Supporting Information

For

Copper-catalyzed oxidation of arene-fused cyclic amines to cyclic imides

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Content

General Considerations

All manipulations were conducted in sealed tube under an atmosphere of air. Unless otherwise noted, all starting materials were commercially available and were used without further purification. Isoindolines **1a-1k** were prepared by reaction of 1,2-bis(bromomethyl)benzene with amine in the present of base.[1-3] Compound **1l** was prepared by reaction of 1,8-bis(bromomethyl)naphthalene with methanamine. N,N-bispropargylamine was prepared by A^3 coupling.[4] ^1H NMR and ^{13}C NMR spectra were recorded on 300 MHz and 400 MHz NMR spectrometer with TMS as internal standard. Mass spectra were obtained using a Bruker Esquire ion trap mass spectrometer in positive ion mode. Flash column chromatography was performed on silica gel and Al_2O_3 (200-300 mesh).

Experimental Procedures

General procedure for copper-catalyzed oxidation of isoindoline

To a 25 mL tube with teflon-coated magnetic stir bar and a rubber septum, was added isoindoline **1** (0.4 mmol), CuCl (0.04 mmol), CH_2Cl_2 1 mL, TBHP (0.55 mL, 4 mmol, 70% in water). The tube was sealed and stirred for 24 h at 50 ^oC. The reaction mixture was quenched by water and extracted by ethyl acetate. The organic extract was dried over $MgSO_4$. Removing the solvent and subsequent purification by column chromatography on Al_2O_3 afforded **2**.

Procedure for copper-catalyzed oxidation of isoindoline on 5 mmol scale

To a 100 mL tube with teflon-coated magnetic stir bar and a rubber septum, was added isoindoline **1** (5 mmol), CuCl (0.5 mmol), CH_2Cl_2 13 mL, TBHP (6.9 mL, 50 mmol, 70% in water). The tube was sealed and stirred for 24 h at 50 ^oC. The reaction mixture was quenched by water and extracted by ethyl acetate. The organic extract was dried over $MgSO_4$. Removing the solvent and subsequent purification by column chromatography on Al_2O_3 afforded **2a** (589 mg).

Procedure for copper-catalyzed oxidation of isoindoline on 10 mmol scale

To a 100 mL tube with teflon-coated magnetic stir bar and a rubber septum, was added isoindoline **1e** or **1g** (10 mmol), CuCl (1 mmol), CH_2Cl_2 25 mL, TBHP (13.7 mL, 100 mmol, 70% in water). The tube was sealed and stirred for 24 h at 50 ^oC. The reaction mixture was quenched by water and extracted by ethyl acetate. The organic extract was dried over $MgSO_4$. Removing the solvent and subsequent purification by column chromatography on Al_2O_3 afforded **2e** (995 mg) or **2g** (825 mg).

2-Butylisoindoline-1,3-dione, 2a[5]

68% isolated yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.84-7.80 (m, 2H), 7.71-7.67 (m, 2H), 3.67 (t, *J* =, 2H), 1.68-1.60 (m, 2H), 1.40-1.31 (m, 2H), 0.93 (t, *J*= , 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 133.9, 132.3, 123.2, 37.9, 30.7, 20.2, 13.7. GC-MS: 203.

2-Octylisoindoline-1,3-dione, 2b[6]

73% isolated yield. ^1H NMR (300 MHz, $CDCl_3$) δ 7.84-7.80 (m, 2H), 7.72-7.68

(m, 2H), 3.66 (t, J = 7.2 Hz, 2H), 1.70-1.62 (m, 2H), 1.43-1.24 (m, 10H), 0.85 (t, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 133.9, 132.3, 123.2, 38.2, 31.9, 29.2, 28.7, 27.0, 22.7, 14.2. GC-MS: 259.

2-(*Tert*-butyl)-isoindoline-1,3-dione, 2c[7]

71% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77-7.74 (m, 2H), 7.69-7.65 (m, 2H), 1.69 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 133.7, 132.2, 122,7, 57.9, 29.2. GC-MS: 203.

2-Allylisoindoline-1,3-dione, 2d[8]

45% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.86-7.83 (m, 2H), 7.73-7.69 (m, 2H), 5.93-5.83 (m, 1H), 5.27-5.17 (m, 2H), 4.30-4.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 134.0, 132.2, 131.6, 123.4, 117.8, 40.1. GC-MS: 187.

2-Benzylisoindoline-1,3-dione, 2e[5]

48% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$)δ 7.85-7.80 (m, 2H), 7.71-7.67 (m, 2H), 7.45-7.25 (m, 5H), 4.84 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 136.5, 134.0, 132.2, 128.8, 128.7, 127.9, 123.4, 41.7. GC-MS: 237.

Methyl 2-(1,3-dioxoisoindolin-2-yl)acetate, 2f[7]

40% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90-7.85 (m, 2H), 7.77-7.73(m, 2H), 4.45 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 167.5, 134.3, 132.1, 123.7, 52.8, 38.9. GC-MS: 219.

2-Phenylisoindoline-1,3-dione, 2g[5]

42% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.94 (m, 2H), 7.81-7.77 (m, 2H), 7.53-7.39 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 134.5, 131.9, 131.8, 129.2, 128.2, 126.7, 123,8. GC-MS: 223.

2-(4-Chlorophenyl)isoindoline-1,3-dione, 2h[5]

47% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98-7.93 (m, 2H), 7.83-7.78 (m, 2H), 7.52-7.46 (m, 2H), 7.44-7.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 134.7, 133.9, 131.7, 130.3, 129.4, 127.8, 124.0. GC-MS: 257.

2-(4-Isopropylphenyl)isoindoline-1,3-dione, 2i

30% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.94(m, 2H),7.80-7.77 (m, 2H), 7.38-7.33 (m, 4H), 3.00-2.94 (m, 1H), 1.29 (d, J = 6.9 Hz, 6H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 167.5, 149.0, 134.4, 131.9, 129.3, 127.3, 126.5, 123.9, 34.0, 24.0. GC-MS: 265.

2-(Naphthalen-2-yl)isoindoline-1,3-dione 2j[9]

57% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.94(m, 4H),7.90-7.88 (m, 2H), 7.82-7.79 (m, 5H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 134.5, 133.4, 132.7, 129.2, 129.1, 128.3, 127.8, 126.8, 126.7, 125.6, 124.3, 123.9. GC-MS: 273.

2-Butyl-5-chloroisoindoline-1,3-dione, 2k

48% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.75 (m, 2H), 7.65 (q, J = 7.8 Hz, 1.8 Hz, 1H), 3.67 (t, J = 7.3 Hz, 2H), 1.68-1.60 (m, 2H), 1.40-1.30 (m, 2H), 0.93 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 167.2, 140.6, 133.9, 130.3, 124.4, 123.7, 38.1, 30.6, 20.1, 13.6. GC-MS: 237.

2-Methyl-1H-benzo[de]isoquinoline-1,3(2H)-dione, 2l[10]

75% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, J = 7.2 Hz, 2H), 8.13 (d, J = 8.3 Hz, 2H), 7.68 (dd, J = 8.3, 7.2 Hz, 2H), 3.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.4, 133.9, 131.5, 131.2, 128.0, 126.9, 122.5, 27.0. GC-MS: 211.

General procedure for preparation of TPD

To a solution of Cp_2ZrCl_2 (702 mg, 2 mmol) in 10 mL of THF, BuLi (1.6 M in hexane, 4.8 mmol), was added at -78 ^{o}C and the mixture was stirred for 1 h at the same temperature. To this solution, N,N-bis(3-phenylprop-2-yn-1-yl)butan-1-amine (2.0 mmol) was added and stirred for 3 h at room temperature. Then, S_2Cl_2 (3 mmol) was added and stirred overnight. The reaction mixture was quenched by water and extracted by ethyl acetate. The organic extract was dried over $MgSO_4$. Removing the solvent and subsequent purification by column chromatography on silica gel afforded **3a** in 64% isolated yield.[11] **3b** was prepared in 57% isolated yield by using similar procedure with *N*,*N*-bis(3-(thiophen-2-yl)prop-2-yn-1-yl)butan-1-amine as starting material.

To a 25 mL tube with teflon-coated magnetic stir bar and a rubber septum, was added **3** (0.4 mmol), CuCl (0.04 mol), CH_2Cl_2 1 mL, TBHP (4 mmol, 70% in water). The tube was sealed and stirred for 24 h at 50^{o}C. The reaction mixture was quenched by water and extracted by ethyl acetate. The organic extract was dried over $MgSO_4$.

Removing the solvent and subsequent purification by column chromatography on Al_2O_3 afforded **4**.

5-Butyl-1,3-diphenyl-4H-thieno[3,4-c]pyrrole-4,6(5H)-dione, 4a.

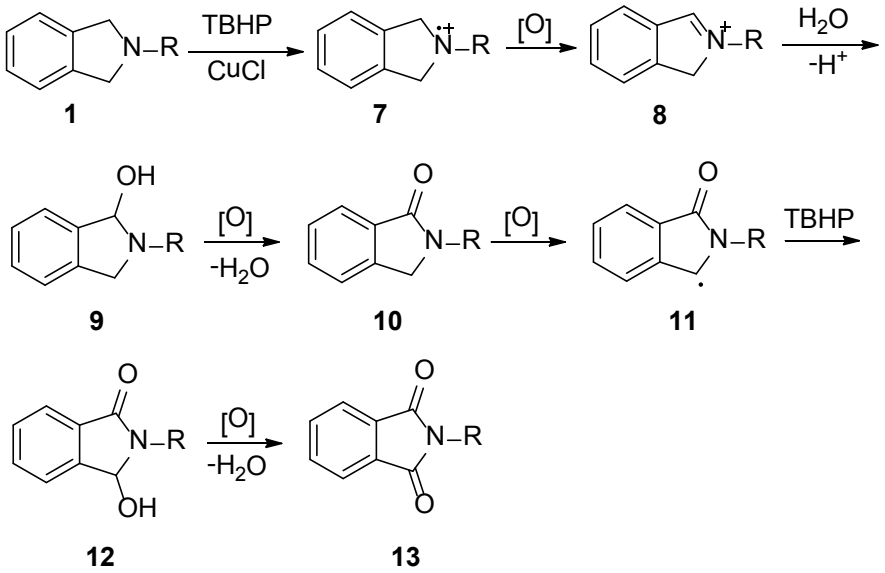
82% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14-8.12 (m, 4H), 7.50-7.41 (m, 6H), 3.68 (t, J = 7.3 Hz, 2H), 1.71-1.63 (m, 2H), 1.42-1.36 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 145.1, 130.7, 130.5, 130.2, 129.1, 128.2, 38.4, 30.6, 20.3, 13.8. HRMS calcd for C22H19NO2S 361.1136, found 361.1131.

5-Octyl-1,3-di(thiophen-2-yl)-4H-thieno[3,4-c]pyrrole-4,6(5H)-dione, 4b.

55% isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J = 3.8 Hz, 2H), 7.43 (d, J = 5.2 Hz, 2H), 7.14-7.10 (m, 2H), 3.66 (t, J = 7.2 Hz, 2H), 1.72-1.63 (m, 2H), 1.42-1.20 (m, 10H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.7, 136.6, 132.5, 130.0, 128.7, 128.5, 38.7, 31.9, 29.3, 29.2, 28.6, 27.0, 22.7, 14.2. HRMS calcd for C22H23NO2S3 429.0891, found 429.0893.

Proposed mechanism

Based on the results, a plausible mechanism was proposed as follow. Firstly, amine **1** was oxidized to radical cation **7** in the present of TBHP and CuCl. **7** was further oxidized to iminium **8**. **8** reacted with water to yield compound **9**, which was then oxidized to amide **10**. **10** was further oxidized to form **11**, which reacted with TBHP to give **12**. Oxidation of **12** afforded imide **13**.



1 **7** **8** **9** **10** **11** **12** **13**

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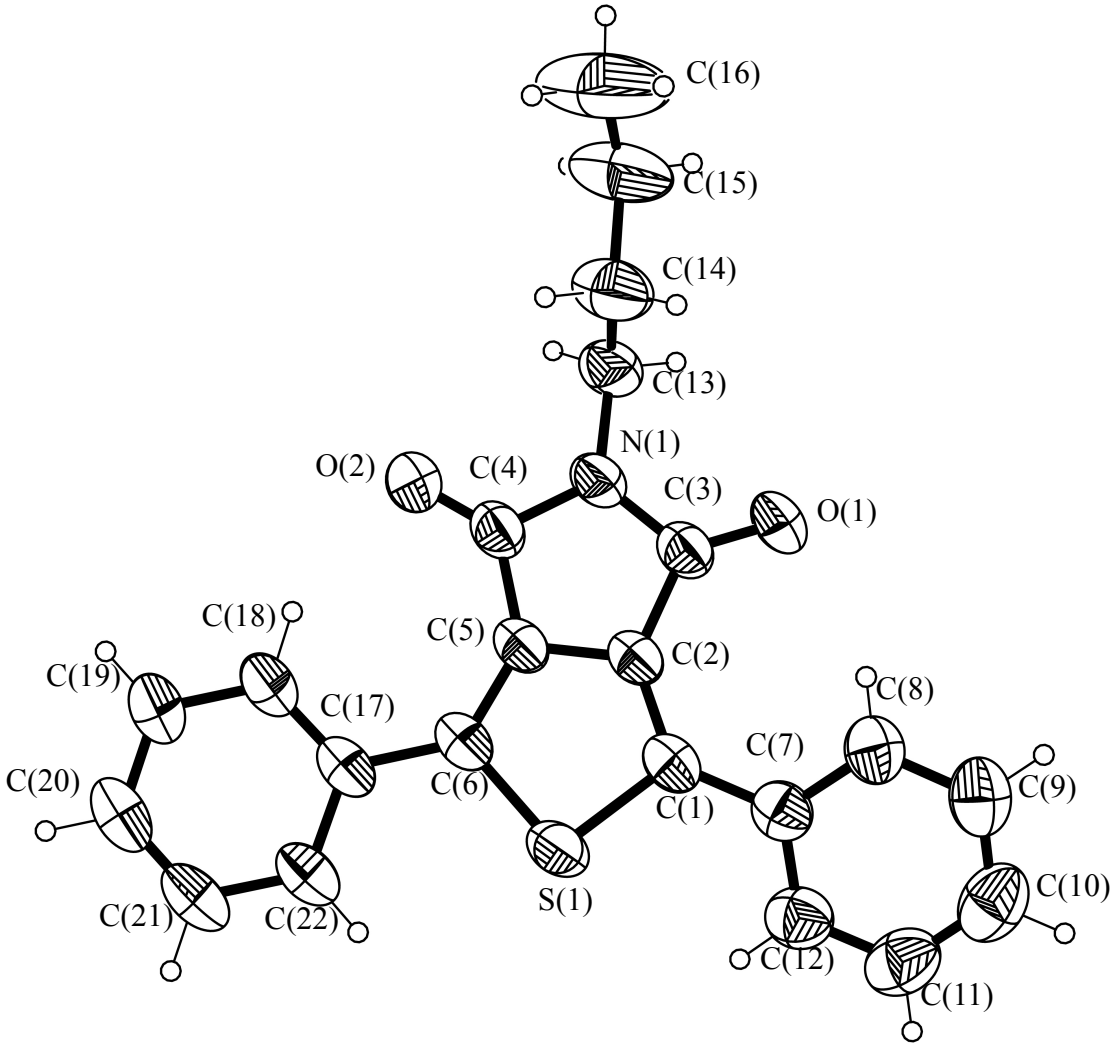
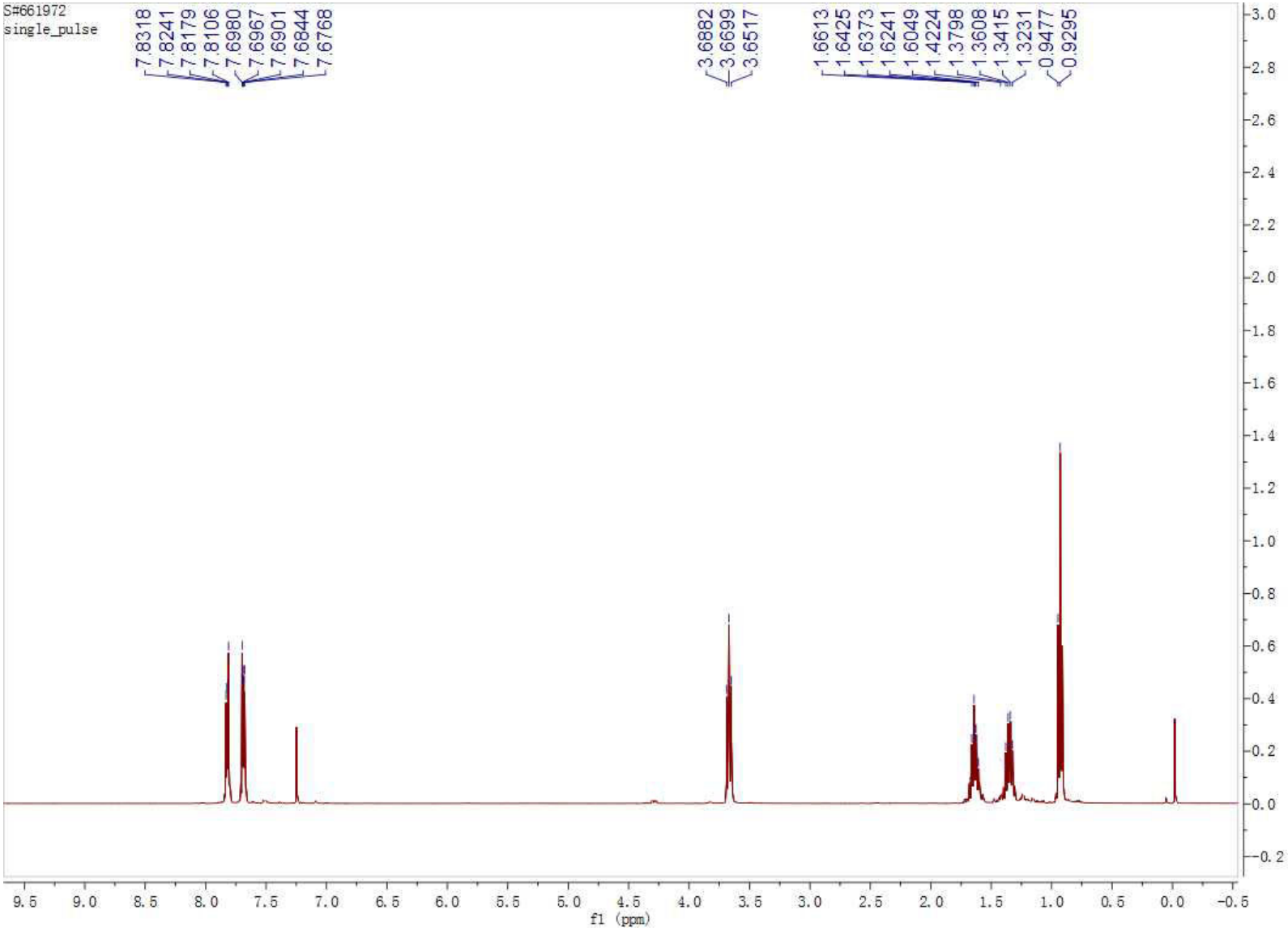
X-ray structure of **4a**

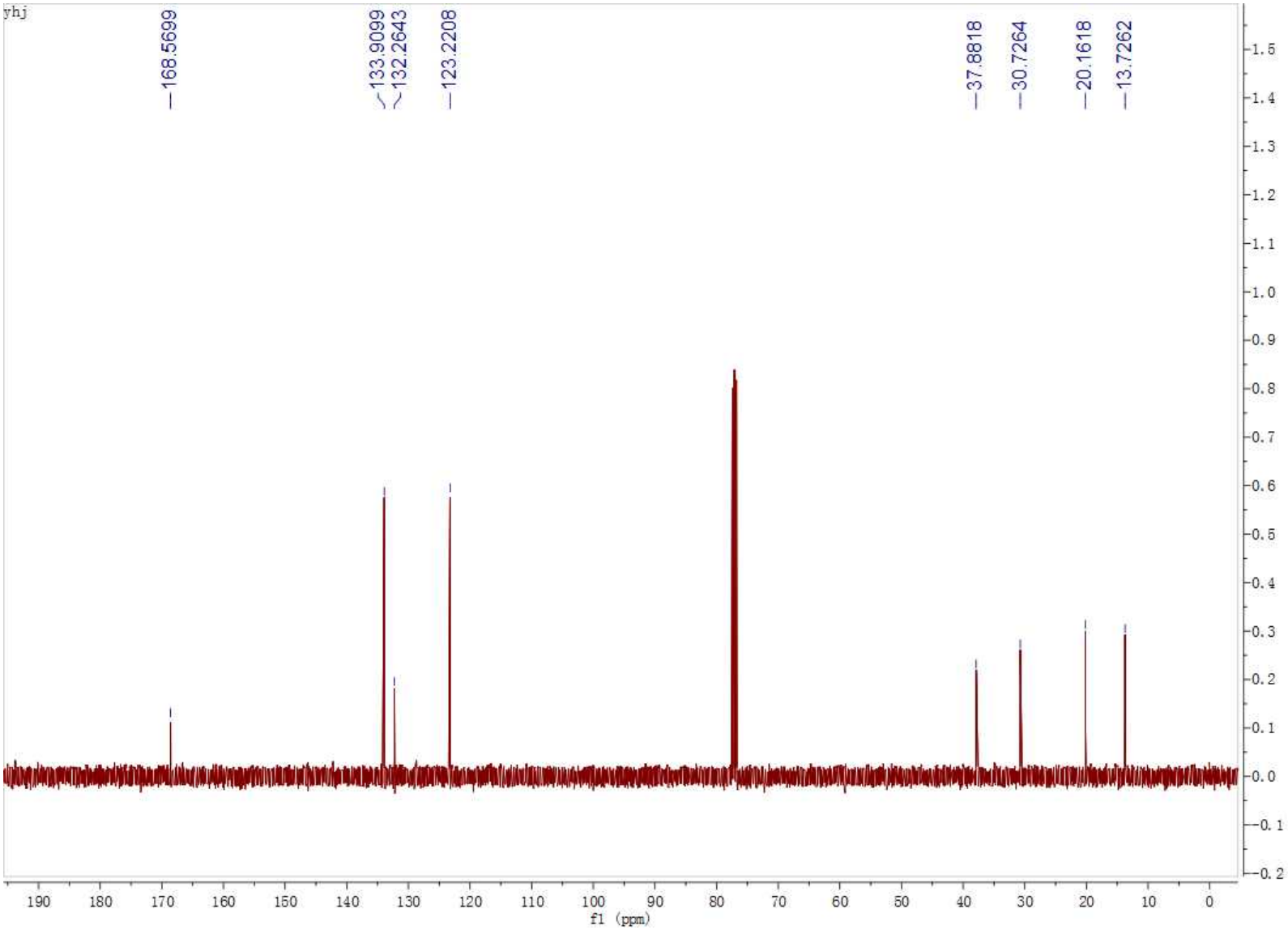


ORTEP drawing of $C_{22}H_{19}NO_2S$ with 35% probability ellipsoids, showing the atomic numbering scheme.

Copies of ^{1}H and ^{13}C NMR Spectra



^{1}H NMR for compound **2a**



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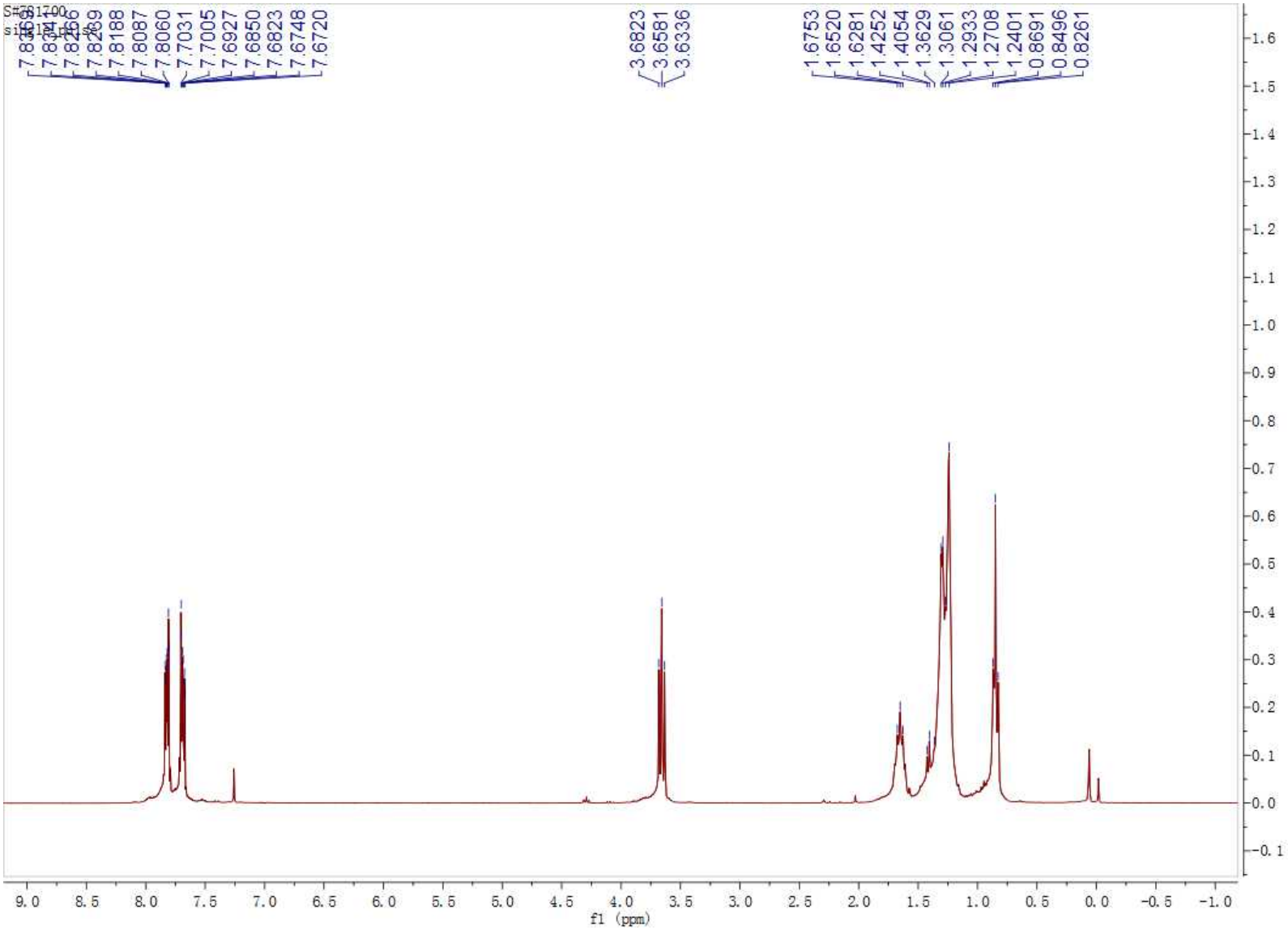

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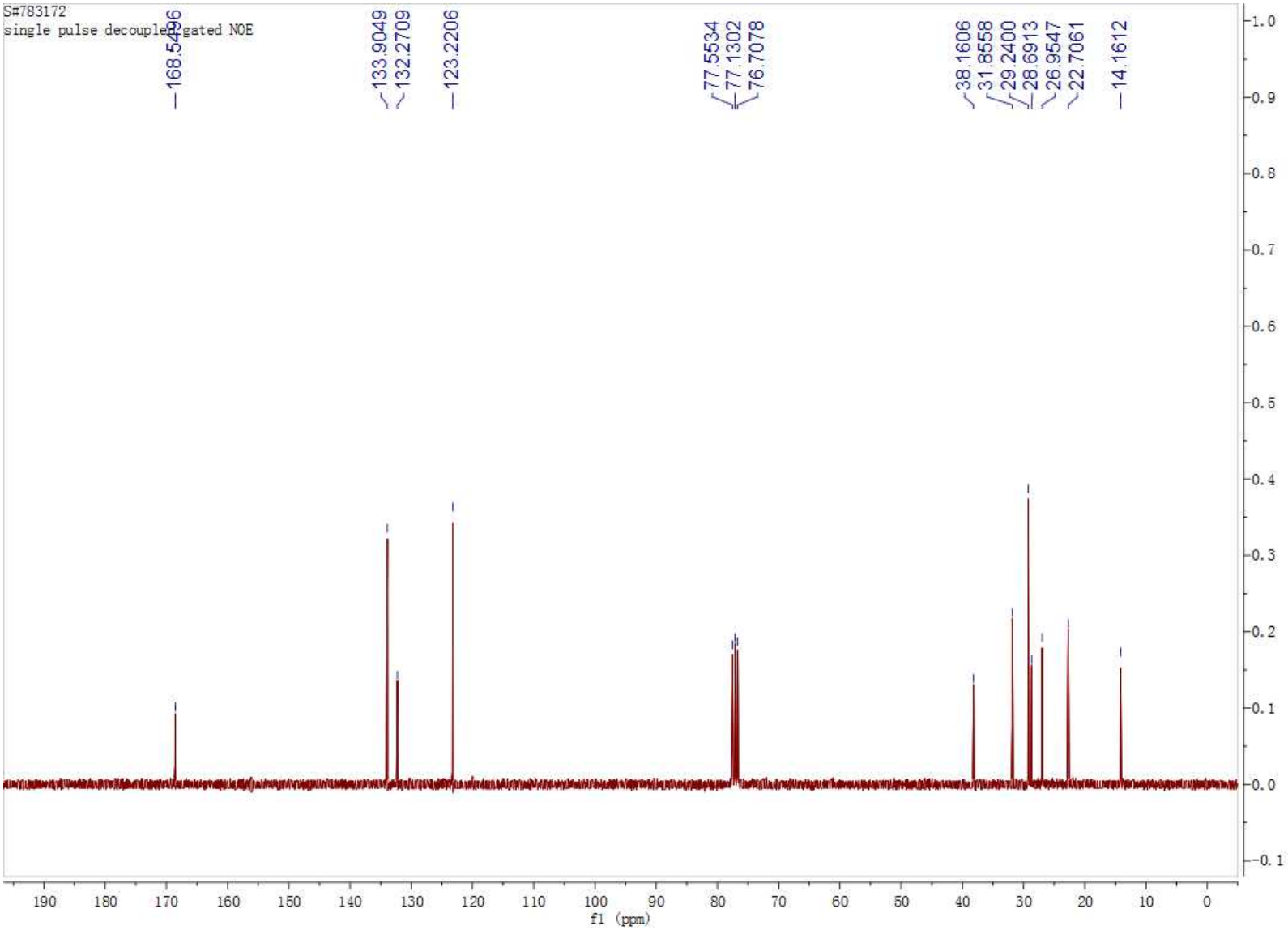

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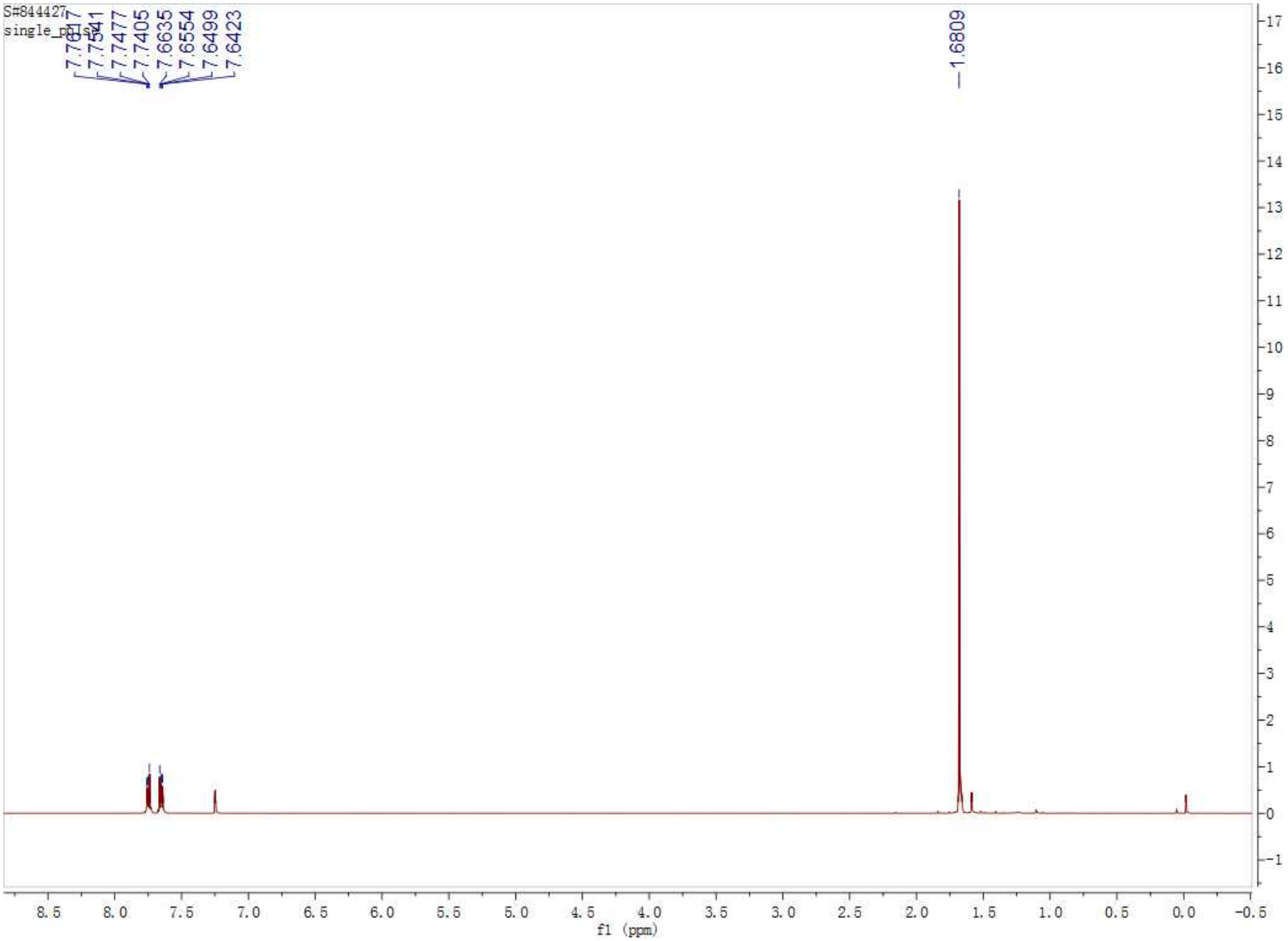

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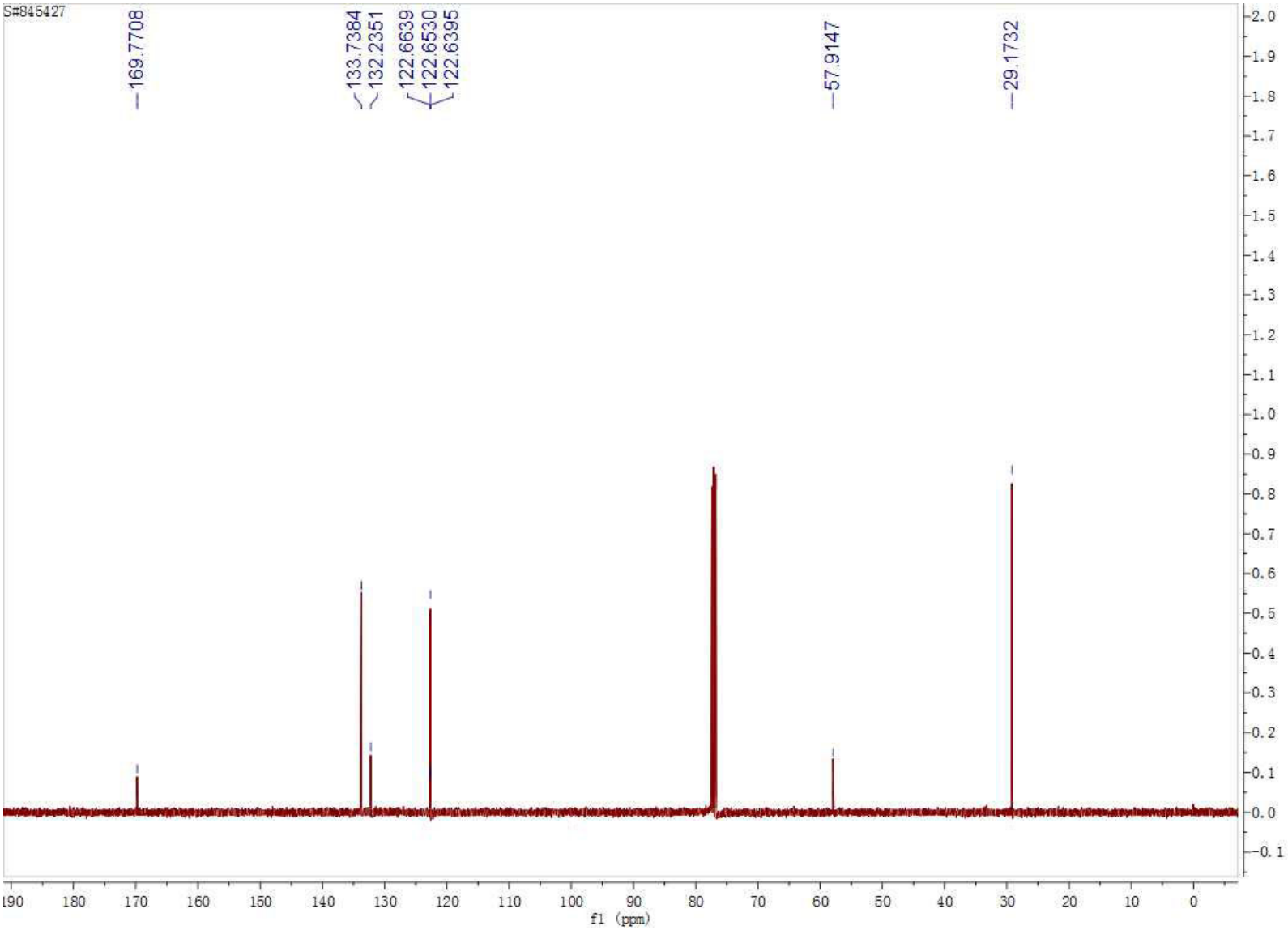

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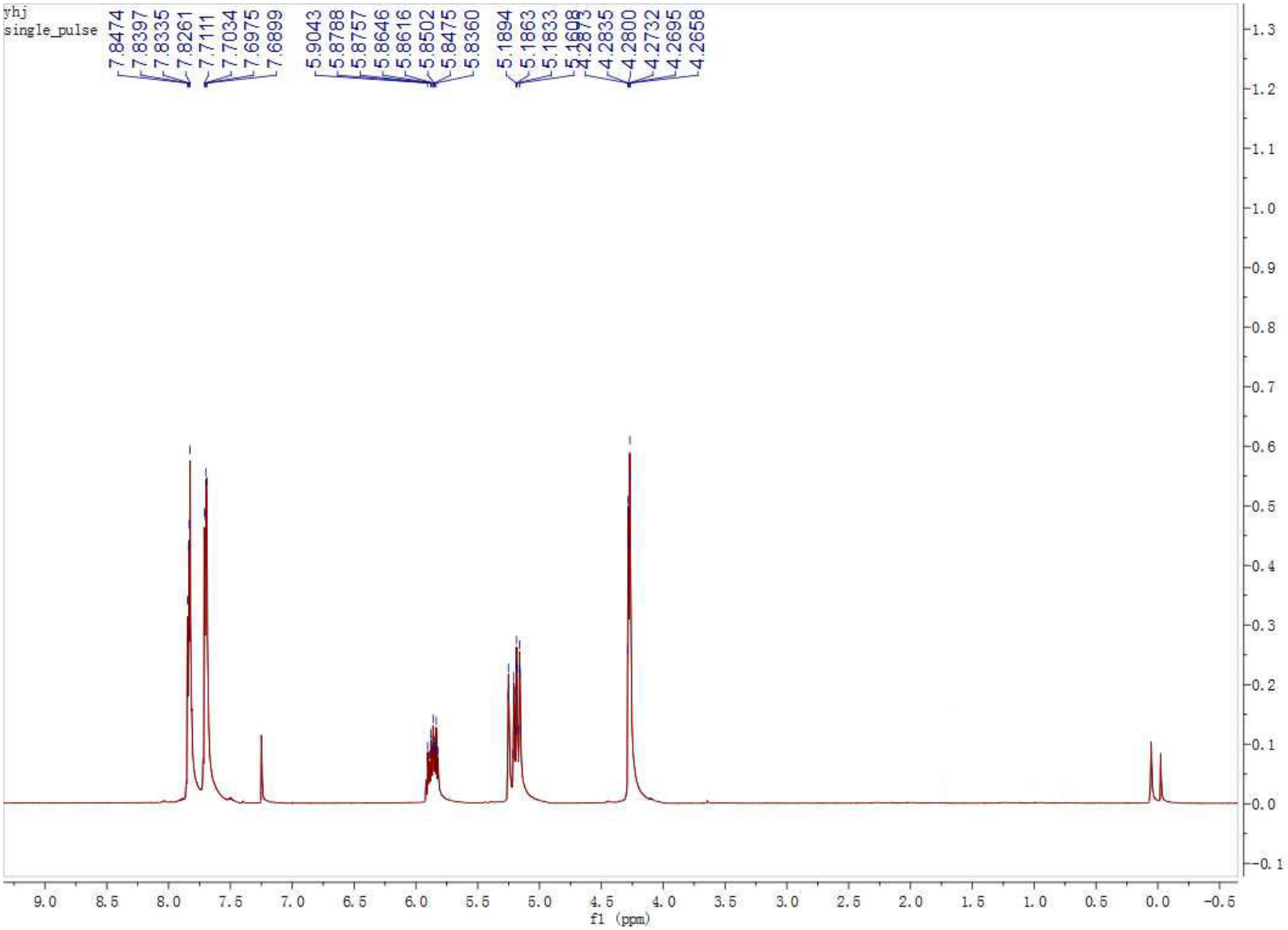

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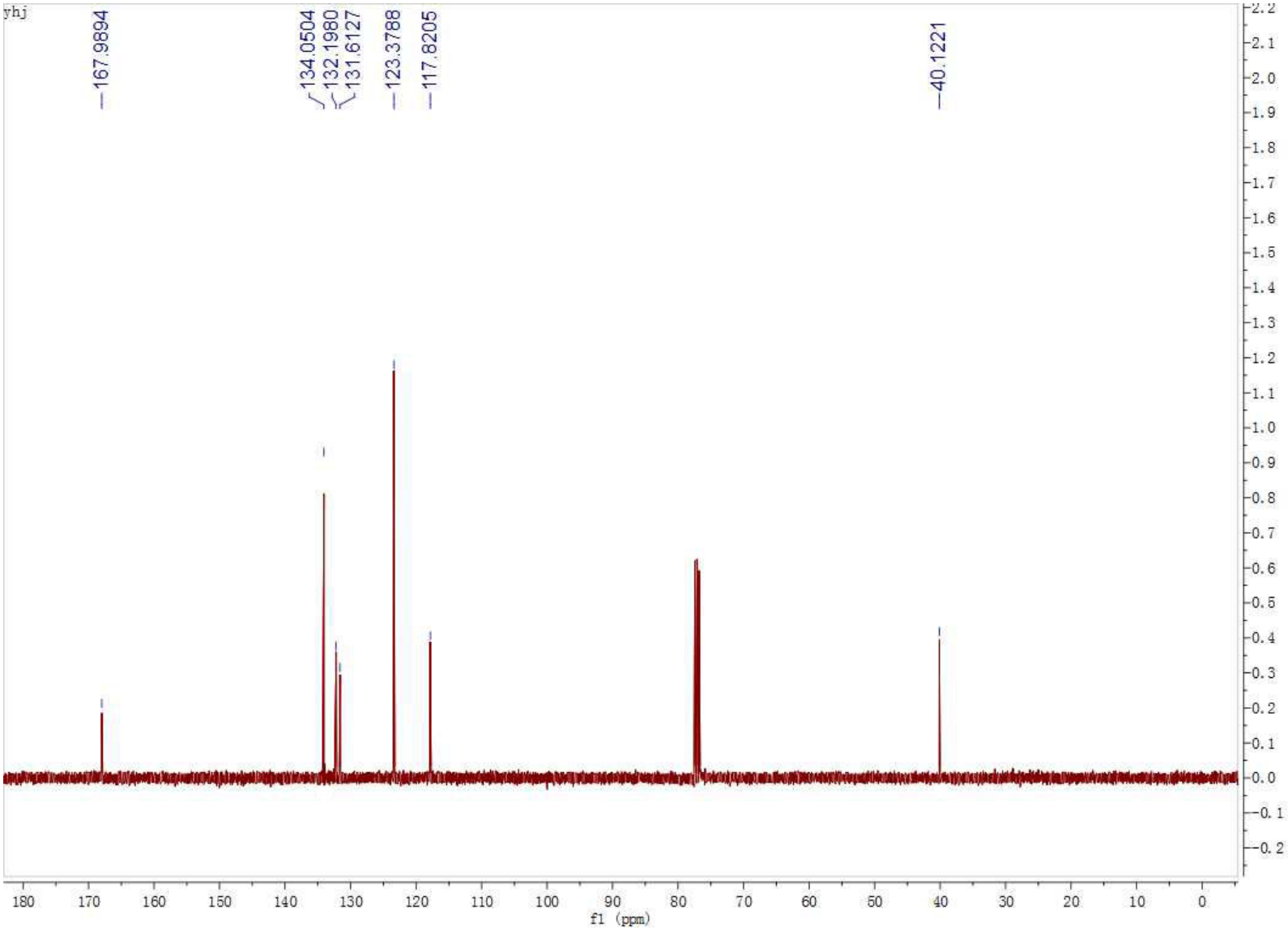

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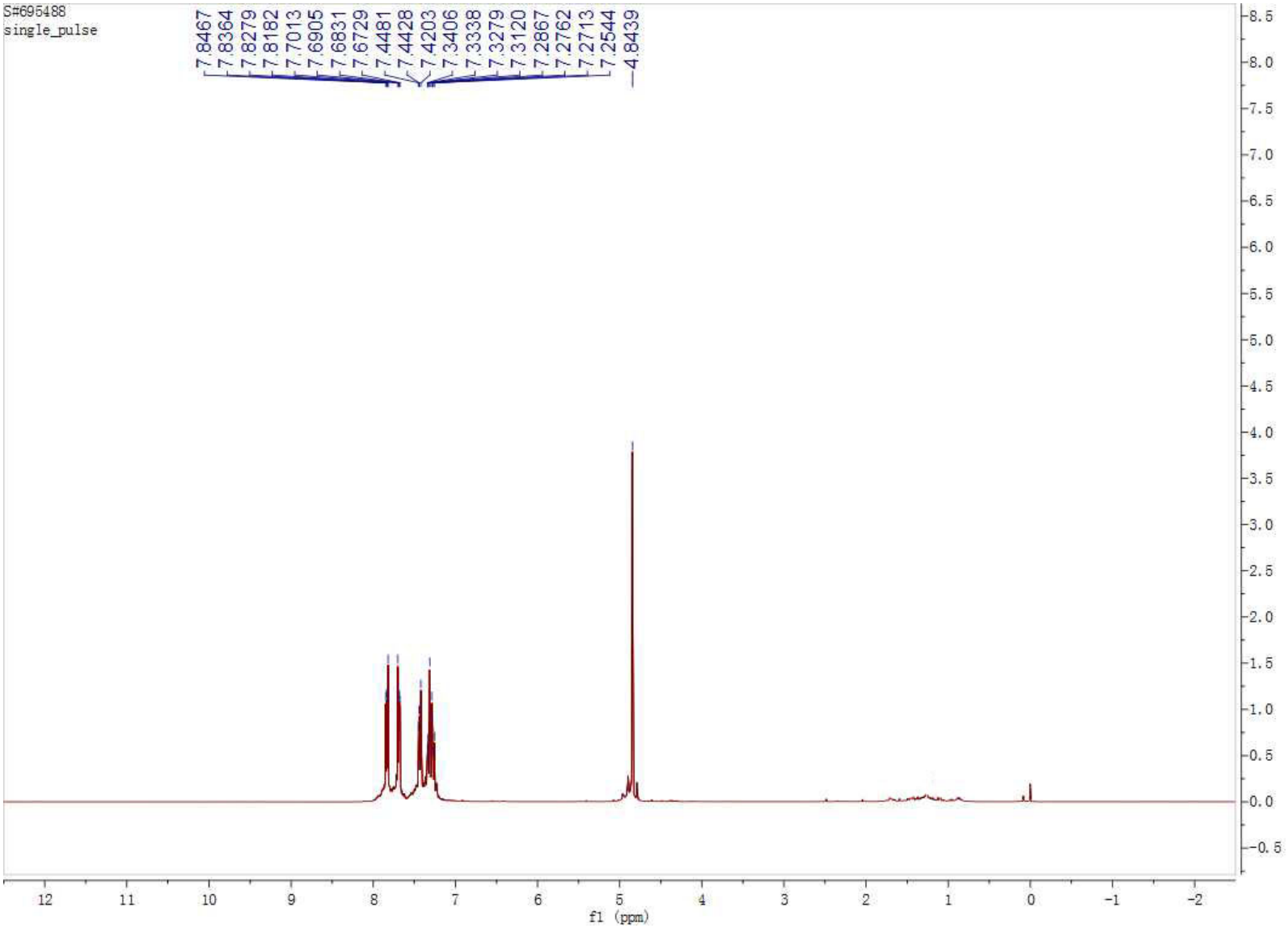

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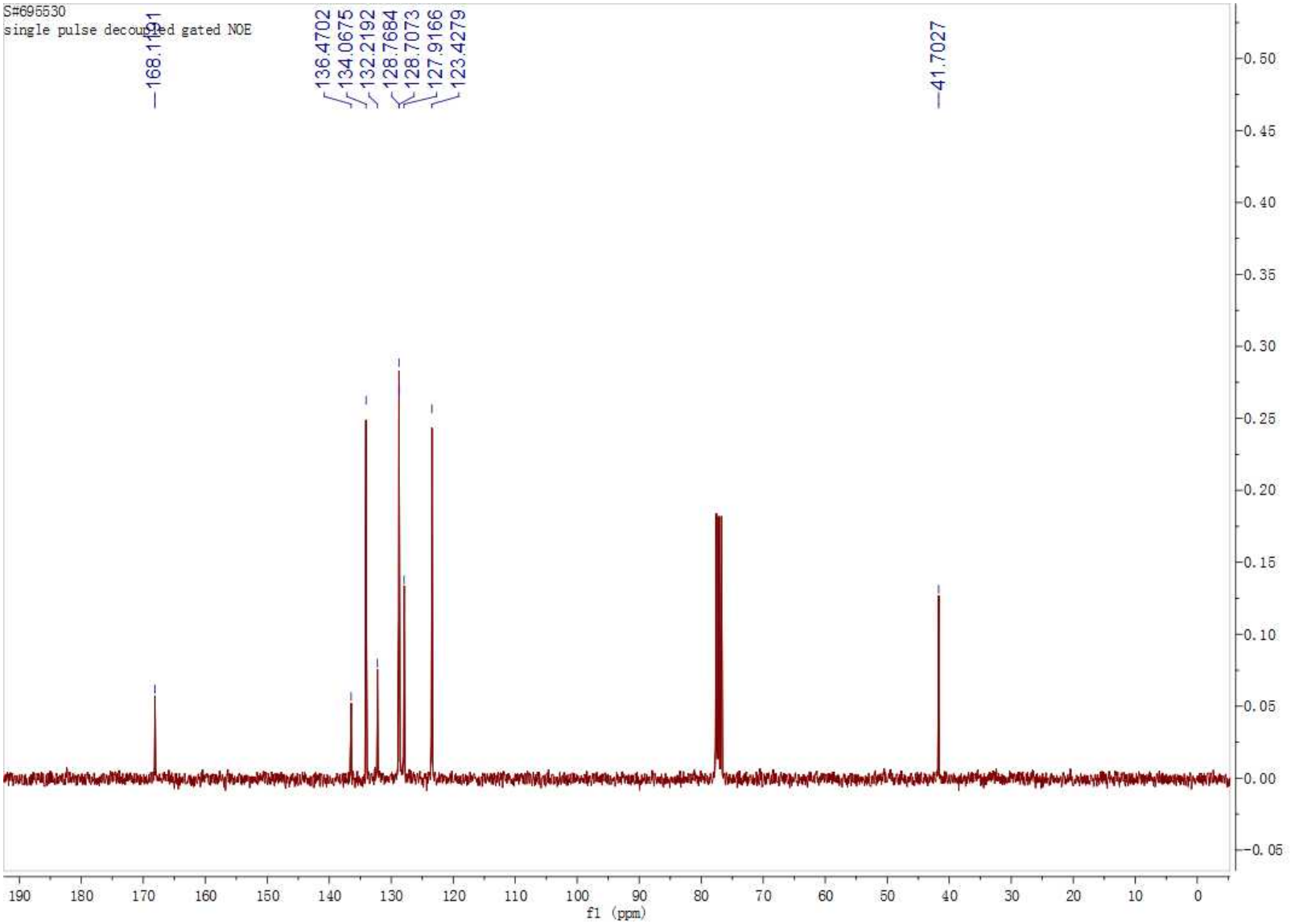

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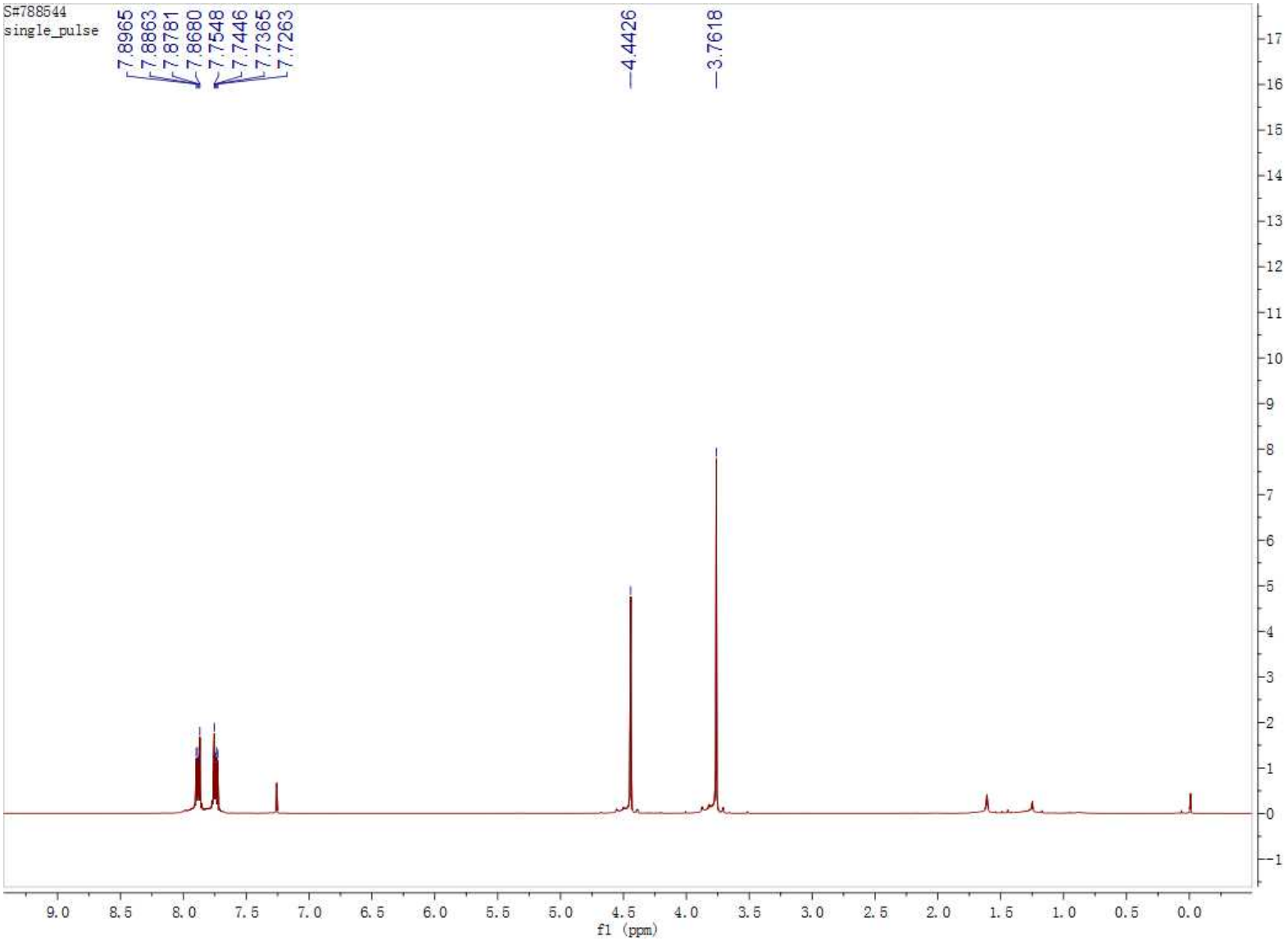

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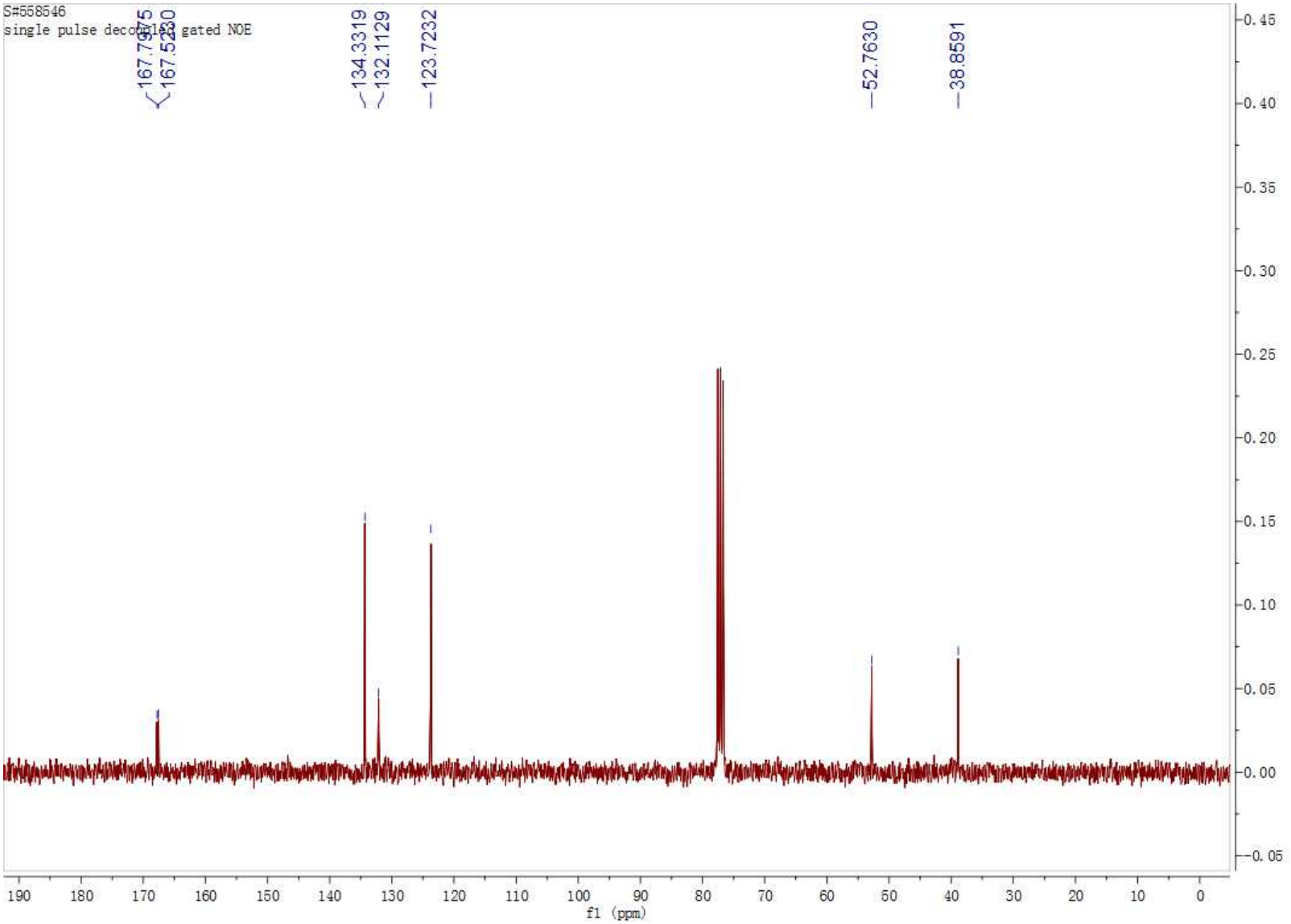

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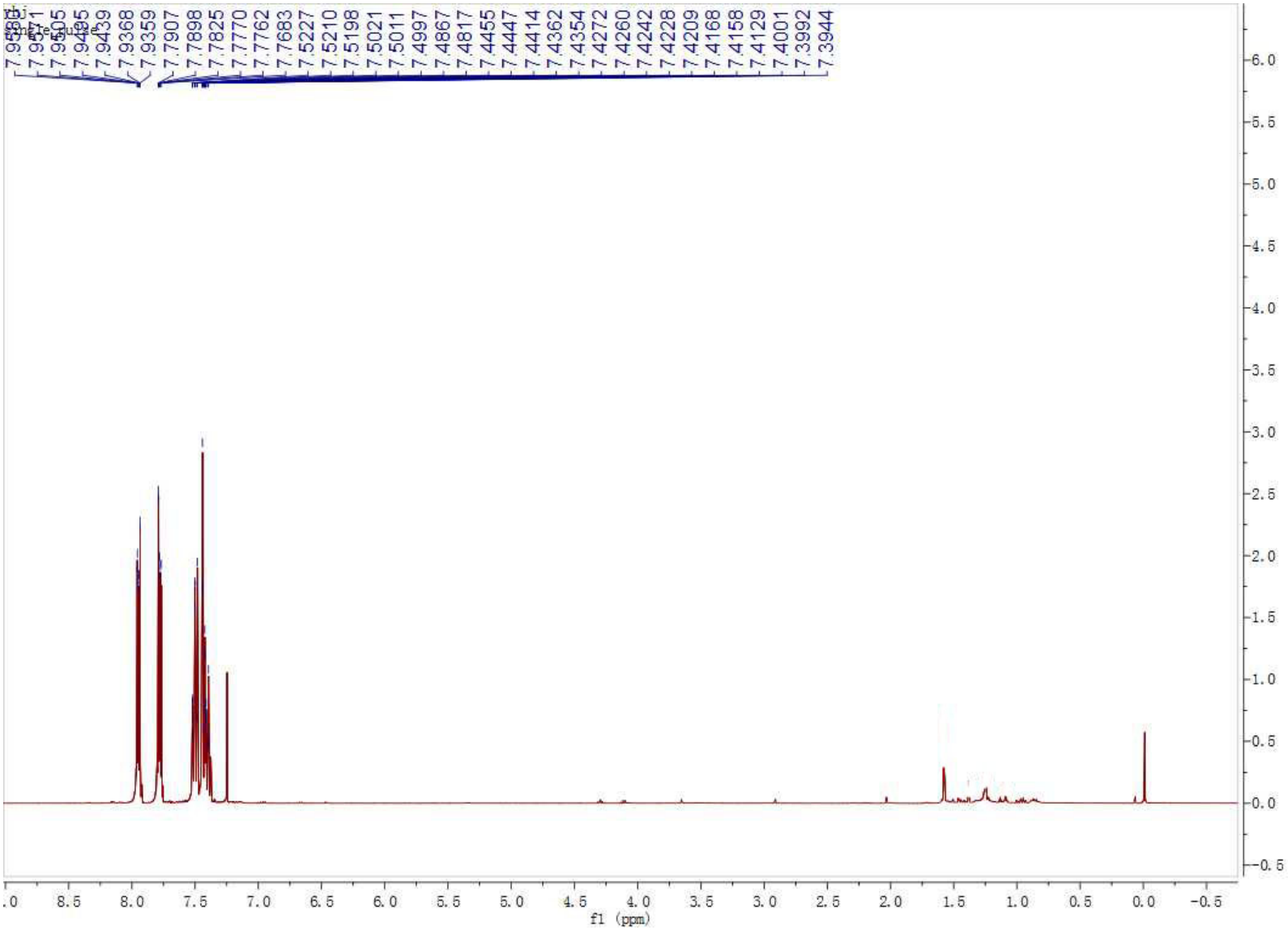

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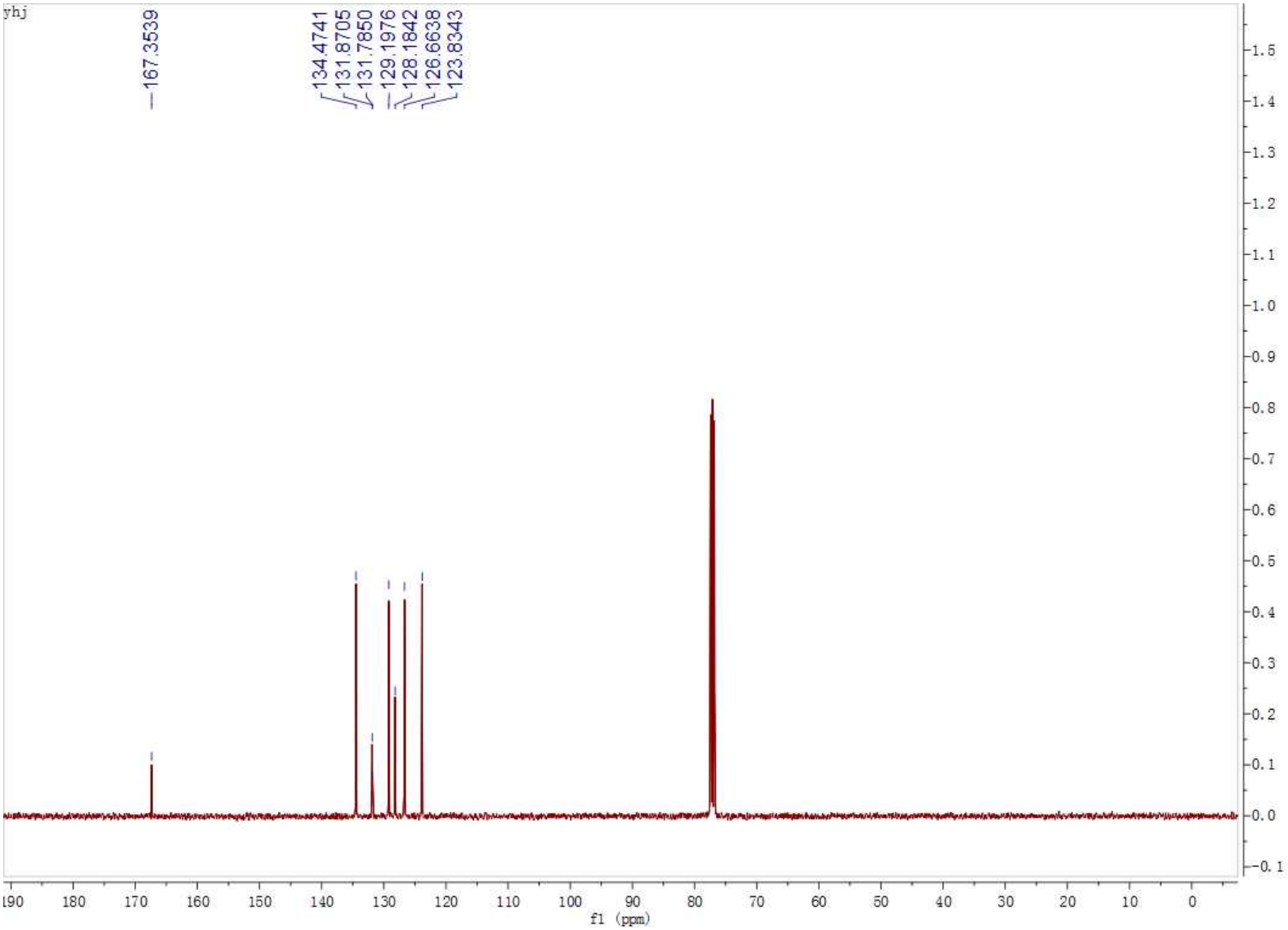

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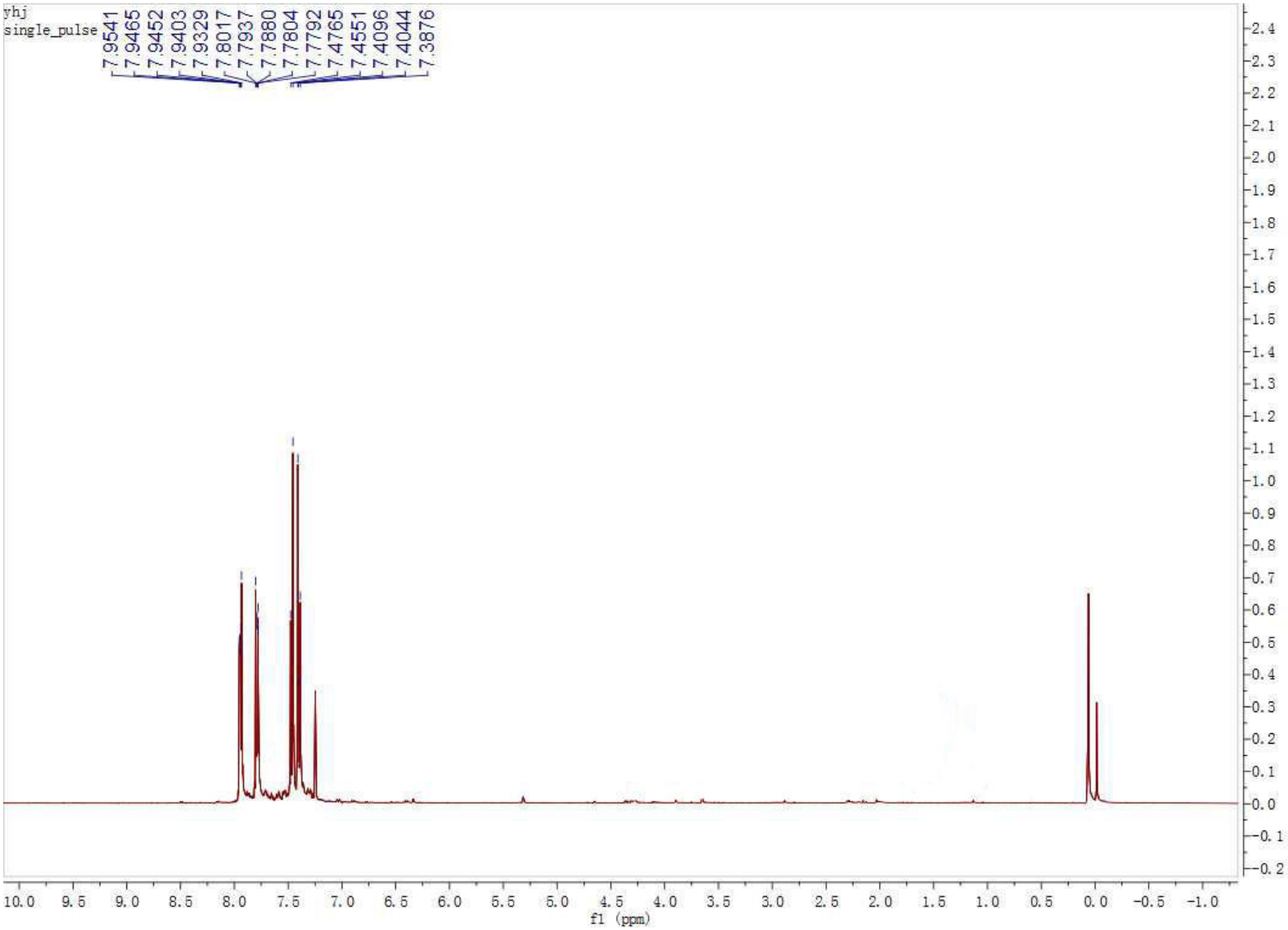

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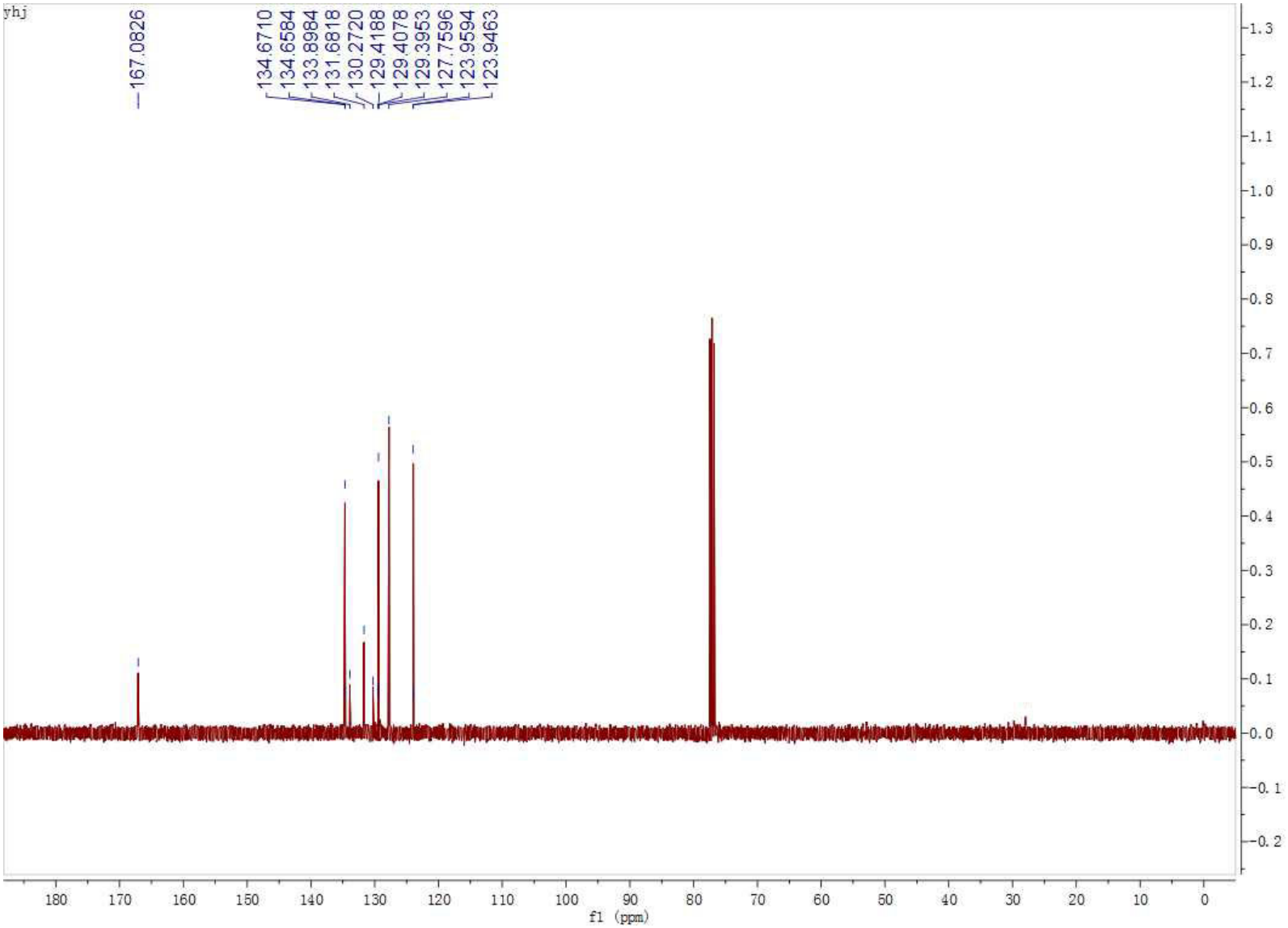

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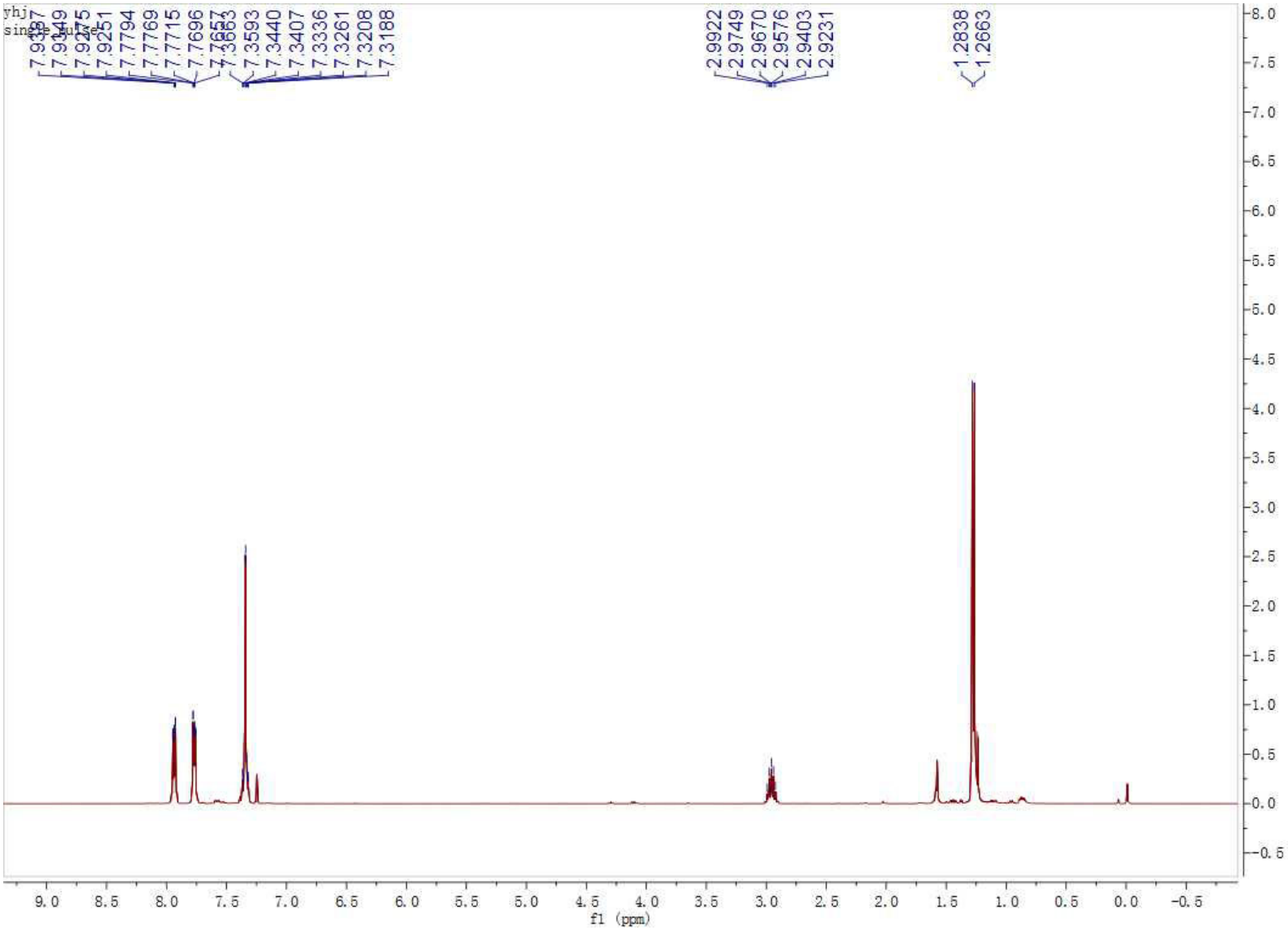

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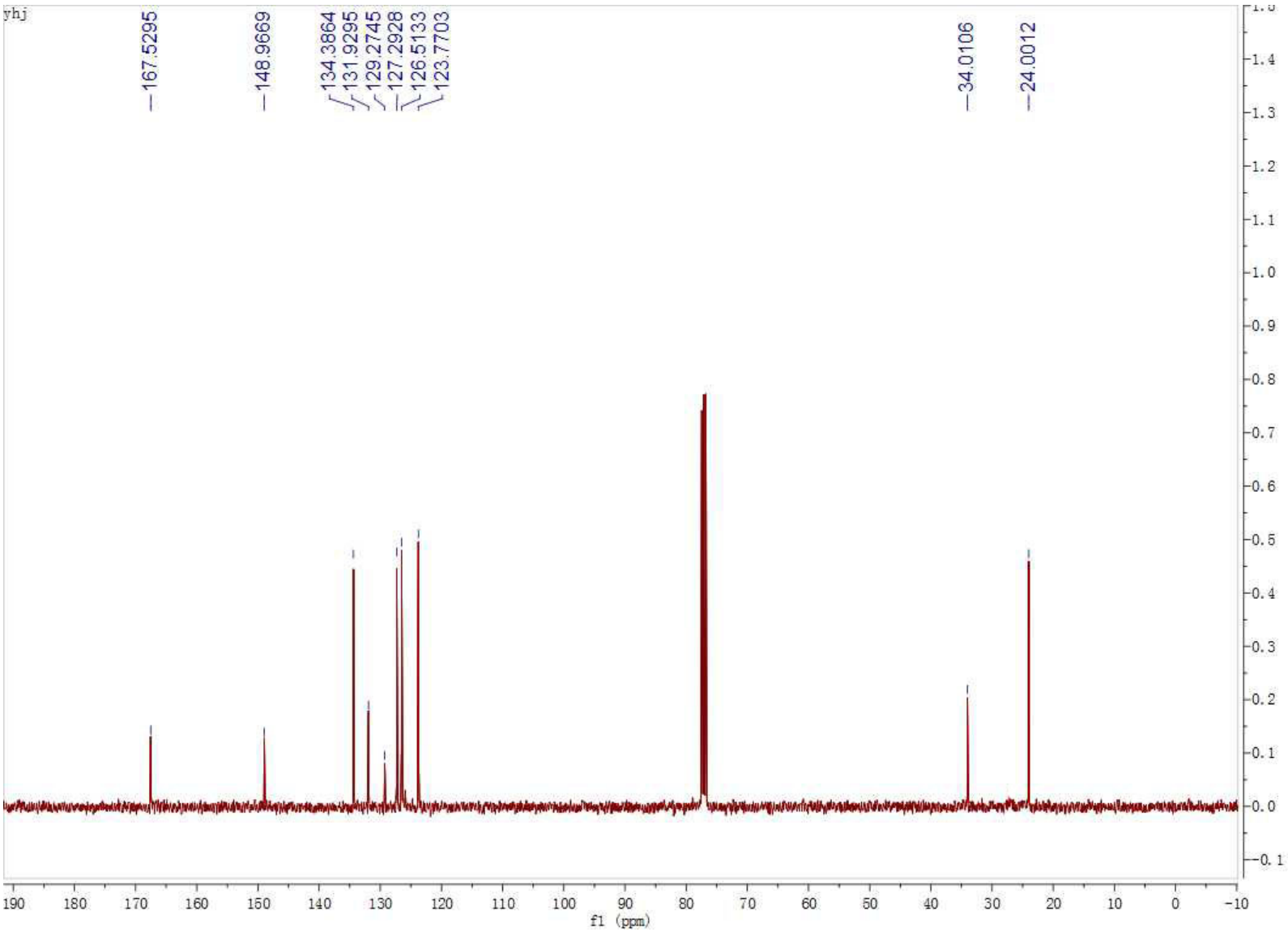

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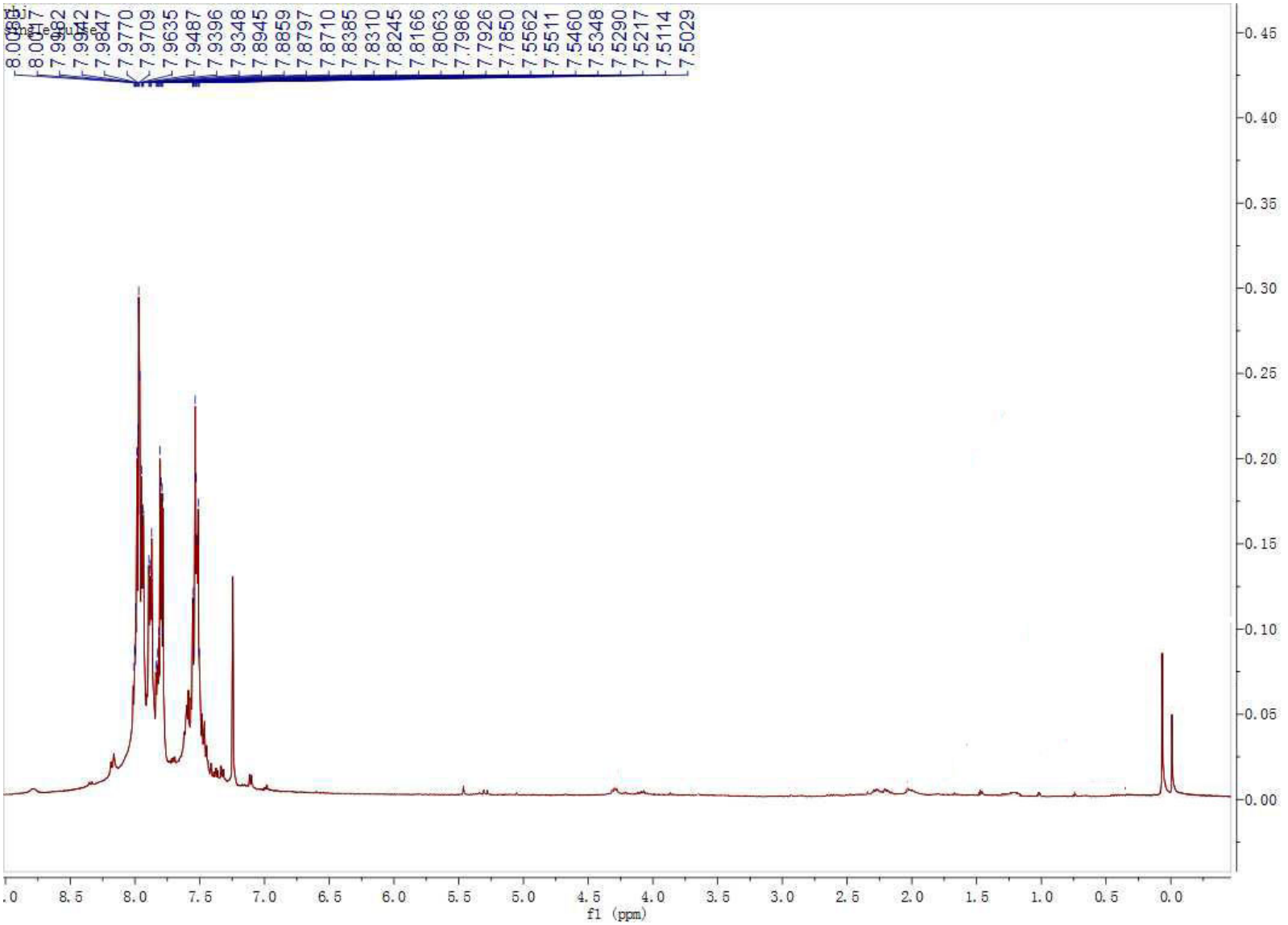

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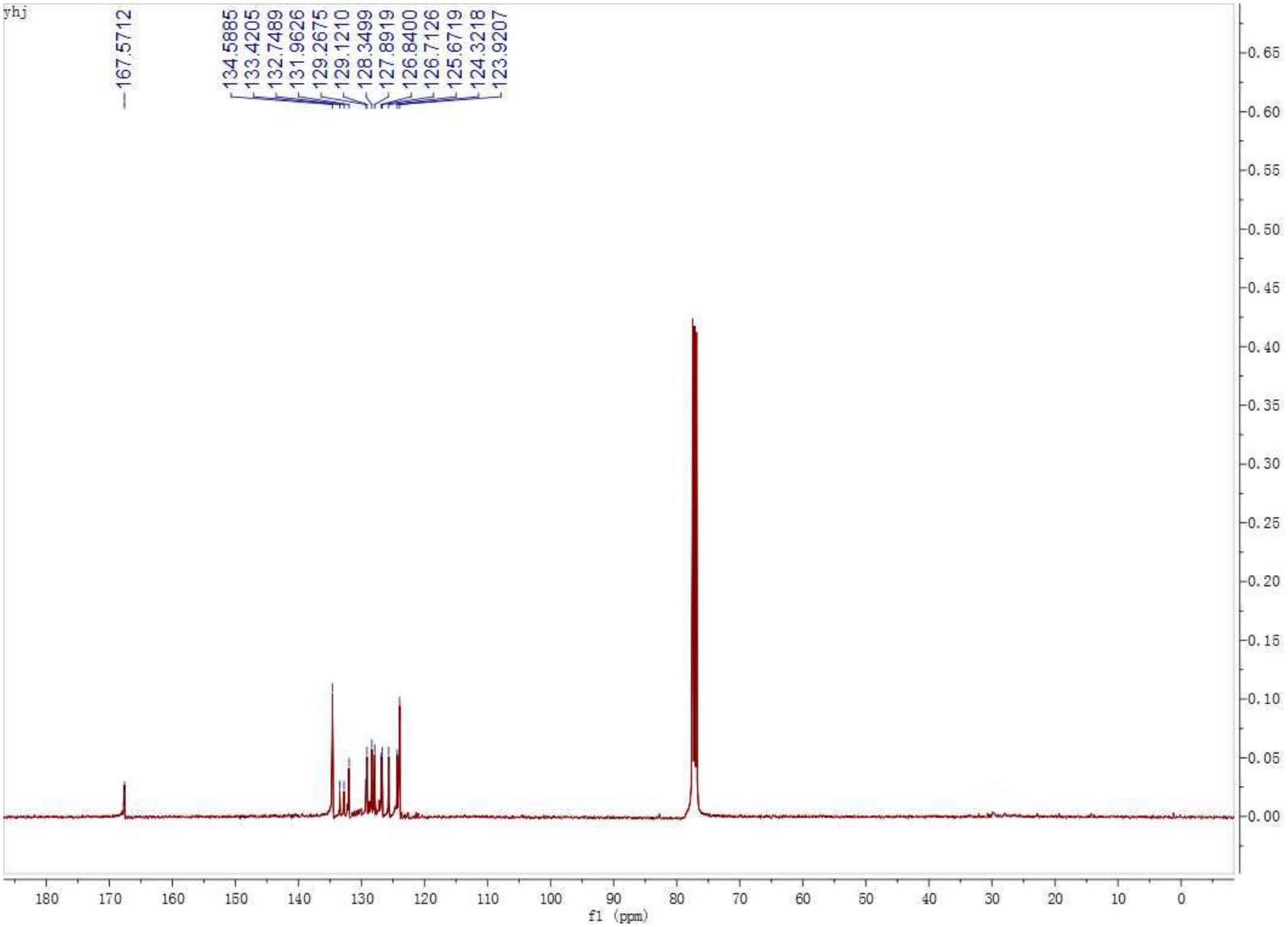

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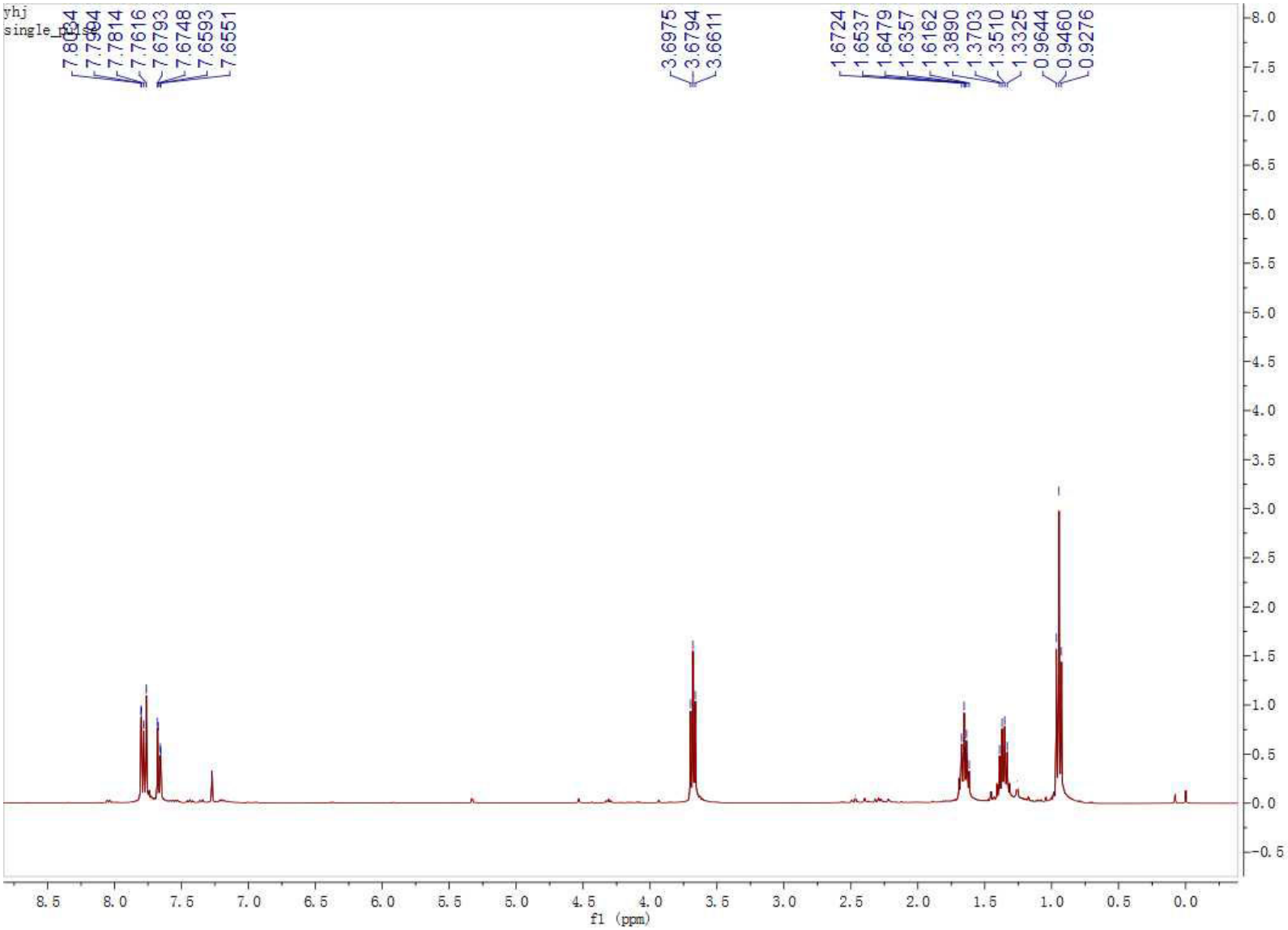

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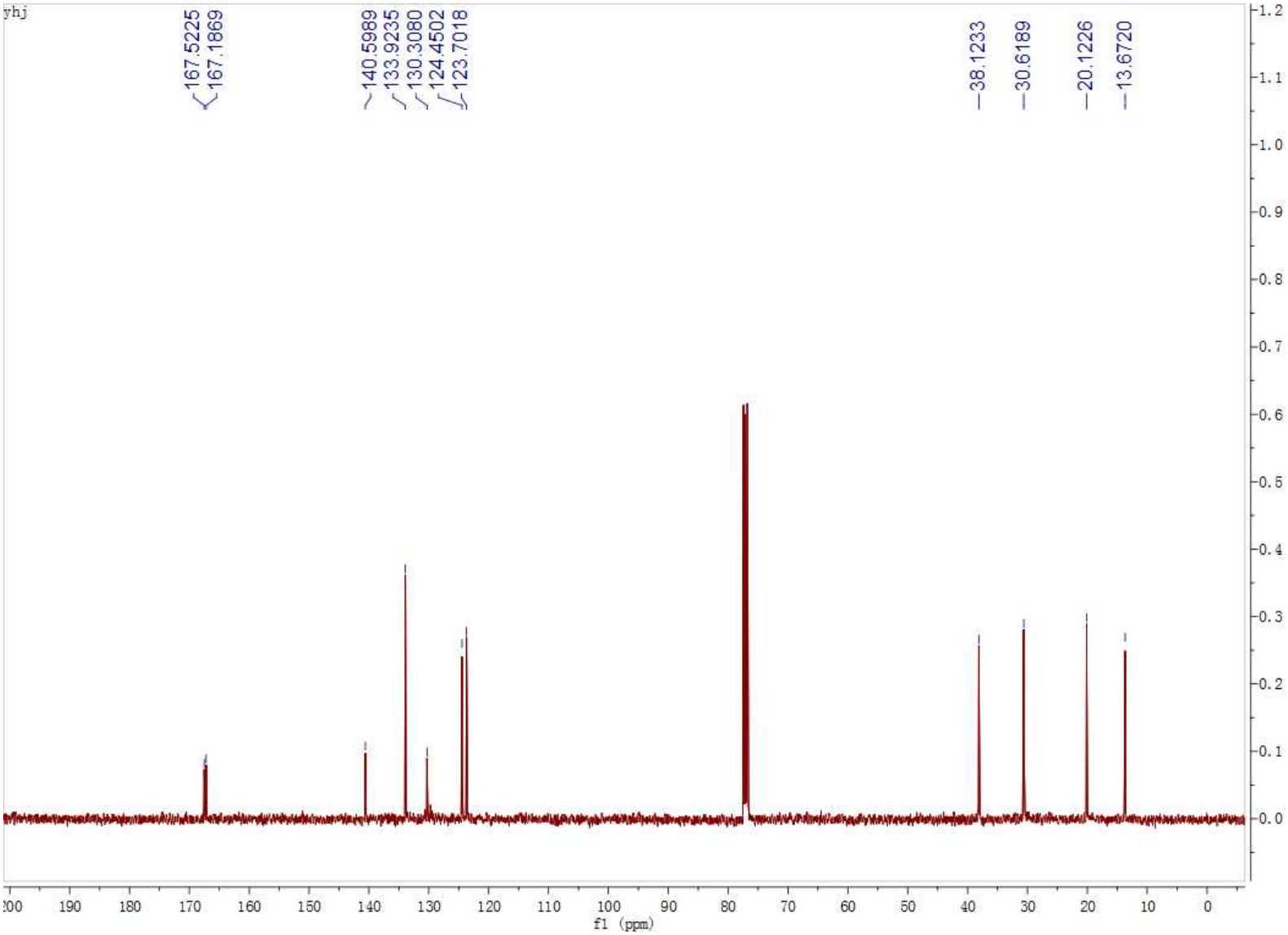

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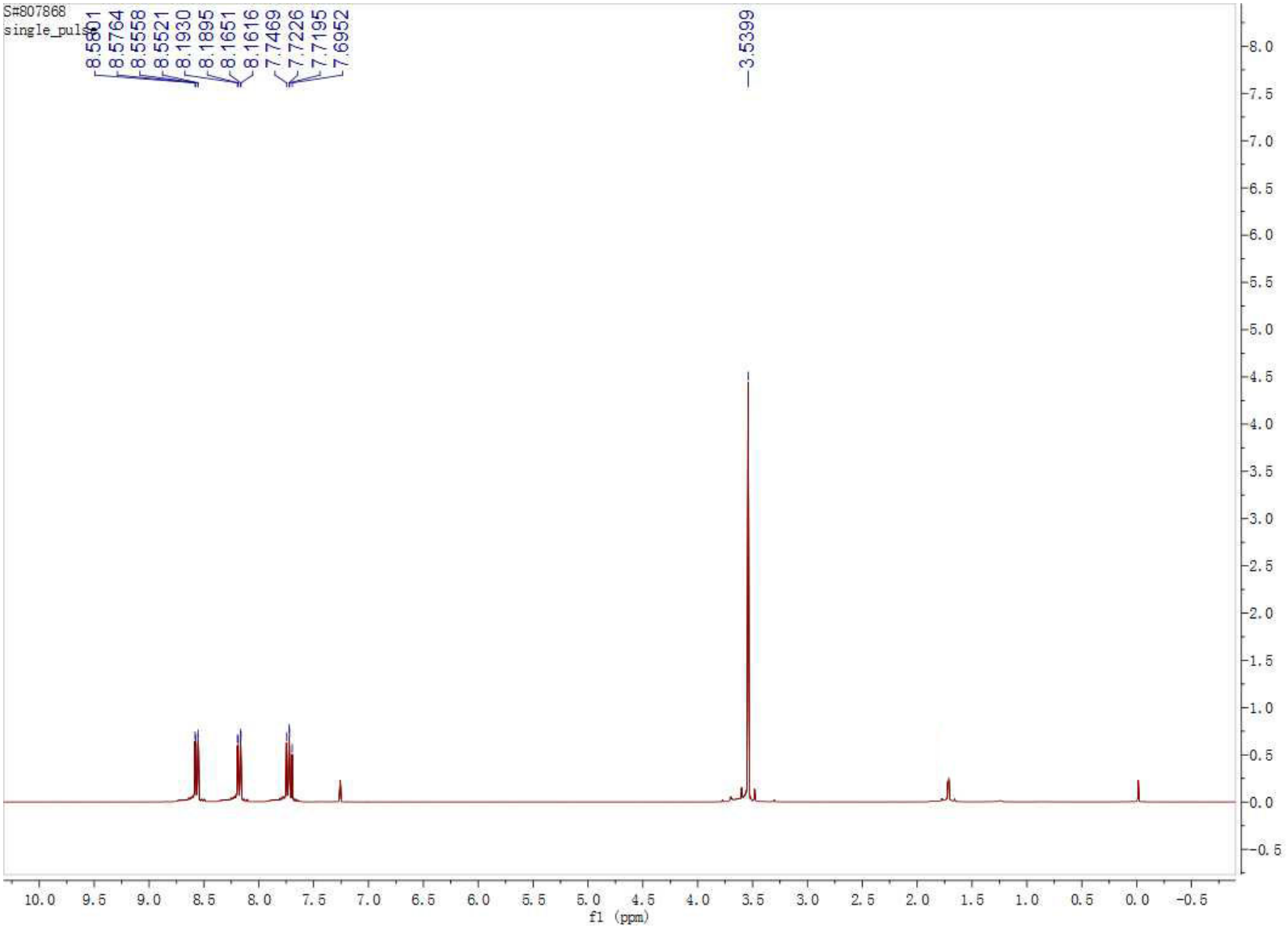

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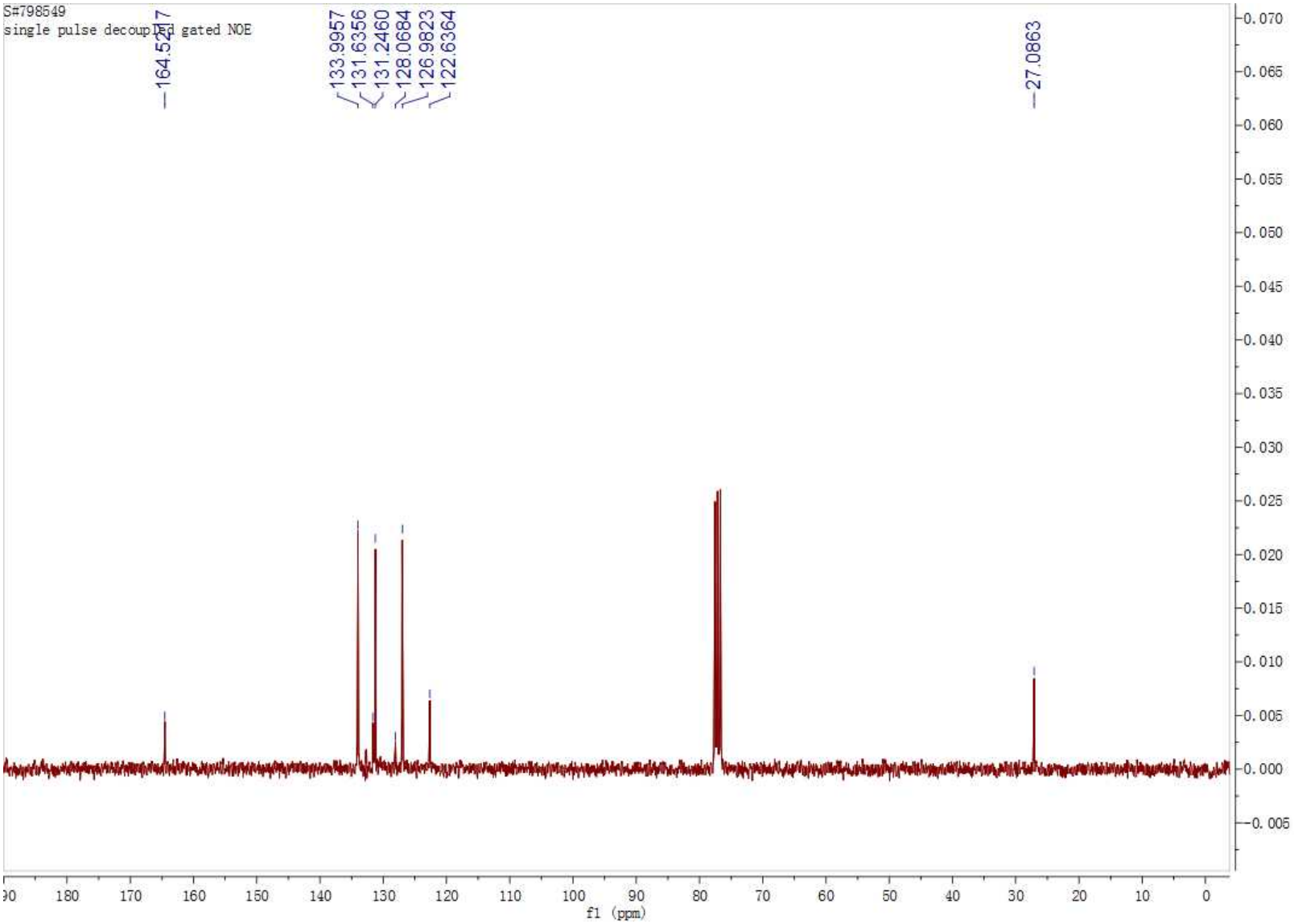

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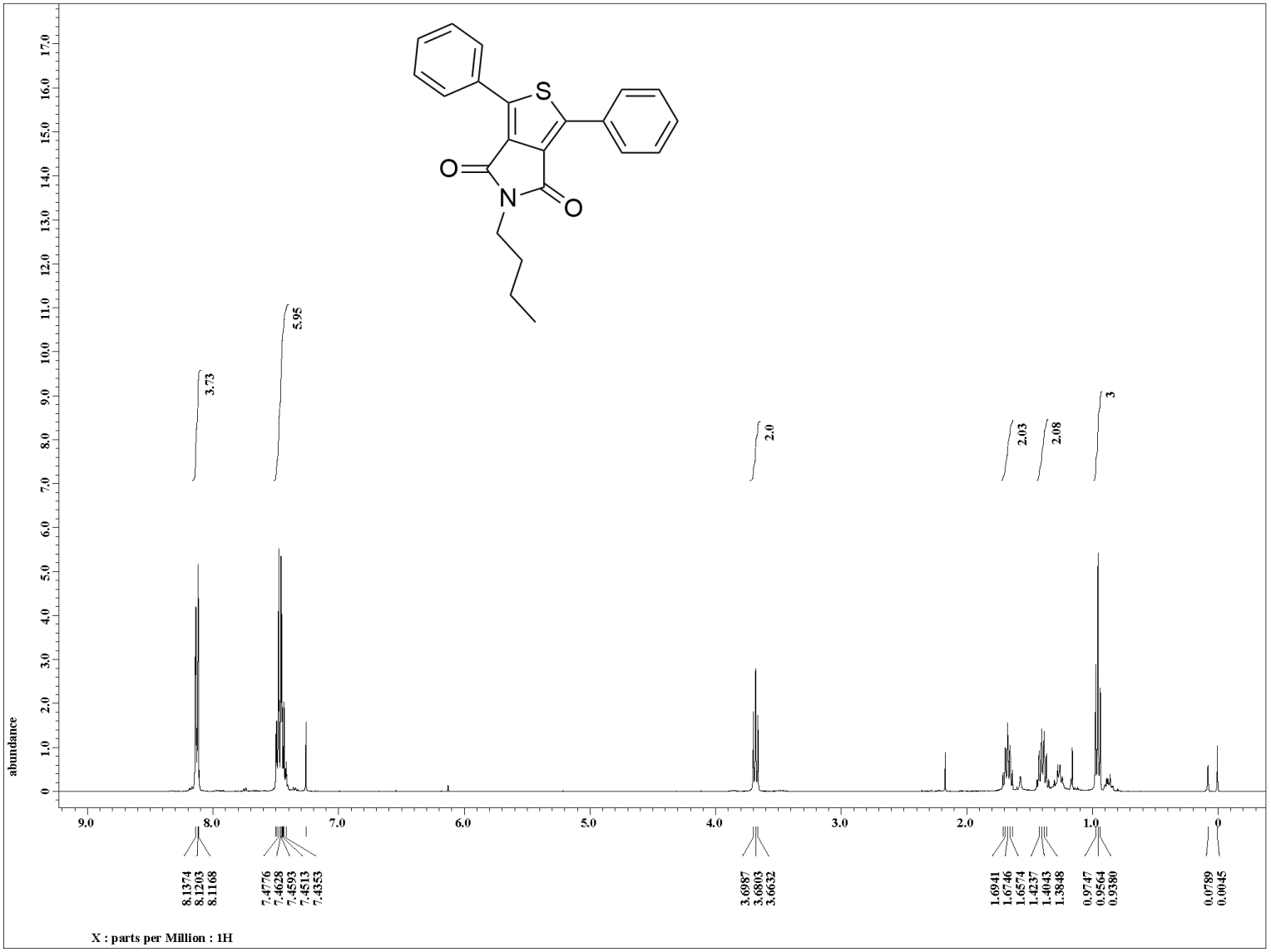
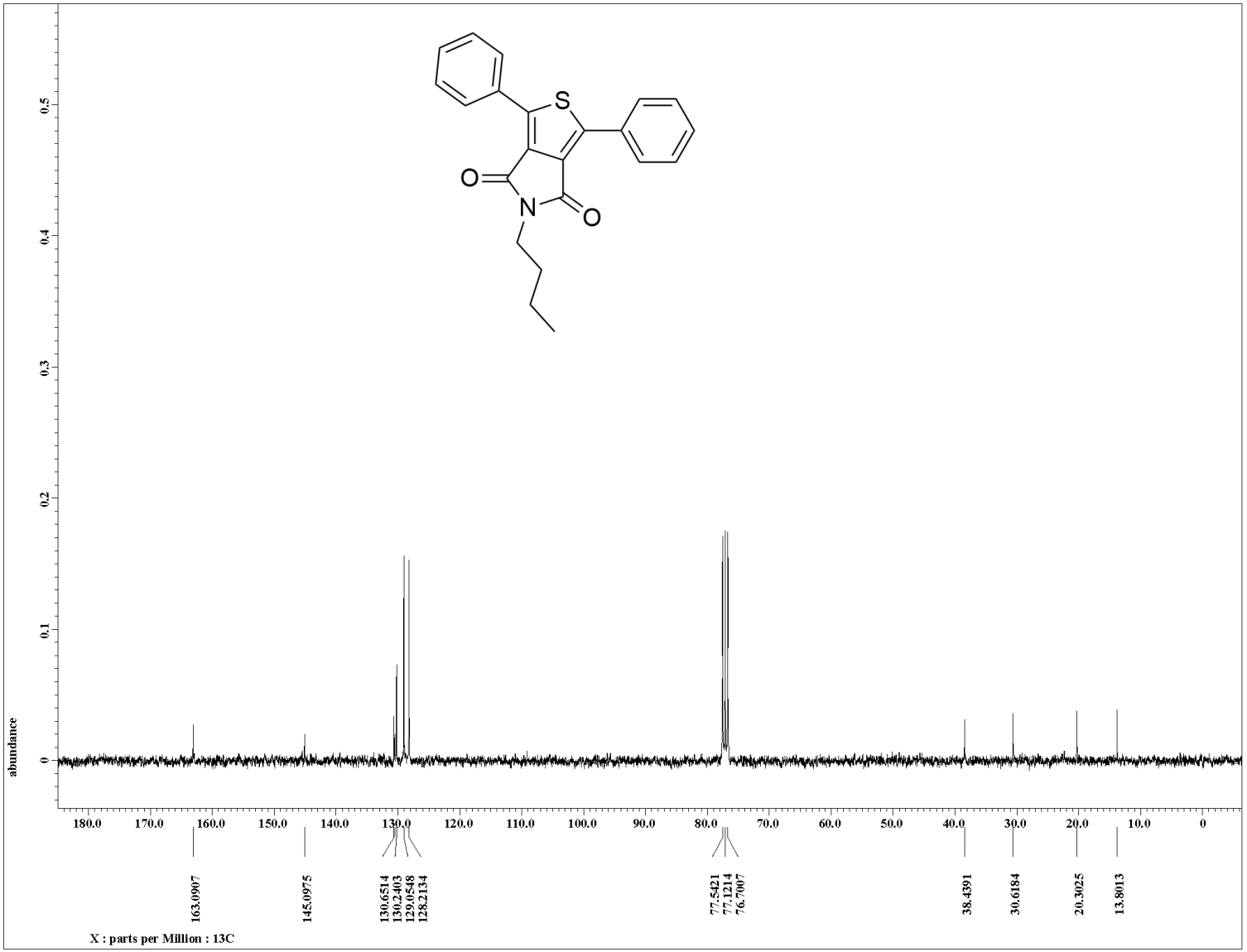
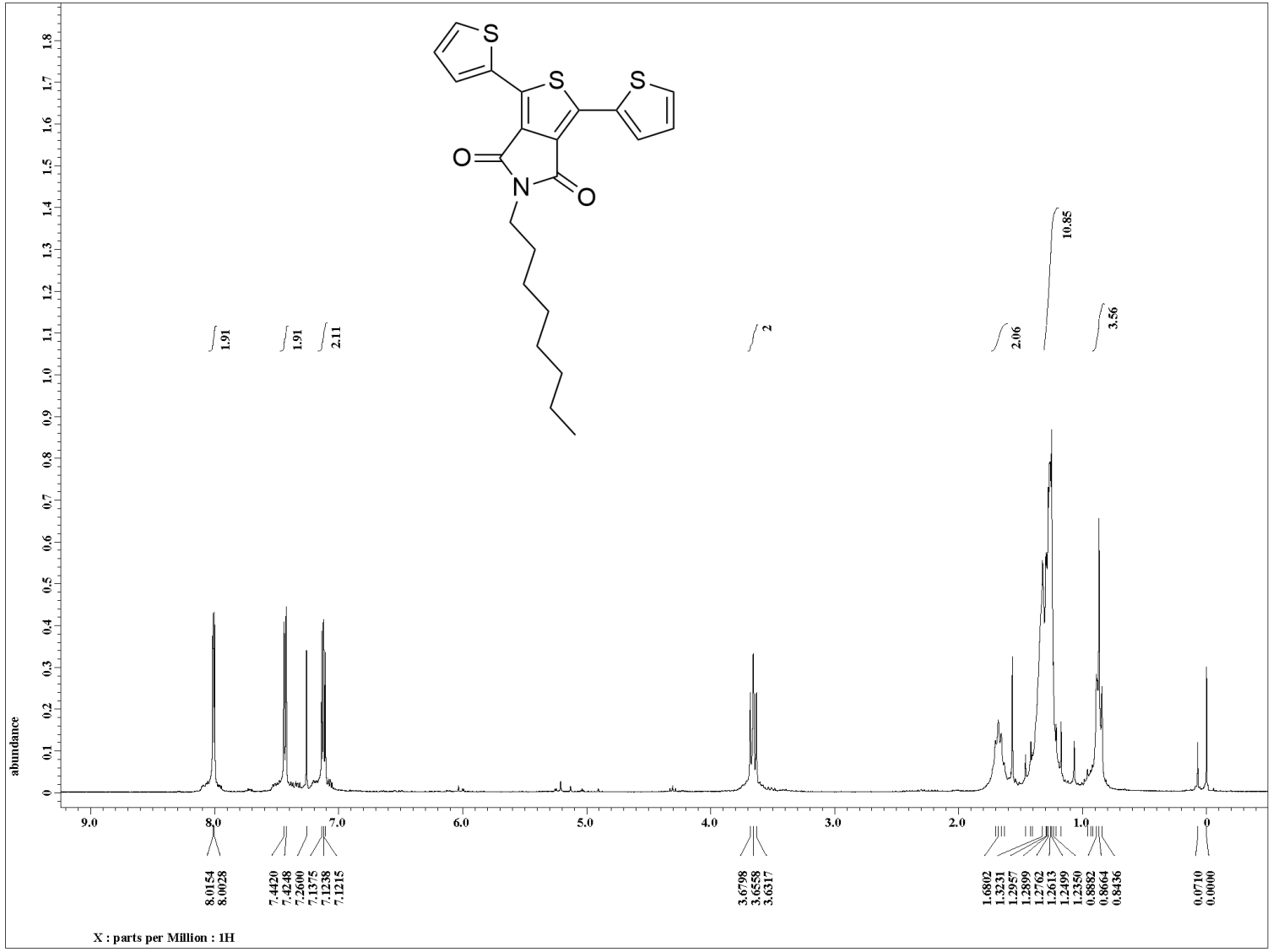


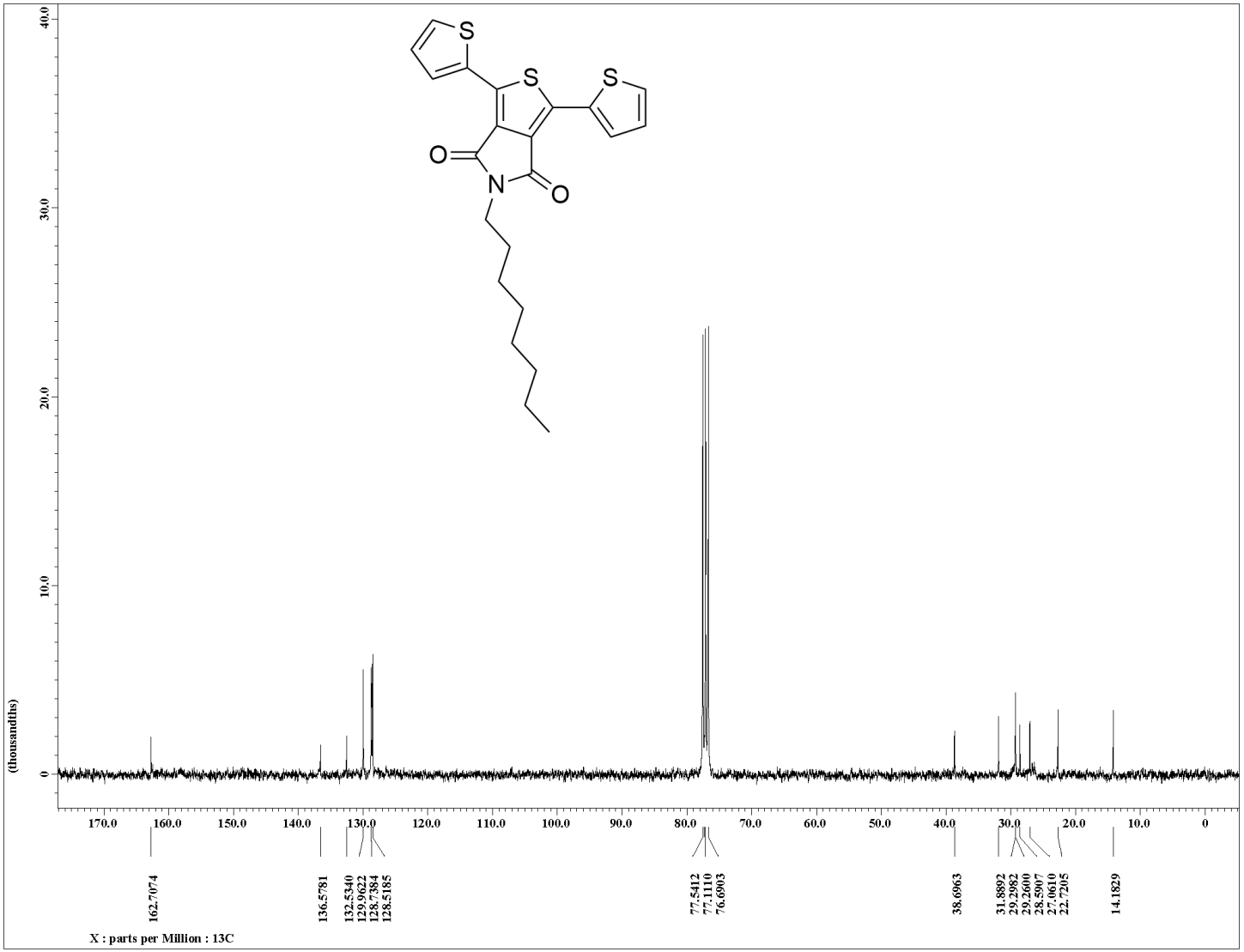
^{1}H NMR for compound **4a**



^{13}C NMR for compound **4a**



^{1}H NMR for compound **4b**



^{13}C NMR for compound **4b**