Supporting Information for

Metal-free aerobic oxidative coupling of amines in dimethyl sulfoxide *via* a radical pathway

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General Information

$CDCl_3$ and CD_3SOCD_3 were purchased from Cambridge Isotope Laboratory Inc; CH_3SOCH_3 was purchased from Aldrich, Acros, Alfa Aesar, TCI, and the yields in DMSO from different sources were the same; tetrahydrothiophene 1-oxide (THTO) was purchased from Alfa Aesar; all amines purchased from Aldrich or Alfa Aesar were distilled and stored at 4°C; and all other chemicals were purchased from Aldrich or Alfa Aesar unless otherwise noted and used as received. ^{1}H NMR spectra were recorded on a Bruker AVII$^+$-400 spectrometer at ambient temperature. GC-MS results were obtained by the Agilent 7890A/5975C GC/MSD system equipped with the DB-17MS (30m, 0.25mm, 0.25μm) column.

NMR spectra were measured on Bruker ARX 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz), Bruker ARX 500 (^{1}H at 500 MHz, ^{13}C at 126 MHz) nuclear magnetic resonance spectrometers. Data for ^{1}H-NMR spectra are reported as follows: chemical shift (ppm, referenced to TMS; s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, dm = doublet of multiplet, ddd = doublet of doublet of doublets, tdd = triplet of doublet of doublets, m = multiplet), coupling constant (Hz), and integration. Data for ^{13}C-NMR are reported in terms of chemical shift (ppm) relative to residual solvent peak (Acetone [$(CD_3)_2CO$]: 2.05 ppm).

General procedure for the aerobic oxidative coupling reactions

In a typical experiment, one atmosphere oxygen is pressurized to a 45 ml Schlenk flask containing amines and solvents. After the reaction mixture is heated for 24 hours, the solution is diluted with methanol to 25 mL and characterized by GC and GC-MS.

For the homo-coupling reactions: Benzylamine 0.065 g (0.6 mmol) and DMSO (1 mL) were added into a Schlenk flask with a high vacuum valve (V = 45 mL) fitting in a Radleys parallel synthesis station.[1] The sample was subjected to three freeze-pump-thaw cycles and then filled with 1 atm O_2. The solution was stirred vigorously and heated at 105 °C for 24 hours.

To obtain the GC results, after it was cooled down to room temperature, the solution was diluted with methanol to 25.00 mL for GC test. The imine products were independently synthesized by condensation of aldehydes and amines, and used as standards for GC measurements.

To obtain the isolated products, the reaction mixture was cooled to room temperature, quenched by water, and extracted with ethyl acetate. The organic phase was dried over Na_2SO_4, filtrated and concentrated. The residue was purified by flash column chromatography on silica gel to afford the final product.[S1] The compounds of P1, P4, P5, P6 can be found in the ref. S3. The compounds of P2 and P3can be found in the

ref. S4. The compound of P7 can be found in the ref. S5. The compound of P8 can be found in the ref. S6. The compounds of P9, P10, P11 can be found in the ref. S7.

For the cross-coupling reactions: benzylamine 0.065 g (0.60 mmol), 1.8 mmol of aliphatic amine and 1.0 mL of DMSO were used instead. The compounds of P12, P13, P14, P15, P16, can be found in the ref. S7.

For the oxidative coupling reactions of aromatic amines: 0.5 mmol of aromatic amines, 1.5 mmol of KOH, 1mL of DMSO, 1 atm oxygen were used instead. The solution was stirred vigorously and heated at 90 ^{o}C for 48 hours. The reaction mixture was cooled to room temperature, quenched by water, and extracted with ethyl acetate. The organic phase was dried over Na_2SO_4, filtrated and concentrated. The residue was purified by flash column chromatography (PE/EA 200:1) on silica gel to afford the final product. The corresponding spectral data can be found in the supporting information of our previous report. [S2] The compounds of P17, P18, P19, P20 can be found in the ref. S8.

Reference

[S1] See a picture of the Radleys parallel synthesis station in the supporting information: Liu L.; Yu M.; Wayland B. B.; Fu X. *Chem. Commun.* **2010**, *46*, 6353.

[S2] Zhang, C.; Jiao, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 6174.

[S3] Zhang, E.; Tian, H.; Xu, S.; Yu, X.; Xu, Q. *Org. Lett.* **2013**, *15*, 2704.

[S4] Marui, K.; Nomoto, A.; Michio, U.; Ogawa, A. *Tetrahedron Lett.* **2015**, *56*, 1200.

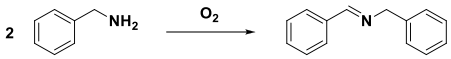
[S5] Semmelhack, M. F.; Schmid, C. R. *J. Am. Chem. Soc*. **1983**, *105*, 6732.

[S6] Dahn, H.; Solms, U.; Zoller, P. *Helv.* **1952**, *35*, 1348.

[S7] Liu, L.; Zhang, S.; Fu, X.; Yan, C.-H. *Chem. Commun.* **2011**, *47*, 10148.

[S8] Kumari, S.; Shekhar, a.; Pathak, D. D. *RSC Adv.*, **2014**, *4*, 61187.

Table 1S. Solvent Effect of Oxidation of Benzylamine[a]



Entry	Solvent	T (°C)	Gas	C (%)[b]	Y (%)[b]	R[c]
1	DMSO	100	O_2	82	80	0.9
2	DMSO-D^6	100	O_2	88	82	-
3	THTO	100	O_2	96	84	-
4	DMF	100	O_2	66	24[d]	-
5	$THTO_2$	100	O_2	12	12	-
6	THS	100	O_2	11	11	-
7	PhSMe	100	O_2	4	4	-
8	PhOMe	100	O_2	11	11	-
9	PhCN	100	O_2	3	3	-
10	CH_3CN	100	O_2	10	10	-
11	Toluene	100	O_2	5	5	-
12	EtOH	100	O_2	12	12	-

[a] Reaction conditions: benzylamine 0.6 mmol, solvent 1 ml, P_{gas} = 1 atm, 24 hours. THTO = tetrahydrothiophene 1-oxide, $THTO_2$ = sulfolane, THS = tetrahydrothiophene. [b] C = conversion, Y = yield, GC results. [c] R = n (sulfone) / n (imine). [d] 42% of $PhCH_2NHCHO$ was detected.

We observed no radical signals by mixing benzyl amine and DMSO at 25 °C (Figure 1S, a). However, after heating the solution (0.6 M benzyl amine in DMSO) under 1 atmosphere of oxygen at 110 °C for 7 hours, we observed a weak radical signal (anisotropic *g*-value equals 2.004) by EPR method (Figure 1S, b). Meanwhile, 7% of N-benzylidene-1-benzylamine was formed.

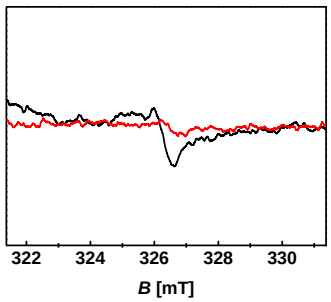
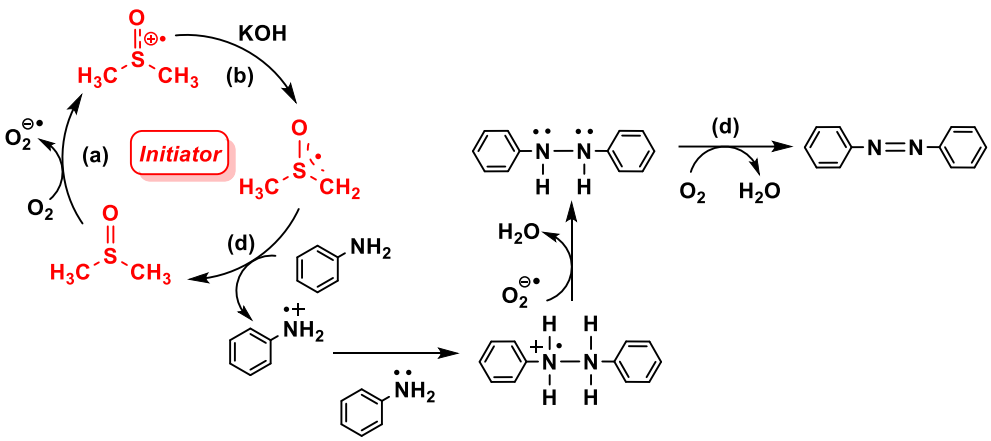


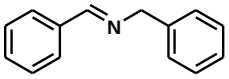
Figure 1S. X-band EPR spectrum of radicals formed in DMSO after adding benzylamine. Experimental details: 77 K, frequency 9.0851 GHz, microwave power 1 mW. (a) red: 7 hours at 25 °C; (b) black: 7 hours at 110 °C.



Scheme S1. Proposed mechanism for synthesis of azo compounds.

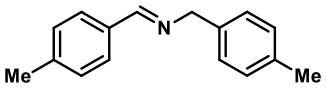
Experimental and Spectral Data

P1



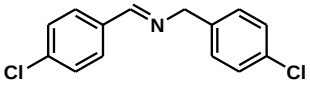
Colorless oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 4.80 (s, 2H), 7.19-7.32 (m, 1H), 7.32-7.33 (m, 4H), 7.37-7.41 (m, 3H), 7.76-7.78 (m, 2H), 8.36 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 65.1, 127.1, 128.1, 128.4, 128.6, 128.7, 130.8, 136.3, 139.4, 162.0.[1]

P2



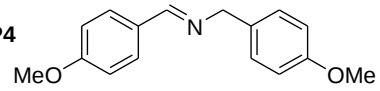
White solid, m. p. = 82-84 ℃. ^{1}H NMR ($CDCl_3$, 400MHz): δ 2.32 (s, 3H), 2.36 (s, 3H), 4.75 (s, 2H), 7.13 (d, J = 7.8 Hz, 2H), 7.20-7.22 (m, 4H), 7.65 (d, J = 8.1 Hz, 2H), 8.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 21.2, 21.6, 64.9, 128.1, 128.4, 129.3, 129.4, 133.8, 136.5, 136.6, 141.0, 161.7.[2]

P3



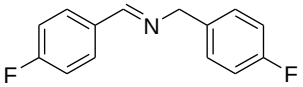
White solid, m. p. = 62-63 ℃. ^{1}H NMR ($CDCl_3$, 400MHz): δ 4.77 (s, 2H), 7.29-7.23 (m, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 7.71 (d, J = 8.4 Hz, 2H), 8.34 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 64.2, 128.7, 129.0, 129.3, 129.5, 132.9, 134.5, 136.9, 137.6, 160.9.[2]

P4



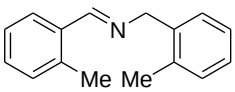
Colorless oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 3.76 (s, 3H), 3.79 (s, 3H), 4.70 (s, 2H), 6.86 (d, J = 8.6 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H), 7.70 (d, J = 8.7 Hz, 2H), 8.28 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 55.3, 55.4, 64.5, 114.0, 114.1, 129.2, 129.3, 129.9, 131.8, 158.7, 161.0, 161.8.[1]

P5



Light yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 4.75 (s, 2H), 6.99-7.04 (m, 2H), 7.06-7.10 (m, 2H), 7.26-7.30 (m, 2H), 7.74-7.77 (m, 2H), 8.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 64.2, 115.3, 115.5, 115.7, 115.9, 129.5, 129.6, 130.2, 130.3, 132.5, 132.5, 135.07, 135.10, 160.6, 160.9, 163.26, 163.3, 165.8. [1]

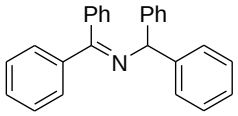
P6



[1] Zhang, E.; Tian, H.; Xu, S.; Yu, X.; Xu, Q. *Org. Lett.* **2013**, *15*, 2704.
[2] Marui, K.; Nomoto, A.; Michio, U.; Ogawa, A. *Tetrahedron Lett.* **2015**, *56*, 1200.

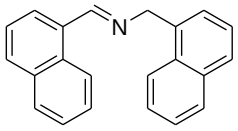
Light yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 2.38 (s, 3H), 2.49 (s, 3H), 4.81 (s, 2H), 7.14-7.30 (m, 7H), 7.90-7.92 (m, 1H), 8.65 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 19.4, 19.5, 63.4, 126.2, 126.3, 127.2, 127.8, 128.4, 130.2, 130.3, 130.9, 134.4, 136.2, 137.7, 137.8, 160.6. [1]

P7



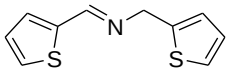
White solid, m. p. = 157-158 ℃. ^{1}H NMR ($CDCl_3$, 400MHz): δ 5.55 (s, 1H), 7.06-7.08 (m, 2H), 7.16-7.20 (m, 2H), 7.24-7.28 (m, 4H), 7.31-7.37 (m, 7H), 7.39-7.43 (m, 3H), 7.74-7.76 (m, 2H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 70.0, 126.8, 127.7, 127.9, 128.1, 128.47, 128.54, 128.6, 128.9, 130.2, 136.9, 140.0, 145.0, 167.0.[3]

P8



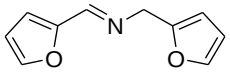
Light yellow solid, m. p. = 157-158 ℃. ^{1}H NMR ($CDCl_3$, 400MHz): δ 5.40 (s, 2H), 7.44-7.58 (m, 7H), 7.79-7.93 (m, 5H), 8.24 (d, J = 8.3 Hz, 1H), 8.93 (d, J = 8.4 Hz, 1H), 9.07 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 63.4, 124.1, 124.6, 125.4, 125.8, 125.8, 126.0, 126.2, 126.3, 127.3, 128.0, 128.75, 128.84, 129.3, 131.3, 131.5, 131.8, 131.9, 134.0, 134.0, 135.7, 162.1[4].

P9



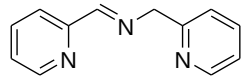
Light yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 4.93 (s, 2H), 7.00 – 6.94 (m, 2H), 7.05 (dd, J = 4.8, 3.8 Hz, 1H), 7.22 (dd, J = 4.9, 1.2 Hz, 1H), 7.31 (d, J = 3.5 Hz, 1H), 7.39 (d, J = 5.0 Hz, 1H), 8.40 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 58.6, 124.9, 125.3, 127.0, 127.5, 129.4, 131.0, 141.7, 142.2, 155.5.[5]

P10



Yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 4.75 (s, 2H), 6.26-6.27 (m, 1H), 6.33-6.34 (m, 1H), 6.45-6.47 (m, 1H), 6.77-6.78 (m, 1H), 7.36-7.37 (m, 1H), 7.50 (s, 1H), 8.11 (m, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 56.9, 107.9, 110.4, 111.7, 114.5, 142.3, 145.0, 151.3, 151.5, 151.9.[5]

P11



Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.67 (d, J = 4.8 Hz, 1H), 8.59 (d, J = 4.9 Hz, 1H), 8.57 (s, 1H), 8.09 (d, J = 7.9 Hz, 1H), 7.75 (td, J = 7.7 and 1.6 Hz, 1H), 7.68 (td, J = 7.7 and 1.8 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.33 (ddd, J = 7.4, 4.9 and 1.0 Hz, 1H), 7.29 (s, 1H), 5.03 (d, J = 0.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 66.7, 121.6, 122.2, 122.5, 125.0, 136.6, 136.8, 149.5, 149.6, 154.5, 158.9, 164.0.[5]

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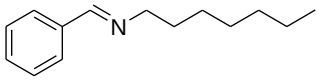
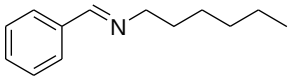
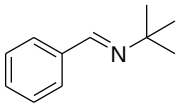
[3] Semmelhack, M. F.; Schmid, C. R. *J. Am. Chem. Soc.* **1983**, *105*, 6732.
[4] Dahn, H.; Solms, U.; Zoller, P. *Helv.* **1952**, *35*, 1348.
[5] Liu, L.; Zhang, S.; Fu, X.; Yan, C.-H. *Chem. Commun.* **2011**, *47*, 10148.

P12 

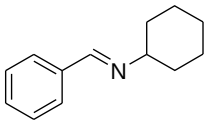
Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 6.7 Hz, 2H), 1.28-1.35 (m, 8H), 1.66-1.73 (m, 2H), 3.59 (t, J = 7.0 Hz, 1H), 7.36-7.41 (m, 3H), 7.70-7.74 (m, 2H), 8.26 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2, 22.8, 27.5, 29.3, 31.1, 32.0, 61.9, 128.1, 128.7, 130.5, 136.6, 160.8.[5]

P13 

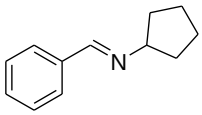
Light yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 0.89 (t, J = 6.8 Hz, 3H), 1.29-1.38 (m, 6H), 1.66-1.73 (m, 2H), 3.61 (t, J = 7.1 Hz, 2H), 7.39 (s, 1H), 7.41 (d, J = 3.0 Hz, 2H), 7.70-7.73 (m, 2H), 8.26 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 14.19, 22.74, 27.16, 31.02, 31.80, 61.94, 128.13, 128.67, 130.53, 136.52, 160.79.[5]

P14 

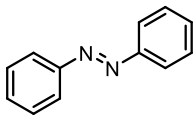
Light yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.30 (s, 2H), 7.36-7.40 (m, 3H), 7.72-7.74 (m, 2H), 8.27 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 29.9, 57.3, 128.0, 128.6, 130.3, 137.3, 155.3.[5]

P15 

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.20-1.42 (m, 3H), 1.54-1.75 (m, 5H), 1.80-1.85 (m, 2H), 3.14-3.22 (m, 1H), 7.36-7.38 (m, 3H), 7.70-7.73 (m, 2H), 8.29 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 24.9, 25.8, 34.5, 70.1, 128.1, 128.6, 130.4, 136.7, 158.6.[5]

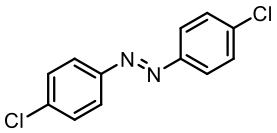
P16 

Light yellow oil. ^{1}H NMR ($CDCl_3$, 400MHz): δ 1.61-1.75 (m, 4H), 1.85-1.95 (m, 4H), 3.72-3.78 (m, 1H), 7.37-7.39 (m, 3H), 7.70-7.73 (m, 2H), 8.28 (s, 1H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 24.75, 34.50, 71.83, 128.00, 128.49, 130.22, 136.62, 158.49.[5]

P17 

Orange solid, m. p. = 65-66 ℃. ^{1}H NMR ($CDCl_3$, 400MHz): δ 7.47-7.51 (m, 4H), 7.85-7.88 (m, 4H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 150.8, 137.2, 129.4, 124.2.[6]

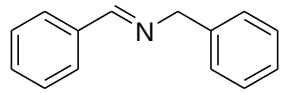
[6] Kumari, S.; Shekhar, a.; Pathak, D. D. *RSC Adv.*, **2014**, *4*, 61187.

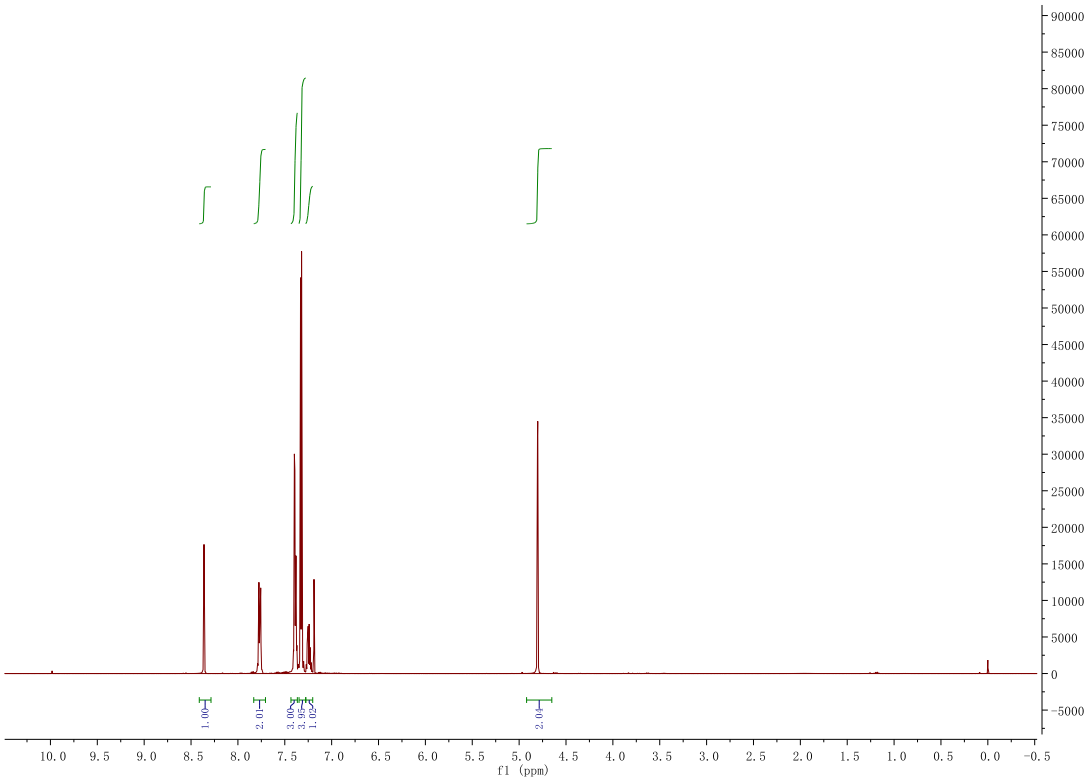
P18 

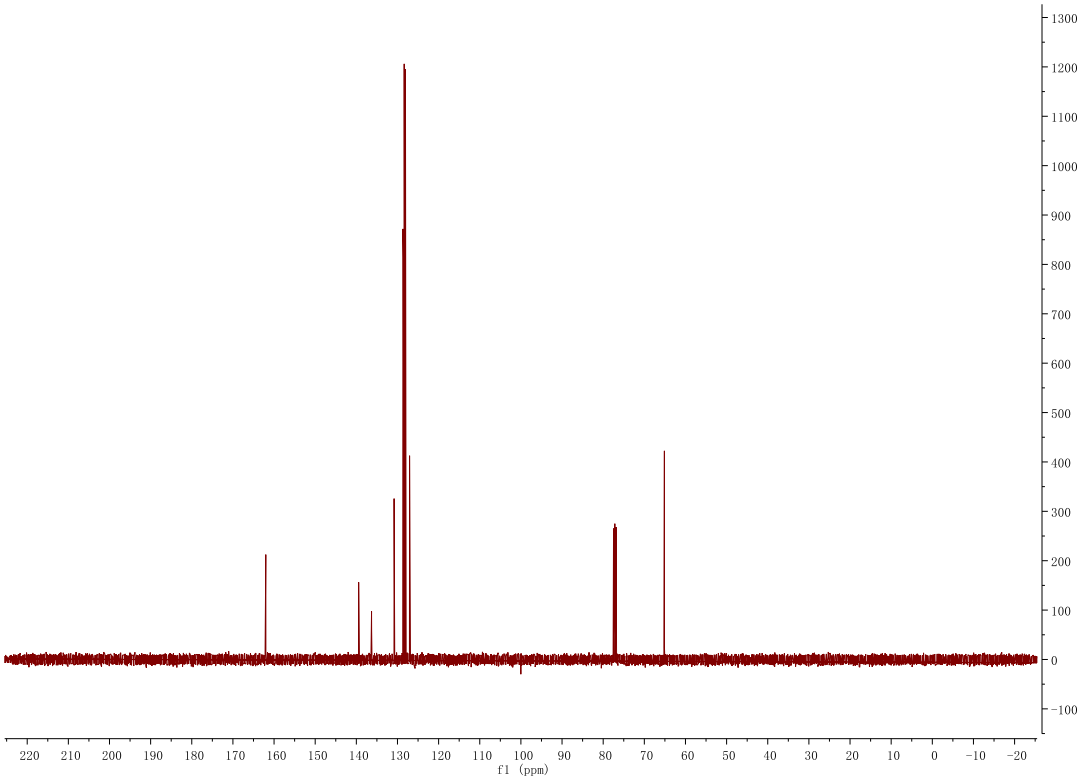
Orange solid, m. p. = 184-185 ℃.^{1}H NMR ($CDCl_3$, 400MHz): δ 7.45-7.54 (m, 6H), 7.91-7.94 (m, 4H). ^{13}C NMR ($CDCl_3$, 100MHz): δ 152.7, 131.0, 129.1, 122.9.[6]

NMR Spectra

P1







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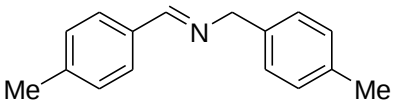

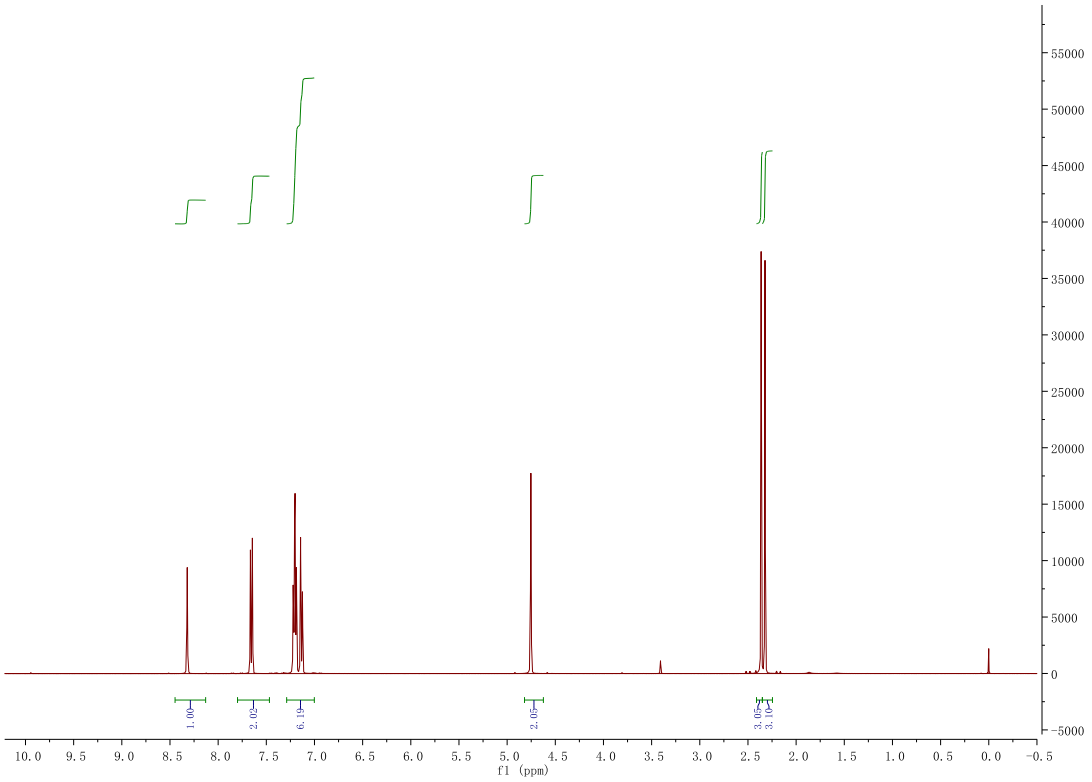

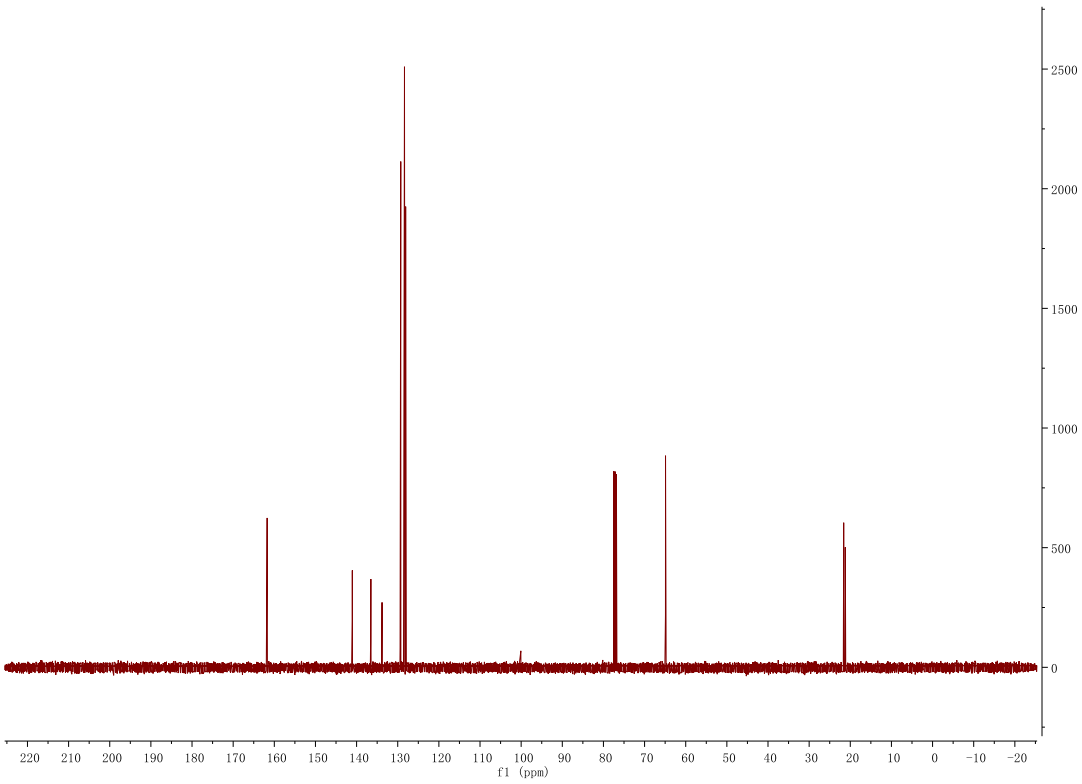

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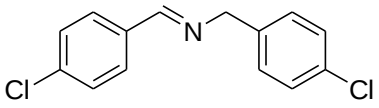

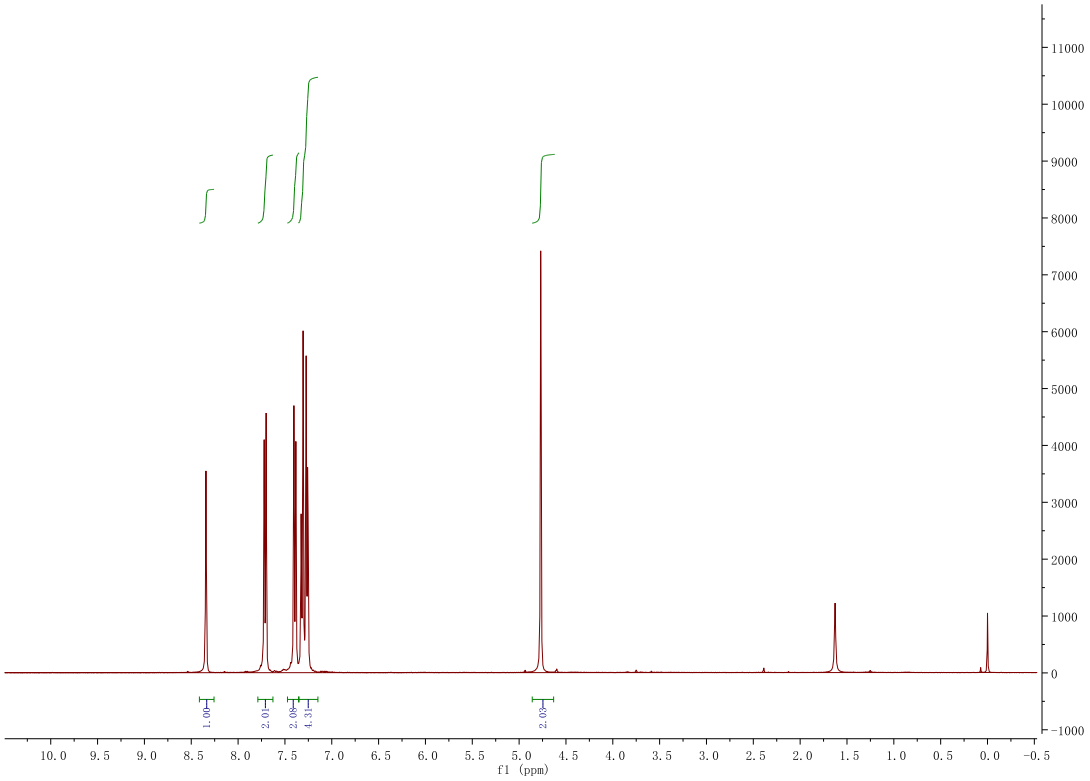

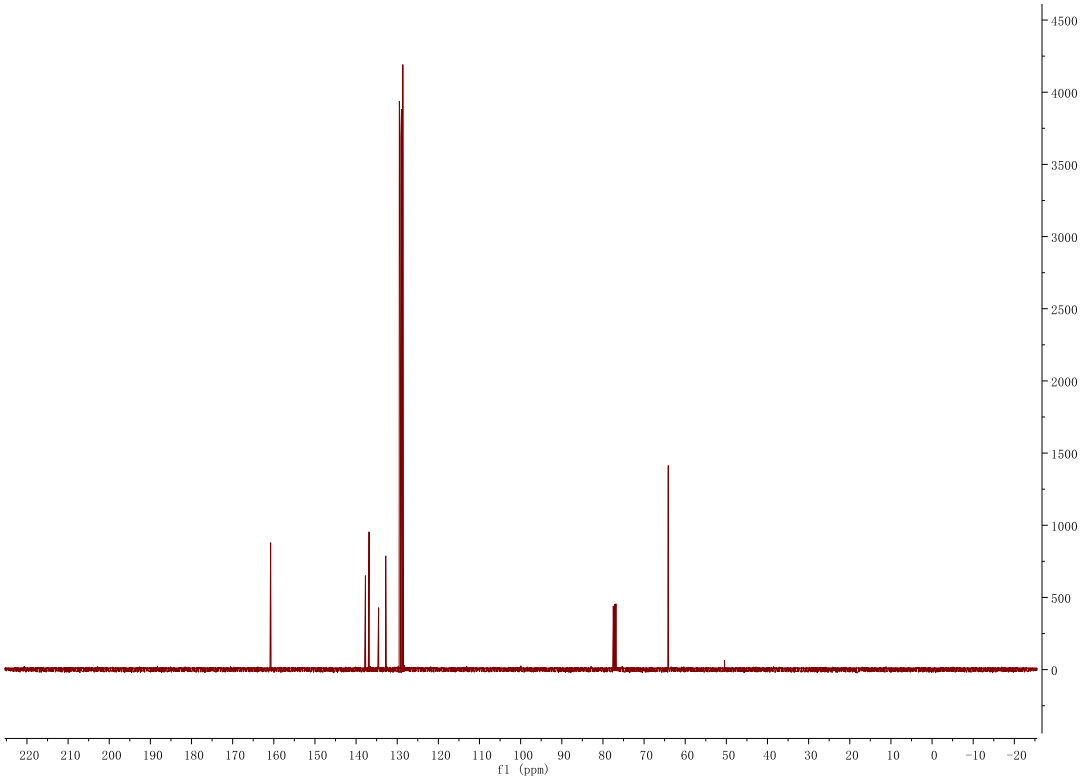

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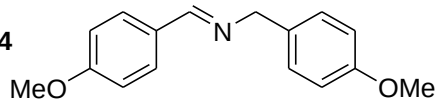

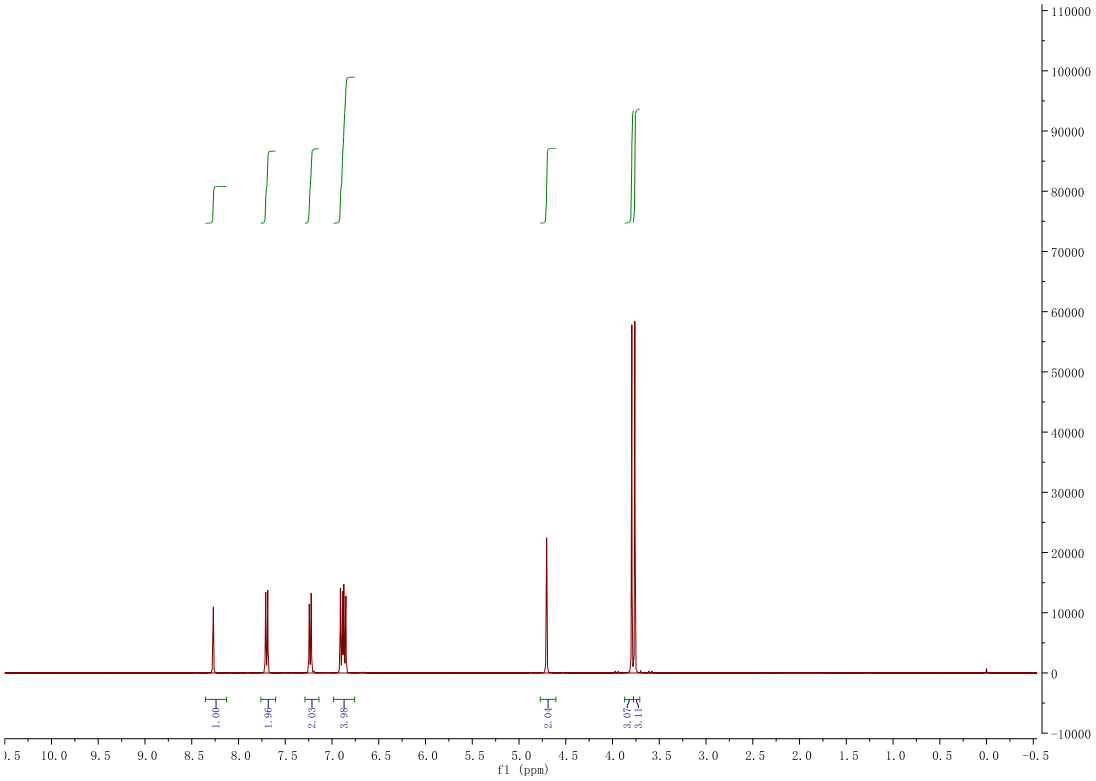

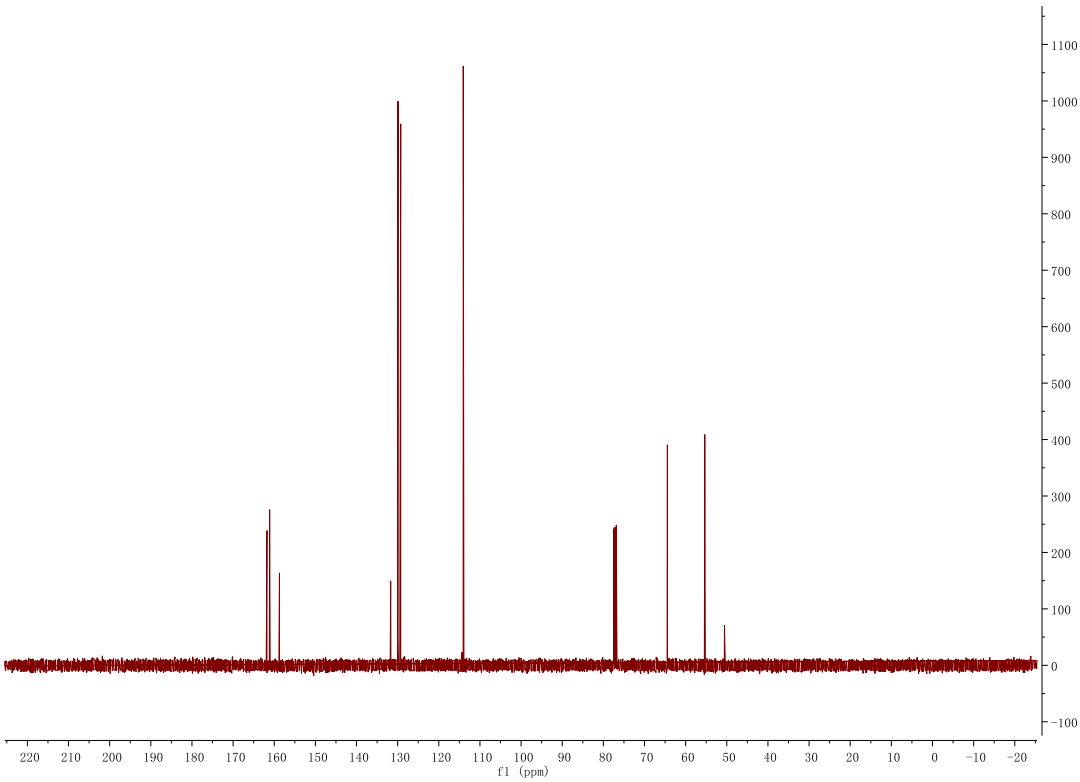

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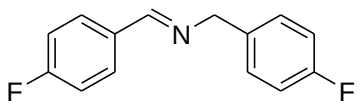

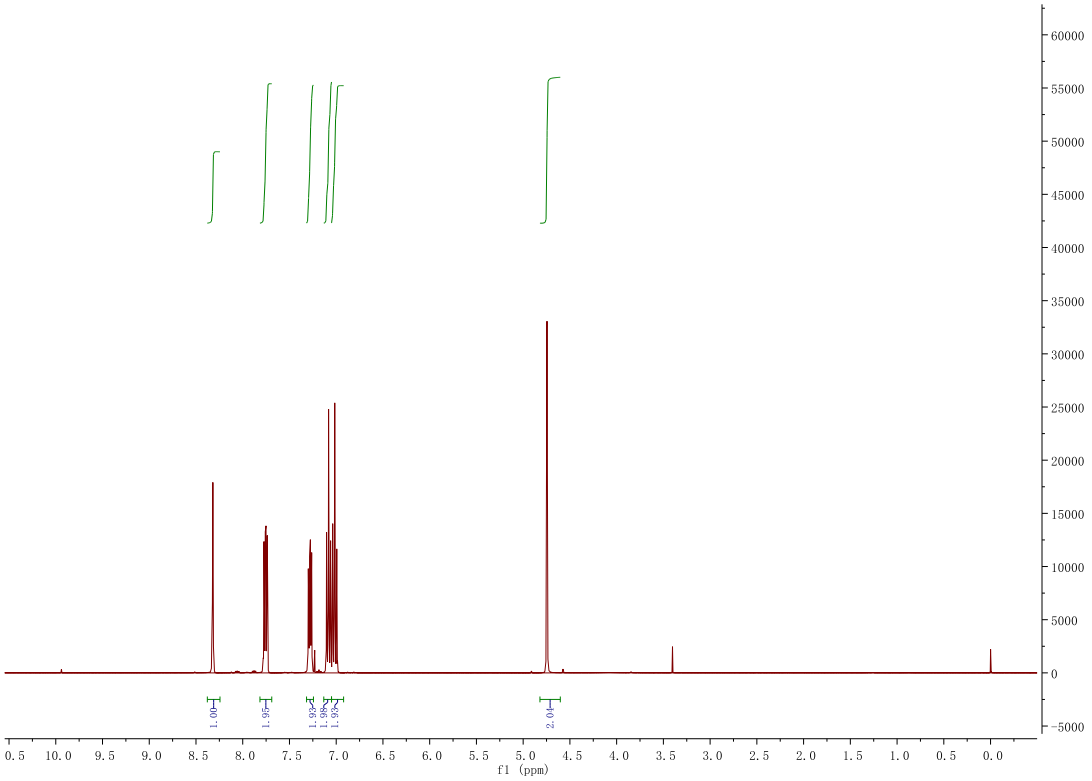

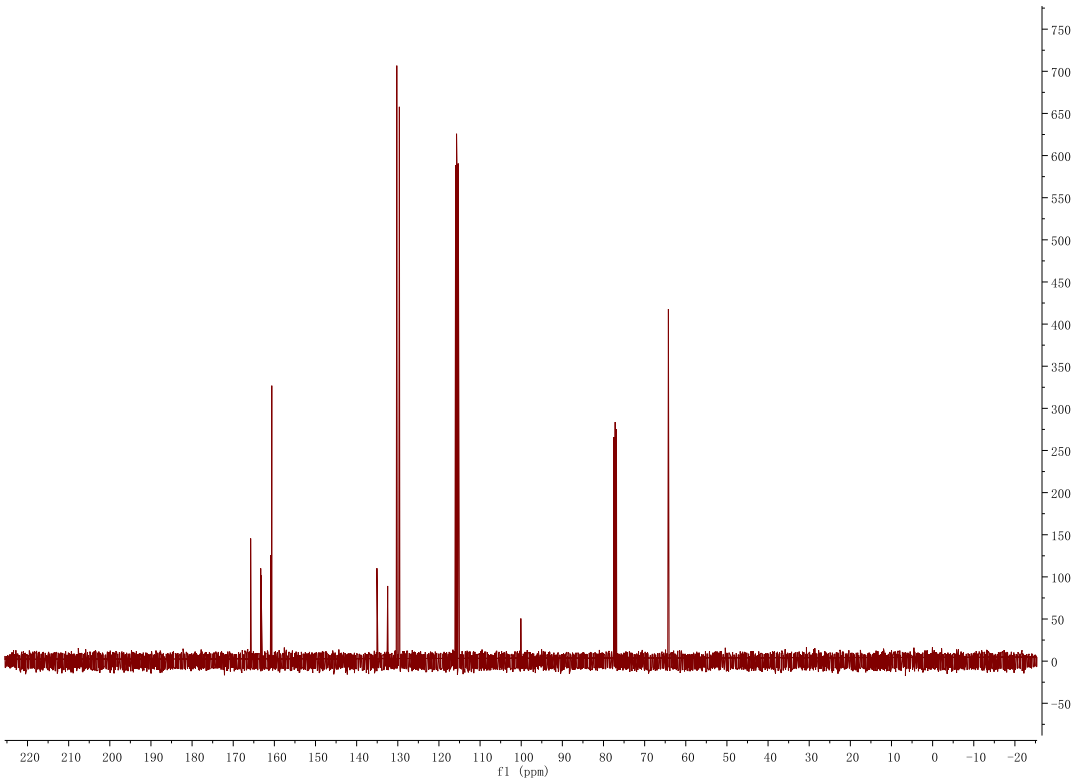

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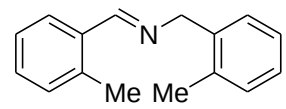

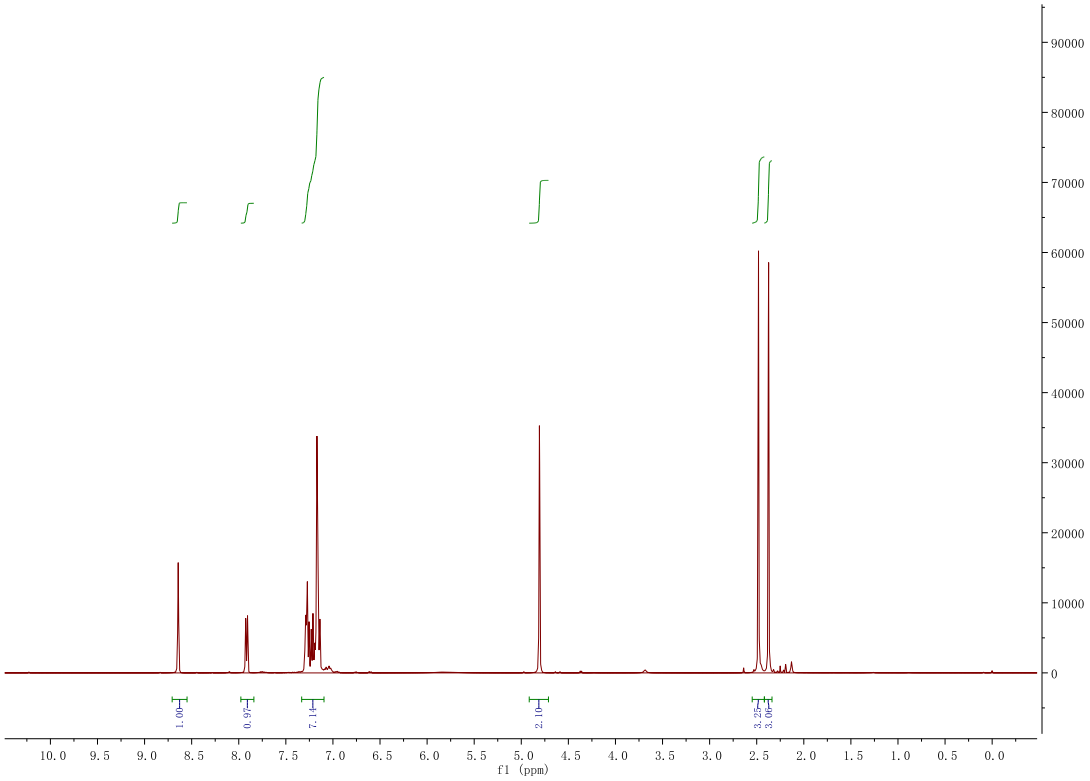

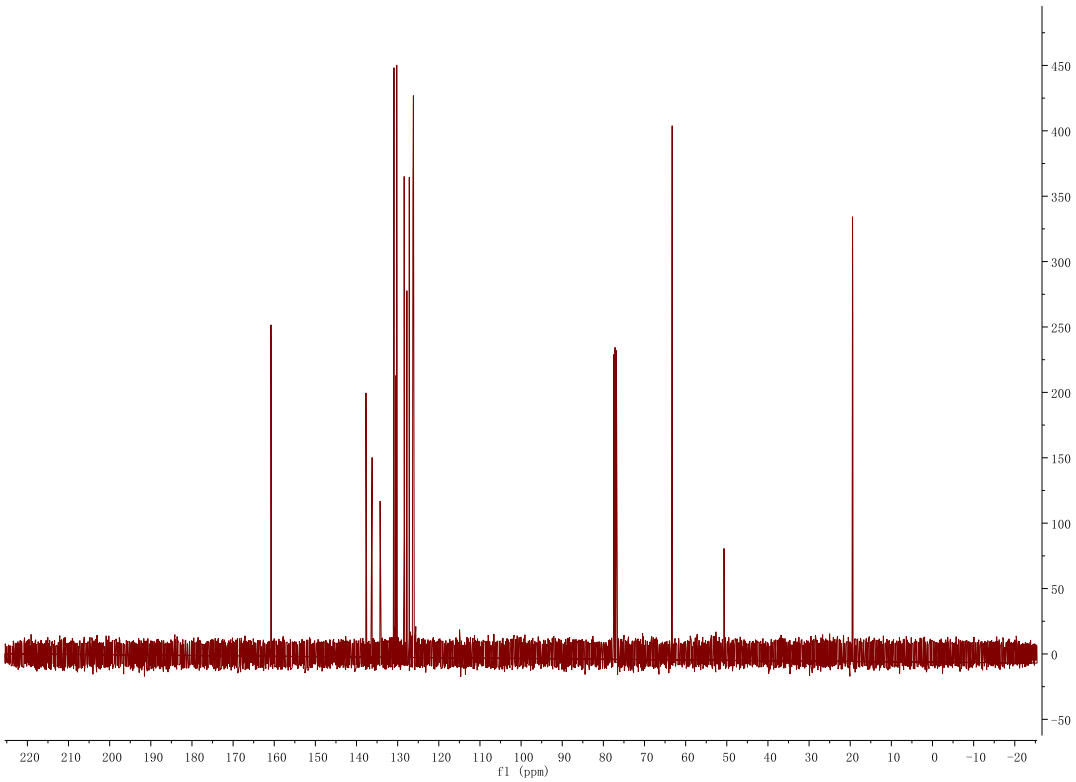

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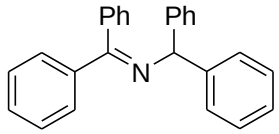

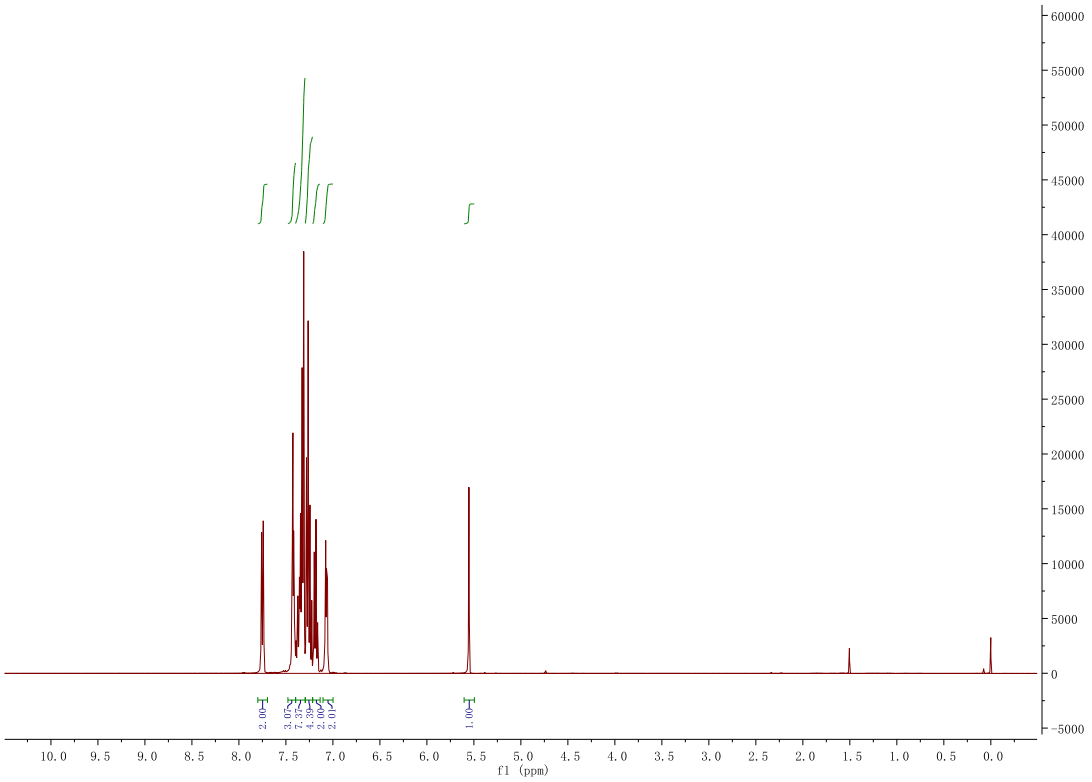

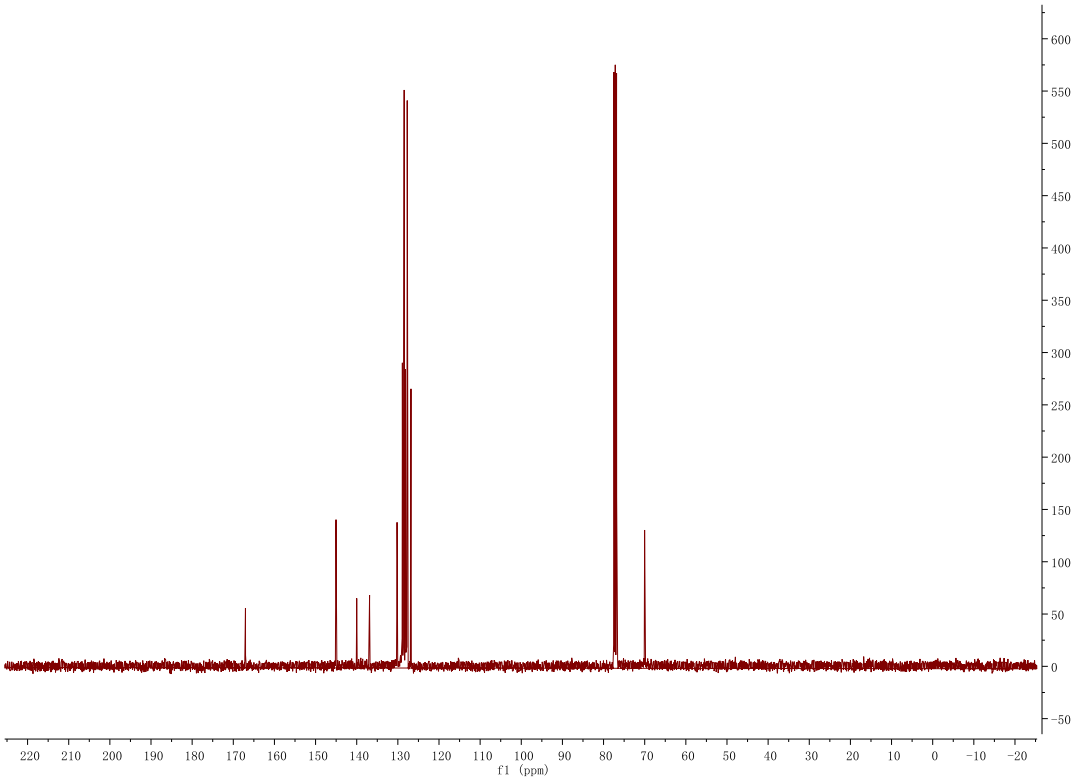

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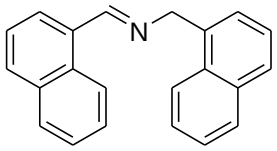
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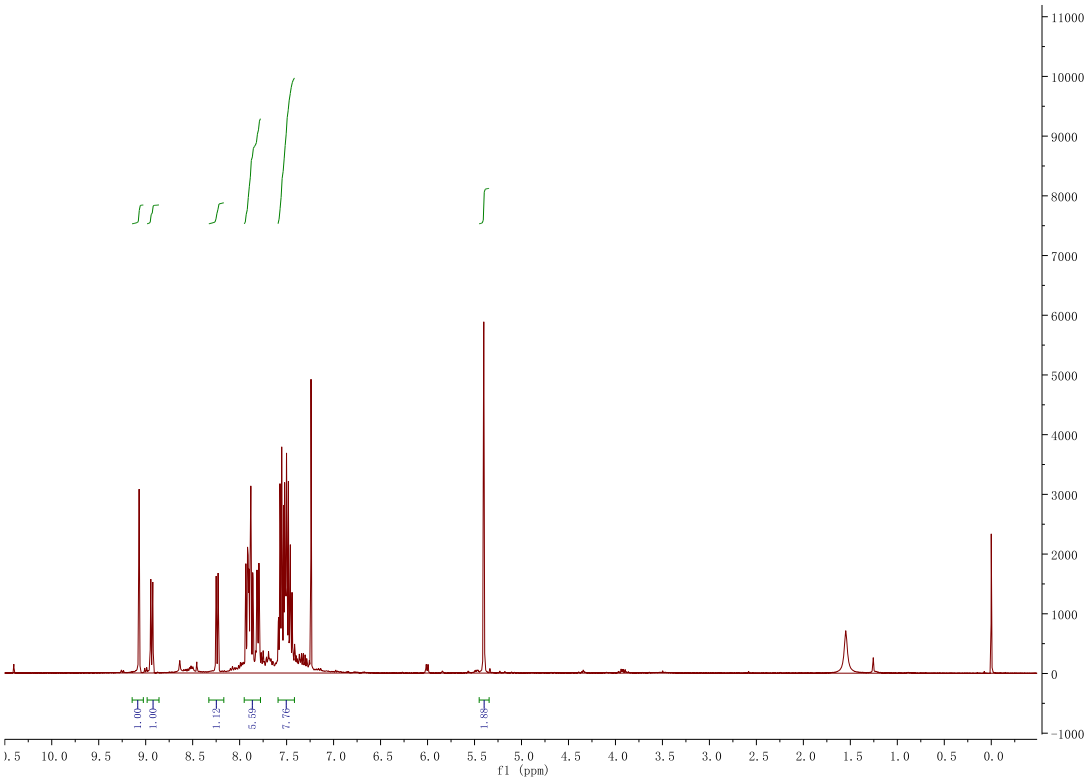
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8000
7000
6000
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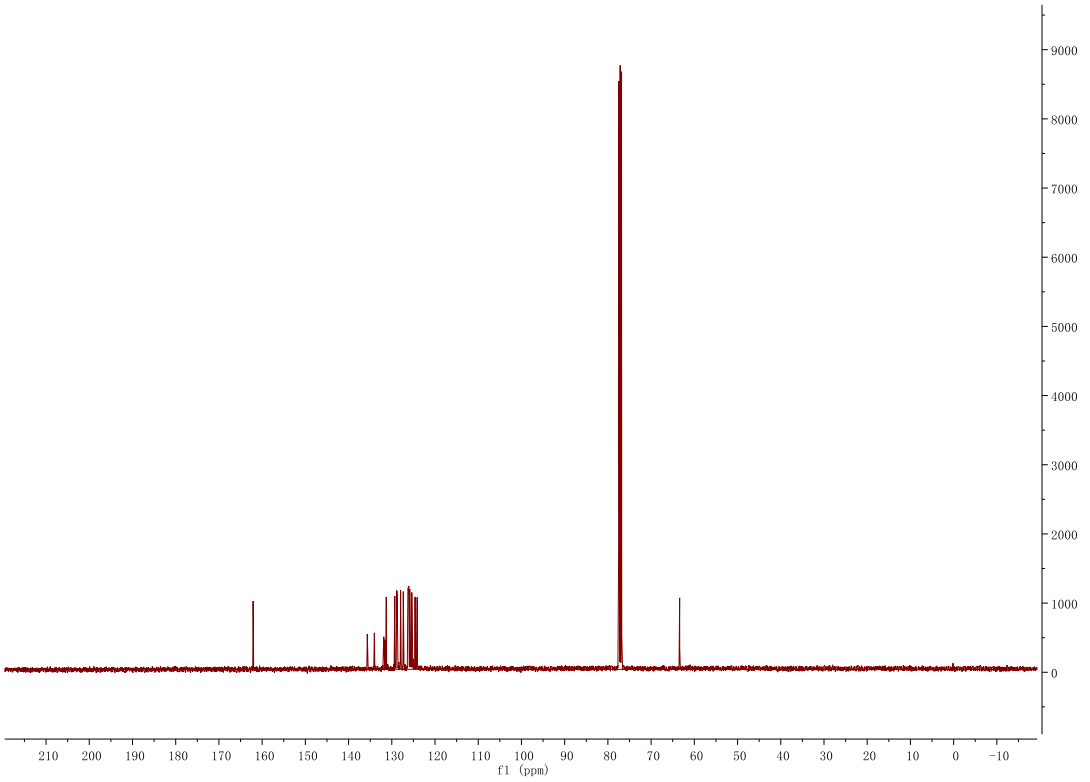
4000
3000
2000
1000
0
-1000
1.00
1.00
1.12
5.59
7.76
1.88
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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60
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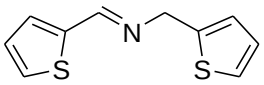
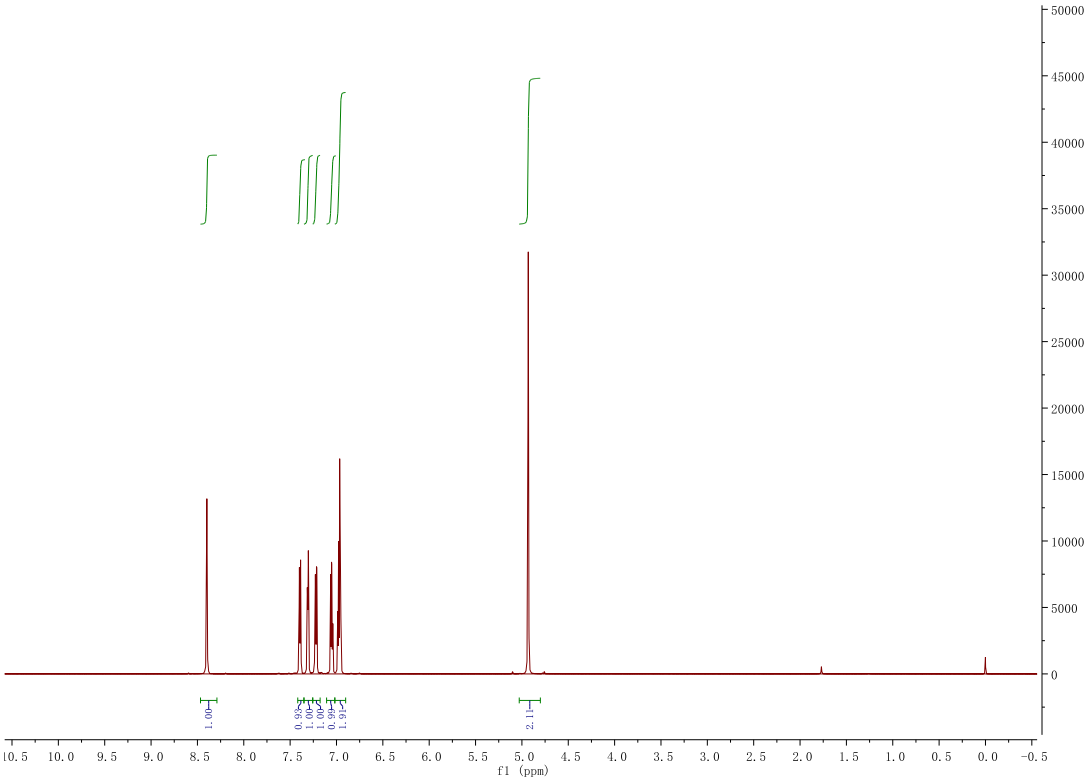
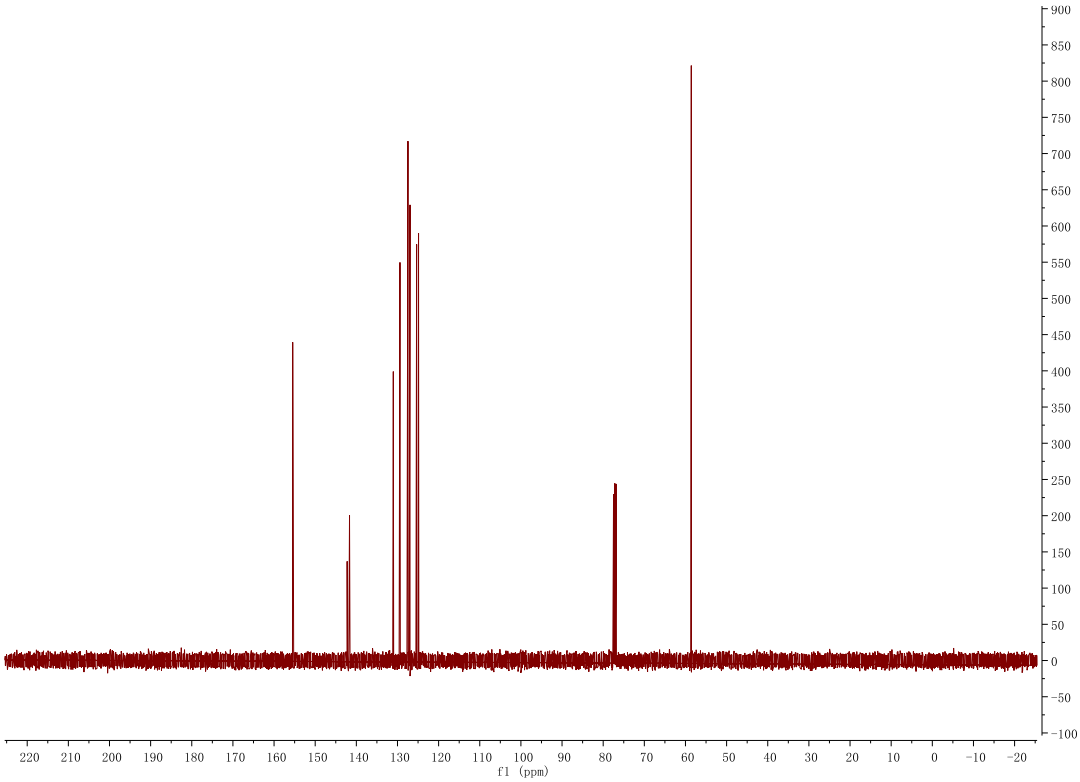
40
30
20
10
0
-10
f1 (ppm)

P9







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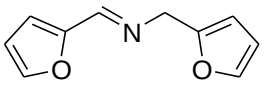

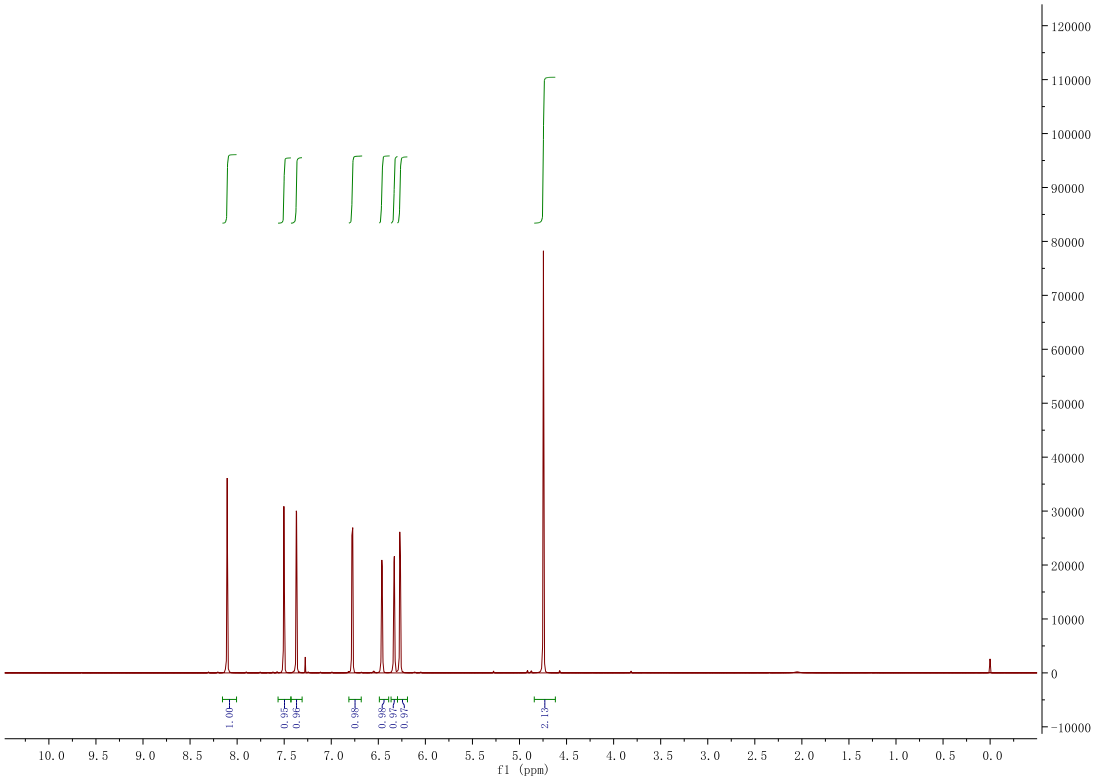

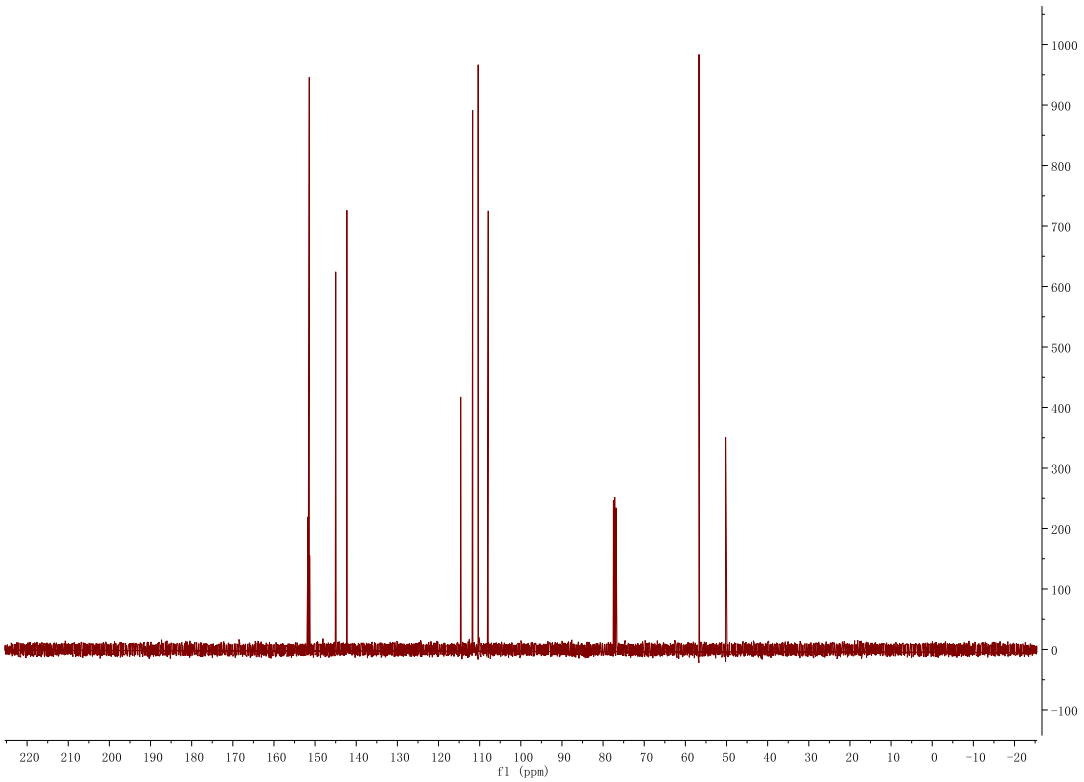

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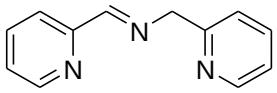

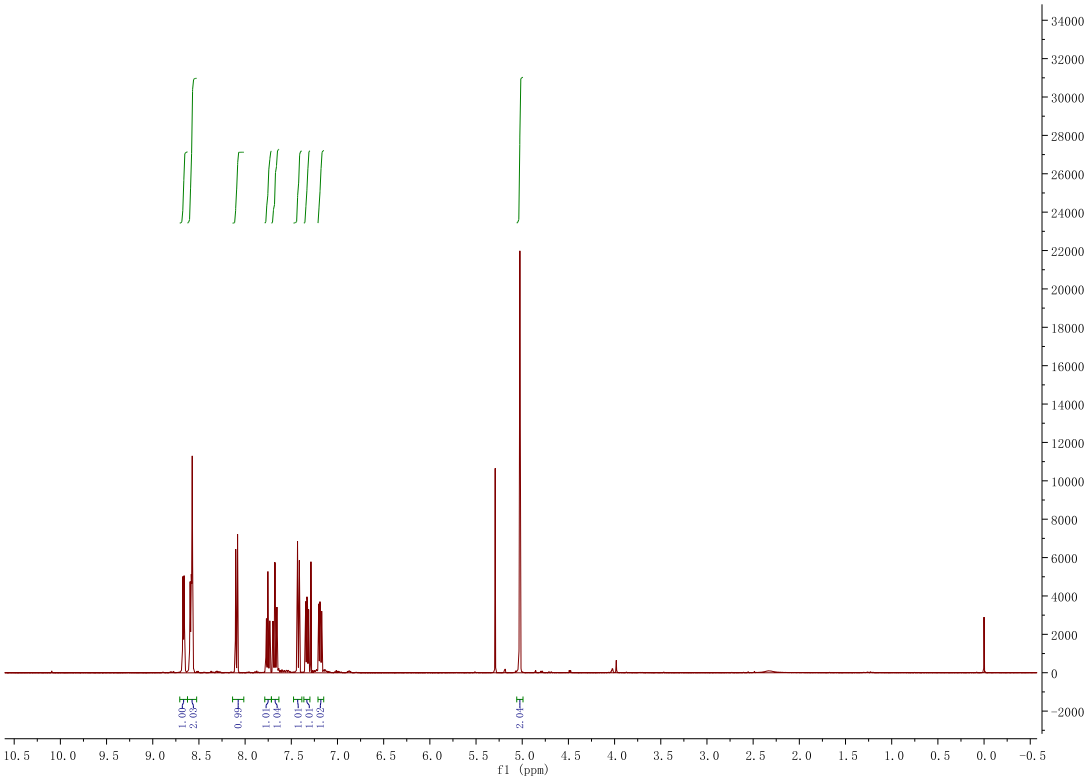

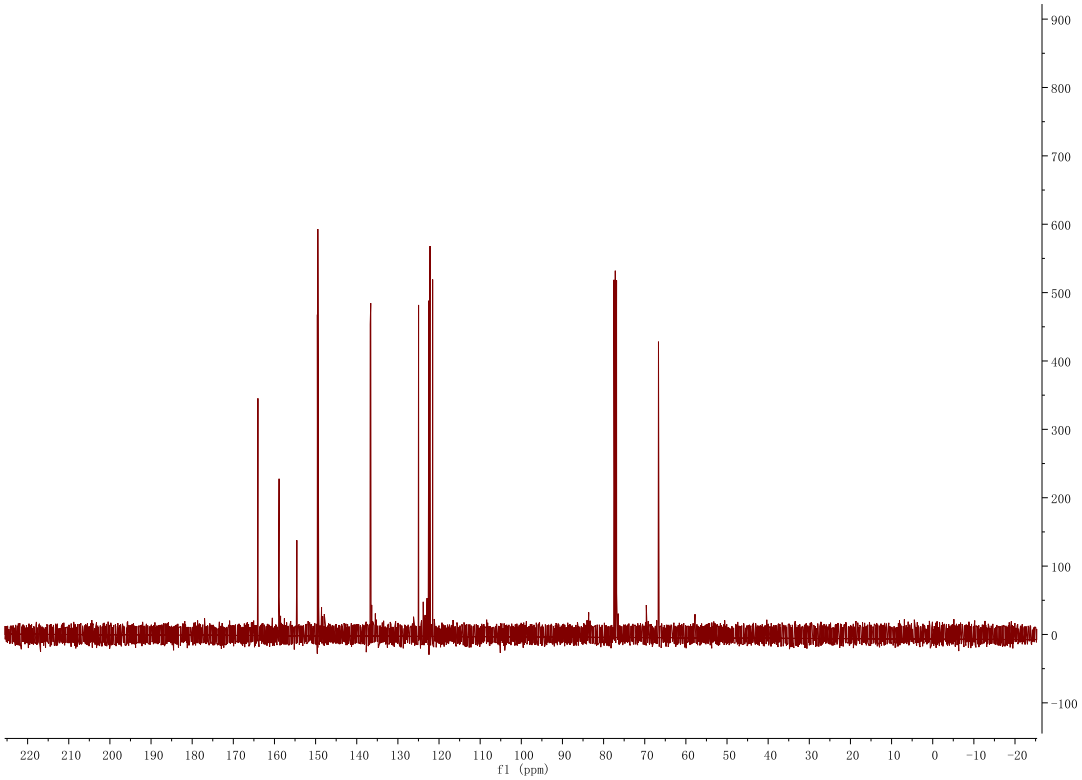

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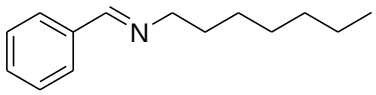
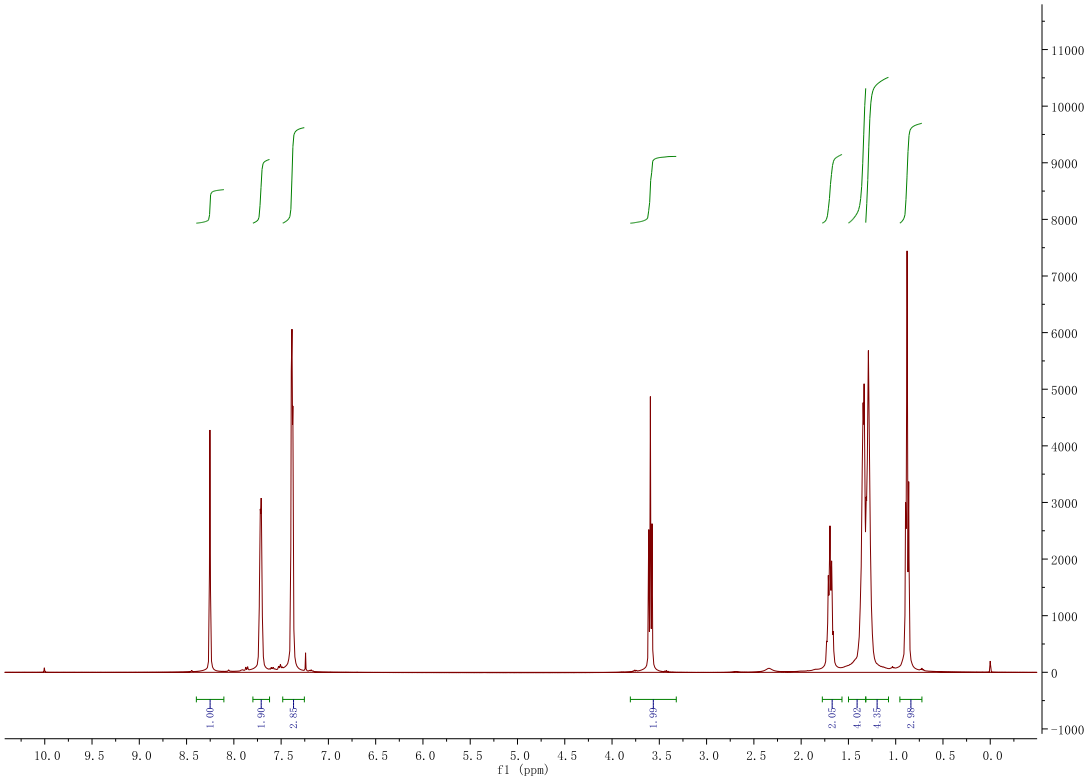
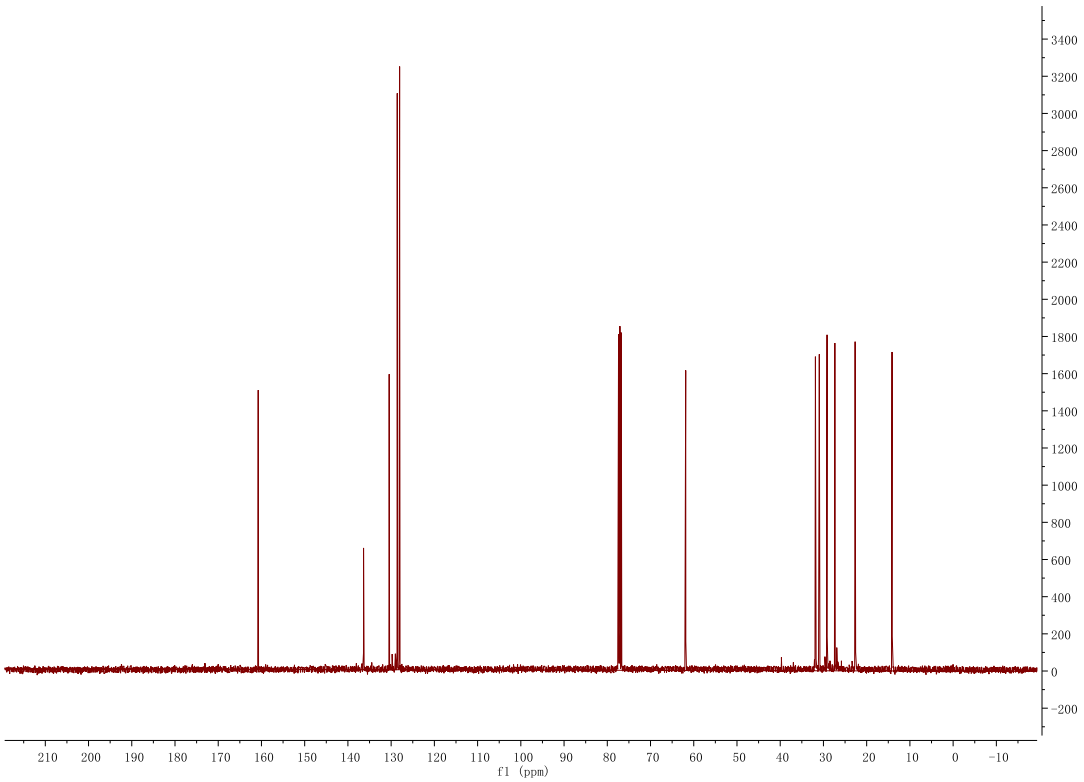
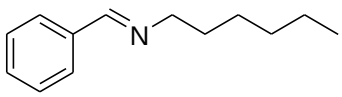
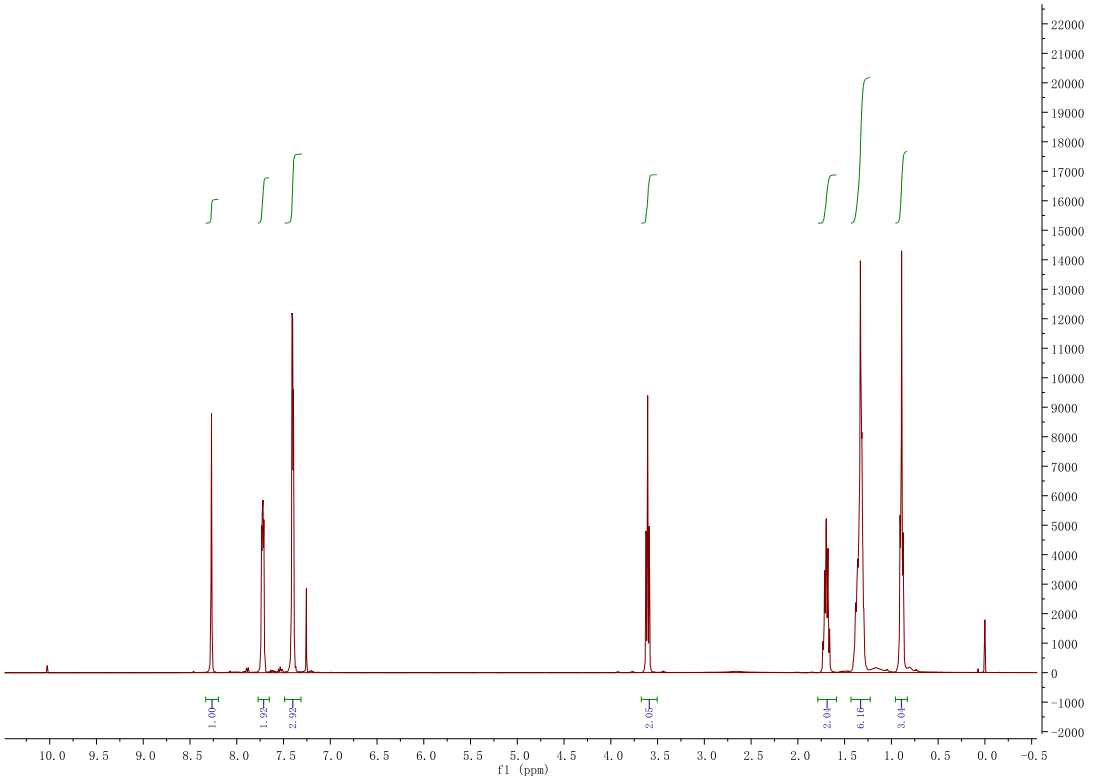


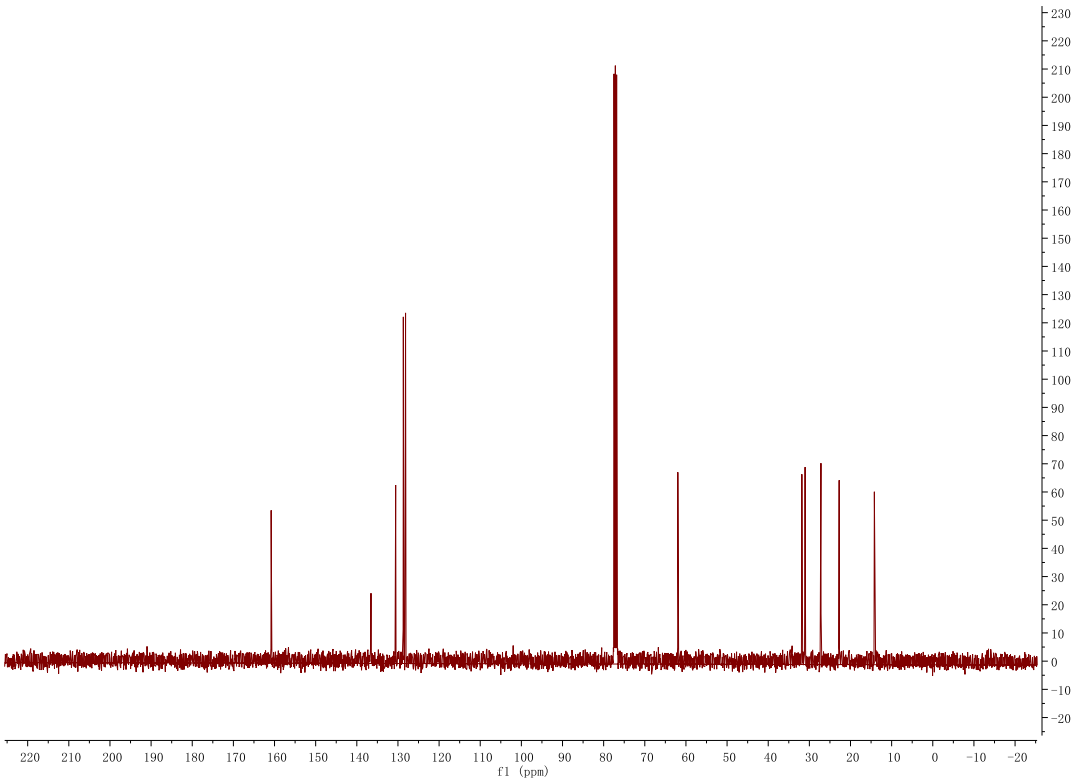




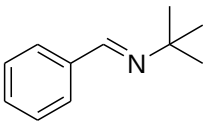
P13

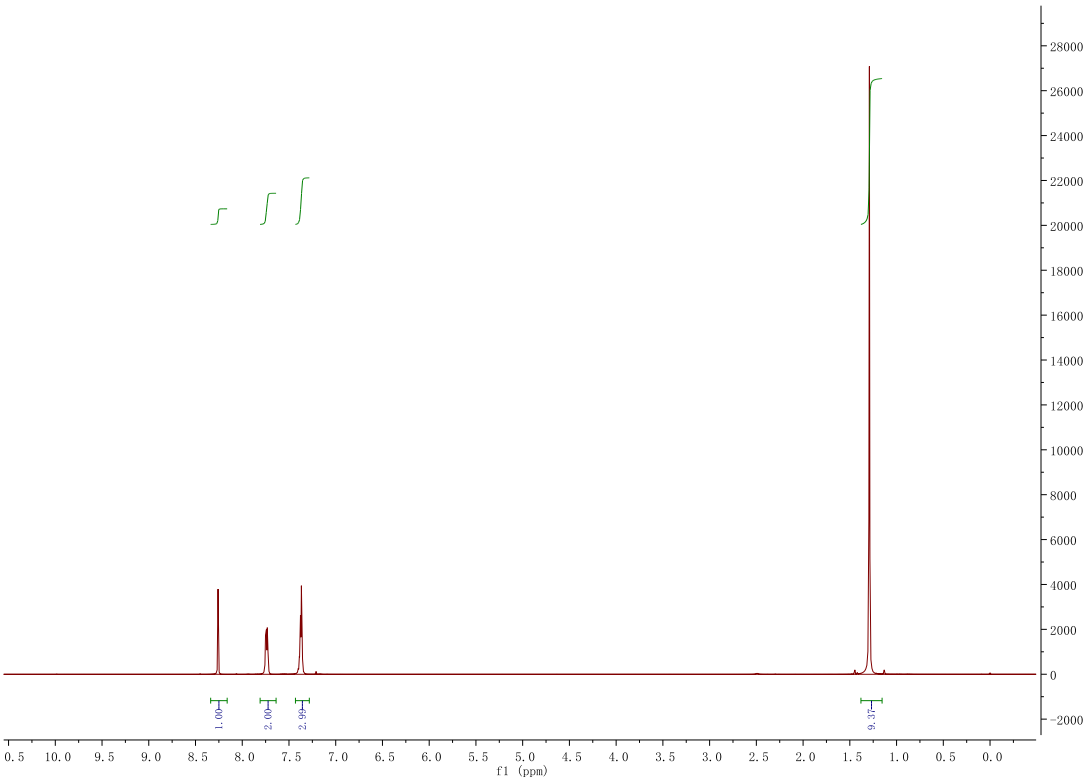






P14





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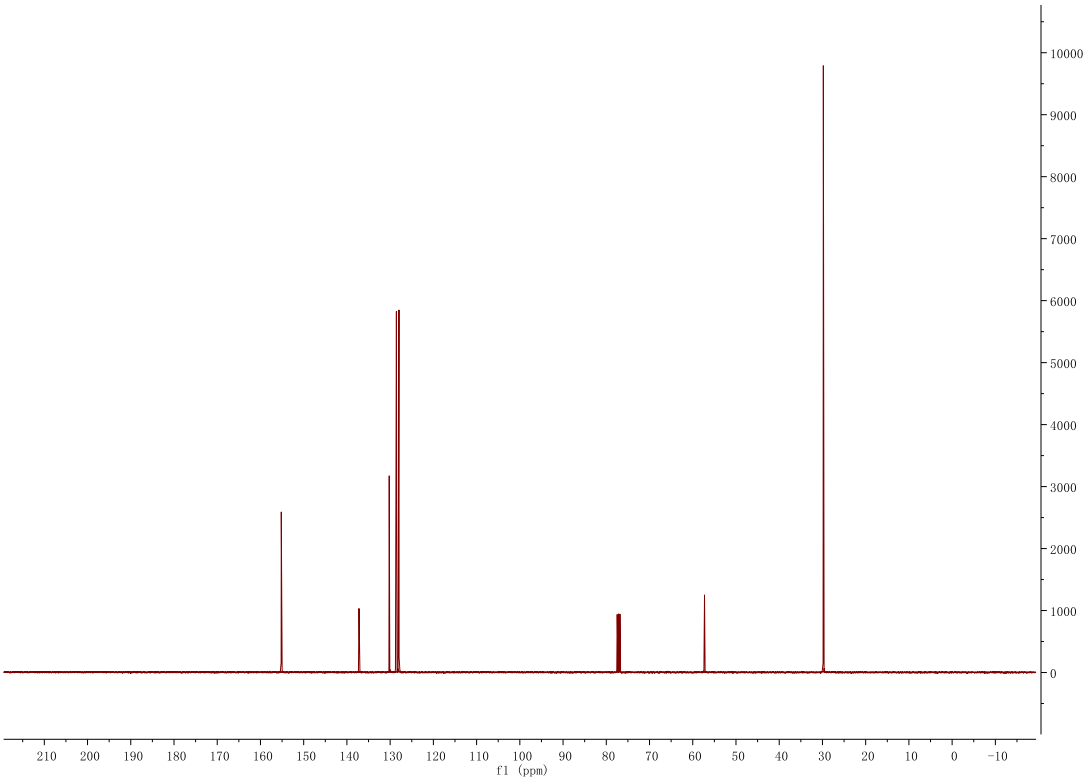
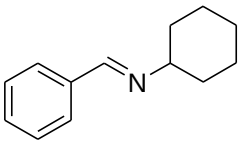


P15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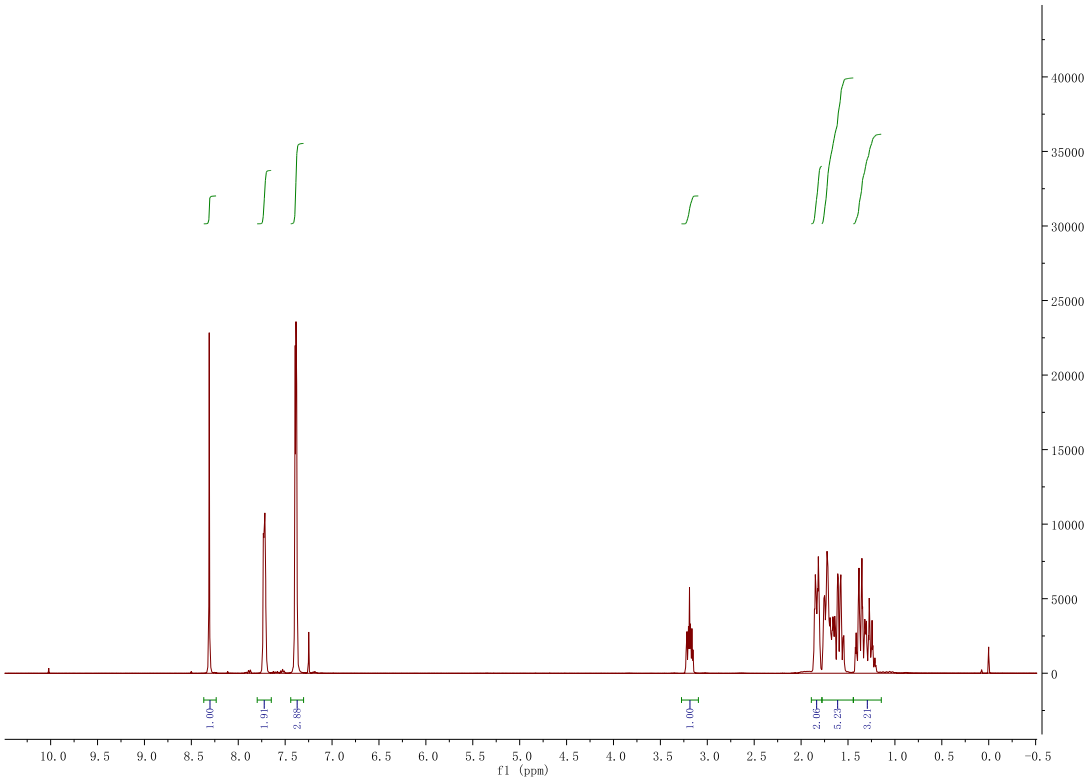
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2.80
1.00
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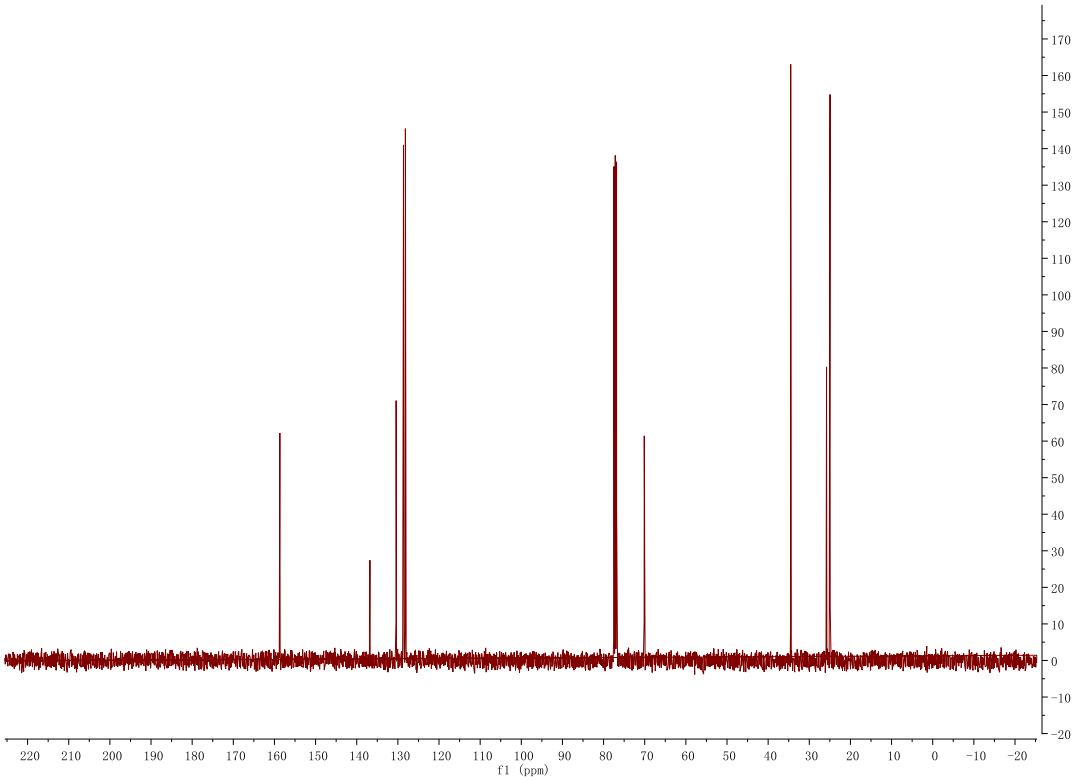
f1 (ppm)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70
60
50
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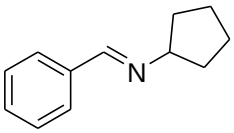
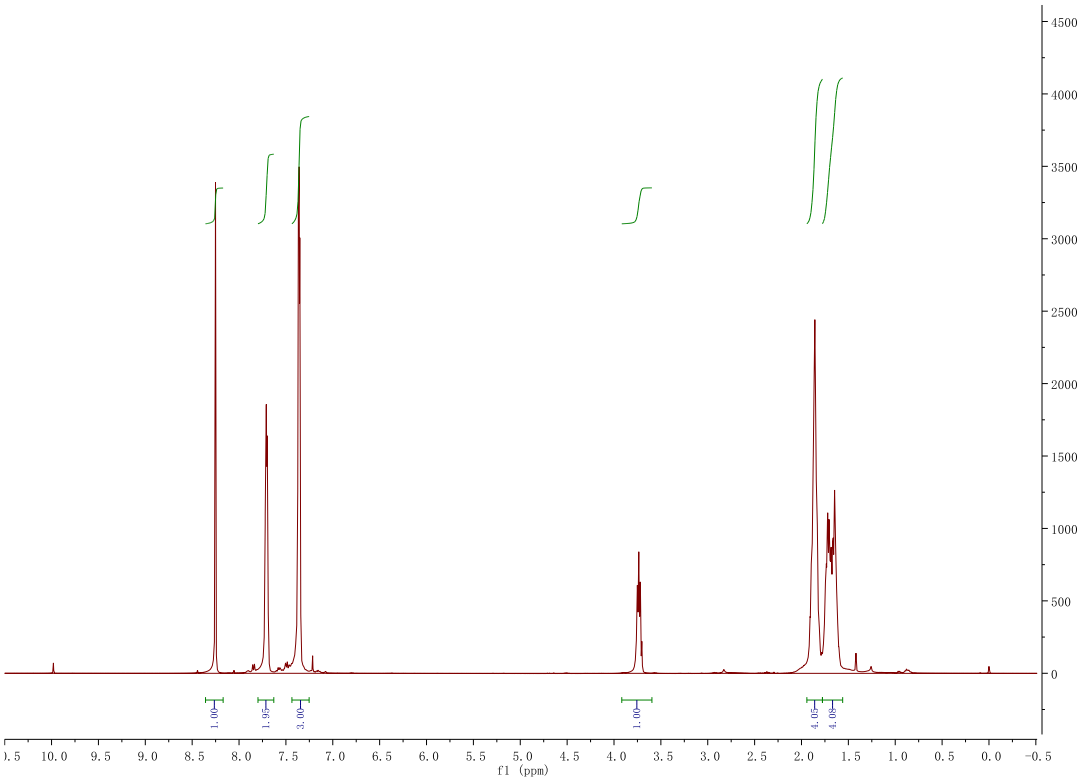
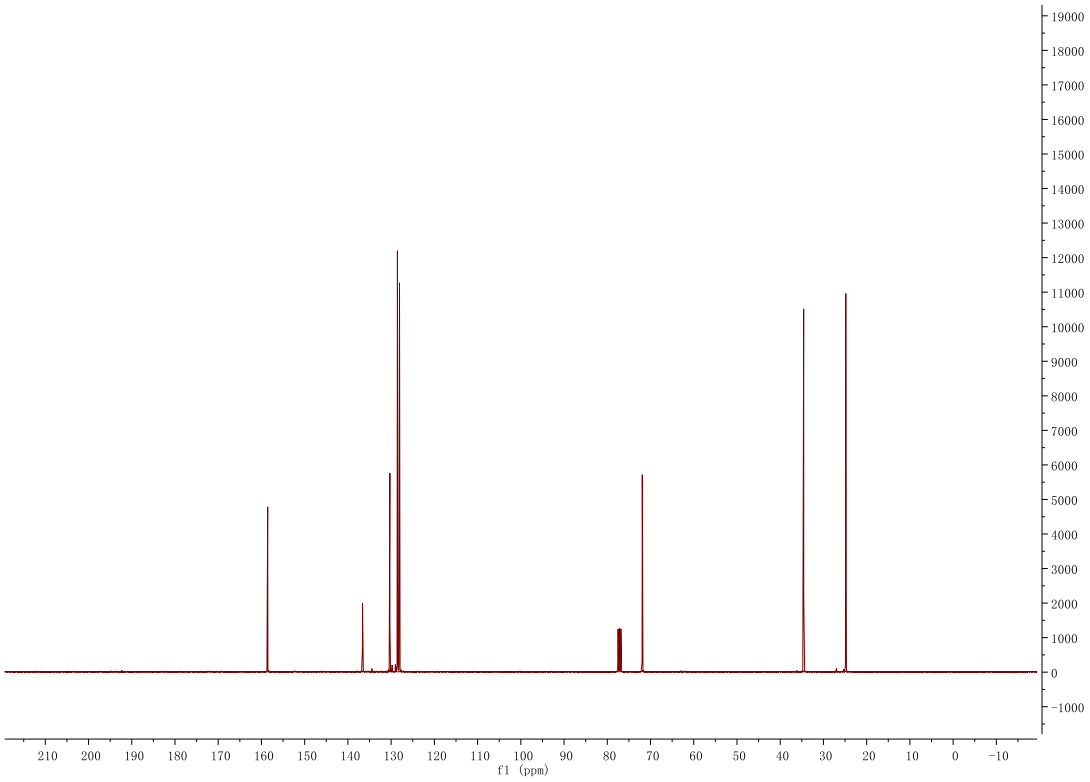
-10
-20
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

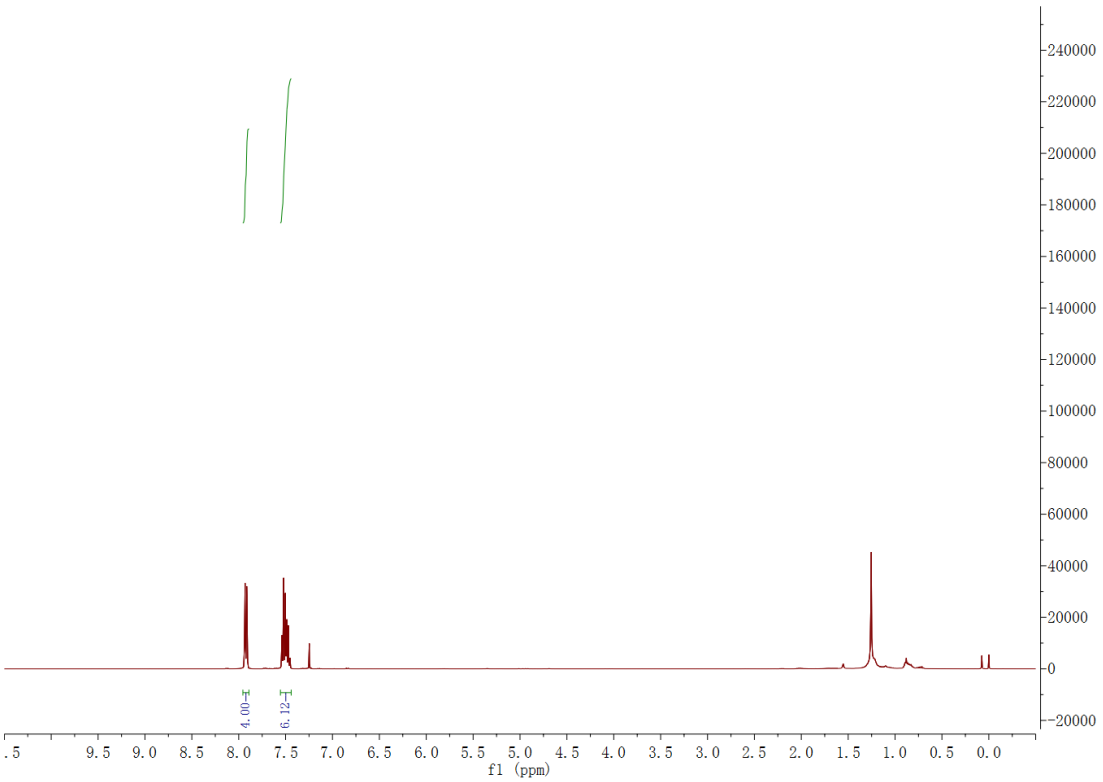
P16

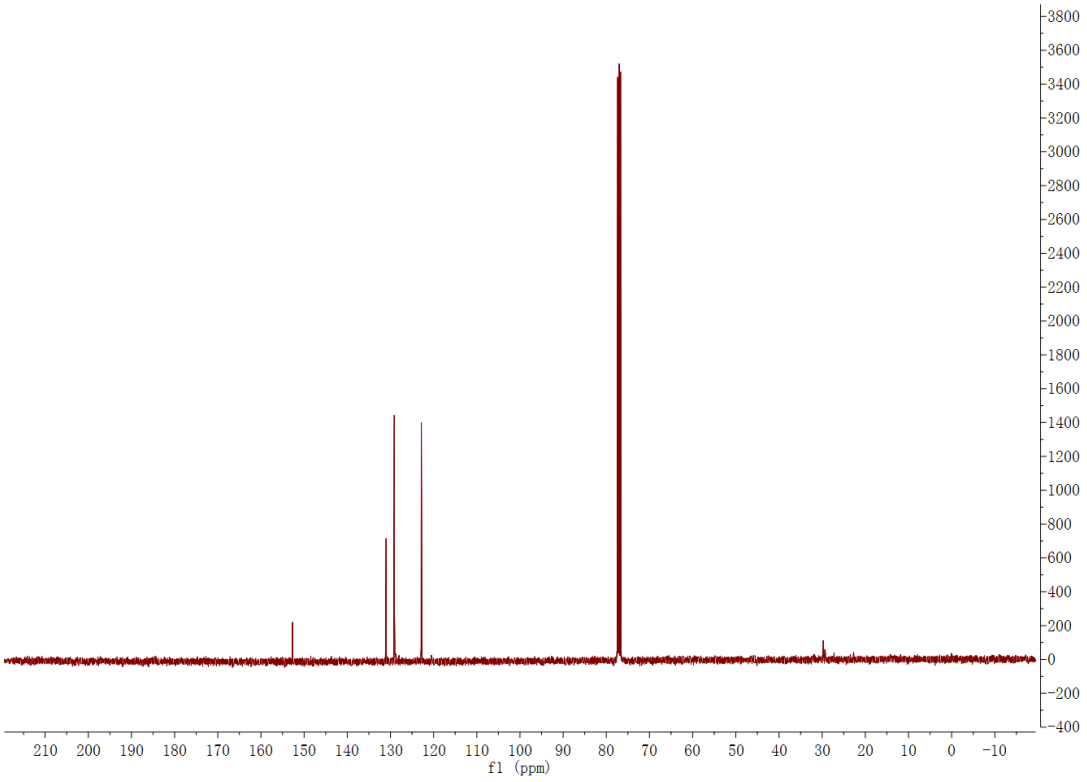






P17





P18