# 2-Azaadamantane N-oxyls (AZADOs): The highly efficient organocatalyst for oxidation of alcohols

Masatoshi Shibuya, Masaki Tomizawa, Iwao Suzuki, and Yoshiharu Iwabuchi*

*Department of Organic Chemistry and Biophysical Chemistry, Graduate School of Pharmaceutical Sciences,*

*Tohoku University, Aobayama, Sendai 980-8578, Japan.*

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**General experimental procedures:**

All reactions were carried out under an atmosphere of argon unless otherwise specified. Anhydrous solvents were transferred via syringe to flame-dried glassware, which had been cooled under a stream of dry nitrogen. Ethereal solvents and dichloromethane (anhydrous; Kanto Chemical Co., Inc) were used as received. All other solvents were dried and distilled by standard procedures. Yields refer to chromatographically and spectroscopically ($^1$H NMR) homogeneous materials unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification unless otherwise stated.

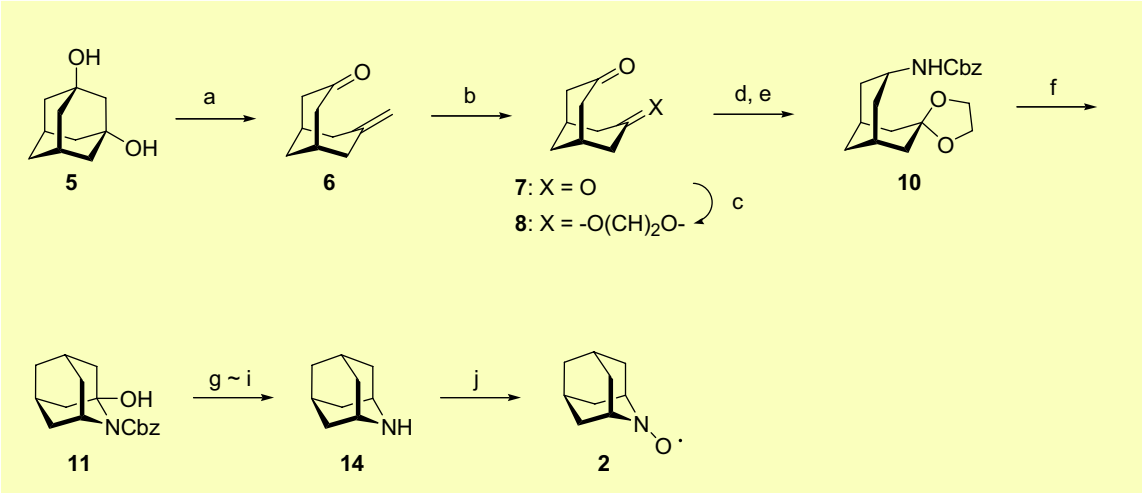
Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as visualizing agent and p-anisaldehyde in ethanol/aqueous $H_2SO_4$/$CH_3CO_2H$ for staining. Column chromatograpy was performed using silica gel 60 particle size 0.063-0.210 mm. The eluents employed are reported as volume : volume percentages.

Proton nuclear magnetic resonance (1H NMR) spectra were recorded using a JEOL JMN-AL400 (400 MHz), and a JEOL 500 (500 MHz) spectrometers. Chemical shift ($\delta$) is reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS). Coupling constants ($J$) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d. doublet; t, triplet; q, quartet; m, multiplet; br, broad; app, Apparent. Carbon-13 nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded using a JEOL JMN-AL400 spectrometer at 100 MHz. Chemical shift is reported in ppm relative to the center line of the triplet of $CDCl_3$ (77.10 ppm).

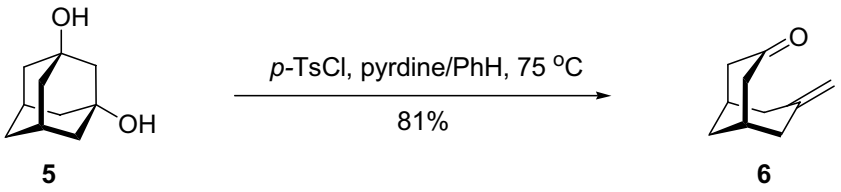
Melting points were determined using Yazawa BY-2 melting point apparatus and are reported uncorrected. Infrared spectra were obtained on a JASCO FT-IR-410 at 4.0 $cm^{-1}$ resolution and are reported in wavenumbers. High resolution mass spectra (HRMS) were recorded on a JMS-AX500 or JMS-700 using electron impact (EI). Low resolution mass spectra (MS) were recorded on JEOL JMS-DX303. Elemental analyses were performed using Yanaco CHN CORDER MT-6.

**An improved synthesis of AZADO**

***Scheme S1***. An improved synthetic route to AZADO starting from 1,3-adamantanediol



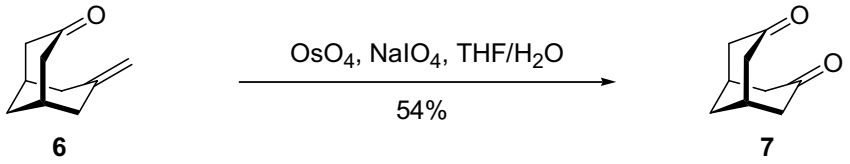

Reagents and conditions: (a) *p*-TsCl, pyridine/PhH, 75 °C, 81%; (b) $OsO_4$, $NaIO_4$, THF/$H_2O$, 54%; (c) $HO(CH_2)_2OH$, *p*-TsOH, PhMe, reflux, 94%; (d) $HCl \cdot NH_2OH$, pyridine, quant; (e) $NaBH_4$, $MoO_3$, MeOH, 0 °C, then $Et_3N$, CbzCl, 75%; (f) 5% aq. HCl MeOH, quant; (g) $H_2$, Pd-C, MeOH; (h) $SOCl_2$, reflux; (i) LAH, DME, reflux; (j) UHP, $Na_2WO_4 \cdot 2H_2O$, MeOH, 60% over four steps.




**7-Methylene-bicyclo[3.3.1]nonan-3-one (6)**

A mixture of 1,3-adamantanediol (**5**) (1 g, 5.95 mmol), *p*-TsCl (2.84 g, 14.9 mmol) in benzene-pyridine (40 ml, 1:1 v/v) was stirred at 75 ºC for 12 h. After cooling to 0 ºC, the reaction mixture was poured into $H_2O$ and extracted with cold $Et_2O$. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by column chromatography ($SiO_2$, 1:8 AcOEt: hexane) to give **6** (720 mg, 4.8 mmol, 81 %) as a white solid. [a)]

mp 158-159 °C (recrystallized from pet. ether), $^1$H-NMR (400 MHz, $CDCl_3$): δ 4.78 (br s, 2H), 2.45-2.35 (m, 8H), 2.28 (d, *J* = 13.7 Hz, 2H), 1.97-1.88 (m, 1H). $^{13}$C-NMR (100 MHz, $CDCl_3$) : δ 211.1, 141.8, 114.6, 47.2, 41.3, 31.9, 30.7. IR ($CHCl_3$, $cm^{-1}$): 1716. MS *m/z*: 150 ($M^+$), 93 (100%). HRMS (EI): Calcd. for $C_{10}H_{15}NO$ 150.1045 ($M^+$), found: 150.1061.

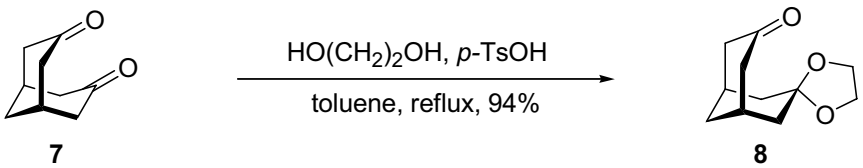



**6** **7**

**Bicyclo[3.3.1]nonane-3,7-dione (7)**

To a solution of ketone **6** (1 g, 6.7 mmol) in THF- $H_2O$ (34 ml, 5 : 1 v/v) at 0 ºC was added $NaIO_4$ (3.6 g, 16.8 mmol), $OsO_4$ in THF (0.1967 M, 1.7 ml, 0.335 mmol). The mixture was allowed to stir at room temperature for 5 h and then quenched with a saturated aqueous solution of $NaHCO_3$ and a saturated aqueous solution of $Na_2S_2O_3$. The mixture was extracted ten times with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 4:1 AcOEt: hexane) to give **7** (550 mg, 3.6 mmol, 54 %) as a white solid.

mp 253-256 °C (recrystallized from pet. ether), $^1$H-NMR (400 MHz, $CDCl_3$): δ 2.86 (br s, 2H), 2.60 (dd, *J* = 15.4, 5.6 Hz, 4H), 2.42 (br d, *J* = 15.4 Hz, 4H), 2.20 (br s, 2H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 208.3, 47.7, 32.6, 31.4. IR (neat, $cm^{-1}$): 1696.0. MS *m/z*: 152 ($M^+$), 152 (100%). HRMS (EI): Calcd. for $C_9H_{12}O_2$ 152.0837. ($M^+$), found: 152.0846.

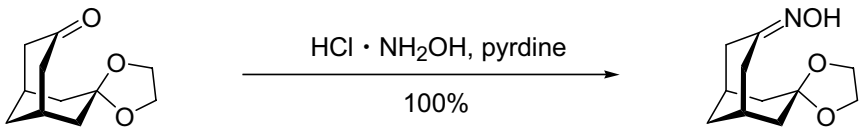



**7** **8**

**7,7-Ethylenedioxybicyclo[3.3.1]nonan-3-one (8)**

A solution of diketone **7** (300 mg, 1.97 mmol), $HO(CH_2)_2OH$ (0.44 ml, 7.89 mmol) and *p*-TsOH·$H_2O$ (37 mg, 0.197 mmol) in toluene (6.7 ml) was heated at reflux during 2 h under continuous removal of water by means of a Dean-Stark trap. After cooling to room temperature, the reaction was quenched a saturated aqueous solution of $NaHCO_3$. The mixture was extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 2:1 AcOEt: hexane) to give **8** (363 mg, 1.85 mmol, 94 %) as a white solid.

mp 79-80 °C (recrystallized from pet. ether), $^1$H-NMR (400 MHz, $CDCl_3$): δ 3.93-3.91 (ddd, *J* = 7.2, 6.3, 1.5 Hz, 2H), 3.85-3.83 (ddd, *J* = 7.2, 6.3, 1.5 Hz, 2H), 2.52-2.46 (m, 4H), 2.37 (br d, *J* = 6.8 Hz, 1H), 2.33 (br d, *J* = 6.5 Hz, 1H), 1.87-1.75 (m, 6H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 208.8, 107.3, 64.3, 63.3, 45.8, 40.0, 31.5, 29.1. IR (neat, $cm^{-1}$): 1700.9. MS *m/z*: 196 ($M^+$), 139 (100%). HRMS (EI): Calcd. for $C_{11}H_{16}O_3$ 196.1099 ($M^+$), found: 196.1086. Anal: Calcd. for $C_{11}H_{16}O_3$ : C, 67.32; H, 8.22, found: C, 67.22; H, 8.10.



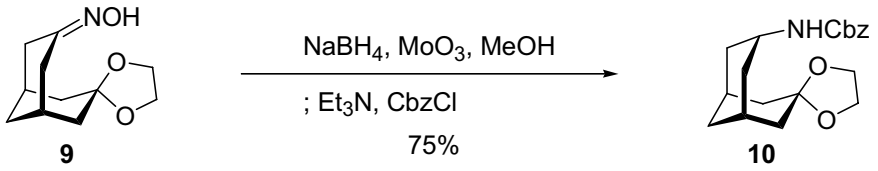

**8** **9**

**7, 7-Ethylenedioxybicyclo[3.3.1]nonan-3-one oxime (9)**

To a solution of ketone **8** (325 mg, 1.66 mmol) in pyridine (17 ml) was added HCl·$NH_2OH$ (344 mg, 5 mmol) at room temperature. After stirring at 40 ºC for 4 h, pyridine was removed *in vacuo*. The residue was poured into $H_2O$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 5:2 AcOEt: hexane) to give **9** (350 mg, 1.66 mmol, 100 %) as a white solid.

mp 135-138 °C (recrystallized from $Et_2O$-hexane), $^1$H-NMR (400 MHz, $CDCl_3$): δ 3.96 (t, *J* = 6.4 Hz, 2H), 3.82 (t, *J* = 6.4 Hz, 2H), 3.09 (d, *J* = 17.9 Hz, 1H), 2.48 (br s, 1H), 2.44 (br dd, *J* = 17.9, 5.8 Hz, 1H), 2.34 (br s, 2H), 2.2 (br dd, *J* = 17.6, 5.8 Hz, 1H), 1.84 (d, *J* = 3.6, 2H), 1.78 (d, *J* = 3.6, 2H), 1.69 (s, 2H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 157.1, 107.1, 64.2,

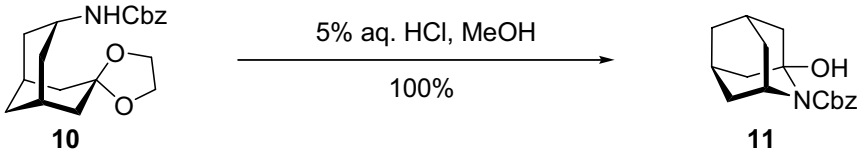
62.9, 40.3, 39.8, 34.7, 31.5, 29.4, 27.7, 26.5. IR (neat, $cm^{-1}$): 3190.7, 3077.8, 1651.7. MS *m/z*: 211 ($M^+$), 194 (100%). HRMS (EI): Calcd. for $C_{11}H_{17}NO_3$ 221.1208 ($M^+$), found: 221.1222.




**9** **10**

**(7,7-Ethylenedioxybicyclo[3.3.1]nonan-3-yl)-carbamic acid benzyl ester (10)**

To a solution of oxime **9** (348 mg, 1.65 mmol), $MoO_3$ [b)] (403 mg, 2.8 mmol) in MeOH (16 ml) at 0 ºC was added $NaBH_4$ (187 mg, 4.95 mmol) portionwise. The mixture was then allowed to stir until the oxime was no longer detectable (TLC), and then it was added $Et_3N$ (0.35 ml, 2.48 mmol), CbzCl (0.35 ml, 0.28 mmol) at 0 ºC. The mixture was stirred for an additional 1 h, and then filtered through Celite®. The filtrate was concentrated under reduced pressure. The residue was poured into $H_2O$ and extracted with AcOEt. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:3 AcOEt: hexane) to give **10** (410 mg, 1.24 mmol, 75 %) as a colorless oil. $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.36-7.29 (m, 5H), 5.07 (s, 2H), 4.64 (br d, *J* = 8.5 Hz, 1H), 3.97 t, *J* = 6.3 Hz, 2H), 3.81 (t, *J* = 6.3 Hz, 2H), 2.28 (br s, 2H), 2.16-2.07 (m, 2H), 1.84 (br d, *J* = 13.0 Hz, 1H), 1.76 (br d, *J* = 13.0 Hz, 2H), 1.73 (br d, *J* = 13.0 Hz, 1H), 1.66-1.57 (m, 4H), 1.13 (d, *J* = 13.0 Hz, 1H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 136.8, 128.5, 128.1, 128.0, 108.9, 66.4, 64.3, 62.6, 43.8, 41.8, 31.8, 27.6, 26.1. IR (neat, $cm^{-1}$): 3329.5, 1715.4, 1527.4. MS *m/z*: 331 ($M^+$), 91 (100%). HRMS (EI): Calcd. for $C_{19}H_{25}NO_4$ 331.1784 ($M^+$), found: 331.1784. Anal: Calcd. for $C_{19}H_{25}NO_4$: C, 68.86; H, 7.60; N, 4.23, found: C, 68.71; H, 7.69; N, 4.16.

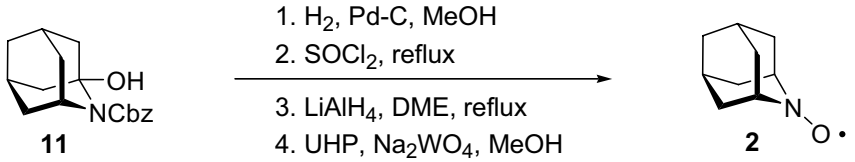



**10** **11**

***N*-Benzyloxycarbonyl-2-azaadamantane-1-ol (11)**

To a solution of carbamate **10** (300 mg, 0.91 mmol) in MeOH (2.3 ml) at room temperature was added 5% aq. HCl (2.3 ml). The mixture was allowed to stir at room temperature for 2 h, and then quenched with a saturated aqueous solution of $NaHCO_3$. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:3 AcOEt: hexane) to give **11** (261 mg, 0.91 mmol, 100 %) as a colorless oil.

$^1$H-NMR (400 MHz, $CDCl_3$): δ 7.36-7.32 (m, 5H), 5.13 (s, 2H), 4.50 (br s, 1H), 2.24 (br s, 2H), 2.02 (br d, *J* = 12.7 Hz, 2H), 1.81 (br d, *J* = 15.4 Hz, 2H), 1.74 (br s, 2H), 1.72 (br d, *J* = 13.0 Hz, 1H), 1.62 (br d, *J* = 12.7 Hz, 1H), 1.55 (br d, *J* = 13.0, 1H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 157.7, 136.2, 128.5, 128.1, 127.9, 83.9, 66.9, 51.0, 43.2, 35.0, 34.4, 29.0. IR (neat, $cm^{-1}$): 3341.1, 1663.3, 1447.3. MS *m/z*: 287 ($M^+$), 91 (100%). HRMS (EI): Calcd. for $C_{17}H_{21}NO_3$ 287.1521 ($M^+$), found: 287.1514.




**2-Azaadamantane-*N*-oxyl (2)**

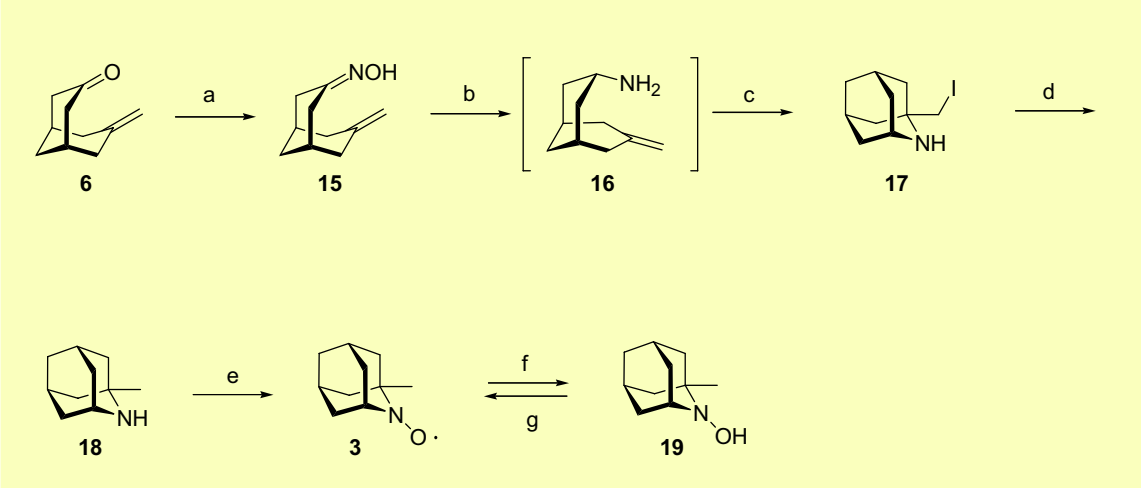
To a solution of carbamate **11** (130 mg, 0.457 mmol) in MeOH (4.6 ml) was added 10% Pd-C (12 mg) under Ar atmosphere. The reaction flask was evacuated and purged with $H_2$ three times and then the reaction was stirred at room temperature under $H_2$ atmosphere for 2h. The catalyst was removed by filtration through Celite®. The filtrate was concentrated under reduced pressure to give **12** as a white solid. Aminoalcohol **12** was used directory for further reaction. To a 10 ml flask charged with crude aminoalcohol **12** at 0 ºC was added dropwise $SOCl_2$ (0.4 ml, 5.7 mmol) over 10 min. The solution was heated to reflux for 1 h, and then the excess $SOCl_2$ was removed by distillation. The resulting solid was cooled, after which $CH_2Cl_2$ (3.8 ml) was added, followed by $H_2O$ (7.6 ml). The two-phase mixture was rapidly stirred at 0 ºC for 30 min. A 10% aqueous

solution of NaOH was added dropwise until the aqueous phase became strongly basic. The layers were separated, and the aqueous phase was extracted with $CHCl_3$. The combined organic layers were dried over $K_2CO_3$ and concentrated under reduced pressure to give **13** as a white solid. Chloroamine **13** was used directly for further reaction. A solution of crude chloroamine **13** in dry dimethoxyethane (2.3 ml) at 0 ºC was added $LiAlH_4$ (28 mg, 0.74 mmol) portionwise. The mixture was allowed to heat at reflux for 1 h, then cooled to 0 ºC. To the mixture was diluted with $Et_2O$ and added dropwise aq. $NH_3$. After stirring at room temperature for an additional 1h, the mixture was filtered through Celite®. The filtrate was concentrated under reduced pressure. The residue was poured into a saturated aqueous solution of $Na_2CO_3$ and extracted with $CHCl_3$. The organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure to give **14** as a pale yellow oil. The crude product was not further purified. A mixture of crude amine **14** and $Na_2WO_4 \cdot 2H_2O$ (75 mg, 0.23 mmol) in MeOH (0.9 ml) was stirred at room temperature for 30 min. To the reaction mixture was added urea hydrogen peroxide [c] (172 mg, 1.83 mmol) at room temperature. After stirring for 3.5 h, the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$. The mixture was extracted with $CHCl_3$, and the organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:3 AcOEt: hexane) to give **2** (42 mg, 0.27 mmol, 60 %) as a red solid.

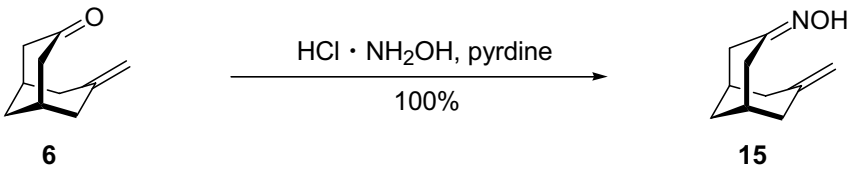
IR (neat, $cm^{-1}$): 1446.4, 1280.5. MS *m/z*: 152 ($M^+$), 152 (100%). HRMS (EI): Calcd. for $C_9H_{14}NO$ 152.1075 ($M^+$), found: 152.1073. Anal: Calcd. for $C_9H_{14}NO$: C, 71.02; H, 9.27; N, 9.20, found: C, 70.68; H, 9.22; N, 8.88.

**Synthesis of 1-Me-AZADO**

***Scheme S2.***




Reagents and Conditions: (a) $HCl \cdot NH_2OH$, pyridine, quant; (b) $NaBH_4$, $MoO_3$, MeOH, 0 $^oC$; (c) $I_2$, MeCN, 48% over two steps; (d) LAH, THF, reflux; (e) 30% $H_2O_2$, $Na_2WO_4 \cdot 2H_2O$, $MeOH/H_2O$, 39% over two steps; (f) $H_2$, Pd-C, MeOH, 34%; (g) $O_2$, $Et_2O$, 54%.

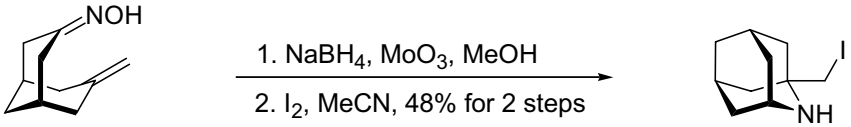



**7-Methylene-bicyclo[3.3.1]nonan-3-one oxime (15)**

To a solution of ketone **6** (3 g, 20 mmol) in pyridine (30 ml) was added $HONH_2 \cdot HCl$ (2.8 g, 40 mmol). After stirring at room temperature for 4h, the solvent was removed *in vacuo*. The residue was diluted with AcOEt and then $H_2O$ was added. The layers were separated and the aqueous layer was extracted with AcOEt. The organic layers were combined and washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by column chromatography ($SiO_2$, 1:6 AcOEt: hexane) to give **15** (3.3 g, 20 mmol, 100 %) as a colorless solid.

mp 123-124 $^oC$ (recrystallized from pet. ether), $^1$H-NMR (400 MHz, $CDCl_3$): δ 4.73 (s, 1H), 3.17 (d, $J$ = 15.8 Hz, 1H), 2.43-2.23 (m, 8H), 1.96 (dd, $J$ = 16.1, 5.4 Hz, 1H), 1.76 (s, 2H).

$^{13}$C-NMR (100 MHz, $CDCl_3$): δ 158.4, 143.0, 111.6, 41.6, 40.6, 37.4, 33.2, 30.3, 29.7, 28.6. IR ($CHCl_3$, $cm^{-1}$): 3590. MS *m/z:* 165 ($M^+$), 93 (100%). HRMS Calcd. for $C_{10}H_{15}NO$ : 165.1154($M^+$), found: 165.1149. Anal: Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48, found: C, 72.61; H, 9.11; N, 8.48.

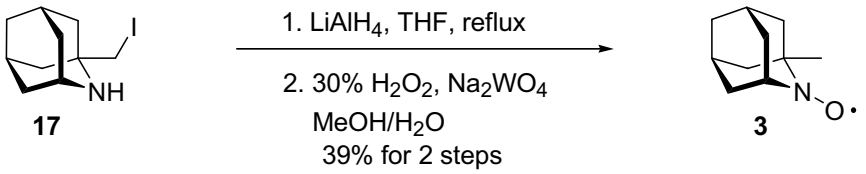



**15** **17**

**1-Iodomethyl-2-azaadamantane (18)**

A mixture of oxime **15** (200 mg, 1.2 mmol), $MoO_3$ (240 mg, 1.7 mmol) in MeOH (12 ml) at 0 ºC was added $NaBH_4$ (450 mg, 1.2 mmol) portionwise. After stirring at 0 ºC for 2 h, the reaction was quenched with acetone and then filtered through Celite®. The filtrate was concentrated under reduced pressure. The resulting residue was poured into $H_2O$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give **16** as a pale yellow oil. The crude product was not further purified. To a solution of crude amine **16** in $CH_3CN$ (6 ml) at 0 ºC was added $I_2$ (304 mg, 1.2 mmol). The mixture was allowed to stir at room temperature for 3 h and then quenched with a saturated aqueous solution of $NaHCO_3$ and a saturated aqueous solution of $Na_2S_2O_3$. The resulting mixture was extracted with $CHCl_3$, dried over $K_2CO_3$ and concentrated under reduced pressure. The crude material was purified by column chromatography ($SiO_2$, 1:4 $CHCl_3$: MeOH) to give **17** (159 mg, 0.58 mmol, 48 %) as a yellow solid.

mp 48 $^o$C (recrystallized from $Et_2O$-hexane), $^1$H-NMR (400 MHz, $CDCl_3$): δ 3.25 (br, 1H), 3.15 (s, 2H), 2.10 (br s, 2H) 1.91 (br, 1H), 1.79-1.72 (m, 8H), 1.66 (br d, *J* = 13.7 Hz, 2H), 1.59 (br d, *J* = 11.7 Hz, 2H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 48.9, 48.0, 41.1, 36.2, 36.0, 27.9, 25.1. IR ($CHCl_3$, $cm^{-1}$): 3300. MS *m/z*: 277 ($M^+$), 93 (100%). HRMS (EI): Calcd. for $C_{10}H_{16}I$ 277.0327 ($M^+$), found: 277.0323.



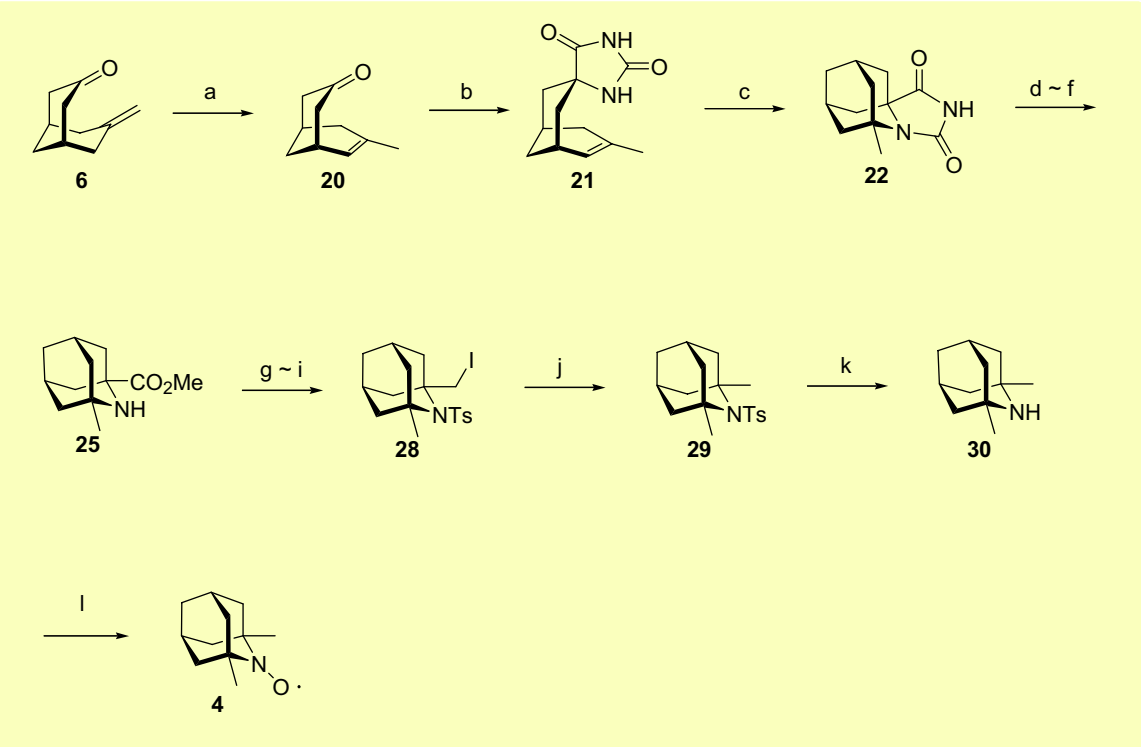

**1-Methyl-2-azaadamntane-*N*-oxyl (3)**

To a solution of amine **17** (3.35 g, 12 mmol) in THF (60 ml) at 0 ºC was added $LiAlH_4$ (550 mg, 14.4 mmol) portionwise. After stirring at 70 ºC for 30 min, the reaction was cooled to 0 ºC and diluted with $Et_2O$ and quenched with 30% aq. $NH_3$. The resulting mixture was filtered through Celite®. The filtrate was concentrated under reduced pressure. The residue was diluted with $CHCl_3$ and a saturated aqueous solution of $Na_2CO_3$ was added and extracted with $CHCl_3$. The organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure to give **18** as a pale yellow oil. The crude product was not further purified. A mixture of crude amine **18** and $Na_2WO_4 \cdot 2H_2O$ (404 mg, 1.23 mmol) in $H_2O$-MeOH (20 ml, 1:4 v/v) was stirred at room temperature for 30 min. To the reaction mixture was added 30% $H_2O_2$ (5.6 ml, 51.2 mmol) at 0 ºC and stirred for 30 min. After stirring at room temperature for 3 h, MeOH was removed by rotary evaporation. The residue was poured into a saturated aqueous solution of $NaHCO_3$ and extracted with $Et_2O$. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:4 AcOEt: hexane) to give **3** (777 mg, 4.68 mmol, 39 %) as a red solid.

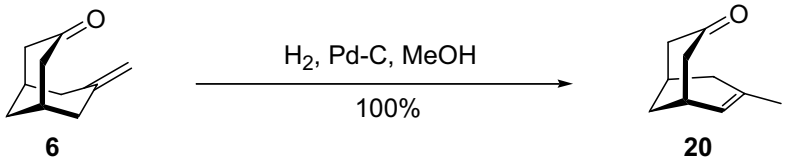
IR ($CHCl_3$, $cm^{-1}$): 3432. MS *m/z*: 166 ($M^+$), 93 (100%). HRMS (EI): Calcd. for $C_{10}H_{16}NO$ 166.1232 ($M^+$), found: 166.1194. Anal: Calcd. for $C_{10}H_{16}NO$: C, 72.25; H, 9.70; N, 8.43, found: C, 72.55; H, 9.60; N, 8.28.

**Synthesis of 1,3-dimethyl-AZADO**

***Scheme S3.***



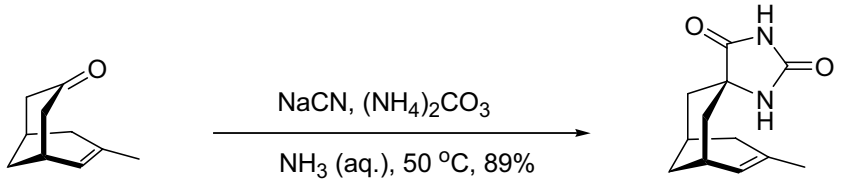

Reagents and conditions: (a) $H_2$, Pd-C, MeOH, quant; (b) NaCN, $(NH_4)_2CO_3$, aq. $NH_3$, 50 $^oC$, 89%; (c) TfOH, $CH_2Cl_2$, 0 $^oC$, quant; (d) $Boc_2O$, $Et_3N$, 4-DMAP, $CH_2Cl_2$, 0 $^oC$, 98%; (e) 10N KOH/EtOH, reflux; (f) AcCl, MeOH, reflux, 74% over two steps; (g) *p*-TsCl, pyridine, reflux, 40%; (h) DIBAL, PhMe, 0 $^oC$, 82%; (i) $PPh_3$, imidazole, $I_2$, $CH_2Cl_2$, 77%; (j) NaI, *i*-PrOH, reflux, 65%; (k) $Na/NH_3$, $Et_2O$, -78 $^oC$, then $EtOH/H_2O$; (l) UHP, $Na_2WO_4 \cdot 2H_2O$, MeOH, 41% over two steps.




**7-Methyl-bicyclo[3.3.1]non-6-en-3-one (20)**

To a solution of ketone **6** (2 g, 13.3 mmol) in MeOH (133 ml) was added 10% Pd-C (200 mg) under Ar atmosphere. The reaction flask was evacuated and purged with $H_2$ three times and then the reaction was stirred at room temperature under $H_2$ atmosphere for 3h. The catalyst was removed by filtration through Celite®. The filtrate was concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:8 AcOEt: hexane) to give **20** (2 g, 13.3 mmol, 100 %) as a colorless oil.

$^1$H-NMR (400 MHz, $CDCl_3$): δ 5.42 (br d, $J$ = 5.6 Hz, 2H), 2.65 (br s, 1H), 2.56 (br s, 1H), 2.36-2.22 (m, 3H), 2.00-1.90 (m, 2H), 1.79 (d, $J$ = 17.9 Hz, 1H), 1.58 (s, 3H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 212.2, 132.8, 124.6, 49.1, 46.5, 37.4, 31.1, 30.24, 30.21, 23.1. IR (neat, cm$^{-1}$): 1714.4. MS *m/z*: 150 ($M^+$), 93 (100%). HRMS (EI): Calcd. for $C_{10}H_{14}O$ 150.1045 ($M^+$), found: 150.1047.



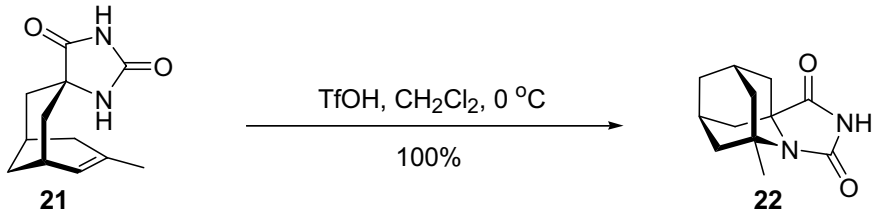

**20** **21**

**7-Methyl-bicyclo[3.3.1]non-6-en-3-spiro-5'-hydantoin (21)**

To a 100 ml sealed tube charged with NaCN (4.9 g, 100 mmol), $(NH_4)_2CO_3$ (22.4 g, 233 mmol) was added 30% aq. $NH_3$ (55 ml) at room temperature [d]. The mixture was vigorously stirred for 10 min, and then ketone **20** (5 g, 33.3 mmol) was added. The solution was allowed to stir at 50 ºC for 37 h. After cooling to room temperature, the mixture was diluted with $H_2O$ and extracted with $CHCl_3$. The organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:2 AcOEt: hexane) to give **21** (6.5 g, 29.6 mmol, 89 %) as a white solid.

mp 205-207 °C (recrystallized from $CHCl_3$-hexane), $^1$H-NMR (400 MHz, $CDCl_3$): δ 8.79 (br s, 1H), 5.92 (br s, 1H), 5.68 (br d, $J$ = 6.1 Hz, 1H), 2.50 (br s, 1H), 2.43 (br dd, $J$ = 18.1, 6.8 Hz, 1H), 2.37 (br s, 1H), 2.24 (dd, $J$ = 14.4, 4.9 Hz, 1H), 2.07 (dd, $J$ = 13.9, 3.7 Hz,

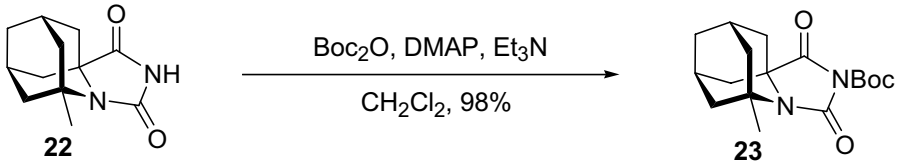
1H),1.94 (d, $J$ = 18.1 Hz, 1H), 1.76-1.71 (m, 7H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 178.8, 156.1, 135.8, 127.3, 62.9, 40.2, 37.3, 36.7, 30.2, 27.5, 25.8, 23.3. IR (neat, $cm^{-1}$): 3447.1, 3391.2, 3156.9, 3064.3, 1774.2, 1721.2, 1417.4. MS *m/z*: 220 ($M^+$), 220 (100%). HRMS (EI): Calcd. for $C_{12}H_{16}N_2O_2$ 220.1212 ($M^+$), found: 220.1201.




**1,2-(1',3'-Diketoimidazo)-3-Methyl-2-azaadamantane (22)**

To a solution of hydantoin **21** (835 mg, 3.8 mmol) in $CH_2Cl_2$ (38 ml) at 0 ºC was added TfOH (1 ml, 11.4 mmol). The mixture was allowed to stir at 0 ºC for 2h and then quenched with a saturated aqueous solution of $Na_2CO_3$ and extracted with $CHCl_3$. The organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:2 AcOEt: hexane) to give **22** (830 mg, 3.8 mmol, 100 %) as a white solid.

mp 227-229 °C (recrystallized from $CHCl_3$-hexane), $^1$H-NMR (400 MHz, $CDCl_3$): δ 8.59 (br s, 1H), 2.30 (br s, 1H), 2.04 (d, $J$ = 12.2 Hz, 2H), 1.86-1.73 (m, 6H), 1.66 (s, 3H), 1.59 (d, $J$ = 12.7 Hz, 2H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 176.3, 151.7, 61.8, 54.6, 43.2, 36.4, 33.8, 27.6, 26.3. IR (neat, $cm^{-1}$): 3163.7, 3047.9, 1763.6, 1698.0. MS *m/z*: 220 ($M^+$), 220 (100%). HRMS (EI): Calcd. for $C_{12}H_{16}N_2O_2$ 220.1212 ($M^+$), found: 220.1219.

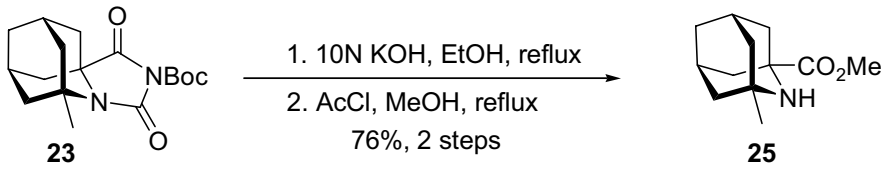



**1,2-(2'-*t*-Butoxycarbonyl-1',3'-diketoimidazo)- 3-methyl-2-azaadamantane (23)**

Hydantoin **22** (216 mg, 0.98 mmol) was dissolved in $CH_2Cl_2$ (5 ml) and cooled to 0 ºC. $Et_3N$ (0.27 ml, 1.96 mmol), $Boc_2O$ (430 mg, 1.96 mmol), 4-DMAP (12 mg, 0.1 mmol) was

added and the mixture was stirred at 0 ºC for 10 min and then quenched with $H_2O$. The resulting biphasic mixture was extracted $Et_2O$. The combined organic layers were washed with brine and dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:2 AcOEt: hexane) to give **23** (313 mg, 0.97 mmol, 98 %) as a white solid.

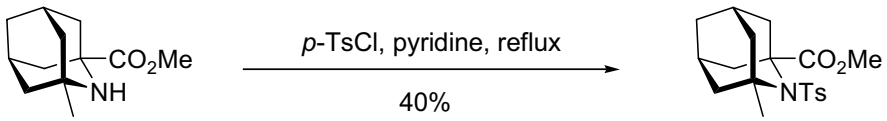
$^1$H-NMR (400 MHz, $CDCl_3$): δ 2.39 (br s, 2H), 2.06 (br d, $J$ = 12.1 Hz, 2H), 1.84 (m, 3H), 1.76 (m, 3H), 1.69 (s, 3H), 1.60 (br d, $J$ = 11.6 Hz, 2H), 1.57 (s, 9H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 172.1, 147.4, 146.8, 85.1, 59.9, 55.0, 43.0, 36.5, 33.7, 27.8, 27.4, 26.3. IR (neat, $cm^{-1}$): 1800.2, 1767.4, 1721.2, 1454.1, 1385.6. MS *m/z*: 320 ($M^+$), 220 (100%). HRMS (EI): Calcd. for $C_{17}H_{24}N_2O_4$ 320.1736 ($M^+$), found: 320.1756.




**3-Methyl-1-methoxycarbonyl-2-azaadamantane (25)**

Carbamate **23** (313 mg, 0.98 mmol) was dissolved in mixture of EtOH-10N *aq.*KOH (5 ml, 1 : 1 v/v) and heated at reflux for 15 h. After cooling to room temperature, solvent was removed *in vacuo*. The residue was poured into $H_2O$ and extracted three times with $CHCl_3$. The aqueous layer was concentrated under reduced pressure to give amino acid **24**. The crude product was not further purified. To a 20 ml flask charged with MeOH (2.5 ml) at 0 ºC was added AcCl (0.33 ml, 4.7 mmol). The reaction mixture was allowed to stir at room temperature for 10 min, and then crude amino acid **24** was added. After stirring at 80 ºC for 5 h, solvent was removed *in vacuo*. The residue was poured into $H_2O$ and extracted three times with $CHCl_3$. The aqueous layer was added a saturated aqueous solution of $Na_2CO_3$ until it became strongly basic. The aqueous phase was extracted with $CHCl_3$ and dried over $K_2CO_3$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:4 MeOH:$CHCl_3$) to give **25** (156 mg, 0.76 mmol, 74 %) as a white solid.

$^1$H-NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 3H), 2.20 (br s, 1H), 1.97 (br d, *J* = 12.1 Hz, 2H), 1.81-1.69 (m, 4H), 1.57 (br s, 4H), 1.06 (s, 3H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 175.4, 57.2, 51.9, 48.9, 42.4, 38.1, 35.0, 30.4, 27.9. IR (neat, $cm^{-1}$): 1735.6, 1435.7, 1245.8. MS *m/z*: 209 ($M^+$), 150 (100%). HRMS (EI): Calcd. for $C_{12}H_{19}NO_2$ 209.1416 ($M^+$), found: 209.1397.

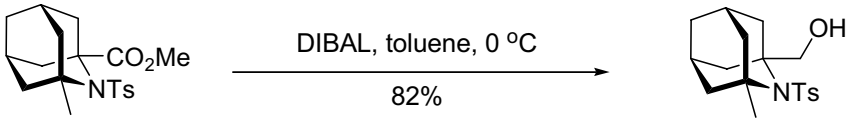



**25** **26**

***N*-*p*-Toluenesulfonyl-3-methyl-1-methoxycarbonyl-2-azaadamantane (26)**

To a solution of amine **25** (1g, 4.79 mmol) in pyridine (24 ml) at 0 ºC was added *p*-TsCl (4.6 g, 23.9 mmol). The mixture was heated at reflux for 19 h. After cooling to room temperature, the reaction mixture was poured into $H_2O$ and extracted with $CHCl_3$. The organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:4 AcOEt: hexane) to give **26** (605 mg, 1.9 mmol, 40 %) as a white solid.

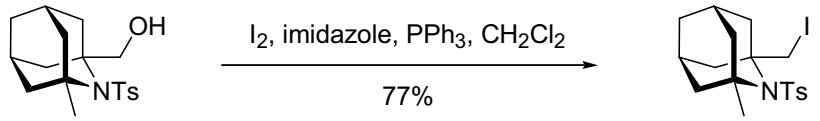
mp 198-199 ºC (recrystallized from AcOEt-hexane), $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.5 Hz, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 3.71 (s, 3H), 2.33-2.04 (m, 6H), 1.99 (br d, *J* = 12.3 Hz, 1H), 1.96 (br d, *J* = 12.3 Hz, 1H), 1.75 (br d, *J* = 12.7 Hz, 1H), 1.70 (br d, *J* = 12.7 Hz, 1H), 1.45 (br d, *J* = 13 Hz, 1H), 1.42 (br d, *J* = 13 Hz, 1H), 1.15 (s, 3H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 174.1, 142.7, 141.9, 129.2, 127.3, 77.2, 63.4, 59.1, 52.1, 34.2, 28.1, 27.0, 21.5. IR (neat, $cm^{-1}$): 1740.4, 1597.7, 1448.3, 1323.9, 1309.4. MS *m/z*: 363 ($M^+$), 363 (100%). HRMS (EI): Calcd. for $C_{19}H_{25}NO_4S$ 363.1504 ($M^+$), found: 363.1503.




**26** **27**

***N*-*p*-Toluenesulfonyl-1-hydroxymethyl-3-methyl-2-azaadamantane (27)**

To a solution of sulfonamide **26** (605 mg, 1.9 mmol) in toluene (10 ml) at 0 ºC was added DIBAL in toluene (7.5 ml, 7.5 mmol). The mixture was allowed to stir at 0 ºC for 30 min, and then quenched with AcOEt, $H_2O$. After stirring at room temperature for an additional 2 h, the mixture was filtered through Celite®. The filtrate was concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:5 AcOEt: hexane) to give **27** (520 mg, 1.56 mmol, 82 %) as a white solid.
mp 166-168 °C (recrystallized from $CHCl_3$-$Et_2O$), $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.3 Hz, 2H), 3.88 (d, *J* = 7.8 Hz, 2H), 3.31 (t, *J* = 8.1 Hz, 1H), 2.41 (s, 3H), 2.25 (d, *J* = 12.5 Hz, 2H), 2.16 (br s, 2H), 2.04 (d, *J* = 8.3 Hz, 2H), 1.78-1.67 (m, 2H), 1.54 (br d, *J* = 13 Hz, 2H), 1.39 (br d, *J* = 13 Hz, 2H), 1.26 (s, 3H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 142.9, 142.3, 129.3, 129.1, 71.7, 65.0, 59.0, 43.2, 39.8, 34.4, 29.5, 26.5, 21.4. IR (neat, $cm^{-1}$): 3575.4, 1596.8, 1445.4, 1321.0, 1302.7. MS *m/z*: 335 ($M^+$), 180 (100%). HRMS (EI): Calcd. for $C_{18}H_{25}NO_3S$ 335.1555 ($M^+$), found: 335.1526.

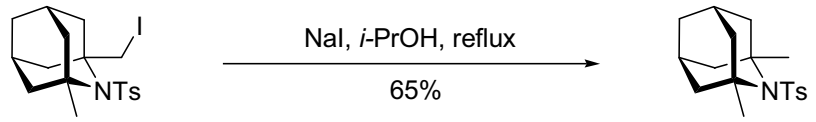



**27** **28**

***N*-*p*-Toluenesulfonyl-1-iodomethyl-3-methyl-2-azaadamantane (28)**

To a mixture of $PPh_3$ (820 mg, 3.13 mmol) and imidazole (213 mg, 3.13 mmol) in $CH_2Cl_2$ (3 ml) at room temperature was added $I_2$ (796 mg, 3.13 mmol). After stirring at room temperature for 30 min, sulfonamide **27** (350 mg, 1.05 mmol) in $CH_2Cl_2$ (2 ml) was cannulated into the reaction mixture. The reaction was stirred for an additional 2 h then quenched with a saturated aqueous solution of $NaHCO_3$, which was extracted with AcOEt. The organic layer was washed with brine and dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:18 AcOEt: hexane) to give **28** (360 mg, 0.81 mmol, 77 %) as a white solid.
mp 128-130 °C (recrystallized from $CHCl_3$-$Et_2O$), $^1$H-NMR (400 MHz, $CDCl_3$): δ 8.0 (d, *J* = 7.2 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 2H), 3.95 (s, 2H), 2.39 (s, 3H), 2.24 (br d, *J* = 12.6 Hz, 2H), 2.13 (br s, 2H), 1.70-1.61 (m, 4H), 1.37 (br d, *J* = 12.6 Hz, 2H), 1.09 (s, 3H).
$^{13}$C-NMR (100 MHz, $CDCl_3$): δ 143.2, 142.4, 129.1, 127.1, 61.0, 60.0, 43.1, 42.9, 34.3,

29.7, 27.1, 22.3, 21.4. IR (neat, $cm^{-1}$): 1586.2, 1457.9, 1323.9, 1311.4. MS *m/z*: 445 ($M^+$), 319 (100%). HRMS (EI): Calcd. for $C_{18}H_{24}INO_2S$ 445.0572 ($M^+$), found: 445.0564.

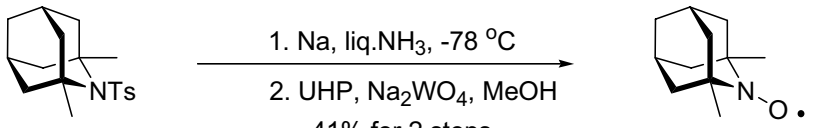



**28** **29**

***N*-*p*-Toluenesulfonyl-1,3-dimethyl-2-azaadamantane (29)**

A mixture of sulfonamide **28** (200 mg, 0.45 mmol) and NaI (4.45 g, 22.5 mmol) in 2-propanol (2 ml) was heated at reflux until the starting material was no longer detectable (TLC, SM $R_f$ = 0.3 ; 1:1 $CHCl_3$:benzene). The reaction was cooled to room temperature and then 2-propanol was removed *in vacuo*. The residue was poured into a saturated aqueous solution of $NaHCO_3$ and extracted with $Et_2O$. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:18 AcOEt: hexane) to give **29** (93 mg, 0.29 mmol, 65 %) as a white solid.

mp 116-119 °C (recrystallized from $CHCl_3$-$Et_2O$), $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 2.39 (s, 3H), 2.11-2.09 (m, 6H), 1.68 (s, 2H), 1.51 (m, 4H), 1.43 (s, 6H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 143.9, 141.8, 129.2, 126.2, 59.8, 44.2, 34.2, 30.8, 27.2, 21.3. IR (neat, $cm^{-1}$): 1598.7, 1439.6, 1347.0, 1308.5. MS *m/z*: 319 ($M^+$), 164 (100%). HRMS (EI): Calcd. for $C_{18}H_{25}NO_2S$ 319.1606 ($M^+$), found: 319.1612.




**29** **4**

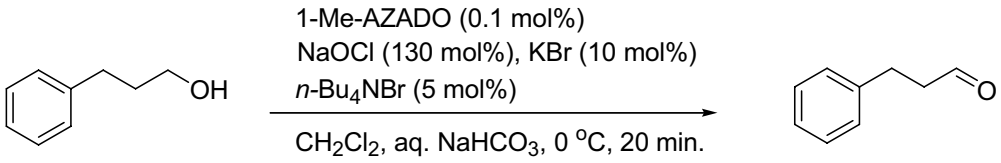
**1,3-Dimethyl-2-azaadamantane *N*-oxyl (4)**

To a mixture of dry $Et_2O$ (0.5 ml), liquid ammonia (2 ml) and sodium metal (excess amount) was added a dry $Et_2O$ (2 ml) solution of sulfonamide **29** (70 mg, 0.22 mmol) at -78 °C, and the mixture was stirred for 1 h. To this was added EtOH-$H_2O$ (5 ml, 1:4 v/v), and

the mixture was warmed to room temperature with evaporation of ammonia and stirred for 2 h. The reaction was quenched with a saturated aqueous solution of $NH_4Cl$. The layers were separated, and the aqueous layer was extracted seven times with $CHCl_3$. The combined organic layers were dried over $K_2CO_3$ and concentrated under reduced pressure. The residue was dissolved in EtOH (1 ml) and added 7N EtOH solution of HCl (3 ml) at 0 ºC. The mixture was allowed to stir for 1 h and then solvent was removed under reduced pressure. The residue was poured into $H_2O$ and extracted three times with $CHCl_3$. The aqueous layer was added 10% aq. NaOH until it became strongly basic, which was extracted with $CHCl_3$. The organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure.to give **30** as a colorless oil. Amine **30** was then used directly for further reaction. A mixture of amine **30** and $Na_2WO_4 \cdot 2H_2O$ (30 mg, 0.091 mmol) in MeOH (0.9 ml) was stirred at room temperature for 30 min. To the reaction mixture was added urea hydrogen peroxide (69 mg, 0.73 mmol) at room temperature. After stirring for 3 h, the reaction mixture was quenched with a saturated aqueous solution of $NaHCO_3$. The mixture was extracted with $CHCl_3$. The organic layer was dried over $K_2CO_3$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:10 $Et_2O$: hexane) to give **4** (16.2 mg, 0.09 mmol, 41 %) as a red solid.

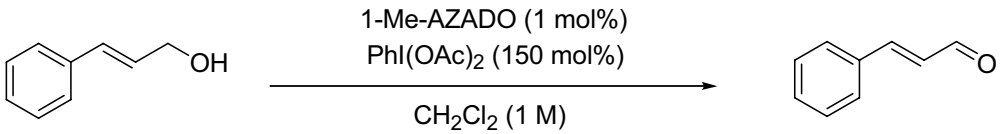
IR (neat, $cm^{-1}$): 1448.3, 1369.2, 1343.2. MS *m/z*: 180 ($M^+$), 93 (100%). HRMS (EI): Calcd. for $C_{11}H_{18}NO$ 180.1388 ($M^+$), found 180.1380. Anal: Calcd. for $C_{11}H_{18}NO$: C, 73.29; H, 10.06; N, 7.77, found: C, 73.00; H, 9.92; N, 7.84.

**General procedure A: Anelli's oxidation conditions** [e)]




A 20 ml flask was charged with a solution of 3-phenyl propanol (200 mg, 1.47 mmol), 1-Me-AZADO (**3**) (0.244 mg, 1.47 μmol) in $CH_2Cl_2$ (3.9 ml) and a sat. aqueous solution of $NaHCO_3$ (2 ml) containing KBr (17.5 mg, 0.074 M) and *n*-$Bu_4NBr$ (23.7 mg, 0.037 M). To this cooled (0 ºC, a water-ice bath) and well stirred mixture, a pre-mixed solution of aqueous NaOCl (8% Cl, purchased from Junsei Chemical Co.) and sat. aqueous solution of $NaHCO_3$ (3.3 ml, 1:1.4 v/v) was added dropwise during 6 min. The reaction was stirred for 20 min at 0 ºC, then quenched with a sat. aqueous solution of $Na_2S_2O_3$ (4 ml). The aqueous layer was separated and extracted with $Et_2O$. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:6 $Et_2O$: hexane) to give 3-phenyl propanal (177 mg, 1.32 mmol, 90 %) as a colorless oil.

**General procedure B: Margarita's oxidation conditions** [f)]




To a solution of cinnamyl alcohol (200 mg, 1.49 mmol) and 1-Me-AZADO (**3**) (2.47 mg, 14.9 μmol) in $CH_2Cl_2$ (1.5 ml) was added $PhI(OAc)_2$ (720 mg, 2.24 mmol) at one stroke. The reaction mixture was allowed to stir until the alcohol was no longer detectable (TLC), then it was diluted with $Et_2O$ and quenched with a sat. aqueous solution of $NaHCO_3$ (4 ml), followed by a sat. aqueous solution of $Na_2S_2O_3$ (4 ml). The layer was separated and the aqueous layer was extracted with $Et_2O$. The combined organic layers were washed

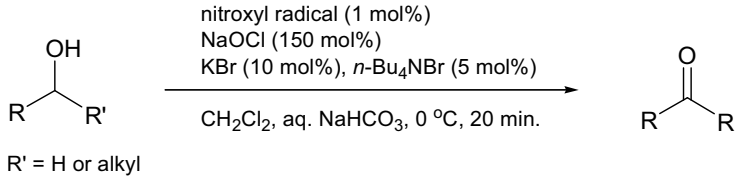
with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:9 $Et_2O$: hexane) to give cinnamaldehyde (183 mg, 1.39 mmol, 93 %) as a colorless oil.

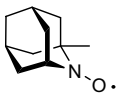
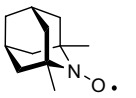
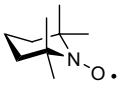
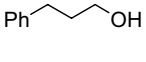
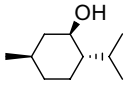
<note> 1-Me-AZADO was added accurately as a $CH_2Cl_2$ solution.

**Catalytic efficiencies of 1,3-dimethyl-AZADO:**

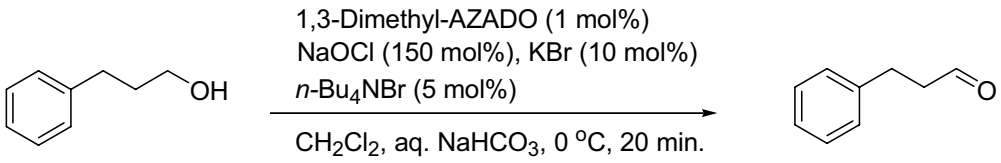
Catalytic efficiencies of 1,3-dimethyl-AZADO (**4**) were evaluated by monitoring the oxidation of 3-phenylpropanol and *l*-menthol under Anelli's condition. As shown in Table S1, 1, 3-dimentyl-AZADO (**4**) exhibited comparable catalytic activity towards the oxidation of 3-phenylpropanol to give 3-phenylpropanal in 92% yield after 20min. On the other hand, 1,3-dimethyl-AZADO (**4**) does not efficiently oxidize *l*-menthol similar to TEMPO (**1**), showing a remarkable difference from 1-Me-AZADO (**3**).

*Table S1*



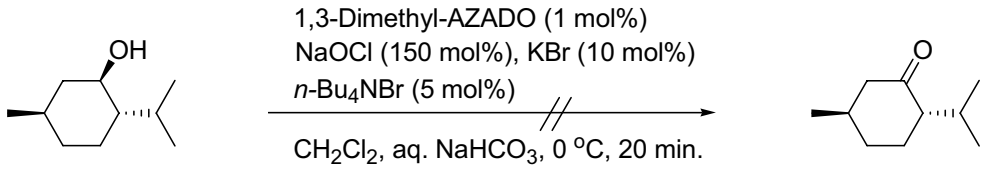

| substrate \ catalyst |  1-Me-AZADO (**3**) |  1,3-dimethyl-AZADO (**4**) |  TEMPO (**1**) |
|---|---|---|---|
|  | 91% | 92% | 90% |
|  | 95% | trace | trace |

**Procedure for the oxidation of 3-phenyl propanol**




A 20 ml flask was charged with a solution of 3-phenyl propanol (200 mg, 1.47 mmol), 1,3-dimethyl-AZADO (**4**) (2.65 mg, 14.7 μmol) in $CH_2Cl_2$ (3.9 ml) and a sat. aqueous solution of $NaHCO_3$ (2 ml) containing KBr (17.5 mg, 0.074 M) and *n*-$Bu_4NBr$ (23.7 mg, 0.037 M). To this cooled (0 ºC, a water-ice bath) and well stirred mixture, a pre-mixed solution of aqueous solution of NaOCl and sat. aqueous solution of $NaHCO_3$ (3.3 ml, 1:1.4 v/v) was added dropwise during 6 min. The reaction was stirred for 20 min at 0 ºC, then quenched with a sat. aqueous solution of $Na_2S_2O_3$ (4 ml). The aqueous layer was separated and extracted with $Et_2O$. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography ($SiO_2$, 1:6 $Et_2O$: hexane) to give 3-phenyl propanal (183 mg, 1.35 mmol, 92 %) as a colorless oil.

**Procedure for the oxidation of *l*-menthol**




A 20 ml flask was charged with a solution of *l*-menthol (200 mg, 1.28 mmol), 1,3-dimethyl-AZADO (**4**) (2.3 mg, 1.47 μmol) in $CH_2Cl_2$ (1.7 ml) and a sat. aqueous solution of $NaHCO_3$ (1.7 ml) containing KBr (15 mg, 0.074 M) and *n*-$Bu_4NBr$ (20.3 mg, 0.037 M). To this cooled (0 ºC, a water-ice bath) and well stirred mixture, a pre-mixed solution of aqueous solution of NaOCl and sat. aqueous solution of $NaHCO_3$ (3.1 ml, 1:1.2

v/v) was added dropwise during 6 min. The reaction was stirred for 20 min at 0 ºC, then quenched with a sat. aqueous solution of $Na_2S_2O_3$ (4 ml). The aqueous layer was separated and extracted with $Et_2O$. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude material was purified by flash column chromatography to give trace amount of *l*-menthone and *l*-menthol (recovered yield : 49~56%).

**Electrochemical measurements**

We carried out cyclic voltammetric measurements to get insight into the electrochemical behaviors of the nitroxyl radicals used in this study. Although *E*º' values of nitroxyl radicals have been summarized by Schukin and his coworkers (57 species) as well as by Bobbit,[g] those of AZADO, 1-Me-AZADO, and 1,3-dimethyl-AZADO were unavailable. The cyclic voltammograms were measured on a Cypress CS-2010 electrochemical analyzer with a conventional three-electrode configuration at room temperature (approximately 23 ºC). $CH_3CN$ solutions of TEMPO, AZADO, 1-Me-AZADO, and 1,3-dimethyl-AZADO (2 mM) were used throughout the cyclic voltammetric measurements. Glassy carbon (BAS, 3 mm diameter), platinum wire, and Ag/Ag+ (BAS type RE-5) were used as working, auxiliary, and reference electrodes, respectively. Electric potential values reported herein referred to this reference electrode. $NaClO_4$ (0.1 M) was used as supporting electrolyte.

The cyclic voltammograms of TEMPO, AZADO, 1-Me-AZADO, and 1,3-dimethyl-AZADO are shown in Fig. S1, and the cyclic voltammograms obtained at various potential sweep rate ($v$) are independently given in Fig. S2 (TEMPO), Fig. S3 (AZADO), Fig. S4 (1-Me-AZADO), and Fig. S5 (1,3-dimethyl-AZADO). Obviously, these nitroxyl radicals showed c cyclic voltammograms within $v$ = 200 mV $s^{-1}$, with peak-to-peak separation ($\Delta E_p = E_{pa} - E_{pc}$; $E_{pa}$ and $E_{pc}$ denote anodic and cathodic peak potentials, respectively) being approximately 60 mV. These $\Delta E_p$ values establish that the electrochemical reactions of the nitroxylradicals reversibly proceed by one-electron transfer. The $i_{pa}$ (electric current at $E_{pa}$) values of the nitroxylradicals linearly correlate with $v^{1/2}$.[h] This indicates that the electrochemical reactions of the nitroxylradicals are of fusion-controlled. The highly reversible nature in electrochemical oxidation of the nitroxylradicals implies that they can intrinsically function as catalysts for the oxidation of alcohols. It is noteworthy that such well-defined redox waves were retained after more than 100-cycle measurements with neither decreasing the $i_{pa}$ values nor shifting the $E_{pa}$ and $E_{pc}$ values. The observed marked durability of the nitroxylradicals would result in the high turnover numbers prerequisite to efficient catalysts.

The $E^{o}$' values of the nitroxylradicals, which were calculated by ($E_{pa}$ + $E_{pa}$) / 2, are summarized in Table 1. The $E^{o}$' values of the nitroxylradicals is in the order of 1,3-dimethyl-AZADO < 1-Me-AZADO < AZADO < TEMPO. However, the total efficiency of the nitroxylradicals as catalysts was in the order of 1,3-dimethyl-AZADO << TEMPO < 1-Me-AZADO. No obvious correlation between the two orders is found. Thus, we conclude that at least a part of the high efficiency of 1-Me-AZADO as an oxidative catalyst is due to kinetic factors, presumably decreased steric hindrance around the reaction center.

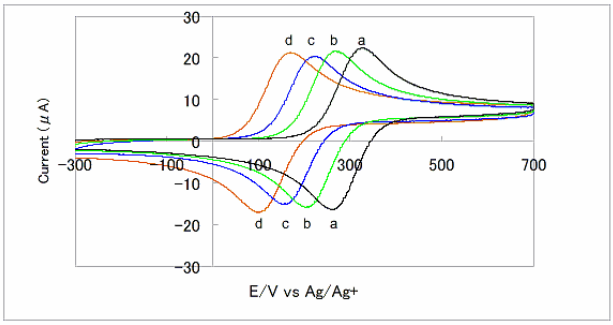



Fig. S1 Cyclic voltammograms of various nitroxyl radicals (2 mM) at scan rate of 50 mV $s^{-1}$ (a; TEMPO, b; AZADO, c; 1-Methyl-AZADO, d; 1,3-dimethyl-AZADO)

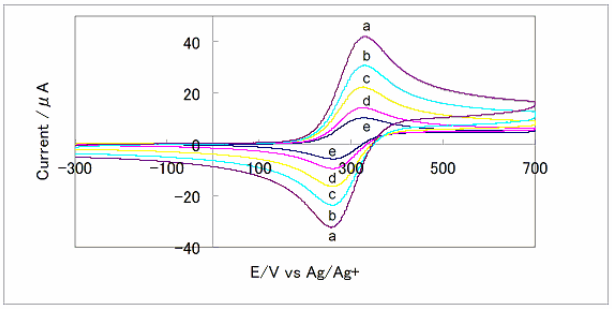



Fig. S2 Cyclic voltammograms of TEMPO (2 mM) at varying scan rates. (a; 10 mV $s^{-1}$, b; 20 mV $s^{-1}$, c; 50 mV $s^{-1}$, d; 100 mV $s^{-1}$ e; 200 mV $s^{-1}$)

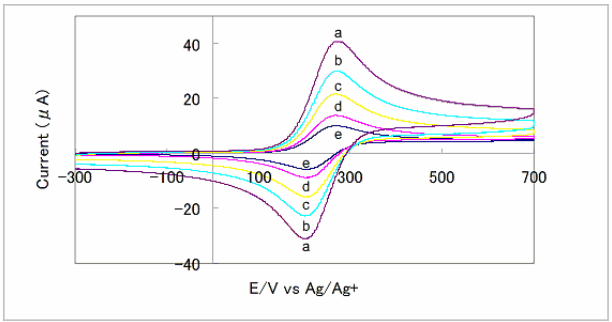



Fig. S3 Cyclic voltammograms of AZADO (2 mM) at varying scan rates. (a; 10 mV $s^{-1}$, b; 20 mV $s^{-1}$, c; 50 mV $s^{-1}$, d; 100 mV $s^{-1}$ e; 200 mV $s^{-1}$)

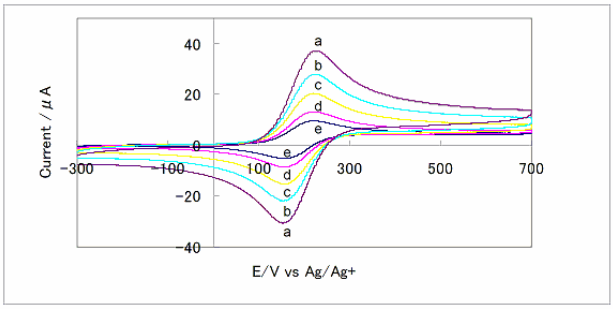



Fig. S4 Cyclic voltammograms of 1-Me-AZADO (2 mM) at varying scan rates. (a; 10 mV $s^{-1}$, b; 20 mV $s^{-1}$, c; 50 mV $s^{-1}$, d; 100 mV $s^{-1}$ e; 200 mV $s^{-1}$)

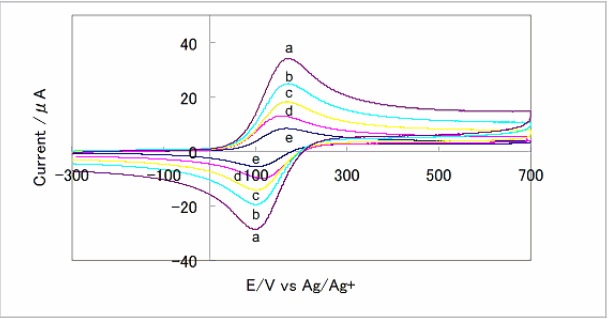



Fig. S5 Cyclic voltammograms of 1,3-dimethyl-AZADO (2 mM) at varying scan rates. (a; 10 mV $s^{-1}$, b; 20 mV $s^{-1}$, c; 50 mV $s^{-1}$, d; 100 mV $s^{-1}$ e; 200 mV $s^{-1}$)

*Table S2* The formal potential of various nitroxylradicals

| **Nitroxyl radical** | $E^{0\prime}$ **vs Ag/Ag$^+$** |
|---|---|
| TEMPO | + 294 mV |
| AZADO | + 236 mV |
| 1-Me-AZADO | + 186 mV |
| 1,3-Dimethyl-AZADO | + 136 mV |

**References and notes**

(a) Muraoka, O.; Wang, Y.; Okamura, M.; Nishimura, S.; Tanabe, G.; Momose, T. *Synth. Commn*. **1996**, *26*, 1555-1562.

(b) Ipaktschi, J. *Chem. Ber.* **1984**, *117*, 856-858.

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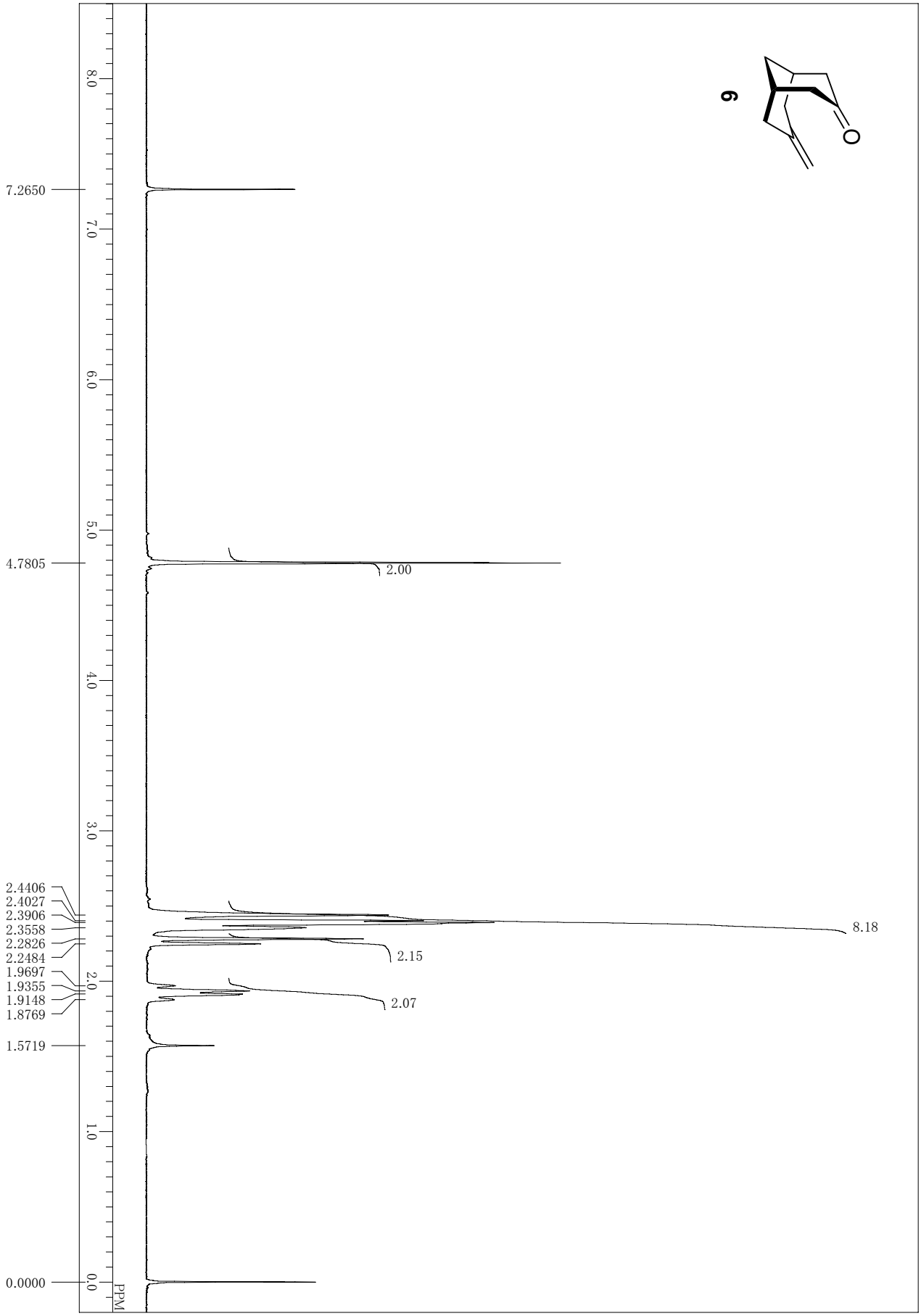
(e) Anelli, P. L.; Banfi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, *52*, 2559-2562.

(f) De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. *J. Org. Chem.* **1997**, *62*, 6974-6977.

(g) Bobbit, J. M.; Flores, M. C. L. *Heterocycles* **1988**, *27*, 509-533.

(h) Bard, A. J.; Faulkner, L. R. Electrochemical Methods, Fundamentals and Application: Wiley: New York, 1980; Chapter 6.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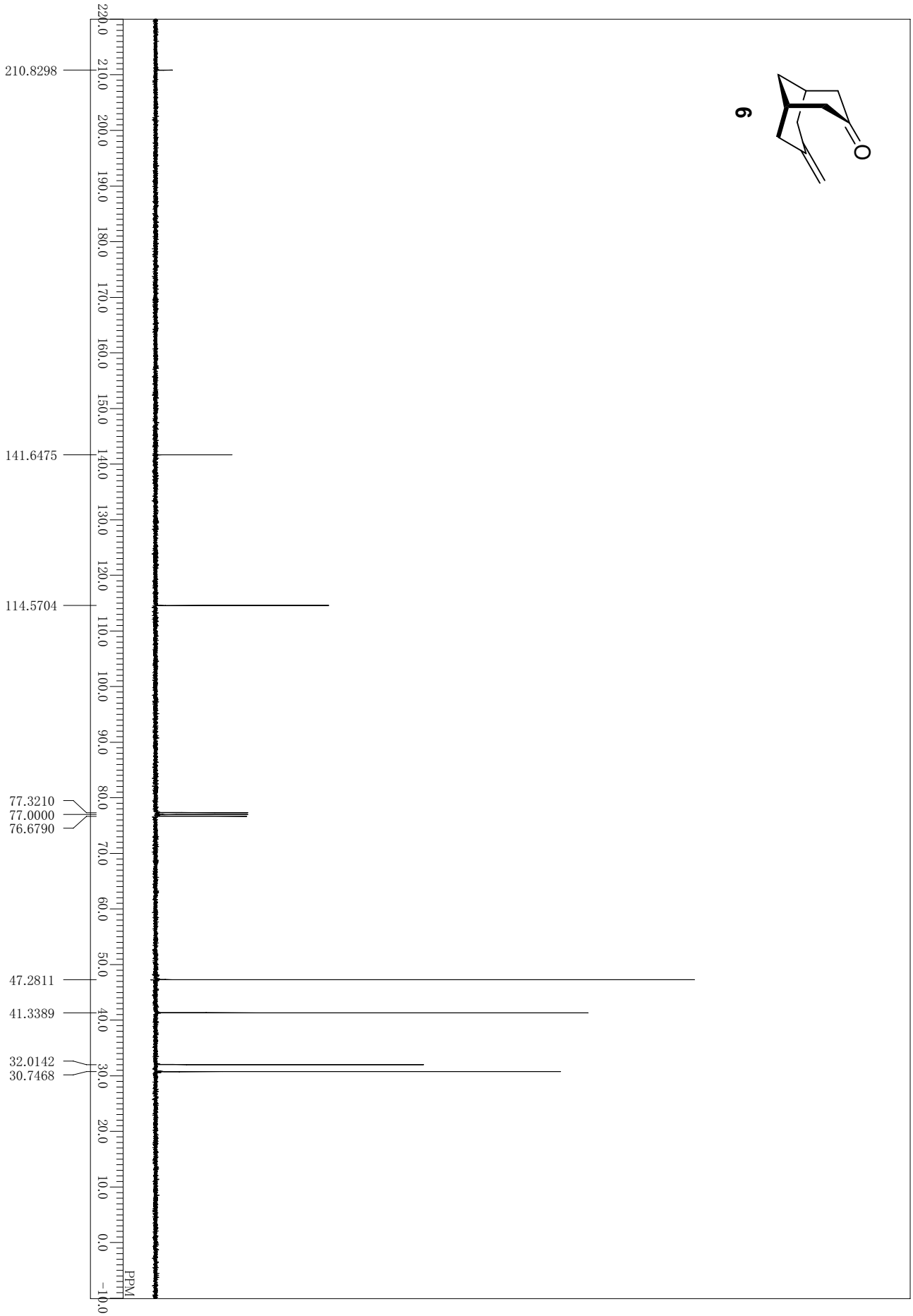
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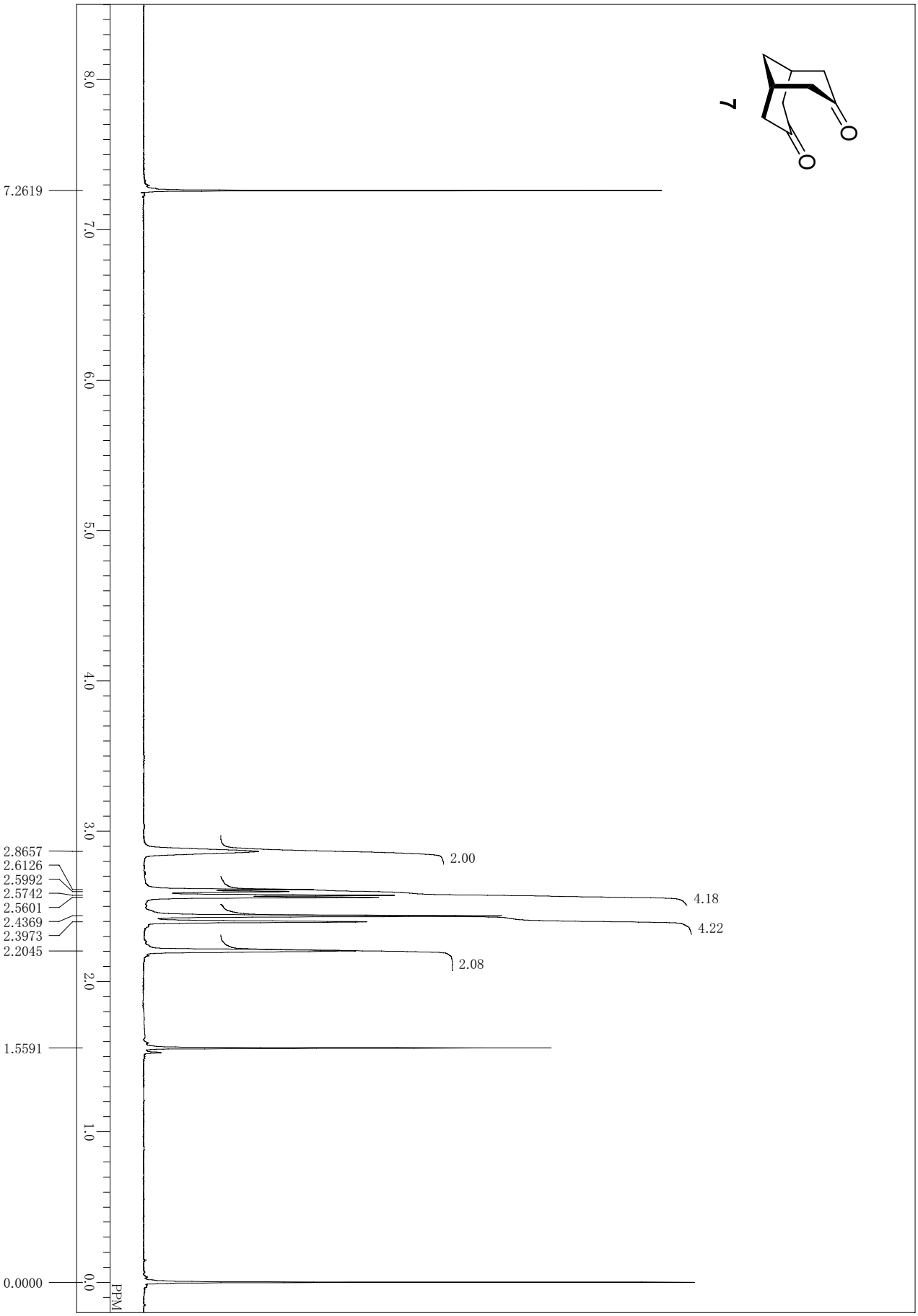
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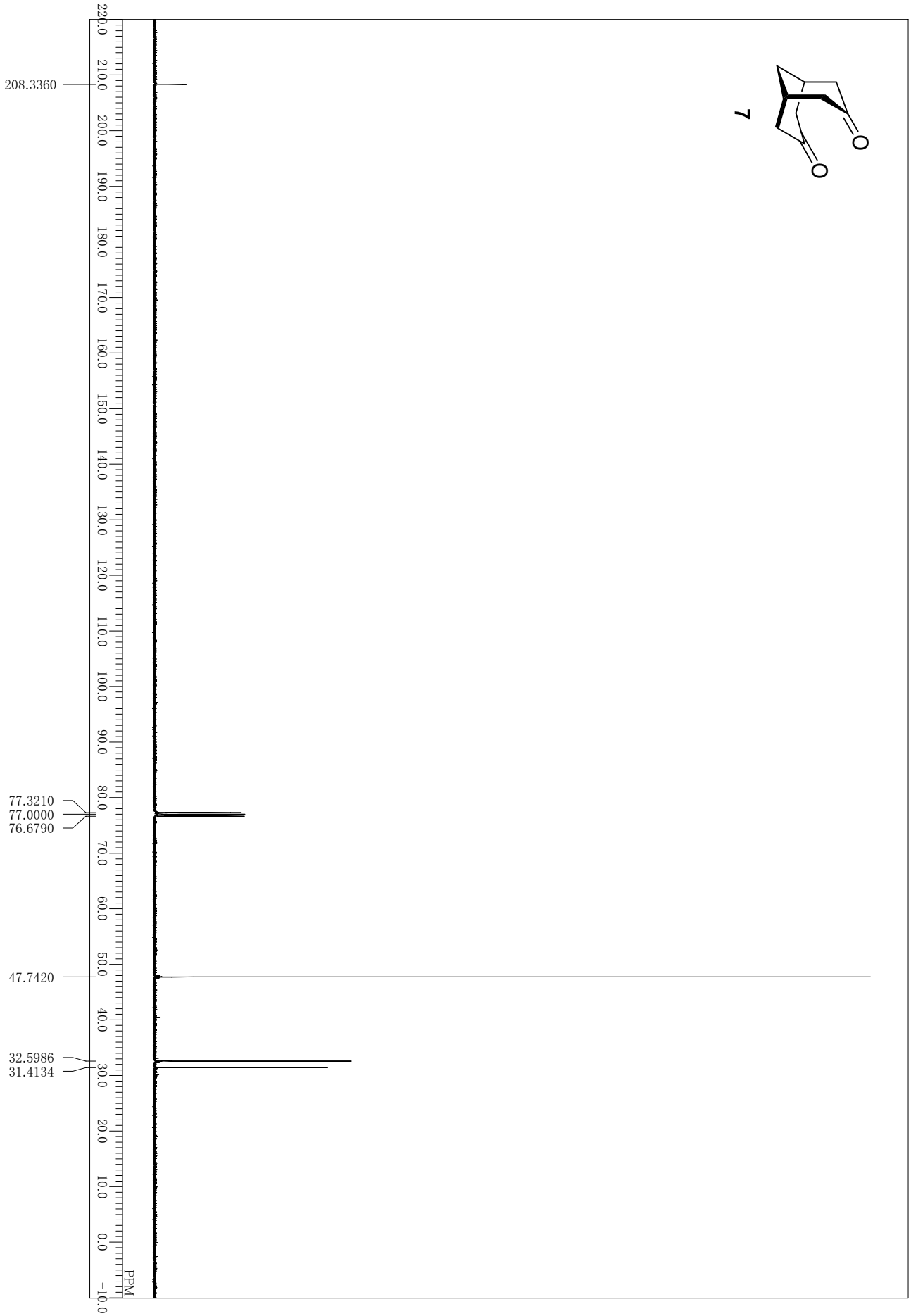
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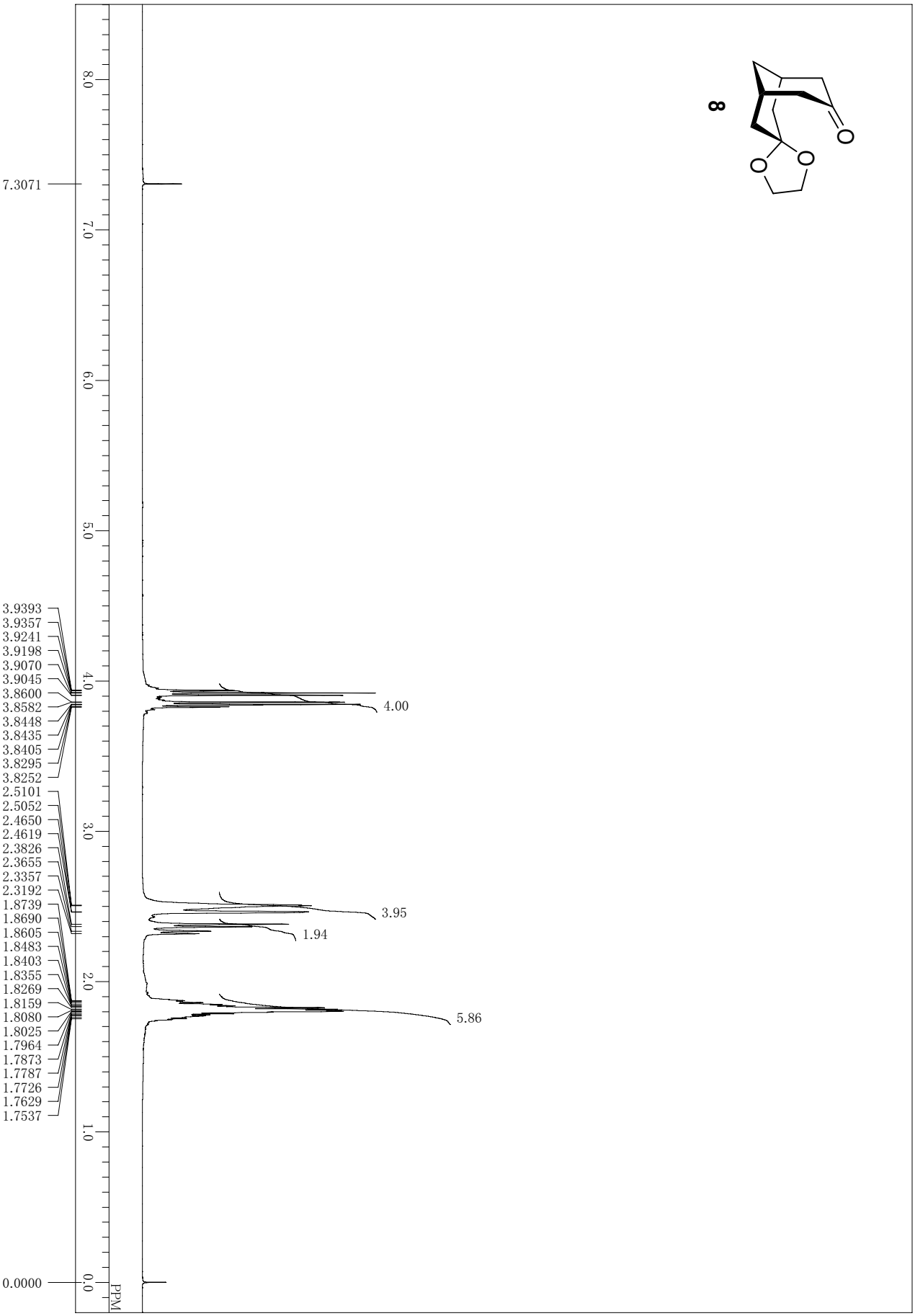
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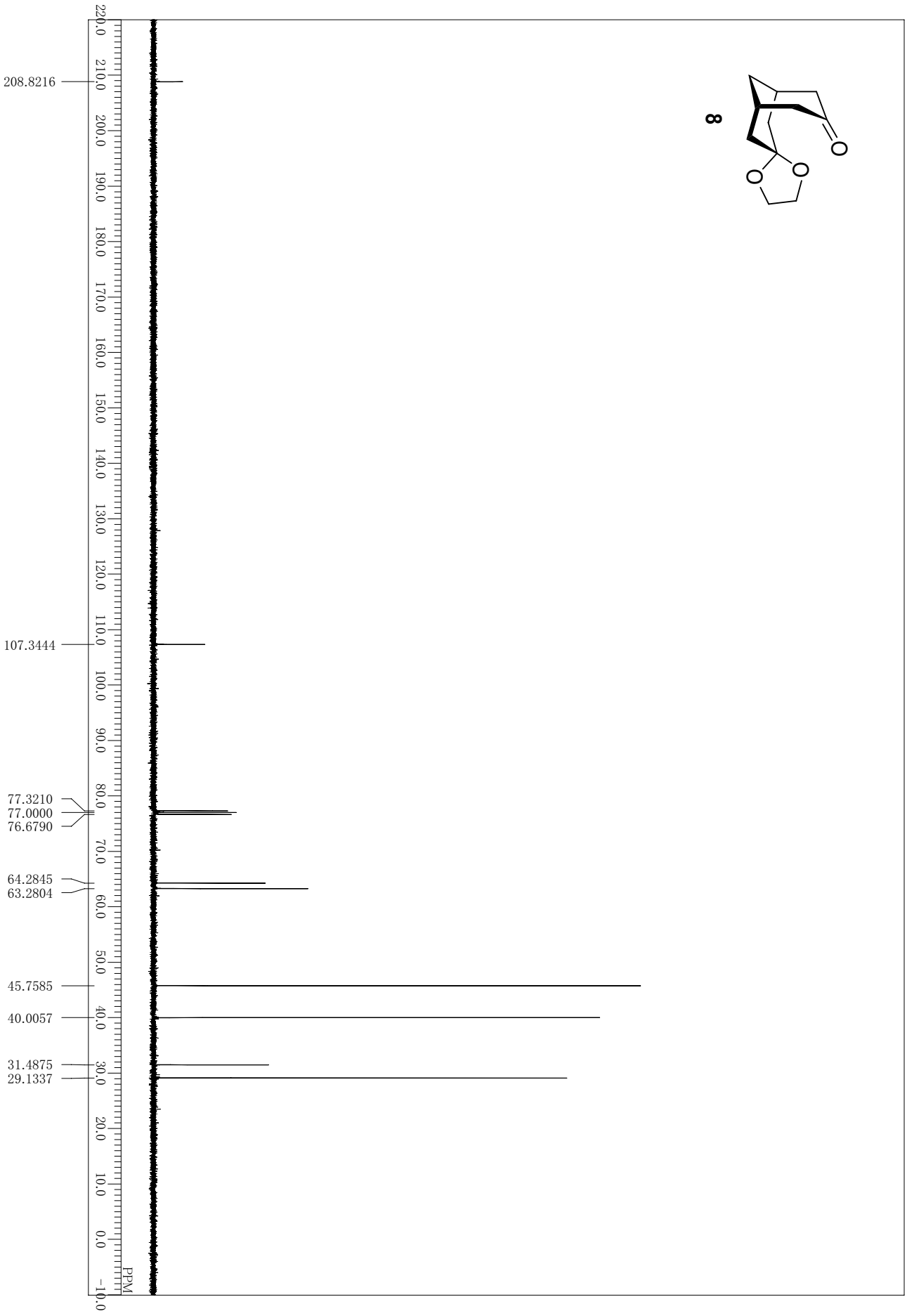
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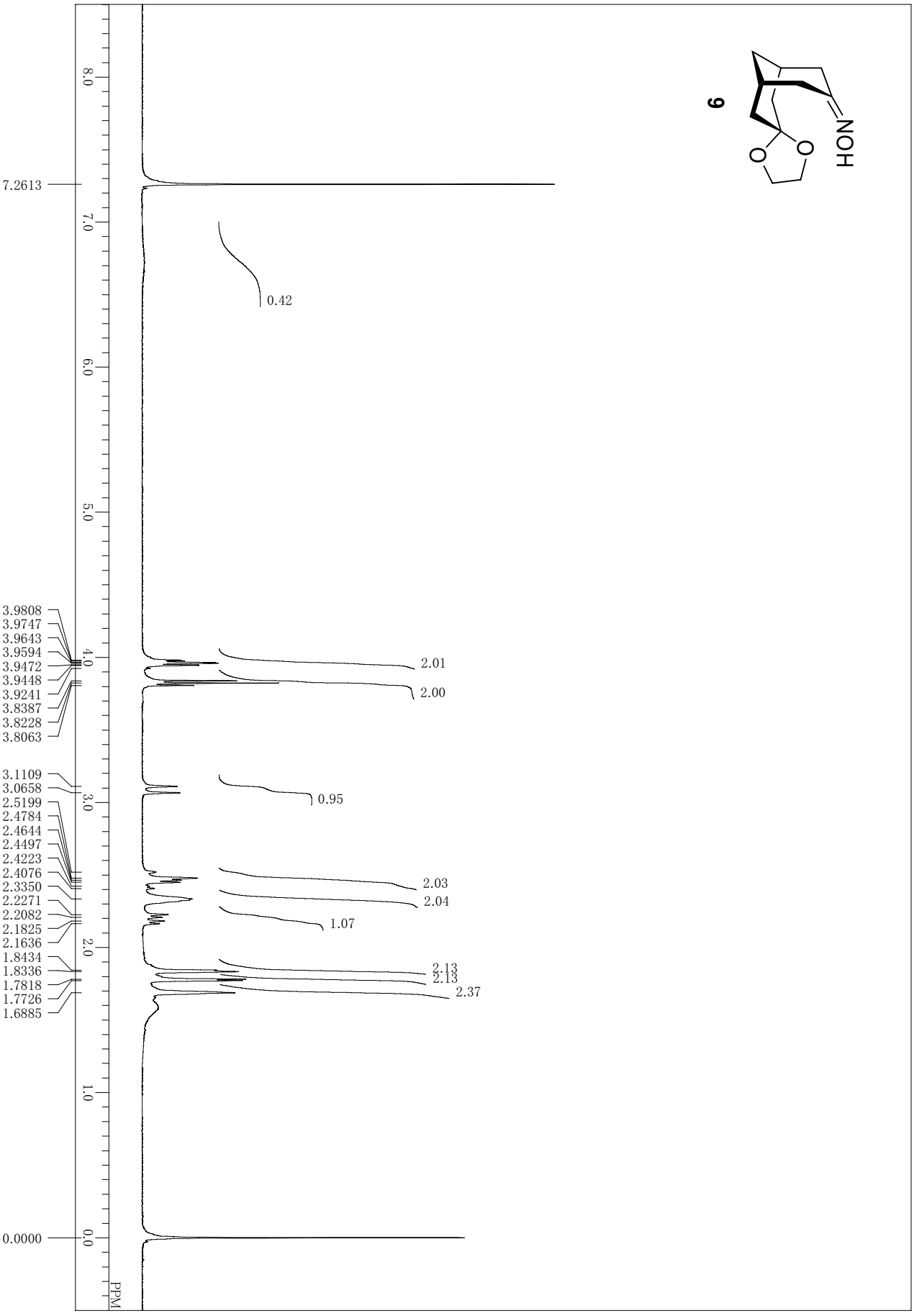
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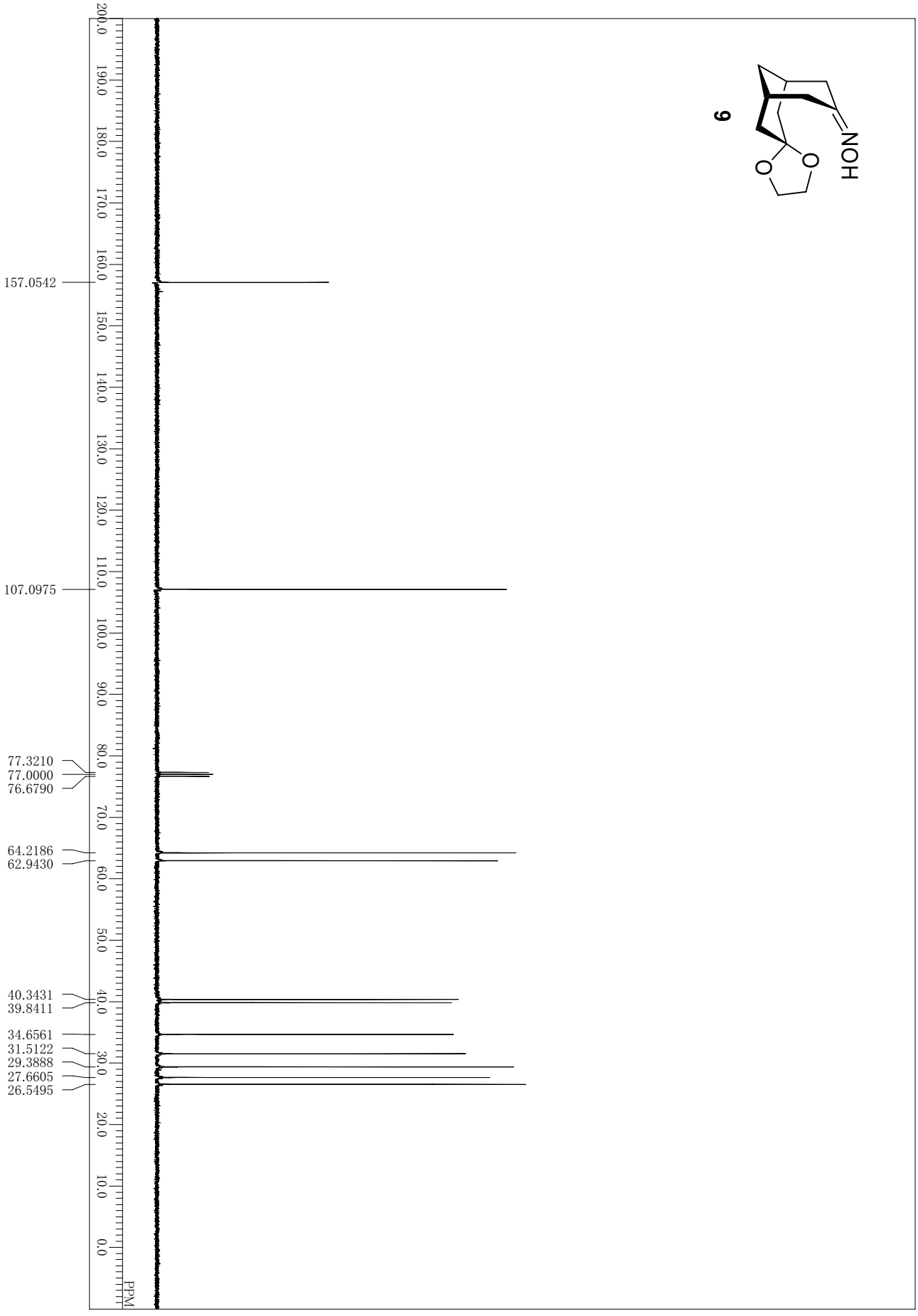
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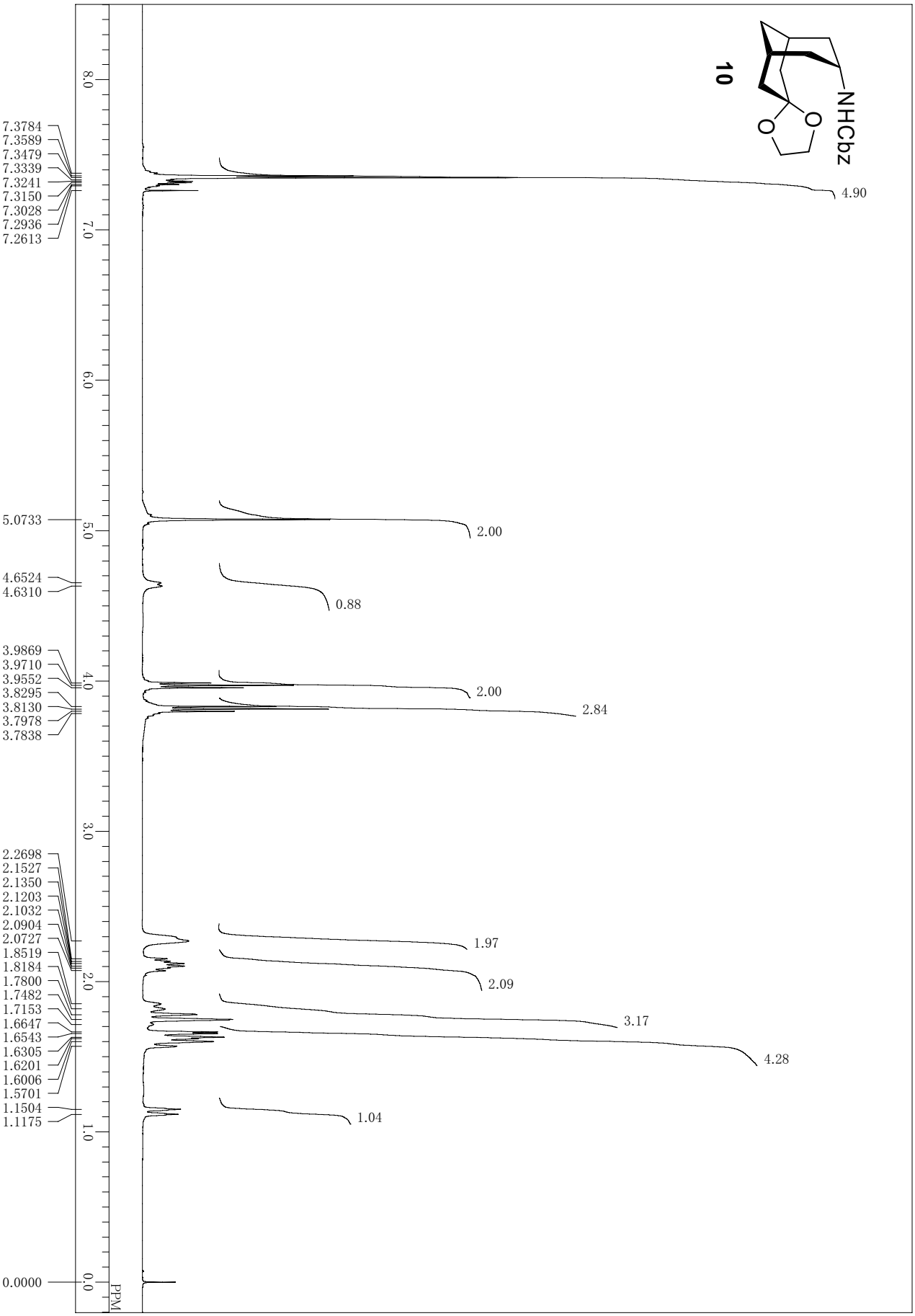
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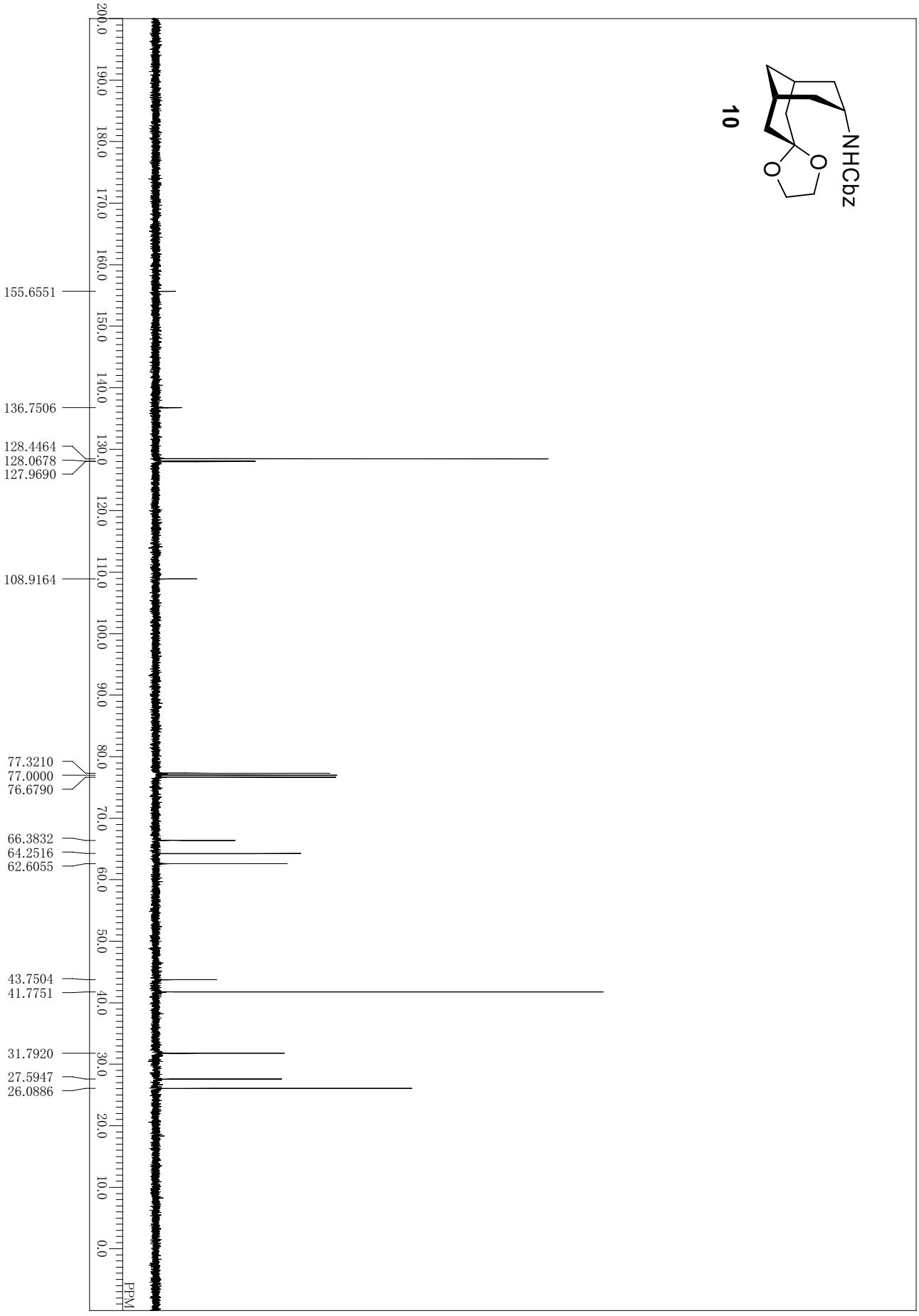
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127.9690
108.9164
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26.0886
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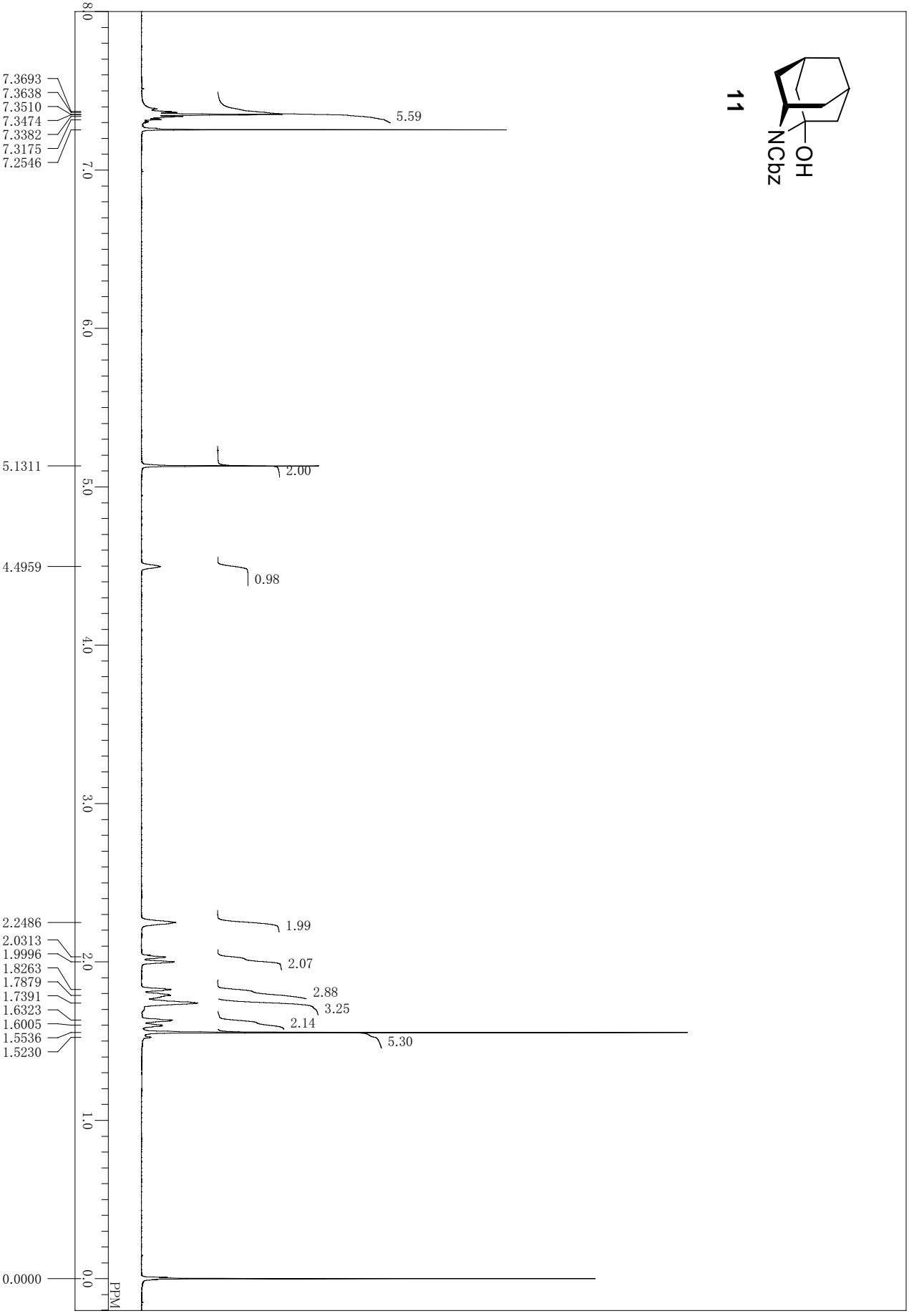
11
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7.3510
7.3474
7.3382
7.3175
7.2546
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4.4959
2.2486
2.0313
1.9996
1.8263
1.7879
1.7391
1.6323
1.6005
1.5536
1.5230
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5.59
2.00
0.98
1.99
2.07
2.88
3.25
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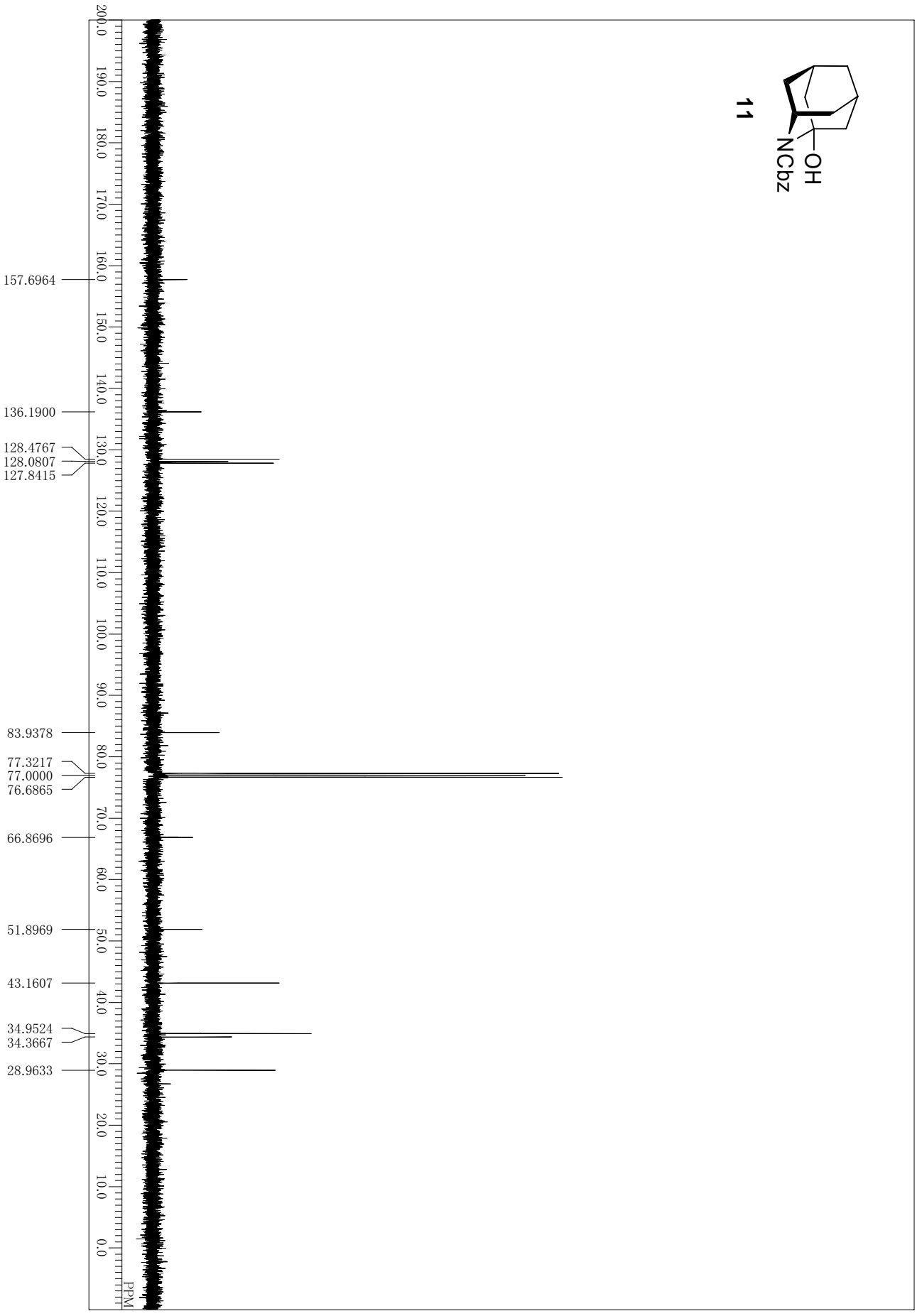
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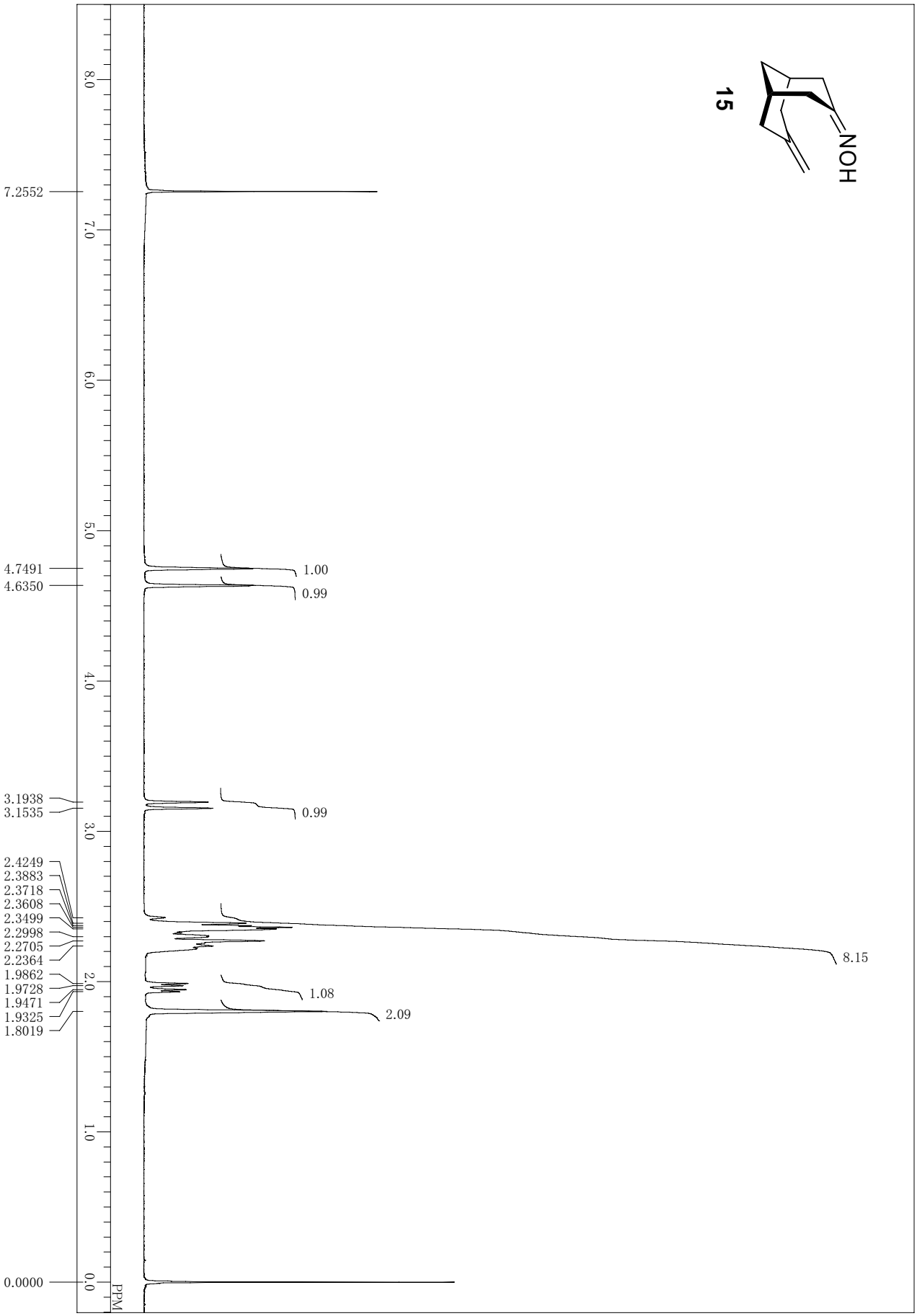
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3.1535
2.4249
2.3883
2.3718
2.3608
2.3499
2.2998
2.2705
2.2364
1.9862
1.9728
1.9471
1.9325
1.8019
0.0000
1.00
0.99
0.99
8.15
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2.09
8.0
7.0
6.0
5.0
4.0
3.0
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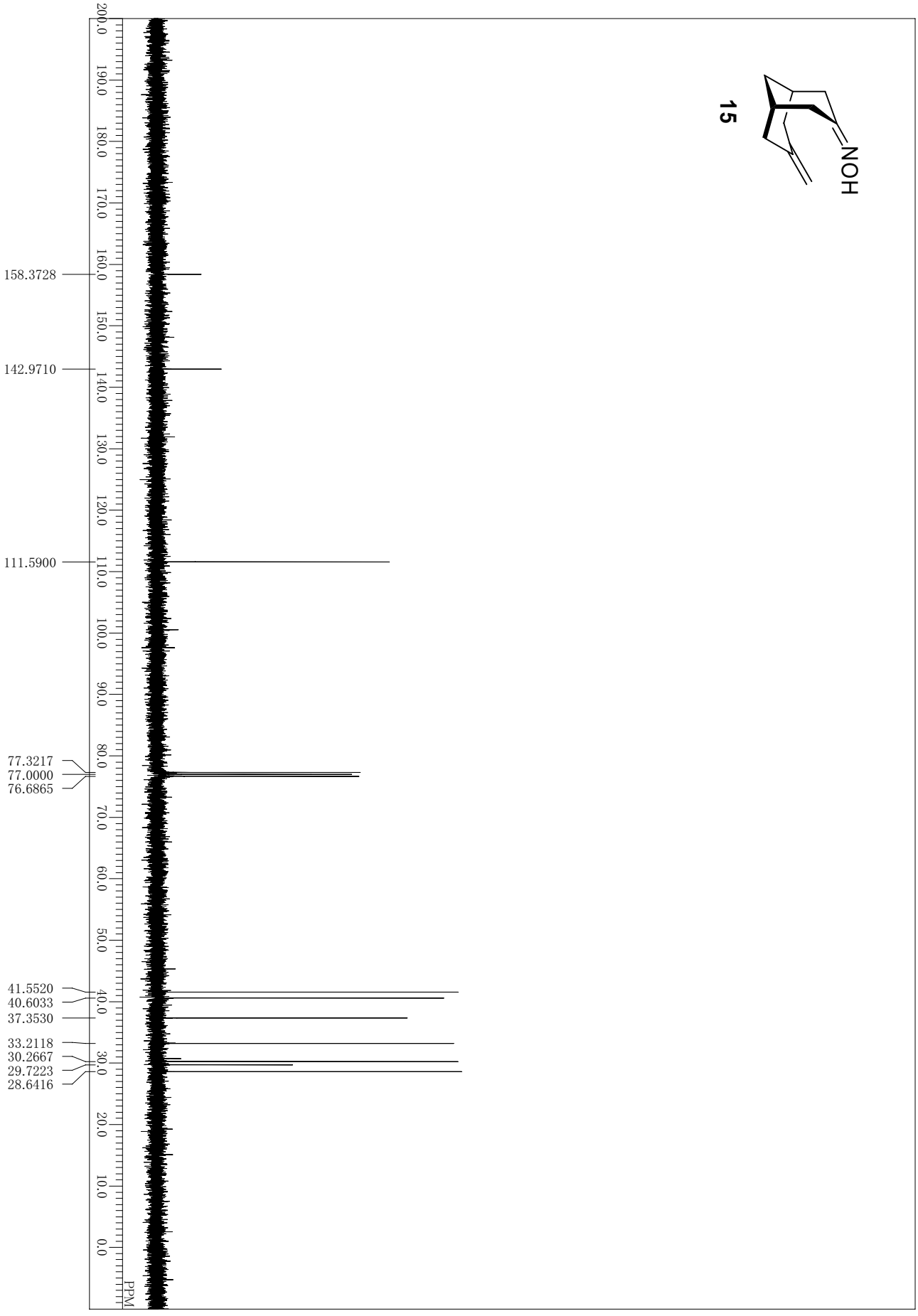
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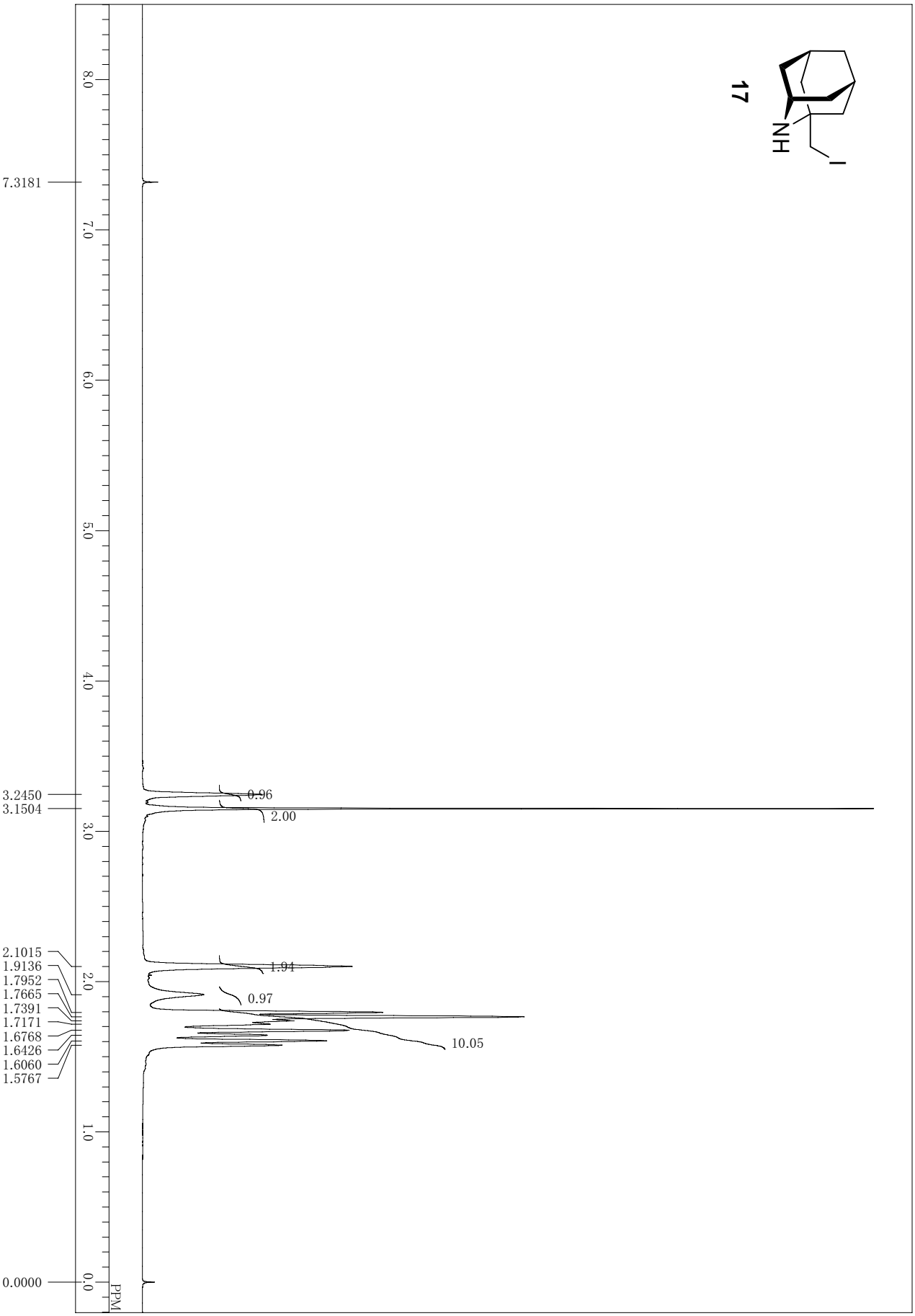
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1.6426
1.6060
1.5767
0.0000
0.96
2.00
1.94
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5.0
4.0
3.0
2.0
1.0
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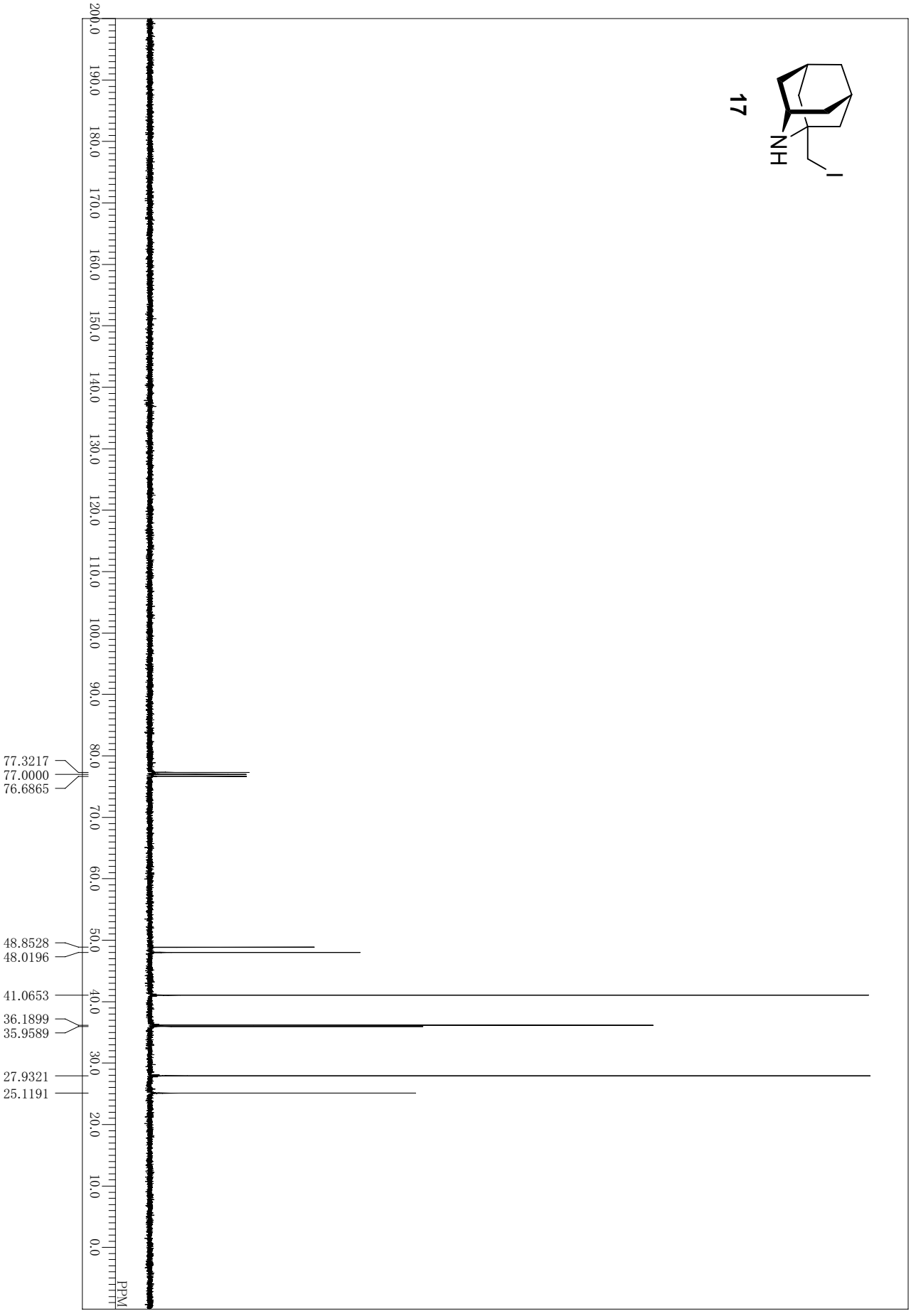
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I
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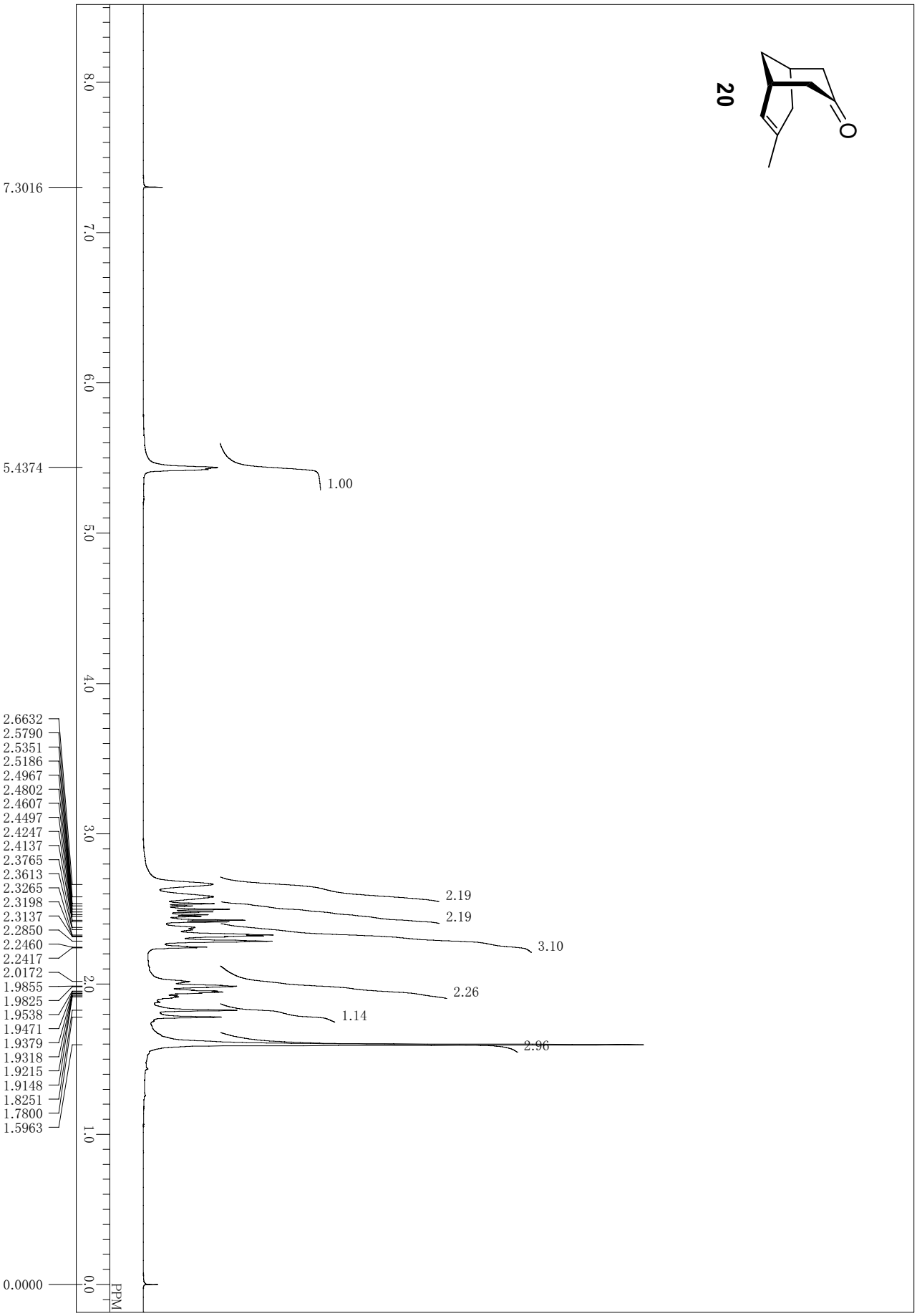
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2.4607
2.4497
2.4247
2.4137
2.3765
2.3613
2.3265
2.3198
2.3137
2.2850
2.2460
2.2417
2.0172
1.9855
1.9825
1.9538
1.9471
1.9379
1.9318
1.9215
1.9148
1.8251
1.7800
1.5963
1.00
2.19
2.19
3.10
2.26
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3.0
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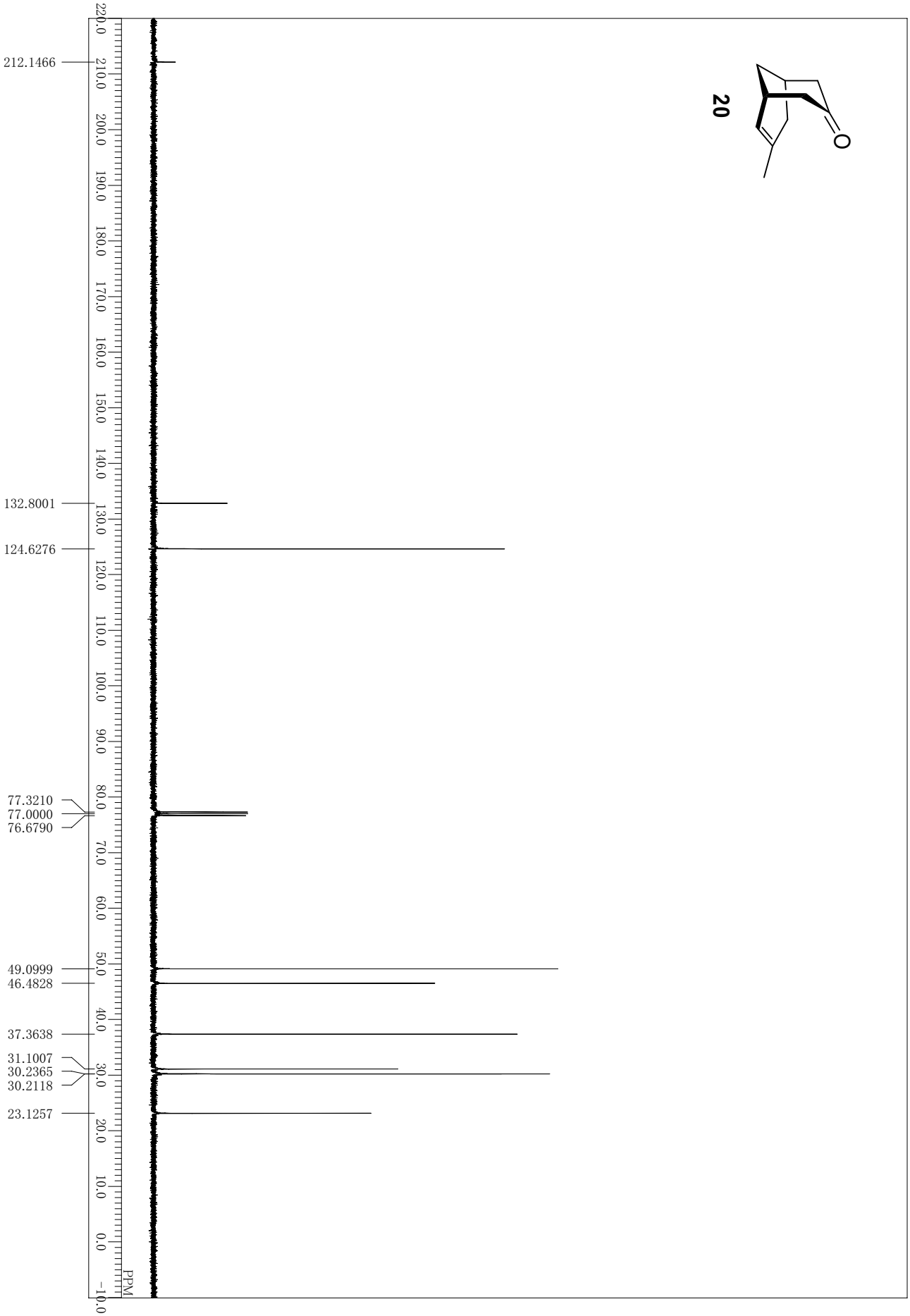
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46.4828
37.3638
31.1007
30.2365
30.2118
23.1257
PPM
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
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10.0
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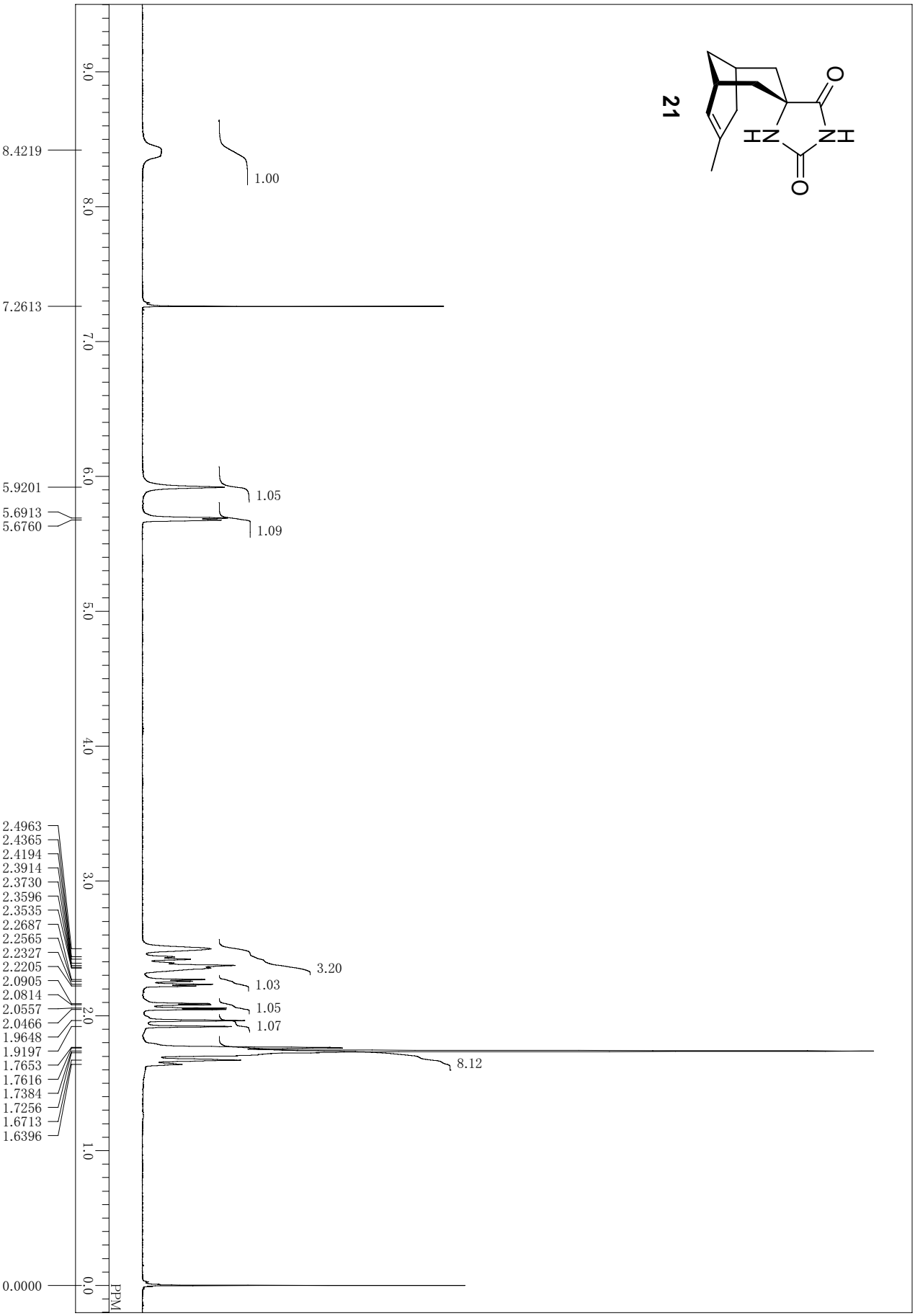
-10.0
20
O


21
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5.6913
5.6760
2.4963
2.4365
2.4194
2.3914
2.3730
2.3596
2.3535
2.2687
2.2565
2.2327
2.2205
2.0905
2.0814
2.0557
2.0466
1.9648
1.9197
1.7653
1.7616
1.7384
1.7256
1.6713
1.6396
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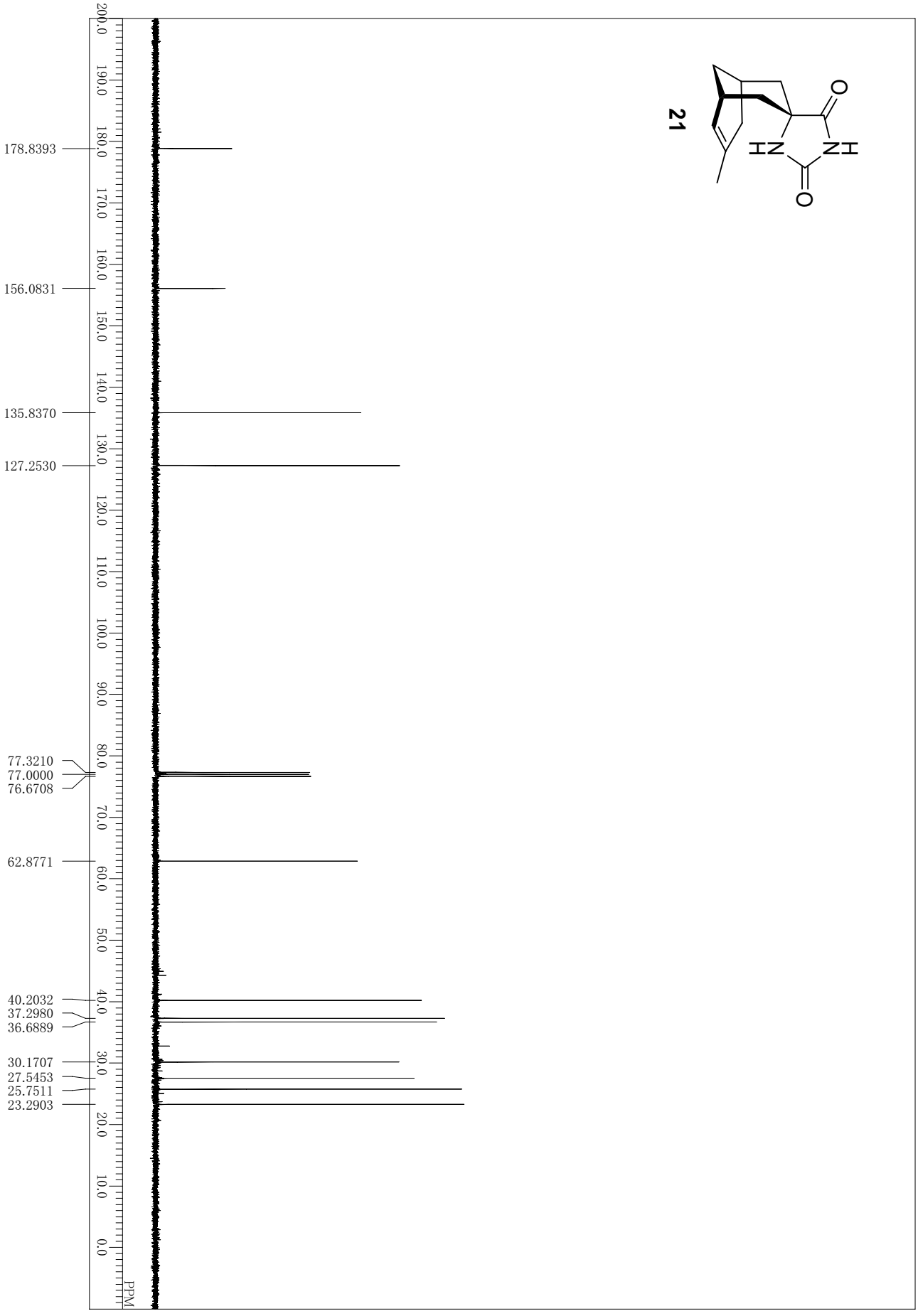
1.05
1.09
3.20
1.03
1.05
1.07
8.12
PPM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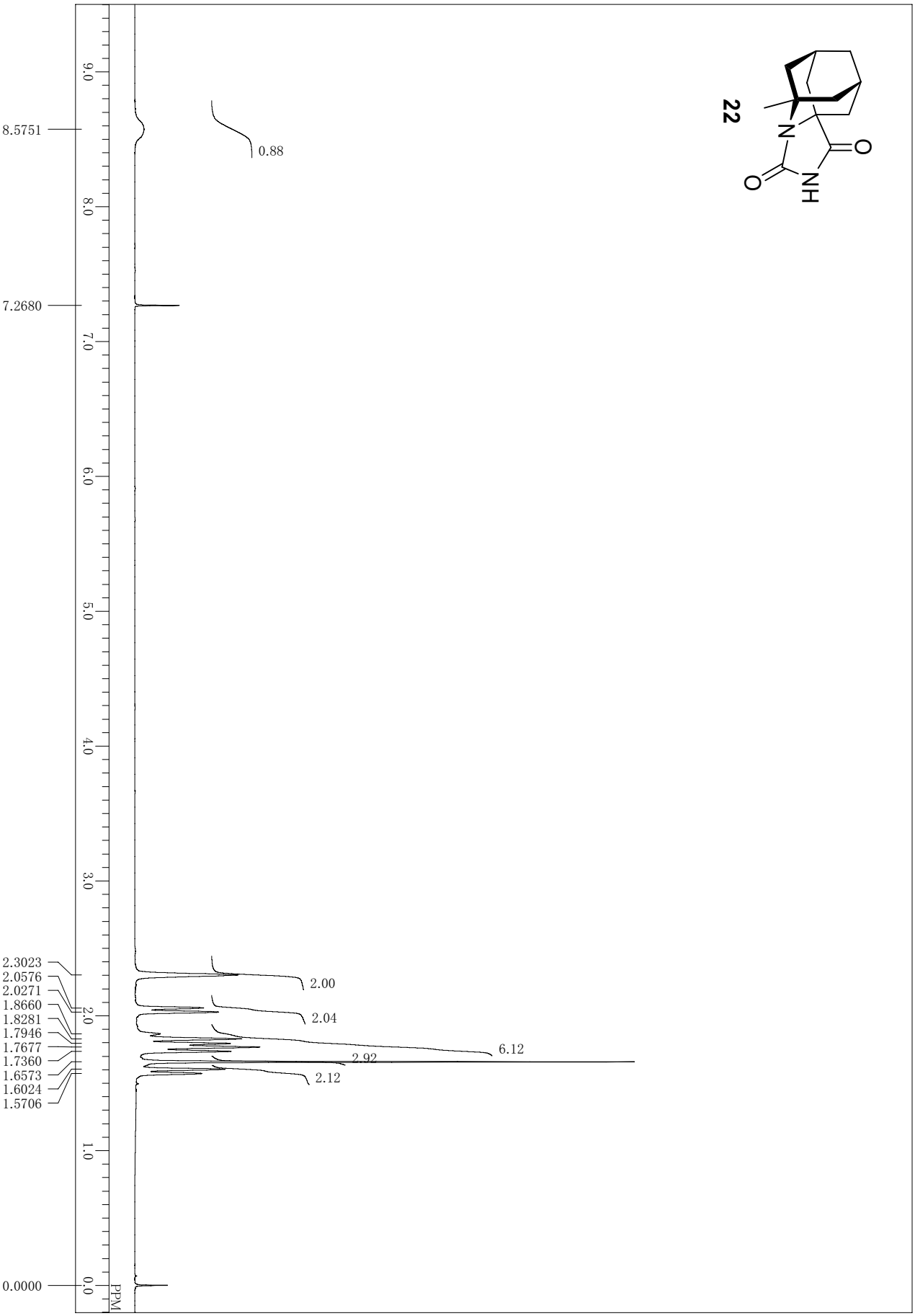
22
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O
O
NH
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2.00
2.04
6.12
2.92
2.12
2.3023
2.0576
2.0271
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1.8281
1.7946
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1.6024
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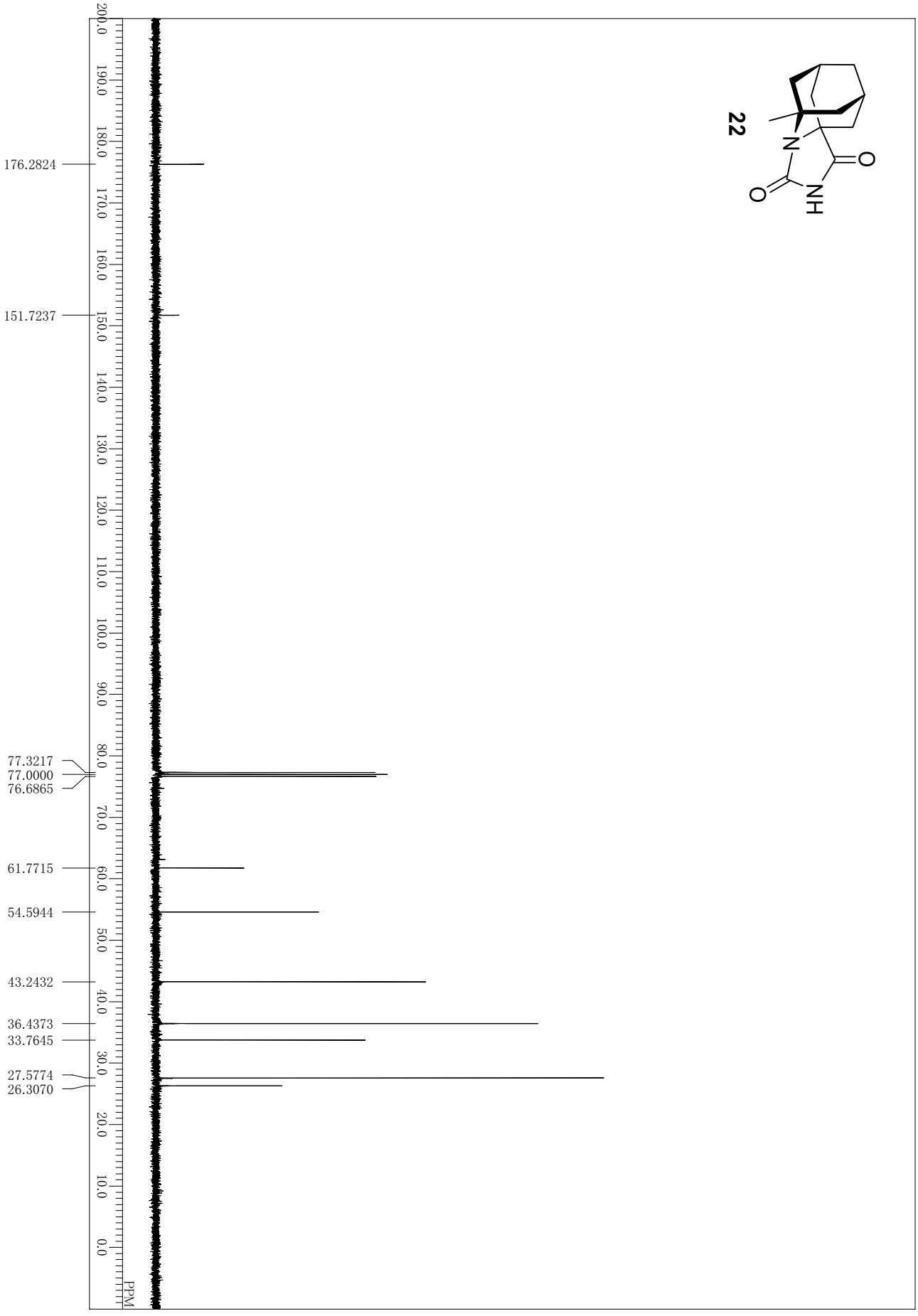
22
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O
O
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61.7715
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27.5774
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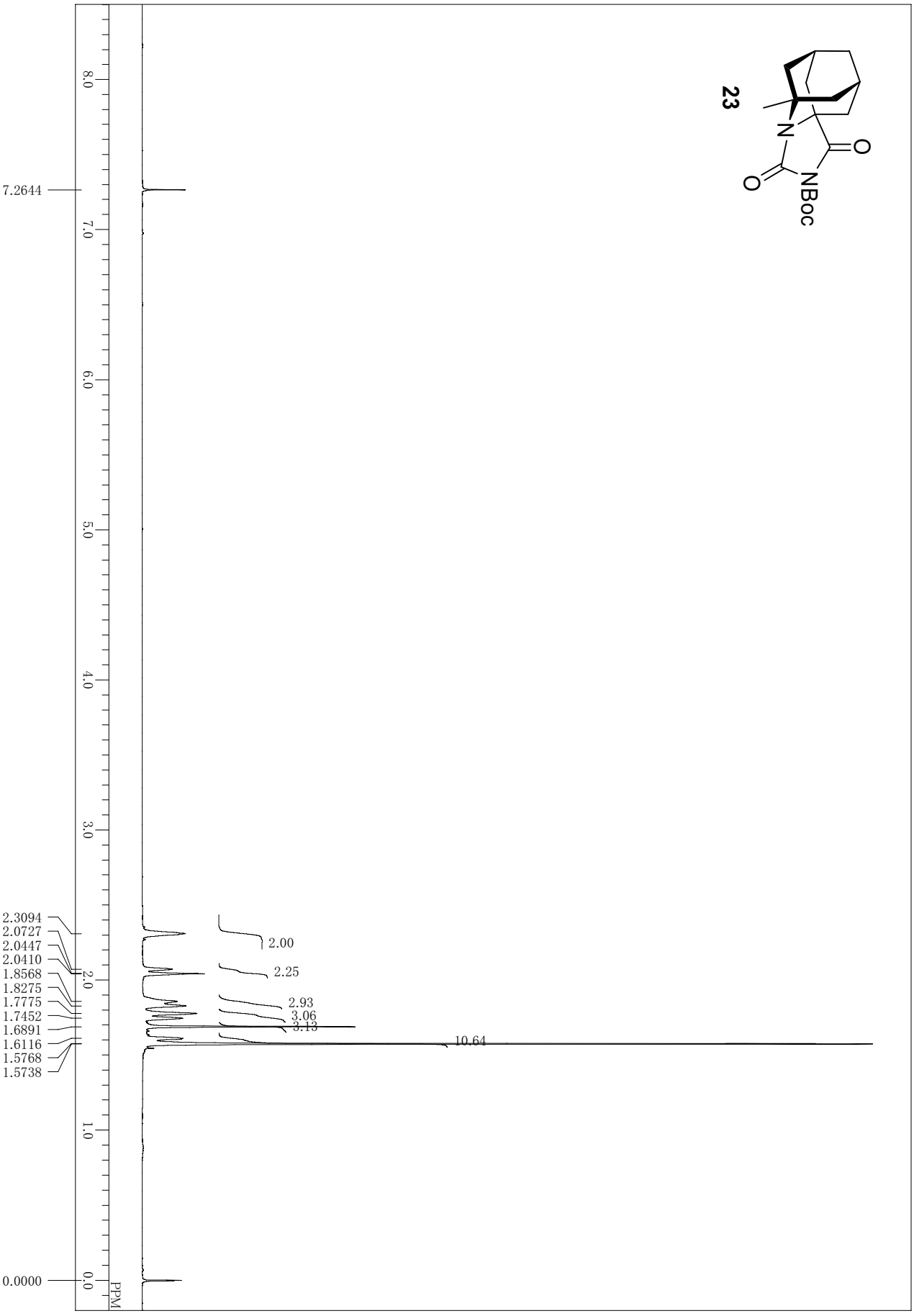
23
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2.0447
2.0410
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1.7775
1.7452
1.6891
1.6116
1.5768
1.5738
0.0000
2.00
2.25
2.93
3.06
3.13
10.64
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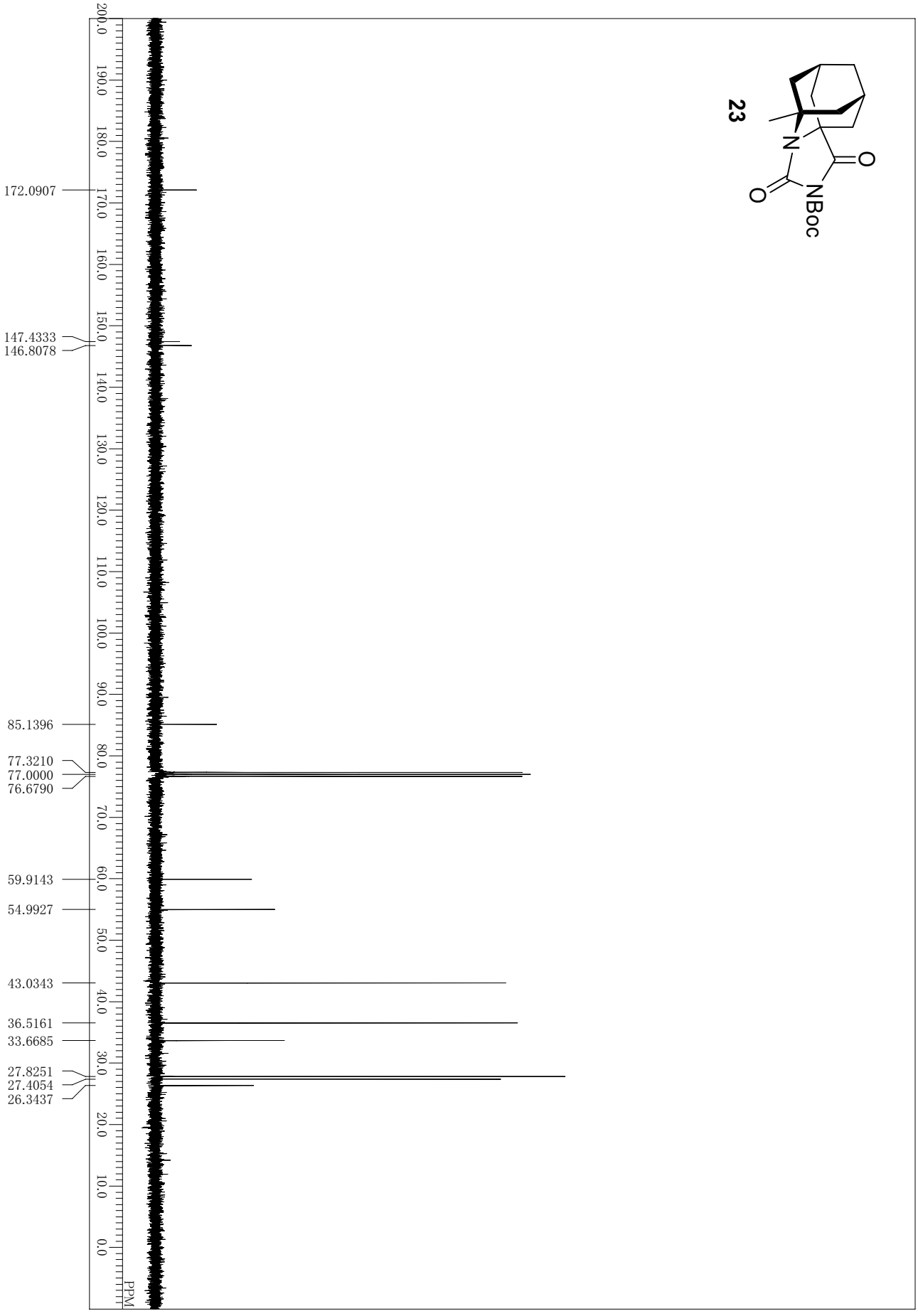
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
PPM


23
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NBoc
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76.6790
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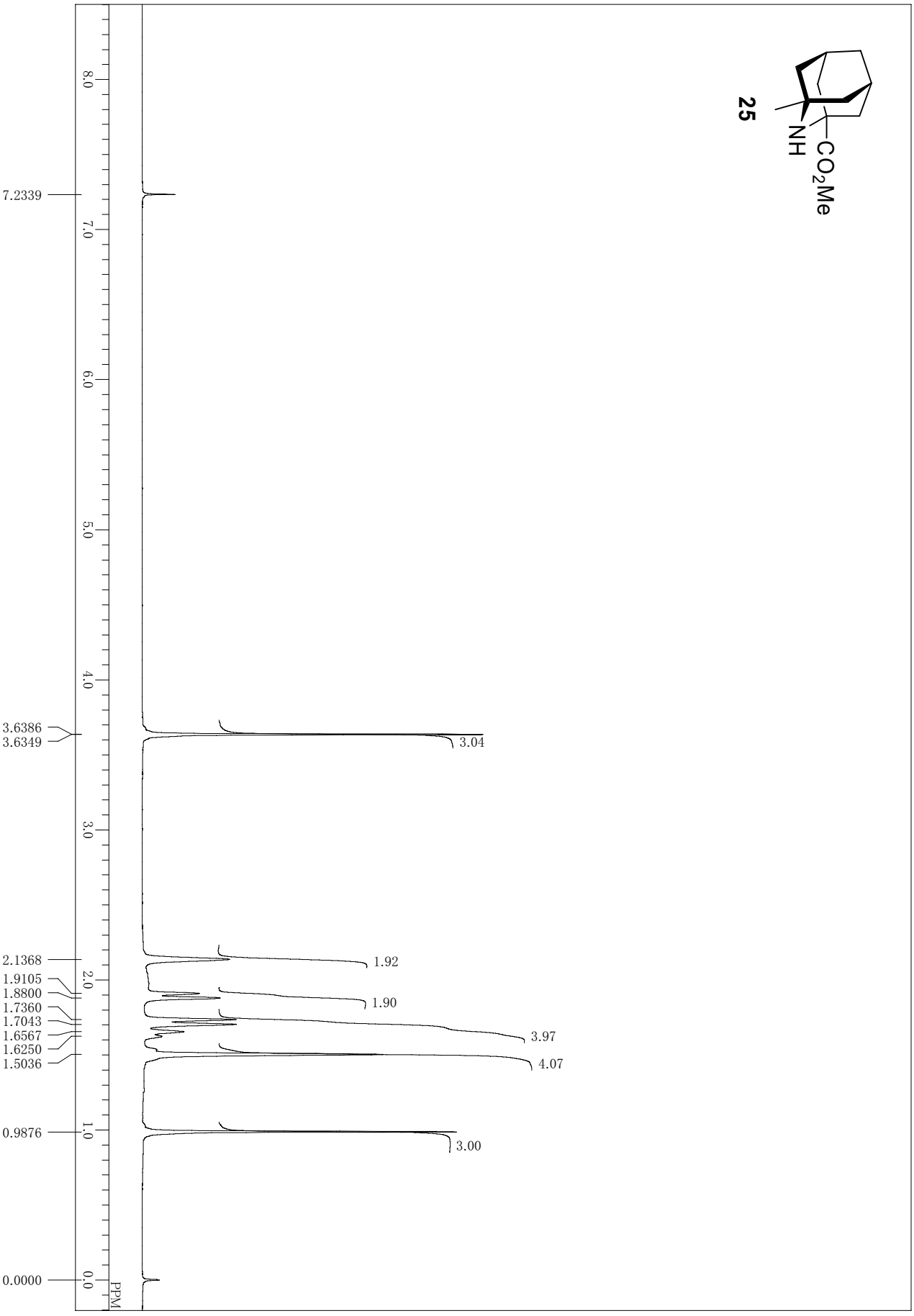
27.4054
26.3437
PPM


25
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1.7360
1.7043
1.6567
1.6250
1.5036
0.9876
0.0000
3.04
1.92
1.90
3.97
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3.00
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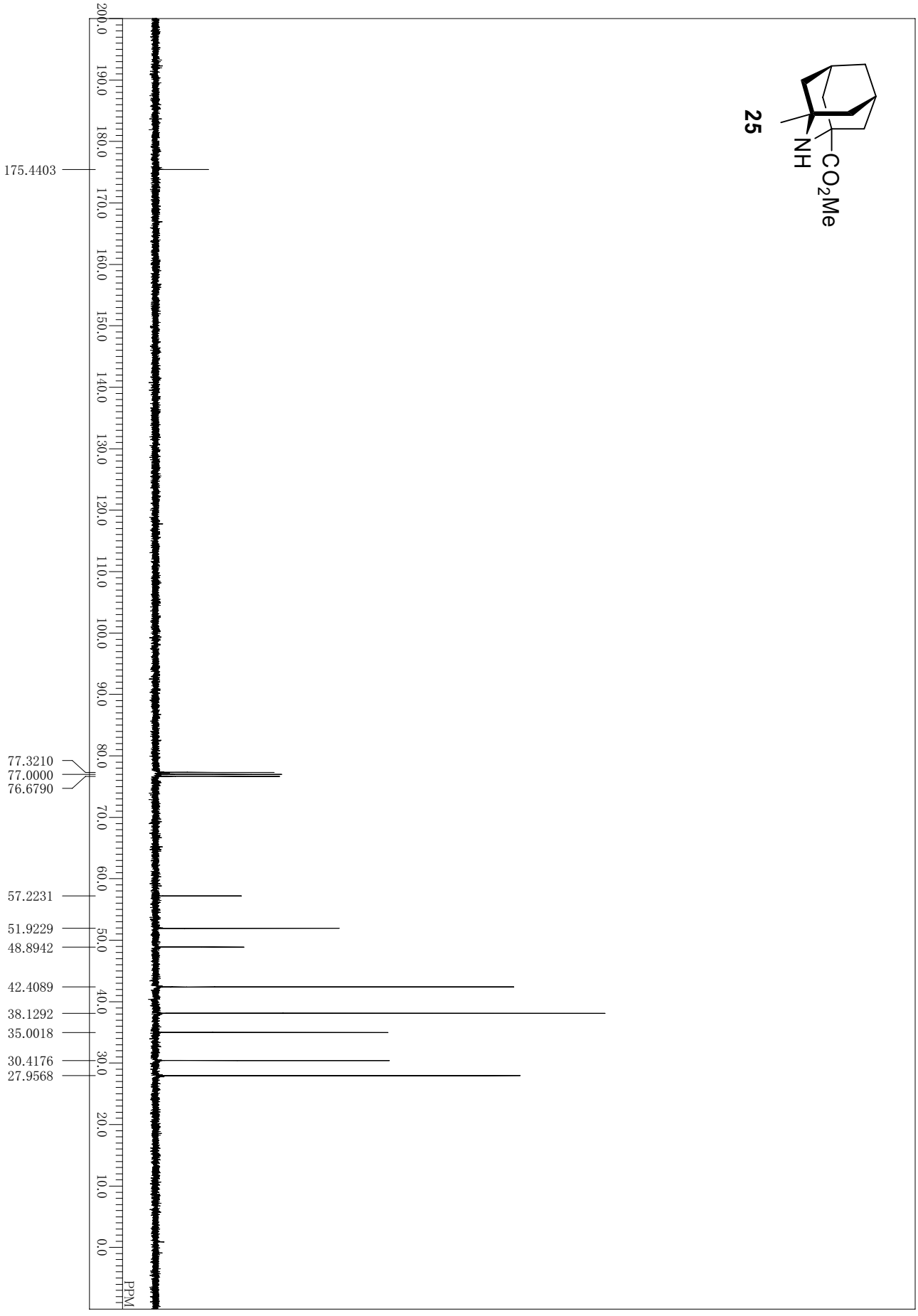
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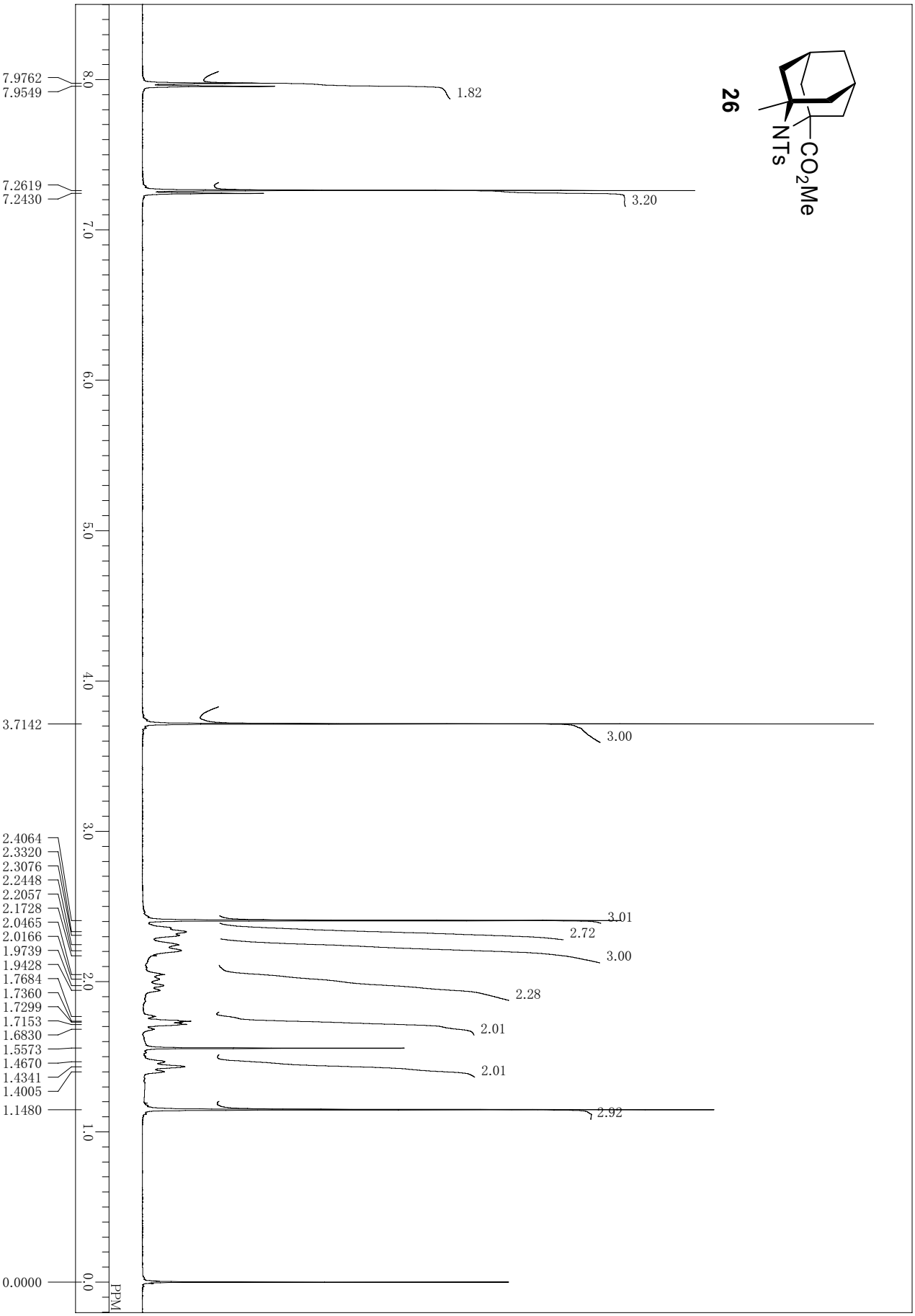
26
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2.2057
2.1728
2.0465
2.0166
1.9739
1.9428
1.7684
1.7360
1.7299
1.7153
1.6830
1.5573
1.4670
1.4341
1.4005
1.1480
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1.82
3.20
3.00
3.01
2.72
3.00
2.28
2.01
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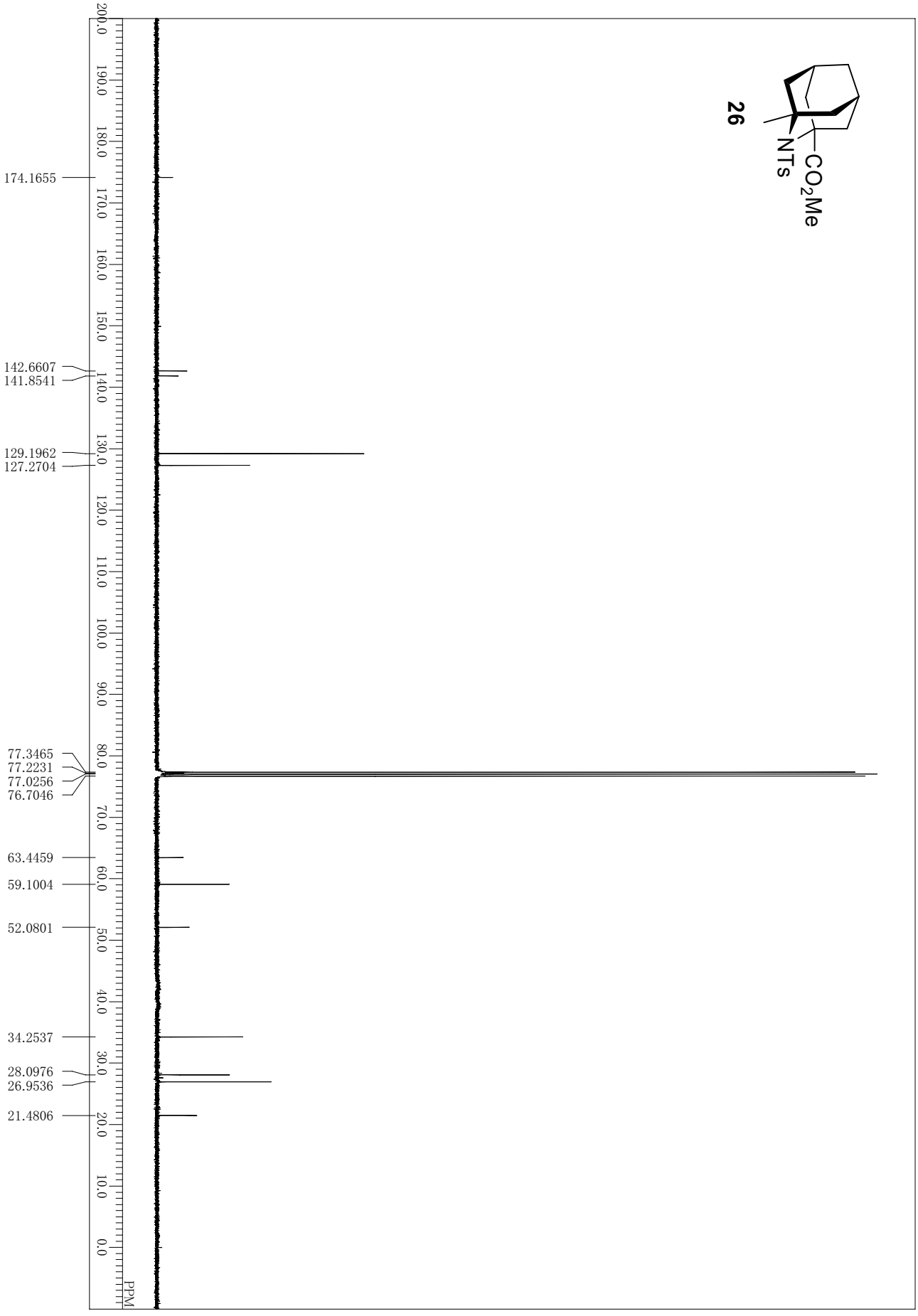
26
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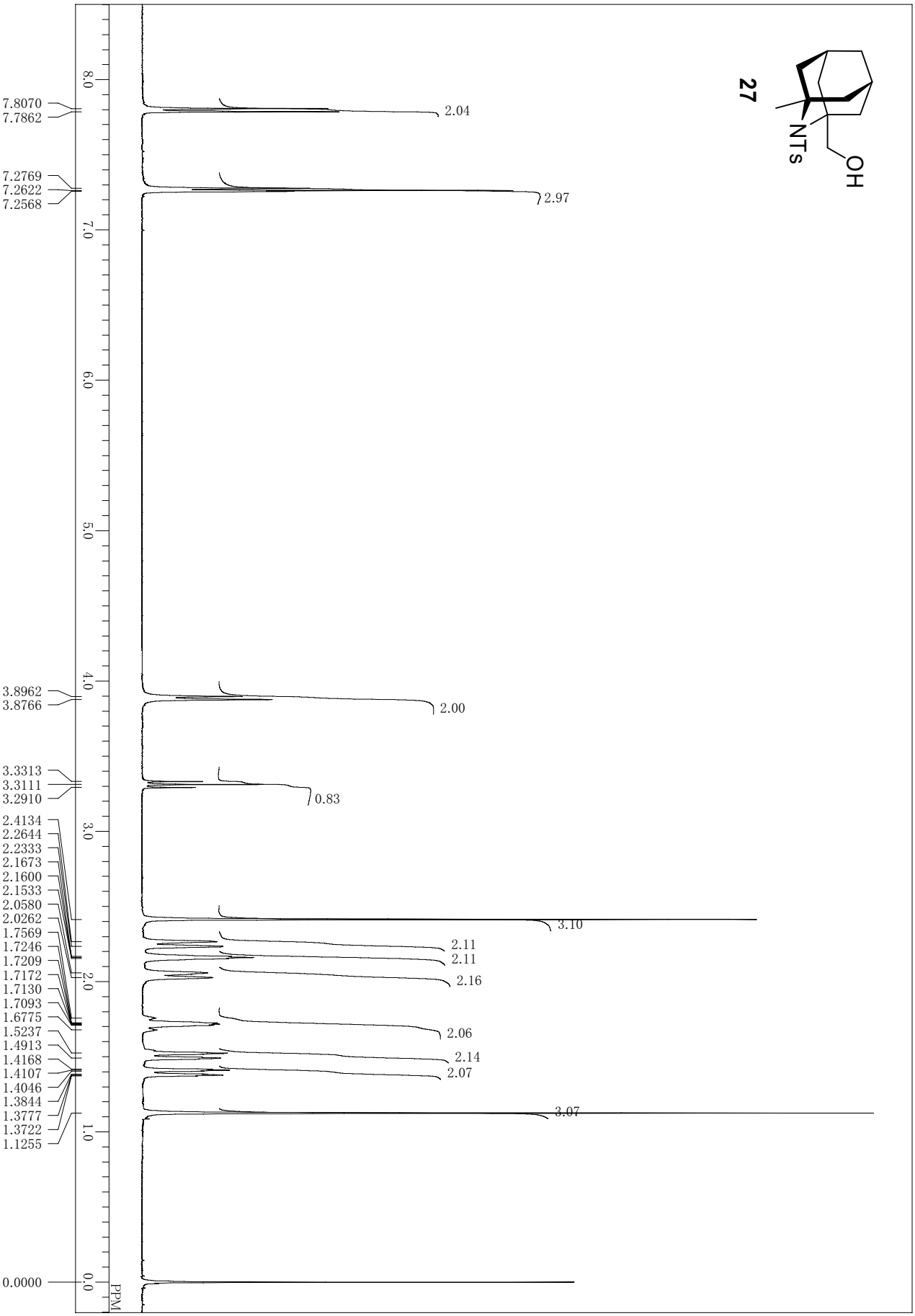
27
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3.2910
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2.2644
2.2333
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2.1533
2.0580
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1.7209
1.7172
1.7130
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1.4913
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1.4107
1.4046
1.3844
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1.3722
1.1255
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2.11
2.16
2.06
2.14
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3.07
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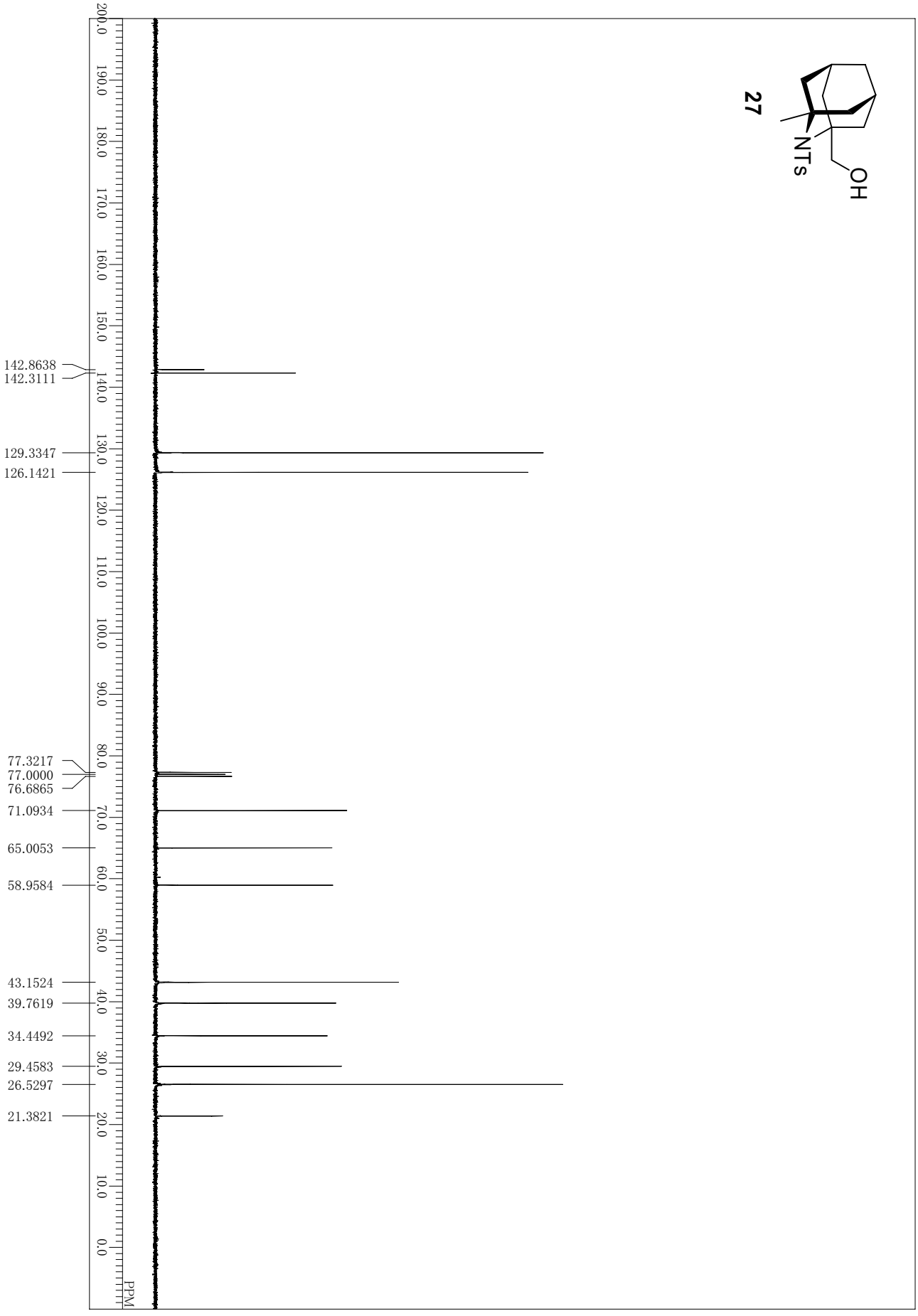
27
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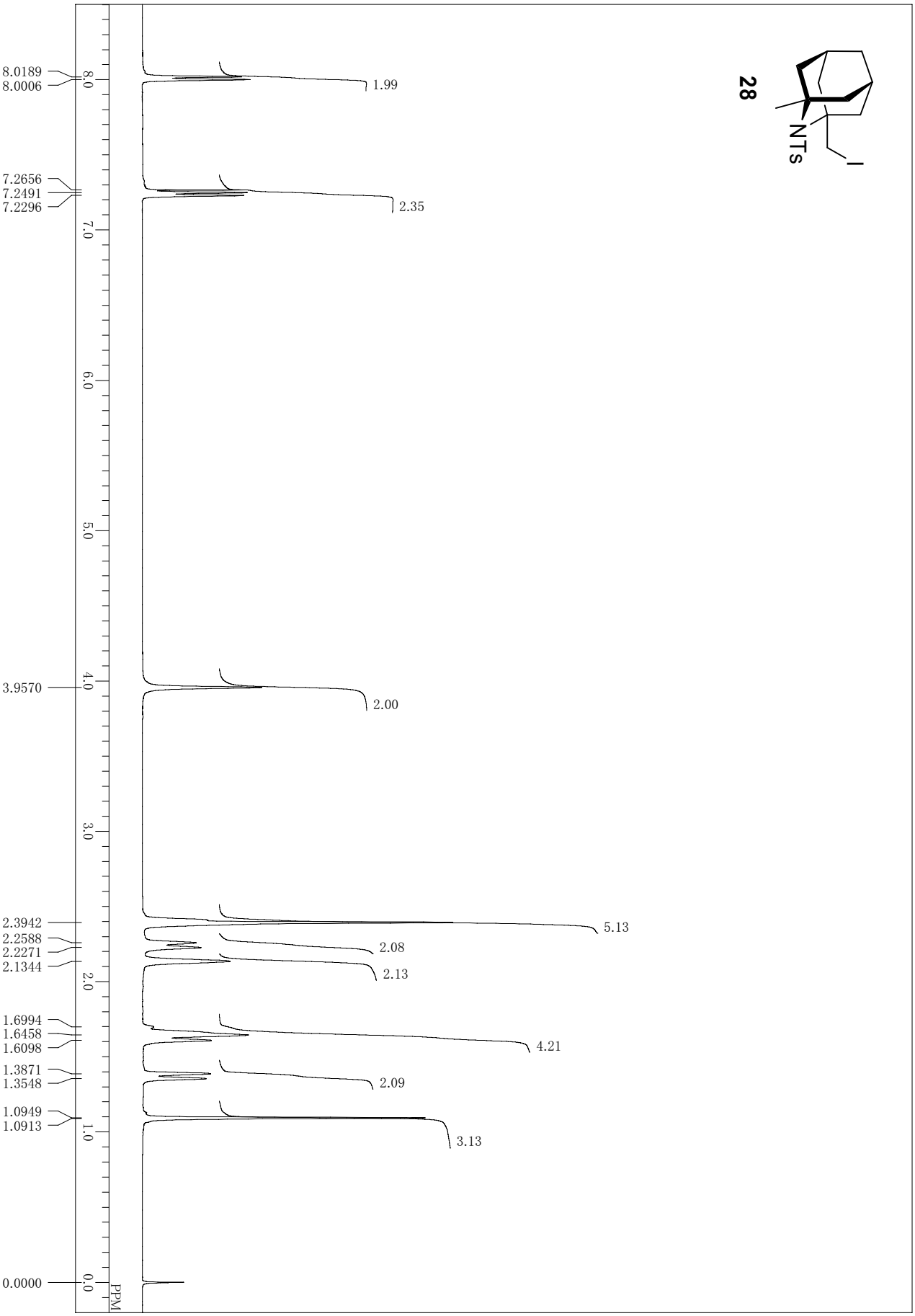
28
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1.6458
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1.3871
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1.0913
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2.00
5.13
2.08
2.13
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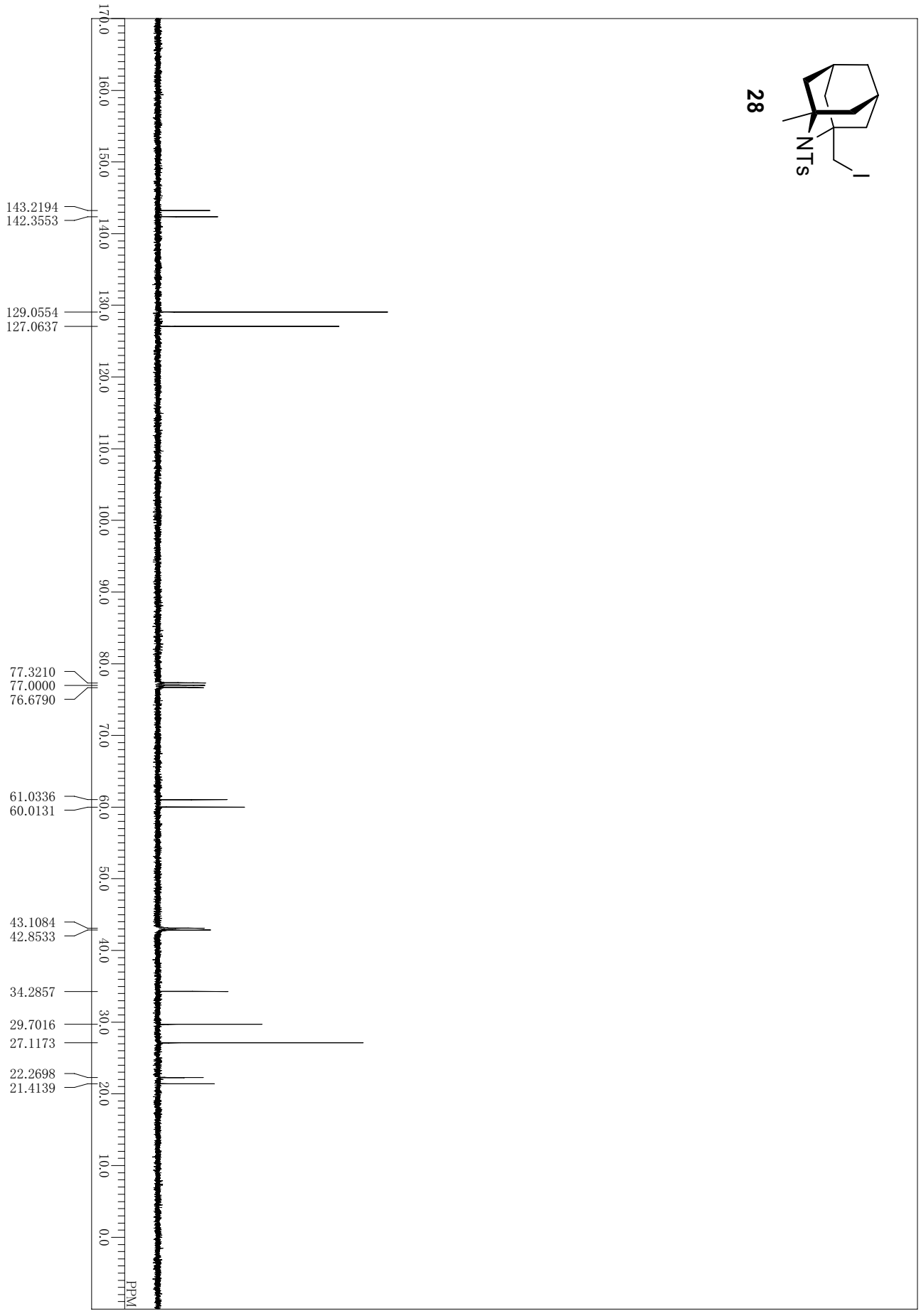
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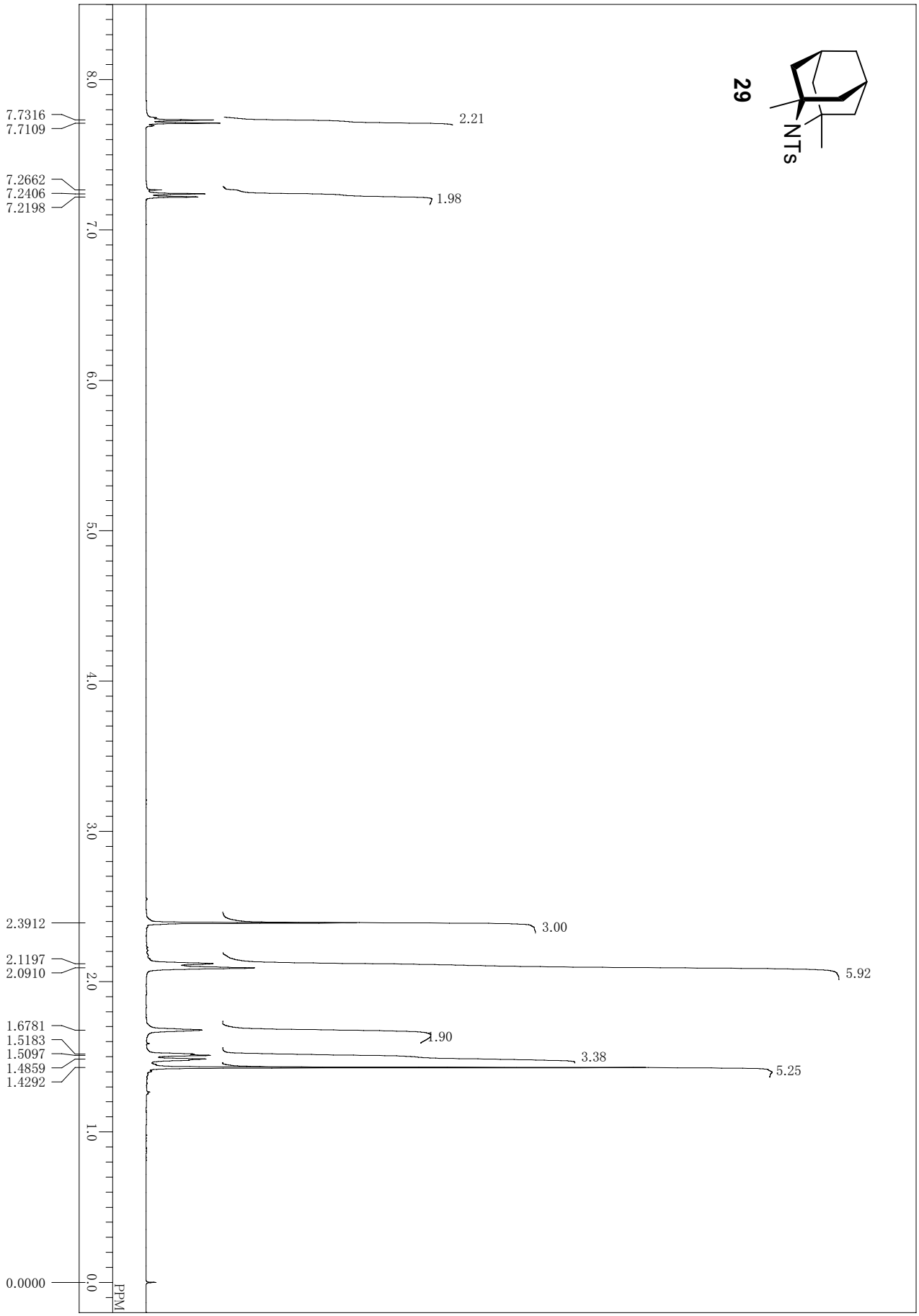
29
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7.2662
7.2406
7.2198
2.3912
2.1197
2.0910
1.6781
1.5183
1.5097
1.4859
1.4292
0.0000
2.21
1.98
3.00
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1.90
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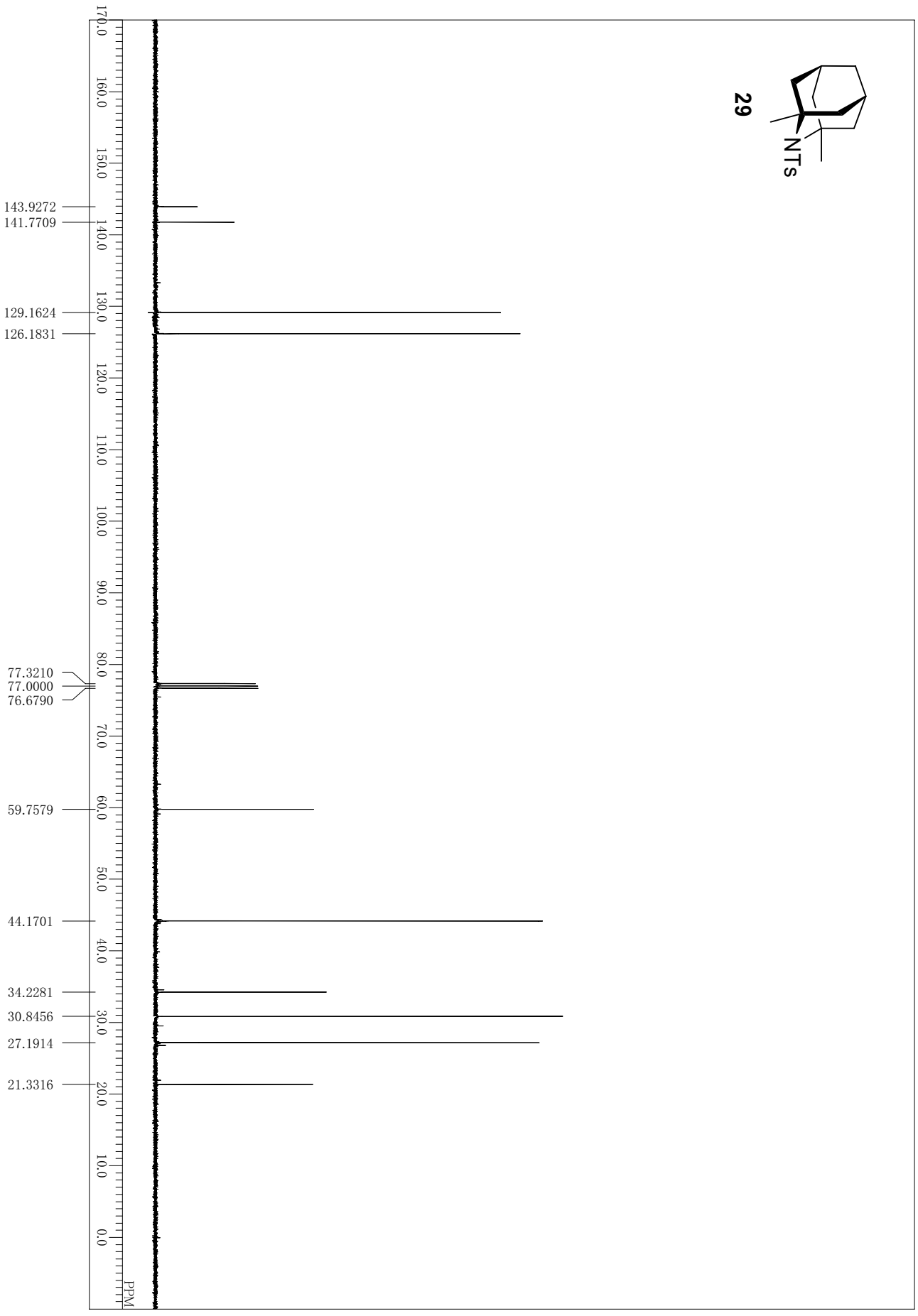
29
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30.8456
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130.0
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