SUPPORTING INFORMATION

Design of hydrazide-bearing HDACIs based on panobinostat and their p53 and FLT3-ITD dependency in anti-leukemia activity

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[5]Department of Cellular and Molecular Pharmacology & Experimental Therapeutics, Medical University of South Carolina, Charleston, SC29425, USA

[6]Section of Hematology, Department of Internal Medicine and Yale Cancer Center, Yale University School of Medicine, New Haven, CT 06511, USA.

Contents

Inhibition curves and ratios for representative compounds

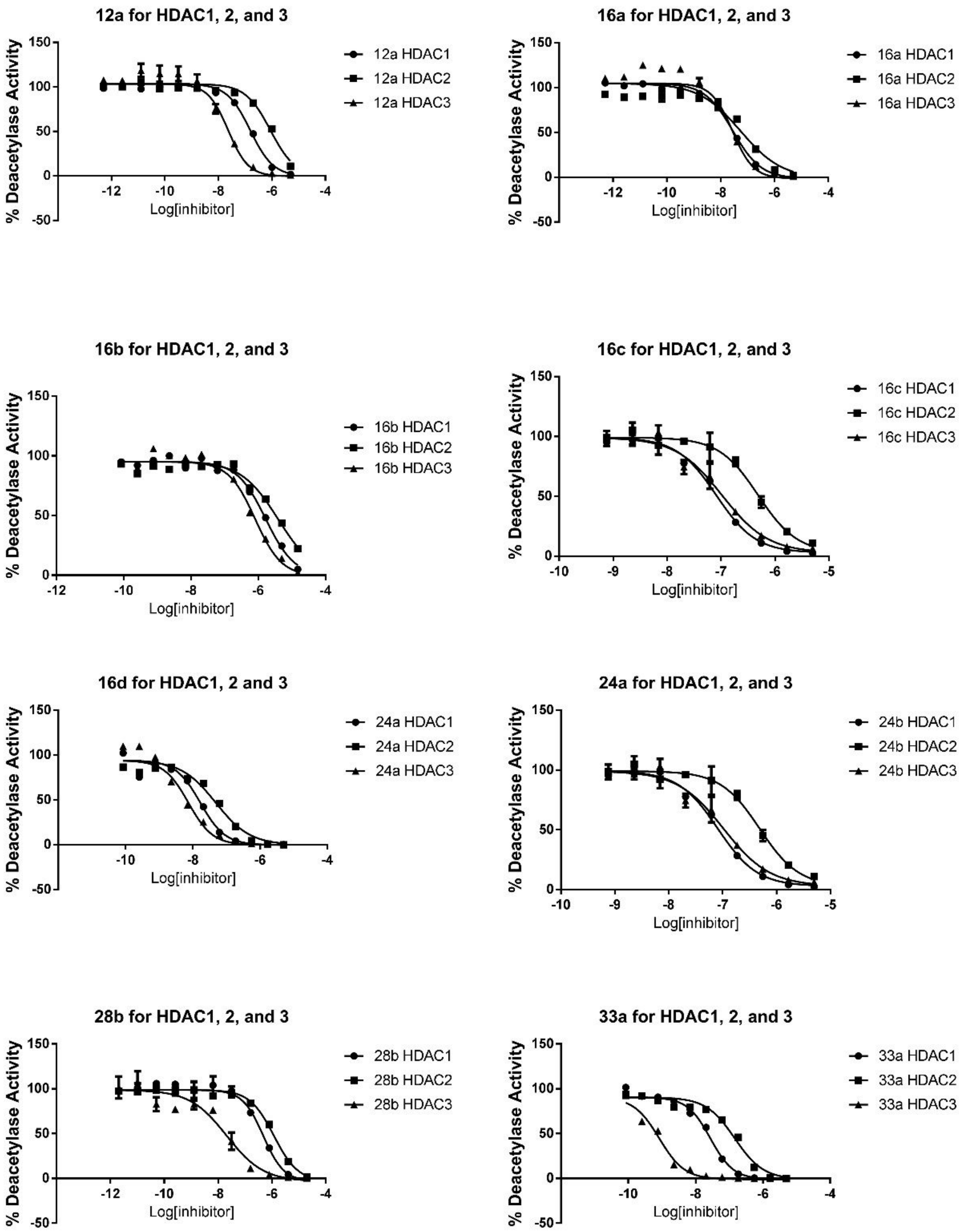


Figure S1. IC_{50} curves of representative compounds against HDAC1, 2, and 3.

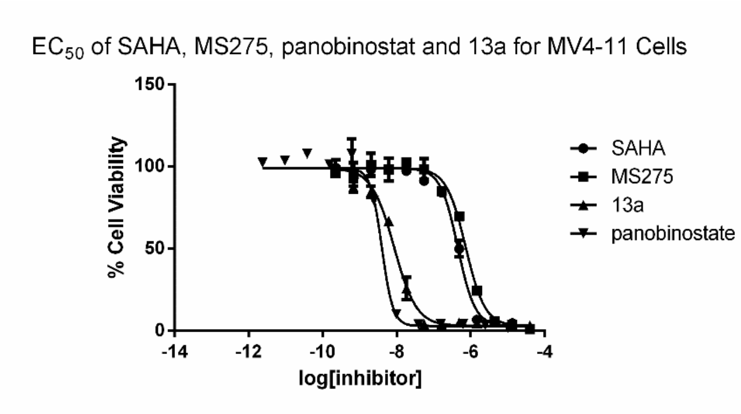


Figure S2. EC_{50} curves of SAHA, MS275, panobinostat and 13a for MV4-11 cells.

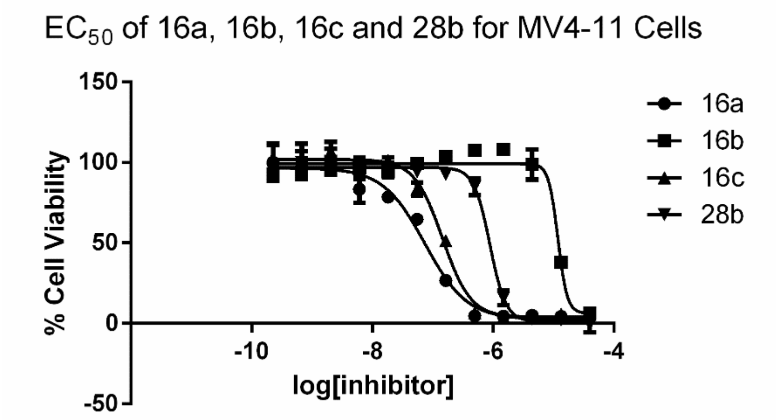


Figure S3. EC_{50} curves of 16a, 16b, 16c and 28b for MV4-11 cells.

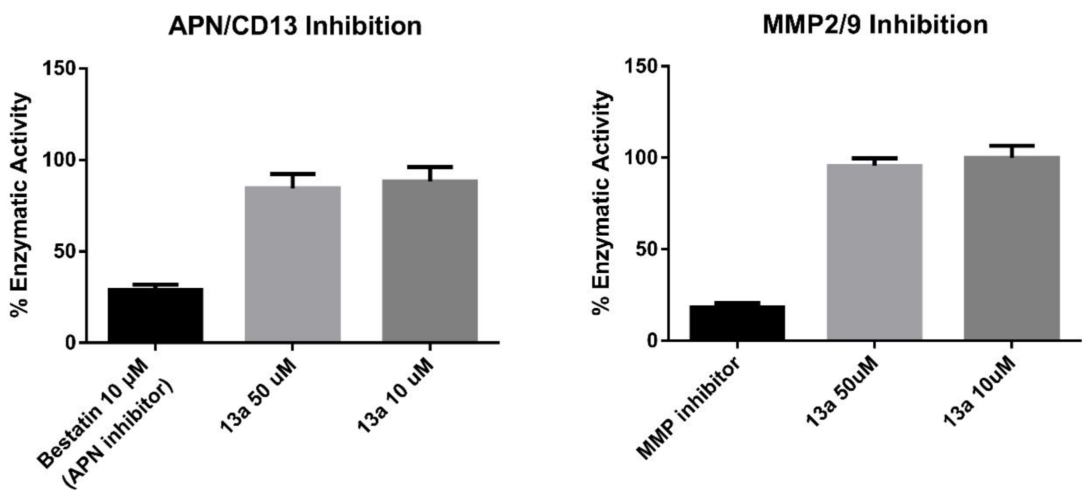


Figure S4. Inhibitory activity of 13a against APN/CD13 and MMP2/9.

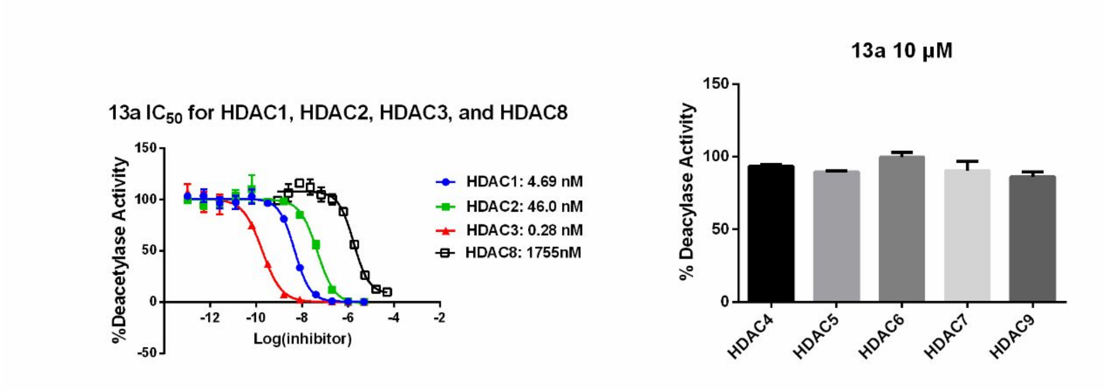


Figure S5. Inhibitory activity of 13a against HDAC1-9.

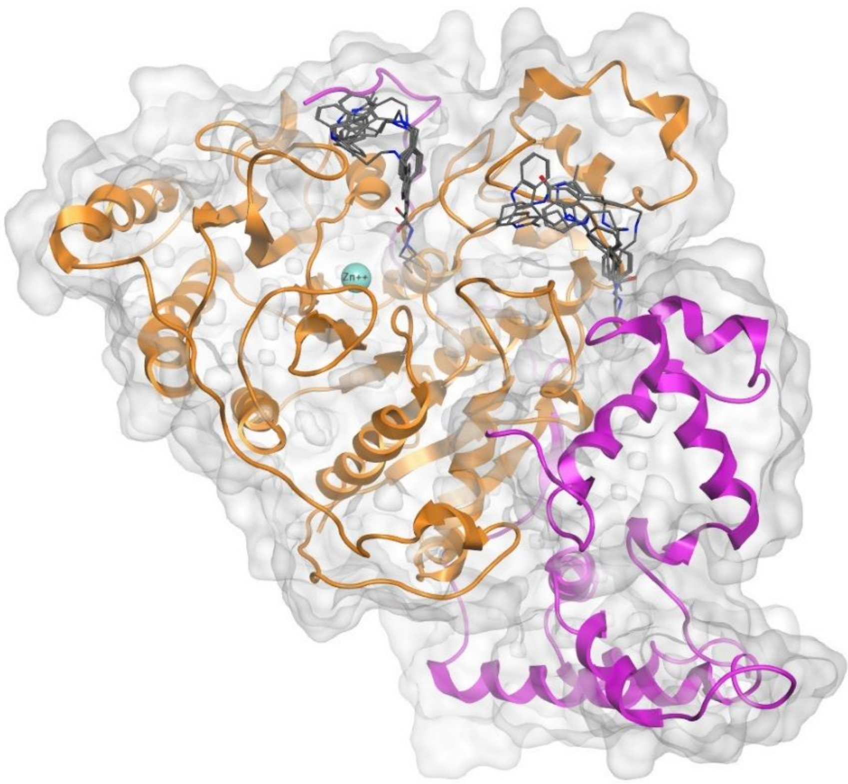


Figure S6. Binding mode of **13a** with catalytic site and allosteric site of HDAC1 in silico. Top 5 docking poses for each site are displayed. **13a** failed to chelate Zn metal in the catalytic site because of the long distance.

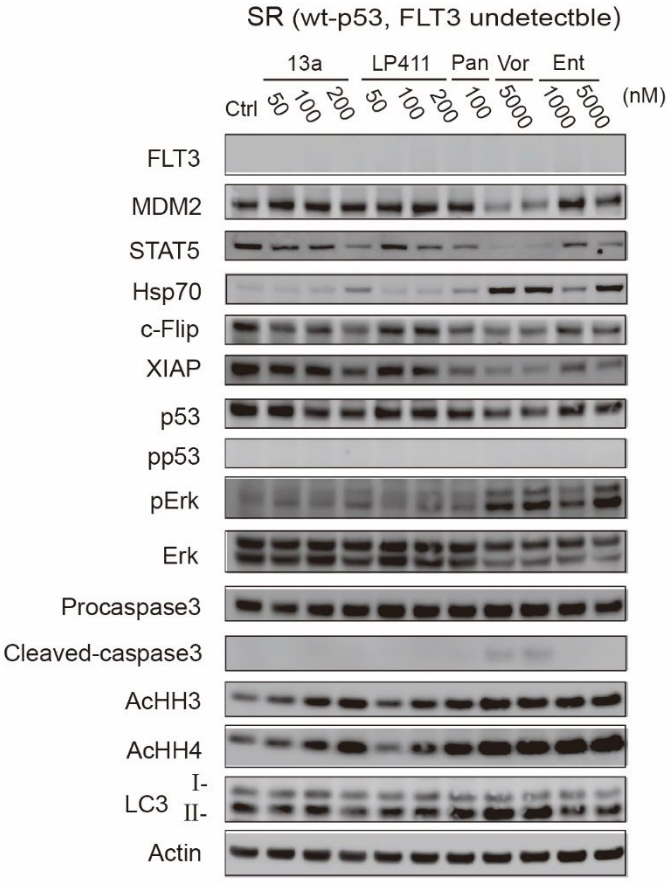


Figure S7. Treatment of **13a**, LP411, panobinostat (Pan), vorinostat (Vor) and entinostat (Ent) in wt-p53 SR cell line for 24 h.

Dose 13a (nM)	Dose 17AAG (nM)	Effect	Combination Index (CI)
9.87	59.0	0.279	1.68712
9.87	88.0	0.346	1.57667
9.87	133.0	0.572	1.03593
9.87	200.0	0.762	0.78417
9.87	300.0	0.968	0.28069

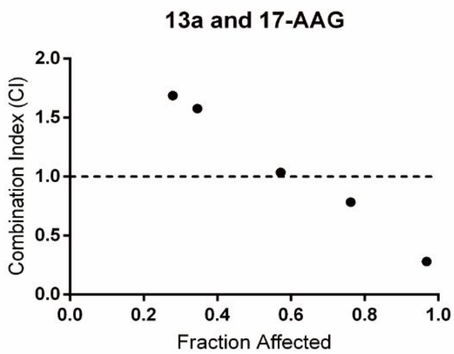
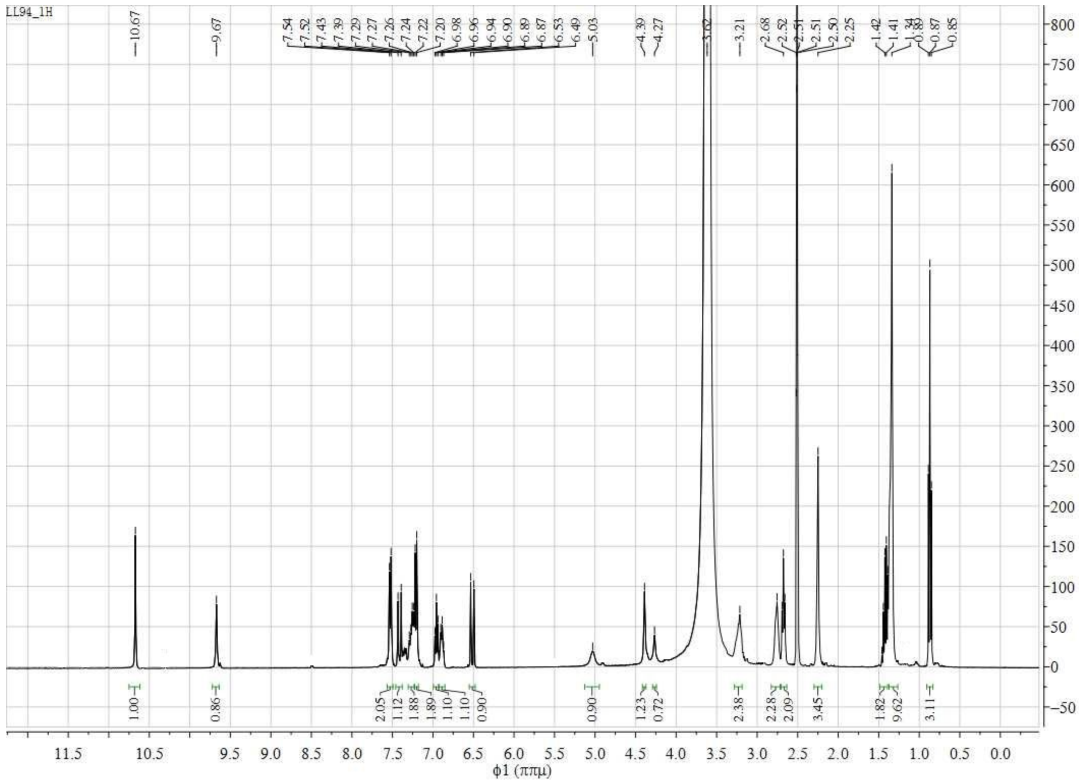


Figure S8. Combination Index (CI) for **13a** and 17-AAG after treatment for 48 h. Data is analysed by CompuSyn Software. CI < 1, = 1, and > 1 indicate synergism, additive effect, and antagonism, respectively.



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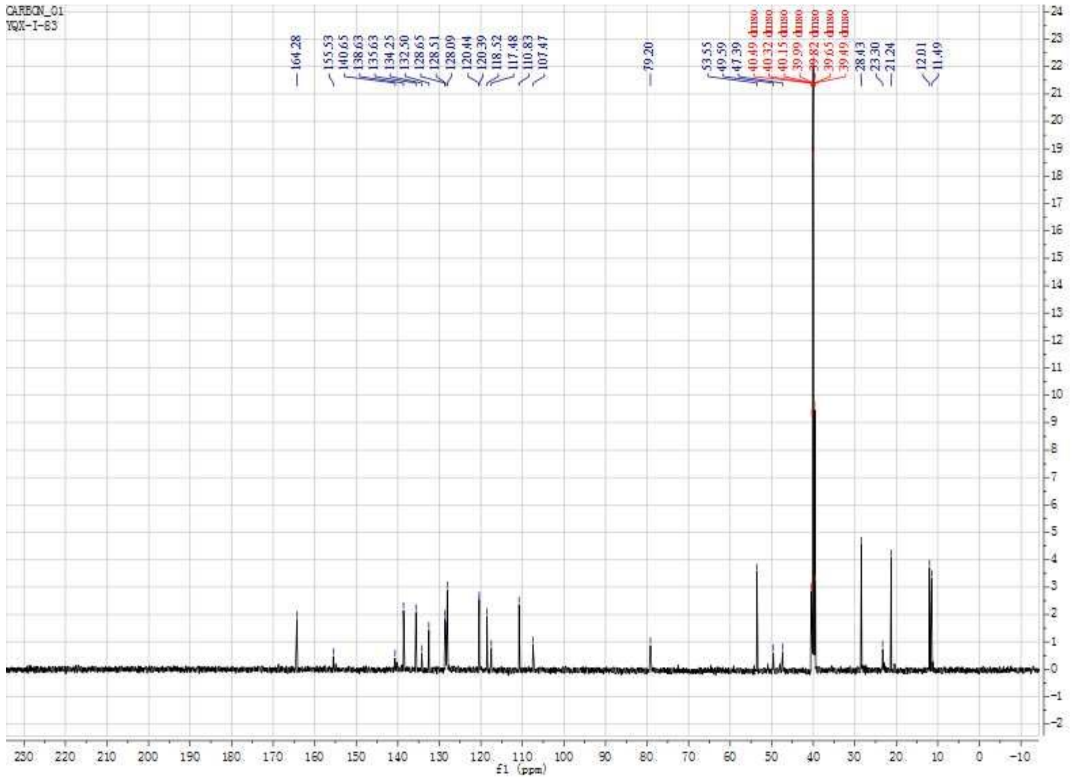

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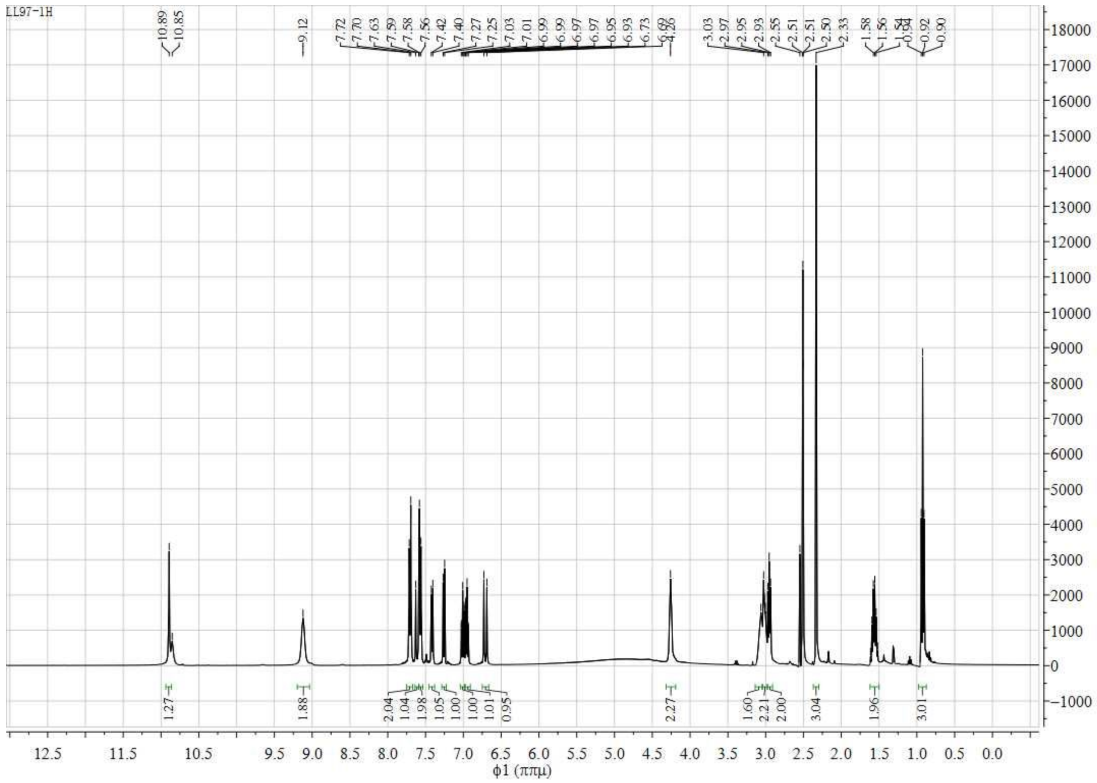

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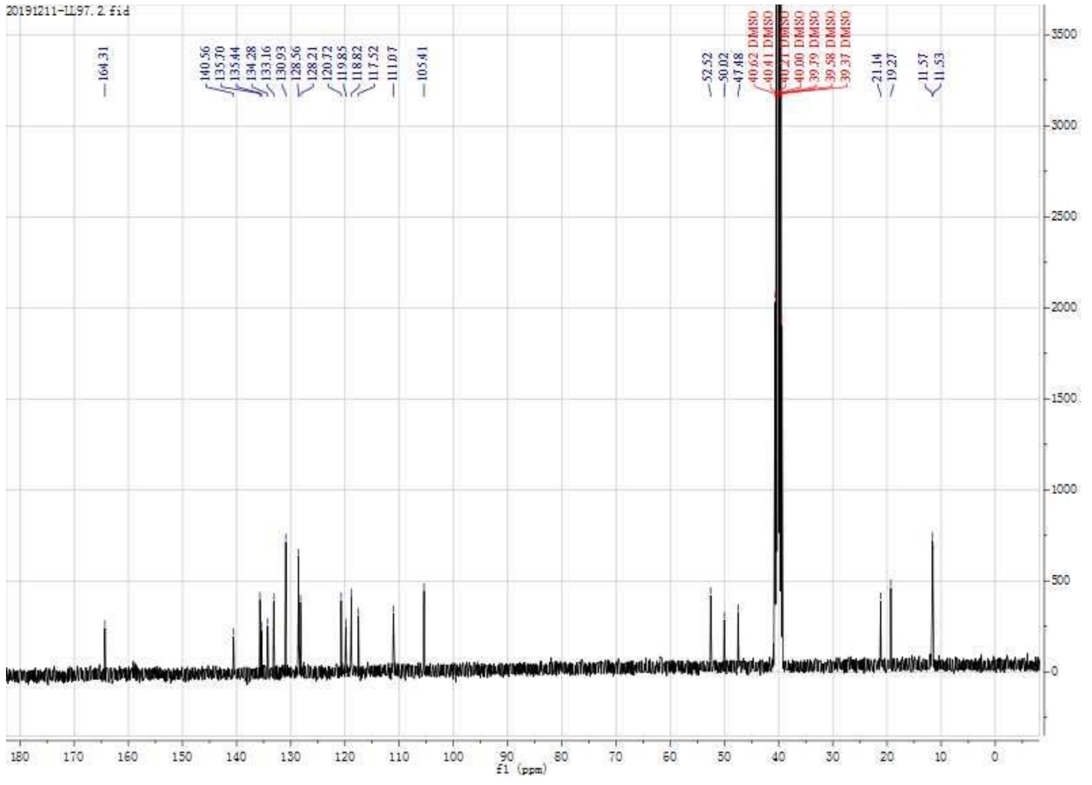

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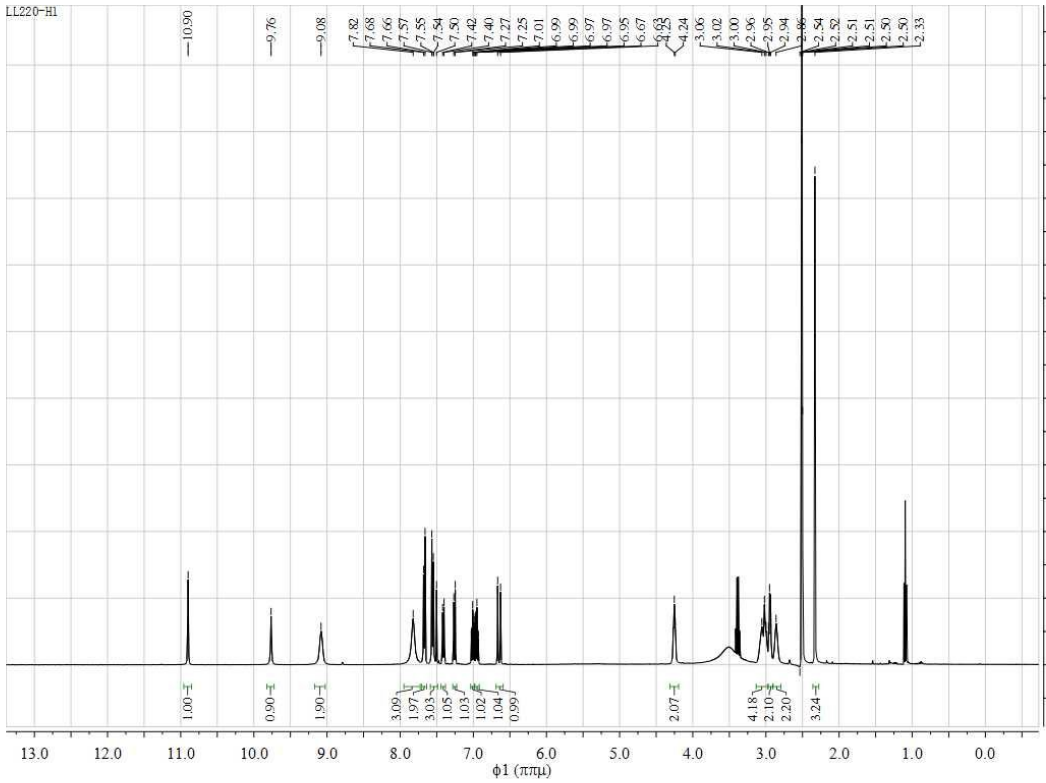

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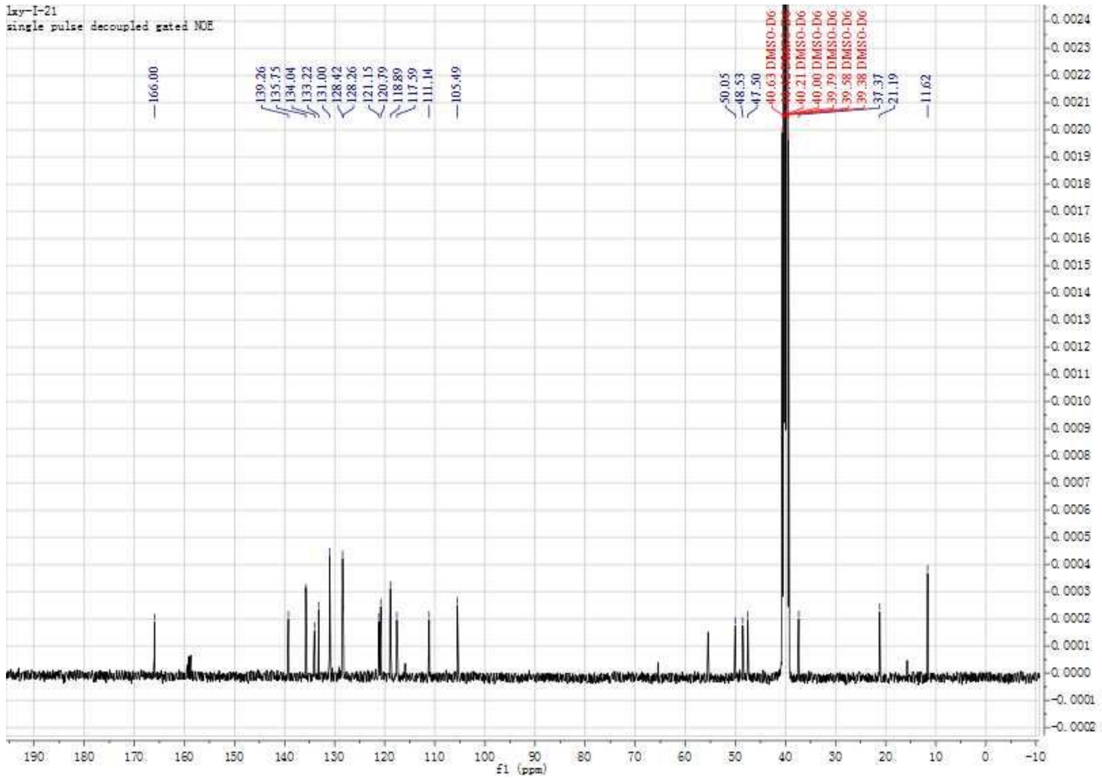

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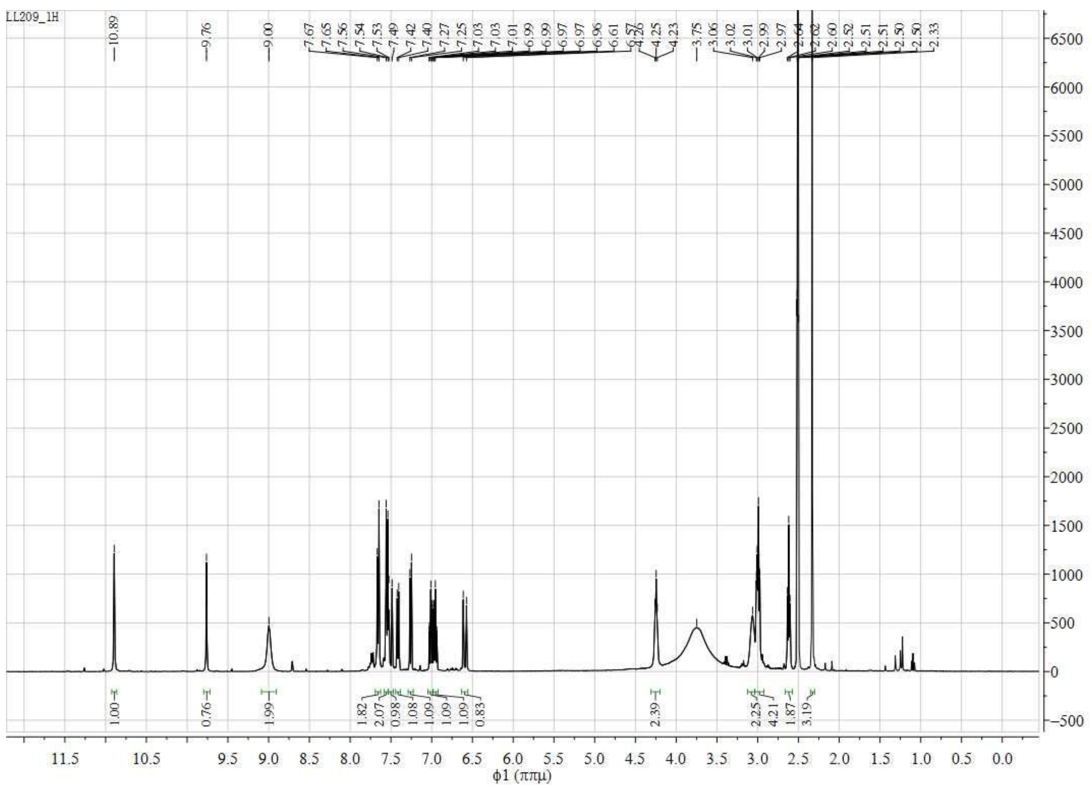

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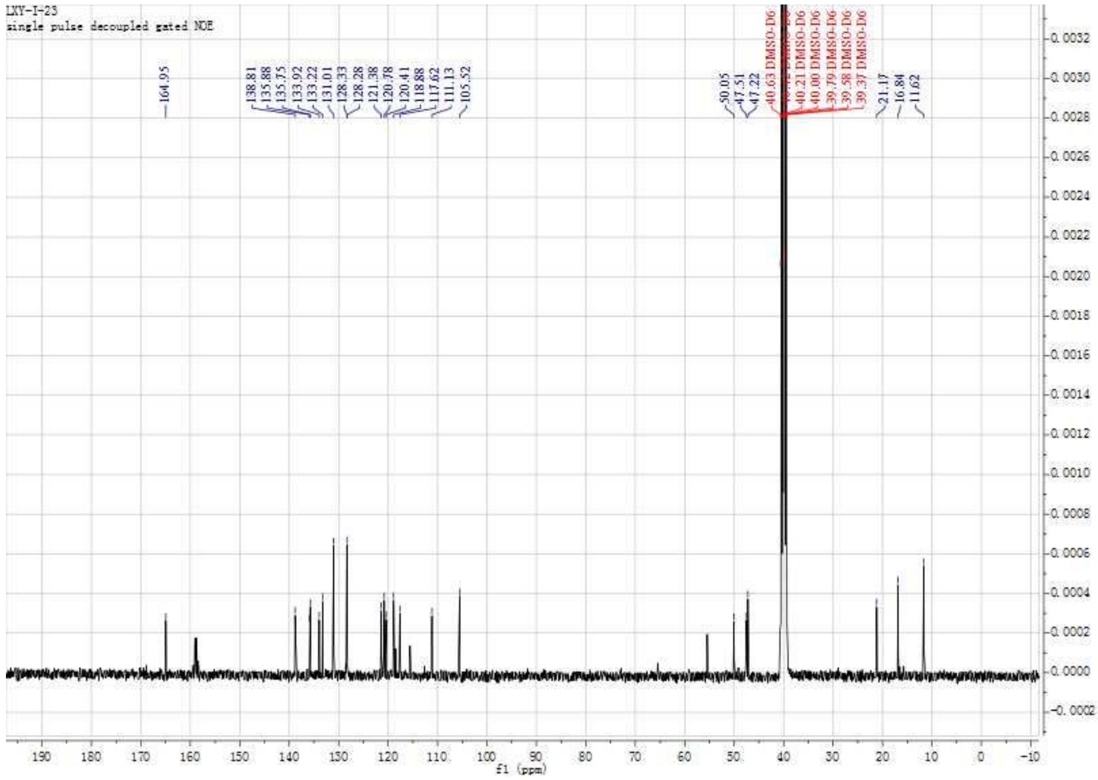

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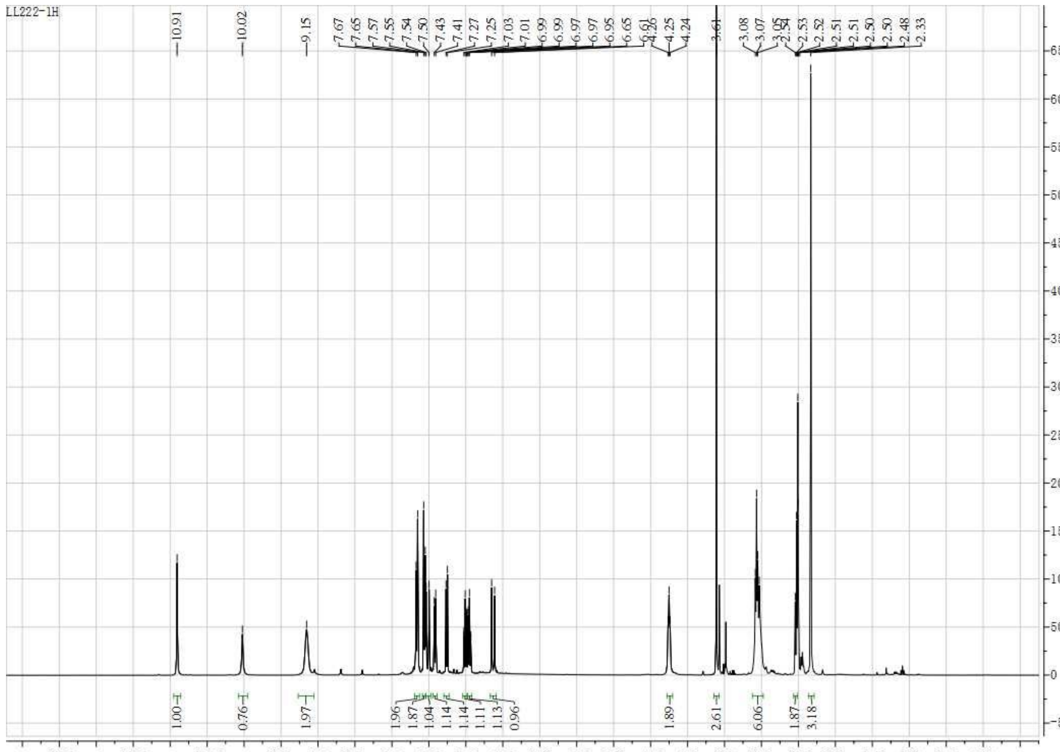

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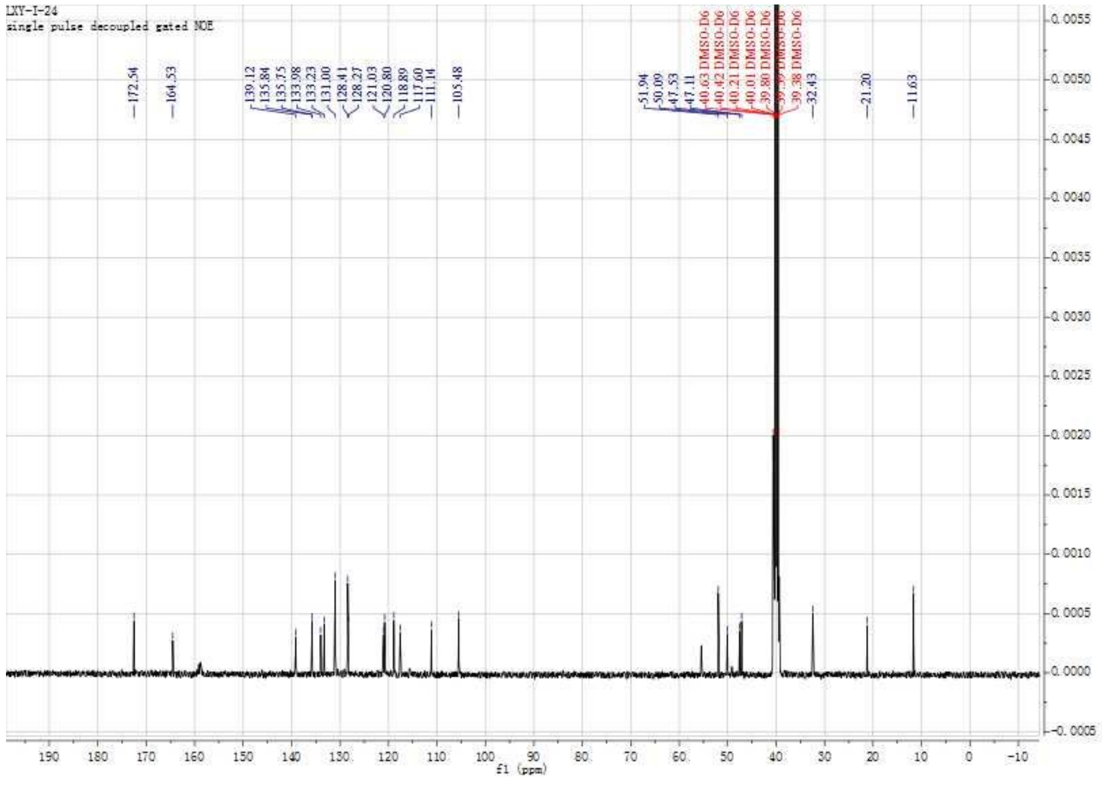

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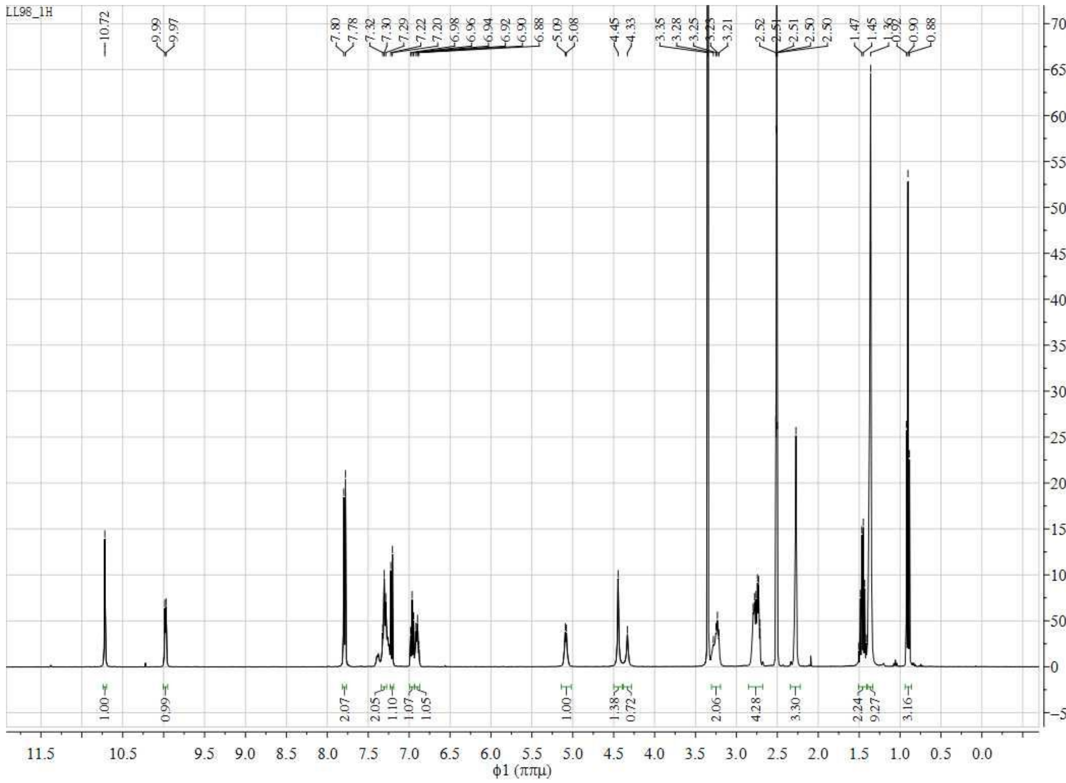

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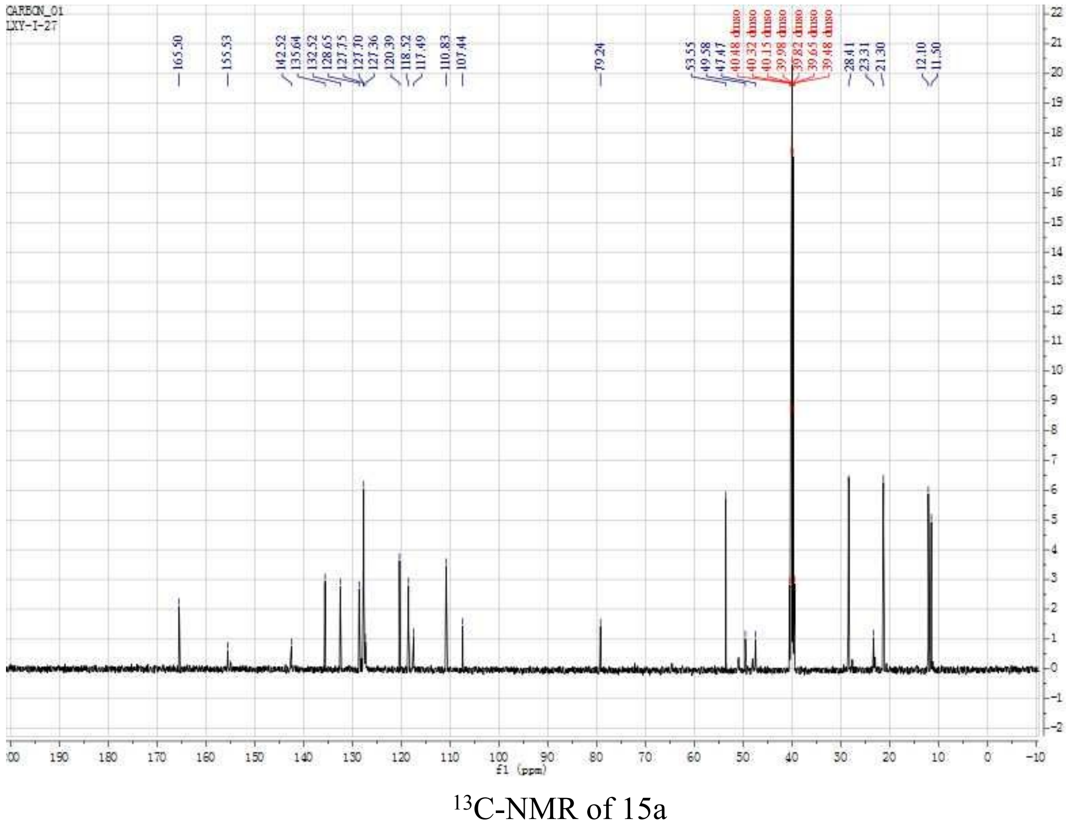

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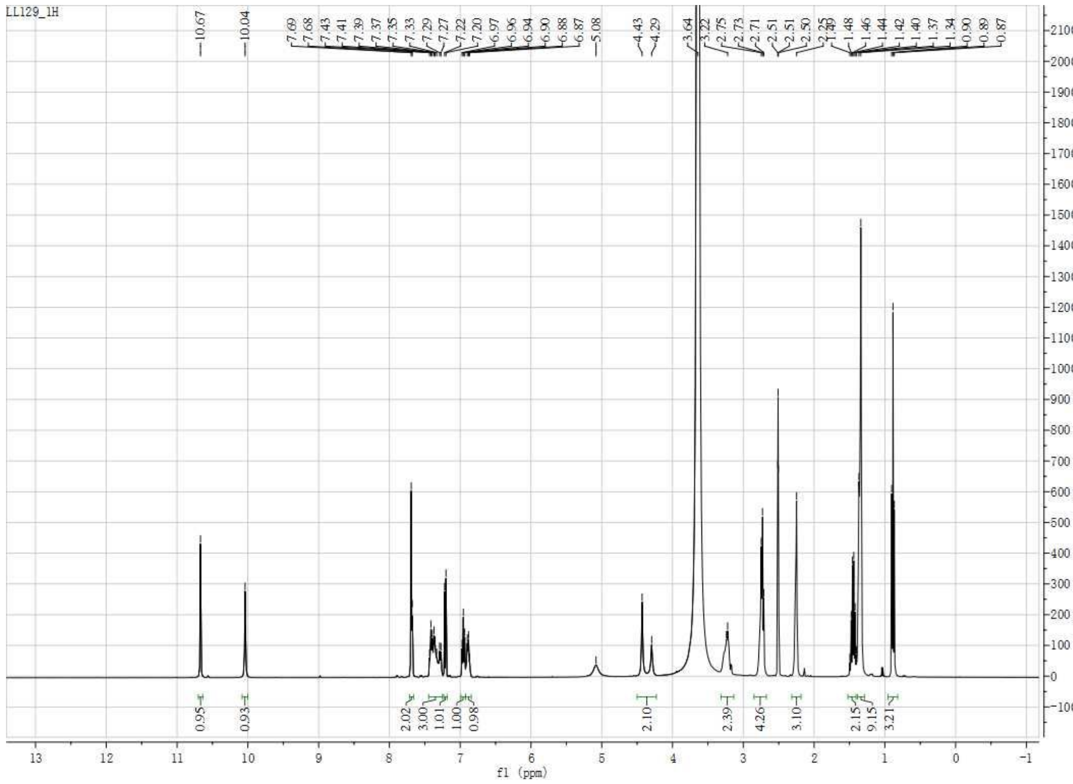

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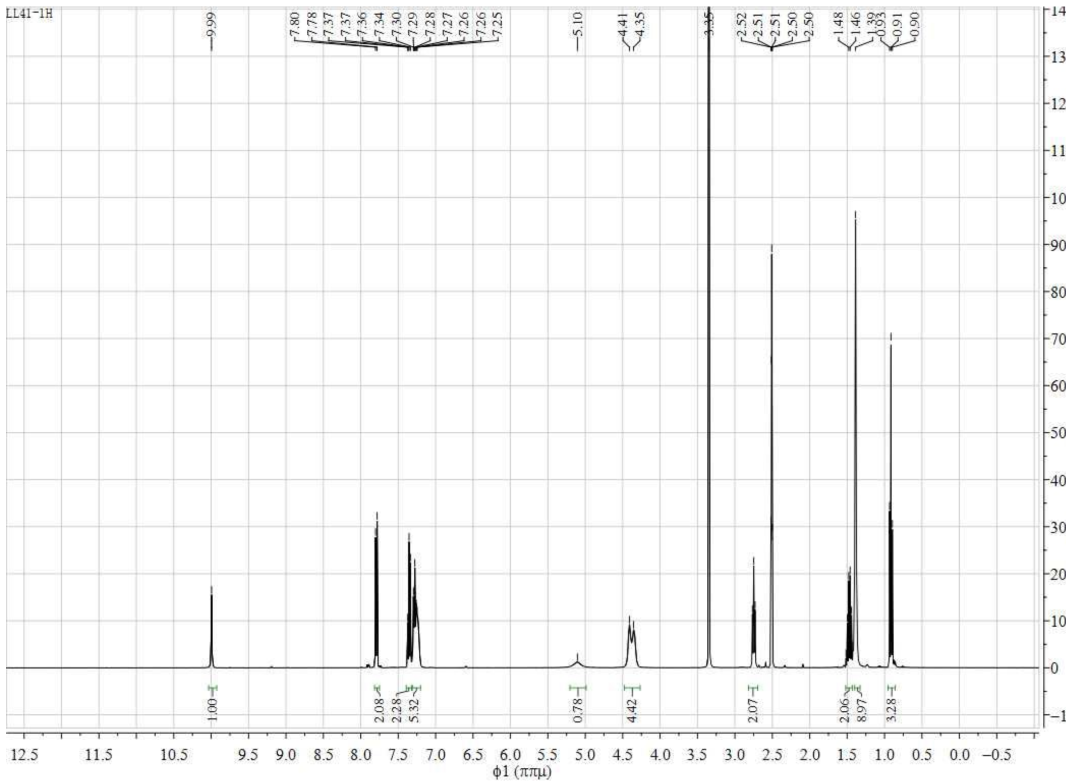

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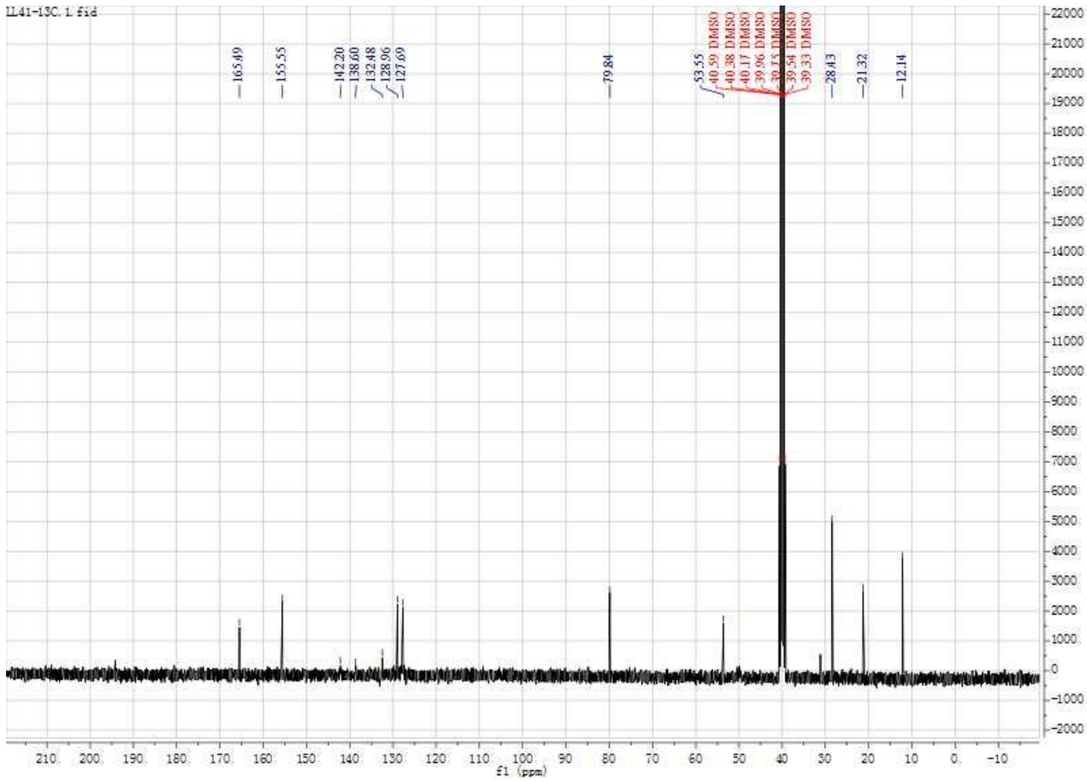

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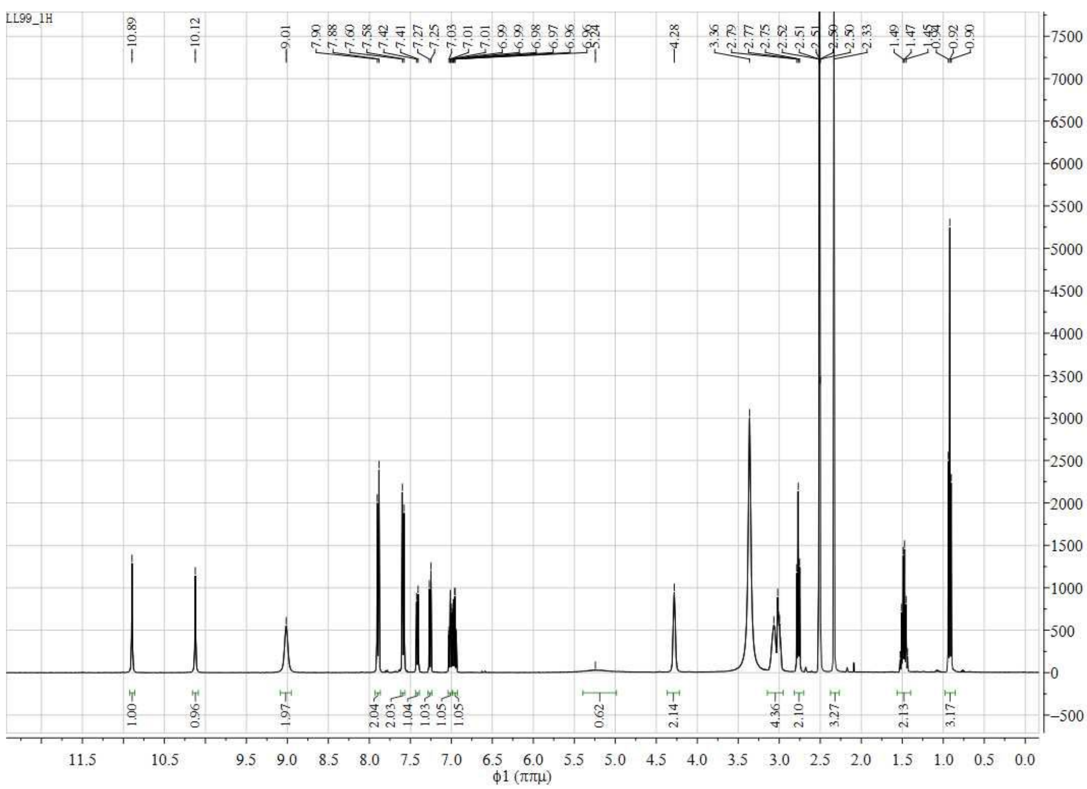

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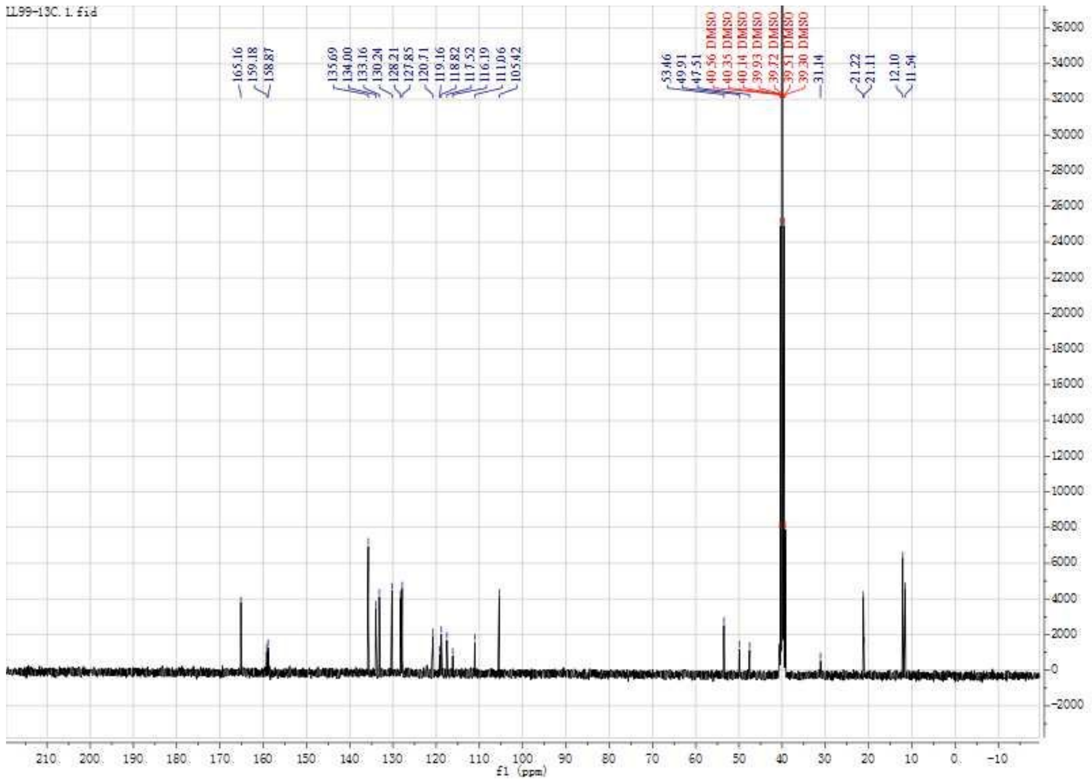

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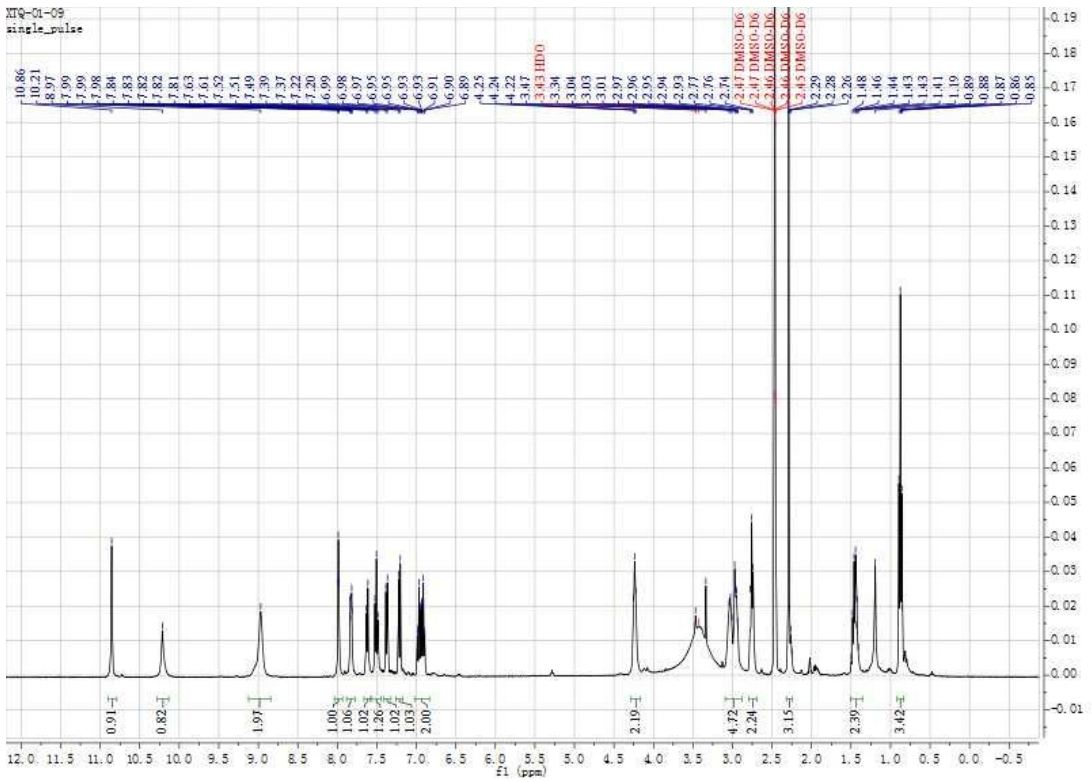

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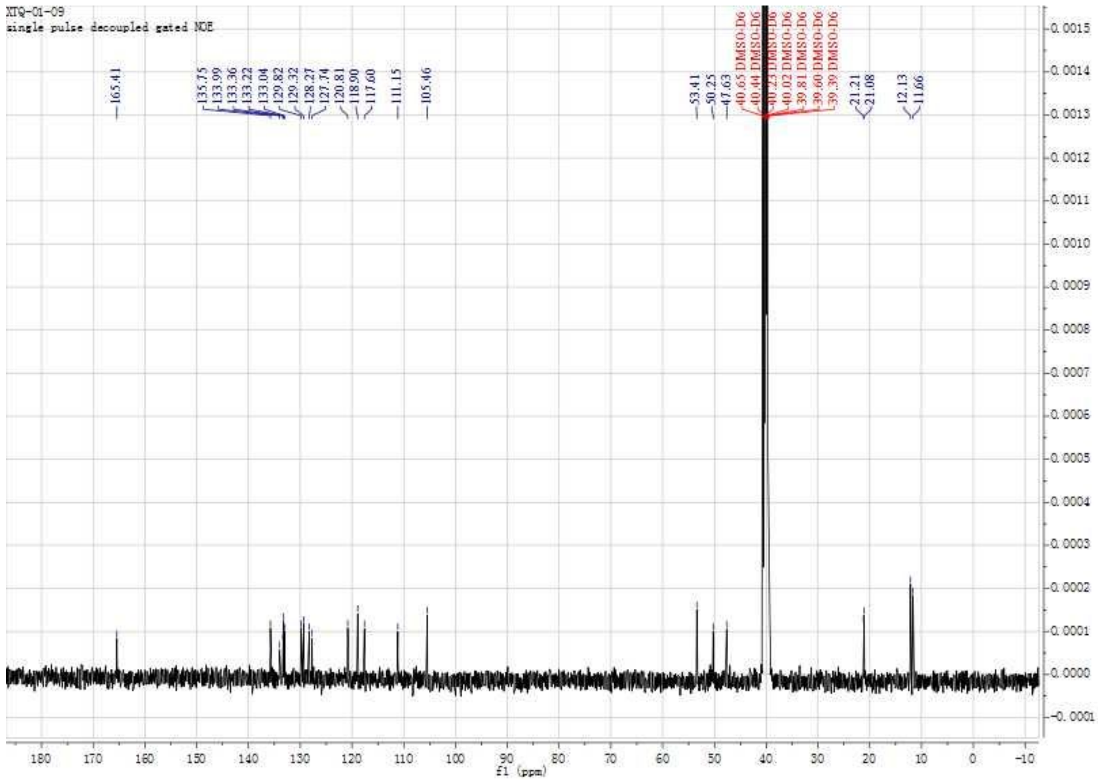

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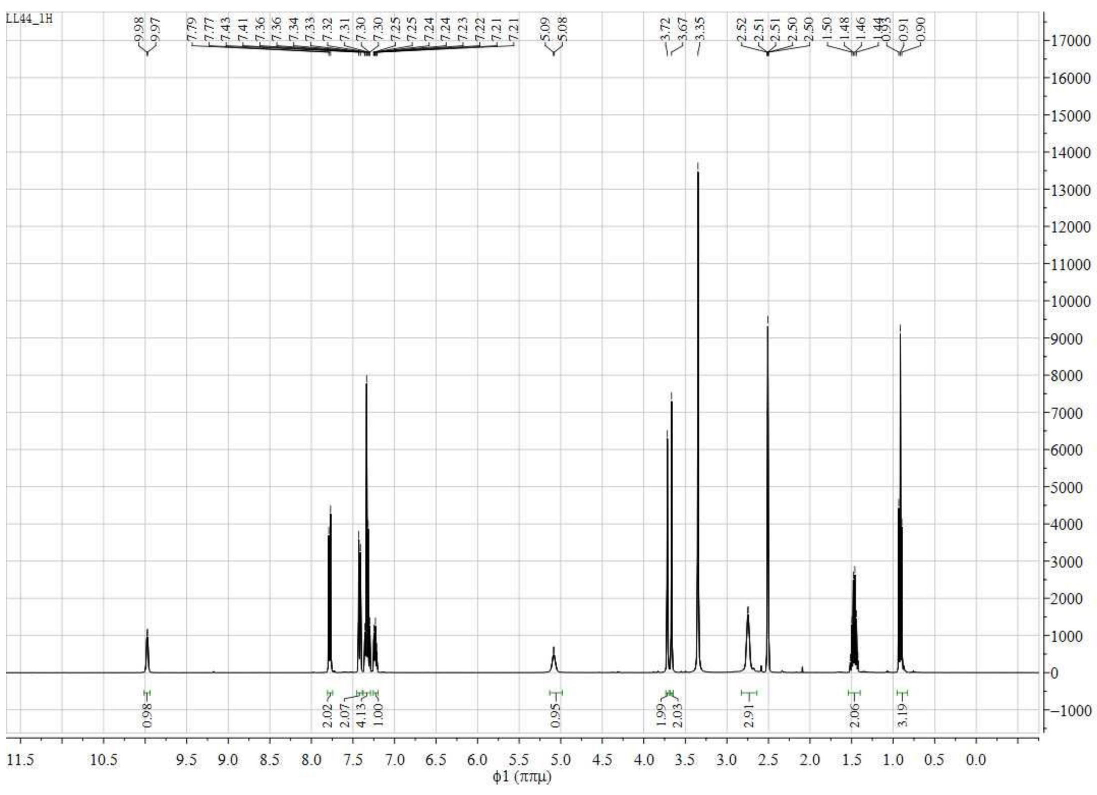

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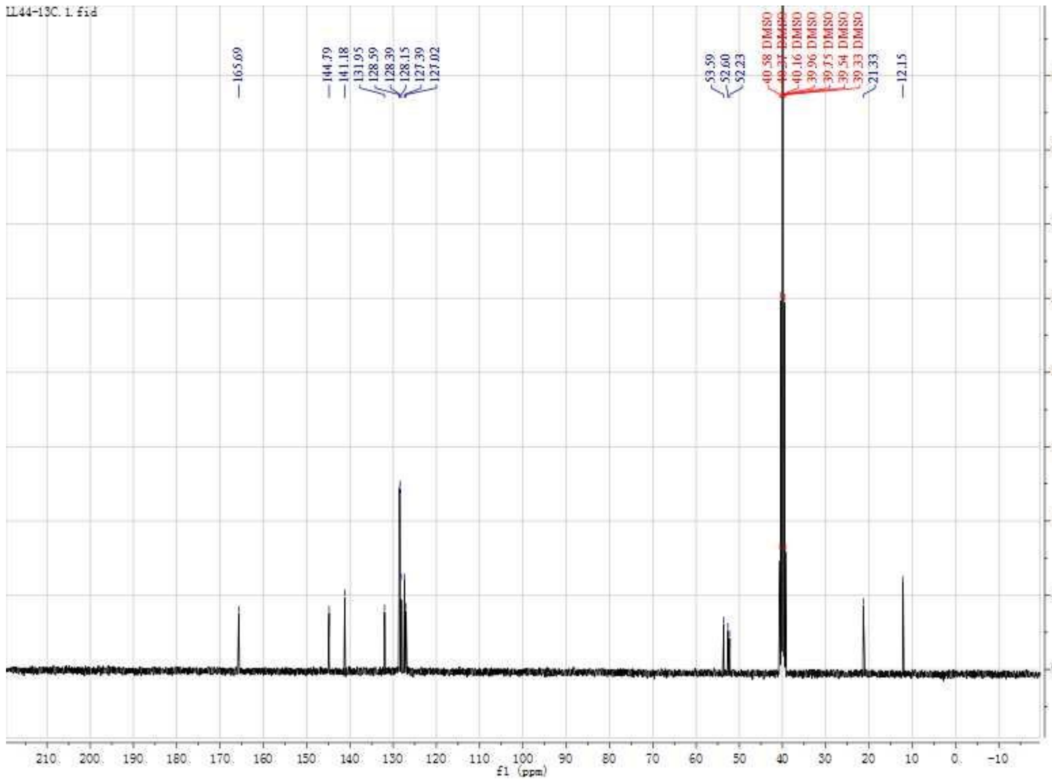

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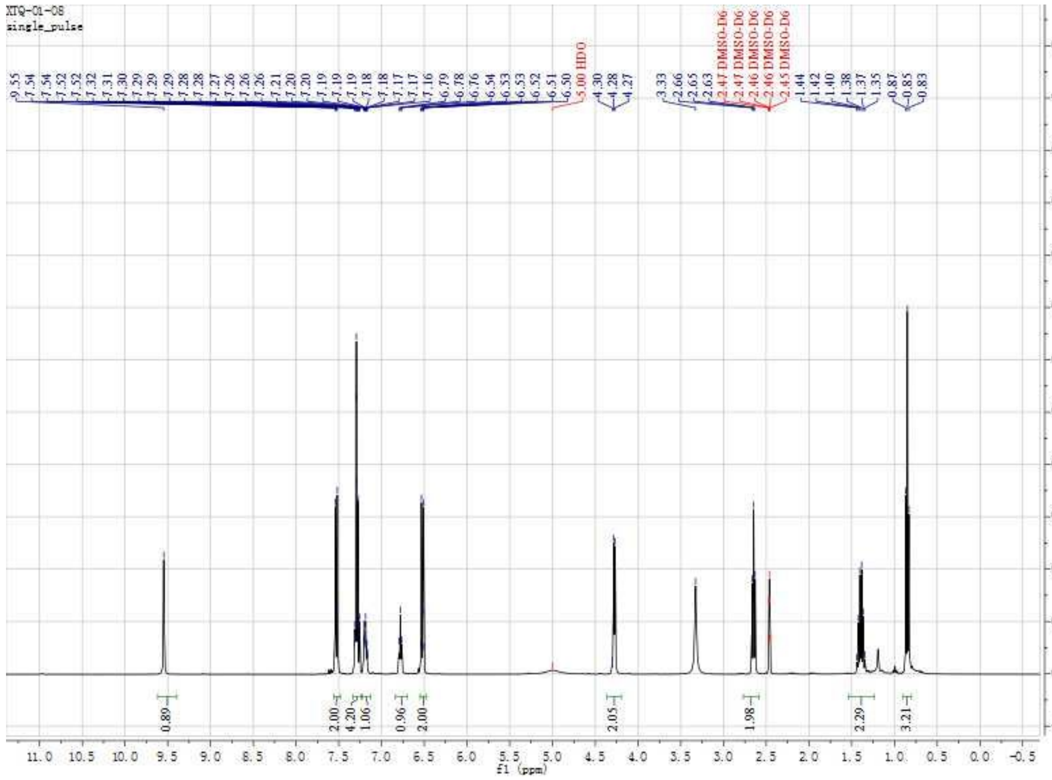

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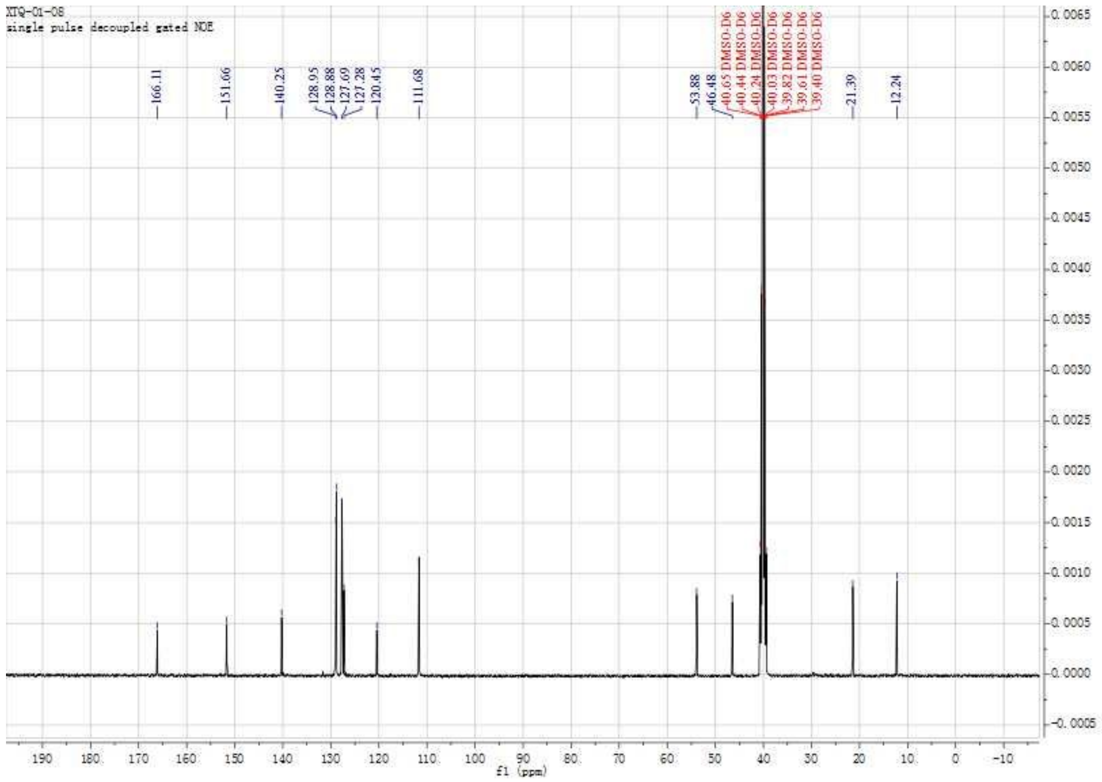

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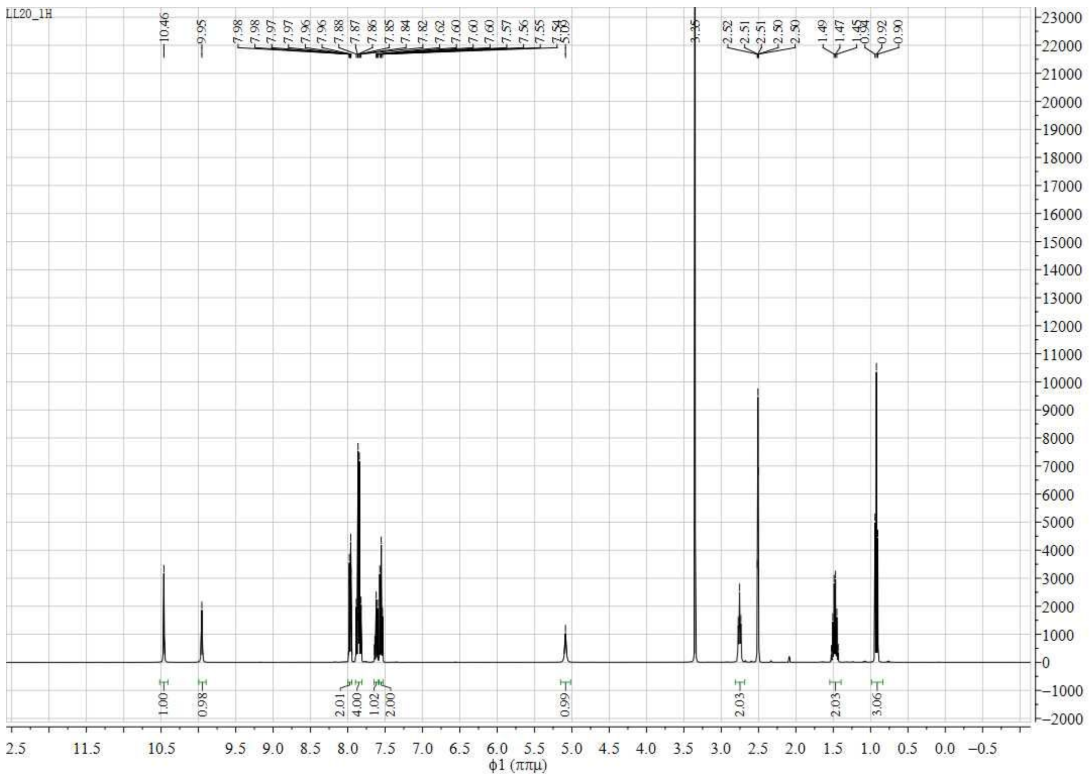

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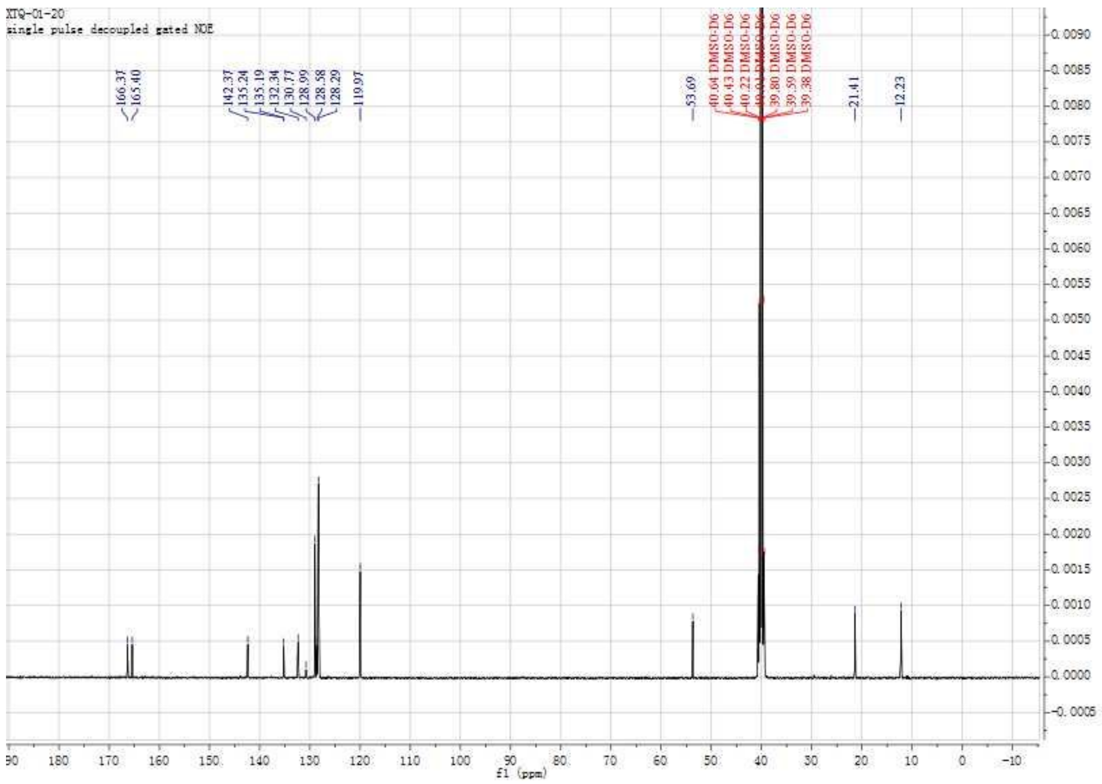

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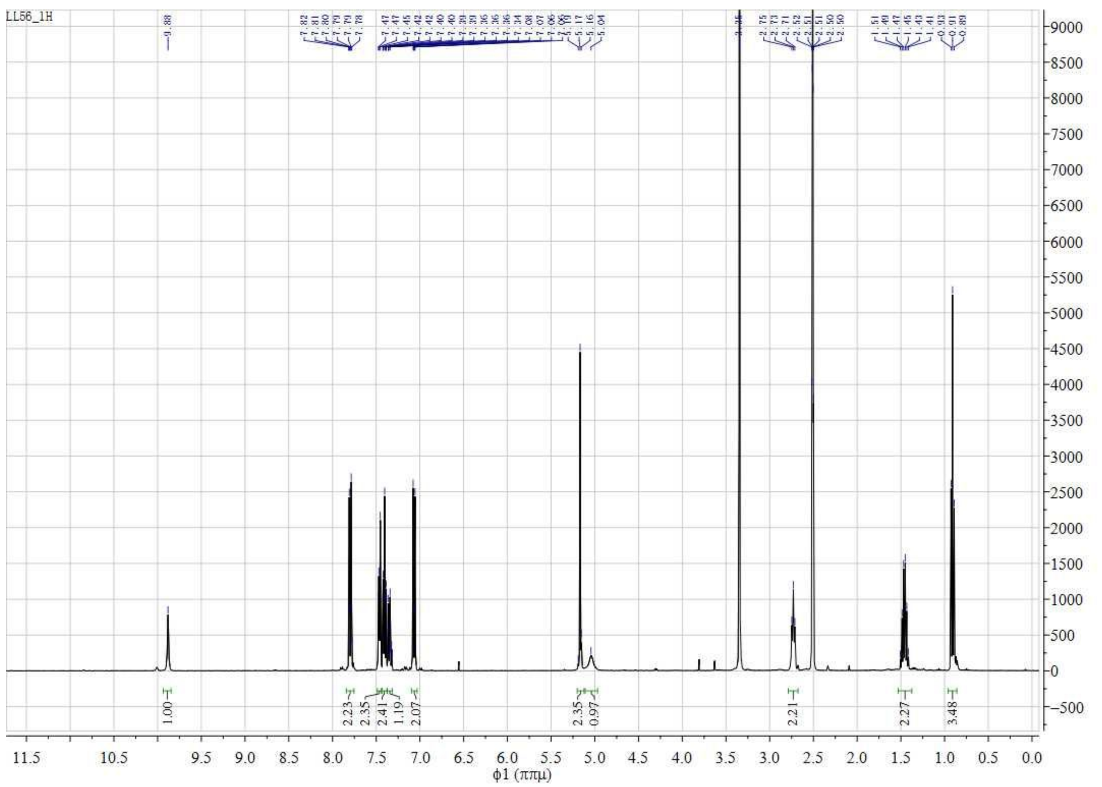

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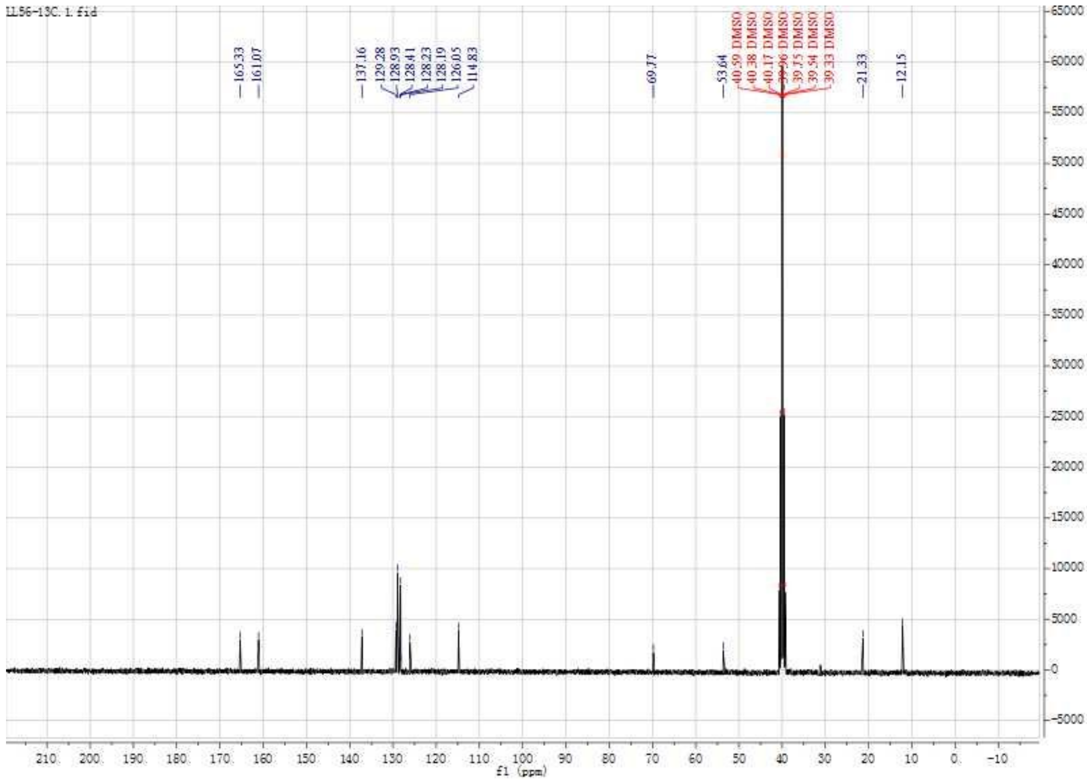

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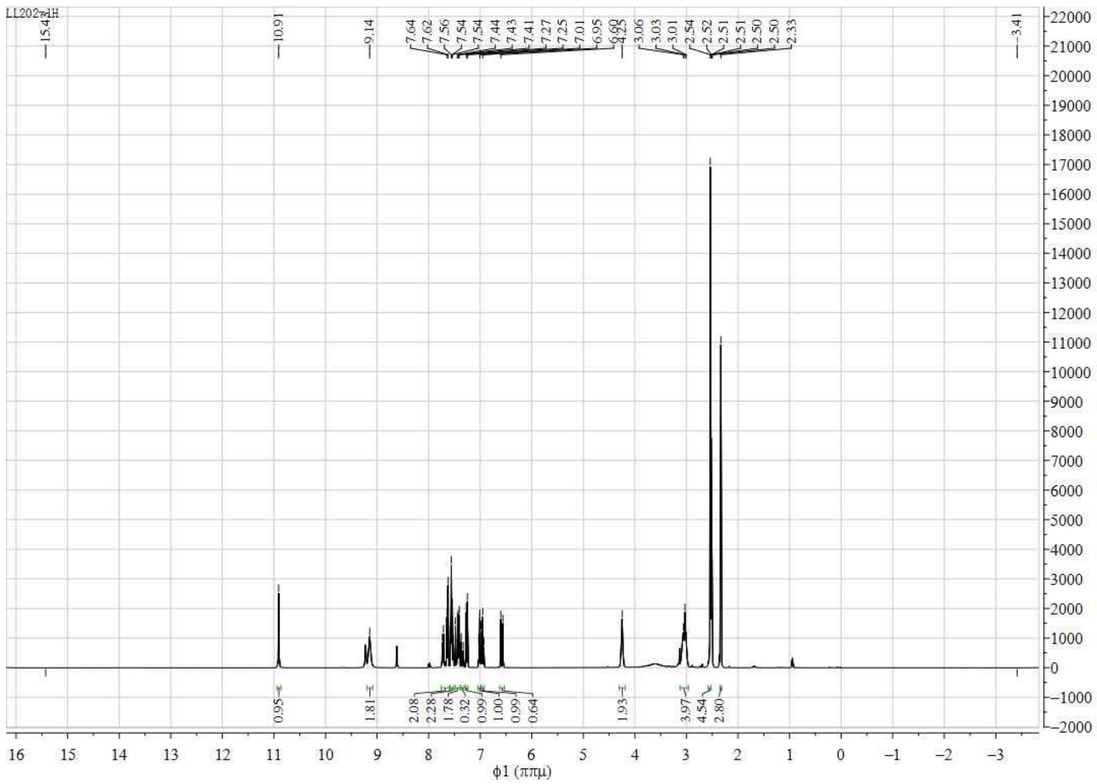

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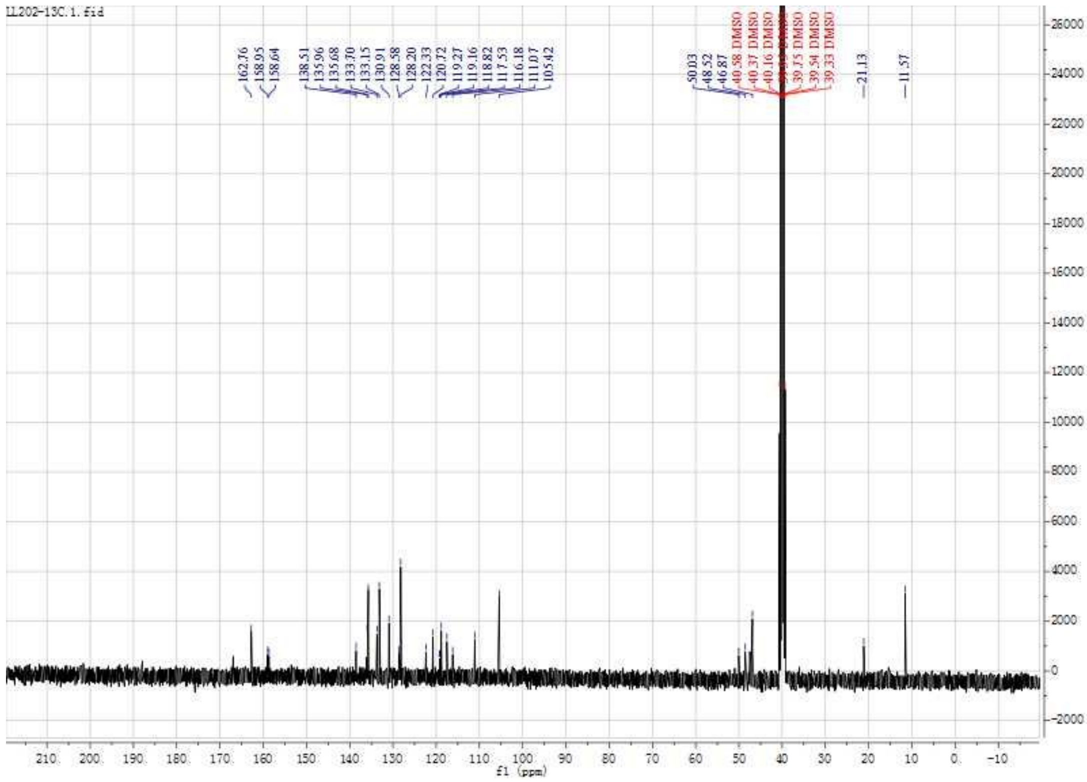

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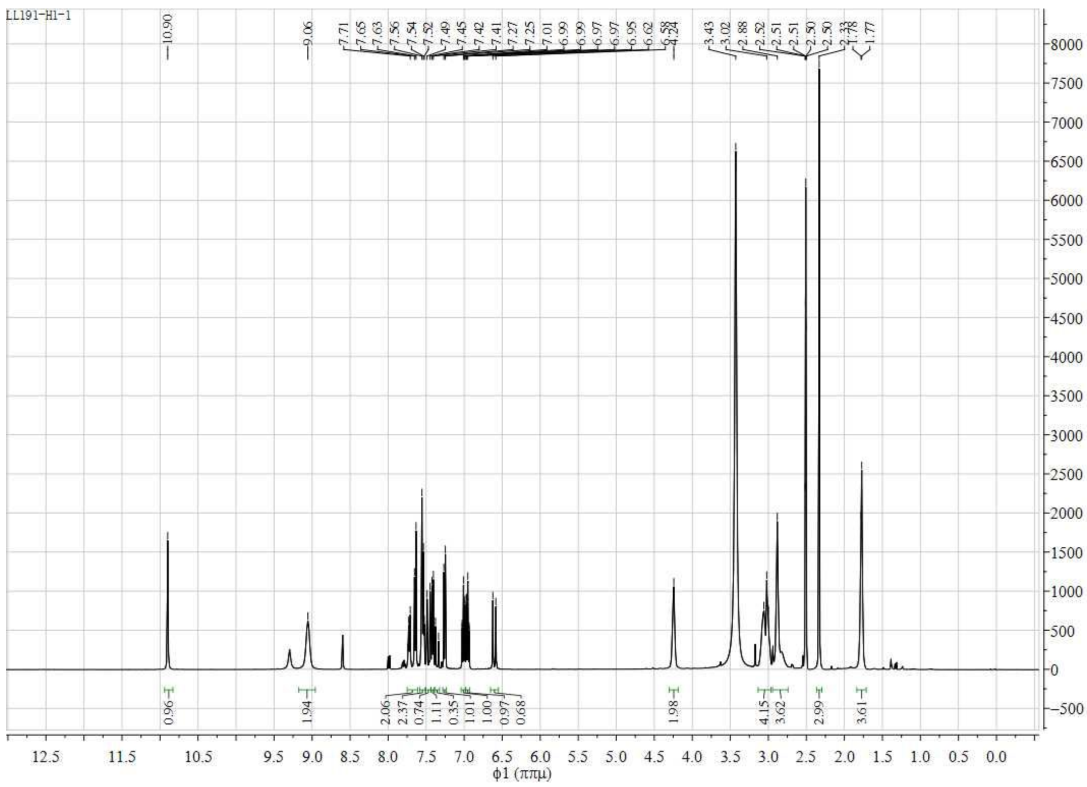

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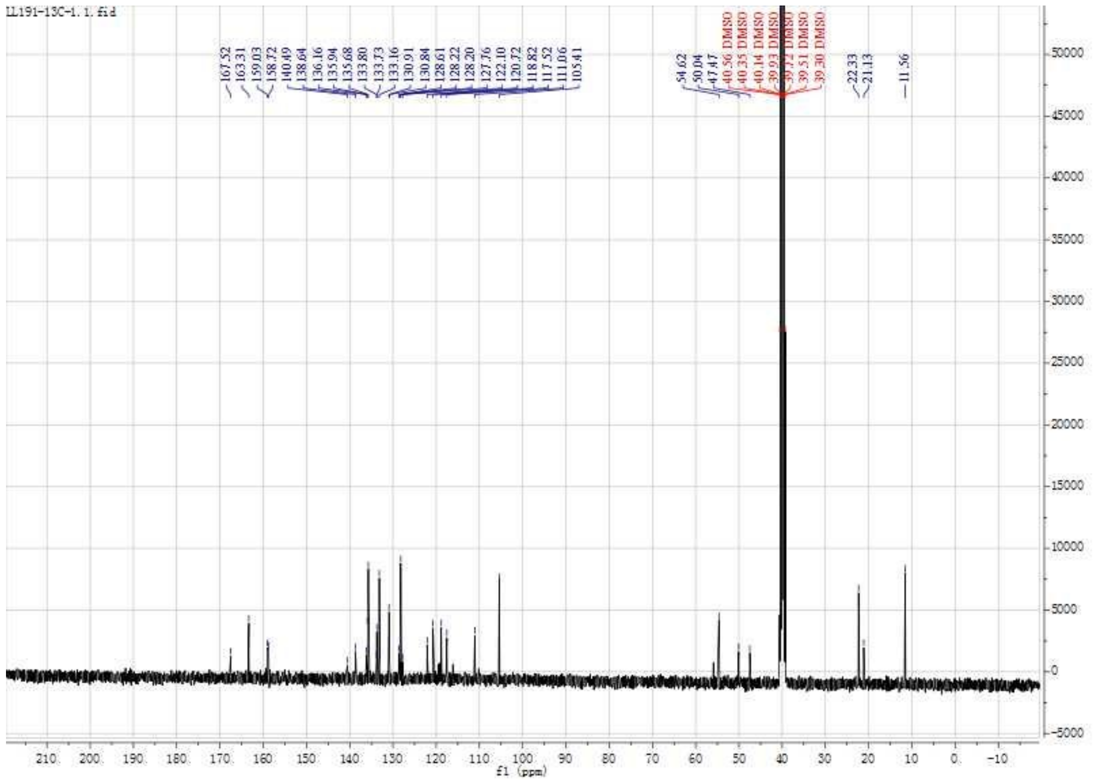

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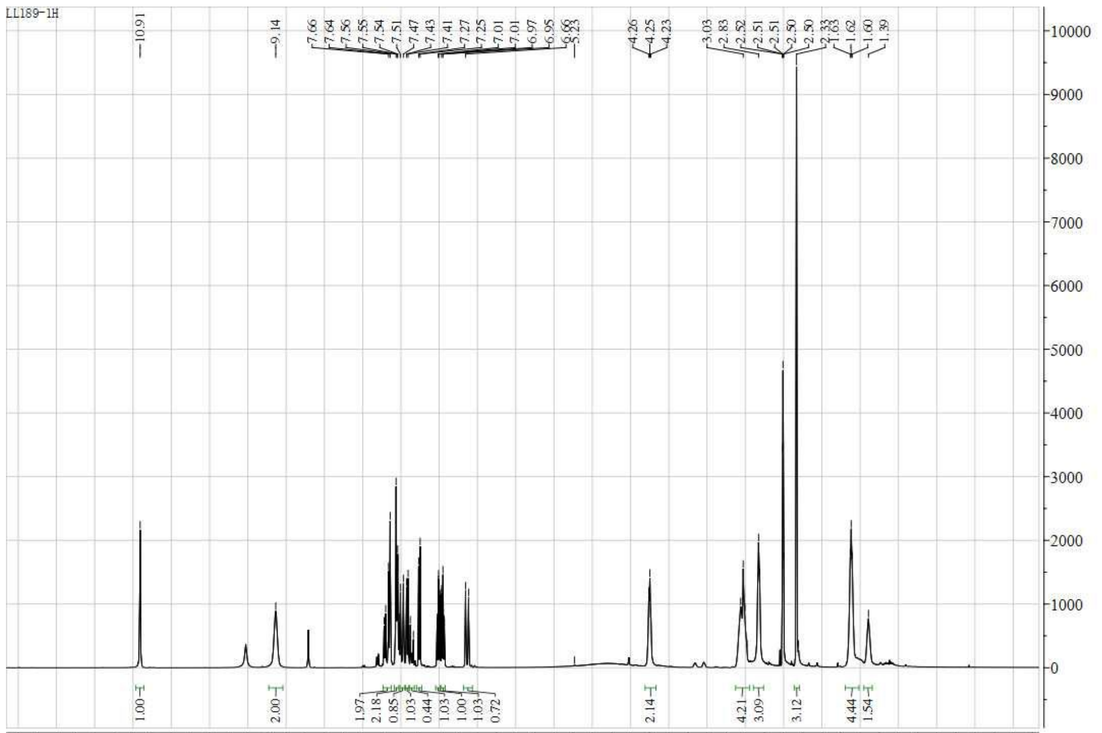

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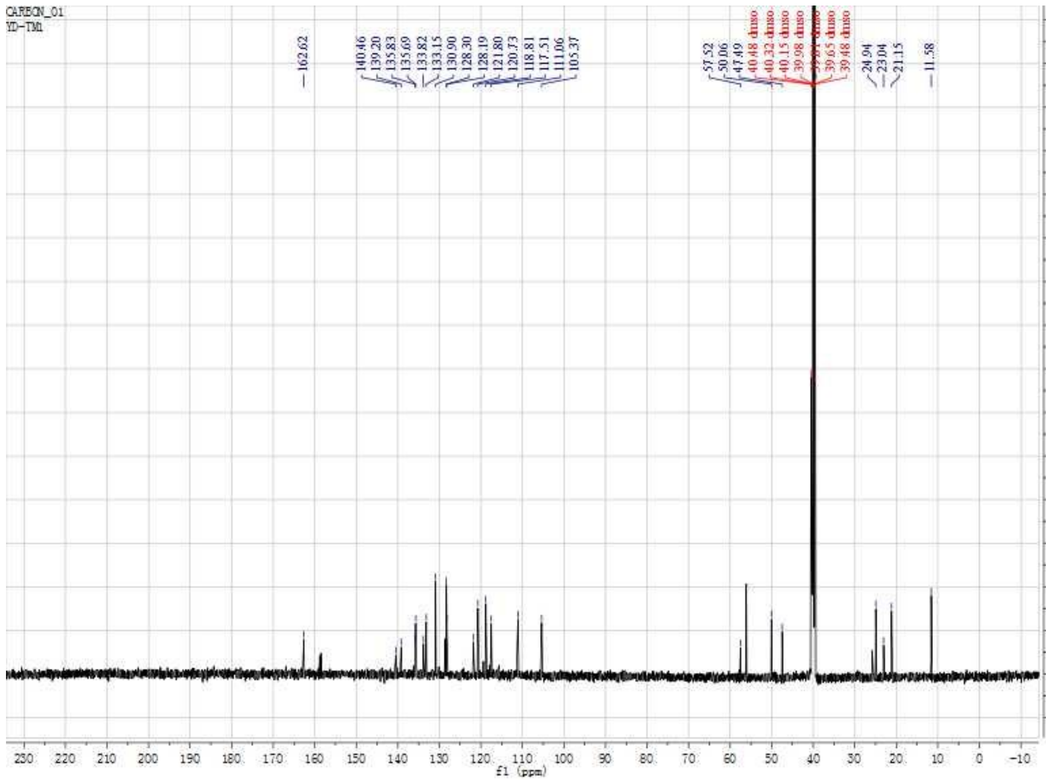

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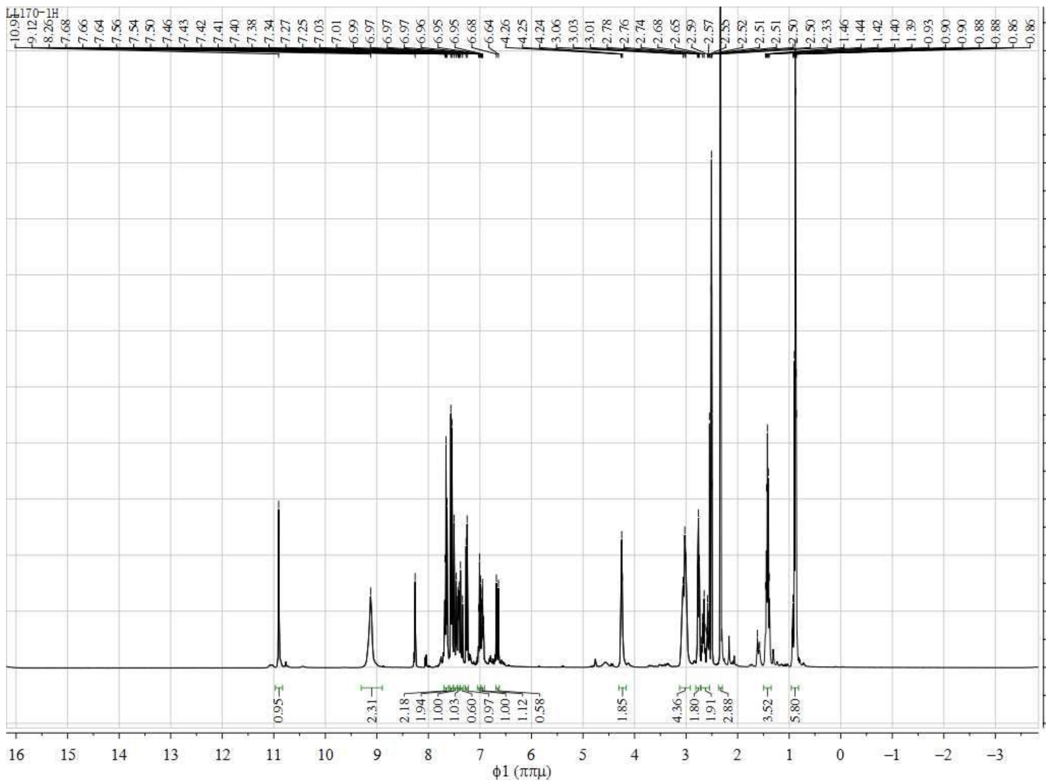

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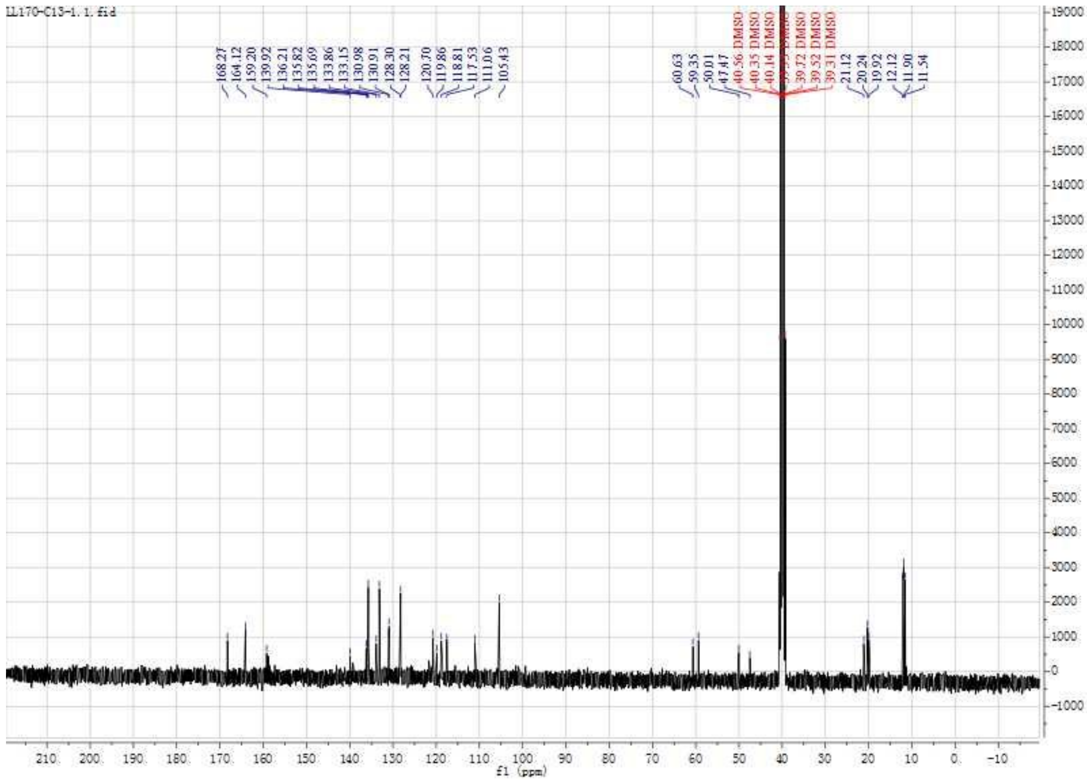

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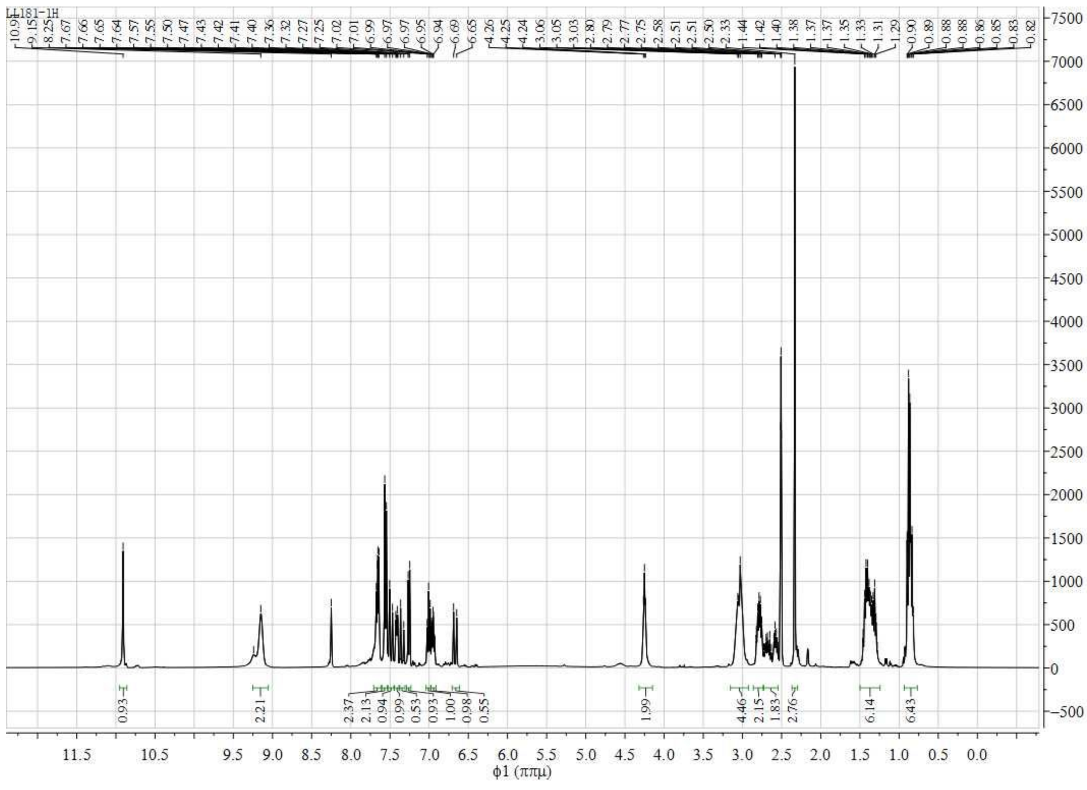

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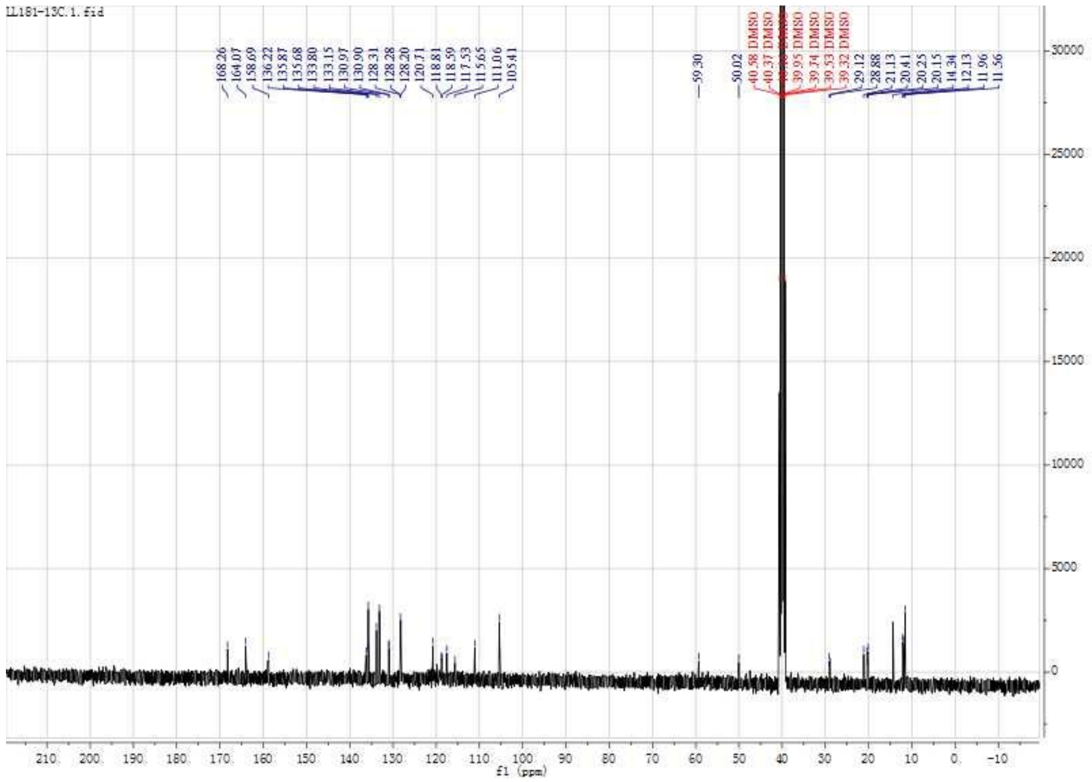

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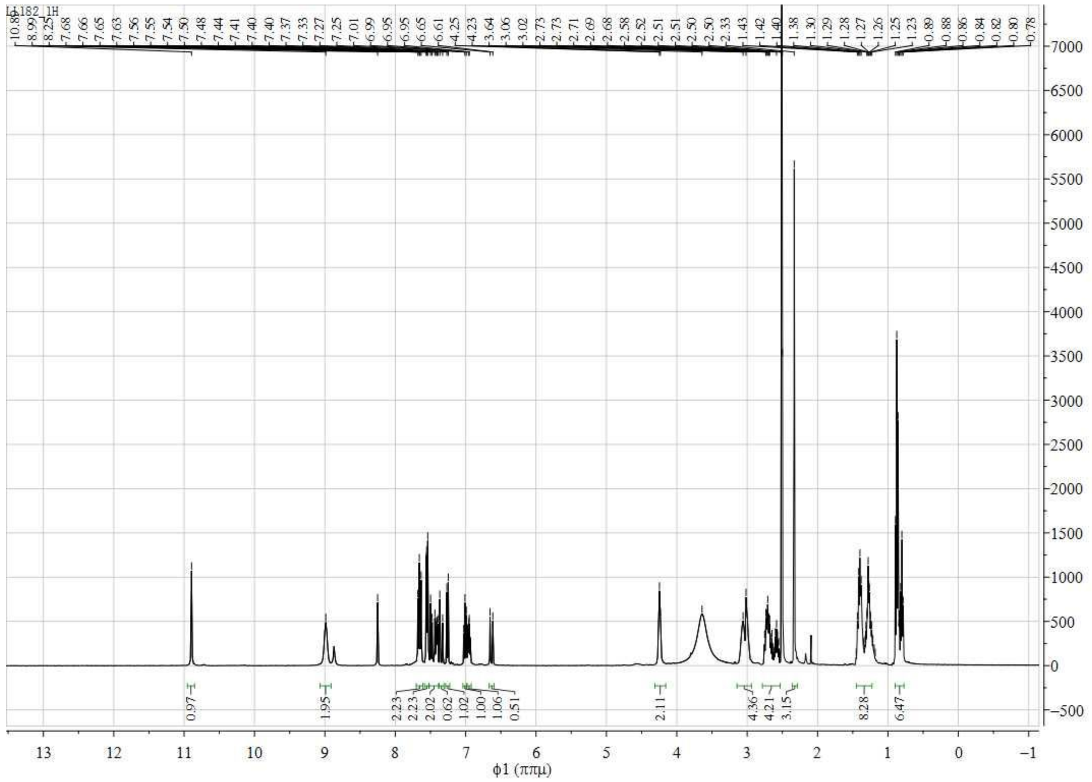

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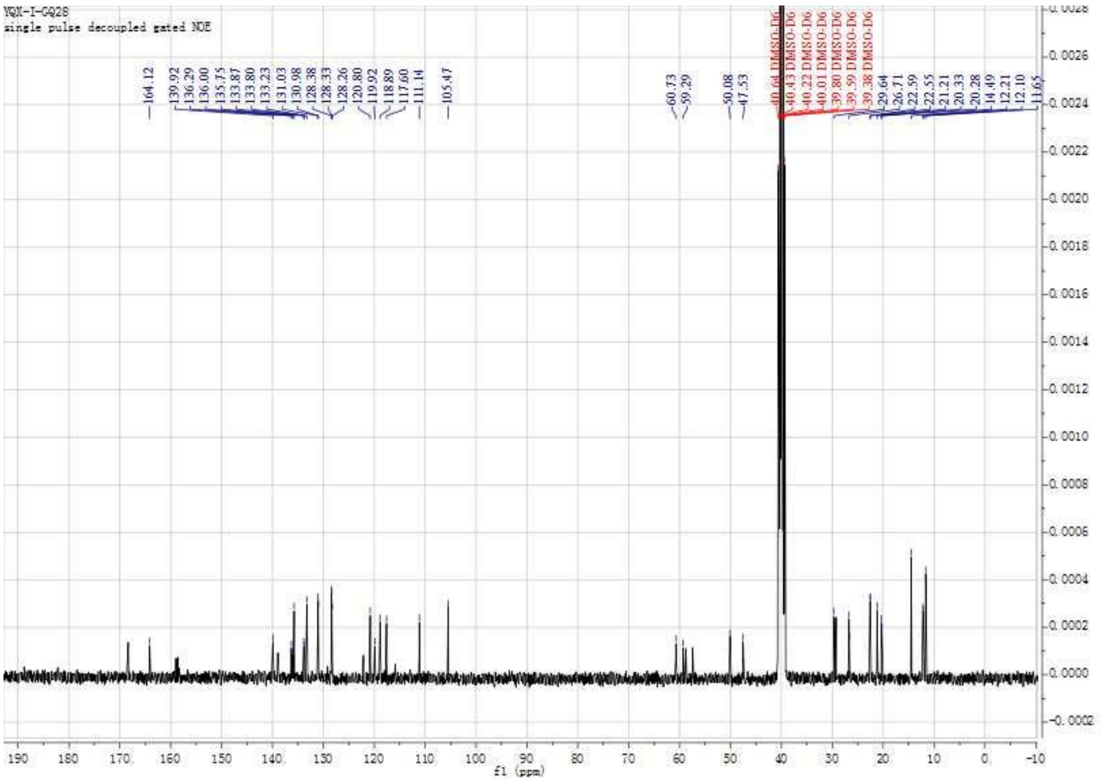

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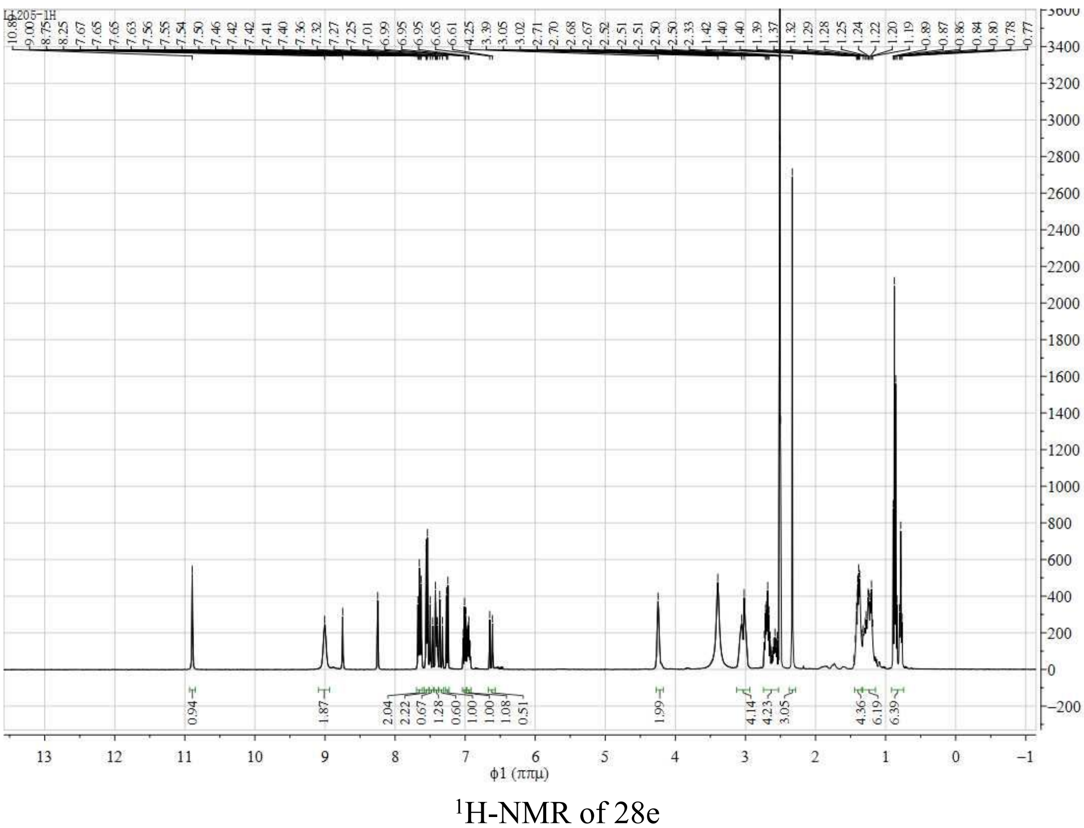

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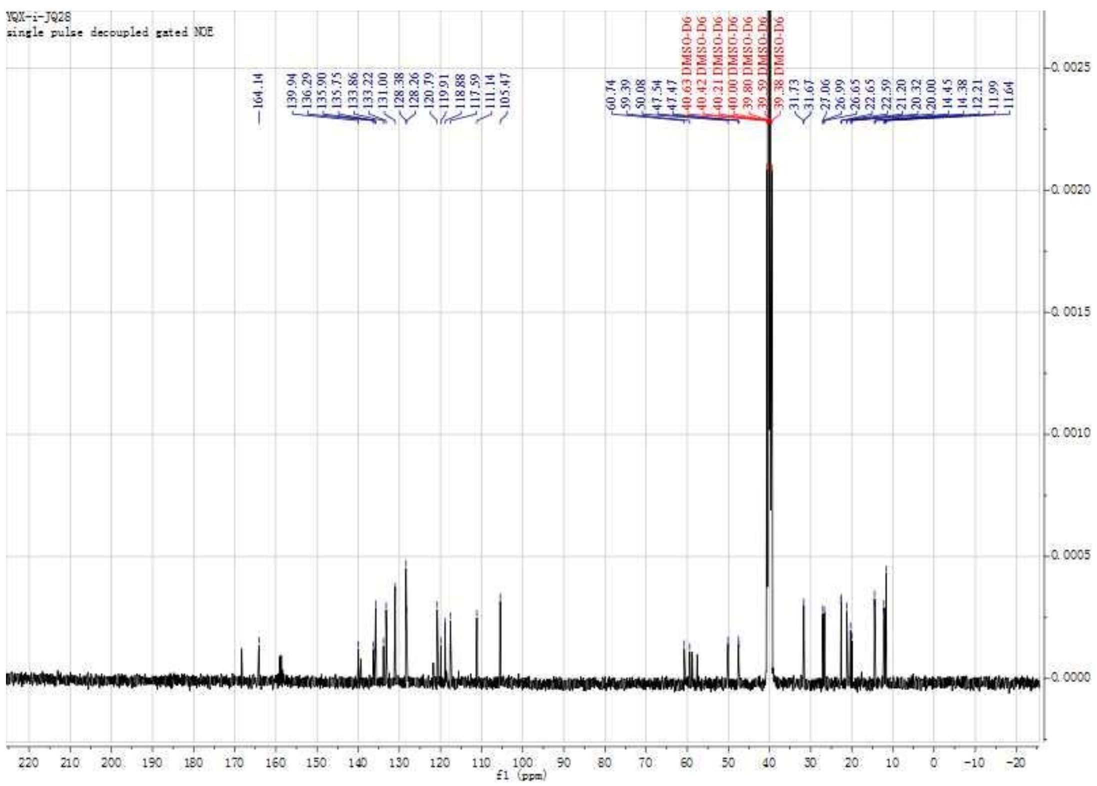

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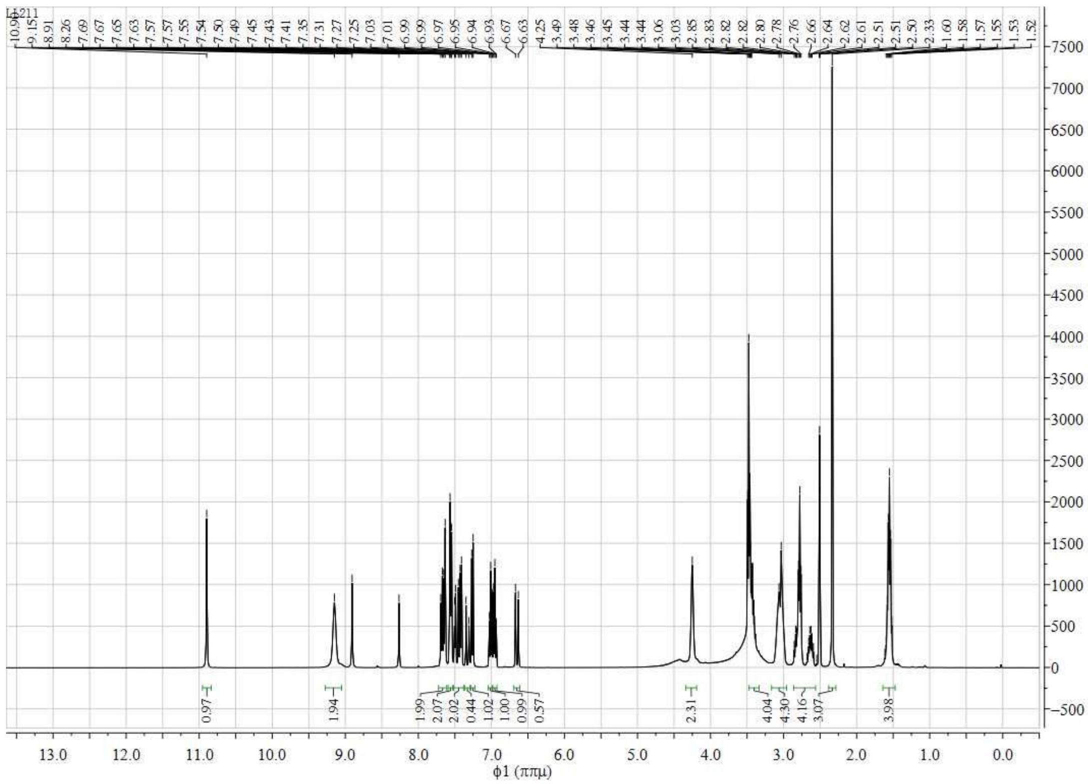
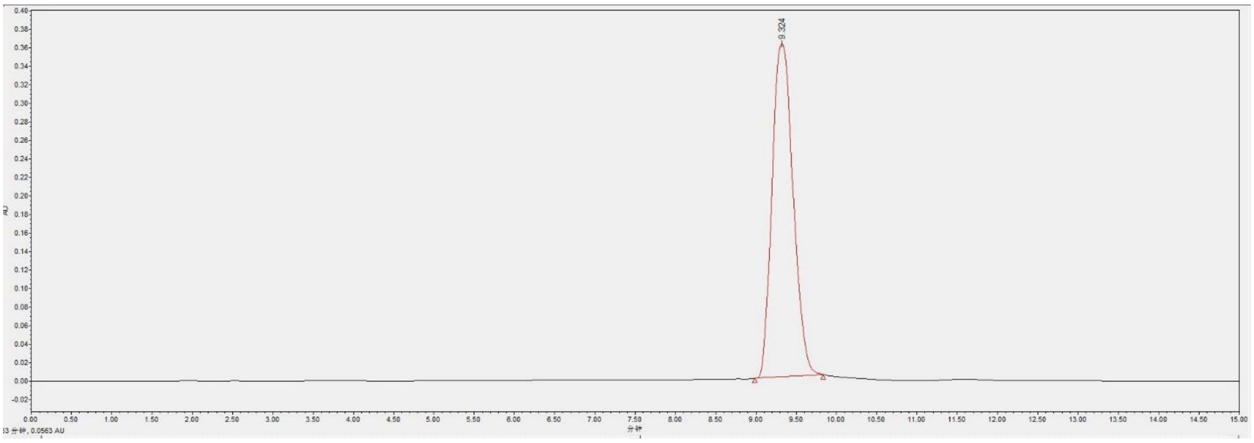


^{1}H-NMR of 30

HPLC traces and purity of the target compounds

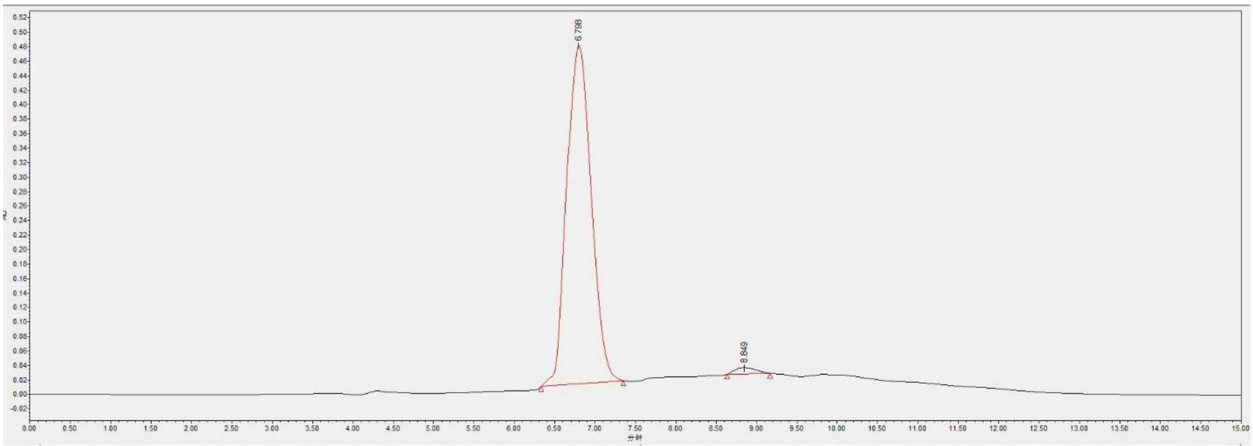
All target compounds were at least 95% pure as confirmed via UV detection of ESI LCMS, performed on an Waters e2695 HPLC instrument using an XBridge C18 column (5μm, 4.6 mm × 150 mm) using a gradient of water/methanol plus 0.1% formic acid (0-1 mins from 0-50% methanol, 1-12 mins from 50% to 100% methanol, 12-14 min to 0% methanol, and maintained at 0% for 1 minute).

12a



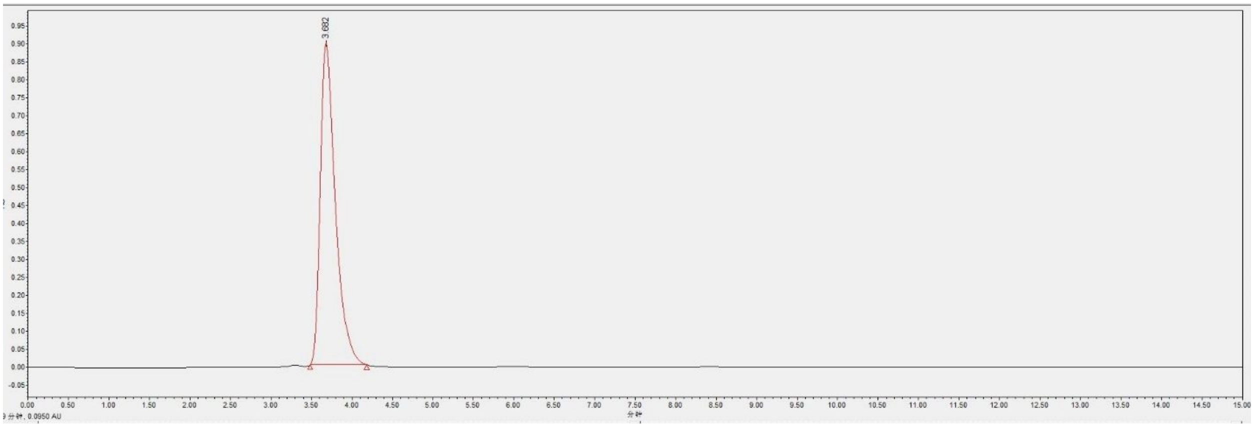
Purity: 100%

13a



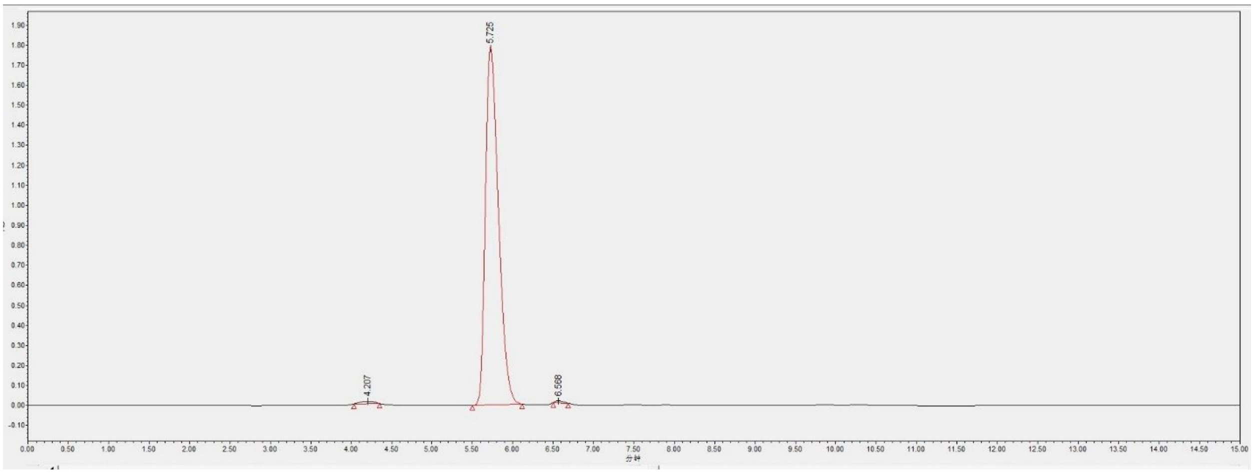
Purity: 98.5%

13b



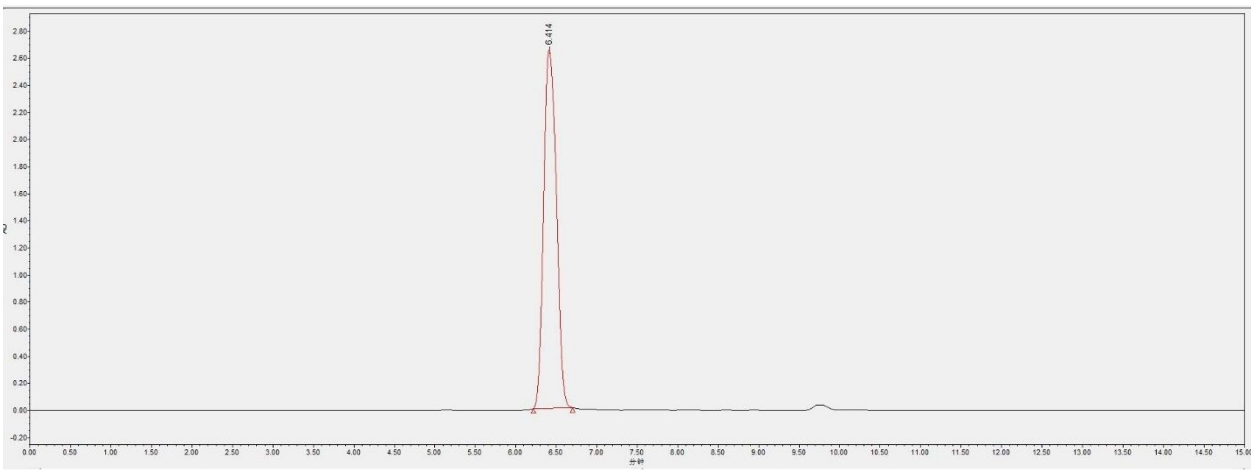
Purity: 100%

13c



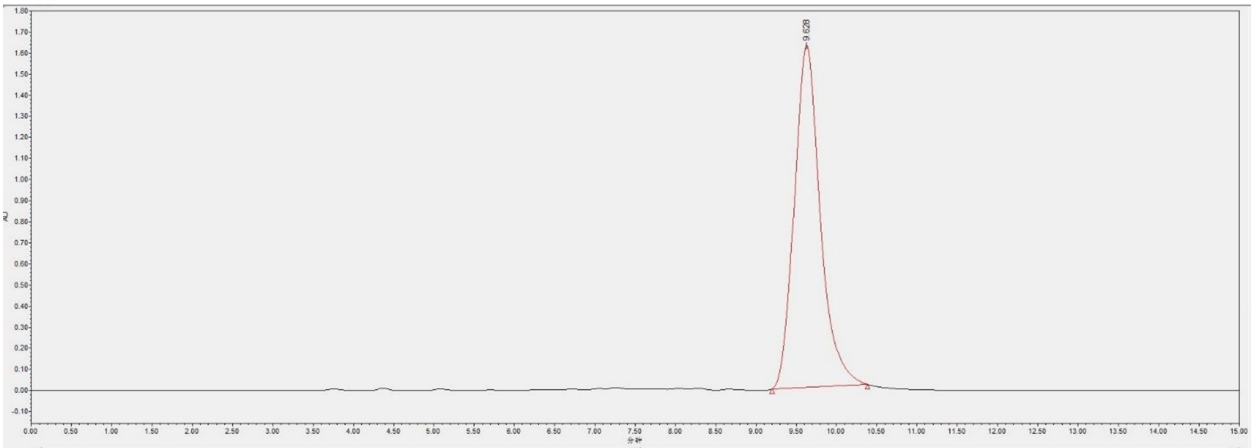
Purity: 99.0%

13d



Purity: 100%

15a



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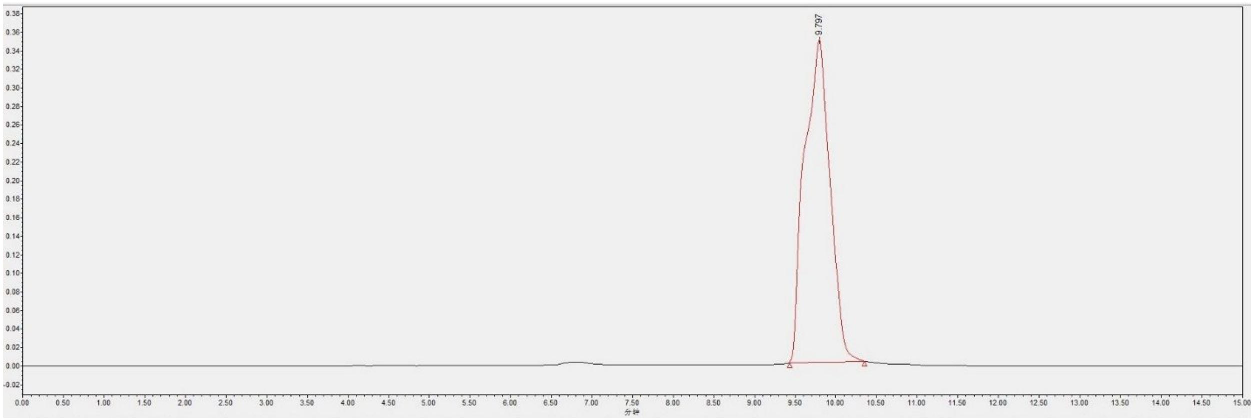
15b



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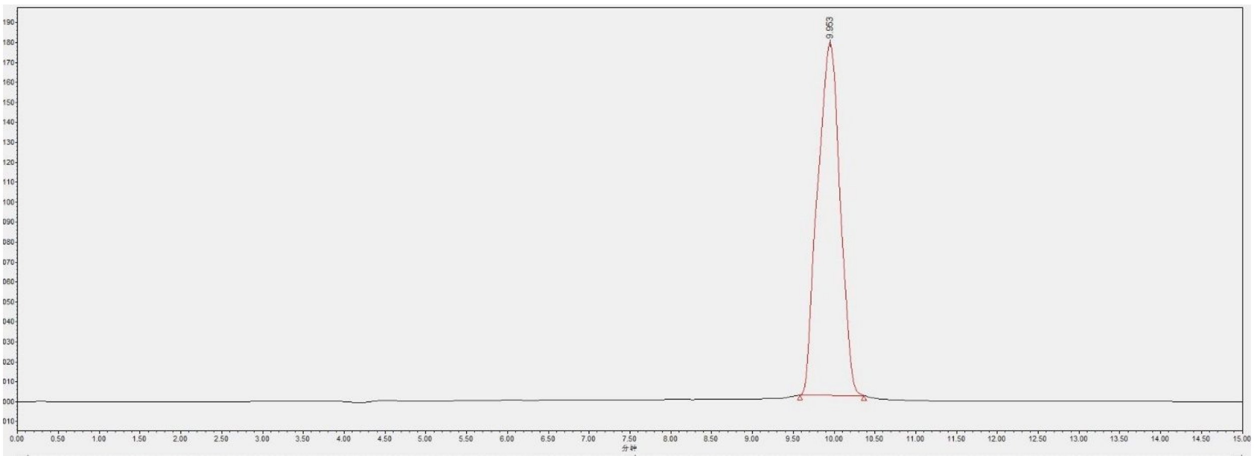
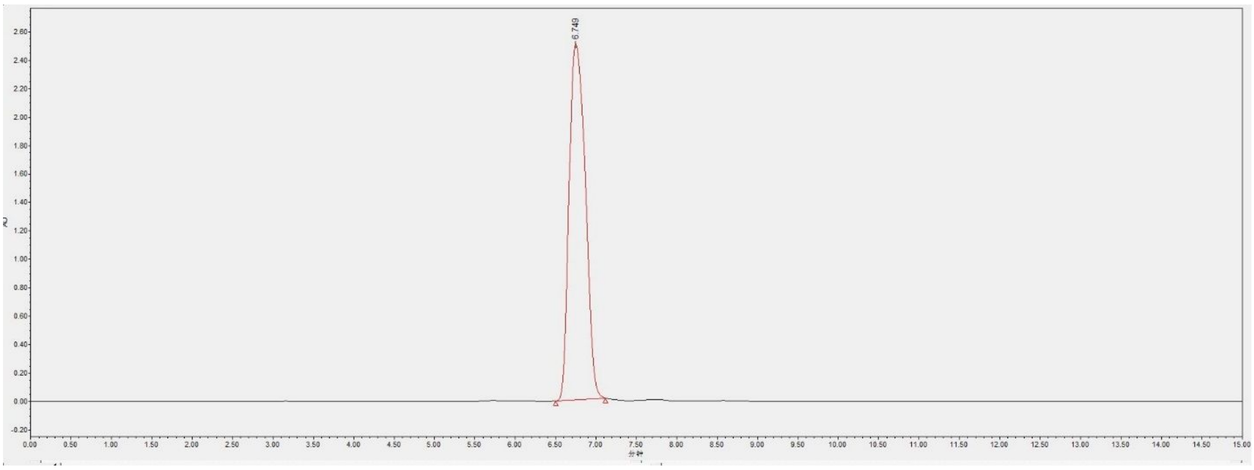
15c



Purity: 100%

16a



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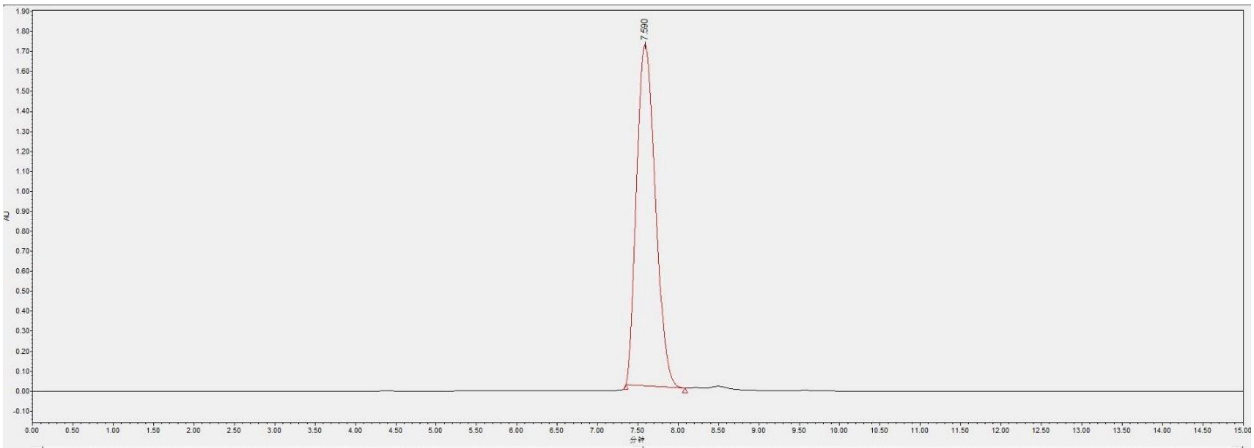
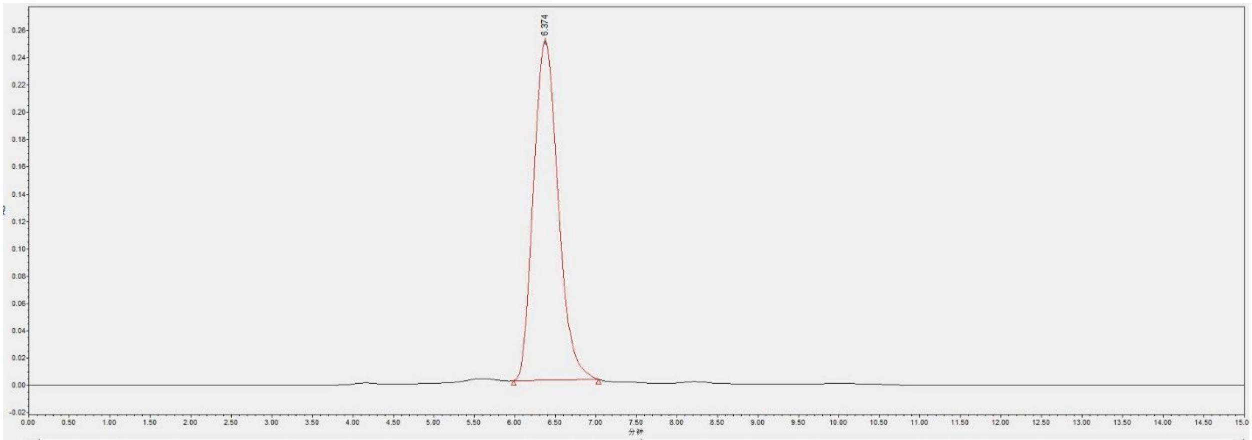
16b



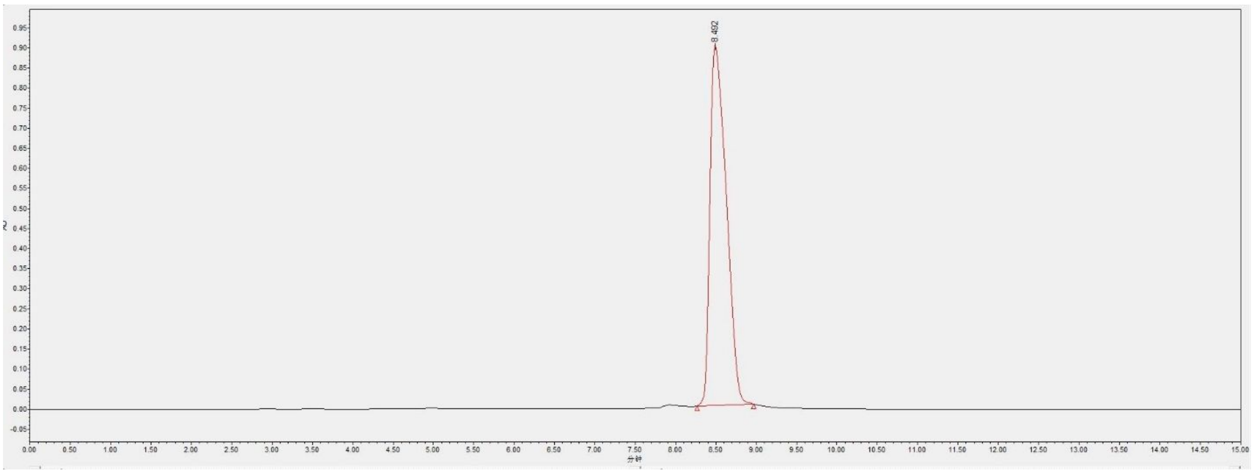
Purity: 100%

16c



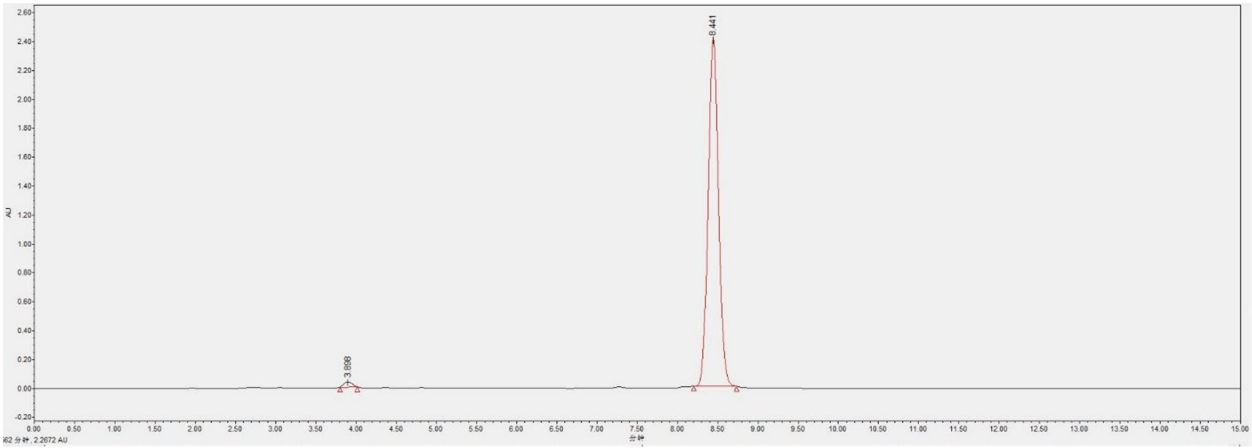
Purity: 100%

24a



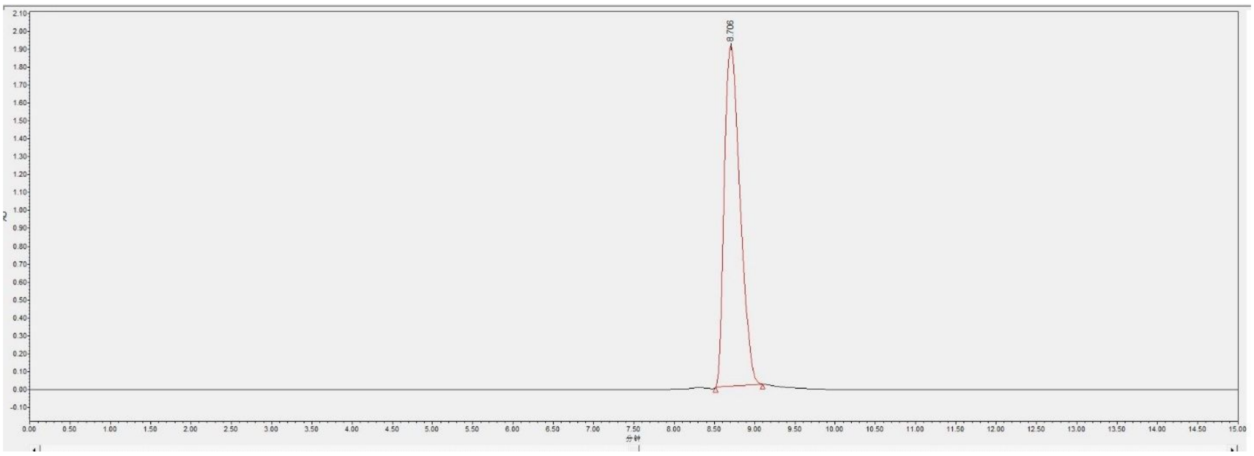
Purity: 100%

24b



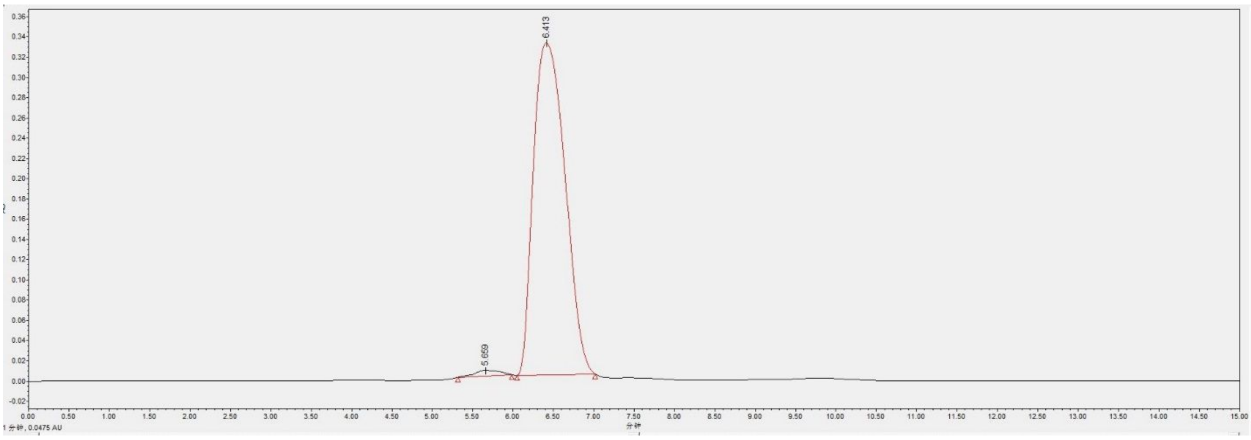
Purity: 98.7%

24c



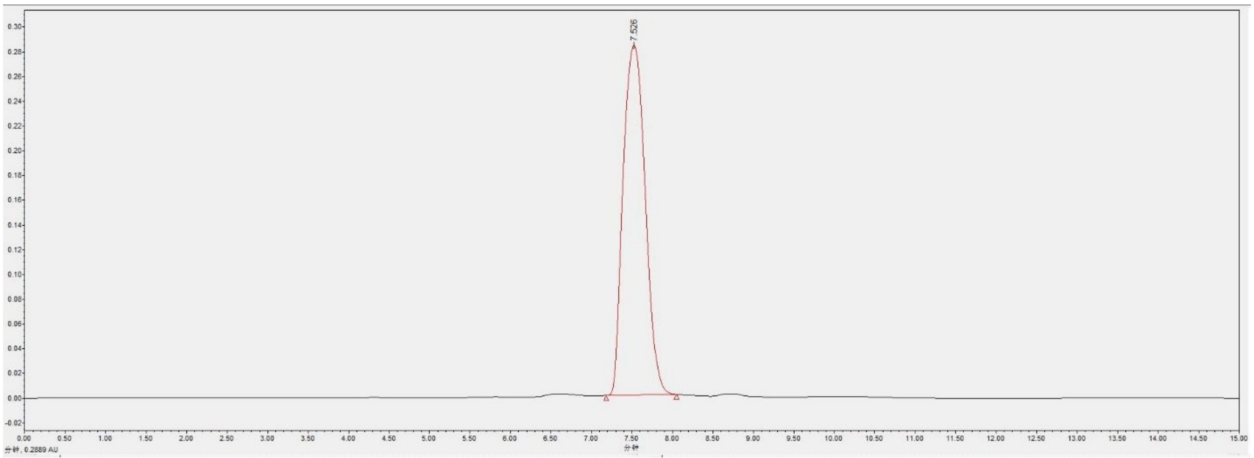
Purity: 100%

26a



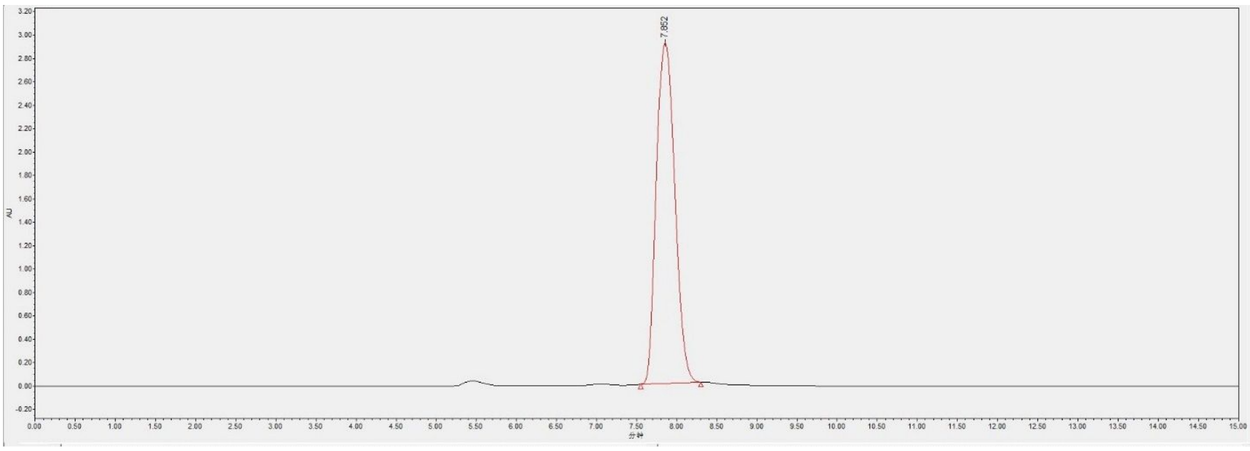
Purity: 98.7%

26b



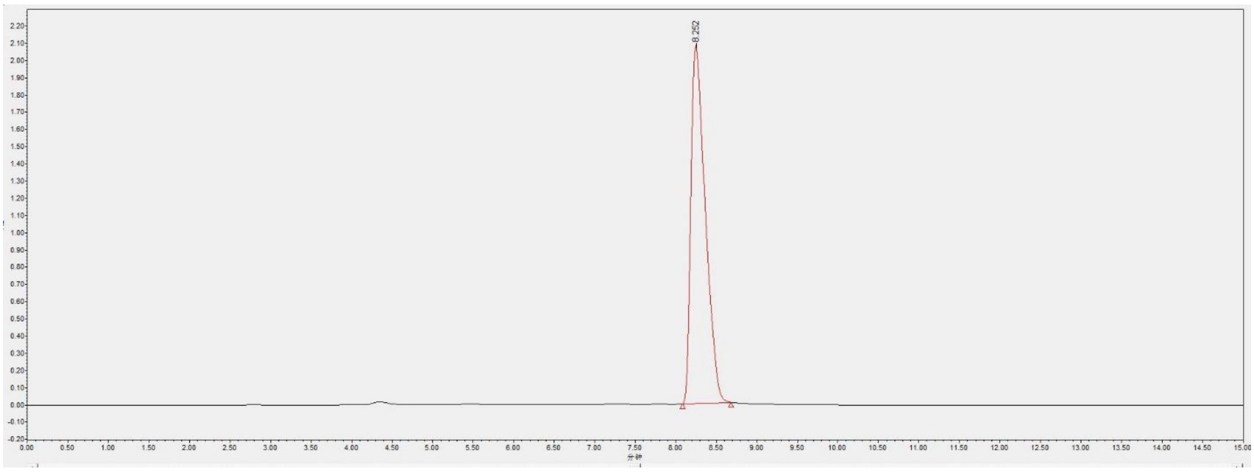
Purity: 100%

26c



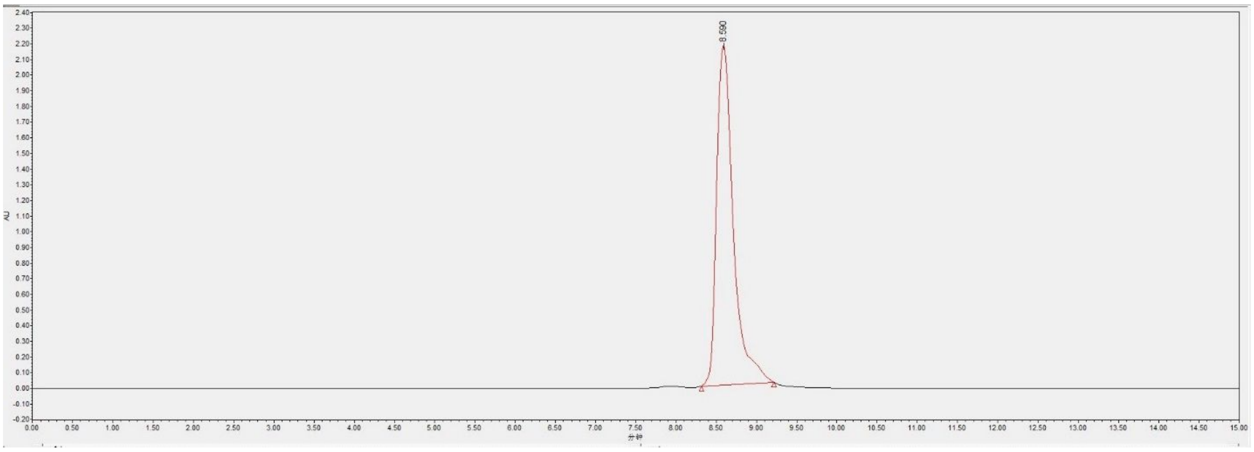
Purity: 99.5%

28a



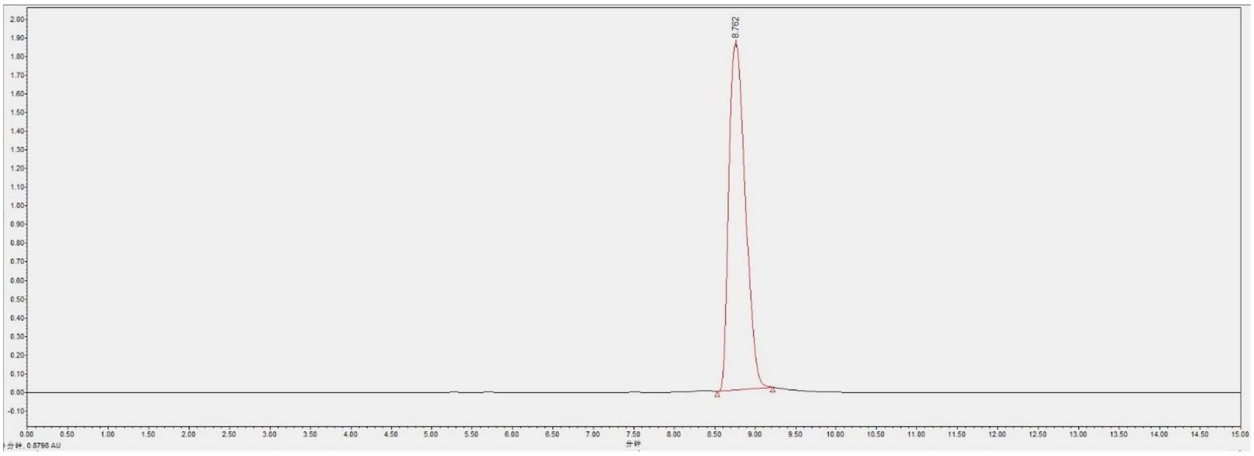
Purity: 100%

28b



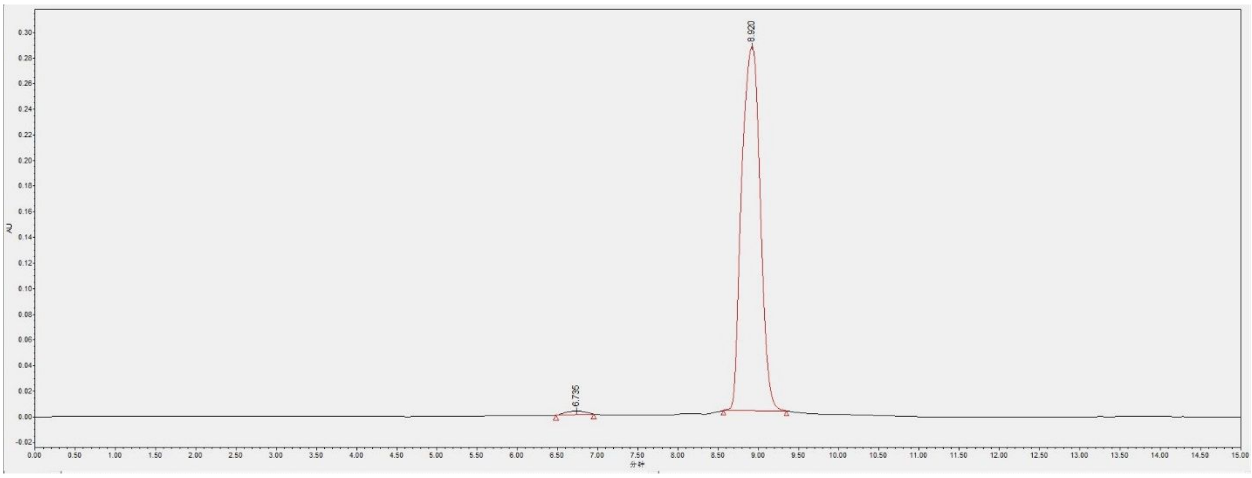
Purity: 100%

28c



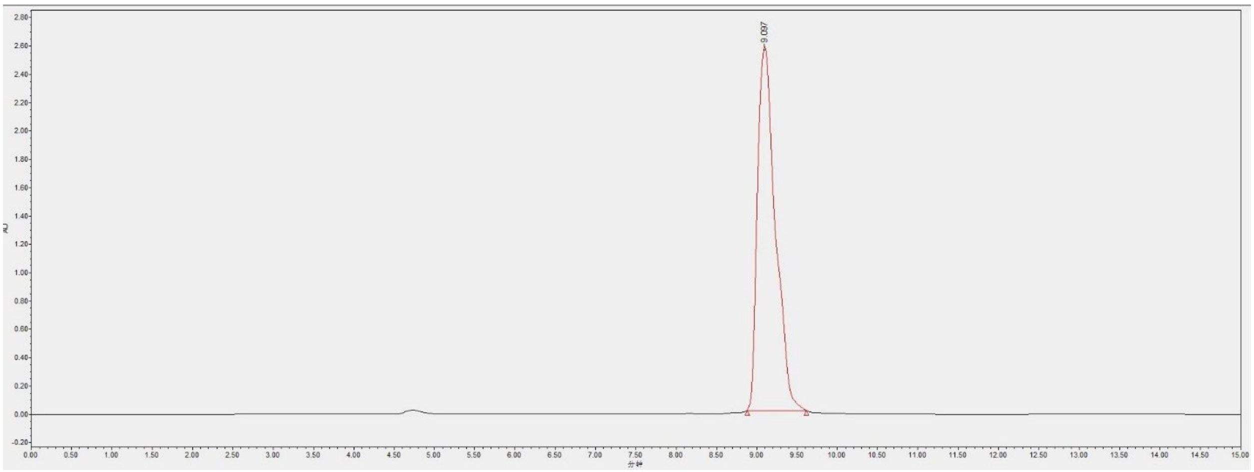
Purity: 100%

28d



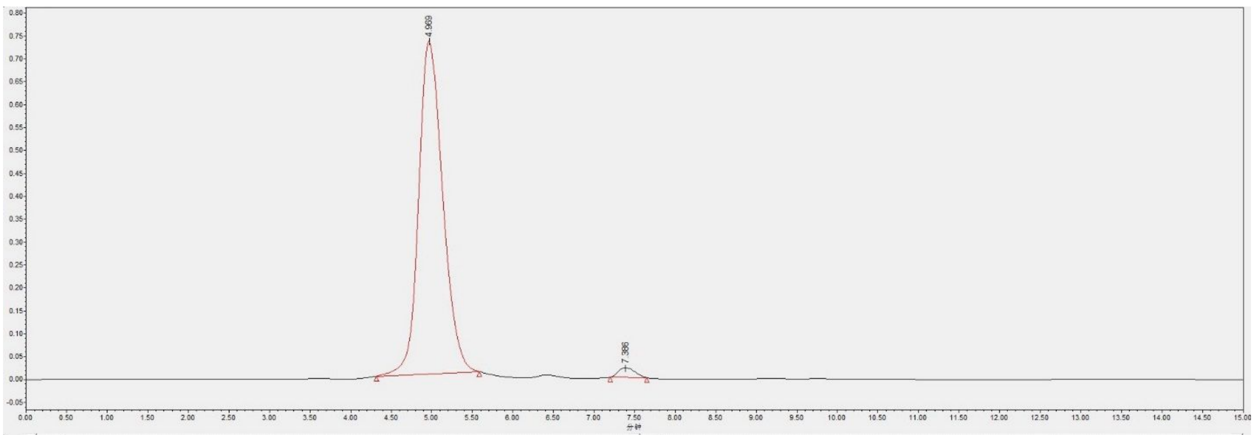
Purity: 99.4%

28e



Purity: 100%

30



Purity: 98.0%