMR spectroscopy methods in which 1,3,5-trimethoxybezene was used as the internal standard; [c]the ratio of **2a** and **3a**, determined by ^{1}HNMR; [d]DMF as the solvent; [e]DMSO as the solvent; [f]50 °C; [g]MA = maleic anhydride; [h]BQ =benzoquinone; [i]nbd = 2,5-Norbornadiene; [j]Including other isomers.

(salen)Cr^{III}Cl:



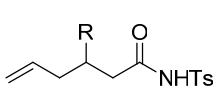
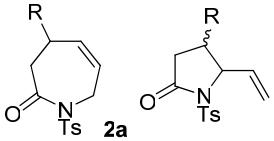
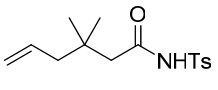
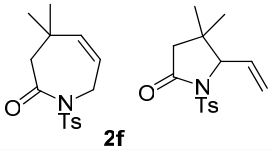
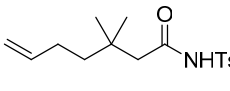
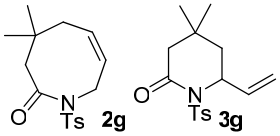
General procedure for the intramolecular reaction of 1.

Condition A:

In a glass tube, substrate **1** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol), maleic anhydride (MA, 0.08 mmol), NaOBz (0.2 mmol) and 4Å molecular seives (30 mg) were combined in 2.0 mL *N*,*N*-dimethylacetamide (DMA). The reaction tubes were placed into a custom 9-well parallel reactor mounted in a 300 mL Parr bomb and sealed. The whole system was purged with molecular oxygen for ca. 10 times. Then the oxygen pressure was increased to 1.0 atm and the reactor was warmed to 70° C;

Condition **B**: In a glass tube, substrate **1** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol), (salen)Cr(III)Cl (0.02 mmol) were dissolved in 2.0 mL DMA. The reaction tubes were placed into a custom 9-well parallel reactor mounted in a 300 mL Parr bomb and sealed. The whole system was purged with molecular oxygen for ca. 10 times. The oxygen pressure was increased to 1.0 atm and the reactor was warmed to 50° C;
The reaction was stirred for 8-12 hours. After the reaction was complete, the mixture was concentrated *in vacuo*. The crude mixture was purified by column chromatography. The results were summarized in Table S2.

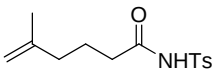
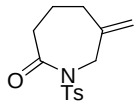
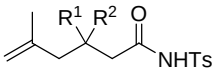
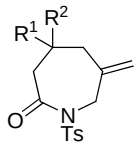
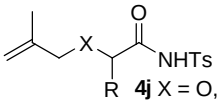
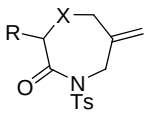
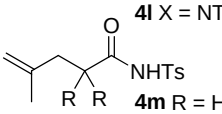
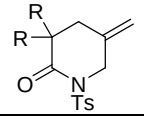
Table S2. Palladium-catalyzed oxidative allylic C-H amination.[a]

Entry	Sub		Condition	major Product		Yield (**2**:**3**)[b]
						
1	**1a**	R = H	**A**	**2a**		90% (86:14)
2			**B**		**3a**	64% (<3:97)
3	**1b**	Me	**A**	**2b**		83% (82:18)
4			**B**		**3b** (10:1)[c]	66% (<3:97)
5	**1c**	C_5H_{11}	**A**	**2c**		64% (81:19)
6			**B**		**3c** (6:1)[c]	71% (6:94)
7	**1d**	^{i}Pr	**A**	**2d**		45% (81:19)
8			**B**		**3d** (9:1)[c]	41% (<3:97)
9	**1e**	CH_2OBn	**A**	**2e**		67% (79:21)
10			**B**		**3e** (17:1)[c]	61% (5:95)
						
11	**1f**		**A**	**2f**		74% (84:16)
12			**B**		**3f**	71% (<3:97)
						
13	**1g**		**A**	**2g**	**3g**	80% (15:85)

[a]The reaction was conducted at 0.2 mmol scale at 2 mL DMA under 1 atm dioxygen; condition **A**: $Pd(OAc)_2$ (10 mol %), NaOBz (1 equiv), MA (40 mol %), 4 A MS (30 mg), 70 °C; Condition **B**: $Pd(OAc)_2$ (10 mol %), (salen)Cr(III)Cl (10 mol %), 50 °C; [b]Isolated Yield, the data in parenthesis is the ratio of **2** and **3**; [c]the ratio of *trans*-**3** and *cis*-**3.**

General procedure for the intramolecular reaction of 4 to synthesize seven-membered product 5. In a glass tube, substrate **4** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol), maleic anhydride (0.08 mmol), NaOBz (0.2 mmol) and 4Å molecular seives (30 mg) were combined in 2.0 mL DMA. The reaction tubes were placed into a custom 9-well parallel reactor mounted in a 300 ML Parr bomb and sealed. The whole system was purged with molecular oxygen for ca. 10 times. Then the oxygen pressure was increased to 1.0 atm and the reactor was warmed to 70° C; The reactions were stirred for 8-12 hours. After the reactions were stopped they were concentrated *in vacuo*. The crudes mixture was purified by column chromatography. The results were summarized in Table S3.

Table S3. Palladium-catalyzed oxidative allylic C-H amination of **4**.[a]

Entry	Substrate	Product	Yield[b]
1[c]	 **4a**	 **5a**	71% (87:13)[d]
2[e]	 **4b** R^1 = H, R^2 = Me	 **5b**	76%
3[c]	**4c** R^1 = H, R^2 = Ph	**5c**	58%
4	**4d** R^1 = H, R^2 = OMe	**5d**	82%
5	**4e** R^1 = H, R^2 = COOMe	**5e**	70%
6	**4f** R^1 = Me, R^2 = Me	**5f**	91%
7	**4f**	**5f**	(88%)[f]
8	**4g** R^1 = Me, R^2 = OMe	**5g**	93%
9	**4h** R^1 = R^2 = $(CH_2)_4$	**5h**	82%
10	**4i** R^1 = R^2 = $(CH_2)_5$	**5i**	81%
11	 **4j** X = O, R = H	 **5j**	54%
12	**4k** X = NTs, R = H	**5k**	62%
13	**4l** X = NTs, R = Me	**5l**	68%
14	 **4m** R = H	 **5m**	72%
15	**4n** R = Me	**5n**	77%

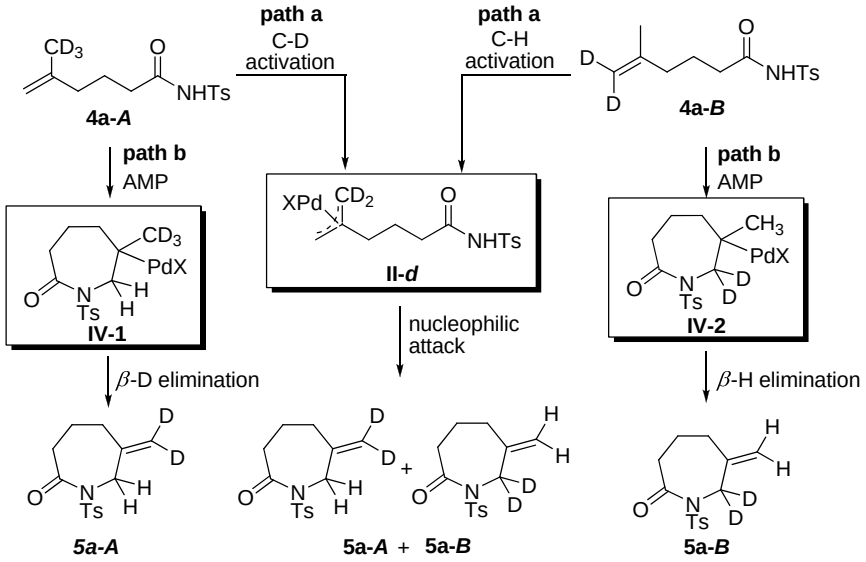
[a]The reaction condition: **4** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), NaOBz (1 equiv), MA (40 mol%), 4A MS (30 mg) in DMA (2 mL) under 1 atm O_2, 70 °C; [b]Isolated Yield; [c] NaOBz (2.5 equiv); [d]ratio of **5a**:**6a** (5-membered ring); [e]NaOBz (1.5 equiv), 20 h; [f]1.5 mmol scale.

Mechanistic studies:

Hypothesis of allylic C-H activation/reductive elimination or aminopalladation/*β*-hydride elimination pathway:

We hypothesized that the deuterium labeled substrate **4a-*A*** and **4a-*B*** might be helpful to gain insights into the mechanism. If the reaction involves allylic C—H activation, both the reaction of **4a-*A*** and **4a-*B*** will result the same π-allyl-Pd^{II} intermediate **II-*d*** and afford the similar results containing the mixture of equal amount **5a-*A*** and **5a-*B*** (Scheme 4, path a). Otherwise, if the reaction goes through aminopalladation /β-H elimination pathway, the reactions of **4a-*A*** and **4a-*B*** would be formed seven-membered products **5a-*A*** and **5a-*B*** respectively (path b)

Scheme S1. the hypothesis of two possible mechanism (AMP = aminopalladation).



Procedure of deuterium-labeled reaction of 4a-*A* and 4a-*B*

The deuterium-labeled substrates **4a-*A*** and **4a-*B*** were treated under the standard reaction condition: In a glass tube, substrates **4a-*A*** or **4a-*B*** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol), Melanie anhydride (0.08 mmol), NaOBz (0.4 mmol) and 4Å Molecular Seives (30 mg) were combined in 2.0 mL DMA. The reaction tubes were placed into a custom 9-well parallel reactor mounted in a 300 ML Parr bomb and sealed. The whole system was purged with molecular oxygen for ca. 10 times. Then the oxygen pressure was increased to 1.0 atm and the reactor was warmed to 70° C. The reactions were stirred for 8-12 hours. After the reactions were stopped they were concentrated *in vacuo*. The crudes mixture was purified by column chromatography. The results were summarized in eq S1 and eq S2.

Those results, the formation of mixture of **5a-*A*** and **5a-*B*** with roughly 1:1 ratio, strong supports that the reactions go thought allylic C—H activation/nucleophilic attack pathway. On the other hand, the formation of five-membered products **6a-*A*** and **6a-*B*** from **4a-*A*** and **4a-*B*** respectively, were also the strong evidence to support the allylic C-H activation mechanism (eq S1 and S2). For the case of **4a-*A***, except the formation of intermediate **III-*d*** via C-D activation, the reaction also generated the intermediate **II-*d*,** via allylic C-H activation at methylene position. Then the nucleophilic attack afforded product **6a-*A***. In contrast, if the reaction proceeded via the isomerization/aminopalladation pathway, the reaction should give raise to the mixture of **6a-*A*** and **6a-*B*.** On the other hand, no observation of the double bond isomerization within the recovered **4a-*A*** rules out the possibility of isomeriztion between **5a'-d_3** and **5a-A** (or **5a-*B*)**, which also supported that intermediate **II-*d*** exclusively generated five-membered product **6a-*A*** (Scheme S2).

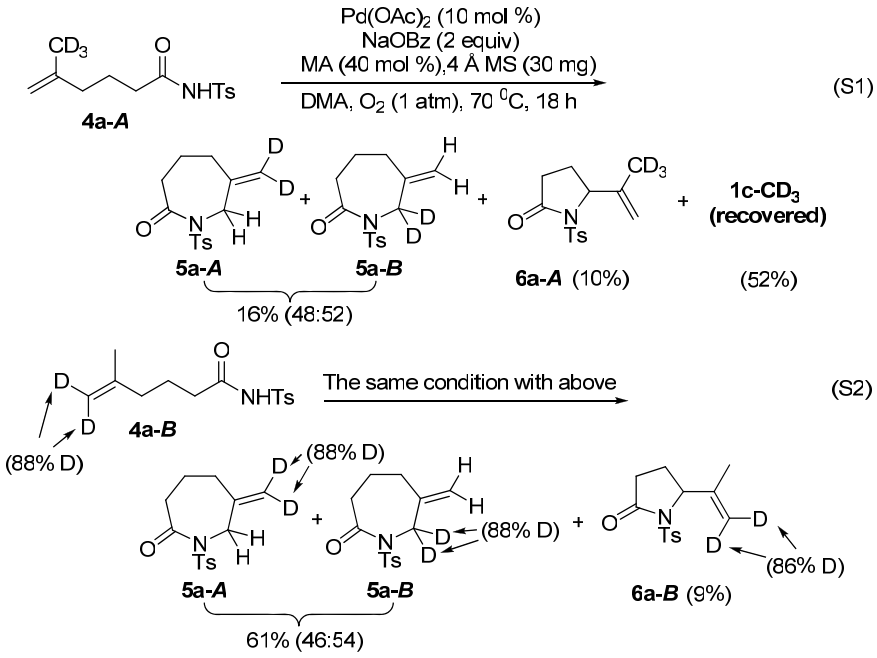
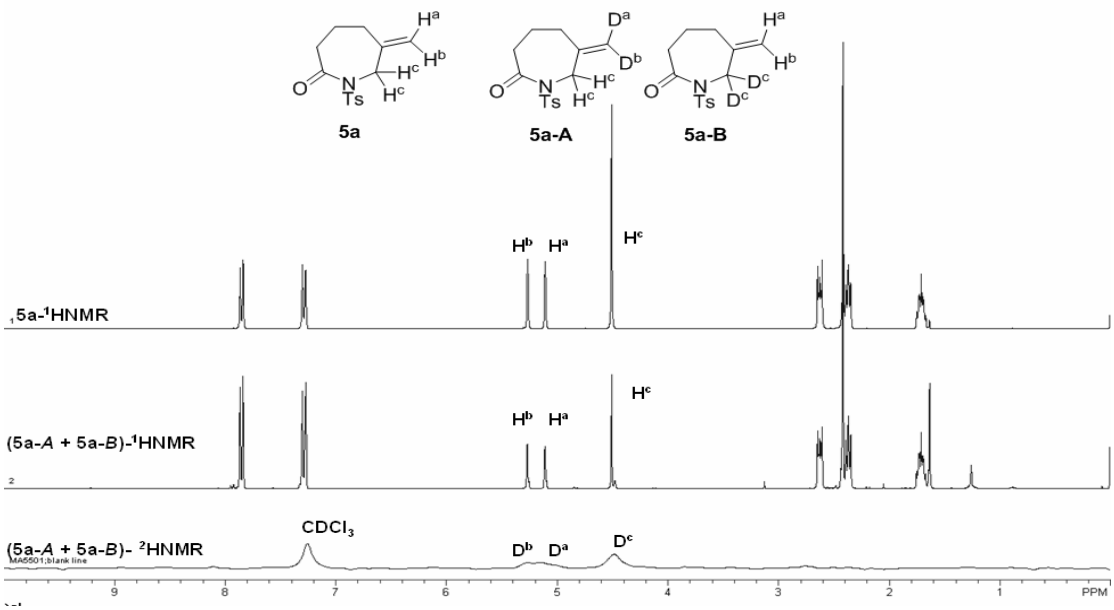
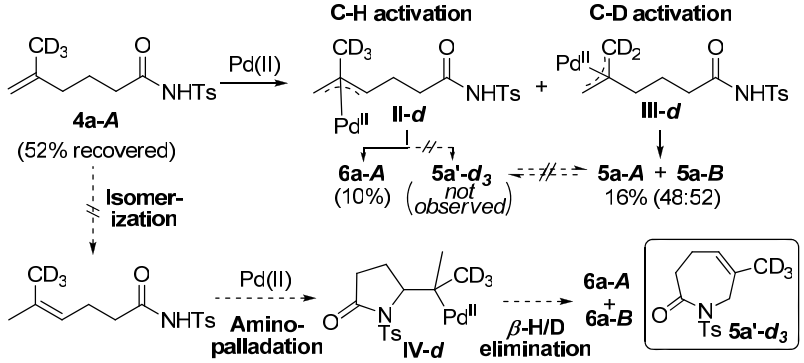


Figure S1. **Representive spectrum of deuterium-labeled products 5a-A and 5a-B (Structure of 5a was determined by H-H cosy).**



Scheme S2. the formation of seven- and five-membered products.



Studies of Kinetic Isotopic Effect: In a glass tube, substrates **4a** (0.1 mmol) and **4a-*A*** (0.1 mmol), $Pd(OAc)_2$ (0.02 mmol), Melanie anhydride (0.08 mmol), NaOBz (0.4 mmol) and 4Å Molecular Seives (30 mg) were combined in 2.0 mL DMA. The reaction tubes were placed into a custom 9-well parallel reactor mounted in a 300 ML Parr bomb and sealed. The whole system was purged with molecular oxygen for ca. 10 times. Then the oxygen pressure was increased to 1.0 atm and the reactor was warmed to 70° C for 4 hours. After the reactions were stopped they were concentrated *in vacuo*. The crude was detected by HNMR with 1,3,5-trimethoxybenzene as internal standard. The result was summarized in eq S3.

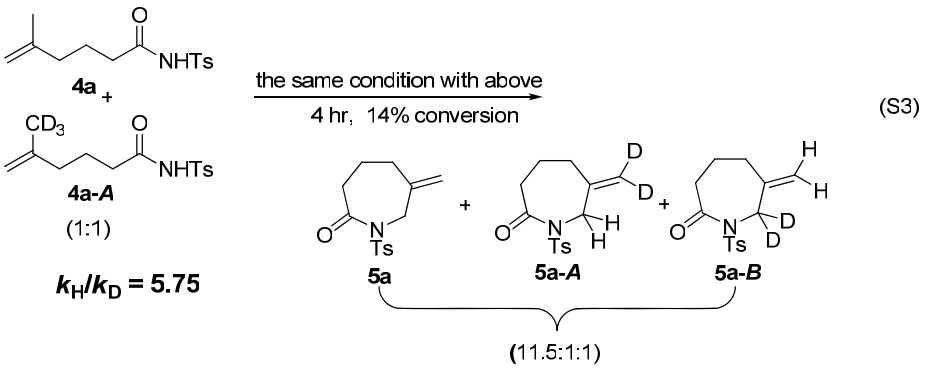
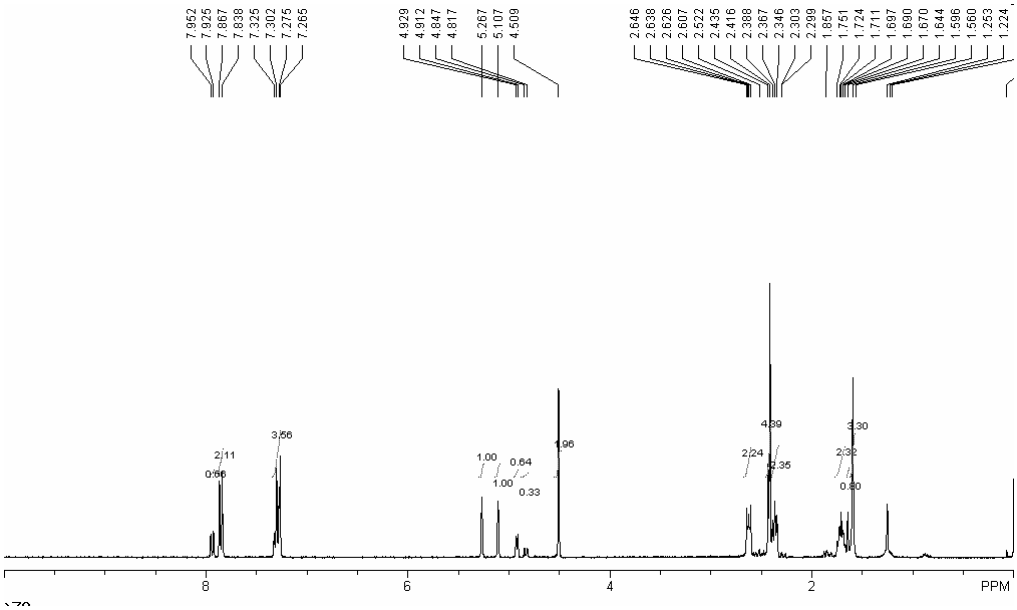


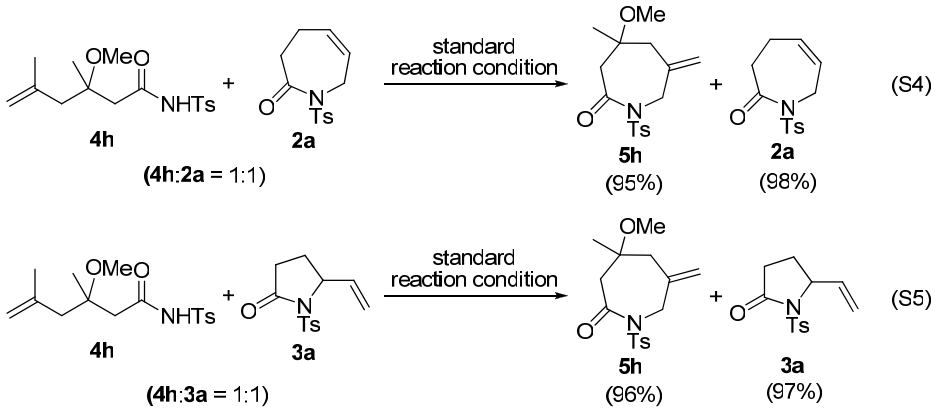
Figure S2. **The HNMR of mixture products of the reaction of 4a and 4a-*A* with 1:1 ratio**



Controlled reaction: In a glass tube, substrates **4h** (0.2 mmol) and **2a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol), melanie anhydride (0.08 mmol), NaOBz (0.4 mmol) and 4Å Molecular Seives (30 mg) were combined in 2.0 mL DMA. The reaction tubes were placed into a custom 9-well parallel reactor mounted in a 300 ML Parr bomb and sealed. The whole system was purged with molecular oxygen for ca. 10 times. Then the oxygen pressure was increased to 1.0 atm and the reactor was warmed to 70° C for

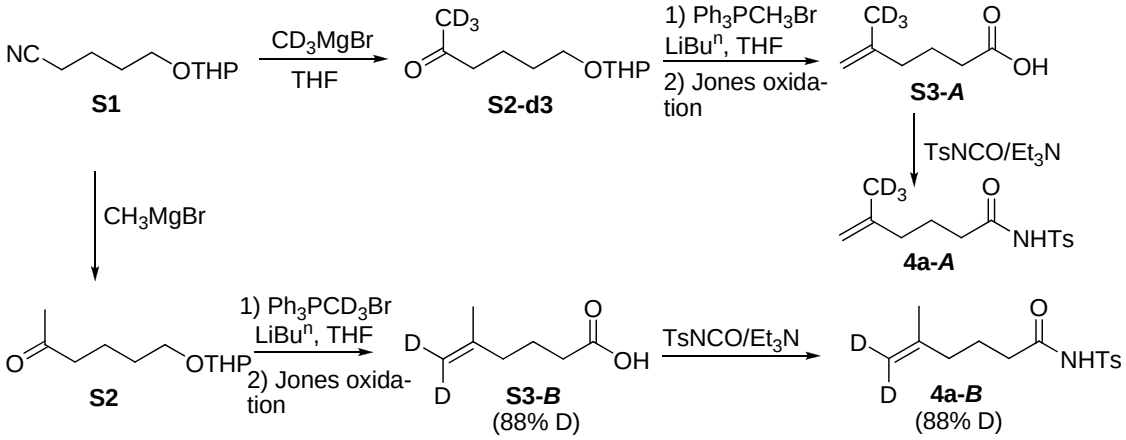
4 hours. After the reactions were stopped they were concentrated *in vacuo*. The residue was detected by HNMR with 1,3,5-trimethoxybenzene as internal standard. The result was summarized in eq S4 and S5.

No observation of transformation between **2a** and **3a** indicated that the formation of seven-membered product **2a** is the kinetically preferred product and the C—N bond formation is irreversible



Synthesis of deuterium-labeled substrates 4a-*A* and 4a-*B*:

Scheme S1.

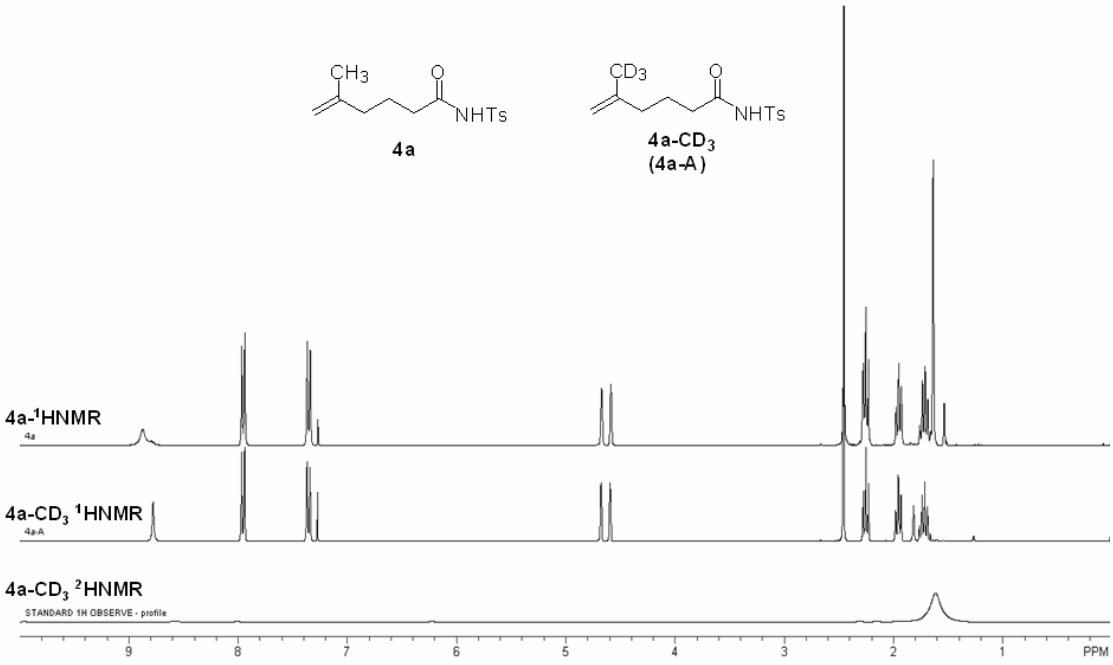


Compound **S1** was synthesized by the literature procedure.[1] To a solution of **S1** (1.8 g, 10.0 mmol） in dry diethyl ether (100 mL)，CD_3MgI (20 mL, 1.0 M in Et_2O) was added slowly at 0 ^oC. The mixture was stirred overnight and saturation NH_4Cl aqueous was added at low temperature, then extracted by Et_2O, dried by $MgSO_4$. After the solvent was removed under vacumm, the residue was purified by silical gel column to afford the ketone **S2** (1.3g, 65%). [S2]

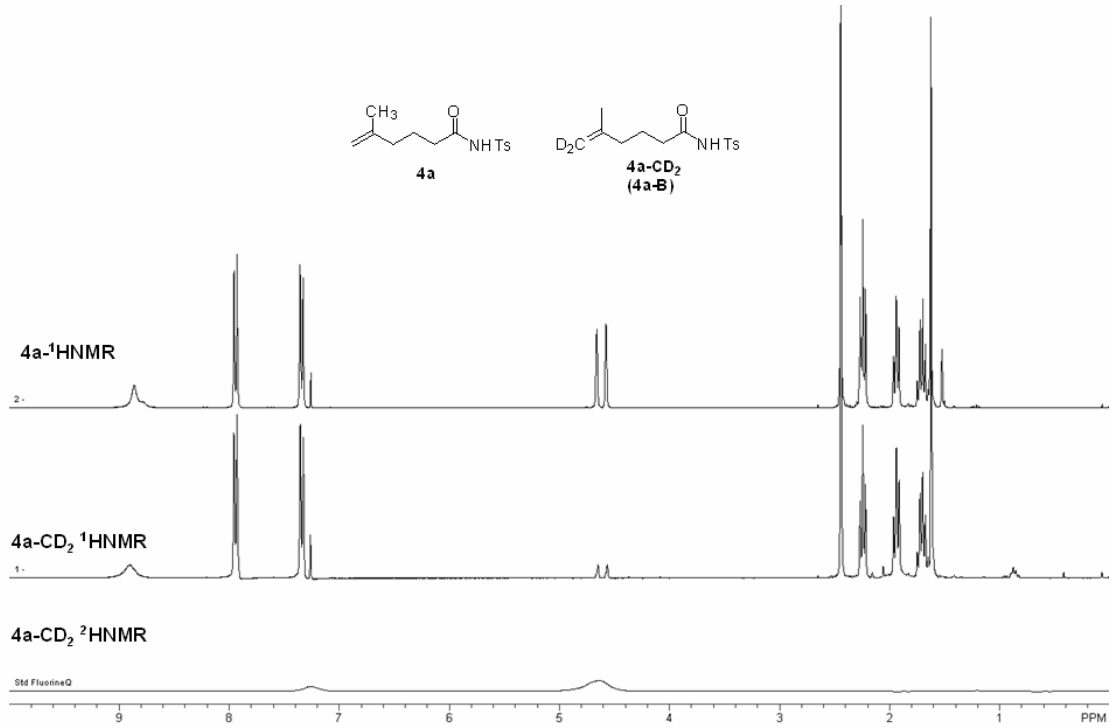
To a suspension Ph_3PCH_3Br in THF (7.14 g, 20 mmol), n-butyl lithium (12.5 mL, 1.6 M in hexane) was slowly added at 0 ^oC. The mixture became to clear solution. Then **S2** (1.6 g, 6 mmol) was added and the mixture was stirred for over night. After the workup as above, the residue was redissoved in actone, then Jone's reagent (24

mmol) was added slowly at -10 ~ 0 °C. After two hours, the acetone was removed under vacumm, and the mixture was extracted by methylene chloride. The organic layer washed with brine, dried by $MgSO_4$, filtered and concentrated under vacumm to give oil **S3-*A*** 430 mg (55% yield, >99% D). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.75 (m, 1H), 4.70 (m, 1H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.07 (t, *J* = 7.2 Hz, 2H), 1.79 (tt, *J* = 7.5, 7.2 Hz, 2H).

In a solution of **S3-*A*** (300 mg, 2.3 mmol） in dry THF (5 mL), TsNCO (0.5 g, 2.5 mmol） was added under Nitrogen. The mixture was stirred for 10 min, then Et_3N (0.5 mL) was added. The mixture was stirred overnight, and a 2N HCl solution (10 mL) was added. The mixture was extracted with diethyl ether. The combined organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by silica gel chromatography to give **4a-*A*** (594 mg, 91% yield). **4a-*A*** (>99% D)**:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.25 (s,1H), 7.96(d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.66 (s, 1H), 4.58 (s, 1H), 2.44 (s, 3H), 2.27 (t, *J* = 7.5 Hz, 2H), 1.94 (t, *J* = 7.5 Hz, 2H), 1.70 (M, 2H). ^{2}H NMR (100 MHz, $CHCl_3$) δ 1.61 (s). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.7, 145.1, 144.2, 135.6, 129.6, 128.3, 111.0, 36.6, 35,5, 21.9, 21.6.. HRMS: m/z (ESI) calculated $[M+H]^+$ 285.1347, measured 285.1354.

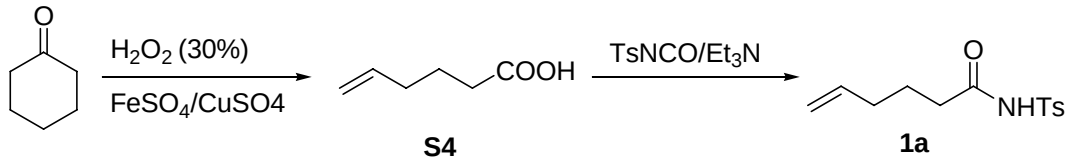


Synthetic procedure of 4a-B is the same with that of **4a-A** which using CH_3MgBr instead of CD_3MgI, and Ph_3PCD_3Br instead of Ph_3PCH_3Br. The synthesis of Ph_3PCD_3Br is according to the literature procedure. **4a-*B*** (88% D): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.91 (s,1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 2.44 (s, 3H), 2.27 (t, *J* = 7.5 Hz, 2H), 1.94 (t, *J* = 7.5 Hz, 2H), 1.70 (M, 2H)， 1.63 (s, 3H). ^{2}H NMR (100 MHz, $CHCl_3$) δ 4.60 (br s, 2H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 170.8, 145.1, 144.1, 135.5, 129.6, 128.3, 111.0, 36.5, 35.4, 21.9, 21.8, 21.7.. HRMS: m/z (ESI) calculated $[M+H]^+$ 284.1284, measured 284.1296.



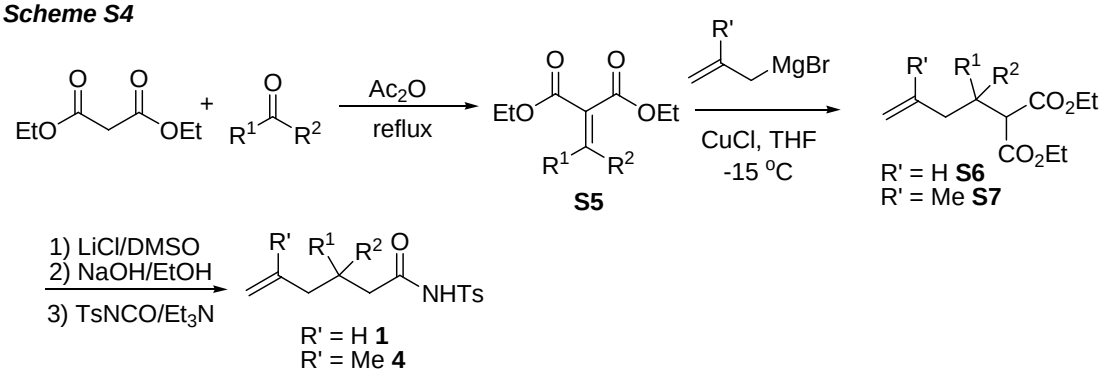
Starting material synthesis:

Scheme S3

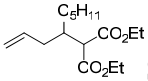


Synthesis 1a from S4[3]: The same protocol used in the preparation of **4a-*A*** from **S3-*A*** was employed (see above) (73% yield). **1a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.68 (m, 1H), 4.96 (d, J = 17.1 Hz, 1H), 4.92 (d, J = 9.3 Hz, 1H), 2.45 (s, 3H), 2.27 (t, *J* = 7.2 Hz, 2H), 2.00 (m, 2H), 1.66 (m, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 171.1, 145.1, 137.2, 135.4, 129.6, 128.2, 115.6, 35.3, 32.6, 23.2, 21.6. Anal. Calcd. for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.41; N. 5.24. Found: C, 58.23; H, 6.17; N. 5.18.

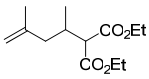
Scheme S4



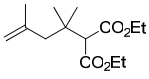
Synthesis of S6 is modified from the literature procedure,[S4] and the NMR spectrums of S6b,[S5] S6d,[6] S6f,[S7] S6g[S8] and S7d[S9] are consisted with literatures: To a solution of CuCl (2.5 g, 25 mmol) in dry THF (100 mL), the solution of allylic Magnesiumbromide (30 mmol, 0.3 M in THF) was added at -15 °C, and the mixture was stirred for 15 min. Then **S5b** (R^1 = H, R^2 = Me)[10] (4.6 g, 25 mmol) was added. After 2 hours, the mixture was quenched by aqueous of NH_4Cl, extracted by ether, dried by $MgSO_4$ and concentrated under vacumm. The residue was purified by silic gel chromatography to give **S6b** (4.95 g, 87% yield).



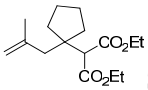
S6c (72%) ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76(m, 1H), 5.05 (m, 1H), 4.20 (q, *J* = 7.2 Hz, 4H), 3.41 (d, *J* = 6.9 Hz, 1H), 1.40-1.21 (m, 14H), 0.87 (t, *J* = 6.3 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ168.9, 135.8, 117.1, 61.0, 54.8, 37.8, 35.2,3, 31.8, 30.5, 26.2, 22.4, 14.0, 13.9. HRMS: m/z (ESI) calculated $[M]^+$ 284.1988, measured 284.1987.



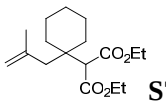
S7c (42% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.79 (s, 1H), 4.70 (s, 1H), 4.21 (m, 4H), 3.25 (d, *J* = 7.2 Hz, 1H), 2.42 (m, 1H), 2.16 (m, 1H), 1.85 (m, 1H), 1.65 (s, 3H), 1.02 (m, 6H), 0.97 (m, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 169.0, 168.7, 143.2, 112.8, 61.2, 61.1, 57.1, 43.1, 31.2, 21.9, 16.7, 14.1. HRMS: m/z (ESI) calculated $[M+H]^+$ 243.1510, measured 243.1595.



S7g (45% yield) ^{1}H NMR (300 MHz, CDCl3) δ 4.91 (s, 1H), 4.70 (s, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.36 (s, 1H), 2.25 (s, 2H), 1.79 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 6H), 1.14 (s, 3H). ^{13}C{1H}NMR (75 MHz, CDCl3) δ 168.4, 142.4, 115.6, 60.8, 59.8, 47.5, 36.8, 25.7, 25.4, 14.1. HRMS: m/z (ESI) calculated $[M+H]^+$ 257.1747, measured 257.1748.

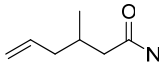


S7i (38% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.86 (s, 1H), 4.68 (s, 1H), 4.17 (q, *J* = 7.2 Hz, 4H), 3.57 (s, 1H), 2.35 (s, 2H), 1.93 (m, 2H), 1.78 (s, 3H), 1.66 (m, 6H), 1.24 (t, *J* = 7.2 Hz, 4H). ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ 168.9, 143.0, 115.4, 60.8, 57.5, 47.0, 46.0, 35.7, 24.8, 24.8, 14.0. HRMS: m/z (ESI) calculated $[M+H]^+$ 283.1904, measured 283.1915.

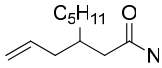


S7j (35% yield) ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.91 (s, 1H), 4.71 (s, 1H), 4.18 (q, *J* = 7.5 Hz, 4H), 2.46 (s, 2H), 1.79 (s, 3H), 1.51 (m, 10H), 1.27 (t, *J* = 7.5 Hz, 6H). ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ 168.7, 142.6, 115.8, 60.8, 56.1, 41.4, 40.0, 32.7, 25.7, 25.6, 21.5, 14.1. HRMS: m/z (EI) calculated $[M]^+$ 296.1988, measured 296.1992.

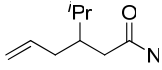
Synthesis of 1b: To a solution of **S6b** (2.3 g, 10.0 mmol) in DMSO (25 mL), LiCl (1.5 g, 36 mmol) and H_2O (1 mL) were added and the mixture was refluxed. The reaction was monitored by TLC. After the reaction completed, H_2O (50 mL) was added and the mixture was extracted by ether. The organic layer was washed with brine and dried with $MgSO_4$. The solvent was removed under vacumm to give crude oil 1.27 g. The oil was dissolved in the mixture of ethanol (10 mL) and NaOH aqueous solution (2N, 6 mL). The mixture was stirred for overnight at 50 ^{o}C. The ethanol was removed under vacumm. The water (10 mL) was added and the mixture was extracted with ether for twice. Then the water phase was acidified with HCl solution (2N) and extracted with ether. The organic layer was dried with $MgSO_4$, filtered and concentrated to afford acid 0.97 g. To a solution of acid (0.97 g, 7.5 mmol） in dry THF (5 mL), TsNCO (1.6 g, 8 mmol） was added under Nitrogen. The mixture was stirred for 10 min, then Et_3N (0.5 mL) was added. The mixture was stirred overnight, and a 2N HCl solution (10 mL) was added. The mixture was extracted with diethyl ether. The combined organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by silica gel chromatography to give **1b** (1.82 g, 65% yield for three steps).



1b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (br s, 1H), 7.95 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 5.67(m, 21), 4.95 (d, *J* = 9.9 Hz, 1H), 4.93 (d, *J* = 17.7 Hz, 1H), 2.45 (s, 3H), 2.26 (m, 1H), 2.10-1.86 (m, 4H), 0.85 (d, *J* = 6.3 Hz, 3H), ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ 170.4, 145.1, 135.9, 135.5, 129.6, 128.3, 116.9, 42.8, 40.6, 29.8, 21.6, 19.3. HRMS: m/z (ESI) calculated $[M+Na]^+$ 304.0978 measured 304.0983.

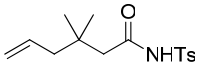


1c (61% yield for three steps)**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (br s, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 5.61(m, 1H), 4.94 (d, *J* = 11.6 Hz, 1H), 4.92 (d, *J* = 15.6 Hz, 1H), 2.44 (s, 3H), 2.20-1.84 (m, 5H), 1.30-1.11 (m, 8H), 0.85 (t, *J* = 7.2 Hz, 3H), ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ 170.6, 145.1, 135.9, 135.5, 129.6, 128.4, 117.1, 40.7, 37.9, 34.5, 33.4, 31.8, 26.2, 22.5, 21.7, 14.0. HRMS: m/z (ESI) calculated $[M+H]^+$ 338.1784, measured 338.1792.

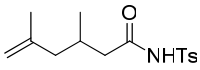


1d (54% yield for three steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (br s, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 5.58(m, 1H), 4.92 (d, *J* = 17.1 Hz, 1H), 4.88 (d, *J* = 10.2 Hz, 1H), 2.45 (s, 3H), 2.24-2.01 (m, 2H), 1.90-1.75 (m, 3H), 1.63 (m, 1H), 0.77 (m, 6H), ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ 171.1, 145.1, 136.7,

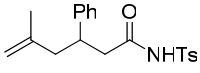
135.4, 129.5, 128.3, 116.7, 40.0, 37.6, 35.3, 29.6, 21.6, 19.1, 18.7. HRMS: m/z (ESI) calculated $[M+H]^+$ 310.1471, measured 310.1476.



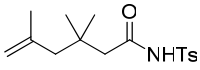
1f (42% yield for three steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.72 (m, 1H), 4.99 (d, *J* = 11.4 Hz, 1H), 4.94 (d, *J* = 17.2 Hz, 1H), 2.45 (s, 3H), 2.09 (s, 2H), 1.98 (d, *J* = 7.5 Hz, 2H), 1.63 (m, 1H), 0.93 (s, 6H), ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ169.8, 145.0, 135.4, 134.4, 129.5, 128.3, 118.0, 47.1, 46.2, 34.0, 26.9, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 296.1315, measured 296.1320.



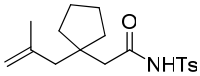
4c (55% yield for three steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.80 (br s, 1H), 7.95 (d, *J* = 8.1 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 4.68 (s, 1H), 4.59 (s, 1H), 2.45 (s, 3H), 2.26 (dd, *J* = 14.7, 4.8 Hz, 1H), 2.16 (m, 1H), 2.09 (dd, J = 14.7, 8.1 Hz, 1H), 1.91 (m, 1H), 1.80 (m, 2H), 1.60 (s, 3H), 0.84 (d, *J* = 6.3 Hz, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.5, 145.1, 143.4, 135.5, 129.6, 128.3, 112.5, 45.3, 43.1, 27.9, 21.9, 21.7, 19.5. HRMS: m/z (ESI) calculated $[M+H]^+$ 296.1315, measured 296.1322.



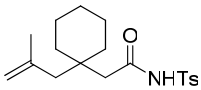
4d (45% yield for three steps): ^{1}H NMR (300 MHz, CDCl3) δ 9.29 (br s, 1H), 7.74 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.14 (m, 3H), 7.04 (m, 2H), 4.59 (s, 1H), 4.53 (s, 1H), 3.25 (m, 1H), 2.58 (dd, *J* = 15.0, 5.7 Hz, 1H), 2.45 (m, 1H), 2,41 (m, 3H), 2.23 (d, *J* = 7.5 Hz, 2H), 1.56 (s, 3H). ^{13}C{1H} NMR (75 MHz, CDCl3) δ 170.2, 144.7, 142.8, 142.5, 135.2, 129.4, 128.3, 127.9, 127.1, 126.4, 113.0, 44.5, 42.6, 39.7, 21.8, 21.5. HRMS: m/z (ESI) calculated $[M+H]^+$ 358.1471, measured 358.1460.



4g (48% yield for three steps): ^{1}H NMR (300 MHz, CDCl3) δ 9.15 (br s, 1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 4.81 (s, 1H), 4.56 (s, 1H), 2.45 (s, 3H), 2.14 (s, 2H), 1.98 (s, 2H), 1.69 (s, 3H), 0.96 (s, 6H). ^{13}C{1H} NMR (75 MHz, CDCl3) δ 169.9, 145.0, 142.5, 135.4, 129.5, 128.3, 115.1, 49.5, 47.6, 34.5, 27.6, 25.1, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 310.1471, measured 310.1475.

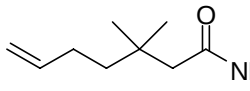


4i (65% yield for three steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (br s, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 4.72 (s, 1H), 4.49 (s, 1H), 2.45 (s, 3H), 2.21 (s, 2H), 2.14 (s, 2H), 1.66 (s, 3H), 1.54 (m, 8H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 169.9, 145.0, 143.9, 135.5, 129.5, 128.3, 114.7, 46.3, 45.0, 43.0, 38.4, 24.3, 23.7, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 336.1628, measured 336.1630.



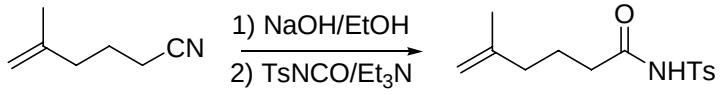
4j (57% yield for three steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (br s, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.80 (s, 1H), 4.57 (s, 1H), 2.45 (s, 3H), 2.21 (s, 2H), 2.11 (s, 2H), 1.70 (s, 3H), 1.50-1.34 (m, 10H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.0, 145.0, 142.8, 135.6, 129.5, 128.3, 115.4, 45.0, 43.0, 37.4, 35.9, 35.7, 25.8, 25.3, 21.7, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$

350.1784, measured 350.1780.



4g (46% yield for three steps): ^{1}H NMR (300MHz, $CDCl_3$) δ 9.34 (br s, 1H), 7.96 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.70 (ddd, *J* = 18.1, 11.4, 6.3 Hz, 1H), 4.94 (d, *J* = 18.1 Hz, 1H), 4.88 (d, *J* = 11.4 Hz, 1H), 2.44 (s, 3H), 2.12 (s, 2H), 1.92 (m, 2H), 1.30 (m, 2H), 0.93 (m, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.0, 145.0, 138.7, 135.4, 129.5, 128.2, 114.1, 47.5, 41.1, 33.8, 28.3, 26.8, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 332.1291, measured 332.1292.

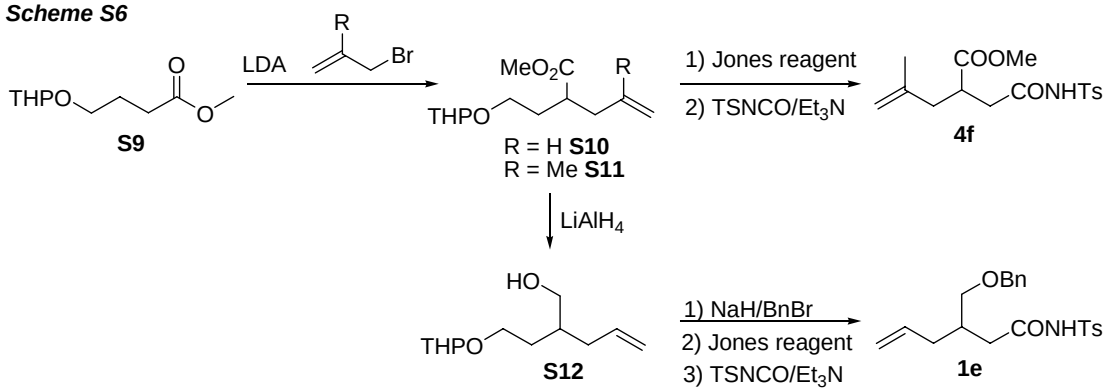
Scheme S5



S8 **4a**

Compound **4a** was synthesized from **S8** [11] with 65% yield. The procedure is the same as above. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.25 (br s,1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.66 (s, 1H), 4.58 (s, 1H), 2.44 (s, 3H), 2.27 (t, *J* = 7.5 Hz, 2H), 1.94 (t, *J* = 7.5 Hz, 2H), 1.70 (m, 2H), 1.62 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.9, 145.2, 144.3, 135.4, 129.6, 128.3, 110.9, 36.5, 35.4, 22.0, 21.8, 21.7. HRMS: m/z (ESI) calculated $[M+H]^+$ 282.1158, measured 282.1165.

Scheme S6



Synthesis of 4f: To a solution of diisopropylamine (5.05g, 50 mmol) in dry THF (50 mL), n-butyllithium (50 mmol, 32 mL 1.6 M in hexane) was added slowly at -50 ^{o}C. The mixture was stirred for 30 min at 0 ^{o}C, then cooled to -78 ^{o}C. **S9** [12] (10g, 50 mmol) was added. The mixture was stirred for 30 min at the same temperature, following 2-methyl allylbromide (9.4 g, 70 mmol) addition. The mixture was allowed to warm to room temperature and stirred for 2 hours. The NH_4Cl aqueous was added to quench reaction. The solution was extracted by ether. The organic layer was washed by brine and dried with MgSO4, filtered and concentrated under vacumm. Purification by flash chromatography (silica gel, diethyl ether/hexane) gave **S11** 8.32 g (65% yield). **S11:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77 (s, 1H), 4.71 (s, 1H), 4.56 (m, 1H), 3.84, (m, 1H), 3.75 (m, 1H), 3.66 (m, 1H), 3.50, (m, 1H), 3.37 (m, 1H), 2.76 (m, 1H), 2.37 (m, 1H) 2.19 (m, 1H), 1.94-1.47 (m, 10H), 1.72 (s, 3H). ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ 176.04, 176.01, 142.68, 142.64, 112.38, 112.34, 98.71, 98.49, 65.25,

65.19, 62.05, 61.82, 51.37, 51.35, 41.12, 40.97, 40.77, 40.62, 31.87, 31.80, 30.49, 25.39, 22.03, 19.33, 19.24. HRMS: m/z (EI) calculated $[M]^+$ 256.1675, measured 256.1671.

S10 (68% yield). **S10:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (m, 1H), 5.06 (d, *J* = 17.2 Hz, 1H), 5.01 (d, *J* = 10.4 Hz, 1H), 4.56 (m, 1H), 3.84, (m, 1H), 3.74 (m, 1H), 3.49 (m, 1H), 3.37, (m, 1H), 2.63 (m, 1H), 2.37 (m, 1H), 2.01-1.48 (m, 8H). ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ 175.79, 175.75, 135.19, 116.95, 98.77, 98.56, 65.21, 65.13, 62.15, 61.89, 51.43, 51.40, 42.48, 42.30, 36.58, 36.38, 31.59, 31.47, 30.53, 25.42, 19.39, 19.27. HRMS: m/z (ESI) calculated $[M+Na]^+$ 265.1410, measured 265.1410.

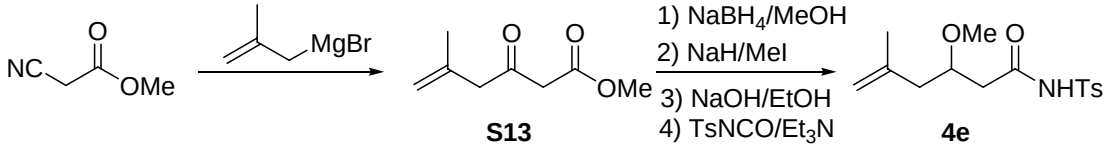
The procedure for oxidation of **S11** by Jones reagent and the preparation of **4f** is the same as that for **4a-*A*** (above). **4f** (67% yield for two steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.69 (br s, 1H), 7.93 (d, *J* = 7.8 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 4.75 (s, 1H), 4.63 (s, 1H), 3.62 (s, 3H), 3.00 (m, 1H), 2.56(dd, *J* = 9.3, 16.2 Hz, 1H), 2.44 (s, 3H), 2.39 (m, 2H), 2.11 (dd, *J* = 9.3, 13.6 Hz, 1H), 1.65 (s, 3H). ^{13}C{1H} NMR (75 MHz, CDCl3) δ 175.2, 169.4, 145.0, 141.6, 135.5, 129.5, 128.3, 113.8, 52.1, 39.9, 38.8, 36.9, 21.7, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 362.1032, measured 362.1028.

Synthesis of 1e: The procedure of synthesis of **S10** is the same as that of **S11**.

To a suspension of LiAlH4 (1.1 g, 30 mmol) in dry THF (50 mL), S10 (3.6 g, 15 mmol) was added. The mixture was stirred for 5 hours. Then the extra of LiAlH4 was quenched by wet THF.. The mixture was extracted with diethyl ether (3x50 mL). The combined organic layer was dried with $MgSO_4$, filtered and concentrated under vacuum. Purification by flash chromatography (silica gel, hexane) gave **S12** 3.0 g (90 yield). **S12**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (m, 1H), 5.05 (d, *J* = 15.2 Hz, 1H), 5.03 (d, *J* = 8.0 Hz, 1H),4.61 (m, 1H), 3.96-3.39, (m, 6H), 2.21-1.49 (m, 10H). ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ 136.80, 136.76, 99.06, 98.92, 66.11, 65.94, 65.73, 65.60, 62.43, 62.38, 39.07, 39.02, 36.38, 36.23, 31.53, 31.49, 30.55, 25.29, 19.51, 19.48. HRMS: m/z (ESI) calculated $[M+Na]^+$ 237.1461, measured 237.1462.

The alcohol (3.0 g, 13.5 mmol) was added to a solution of NaH (0.36 g, 15 mmol) in THF at 0 ^{o}C. After 15 min, BnBr (2.6 g, 15mmol) was added. The mixture was stirred for overnight and 10 mL water was added. The mixture was extracted with diethyl ether (3x50 mL). The combined organic layer was dried with $MgSO_4$, filtered and concentrated under vacuum to give the crude ether 3.4 g. The procedure of synthesis of ether from **S12** is the same as that of 4a-*A*. **1e** (58 % yield for three steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (br s, 1H), 7.87 (d, *J* = 7.8 Hz, 2H), 7.39-7.30 (m, 7H), 5.61 (ddd, *J* = 18.8, 10.4, 5.4 Hz, 1H), 4.97 (d, *J* = 10.4 Hz, 1H), 4.93 (d, *J* = 18.8 Hz, 1H), 4.49 (d, *J* = 11.6 Hz, 2H), 4.45 (d, *J* = 11.6 Hz, 2H), 3.45 (dd, *J* = 9.2, 4.4 Hz, 1H), 3.27 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.41 (s, 3H), 2.30 (m, 2H), 2.18-1.96 (m, 3H). ^{13}C{1H} NMR (100 MHz, CDCl3) δ 170.2, 144.8, 137.4, 135.7, 135.2, 129.4, 128.5, 128.3, 128.0, 127.9, 117.5, 73.3, 72.4, 39.2, 36.0, 35.0, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 338.1577. measured 338.1588.

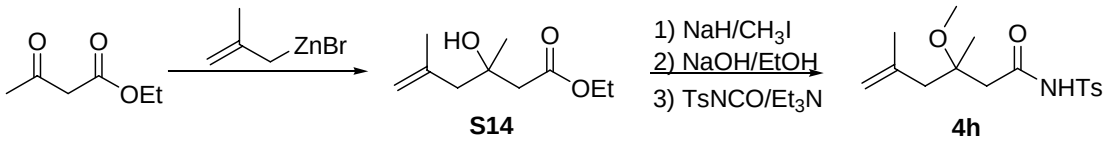
Scheme S7



The procedure is modified from the literature[13]: To a solution of 2-methyl allyl magnesiumbromide (80 mmol) in ether (100 mL), methyl cyanoacetate (4.5g, 40 mmol) was added dropwisely at 0 ^{o}C. The mixture was stirred for overnight and 10% HCl aqueous was added. The mixture was extracted with ether. The organic layer was washed with brine, dried with $MgSO_4$, filtered and concentrated under vacumm. Purification by flash chromatography (silica gel, hexane) gave **S13** 2.7 g (40 % yield). **S13**: ^{1}H NMR (300 MHz, CDCl3) δ 4.99 (s, 1H), 4.86 (s, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.48 (s, 2H), 3.24 (s, 1H), 1.77 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 2H). ^{13}C{1H}NMR (75 MHz, CDCl3) δ 200.8, 167.1, 138.2, 115.8, 61.3, 52.1, 48.1, 22.4, 14.0, 13.9. HRMS: m/z (EI) calculated $[M]^{+}$ 170.0950 measured 170.0943.

To a solution of **S13** (2.0 g, 12 mmol) in methanol (20 mL), NaBH4 (0.6 g, 16.5 mmol) was added in couple potion at 0 ^{o}C. After 1 hour, the NH_4Cl aqueous was added and solvent was removed under vacumm. The mixture was extracted with ether. The organic layer was dried with $MgSO_4$, filtered and concentrated under vacumm to give crude alcohol 1.3g (65% yield). The crude alcohol (1.3 g, 7.6 mmol) dissolved in DMF (10 mL), NaH (0.2 g, 8.3 mmol) was added at -45 ^{o}C. After 10 min, MeI (5.3 g, 38 mmol) was added. The mixture was stirred for 3 hours at the same temperature and slowly raise temperature at 0 ^{o}C, then H_2O (20 mL) was added. The mixture was extracted with ether. The organic layer was washed with brine, dried with $MgSO_4$, filtered and concentrated under vacumm. Purification by flash chromatography (silica gel, hexane) gave methyl ether 0.7 g (55% yield)**.** The methyl ether (0.7 g) was dissolved in mixture of ethanol (5 mL) and NaOH aqueous solution (2N, 3 mL). The mixture was stirred for overnight at 50 ^{o}C. The ethanol was removed under vacumm. The water (10 mL) was added and the mixture was extracted with ether for twice. Then the water phase was acidified with HCl solution (2N) and extracted with ether. The organic layer was dried with $MgSO_4$, filtered and concentrated to afford acid 0.6 g. To a solution of acid (0.6 g, 3.5 mmol） in dry THF (5 mL), TsNCO (0.8 g, 4.0 mmol） was added under Nitrogen. The mixture was stirred for 10 min, then Et_3N (0.5 mL) was added. The mixture was stirred overnight, and a HCl solution (2N, 10 mL) was added. The mixture was extracted with diethyl ether. The combined organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed under vacuum, and the residue was purified by silica gel chromatography to give **4e** 0.9 g (23% yield for four steps). **4e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.26 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.78 (s, 1H), 4.62 (s, 1H), 3.63 (m, 1H), 3.38 (s, 3H), 2.49 (dd, *J* = 15.3, 3.3 Hz, 1H), 2.44 (s, 3H), 2.33 (dd, *J* = 15.3, 7.5 Hz, 1H), 2.28 (dd, *J* = 14.1, 7.5 Hz, 1H), 1.76 (m, 1H), 1.68 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 168.8, 144.9, 140.7, 135.7, 129.4, 128.4, 114.3, 75.9, 56.9, 41.1, 40.7, 22.6, 21.6. HRMS: m/z (ESI) calculated $[M+H]^{+}$ 312.1264, measured 312.1269.

Scheme S8

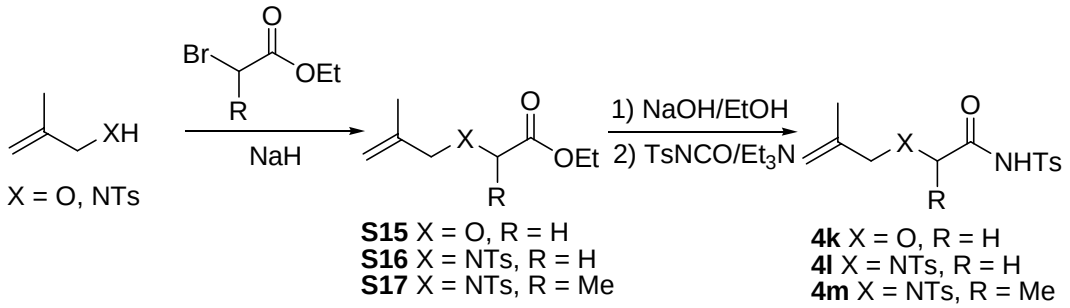


The procedure is modified from the literature: in a 100 ml- three-neck round-bottom flask equipped with a reflux condenser and mechanical stirrer was placed 10.0 g (0.15 mol) of anhydrous Zn powder in 20 mL of anhydrous ether. After the reaction initiated, a mixture solution of ethyl acetoacetate (13.0 g, 0.1 mol) and methyl allyl bromide (16.2 g, 0.12 mol) in 70 mL of 75 % THF-ether (anhydrous) was added dropwisely. The mixture was allowed to stir overnight under nitrogen, decanted from unreacted Zn poured into 100 mL ice water, carefully acidified with 4 N H_2SO_4 and saturated with $(NH_4)_2SO_4$. The mixture was extracted with ether (5 x 50 mL). The combined organic layer were washed with NaOH solution (1 N, 2 x 50 mL) and saturated NaCl solution, dried with $MgSO_4$, and filtered. The ether removed under vacumm to give **S14** 14.6 (85% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.90 (s, 1H), 4.72 (s, 1H), 4.18 (q, *J* = 6.9 Hz, 2H), 3.67 (s, 1H), 2.56 (d, *J* = 15.6 Hz, 1H), 2.42 (d, *J* = 15.6 Hz, 1H), 2.27 (s, 2H), 1.85 (s, 3H), 1.28 (t, *J* = 6.9 Hz, 3H), 1.26 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 173.2, 142.4, 115.1, 71.1, 60.6, 49.5, 44.7, 27.4, 24.5, 14.1. HRMS: m/z (ESI) calculated $[M+Na]^+$ 209.1148, measured 209.1149.

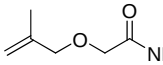
Synthesis of 4h: The procedure of synthesis of **4h** from **S14** is similar as that for **4e**.

4h: (43% yield for three steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.57 (s, 1H), 7.94 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 4.82 (s, 1H), 4.62 (s, 1H), 3.30 (s, 3H), 2.53 (d, *J* = 15.0 Hz, 1H), 2.42 (s, 3H), 2.34 (d, *J* = 13.8 Hz, 1H), 2.25 (d, *J* = 15.0 Hz, 1H), 2.03 (d, *J* = 13.8 Hz, 1H), 1.73 (s, 3H), 1.11 (s, 3H). ^{13}C{1H}NMR (75 MHz, $CDCl_3$) δ 169.0, 144.6, 140.5, 135.7, 129.2, 128.1, 115.8, 76.1, 49.2, 46.5, 44.1, 23.7, 22.0, 21.4. HRMS: m/z (ESI) calculated $[M+Na]^+$ 384.1240, measured 384.1235.

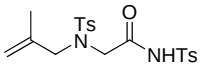
Scheme S9

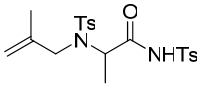


The compounds **4k-4m** were synthesized from **S15-S17** [S14] respectively, according to the same procedure as that of **4h** (see above).

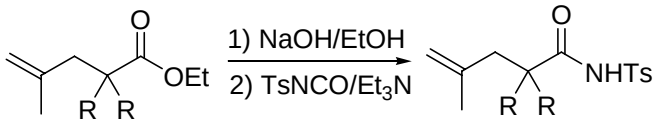


4k (53% yield, two steps) : ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (br s, 1H), 7.98 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.97 (s, 1H), 4.95 (s, 1H), 3.94 (s, 2H), 3.88 (s, 2H), 2.44 (s, 3H), 1.73 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 167.5, 145.2, 134.0, 135.3, 129.5, 128.4, 114.4, 75.6, 68.5, 21.6, 19.2. HRMS: m/z (ESI) calculated $[M+Na]^+$ 306.0771, measured 306.0772.

 **4l** (72% yield, two steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.13 (br s. 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.82 (s, 1H), 4.75 (s, 1H), 3.64 (s, 2H), 3.61 (s, 2H), 2.45 (s, 3H)， 2.43 (s, 3H), 1.68 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 166.4, 145.1, 144.5, 138.4, 135.2, 133.9, 130.0, 129.4, 128.4, 127.4, 117.3, 56.5, 51.0, 21.6, 21.5, 19.8. HRMS: m/z (ESI) calculated $[M+Na]^+$ 459.1019, measured 459.1012.

 **4m** (86% yield, two steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (br s, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 4.73 (s, 1H), 4.64 (s, 1H), 4.27 (q, *J* = 6.8 Hz, 1H), 3.88 (d, *J* = 14.8 Hz, 1H), 3.51 (d, *J* = 14.8 Hz, 1H), 2.45 (s, 3H), 2.44 (s, 3H), 1.64 (s, 3H), 1.00 (d, *J* = 7.2 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 168.2, 145.0, 144.5, 139.1, 135.5, 135.4, 130.1, 129.4, 128.6, 127.1, 116.6, 55.4, 50.4, 21.6, 21.5, 19.9, 11.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 473.1175, measured 473.1158.

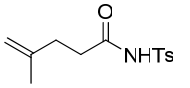
Scheme S10

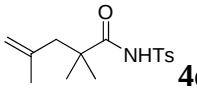


S18 R= H
S19 R = Me

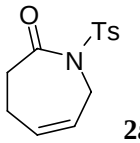
4n R= H
4o R = Me

The compounds **4n-4o** were synthesized from **S18-S19**[S15] respectively, according to the same procedure as that of **4h** (see above).

 **4n:** ^{1}H NMR (300MHz, $CDCl_3$) δ 9.26 (br s, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.68 (s, 1H), 4.58 (s, 1H), 2.44 (s, 3H), 2.41 (t, *J* = 8.1 Hz, 2H), 2.25 (t, *J* = 8.1 Hz, 2H), 1.65 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.8, 145.1, 143.3, 135.4, 129.5, 128.3, 110.8, 34.4, 31.7, 22.3, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 290.0821, measured 290.0824.

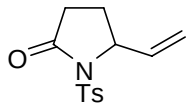
 **4o:** ^{1}H NMR (300MHz, $CDCl_3$) δ 8.92 (br s,1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.71 (s, 1H), 4.49 (s, 1H), 2.44 (s, 3H), 2.22 (s, 2H), 1.47 (s, 3H), 1.15 (s, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 175.6, 145.0, 141.2, 135.2, 129.4, 128.5, 114.8, 47.8, 43.1, 25.1, 23.5, 21.6. HRMS: m/z (EI) calculated $[M]^+$ 295.1242, measured 295.1239.

Product characterized data:



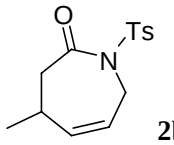
2a

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.89 (m, 1H), 5.78 (dt, *J* = 11.1, 3.6 Hz, 1H), 4.58 (d, *J* = 6.0 Hz, 1H), 2.77 (t, *J* = 6.6 Hz, 2H), 2.42 (s, 3H), 2.36 (m, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 173.4, 144.5, 136.2, 132.1, 129.2, 128.3, 123.7, 42.1, 35.1, 24.9, 21.6. Anal. Calcd. for $C_{13}H_{15}NO_3S$: C, 58.85; H, 5.70; N. 5.28. Found: C, 58.82; H, 5.71; N. 5.26.



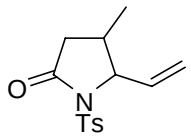
3a

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.84 (ddd, *J* = 16.8, 10.5, 7.2 Hz, 1H), 5.35 (d, *J* = 16.8 Hz, 1H), 5.26 (d, *J* = 10.5 Hz, 1H), 4.91 (t, *J* = 7.2 Hz, 1H), 2.60-2.25 (m, 3H), 2.43 (s, 3H), 1.86(m, 1H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 173.1, 145.0, 135.7, 135.6, 129.3, 128.5, 117.6, 61.8, 30.4, 25.8, 21.6.



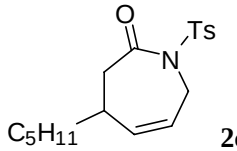
2b

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 5.83 (dt, *J* = 11.2, 6.0 Hz, 1H), 5.67 (dd, *J* = 11.2, 3.6 Hz, 1H), 4.55 (d, *J* = 6.0 Hz, 1H), 2.78 (dd, *J* = 12.8, 3.6 Hz, 1H), 2.62 (m, *J* = 12.8, 4.4Hz, 1H), 2.53 (m, 1H), 2.41 (s. 3H), 0.95 (d, *J* = 6.8 Hz, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 172.2, 144.5, 138.1, 136.3, 129.1, 128.4, 122.3, 42.1, 42.0, 30.7, 21.6, 20.8. HRMS: m/z (ESI) calculated $[M+H]^+$ 280.1002, measured 280.1010.



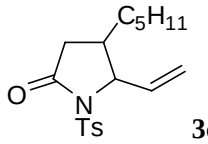
3b

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.81 (ddd, *J* = 16.8, 10.0, 6.8 Hz, 1H), 5.36 (d, *J* = 16.8 Hz, 1H), 5.26 (d, *J* = 10.0 Hz, 1H), 4.39 (d, *J* = 7.2 Hz, 1H), 2.68 (dd, *J* = 17.2, 8.0 Hz, 1H), 2.43 (s, 3H), 2.16 (m, 1H), 1.99 (dd, *J* = 17.2, 3.2 Hz, 1H), 1.07 (d, *J* = 6.8 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 172.8, 145.0, 135.6, 135.5, 129.4, 128.4, 117.4, 69.2, 38.3, 33.2, 21.7, 19.3. HRMS: m/z (ESI) calculated $[M+H]^+$ 280.1002, measured 280.1007.



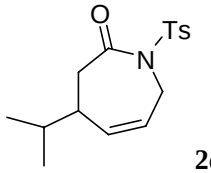
2c

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.86 (m, 1H), 5.72 (dd, *J* = 11.1, 3.0 Hz, 1H), 4.55 (m, 1H), 2.76 (dd, *J* = 13.2, 3.9 Hz, 1H, 1H), 2.63 (dd, *J* = 13.2, 8.4 Hz, 1H), 2.41 (s, 1H), 235 (m. 1H), 1.32-1.17 (m, 9H), 0.84 (t, *J* = 6.6 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 172.4, 144.4, 137.0, 136.3, 129.1, 128.5, 122.7, 42.1, 40.0, 35.5, 34.9, 31.6, 26.0, 22.3, 21.6, 14.0. HRMS: m/z (ESI) calculated $[M+H]^+$ 336.1628, measured 336.1633.



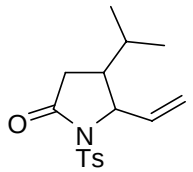
3c

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.82 (ddd, *J* = 17.2, 10.4, 6.8 Hz, 1H), 5.36 (d, *J* = 17.2 Hz, 1H), 5.26 (d, *J* = 10.4 Hz, 1H), 4.49 (d, *J* = 7.2 Hz, 1H), 2.65 (dd, *J* = 8.0, 17.6 Hz, 1H), 2.43 (s, 3H), 2.07 (dd, *J* = 17.6, 2.8 Hz, 1H), 2.00 (m, 1H), 1.36-1.15 (m, 8H), 0.88 (t, *J* = 7.2 Hz, 6H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 172.9, 145.0, 135.9, 135.7, 129.4, 128.4, 117.2, 67.3, 38.4, 36.7, 33.6, 31.5, 26.4, 22.4, 21.6, 13.9. HRMS: m/z (ESI) calculated $[M+H]^+$ 336.1628, measured 336.1633.



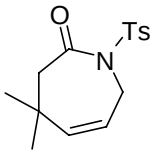
2d

The compound **2d** is difficult to isolate from the mixture of **2d** and **3d**. **2d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 5.95 (m, 1H), 5.71 (d, *J* = 11.6 Hz, 1H), 4.65 (dd, *J* = 16.8, 7.6 Hz, 1H), 4.46 (dq, *J* = 16.8, 2.4 Hz, 1H), 2.87 (dd, *J* = 13.2, 10.8 Hz, 1H), 2.46 (dd, *J* = 13.2, 3.2 Hz, 1H), 2.29 (m, 1H), 1.68 (m, 1H), 0.87 (d, J = 0.66 Hz, 6H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 173.2, 144.5, 136.3, 135.8, 129.2, 128.4, 124.0, 42.4, 41.6, 37.6, 32.6, 21.6, 19.2, 19.0. HRMS: m/z (ESI) calculated $[M+H]^+$ 308.1315 measured 308.1318.



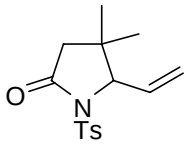
3d

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.81 (ddd, *J* = 16.8, 9.9, 7.5 Hz, 1H), 5.34 (d, *J* = 16.8 Hz, 1H), 5.24 (d, *J* = 9.9 Hz, 1H), 4.65 (d, *J* = 6.6 Hz, 1H), 2.63 (dd, *J* = 17.7, 9 Hz, 1H), 2.43 (s, 3H), 2.23 (dd, *J* = 17.7, 3 Hz, 1H), 1.88 (m, 1H), 1.65 (m, 1H), 0.89 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.9 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 173.0, 145.0, 136.6, 135.8, 129.3, 128.6, 117.1, 64.9, 44.3, 33.9, 30.8, 21.7, 19.6, 18.8. HRMS: m/z (ESI) calculated $[M+H]^+$ 308.1315 measured 308.1314.



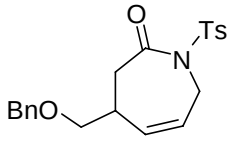
2f

The compound **2f** is difficult to isolate from the mixture of **2f** and **3f**. **2f**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.74 (m, 1H), 5.52 (d, *J* = 11.2 Hz, 1H), 4.53 (d, *J* = 6.8 Hz, 2H), 2.63 (s, 2H), 2.41 (s, 3H), 0.93 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 171.6, 144.5, 142.7, 136.3, 129.1, 128.5, 120.3, 47.9, 42.0, 34.8, 29.2, 23.5, 21.7. HRMS: m/z (ESI) calculated $[M+H]^+$ 294.1158, measured 294.1155.

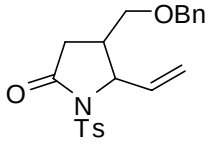


3f

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.6 Hz, 2H), 5.73 (ddd, *J* = 17.2, 10.4, 7.6 Hz, 1H), 5.38 (d, *J* = 17.2 Hz, 1H), 5.33 (d, *J* = 10.4 Hz, 1H), 4.34 (d, *J* = 7.6 Hz, 1H), 2.43 (s, 3H), 2.37 (d, *J* = 16.8 Hz, 1H), 2.06 (d, *J* = 16.8 Hz, 1H), 1.11 (s, 3H), 1.02 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 172.4, 144.9, 135.5, 133.4, 129.3, 128.5, 119.0, 72.0, 44.8, 37.3, 28.2, 23.4, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 294.1158, measured 294.1155.

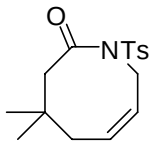


^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.7 Hz, 2H), 7.34-7.25 (m, 7H), 5.98 (m, 1H), 5.75 (d, *J* = 9.9 Hz, 1H), 4.62 (dd, *J* = 6.6, 17.1 Hz, 1H), 4.52 (dd, *J* = 6.6, 17.1 Hz, 1H), 4.43 (d, *J* = 12.11 Hz, 1H), 4.38 (d, *J* = 12.1 Hz, 1H),3.27 (m, 2H), 2.90 (dd, J = 12.6, 9.0 Hz, 1H), 2.72 (dd, J = 12.6, 3.6 Hz, 1H), 2.60 (m, 1H), 2.41 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 172.2, 144.5, 137.8, 136.2, 133.7, 129.2, 128.5, 128.4, 127.7, 127.6, 124.8, 73.1, 72.5, 42.1, 38.0, 36.6, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 386.1421, measured 386.1428.



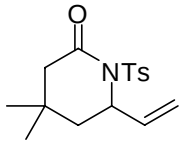
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.39-7.27 (m, 7H), 5.86 (ddd, J = 17.2, 10.0, 6.8 Hz, 1H), 5.38 (d, *J* = 17.2 Hz, 1H), 5.27 (d, *J* = 10.0 Hz, 1H), 4.77 (d, *J* = 7.6 Hz, 1H), 4.44 (d, *J* = 2.4 Hz, 2H), 3.40-3.22 (m, 2H), 2.65 (dd, J = 17.6, 8.4 Hz, 1H), 2.42 (s, 3H), 2.32 (m, 1H), 2.17 (dd, J = 17.6, 2.4 Hz, 1H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 172.5, 144.9, 137.5, 135.8, 135.6，129.4, 128.6, 128.4, 127.9, 127.6, 117.3, 73.2, 70.4, 64.2, 42.1, 38.4, 33.6, 21.7. HRMS: m/z (ESI)

calculated $[M+H]^+$ 386.1421, measured 386.1425.



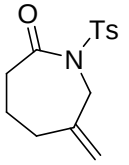
2g

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 5.85 (m, 1H), 5.68 (dt, *J* = 12.0, 4.2 Hz, 1H), 4.55 (m, 1H), 2.42 (s, 3H), 2.32 (s. 2H), 2.02 (d, J = 7.8 Hz, 2H), 0.96 (s, 6H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 173.0, 144.5, 136.4, 129.7, 129.1, 128.7, 126.8, 47.2, 47.1, 39.2, 36.6, 28.6, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 308.1315, measured308.1316.



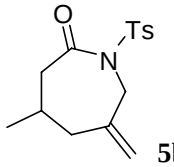
3g

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 5.86 (ddd, *J* = 17.2, 10.4, 5.6 Hz, 1H), 5.29 (d, *J* = 17.2 Hz, 1H), 5.24 (d, *J* = 1.04 Hz, 1H), 5.11 (m, 1H), 2.42 (s, 3H), 2.34 (d, *J* = 16.4 Hz, 1H), 2.15 (d, *J* = 16.1 Hz, 1H), 1.97 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.72 (dd, *J* = 14.0, 5.6 Hz, 1H), 1.04 (s, 3H), 0.94 (s, 3H). ^{13}C{1H} NMR (100 MHz, $CDCl_3$) δ 170.7, 144.6, 138.6, 136.4, 129.1, 129.0, 116.2, 57.6, 47.2, 42.4, 31.0, 30.7, 28.7, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 330.1134, measured 330.1136.



5a

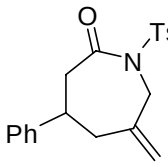
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.26 (s, 1H), 5.10 (s, 1H), 4.50 (s, 2H), 2.63 (m, 2H), 2.41 (s, 3H), 2.37 (t, *J* = 6.3 Hz, 2H), 1.71 (m, 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 173.5, 144.4, 142.3, 136.0, 129.1, 128.6, 116.8, 50.1, 37.8, 36.6, 23.0, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 280.1002, measured 280.1007.



5b

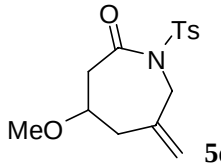
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.29 (s, 1H), 5.10 (s, 1H), 4.63 (d, *J* = 15.3 Hz, 2H), 4.37 (d, *J* = 15.3 Hz, 2H), 2.55 (m, 3H), 2.41 (s, 3H), 2.08 (dd, *J* = 13.8, 8.4 Hz, 1H), 1.92 (m, 1H), 0.88 (d, *J* = 6.6 Hz 2H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 172.5, 144.5, 141.0, 136.0, 129.1, 128.6,

117.4, 50.0, 44.8, 44.6, 29.1, 21.6, 21.0. HRMS: m/z (ESI) calculated $[M+H]^+$ 294.1158, measured 294.1159.



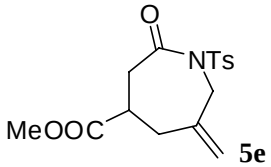
5c

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.24 (m, 5H), 7.09 (d, *J* = 6.6 Hz, 2H), 5.33 (s, 1H), 5.14 (s, 1H), 5.01 (d, *J* = 15.9 Hz, 1H), 4.26 (d, *J* = 15.9 Hz, 1H), 3.07 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.87 (m, 1H), 2.74 (d, *J* = 13.8 Hz, 1H), 2.65 (dd, *J* = 13.8, 3.6 Hz, 1H), 2.48 (d, *J* = 13.8 Hz, 1H), 2.44 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 172.1, 144.7, 144.6, 141.4, 136.1, 129.3, 128.8, 128.7, 126.9, 126.3, 117.7, 50.0, 45.0, 44.8, 40.6, 21.7. HRMS: m/z (ESI) calculated $[M+H]^+$ 356.1315, measured 356.1327.



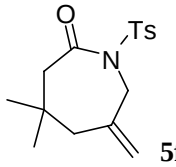
5d

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 5.36 (s, 1H), 5.19 (s, 1H), 4.67 (d, *J* = 15.6 Hz, 1H), 4.45 (d, *J* = 15.6 Hz, 1H), 3.52 (m, 1H), 3.16 (s, 3H), 2.88 (d, *J* = 5.1 Hz 2H), 2.61 (dd, *J* = 14.1, 5.7 Hz, 1H), 2.46 (dd, J = 14.1, 3.6 Hz, 1H), 2.41 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.2, 144.4, 138.5, 135.7, 129.0, 128.7, 119.0, 73.6, 56.1, 49.8, 42.7, 41.8, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 310.1108, measured 310.1114.



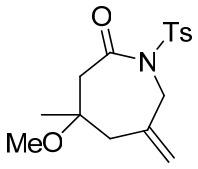
5e

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 5.31 (s, 1H), 5.16, (s, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.24 (d, *J* = 15.6 Hz, 1H), 3.64 (s, 3H), 3.00 (dd, *J* = 14.1, 9.6 Hz, 1H), 2.80-2.50 (m, 4H), 2.42 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 173.0, 171.0, 144.7, 139.6, 135.7, 129.2, 128.7, 118.1, 52.3, 49.7, 39.2, 38.3, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 360.0876, measured 360.0874.



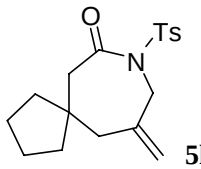
5f

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.30 (s, 1H), 5.08 (s, 1H), 4.52 (s, 2H), 2.48 (s, 2H), 2.42 (s, 2H), 2.16 (s, 2H), 0.84 (s, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 171.8, 144.5, 140.4, 136.0, 129.0, 128.7, 117.7, 50.9, 50.0, 49.9, 32.2, 28.3, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 308.1315, measured 308.1321.



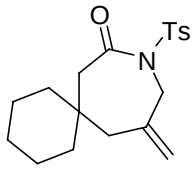
5g

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.38 (s, 1H), 5.18, (s, 1H), 4.73 (d, *J* = 15.6 Hz, 1H), 4.37 (d, *J* = 15.6 Hz, 1H), 3.0 (s, 3H), 2.82 (s, 2H), 2.63 (d, *J* = 14.1 Hz, 1H), 2.41 (s, 3H), 2.28 (d, *J* = 14.1 Hz, 1H), 1.13 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.1, 144.3, 139.2, 135.6, 128.9, 128.8, 119.0, 73.7, 49.6, 49.3, 48.3, 47.8, 24.2, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 346.1084, measured 346.1093.



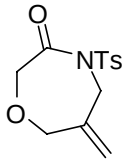
5h

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 5.29 (s, 1H), 5.07 (s, 1H), 4.51 (s, 2H), 2.57 (s, 2H), 2.42 (s, 3H), 2.22 (s, 2H), 1.57 (m, 4H), 1.28 (m, 4H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 172.0, 144.4, 141.0, 136.1, 129.0, 128.6, 117.6, 50.0, 48.9, 48.8, 43.1, 37.8, 23.8, 21.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 334.1471, measured 334.1463.



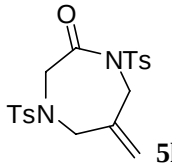
5i

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 5.27 (s, 1H), 5.05 (s, 1H), 4.53 (s, 2H), 2.50 (s, 2H), 2.43 (s, 3H), 2.17 (s, 2H), 1.36-1.11 (m, 10H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 171.9, 144.4, 140.1, 136.0, 129.0, 128.7, 117.3, 50.2, 48.2, 47.3, 36.3, 34.7, 25.6, 21.6, 21.2., HRMS: m/z (ESI) calculated $[M+H]^+$ 348.1628, measured 348.1638.



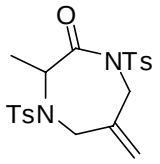
5j

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 5.43 (s, 2H), 5.27 (s, 1H), 4.60 (s, 2H), 4.24 (s, 2H), 4.18 (s, 2H), 2.43(s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 171.1, 144.9, 141.2, 135.8, 129.3, 128.5, 118.6, 74.3, 72.4, 48.2, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 304.0614, measured 304.0623.



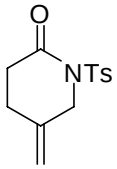
5k

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 4H), 5.34 (s, 1H), 5.24 (s, 1H), 4.38 (s, 2H), 3.92 (s, 2H), 3.91(s, 2H), 2.39 (s, 6H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 167.9, 145.0, 144.3, 138.3, 135.5, 135.0, 130.1, 129.4, 128.6, 127.1, 120.2, 53.6, 52.9, 48.9, 21.7, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 457.0862,measured 457.0850.



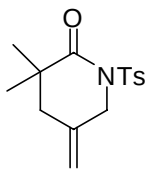
5l

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.1 Hz, 2H), 7.30 (m, 4H), 5.39 (s, 1H), 5.29 (s, 1H), 4.70 (m, 2H), 4.45 (d, *J* = 15.9 Hz, 1H), 4.04 (d, *J* = 14.1 Hz, 1H), 3.62 (d, *J* = 14.1 Hz, 1H), 2.44 (s, 6H), 1.18 (d, *J* = 6.9 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 171.4, 144.9, 144.2, 139.4, 136.4, 135.6, 130.1, 129.4, 128.5, 126.9, 119.0, 57.7, 48.8, 48.6, 21.7, 21.6, 15.9. HRMS: m/z (ESI) calculated $[M+H]^+$ 449.1199, measured 449.1205.



5m

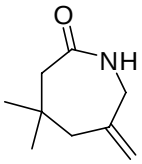
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.15 (s, 1H), 5.04 (s, 1H), 4.50 (s, 2H), 2.48 (s, 4H), 2.43 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 170.3, 144.9, 137.9, 135.8, 129.3, 128.6, 112.8, 51.3, 34.3, 27.3, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 288.0665, measured 288.0671.



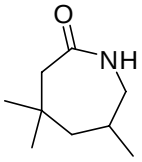
5n

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 5.16 (s, 1H), 5.00 (s, 1H), 4.51 (s, 2H), 2.43 (s, 3H), 2.32 (s, 2H), 1.11 (s, 6H). ^{13}C{1H}

NMR (75 MHz, $CDCl_3$) δ 175.9, 144.6, 136.1, 135.9, 129.3, 128.4, 113.8, 52.3, 43.0, 41.0, 25.8, 21.6. HRMS: m/z (ESI) calculated $[M+Na]^+$ 316.978, measured 316.0977.



^1H NMR (300 MHz, $CDCl_3$) δ 6.27 (br s, 1H), 4.92 (s, 1H), 4.88 (s, 1H), 3.69 (d, J = 5.4 Hz, 2H), 2.39 (s, 2H), 2.20 (s, 2H), 1.03 (s, 6H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 175.4, 142.3, 114.9, 51.2, 47.9, 47.7, 31.4, 28.5. HRMS: m/z (ESI) calculated $[M+H]^+$ 154.1226, measured 154.1220.



^1H NMR (300 MHz, $CDCl_3$) δ 6.72 (s, 1H), 2.96 (t, J = 5.4 Hz, 2H), 2.60 (d, J = 13.5 Hz, 1H), 2.17 (dt, J = 13.5, 2.1 Hz, 1H), 1.85 (m, 1H), 1.62 (d, J = 13.5 Hz, 1H), 1.19 (t, J = 12.6 Hz, 1H), 1.05 (s, 3H), 1.03 (s, 3H), 0.87 (d, J = 6.9 Hz, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 176.5, 53.3, 49.2, 48.6, 33.8, 31.2, 30.8, 24.3, 20.6. HRMS: m/z (ESI) calculated $[M+H]^+$ 156.1383, measured 156.1378.

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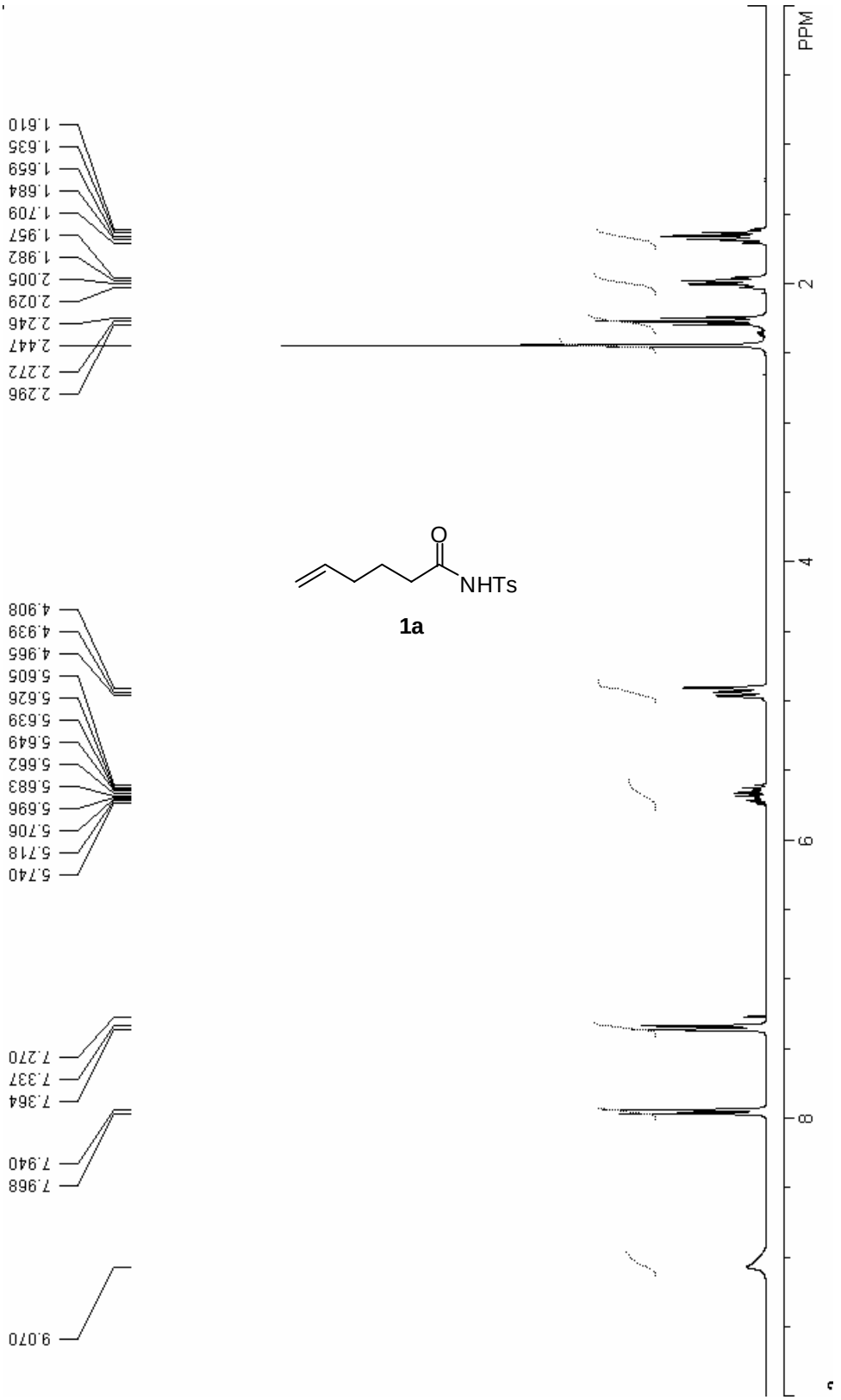
(S15) Donaldson, W. A.; Hossain, M. A.; Cushnie, C. D. *J. Org. Chem.* **1995**, *60*, 1611 – 1618.

New Compound's Spectrum



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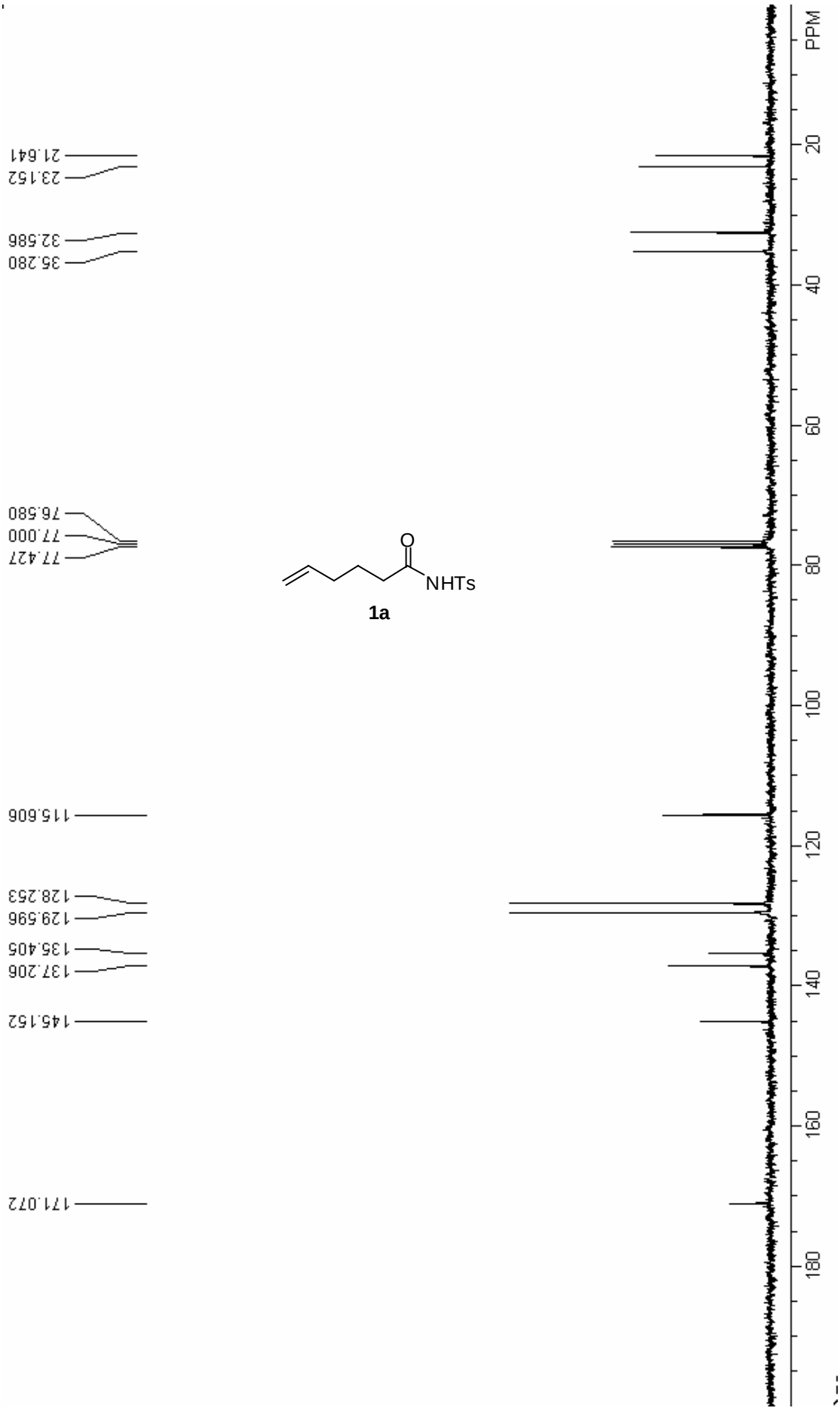
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O
NHTs
PPM
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60
80
100
120
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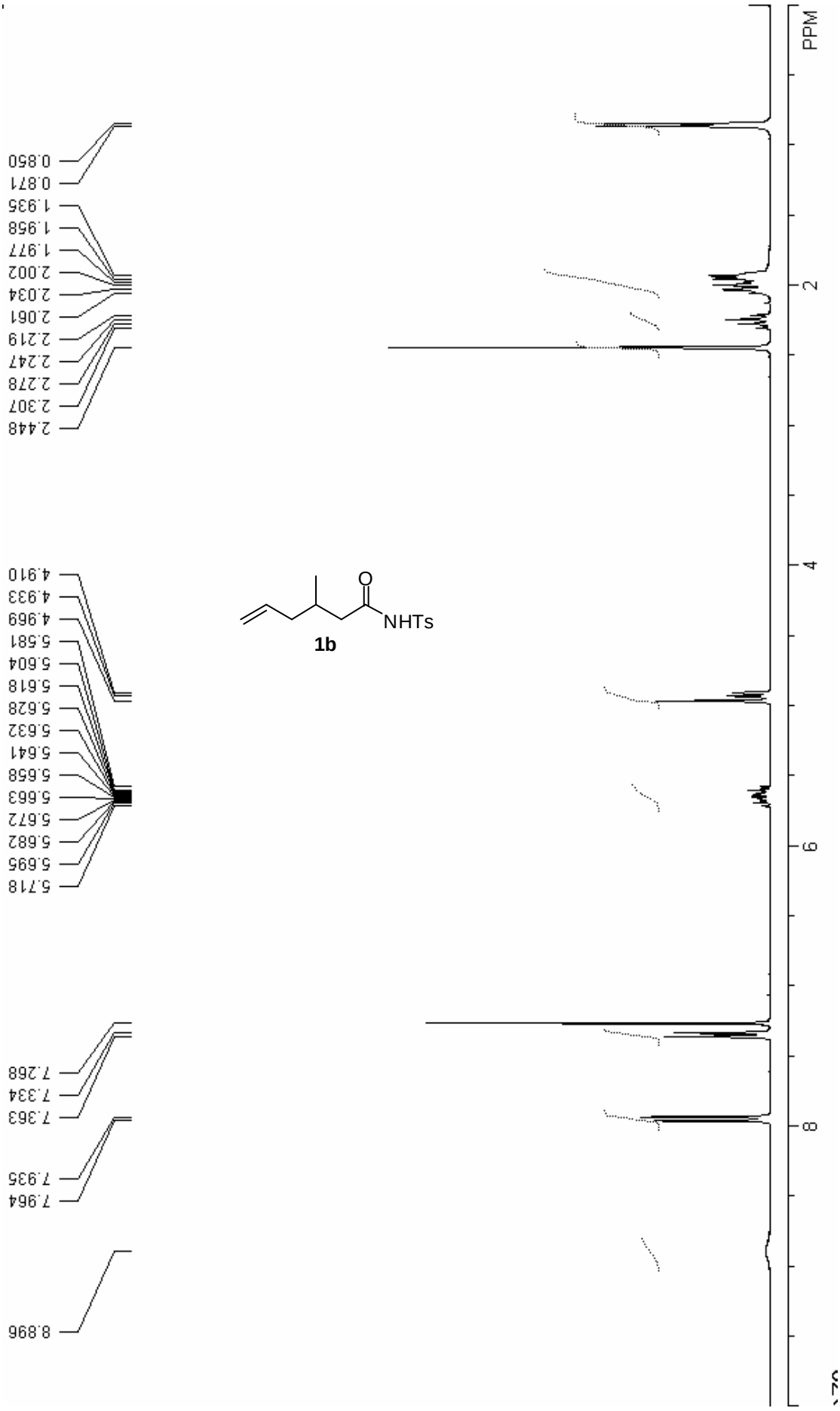
180

1a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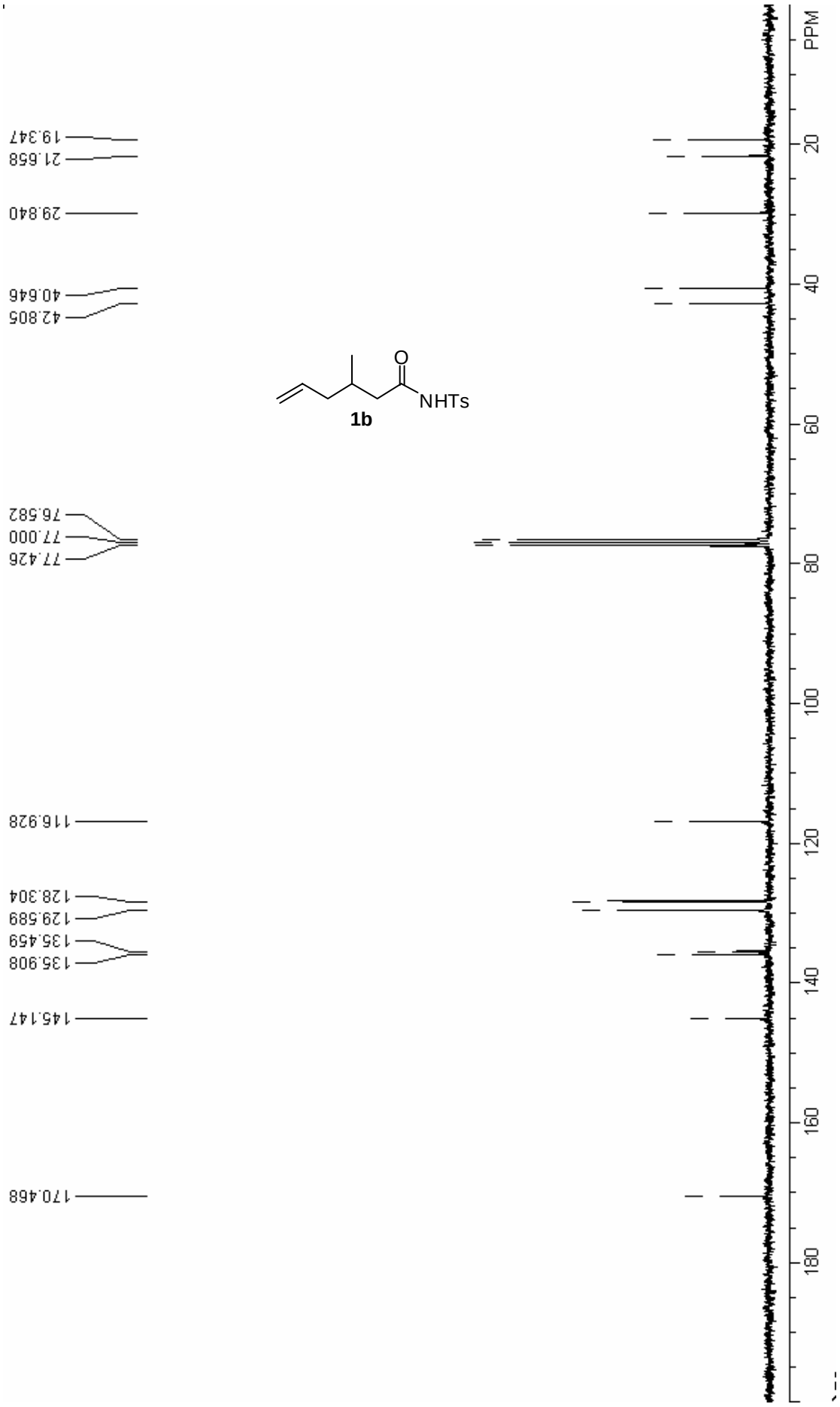
NHTs
1b
PPM
2
4
6
8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1b
PPM
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40
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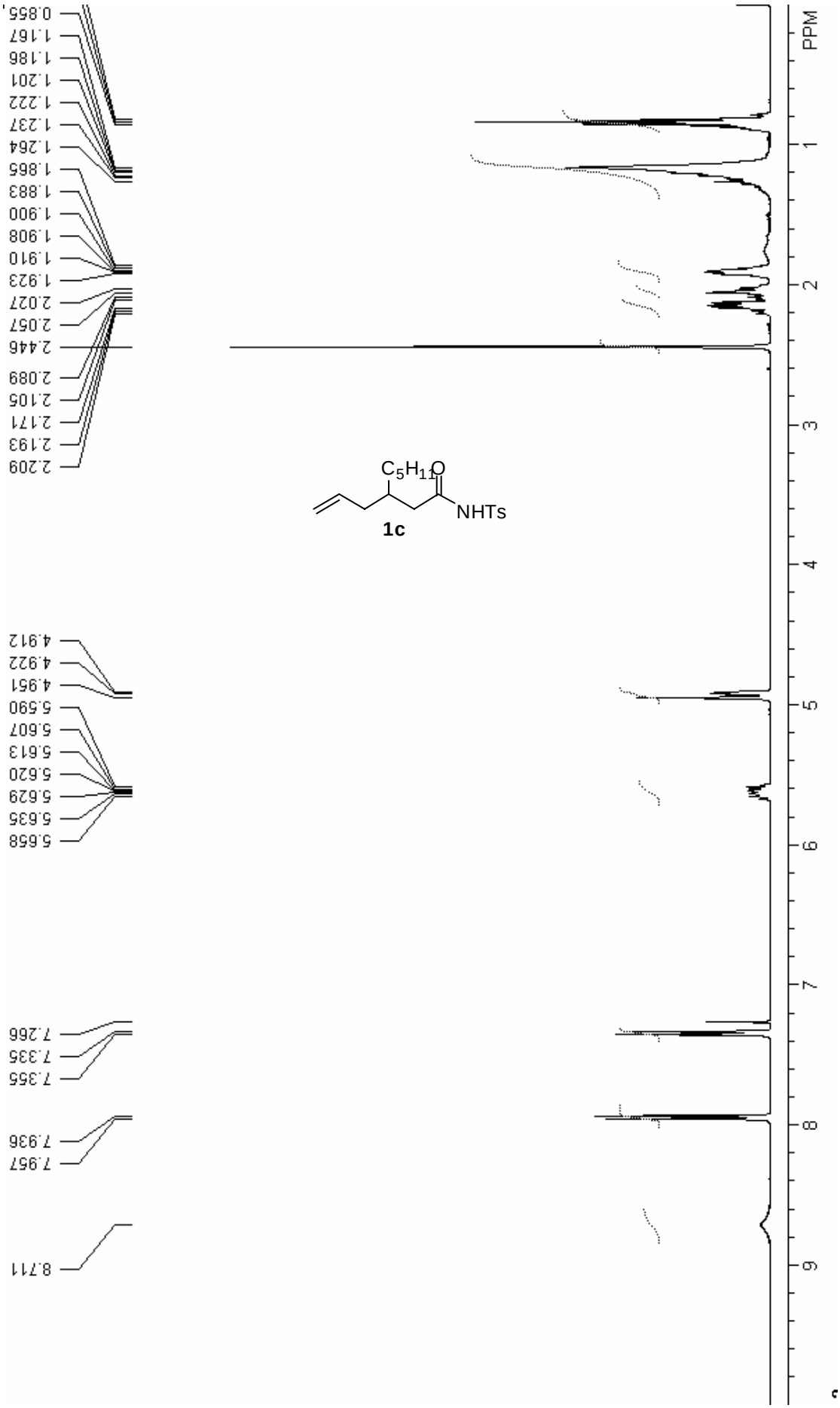
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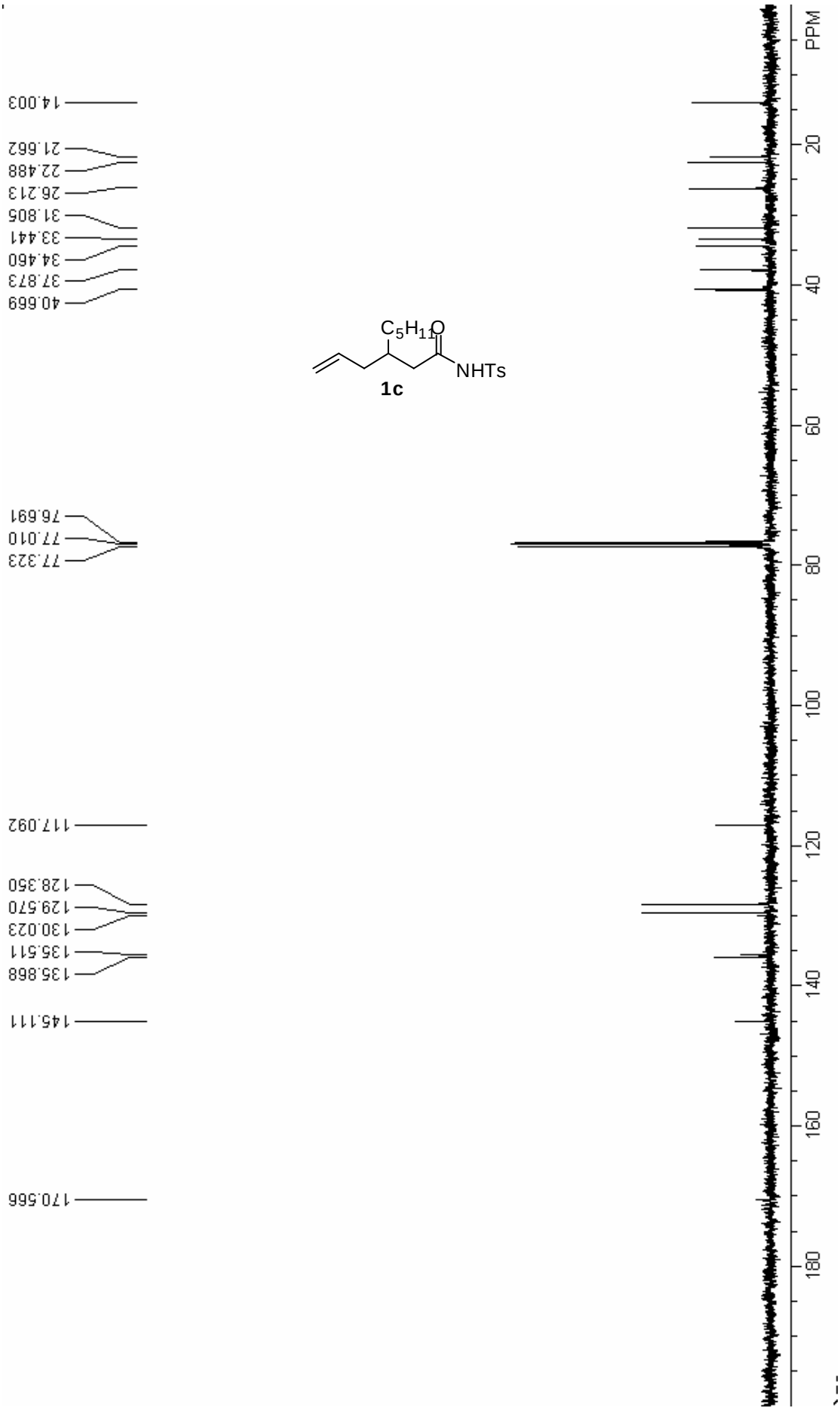
C5H11O
NHTs
1c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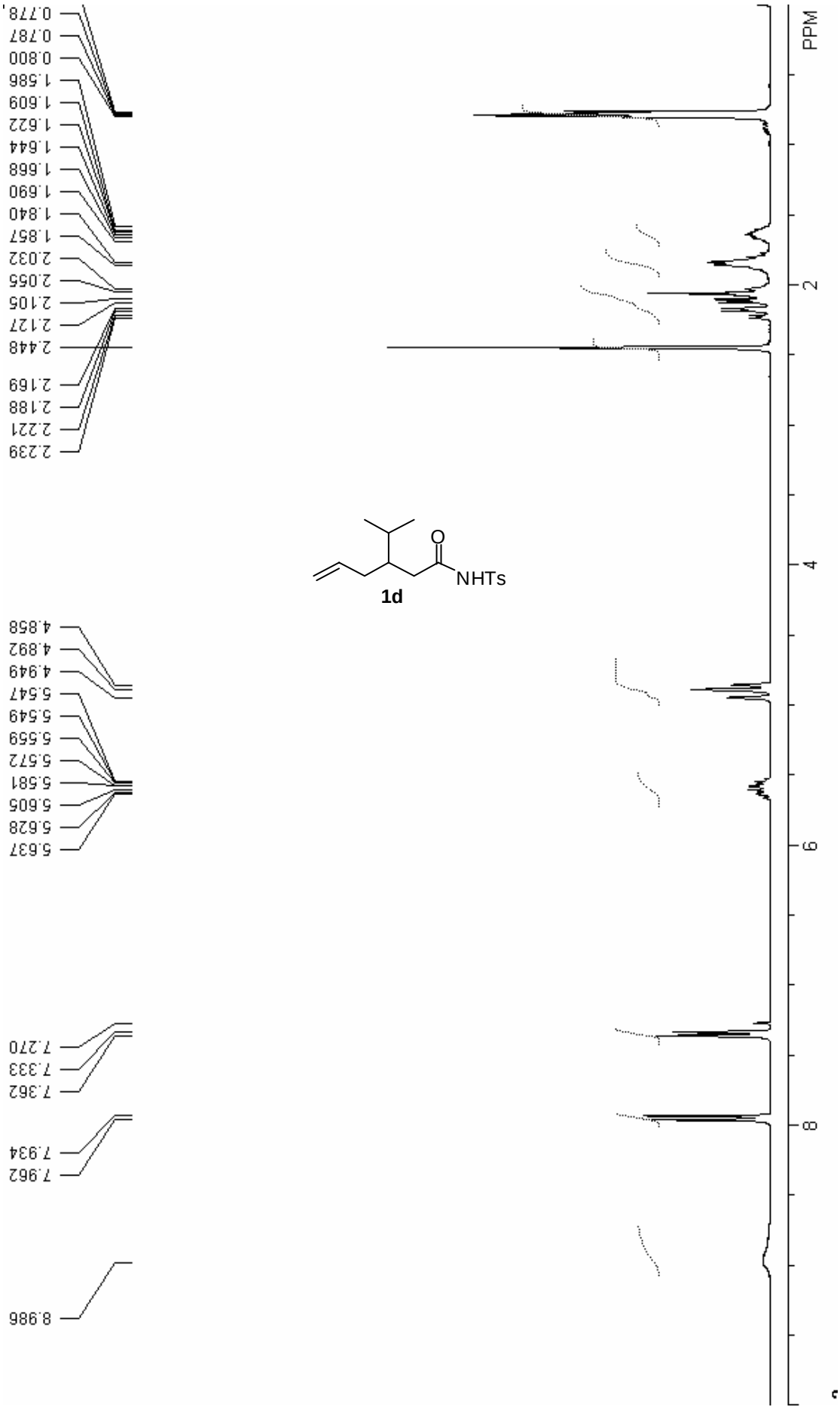
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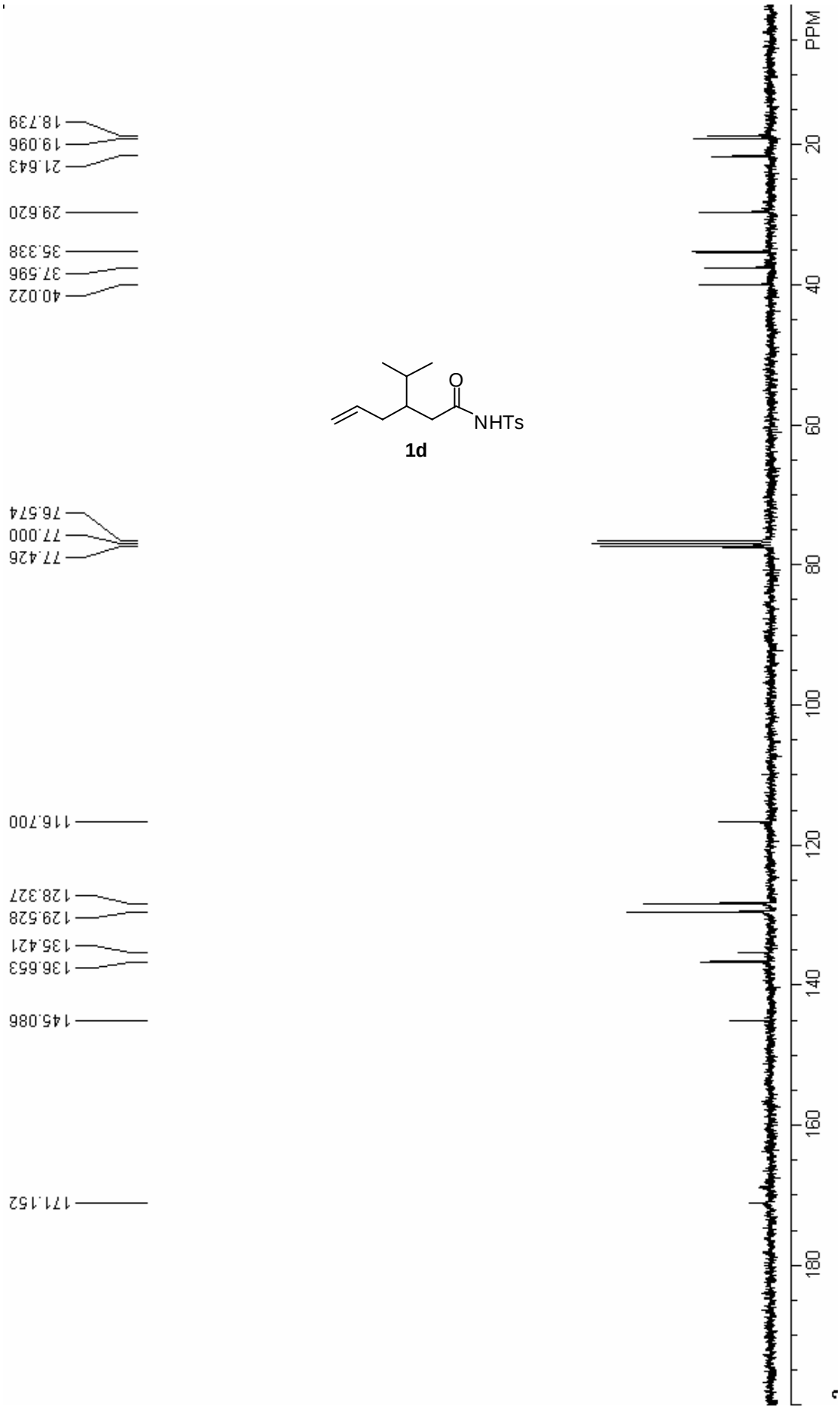
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120
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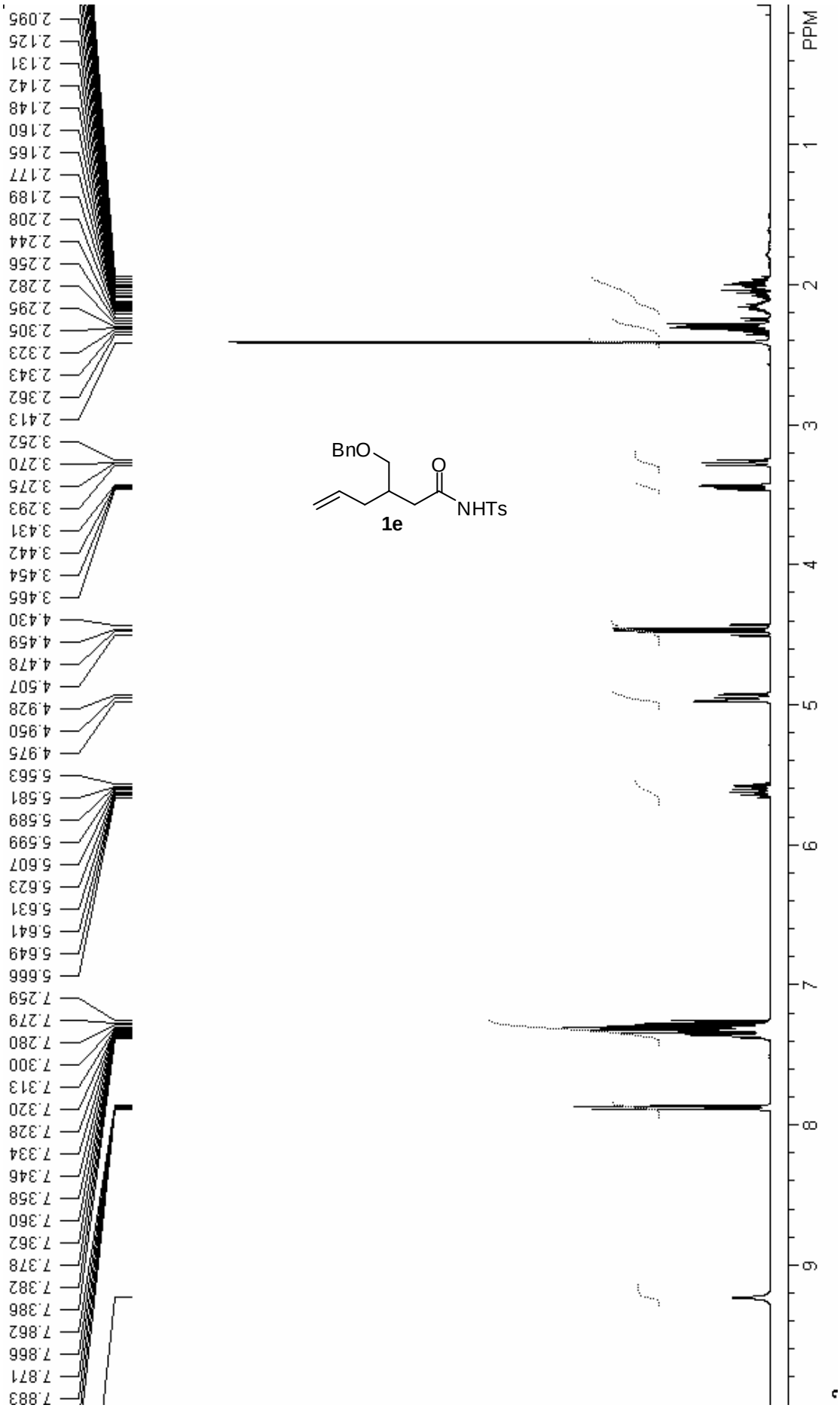
O
NHTs

1d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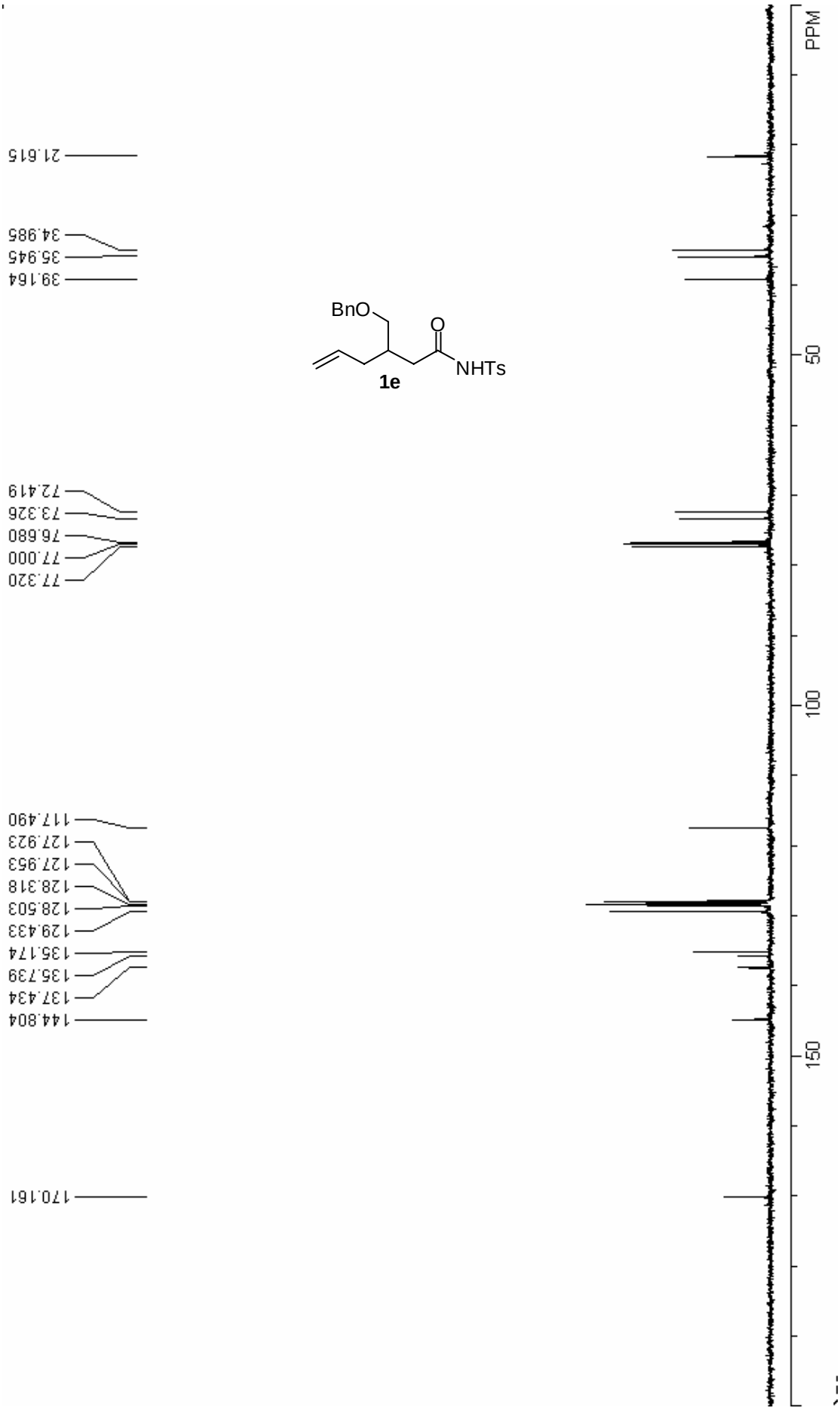
9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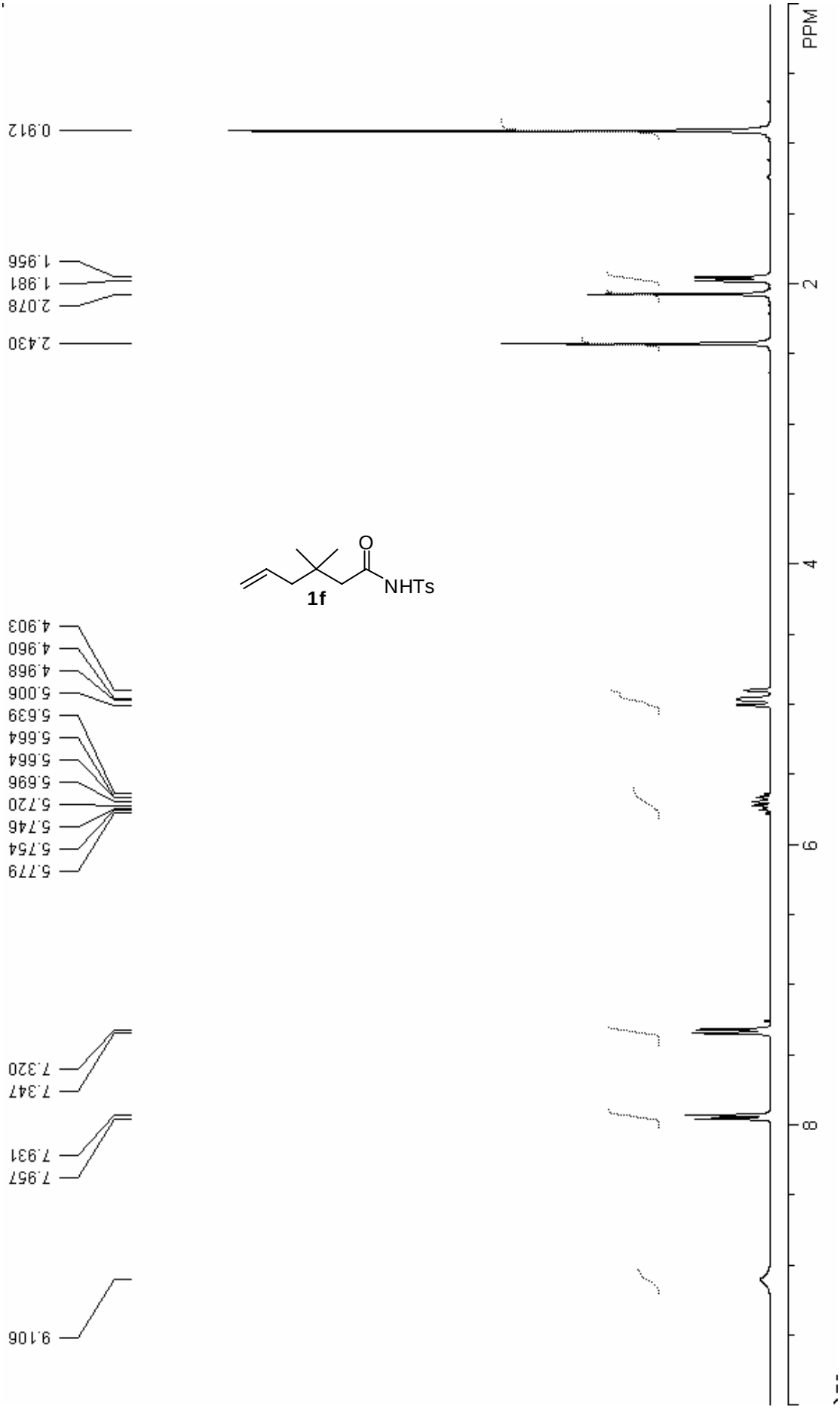
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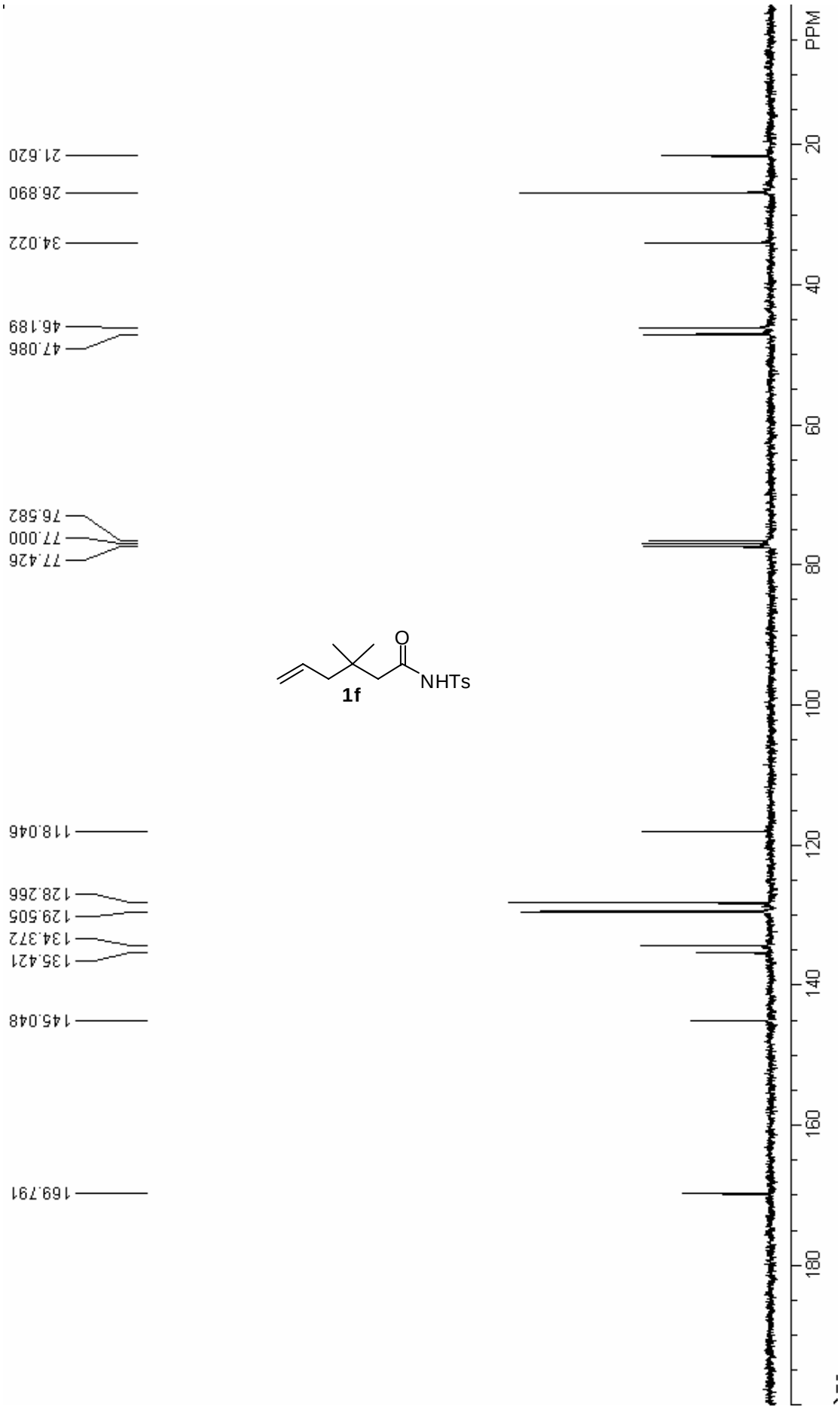
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NHTs
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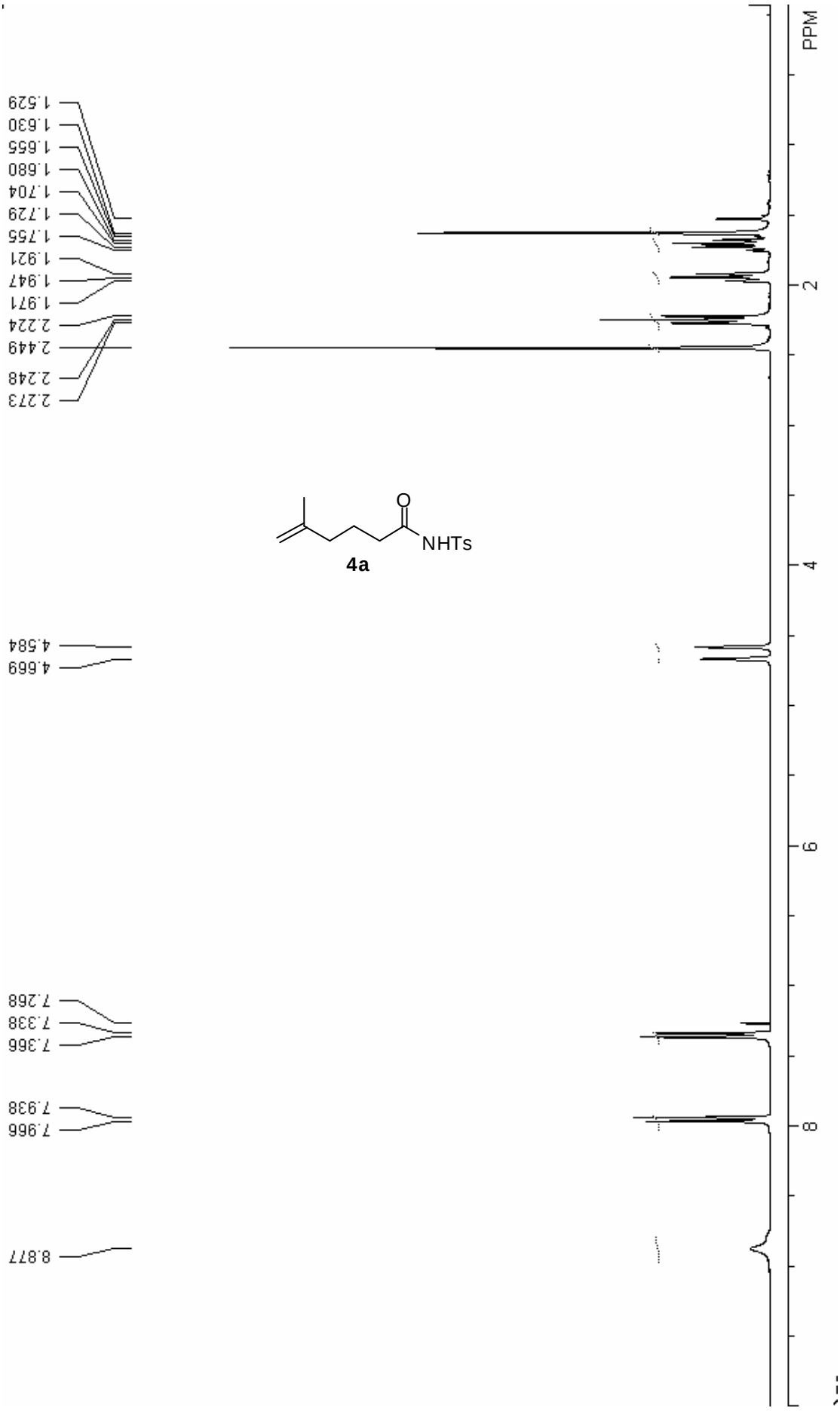
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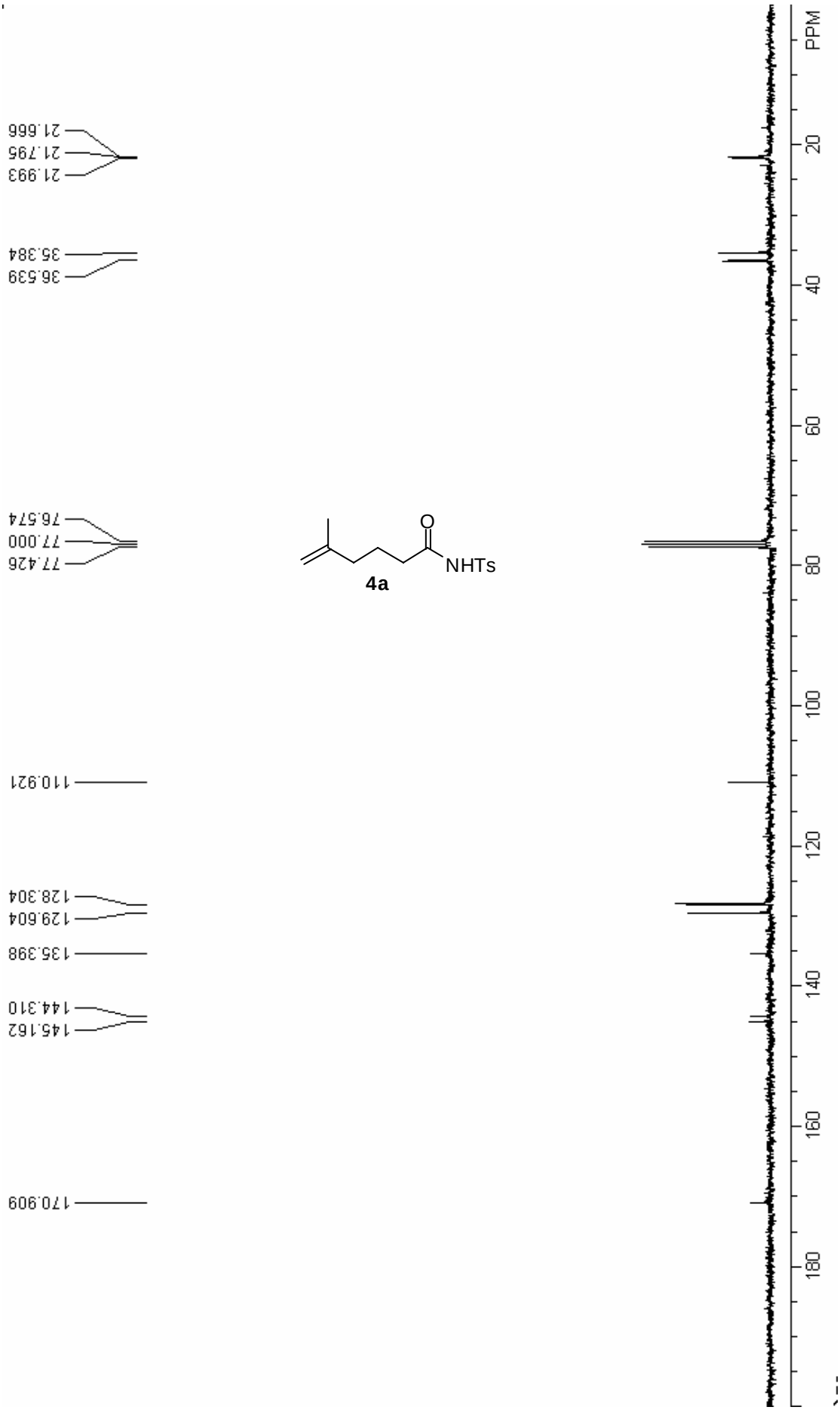
O
NHTs

4a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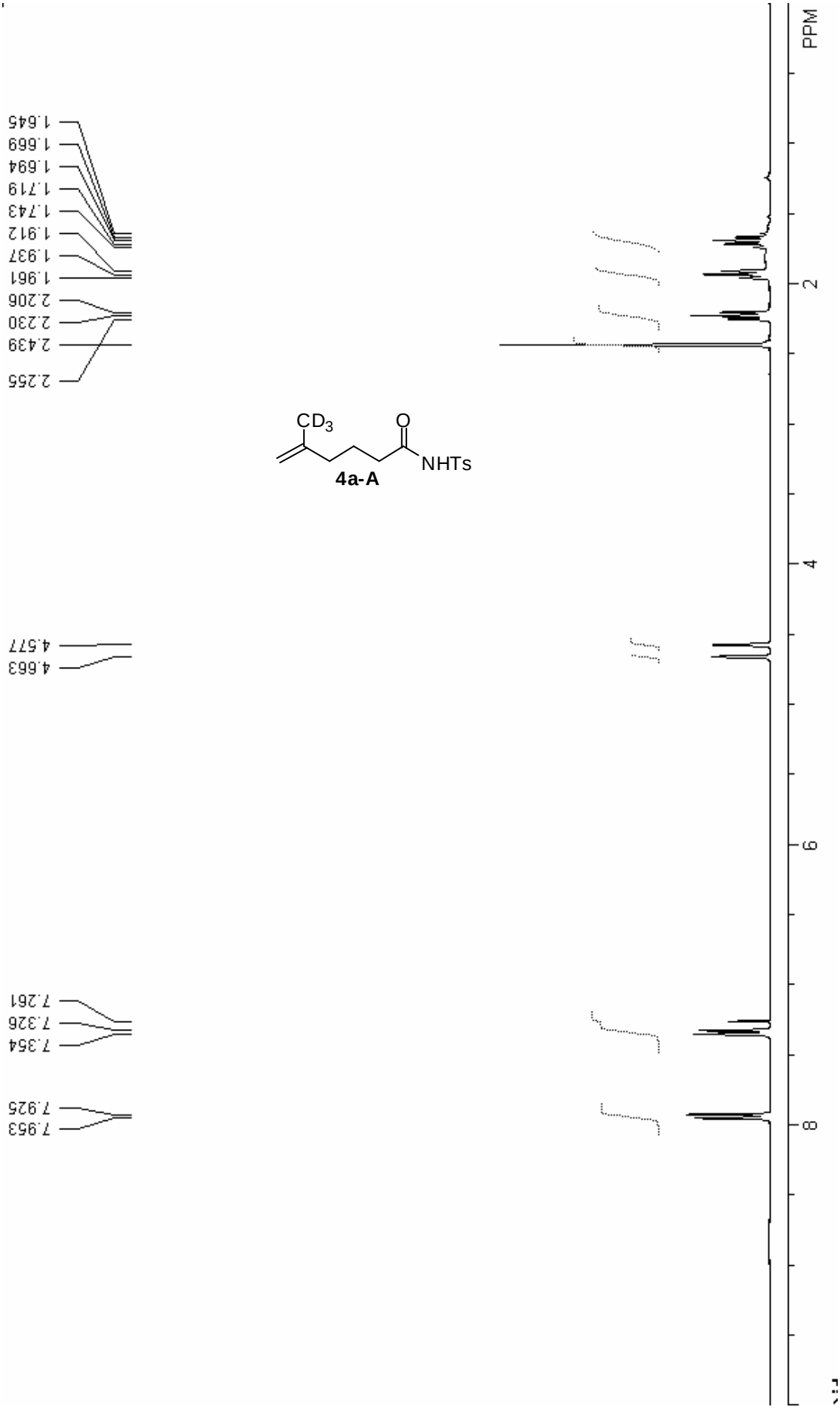
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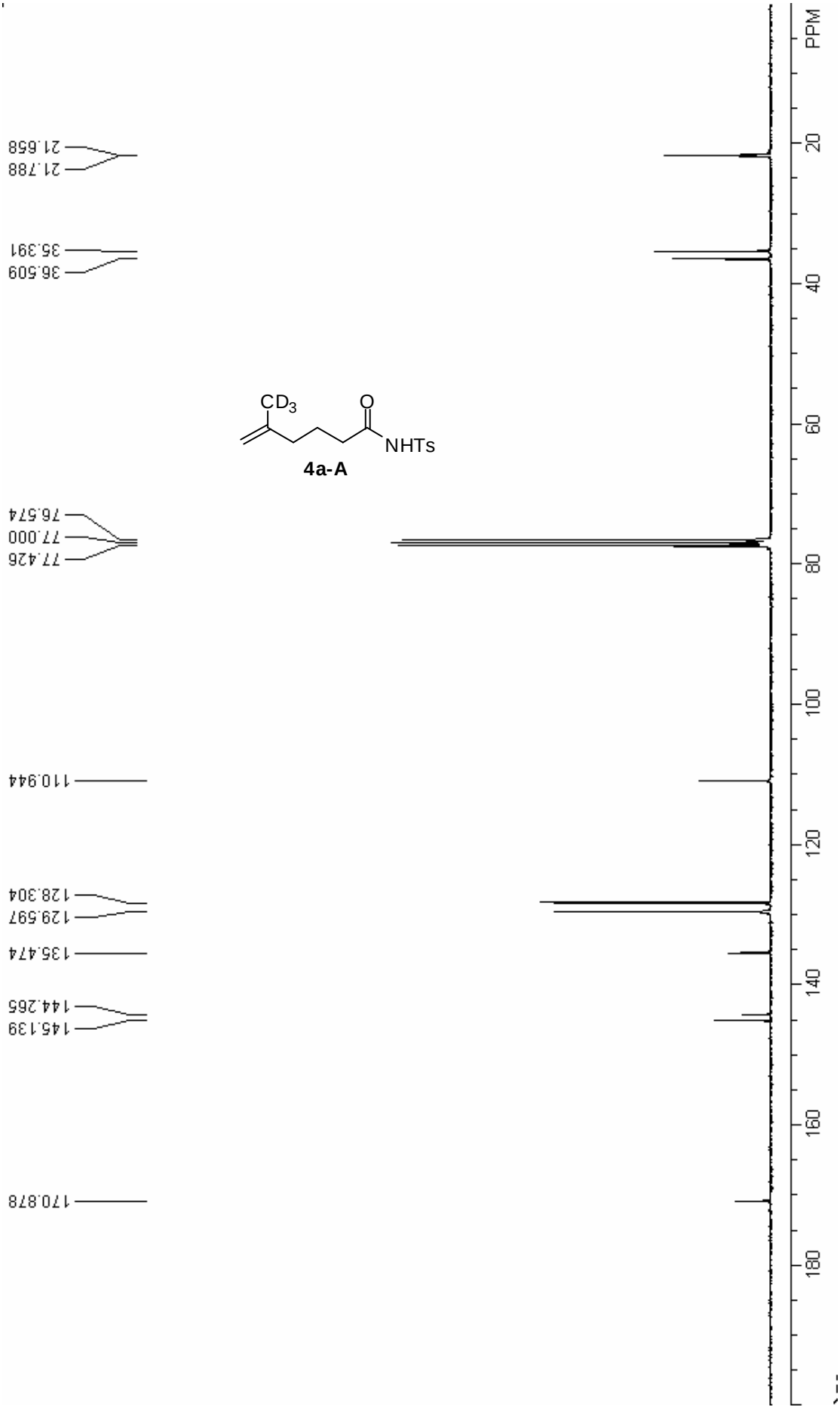
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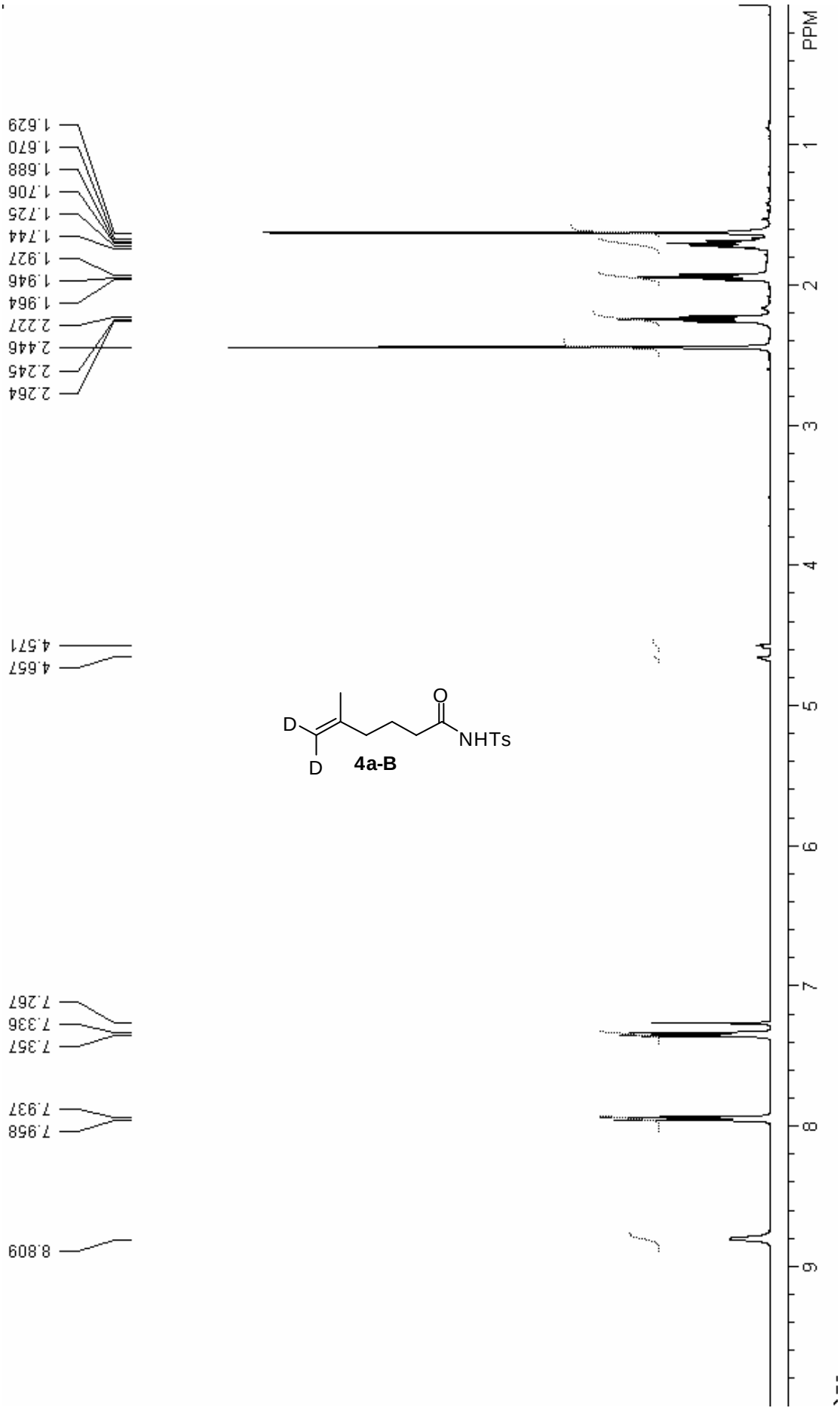
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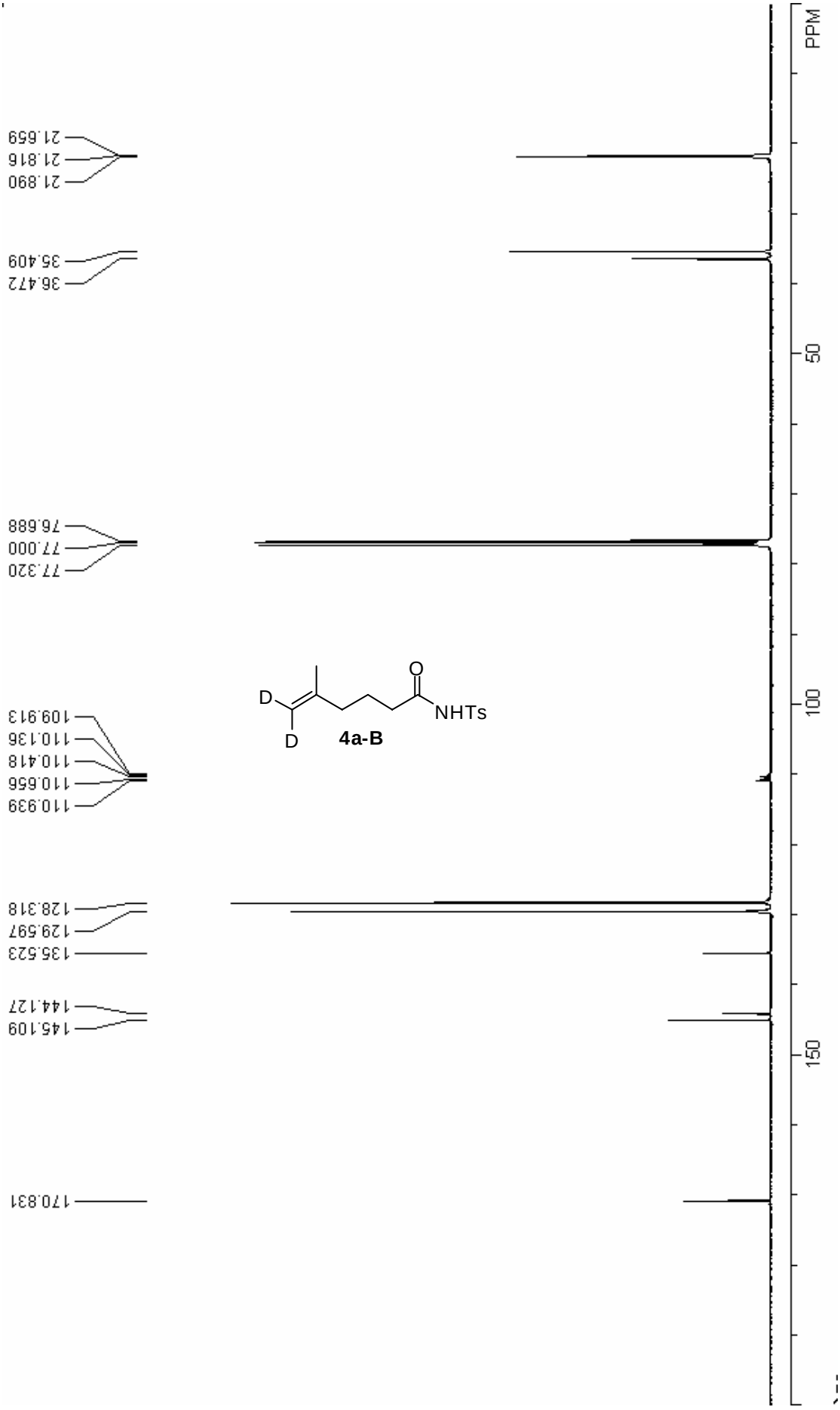
NHTs
D
D

4a-B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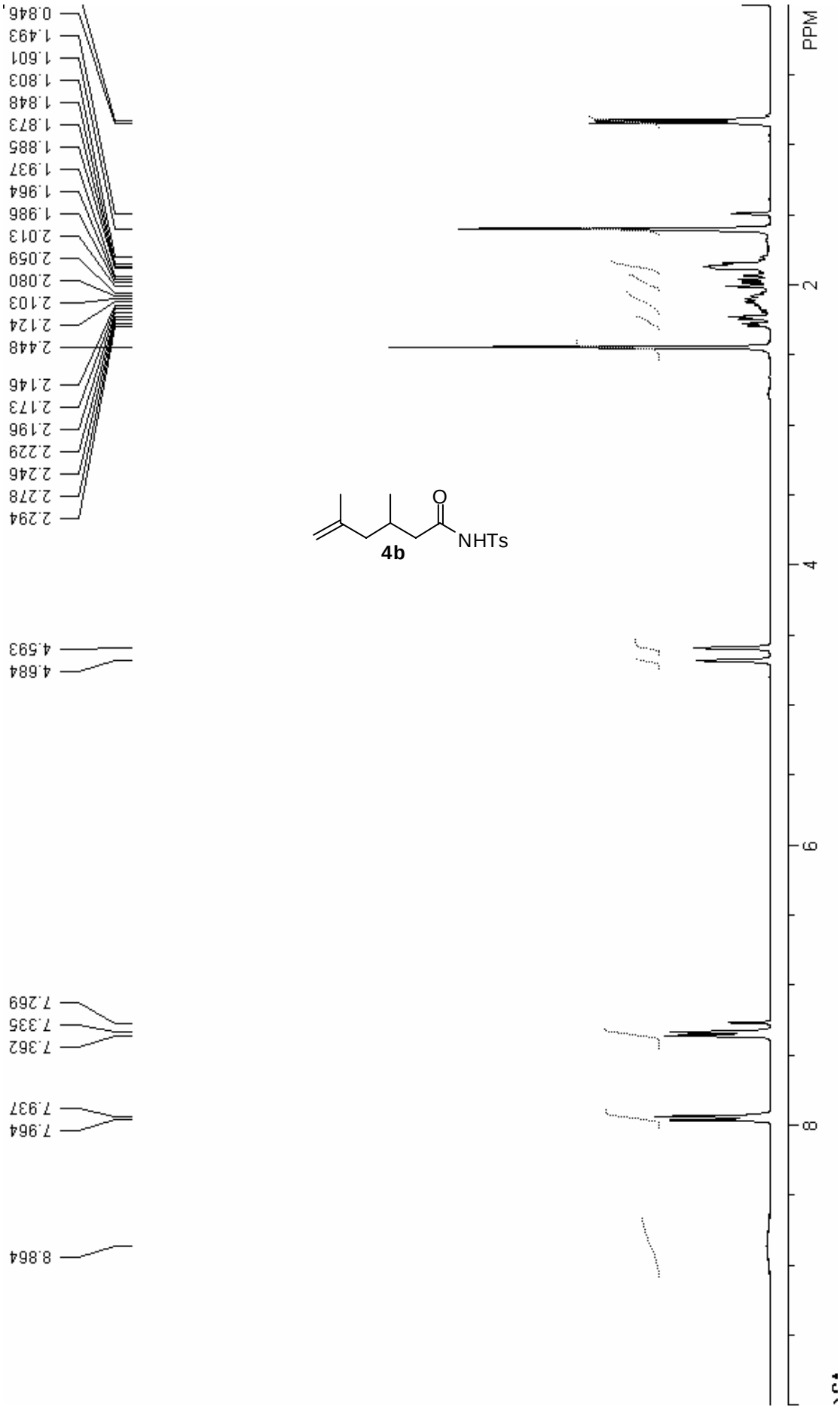
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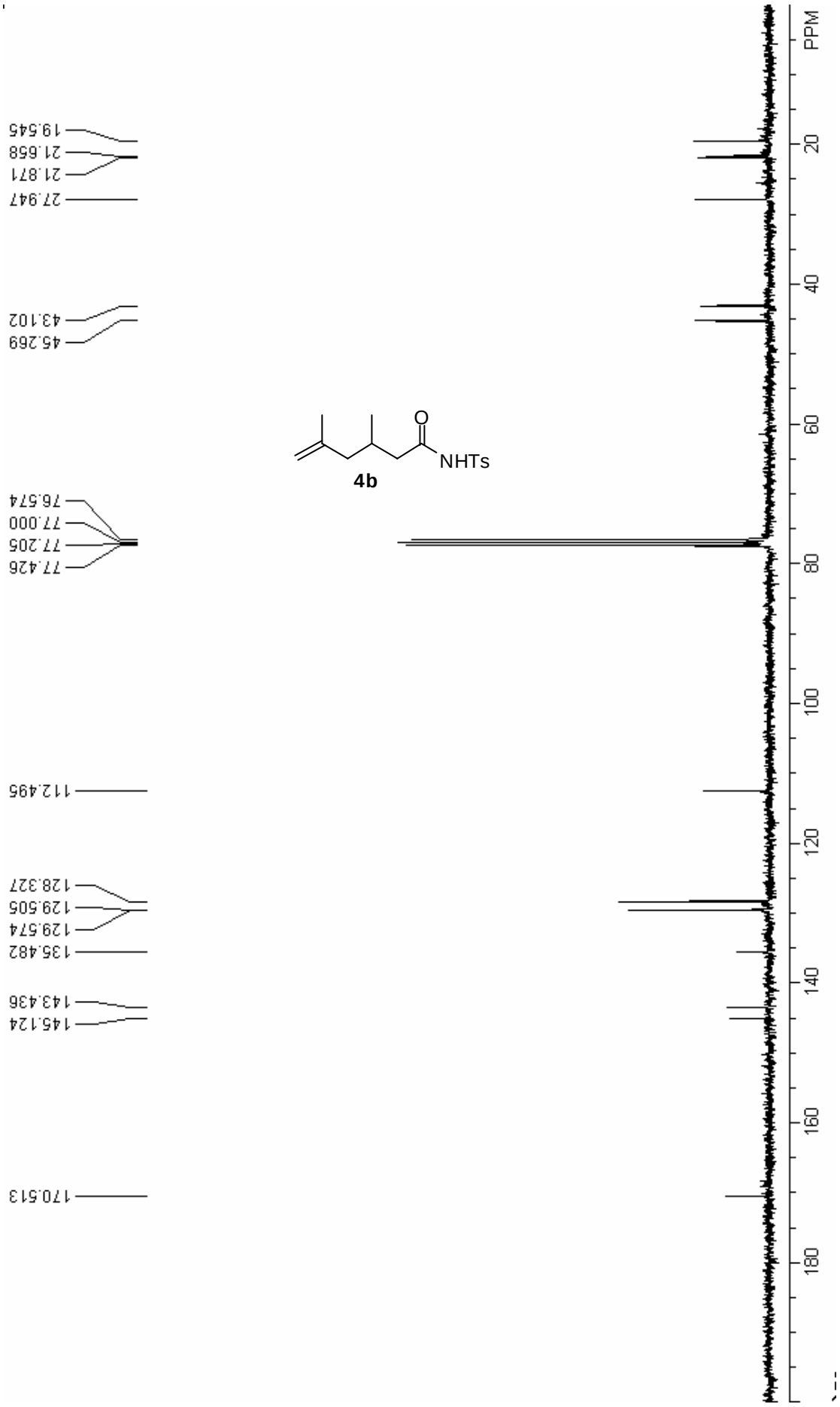
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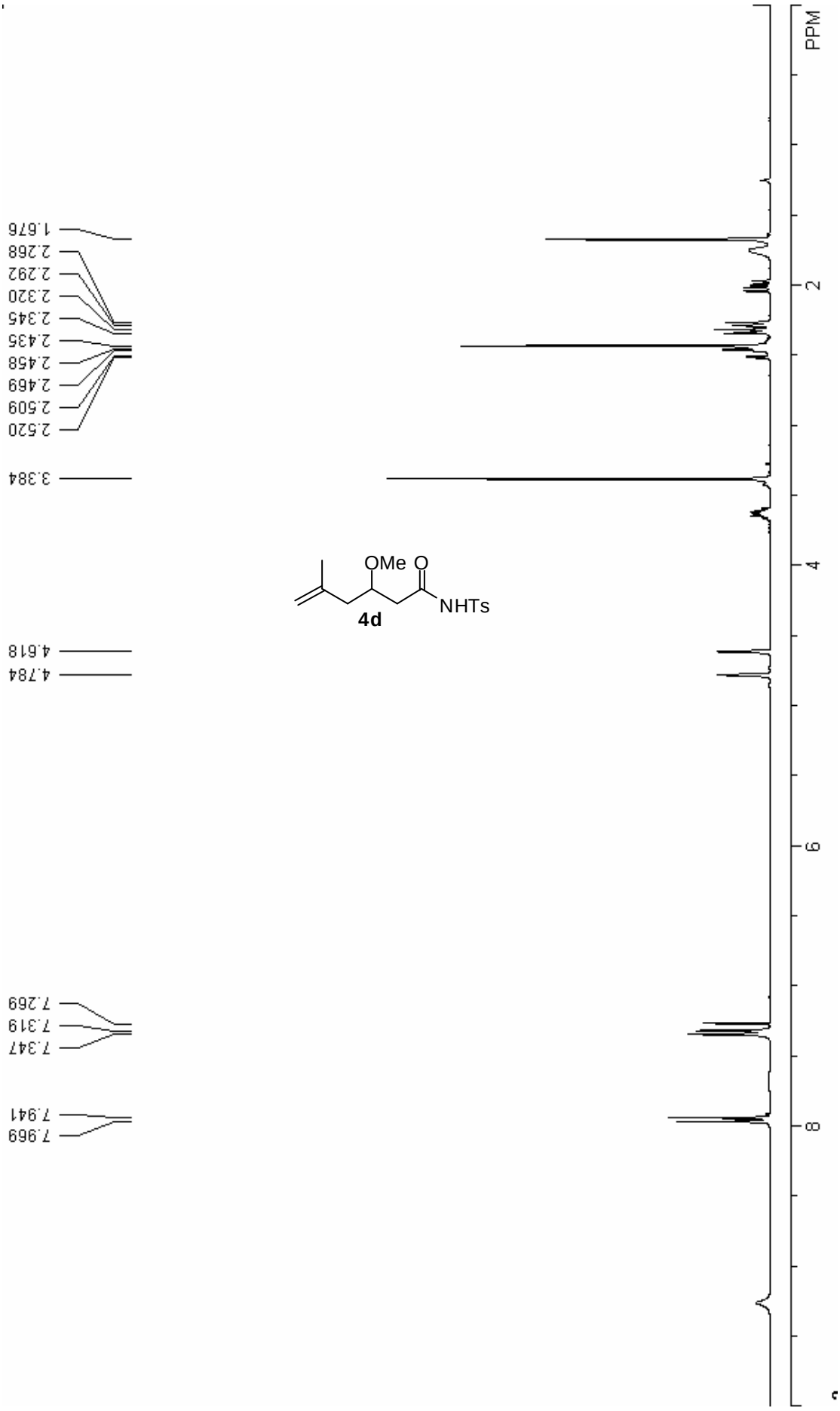
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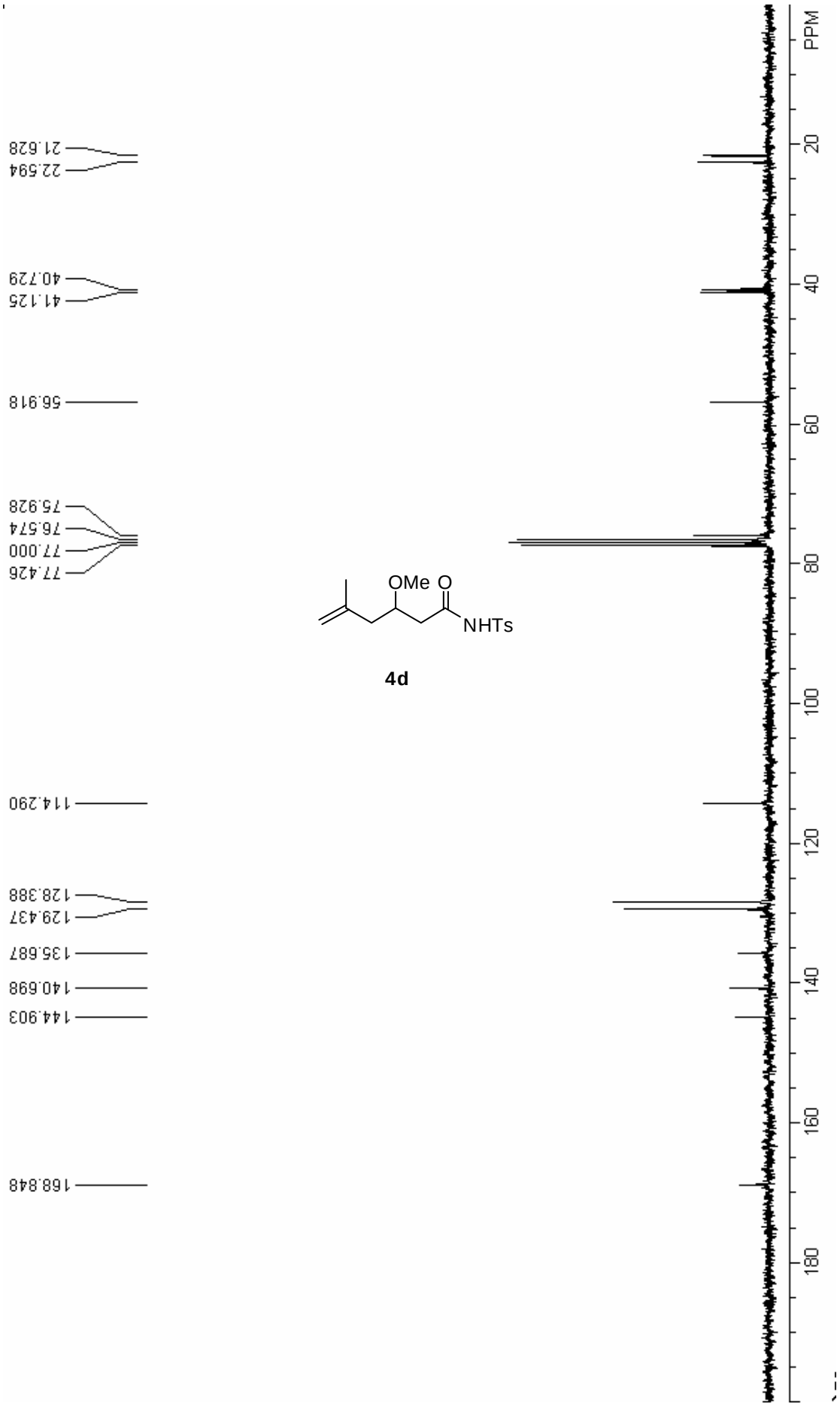
OMe O
NHTs
4d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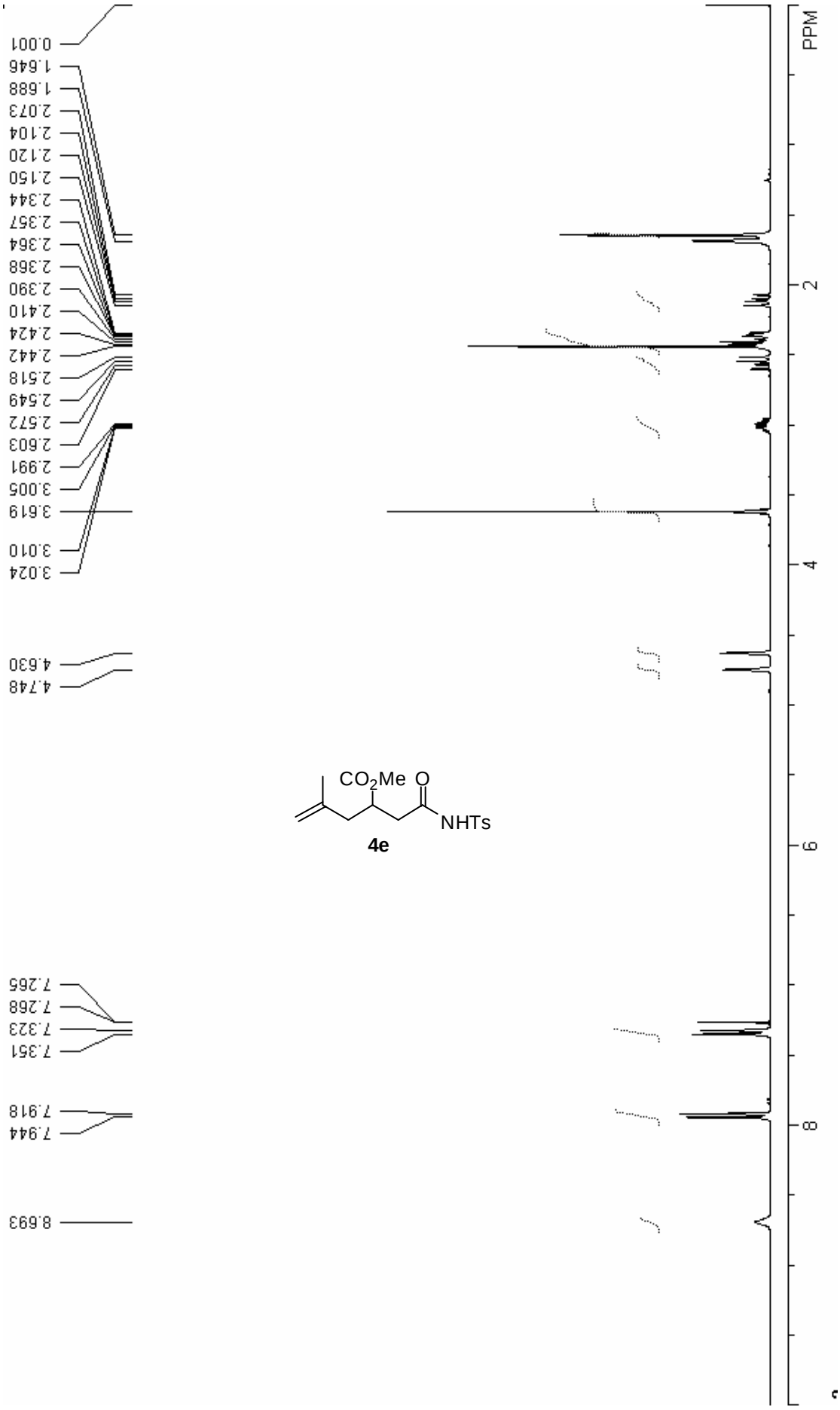
OMe
O
NHTs

4d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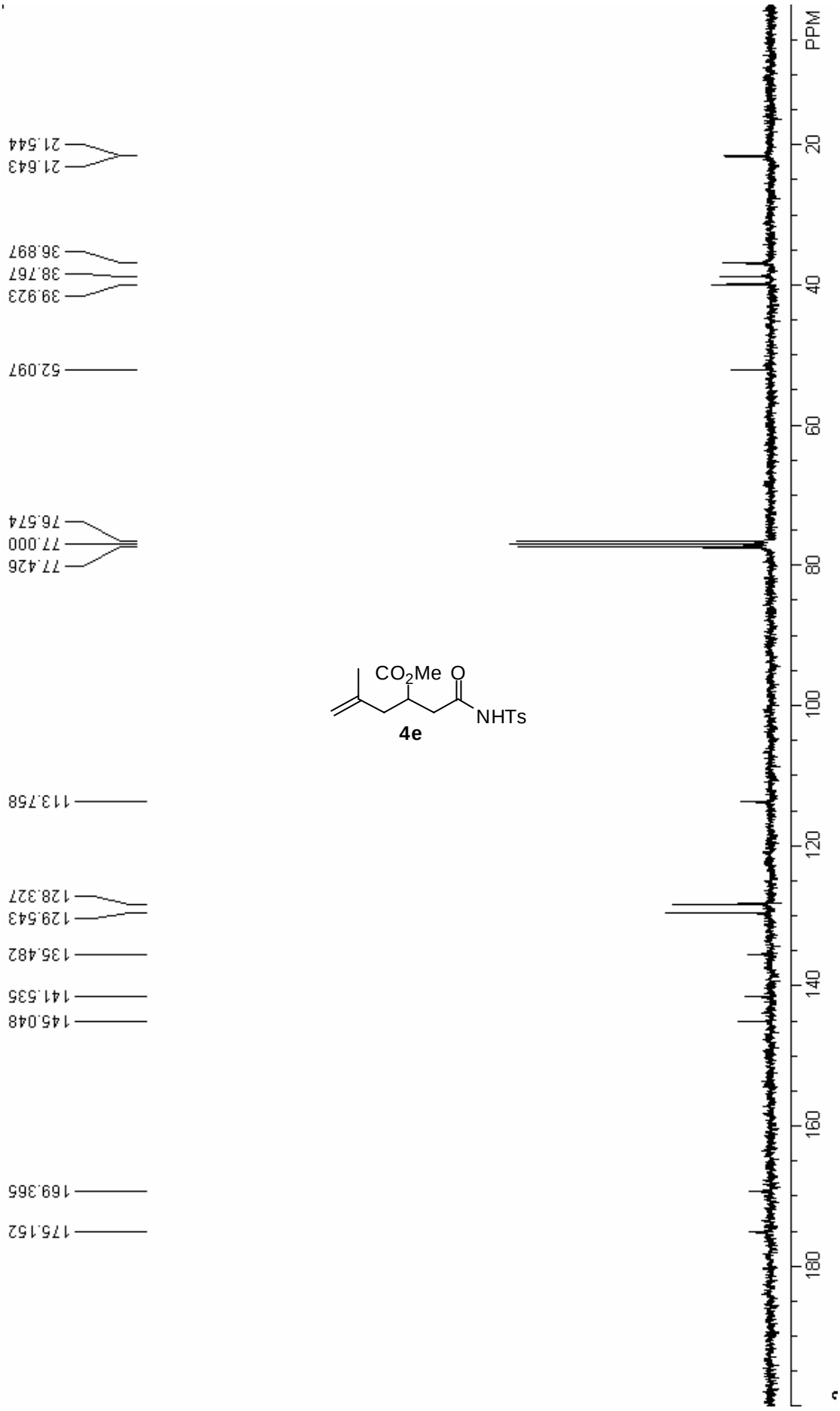
CO2Me
O
NHTs

4e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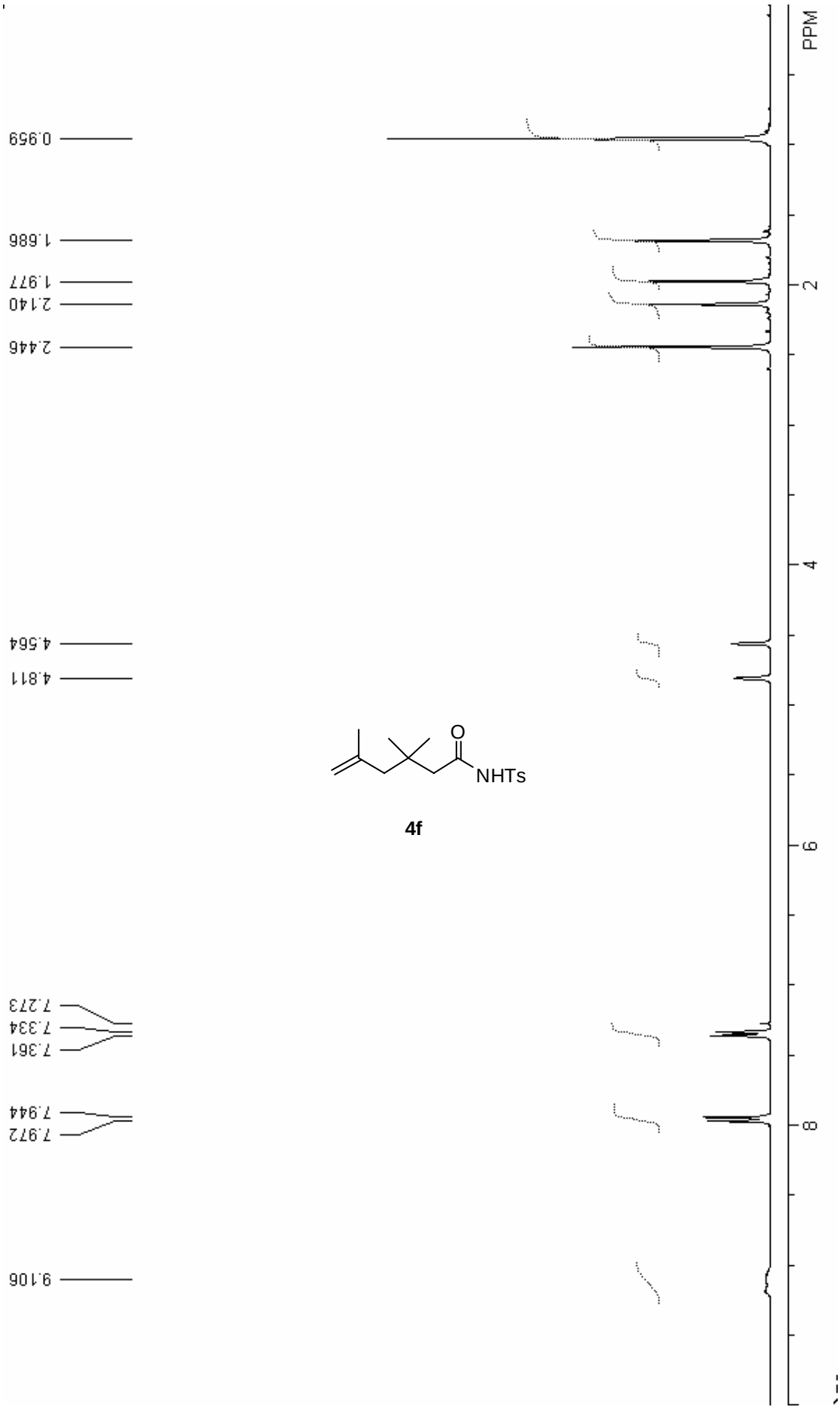
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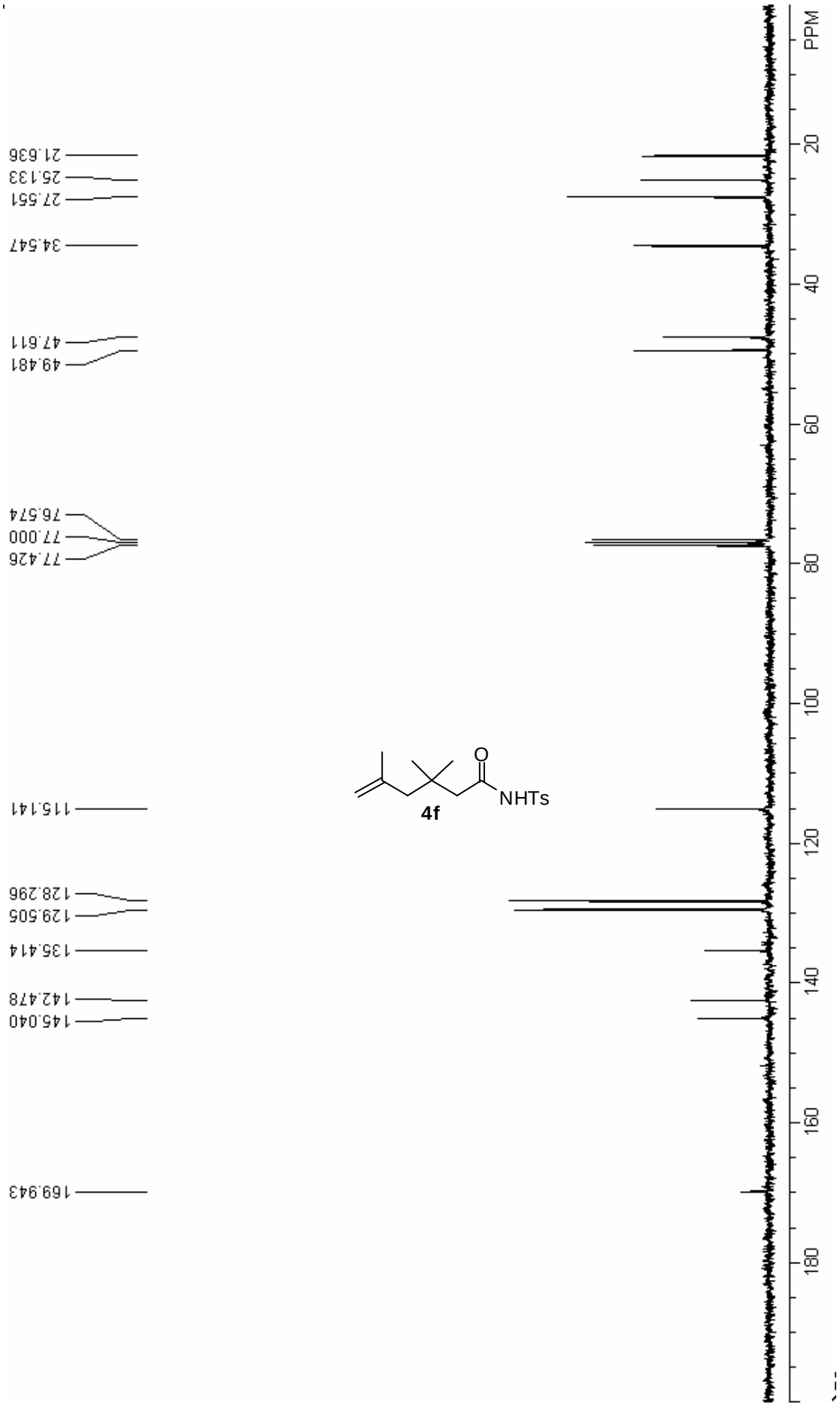
O
NHTs

4f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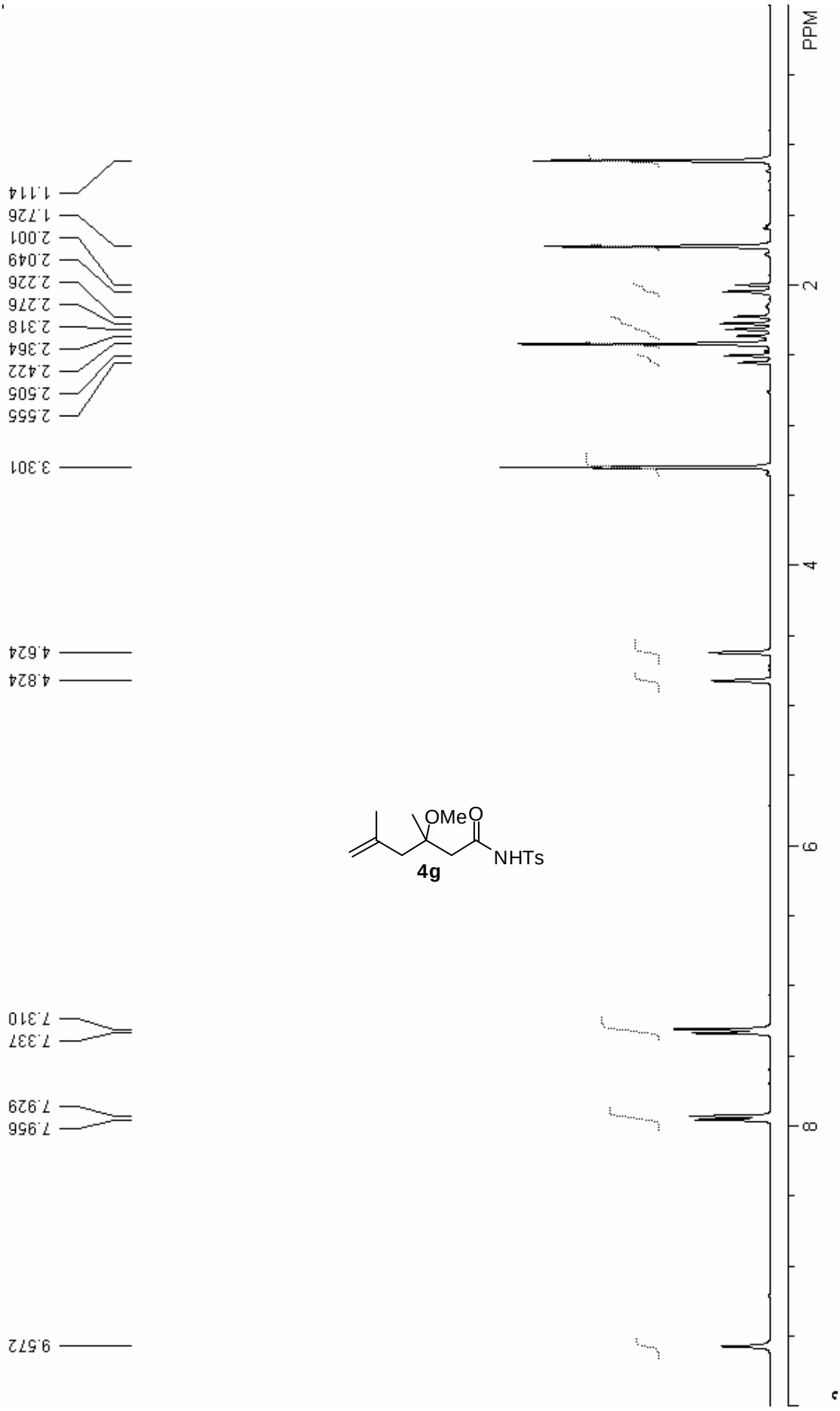
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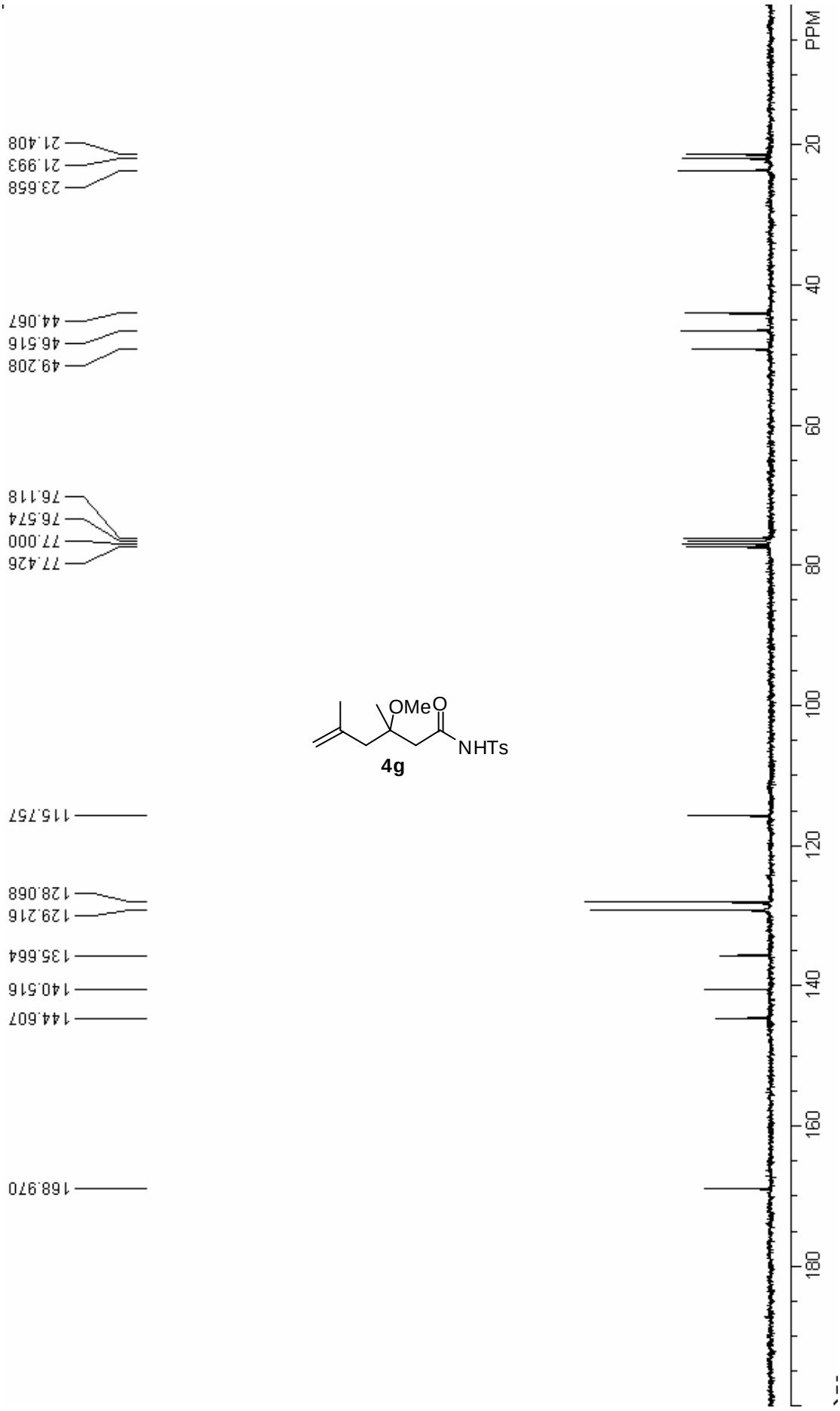
O
NHTs
4g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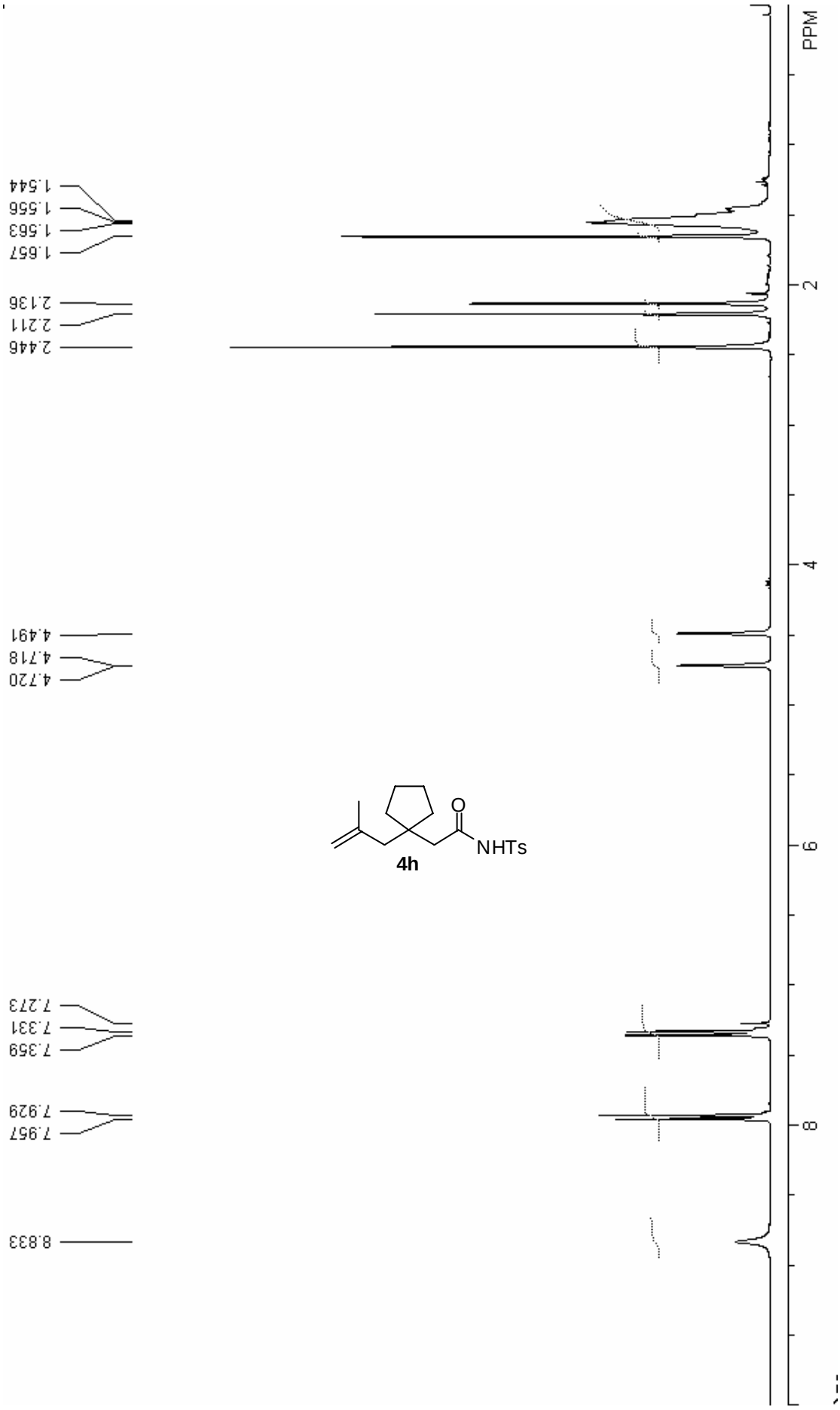
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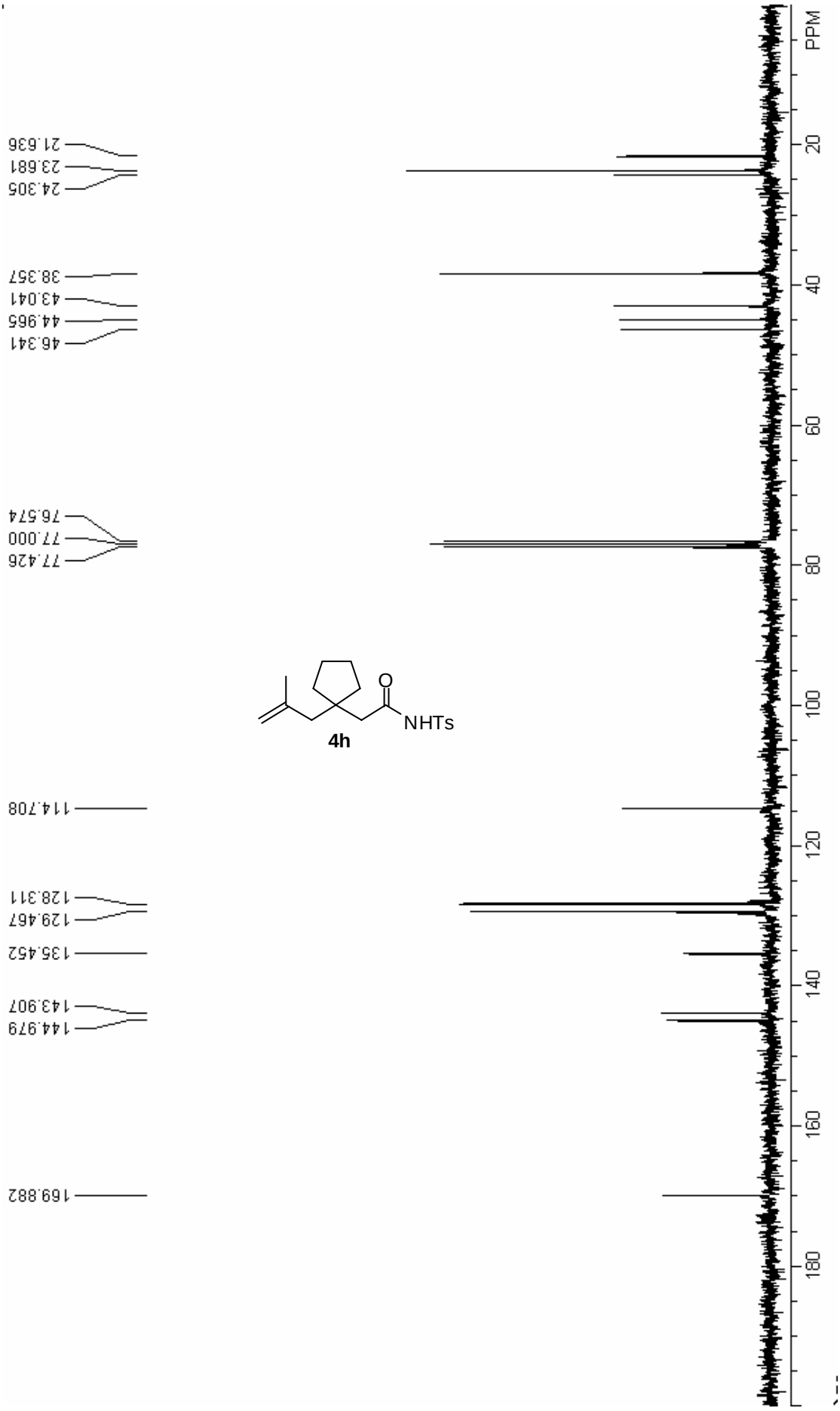
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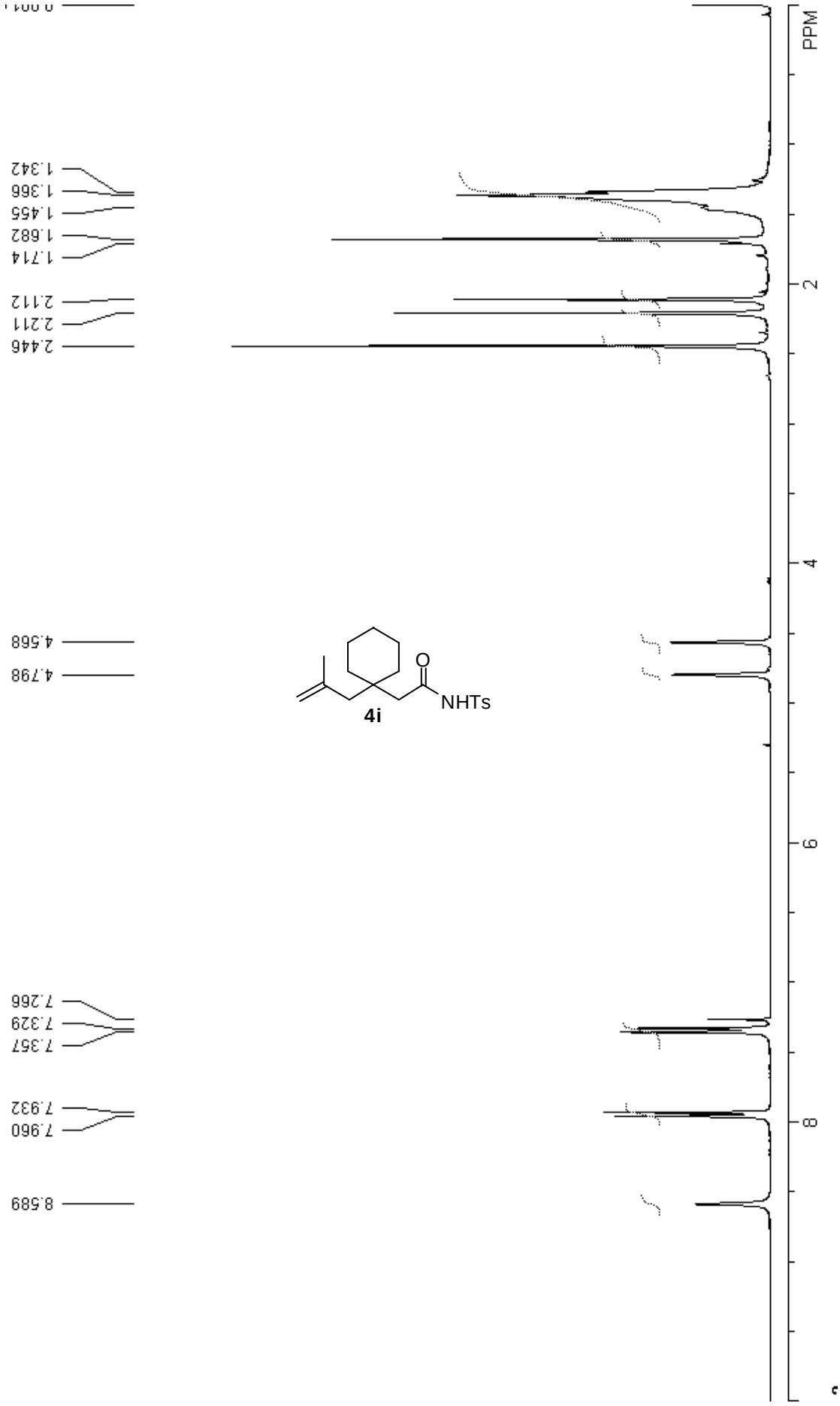
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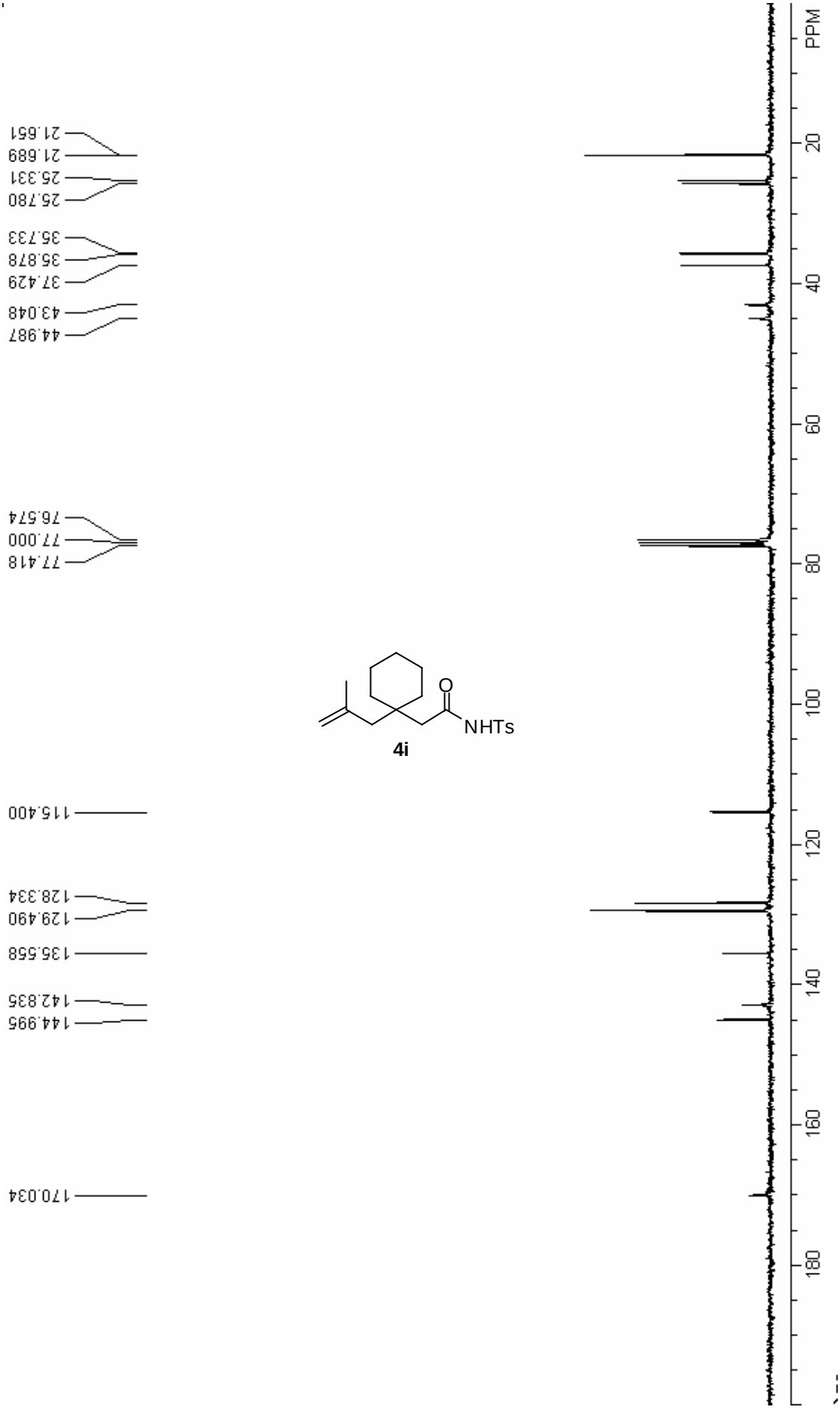
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PPM
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4i


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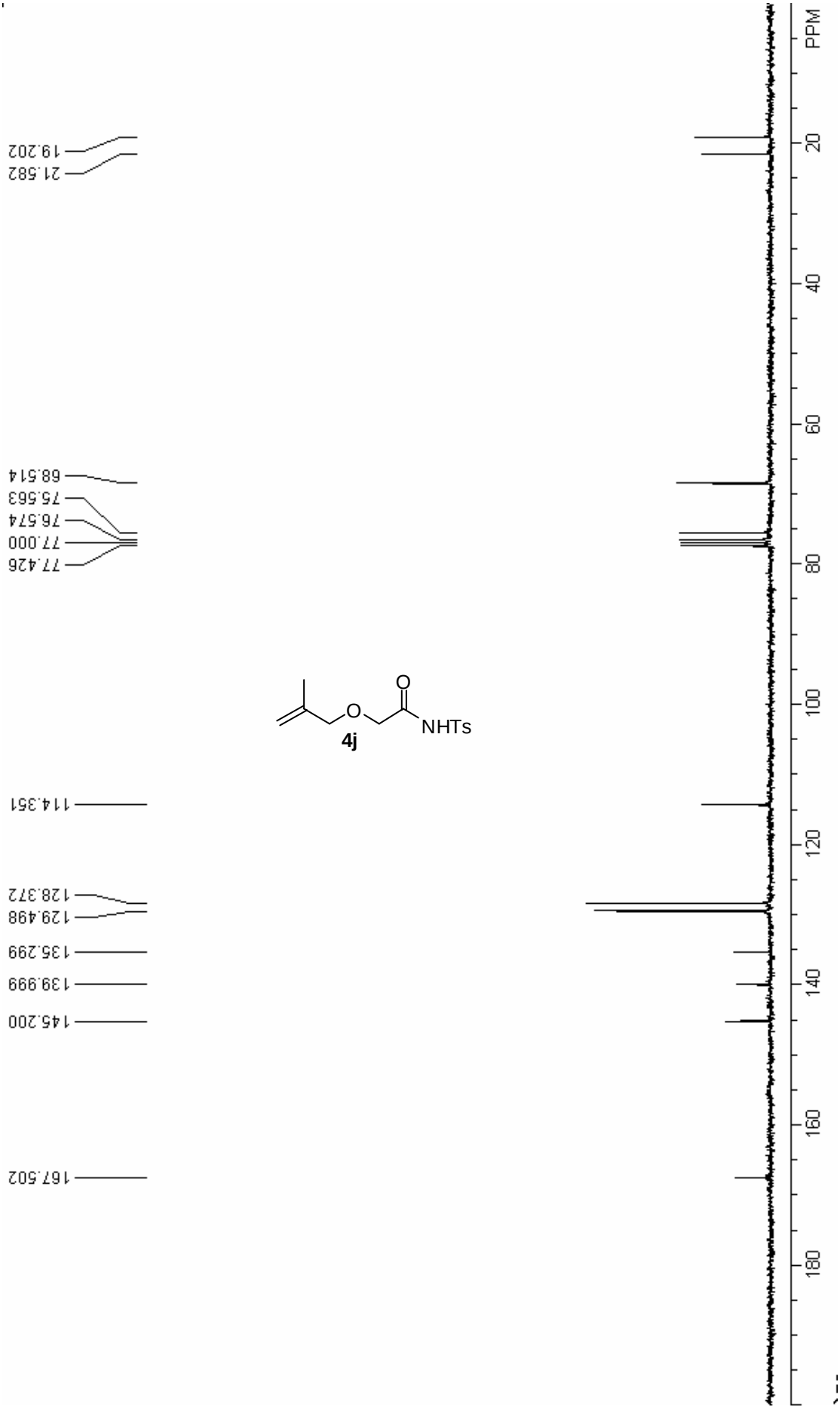
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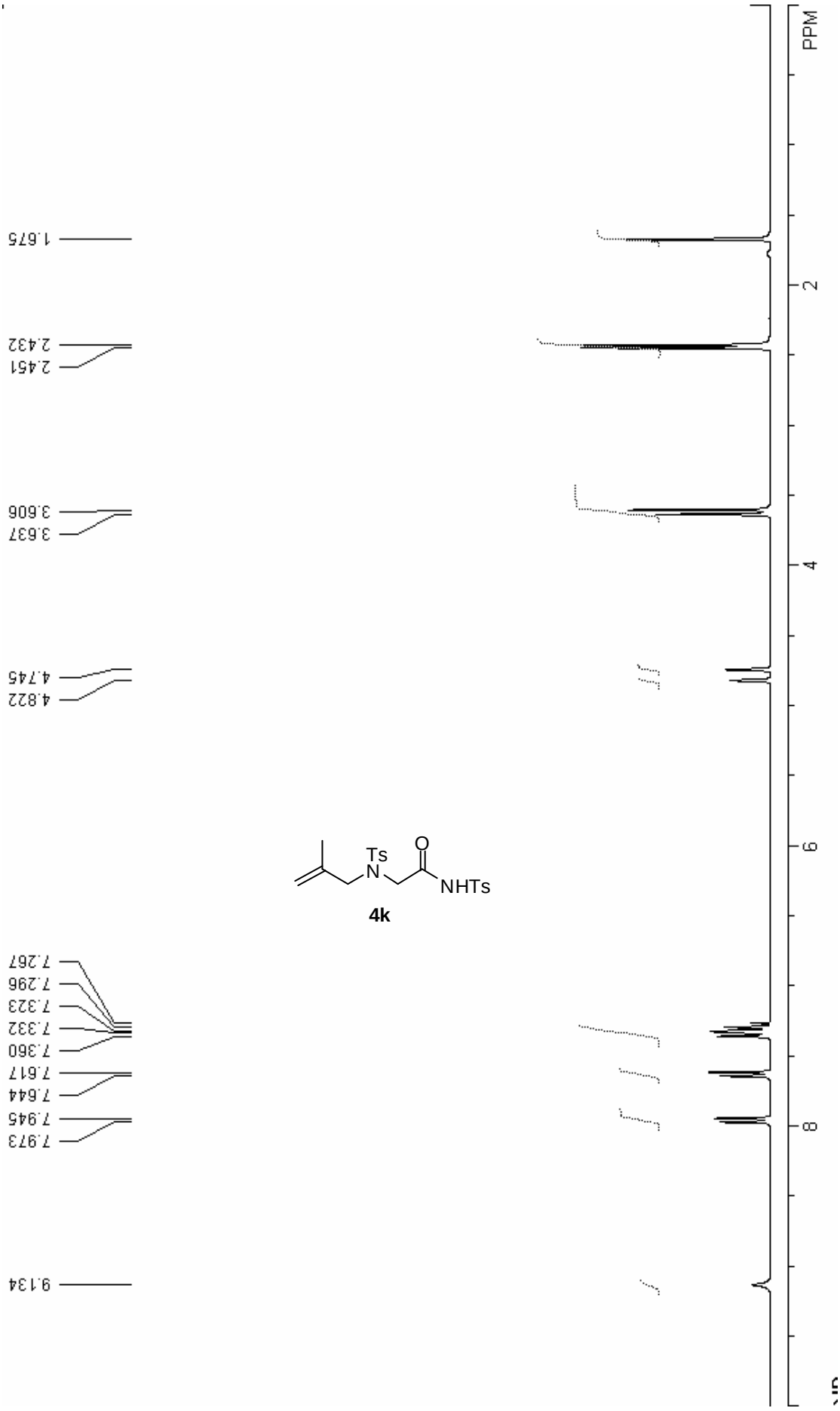
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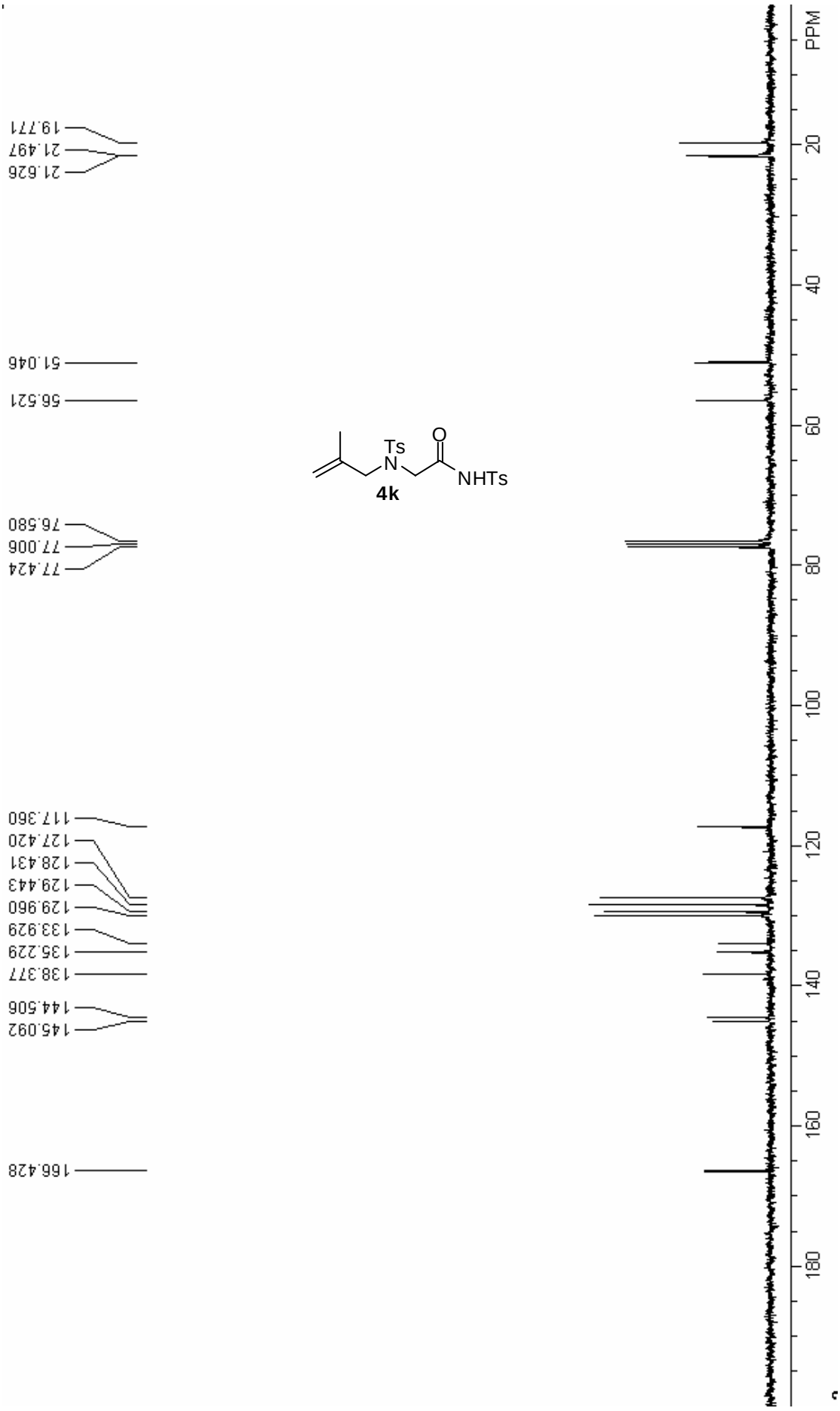
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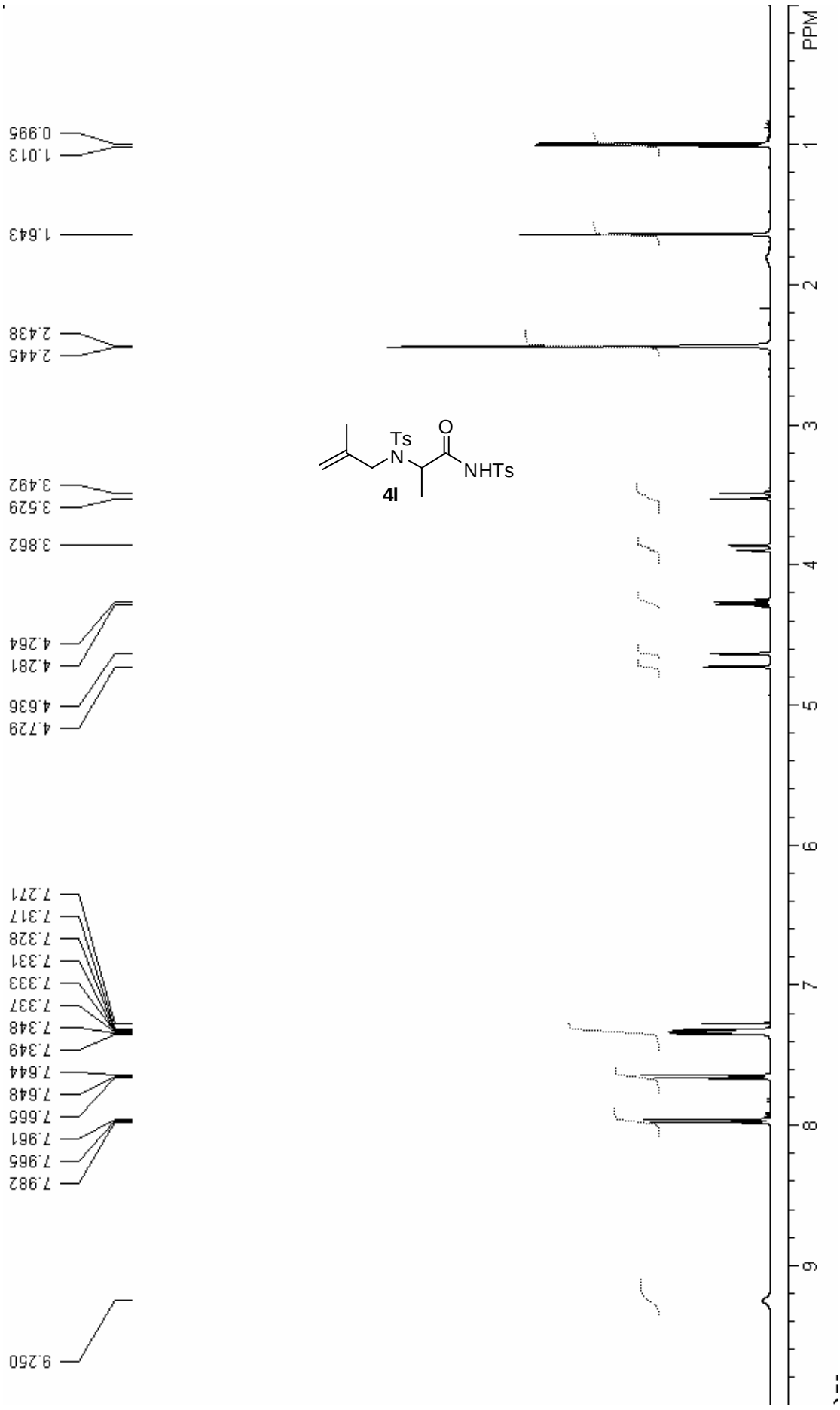
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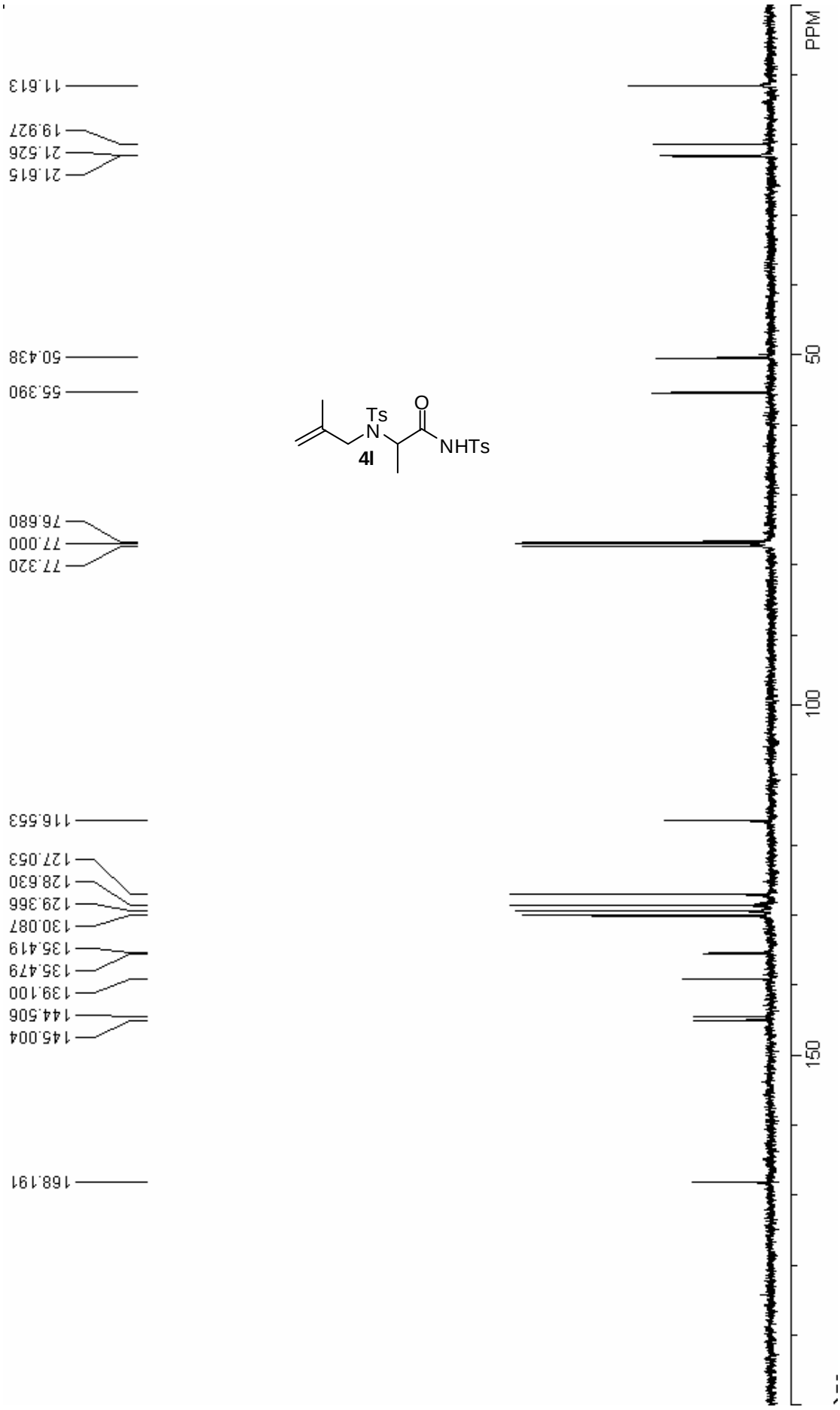
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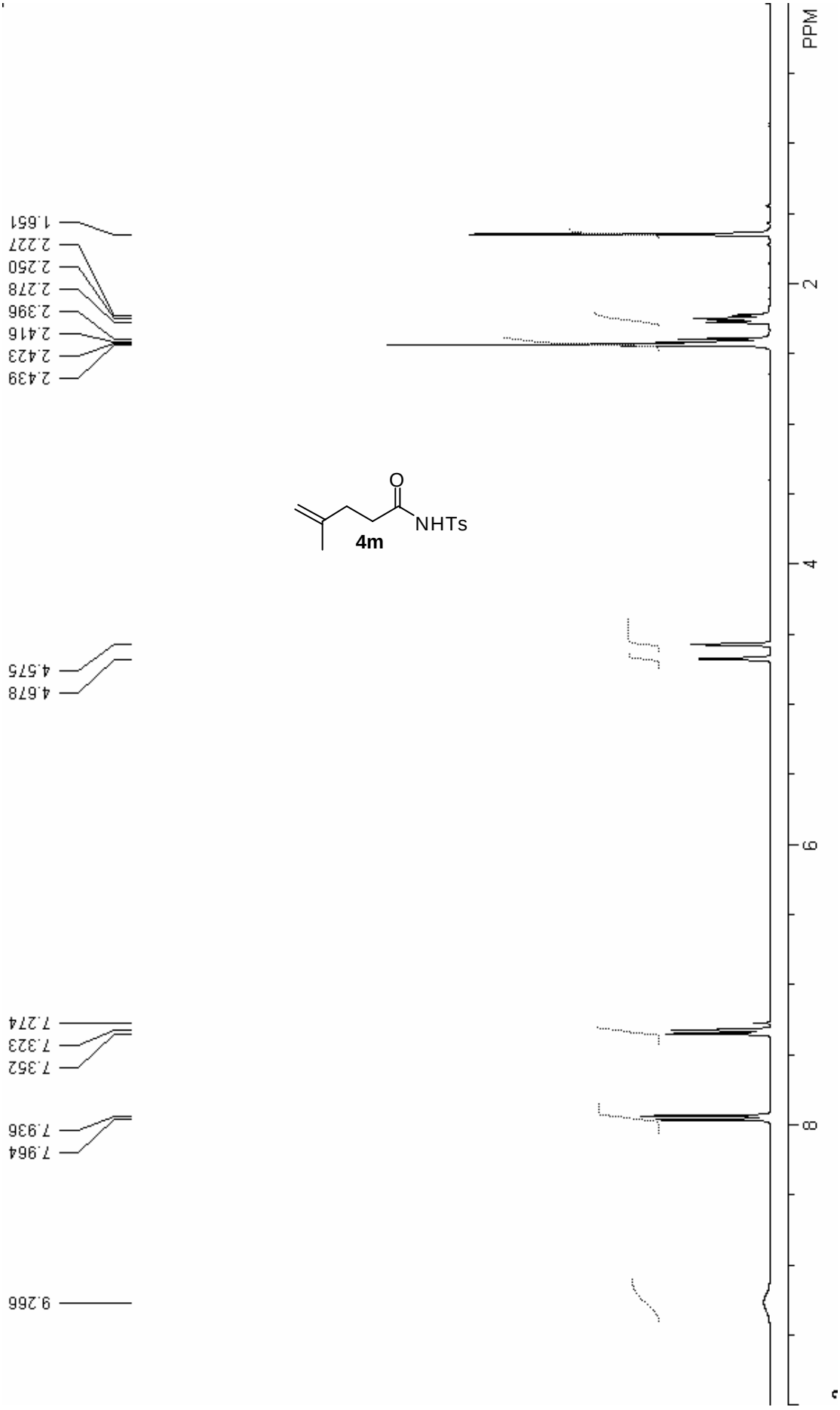
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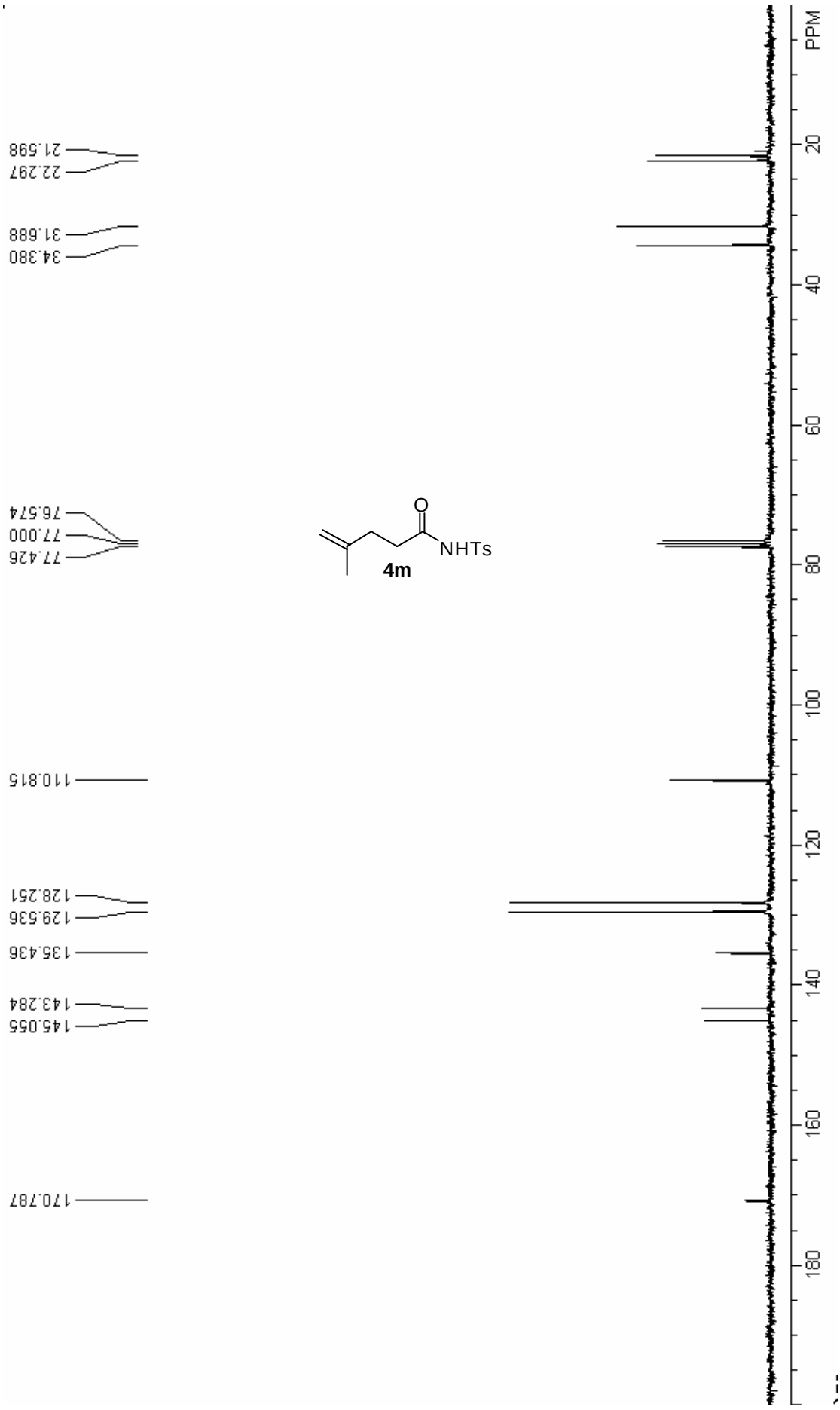
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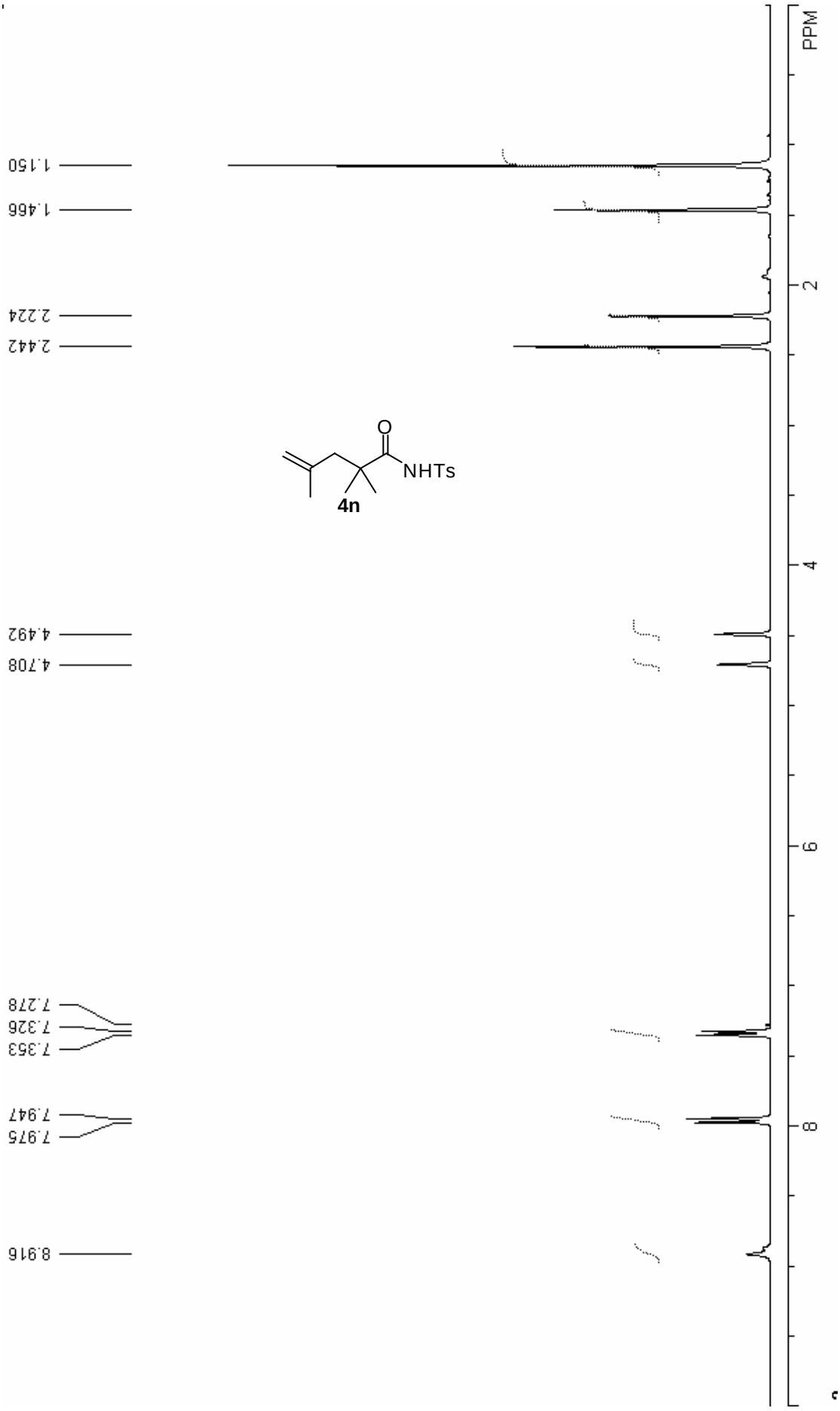
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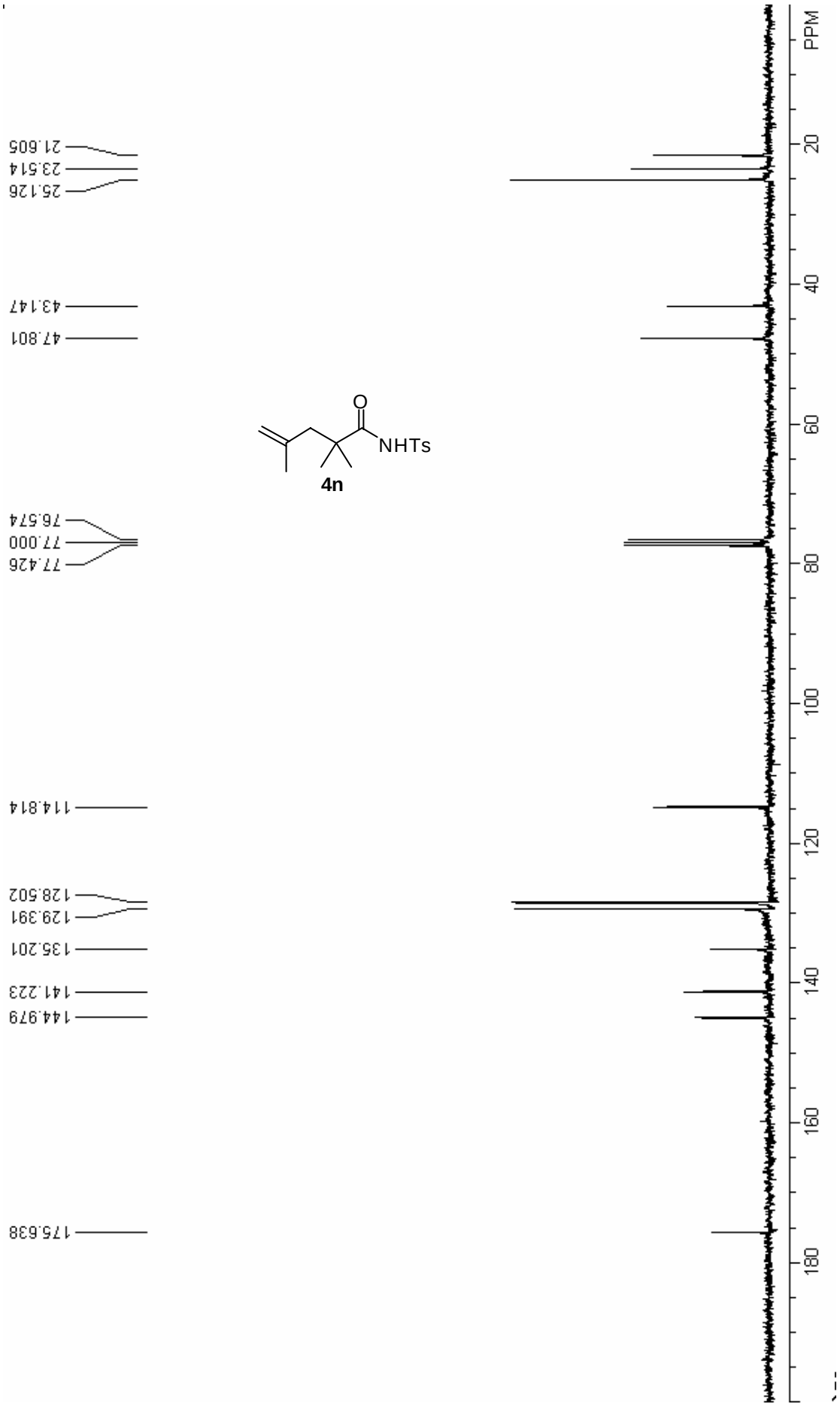
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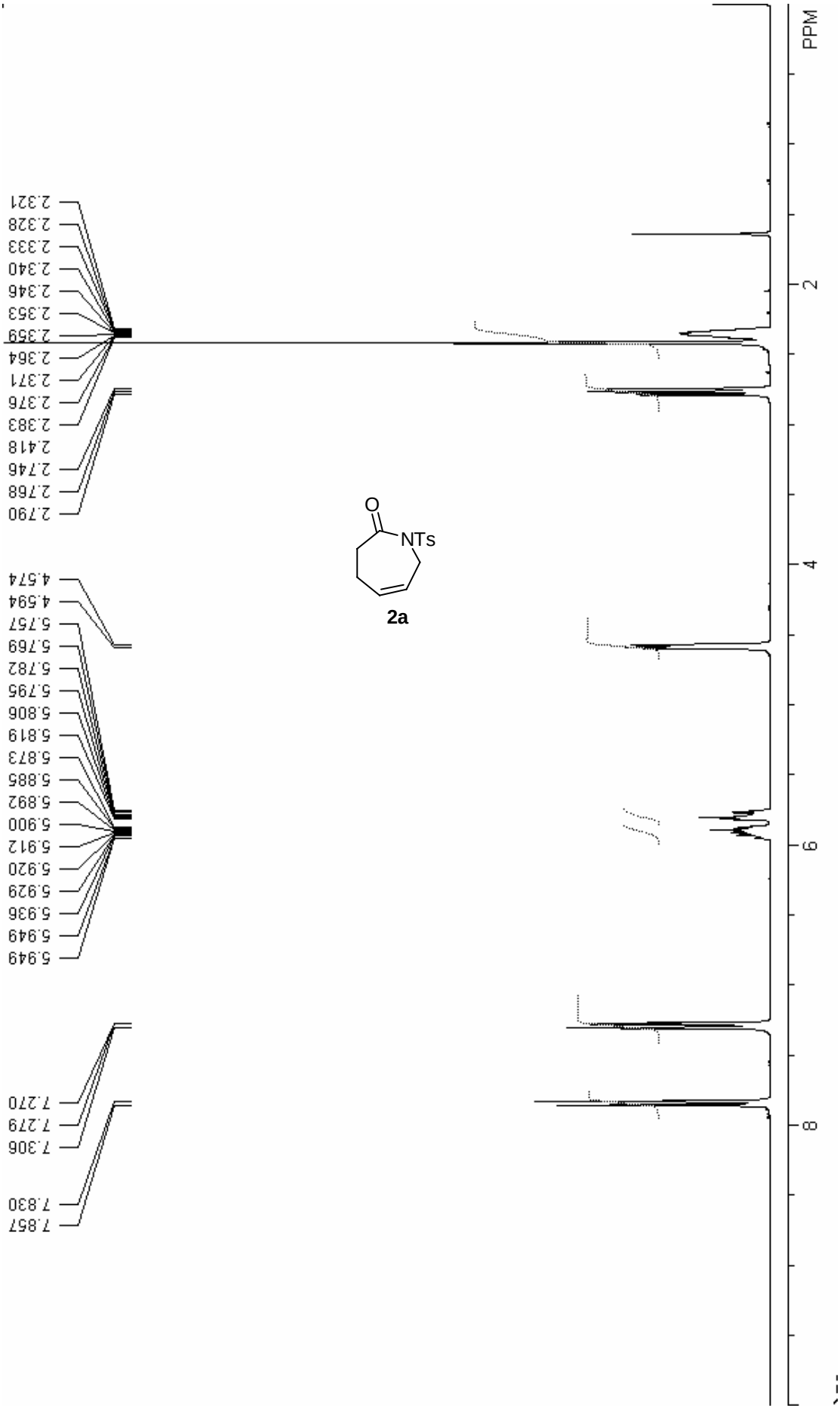
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2.376
2.383
2.418
2.746
2.768
2.790
4.574
4.694
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5.769
5.782
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5.806
5.819
5.873
5.885
5.892
5.900
5.912
5.920
5.929
5.936
5.949
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7.279
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7.830
7.857
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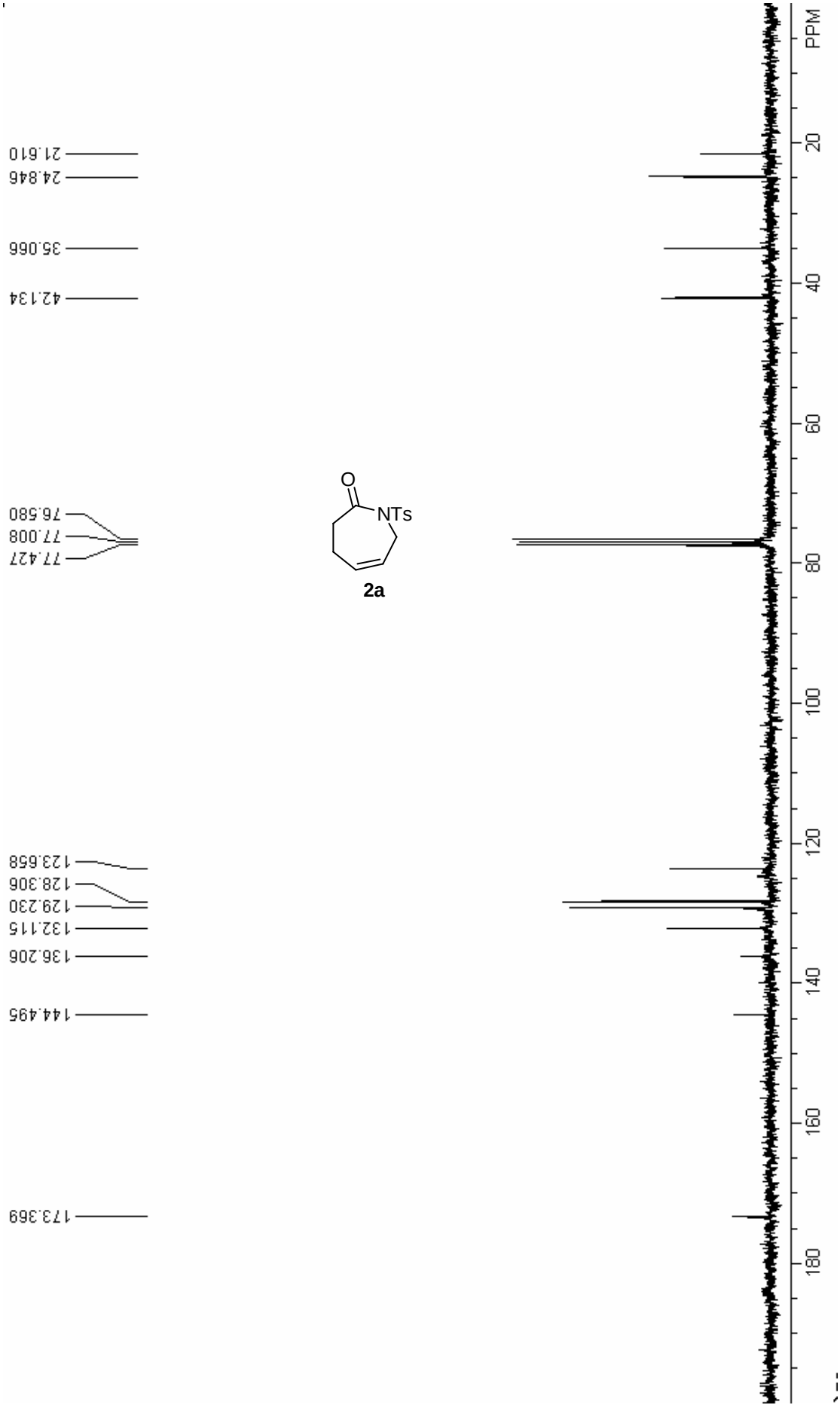
NTs
2a
PPM
2
4
6
8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123.658
128.306
129.230
132.115
136.206
144.495
173.369
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NTs
PPM
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60
80
100
120
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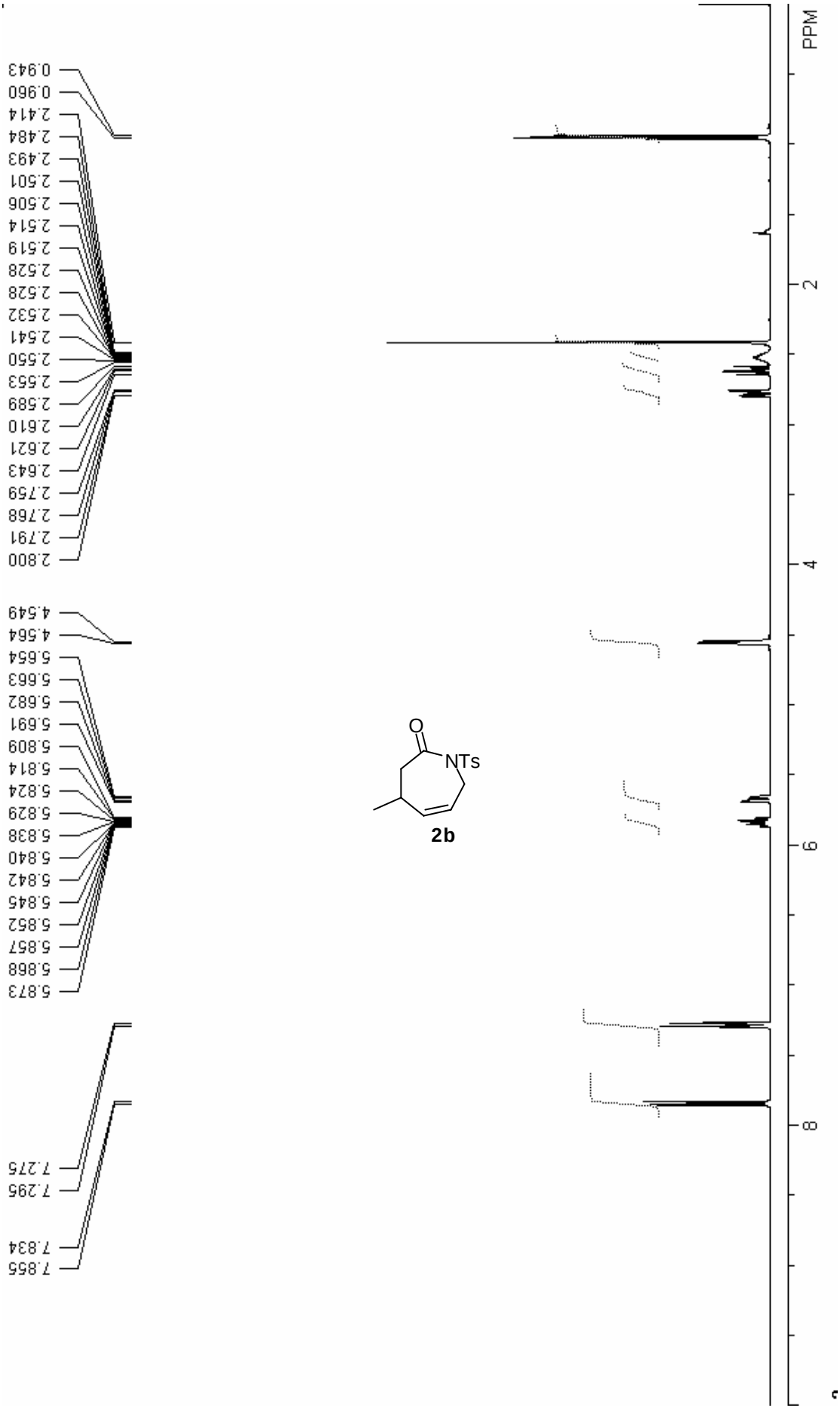
160
180

2a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2.514
2.519
2.528
2.528
2.532
2.541
2.550
2.553
2.589
2.610
2.621
2.643
2.759
2.768
2.791
2.800
4.549
4.564
5.654
5.663
5.682
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5.809
5.814
5.824
5.829
5.838
5.840
5.842
5.845
5.852
5.857
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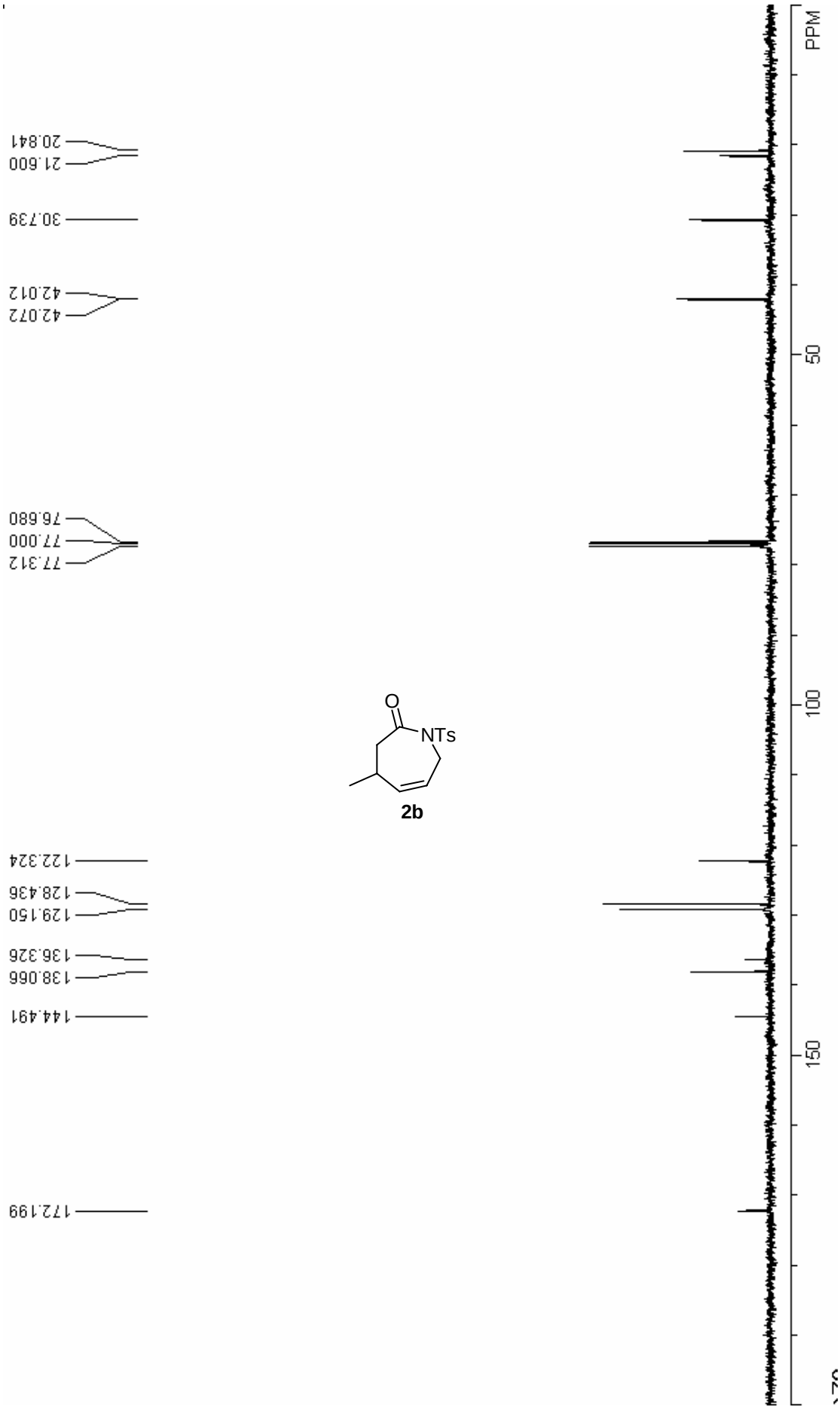
7.275
7.295
7.834
7.855
O
NTs
2b
PPM
2
4
6
8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77.312
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172.199
PPM
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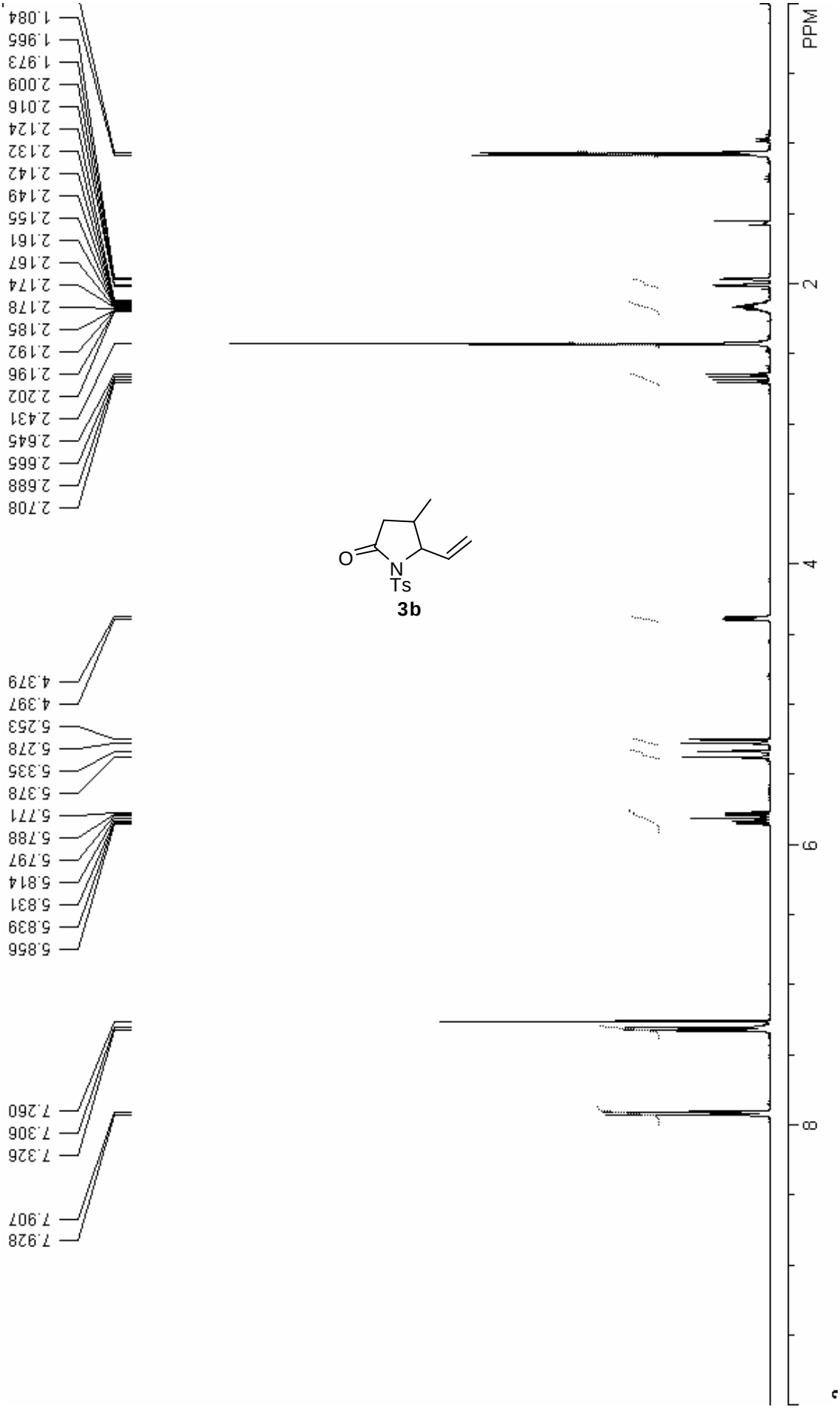
100
150
O
NTs

2b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1.973
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2.142
2.149
2.155
2.161
2.167
2.174
2.178
2.185
2.192
2.196
2.202
2.431
2.645
2.665
2.688
2.708
4.379
4.397
5.253
5.278
5.335
5.378
5.771
5.788
5.797
5.814
5.831
5.839
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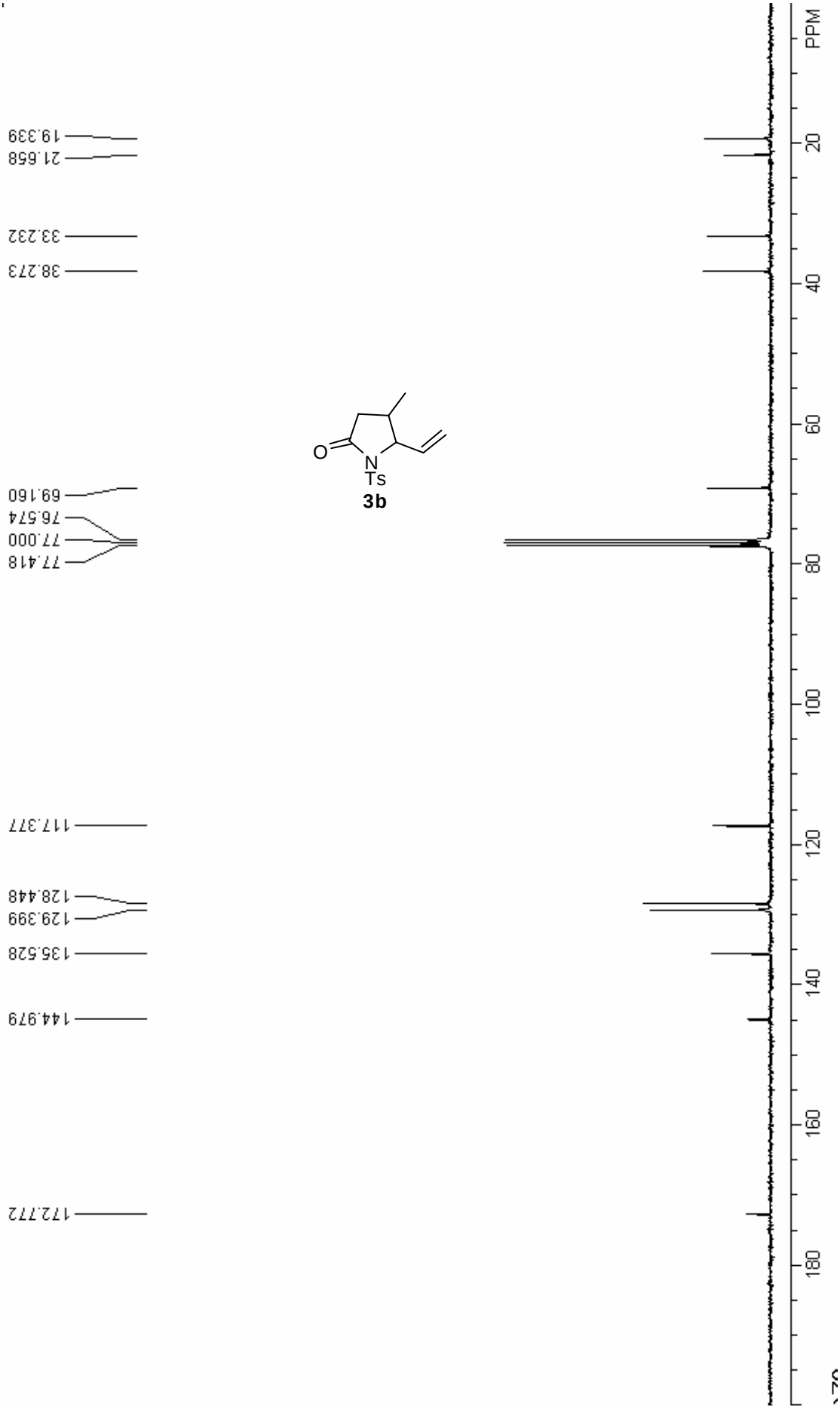
7.326
7.907
7.928
PPM
2
4
6
8
O
N
Ts

3b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O
N
Ts
3b
PPM
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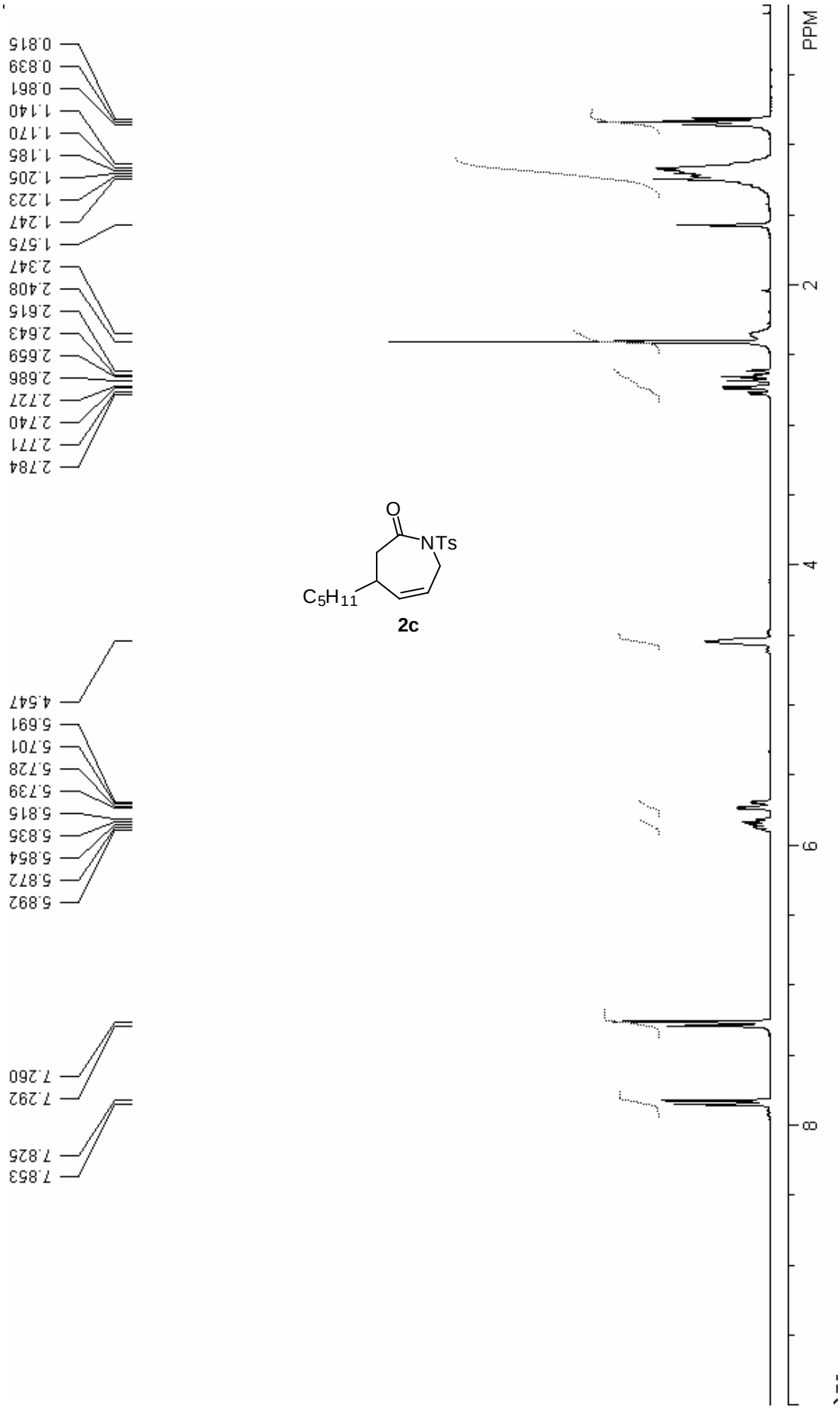
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1.205
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2.615
2.643
2.659
2.686
2.727
2.740
2.771
2.784
4.547
5.691
5.701
5.728
5.739
5.815
5.835
5.854
5.872
5.892
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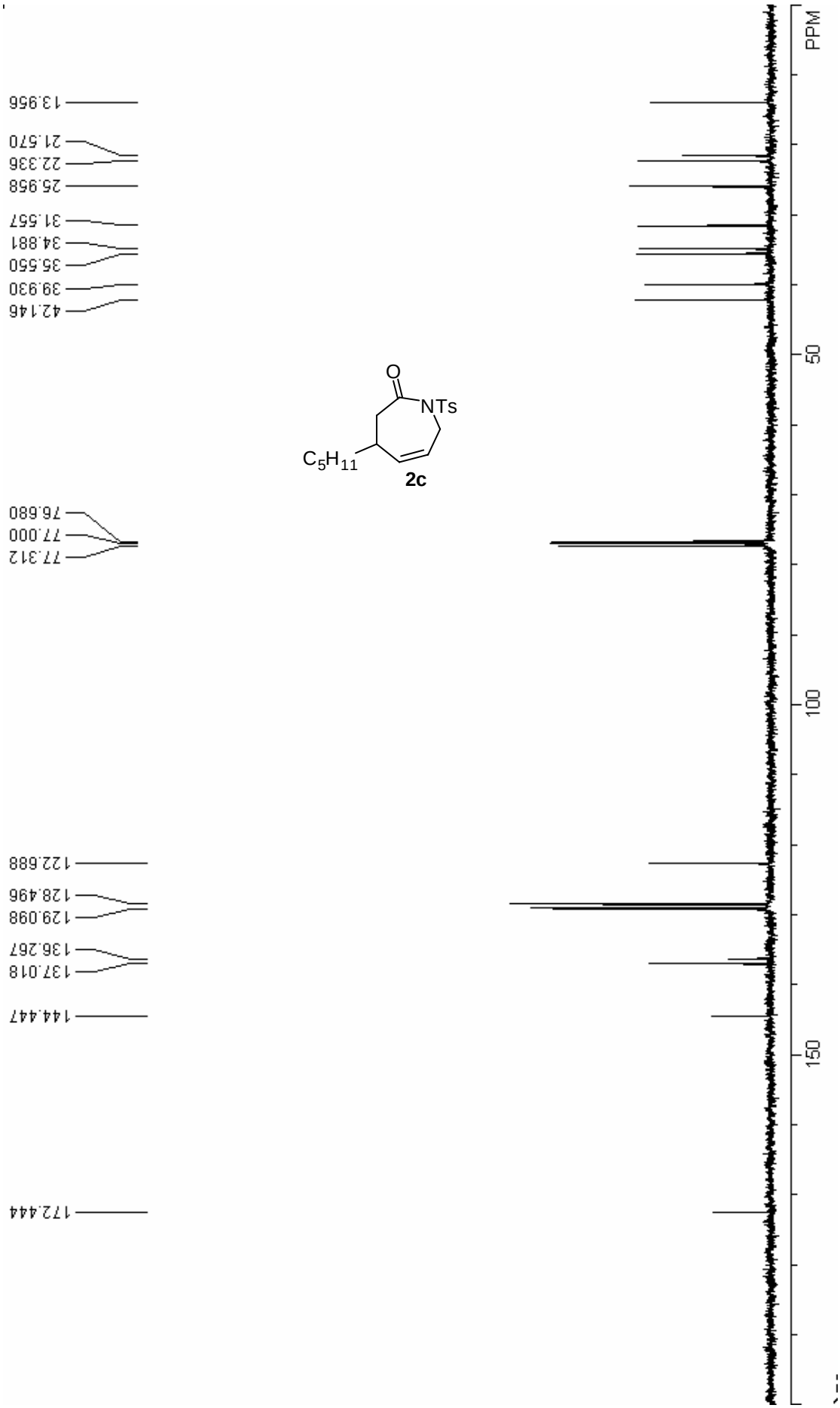
7.292
7.825
7.853
O
NTs
C5H11
2c
PPM
2
4
6
8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77.000
77.312
122.688
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137.018
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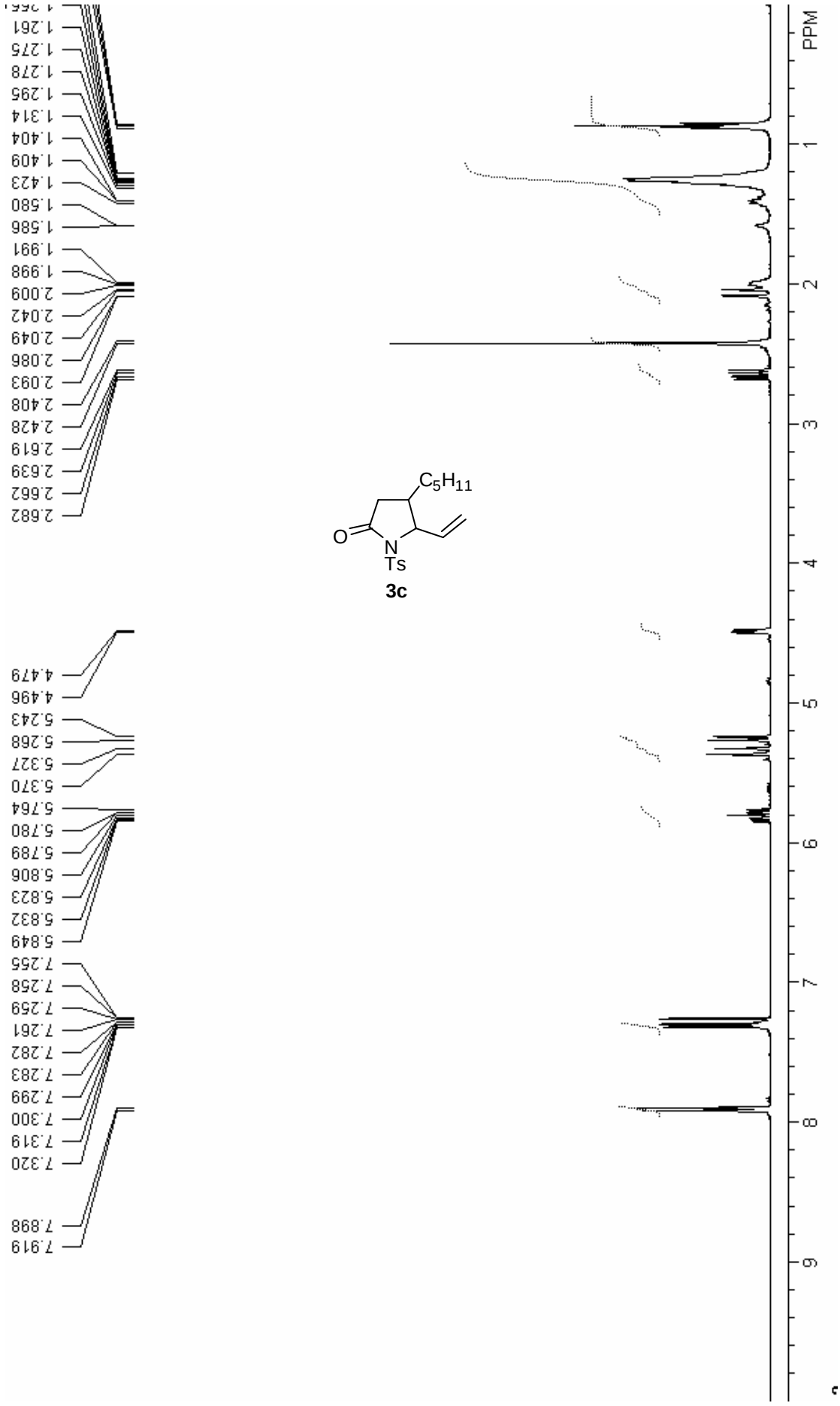
NTs
C5H11
2c
PPM
50
100
150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1.423
1.580
1.586
1.991
1.998
2.009
2.042
2.049
2.086
2.093
2.408
2.428
2.619
2.639
2.662
2.682
4.479
4.496
5.243
5.268
5.327
5.370
5.764
5.780
5.789
5.806
5.823
5.832
5.849
7.255
7.258
7.259
7.261
7.282
7.283
7.299
7.300
7.319
7.320
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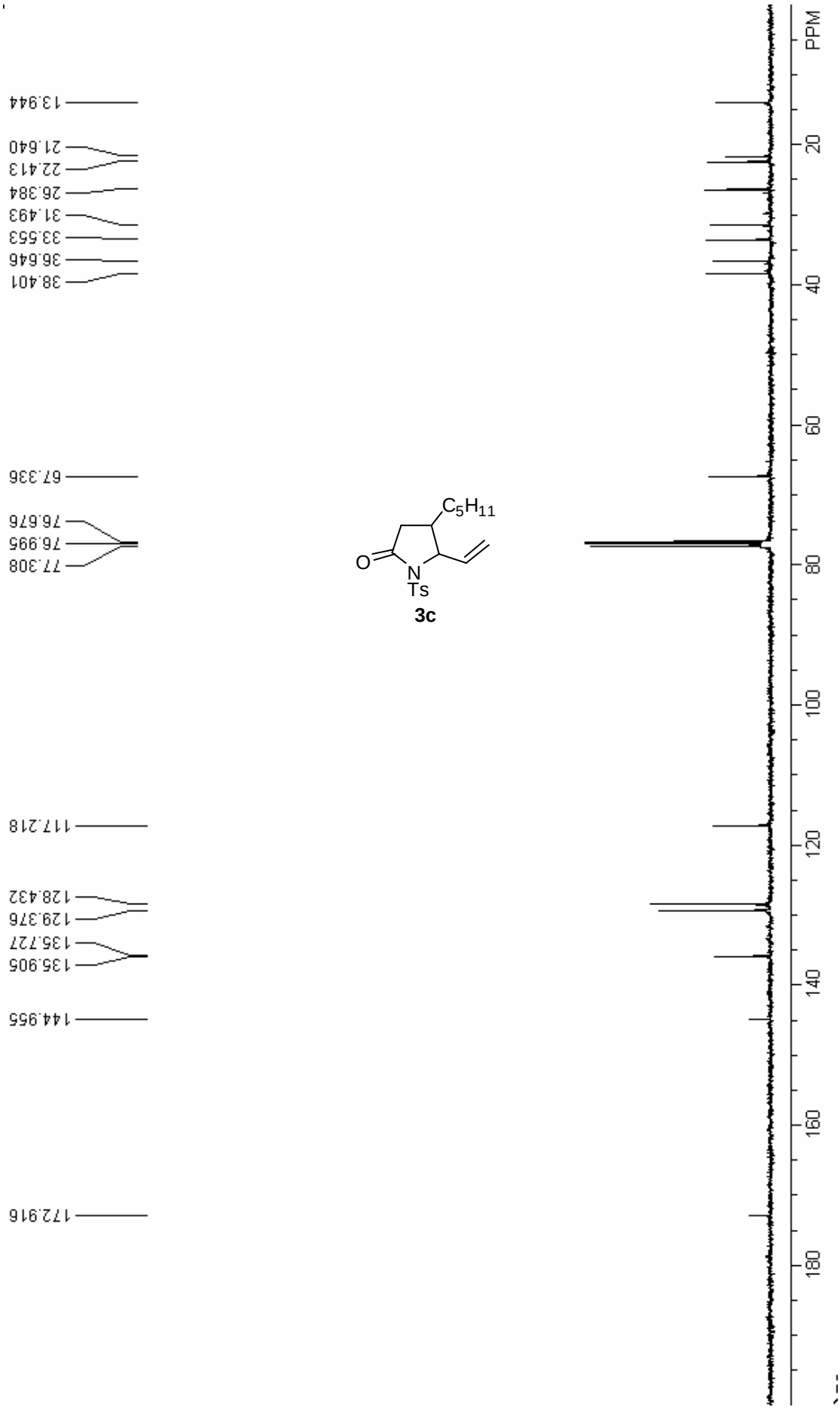
PPM
1
2
3
4
5
6
7
8
9
O
N
Ts
C5H11

3c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33.553
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38.401
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117.218
128.432
129.376
135.727
135.905
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80
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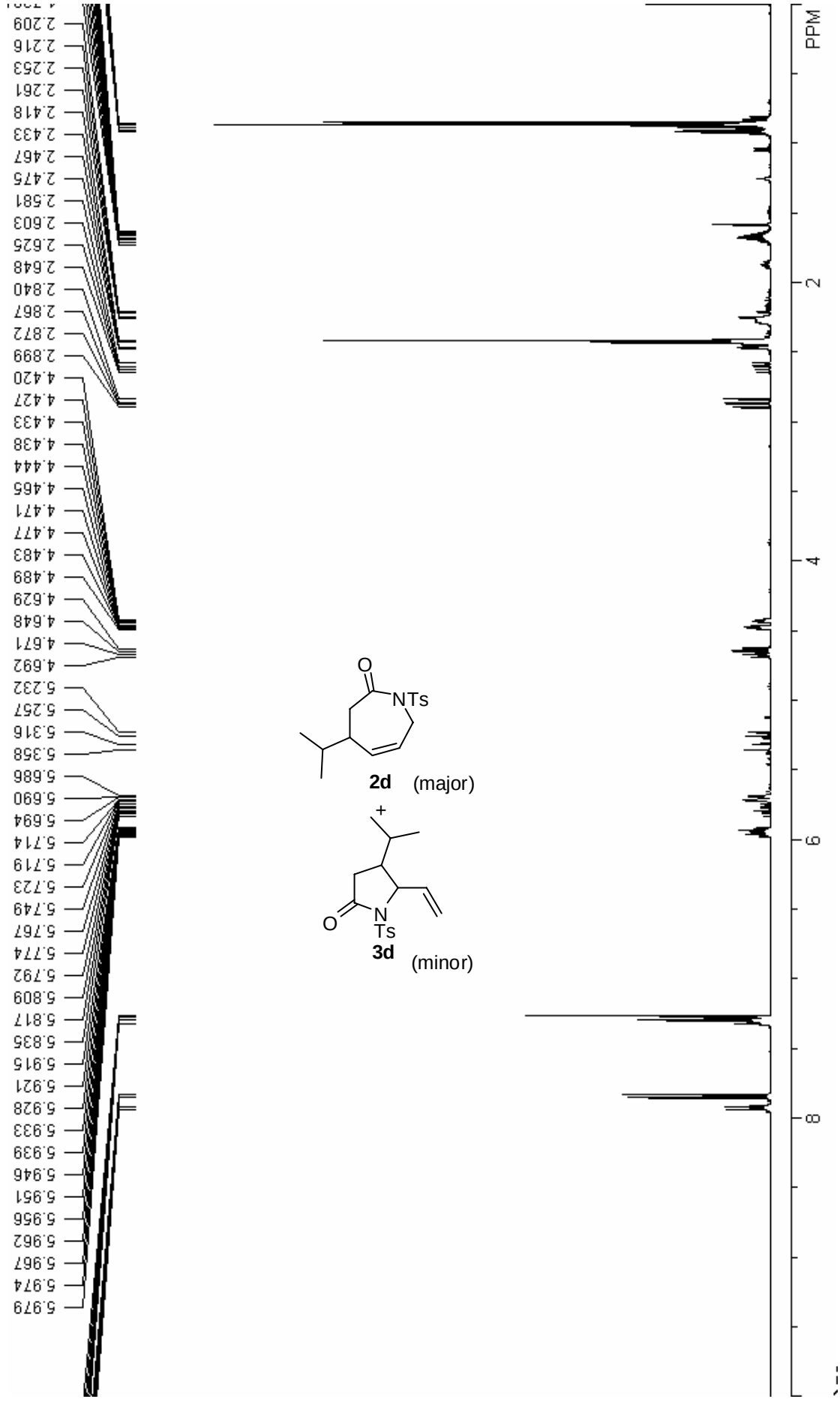
140
160
180
O
N
Ts
C5H11

3c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2.840
2.867
2.872
2.899
4.420
4.427
4.433
4.438
4.444
4.465
4.471
4.477
4.483
4.489
4.629
4.648
4.671
4.692
5.232
5.257
5.316
5.358
5.686
5.690
5.694
5.714
5.719
5.723
5.749
5.767
5.774
5.792
5.809
5.817
5.835
5.915
5.921
5.928
5.933
5.939
5.946
5.951
5.956
5.962
5.967
5.974
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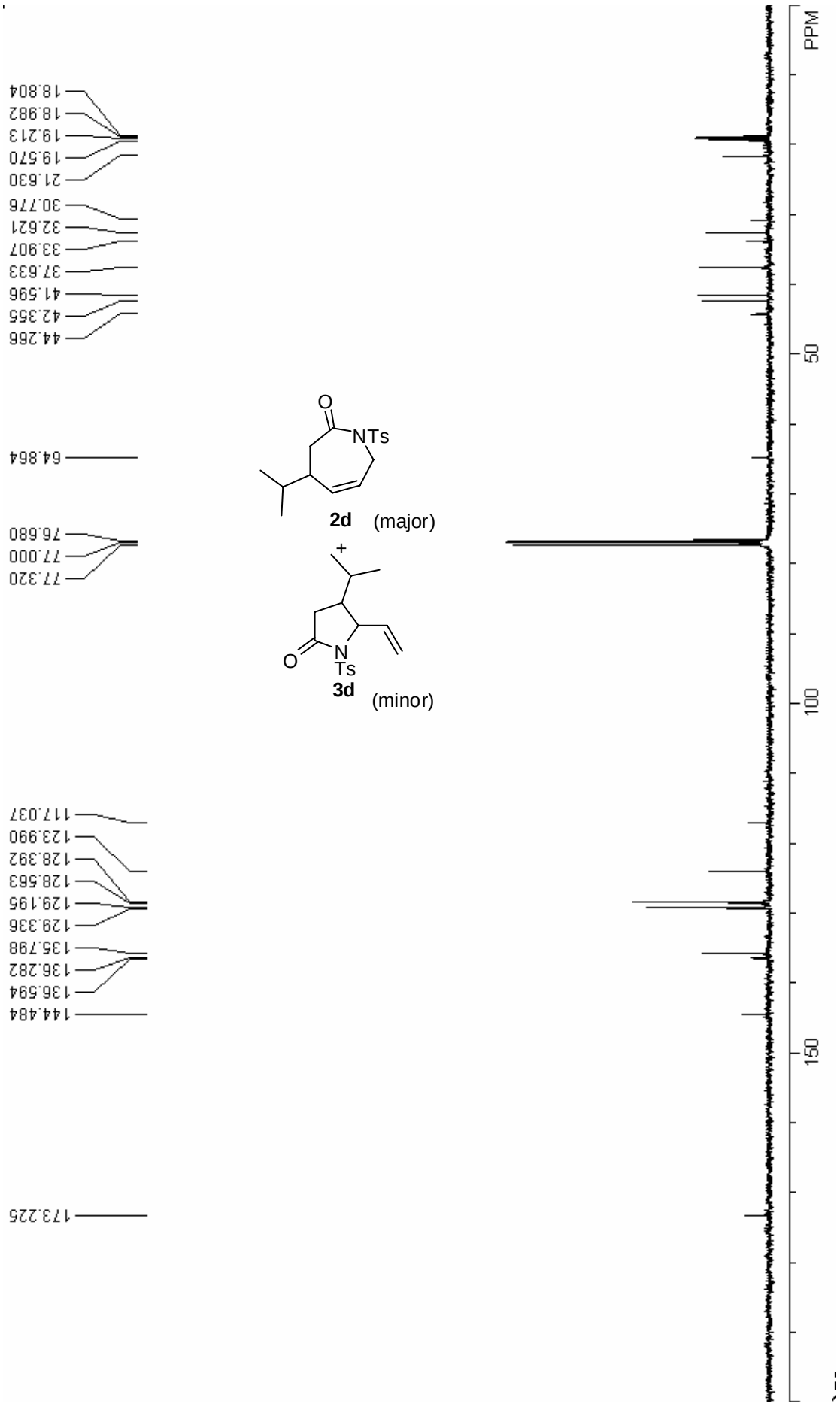
PPM
2
4
6
8
O
NTs
2d (major)
+
O
N
Ts
3d (minor)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19.213
19.570
21.630
30.776
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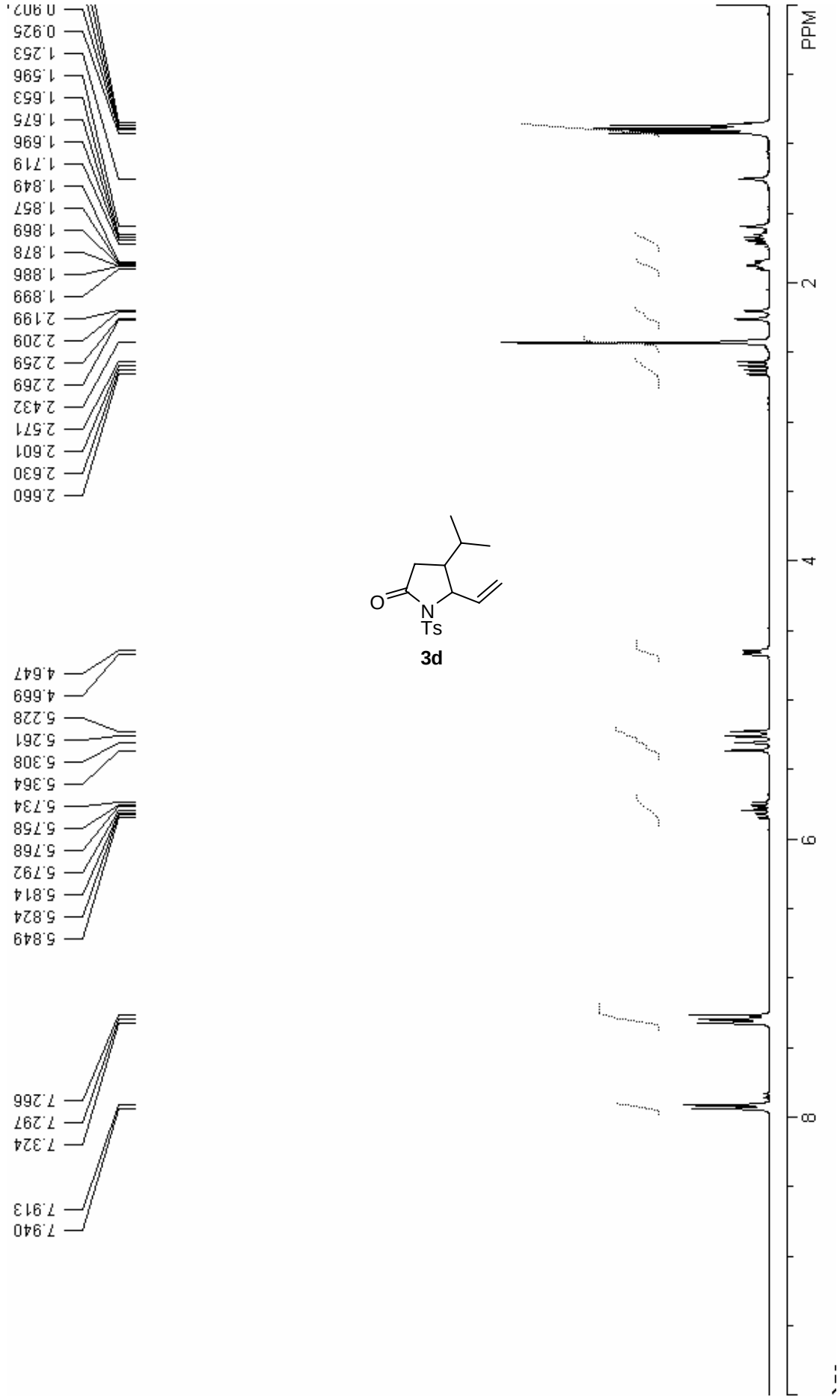
33.907
37.633
41.596
42.355
44.266
64.864
76.680
77.000
77.320
117.037
123.990
128.392
128.563
129.195
129.336
135.798
136.282
136.594
144.484
173.225
O
NTs
2d (major)
+
O
N
Ts
3d (minor)
PPM
50
100
150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1.857
1.869
1.878
1.886
1.899
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2.269
2.432
2.571
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2.630
2.660
4.647
4.669
5.228
5.261
5.308
5.364
5.734
5.758
5.768
5.792
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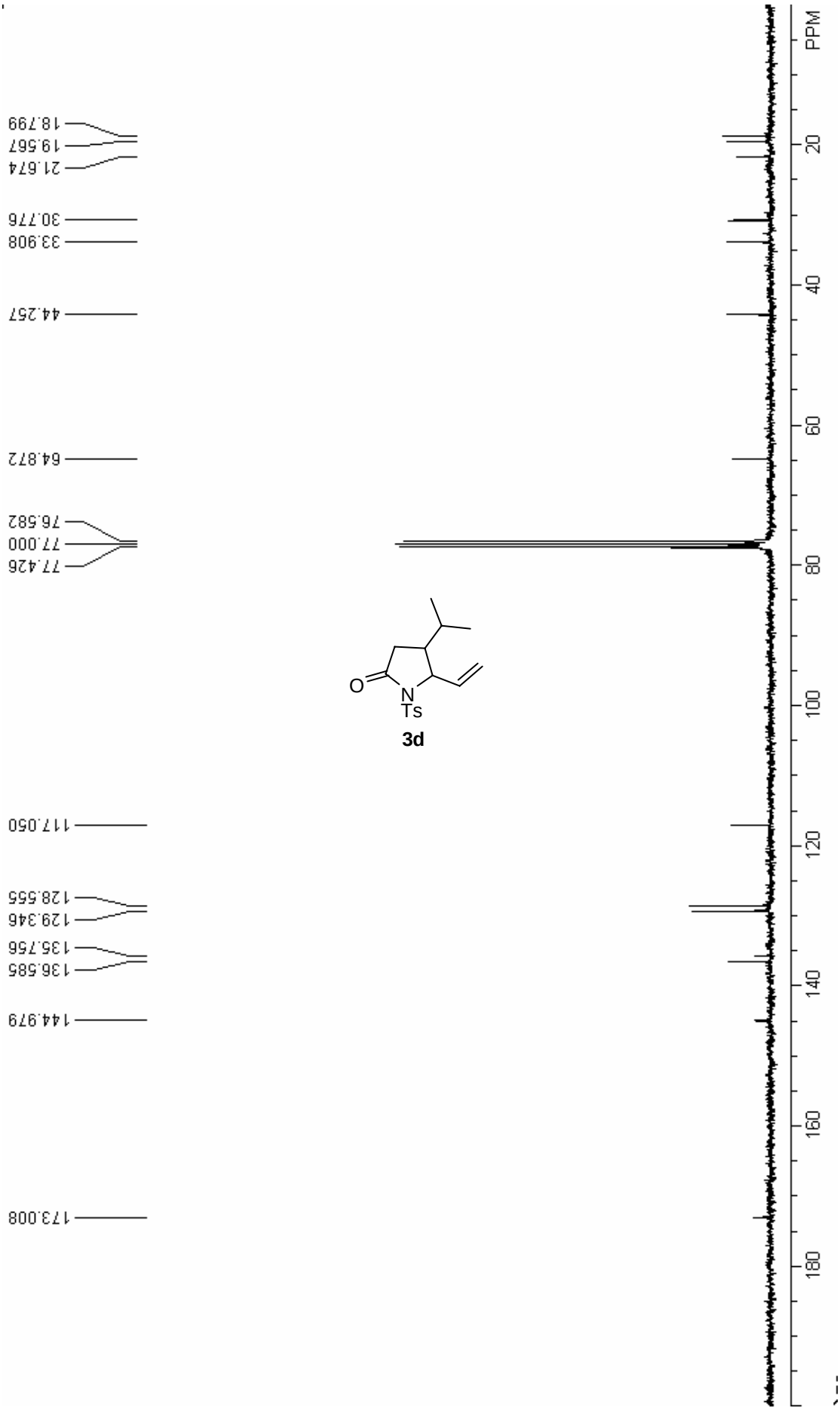
PPM
2
4
6
8

3d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77.426
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128.555
129.346
135.756
136.585
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173.008
PPM
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120
140
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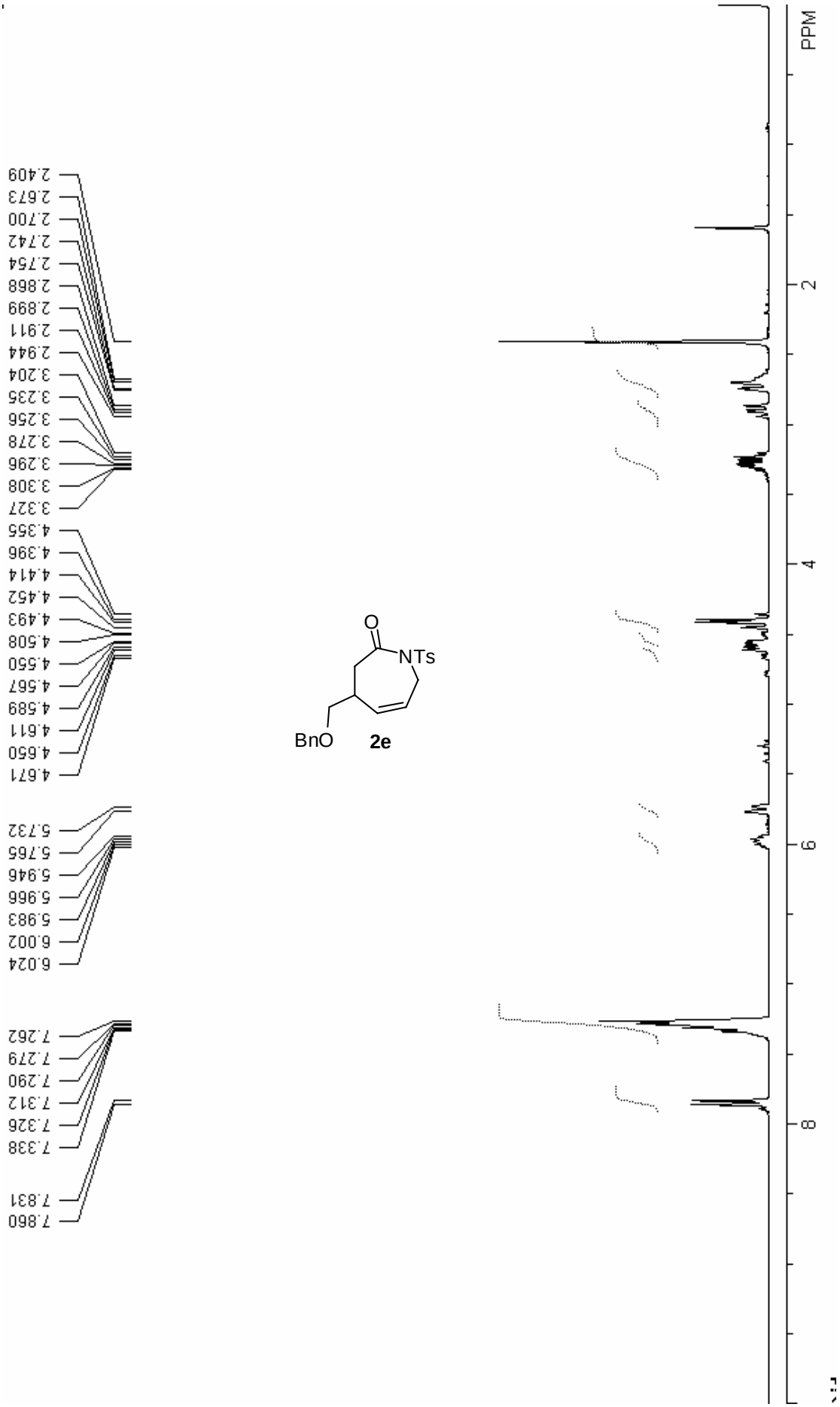
180
O
N
Ts

3d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2.899
2.911
2.944
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3.235
3.256
3.278
3.296
3.308
3.327
4.355
4.396
4.414
4.452
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4.550
4.567
4.589
4.611
4.650
4.671
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6.002
6.024
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7.279
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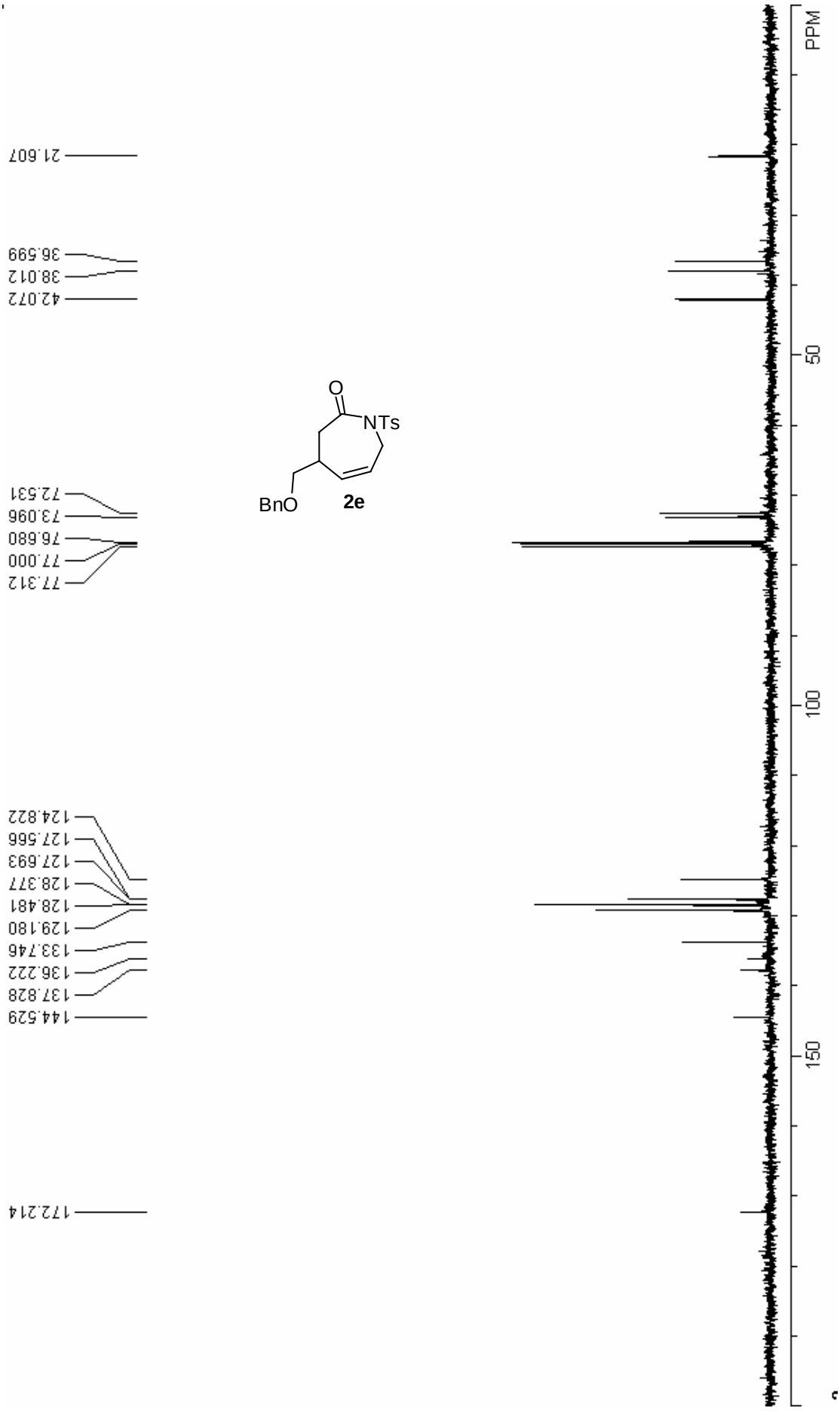
7.860
O
NTs
BnO
2e
PPM
2
4
6
8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77.000
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127.693
128.377
128.481
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NTs
BnO
2e
PPM
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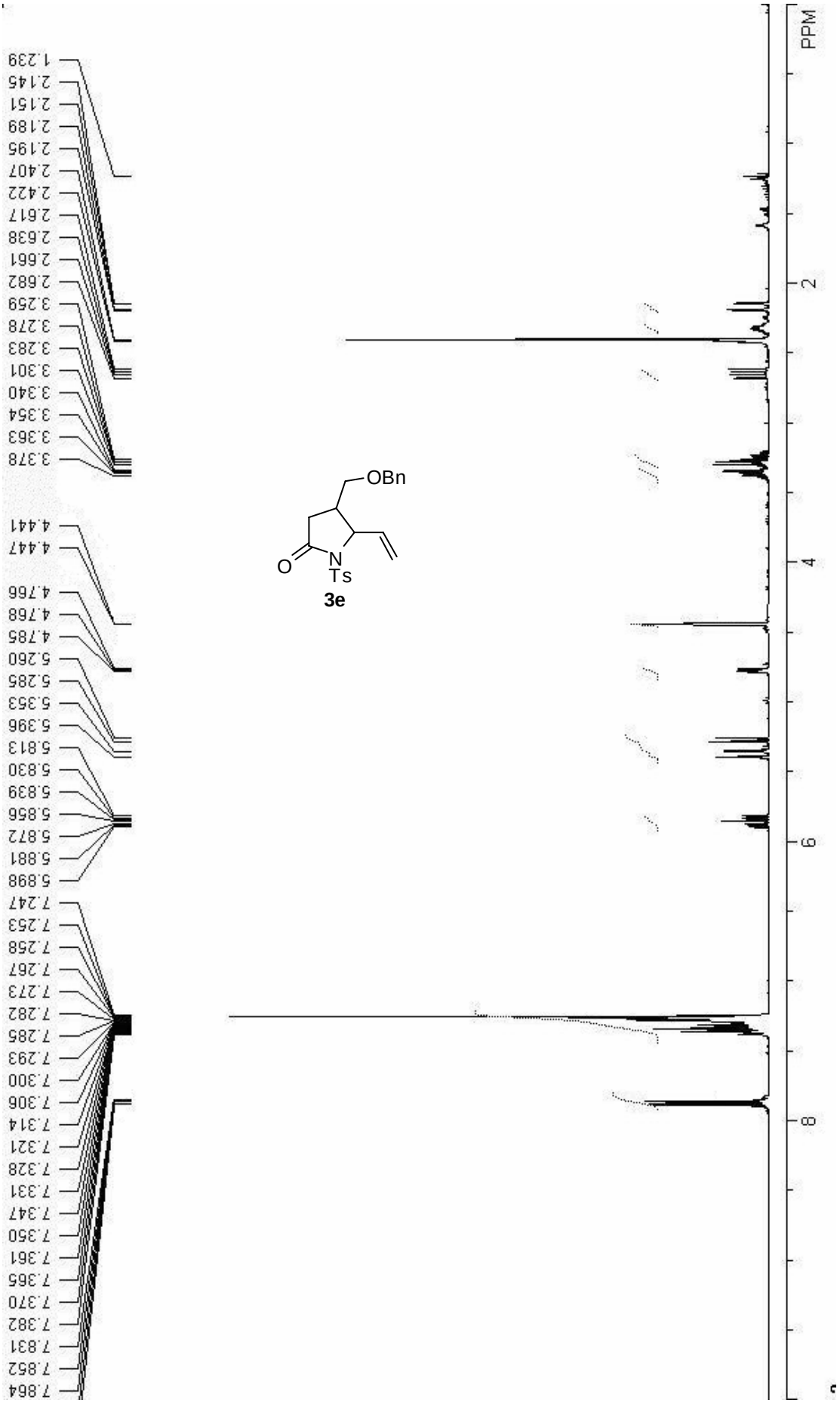
100
150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3.278
3.283
3.301
3.340
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4.768
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5.285
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5.813
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5.856
5.872
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7.273
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7.314
7.321
7.328
7.331
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7.361
7.365
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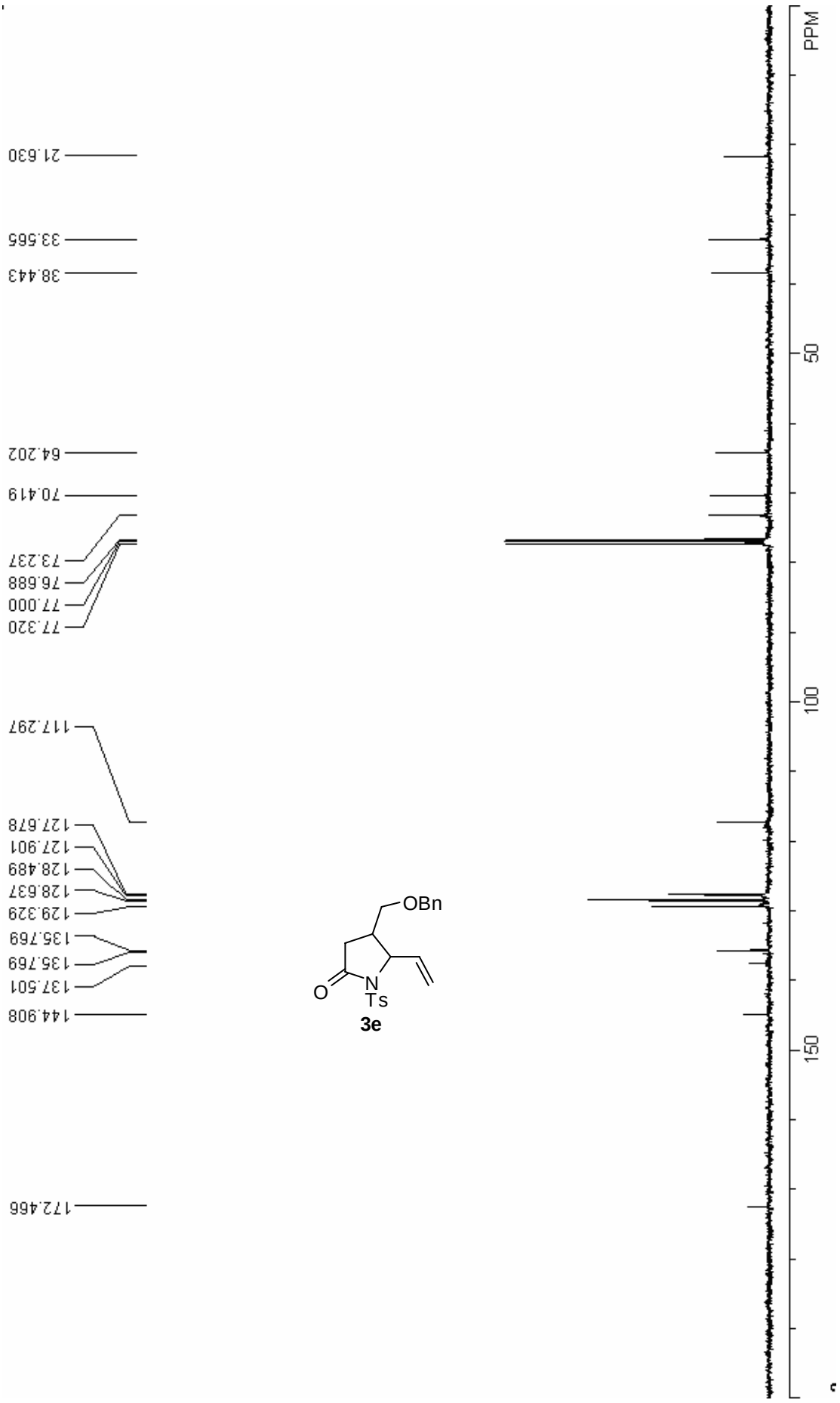
7.852
7.864
OBn
O
N
Ts
PPM
2
4
6
8

3e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117.297
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128.489
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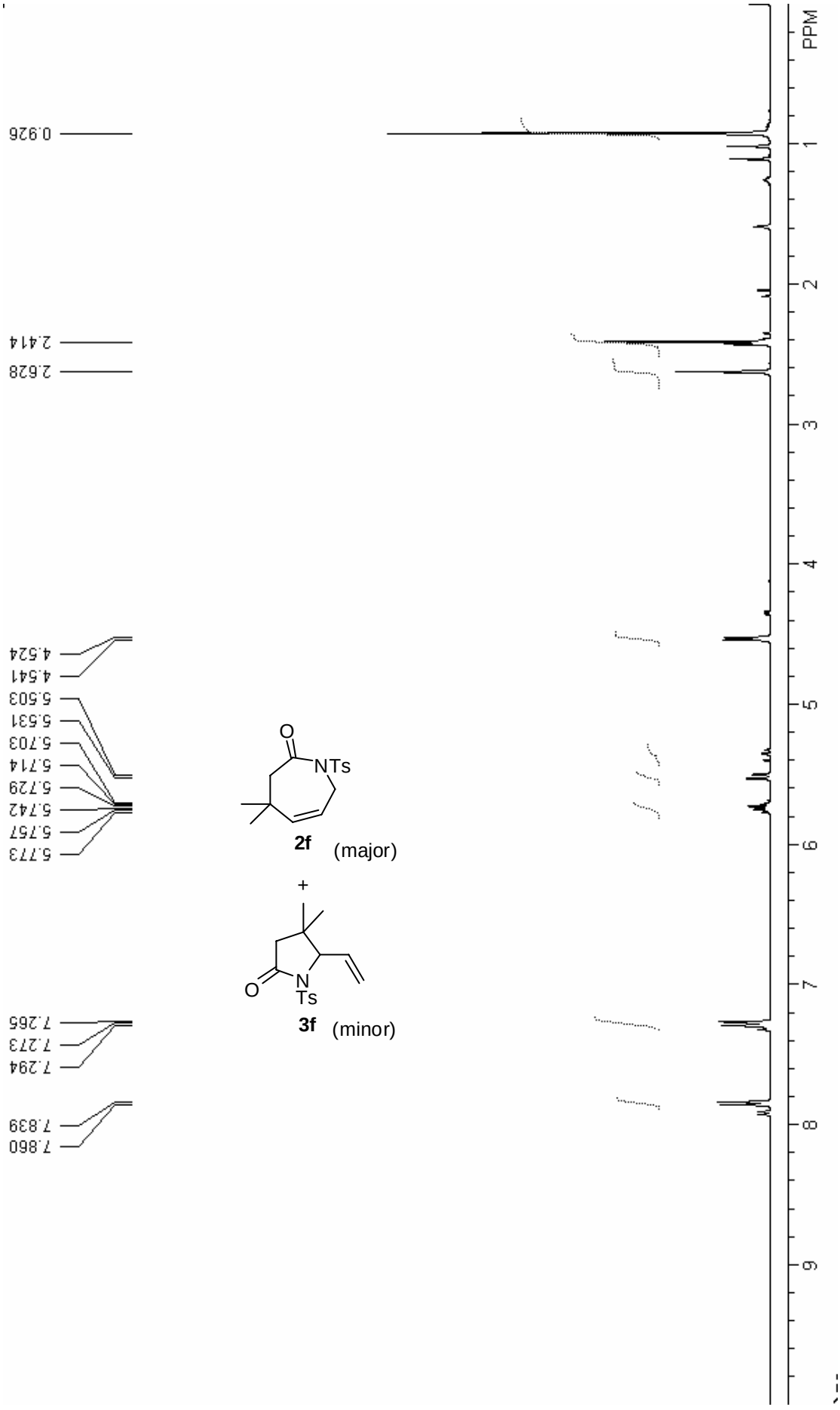
137.501
144.908
172.466
PPM
50
100
150
OBn
O
N
Ts

3e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5.503
5.531
5.703
5.714
5.729
5.742
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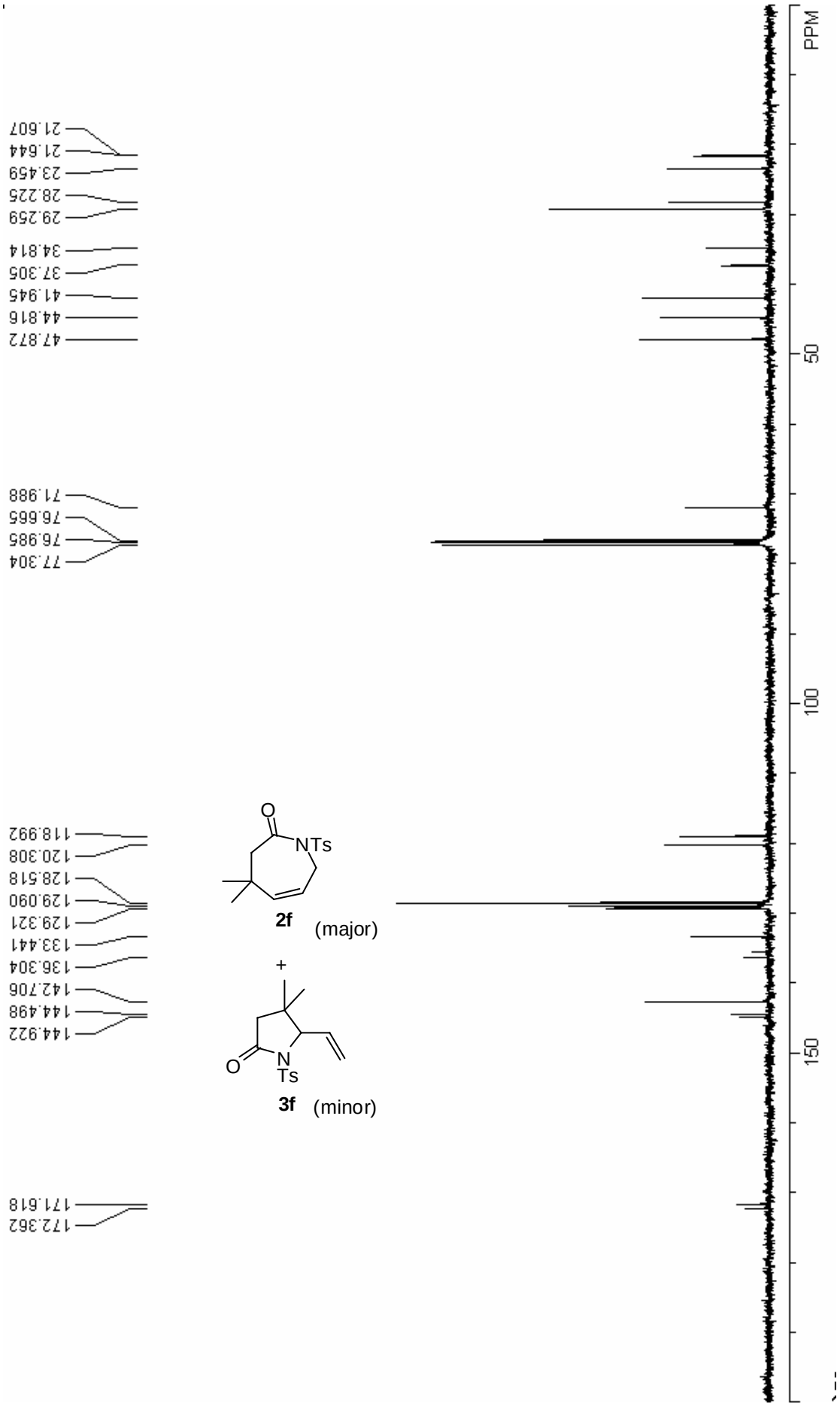
5.773
7.265
7.273
7.294
7.839
7.860
PPM
1
2
3
4
5
6
7
8
9
O
NTs
2f (major)
+
O
N
Ts
3f (minor)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29.259
34.814
37.305
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47.872
71.988
76.665
76.985
77.304
118.992
120.308
128.518
129.090
129.321
133.441
136.304
142.706
144.498
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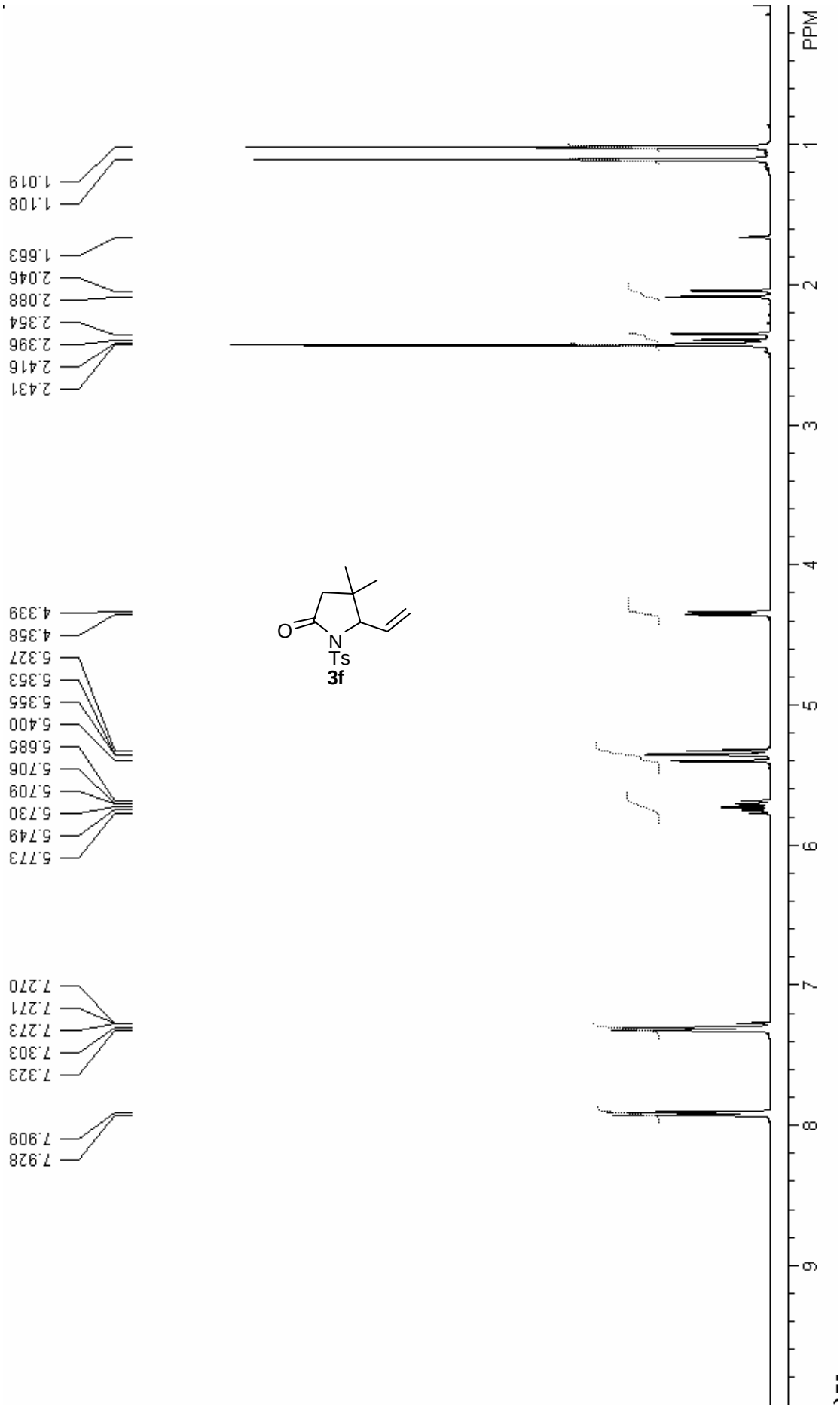
172.362
PPM
50
100
150
O
NTs
2f (major)
+
O
N
Ts
3f (minor)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5.400
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5.706
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5.730
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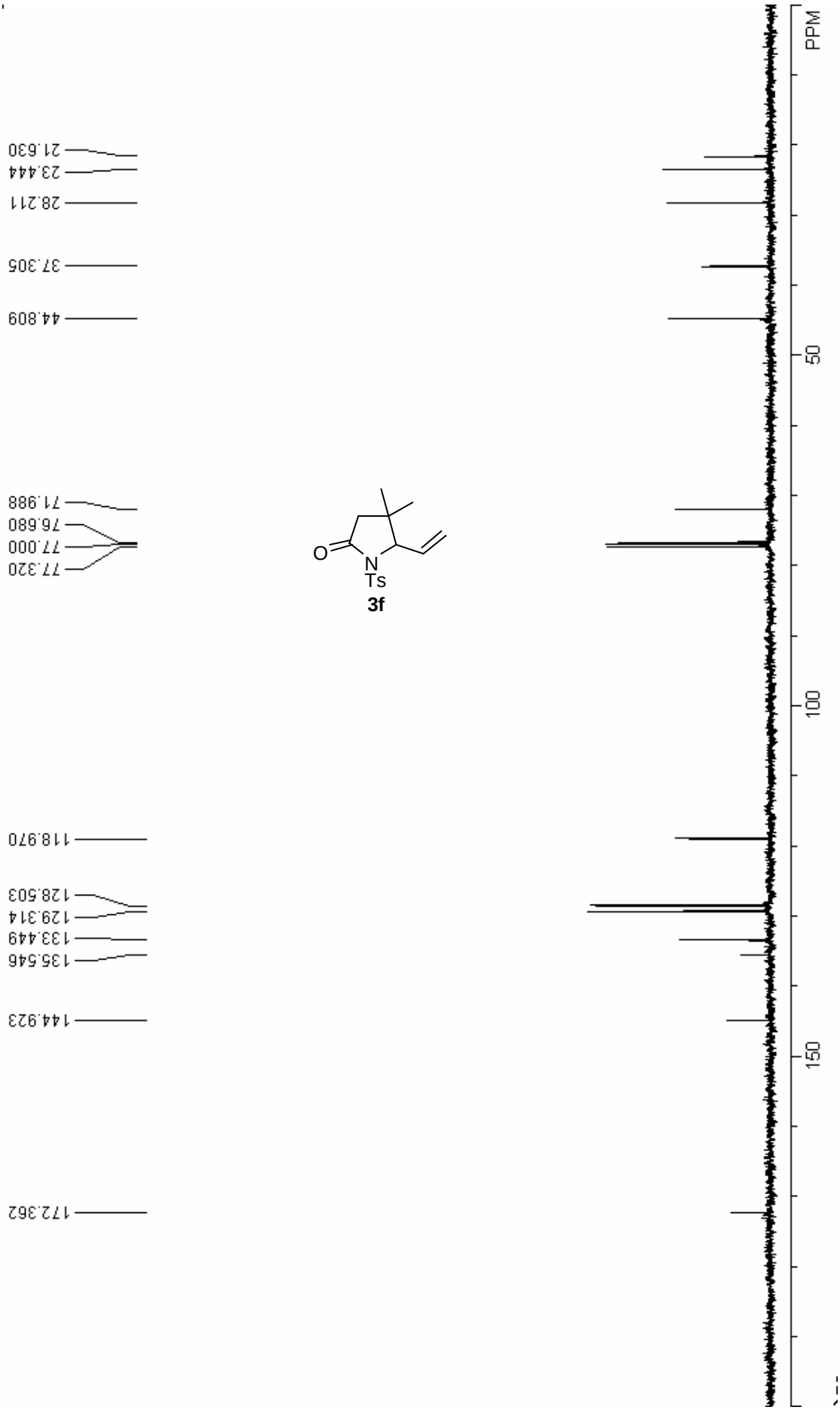
7.271
7.273
7.303
7.323
7.909
7.928
PPM
O
N
Ts
3f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N
Ts
PPM
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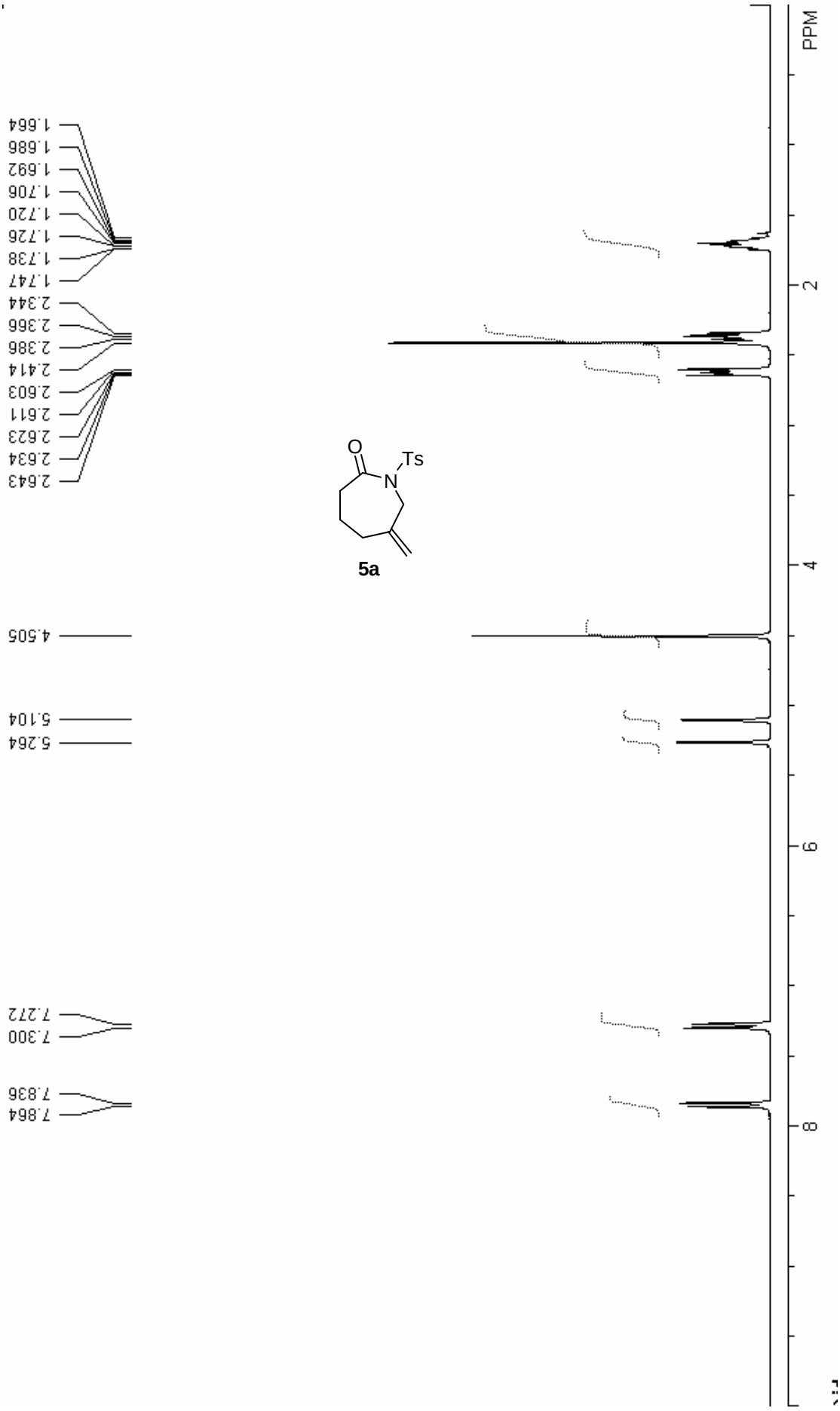
100
150

3f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2.414
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2.611
2.623
2.634
2.643
4.505
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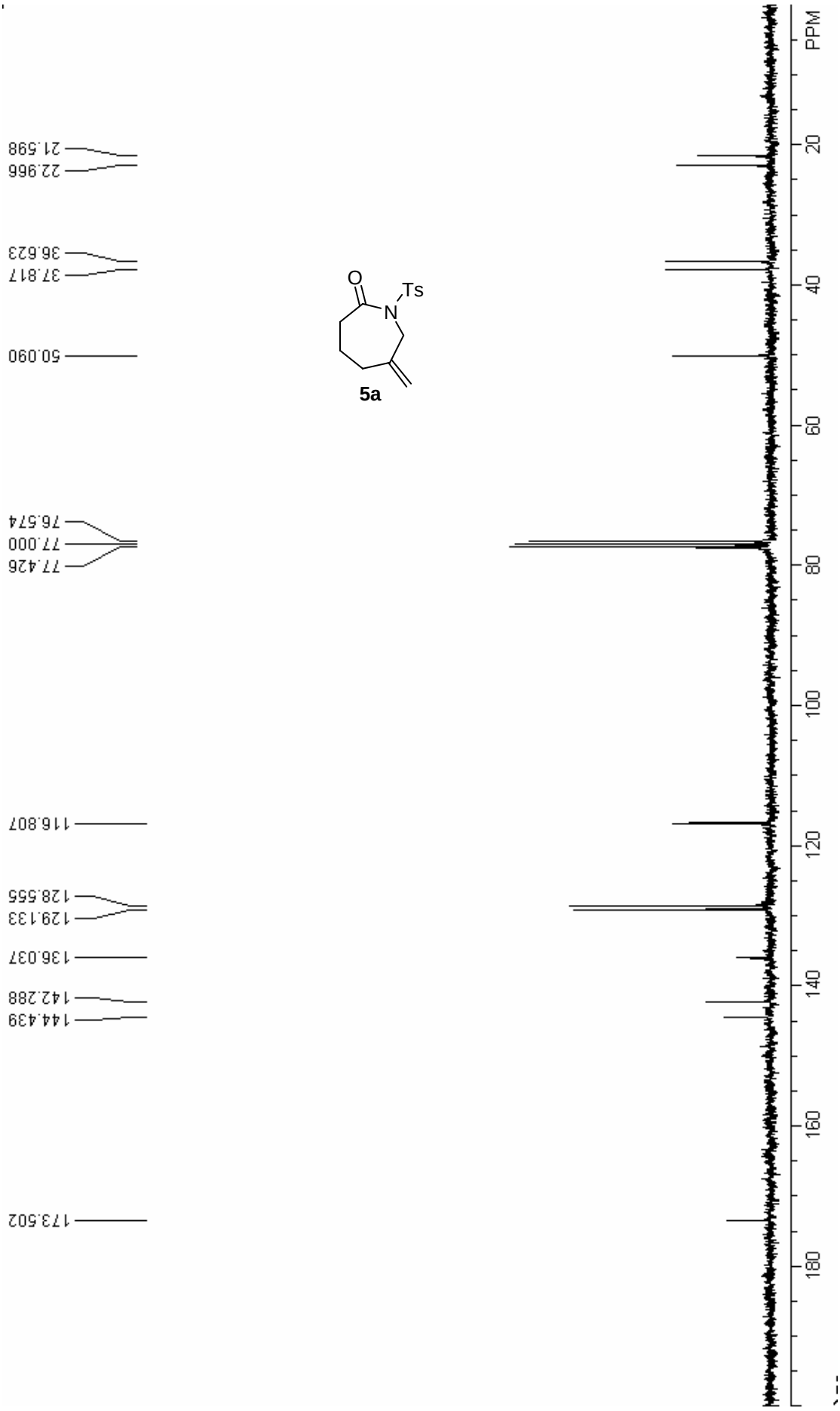
7.300
7.836
7.864
O
N
Ts
5a
PPM
2
4
6
8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O
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Ts
5a
PPM
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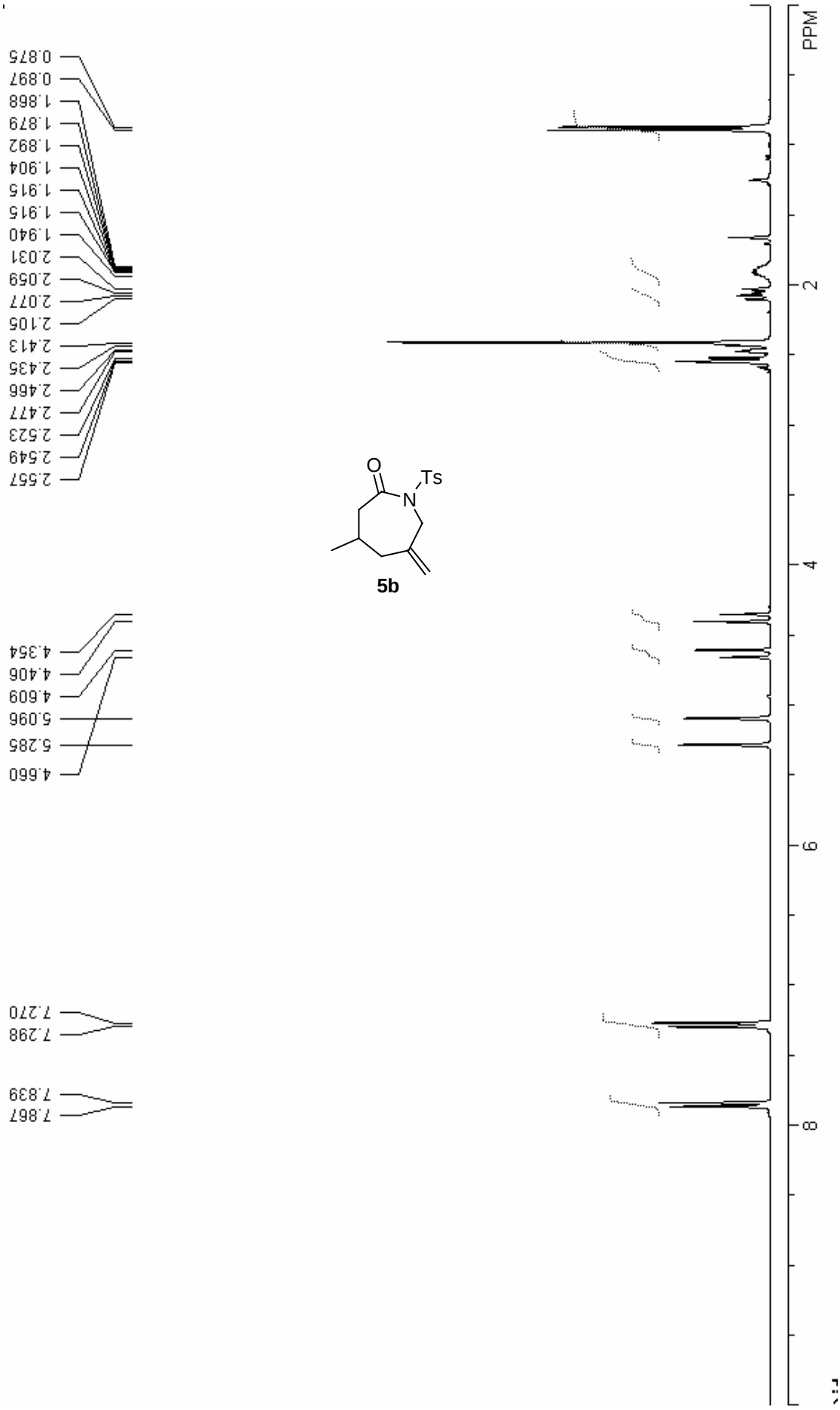
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2.031
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2.523
2.549
2.557
4.354
4.406
4.609
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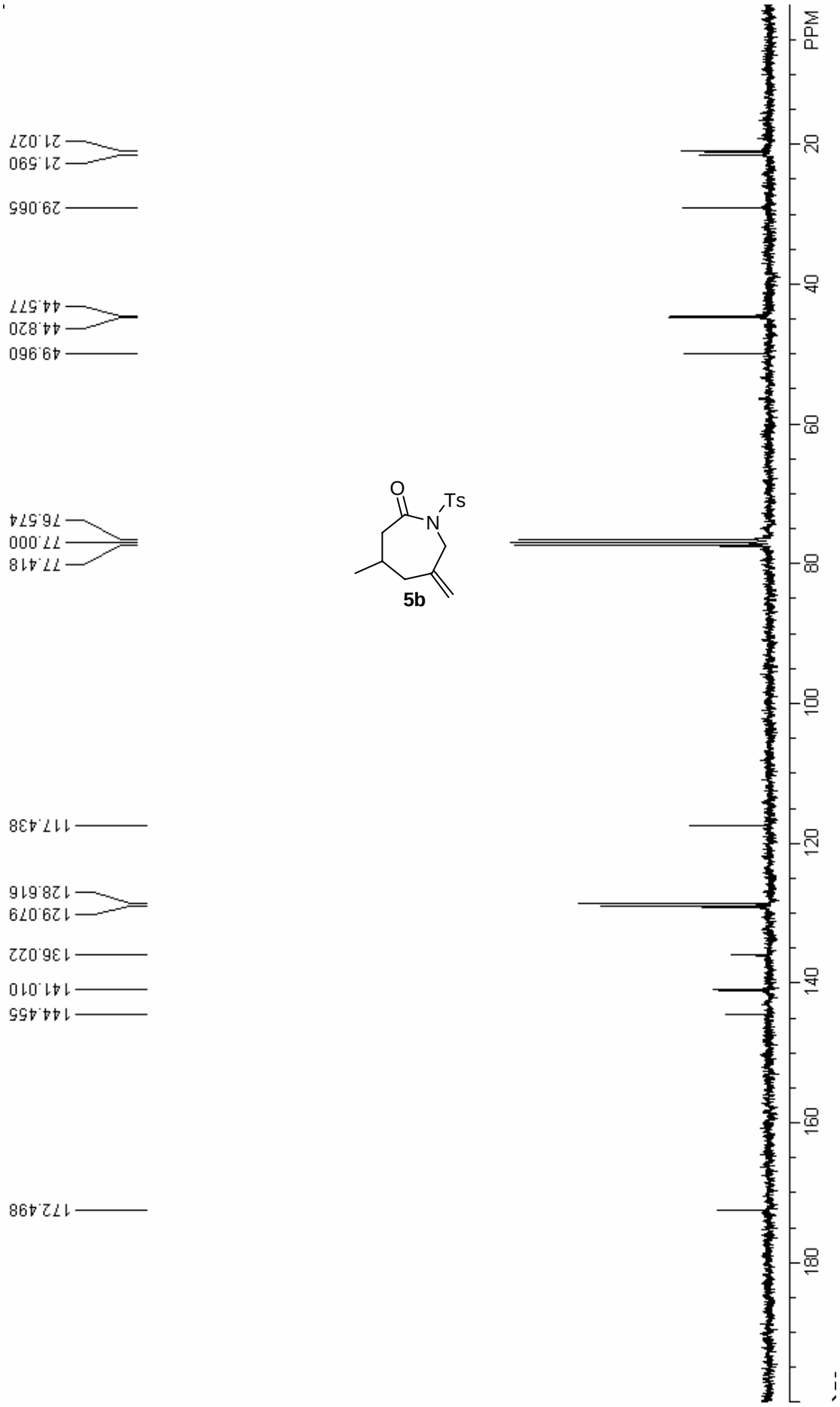
N
Ts
PPM
2
4
6
8

5b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O
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5b
PPM
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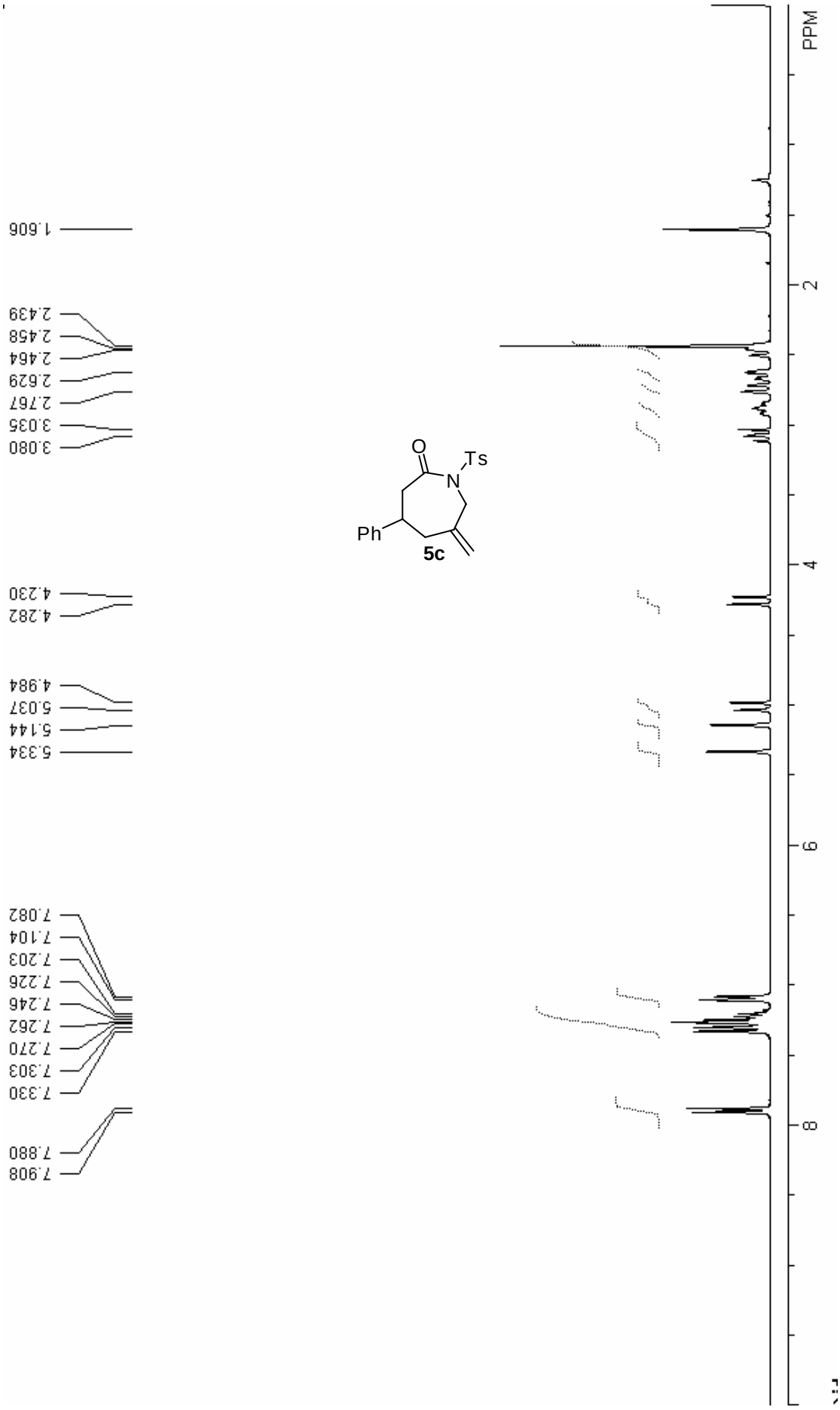
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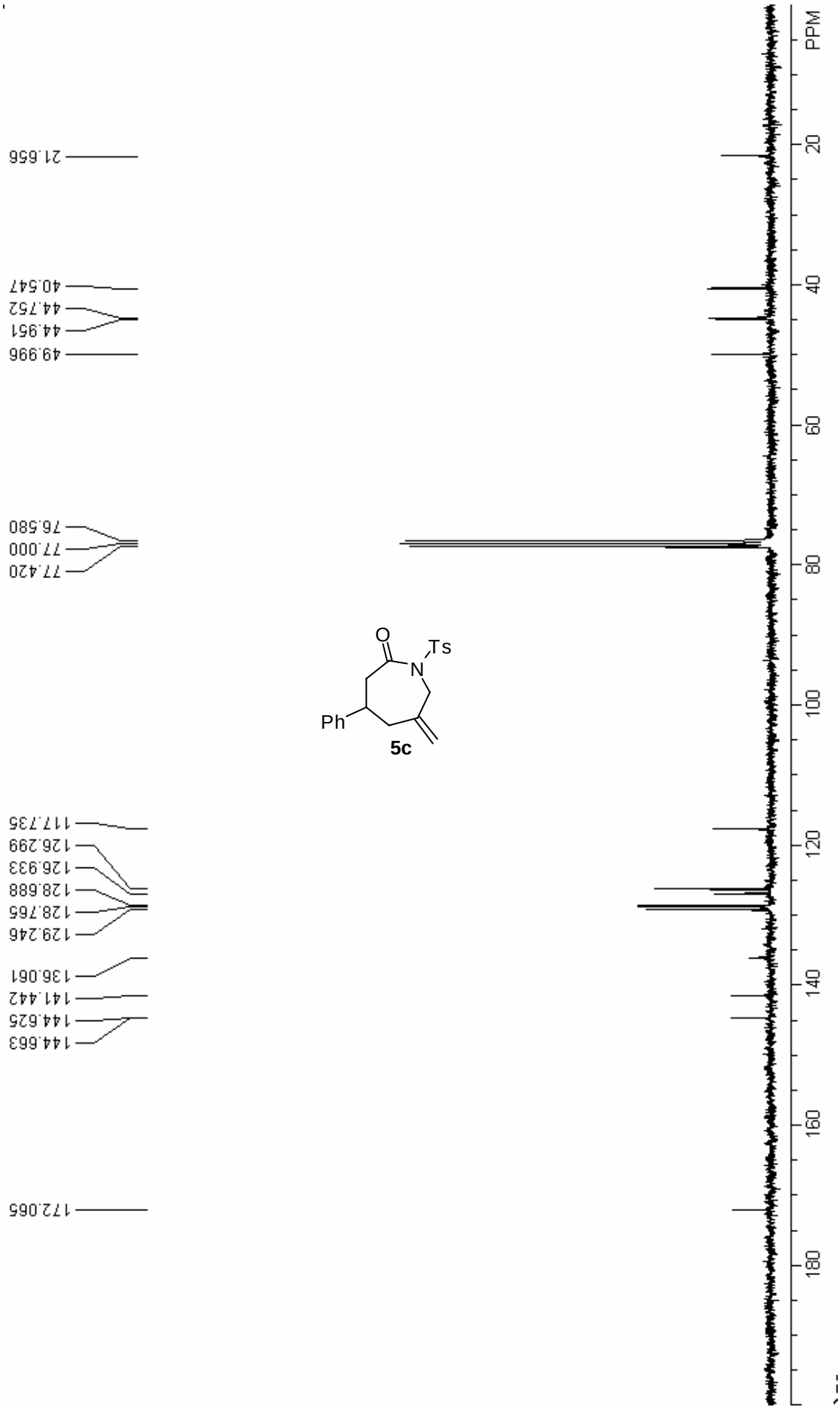
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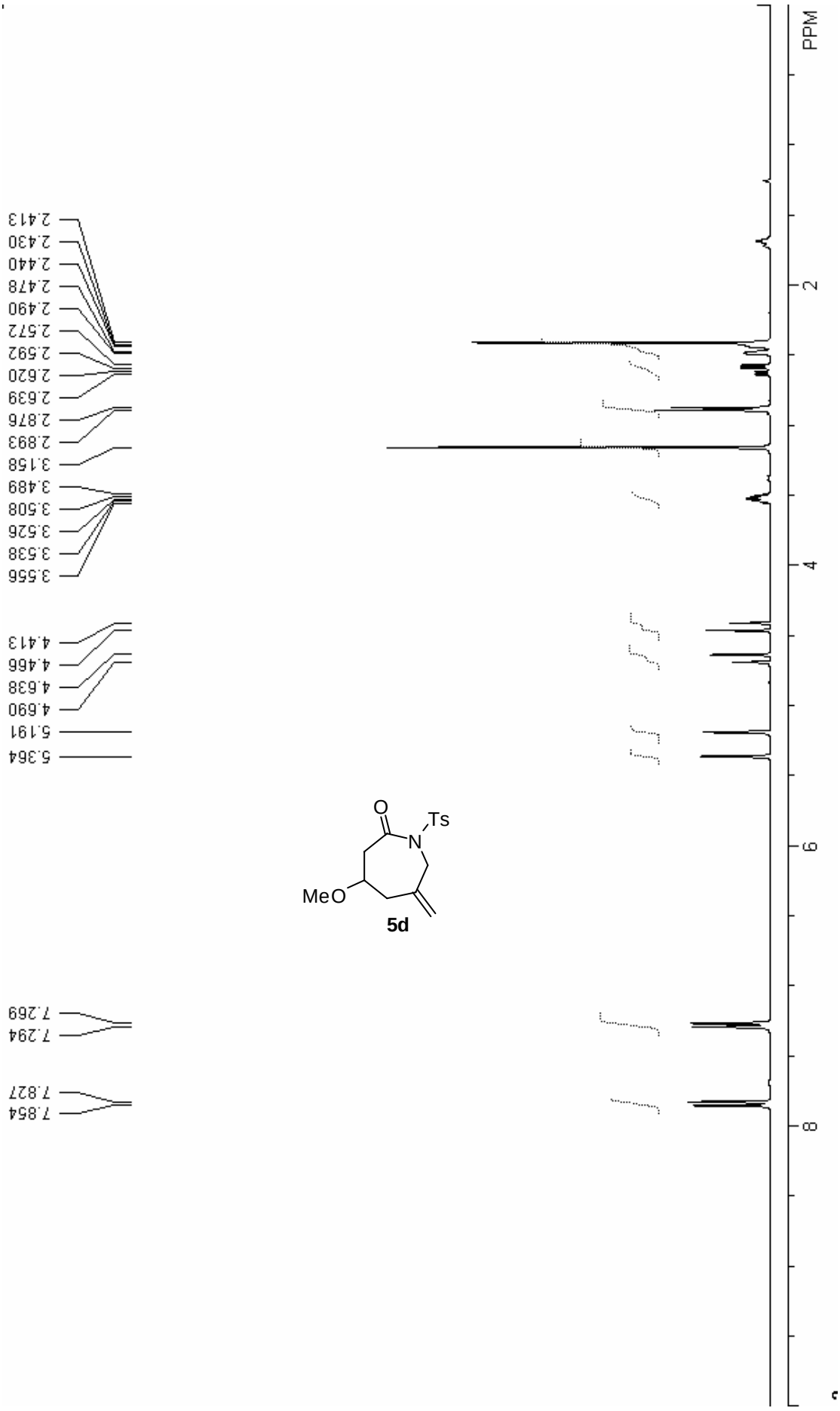
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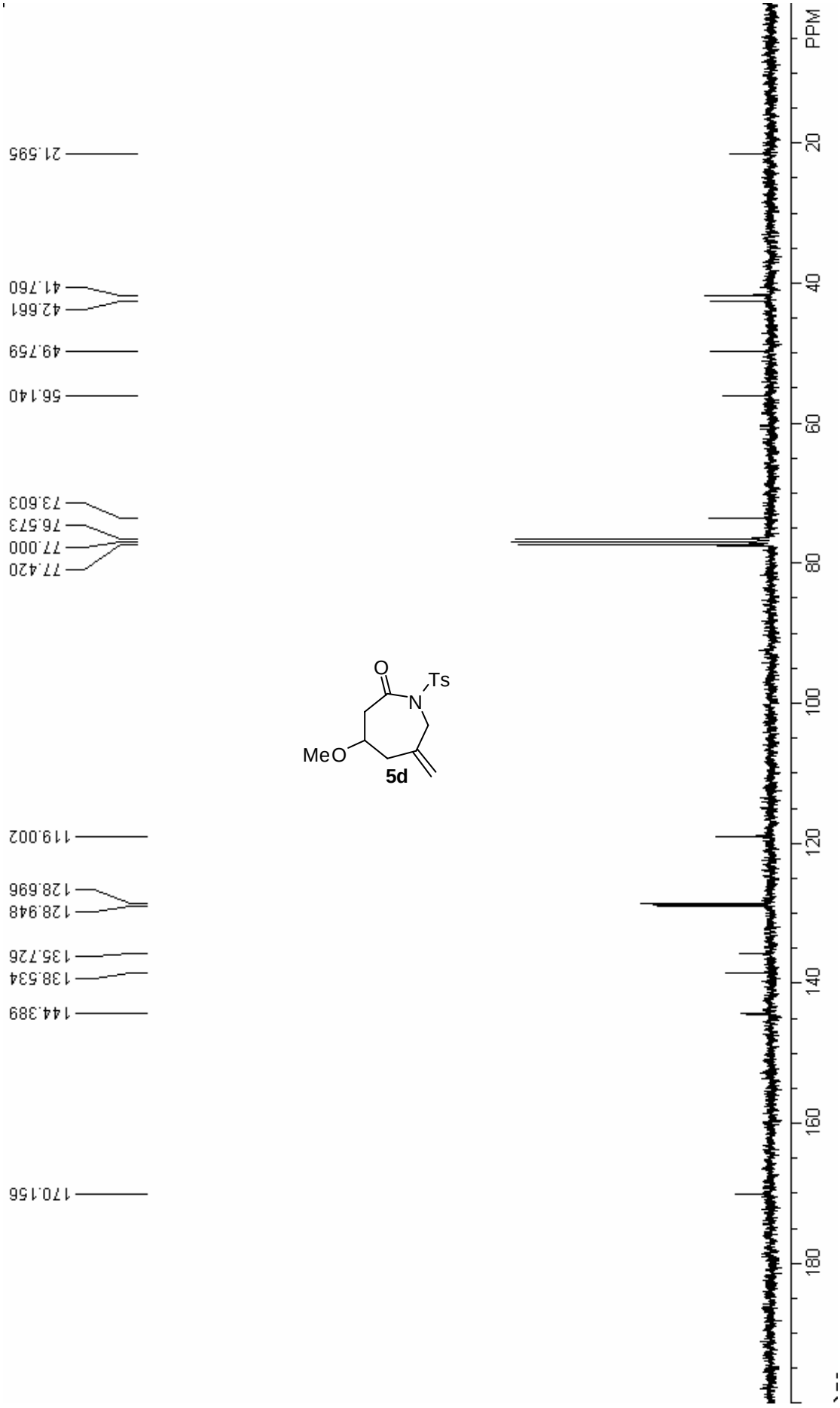
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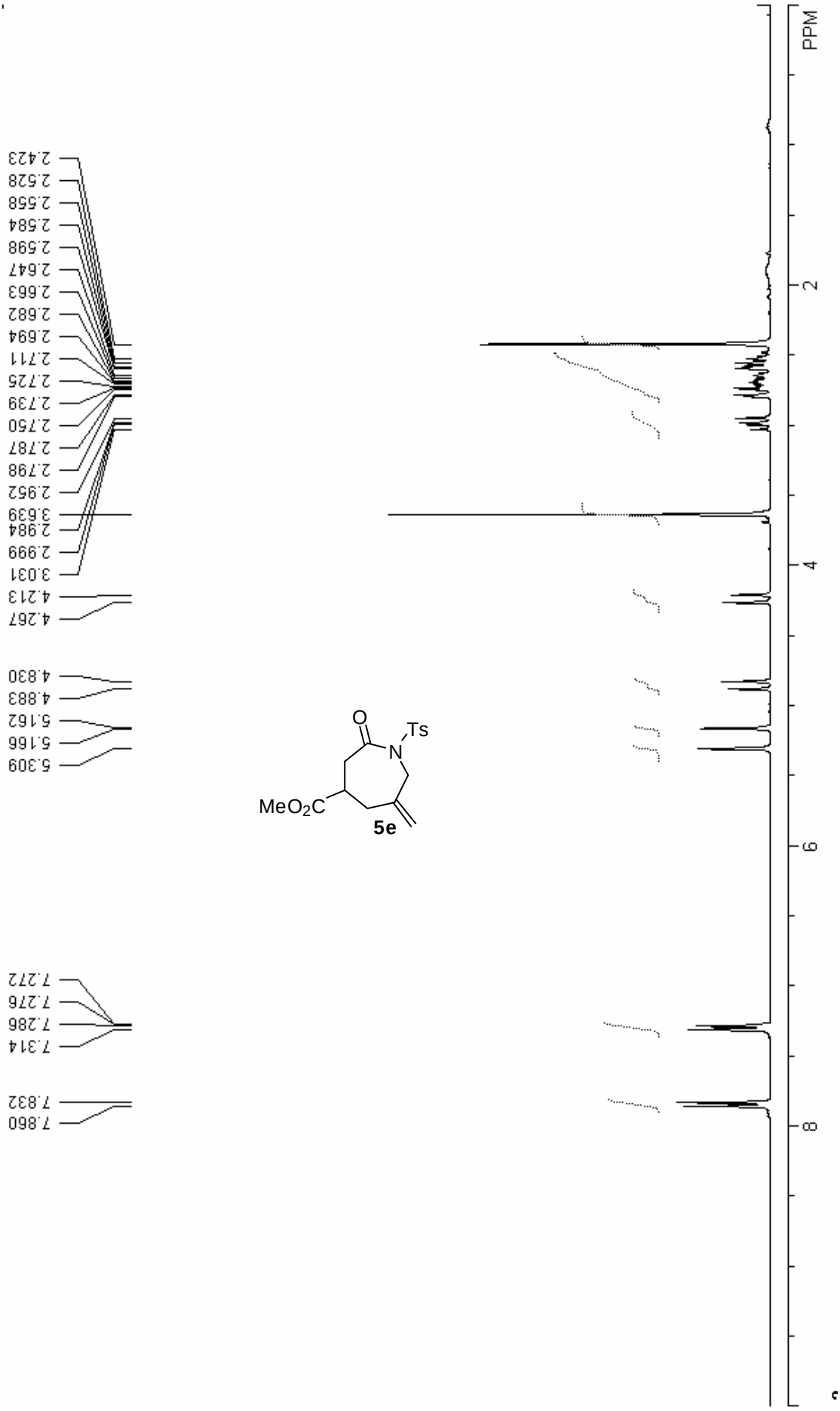
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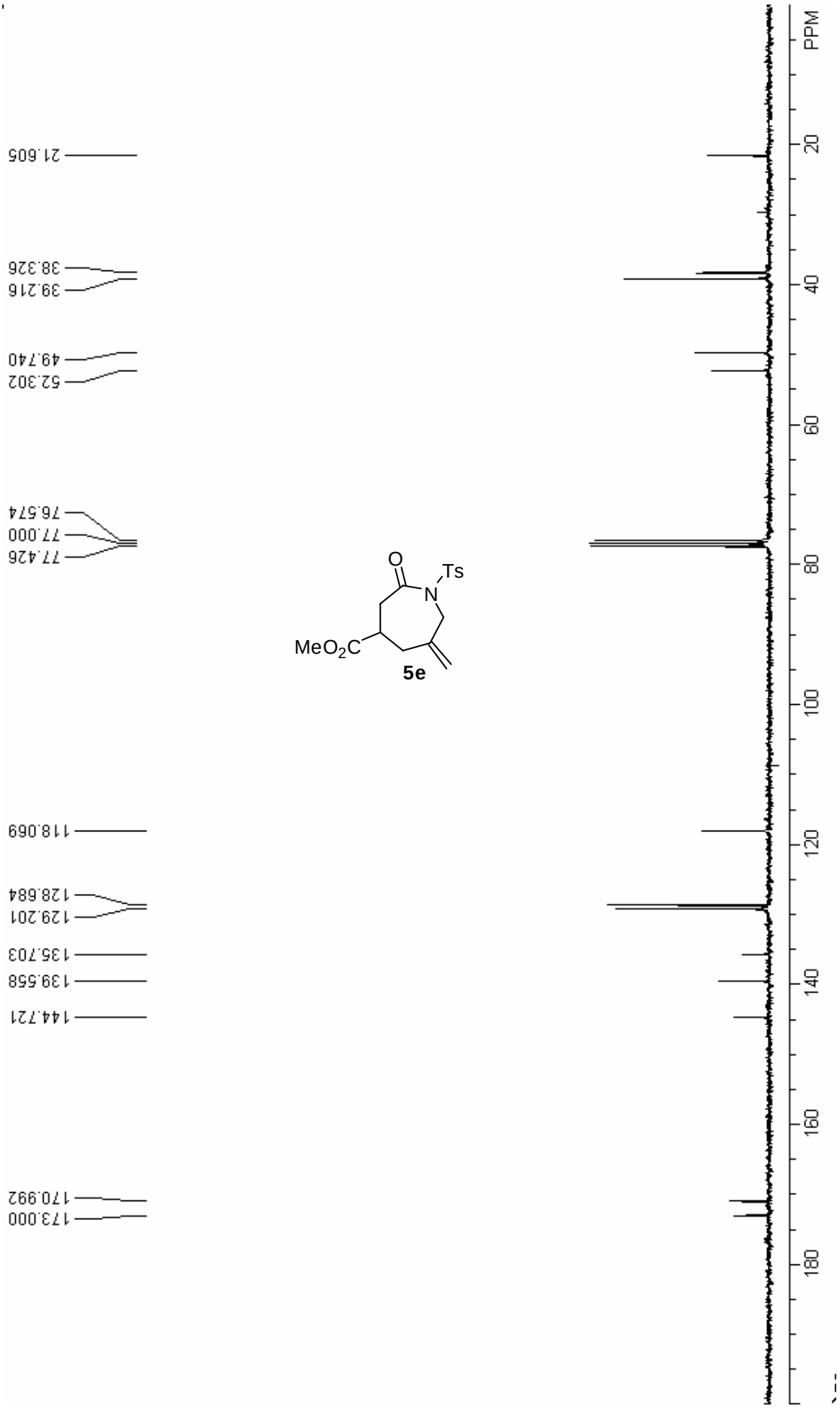
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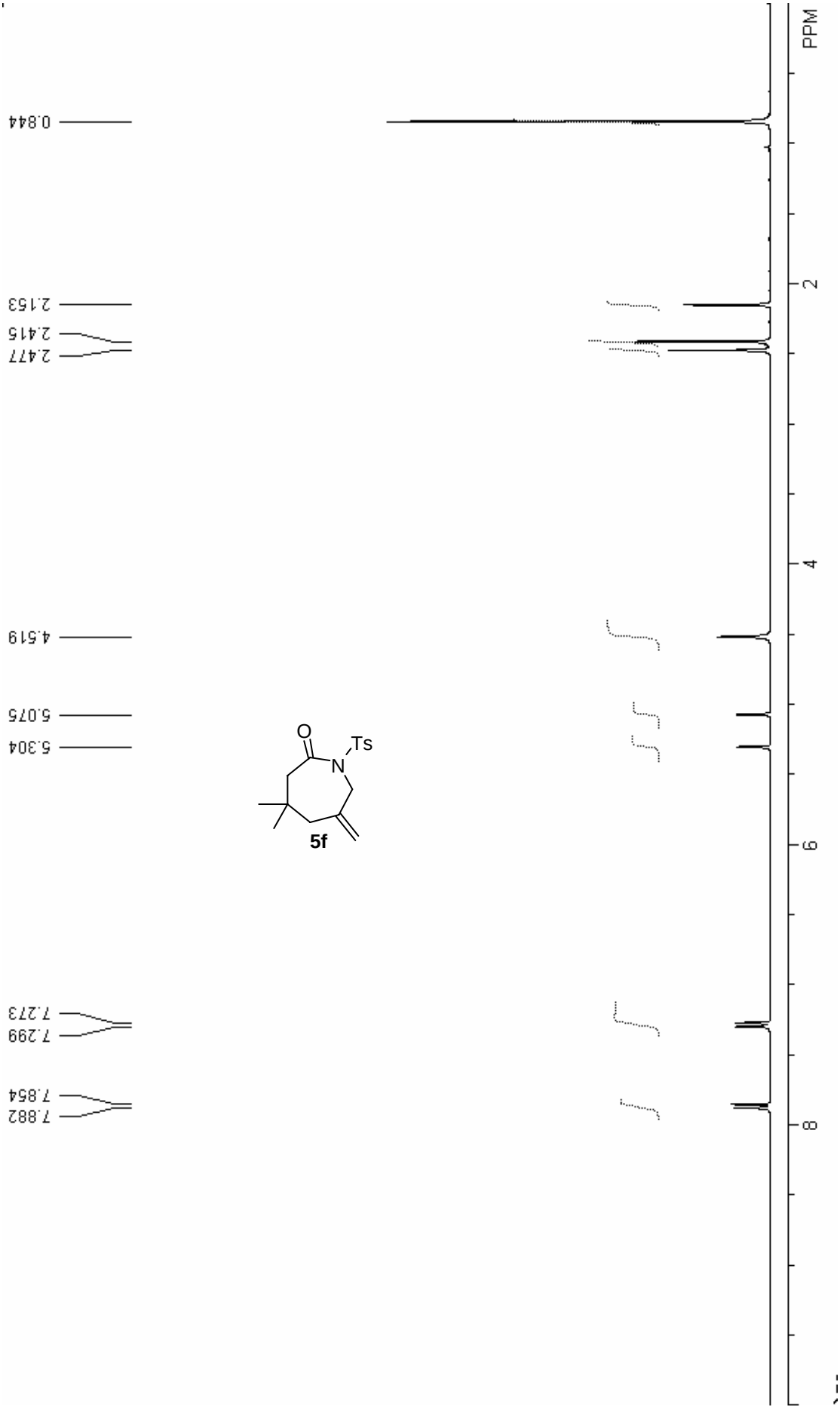
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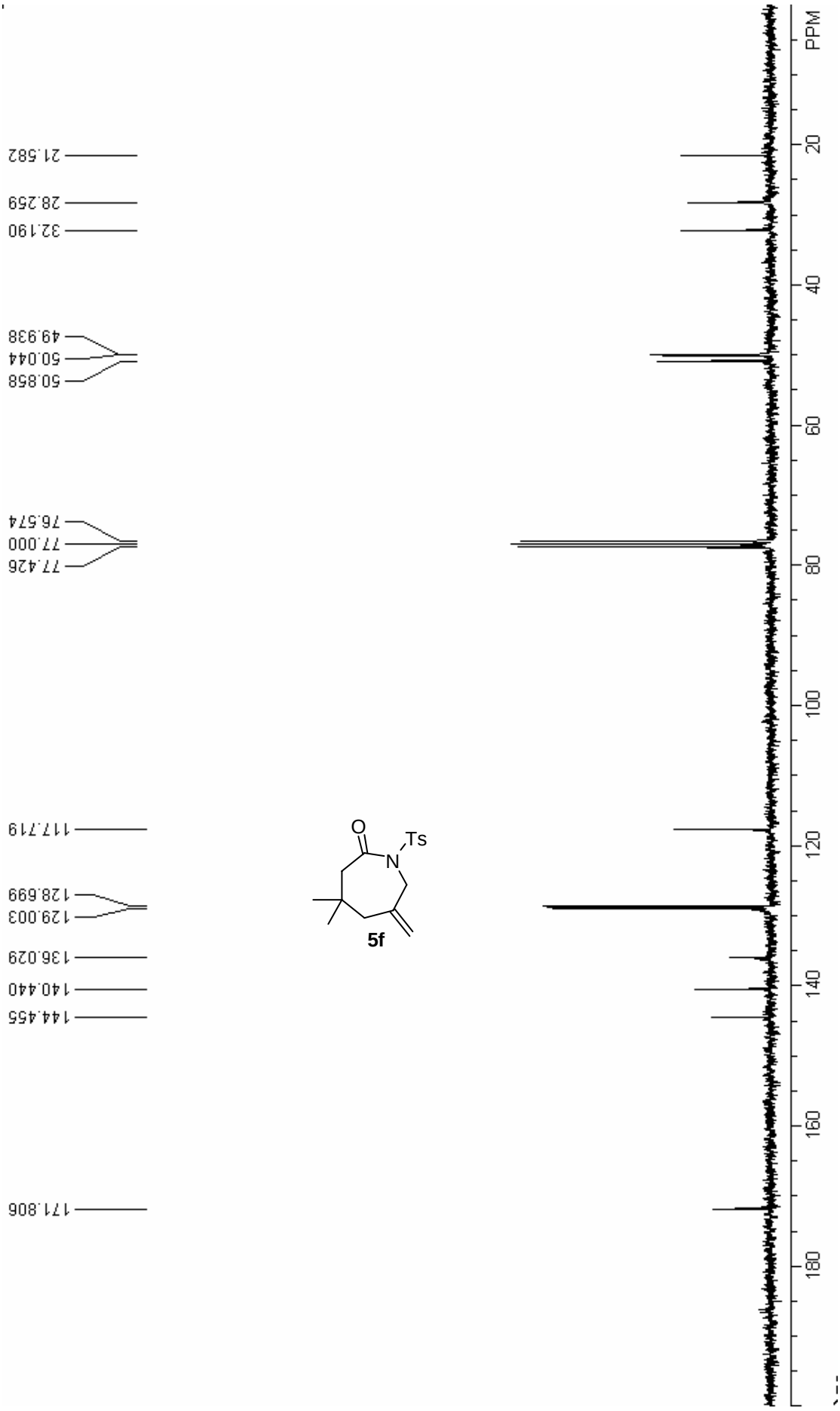
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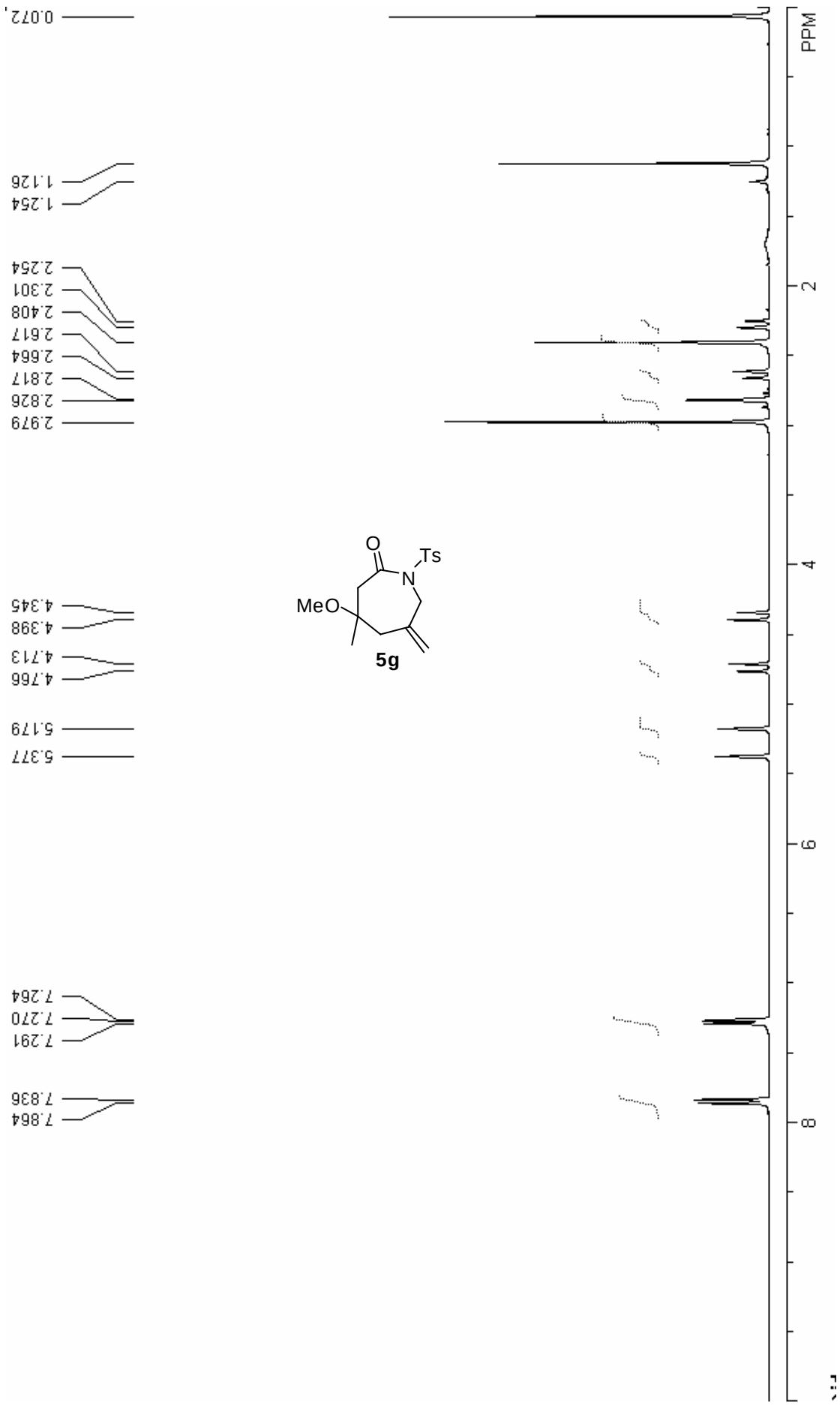
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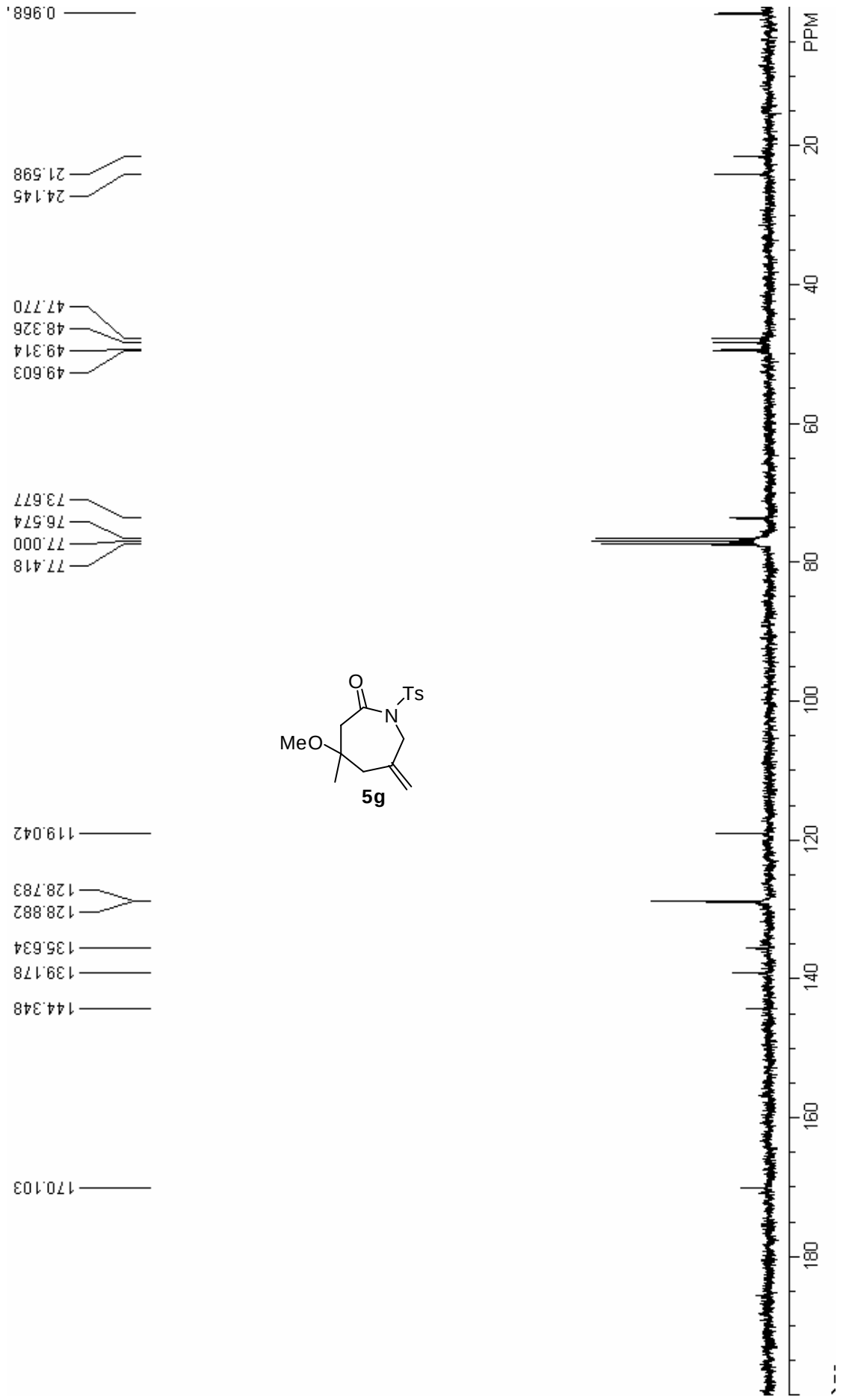
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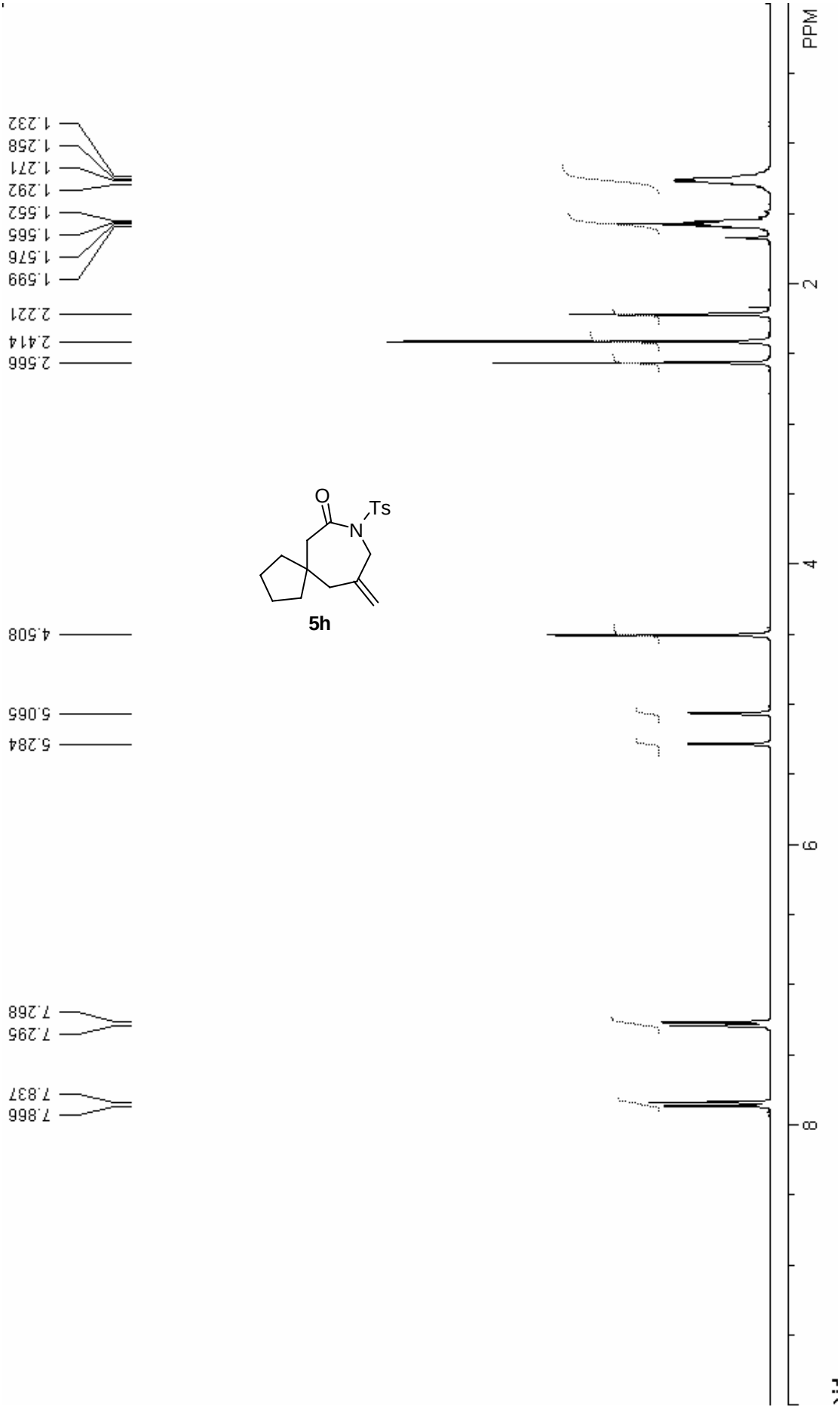
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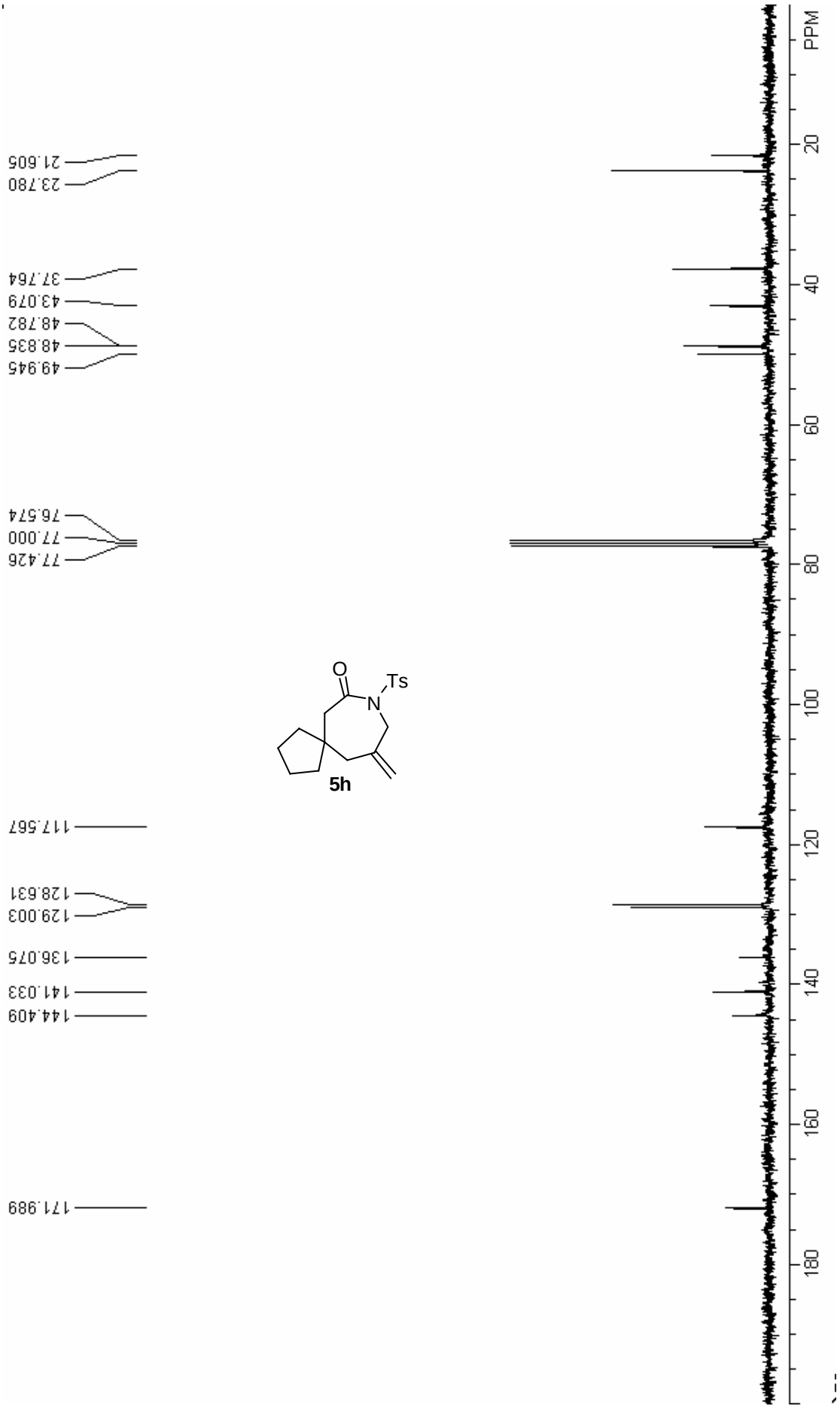
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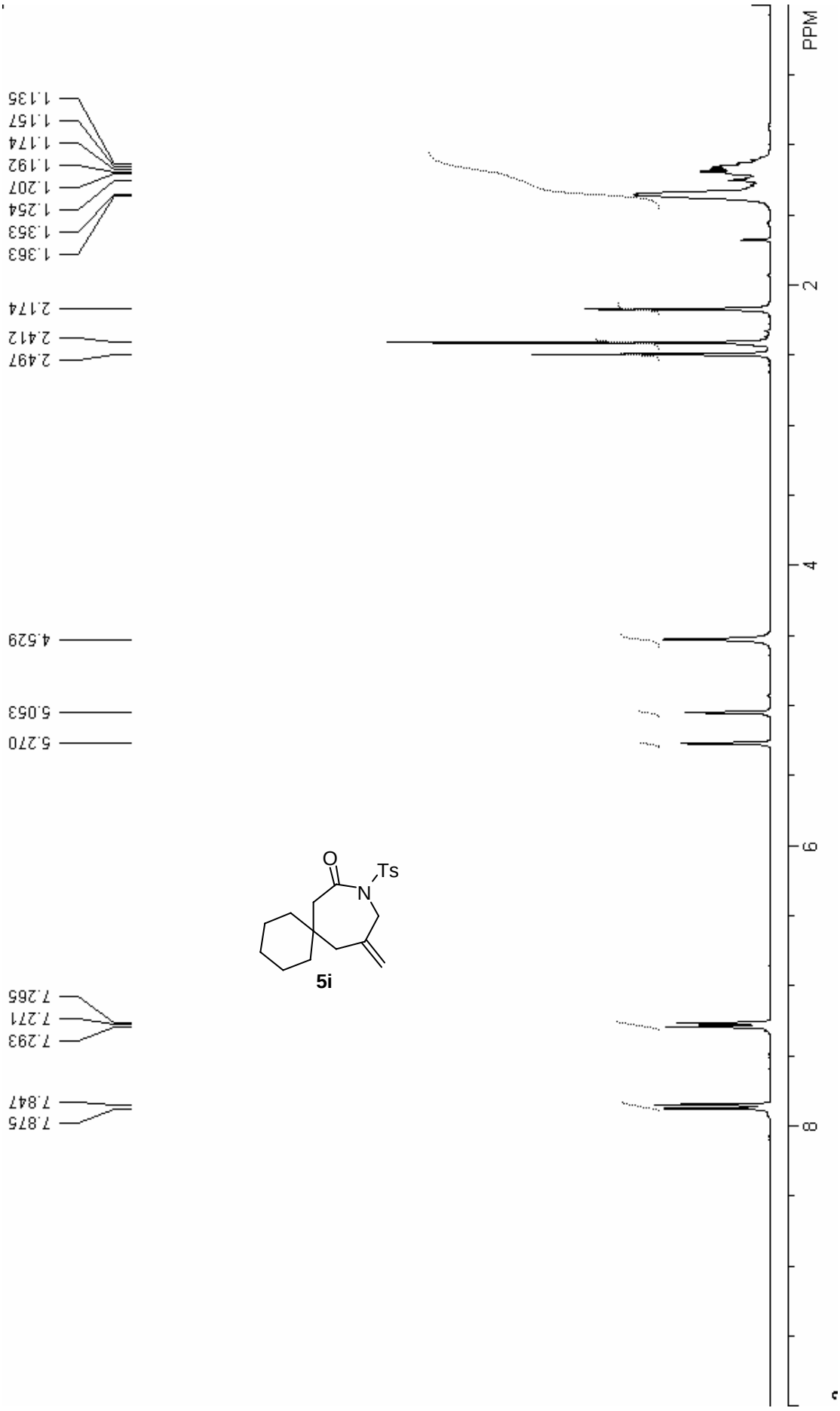
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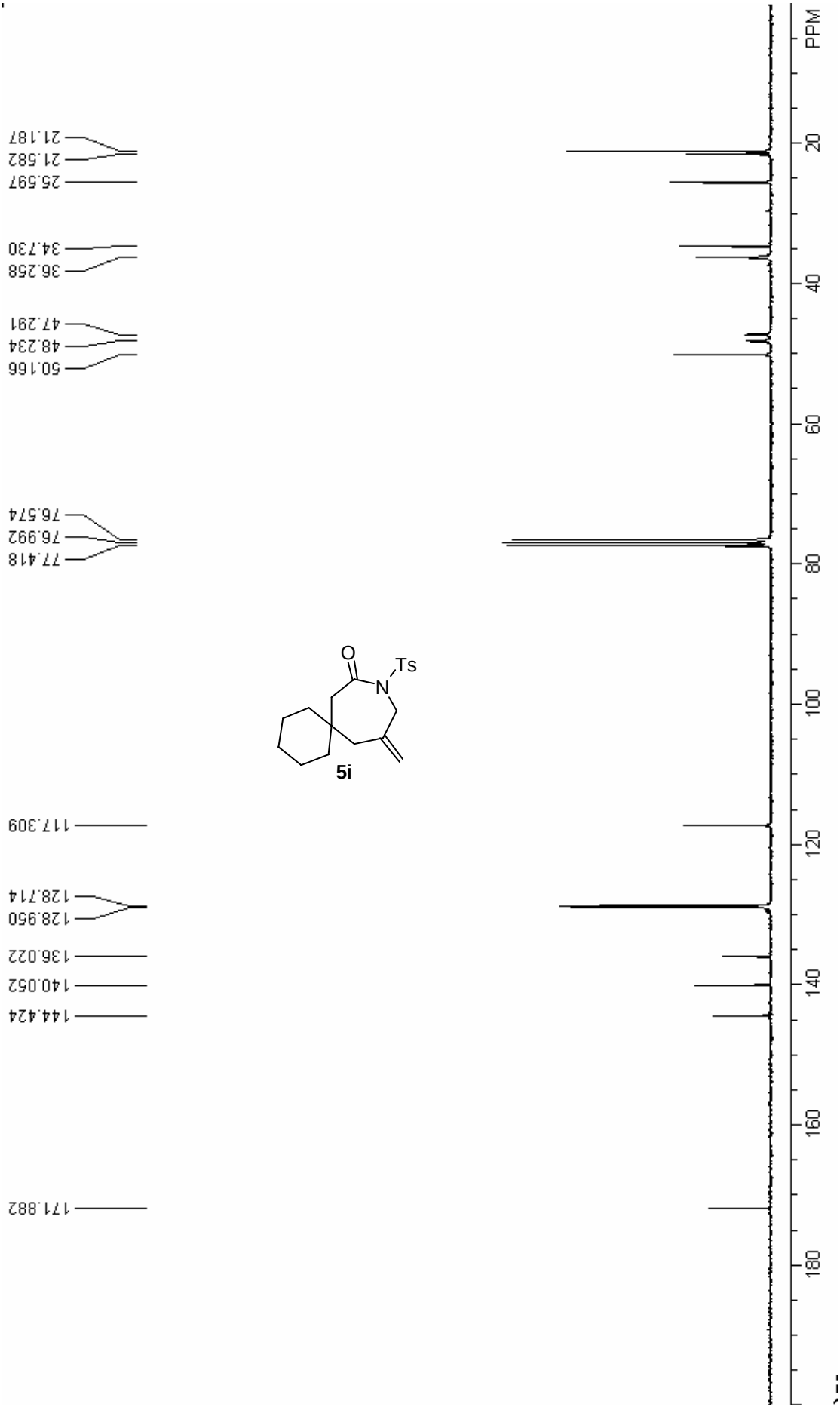
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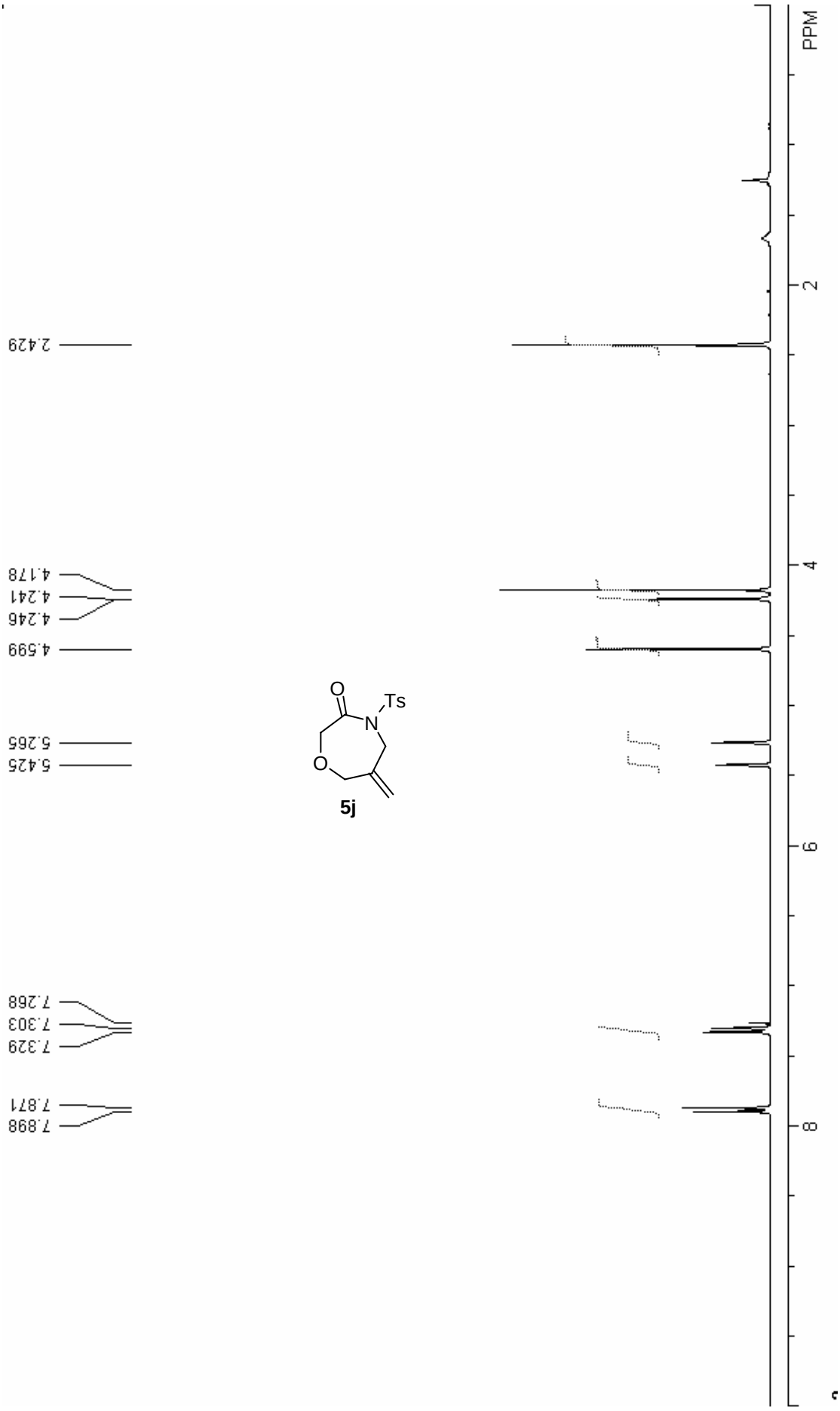
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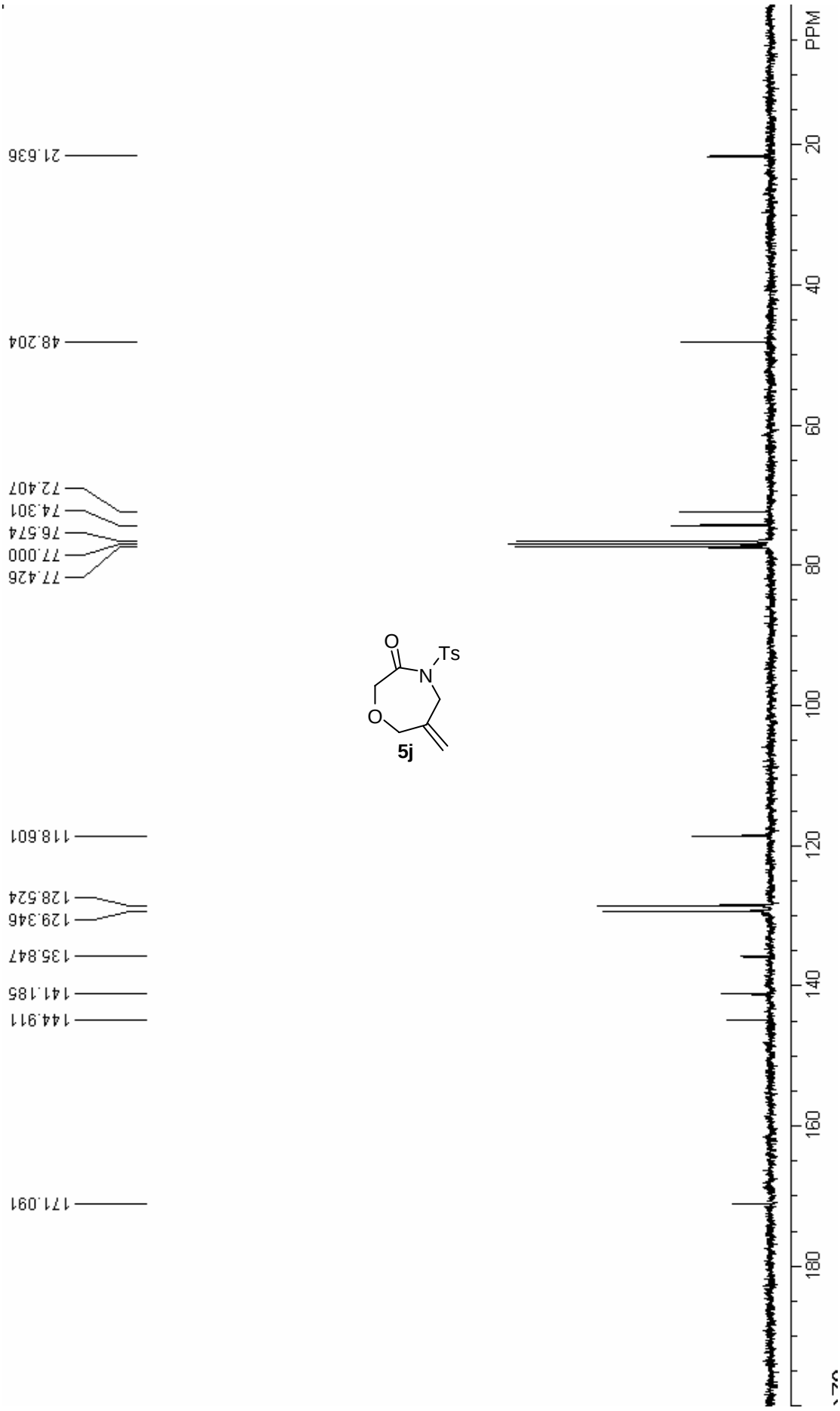
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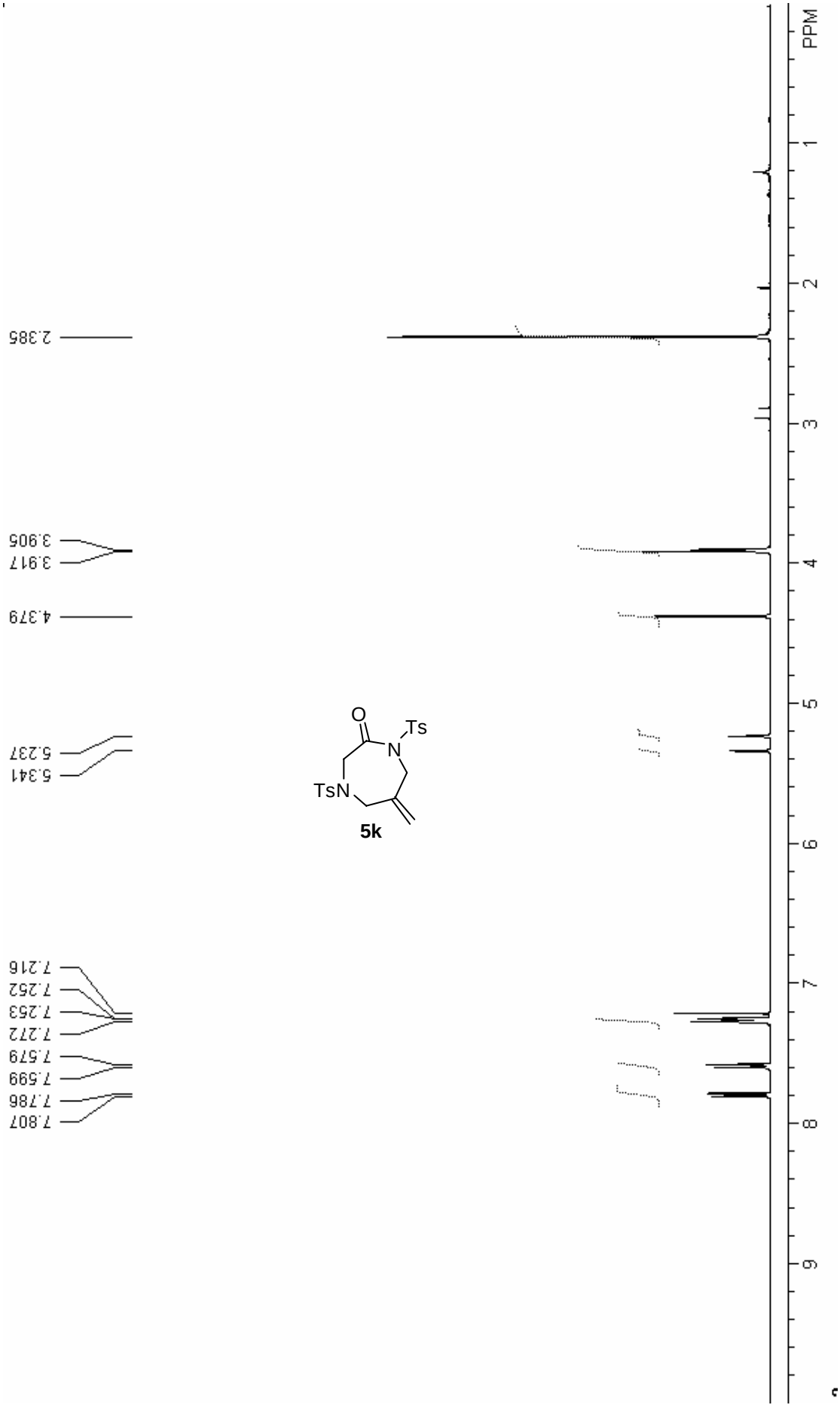
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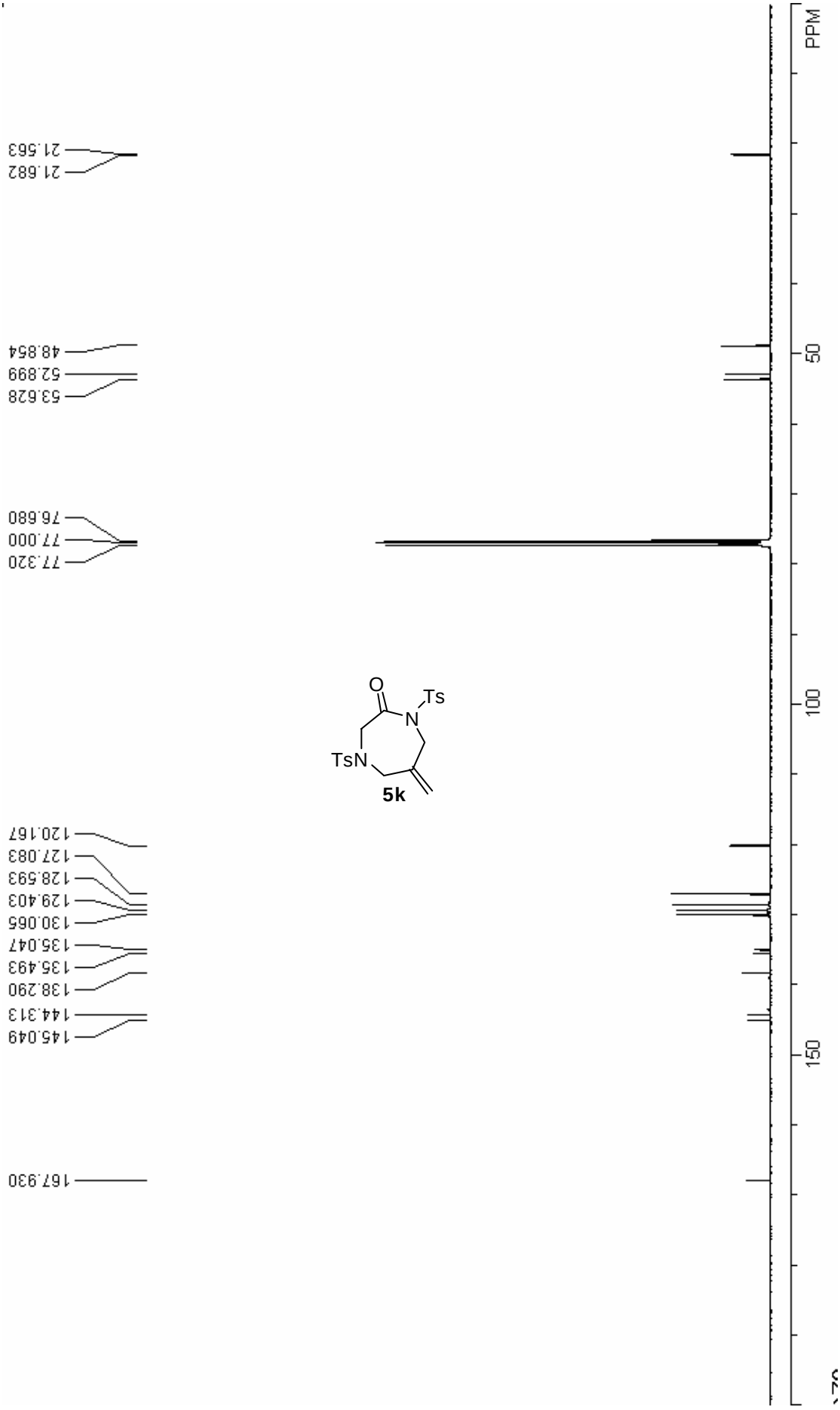
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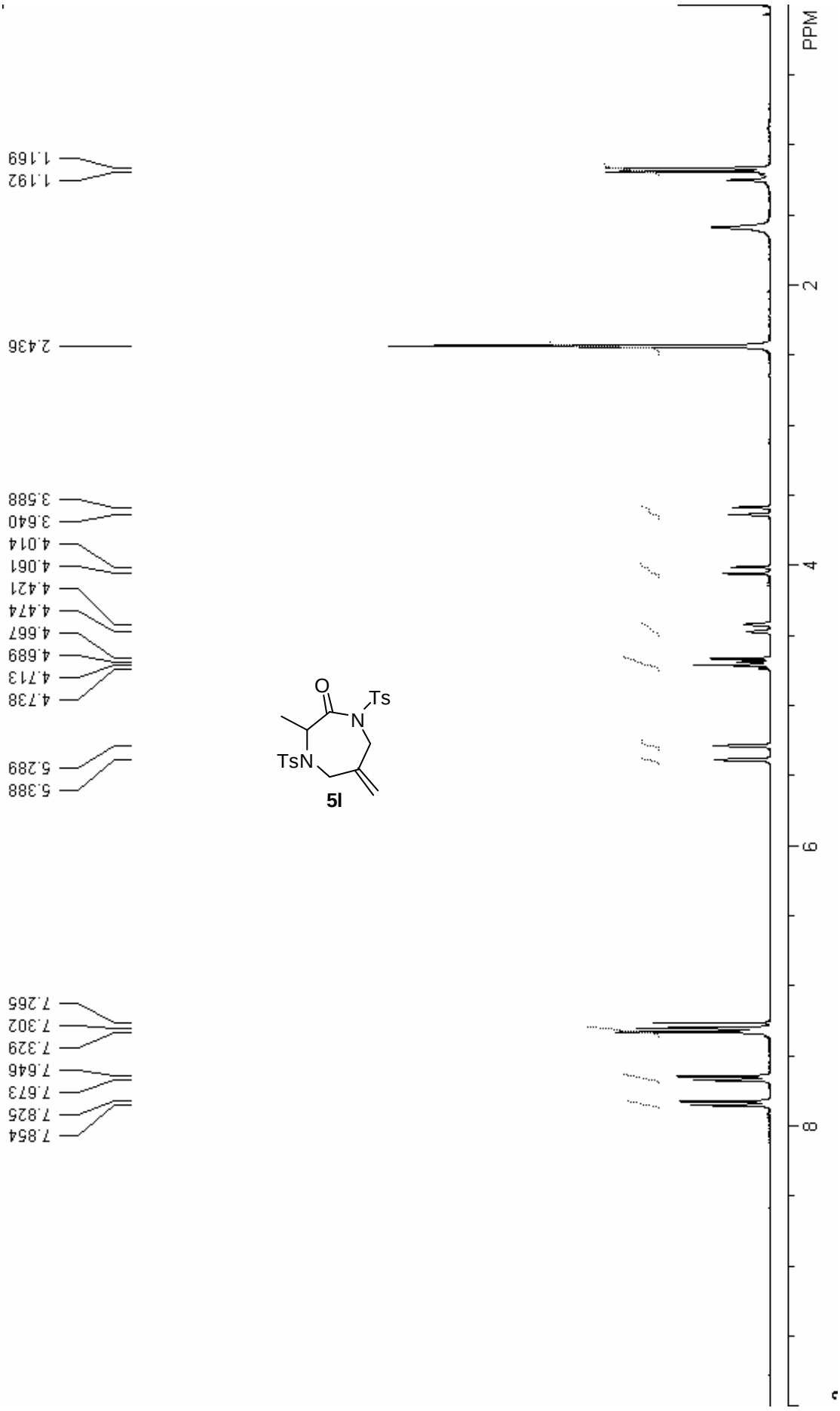
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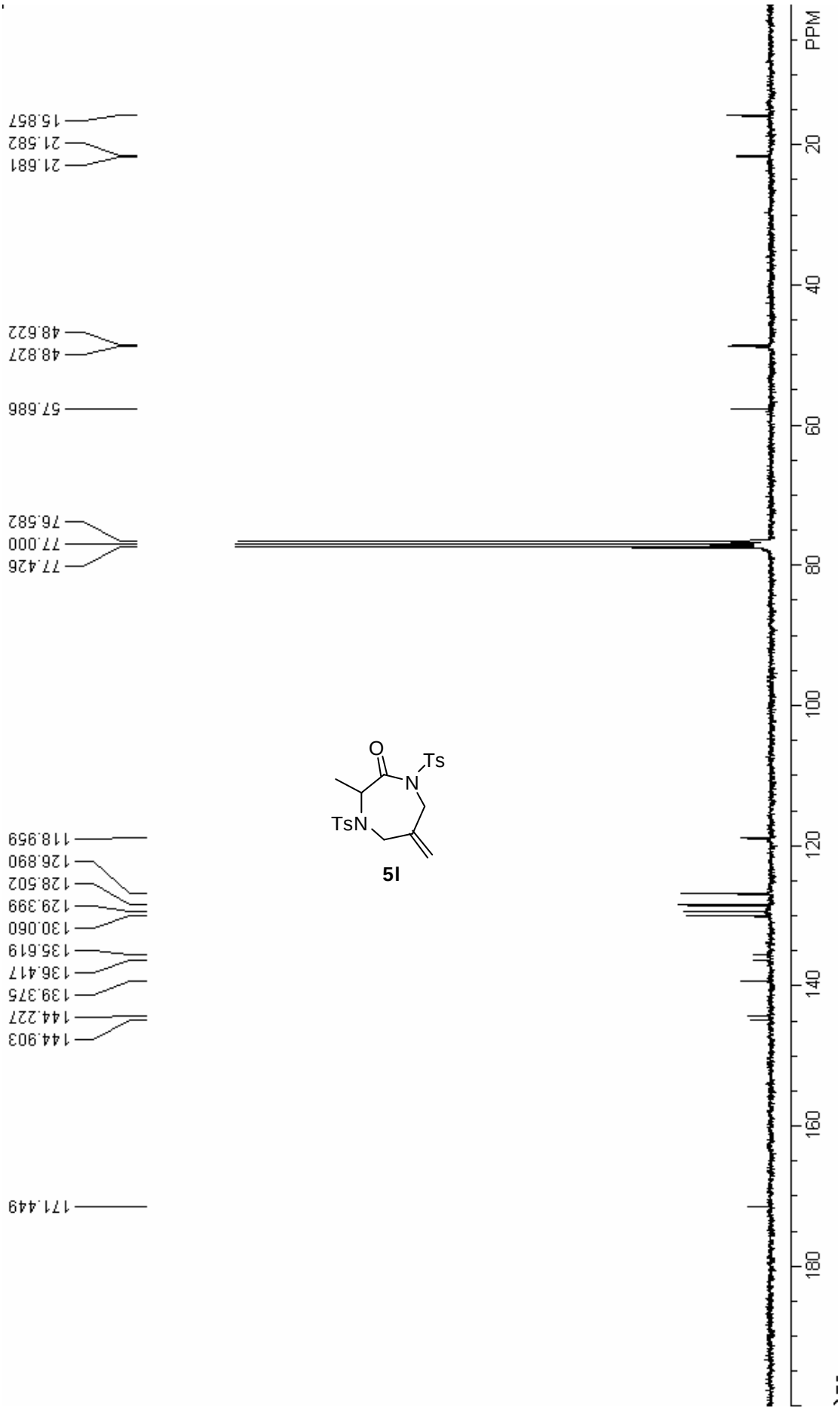
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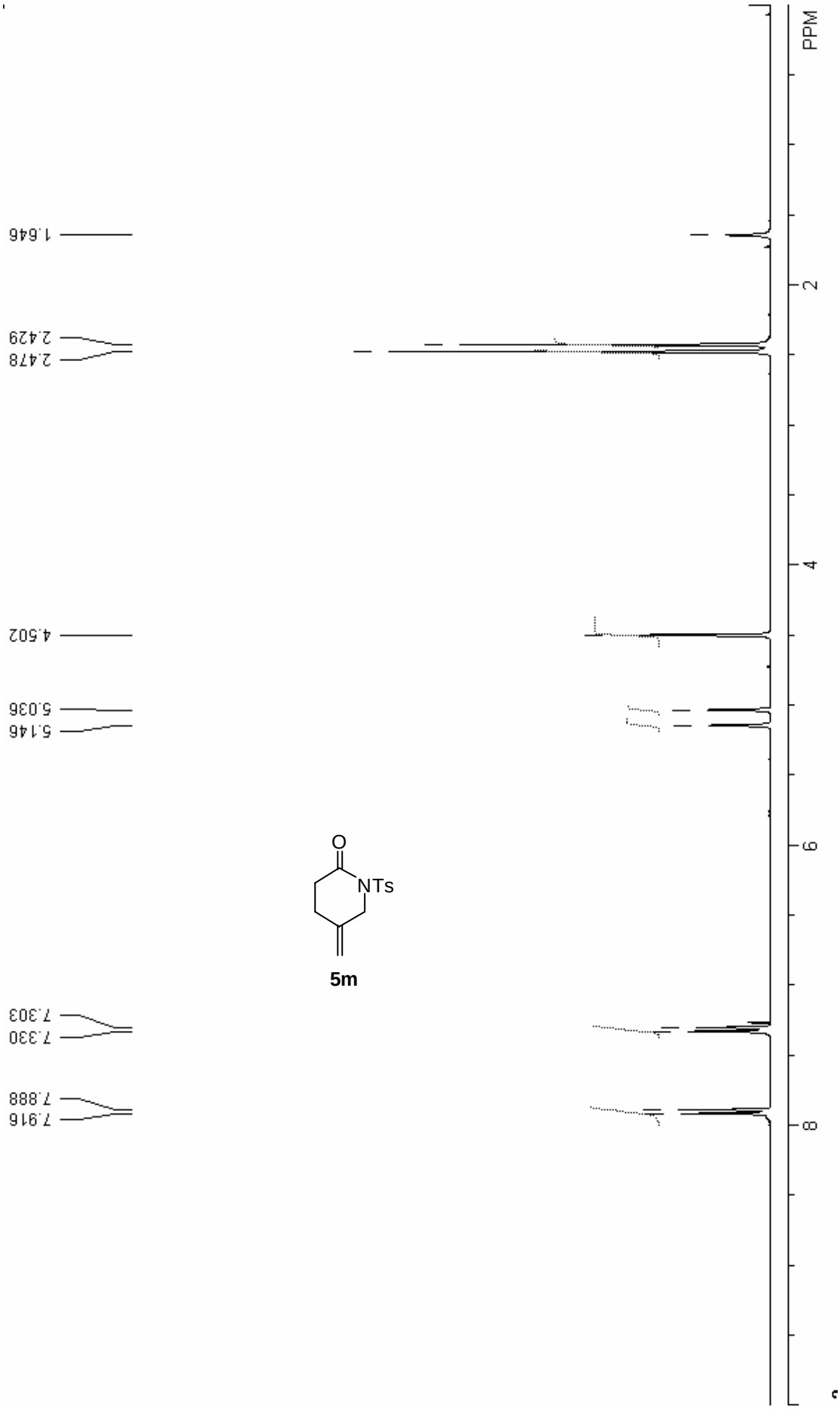
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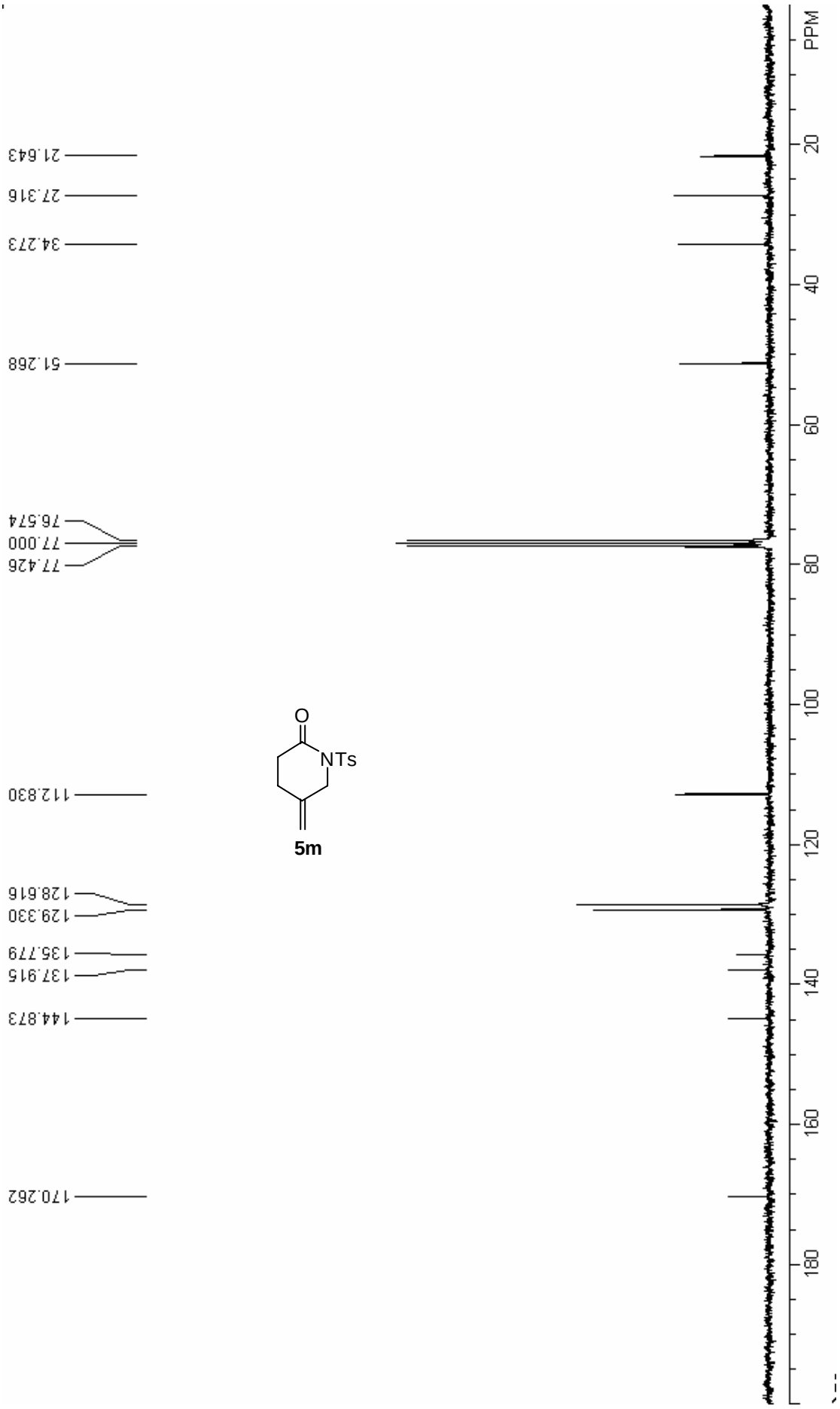
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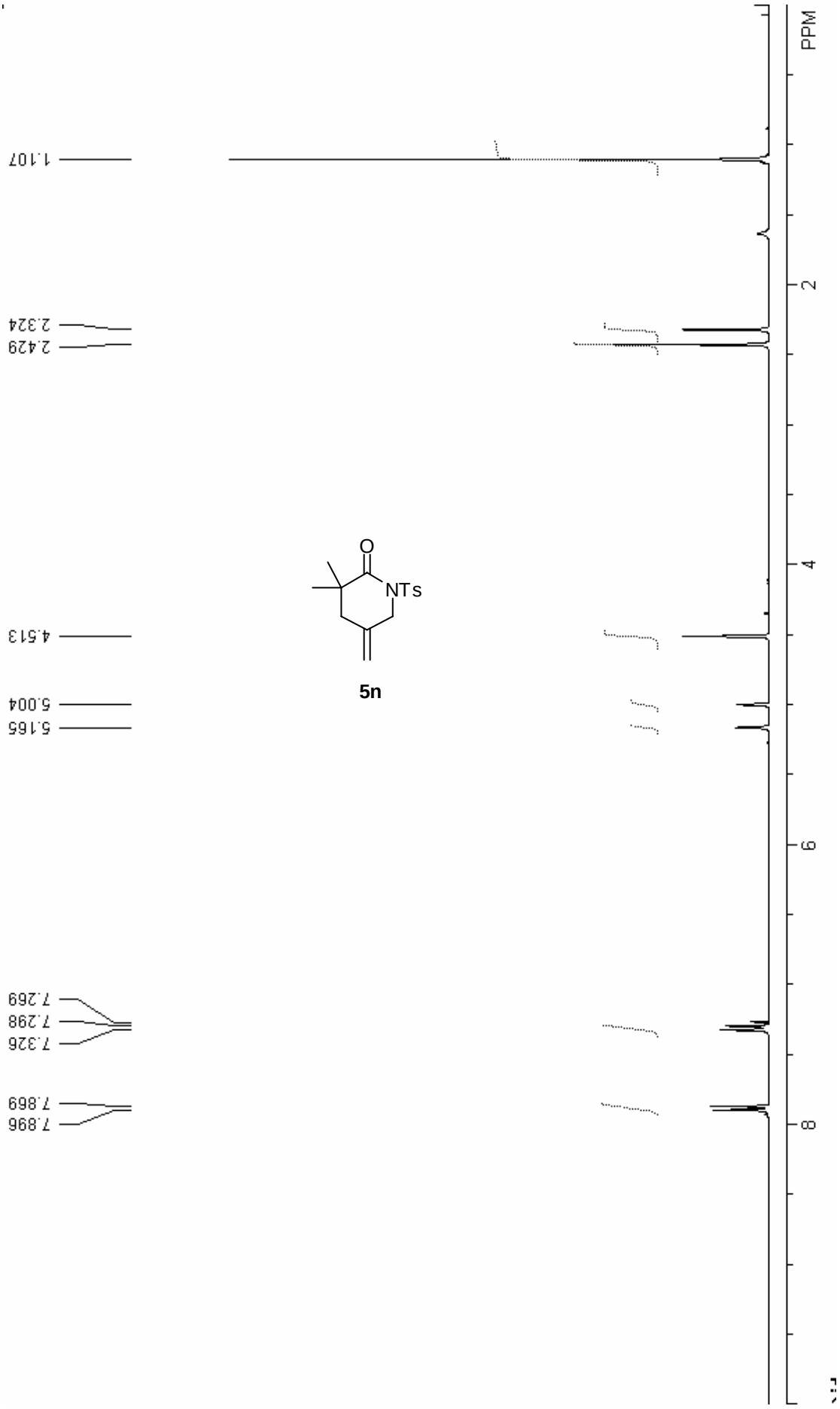
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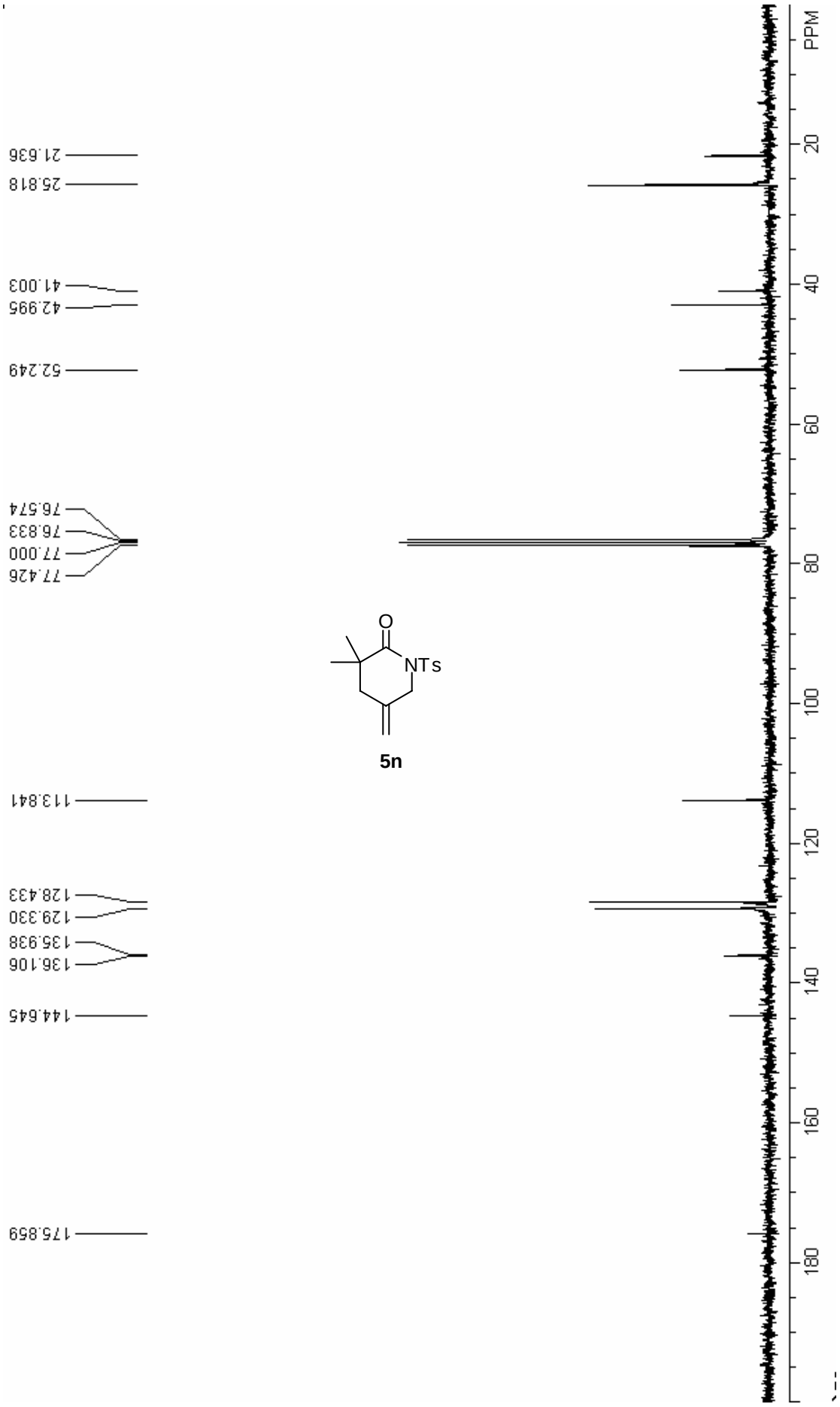
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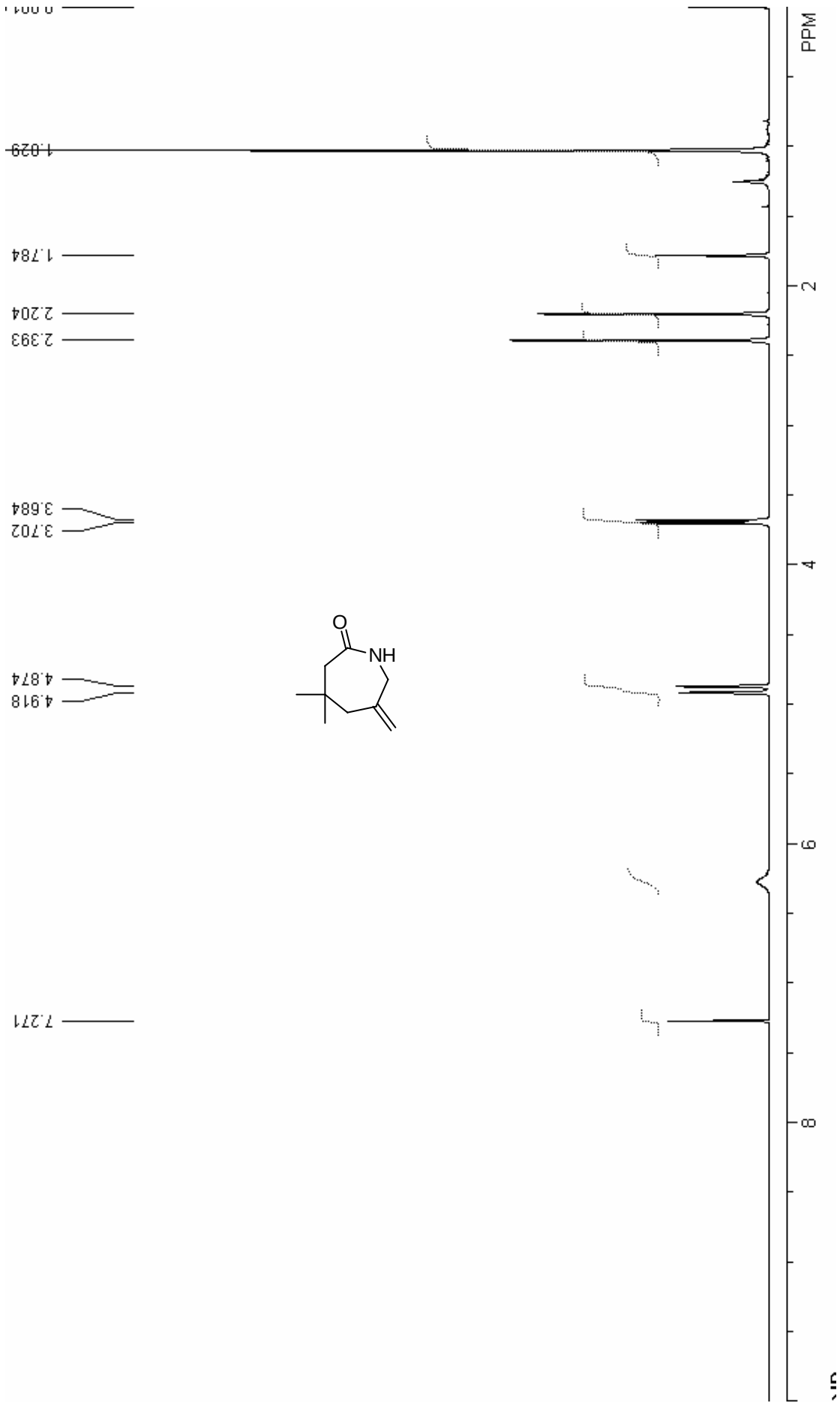
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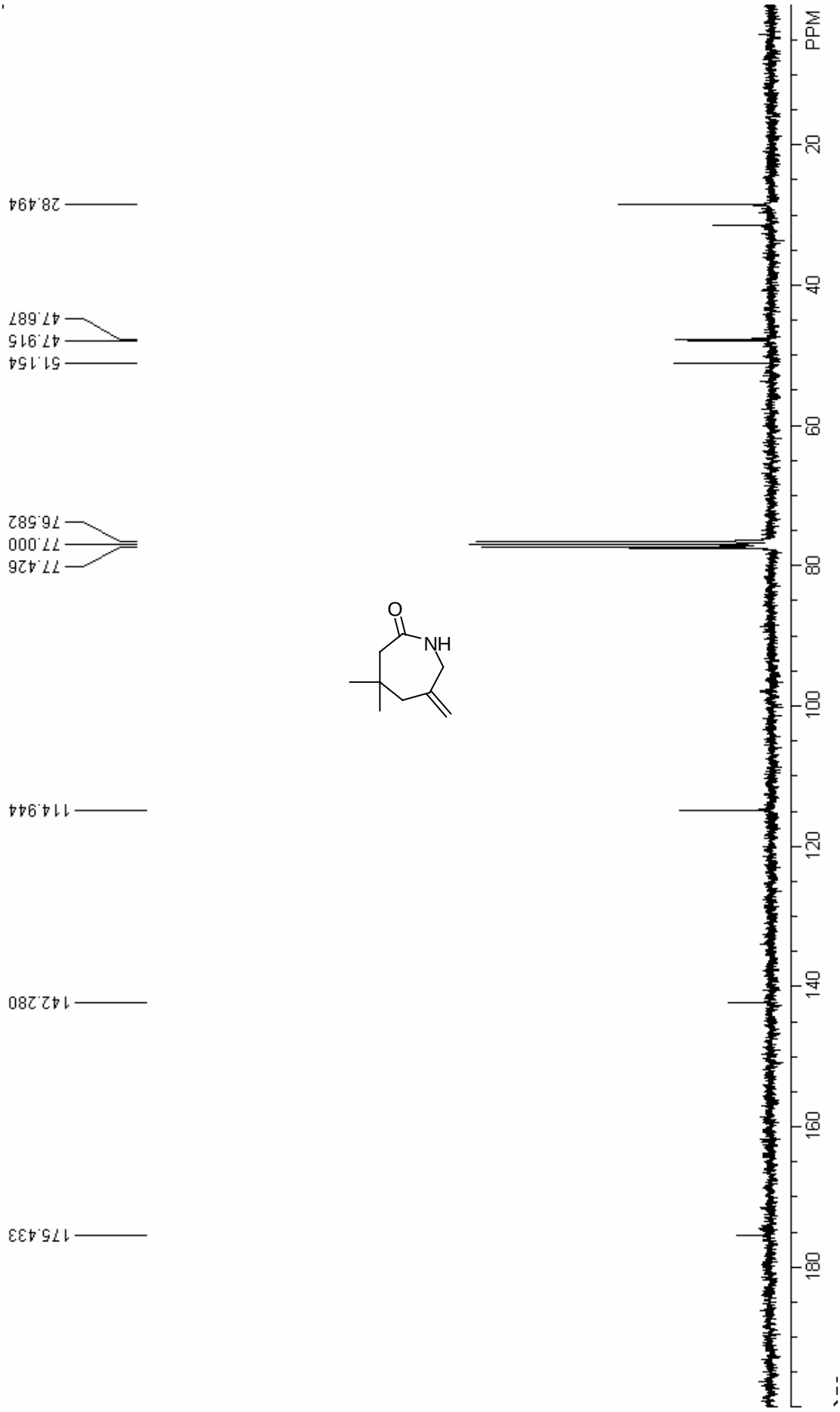
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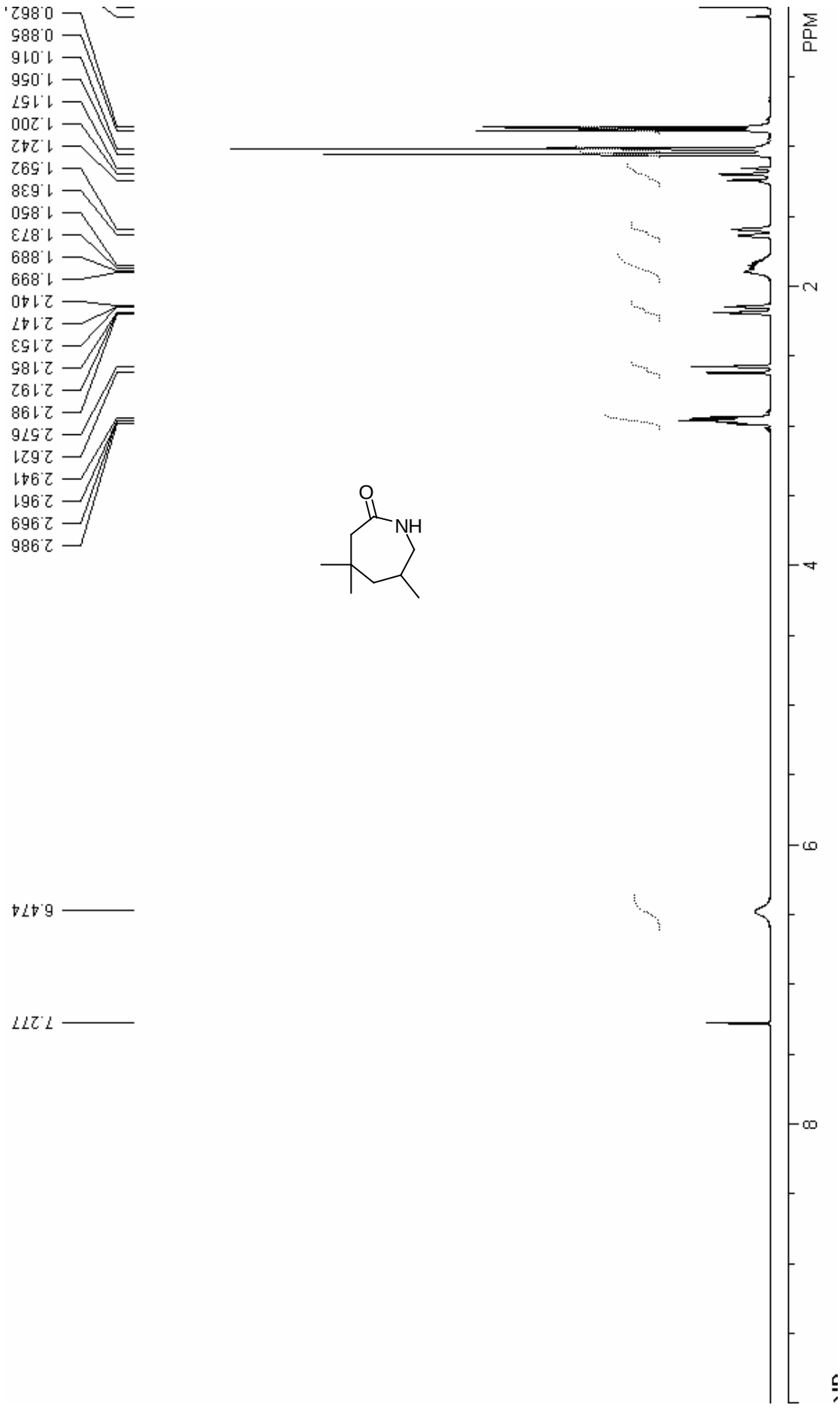
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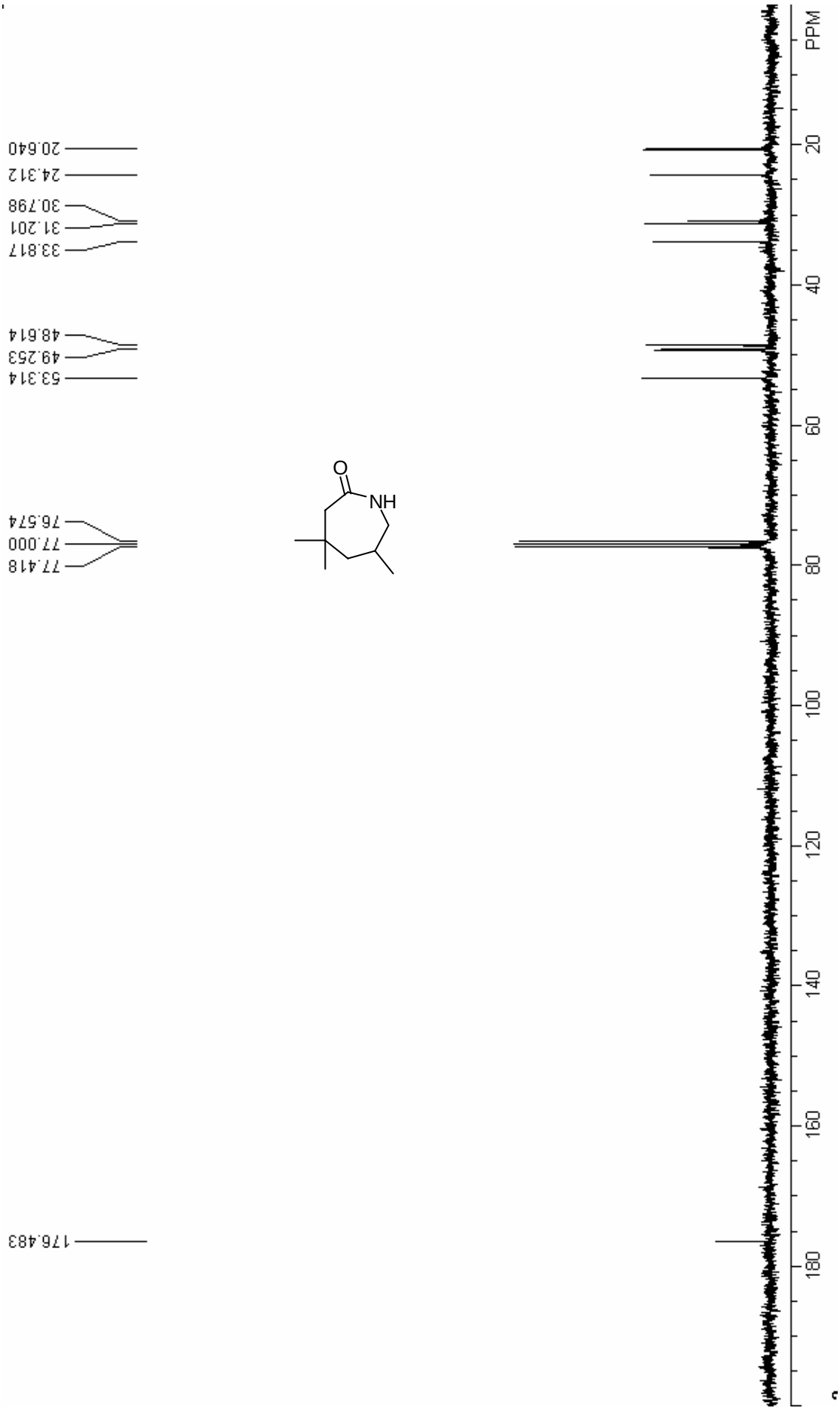
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