Copper-Catalyzed Ligand-Free Amidation of Benzylic Hydrocarbons and Inactive Aliphatic Alkanes

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Supporting Information

Table of contents

General information……...S2

Experimental procedures…….…….….S3

Spectroscopic data of products…….……S4

Copies of NMR spectra of products…….S11

General information

Unless otherwise noted, all solvents and reagents were obtained commercially and used without further purification. 4-Methoxybenzamide, p-tolylamide and lauroicacidamide were purchased from TCI Shanghai Co., Ltd. in China; Butyramide, phthalamide, p-toluenesulfonamide, p-nitrobenzamide, and 4-(trifluoromethyl)benzamide were purchased from J&K Scientific Ltd. in China; 2-oxohexamethylenimine, acetamide, succinamide, cyclohexanecarboxamide, 3,5-dimethoxybenzamide, 2-chlorotoluene 4-fluorobenzamide, 4-bromotoluene, 3-iodotoluene, p-fluorotoluene, p-xylene, 1,2-dimethylbenzene, m-xylene, mesitylene, isopropylbenzene, 4-chlorotoluene, 4-ethyltoluene, ethylbenzene and ^{t}BuOK were purchased from Aladdin Chemistry Co., Ltd. in China; Toluene and cyclohexane were purchased from Guangzhou chemical reagent factory; 4-bromobenzamide was purchased from Adamas-beta; 3-chlorobenzamide and CuCl (99% or 99.999%) was purchased from Alfa-Aesar. $CuCO_3$•$Cu(OH)_2$ was purchased from Acros Organics.

Analytical thin layer chromatography (TLC) plates and the silica gel (200−300 mesh) for column chromatography were phased from Qingdao Haiyang Chemical and Special Silica Gel Co, Ltd.

Proton nuclear magnetic resonance (^{1}H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectroscopy were performed on Bruker Advance III-400 spectrometers (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR). Chemical shifts of ^{1}H NMR and ^{13}C NMR spectra were reported as in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0 ppm) and relative to the signal of chloroform-d (δ 7.26 ppm for ^{1}H NMR and δ 77.2 ppm for ^{13}C NMR). Multiplicities were given as: s (singlet); br s (broad singlet); d (doublet); t (triplet); q (quartet); m (multiplets), etc. The number of protons (n) for a given resonance was indicated by nH.

IR spectra were recorded on Bruker Tensor 27 FTIR spectrometer and only major peaks were reported in cm^{-1}.

Melting points were recorded on BUCHI Melting Point B-545 apparatus (Switzerland) without correction.

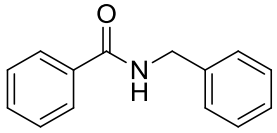
HRMS data were collected on Q-star Elite, ELI-LC-MS/MS (product from ABI, America).

Experimental procedures

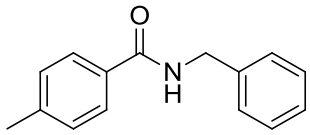
General procedure for the amidation of amides, sulfonamides and imides with toluene: A 25 mL Schlenk tube was added amides **1** (or sulfonamides, imides) (0.5 mmol), ^{t}BuOK (0.001mol%, ^{t}BuOK was dissolved in toluene), toluene **2** (2 mL), CuCl (10 mol %) and DTBP (2 equiv). The tube was then charged with N_2 (1 atm), and was stirred at 120°C for 24 h. After the reaction mixture was cooled to room temperature, the reaction mixture was extracted with ethyl acetate (3×10 mL). The combined organic layer was washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. And the resulting mixture was purified by silica gel column chromatography to afford the desired products **3**.

General procedure for the amidation of primary benzylic hydrocarbons and Inactive aliphatic alkanes with benzamide : A 25.0 mL Schlenk tube was added benzamide **1** (0.5 mmol), ^{t}BuOK(0.001 mol %, ^{t}BuOK was dissolved in toluene), benzylic hydrocarbons **2** (or unactive aliphatic alkanes) (2 mL), CuCl (10 mol %) and DTBP (2 equiv). Then the tube was charged with N_2 (1 atm), and was stirred at 120 °C for 24 h. After the reaction mixture was cooled to room temperature, the reaction mixture was extracted with ethyl acetate (3×10 mL). The combined organic layer was washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. And the resulting mixture was purified by silica gel column chromatography (petroleum ether/ethyl acetate = 3:1) to afford the desired products **4**.

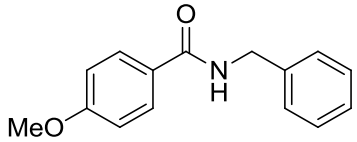
Spectroscopic data of products



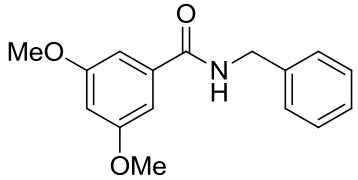
***N*-benzylbenzamide(3a):**The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3a** as white solid (88.7 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J*=8.0Hz, 2H), 7.29 (t, *J*=8.0Hz, 1H), 7.13-7.20 (m, 7H), 4.39 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 167.6, 138.4, 134.3, 131.4, 128.6, 128.4, 127.6, 127.3, 127.1, 43.8.



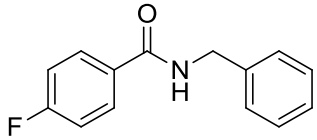
***N*-benzyl-4-methylbenzamide(3b):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3b** as white solid (89.0 mg, 79%). ^{1}H NMR (400 MHz, CDCl3): δ 7.79 (d, *J*=8.0Hz, 2H), 7.26-7.30 (m, 5H), 7.17 (d, *J*=8.0Hz, 2H), 6.74 (br s, 1H), 4.58 (d, *J*=4.0Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 142.0, 138.5, 131.6, 129.3, 128.8, 127.9, 127.5, 127.1, 44.1, 21.5.



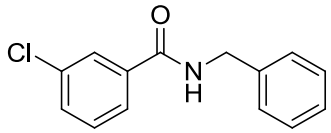
***N*-benzyl-4-methoxybenzamide(3c):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3c** as white solid (100.1 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J*=8.0Hz, 2H), 7.29-7.32 (m, 5H), 6.94 (br s, 1H), 6.88 (d, *J*=8.0Hz, 2H), 4.59 (d, *J*=4.0Hz, 2H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 162.2, 138.6, 128.9, 128.7, 127.8, 127.4, 126.7, 113.7, 55.4, 44.0.



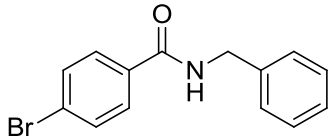
***N*-benzyl-3,5-dimethoxybenzamide(3d):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3d** as white solid (95.0 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29-7.34 (m, 5H), 6.95 (s, 2H), 6.75 (br s, 1H), 6.58 (s, 1H), 4.61 (d, *J*=4.0Hz, 2H), 3.80 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 160.8, 138.3, 136.6, 128.7, 127.8, 127.4, 105.0, 103.7, 55.5, 44.0.



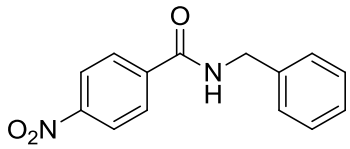
***N*-benzyl-4-fluorobenzamide(3e):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3e** as white solid (81.4 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (t, *J*=4.0Hz, 2H), 7.30-7.33 (m, 5H), 7.07 (t, *J*=4.0Hz, 2H), 6.89 (br s, 1H), 4.60 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 162.4 ($J_{C\text{-}F}$=250.0Hz), 138.3, 130.7 ($J_{C\text{-}F=}$10.0Hz), 129.6 ($J_{C\text{-}F=}$10.0Hz), 128.8, 127.9, 127.7, 115.6($J_{C\text{-}F=}$20.0), 44.2.



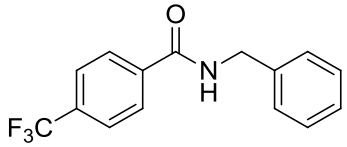
***N*-benzyl-3-chlorobenzamide(3f):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3f** as white solid (63.9 mg, 52%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.63 (d, *J*=8.0Hz, 1H), 7.43 (d, *J*=8.0Hz, 1H), 7.25-7.32 (m, 6H), 6.76 (br s, 1H), 4.58 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 138.0, 136.3, 134.8, 131.7, 130.0, 128.9, 128.0, 127.8, 127.5, 125.3, 44.3.



***N*-benzyl-4-bromobenzamide(3g)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3g** as white solid (103.0 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J*=8.0Hz, 2H), 7.52 (d, *J*=8.0Hz, 2H), 7.29-7.36 (m, 5H), 6.96 (br s, 1H), 4.59 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 138.1, 133.3, 131.8, 128.8, 128.8, 127.9, 127.7, 126.2, 44.2.

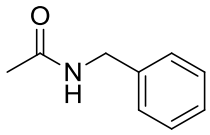


***N*-benzyl-4-nitrobenzamide(3h):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3h** as white solid (70.5 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22(d, *J*=8.0Hz, 2H), 7.93 (d, *J*=8.0Hz, 2H), 7.33 (s, 5H), 6.86 (br s, 1H), 4.63 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 149.7, 140.0, 137.6, 129.0, 128.3, 128.0, 128.0, 123.9, 44.5.

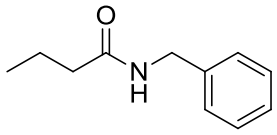


***N*-benzyl-4-trifluoromethylbenzamide(3i)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3i** as yellow solid (93.6 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86(d, *J*=8.0Hz, 2H), 7.64 (d, *J*=4.0Hz, 2H), 7.29-7.32 (m,5H), 6.79 (br s, 1H), 4.61 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 137.8 ($J_{C\text{-}F}$=12.0Hz), 133.4 ($J_{C\text{-}F}$=33.0Hz), 129.0,

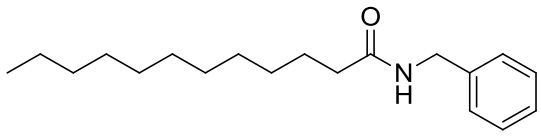
128.0, 127.9, 127.6, 125.7 (J_{C-F}=4.0Hz), 125.1, 122.4, 44.0.



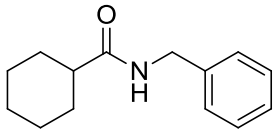
***N*-benzylacetamide(3j)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3j** as white solid (61.2 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23-7.31 (m, 5H), 6.66 (br s,1H), 4.35 (d, J=4.0Hz, 2H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 138.3, 128.4, 127.5, 127.0, 43.2, 22.6.



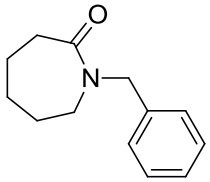
***N*-benzylbutyramide(3k):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3k** as white solid (63.8 mg, 72%). ^{1}H NMR (400MHz, $CDCl_3$): δ 7.21-7.28 (m, 5H), 6.81 (br s, 1H), 4.34 (d, *J*=8.0Hz, 2H), 2.14 (t, *J*=8.0Hz, 2H), 1.58-1.65 (m, 2H), 0.91 (t, *J*=8.0Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) : δ 173.3, 138.6, 128.5, 127.5, 127.2, 43.2, 38.3, 19.1, 13.7.



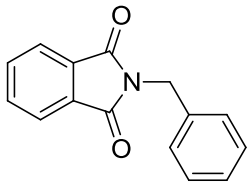
***N*-benzyllaurylamide(3l)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3l** as white solid (98.4 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24-7.32(m, 5H), 6.09 (br s, 1H), 4.40 (d, *J*=4.0Hz, 2H), 2.18 (d, *J*=8.0Hz, 2H), 1.61-1.64 (m, 2H), 1.25 (s, 16H), 0.88 (t, *J*=4.0Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 138.6, 128.7, 127.5, 43.6, 36.8, 32.0, 29.7, 29.6, 29.4, 29.4, 25.9, 22.8, 14.2.



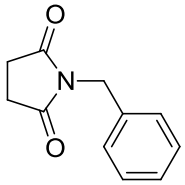
***N*-benzylcyclohexanecarboxamide(3m):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3m** as white solid (86.9 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25-7.35 (m, 5H), 6.04 (br s, 1H), 4.42 (d, *J*=8.0Hz, 2H), 2.13 (t, *J*=12.0Hz, 1H), 1.87-1.90 (m, 2H), 1.79-1.81 (m, 2H), 1.69 (s, 1H), 1.48 (q, *J*=12.0Hz, 2H), 1.20-1.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.1, 138.6, 128.6, 127.7, 127.4, 45.5, 43.3, 29.7, 25.7, 25.7.



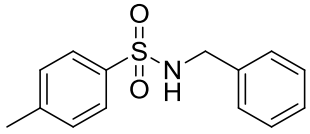
Benzylazepan-2-on(3n): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give **3n** as white solid (71.1 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24-7.30 (m, 5H), 4.58 (s, 2H), 3.27-3.29 (m, 2H), 2.58-2.60 (m, 2H), 1.68 (s, 4H), 1.47 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.0, 137.9, 128.5, 128.1, 127.3, 51.1, 48.9, 37.1, 29.9, 28.1, 23.4.



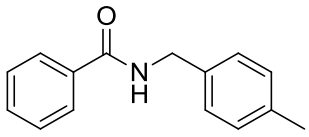
***N*-benzylphthalimide(3o):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3o** as white solid (109.1 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J*=4.0Hz, 2H), 7.50 (s, 2H), 7.30 (d, *J*=8.0Hz, 2H), 7.09-7.18 (m, 3H), 4.69 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 136.4, 133.9, 132.0, 128.6, 128.5, 127.8, 123.2, 41.5.



1-(Phenylmethyl)-2,5-pyrrolidinedione(3p): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **3p** as white solid (80.4 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, J=4.0Hz, 2H), 7.25 (d, J=8.0Hz, 3H), 4.59 (s, 2H), 2.59 (s, 4H)**;** ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0, 135.9, 128.8, 128.6, 127.9, 42.3, 28.2.

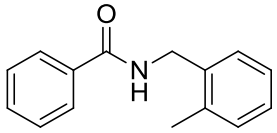


***N*-benzyl-4-methylbenzenesulfonamide(3q)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **3q** as white solid (39.2 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J*=8.0Hz, 2H), 7.14-7.25 (m, 7H), 5.19 (t, *J*=8.0Hz, 1H), 4.06 (d, *J*=8.0Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.4, 137.0, 136.5, 129.7, 128.6, 127.9, 127.8, 127.2, 47.2, 21.5.

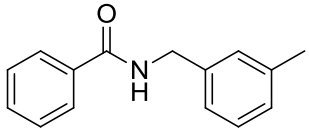


***N*-(4-Methylbenzyl)benzamide(4a):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4a** as white solid (92.4 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J*=8.0Hz, 2H), 7.50 (t, *J*=8.0Hz, 1H), 7.41 (t, *J*=8.0Hz, 2H), 7.21 (dd, J_1=8.0Hz, J_2=36.0Hz, 4H), 6.87 (br s, 1H), 4.58 (d, *J*=8.0Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5,

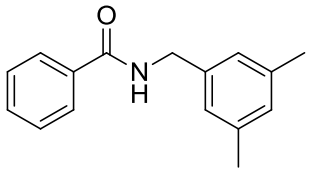
137.2, 135.3, 134.5, 131.5, 129.4, 128.5, 127.9, 127.1, 43.8, 21.2.



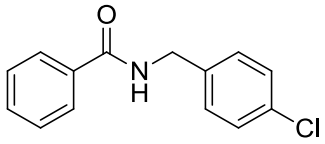
***N*-(2-methylbenzyl)benzamide(4b):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4b** as white solid (75.5 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J*=8.0Hz, 2H), 7.42 (t, *J*=8.0Hz, 1H), 7.32 (t, *J*=8.0Hz, 2H), 7.23 (d, *J*=8.0Hz, 1H), 7.12-7.16 (m, 3H), 6.85 (br s,1H), 4.52 (d, *J*=4.0Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 136.6, 135.8, 134.4, 131.5, 130.6, 128.6, 128.6, 127.9, 127.0, 126.3, 42.3, 19.1.



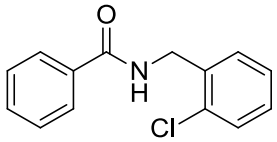
***N*-(3-methylbenzyl)benzamide(4c)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4c** as white solid (90.1 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J*=8.0Hz, 2H), 7.45-7.48 (m, 1H), 7.36-7.40 (m, 2H), 7.19-7.22 (m, 1H), 7.07-7.13 (m, 3H), 6.72 (br s,1H), 5.56 (d, *J*=4.0Hz, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 138.5, 138.2, 134.5, 131.5, 128.7, 128.6, 128.4, 127.1, 125.0, 44.1, 21.4.



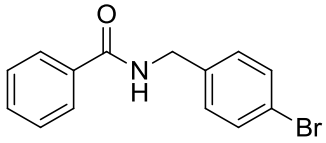
***N*-(3,5-dimethylbenzyl)benzamide(4d):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4d** as white solid (110.1 mg, 92%). Mp 80-81.5 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.78 (d, *J*=8.0Hz, 2H), 7.44 (t, *J*=8.0Hz, 1H), 7.35 (t, *J*=8.0Hz, 2H), 6.88-6.91 (m, 4H), 4.50 (d, *J*=4.0Hz, 2H), 2.26 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 138.3, 138.2, 134.5, 131.5, 129.2, 128.5, 127.1, 125.7, 44.1, 21.3; IR (thin film, cm^{-1}): 3317, 3020, 2920, 1642, 1537, 1486, 1300; HRMS (ESI): m/z ($M+H^+$) calcd. for $C_{16}H_{18}NO$ 240.1388, found: 240.1393.



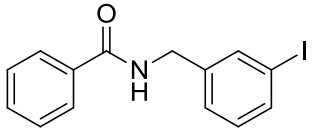
***N*-(4-chlorobenzyl)benzamide(4e)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4e** as white solid (79.9 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J*=8.0Hz, 2H), 7.47 (t, *J*=8.0Hz, 1H), 7.37 (t, *J*=8.0Hz, 2H), 7.23 (dd, J_1=8.0Hz, J_2=20.0Hz, 4H), 7.00 (br s,1H), 4.52 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 137.0, 134.2, 133.3, 131.7, 129.2, 128.8, 128.6, 127.1, 43.3.



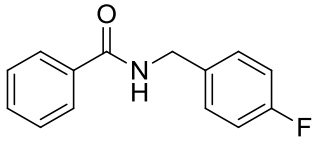
***N*-(2-chlorobenzyl)benzamide(4f)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4f** as light yellow solid (79.9 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J*=8.0Hz, 2H), 7.36-7.40 (m, 1H), 7.27-7.31 (m, 4H), 7.12-7.12 (m, 2H), 6.81 (br s, 1H), 4.60 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 135.7, 134.3, 133.7, 131.6, 130.2, 129.6, 129.0, 128.6, 127.2, 127.1, 42.0.



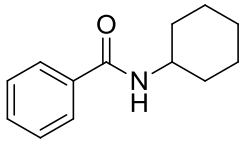
***N*-(4-bromobenzyl)benzamide (4g):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4g** as white solid (116.1 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.8 (d, *J*=4.0Hz, 2H), 7.48-7.49 (m, 1H), 7.36-7.41 (m, 4H), 7.25 (br s,1H), 7.15 (d, *J*=8.0Hz, 2H), 4.50 (d, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 137.5, 134.1, 131.7, 131.7, 129.4, 128.6, 127.1, 121.2, 43.3.



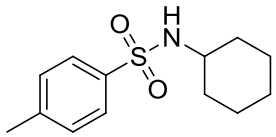
***N*-(3-iodobenzyl)benzamide (4h):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4h** as white solid (119.7 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J*=8.0Hz, 2H), 7.53 (s, 1H), 7.47 (d, *J*=8.0Hz, 1H), 7.37 (t, *J*=8.0Hz, 1H), 7.27 (t, *J*=8.0Hz, 2H), 7.14 (d, *J*=8.0Hz, 1H), 7.08 (br s, 1H), 6.91 (t, *J*=8.0Hz, 1H), 4.39 (t, *J*=4.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 140.9, 136.6, 136.5, 134.1, 131.7, 130.4, 128.6, 127.1, 127.0, 94.6, 43.2.



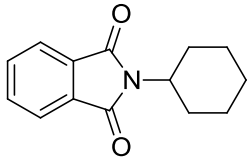
***N*-(4-fluorobenzyl)benzamide (4i):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4i** as white solid (49.3 mg, 43%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J*=8.0Hz, 2H), 7.34 (t, *J*=8.0Hz, 1H), 7.23 (t, *J*=8.0Hz, 2H), 7.17 (br s, 1H), 7.11 (t, *J*=4.0Hz, 2H), 6.83 (t, *J*=8.0Hz, 2H), 4.38 (d, *J*=8.0Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 162.1 ($J_{C\text{-}F}$=244.0Hz), 134.3 ($J_{C\text{-}F}$=4.0Hz), 131.6, 129.4, 129.3, 128.5, 127.1, 115.4 ($J_{C\text{-}F}$=21.0Hz), 43.2.



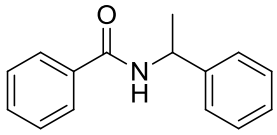
***N*-cyclohexylbenzamide(4j):** The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4j** as white solid (81.3 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J*=8.0Hz, 2H), 7.32-7.43 (m, 3H), 6.38 (br s, 1H), 3.91-3.93 (m, 1H), 1.96 (d, *J*=12.0Hz, 2H), 1.70 (d, *J*=12.0Hz, 2H), 1.60 (d, *J*=12.0Hz, 1H), 1.30-1.39 (m, 2H), 1.09-1.26 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.7, 135.1, 131.1, 128.4, 126.9, 48.8, 33.1, 25.5, 25.0.



***N*-cyclohexyl-4-methylbenzenesulfonamide(4k)**: The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4k** as white solid (88.7 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ7.78 (d, *J*=8.0Hz, 2H), 7.29 (d, *J*=8.0Hz, 2H), 4.95 (d, *J*=8.0Hz, 1H), 3,12 (br s, 1H), 2.42 (s, 3H), 1.72-1.75 (m, 2H), 1.60-1.63 (m, 2H), 1.48-1.51 (m, 1H), 1.08-1.23 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 138.6, 129.6, 126.9, 52.6, 33.7, 25.1, 24.6, 21.5.

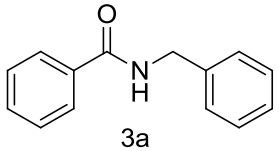


2-cyclohexylisoindoline-1,3-dione(4l): The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4l** as white solid (81.4 mg, 71%).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79-7.81 (m, 2H), 7.69-7.70 (m, 2H), 4.11 (t, *J*=12.0Hz, 1H), 2.21 (q, J_1=12.0Hz, J_2=20.0Hz, 2H), 1.87 (d, *J*=12.0Hz, 2H), 1.68-1.74 (m, 3H), 1.25-1.42 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 133.7, 132.1, 122.9, 50.9, 29.9, 26.0, 25.1.

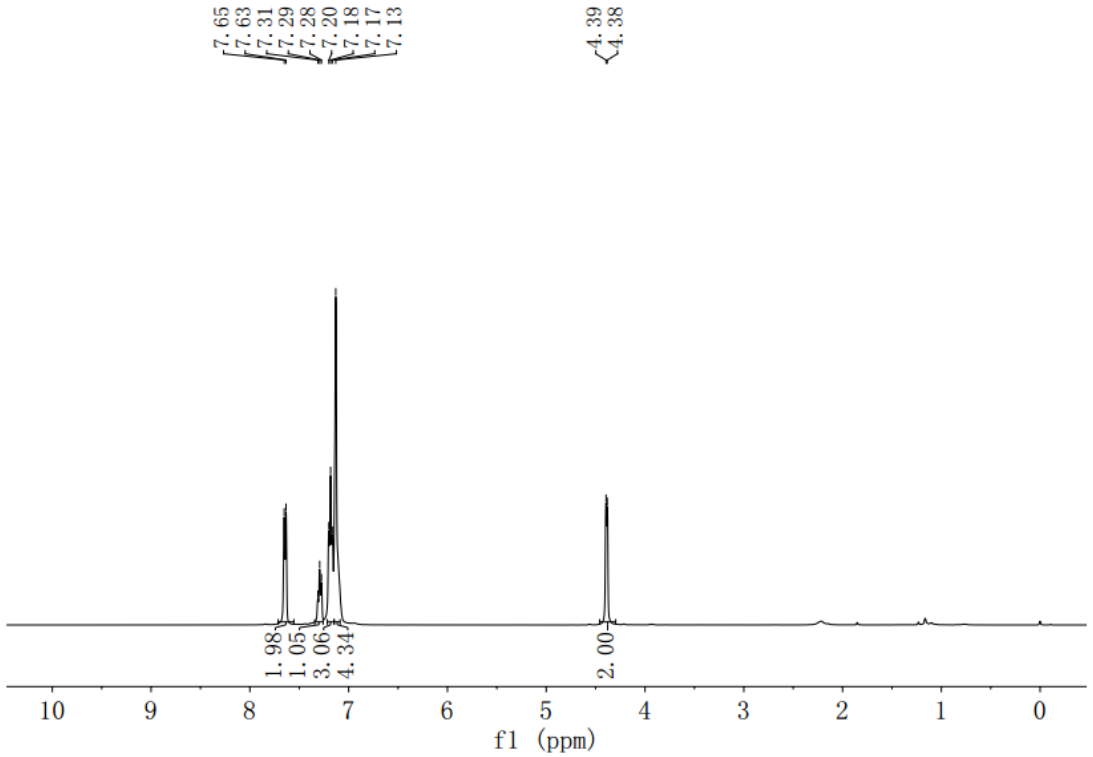


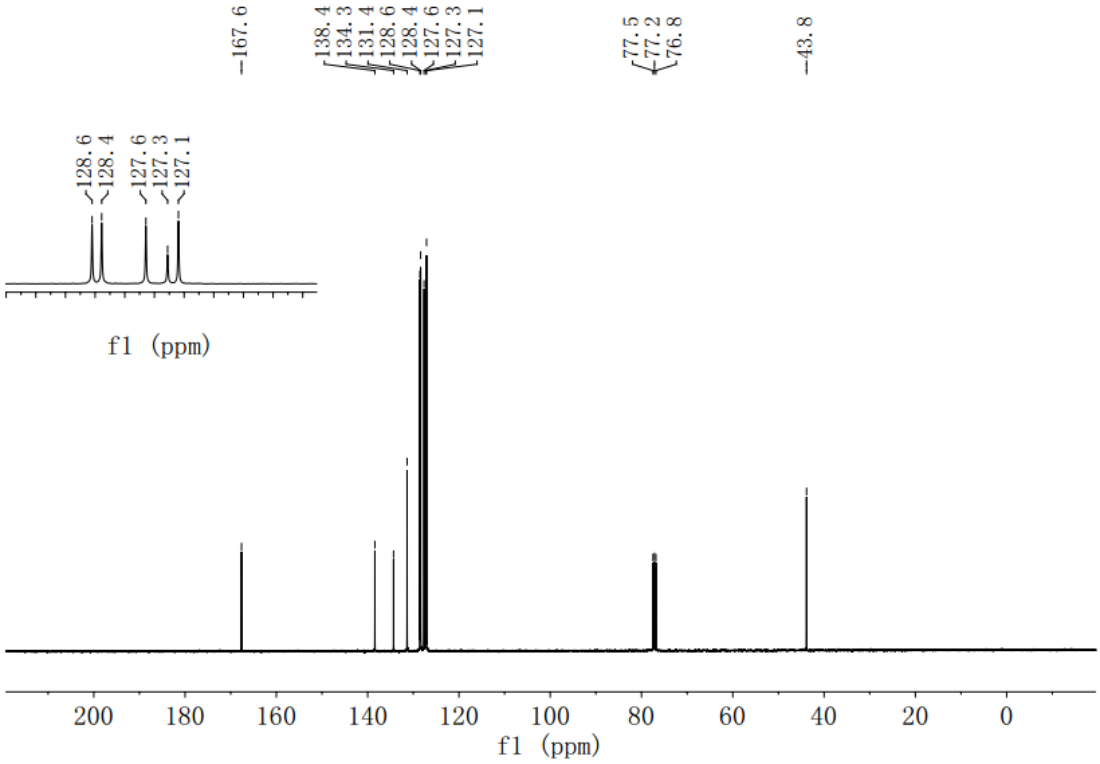
N-(1-Phenylethyl)benzamide(4m) The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **4m** as white solid (34.9 mg, 31%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.68 (m, 2H), 7.34-7.38 (m, 1H), 7.21-7.30 (m, 6H), 7.14-7.18 (m, 1H), 6.52 (br s, 1H), 5.19-5.26 (m, 1H), 1.48 (d, *J*=8.0Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 166.7, 143.3, 134.7, 131.5, 128.8, 128.6, 127.4, 127.1, 126.3, 49.3, 21.8.

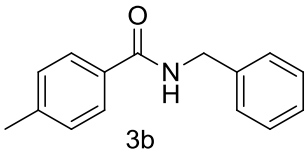
Copies of NMR spectra of products



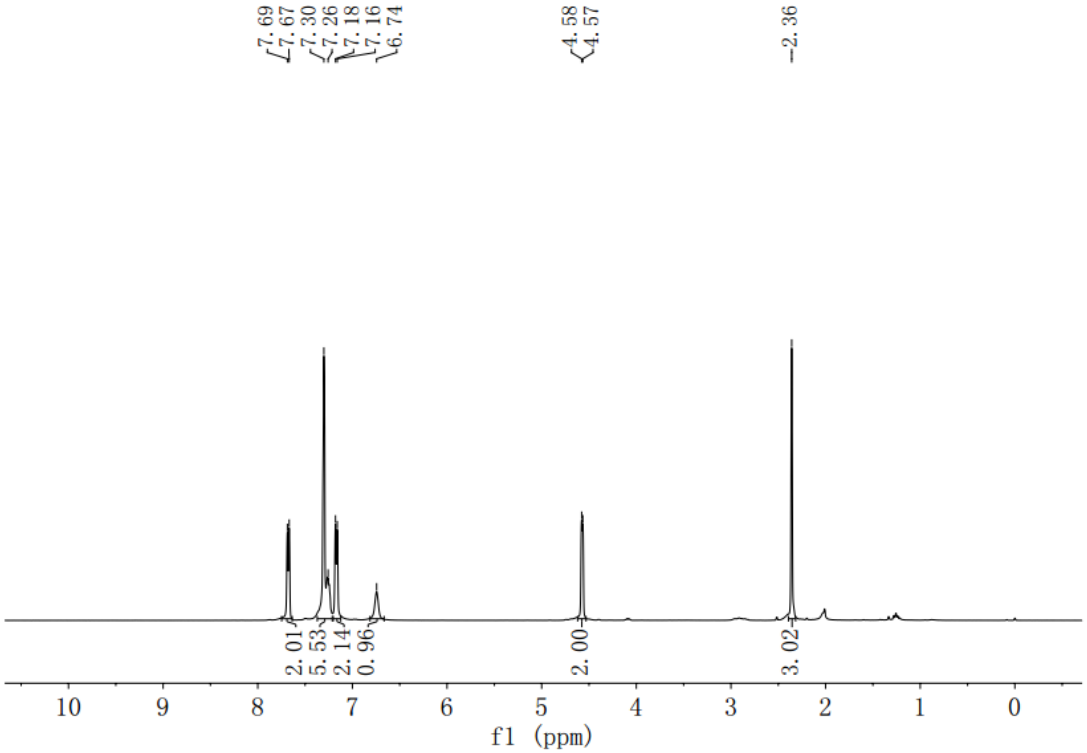
3a






O
N
H

3b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9
8
7
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5
4
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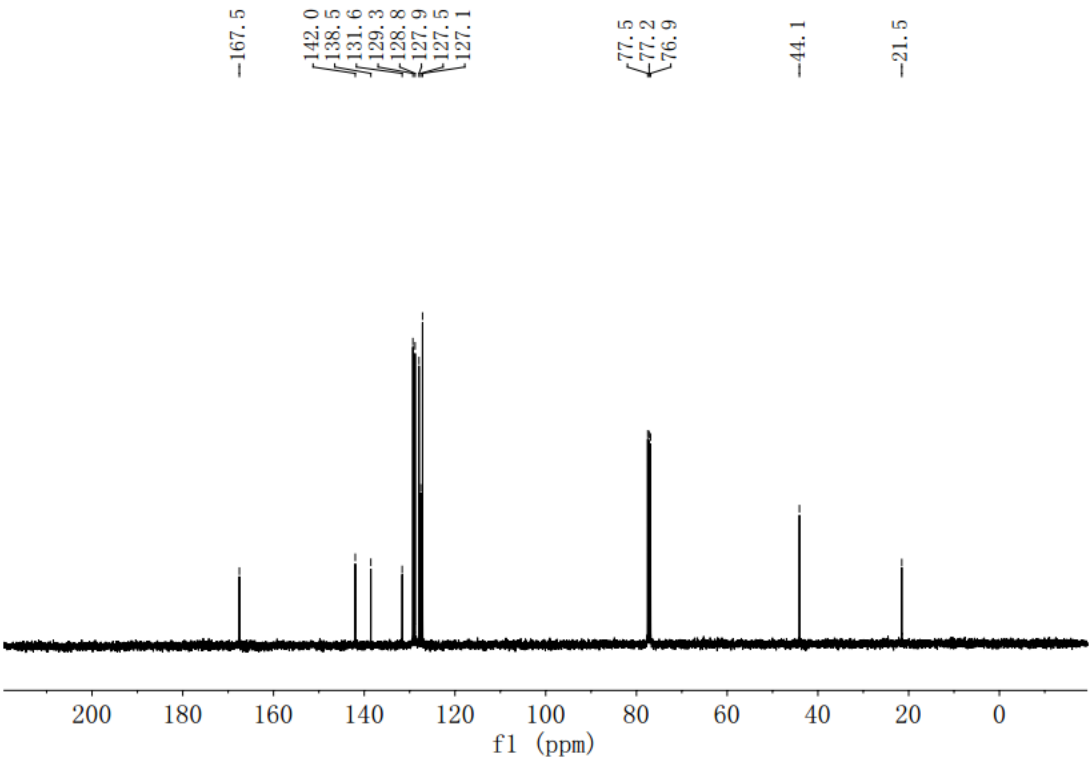
f1 (ppm)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127.9
127.5
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21.5
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80
60
40
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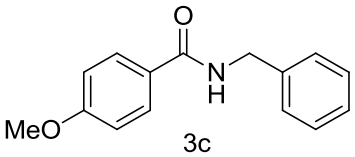
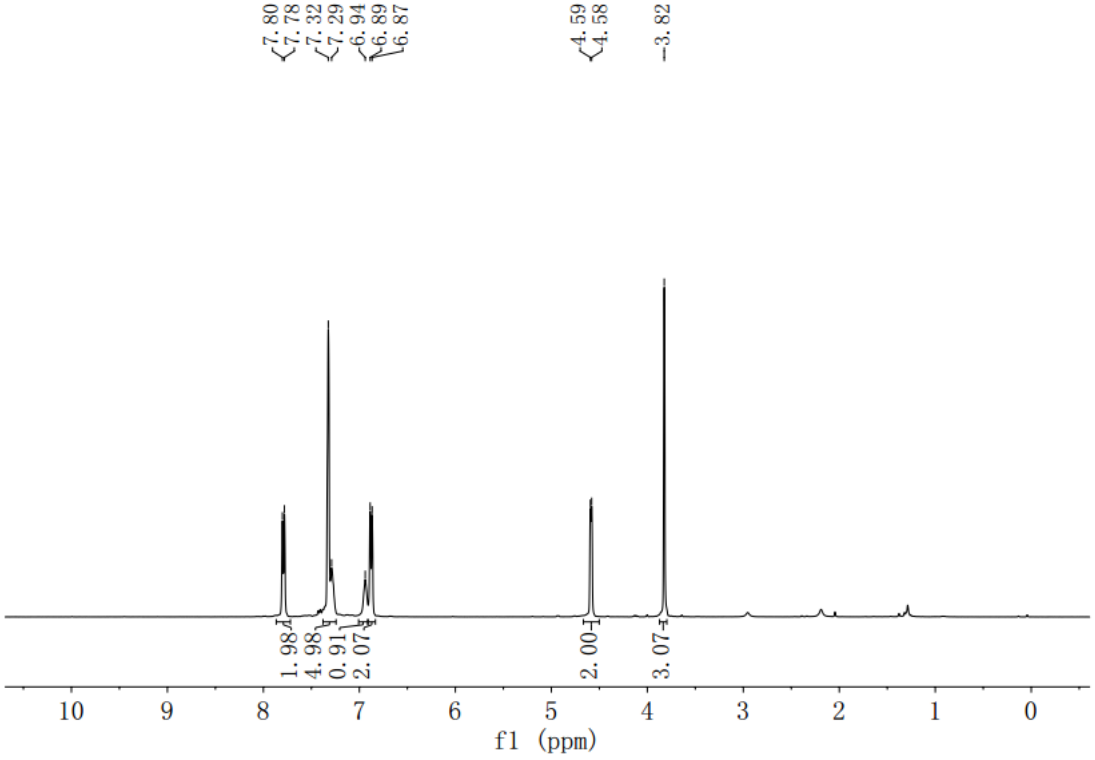
0
f1 (ppm)


O
N
H
MeO

3c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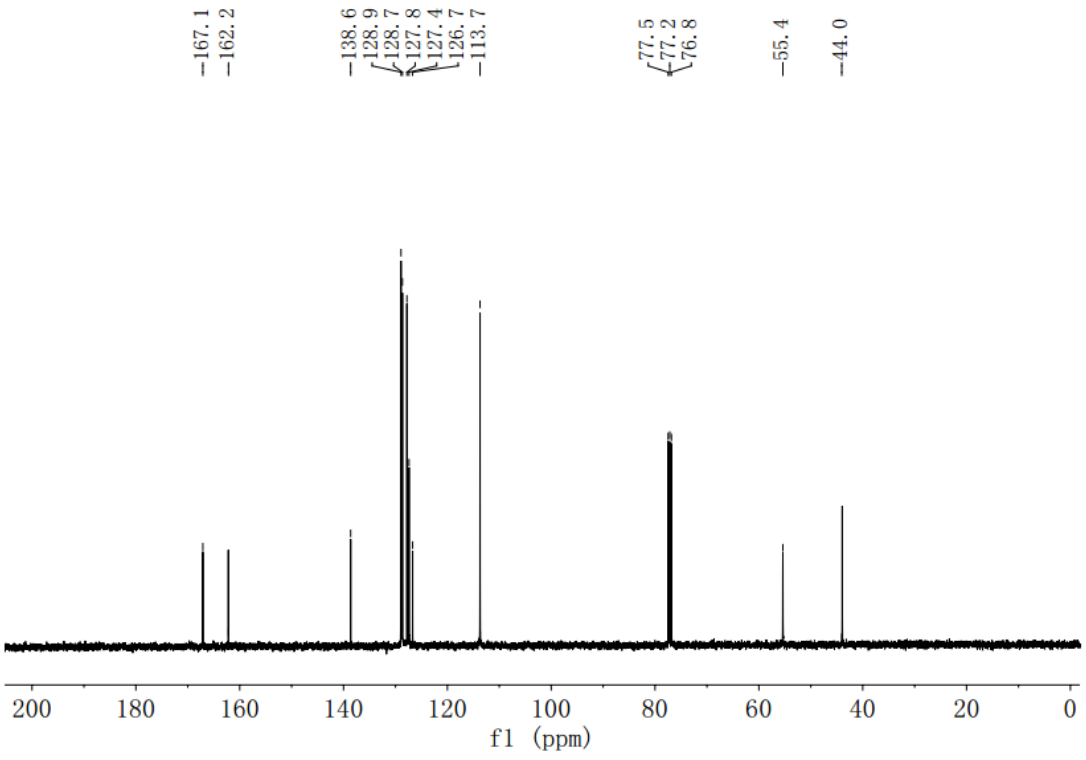
f1 (ppm)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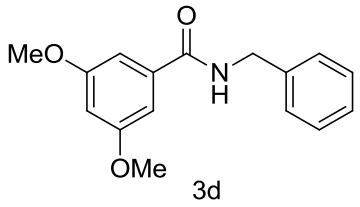
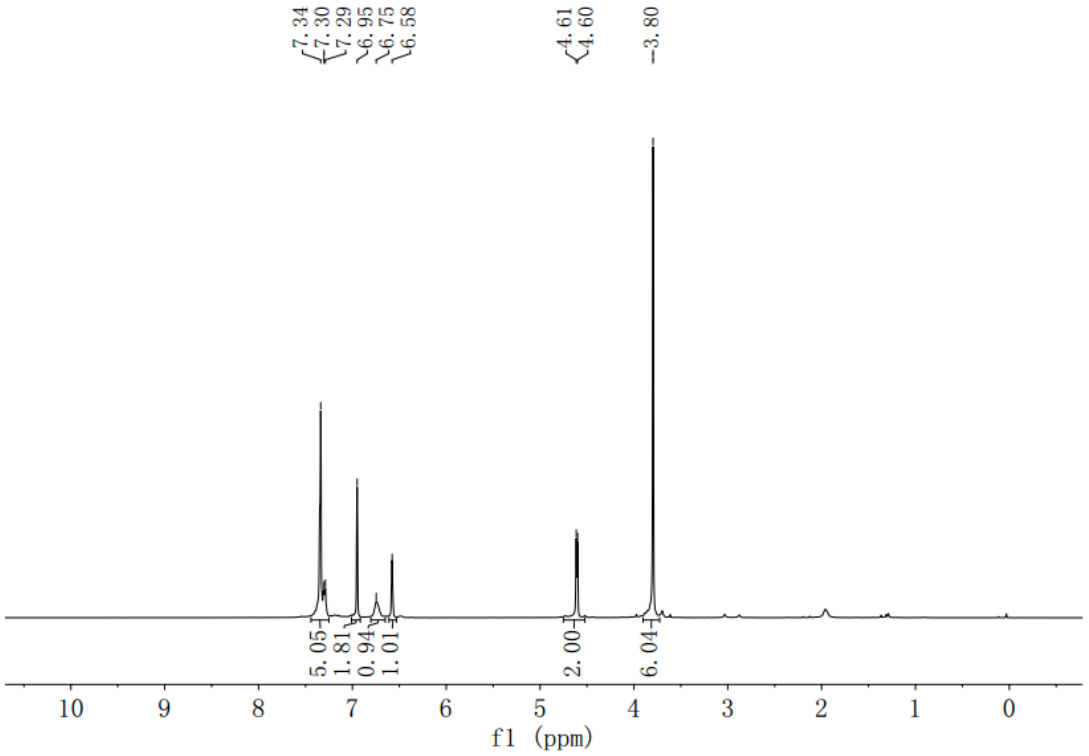

MeO
O
N
H
OMe

3d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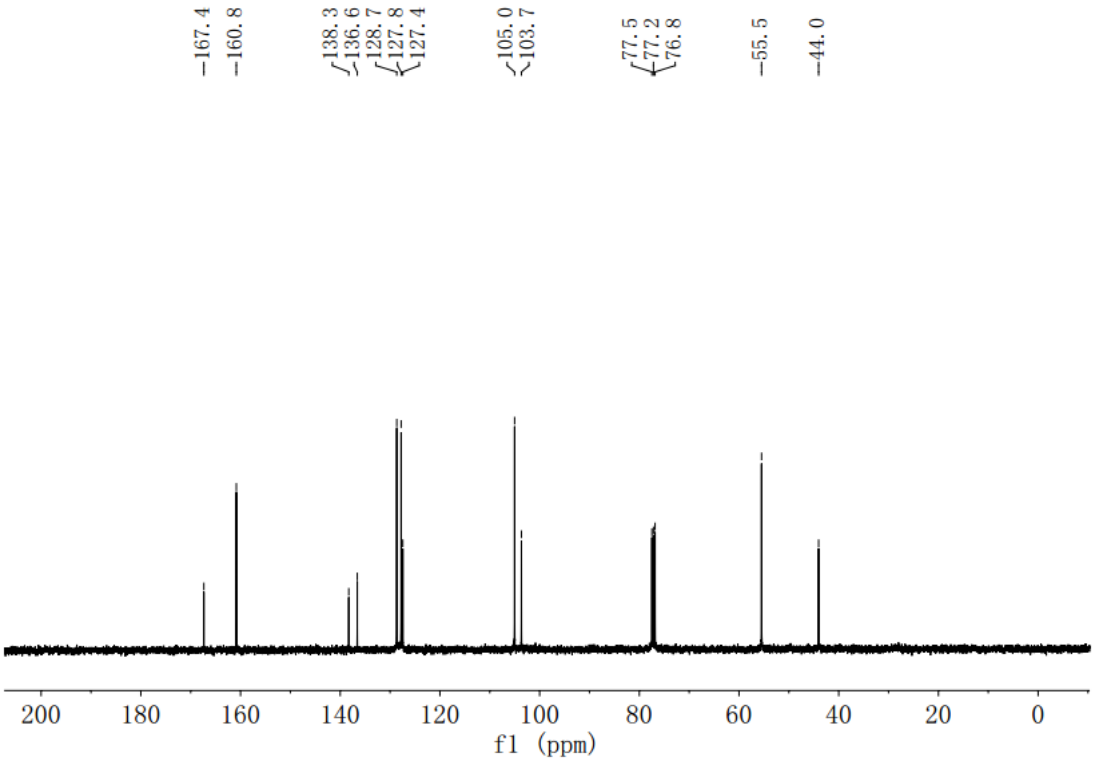
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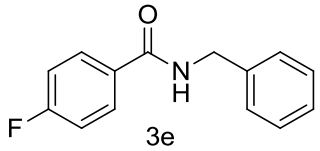
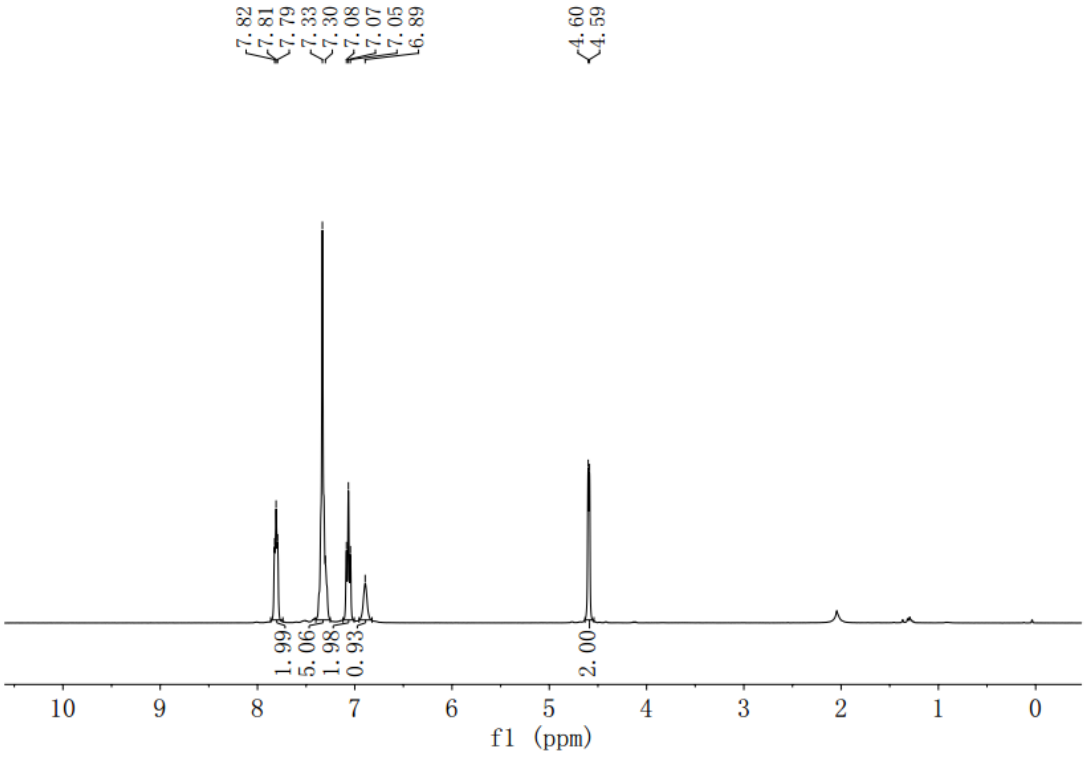
f1 (ppm)


O
N
H
F

3e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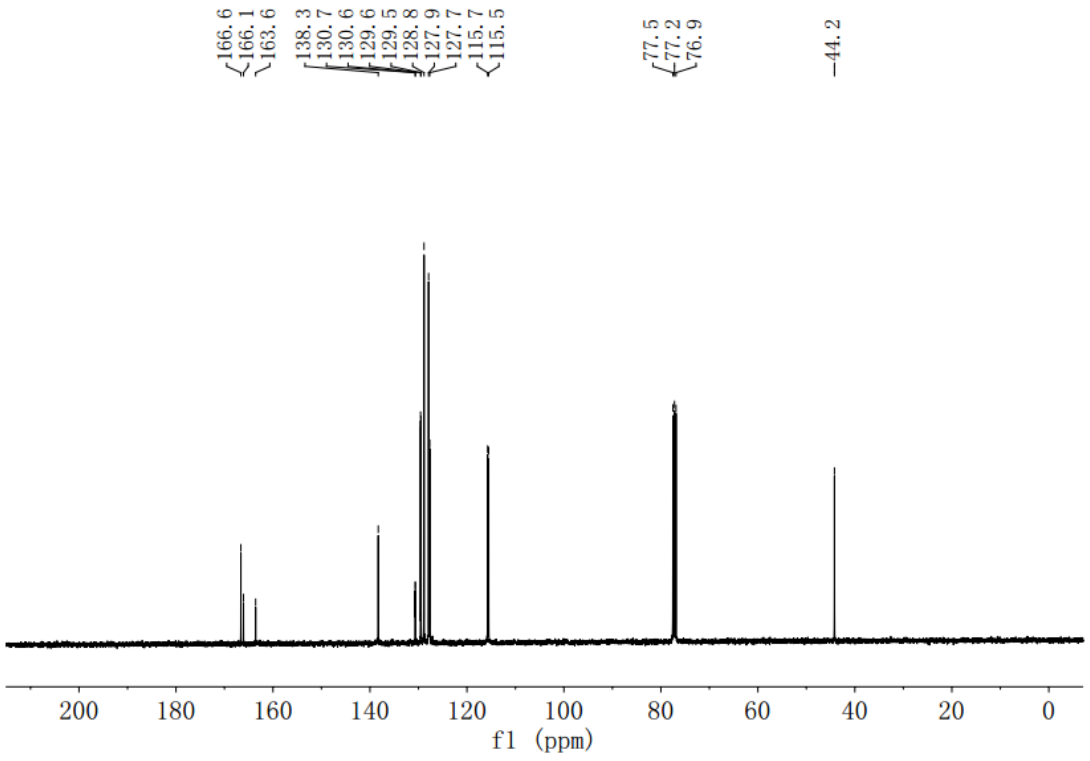
f1 (ppm)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115.5
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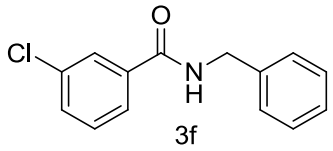
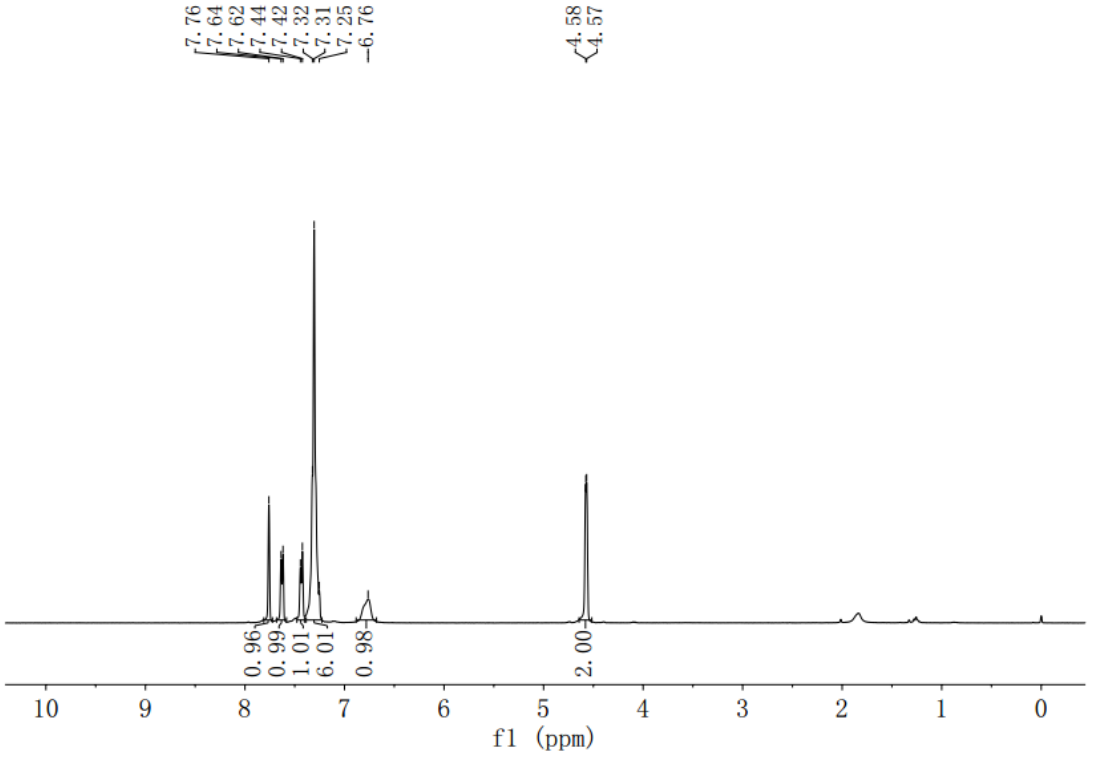
f1 (ppm)


O
Cl
N
H

3f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4.57
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0.99
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0.98
2.00
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6
5
4
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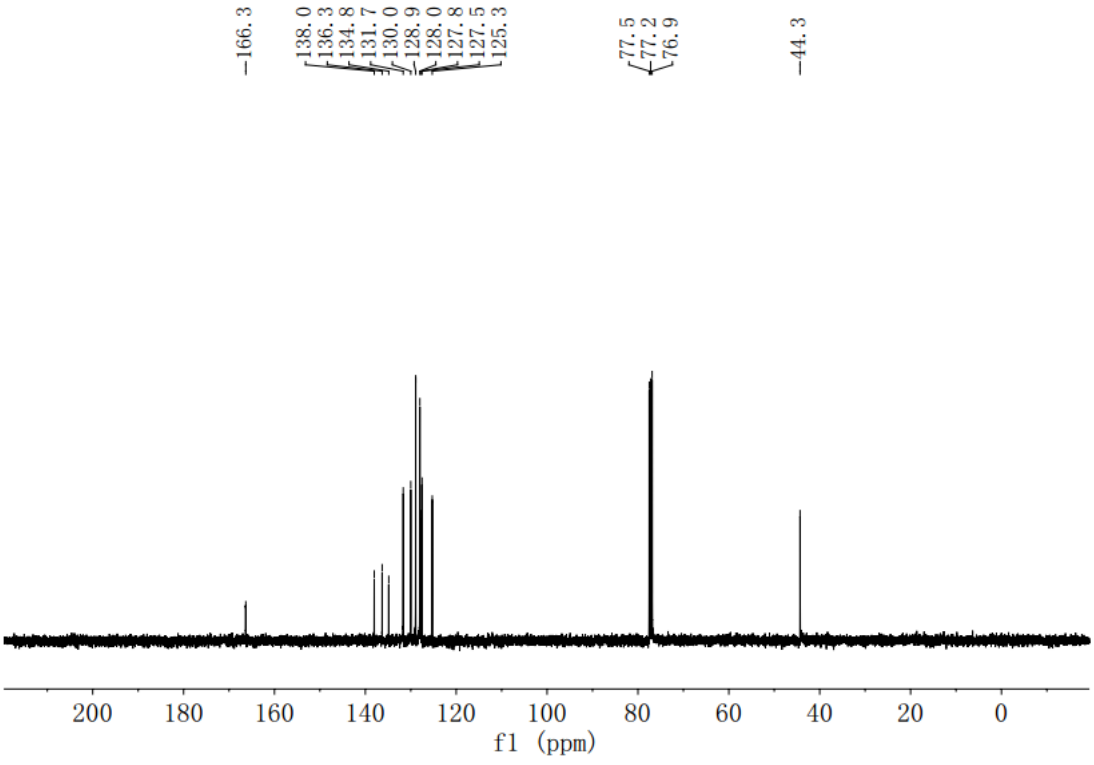
0
f1 (ppm)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140
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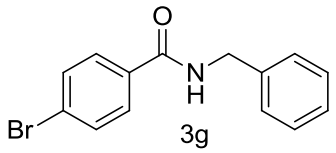
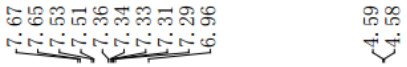
80
60
40
20
0
f1 (ppm)


O
N
H
Br

3g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7.51
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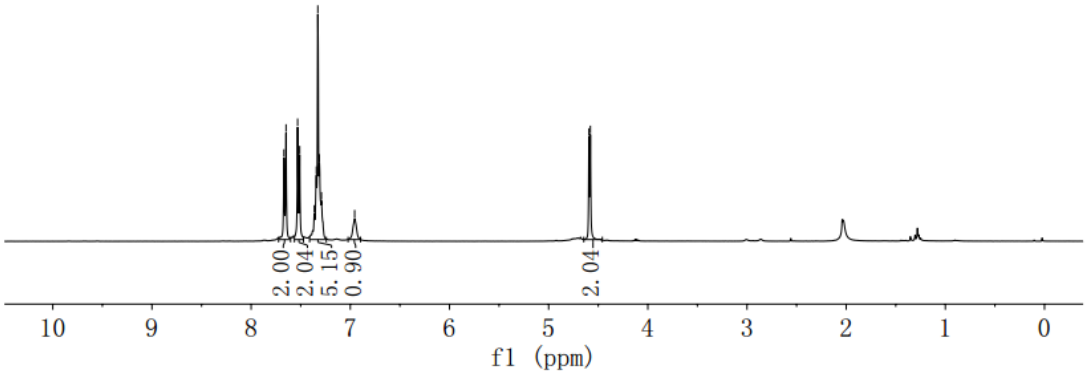
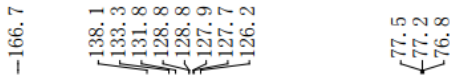
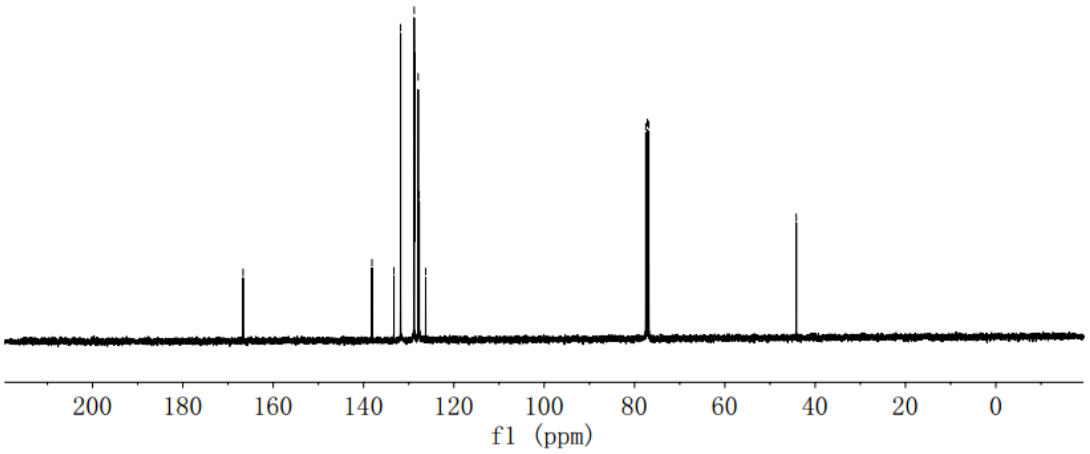
7.34
7.33
7.31
7.29
6.96
4.59
4.58


2.00
2.04
5.15
0.90
2.04
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


166.7
138.1
133.3
131.8
128.8
128.8
127.9
127.7
126.2
77.5
77.2
76.8
44.2


200
180
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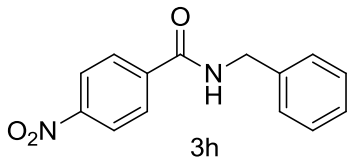
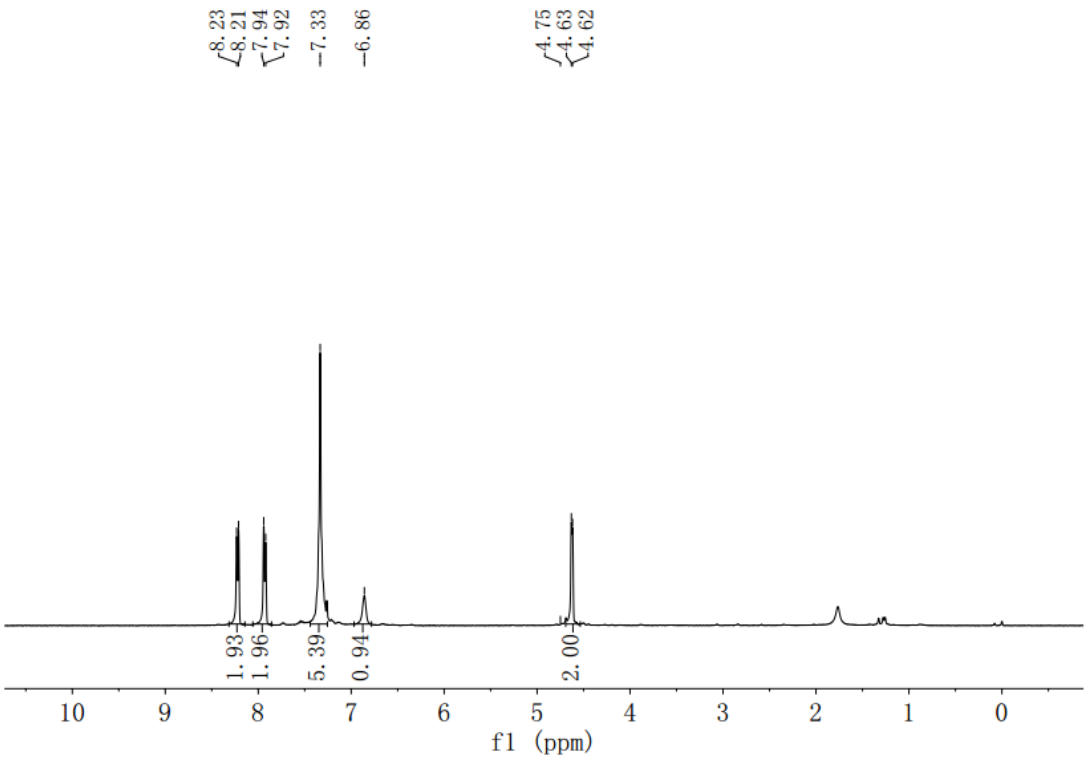
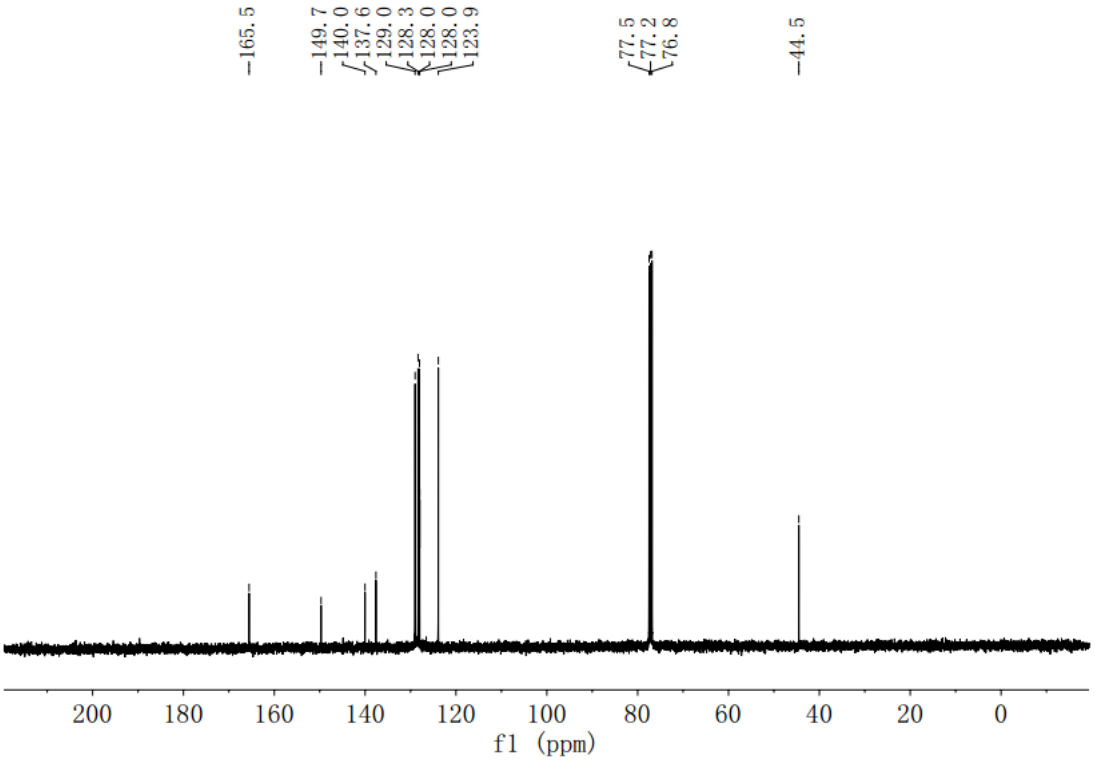
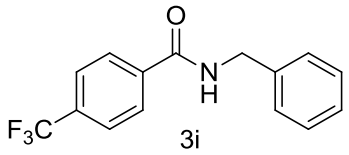
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H
O2N

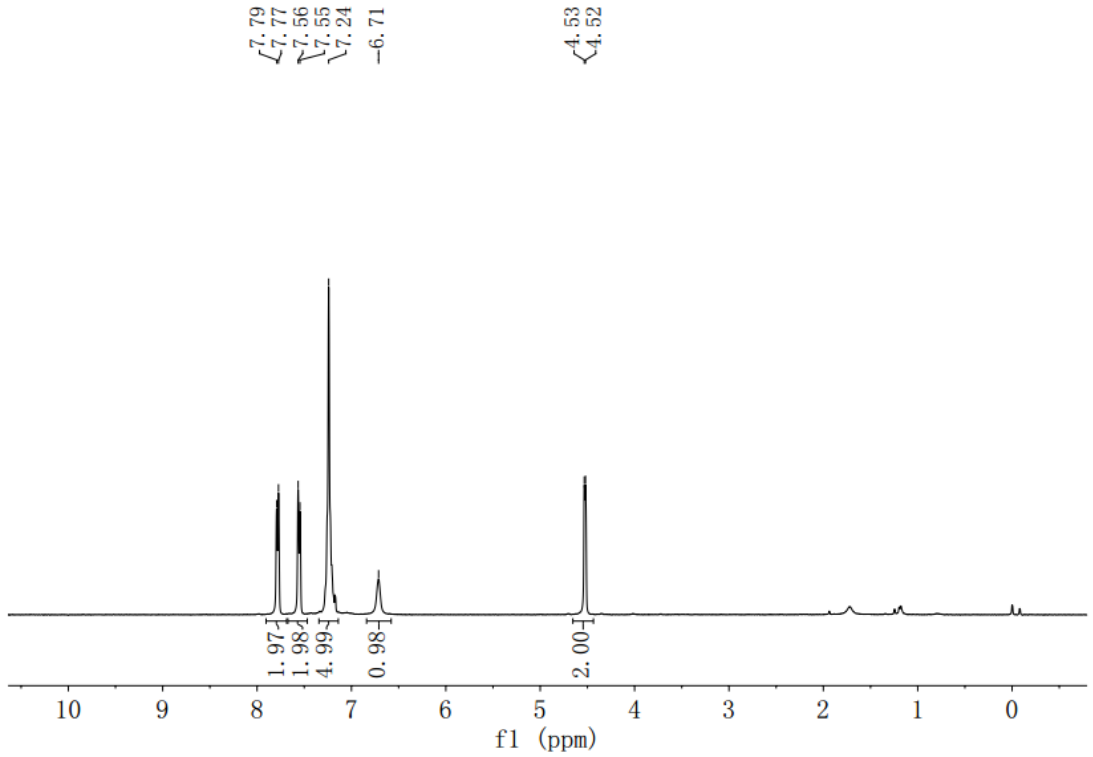
3h

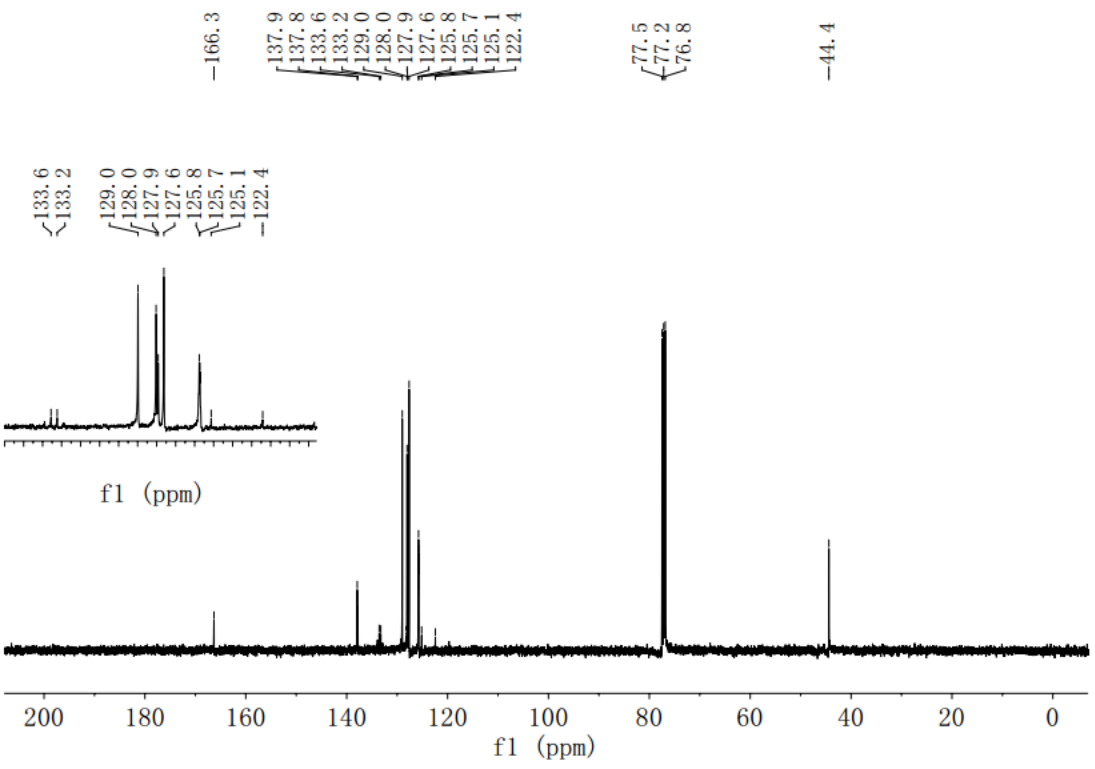

8.23
8.21
7.94
7.92
7.33
6.86
4.75
4.63
4.62
1.93
1.96
5.39
0.94
2.00
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


165.5
149.7
140.0
137.6
129.0
128.3
128.0
128.0
123.9
77.5
77.2
76.8
44.5
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H
F3C

3i


7.79
7.77
7.56
7.55
7.24
6.71
4.53
4.52
1.97
1.98
4.99
0.98
2.00
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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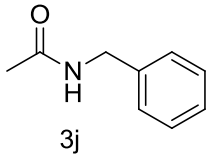
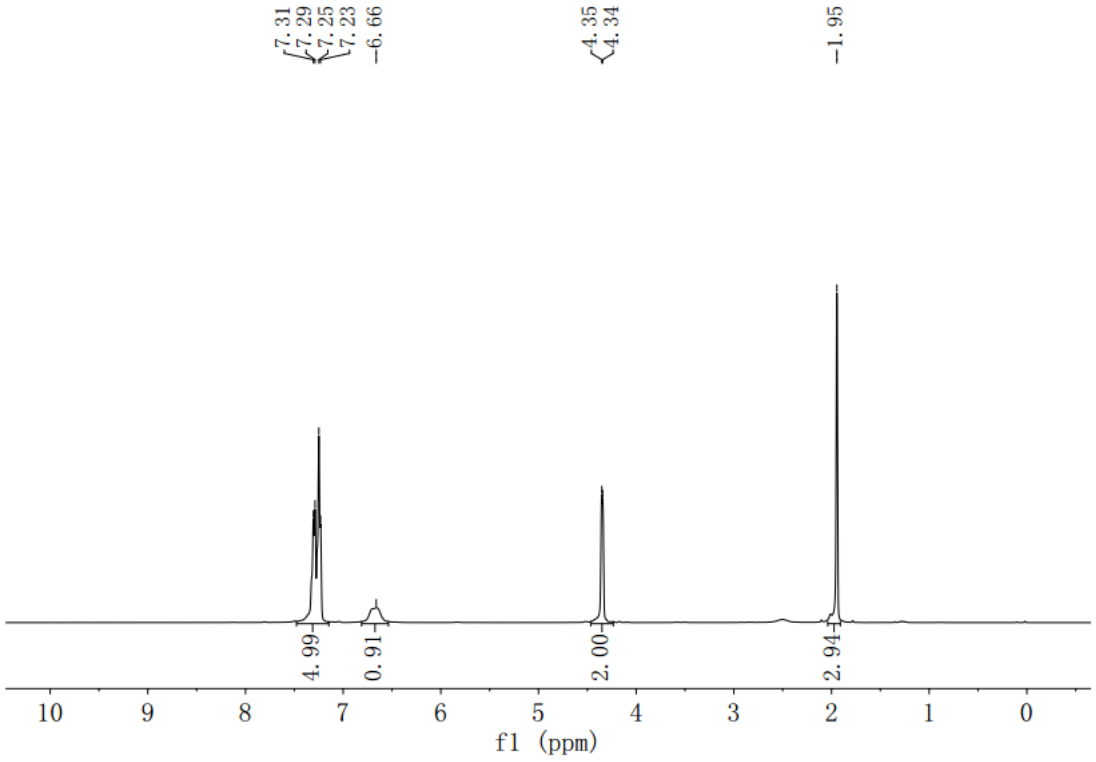
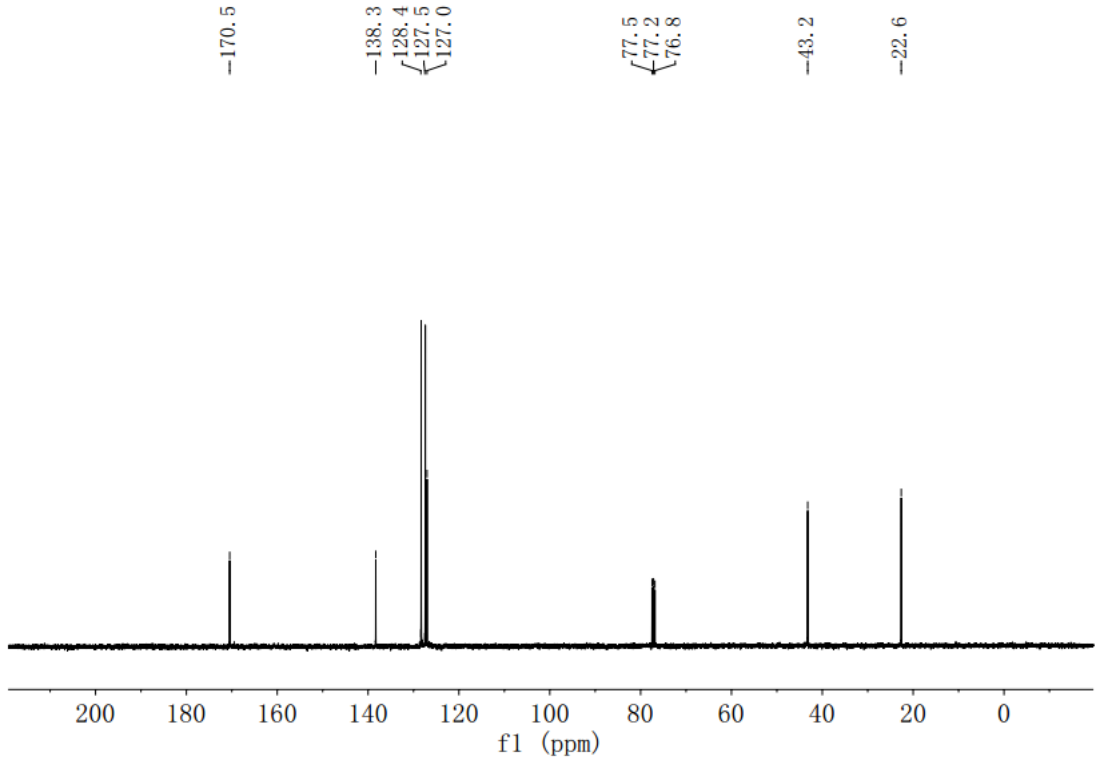
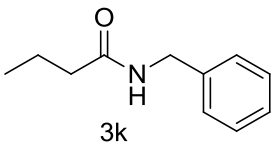
137.9
137.8
133.6
133.2
129.0
128.0
127.9
127.6
125.8
125.7
125.1
122.4
77.5
77.2
76.8
44.4
133.6
133.2
129.0
128.0
127.9
127.6
125.8
125.7
125.1
122.4
f1 (ppm)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



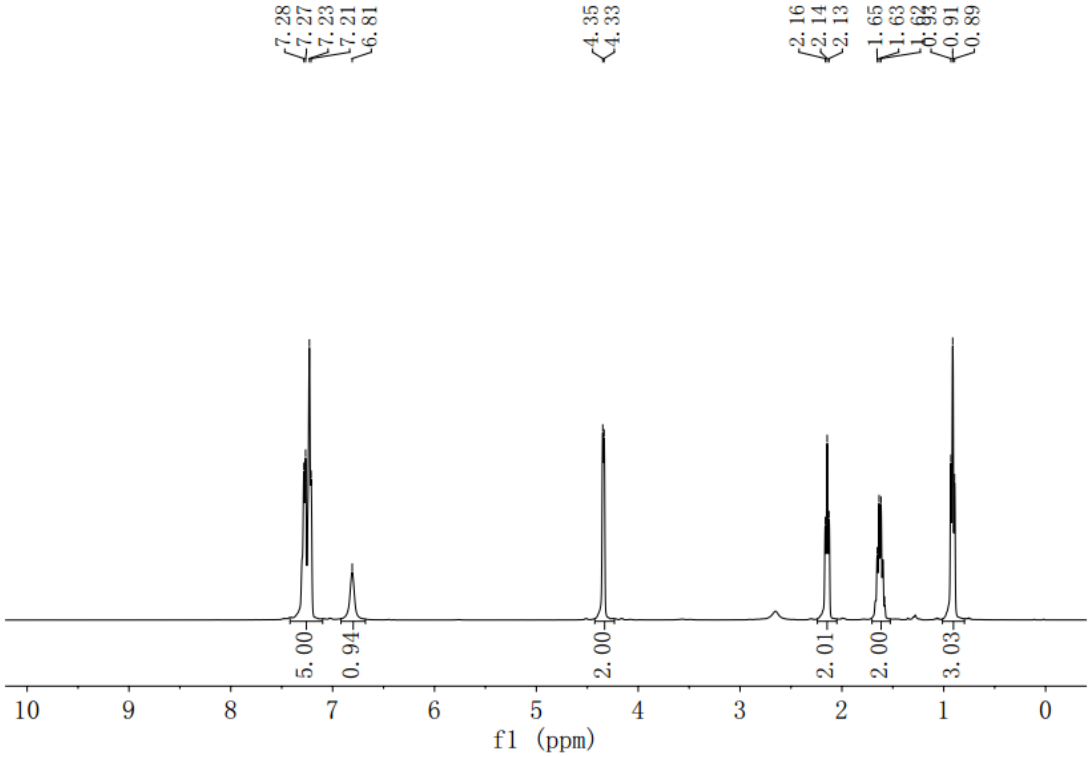
3j

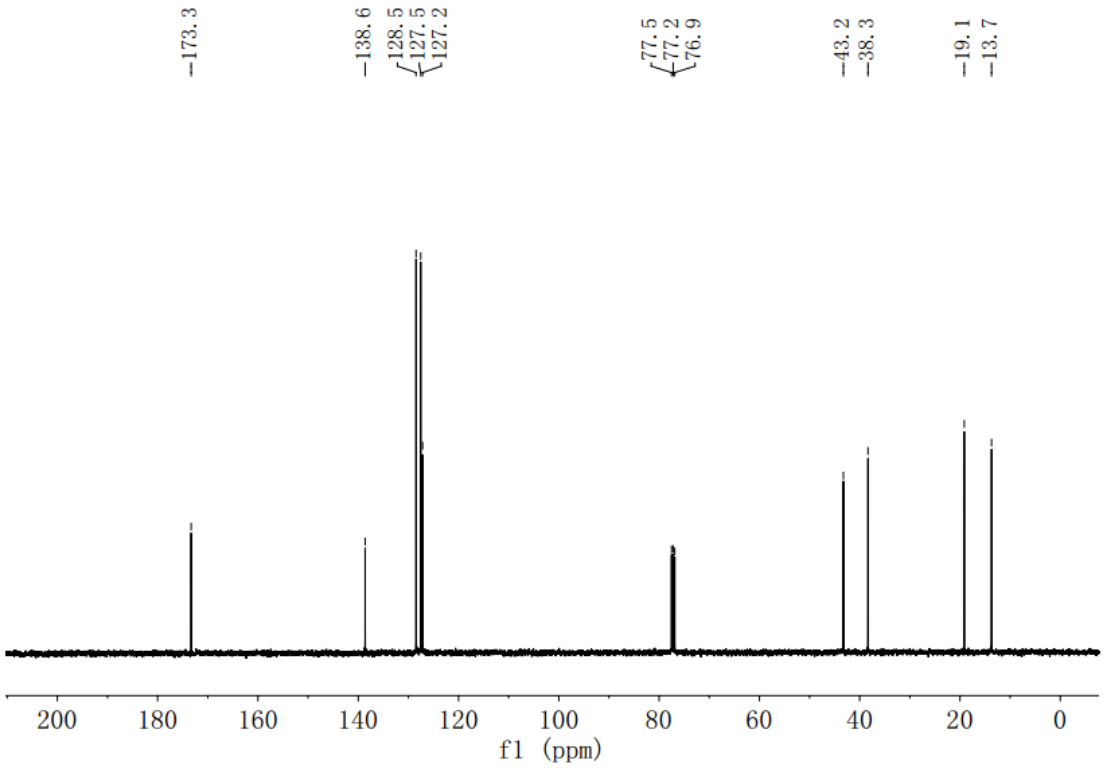

7.31
7.29
7.25
7.23
6.66
4.35
4.34
1.95
4.99
0.91
2.00
2.94
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

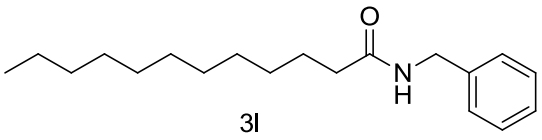

170.5
138.3
128.4
127.5
127.0
77.5
77.2
76.8
43.2
22.6
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H

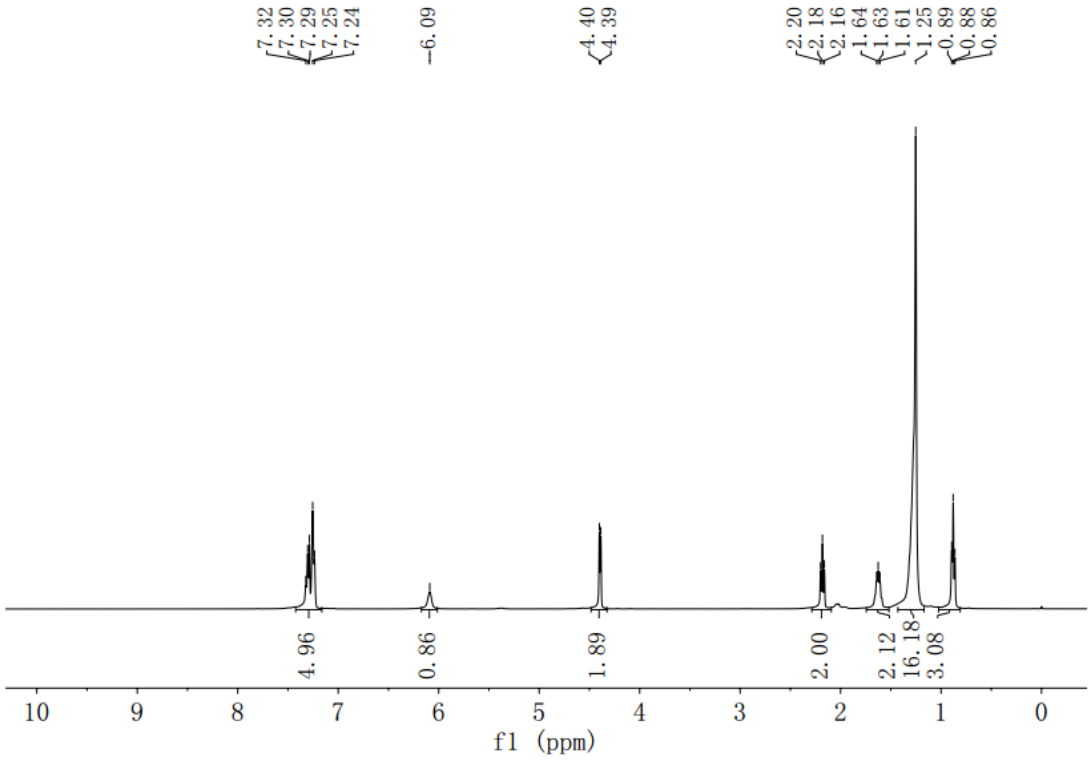
3k

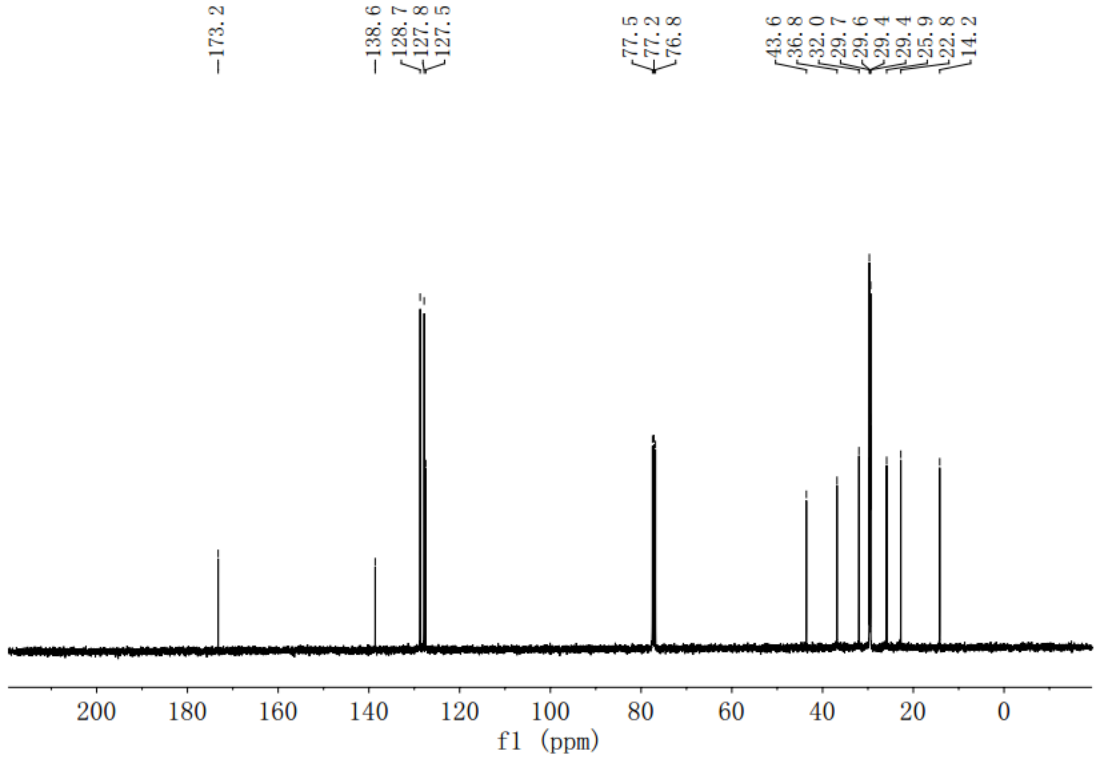

7.28
7.27
7.23
7.21
6.81
4.35
4.33
2.16
2.14
2.13
1.65
1.63
0.93
0.91
0.89
5.00
0.94
2.00
2.01
2.00
3.03
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

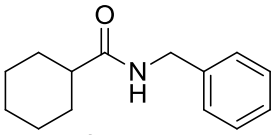

173.3
138.6
128.5
127.5
127.2
77.5
77.2
76.9
43.2
38.3
19.1
13.7
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H

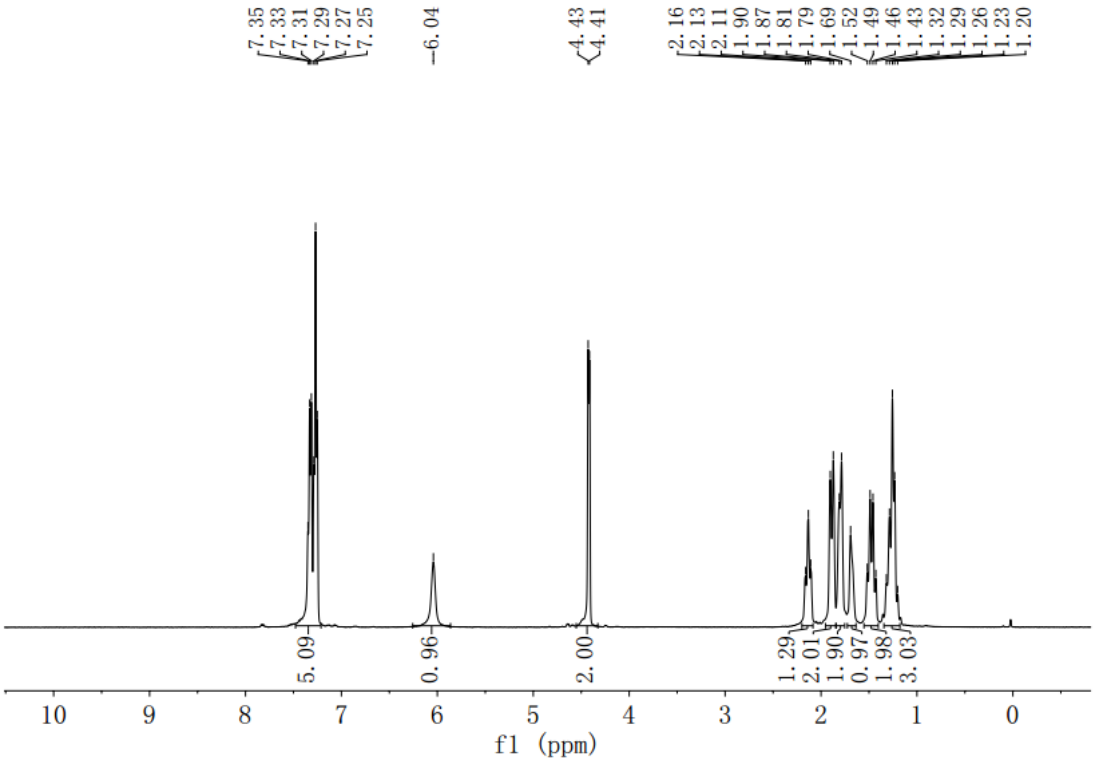
3l

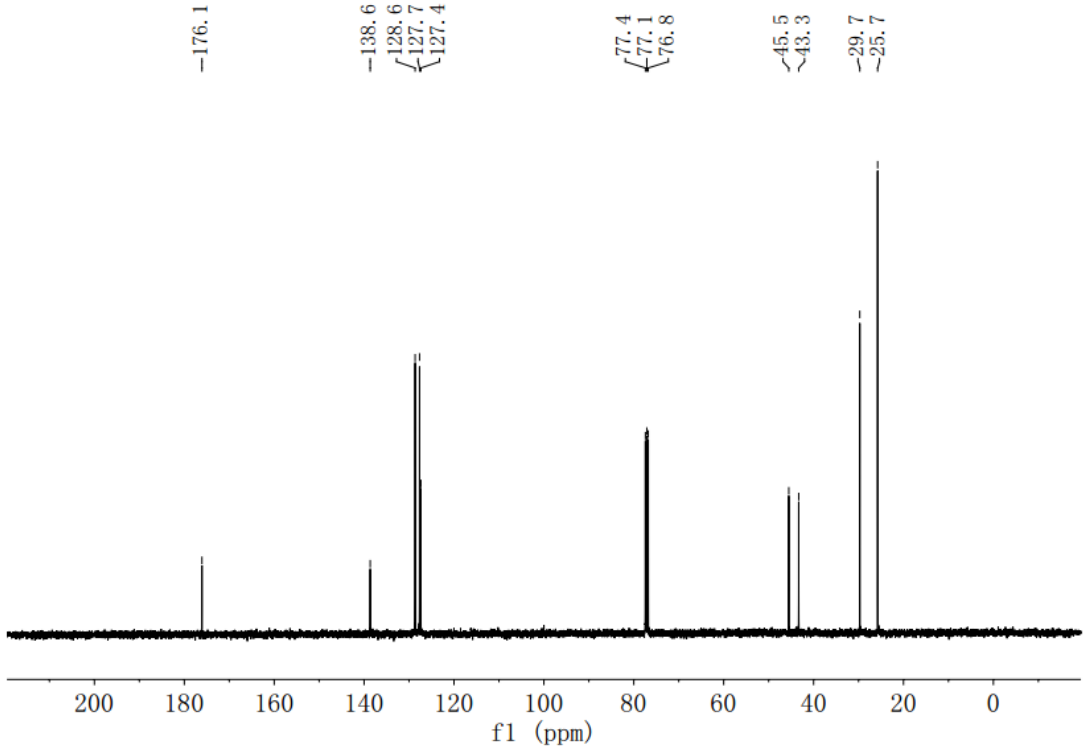

7.32
7.30
7.29
7.25
7.24
6.09
4.40
4.39
2.20
2.18
2.16
1.64
1.63
1.61
1.25
0.89
0.88
0.86
4.96
0.86
1.89
2.00
2.12
16.18
3.08
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

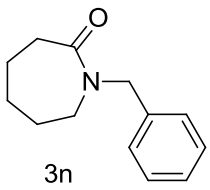

173.2
138.6
128.7
127.8
127.5
77.5
77.2
76.8
43.6
36.8
32.0
29.7
29.6
29.4
29.4
25.9
22.8
14.2
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H

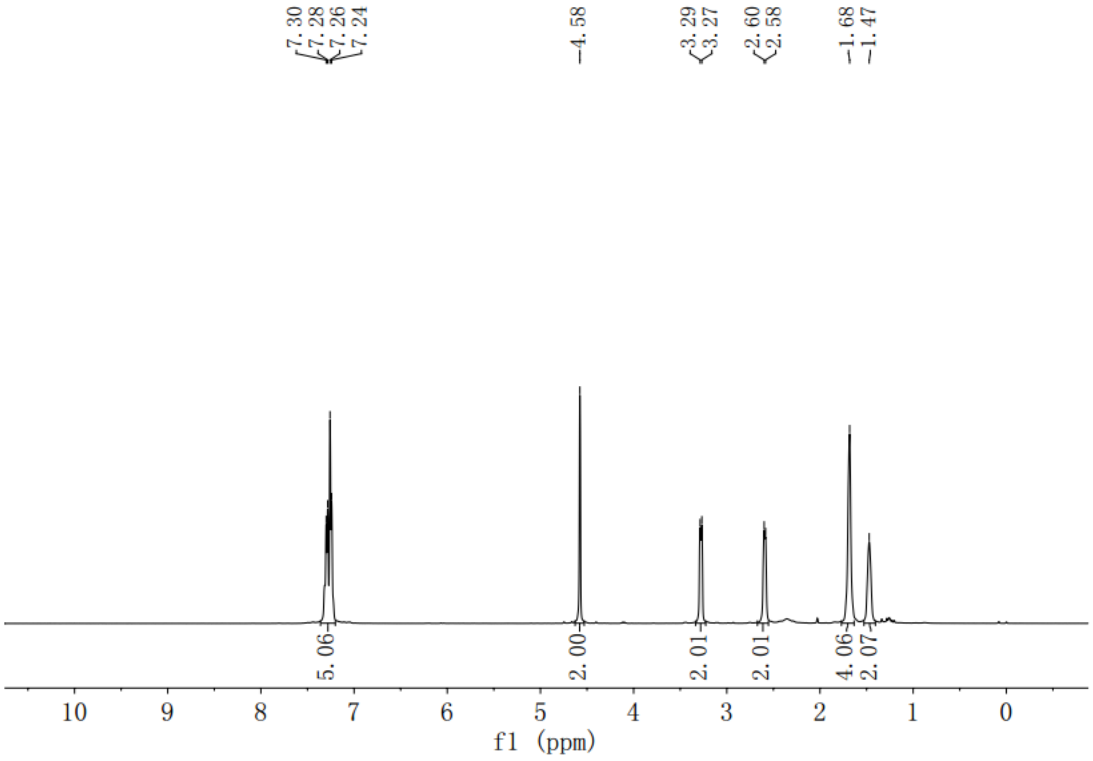
3m


7.35
7.33
7.31
7.29
7.27
7.25
6.04
4.43
4.41
2.16
2.13
2.11
1.90
1.87
1.81
1.79
1.69
1.52
1.49
1.46
1.43
1.32
1.29
1.26
1.23
1.20
5.09
0.96
2.00
1.29
2.01
1.90
0.97
1.98
3.03
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


176.1
138.6
128.6
127.7
127.4
77.4
77.1
76.8
45.5
43.3
29.7
25.7
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N

3n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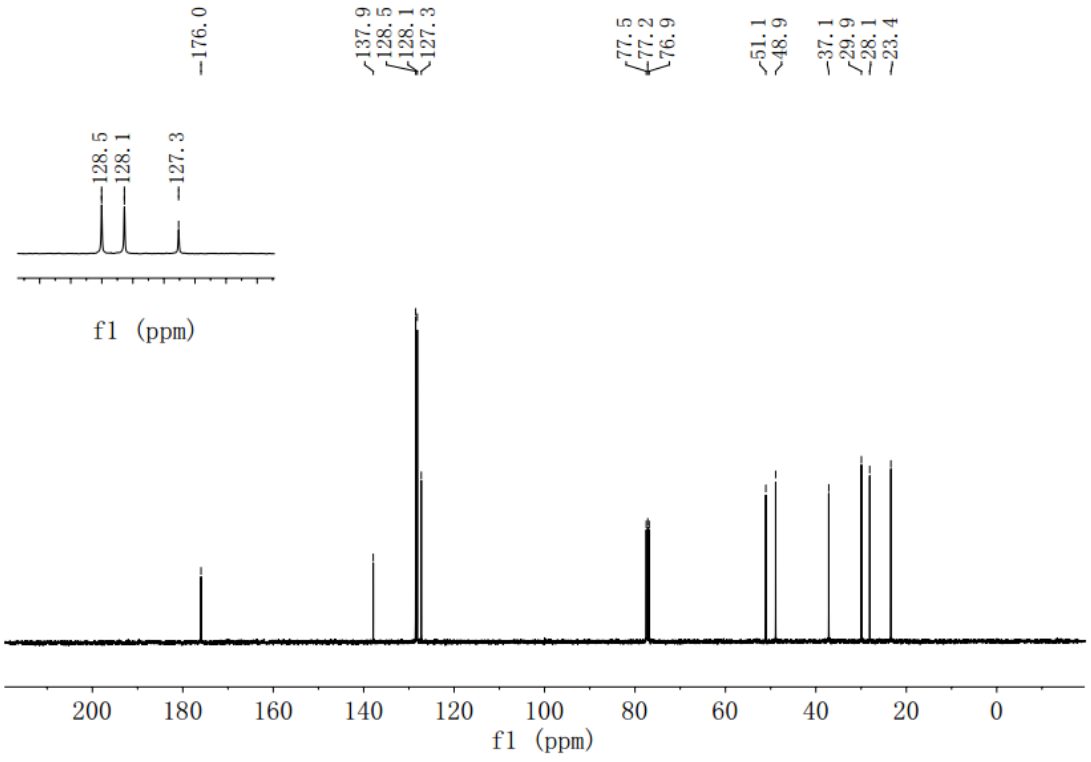
7.28
7.26
7.24
4.58
3.29
3.27
2.60
2.58
1.68
1.47
5.06
2.00
2.01
2.01
4.06
2.07
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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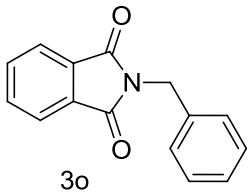
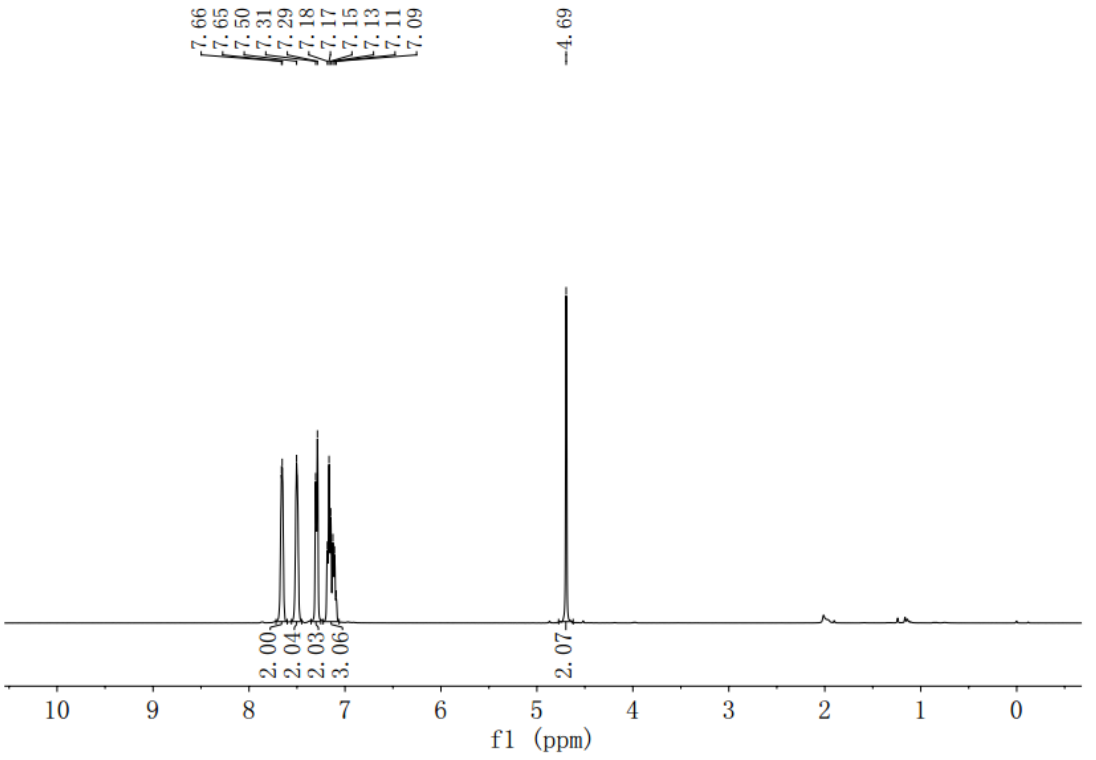
128.5
128.1
127.3
77.5
77.2
76.9
51.1
48.9
37.1
29.9
28.1
23.4
128.5
128.1
127.3
f1 (ppm)
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
O

3o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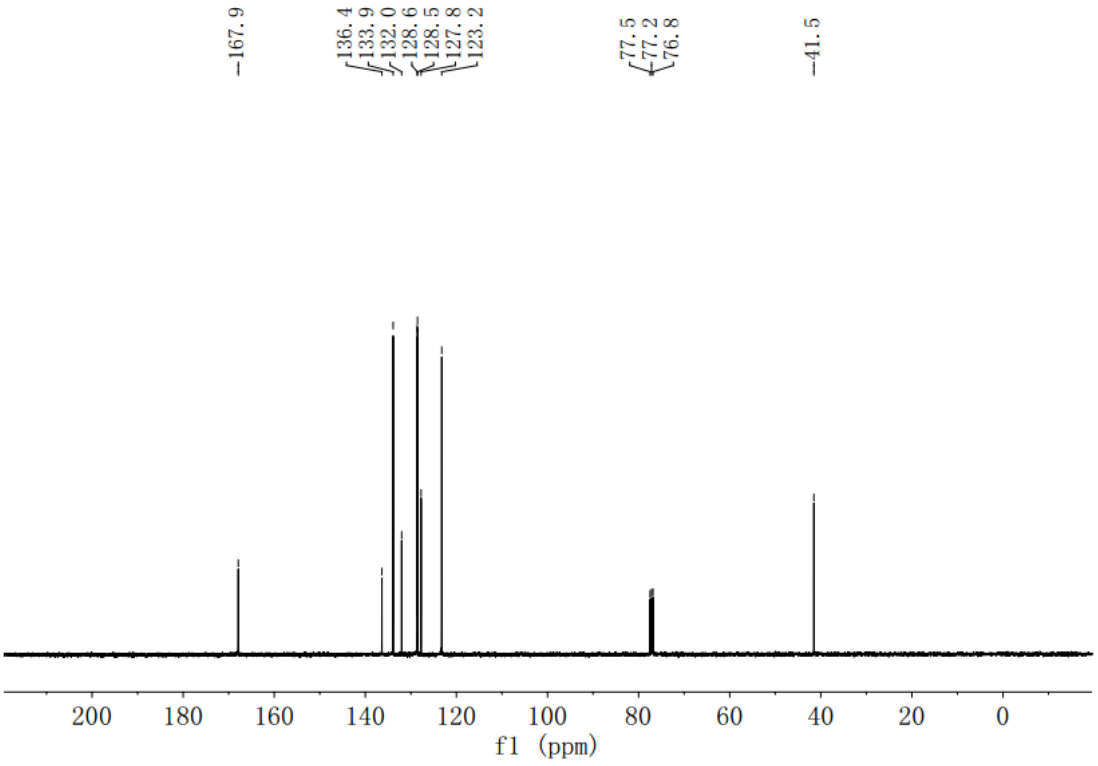
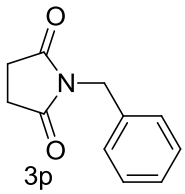
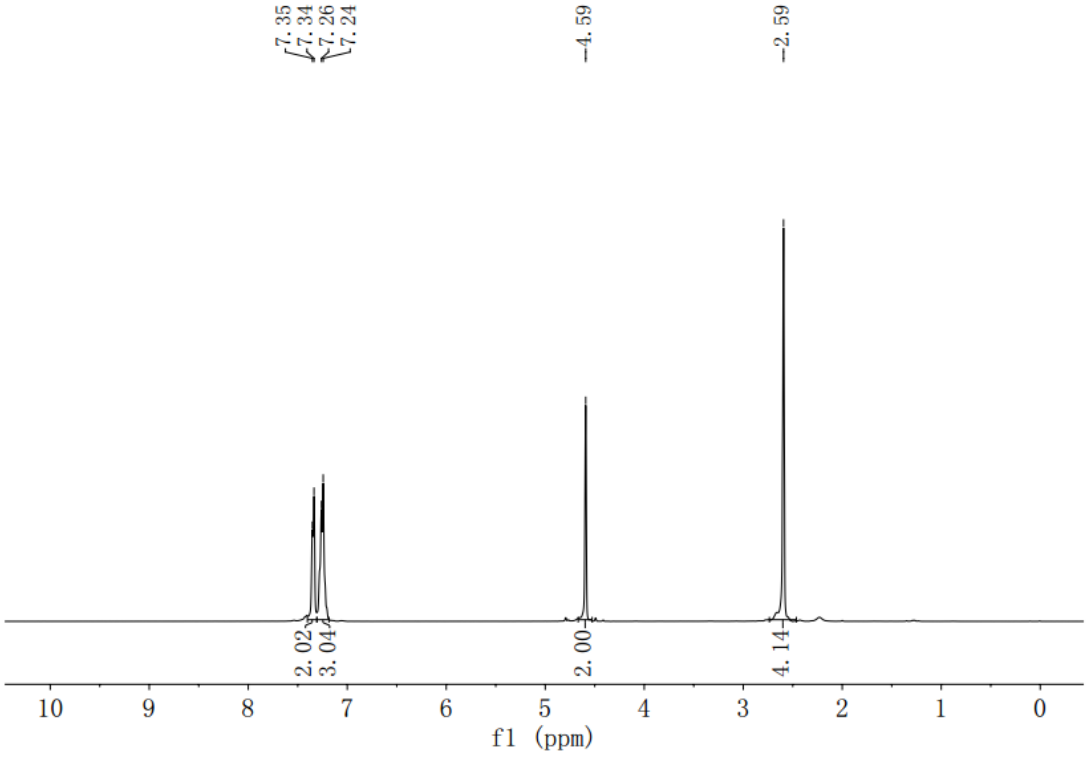
7.65
7.50
7.31
7.29
7.18
7.17
7.15
7.13
7.11
7.09
4.69
2.00
2.04
2.03
3.06
2.07
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


167.9
136.4
133.9
132.0
128.6
128.5
127.8
123.2
77.5
77.2
76.8
41.5
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
O

3p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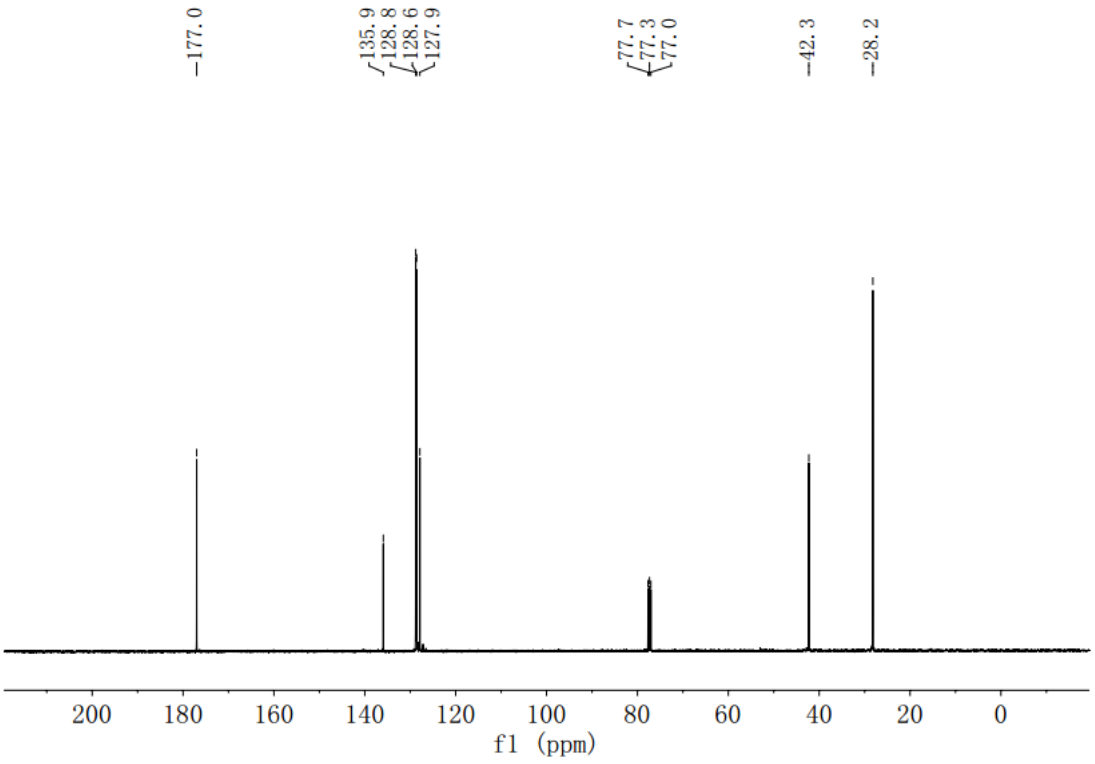
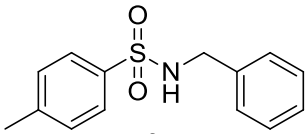
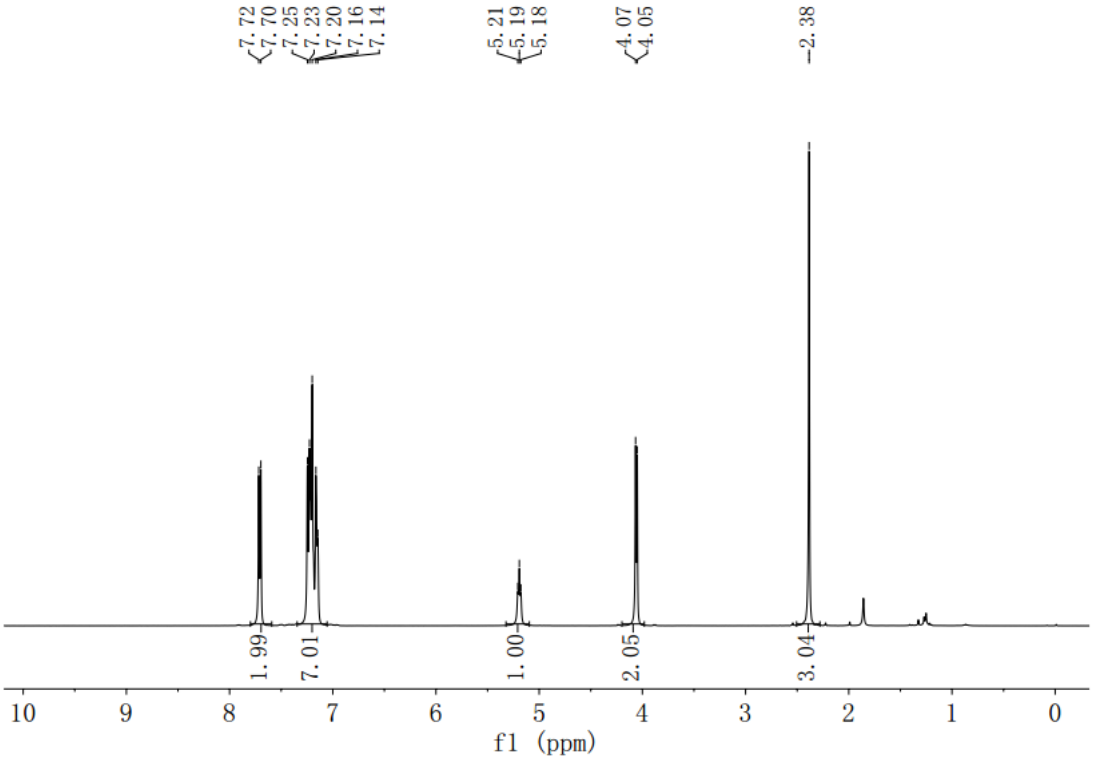
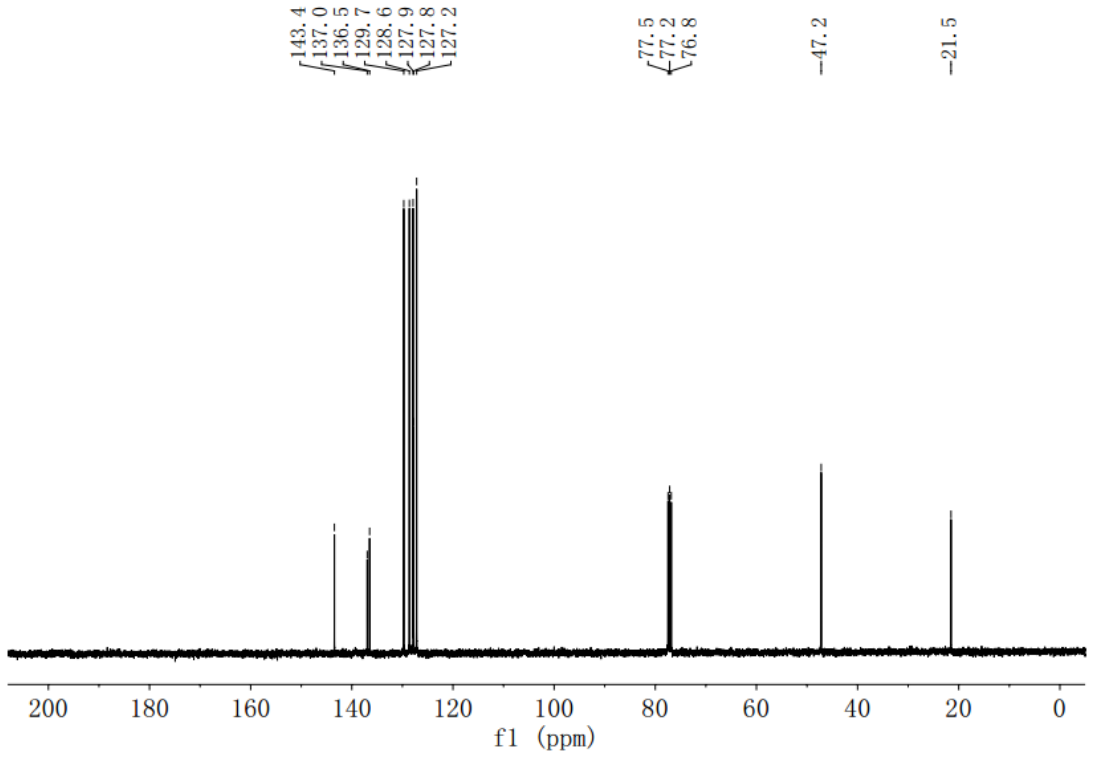
7.34
7.26
7.24
4.59
2.59
2.02
3.04
2.00
4.14
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

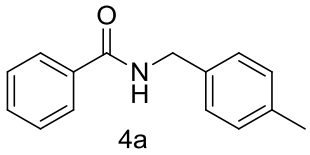

177.0
135.9
128.8
128.6
127.9
77.7
77.3
77.0
42.3
28.2
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



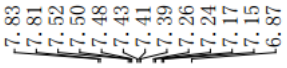
3q


7.72
7.70
7.25
7.23
7.20
7.16
7.14
5.21
5.19
5.18
4.07
4.05
2.38
1.99
7.01
1.00
2.05
3.04
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


143.4
137.0
136.5
129.7
128.6
127.9
127.8
127.2
77.5
77.2
76.8
47.2
21.5
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H

4a


7.83
7.81
7.52
7.50
7.48
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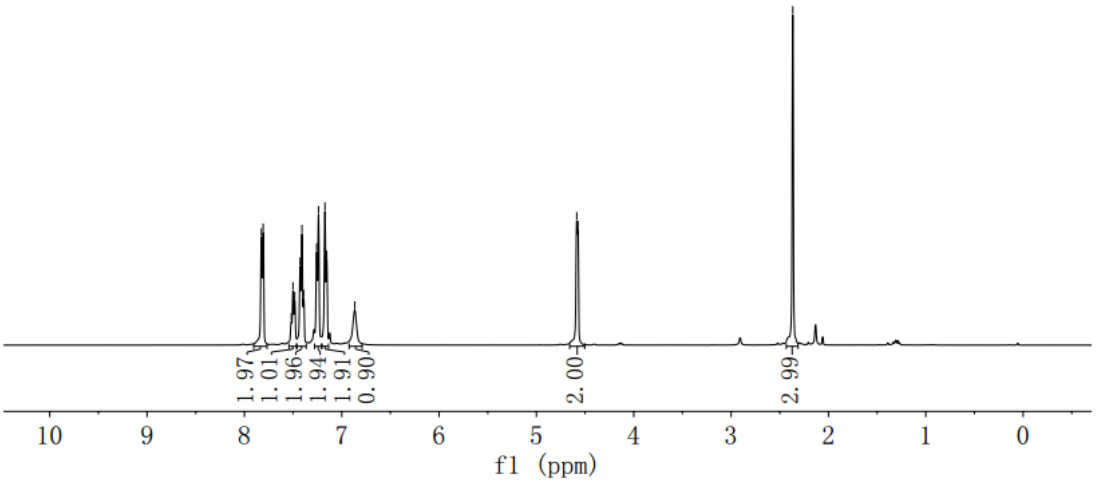
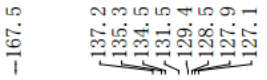
7.41
7.39
7.26
7.24
7.17
7.15
6.87
4.59
4.57
2.37


1.97
1.01
1.96
1.94
1.91
0.90
2.00
2.99
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


167.5
137.2
135.3
134.5
131.5
129.4
128.5
127.9
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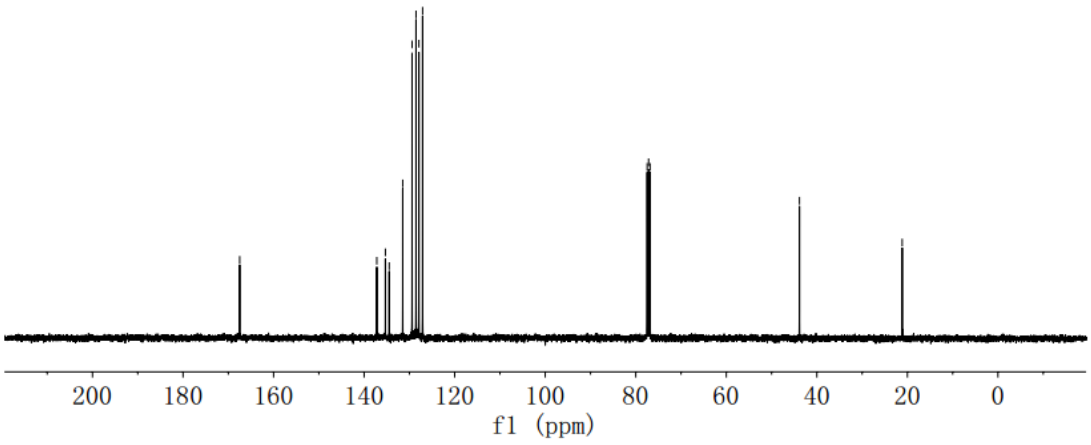
43.8
21.2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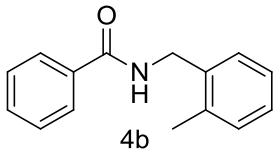
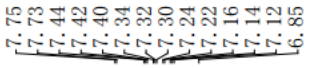
f1 (ppm)


O
N
H

4b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7.16
7.14
7.12
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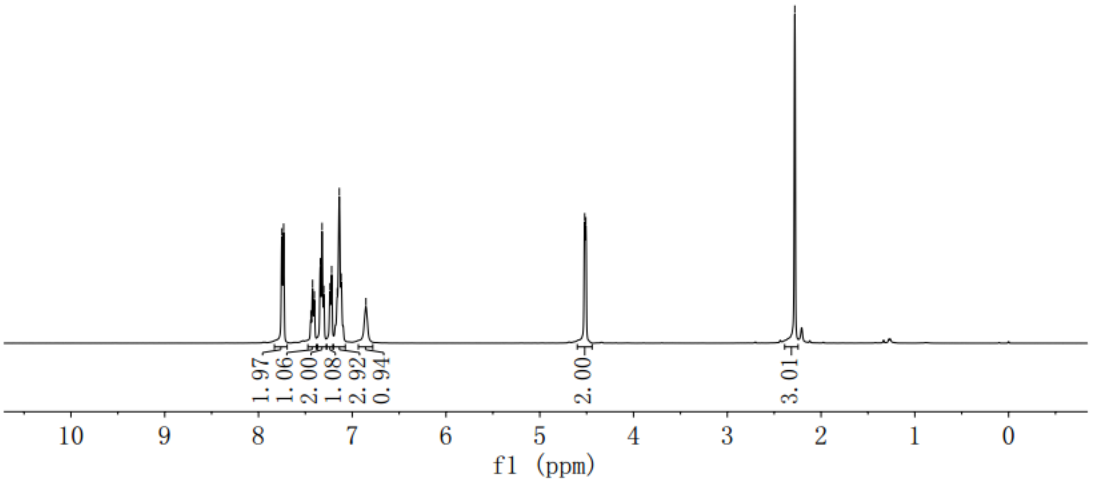
4.51
2.28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1.06
2.00
1.08
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0.94
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3.01
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9
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7
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5
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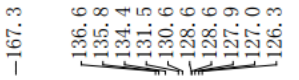
1
0
f1 (ppm)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128.6
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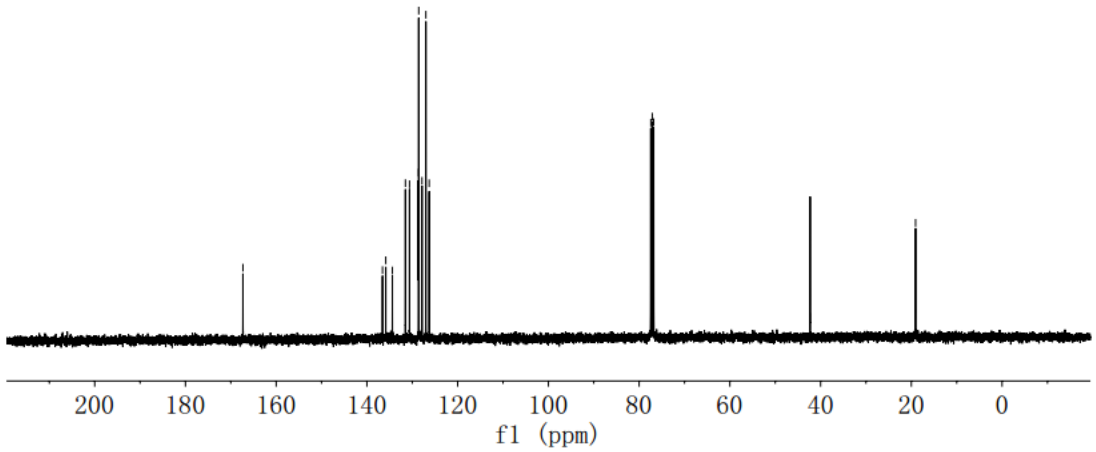
77.1
76.8
42.3
19.1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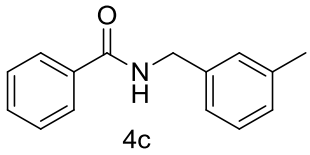
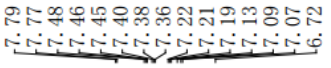
f1 (ppm)


O
N
H

4c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7.77
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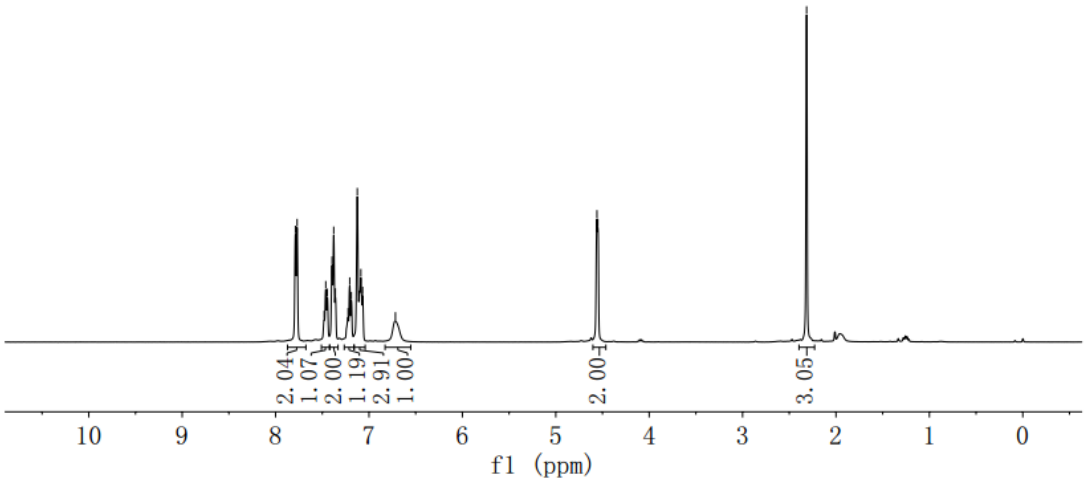
7.46
7.45
7.40
7.38
7.36
7.22
7.21
7.19
7.13
7.09
7.07
6.72
4.56
4.55
2.31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2.00
3.05
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9
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7
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5
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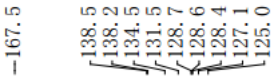
1
0
f1 (ppm)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138.5
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128.6
128.4
127.1
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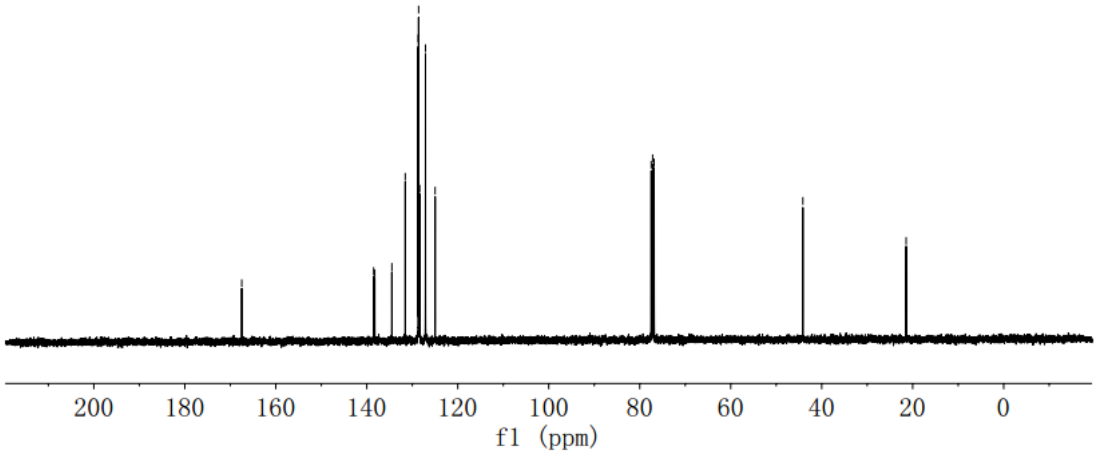
77.5
77.2
76.8
44.1
21.4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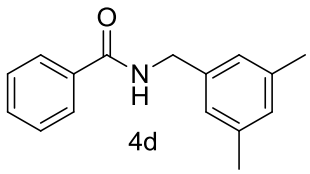
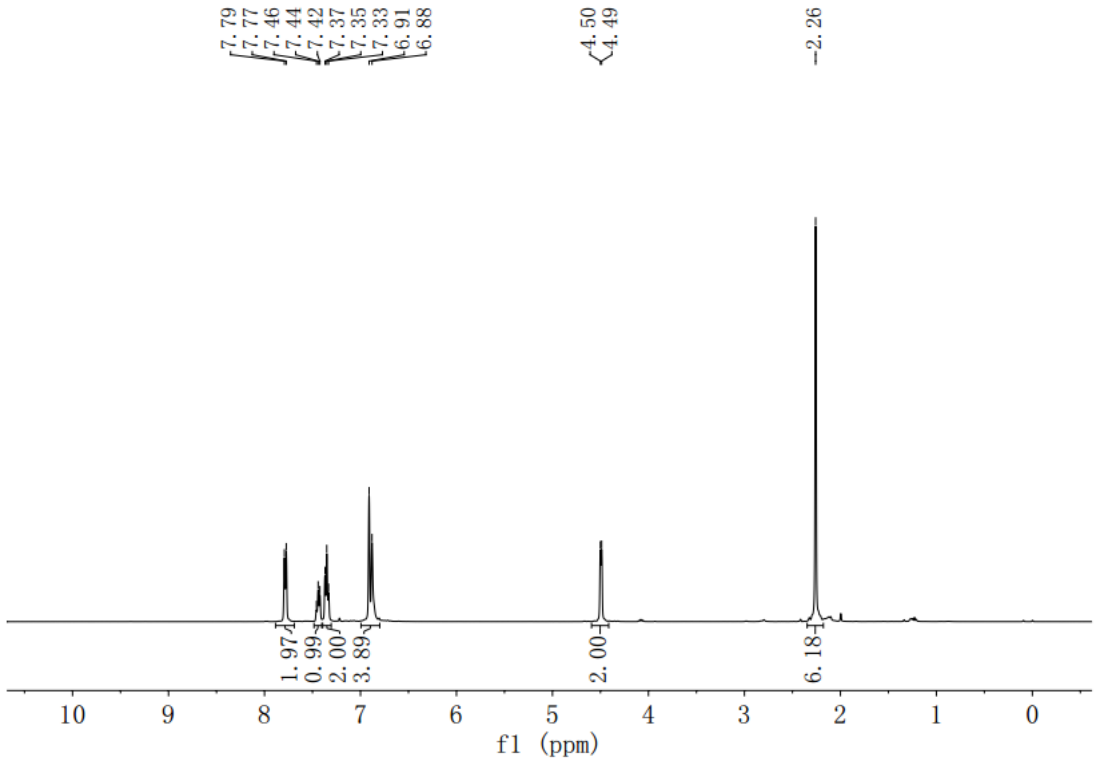
f1 (ppm)


O
N
H

4d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7.42
7.37
7.35
7.33
6.91
6.88
4.50
4.49
2.26
1.97
0.99
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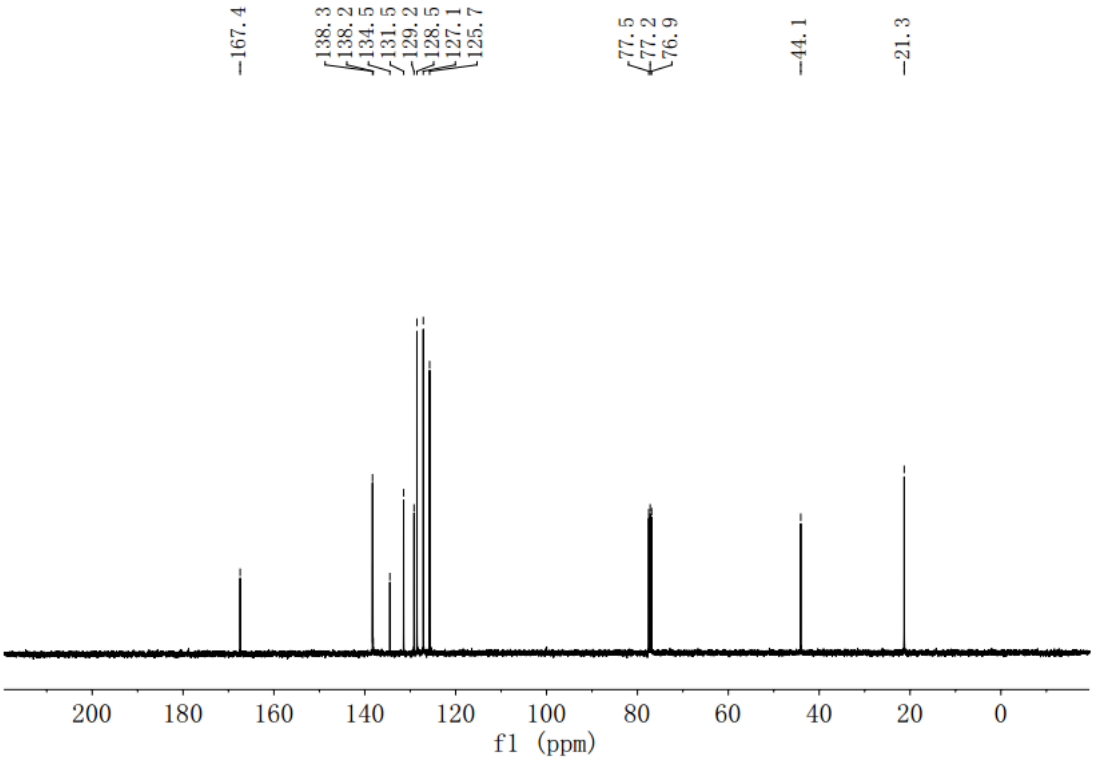
2.00
6.18
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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138.3
138.2
134.5
131.5
129.2
128.5
127.1
125.7
77.5
77.2
76.9
44.1
21.3
200
180
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140
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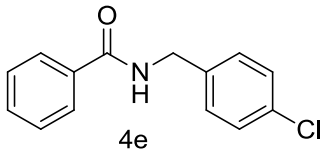
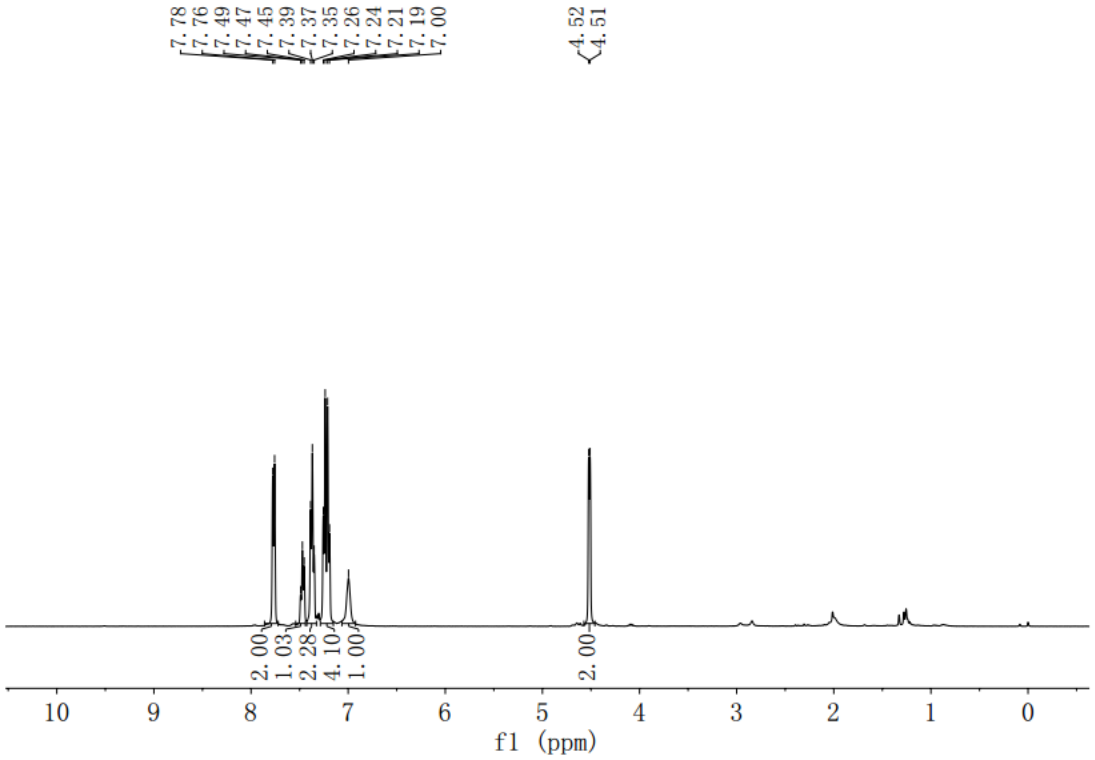
100
80
60
40
20
0
f1 (ppm)


O
N
H
Cl

4e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7.39
7.37
7.35
7.26
7.24
7.21
7.19
7.00
4.52
4.51
2.00
1.03
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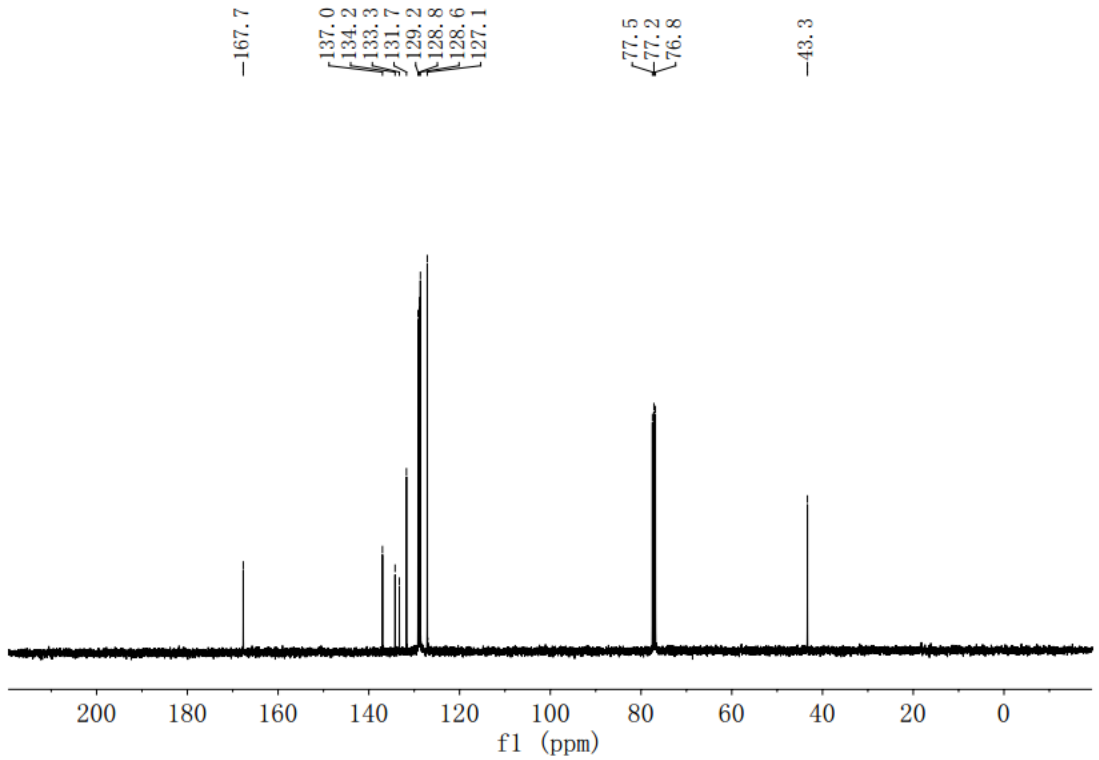
4.10
1.00
2.00
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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137.0
134.2
133.3
131.7
129.2
128.8
128.6
127.1
77.5
77.2
76.8
43.3
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140
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100
80
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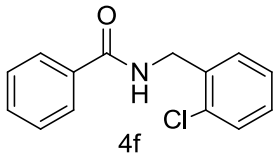
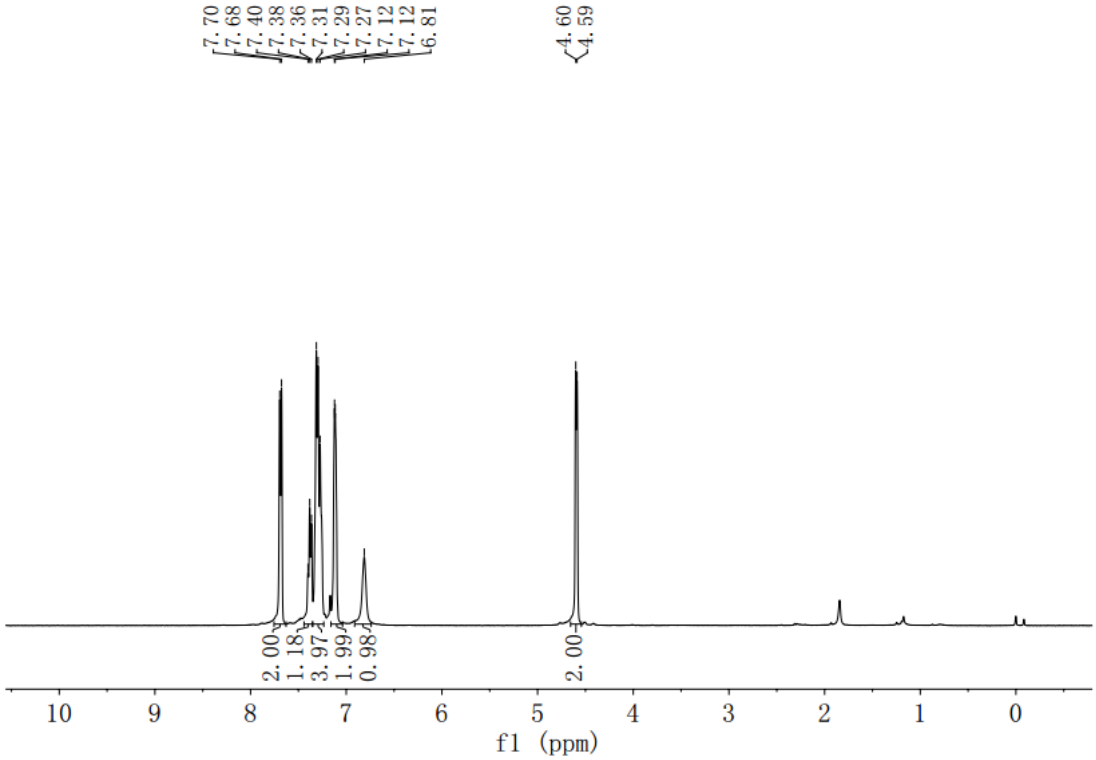
20
0
f1 (ppm)


O
N
H
Cl

4f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7.38
7.36
7.31
7.29
7.27
7.12
7.12
6.81
4.60
4.59
2.00
1.18
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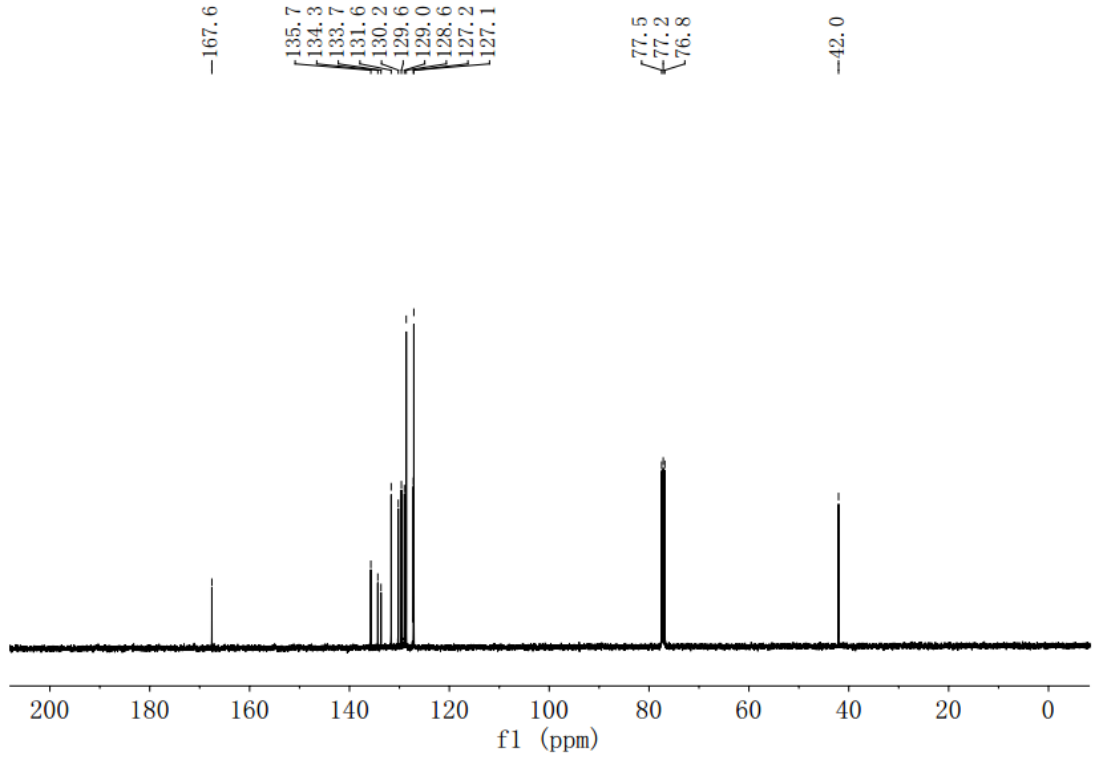
1.99
0.98
2.00
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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134.3
133.7
131.6
130.2
129.6
129.0
128.6
127.2
127.1
77.5
77.2
76.8
42.0
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140
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100
80
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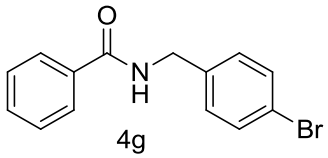
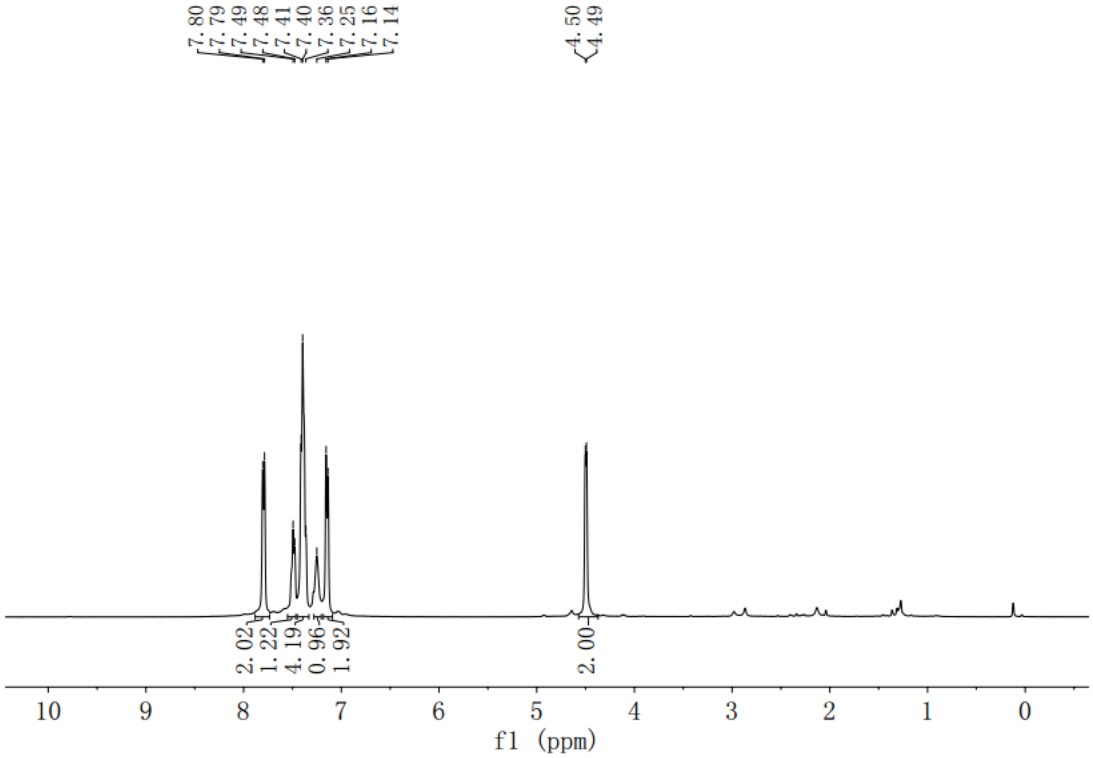
40
20
0
f1 (ppm)


O
N
H
Br

4g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7.25
7.16
7.14
4.50
4.49
2.02
1.22
4.19
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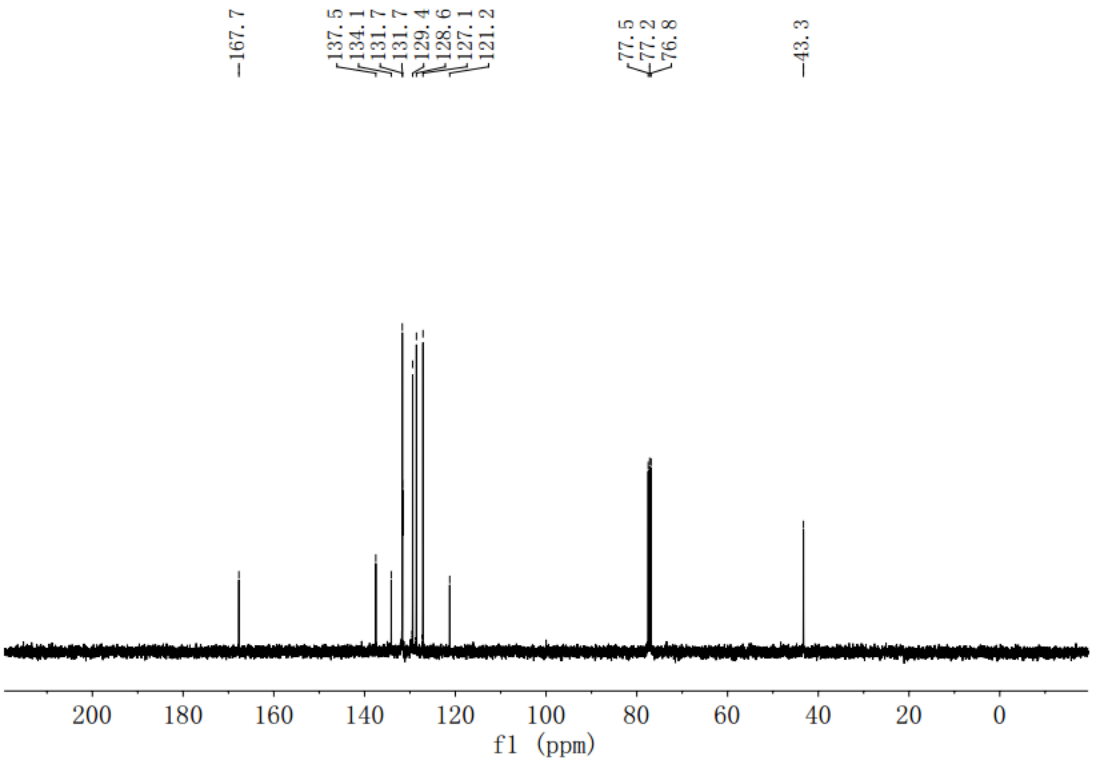
1.92
2.00
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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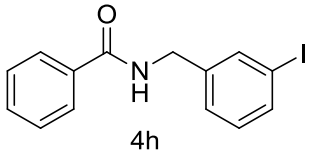
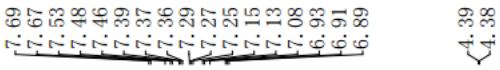
137.5
134.1
131.7
131.7
129.4
128.6
127.1
121.2
77.5
77.2
76.8
43.3
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H
I

4h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7.13
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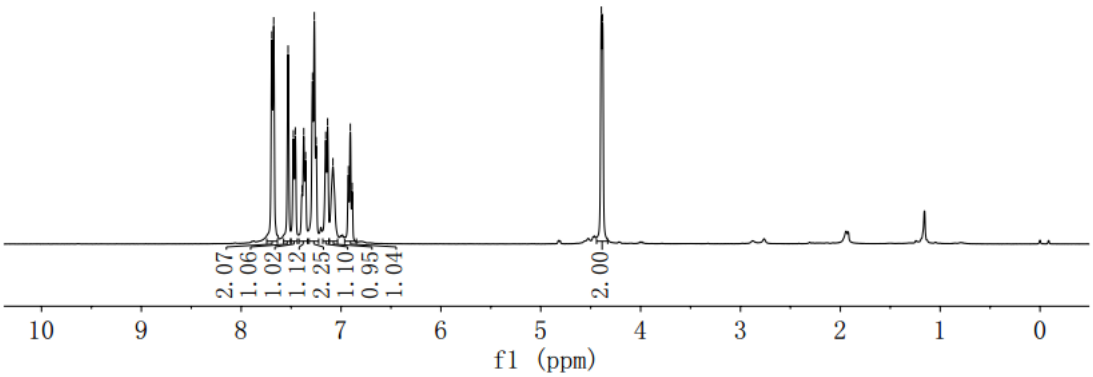
6.93
6.91
6.89
4.39
4.38


2.07
1.06
1.02
1.12
2.25
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1.04
2.00
10
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7
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5
4
3
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1
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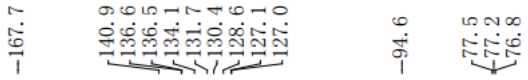
f1 (ppm)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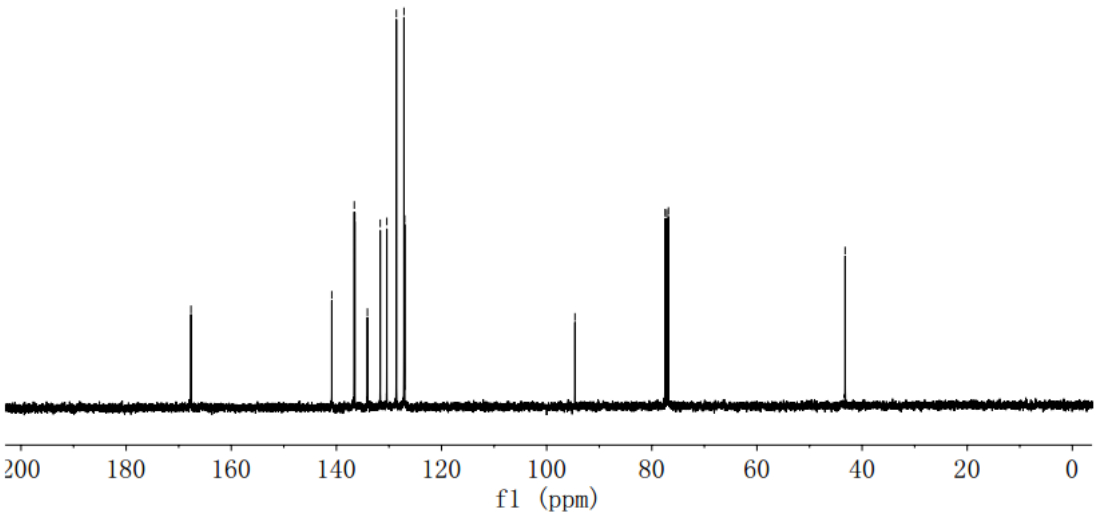
127.1
127.0
94.6
77.5
77.2
76.8
43.2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100
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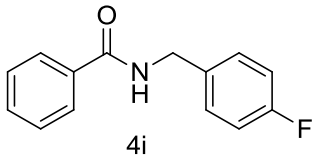
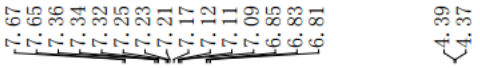
f1 (ppm)


O
N
H
F

4i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7.65
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7.34
7.32
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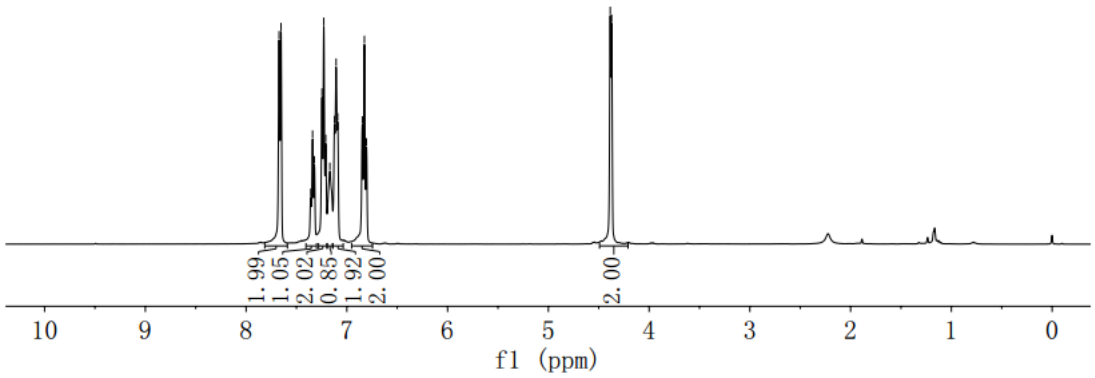
7.17
7.12
7.11
7.09
6.85
6.83
6.81
4.39
4.37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5
4
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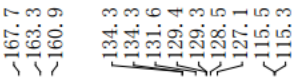
f1 (ppm)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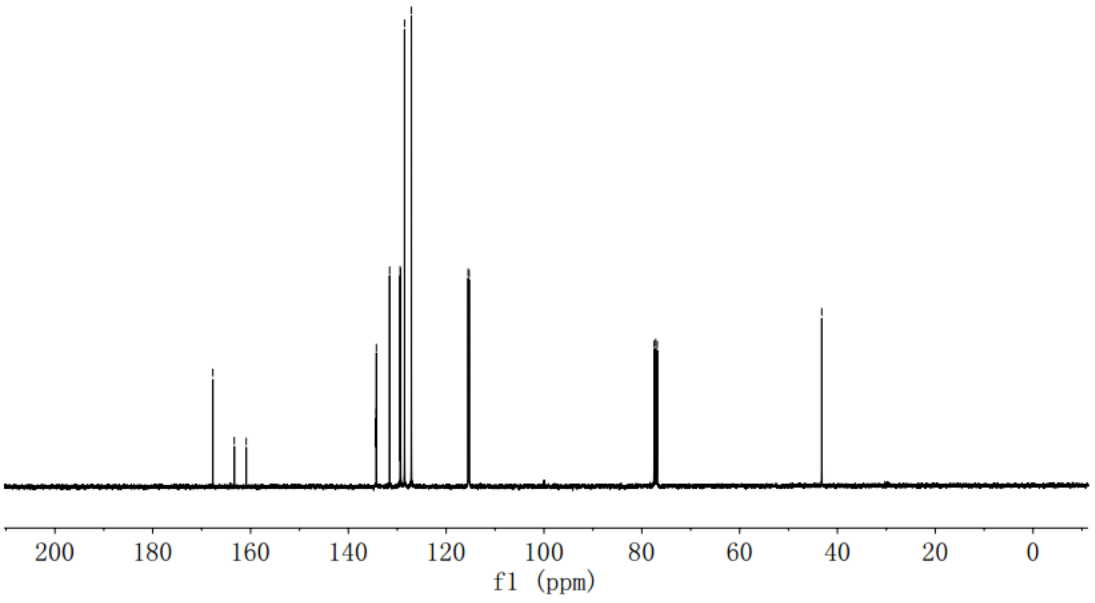
163.3
160.9
134.3
134.3
131.6
129.4
129.3
128.5
127.1
115.5
115.3
77.5
77.2
76.8
43.2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100
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60
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20
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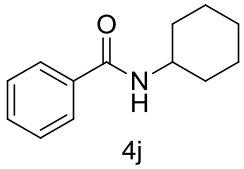
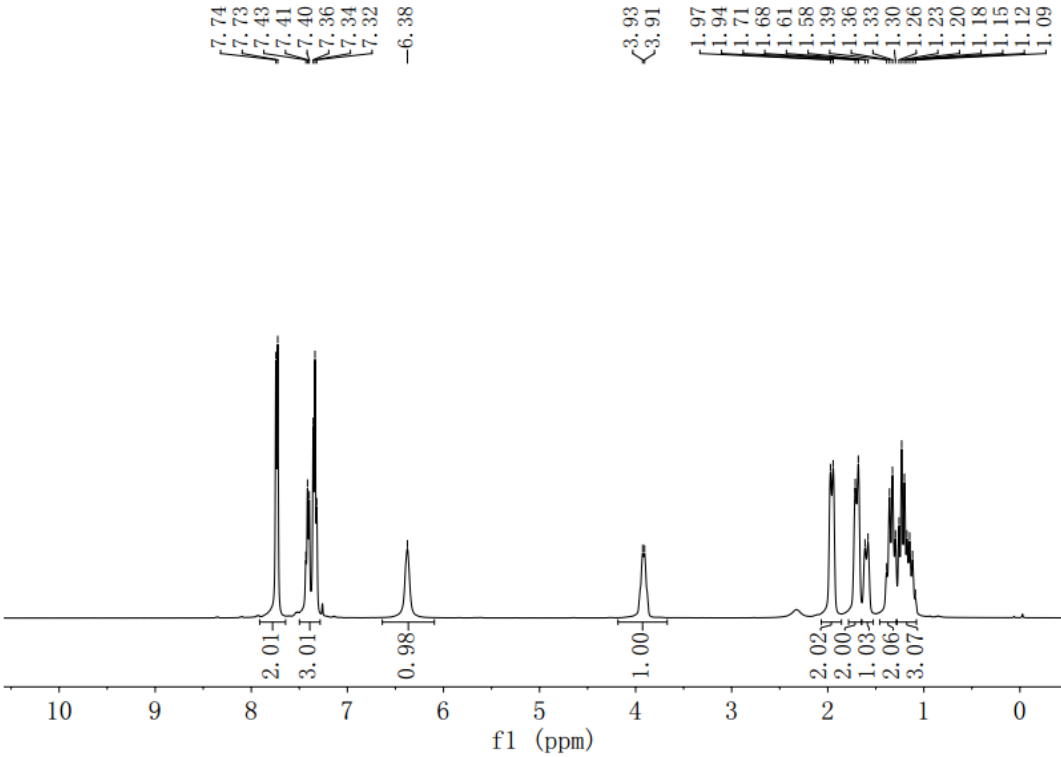
f1 (ppm)


O
N
H

4j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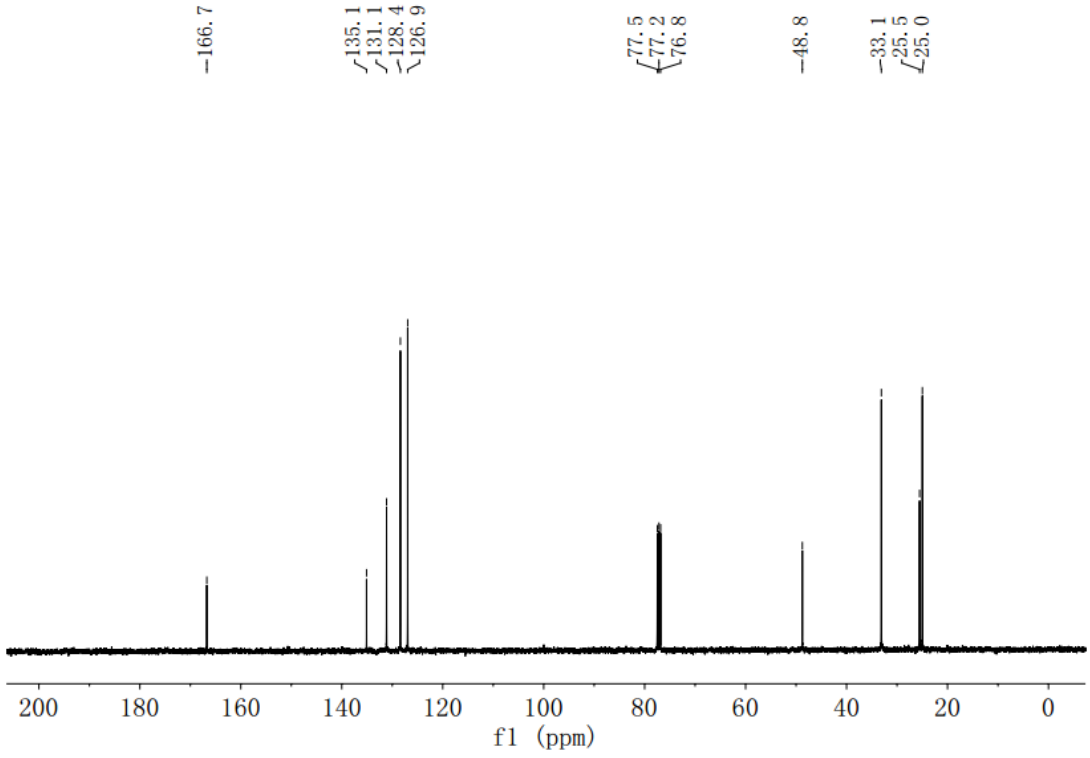
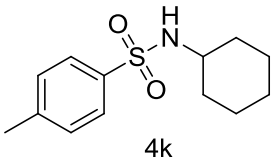
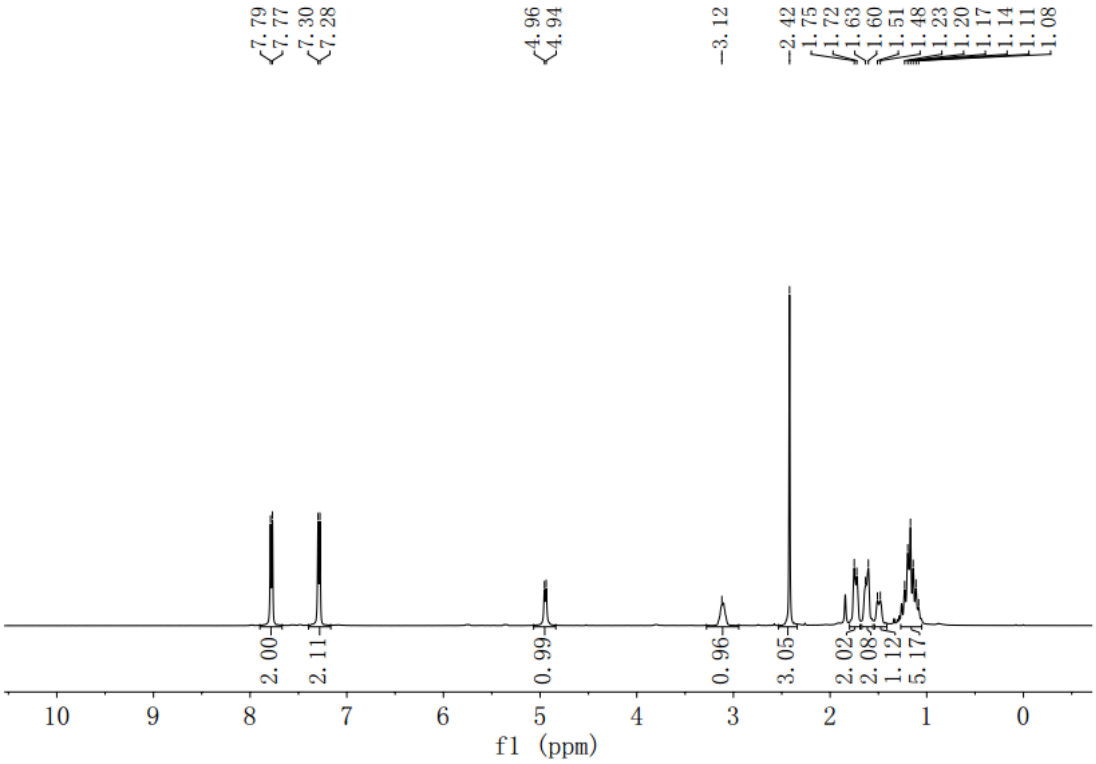
7.34
7.32
6.38
3.93
3.91
1.97
1.94
1.71
1.68
1.61
1.58
1.39
1.36
1.33
1.30
1.26
1.23
1.20
1.18
1.15
1.12
1.09
2.01
3.01
0.98
1.00
2.02
2.00
1.03
2.06
3.07
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


166.7
135.1
131.1
128.4
126.9
77.5
77.2
76.8
48.8
33.1
25.5
25.0
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
H
N
S
O

4k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7.77
7.30
7.28
4.96
4.94
3.12
2.42
1.75
1.72
1.63
1.60
1.51
1.48
1.23
1.20
1.17
1.14
1.11
1.08
2.00
2.11
0.99
0.96
3.05
2.02
2.08
1.12
5.17
10
9
8
7
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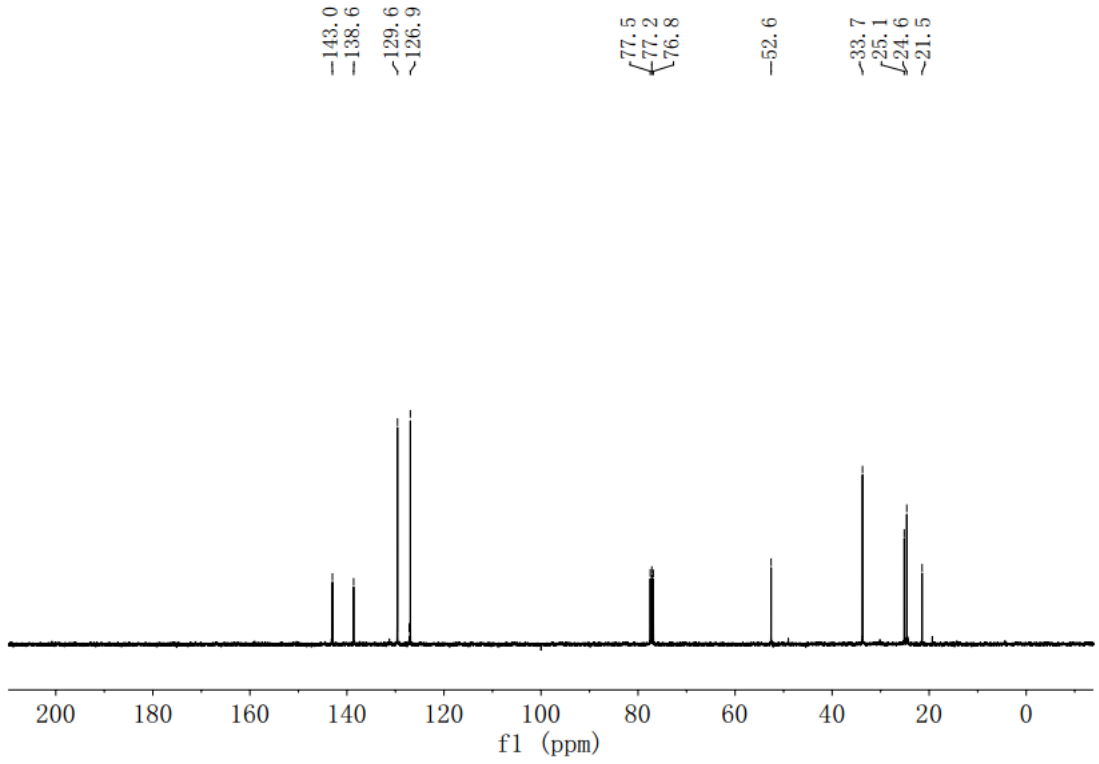
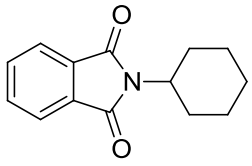
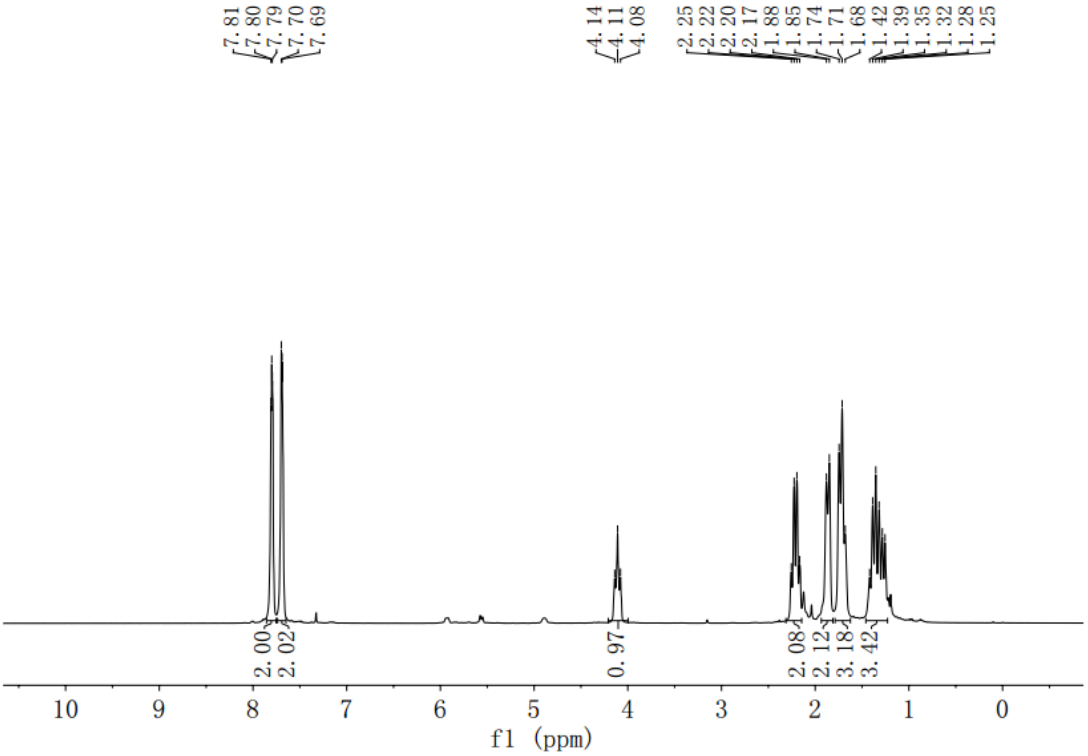
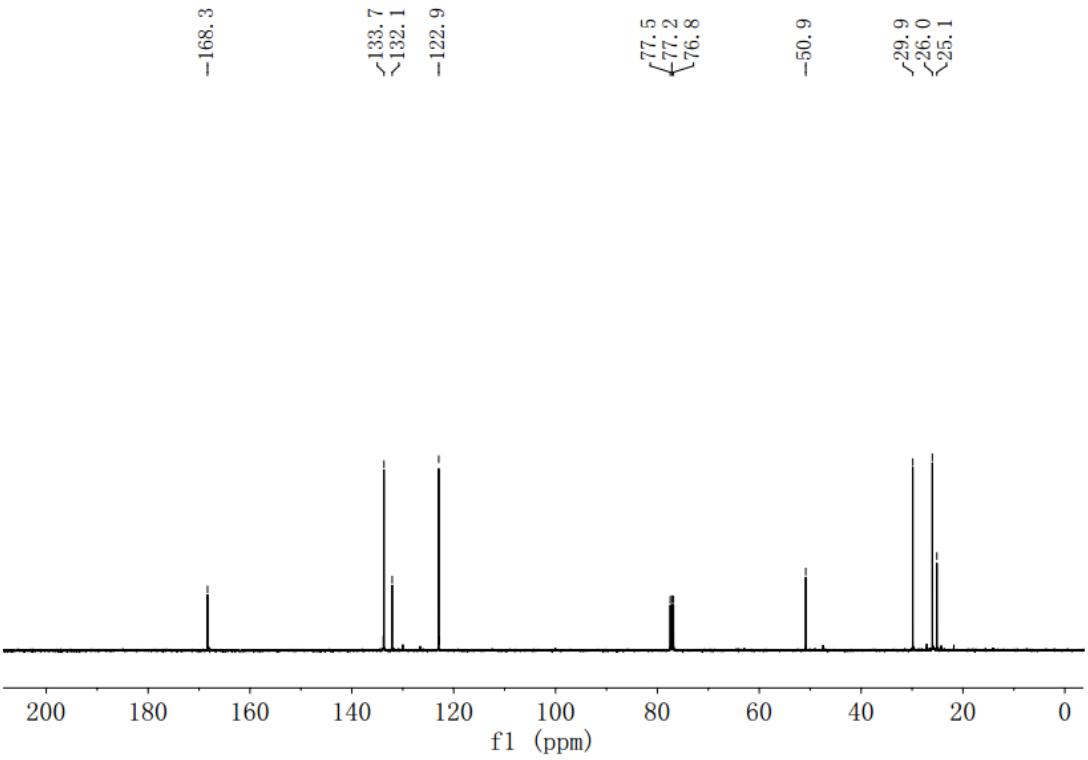
5
4
3
2
1
0
f1 (ppm)

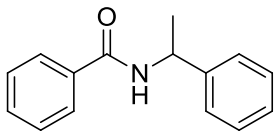

143.0
138.6
129.6
126.9
77.5
77.2
76.8
52.6
33.7
25.1
24.6
21.5
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)



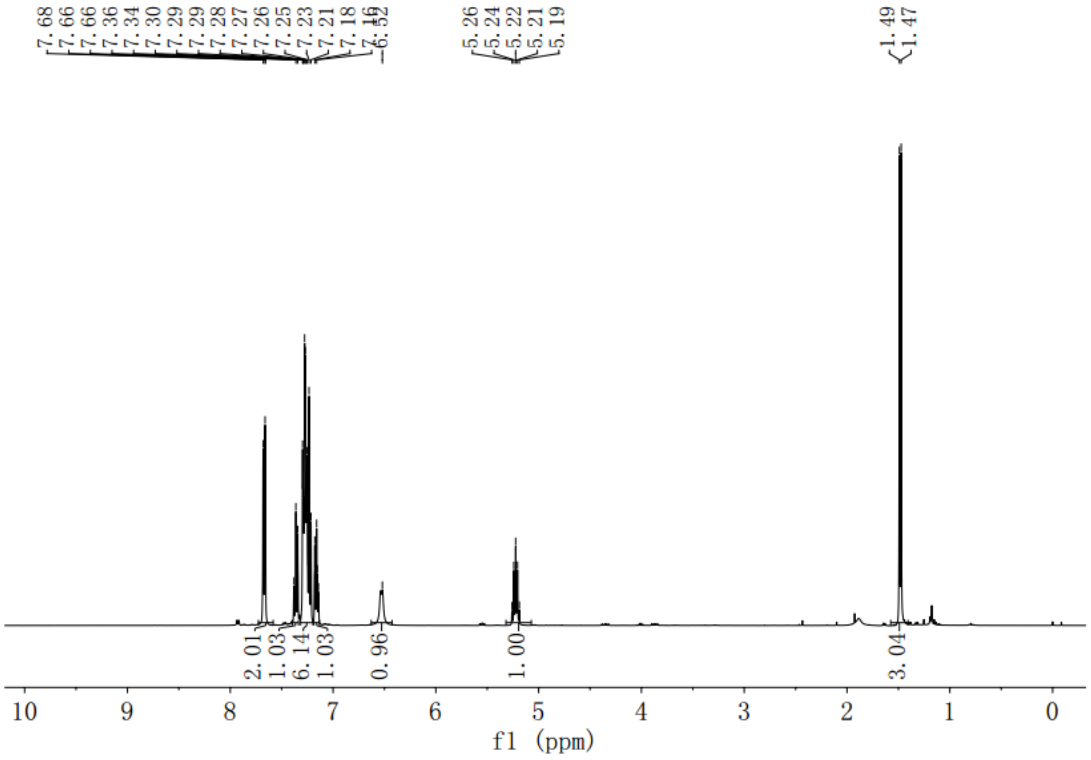
4l

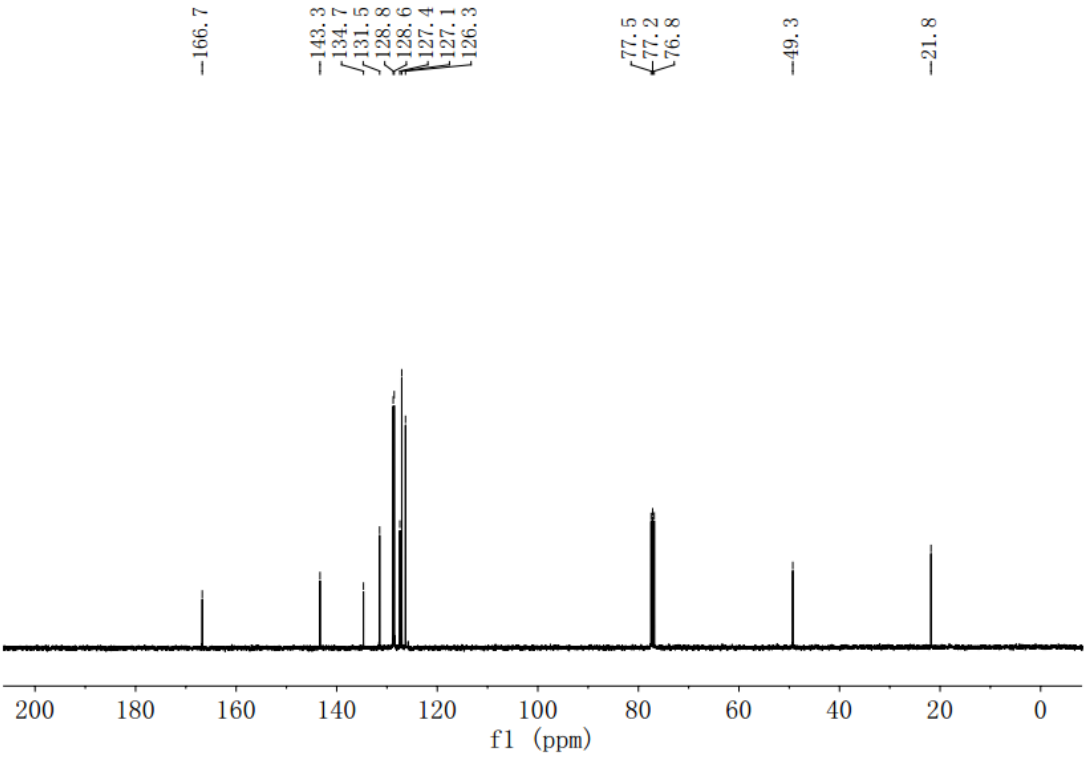

7.81
7.80
7.79
7.70
7.69
4.14
4.11
4.08
2.25
2.22
2.20
2.17
1.88
1.85
1.74
1.71
1.68
1.42
1.39
1.35
1.32
1.28
1.25
2.00
2.02
0.97
2.08
2.12
3.18
3.42
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


168.3
133.7
132.1
122.9
77.5
77.2
76.8
50.9
29.9
26.0
25.1
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


O
N
H

4m


7.68
7.66
7.66
7.36
7.34
7.30
7.29
7.29
7.28
7.27
7.26
7.25
7.23
7.21
7.18
7.16
6.52
5.26
5.24
5.22
5.21
5.19
1.49
1.47
2.01
1.03
6.14
1.03
0.96
1.00
3.04
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


166.7
143.3
134.7
131.5
128.8
128.6
127.4
127.1
126.3
77.5
77.2
76.8
49.3
21.8
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)