**Electronic Supplementary Information**

# Efficient and selective nitrile hydration reaction in water catalyzed by unexpected dimethylsulfinyl anion generated *in situ* from CsOH and DMSO

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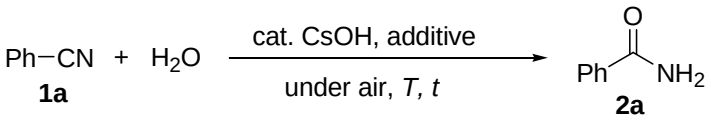
## Contents

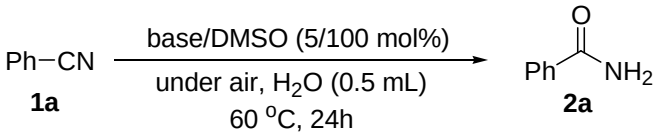
**Table S1.** Detailed Condition Screening for Dimethylsulfinyl Anion-Catalyzed Hydration of Benzonitrile in Water.[a]




| run | CsOH (mol%) | additive | $H_2O$ | *T* | *t* | **2a**%[b] |
|---|---|---|---|---|---|---|
| 1 | 10 | - | $H_2O$ (0.5 mL) | 100 °C | 24 h | (65[c,d]) |
| 2 | 10 | DMF (0.5 mL) | $H_2O$ (0.02 mL, 1.1 equiv.) | 100 °C | 24 h | 10[d] |
| 3 | 10 | dioxane (0.5 mL) | $H_2O$ (0.02 mL, 1.1 equiv.) | 100 °C | 24 h | 72[d] |
| 4 | 10 | THF (0.5 mL) | $H_2O$ (0.02 mL, 1.1 equiv.) | 100 °C | 24 h | 54[d] |
| 5 | 10 | DMSO (0.5 mL) | $H_2O$ (0.02 mL, 1.1 equiv.) | 100 °C | 24 h | >99 (85[c]) |
| 6 | 10 | DMSO (0.5 mL) | $H_2O$ (0.04 mL, 2.2 equiv.) | 100 °C | 24 h | >99 |
| 7 | 10 | DMSO (0.5 mL) | $H_2O$ (0.06 mL, 3.3 equiv.) | 100 °C | 24 h | >99 |
| 8 | 10 | DMSO (0.5 mL) | $H_2O$ (0.24 mL, 13.2 equiv.) | 100 °C | 24 h | >99 |
| 9 | 10 | DMSO (0.5 mL) | $H_2O$ (0.02 mL, 1.1 equiv.) | 100 °C | 12 h | >99 |
| 10 | 10 | DMSO (0.5 mL) | $H_2O$ (0.02 mL, 1.1 equiv.) | 100 °C | 3 h | >99 |
| 11 | 10 | DMSO (0.5 mL) | $H_2O$ (0.02 mL, 1.1 equiv.) | 100 °C | 1 h | >99 (88) |
| 12 | 10 | DMSO (10 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (55[c,d]) |
| 13 | 10 | DMSO (20 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (72[c]) |
| 14 | 10 | DMSO (30 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (78[c]) |
| 15 | 10 | DMSO (40 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (85[c]) |
| 16 | 10 | DMSO (50 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (92) |
| 17 | 5 | DMSO (25 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (60[c,d]) |
| 18 | 5 | DMSO (50 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (89) |
| 19 | 5 | DMSO (100 mol%) | $H_2O$ (0.5 mL) | 100 °C | 1.5 h | (94) |
| 20 | 10 | DMSO (50 mol%) | $H_2O$ (0.5 mL) | 60 °C | 24 h | (62[c,d]) |
| 21 | 5 | DMSO (50 mol%) | $H_2O$ (0.5 mL) | 60 °C | 24 h | (60[c,d]) |
| 22 | 5 | DMSO (100 mol%) | $H_2O$ (0.5 mL) | 60 °C | 24 h | (94) |
| 23 | 5 | DMSO (100 mol%) | $H_2O$ (0.5 mL) | rt[e] | 132 h | (85[c]) |
| 24 | 5 | DMSO (0.25 mL) | $H_2O$ (0.25 mL) | rt[e] | 84 h | (90) |
| 25 | 5 | - | $H_2O$ (0.5 mL) | rt[e] | 84 h | trace |

[a] The mixture of benzonitrile **1a** (2.0 mmol), $CsOH{\cdot}H_2O$ (5-10 mmol%), additive (solvent), and water in a Schlenk tube was sealed under air and then stirred at the indicated temperature. The reaction was then monitored by GC-MS and/or TLC. [b] GC yields (outside the parenthesis) and isolated yields (inside the parenthesis) of **2a** were based on **1a**. [c] Over hydrolysis of **1a** occurred in variant degrees to give byproduct PhCOOH. [d] The reactions were incomplete for **1a** was detected. [e] Room temperature: ca. 30 °C.

**Table S2.** Catalytic Activities of Different Bases under the Optimal Conditions.[a]




| run | base (purity) | **2a**%[b] |
|---|---|---|
| 1 | LiOH (98%) | 50 |
| 2 | NaOH (99.99%) | 46 |
| 3 | KOH (AR) | 30 |
| ***4*** | ***CsOH·H$_2$O (99%)*** | ***94*** |
| 5 | $Na_2CO_3$ (AR) | 7 |
| 6 | $K_2CO_3$ (AR) | 4 |
| 7 | $Cs_2CO_3$ (99.9%) | 7 |

[a] The mixture of **1a** (2 mmol) and base/DMSO (5/100mol%) in $H_2O$ (0.5 mL) in a Schlenk tube was sealed under air and then heated at 60 °C for 24 h. [b] Isolated yields based on **1a**.

## Experimental

**General.** Substrates, catalysts, solvents, and $^{18}O$-$H_2O$ (98% purity) were all purchased and used as received. $^{18}O$-DMSO was prepared according to the reported literature procedure (Fenselau, A. H.; Moffatt, J. G. *J. Am. Chem. Soc.* **1966**, *88*, 1762) and determined to be containing 86% $^{18}O$-DMSO by Secondary Mass analysis. Unless otherwise noted, all reactions were carried out in sealed Schlenk tubes under air and then monitored by TLC. Products of small scale reactions were all purified by column chromatography on silica gel using petroleum ether and ethyl acetate as the eluent. Products of large scale reactions were obtained by simple filtration of the reaction mixtures that include solid amides and liquid reaction media. Absolutely dry DMSO was prepared by distillation from $CaH_2$-predried DMSO and stored under nitrogen in a sealed Schenk flask. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker Avance-III 500 instrument (500 MHz for $^1H$ and 125.4 MHz for $^{13}C$ NMR spectroscopy) by using $d_6$-DMSO or $CDCl_3$ as the solvent. Chemical shifts for $^1H$ and $^{13}C$ NMR were referred to internal $Me_4Si$ (0 ppm). Mass spectra were measured on a Shimadzu GCMS-QP2010 Plus spectrometer (EI). Secondary Mass analysis was conducted at the Analysis Center of Department of Chemistry of Zhejiang University.

**Typical Procedure for Dimethylsulfinyl Anion-Catalyzed Hydration of Organonitriles to Amides in Water.** Benzonitrile **1a** (2.0 mmol) and CsOH (0.0169 g, 0.1 mmol, 5 mol%) were mixed in $H_2O$ (0.5 mL) under air in a Schlenk tube. No any obvious phenomenon of the reaction mixture could be observed at this stage at room temperature. DMSO (0.142 mL, 1.0 equiv.) was then added to the above mixture *via* a syringe. In great difference, upon addition of DMSO, a slight but obvious exothermic phenomenon was observed if touching outward surface of the tube. The reaction mixture was then directly sealed under air and stirred at 60 $^oC$ for 24 h. After completion of the reaction as monitored by TLC (also: forming beautiful crystalline solids in the tube), the mixture was then directly purified, without any workup, through a silica gel column by using ethyl acetate and petroleum ether as the eluent, affording benzamide **2a** in 94% isolated yield.

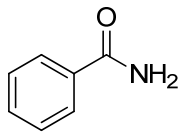
**Additional Comments:**

It should be noted that, no exothermic phenomenon could be observed when mixing **1a**, CsOH, and water at room temperature before addition of DMSO. In great contrast, slight but obvious exothermic phenomenon was observed upon addition of DMSO to the above mixture. Accordingly, no obvious formation of the product could be detected by TLC in the reaction at room temperature without DMSO (Table S1, run 25). On the contrary, slight but obvious exothermic phenomenon was

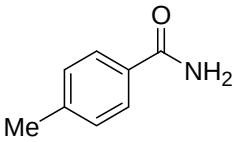
observed in reactions under the same condition upon addition of DMSO (Table S1, runs 23-24). Accordingly, hydration reactions occurred smoothly to give high yields of **2a**. Similarly, exothermic phenomena in varied degrees (from slight/weak to obvious/strong) were also observed in the reactions of other nitriles upon addition of DMSO.

All the above contrastive phenomena and results support that, the true catalyst of the reaction should not be the simple hydroxide anion $OH^-$ derived from CsOH, but a more active new species generated *in situ* from CsOH and DMSO. Since DMSO can be easily deprotonated by bases to form equilibrial ambident dimethylsulfinyl anion (**I**) even at room temperature (ref 16 of the text), we deduce it might be the active catalyst for the reaction.

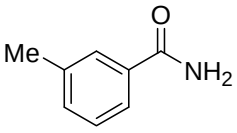
**Characterization of the Products and References.**



**Benzamide.** $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.01 (b, 1H), 7.88-7.86 (m, 2H), 7.54-7.51 (m, 1H), 7.47-7.44 (m, 2H), 7.39 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 168.0, 134.1, 131.2, 128.2, 127.4. MS (EI): m/z (%) 122 (6, M+1), 121 (86, $M^+$), 106 (8), 105 (100), 78 (12), 77 (83), 76 (6), 75 (4), 74 (6), 65 (2), 52 (6), 51 (35), 50 (20), 44 (8), 39 (6), 38 (4), 37 (3), 27 (4). This compound was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal.* **2012**, *354*, 584-588.

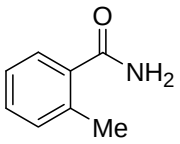


**4-Methylbenzamide.** $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.91 (b, 1H), 7.78 (d, $J$ = 8.0 Hz, 2H), 7.29 (b, 1H), 7.25 (d, $J$ = 8.0 Hz, 2H), 2.35 (s, 3H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 167.7, 141.0, 131.4, 128.7, 127.5, 20.9. MS (EI): m/z (%) 136 (5, M+1), 135 (60, $M^+$), 120 (8), 119 (100), 117 (3), 92 (5), 91 (74), 90 (8), 89 (10), 65 (33), 64 (4), 63 (13), 51 (9), 50 (6), 44 (12), 41 (5), 40 (9), 39 (20), 38 (4). This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.

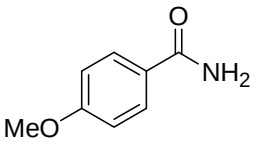


**3-Methylbenzamide**. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.65 (s, 1H), 7.59-7.57 (m, 1H ), 7.34-7.30 (m, 2H), 6.19 (b, 2H), 2.39 (s, 3H). $^{13}$C NMR (125.4 MHz, $CDCl_3$): $\delta$ 169.8, 138.5, 133.4, 132.7, 128.5, 128.1, 124.3, 21.3. MS (EI): m/z (%) 136 (6, M+1), 135 (63, $M^+$), 120 (9), 119 (100), 117 (4), 116 (2), 92 (6), 91 (77), 90 (5), 89 (7), 65 (18), 63 (6), 62 (2), 51(4), 44 (3), 39 (6). This product was

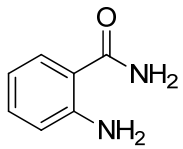
known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.



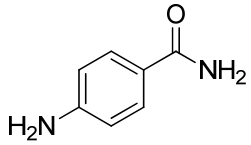

**2-Methylbenzamide.** $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.71 (b, 1H), 7.36-7.30 (m, 3H), 7.24-7.20 (m, 2H), 2.37 (s, 3H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 176.3, 142.3, 140.3, 135.7, 134.4, 132.2, 130.6, 24.8. MS (EI): m/z (%) 136 (6, M+1), 135 (66, $M^+$), 120 (9), 119 (99), 92 (8), 91 (100), 89 (14), 77 (4), 66 (3), 65 (42), 64 (6), 63 (21), 62 (10), 51 (12), 44 (18), 41 (5), 39 (28), 38 (6), 27 (4), 16 (3). This compound was known: Liu, Y. M.; Lin, H.; Fan, K. N. *ChemSusChem*. **2012**, *5*, 1392-1396.




**4-Methoxybenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.78 (d, $J$ = 8.5 Hz, 2H), 7.74 (b, 1H), 7.08 (b, 1H), 6.91 (d, $J$ = 8.0 Hz, 2H), 3.74 (s, 3H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 167.9, 162.1, 129.8, 127.0, 113.9, 55.8. MS (EI): *m/z* (%) 152 (5, M+1), 151 (54, $M^+$), 136 (9), 135 (100), 108 (3), 107 (14), 92 (13), 77 (18), 65 (3), 64 (8), 63 (8), 50 (4), 44 (4), 39 (3), 38 (3), 15 (3). This product was known: Tu, T.; Wang, Z.; Liu, Z.; Feng. X.; Wang, Q. *Green. Chem.* **2012**, *14*, 921-924.

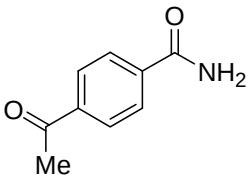



**2-Aminobenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.73 (b, 1H), 7.52 (d, $J$ = 8.0 Hz, 1H), 7.13 (t, $J$ = 8.0 Hz, 1H), 7.07 (b, 1H), 6.67 (d, $J$ = 8.0 Hz, 1H), 6.57 (b, 2H), 6.48 (t, $J$ = 7.5 Hz, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 171.2, 150.2, 131.8, 128.7, 116.3, 114.3, 113.6. MS (EI): m/z (%) 137 (6, M+1), 136 (74, $M^+$), 120 (15), 119 (100), 118 (6), 93 (4), 92 (52), 91 (15), 66 (4), 65 (24), 64 (9), 63 (6), 52 (5), 39 (9). This product was known: Tu, T.; Wang, Z.; Liu, Z.; Feng, X.; Wang, Q. *Green. Chem.* **2012**, *14*, 921-924.

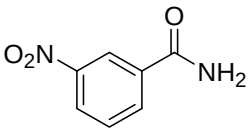



**4-Aminobenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.59 (d, $J$ = 8.5 Hz, 2H), 7.53 (b, 1H), 6.84 (b, 1H), 6.53 (d, $J$ = 8.5 Hz, 2H), 5.60 (b, 2H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 173.3, 156.9, 134.3, 126.2, 117.7. MS (EI): m/z (%) 137(6, M+1), 136 (75, $M^+$), 121 (8), 120 (100), 118 (3), 107

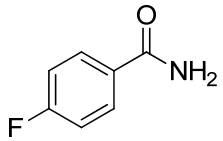
(4), 93 (4), 92 (40), 91 (5), 66 (6), 65 (37), 63 (6), 54 (6), 52 (4), 44 (4), 41 (4), 39 (13), 38 (4), 28 (4). This compound was known: Liu, Y. M.; Lin, H.; Fan, K. N. *ChemSusChem.* **2012**, *5*, 1392-1396.



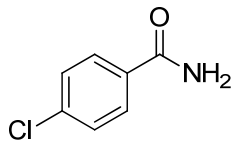

**4-Acetylbenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.15 (b, 1H), 8.02 (d, $J$ = 8.5 Hz, 2H), 7.98 (d, $J$ = 8.5 Hz, 2H), 7.56 (b, 1H), 2.62 (s, 3H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 203.0, 172.4, 143.9, 143.3, 133.3, 133.0, 32.1. MS (EI): m/z (%) 164 (7, M+1), 163 (66, $M^+$), 149 (10), 148 (100), 120 (28), 117 (4), 92 (4), 89 (5), 79 (11), 77 (7), 76 (4), 66 (6), 65 (13), 63 (6), 62 (7), 54 (4), 53 (4), 51 (6), 50 (4), 39 (3), 38 (3). This compound was known: Liu, Y. M.; Lin, H.; Fan, K. N. *ChemSusChem.* **2012**, *5*, 1392-1396.



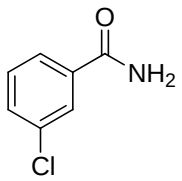

**3-Nitrobenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.69 (s, 1H), 8.39 (b, 1H), 8.36 (d, $J$ = 8.0 Hz, 2H), 8.31 (d, $J$ = 7.5 Hz, 1H), 7.77 (m, 1H), 7.73 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 165.8, 147.8, 135.7, 133.8, 130.1, 125.9, 122.2. MS (EI): m/z (%) 167 (6, M+1), 166 (67, $M^+$), 151 (8), 150 (100), 105 (3), 104 (33), 92 (17), 77 (14), 76 (54), 75 (30), 74 (30), 73 (6), 65 (26), 64 (6), 63 (9), 62 (5), 53 (4), 51 (20), 50 (52), 46 (20), 44 (50), 39 (9), 38 (7), 37 (5), 30 (31) . This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.



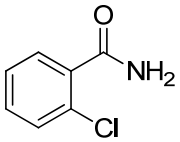

**4-Fluorobenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.02 (b, 1H), 7.96-7.93 (m, 2H), 7.41 (b, 1H), 7.28 (m, 2H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.9, 163.9 (d, $J_{C\text{-}F}$ = 248 Hz), 130.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 130.1 (d, $J_{C\text{-}F}$ = 9.0 Hz), 115.1 (d, $J_{C\text{-}F}$ = 21.6 Hz). MS (EI): m/z (%) 140 (6, M+1), 139 (62, $M^+$), 124 (8), 123 (100), 122 (2), 121 (5), 96 (10), 95 (80), 94 (8), 93 (3), 83 (3), 76 (4), 75 (35), 74 (10), 70 (4), 69 (8), 68 (6), 63 (4), 62 (3), 61 (3), 57 (4), 51 (7), 50 (14), 44 (11), 39 (3), 38 (3), 37 (4), 31 (3). This product was known: Tu, T.; Wang, Z.; Liu, Z.; Feng, X.; Wang, Q. *Green. Chem.* **2012**, *14*, 921-924.



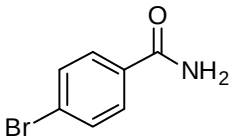
**4-Chlorobenzamide.** $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.07 (b, 1H), 7.91-7.88 (m, 2H), 7.53 (d, $J$ = 9.0 Hz, 2H), 7.49 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.8, 136.0, 133.0, 129.4, 128.3. MS (EI): m/z (%) 157 (16, M+2), 155 (50, $M^+$), 141 (29), 140 (8), 139 (100), 137 (8), 113 (16), 112 (5), 111 (51), 85 (4), 77 (5), 76 (8), 75 (35), 74 (15), 73 (5), 51 (10), 50 (21), 44 (10), 38 (5), 28 (4). This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.



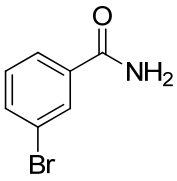

**3-Chlorobenzamide.** $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.10 (b, 1H), 7.92 (s, 1H), 7.84 (d, $J$ = 7.5 Hz, 1H), 7.60 (d, $J$ = 8.0 Hz, 1H), 7.54 (b, 1H), 7.50 (t, $J$ = 7.5 Hz, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.4, 136.3, 133.1, 131.0, 130.2, 127.3, 126.1. MS (EI): m/z (%) 157 (19, M+2), 155 (53, $M^+$), 141 (27), 140 (11), 139 (100), 137 (9), 113 (16), 112 (5), 111 (51), 85 (5), 77 (7), 76 (9), 75 (35), 74 (15), 73 (5), 51 (10), 50 (23), 44 (9), 38 (4), 28 (3). This compound was known: Liu, Y. M.; Lin, H.; Fan, K. N. *ChemSusChem*. **2012**, *5*, 1392-1396.



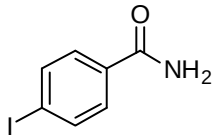

**2-Chlorobenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.94 (b, 1H), 7.66 (b, 1H), 7.55-7.53 (m, 1H), 7.51-7.46 (m, 2H), 7.45-7.42 (m, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 168.1, 137.1, 130.5, 129.58, 129.56, 128.6, 127.0. MS (EI): m/z (%) 157 (18, M+2), 156 (4, M+1), 155 (58, $M^+$), 142 (2), 141 (32), 140 (8), 139 (100), 113 (12), 112 (6), 111 (38), 85 (3), 77 (9), 76 (8), 75 (26), 74 (8), 51 (9), 50 (16), 44 (11), 38 (4), 37 (3). This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.



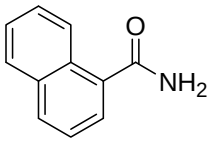

**4-Bromobenzamide.** $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.07 (d, 1H), 7.82 (d, $J$ = 8.5 Hz, 2H), 7.67 (d, $J$ = 7.0 Hz, 2H), 7.49 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.9, 133.3, 131.2, 129.5, 125.0. MS (EI): m/z (%) 201 (51, M+2), 199 (53, $M^+$), 185 (94), 184 (7), 183 (100), 157 (37), 155 (38), 77 (20), 76 (46), 75 (45), 74 (26), 73 (6), 65 (6), 51 (22), 50 (67), 49 (6), 44 (25). This product was known: Tu, T.; Wang, Z.; Liu, Z.; Feng, X.; Wang, Q. *Green. Chem.* **2012**, *14*, 921-924.



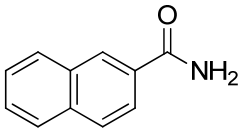
**3-Bromobenzamide.** $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.11 (b, 1H), 8.06-8.05 (m, 1H), 7.89-7.87 (m, 1H), 7.73-7.71 (m, 1H), 7.53 (b, 1H), 7.43 (t, $J$ = 8.0 Hz, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 171.6, 141.7, 139.2, 135.7, 135.4, 131.8, 126.8. MS (EI): m/z (%) 202 (5), 201 (58, M+2), 200 (5, M+1), 199 (59, $M^+$), 186 (8), 185 (96), 184 (8), 183 (100), 157 (31), 156 (4), 155 (32), 139 (6), 102 (3), 77 (17), 76 (26), 75 (25), 74 (11), 65 (4), 51 (11), 50 (26), 44 (12), 38 (6), 37 (4). This compound was known: Liu, Y. M.; Lin, H.; Fan, K. N. *ChemSusChem.* **2012**, *5*, 1392-1396.



**4-Iodobenzamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.03 (b, 1H), 7.84 (d, $J$ = 8.5 Hz, 2H), 7.66 (d, $J$ = 8.0 Hz, 2H), 7.44 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 167.2, 137.1, 133.7, 129.4, 98.8. MS (EI): m/z (%) 248 (8, M+1), 247 (100, $M^+$), 232 (4), 231 (72), 203 (29), 127 (5), 104 (5), 103 (4), 92 (3), 77 (8), 76 (38), 75 (12), 74 (13), 73 (3), 65 (7), 56 (4), 51 (9), 50 (28), 44 (13). This compound was known: Sahnoun, S.; Messaoudi, S.; Peyrat, J.-F.; Brion, J.-D. *Tetrahedron Lett.* **2012**, *53*, 2860-2863.

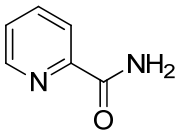


**1-Naphthamide**. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.43 (d, $J$ = 8.5 Hz, 1H), 7.95 (d, $J$ = 8.5 Hz, 1H), 7.88 (d, $J$ = 8.0 Hz, 1H), 7.71 (d, $J$ = 7.0 Hz, 1H), 7.60-7.53 (m, 2H), 7.49-7.46 (m, 1H), 5.96 (b, 1H). $^{13}$C NMR (125.4 MHz, $CDCl_3$): $\delta$ 171.3, 133.7, 133.1, 131.2, 130.0, 128.3, 127.3, 126.5, 125.4, 125.3, 124.6. MS (EI): m/z (%) 172 (9, M+1), 171 (72, $M^+$), 170 (26), 156 (9), 155 (75), 154 (7), 153 (4), 128 (15), 127 (100), 126 (28), 125.4 (3), 115 (9), 101 (9), 85 (4), 77 (12), 76 (5), 75 (10), 63 (12), 51 (8), 50 (6), 44 (4). This product was known: Tu, T.; Wang, Z.; Liu, Z.; Feng, X.; Wang, Q. *Green. Chem.* **2012**, *14*, 921-924.

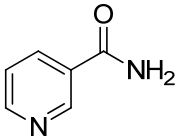


**2-Naphthamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.49 (s, 1H), 8.15 (b, 1H), 8.01 (d, $J$ = 7.5 Hz,

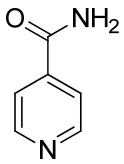
1H), 7.99-7.95 (m, 3H), 7.64-7.58 (m, 2H), 7.47 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 168.0, 134.1, 132.1, 131.7, 128.8, 127.8, 127.7, 127.6, 127.5, 126.6, 124.4. MS (EI): m/z (%) 172 (9, M+1), 171 (71, $M^+$), 170 (23), 156 (10), 155 (73), 154 (8), 153 (7), 128 (15), 127 (100), 126 (28), 125.4 (3), 115 (11), 101 (8), 85 (5), 77 (14), 76 (5), 75 (13), 63 (12), 51 (8), 50 (6), 44 (3). This compound was known: Wu, X.-F.; Sharif, M.; Feng, J.-B.; Neumann, H.; Langerb, P.; Beller, M. *Green. Chem*. **2013**, *15*, 1956-1961.



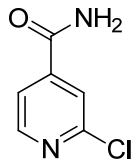

**Picolinamide**. $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.64-8.62 (m, 1H), 8.16 (b, 1H), 8.06-8.04 (m, 1H), 8.00-7.97 (m, 1H), 7.67 (b, 1H), 7.60-7.57(m, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.0, 150.3, 148.4, 137.6, 126.4, 121.9. MS (EI): m/z (%) 123 (2, M+1), 122 (29, $M^+$), 80 (6), 79 (100), 78 (34), 76 (5), 53 (7), 52 (50), 51 (39), 50 (20), 49 (5), 44 (19), 39 (8), 38 (6), 37 (4), 28 (7), 27 (8), 26 (7), 16 (5). This product was known: Tamura, M.; Wakasugi, H.; Shimizu, K.; Satsuma, A. *Chem. Eur. J.* **2011**, *17*, 11428-11431.



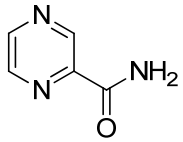

**Nicotinamide**. $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 9.04-9.03 (m, 1H), 8.71 (dd, $J$ = 1.5, $J$ = 5.0 Hz, 1H), 8.22-8.20 (m, 1H), 8.18 (b, 1H), 7.63 (b, 1H), 7.52-7.49 (m, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.4, 151.9, 148.6, 135.1, 129.6, 123.4. MS (EI): m/z (%) 123 (8, M+1), 122 (100, $M^+$), 106 (60), 105 (6), 104 (3), 94 (3), 79 (8), 78 (69), 77 (7), 76 (3), 75 (2), 53 (3), 52 (12), 51 (30), 50 (13), 49 (2), 44 (8), 39 (3), 38 (2). This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.



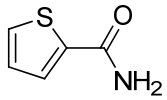

**Isonicotinamide**. $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.72 (d, $J$ = 6.0 Hz, 2H), 8.27 (b, 1H), 7.77 (d, $J$ = 4.5 Hz, 2H), 7.76 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.3, 150.2, 141.2, 121.4. MS (EI): m/z (%) 123 (8, M+1), 122 (100, $M^+$), 107 (2), 106 (40), 79 (12), 78 (56), 77 (2), 53 (2), 52 (15), 51 (36), 50 (14), 49 (2), 44 (13), 39 (3), 28 (3), 26 (2). This product was known: Tu, T.; Wang, Z.; Liu, Z.; Feng, X.; Wang, Q. *Green. Chem.* **2012**, *14*, 921-924.



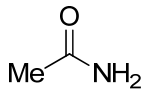
**2-Chloroisonicotinamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.56 (d, $J$ = 5.0 Hz, 1H), 8.33 (b, 1H), 7.88 (b, 2H), 7.78 (dd, $J$ = 5.5, J = 1.5 Hz, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 164.8, 150.9, 150.6, 144.9, 122.1, 121.0. MS (EI): m/z (%) 158 (20, M+2), 157 (9, M+1), 156 (75, $M^+$), 142 (30), 141 (7), 140 (100), 114 (16), 112 (48), 85 (14), 78 (9), 76 (19), 75 (4), 51 (15), 50 (19), 44(18), 28 (6). This product was known: Sahnoun, S.; Messaoudi, S.; Peyrat, J.; Brion, J.; Alami, M. *Tetrahedron Lett.* **2012**, *53*, 2860-2863



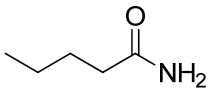
**Pyrazine-2-Carboxamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 9.20 (d, $J$ = 1.5 Hz, 1H), 8.86 (d, $J$ = 2.5 Hz, 1H), 8.72 (dd, $J$ = 2.5, $J$ = 1.5 Hz, 1H), 8.29 (b, 1H), 7.89 (b, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 165.0, 147.4, 145.1, 143.6, 143.4. MS (EI): m/z (%) 124 (7, M+1), 123 (100, $M^+$), 81 (4), 80 (80), 79 (18), 54 (2), 53 (51), 52 (32), 51 (9), 44 (18), 40 (2), 28 (12), 26 (15). This product was known: Tamura, M.; Wakasugi, H.; Shimizu, K.; Satsuma, A. *Chem. Eur. J.* **2011**, *17*, 11428-11431.



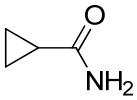
**Thiophene-2-Carboxamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 8.03 (b, 1H), 7.80 (d, $J$ = 4.5 Hz, 2H), 7.45 (b, 1H), 7.19 (t, $J$ = 7.5 Hz, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 162.8, 140.3, 130.9, 128.6, 127.9. MS (EI): m/z (%) 129 (4, M+2), 128 (5, M+1), 127(75, $M^+$), 113 (6), 112 (7), 111 (100), 83 (13), 82 (8), 81 (7), 58 (13), 57 (18), 54 (4), 53 (4), 50 (5), 45 (19), 44 (18), 39 (60), 38 (10). This product was known: Rocío, G.-Á.; Josefina, D.; Pascale, C.; Victorio, C. *Organometallics.* **2011**, *30*, 5442-5451.



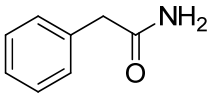
**Acetamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.30 (b, 1H), 6.70 (b, 1H), 1.76 (s, 3H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 176.9, 27.7. MS (EI): m/z (%) 59 ($M^+$). This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.



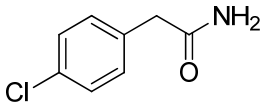
**Pentanamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.24 (b, 1H), 6.70 (b, 1H), 2.03 (t, $J$ = 7.5 Hz, 2H), 1.49-1.43 (m, 2H), 1.30-1.22 (m, 2H), 0.87 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 174.3, 34.8, 27.2, 21.8, 13.7. MS (EI): m/z (%) 86 (7), 85 (5), 73 (4), 72 (18), 60 (8), 59 (100), 57 (16), 55 (9), 44 (30), 43 (7), 42 (6), 41 (10), 39 (5), 29 (19), 28 (9). This product was known: Das, R.; Chakraborty, D. *Catal. Commun.* **2012**, *26*, 48-53.



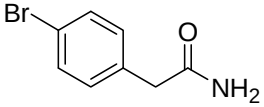
**Cyclopropanecarboxamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.53 (b, 1H), 6.78 (b, 1H), 1.53-1.48 (m, 1H), 0.64-0.61 (m, 4H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 174.6, 13.2, 6.2. MS (EI): m/z (%) 85 (8, $M^+$), 84 (61), 69 (25), 68 (8), 54 (5), 44 (100), 43 (8), 42 (41), 41 (70), 40 (14), 39 (90), 38 (27), 37 (15), 28 (26), 27 (26), 26 (12), 16 (17), 15 (9), 14 (8). This product was known: Jiang, D.; Yuan, F.; Jiang, B.; Li, C. *Faming Zhuanli Shenqing*. **2011**, *CN*, 102249949 A 20111123.



**2-Phenylacetamide**. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 7.48 (b, 1H), 7.32-7.26 (m, 4H), 7.24-7.21 (m, 1H), 6.89 (b, 1H), 3.38 (s, 2H). $^{13}$C NMR (125.4 MHz, $CDCl_3$): $\delta$ 172.2, 136.5, 129.0, 128.1, 126.2, 42.2. MS (EI): m/z (%) 135 (18, $M^+$), 93 (7), 92 (92), 91 (100), 90 (5), 89 (8), 65 (27), 64 (9), 63 (11), 51 (5), 50 (6), 44 (11), 41 (3), 39 (14), 38 (5). This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal.* **2012**, *354*, 584-588.

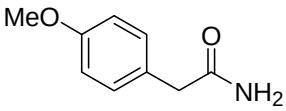


**2-(4-Chlorophenyl)acetamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.50 (b, 1H), 7.36-7.35 (m, 2H), 7.28 (d, $J$ = 8.5 Hz, 2H), 6.93 (b, 1H), 3.37 (s, 2H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 171.8, 135.5, 131.0, 130.90, 128.0, 41.3. MS (EI): m/z (%) 158 (14), 156 (41), 128 (15), 127 (24), 126 (46), 125 (63), 112 (4), 99 (6), 92 (8), 91 (100), 90 (9), 89 (6), 77 (16), 65 (15), 63 (9), 51 (6), 39 (7), 31 (17). This product was known: Khodaei, M. M.; Nazari, E. *Tetrahedron Lett.* **2012**, *53*, 2881-2884.

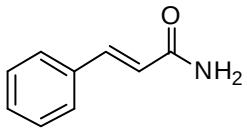


**2-(4-Chlorophenyl)acetamide**. $^{1}$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.50-7.48 (m, 3H), 7.22 (d, $J$ = 8.5 Hz, 2H), 6.93 (b, 1H), 3.36 (s, 2H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 171.7, 135.9, 131.3,

130.9, 119.4, 41.4. MS (EI): m/z (%) 215 (27, M+2), 213 (28, $M^+$), 174 (7), 173 (96), 172 (11), 171 (100), 145 (8), 143 (8), 119 (5), 92 (44), 91 (22), 90 (9), 75 (6), 65 (31), 64 (20), 63 (35), 62 (12), 61 (5), 52 (6), 50 (10), 43 (70), 39 (14), 38 (12), 28 (3). This product was known: Yoshimura, A.; Middleton, K. R.; Luedtke, M. W.; Zhu, C. J.; Zhdankin, V. *J. Org. Chem.* **2012**, *77*, 11399-11404.




**2-(4-Methoxyphenyl)acetamide**. $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.39 (b, 1H), 7.17 (d, $J$ = 8.5 Hz, 2H), 6.86 (d, $J$ = 8.5 Hz, 2H), 6.82 (b, 1H), 3.73 (s, 3H), 3.29 (s, 2H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 172.6, 157.8, 130.0, 128.4, 113.6, 55.0, 41.3. MS (EI): m/z (%) 166 (2, M+1), 165 (20, $M^+$), 122 (12), 121 (100), 107 (4), 91 (8), 89 (4), 78 (12), 77 (16), 65 (4), 63 (4), 52 (6), 51 (8), 50 (4), 44 (8), 39 (4). This product was known: Yoshimura, A.; Middleton, K. R.; Luedtke, M. W.; Zhu, C. J.; Zhdankin, V. *J. Org. Chem.* **2012**, *77*, 11399-11404.




**Cinnamamide**. $^1$H NMR (500 MHz, $d_6$-DMSO): $\delta$ 7.58-7.56 (m, 3H), 7.45-7.38 (m, 4H), 7.14 (b, 1H), 6.62 (d, $J$ = 16.0 Hz, 1H). $^{13}$C NMR (125.4 MHz, $d_6$-DMSO): $\delta$ 166.7, 139.1, 134.9, 129.4, 128.9, 127.5, 122.3. MS (EI): m/z (%) 148 (6, M+1), 147 (59, $M^+$), 146 (100), 131 (60), 130 (22), 129 (65), 128 (19), 104 (12), 103 (80), 102 (35), 78 (12), 77 (49), 76 (10), 63 (11), 51 (32), 50 (13), 44 (11), 39 (7). This product was known: Li, Z.; Wang, L.; Zhou, X. *Adv. Synth. Catal*. **2012**, *354*, 584-588.

# Mechanistic studies and Secondary Mass Analysis of $^{16}O$- and $^{18}O$-Isotopic Products:

## 1. Quality report of commercial $^{18}O$-$H_2O$ ($^{18}O$: 98%):

**Huayi Isotopes Co.**

*The leading manufacturer of Oxygen 18 Water & PET Precursors*

### Certificate of Analysis

**Product Name:** Oxygen-18 Water 98 %
**CAS No.:** [14314-42-2]
**Lot No.:** WT-121201
**Manufacturing Date:** Dec 2012
**Expiry Date:** Dec 2014

| Test | Method | Specifications | Results | Units |
|---|---|---|---|---|
| **Isotopic composition** | | | | |
| $O_{18}$ | MS | >98.00 | 98.03 | Atom % |
| $O_{17}$ | MS | <1.00 | 0.52 | Atom % |
| $O_{16}$ | MS | <2.00 | 1.45 | Atom % |
| Deuterium(D) | | Normalized | Normalized | |
| | | | | |
| **Chemical composition** | | | | |
| Chemical Purity | | >99.9 | 99.99 | % |
| Sodium ( $Na^+$ ) | ICP-MS | <0.1 | 0.014 | mg/L |
| Potassium ( $K^+$ ) | ICP-MS | <0.1 | 0.004 | mg/L |
| Calcium ( $Ca^{2+}$ ) | ICP-MS | <0.05 | 0.01 | mg/L |
| Magnesium ( $Mg^{2+}$ ) | ICP-MS | <0.05 | 0.0002 | mg/L |
| Iron ( $Fe^{2+}$ ) | ICP-MS | <0.05 | 0.005 | mg/L |
| Copper ( $Cu^{2+}$ ) | ICP-MS | <0.05 | 0.0009 | mg/L |
| Zinc ( $Zn^{2+}$ ) | ICP-MS | <0.05 | 0.0012 | mg/L |
| Fluoride ( $F^-$ ) | IC | <0.1 | <0.01 | mg/L |
| Chloride ( $Cl^-$ ) | IC | <0.5 | <0.02 | mg/L |
| Bromide ( $Br^-$ ) | IC | <0.5 | <0.04 | mg/L |
| Iodide ( $I^-$ ) | IC | <0.5 | <0.03 | mg/L |
| Nitrate ( $NO_3^-$ ) | IC | <0.5 | <0.05 | mg/L |
| Sulfur ( $SO_4^{2-}$ ) | IC | <0.5 | <0.1 | mg/L |
| Phosphate ( $PO_4^{3-}$ ) | IC | <0.5 | <0.1 | mg/L |
| Ammonium ( $NH_4^+$ ) | IC | <0.5 | <0.1 | mg/L |
| Total Organic Carbon ( TOC ) | TOC | <1.0 | 0.97 | mg/L |
| | | | | |
| Appearance | Organoleptic | Clear and colorless liquid | Clear and colorless liquid | |
| PH | PH meter | 6.0 -8.0 | 7.65 | |
| Conductivity | Cond. meter | <1.00 | 0.95 | μS/cm |
| Pyrogen | LAL | <0.25 | <0.03 | I.U./ml |
| Sterility | USP | Sterile | Sterile | |

**Note**
- Manufactured according to requirements of cGMP, ISO 9001:2008 and ISO 14001:2004.
- Store the product at room temperature.
- For use by qualified personnel only.

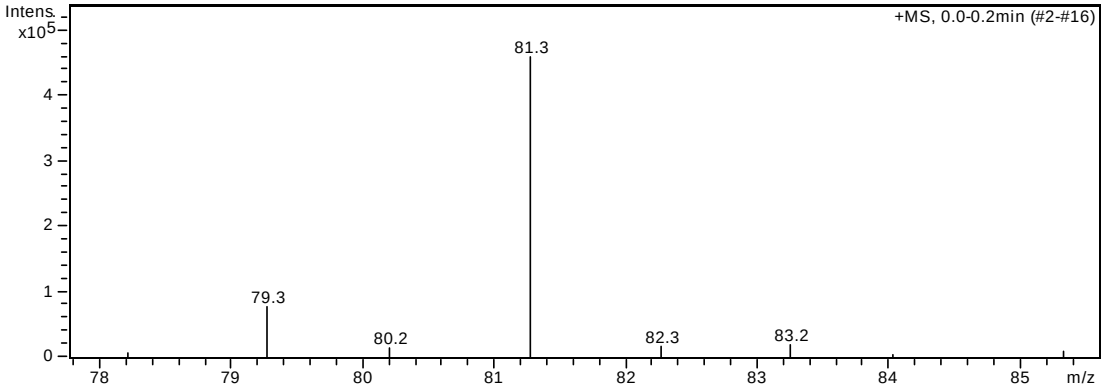
**Quality Control**
Wanwan Liang Date: 2012.12.18

**Quality Assurance**
Dr. Zhihong Xu Date: 2012.12.18

Version 3.0 Lot No.: WT-121201 Page 1 of 1

18 Fuyu Road, Haiyu Town, Changshu City, Jiangsu Province, P.R.CHINA Zip: 215522
Tel: +86 512 52491118 Fax: +86 512 52451806 E-mail: info@huayi-isotopes.com Http:// www.huayi-isotopes.com

**2. Preparation of $^{18}$O-DMSO and Purity Determination of by Secondary Mass Analysis:** $^{18}$O-DMSO was prepared according to the literature method (Fenselau, A. H.; Moffatt, J. G. *J. Am. Chem. Soc.* **1966**, *88*, 1762) by using above commercial $^{18}$O-$H_2O$ (98%) and then its purity determined by secondary mass.

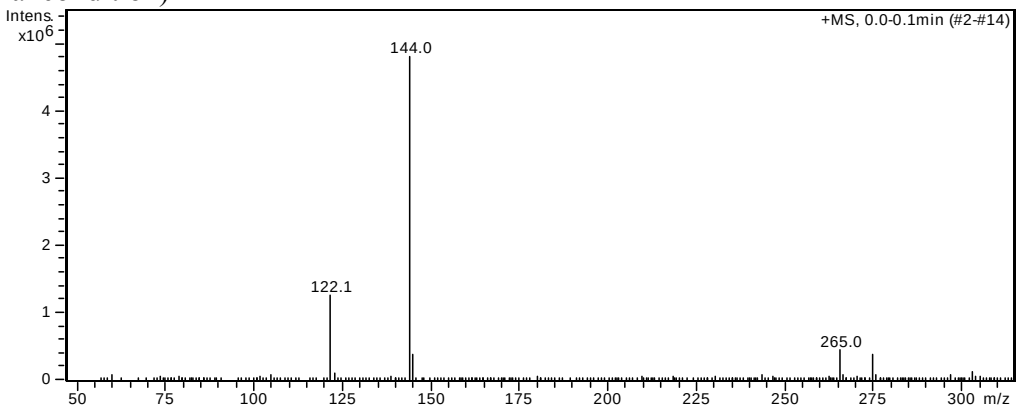



| m/z | Intensity | Ratio% | O% | DMSO | DMSO% |
|---|---|---|---|---|---|
| 79.3 | 74910 | 0.76 | 14.02 | $^{16}$O-DMSO | **14** |
| 81.3 | 456707 | 4.66 | 85.98 | $^{18}$O-DMSO | **86** |

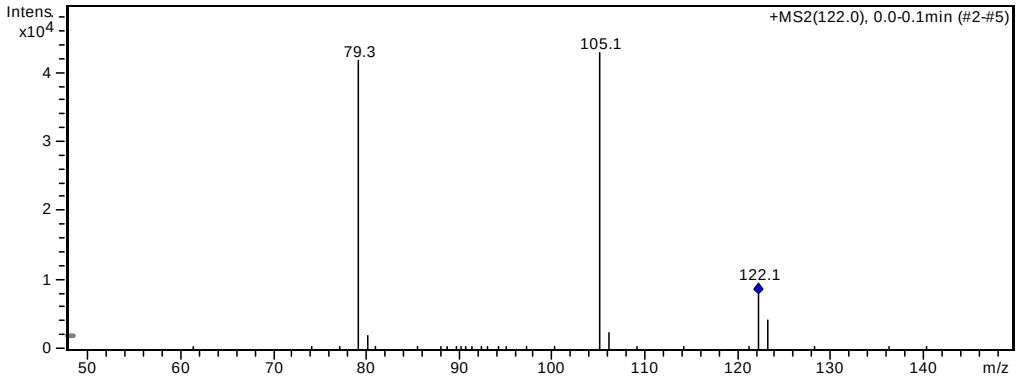
**3. Comparison of $PhCONH_2$ (2a) obtained from hydration reactions of PhCN (1a) using $^{16}O$- or $^{18}O$-DMSO and $^{16}O$-$H_2O$.**

**3.1 $^{16}O$-$PhCONH_2$ (2a) obtained under standard conditions using normal $^{16}O$-DMSO and normal $^{16}O$-$H_2O$.**

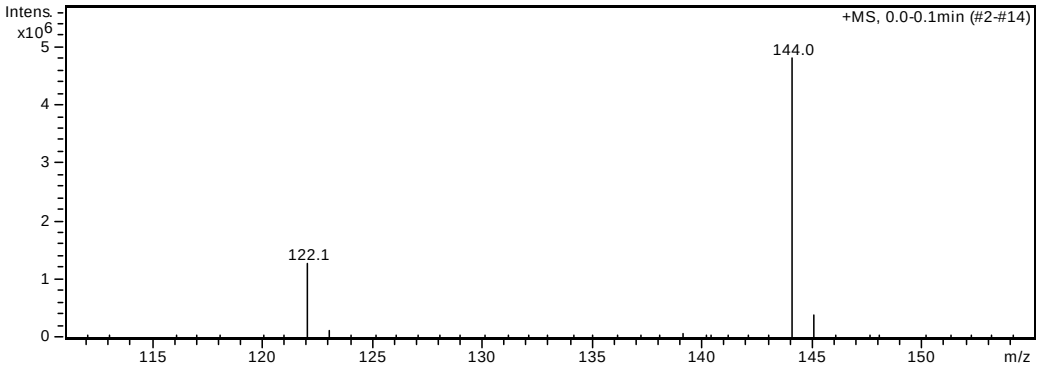
MS (original condition)




2+MS

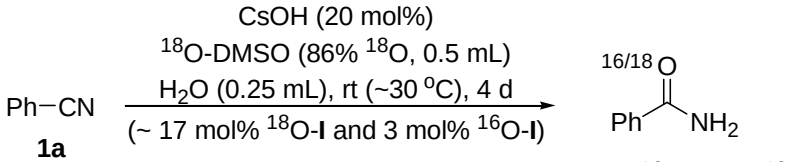



122/124, 144/146



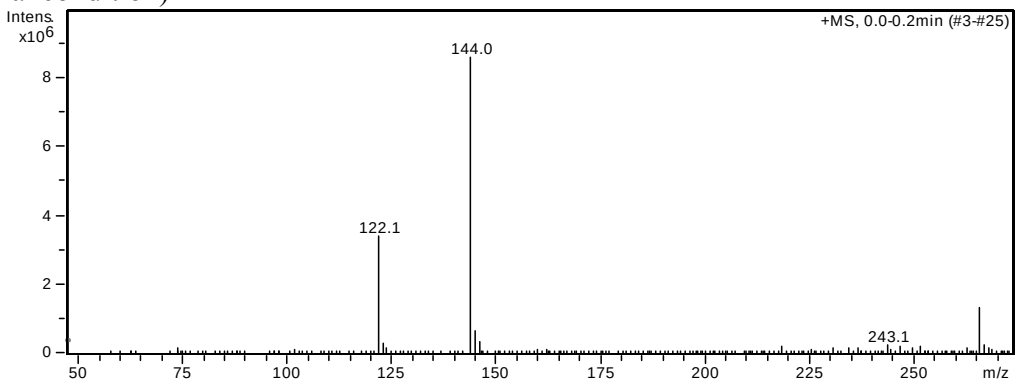

| m/z | Intensity | Ratio | O% | $PhCONH_2$ | $PhCONH_2$% |
|---|---|---|---|---|---|
| 122.1 | 1231244 | 25.83 | $^{16}O$: 100 | $^{16}O$-$PhCONH_2$ + H | **100** |
| 124.1 | 0 | | $^{18}O$: 0 | $^{18}O$-$PhCONH_2$ + H | **0** |
| 144.0 | 4765954 | 100 | $^{16}O$: 100 | $^{16}O$-$PhCONH_2$ + Na | **100** |
| 146.0 | 0 | | $^{18}O$: 0 | $^{18}O$-$PhCONH_2$ + Na | **0** |

**3.2 $^{16/18}$O-PhCONH$_2$ (2a) obtained from hydration reaction using $^{18}$O-DMSO (86% $^{18}$O) and normal $^{16}$O-H$_2$O at room temperature.**

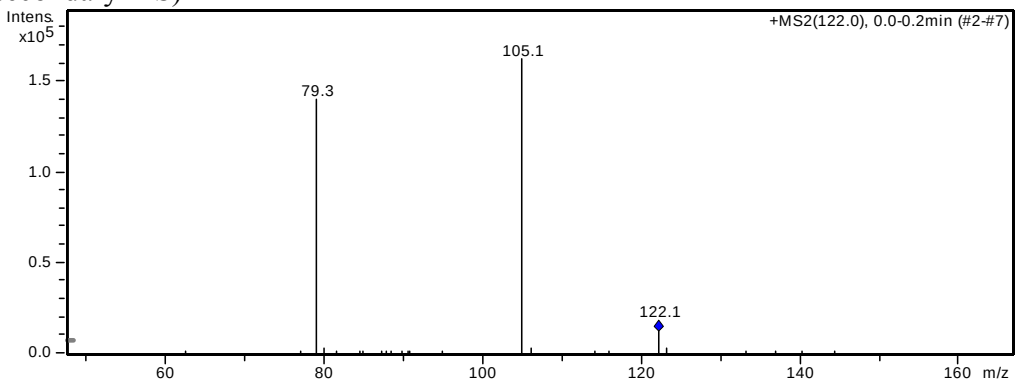



**2a**: 96.7% $^{16}$O; 3.3% $^{18}$O

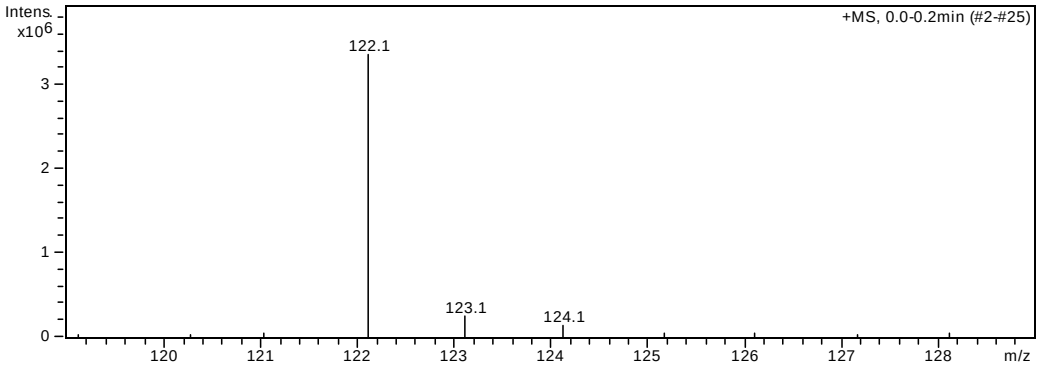
MS (original condition)



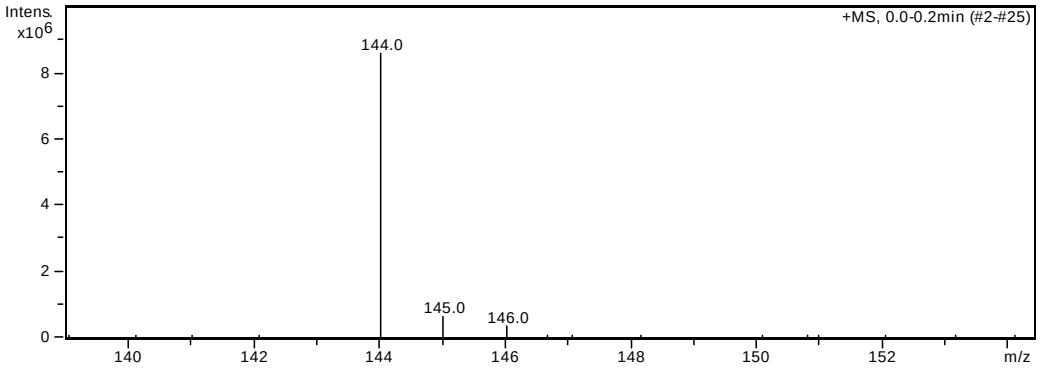

2+MS (secondary MS)




122/124



144/146



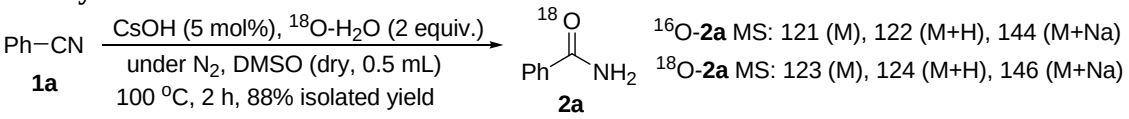

| m/z | Intensity | Ratio % | O% | $PhCONH_2$ | $PhCONH_2$% |
|---|---|---|---|---|---|
| 122.1 | 3336790 | 39.22 | $^{16}O$: 96.67 | $^{16}O$-$PhCONH_2$ + H | **96.7** |
| 124.1 | 115190 | 1.35 | $^{18}O$: 3.33 | $^{18}O$-$PhCONH_2$ + H | **3.3** |
| 144.0 | 8508856 | 100 | $^{16}O$: 96.61 | $^{16}O$-$PhCONH_2$ + Na | **96.6** |
| 146.0 | 298392 | 3.51 | $^{18}O$: 3.39 | $^{18}O$-$PhCONH_2$ + Na | **3.4** |

### 3.3 Comparison and Tentative Conclusion:

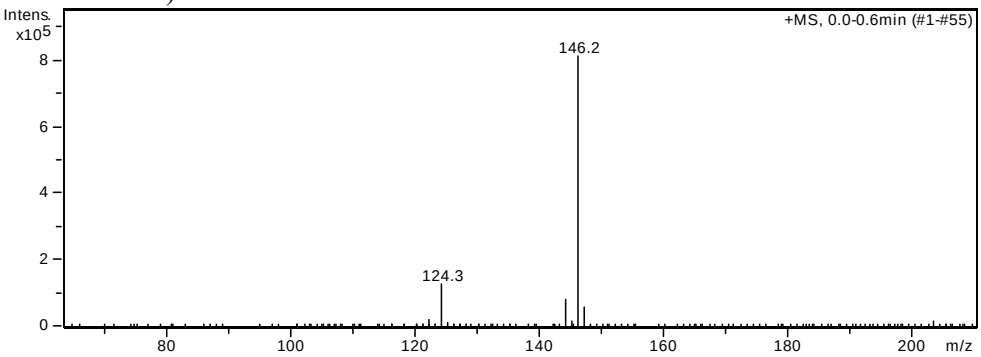
In the case of a normal sample of **2a** (results in section 3.1), since no any $^{18}O$ sources were available in the reaction, secondary mass analysis showed that it contains no $^{18}O$-**2a** at all. In contrast, by using prepared $^{18}O$-DMSO (containing 86% $^{18}O$), the product obtained was determined to contain 3.3% $^{18}O$-**2a** as analyzed by secondary mass (results in section 3.2). Addition of 20 mol% CsOH equals to generation of at best ~17 mol% $^{18}O$-dimethylsulfinyl anion (**I**) and ~3 mol% $^{16}O$-**I** as catalysts, which may suggested that a considerable extent of $^{18}O$-DMSO-participated reaction have occurred. Since $^{18}O$-DMSO is the only $^{18}O$ source in the reaction, this amount of $^{18}O$-**2a** must have been generated from the reaction of $^{18}O$-DMSO. Since O-attack reactions of DMSO and other sulfoxides toward various electrophiles and O-transfer reactions have been the common reactions among DMSO and other sulfoxides (ref. 18 of the text), *the only explanation for the formation of $^{18}O$-**2a** is that an O-transfer reaction from DMSO to **1a** have occurred to give $^{18}O$-**2a** (path a in Scheme 1 of the text) in the present nitrile hydration reaction.*

## 4. Direct hydration reactions of PhCN (1a) with $^{18}O$-$H_2O$ and secondary mass analysis of product benzamide (2a).

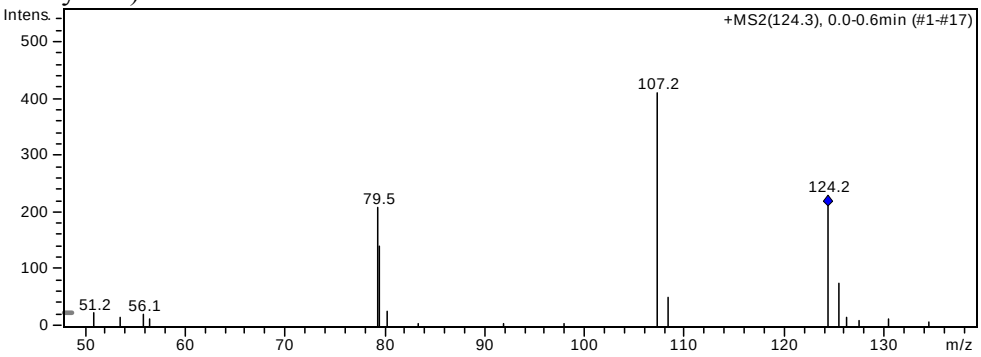
### 4.1: hydration at 100 °C.



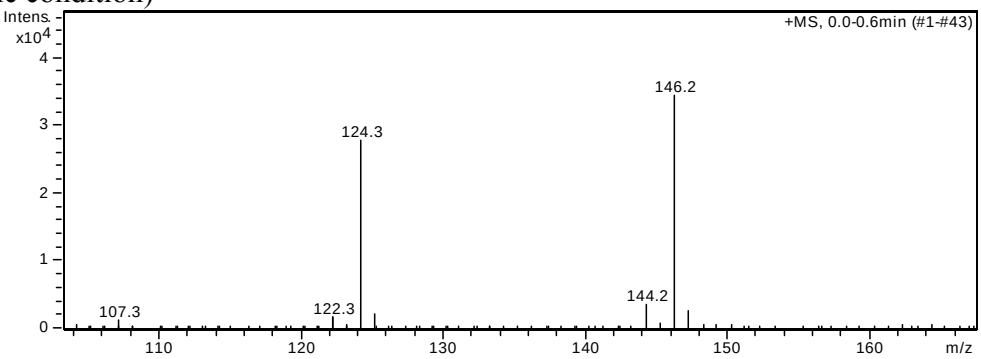

MS-1 (original condition)




2+MS (secondary MS)

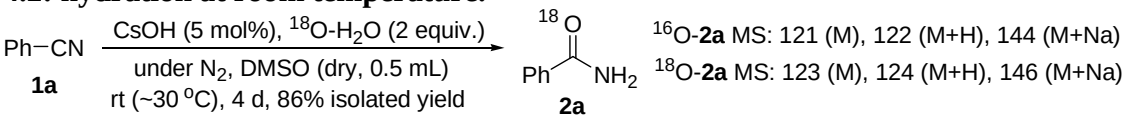



MS-2 (acidic condition)

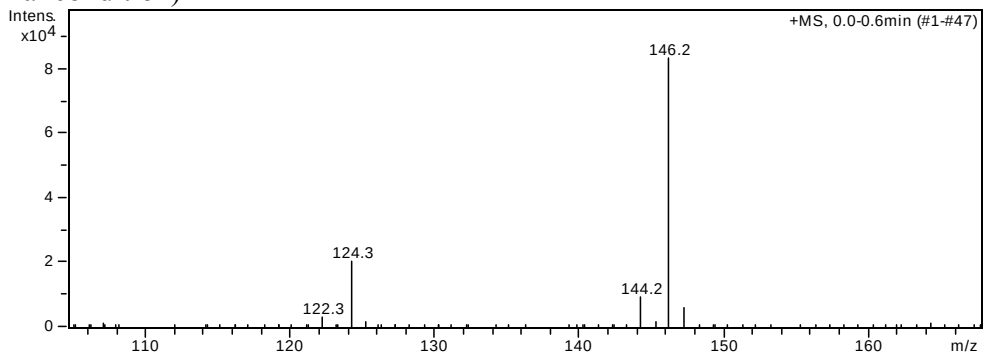



| m/z | Intensity | Ratio (%) | O% |
|---|---|---|---|
| 122.3 ($^{16}O$: M+H) | 1587 | 4.67 | **$^{16}O$: 5.5** |
| 124.3 ($^{18}O$: M+H) | 27359 | 80.43 | $^{18}O$: 94.5 |
| 144.2 ($^{16}O$: M+Na) | 3251 | 9.56 | **$^{16}O$: 8.7** |
| 146.2 ($^{18}O$: M+Na) | 34017 | 100 | $^{18}O$: 91.3 |

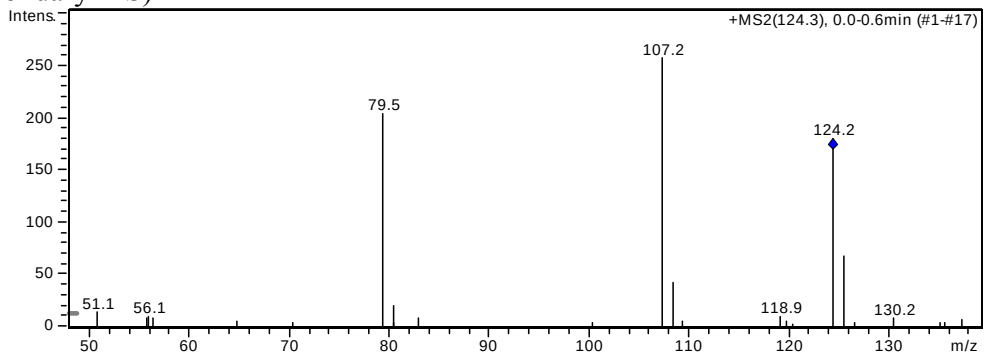
**4.2: hydration at room temperature.**



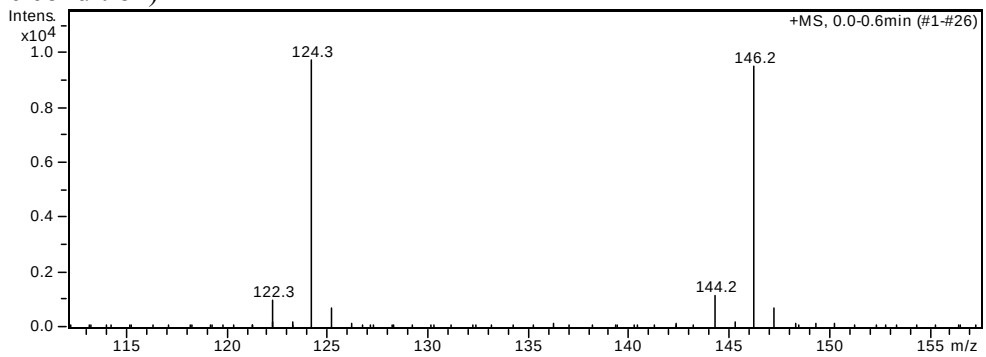

MS-1 (original condition)




2+ MS (secondary MS)




MS-2 (acidic condition)

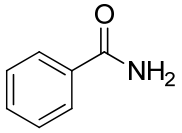



| m/z | Intensity | Ratio (%) | O% | VS reaction at 100 °C |
|---|---|---|---|---|
| 122.3 ($^{16}$O: M+H) | 922 | 9.64 | **$^{16}$O: 8.8** | **60% increase** |
| 124.3 ($^{18}$O: M+H) | 9560 | 100 | $^{18}$O: 91.2 | |
| 144.2 ($^{16}$O: M+Na) | 1056 | 11.05 | **$^{16}$O: 10.2** | **17% increase** |
| 146.2 ($^{18}$O: M+Na) | 9289 | 97.17 | $^{18}$O: 89.8 | |

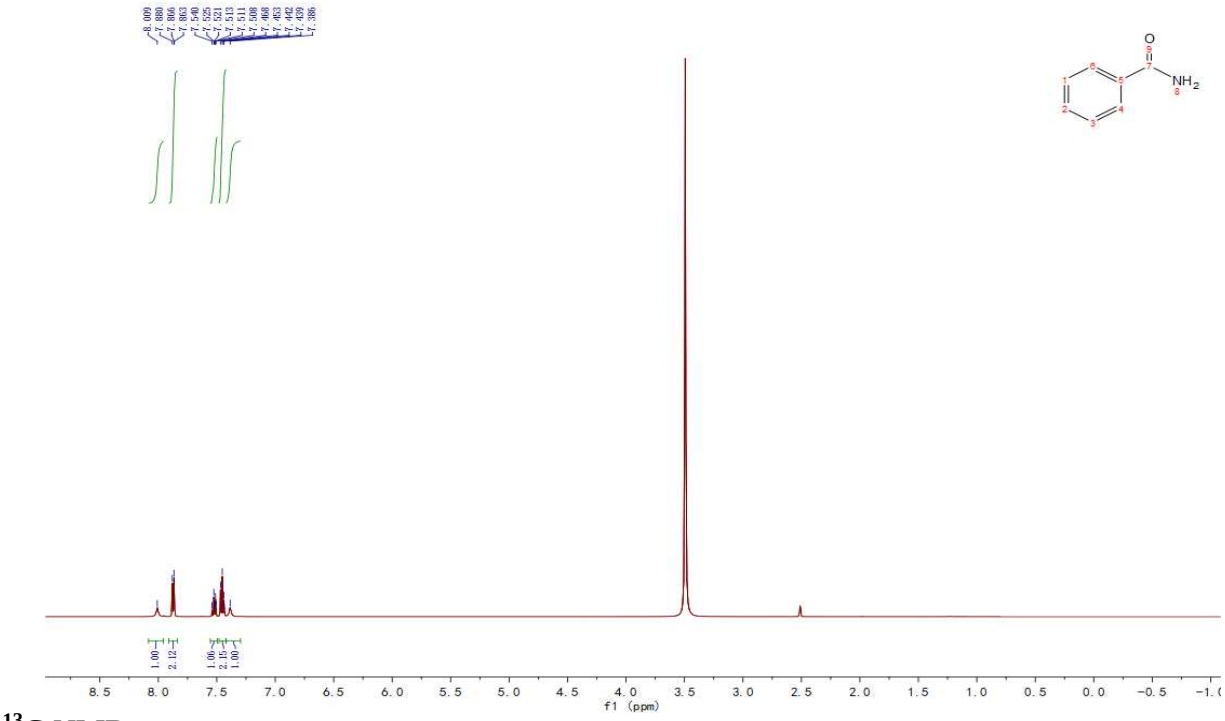
**4.3 Comparison and Tentative Conclusion:**

In the above two parallel reactions, $^{16}$O-DMSO-participated indirect hydration of **1a** involving $^{16}$O-transfer from $^{16}$O-DMSO to **1a** to give $^{16}$O-**2a** increased by 17~60% from the reaction at 100 $^{o}$C (reaction 4.1) to the reaction at room temperature (reaction 4.2). This is most possibly due to the lower reactivity of $^{18}$O-$H_2O$ toward **1a** at room temperature than the one at higher temperature, and stronger interaction between $^{16}$O-dimethylsulfinyl anion (**I**) and **1a**, which consequently led to more effective O-attack of $^{16}$O-**I** at **1a** to give enhanced yields of $^{16}$O-**2a** at room temperature. *These results also support that DMSO-participated indirect hydration process involving O-transfer from DMSO to nitriles to give amides (path a in Scheme 1 of the text) is a possible process in the present nitrile hydration reaction.*

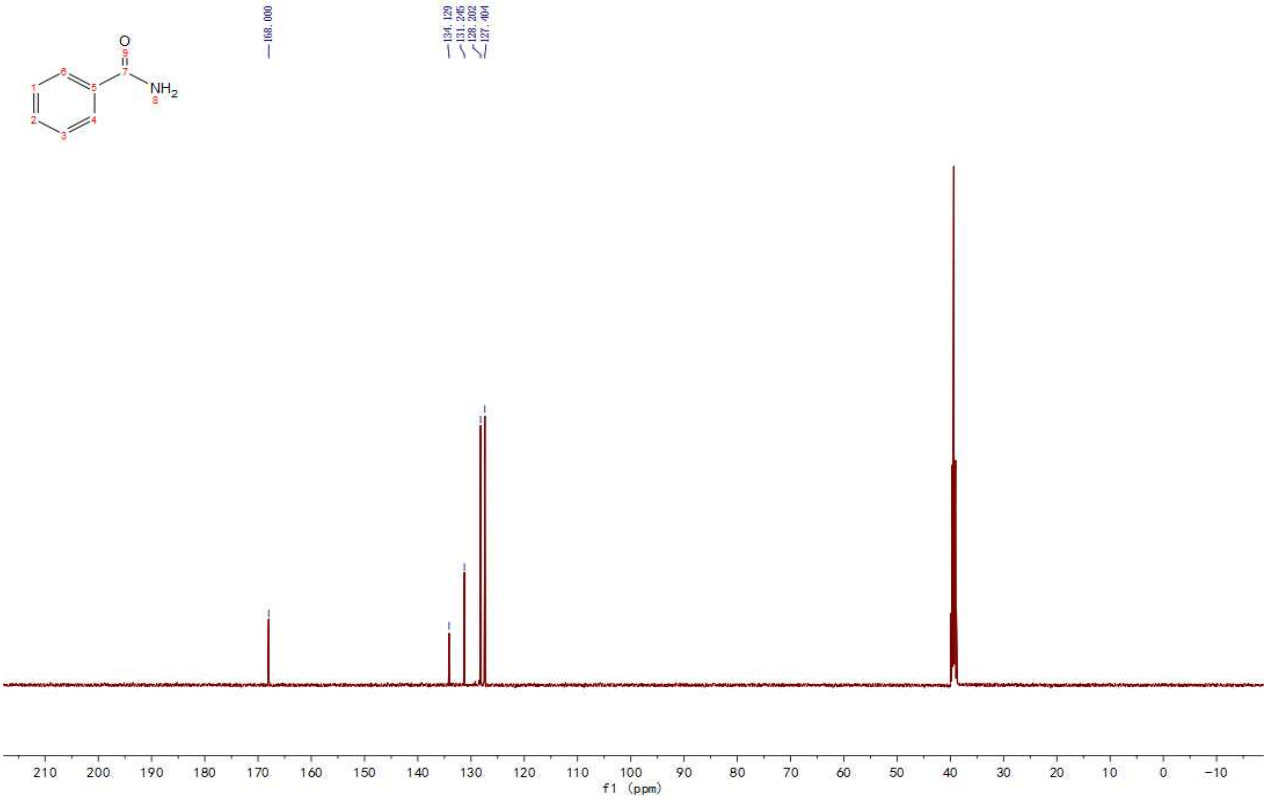
# $^{1}$H NMR and $^{13}$C NMR Spectra of All Products

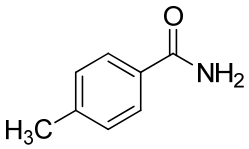



## $^{1}$H NMR

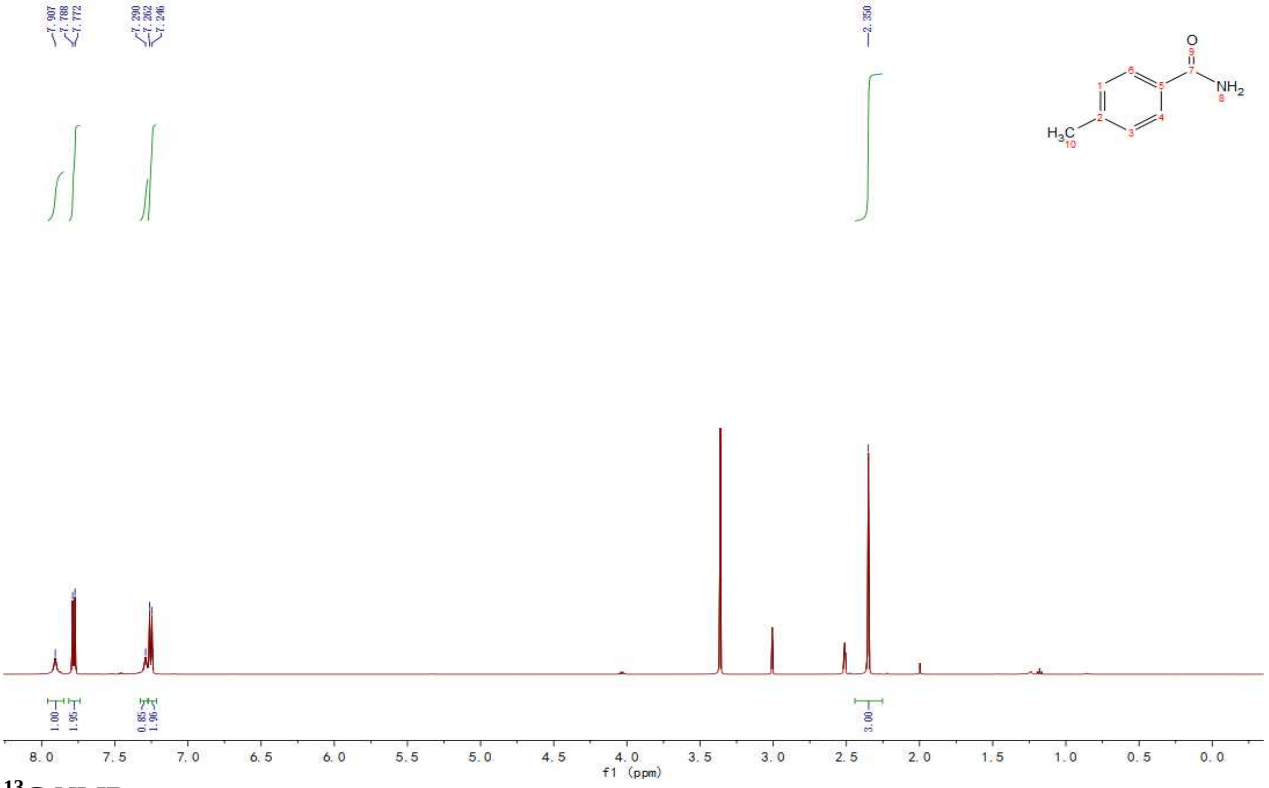



## $^{13}$C NMR

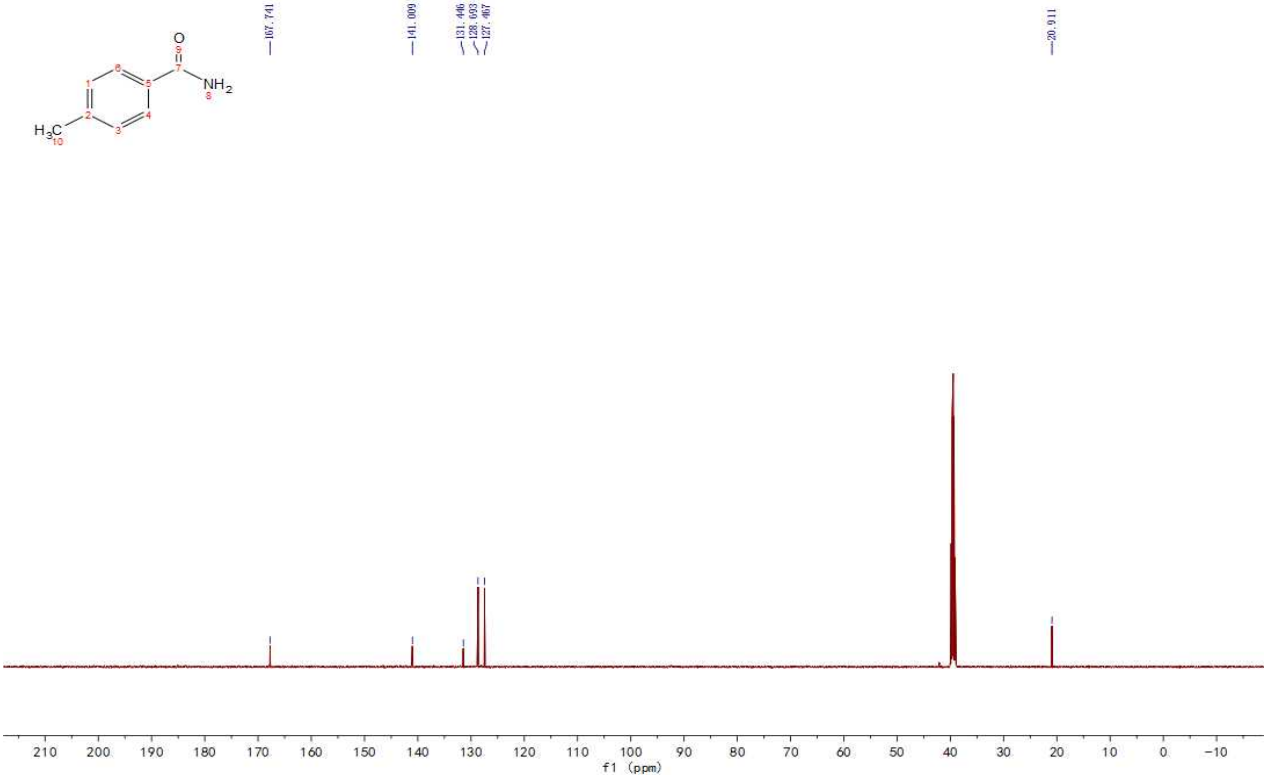


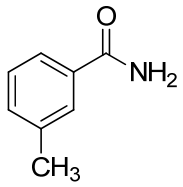



**$^{1}$H NMR**

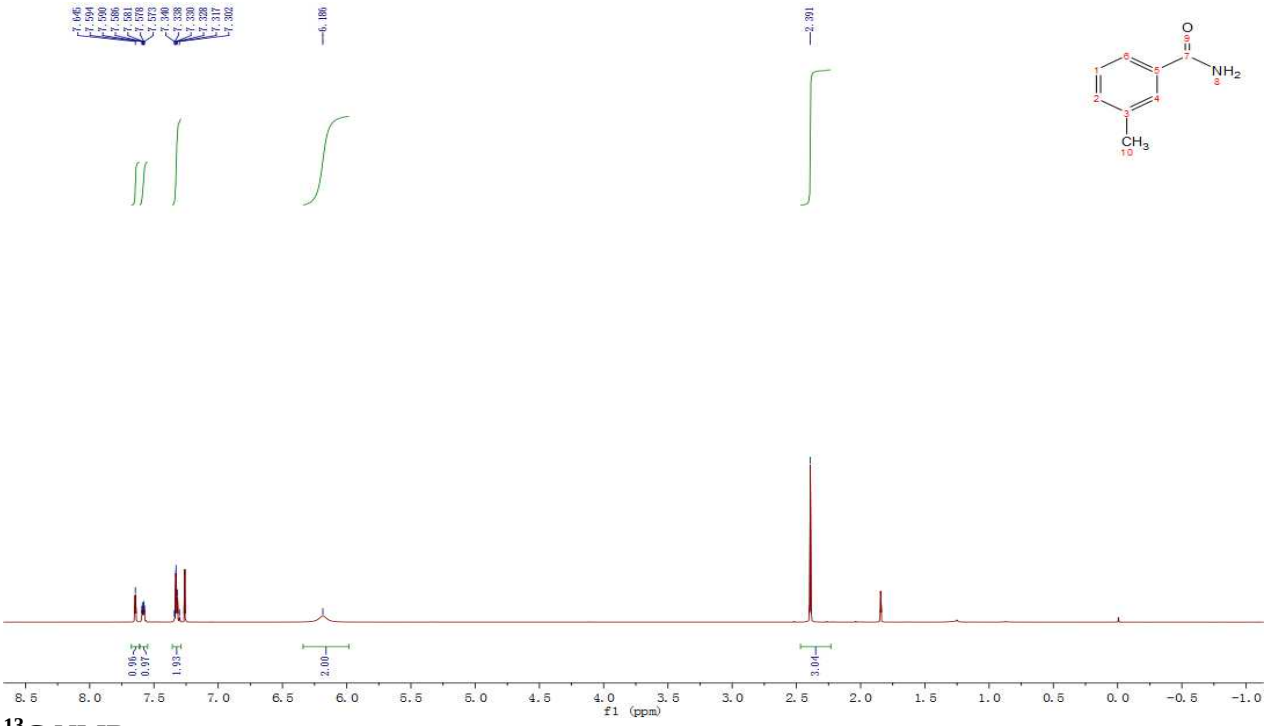



**$^{13}$C NMR**

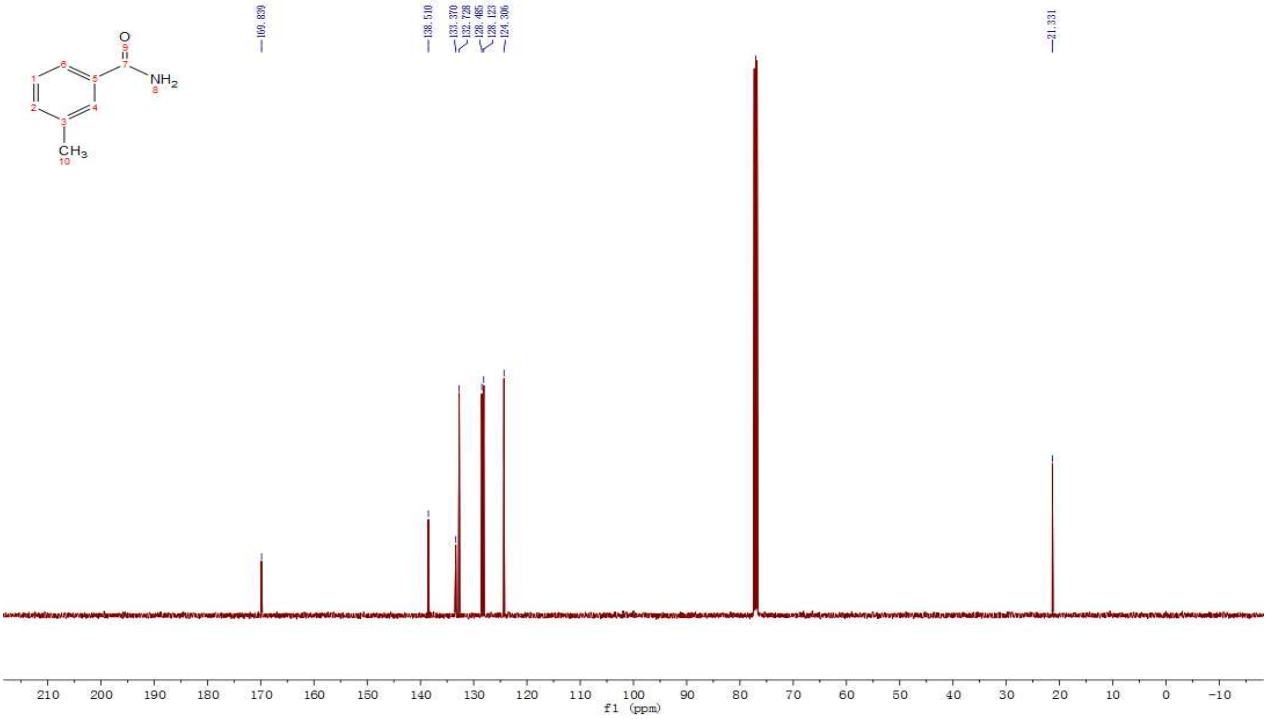


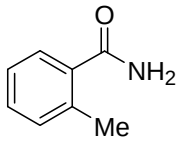



**$^{1}$H NMR**

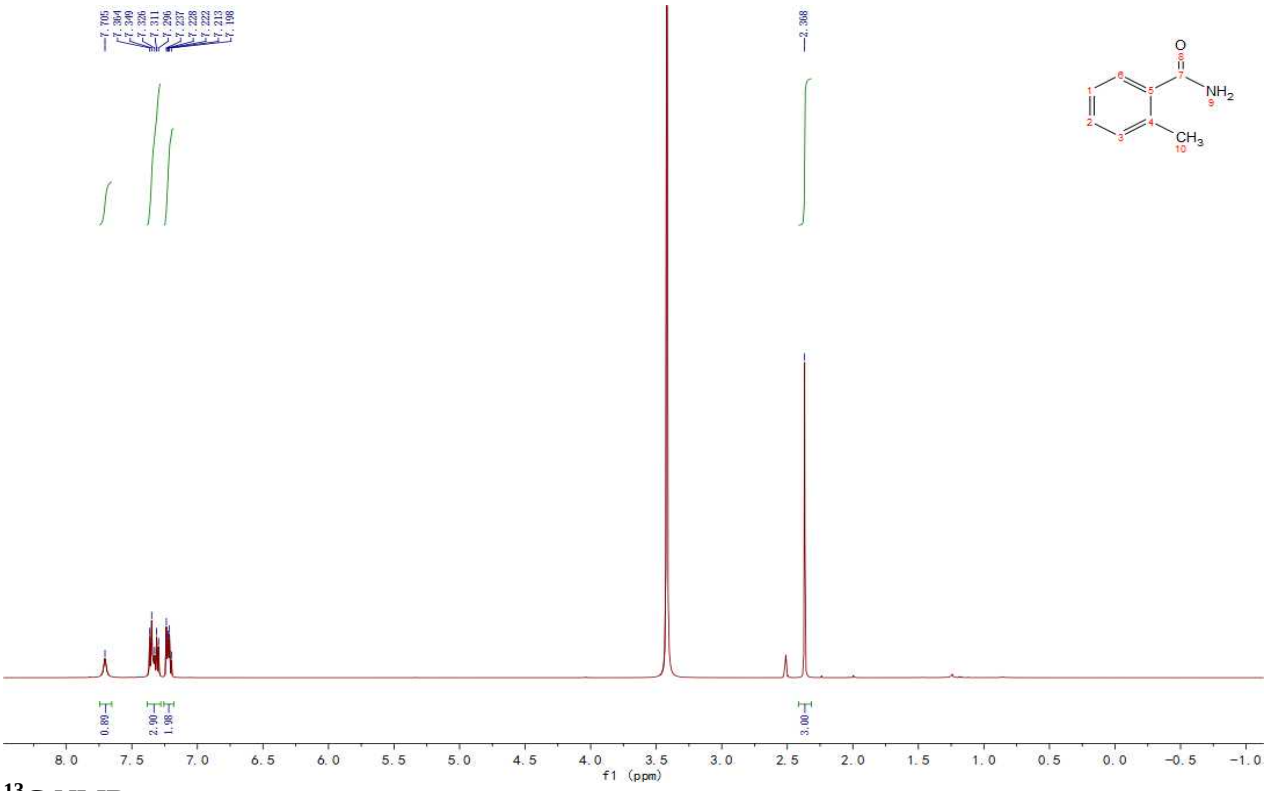



**$^{13}$C NMR**

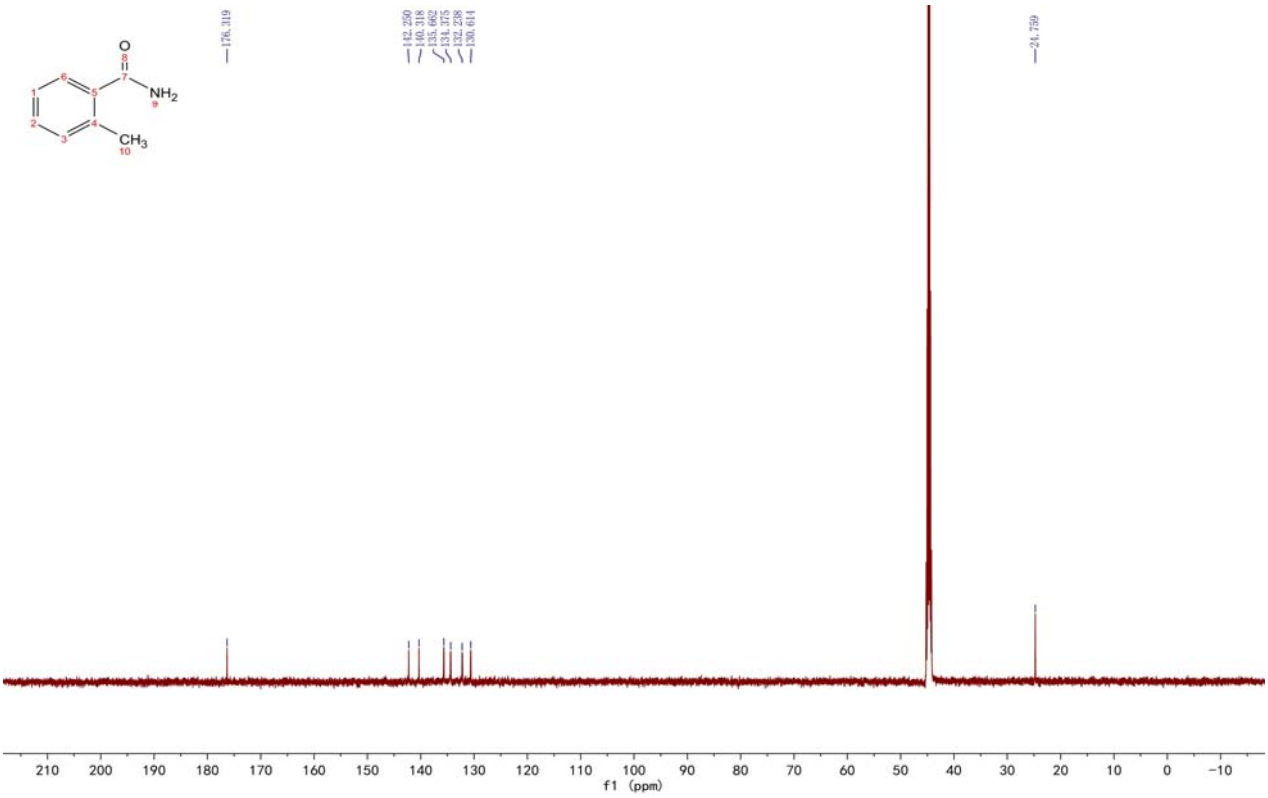


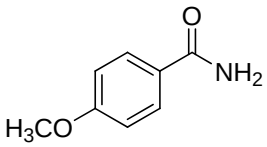



**$^{1}$H NMR**

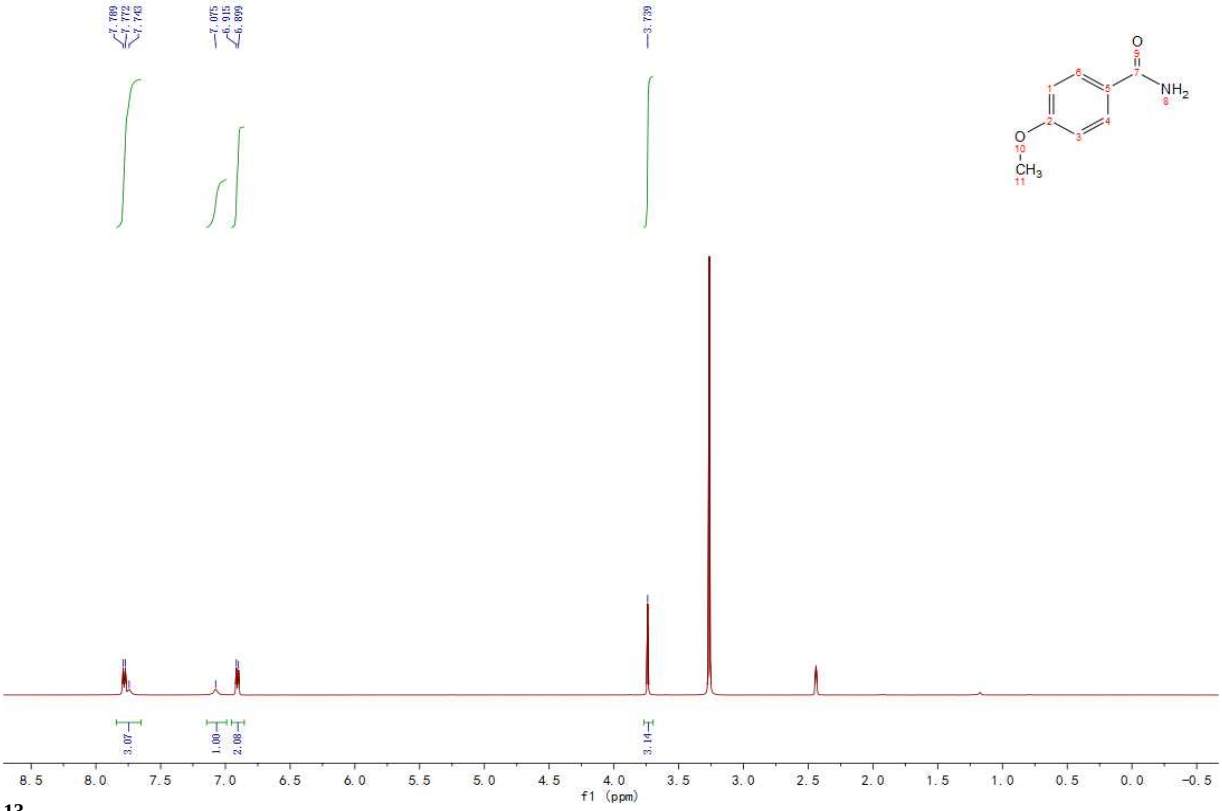



**$^{13}$C NMR**

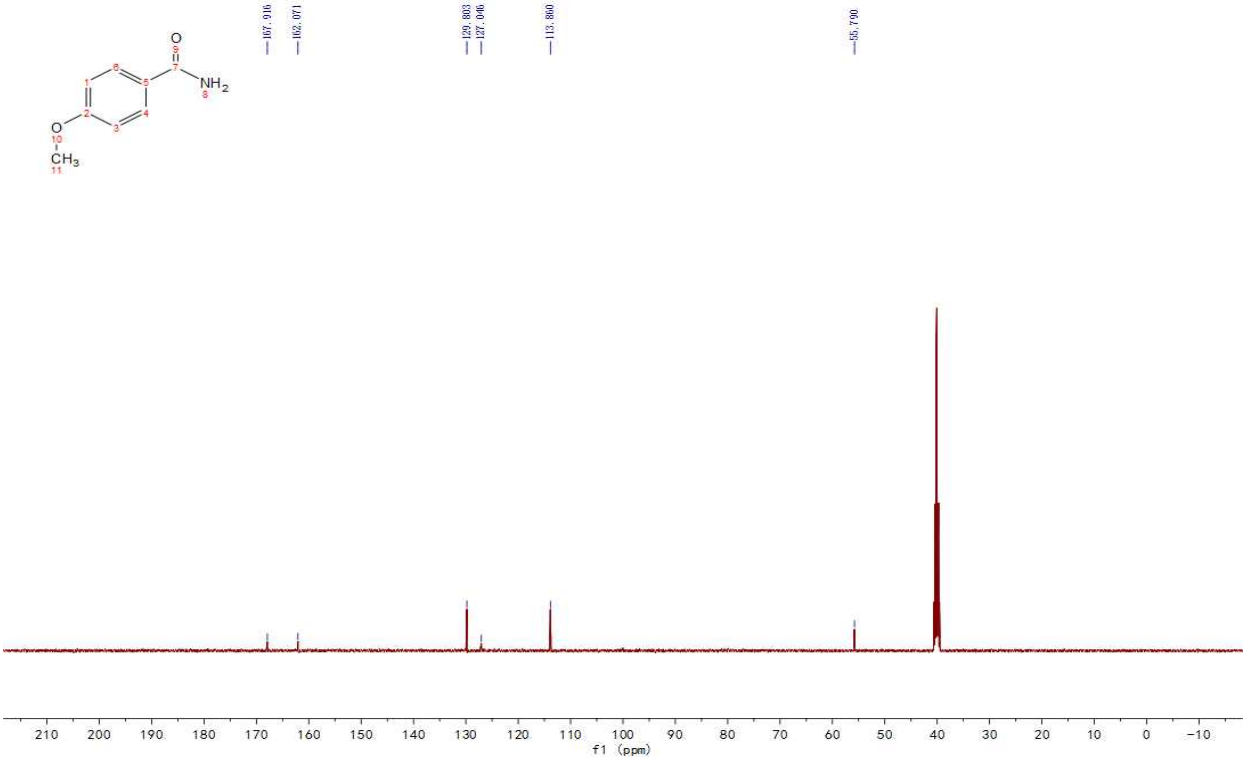


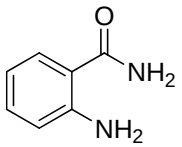



**$^{1}$H NMR**

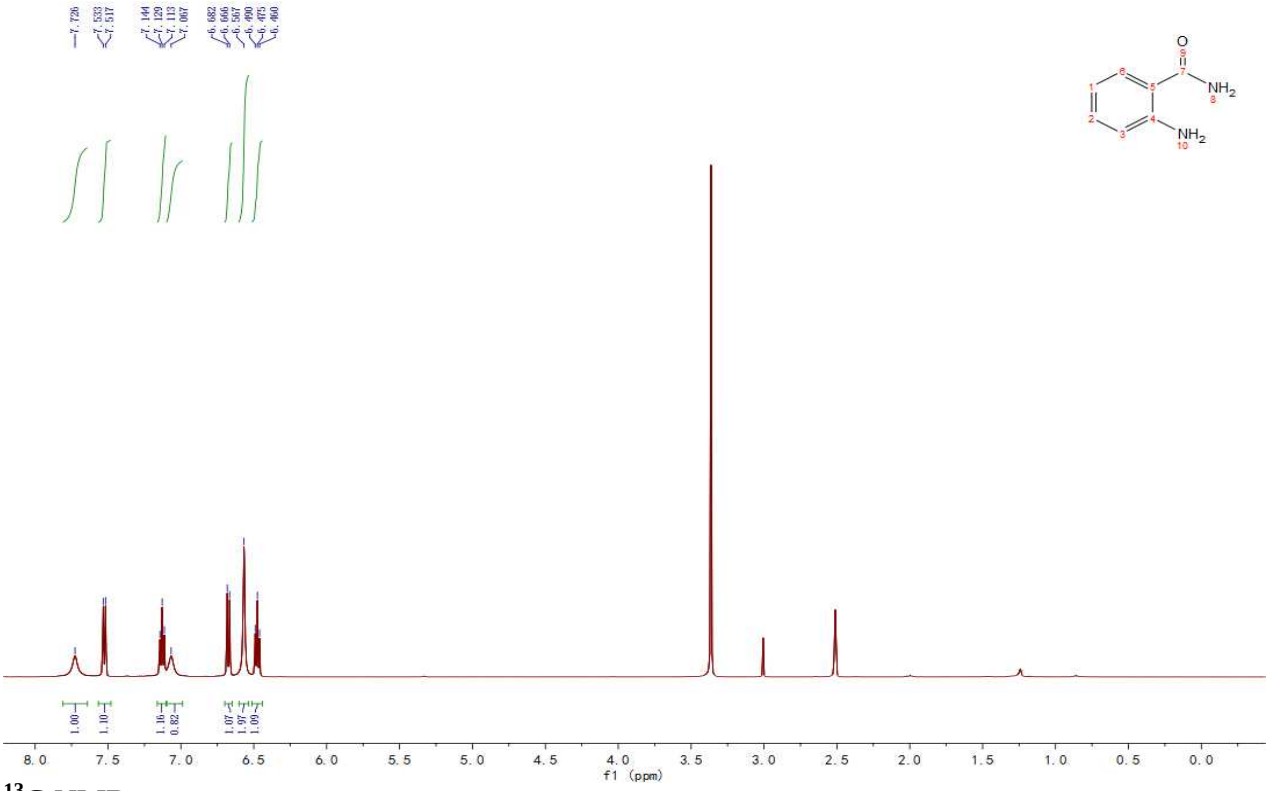



**$^{13}$C NMR**

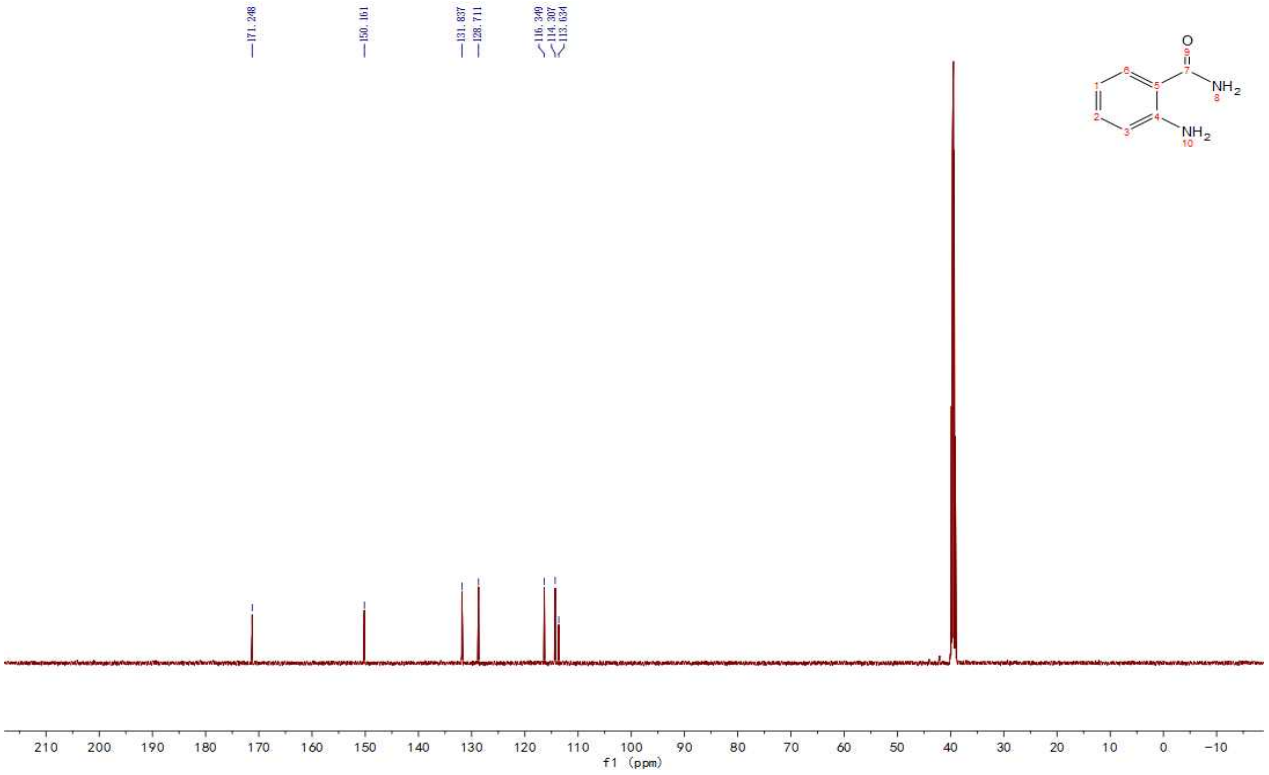


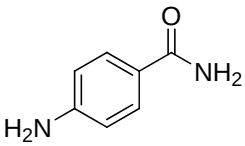



**$^{1}$H NMR**




**$^{13}$C NMR**



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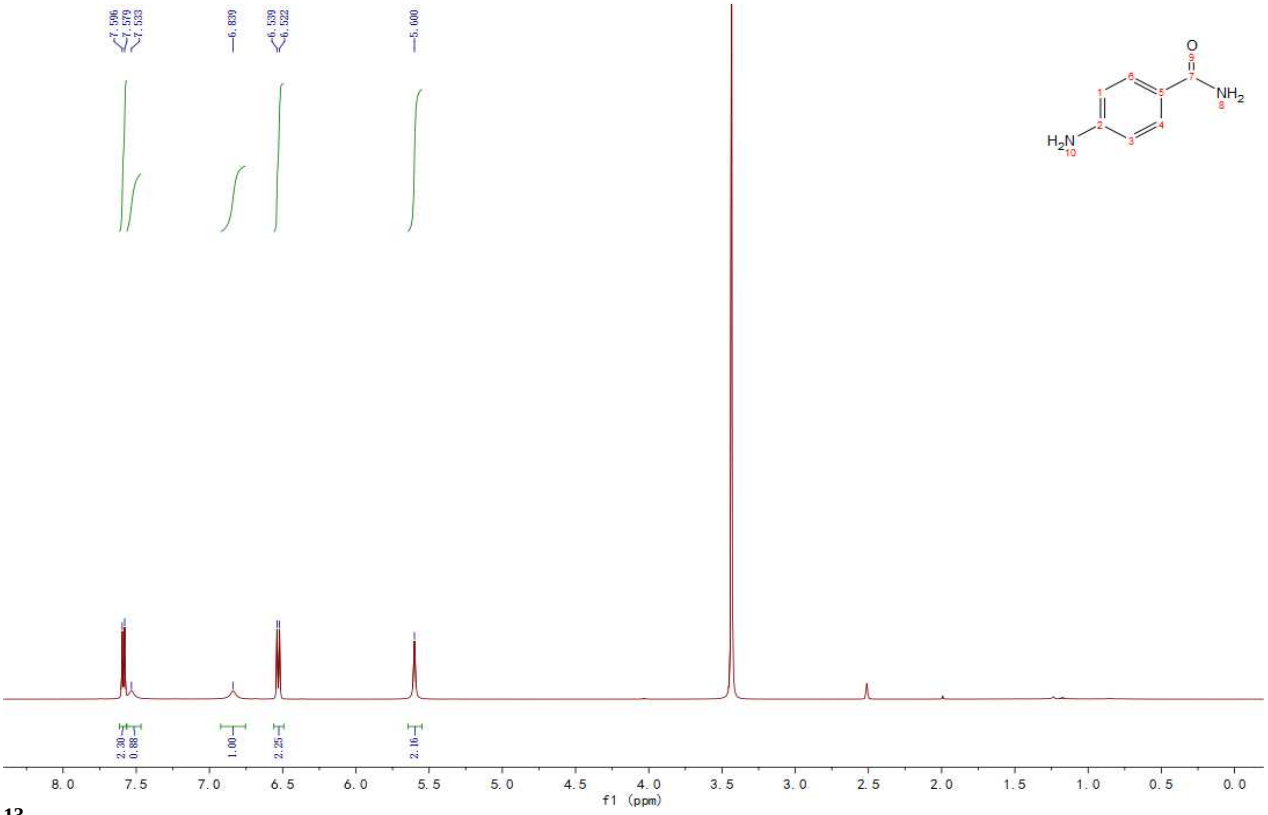
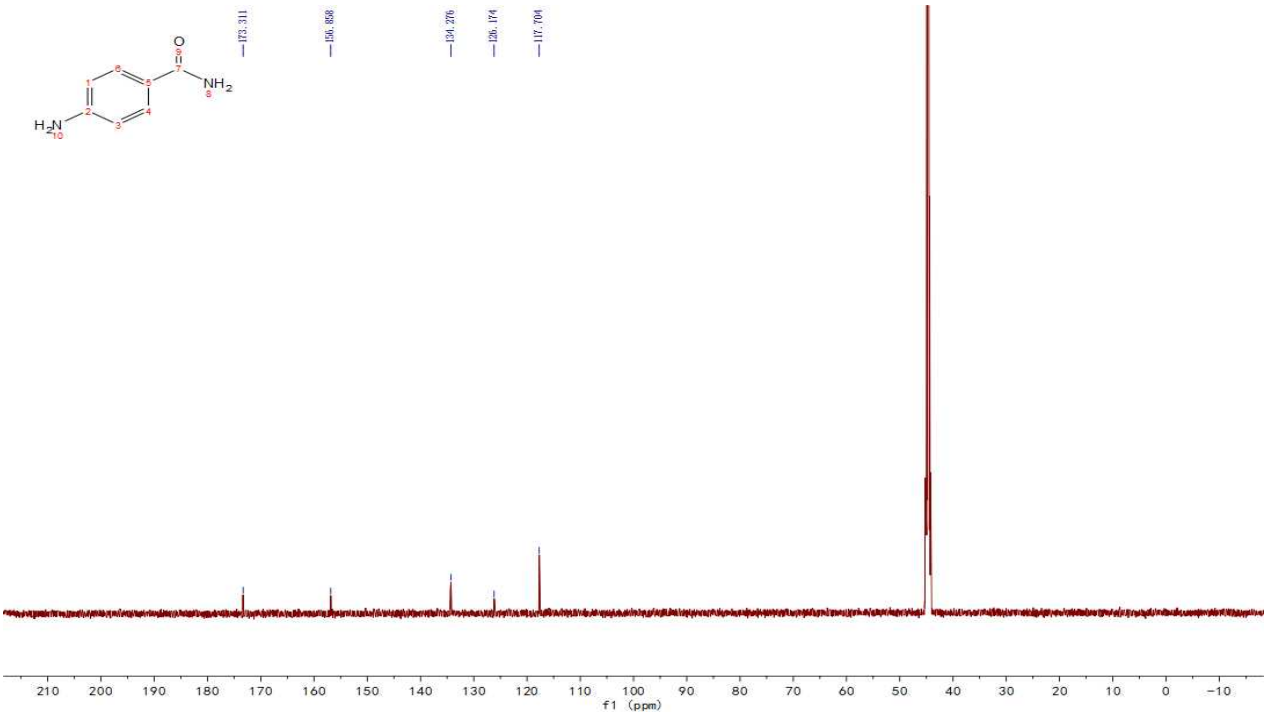
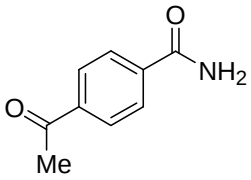



**$^{13}$C NMR**



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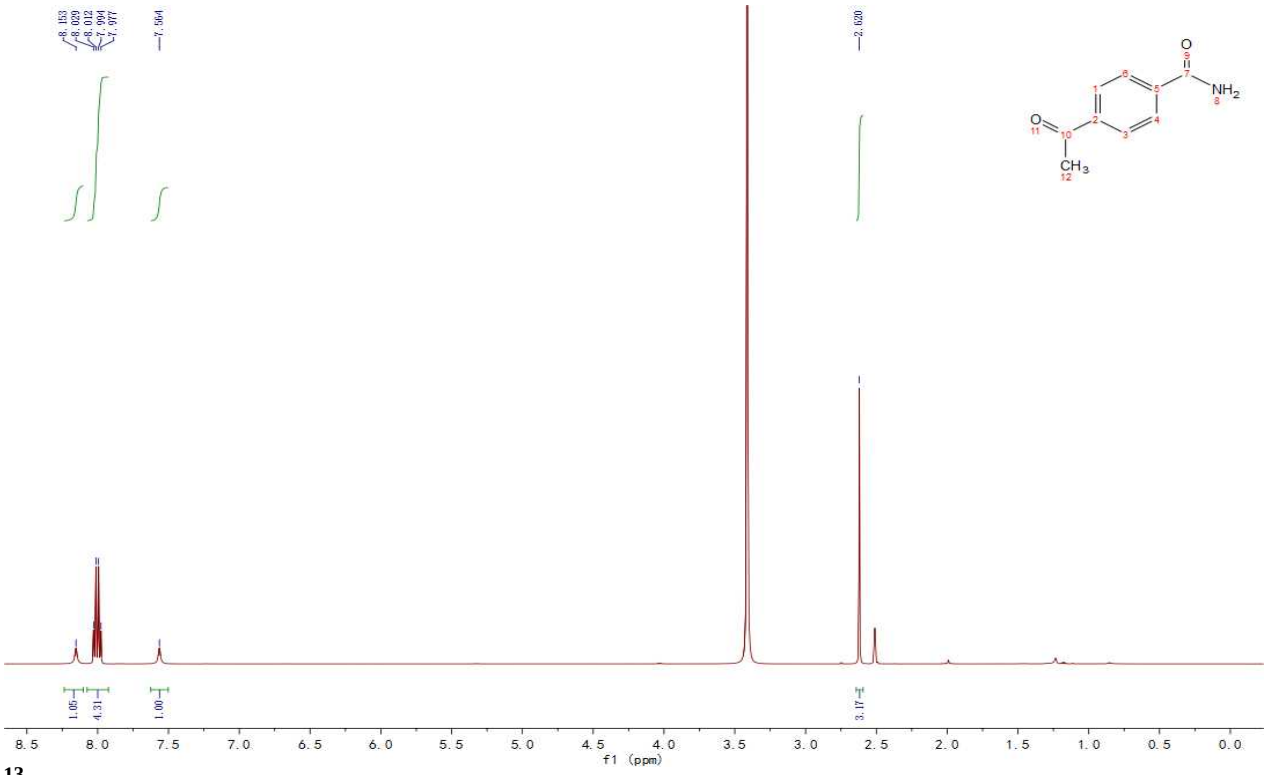


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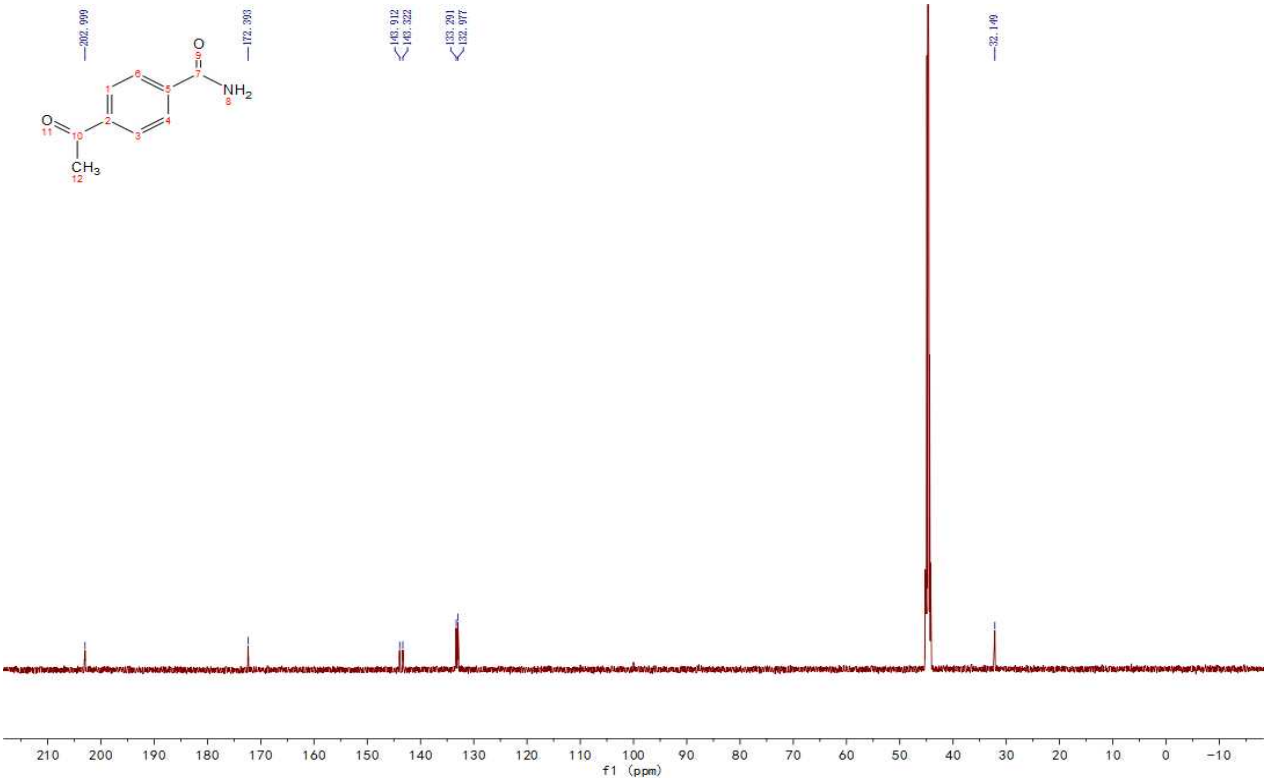

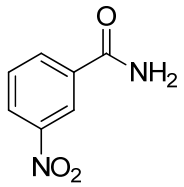


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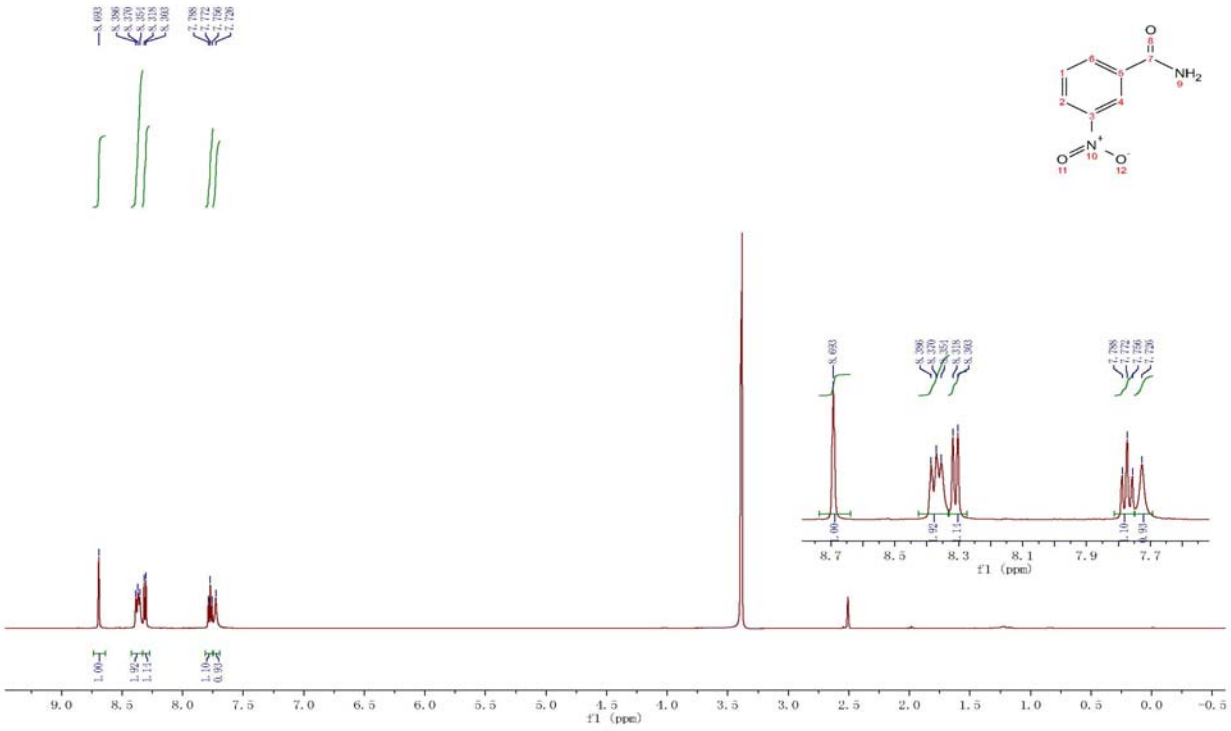


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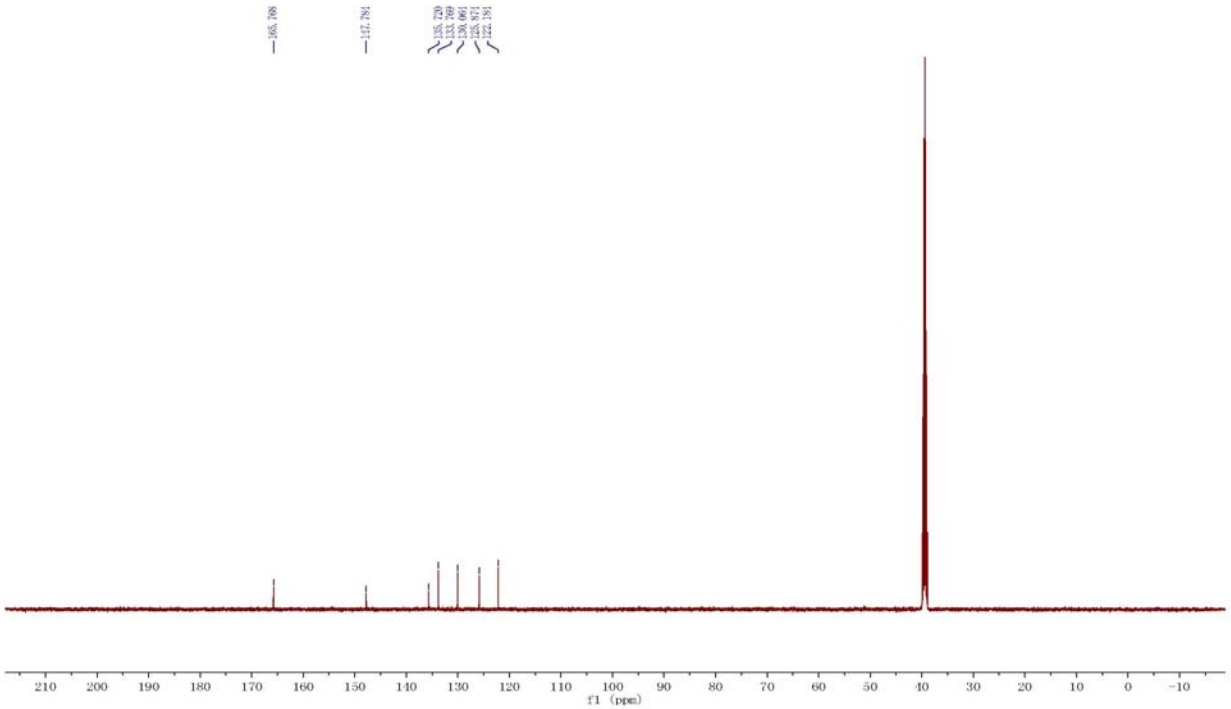

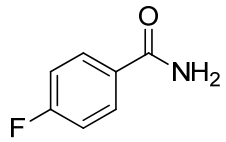


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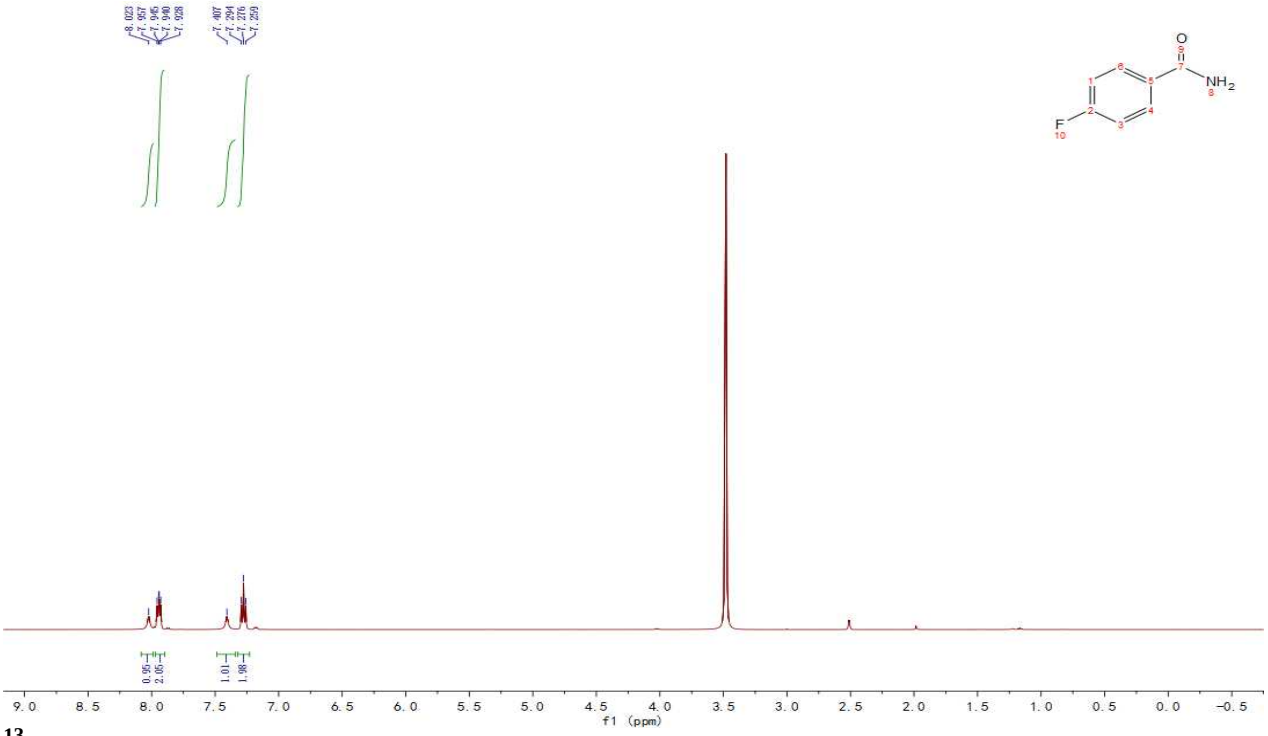


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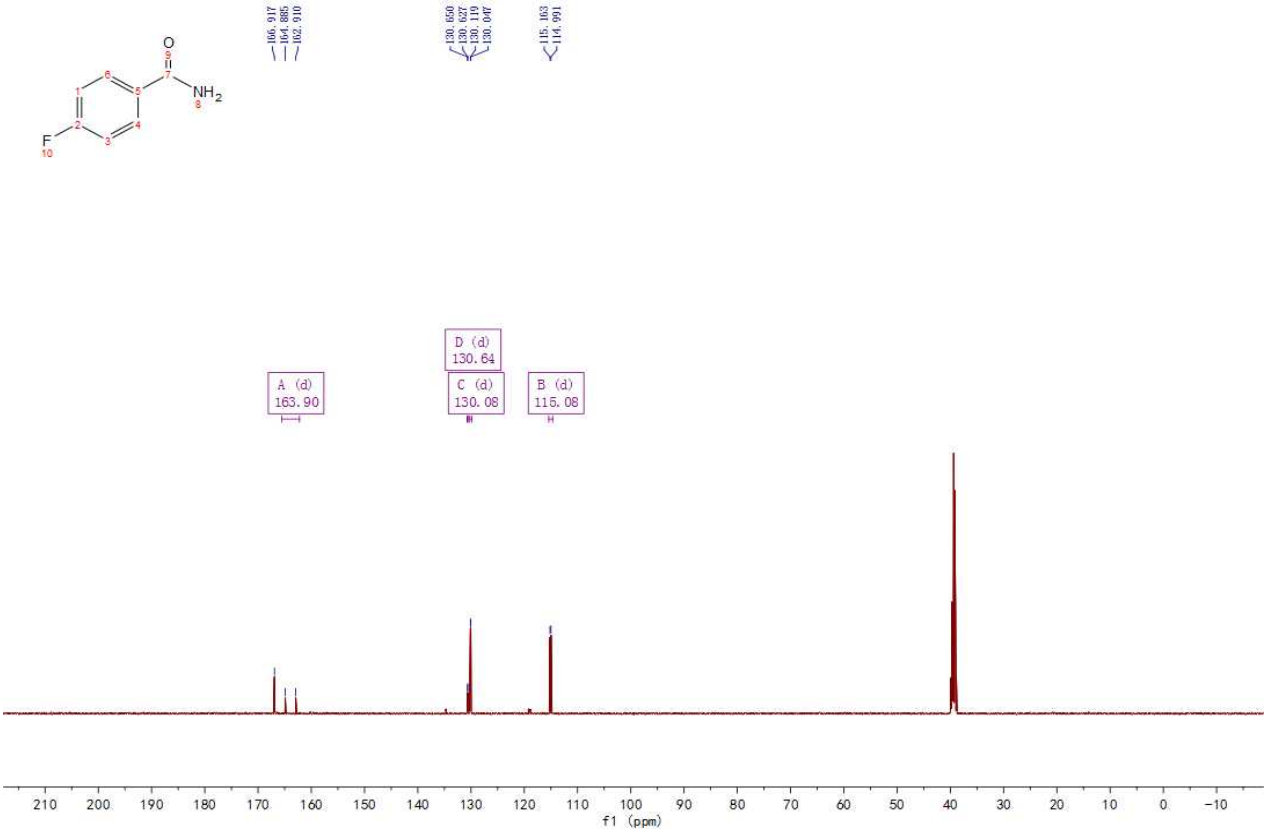

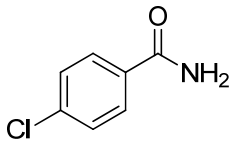


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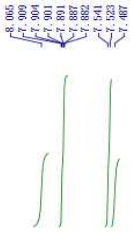
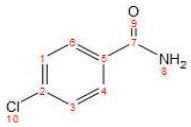
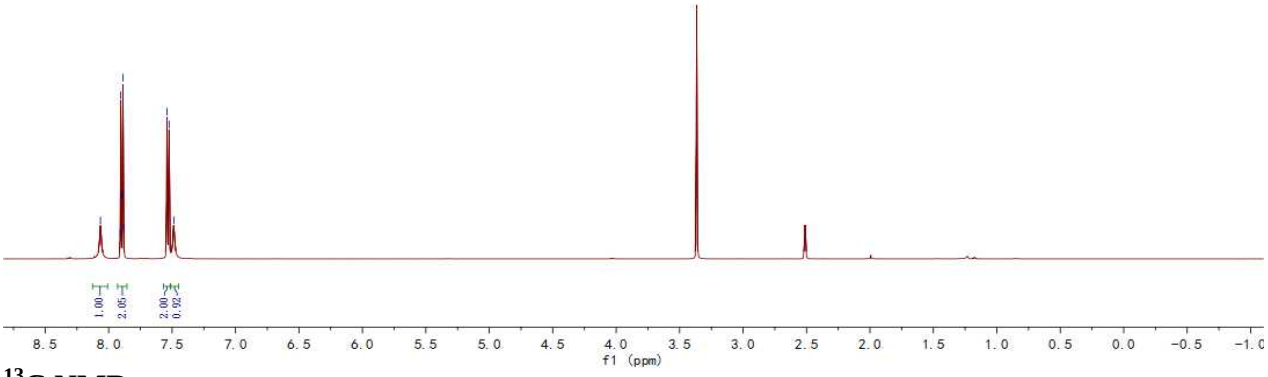
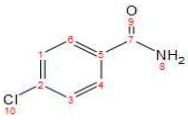


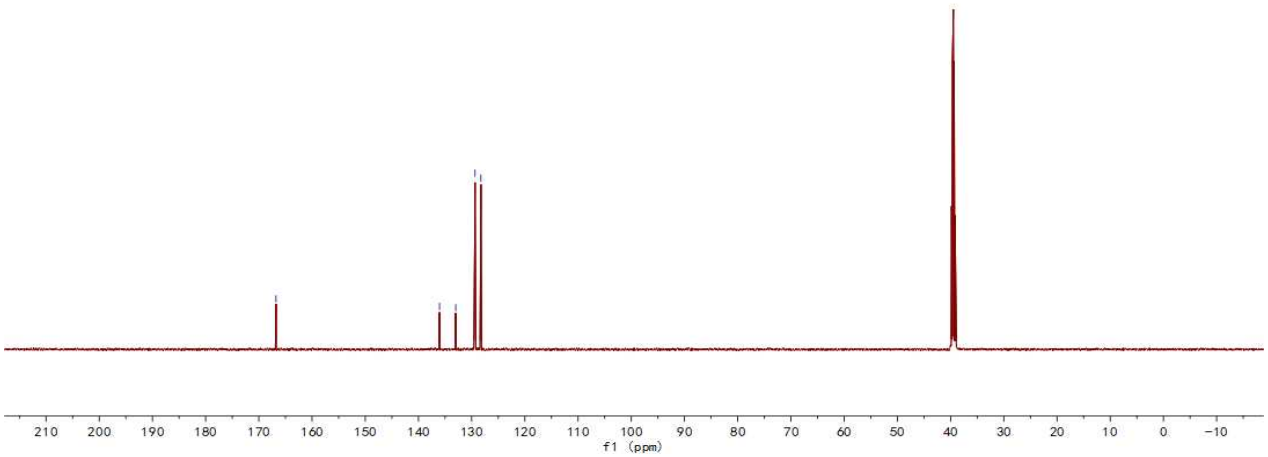



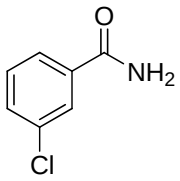




**$^{13}$C NMR**







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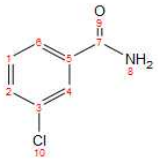

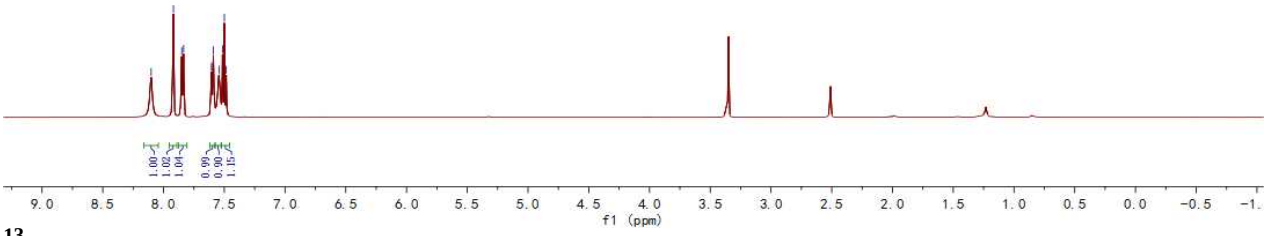


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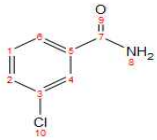

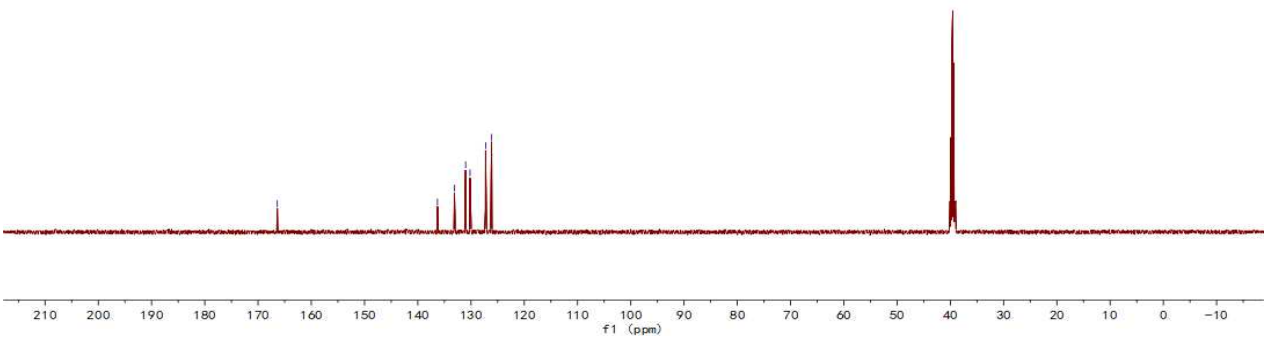

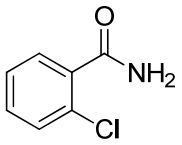


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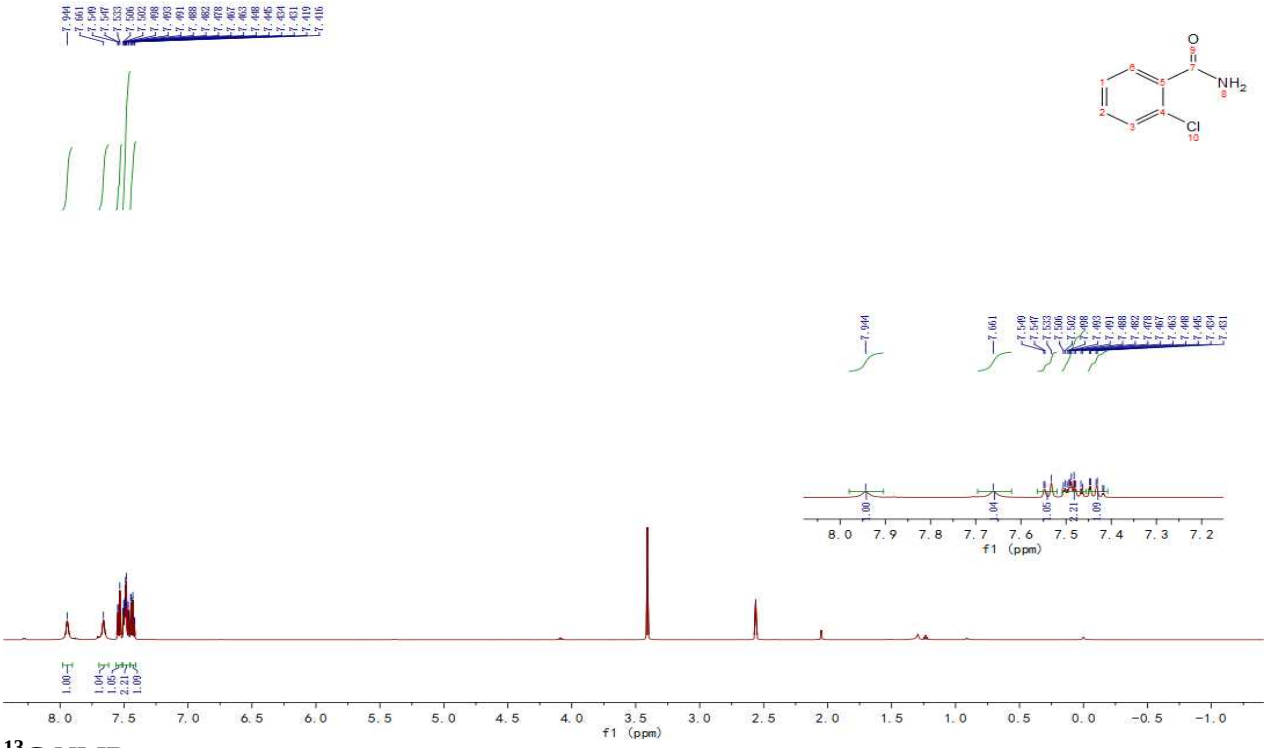


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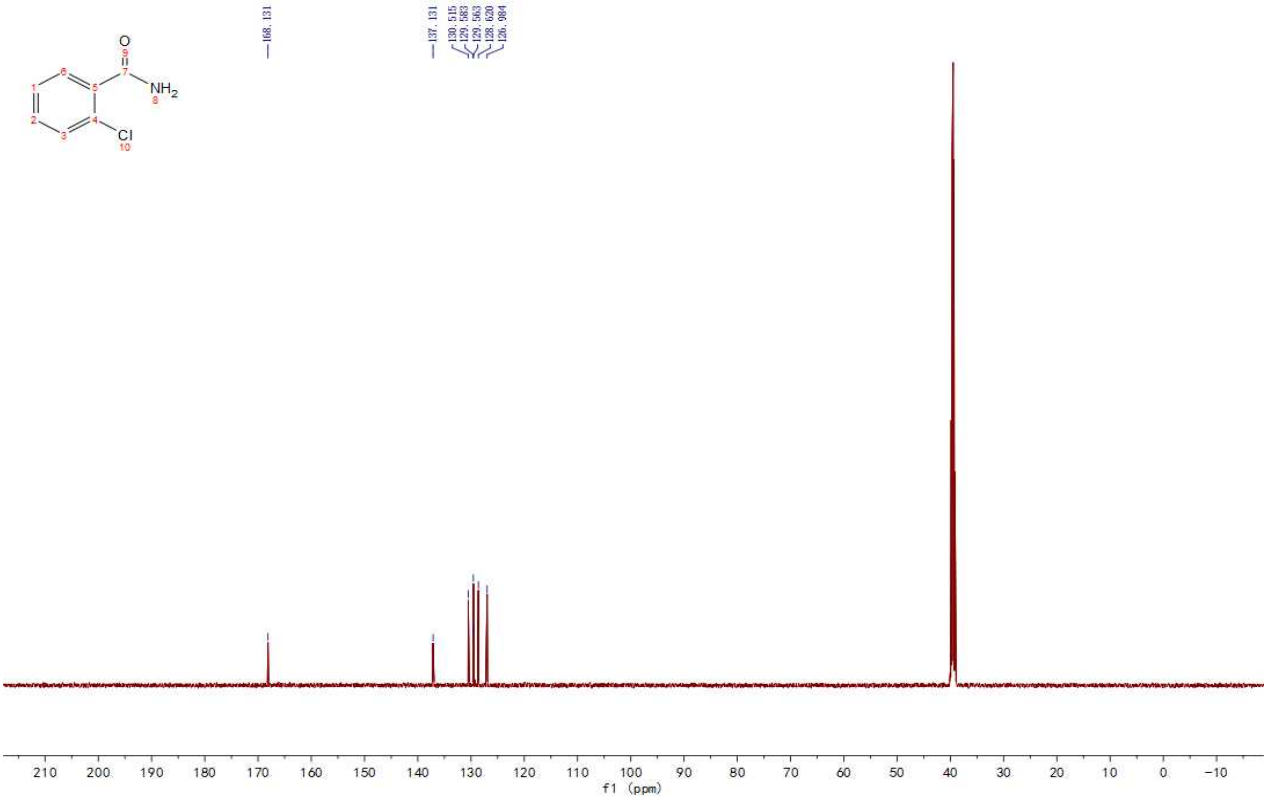

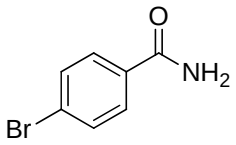


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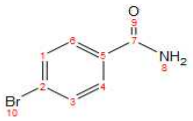


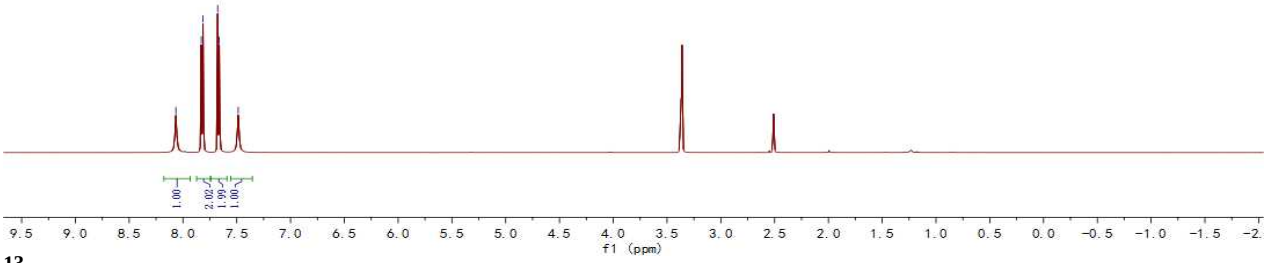


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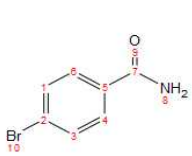



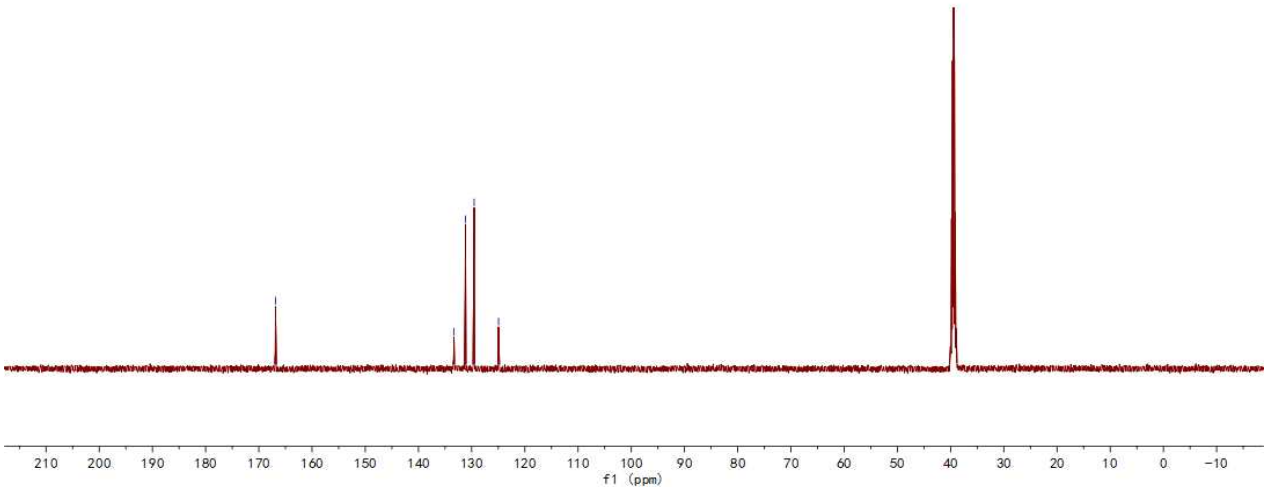

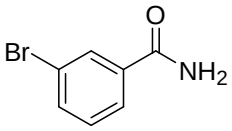


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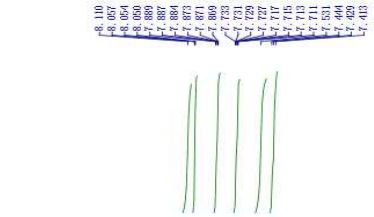
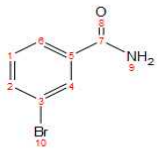
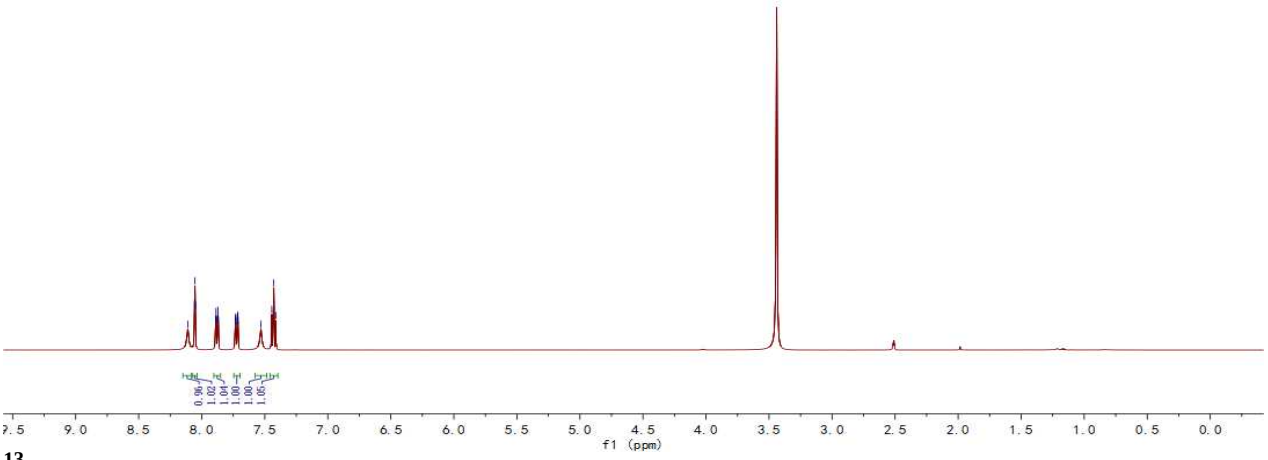
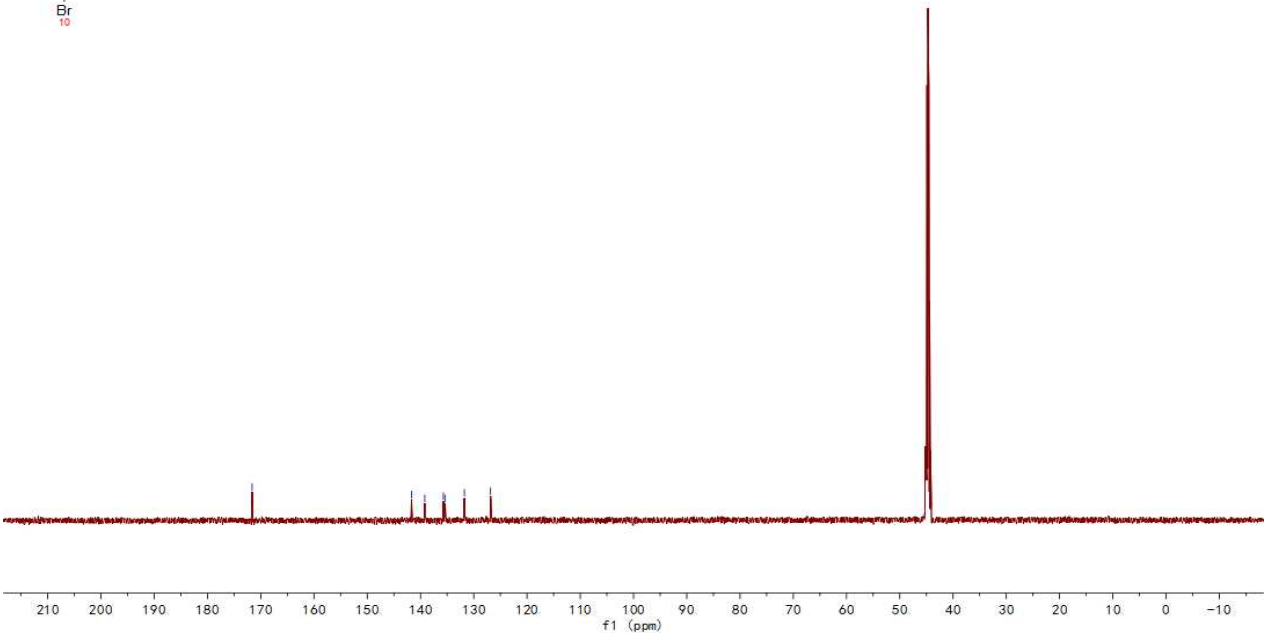
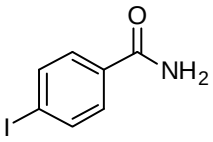





**$^{13}$C NMR**

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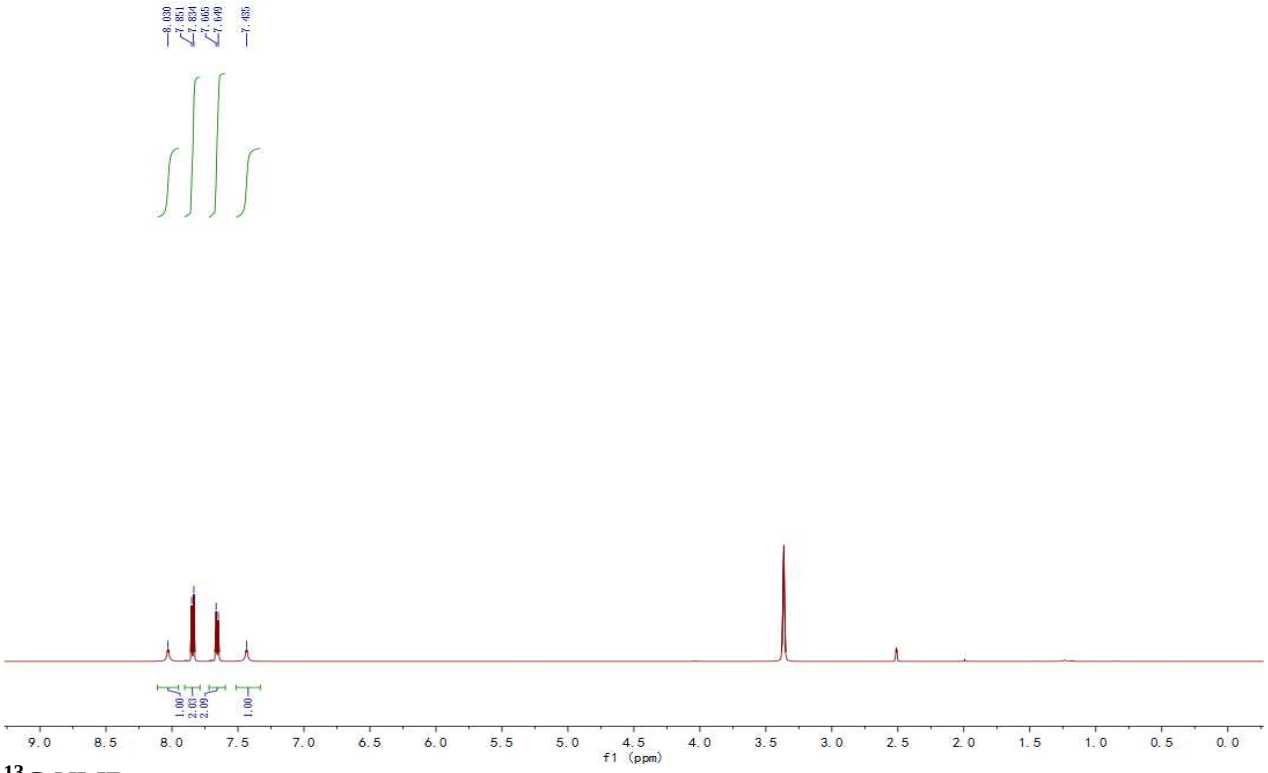


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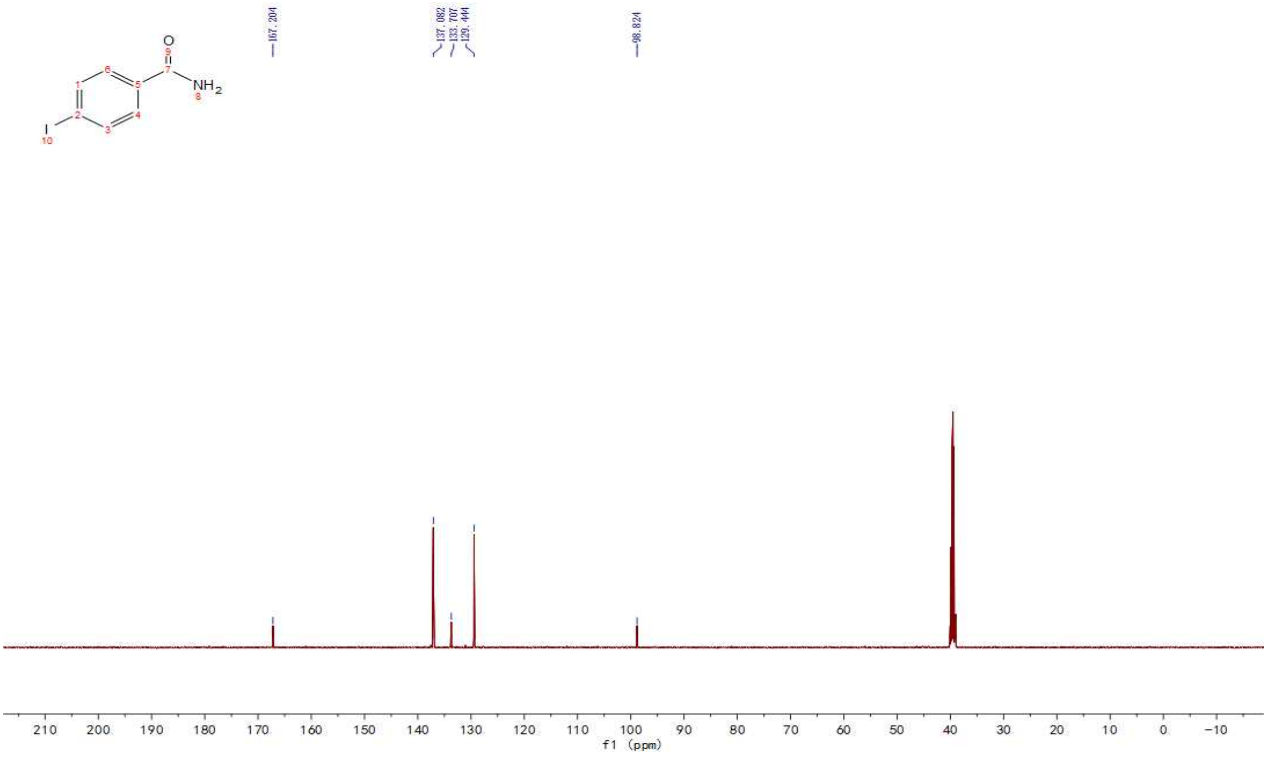

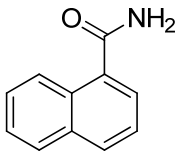


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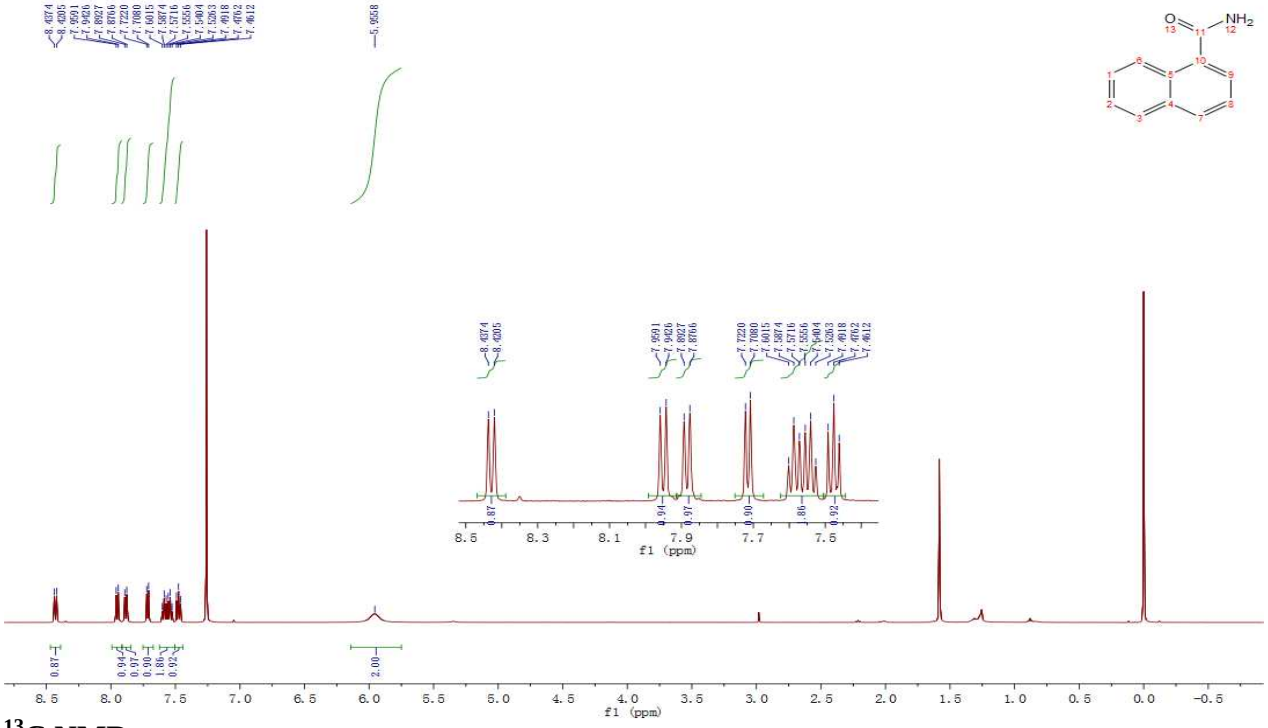
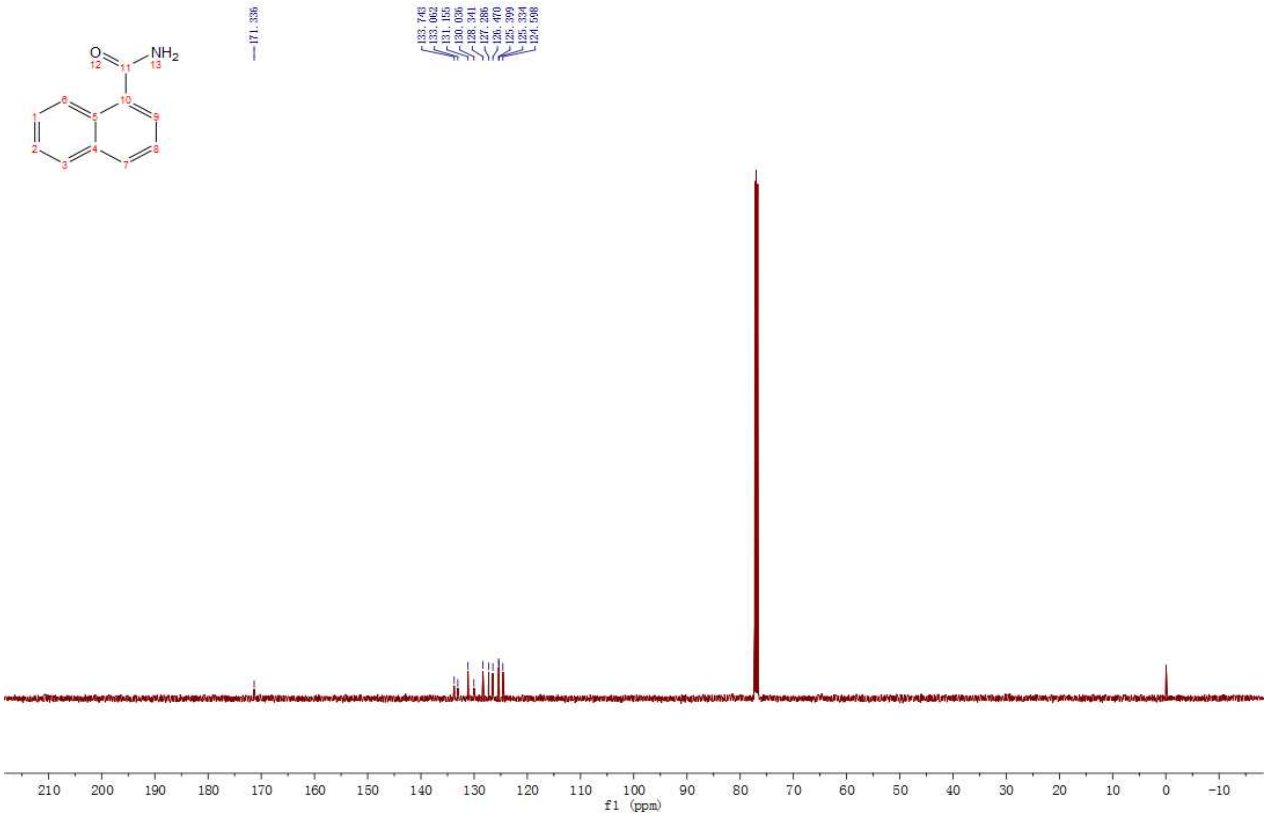
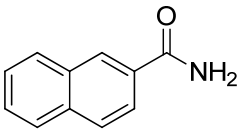



**$^{13}$C NMR**



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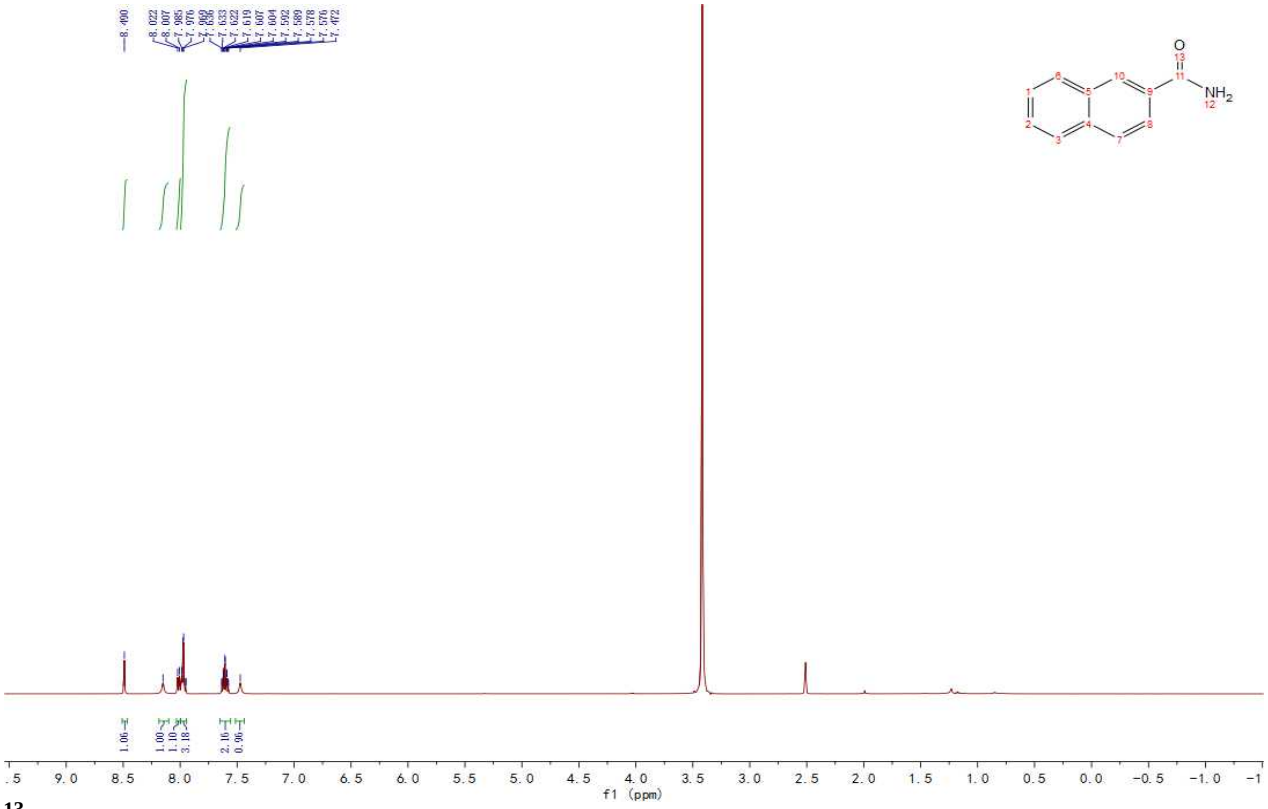


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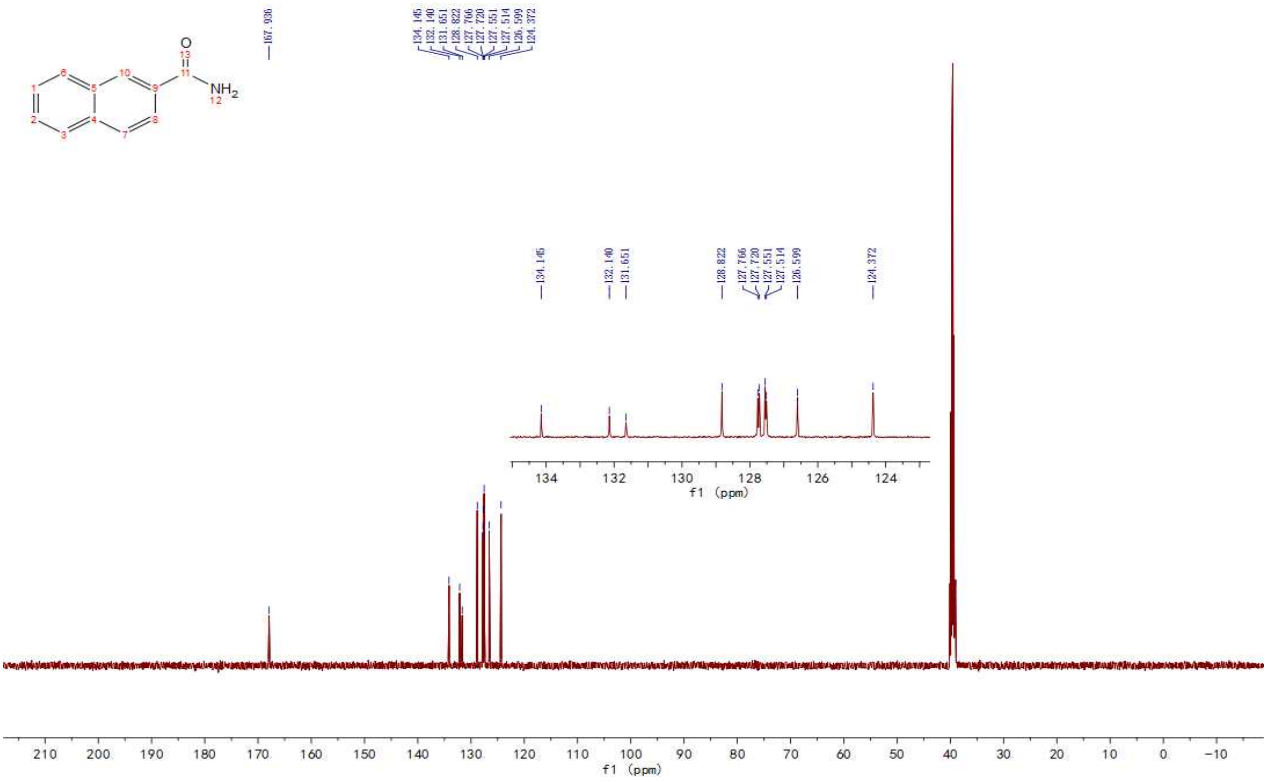

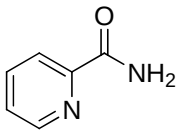


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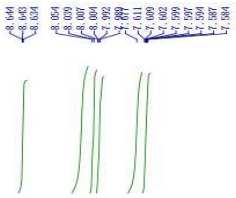

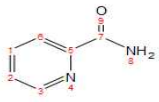

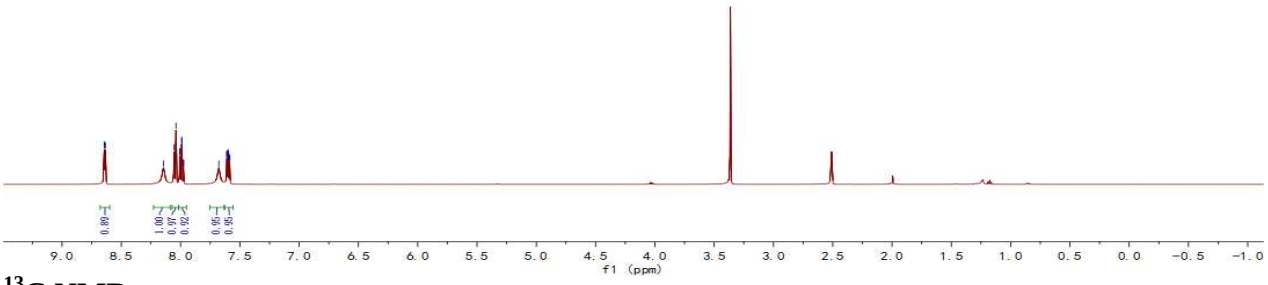


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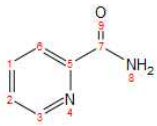
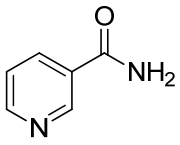
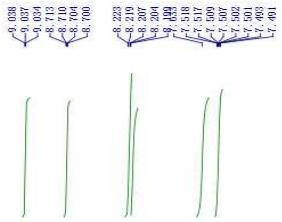
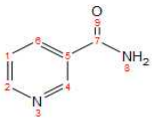
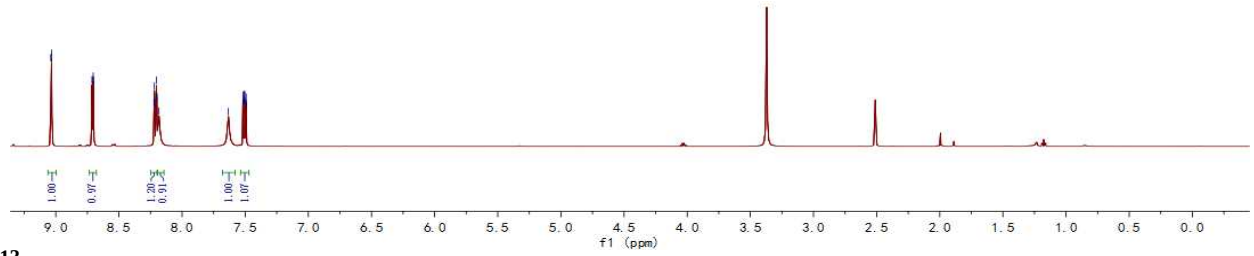





**$^{1}$H NMR**



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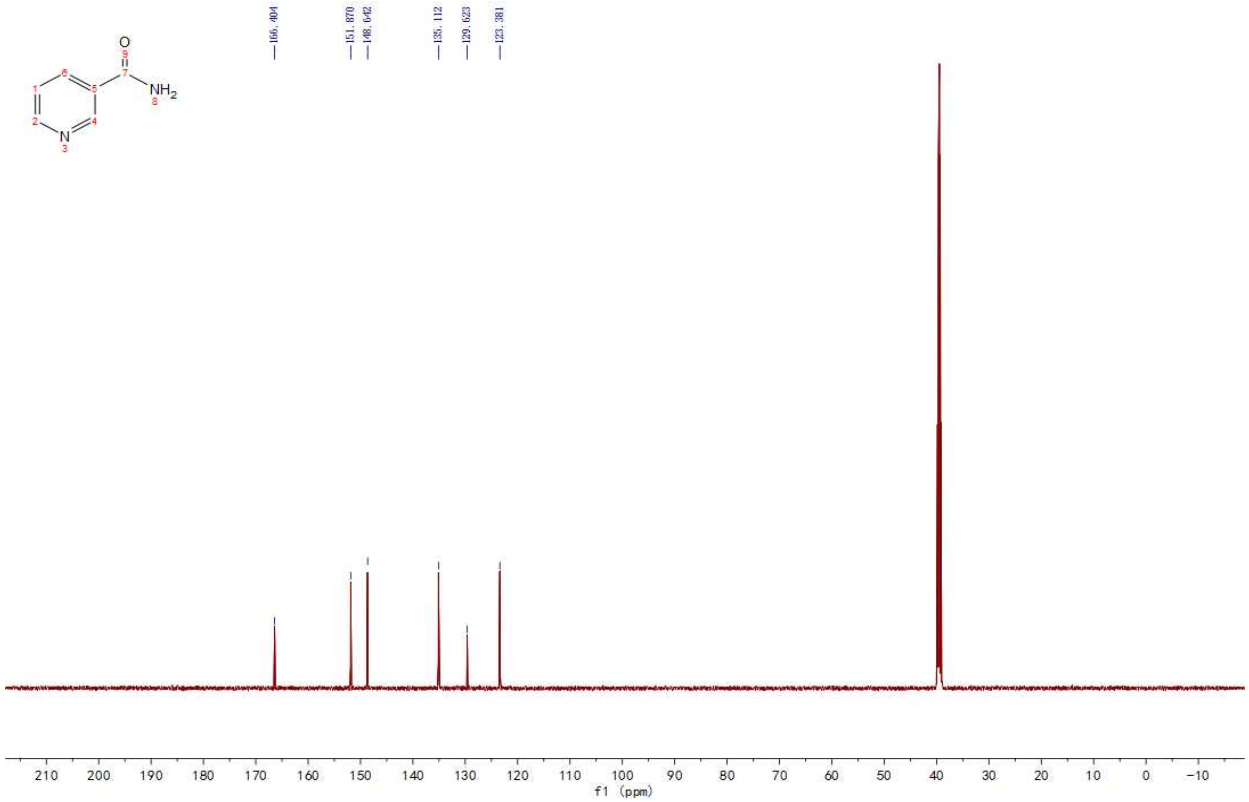
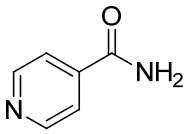
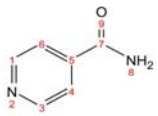
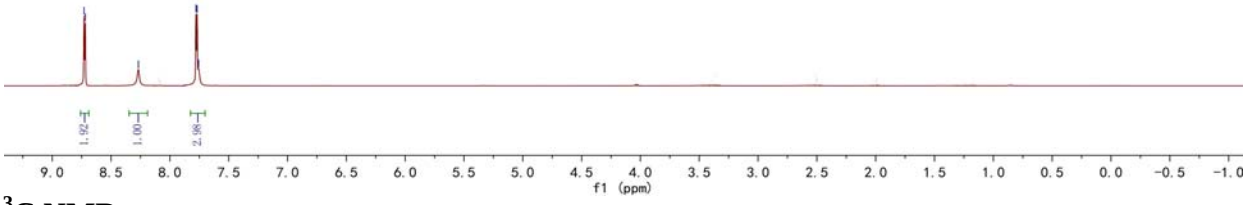


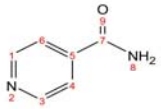



**$^{1}$H NMR**

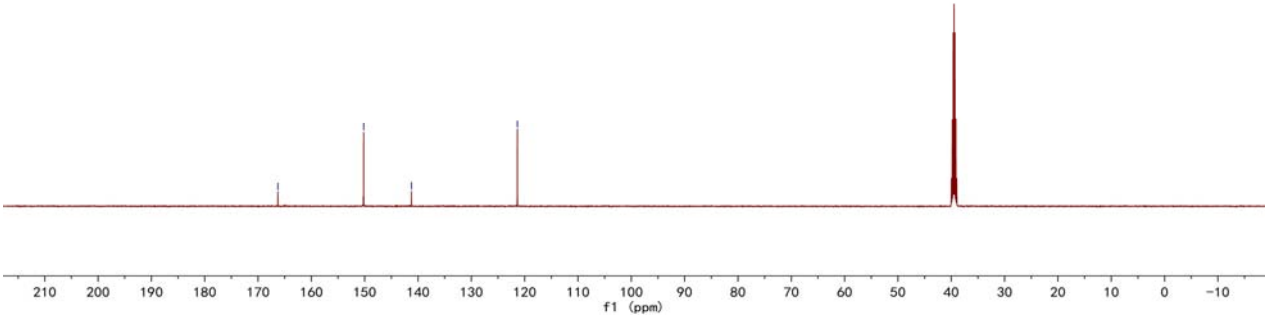



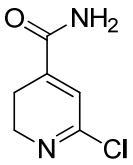




**$^{13}$C NMR**







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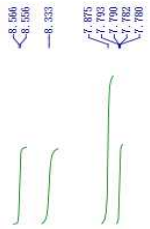
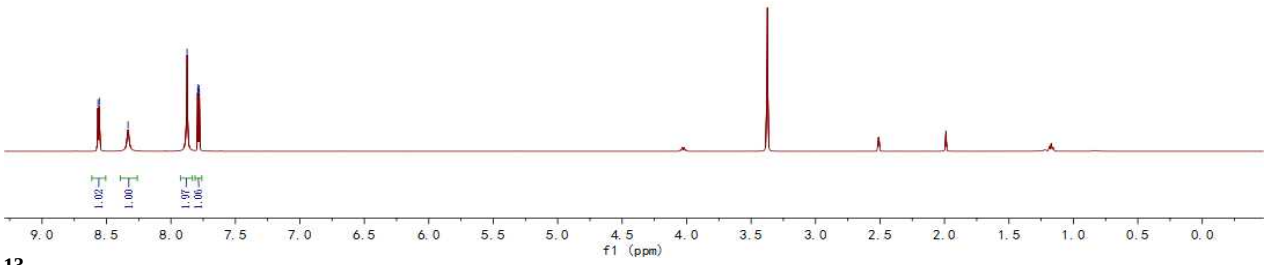
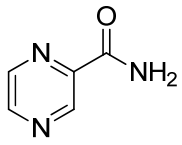







**$^{13}$C NMR**



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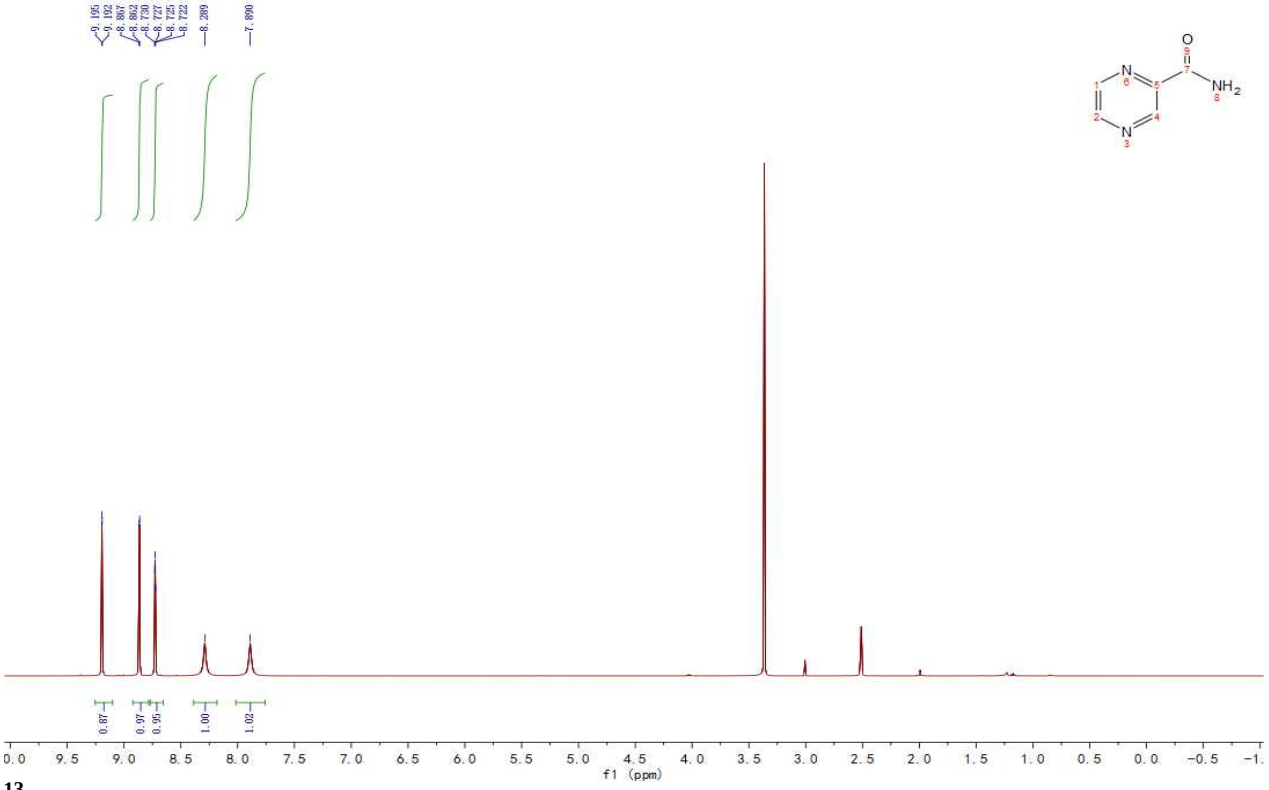

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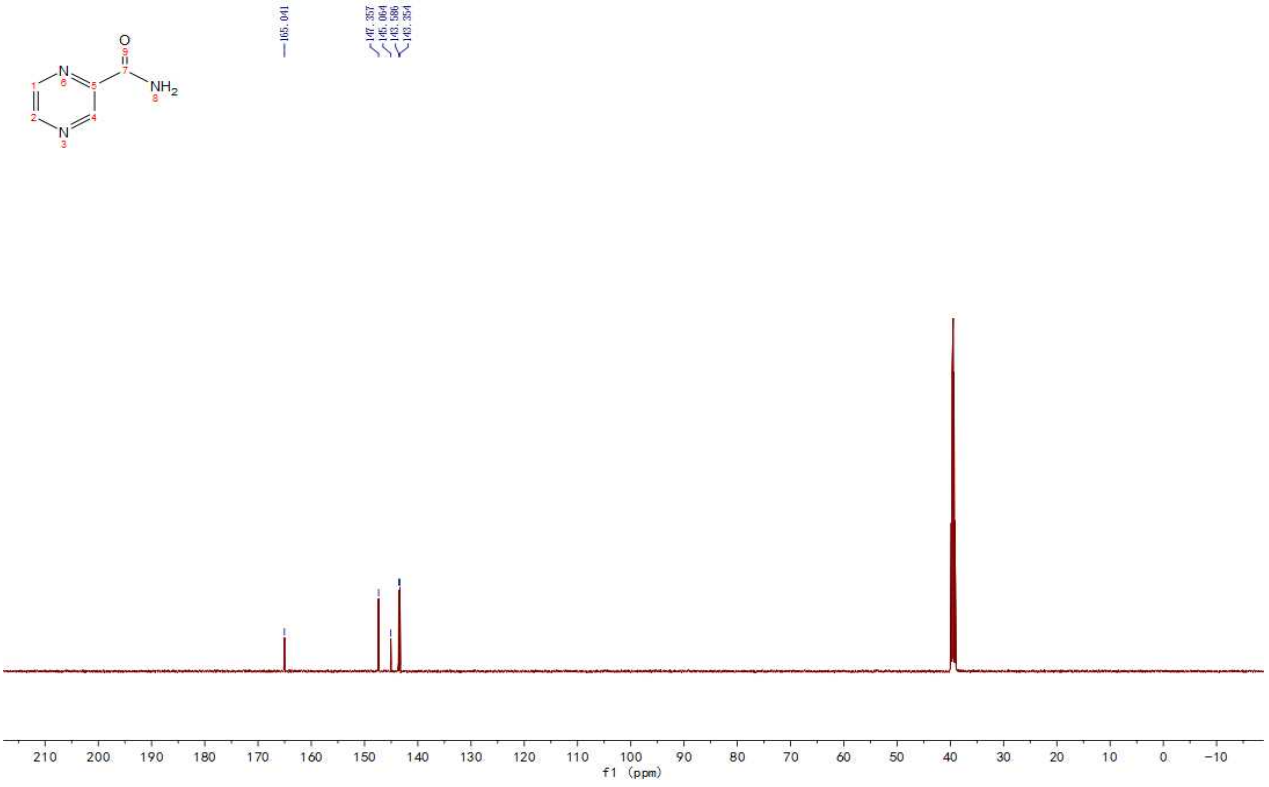

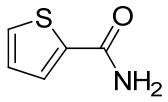


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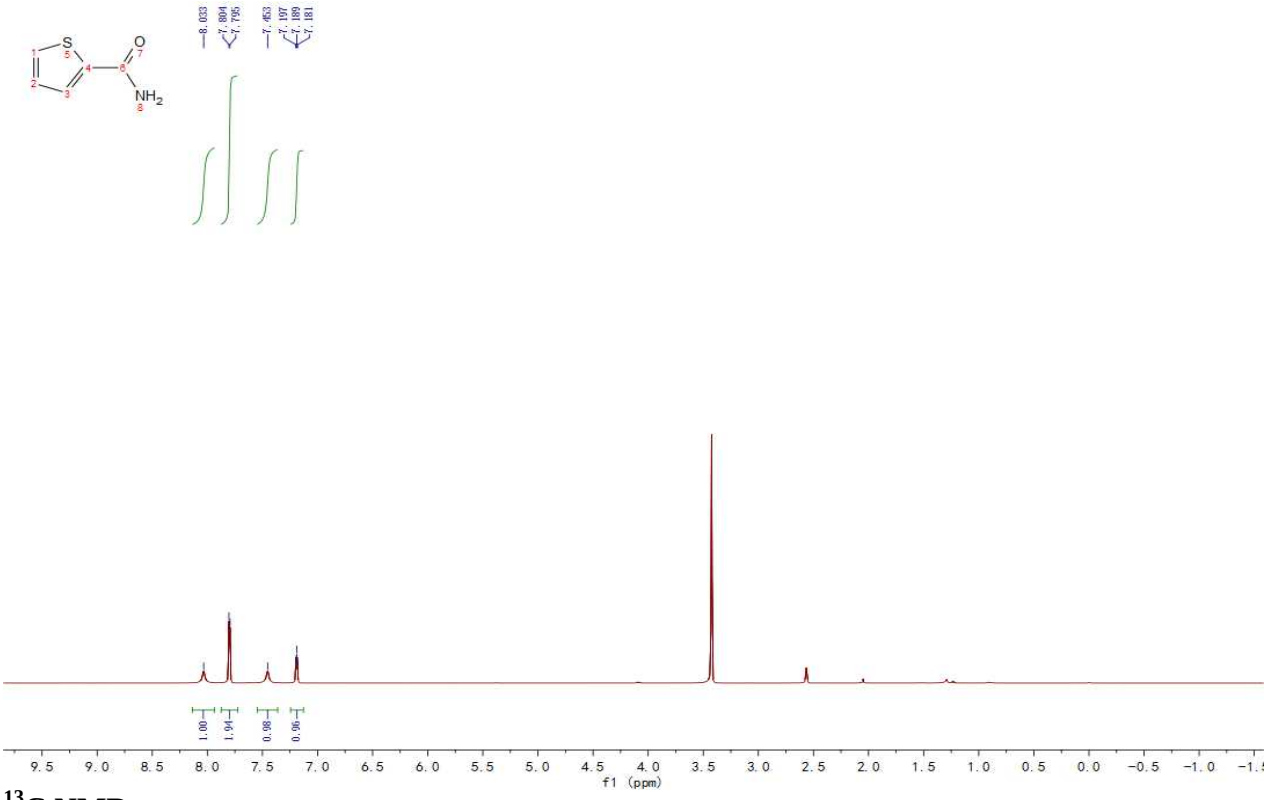


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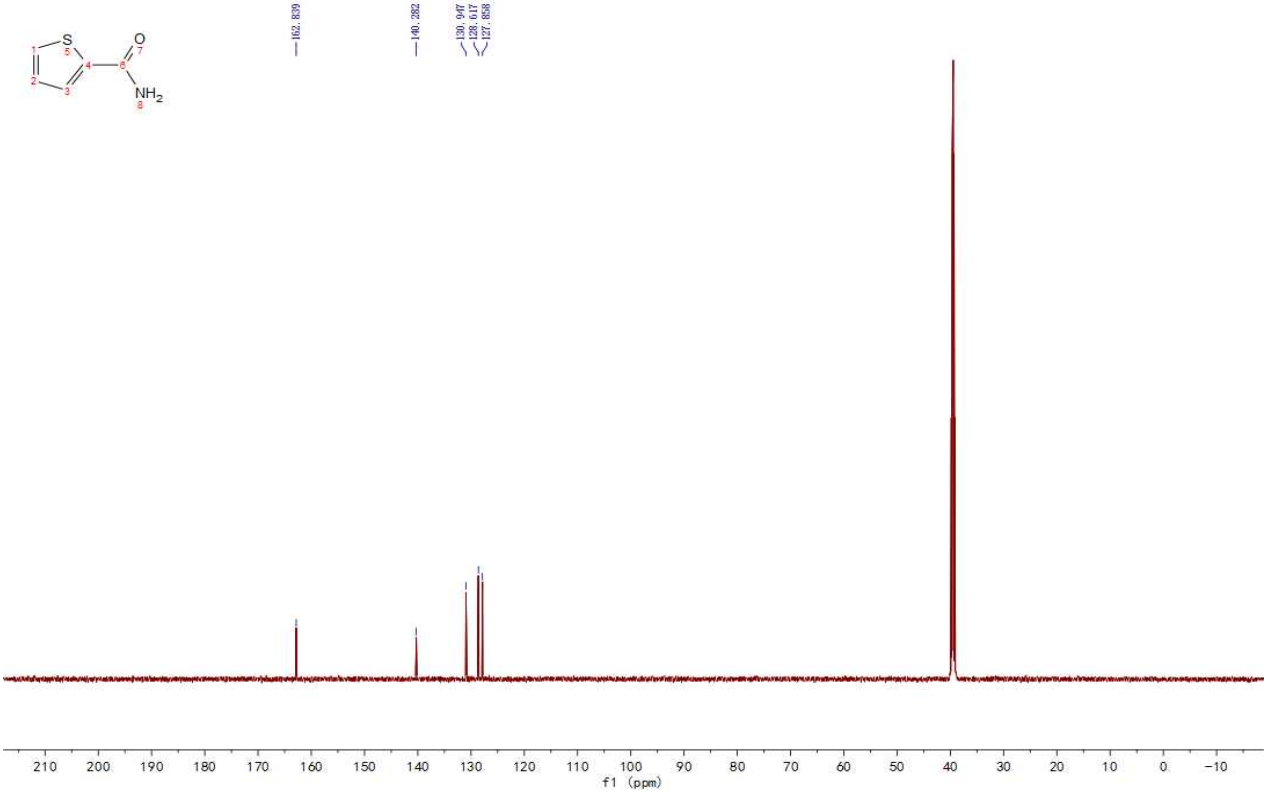

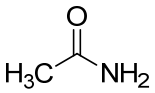

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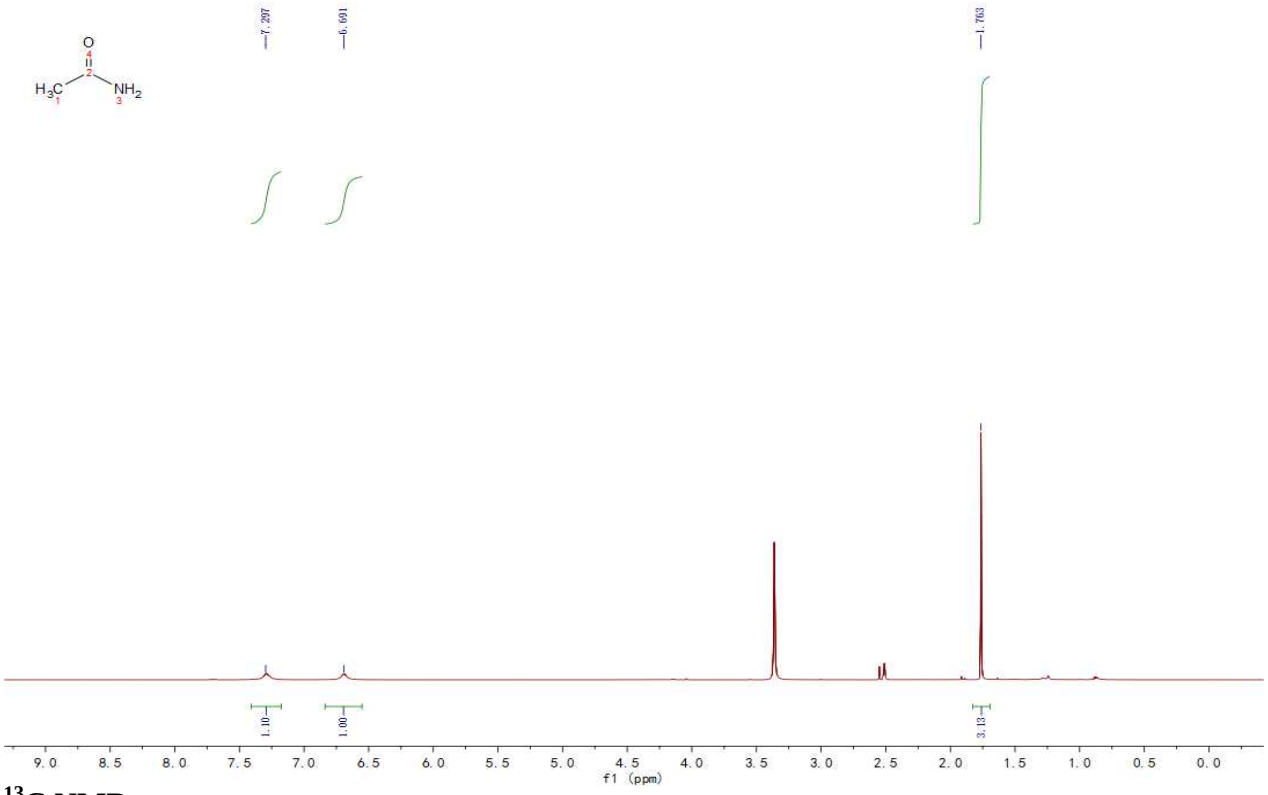


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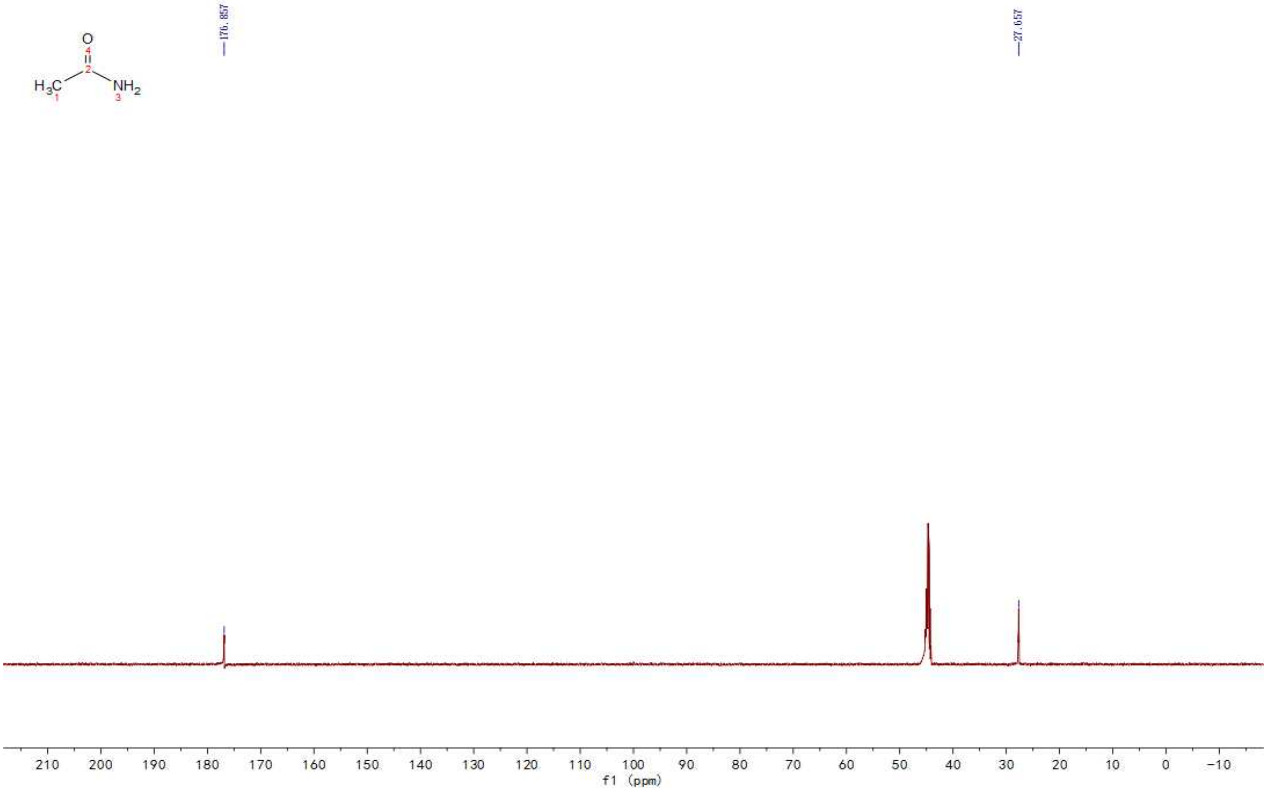

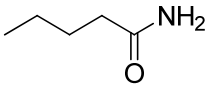


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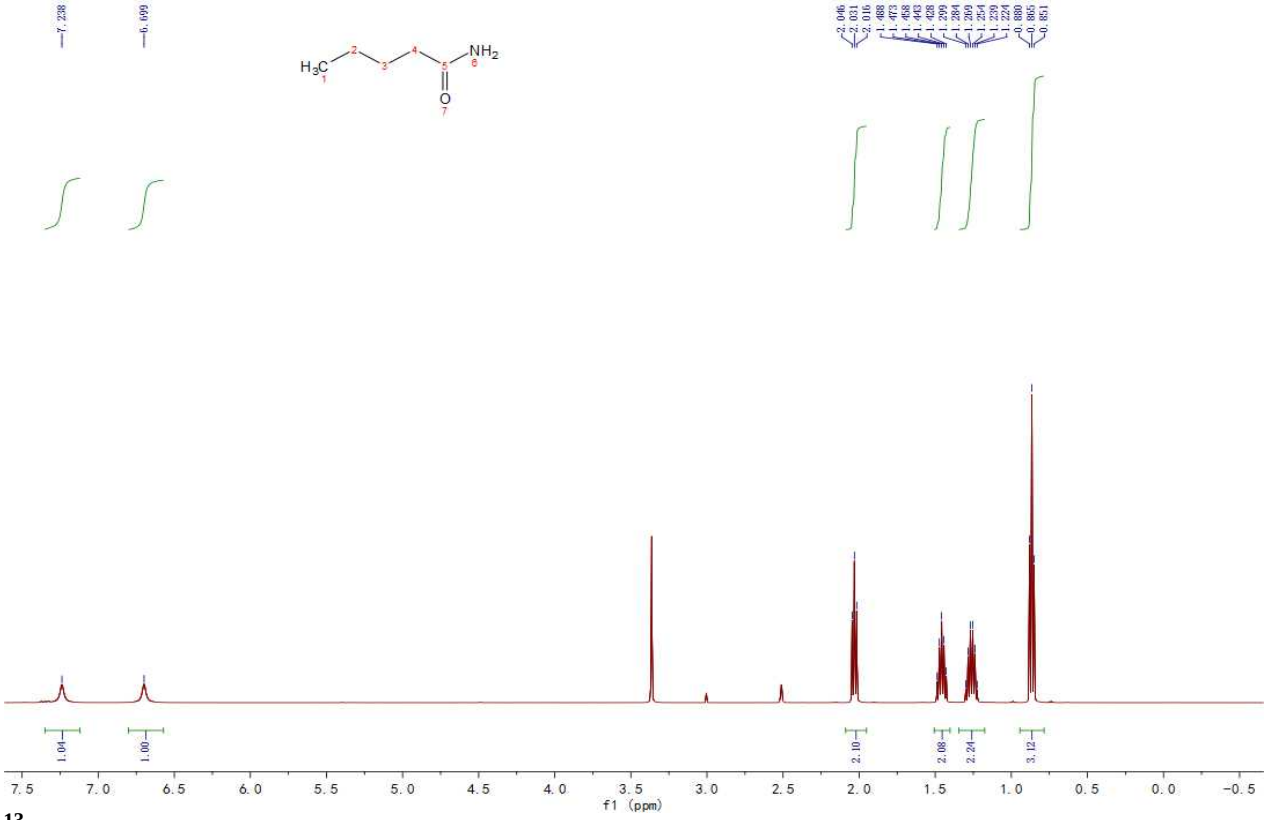


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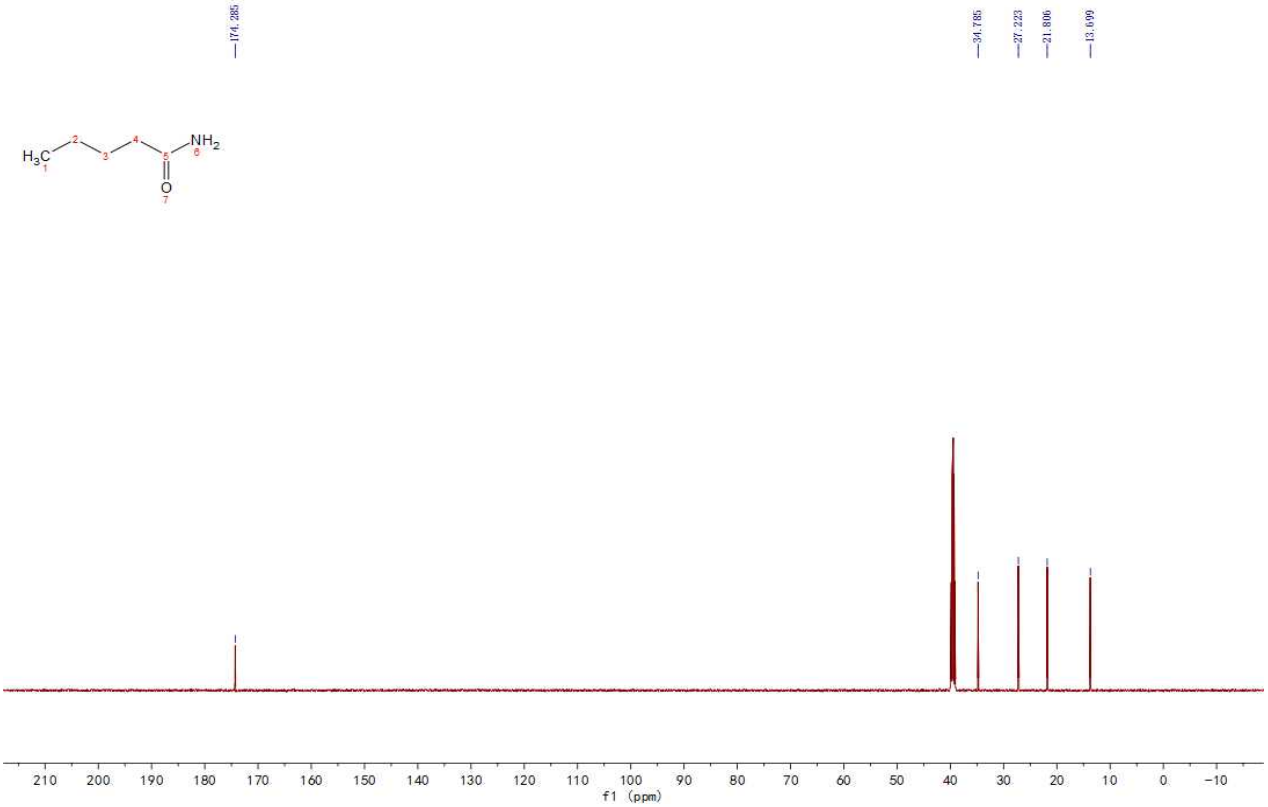

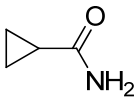


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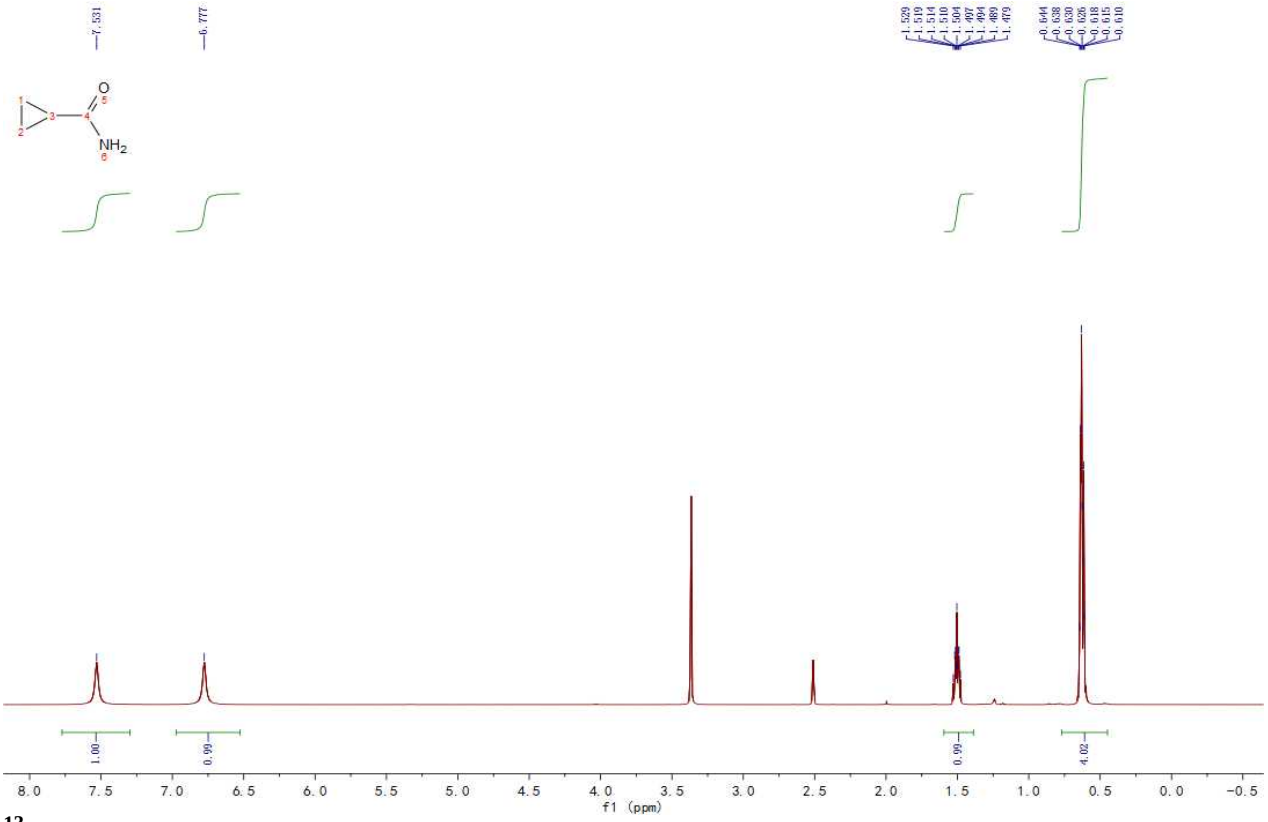


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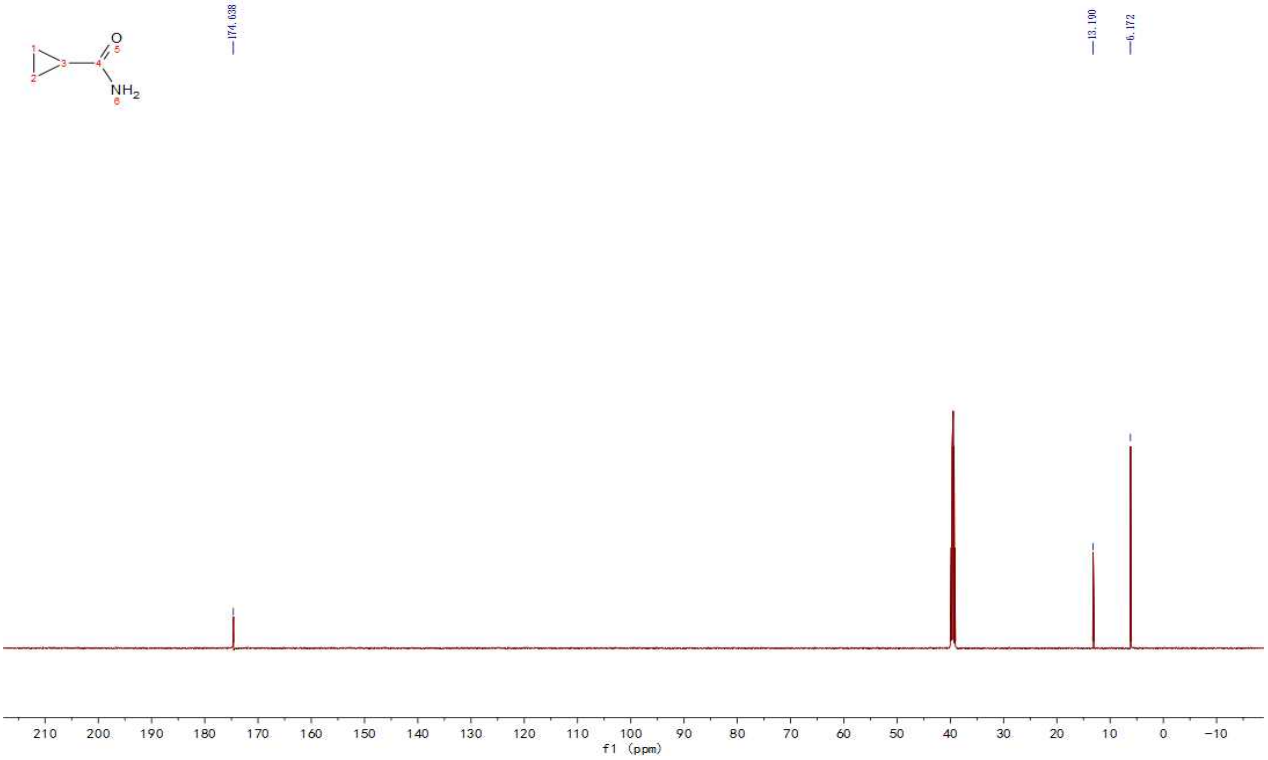

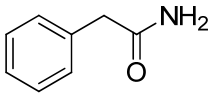


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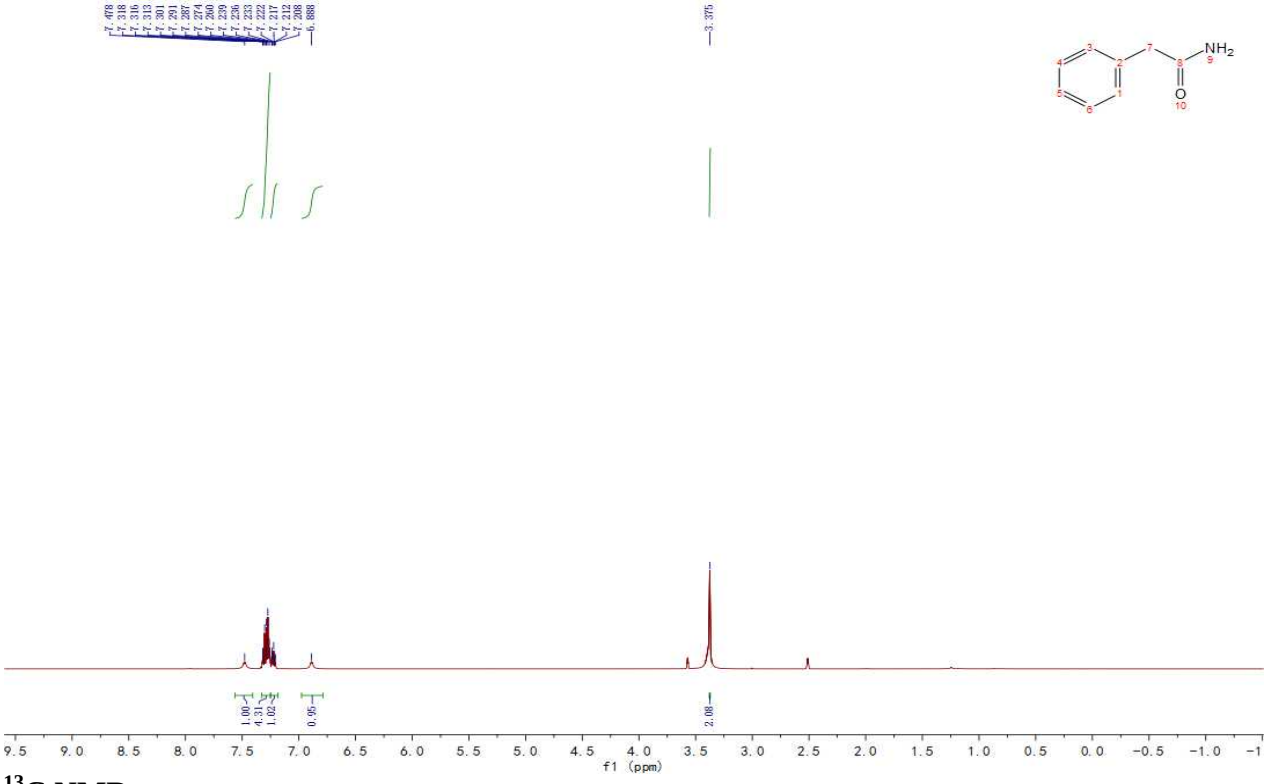


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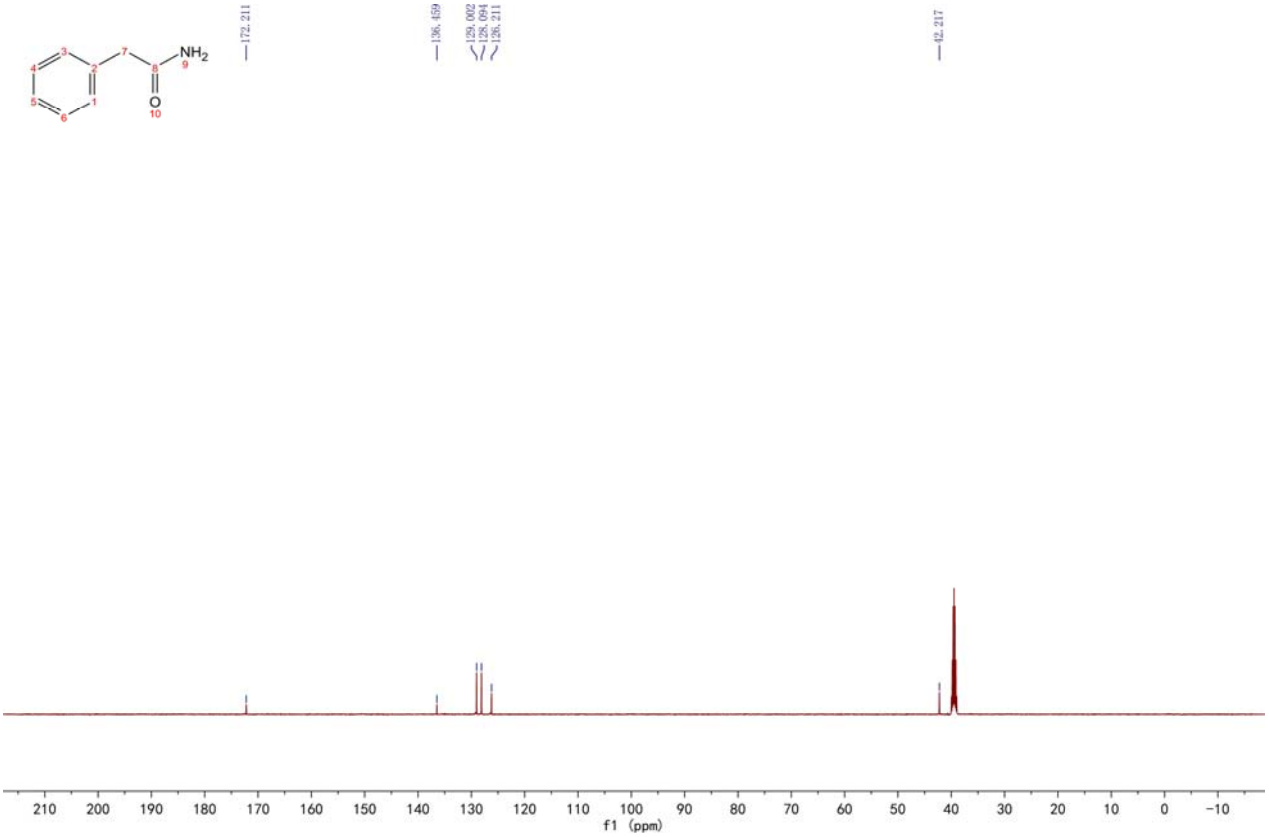

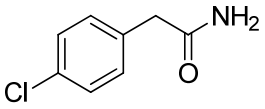


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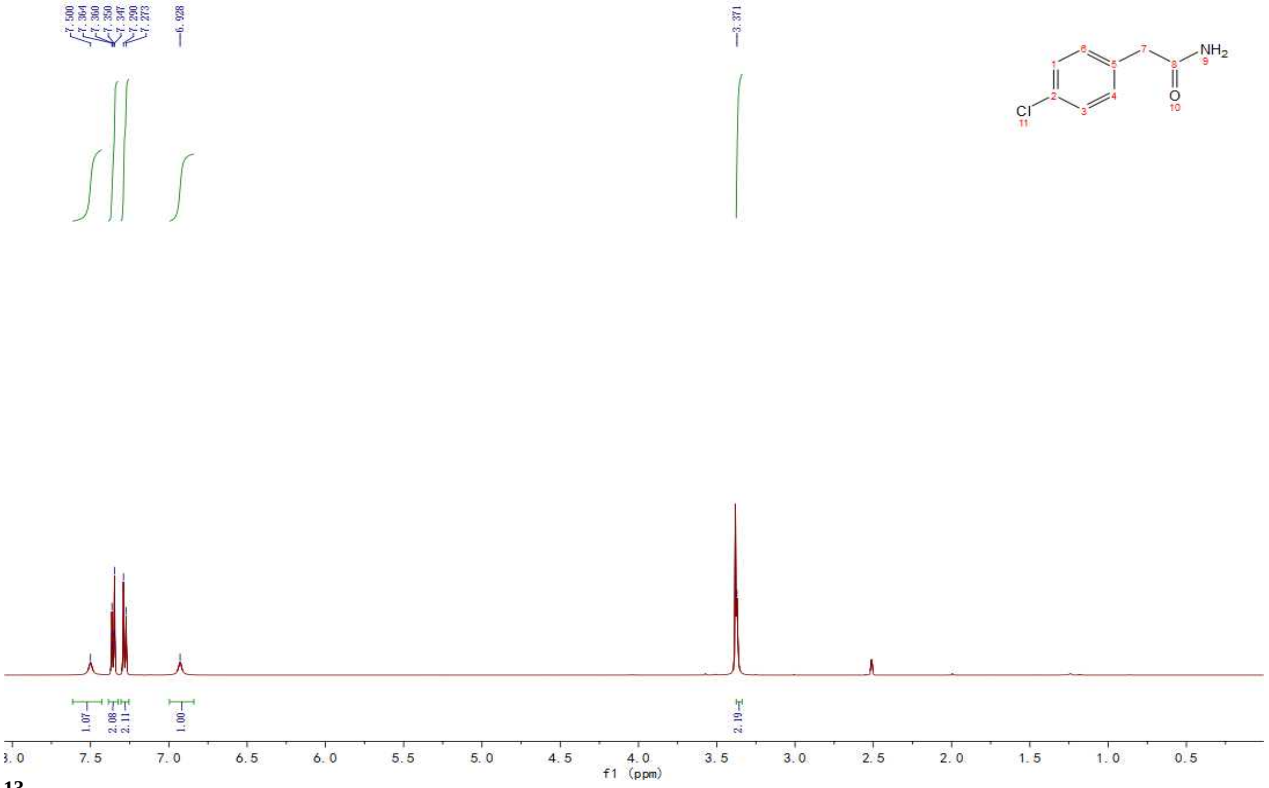


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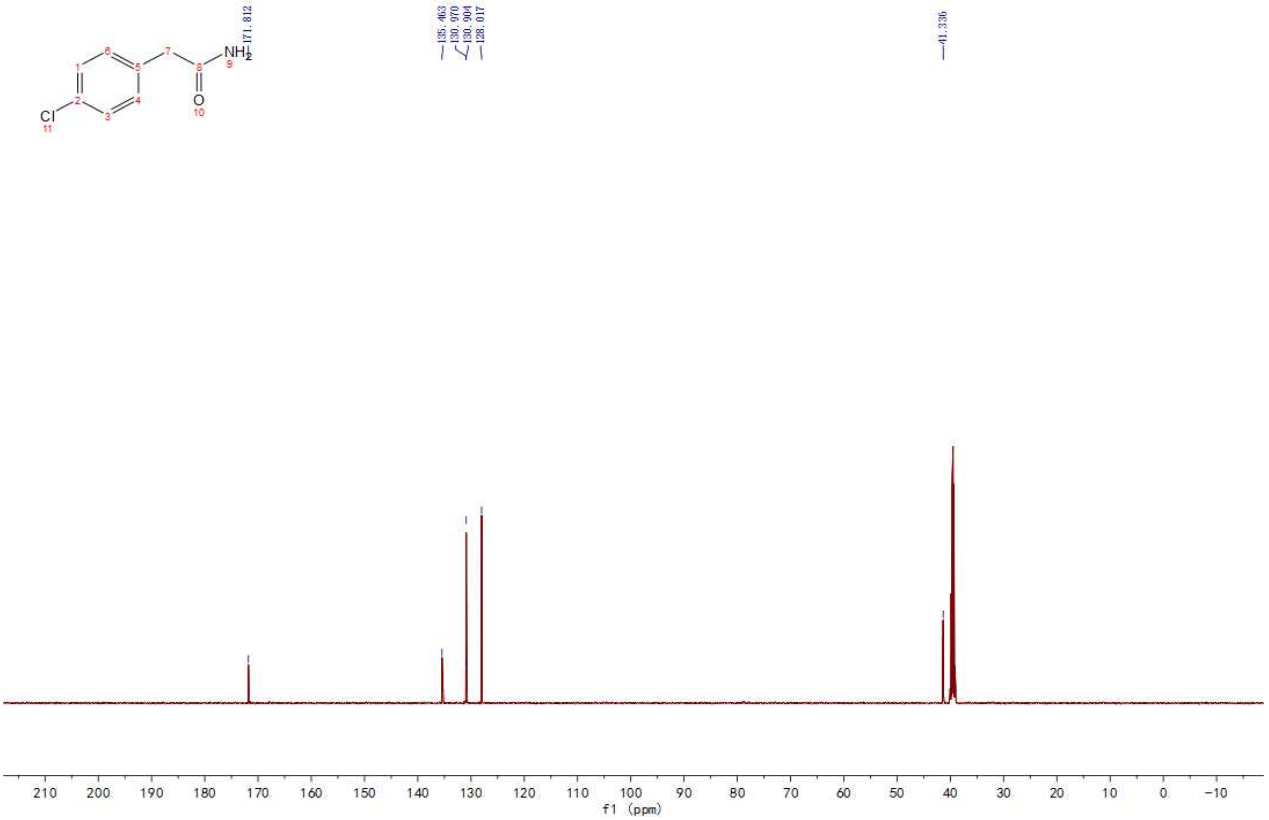

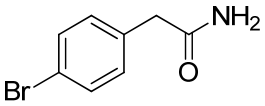


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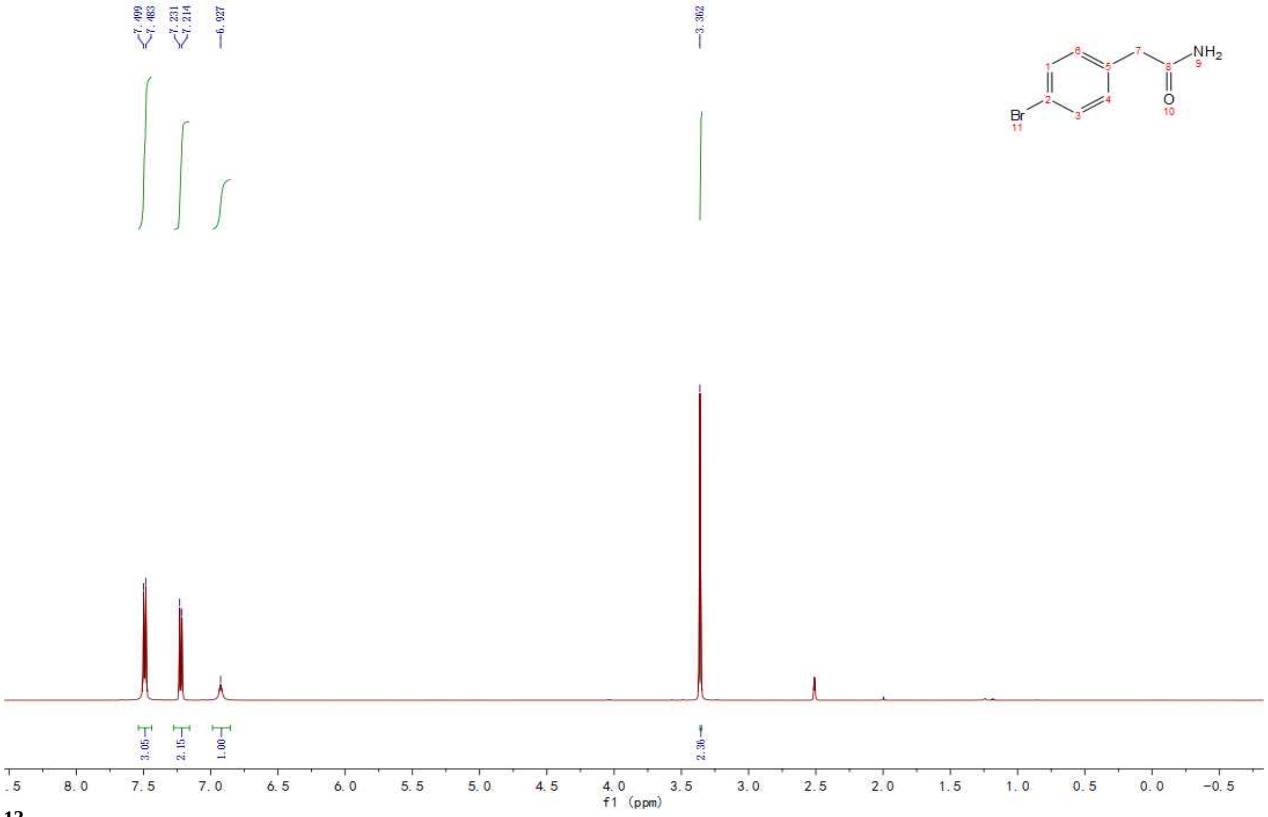


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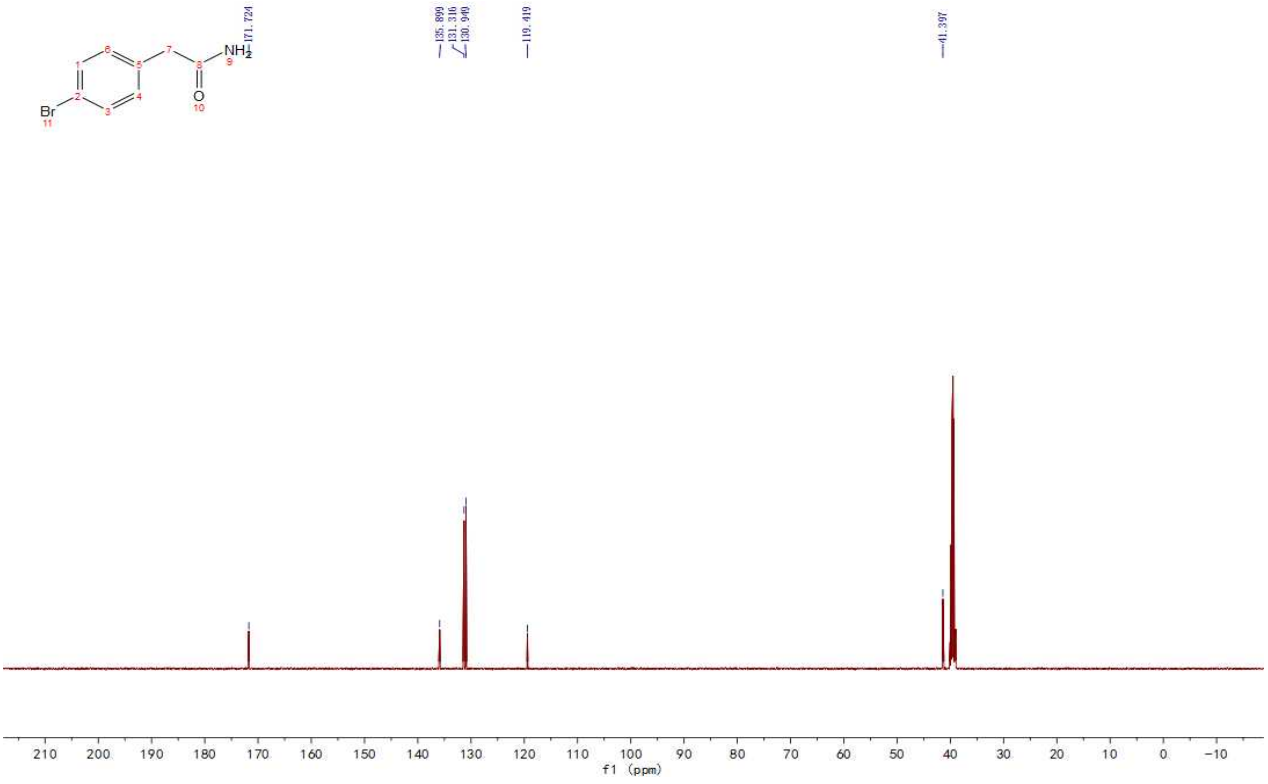

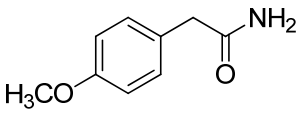


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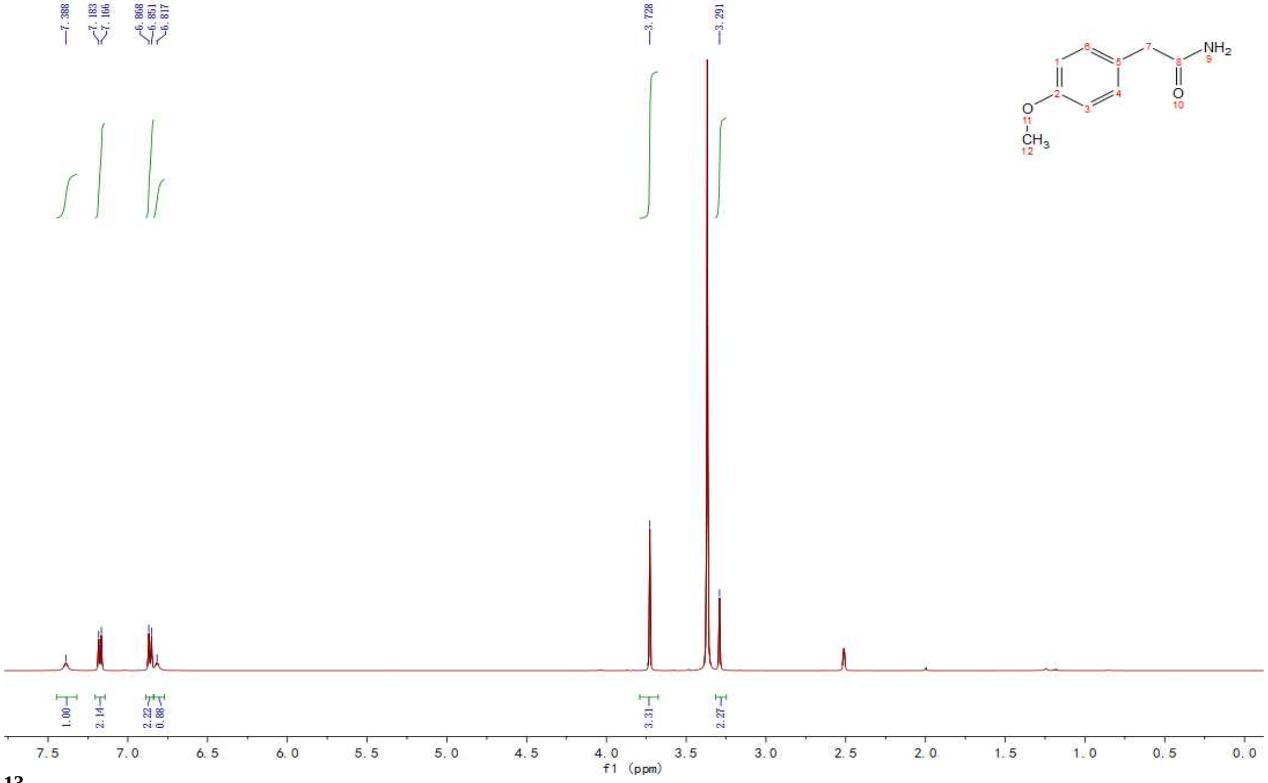


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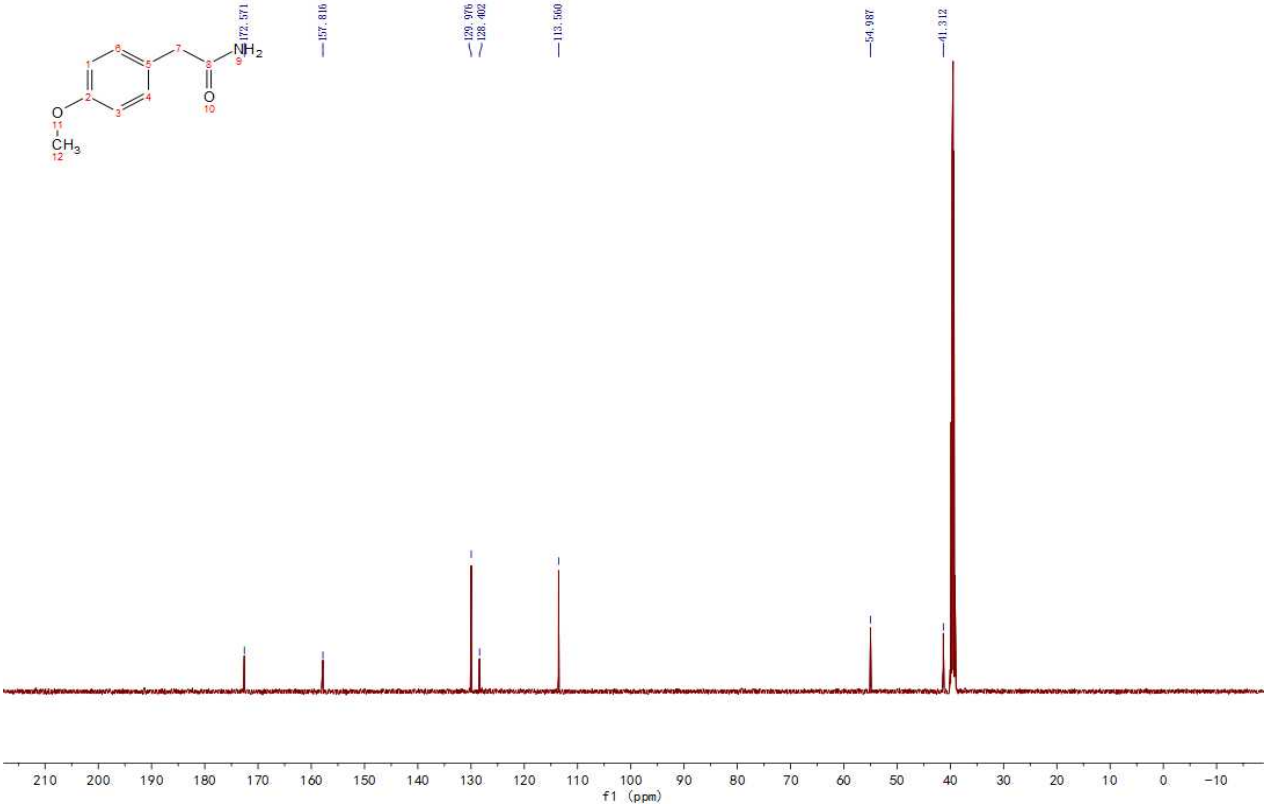

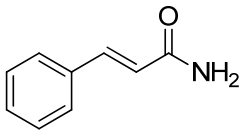


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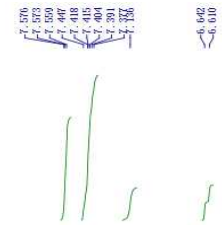

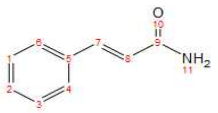

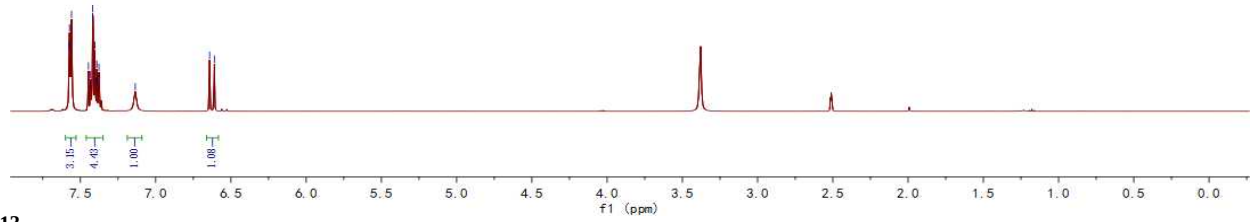


**$^{13}$C NMR**