

Copper-catalyzed formation of *N,N*-dimethyl benzamide from nitrile and DMF under O₂ atmosphere

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General Methods

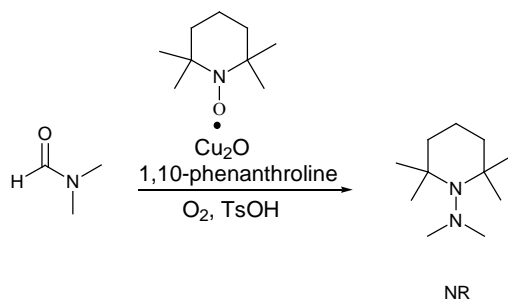
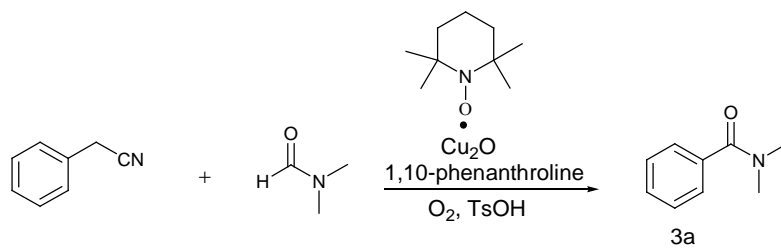
All reagents were purchased from commercial suppliers and used without further purification. Column chromatography was carried out with silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. Thin layer chromatography was carried out using Merck silica gel GF254 plates. ^1H NMR and ^{13}C NMR (400 MHz and 100 MHz, respectively) spectra were recorded in CDCl_3 . Chemical shifts are reported in ppm using TMS as internal standard. Gas chromatography/Mass spectra (GC/MS) were recorded on an Agilent Technologies 6890N instrument with an Agilent 5973N mass detector (EI) and a HP5-MS 30 m \times 0.25 mm capillary apolar column (Stationary phase: 5% diphenyldimethylpolysiloxane film, 0.25 μm).

General procedure for the catalytic reaction

Nitrile (1 mmol), DMF (2 mL), Cu_2O (0.1 mmol), 1,10-phenanthroline (0.2 mmol) and TsOH (1 mmol) were added into a sealed tube. The reaction mixture was stirred at 140 $^\circ\text{C}$ for 24 h. After completion of the reaction, the reaction mixture was allowed to cool to room temperature, quenched with water, and extracted with ethyl acetate. The organic layer was then dried over anhydrous MgSO_4 and the solvent was removed in vacuo. The residue was finally purified by column chromatography on silica gel using petroleum ether-ethyl acetate mixture as eluent.

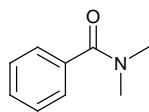
Reaction pathway studies:

To gain insight into the mechanism of the reaction, benzyl cyanide was treated with DMF under the optimized conditions with the addition of 2,2,6,6-tetramethylpiperidin-1-yloxy (TEMPO). The product was also observed with similar yield. Meanwhile, DMF was also treated with TEMPO under the optimized conditions in the absence of benzyl cyanide and provided no corresponding radical products, which indicates that the reaction might not go through a radical process.



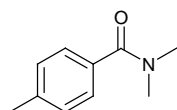
Characterization data

N,N-dimethylbenzamide (3a)¹



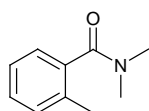
Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a white solid (83% yield). ¹H NMR (400 MHz, CDCl₃): 2.85 (s, 3H), 2.99 (s, 3H), 7.28-7.29 (m, 5H). ¹³C NMR (100 MHz, CDCl₃): 35.10, 39.36, 126.79, 128.13, 129.33, 136.01, 171.45.

N,N,4-trimethylbenzamide (3b)¹



Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a colorless oil (81% yield). ¹H NMR (400 MHz, CDCl₃): 2.37 (s, 3H), 2.99 (s, 3H), 3.09 (s, 3H), 7.20 (d, 2H), 7.33 (d, 2H). ¹³C NMR (100 MHz, CDCl₃): 26.65, 35.17, 39.27, 125.39, 125.42, 127.34, 139.89, 170.07.

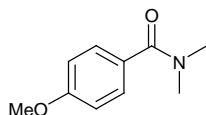
N,N,2-teimethylbenzamide (3c)¹



Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a colorless oil (68% yield). ¹H NMR (400 MHz, CDCl₃): 2.28 (s, 3H), 2.81 (s, 3H), 3.12 (s, 3H), 7.14-7.28 (m, 4H). ¹³C NMR (100

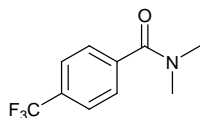
MHz, CDCl₃): 18.55, 34.14, 38.00, 125.41, 125.57, 128.39, 129.98,
133.56, 136.41, 171.11.

N,N-Dimethyl-4-methoxybenzamide (3d)¹



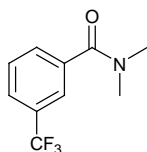
Purified by column chromatography (Petroleum Ether : Ethyl Acetate=
5:6) to give a colorless oil (77% yield). ¹H NMR (400 MHz, CDCl₃): 2.93
(s, 6H), 3.71 (s, 3H), 6.79 (d, 2H), 7.29 (d, 2H). ¹³C NMR (100 MHz,
CDCl₃): 35.22, 39.51, 55.02, 113.25, 128.08, 128.84, 160.31, 171.18.

N,N-dimethyl-4-(trifluoromethyl)benzamide (3e)¹



Purified by column chromatography (Petroleum Ether : Ethyl Acetate=
5:6) to give a paleyellow oil (78% yield). ¹H NMR (400 MHz, CDCl₃):
2.86 (s, 3H), 3.02 (s, 3H), 7.42 (d, 2H), 7.56 (d, 2H). ¹³C NMR (100 MHz,
CDCl₃): 35.17, 39.27, 125.08, 127.34, 139.89, 170.07.

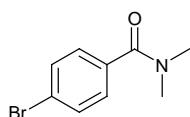
N,N-dimethyl-3-(trifluoromethyl)benzamide (3f)²



Purified by column chromatography (Petroleum Ether : Ethyl Acetate=

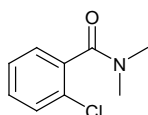
5:6) to give a colorless oil (84% yield). ^1H NMR (400 MHz, CDCl_3): 2.99 (s, 3H), 3.14 (s, 3H), 7.55 (t, 1H), 7.61 (d, 1H), 7.67(d, 2H). ^{13}C NMR (100 MHz, CDCl_3): 35.52, 39.60, 124.15, 126.37, 129.11, 129.24, 137.17, 170.14.

4-bromo-*N,N*-dimethylbenzamide (3g)³



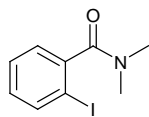
Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a colorless oil (74% yield). ^1H NMR (400 MHz, CDCl_3): 2.97 (s, 3H), 3.10 (s,3H), 7.30 (d, 2H), 7.55 (t, 2H). ^{13}C NMR (100 MHz, CDCl_3): 35.40, 39.54, 123.80, 128.80, 131.55, 135.05, 170.55.

2-Chloro-*N,N*-dimethylbenzamide (3h)³



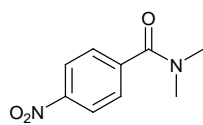
Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a colorless oil (64% yield). ^1H NMR (400 MHz, CDCl_3): 2.86 (s, 3H), 3.13 (s, 3H), 7.27-7.40 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3): 34.64, 38.08, 127.20, 127.73, 129.54, 130.09, 136.29, 168.44.

2-Iodo-*N,N*-dimethylbenzamide (3i)⁴



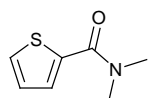
Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a colorless oil (53% yield). ¹H NMR (400 MHz, CDCl₃): 2.85 (s, 3H), 3.14 (s, 3H), 7.07 (t, 1H), 7.21 (d, 1H), 7.39 (t, 1H), 7.82 (d, 1H). ¹³C NMR (100 MHz, CDCl₃): 34.75, 38.45, 127.06, 128.44, 130.10, 139.10, 170.80.

N,N-dimethyl 4-nitrobenzamide (3j)⁵



Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a yellow oil (74% yield). ¹H NMR (400 MHz, CDCl₃): 2.86 (s, 3H), 3.02 (s, 3H), 7.44 (t, 2H), 7.57 (d, 2H). ¹³C NMR (100 MHz, CDCl₃): 35.23, 39.23, 123.86, 128.00, 142.46, 148.11, 169.17.

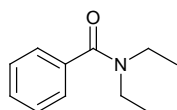
N,N-dimethylthiophene-2-carboxamide (3k)¹



Purified by column chromatography (Petroleum Ether : Ethyl Acetate= 5:6) to give a pale yellow oil (73% yield). ¹H NMR (400 MHz, CDCl₃): 3.19 (s, 6H), 7.04-7.06 (m, 1H), 7.35-7.36 (m, 1H), 7.44-7.51 (m, 1H).

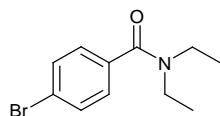
^{13}C NMR (100 MHz, CDCl_3): 29.81, 31.07, 126.80, 128.93, 129.30,
138.04, 164.57.

N,N-diethylbenzamide (5a)⁵



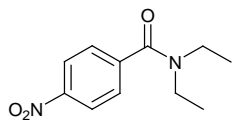
Purified by column chromatography (Petroleum Ether : Ethyl Acetate=
5:6) to give a colorless oil (60% yield). ^1H NMR (400 MHz, CDCl_3): 1.09
(s, 3H), 1.24 (s, 3H), 3.24 (d, 2H), 3.54 (d, 2H), 7.35-7.46 (m, 4H), 8.05
(t, 1H). ^{13}C NMR (100 MHz, CDCl_3): 11.83, 13.14, 38.36, 42.36, 125.20,
127.38, 128.18, 135.88, 170.54.

4-bromo-*N,N*-diethylbenzamide (5g)⁶



Purified by column chromatography (Petroleum Ether : Ethyl Acetate=
5:6) to give a colorless oil (20% yield). ^1H NMR (400 MHz, CDCl_3):
1.09-1.26 (m, 6H), 3.25 (d, 2H), 3.45-3.55 (m, 2H), 7.24-7.43 (m, 4H).
 ^{13}C NMR (100 MHz, CDCl_3): 13.02, 14.31, 39.36, 43.41, 126.36, 128.51,
131.74, 137.32, 171.46.

N,N-diethyl-4-nitrobenzamide (5j)⁷



Purified by column chromatography (Petroleum Ether : Ethyl Acetate=

5:6) to give a colorless oil (40% yield). ¹H NMR (400 MHz, CDCl₃): 1.04

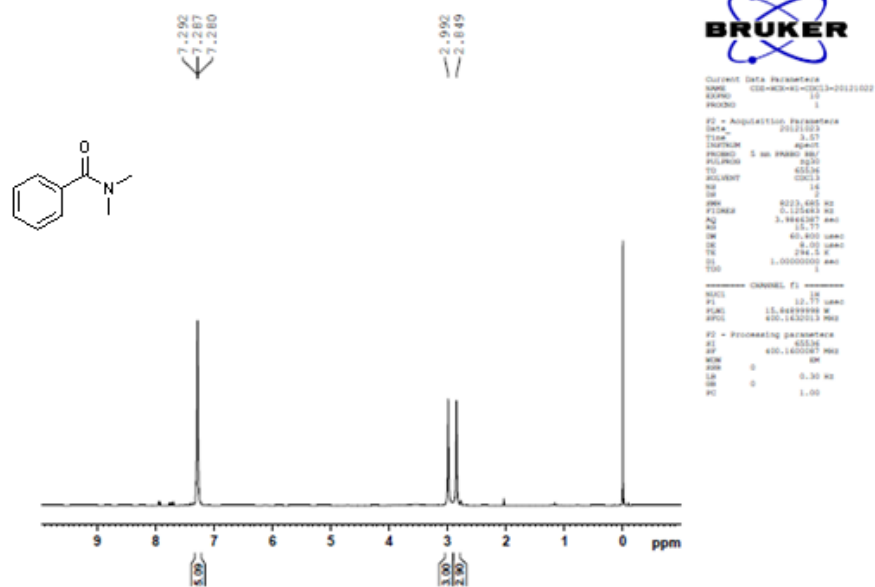
(d, 3H), 1.18 (d, 3H), 3.14 (d, 2H), 3.49 (d, 2H), 7.45-7.48 (m, 2H),

8.17-8.20 (m, 2H). ¹³C NMR (100 MHz, CDCl₃): 11.83, 13.19, 38.50,

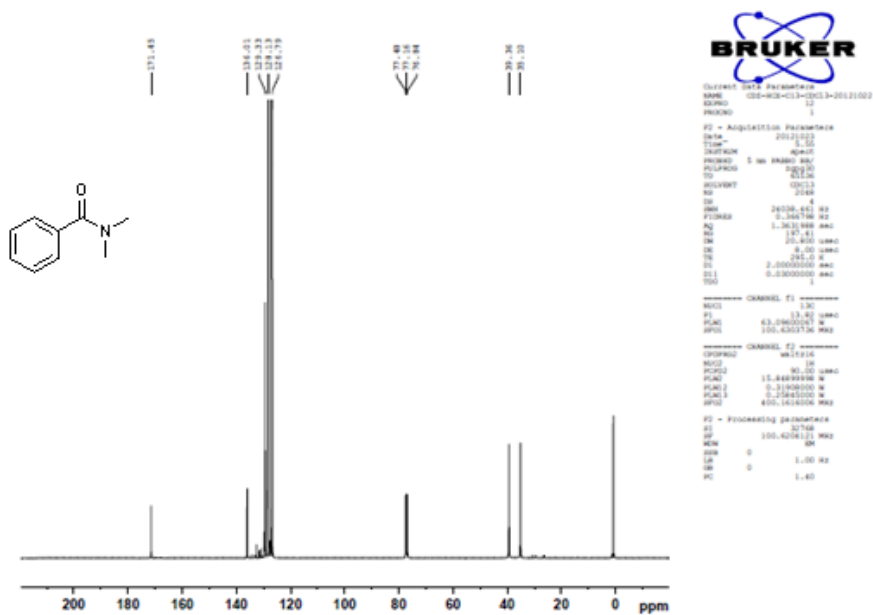
42.28, 122.58, 126.33, 142.34, 147.01, 167.95.

NMR spectra of compounds

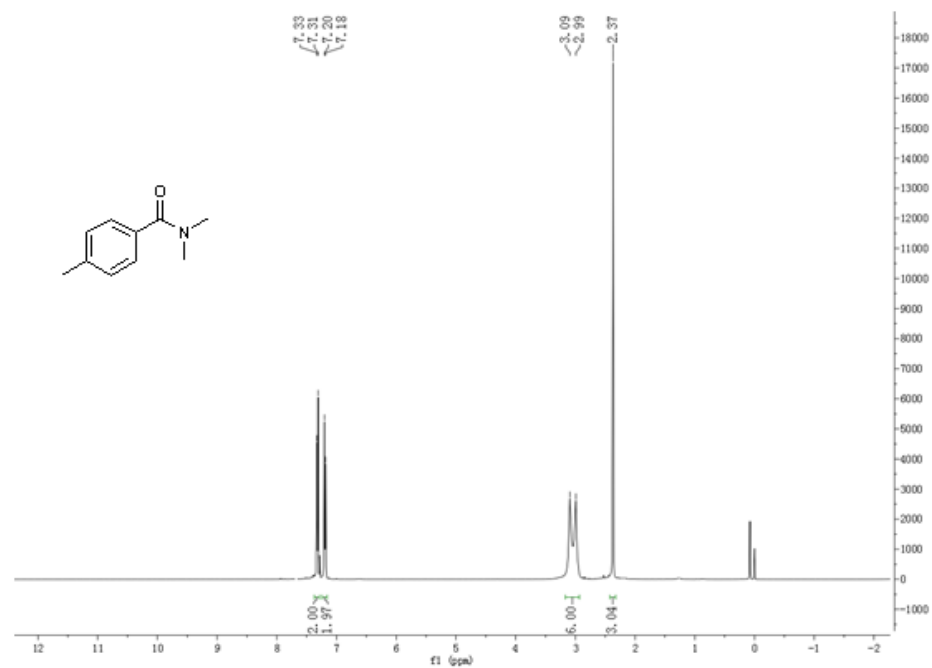
^1H NMR of 3a:



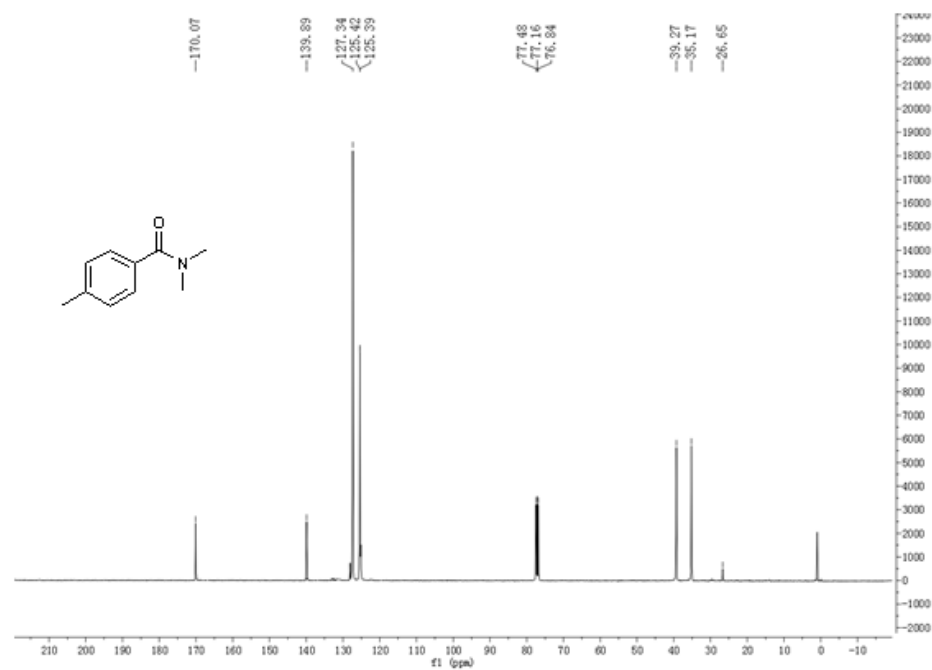
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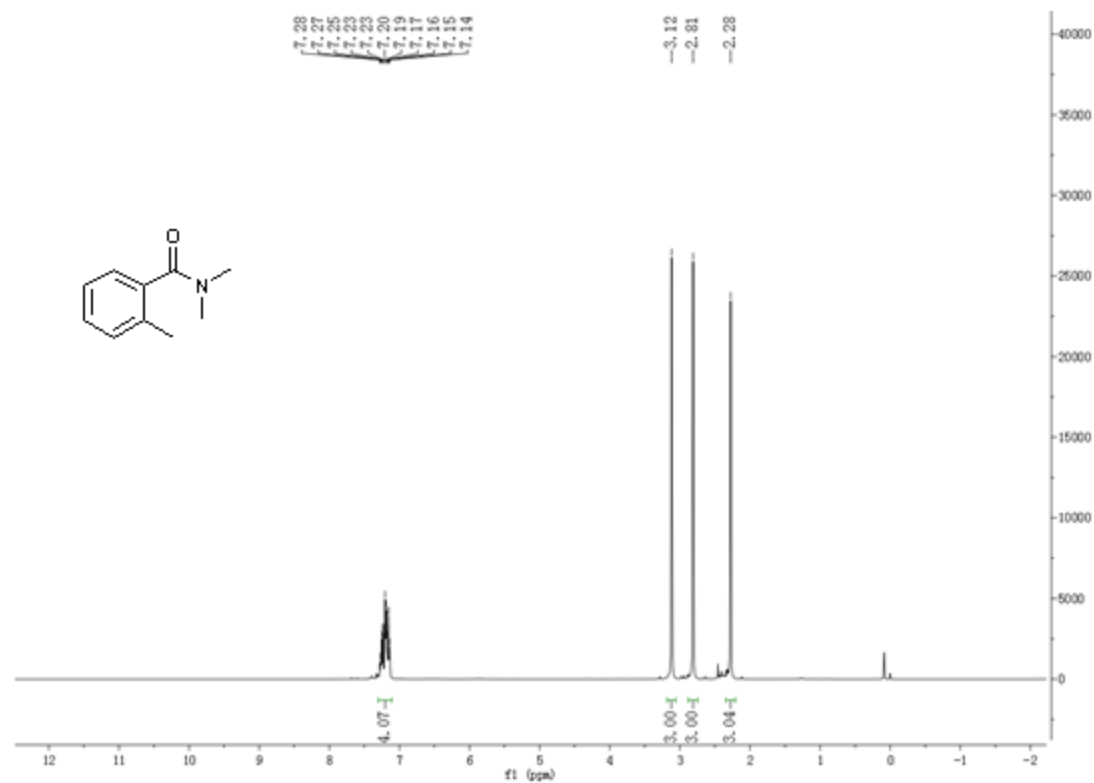
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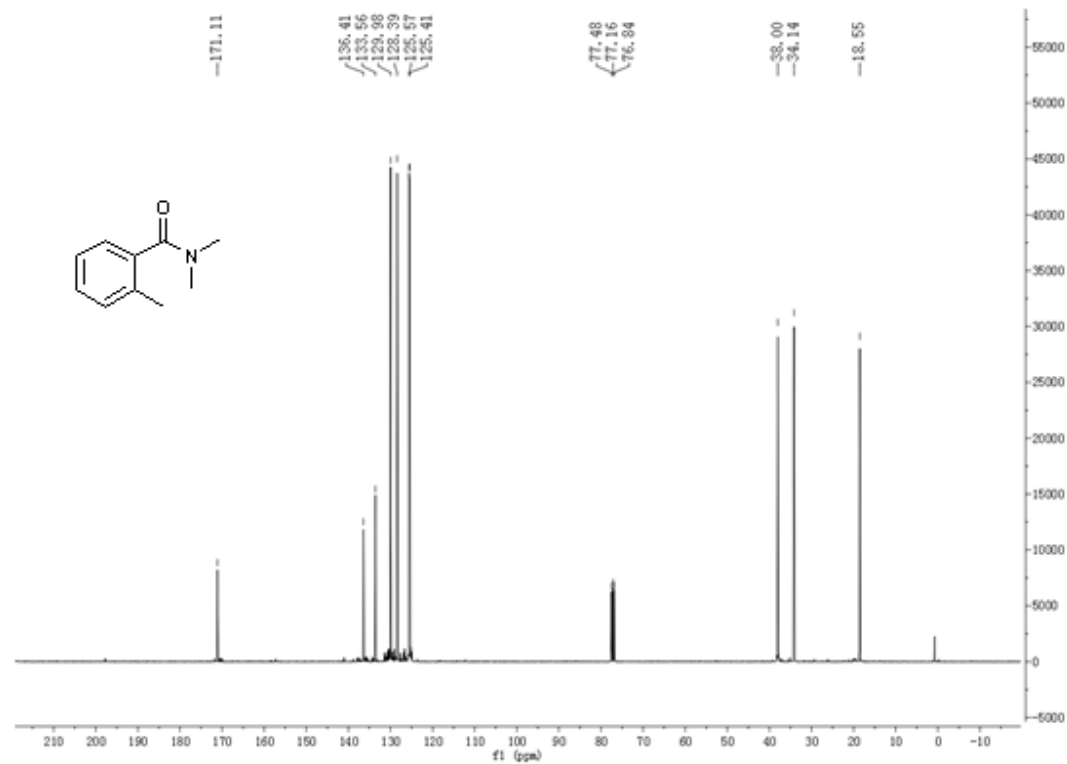
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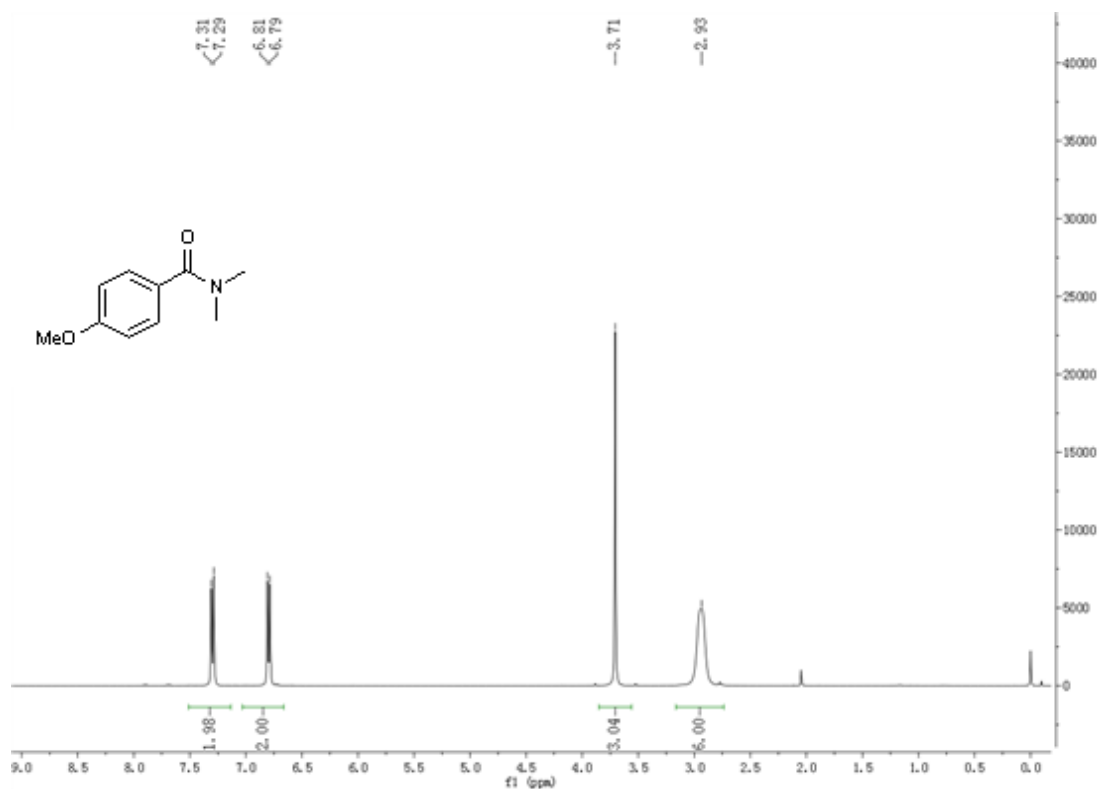
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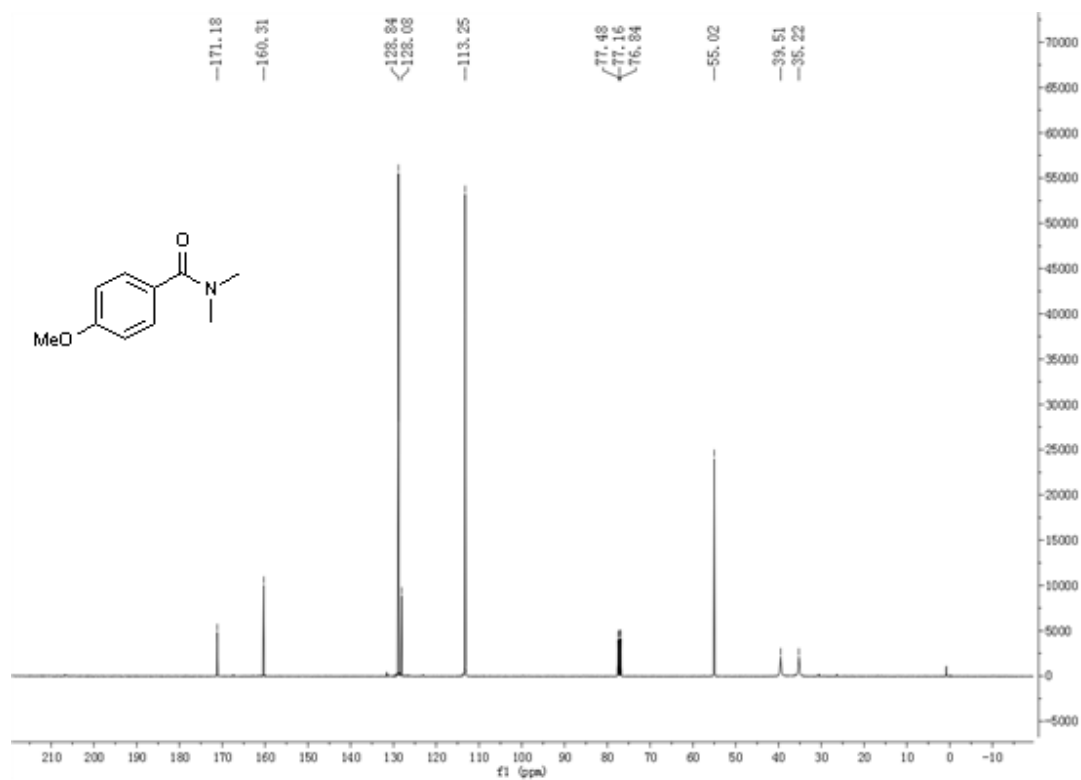
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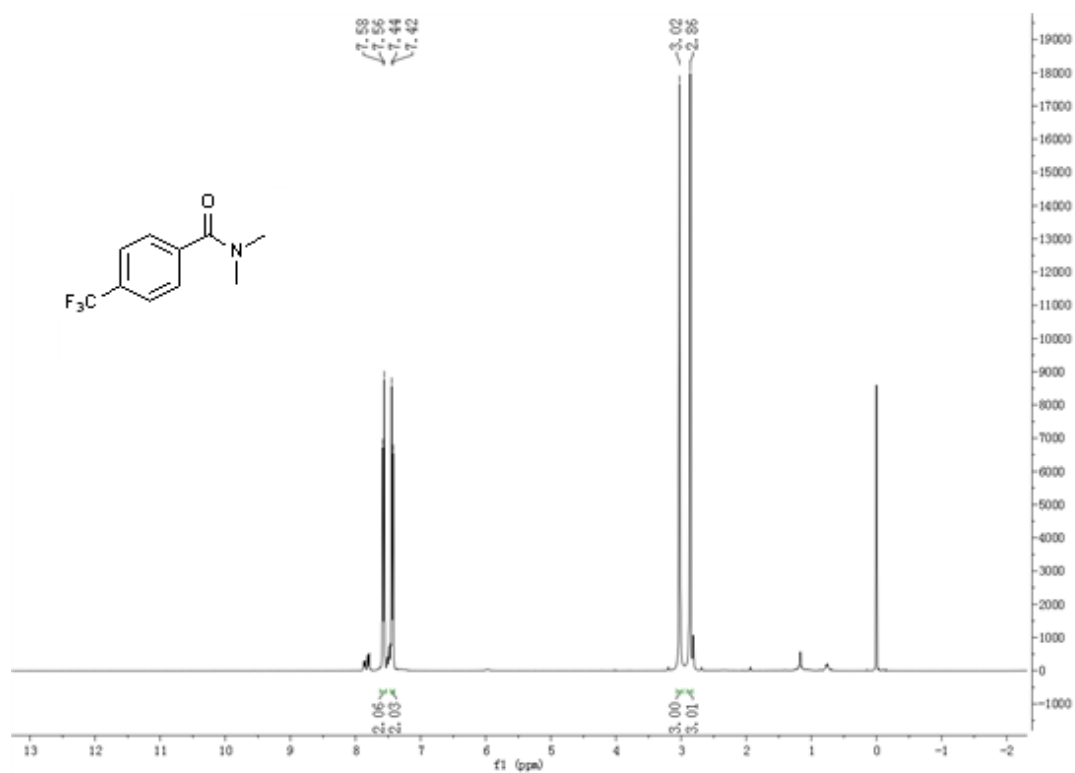
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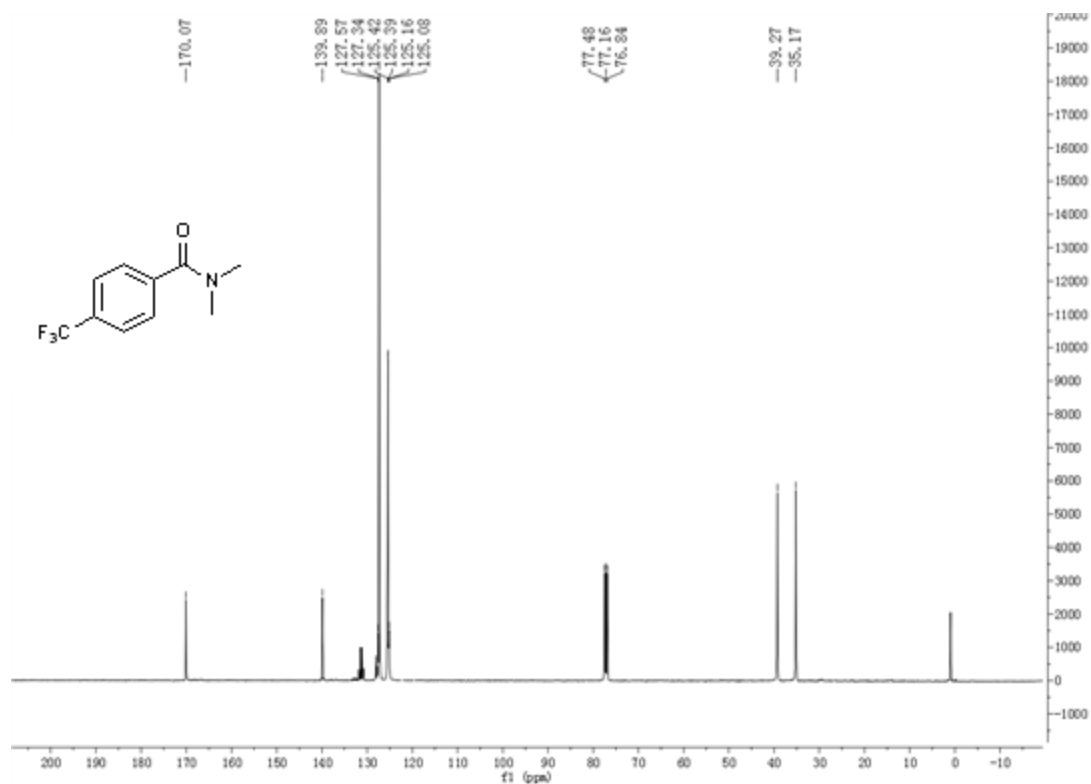
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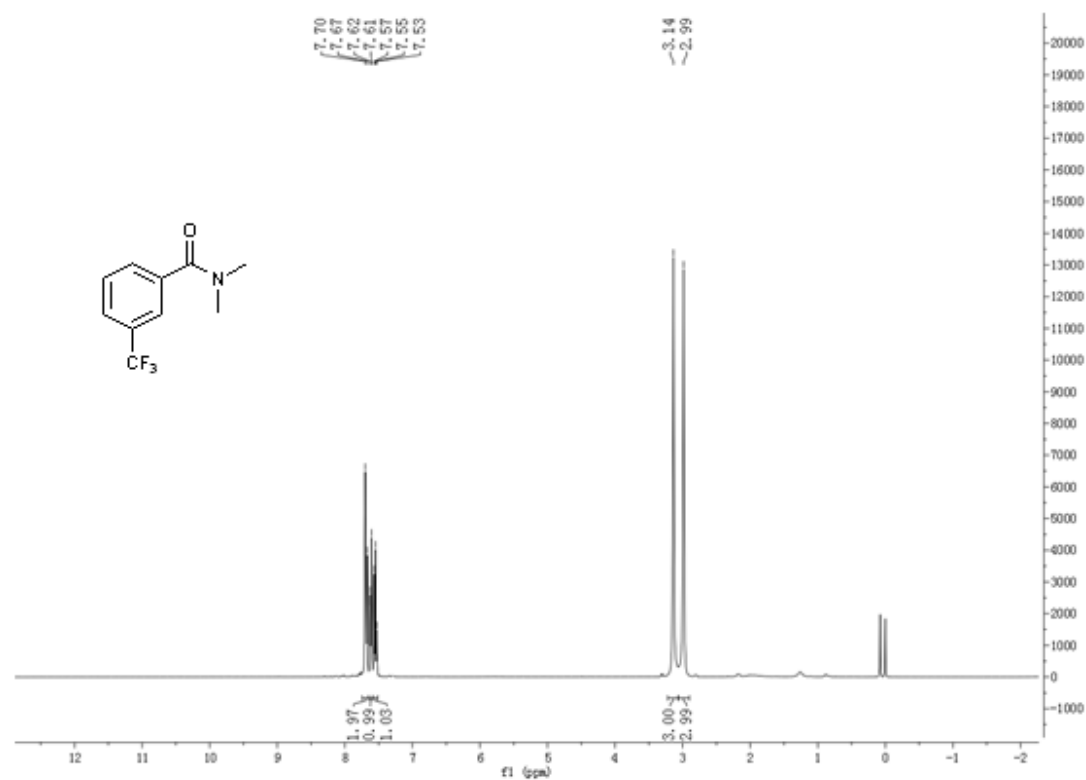
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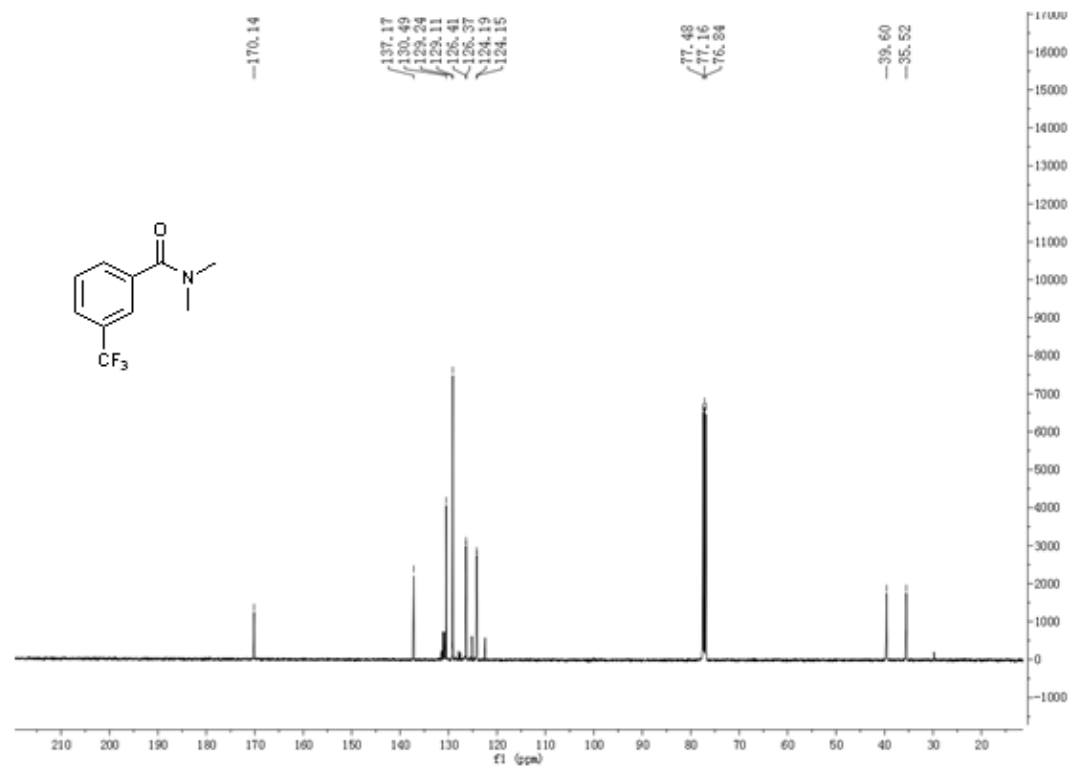
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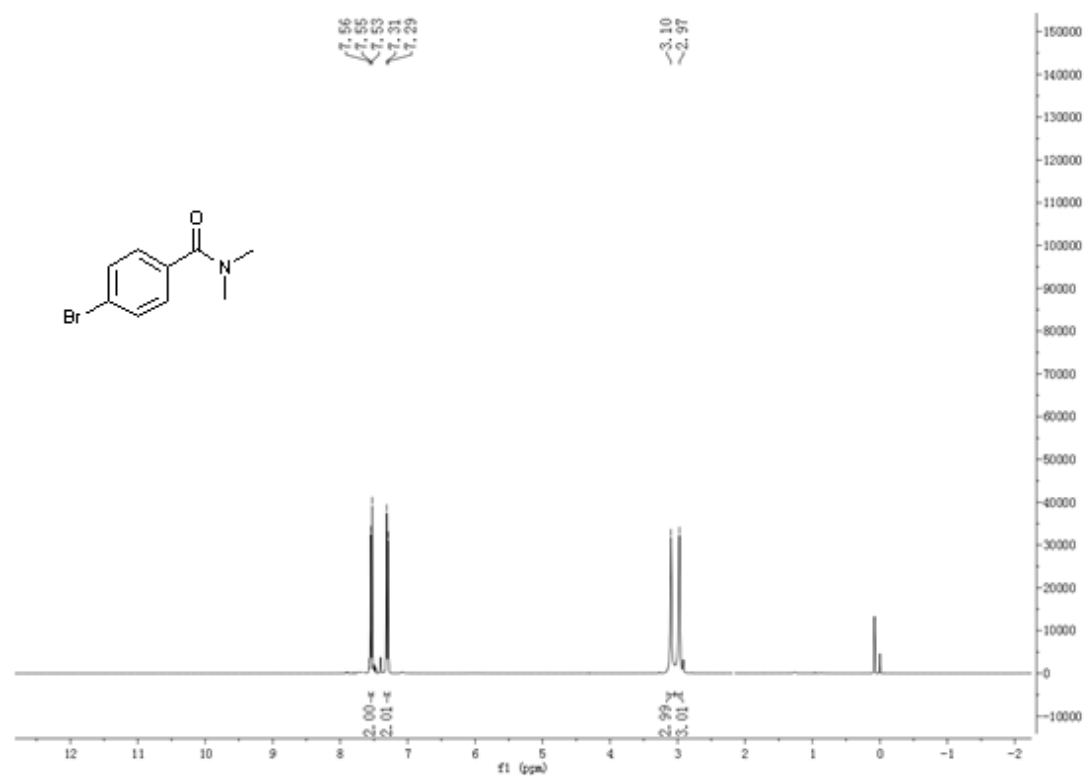
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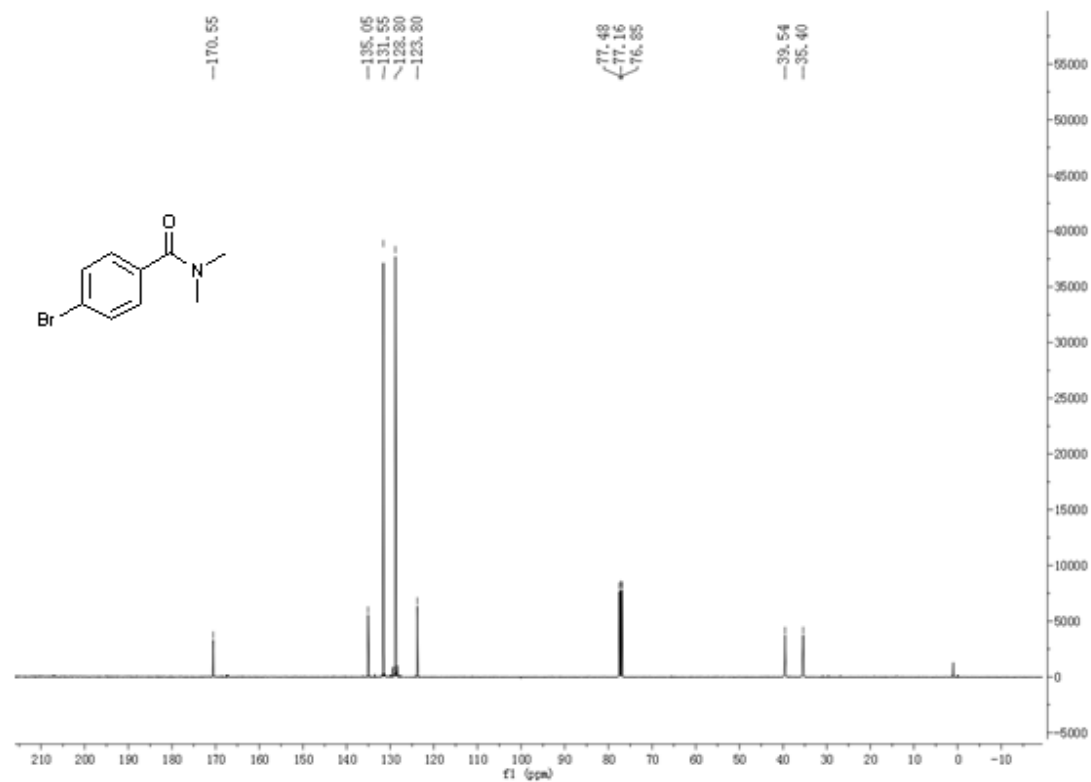
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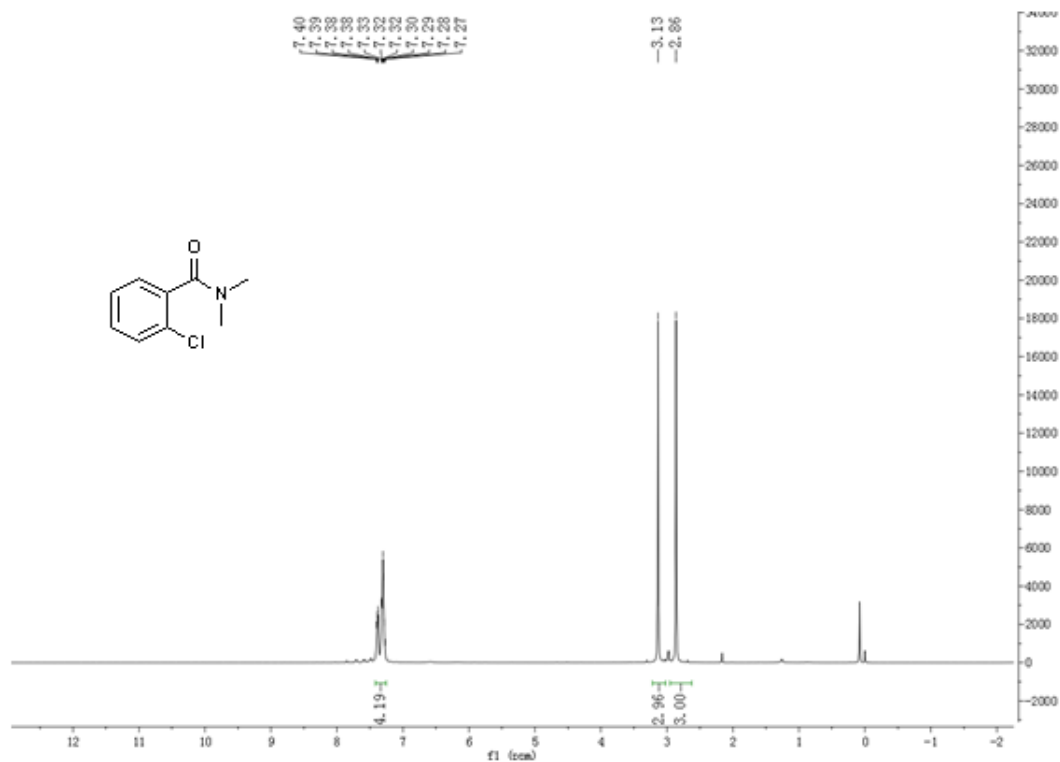
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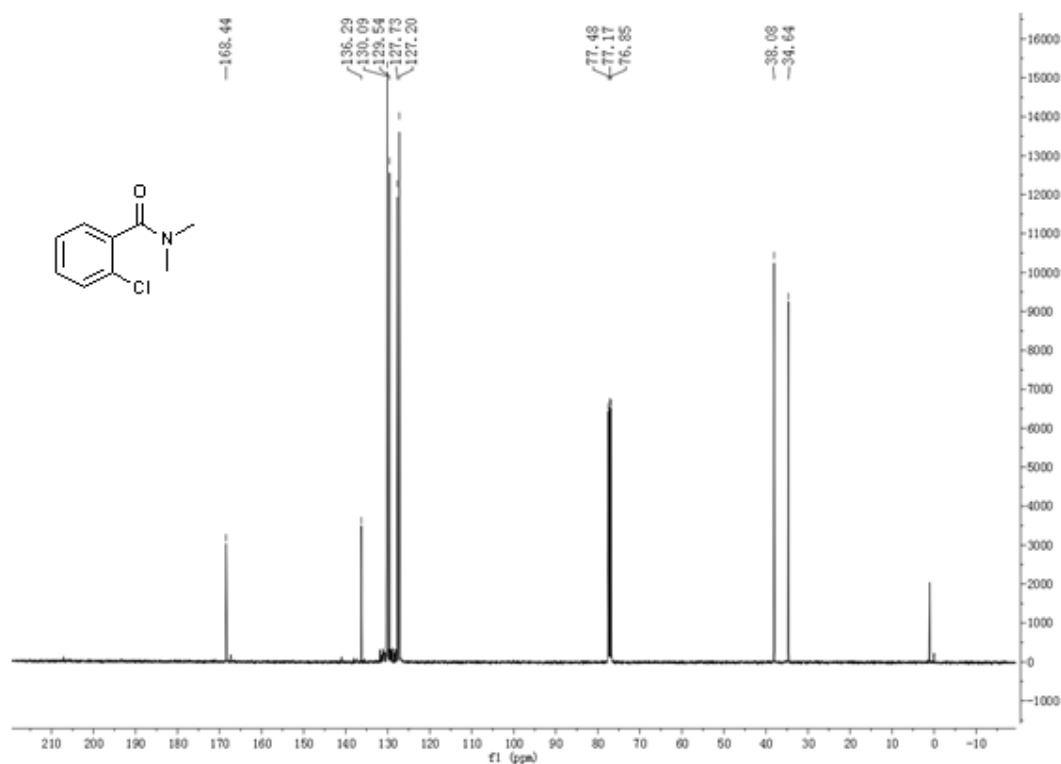
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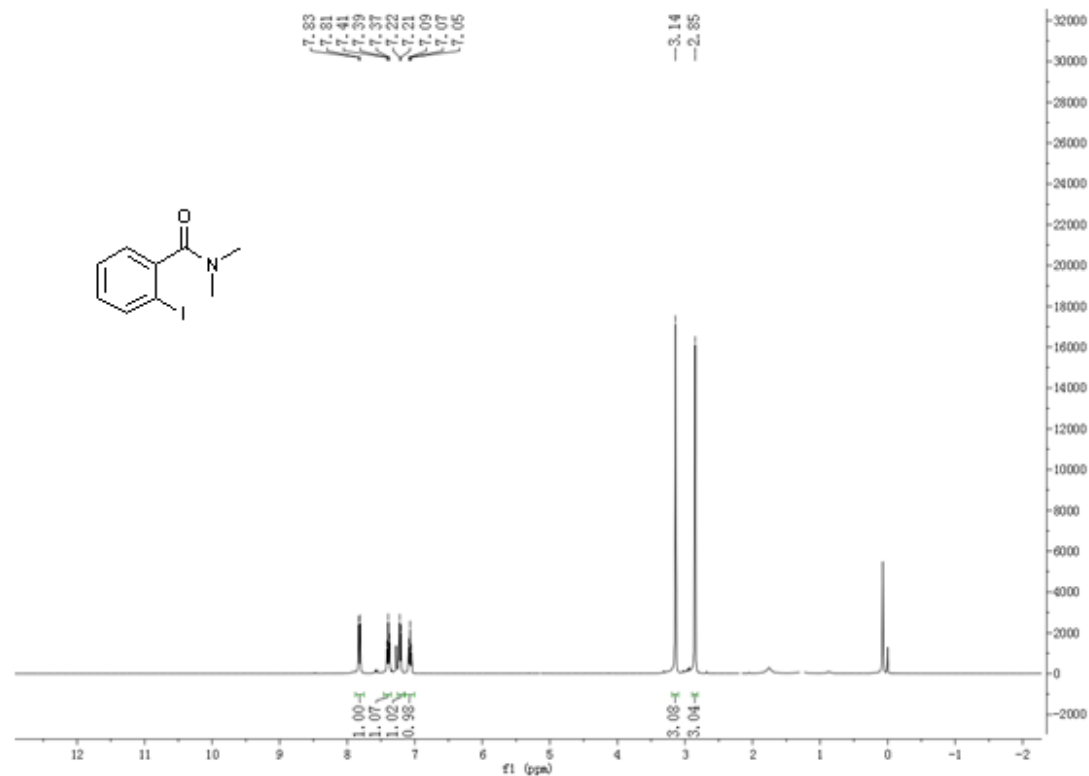
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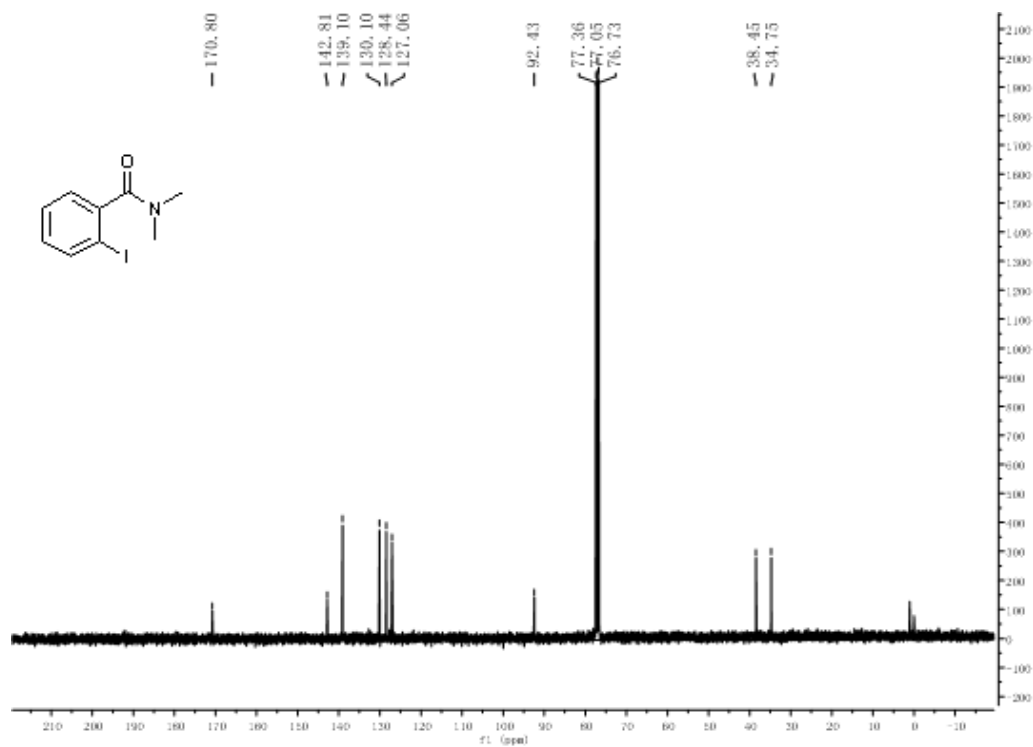
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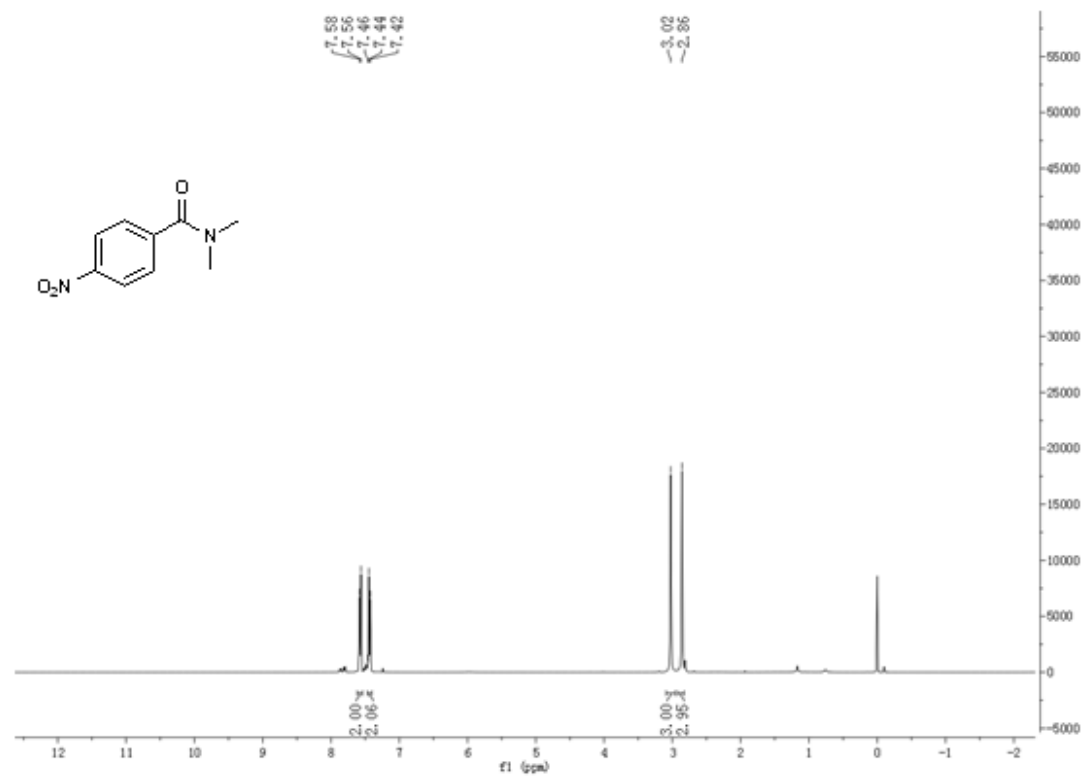
^1H NMR of 3i:



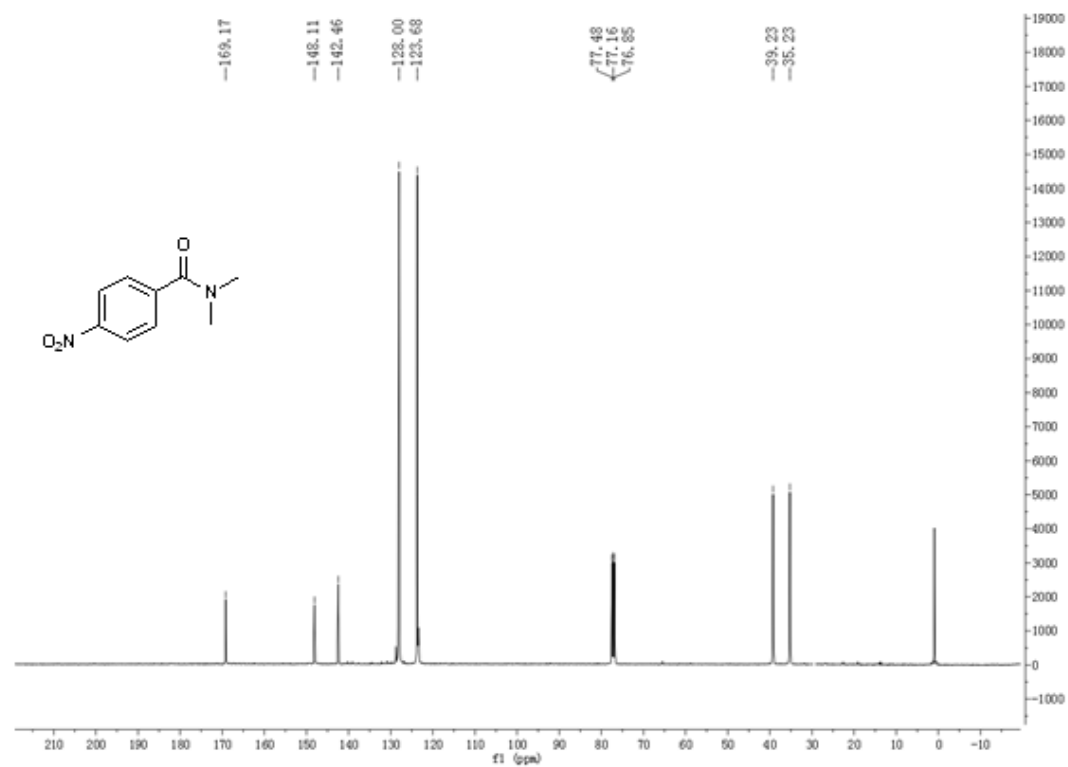
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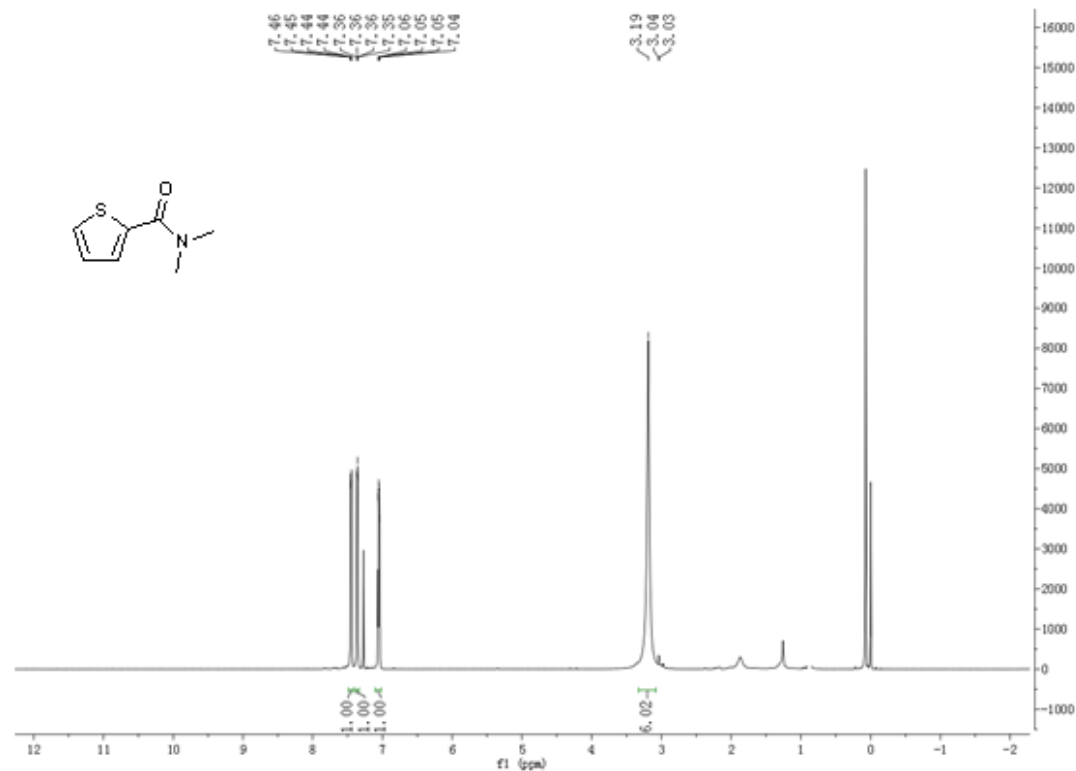
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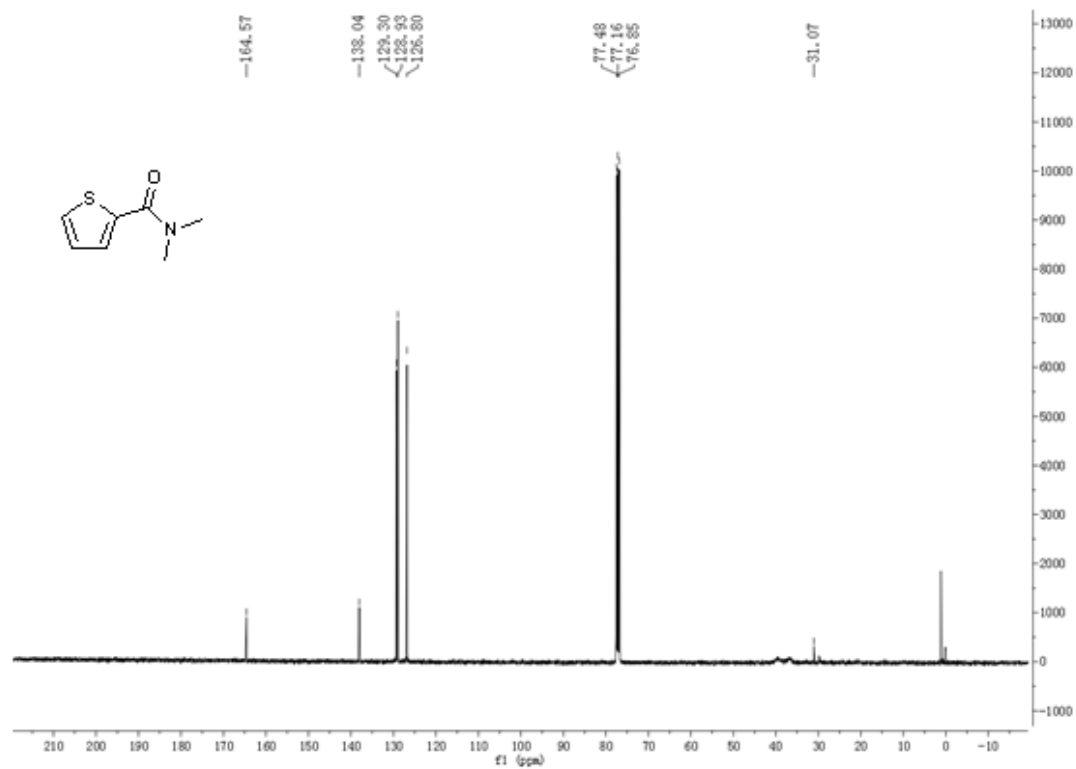
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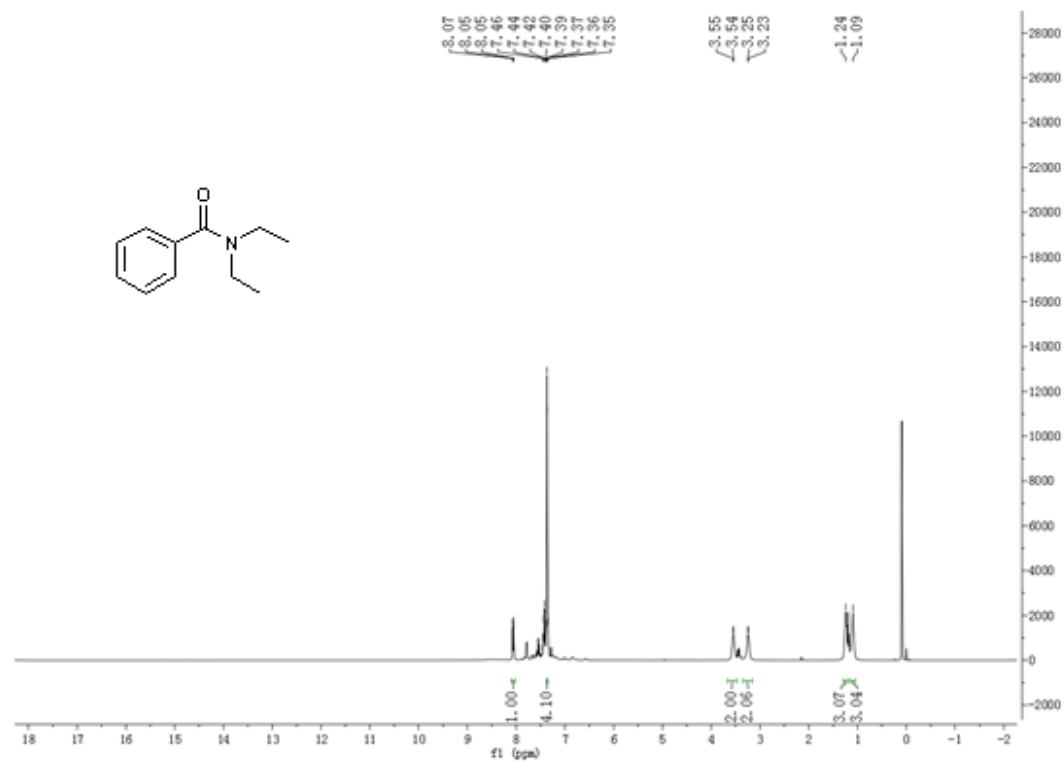
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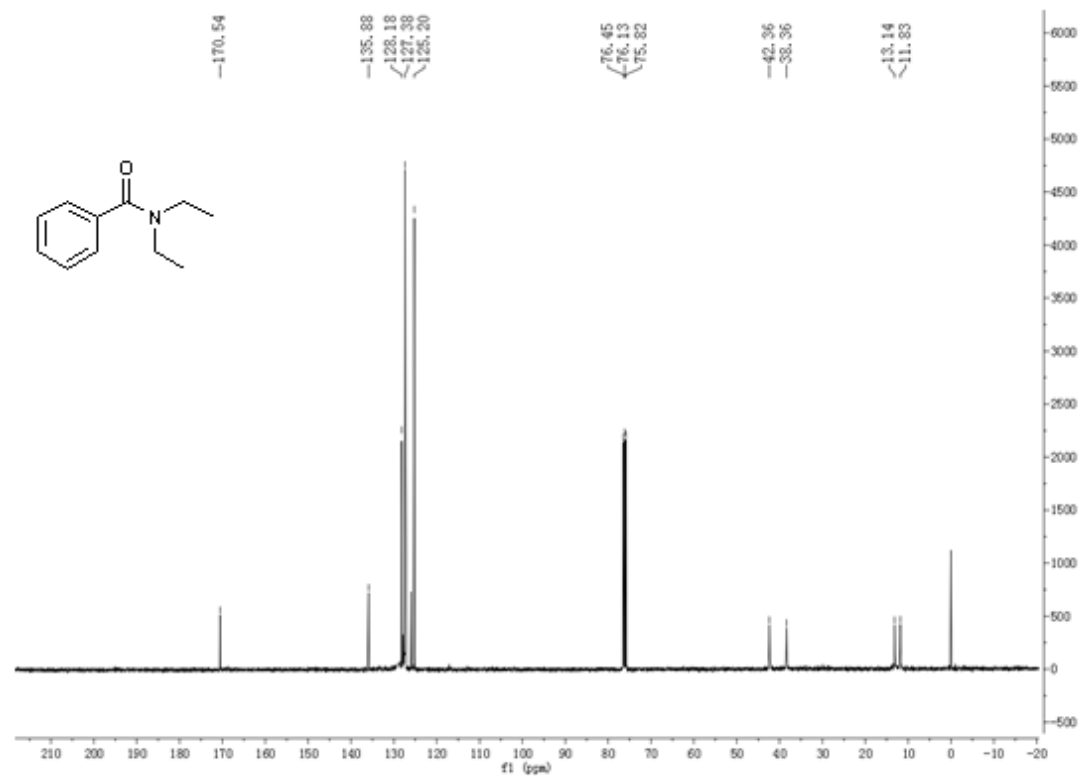
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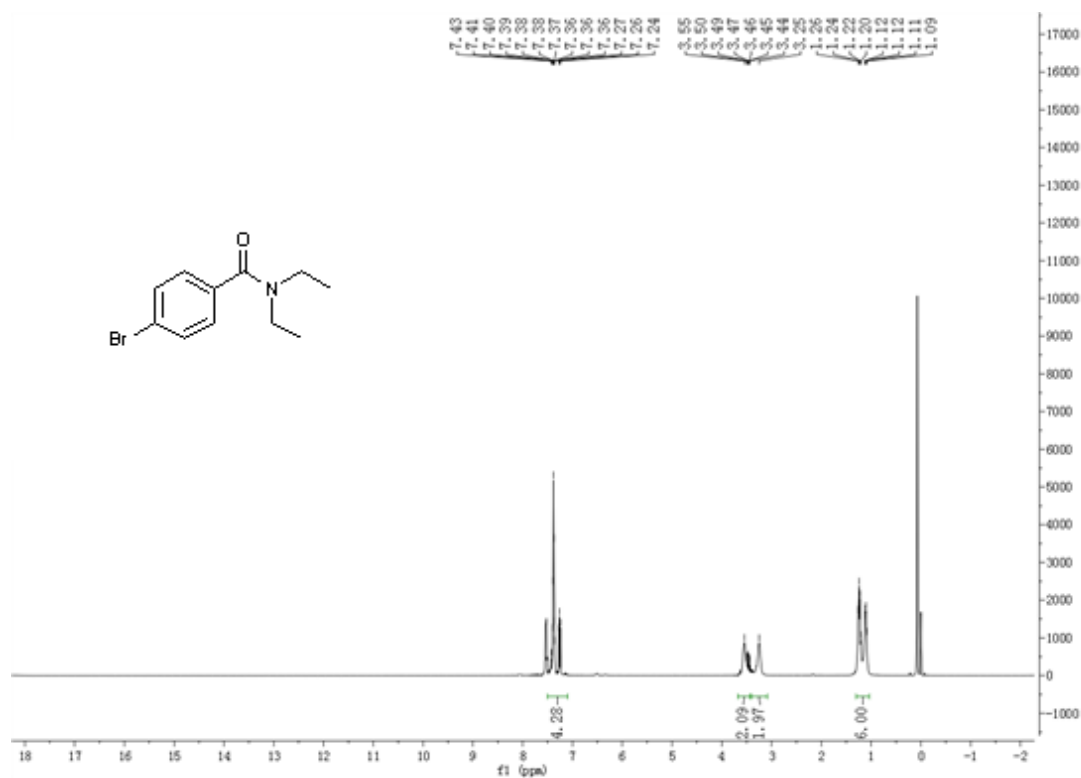
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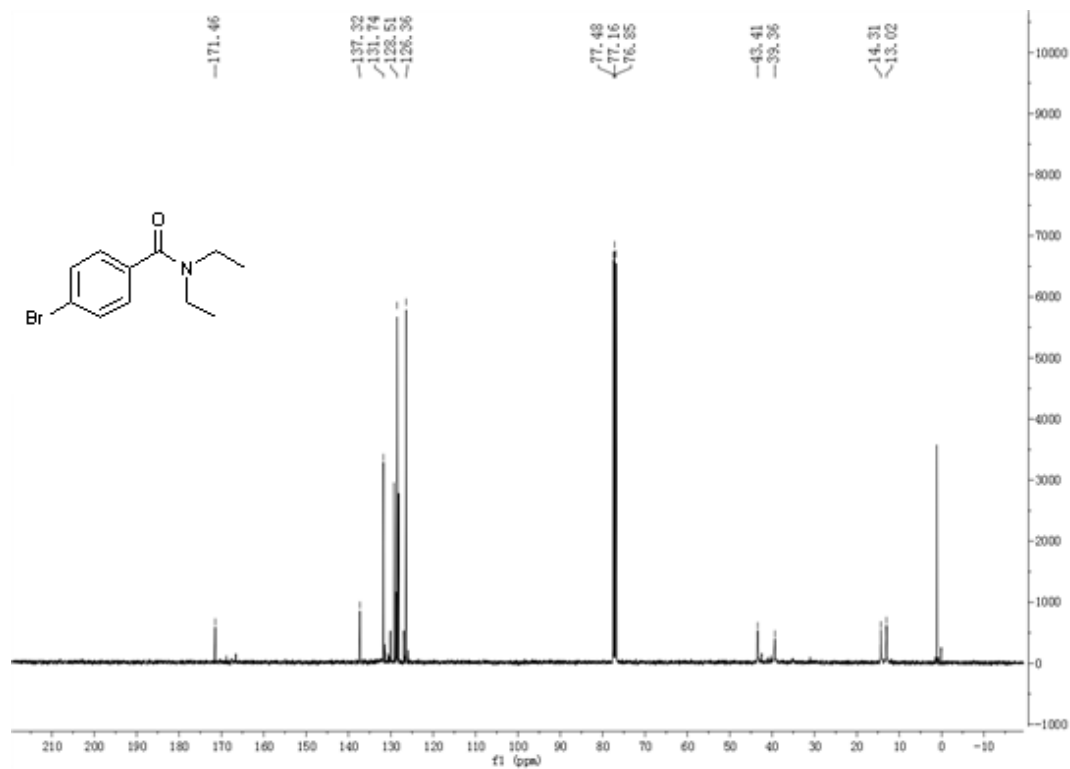
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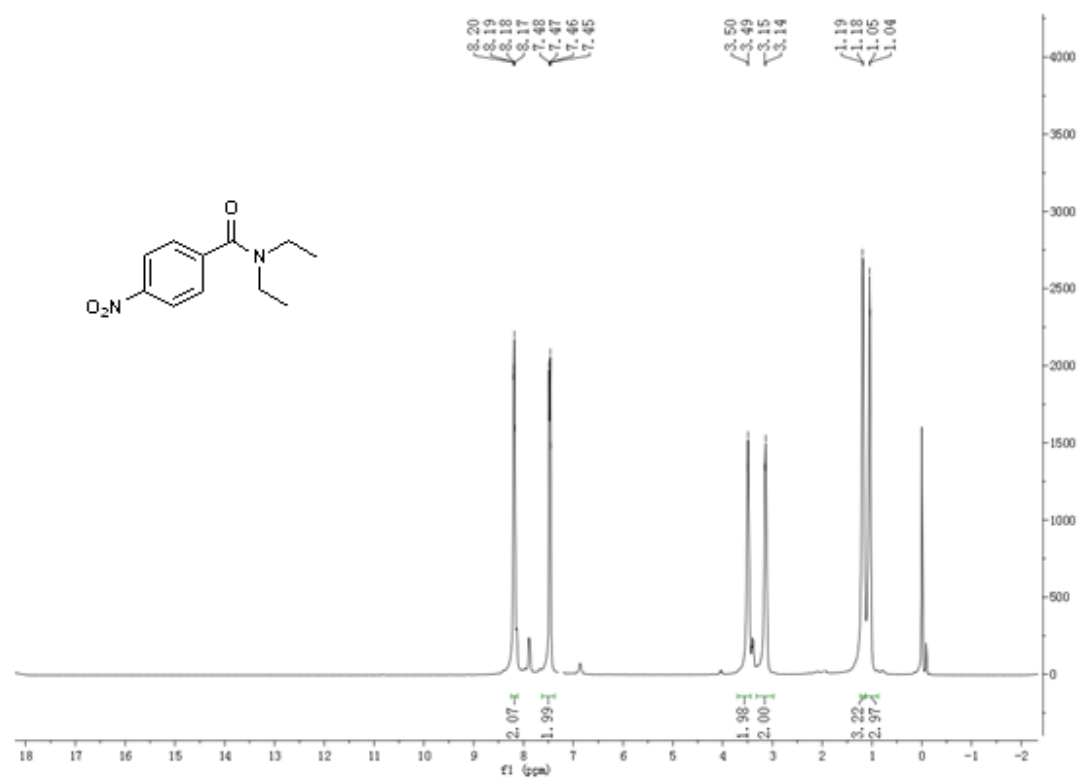
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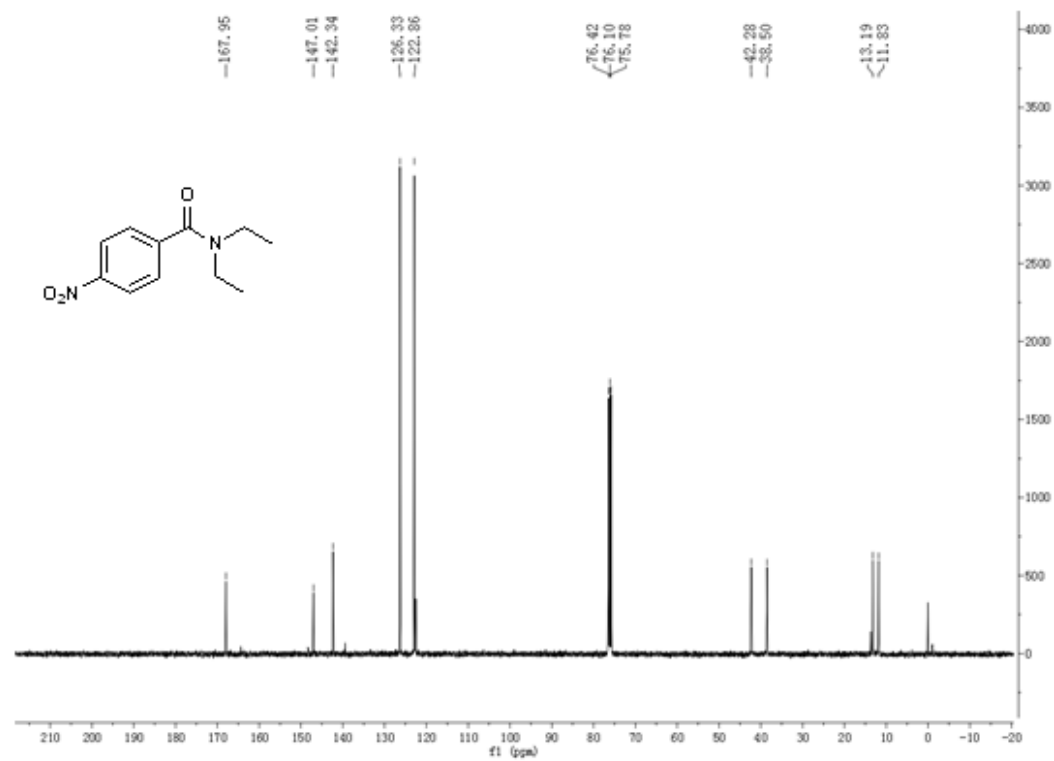
^{13}C NMR of 5g:



^1H NMR of 5j:



^{13}C NMR of 5j:



Reference:

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