Supporting Information

A lipase-glucose oxidase system for the efficient oxidation of *N*-heteroaromatic compounds and tertiary amines

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1 EXPERIMENTAL SECTION

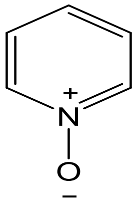
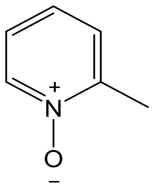
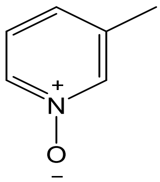
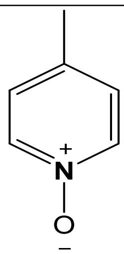
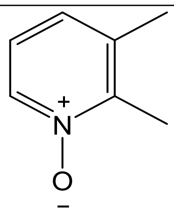
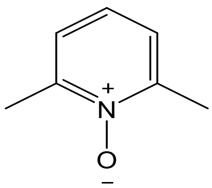
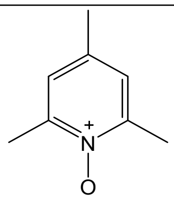
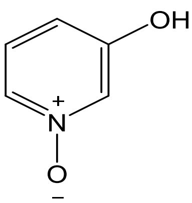
1.1 Materials

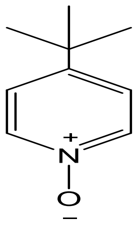
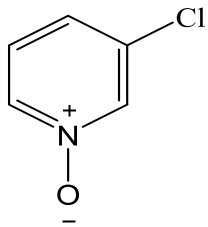
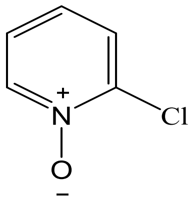
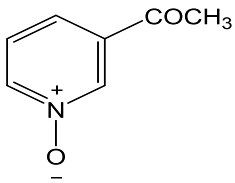
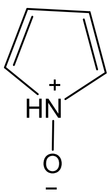
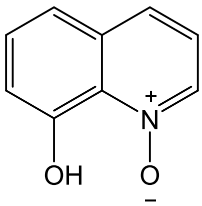
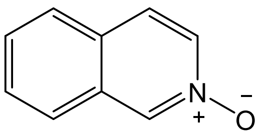
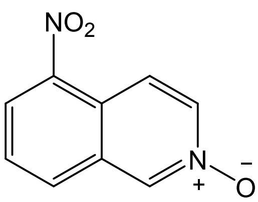
Candida antarctica lipase B (CalB, 10000U/mL) was purchased from Sigma (Beijing, China). One unit of CalB activity was defined as the amount of enzymerequired to hydrolyze 1 μmol of *p*-nitrophenyl acetate per minute at 30 ^{o}C. Glucose oxidase from *A. Niger* (GOX, 200U/mg) was purchased from Sigma (Beijing, China), and one unit of GOX activity was defined as the amount of enzyme required to oxidise 1 μmol of β-d-glucose to d-gluconic acid and hydrogen peroxide per min at 35°C and pH 7.0. Glucose, hydrogen peroxide, *N*-heteroaromatic compounds and tertiary aminesused in this study were purchased from J&K Scientific (Beijing, China). All the other chemical reagents were purchased from Shanghai Chemical Reagent Company (Shanghai, China). All the commercially available reagents and solvents were used without further purification. NMR spectra were recorded on an Inova 500 (500 MHz) spectrometer.

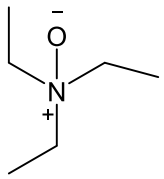
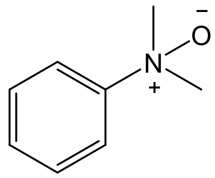
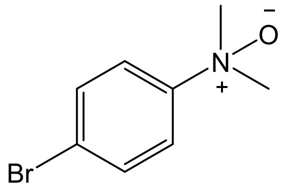
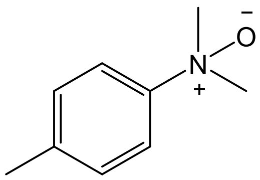
1.2 General Procedure of the dual enzyme system for the oxidation of *N*-heteroaromatic compounds and tertiary amines

A mixture of *N*-heteroaromatic compound or tertiary amine (1 mmol), glucose (1.2 mmol), CalB (30 U/mL) and GOX (42U/mL) in a two-phase reaction medium (3 mL, phosphate buffer/ethyl acetate = 1/2) was stirred at room temperature in a round-bottom flask for 1h when the oxygen (1 mL/min) was bubbled into the reaction mixture.The reaction was monitored by TLC. Then, the mixture was filtered and extracted with Dichloromethane. The combined organic phases were dried over Na_2SO_4 (anhydrous) and concentrated under vacuum, and the resulting residue was purified by flash column chromatography on silica gel with methanol/trichloromethane (1/10) to afford the desired *N*-oxide. All the isolated products were well characterized by their ^{1}H-NMR spectral analysis according to the references (J. Org. Chem., 1998, 63(5), 1740-1741; New J. Chem., 2013, 37, 2614-2618; Chem. Eur. J. 2014, 20, 559-563; RSC Adv., 2015, 5, 36809-36812). Each experiment was performed triplicate, and all the data were obtained based on the average values.

DATA OF PRODUCTS

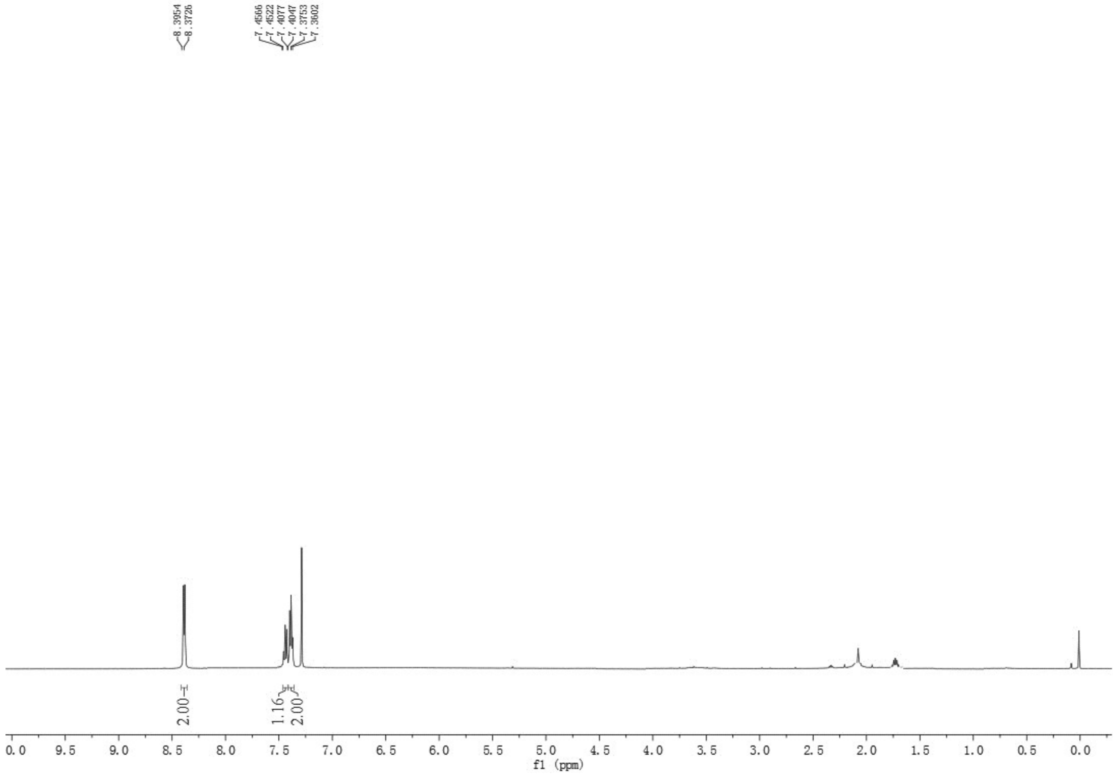
2a		Pyridine-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 7.36-7.41 (t, 2H), 7.41-7.46 (d, 1H),8.37-8.40 (d, 2H);
2b		2-Picoline-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 2.54 (s, 3H), 7.16-7.25 (m, 2H), 7.28-7.31 (m, 1H), 8.35 (d, 1H);
2c		3-Picoline-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 2.31 (s, 3H), 7.09-7.18 (m, 2H), 8.06 (d, 2H);
2d		4-Picoline-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 2.37 (s, 3H), 7.10 (d, 2H), 8.14 (d, 2H);
2e		2,3-Lutidine-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 2.26 (s, 3H), 2.42 (s, 3H), 6.95-6.98 (m, 2H), 8.08 (d, 1H);
2f		2,6-Lutidine-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 2.54 (s, 6H), 7.10-7.06 (m, 1H), 7.15 (d, 2H);
2g		2,4,6-Trimethylpyridine-N-oxide ^{1}H NMR ($CDCl_3$, 500MHz) 2.31 (s, 3H), 2.53 (s, 6H), 7.01 (s, 2H);
2h		3-Hydroxypyridine N-oxide ^{1}H-NMR($CDCl_3$,500MHz)6.79(m,1H),7.18(m,1H),7.67(m,2H),10.51(s,1H);

2i		4-(tert-butyl)Pyridine 1-oxide ^{1}H NMR($CDCl_3$, 500 MHz) 1.33 (s, 9H), 7.36 (d, 2H), 8.30 (d, 2H);
2j		3-Chloropyridine-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 7.27 (m, 1H), 7.35 (d, 1H), 8.21 (d, 1H), 8.33 (s, 1H).
2k		2-Chloropyridine-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 7.24 (s, 2H), 7.53 (s, 1H), 8.35 (s, 1H);
2l		3-Acetylpyridine-N-oxide. ^{1}H NMR ($CDCl_3$, 500 MHz): 2.58 (s, 3H), 7.43-7.45 (m, 1H), 7.75 (d, 1H), 8.32 (d, 1H), 8.69 (s, 1H);
2m		1H-pyrrole N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 6.21 (d, 2H), 7.20 (m, 2H);
2n		8-hydroxy-quinoline-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 6.99 (d, 1H), 7.15-7.19 (m, 2H), 7.39-7.43 (m, 1H), 7.71 (d, 1H), 8.17 (d, 1H), 15.0 (s, 1H);
2o		Isoquinoline-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 7.53-7.60 (m, 2H), 7.63-7.70 (m, 2H), 7.74-7.76 (m, 1H), 8.10 (d, 1H), 8.73 (s, 1H);
2p		5-Nitroisoquinoline-N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 7.74 (m, 1H), 8.00 (d, 1H), 8.30 (d, 1H), 8.41 (d, 1H), 8.61 (d, 1H), 8.84 (s, 1H);

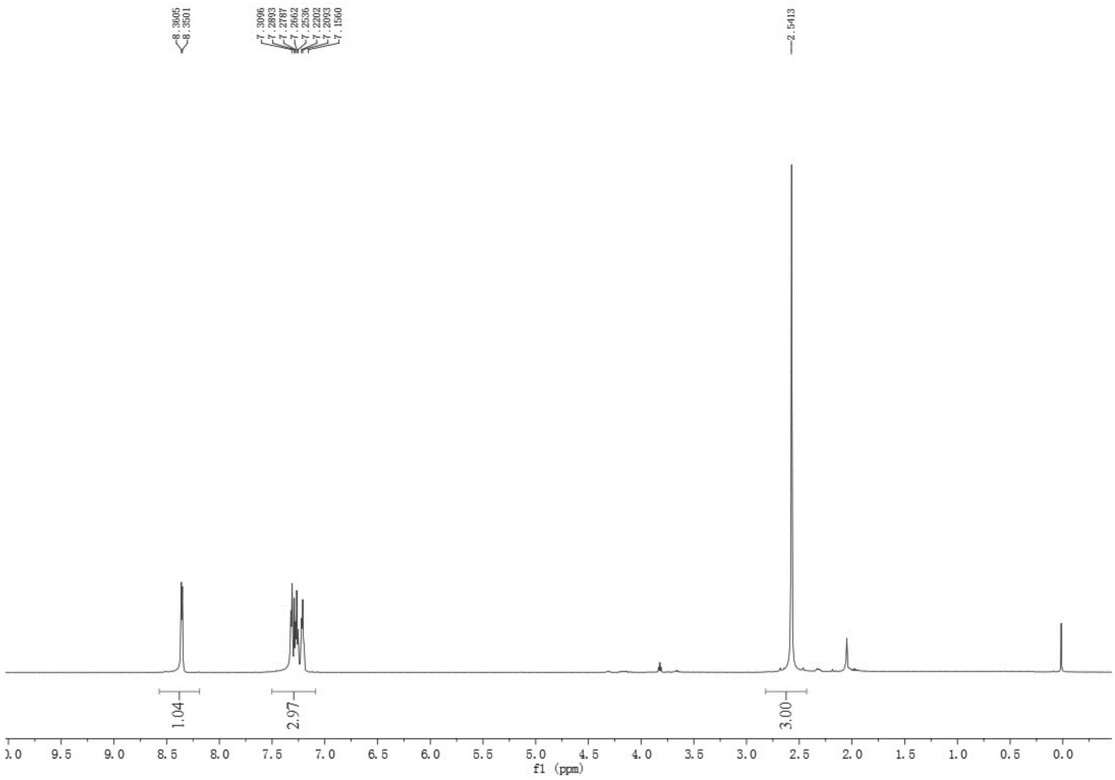
2q		Triethylamine N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 1.13 (t, 9H), 3.02 (m, 6H);
2r		N,N-Dimethyl aniline N-oxide ^{1}H NMR ($CDCl_3$, 500MHz) 3.32 (s, 6H), 7.18-7.21 (m, 4H), 7.55-7.59 (m, 1H);
2s		4-bromo-N,N-dimethylaniline N-oxide ^{1}H NMR($CDCl_3$, 500 MHz) 3.69 (s, 6H), 7.63 (d, 2H), 7.84 (d, 2H);
2t		N,N-Dimethyl-p-toluidine N-oxide ^{1}H NMR ($CDCl_3$, 500 MHz) 2.41 (s, 3H), 3.65 (s, 6H), 7.27 (m, 2H), 7.79 (d, 2H);

^{1}H-NMR SPECTRA OF PRODUCTS

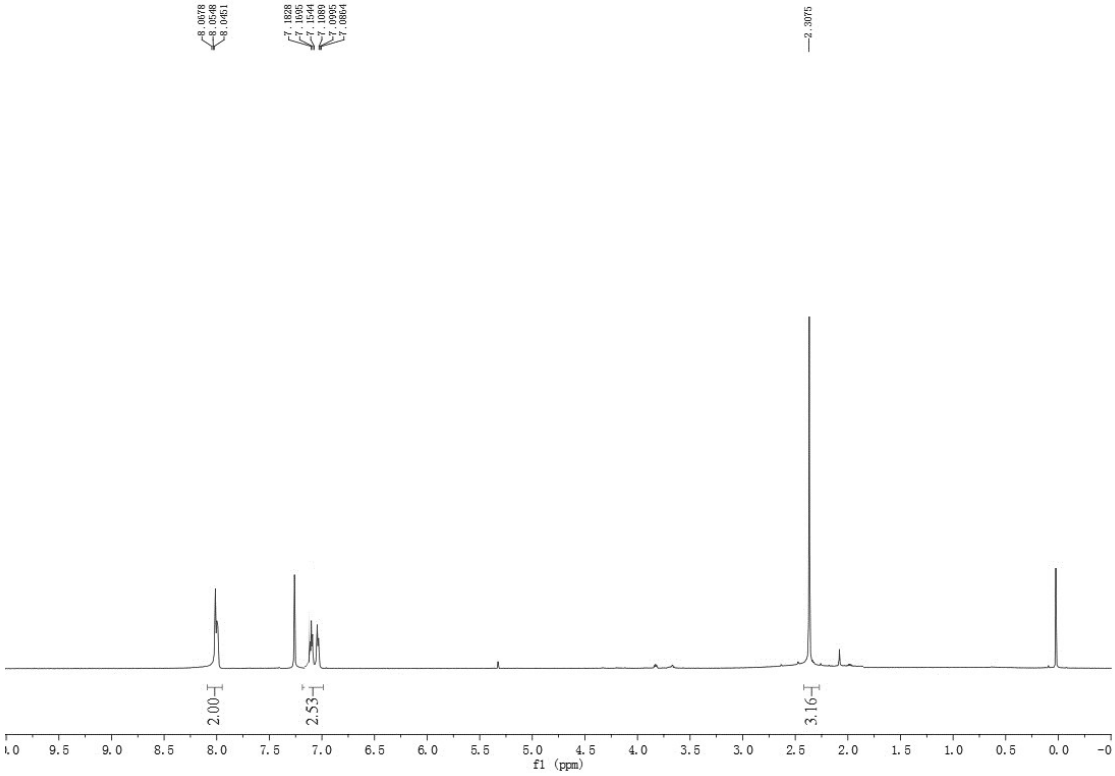
2a



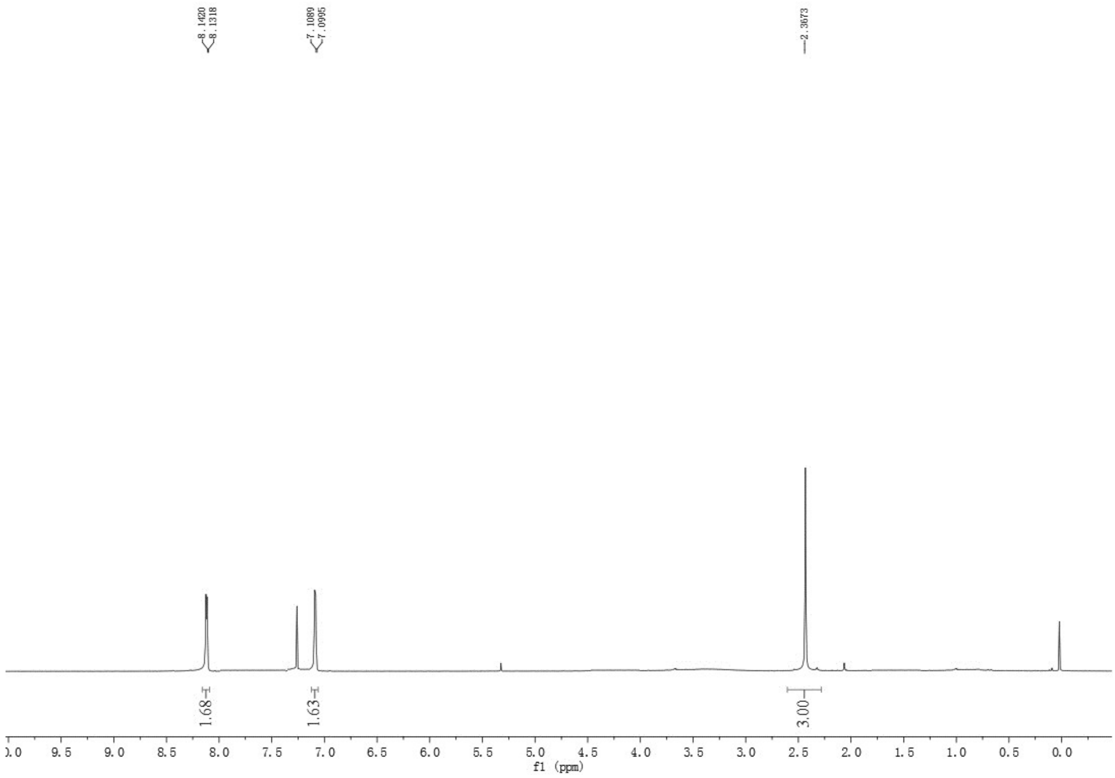
2b



2c


8.0678
8.0548
8.0451
7.1828
7.1695
7.1544
7.1080
7.0995
7.0864
2.3075
2.00
2.53
3.16
f1 (ppm)

2d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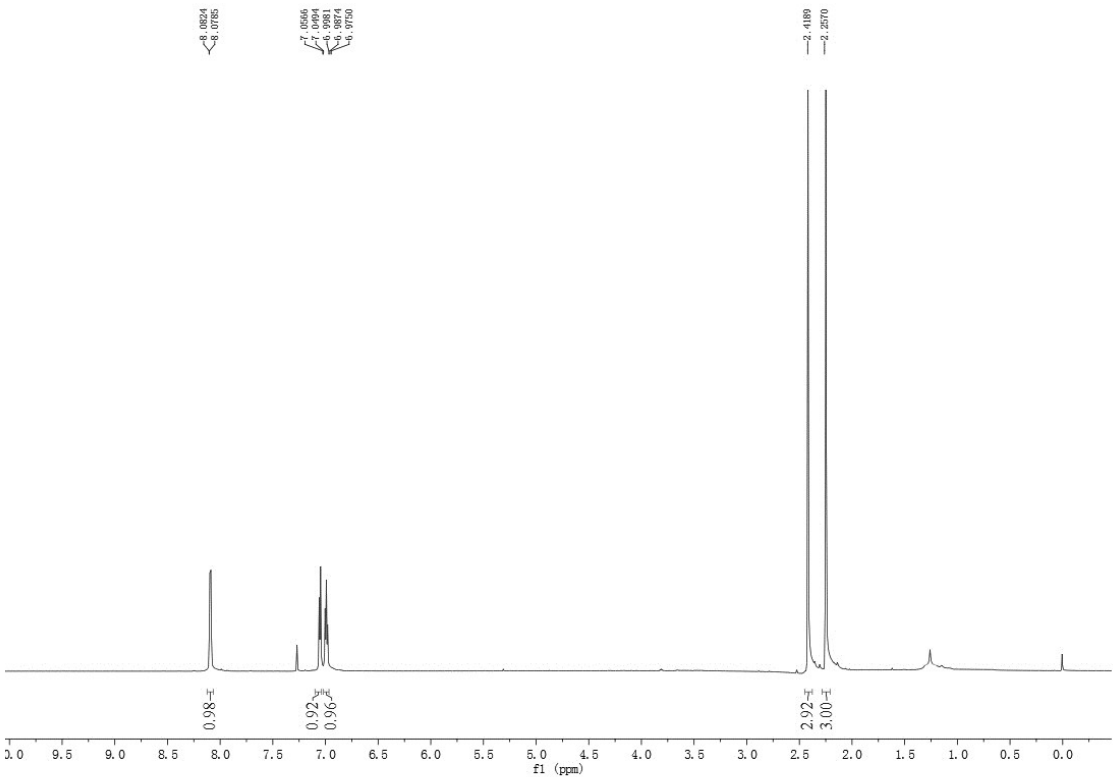
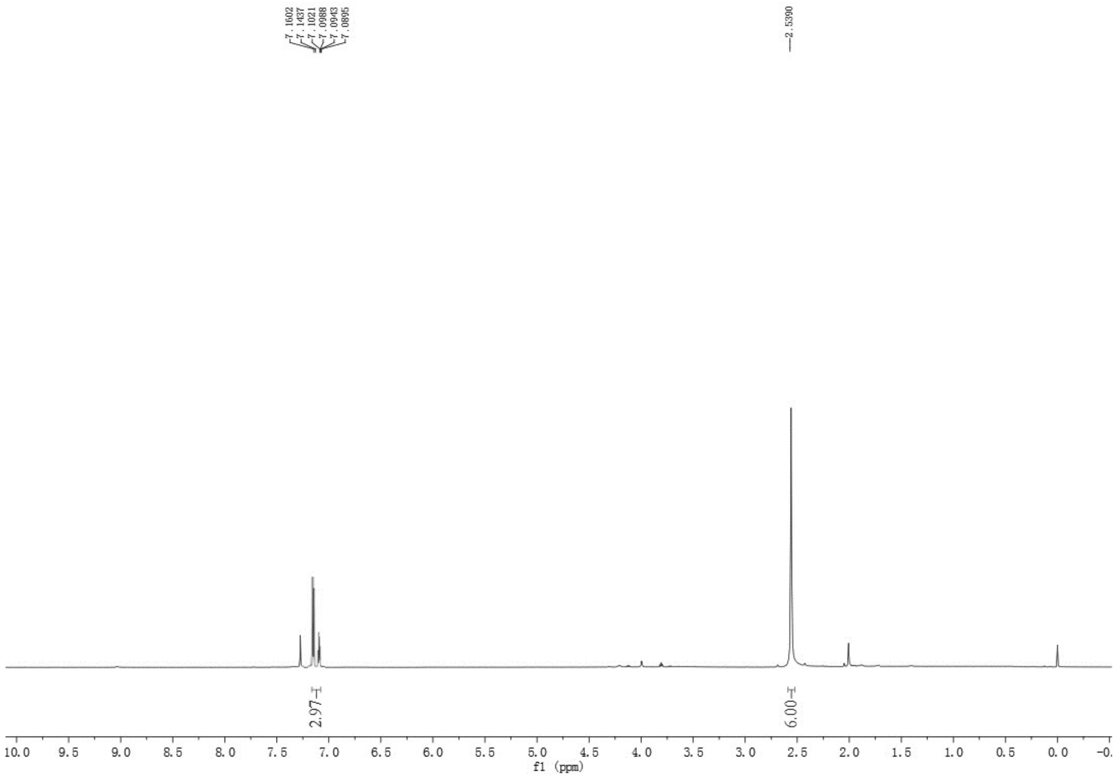
8.1318
7.1080
7.0995
2.3673
1.68
1.63
3.00
f1 (ppm)

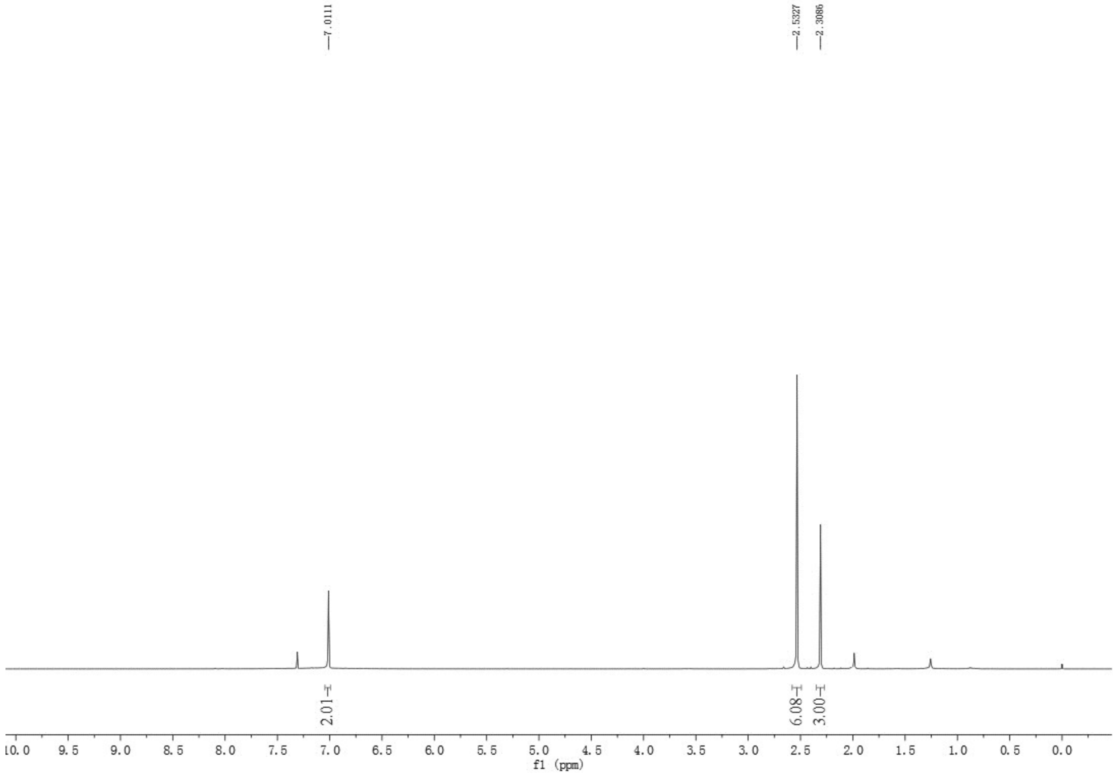
2e



2f

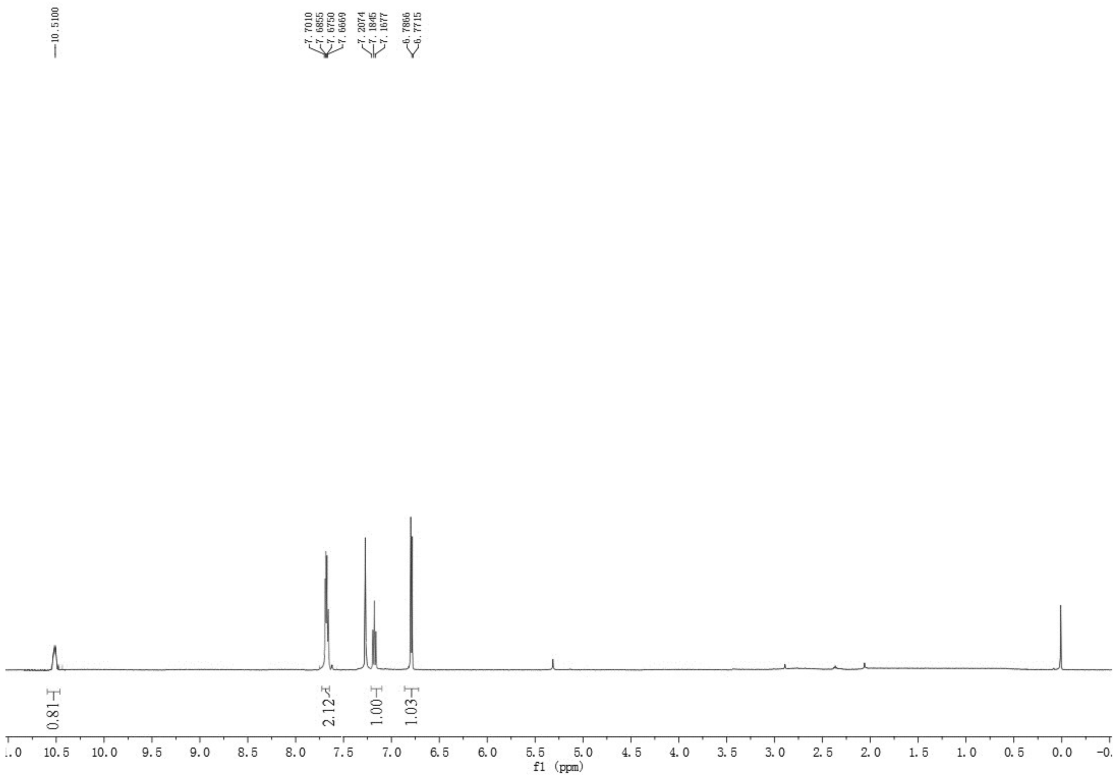


2g



7.0111
2.5327
2.3086
2.01
6.08
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

2h



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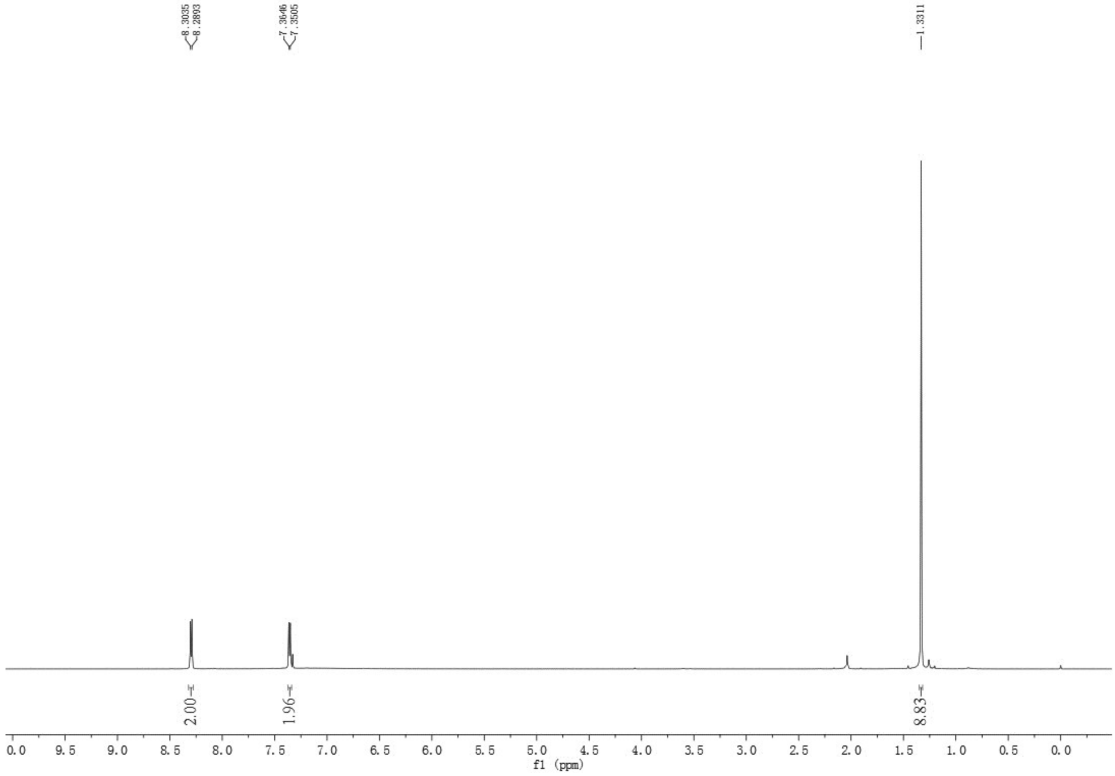
7.7010
7.6855
7.6750
7.6669
7.2074
7.1845
7.1677
6.7866
6.7715
0.81
2.12
1.00
1.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

2i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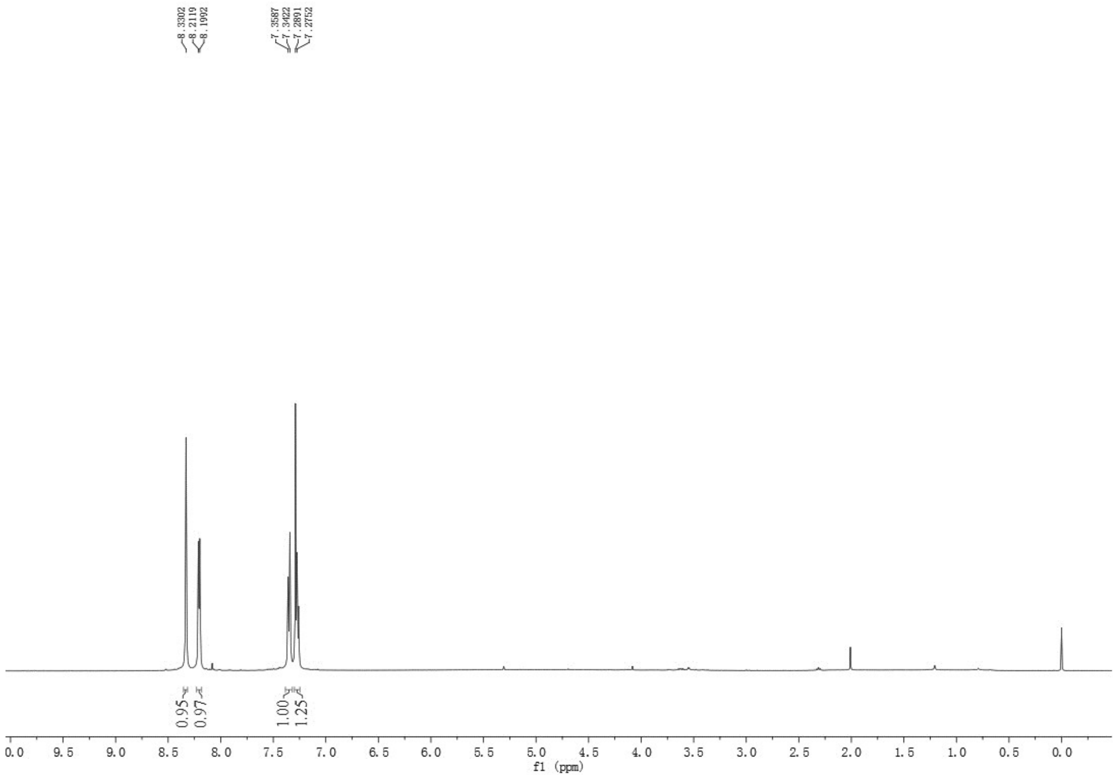
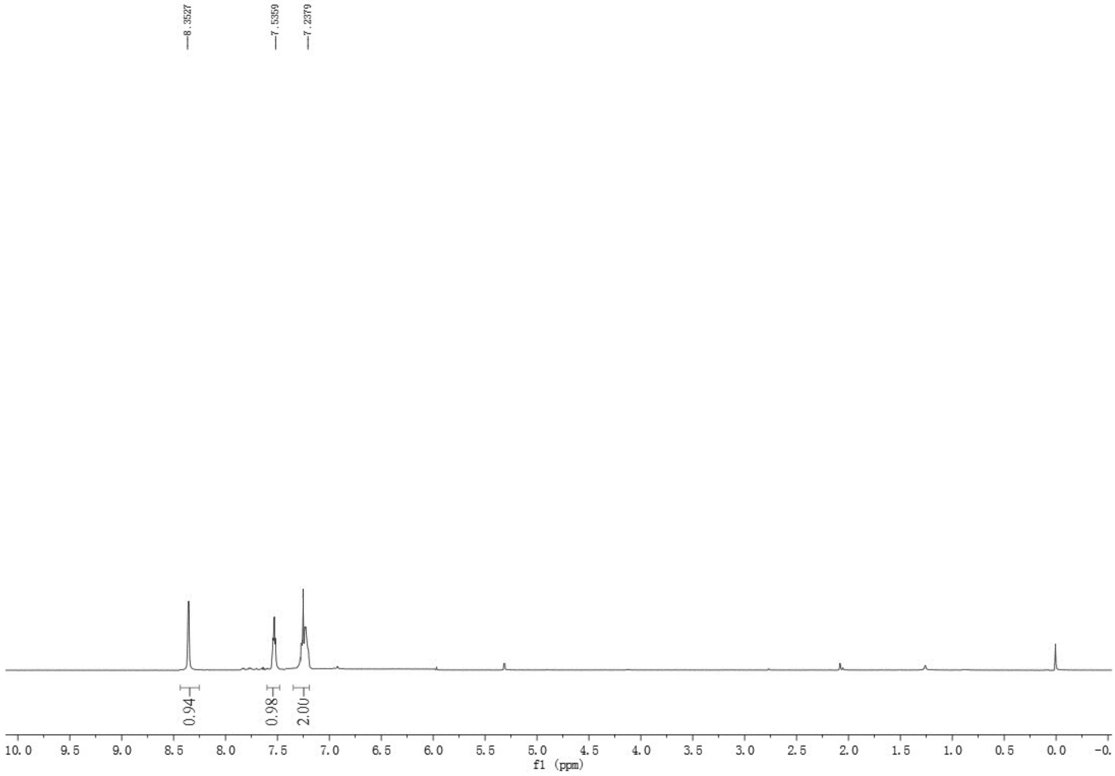
8.2893
7.3646
7.3505
1.3311
2.00
1.96
8.83
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

2j

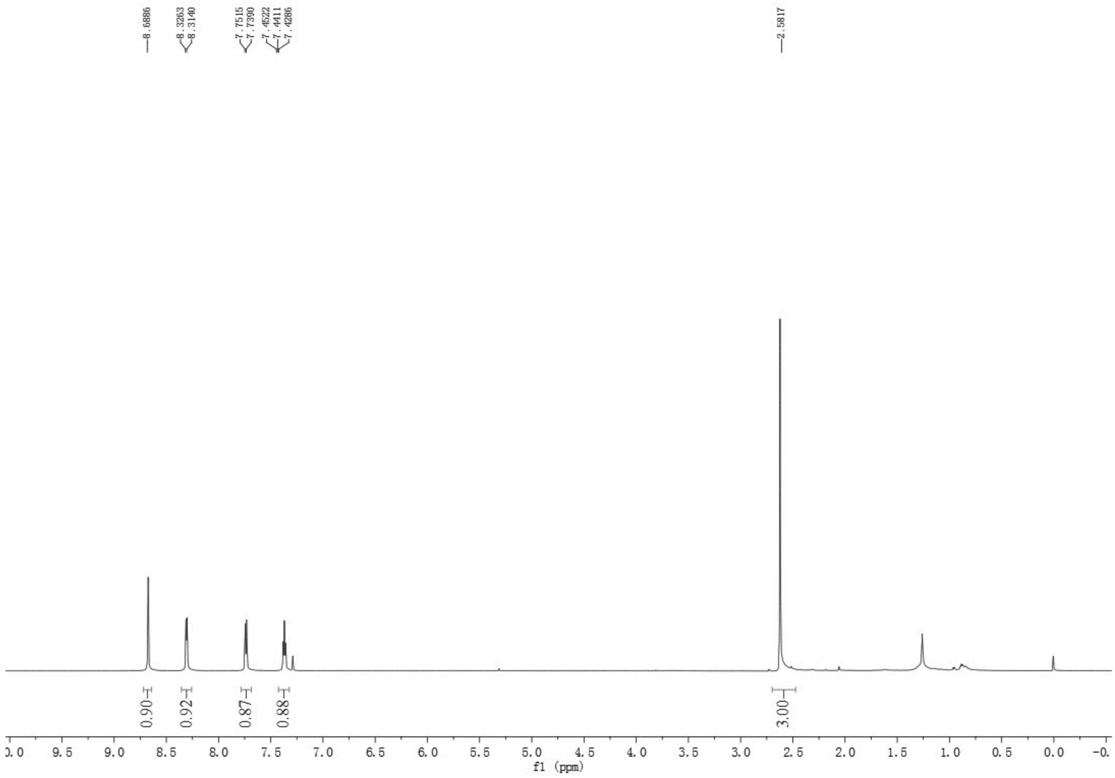

8.3302
8.2119
8.1992
7.3587
7.3422
7.2891
7.2752
0.95
0.97
1.00
1.25
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

2k



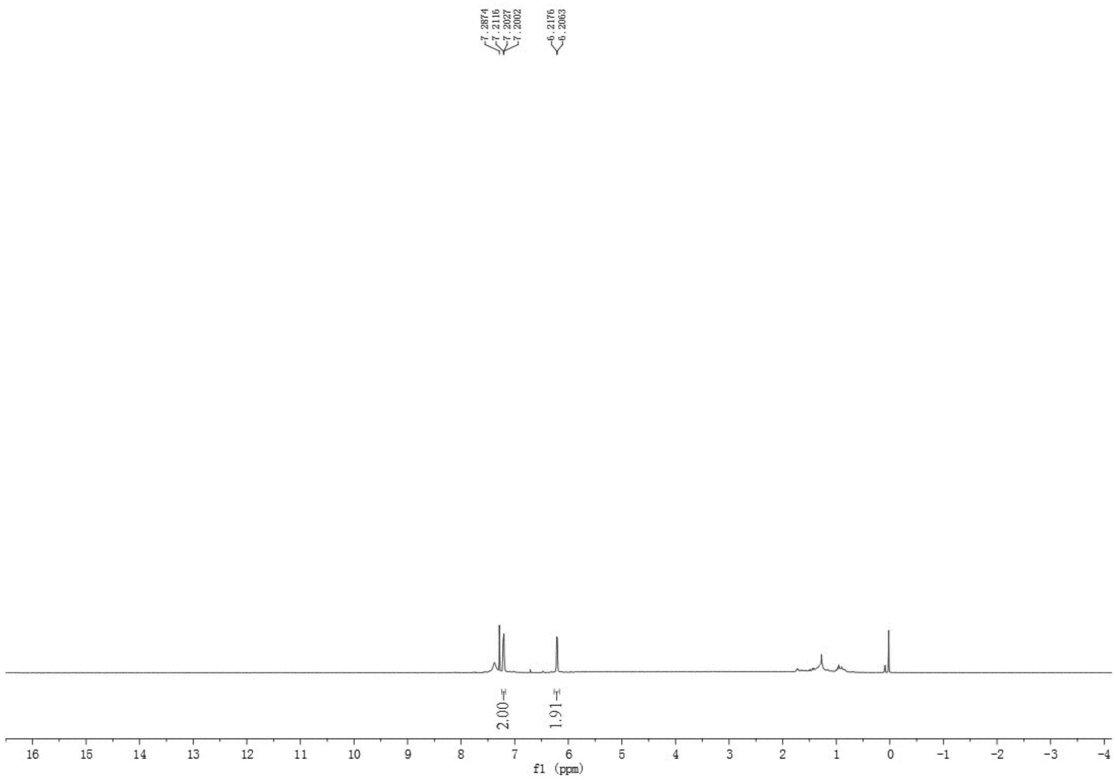
8.3527
7.5359
7.2379
0.94
0.98
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

2l

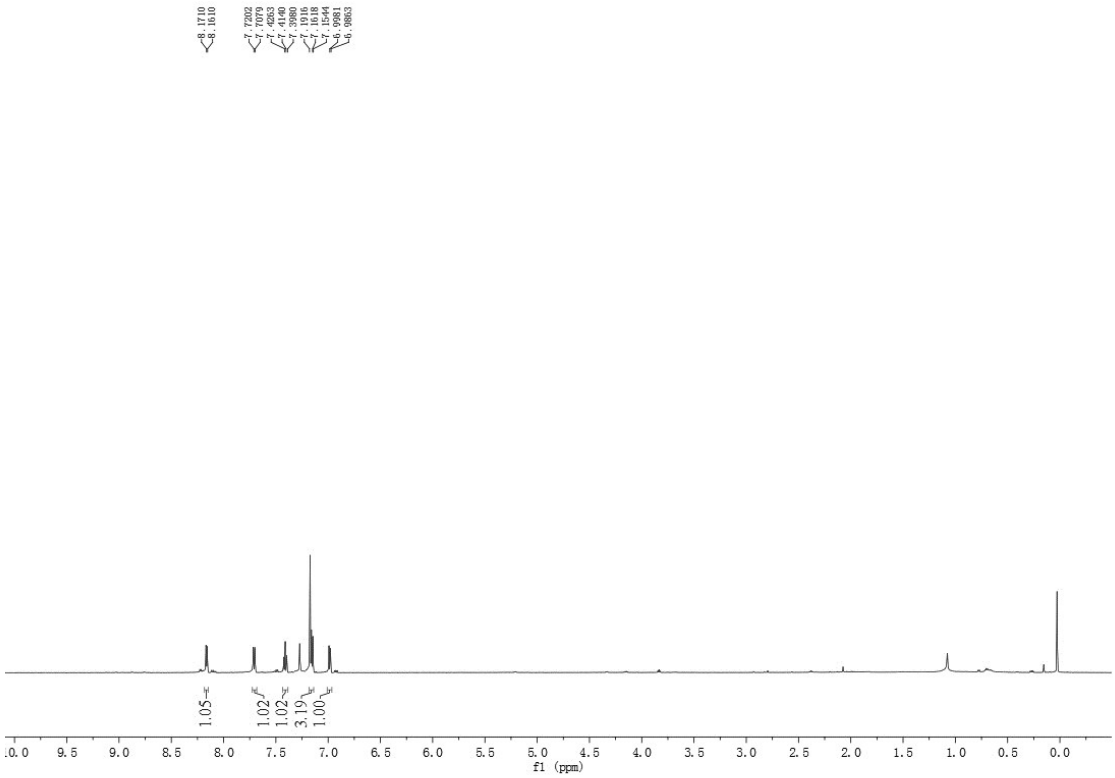


8.6886
8.3263
8.3140
7.7515
7.7390
7.4522
7.4411
7.4286
2.5817
0.90
0.92
0.87
0.88
3.00
f1 (ppm)

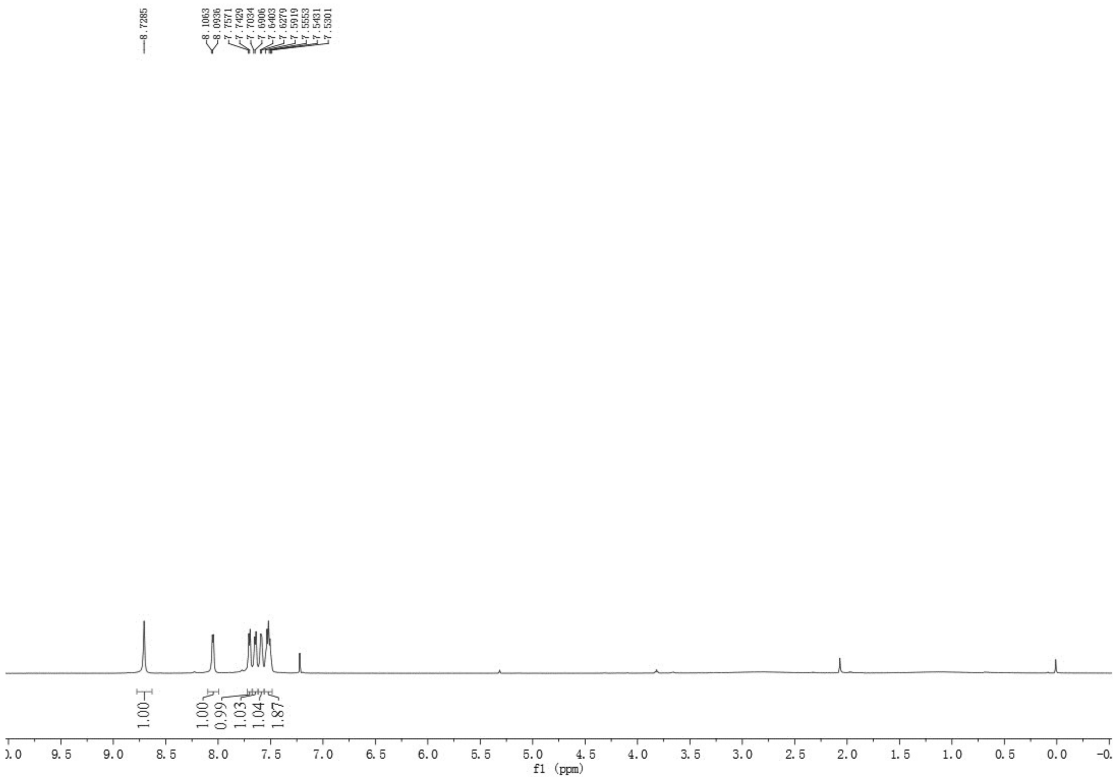
2m



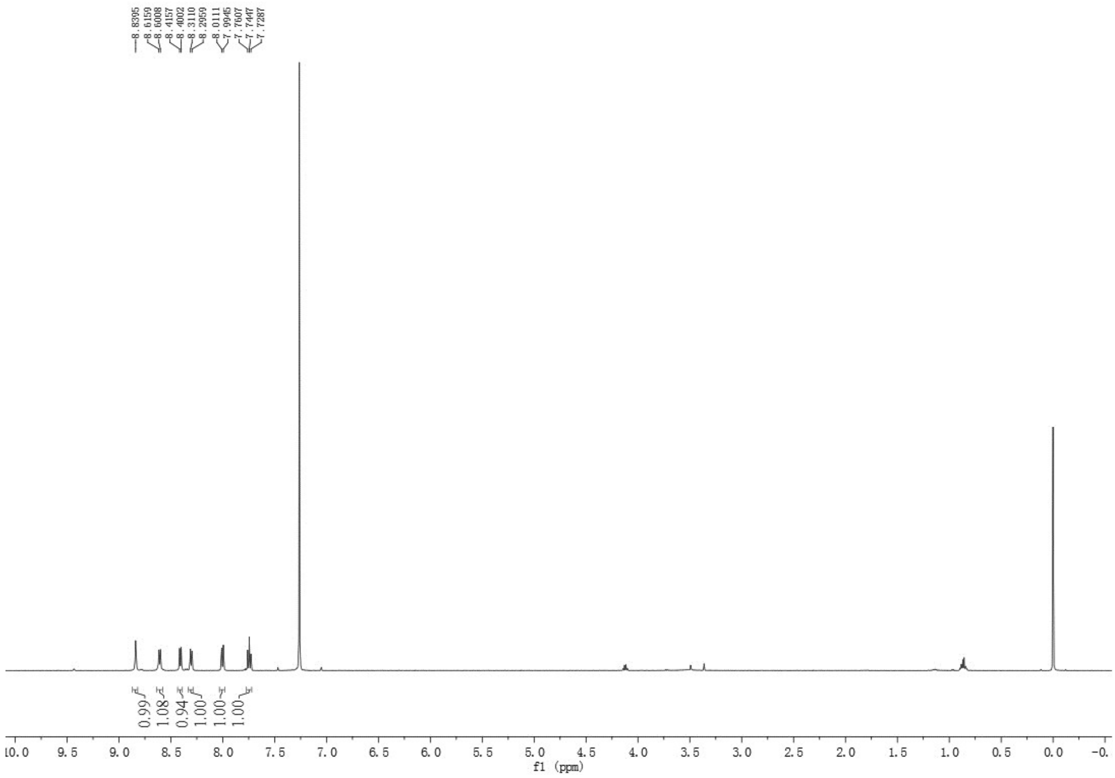
2n



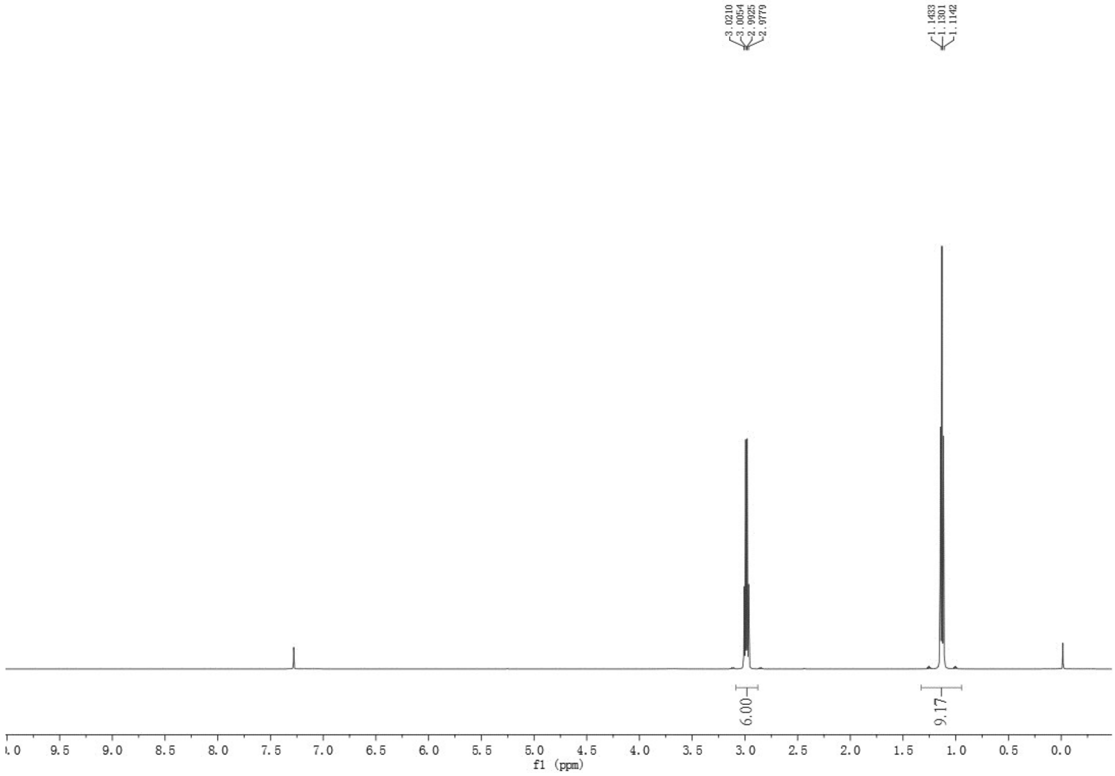
2o



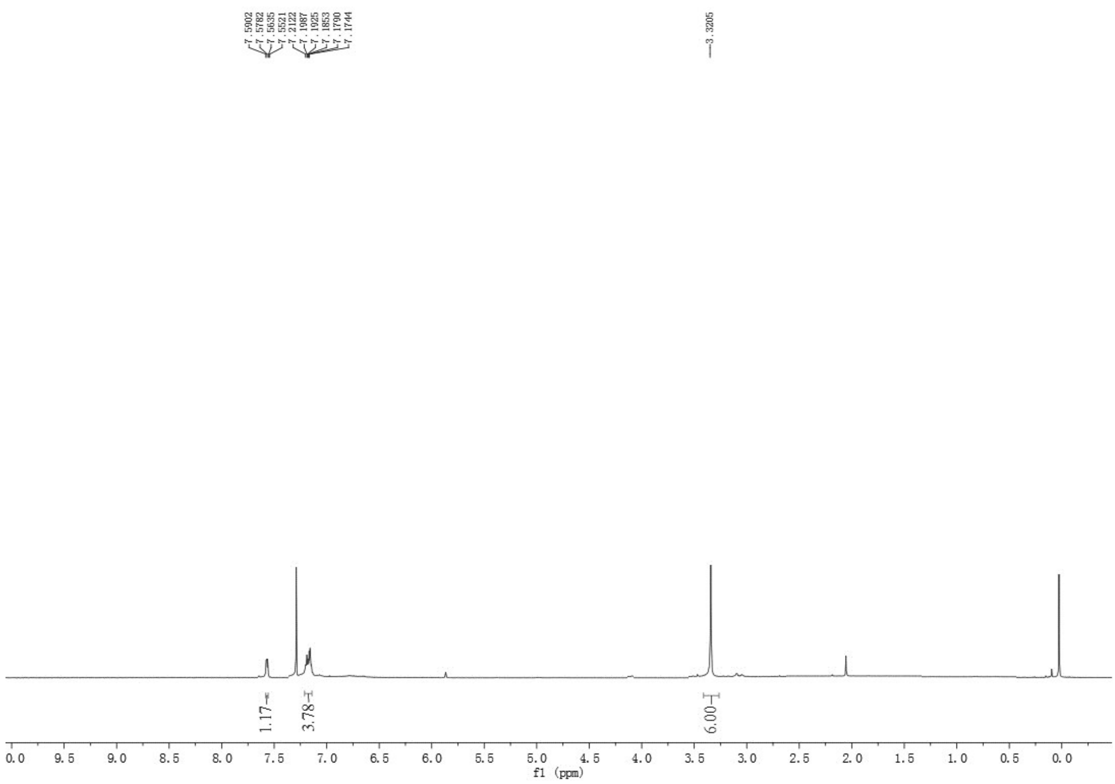
2p



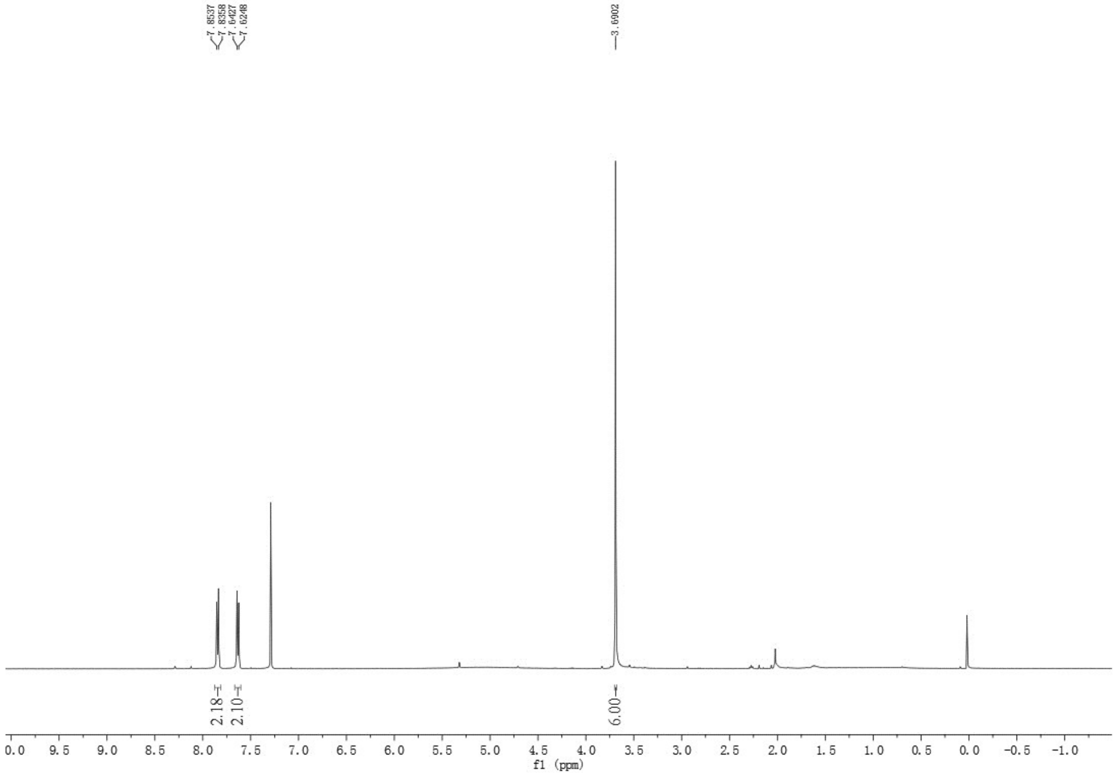
2q


3.0210
3.0054
2.9925
2.9779
1.1433
1.1301
1.1142
6.00
9.17
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

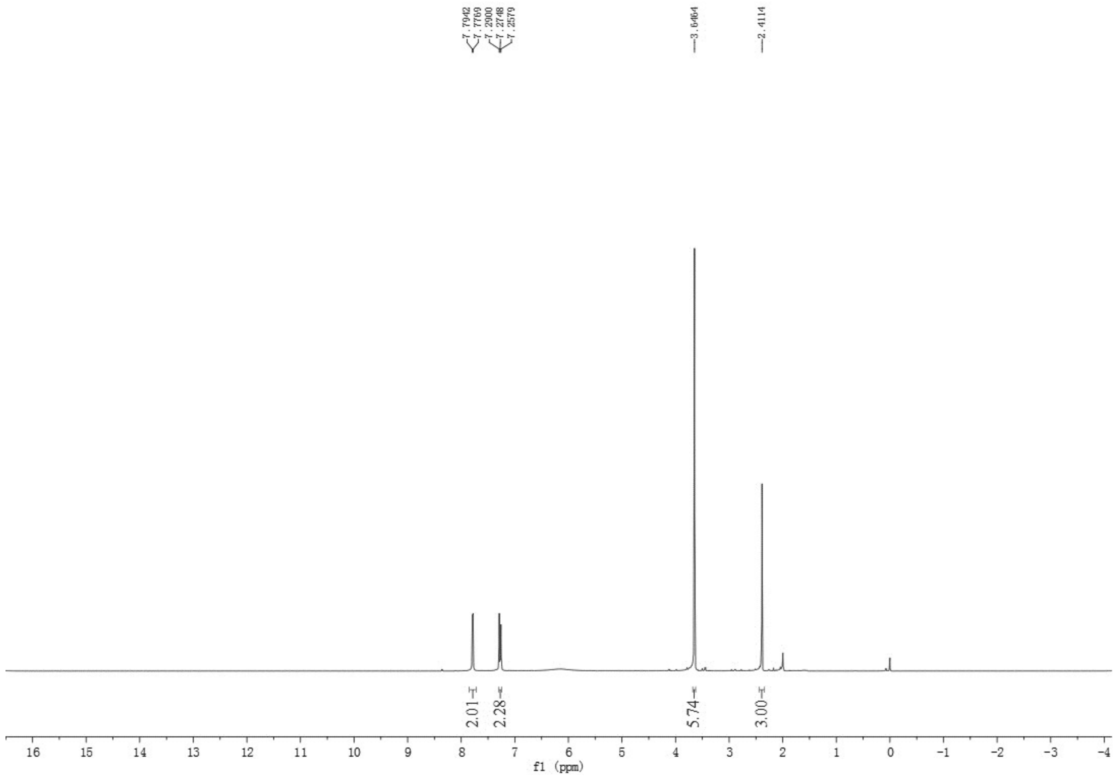
2r


7.5902
7.5782
7.5635
7.5521
7.2122
7.1987
7.1925
7.1853
7.1790
7.1744
3.3205
1.17
3.78
6.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

2s


7.8537
7.8358
7.6427
7.6248
3.6902
2.18
2.10
6.00
f1 (ppm)

2t


7.7942
7.7769
7.2900
7.2748
7.2579
3.6464
2.4114
2.01
2.28
5.74
3.00
f1 (ppm)