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Efficient synthesis of new asymmetric tripodal ligands using microwave irradiation, and their crystal structures

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General Remarks

1. Materials.

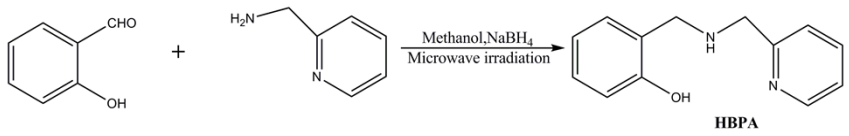
All chemical reagents and solvents were purchased from J&K and used without further purification.

2. Instrumentation

NMR Spectroscopy: NMR spectra were recorded on Agilent-400MRDD2 spectrometers at 298 K; H RMS**:** Mass spectra were recorded on a Time-of-Flight Micromass LCT PremierXE Spectrometer;FT-IR **:**Spectra were recorded on Vary-1000;Melting points were measured on a melting point apparatus and are uncorrected;The apparatus used for the condensation was an XH-100B microwave oven purchased from Beijing Xianggu Science and Technology Development Co., Ltd. (2450 MHz and 100–1000W, Beijing, China).

The crystal data were collected on CCD SMART APEX diffractometer with graphite-mono chromated Mo Ka radiation (l¼0.71073 Å) at 293 K, 9637 reflections for **3**, 12,490 for **4** and 10,141 reflections for **5**. Cell refinements and the data reductions were obtained from SAINT[1]. Absorption corrections were applied by using multi-scan program SADABS[1]. Structural solutions were performed by direct methods and full-matrix least-square refinement based on F^2 with the SHELXTL program packages.[2] Anisotropic thermal parameters were applied to all non-hydrogen. All atoms and all hydrogen atoms of carbon atoms were placed by geometric calculation. Hydrogen atoms on both nitrogen and oxygen atoms were located in a difference map and were restrained. The SHELXTL[2] and Mercury[3] programs were used to prepare materials for publication and the molecular graphics. CCDC-966462 for **3** ,CCDC-966463 for **4** and CCDC-966464 for **5** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge fromThe Cambridge Crystallographic Data Center via http://www.ccdc. cam.ac.uk /Community/Requestastructure/Pages/DataRequest.aspx (or from the Cambridge Crystallographic Data Centre, 12Union Road, Cambridge CB21EZ, U.K.; fax: t44 1223 336 033 or email deposit@ccdc.cam.uk).

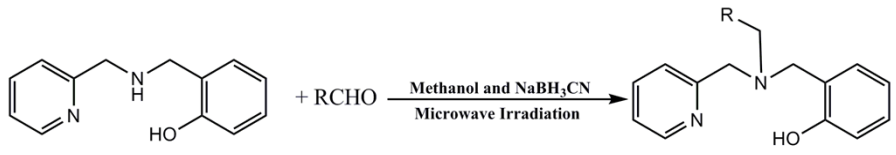
General Procedure I: Microwave-assisted synthesis of HBPA



HBPA

Salicylaldehyde(5 mmol) was placed in a microwave vessel. Methanol(5 mL) and 2-pyridyl - methylamine(5 mmol) were added consecutively. The resultant mixture was heated in a microwave oven(XH-100B microwave oven, which is a monomode instrument) at 60°C with low stirring and 300 W for 10 min. Meanwhile, the system was run at constant temperature operation mode by using the circular water cooling feature of the apparatus. Then, $NaBH_4$(5 mmol) was added and the mixture was irradiated at 200 W for another 30 min. After removal of the solvent, the product is redissolved in 15 mL water, and then extracted with $CHCl_3$. The chloroform extract was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure to give an oily mass. The oily mass is allowed to stand for several days, after which the product precipitates was recrystallized from hot ethylacetate to give the colourless crystalline solid. Yield: 96%.M.p.:62-63 ℃.

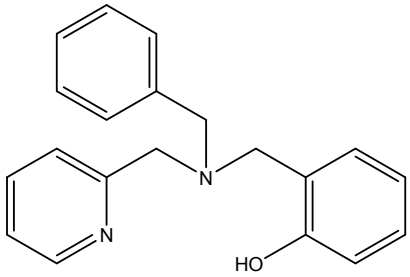
General Procedure II: Microwave-assisted synthesis of asymmetric tripodal ligands(1-7)



HBPA **1-7**

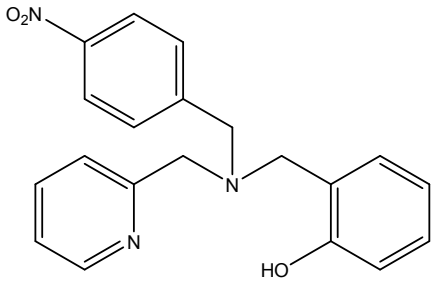
Aromatic aldehyde(5.1 mmol) was placed in a microwave vessel. HBPA (5 mmol) and methanol (5 mL) were added consecutively. The resultant mixture was heated in a microwave oven(XH-100B microwave oven, which is a monomode instrument) at 60°C with low stirring and 300 W for 30 min. Meanwhile, the system was run at constant temperature operation mode by using the circular water cooling feature of the apparatus. Then, $NaBH_3CN$ (6 mmol) was added and the mixture was irradiated of 300 W at 60 ℃(time see Table 2). Basic workup using a saturated aqueous sodium carbonate solution and subsequent extraction using CH_2Cl_2 was performed. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The product was purified by recrystallization using proper solvents (yield see Table 2).

Ligand 1(Table 2 ,Entry 1)



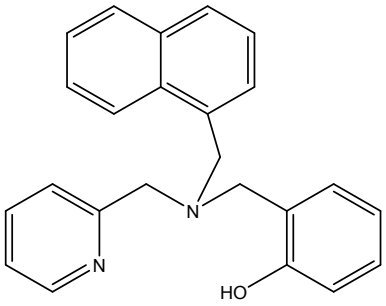
Following Procedure **II**, the product was purified by recrystallization using EtOH and little diethyl ether..m.p. 120-124 ℃. ^{1}H NMR (400MHz,$CDCl_3$) δ: 3.71(s, 2H), 3.80(d, *J*= 5.9 Hz, 4H), 6.80-6.84(td, *J*= 7.4, 1.1 HZ, 1H), 6.95-6.97(dd, *J*= 8.1, 0.9 Hz,1H), 7.06-7.08(dd, *J*= 7.4 Hz, 1H), 7.16-7.28(m, 4H), 7.31-7.39(m, 4H), 7.60-7.65(td, *J*=7.1, 1.3 Hz, 1H), 8.63(dd, *J*=4.9, 0.7 Hz, 1H), 10.88(s, 1H); ^{13}C NMR ($CDCl_3$) δ: 53.1, 54.7, 55.7, 115.5, 116.2, 120.9, 125.5, 128.3, 130.6, 133.6, 136.6, 148.7, 157.7.; HRMS (ESMS) calculated for $C_{20}H_{21}N_2O$(M + H)$^+$: 305.1648;found *m/z:* 305.1648.; FT-IR:3549, 3472, 3414, 3133, 2835, 1583, 1432, 1400, 760.

Ligand 2(Table 2 ,Entry 2)



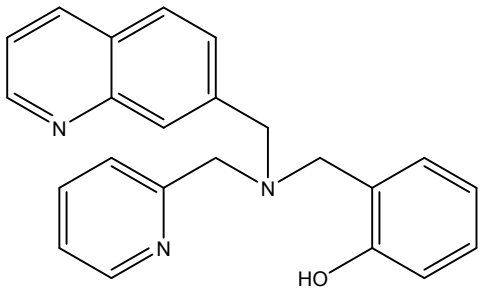
Following Procedure **II**, the product was purified by recrystallization using EtOH and little diethyl ether. m.p.93-94 ℃. ^{1}H NMR($CDCl_3$) δ: 3.78-3.80(d, *J*= 6.3 Hz,6H),6.76-6.79(td, *J*=7.4, 1.1 Hz, 1H), 6.91-6.94(dd, *J*= 8.1, 0.9 Hz, 1H), 7.04-7.06(dd, *J*= 7.4, 1.4 Hz, 1H), 7.16-7.24(m, 3H), 7.51-7.53(d, *J*= 8.7Hz, 2H), 7.64-7.68(td, *J*=7.7, 1.8 Hz,1H), 8.11-8.13(m, 2H), 8.64-8.66(dd, *J*=4.9, 0.7 Hz, 1H), 10.88(s, 1H); ^{13}C NMR($CDCl_3$) δ: 56.8, 56.9, 58.1, 116.4, 118.8, 122.1, 123.4, 129.1, 136.8, 145.8, 156.9; HRMS (ESMS) calculated for $C_{20}H_{20}N_3O_3$(M + H)$^+$: 350.1499, found: 350.1499; FT-IR: 3548, 3471, 3415, 3134, 2817, 1598, 1515, 1400, 1344, 893, 757.

Ligand 3(Table 2 ,Entry 3)



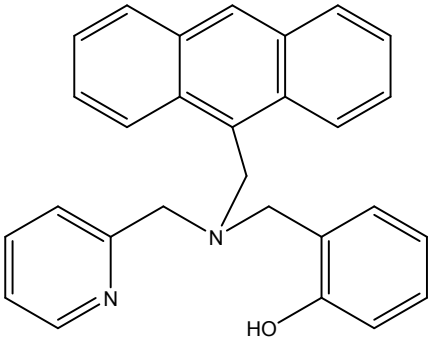
Following Procedure **II**, the product was purified by recrystallization using EtOH and little diethyl ether. m.p. 155-156℃. ^{1}H NMR($CDCl_3$) δ: 3.68-3.71(d, *J*= 13.5 Hz, 1H), 3.83-3.89(dd, *J*=15.6, 9.8 Hz, 2H), 4.05- 4.14(dd, *J*=34.5, 14.4 Hz, 2H), 4.40- 4.44(d, *J*=13.4Hz, 6H), 6.89-6.94(m, 1H), 7.02-7.04(d, *J*= 7.8 Hz, 1H), 7.08-7.24(m, 3H), 7.34-7.47(m, 4H), 7.54-7.56(td, *J*=7.7, 1.8 Hz, 1H), 7.55-7.65(m, 1H), 7.72-7.81(m, 2H), 7.81-7.92(m, 1H), 8.49-8.50(d, *J*= 4.4 Hz, 1H), 11.24(s, 1H); ^{13}C NMR($CDCl_3$) δ: 53.10, 54.7, 55.7, 115.5, 116.9, 118.8, 119.0, 122.1, 123.5, 124.2, 125.5, 126.4, 127.2, 128.2, 129.7, 130.1, 131.1, 133.6, 136.9, 148.7, 157.7; HRMS (ESMS) calculated for $C_{24}H_{22}N_2O(M + H)^+$:355.1805, found:355.1804; FT-IR: 3467, 3415, 3127, 2832, 1602, 1582, 1489, 1399, 1249, 780.

Ligand 4 (Table 2 ,Entry 4)



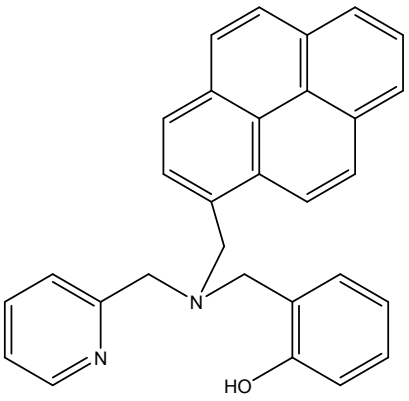
Following Procedure **II**, the product was purified by recrystallization using EtOH and little diethyl ether. m.p.147-148 ℃. ^{1}H NMR($CDCl_3$) δ: 3.87-3.91(d, *J*=19.1 Hz,4H), 4.06(s, 2H), 6.77 -6.81(m, 1H), 6.99-7.01(d, *J*=8.0Hz, 1H), 7.10-7.13(dd, *J*= 9.8, 5.9Hz, 2H), 7.19-7.23(m, 2H), 7.36-7.42(m, 1H), 7.48-7.59(m, 2H), 7.69-7.7.76(m, 2H), 8.05-8.07 (d, *J*= 8.5 Hz, 2H), 8.23 -8.25(d, *J*=8.5 Hz, 1H), 8.55-8.56(d, *J*= 4.3Hz,1H), 11.24(s, 1H); ^{13}C NMR($CDCl_3$) δ: 56.9, 58.6, 59.5, 116.4, 118.5, 120.5, 122.7, 126.1, 127.0, 128.5, 129.4, 130.2, 147.1, 148.5, 157.4, 158.3; HRMS (ESMS) calculated for $C_{23}H_{22}N_3O$ $(M +H)^+$: 356.1763, found:356.1760. FT-IR: 3467, 3415, 3134, 2813, 1596, 1488, 1234, 759.

Ligand 5 (Table 2 ,Entry 5)



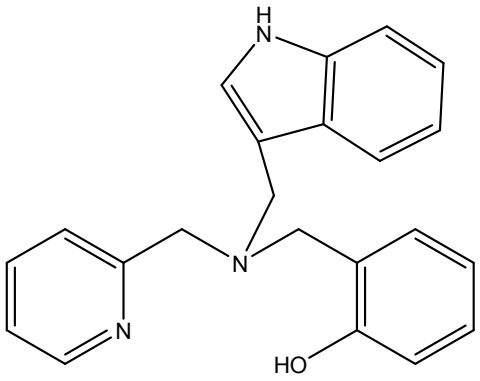
Following Procedure **II**, the product was purified by recrystallization using EtOH. m.p. 204-205 ℃. ^{1}H NMR($CDCl_3$) δ: 3.84-3.94 (m, 4H), 4.68(s, 2H), 6.74-6.77(t, *J*= 7.1Hz, 1H), 6.84-6.86(d, *J*= 8.0 Hz, 1H), 7.05-7.06(d, *J*= 6.5 Hz, 1H), 7.14-7.15(dd, *J*=11.1, 1.9 Hz, 1H), 7.20-7.24(m, 1H), 7.42-7.49(m, 5H), 7.64-7.68(t, *J*= 7.7 Hz, 1H), 7.96-7.97(d, *J*=8.2Hz, 2H), 8.18-8.20(d, *J*=8.8Hz, 2H), 8.389(s, 1H), 8.62-8.63(d, *J*= 4.5Hz, 1H), 10.78(s,1H); ^{13}C NMR($CDCl_3$) δ: 50.1, 57.3, 59.5, 116.3, 119.1, 122.4, 124.2, 126.1, 129.8, 131.3, 136.7, 148.8, 157.6; HRMS (ESMS) calculated for $C_{28}H_{25}N_2O$ $(M+H)^+$:405.1967, found:405.1965; FT-IR: 3471, 3414, 3135, 2805, 1617, 1583, 1400, 1241, 780.

Ligand 6 (Table 2 ,Entry 6)



Following Procedure **II**, the product was purified by recrystallization using EtOH. m.p.181-182 ℃. ^{1}H NMR($CDCl_3$) δ: 3.86-3.87(d, *J*= 2.6 Hz, 4H), 4.35(s, 2H), 6.84-6.88(m, 1H), 6.99-7.01 (d, *J*= 7.9 Hz, 1H), 7.13-7.16(m, 3H), 7.24-7.28(m, 1H), 7.55-7.59(td, *J*=7.7, 1.6 Hz, 1H), 7.95 -7.99(m, 4H), 8.00-8.08(dd, *J*= 8.5, 2.5 Hz, 2H), 8.12-8.16(m, 3H), 8.64-8.65(d, *J*= 4.3 Hz, 1H), 10.82(s, 1H) ;^{13}C NMR($CDCl_3$) δ: 56.1, 57.2, 58.7, 116.3, 125.7, 130.8, 148.6, 157.4; HRMS (ESMS) calculated for $C_{30}H_{25}N_2O(M+H)^+$: 429.1967, found:429.1961; FT-IR: 3464, 3416, 3143, 2816, 1581, 1488, 1400, 841, 707.

Ligand 7 (Table 2 ,Entry 7)



Following Procedure **II**, the product was purified by recrystallization using EtOH. m.p. 178-179 ℃. ^{1}H NMR($CDCl_3$) δ: 3.86-3.89(d, *J*= 9.6 Hz, 4H), 3.94(s, 2H), 4.02-4.09(m, 1H), 6.77-6.79(m, 1H), 6.80-6.90(m, 1H), 7.03-7.04(m, 1H), 7.11-7.21(m, 2H), 7.32-7.36(m, 2H), 7.57-7.59(m, 2H), 7.64-7.68(m, 1H), 8.34(s, 1H), 8.53-8.61(d, *J*= 4.2Hz, 1H), 10.81(s, 1H); ^{13}C NMR($CDCl_3$) δ: 48.2, 56.7, 58.7, 111.0, 116.8, 118.7, 122.2, 127.4, 128.6, 129.2, 136.0, 136.6, 148.8, 157.3; HRMS (ESMS) calculated for $C_{22}H_{22}N_3O$ $(M+H)^+$: 344.1763, found: 344.1760.; FT-IR: 3545, 3468, 3415, 3140, 2891, 1617, 1597, 1401, 1254, 876, 748.

References and notes

1. Bruker. SMART, SAINT and SADABS; Bruker AXS: Madison, WI, USA, 2003.
2. G. M. Sheldrick, *Acta. Crystallogr.,* 2008, **A64**, 112.
3. C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L . Rodriguez-Monge, R. Taylor, J. Vande-Streek and P. A. Wood, *J. Appl. Crystallogr.*, 2008, **41**, 466.

X-Ray data for ligands 3, 4 and 5

Table S1 Crystal data and structure refinement for **3, 4** and **5**

Formula	$C_{24}H_{22}N_2O$(**3**)	$C_{23}H_{21}N_3O$(**4**)	$C_{28}H_{24}N_2O$(**5**)
Molecular weight	354.44	355.43	404.49
space group	P 21/n	P2(1)/c	P 21/n
***a* (A,)**	13.197(11)	9.929(10)	13.918(18)
***b* (A,)**	11.102(9)	12.099(12)	11.138(14)
***c* (A,)**	14.265(12)	16.261(16)	14.314(17)
***β* (°)**	111.786(14)	96.512(11)	110.04(2)
***V* (Å^3)**	1941(3)	1941(3)	2085(4)
Z	4	4	4
D_{calc} **(g cm^{-3})**	1.213	1.216	1.289
Absorption corr Ψ-scan max., min	0.9845,0.9809	0.9857,0.9827	0.9784,0.9853
***F*(000)**	752.0	752.0	856.0
Crystal size (mm)	0.26×0.21×0.21	0.23×0.21×0.19	0.28×0.21×0.19
***θ* range data collection**	1.00-24.99	2.06-25.00	1.76-24.99
Index ranges	-15≤ h≤15 -10≤ k ≤13 -16 ≤ l ≤ 16	-10≤ h≤11 -14≤ k ≤14 -17 ≤ l ≤ 19	-13≤ h≤ 16 -13 ≤ k ≤12 -16≤ l ≤11
Reflections measured	3421	3386	3674
Reflections [*I*>2δ(*I*)]	2061	2267	1901
Data/parameters	3421/245	3386/245	3674/281
Goodness-of-fit on F^2	0.999	0.972	0.966
***R* [*I*>2δ(*I*)]**	0.044	0.0801	0.0819
***wR*^{2} (all data)**	0.1374	0.1533	0.2617

Table S2 Selected bonds lengths(Å) and angles (°) of **3, 4** and **5**

3		**4**		**5**	
Bond lengths					
N1-C5	1.4459 (0.0024)	N1-C5	1.4682 (0.0024)	N1-C5	1.4431 (0.0046)
N1-C1	1.4679 (0.0021)	N1-C1	1.4730 (0.0023)	N1-C1	1.4496 (0.0043)
N2-C14	1.4718 (0.0021)	N2-C14	1.4894 (0.0024)	N2-C14	1.4468 (0.0042)
N2-C6	1.3266 (0.0023)	N2-C6	1.3506 (0.0025)	N2-C6	1.3228 (0.0047)
N2-C7	1.3376 (0.0022)	N2-C7	1.3537 (0.0027)	N2-C7	1.3494 (0.0053)
O1-C13	1.371(2)	O1-C13	1.3825 (0.0028)	O1-C13	1.3922 (0.0049)
O1-H1	0.8200	N3- C15	1.3950 (0.0024)	O1-H1	0.8200
		O1-H1	0.8200		
Bond angles					
C(13)-O(1)-H(1)	109.5	C(13)-O(1)-H(1)	109.5	C(13)-O(1)-H(1)	109.5
C(1)-N(1)-C(5)	111.97(15)	C(1)-N(1)-C(5)	118.3 (5)	C(1)-N(1)-C(5)	112.3(3)
C(8)-N(1)-C(14)	110.93(14)	C(6)-N(1)-C(5)	121.09(3)	C(16)-N(1)-C(22)	111.7(3)
C(6)-N(2)-C(7)	117.39(17)	N(1)-C(2)-C(3)	110.71(4)	C(6)-N(2)-C(7)	118.1(4)
N(2)-C(7)-C(8)	121.41(16)	C(5)-N(2)-C(6)	110.71(9)	N(2)-C(7)-C(8)	121.1(3)
N(2)-C(6)-C(7)	118.74(16)	C(7)-N(2)-C(8)	118.00(9)	N(2)-C(5)-C(6)	118.7(3)
N(2)-C(14)-C(15)	123.96(19)	N(2)-C(14)-C(15)	111.68(8)	N(2)-C(14)-C(15)	123.8(4)

Table S3 Hydrogen-bond geometry(Å) parameters for **3, 4** and **5**

Ligand	**D-H...A**	**d(D-H)**	**d(H..A)**	**<DHA**	**d(D..A)**
3	O1-H1…N1	0.820	2.498	133.64	3.121
	O1-H1…N2	0.820	2.061	152.04	2.811
4	O1-H1…N1	0.820	2.108	154.56	2.870
	O1-H1…N2	0.820	2.478	126.85	3.042
5	O1-H1…N1	0.820	2.360	135.36	2.999
	O1-H1…N2	0.820	2.030	145.78	2.747

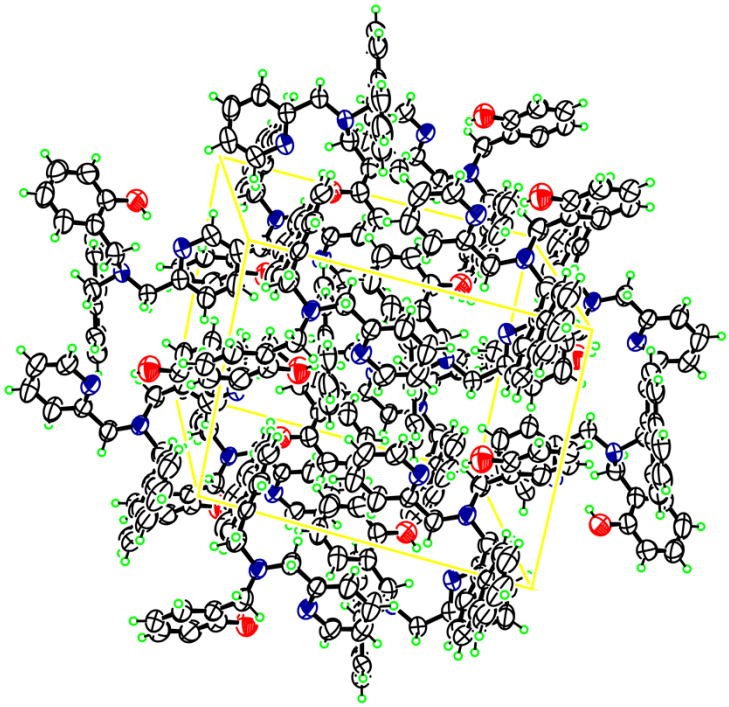


Fig. S1 The hydrogen bond interaction in ligand **3** (c-axis projection)

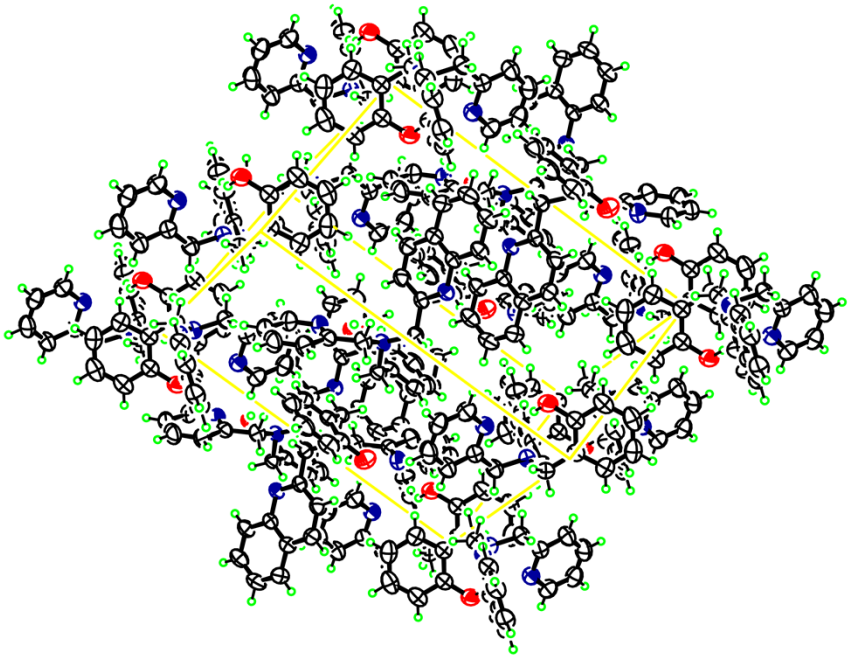


Fig. S2 The hydrogen bond interaction in ligand **4** (c-axis projection)

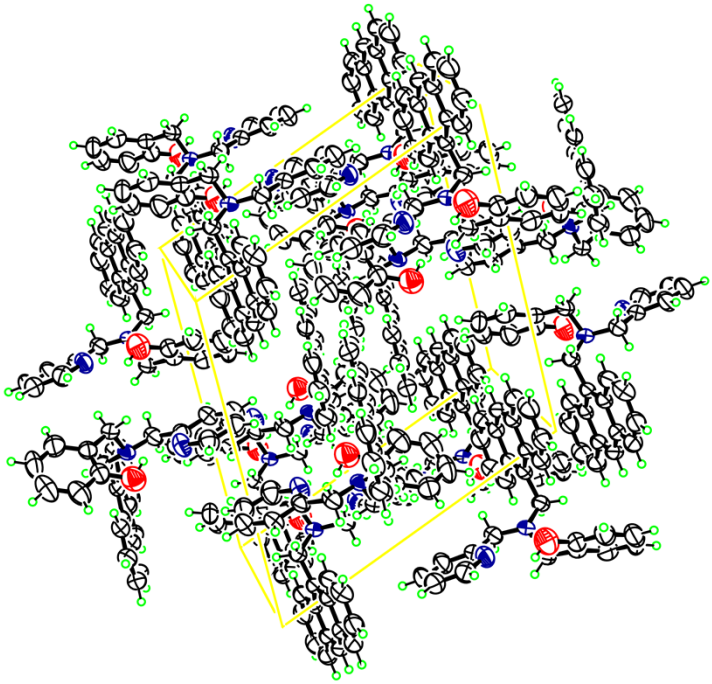


Fig. S3 The hydrogen bond interaction in ligand **5 (c-axis projection)**

NMR data

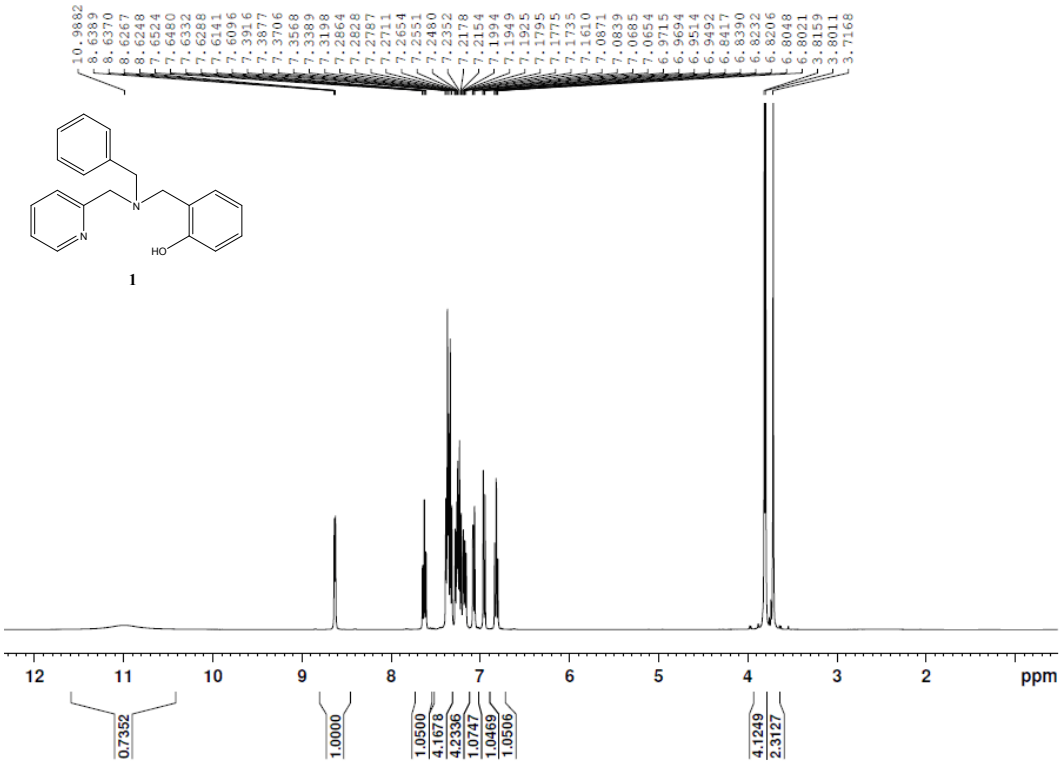


Fig. S4 The ^{1}H NMR spectroscopy of **1**

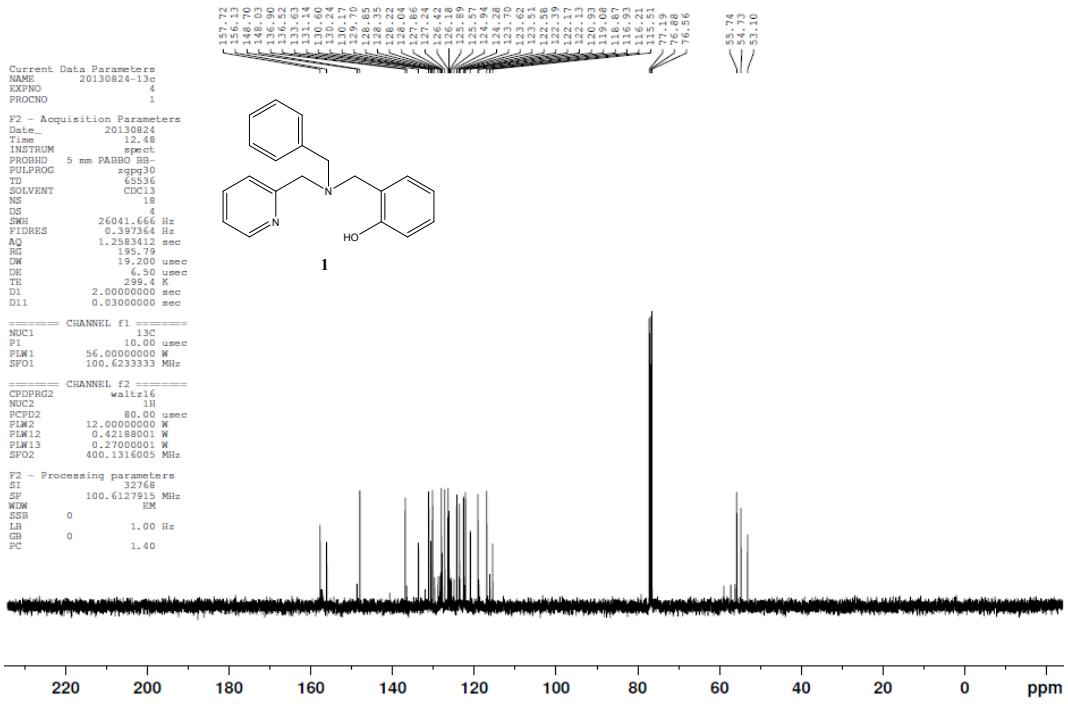


Fig. S5 The ^{13}C NMR spectroscopy of **1**

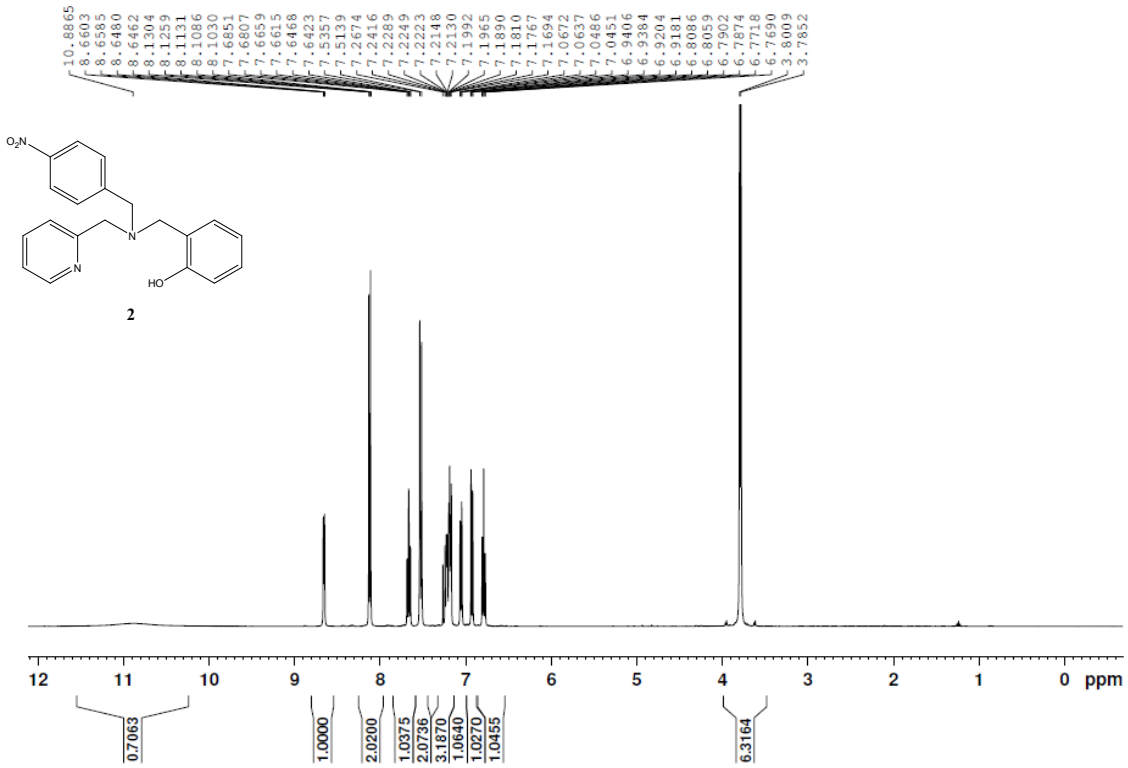


Fig. S6 The ^{1}H NMR spectroscopy of **2**

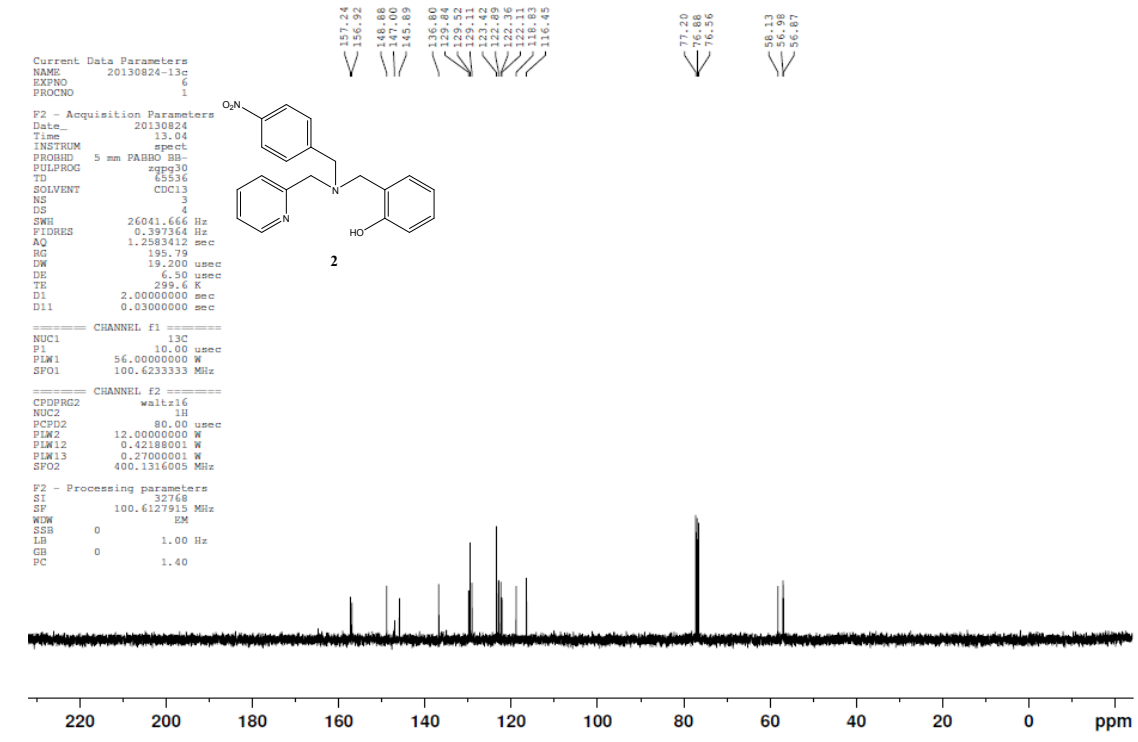


Fig. S7 The ^{13}C NMR spectroscopy of **2**

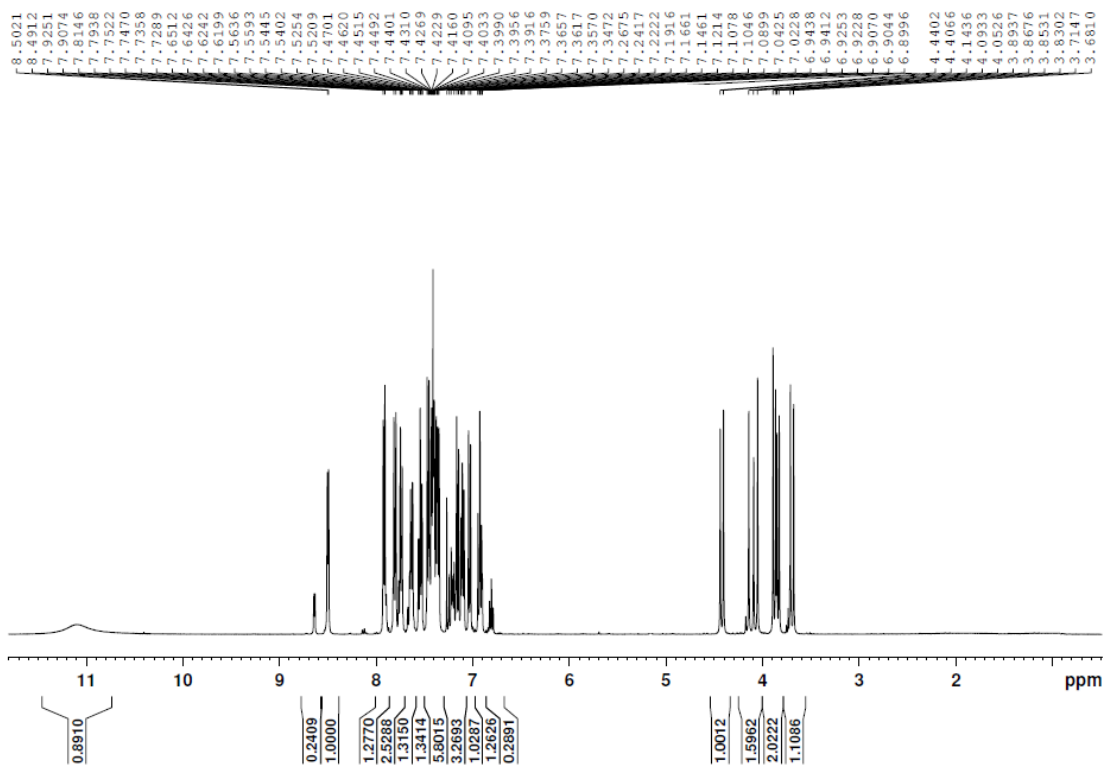


Fig. S8 The ^{1}H NMR spectroscopy of **3**

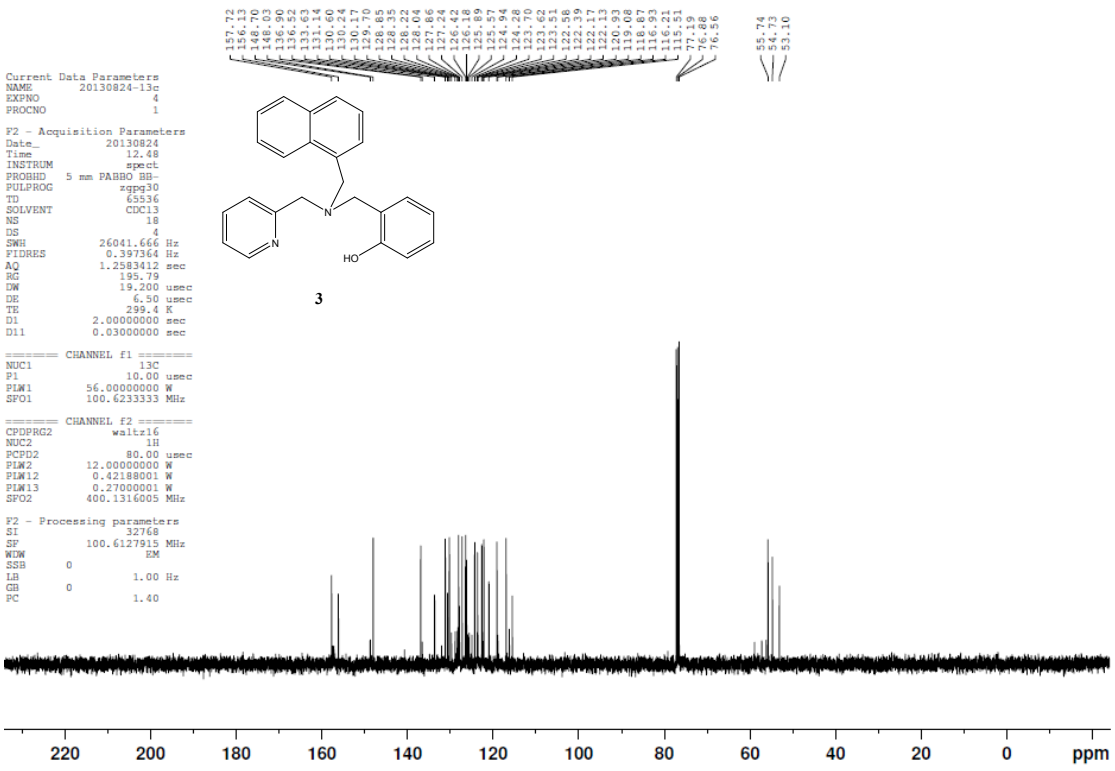


Fig. S9 The ^{13}C NMR spectroscopy of **3**

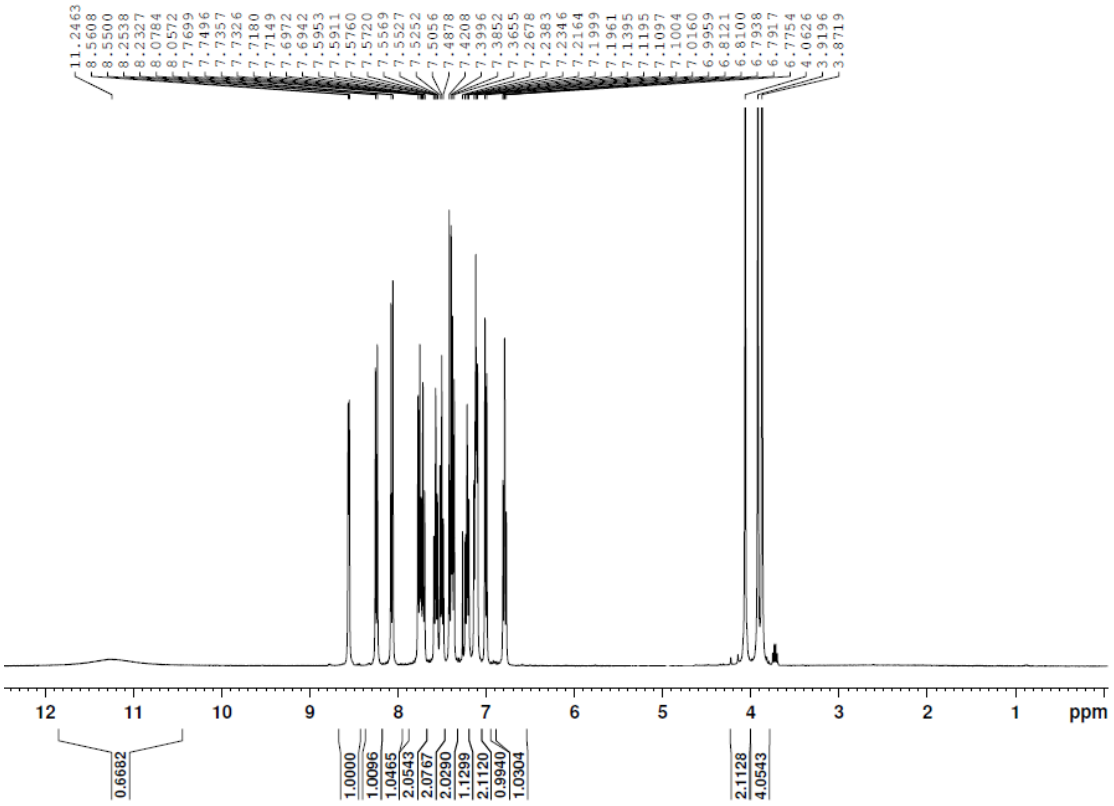


Fig. S10 The ^{1}H NMR spectroscopy of **4**

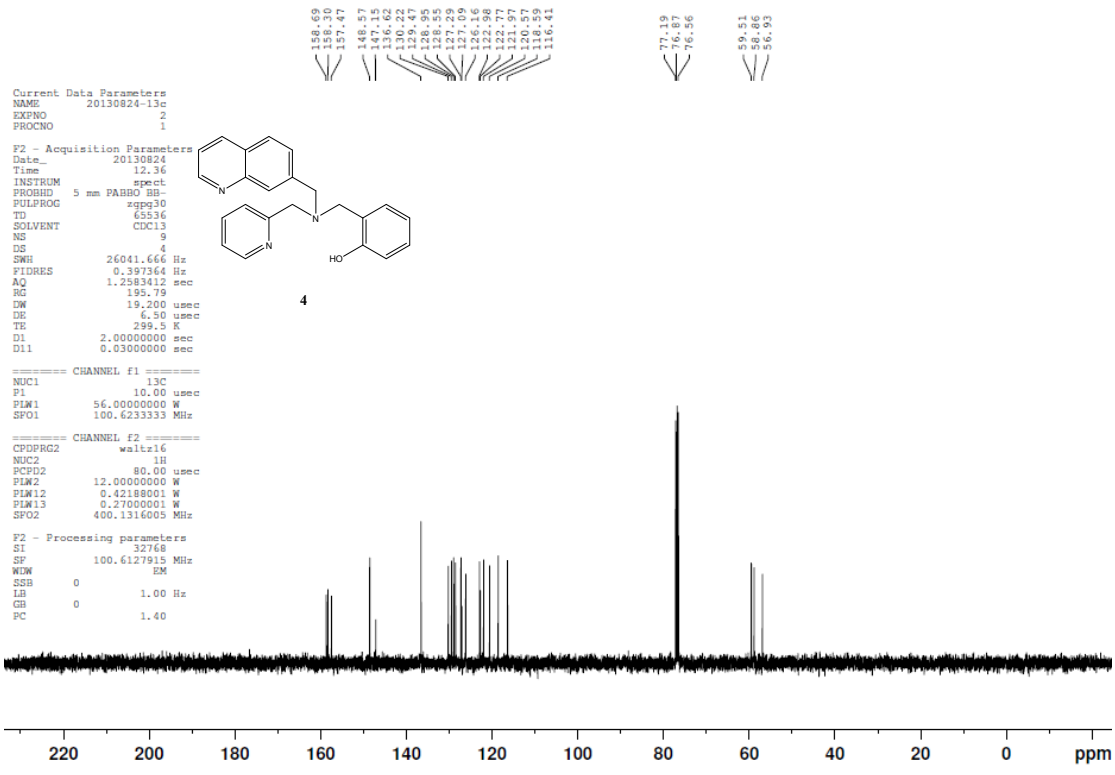


Fig. S11 The ^{13}C NMR spectroscopy of **4**

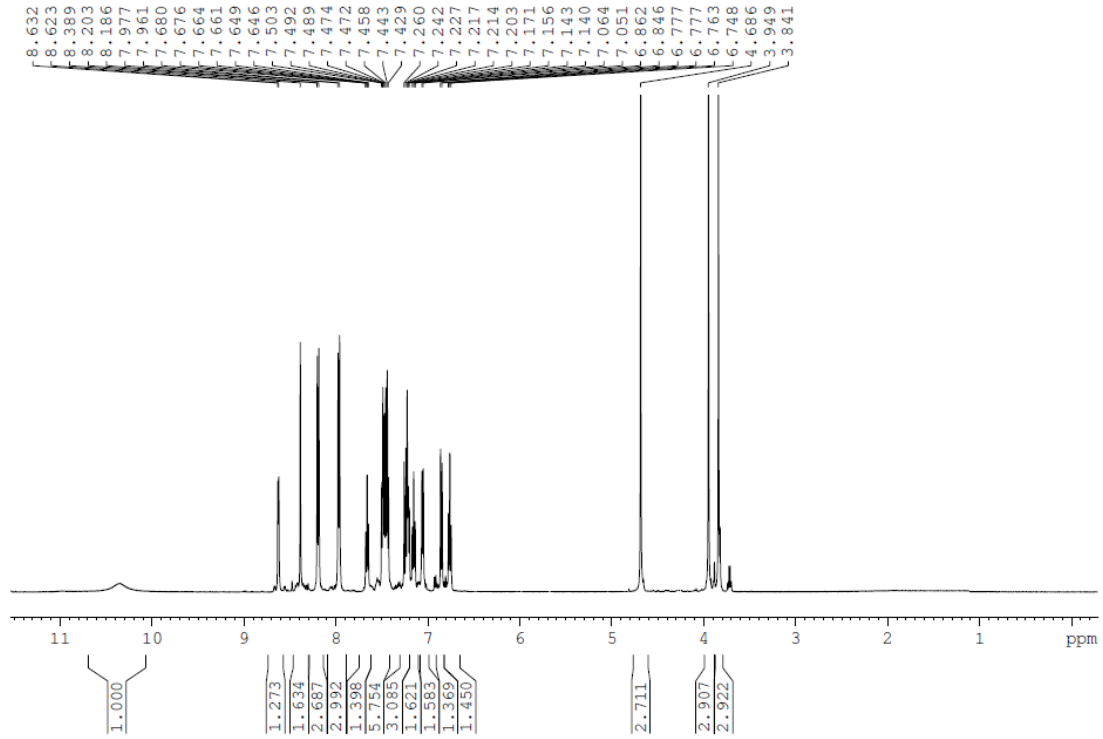


Fig. S12 The ^{1}H NMR spectroscopy of **5**

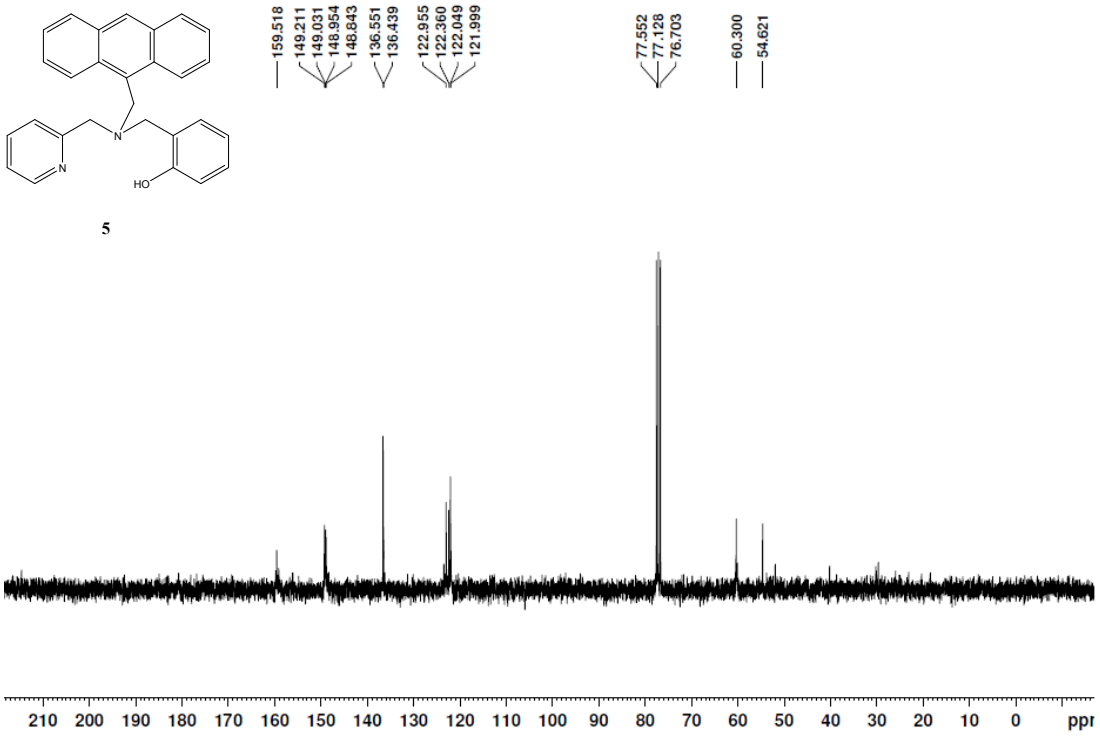


Fig. S13 The ^{13}C NMR spectroscopy of **5**

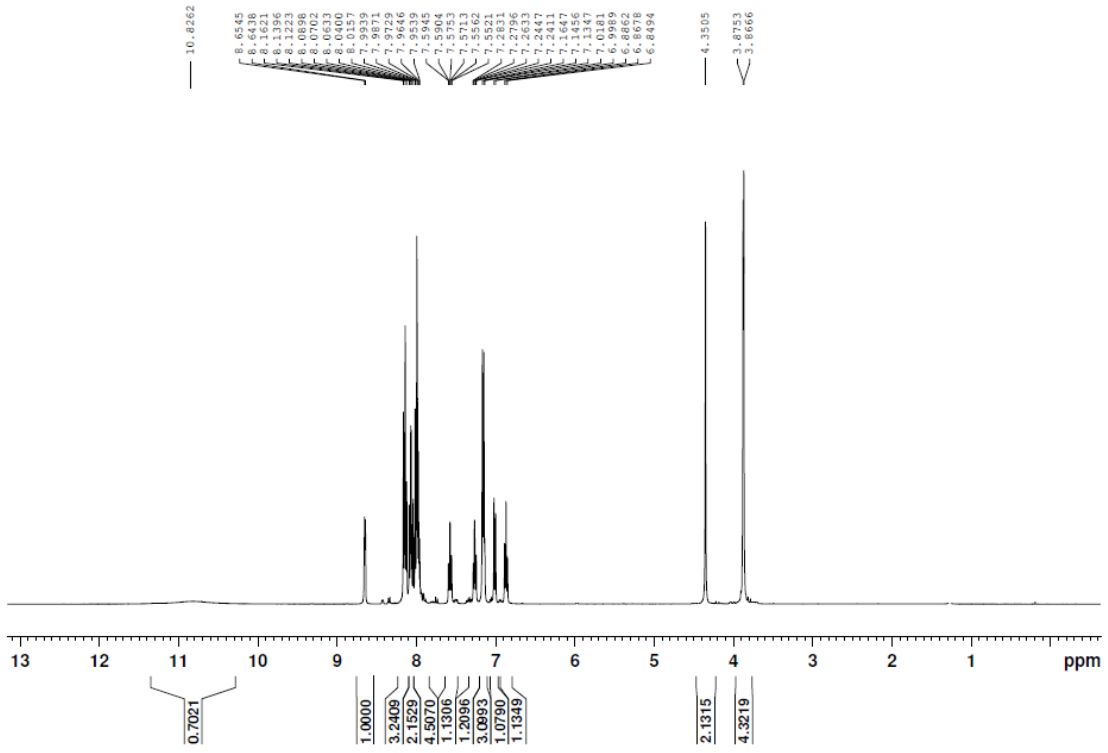


Fig. S14 The [1]H NMR spectroscopy of **6**

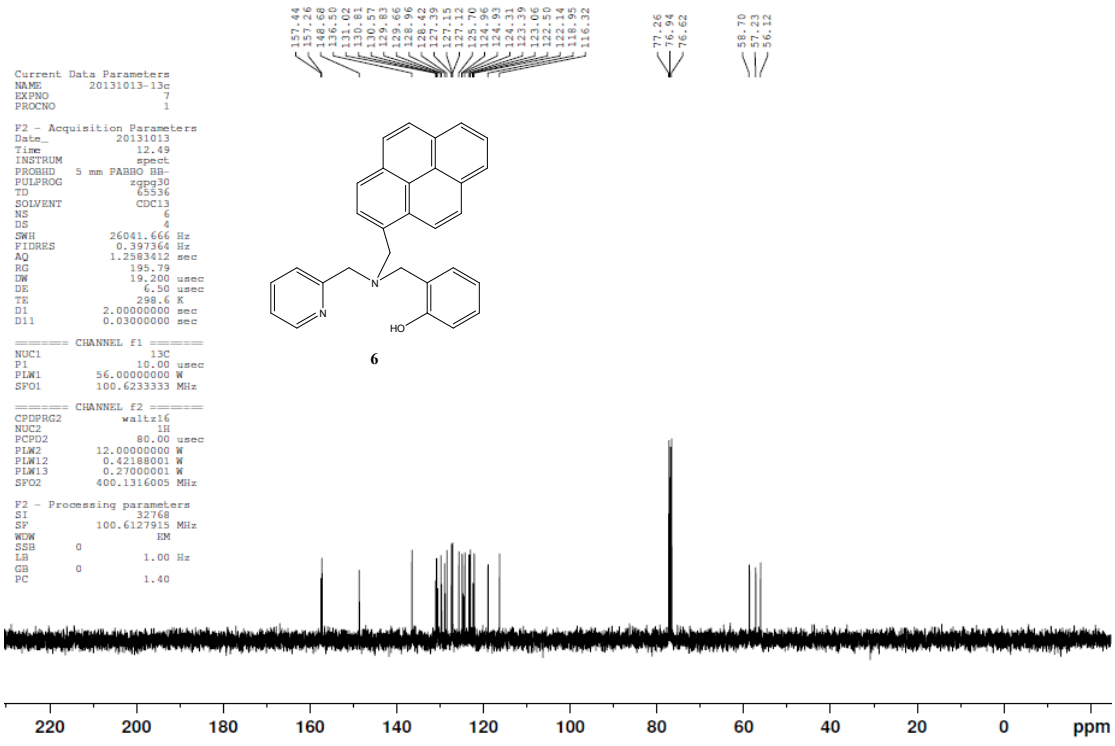


Fig. S15 The [13]C NMR spectroscopy of **6**

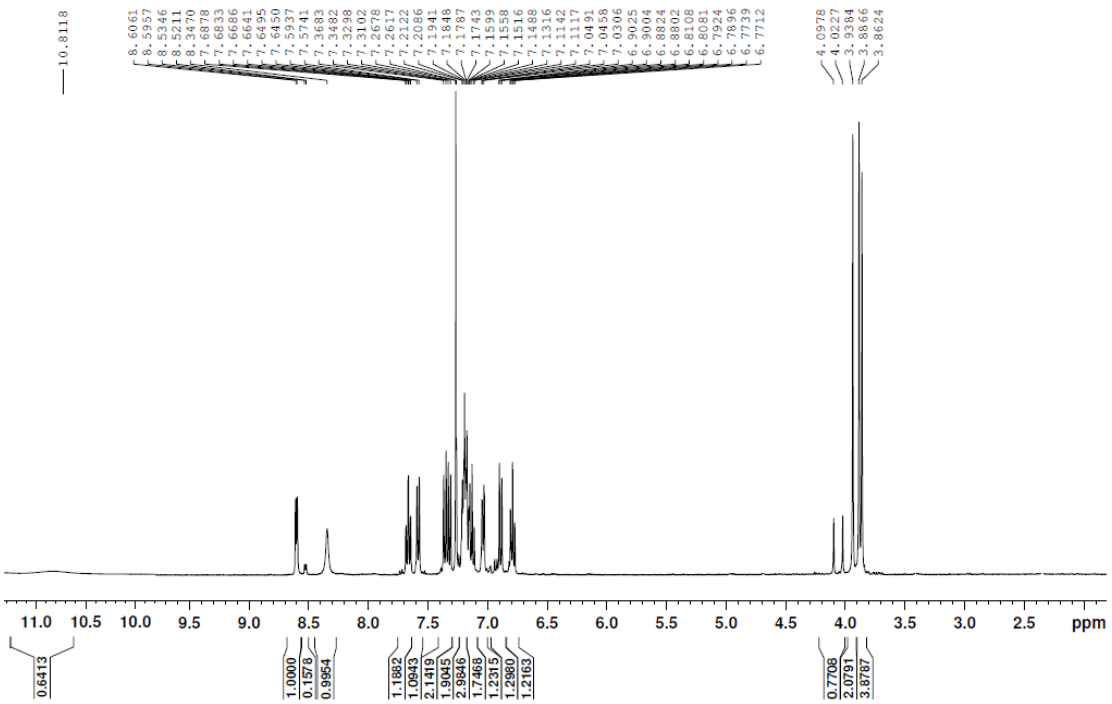


Fig. S16 The ^{1}H NMR spectroscopy of **7**

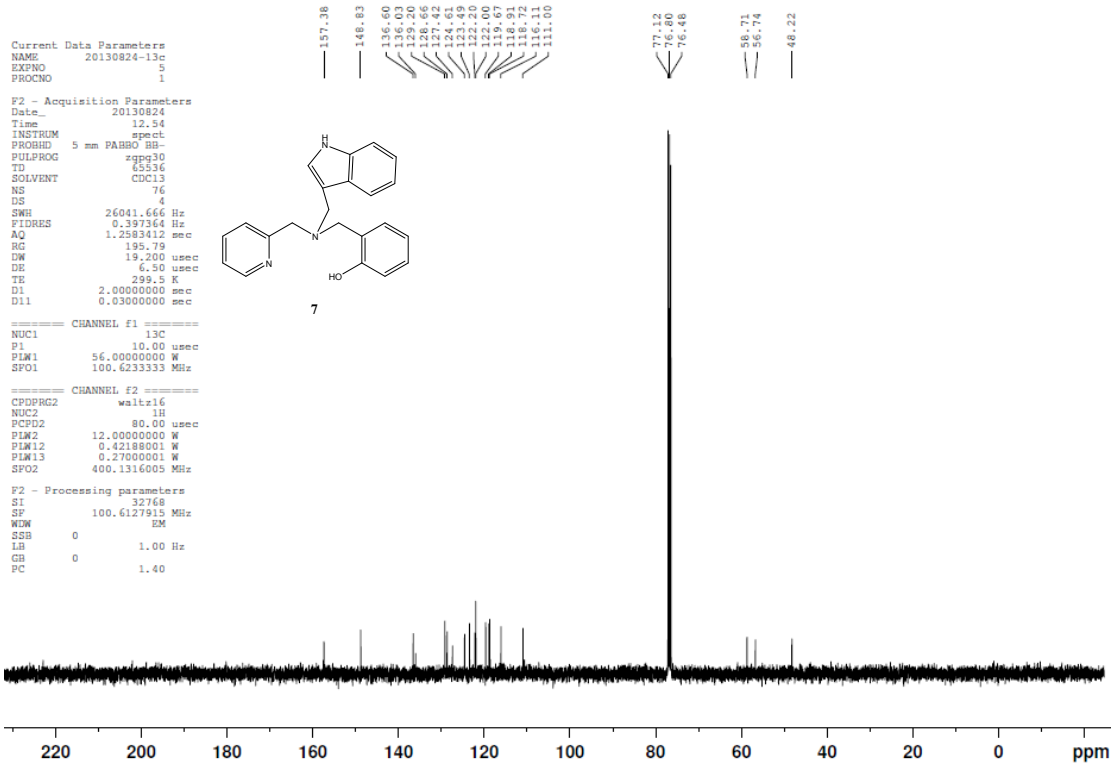


Fig. S17 The ^{13}C NMR spectroscopy of **7**

H RMS data

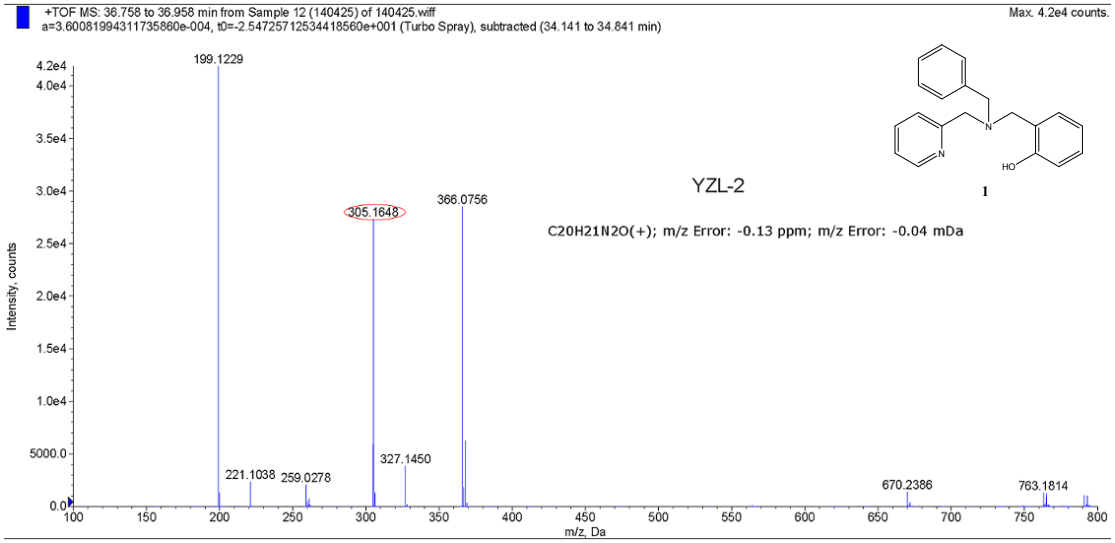


Fig. S18 The HR-MS spectroscopy of **1**

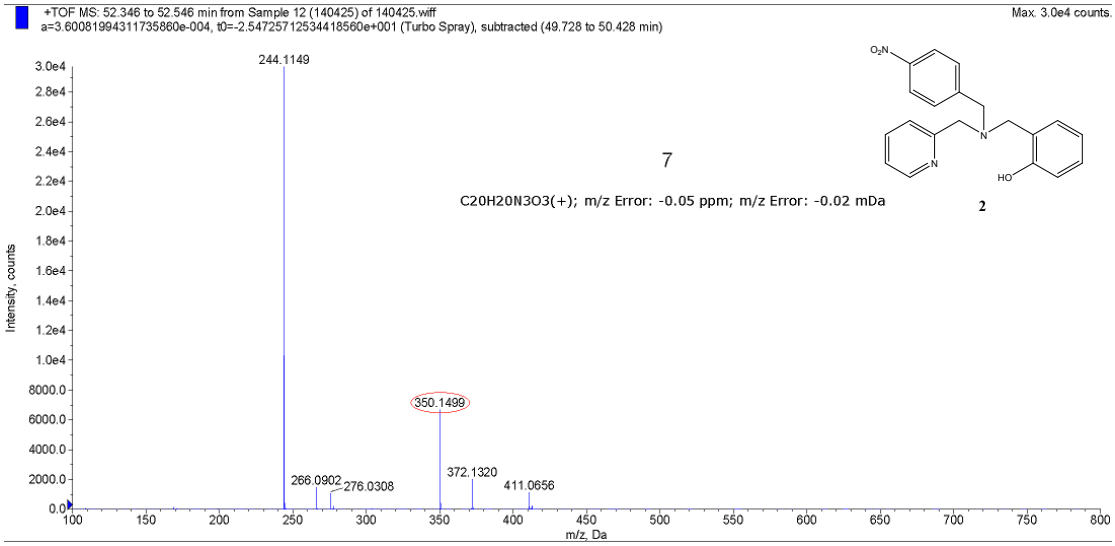


Fig. S19 The HR-MS spectroscopy of **2**

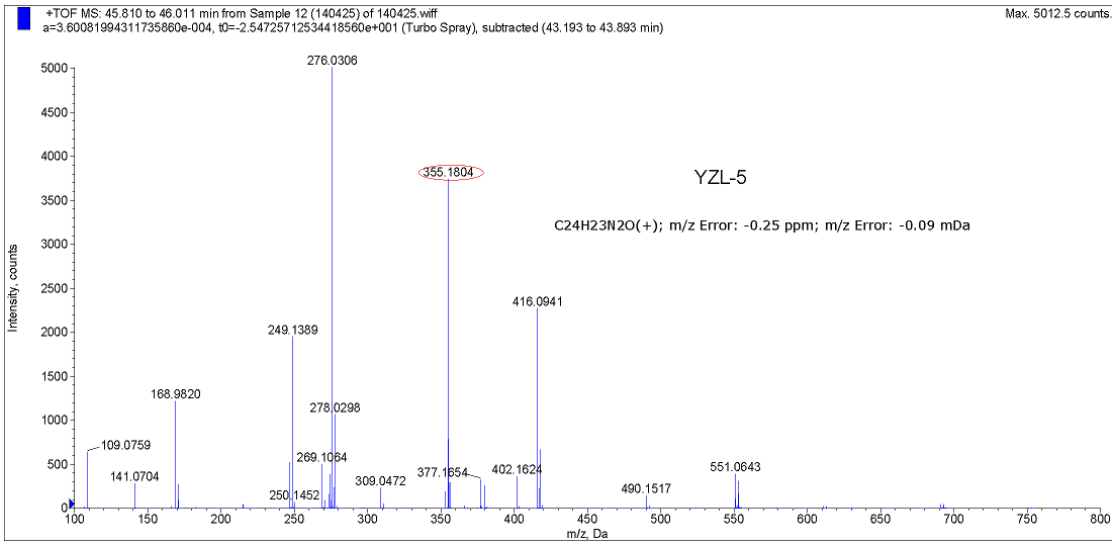


Fig. S20 The HR-MS spectroscopy of **3**

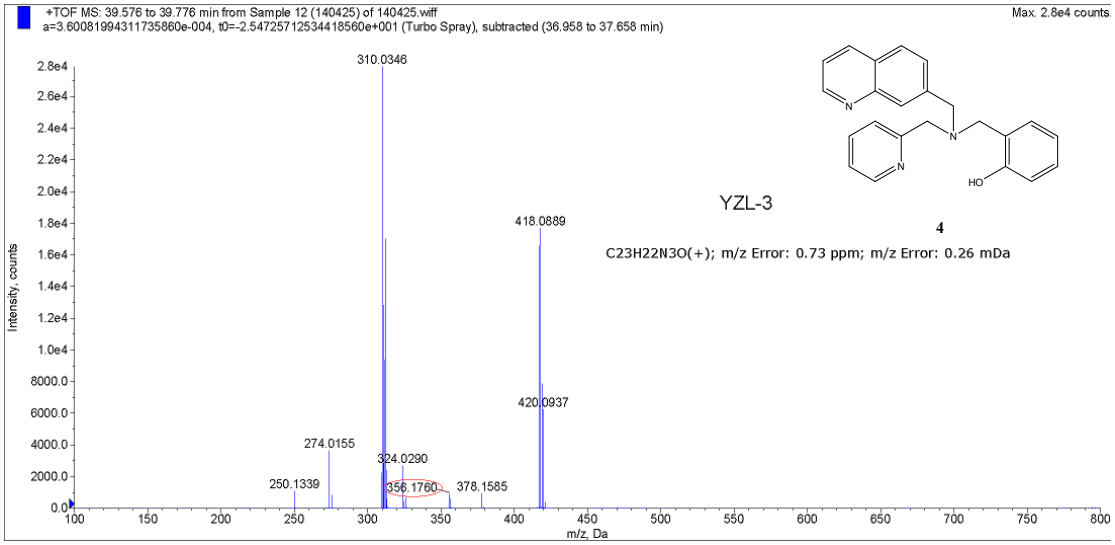


Fig. S21 The HR-MS spectroscopy of **4**

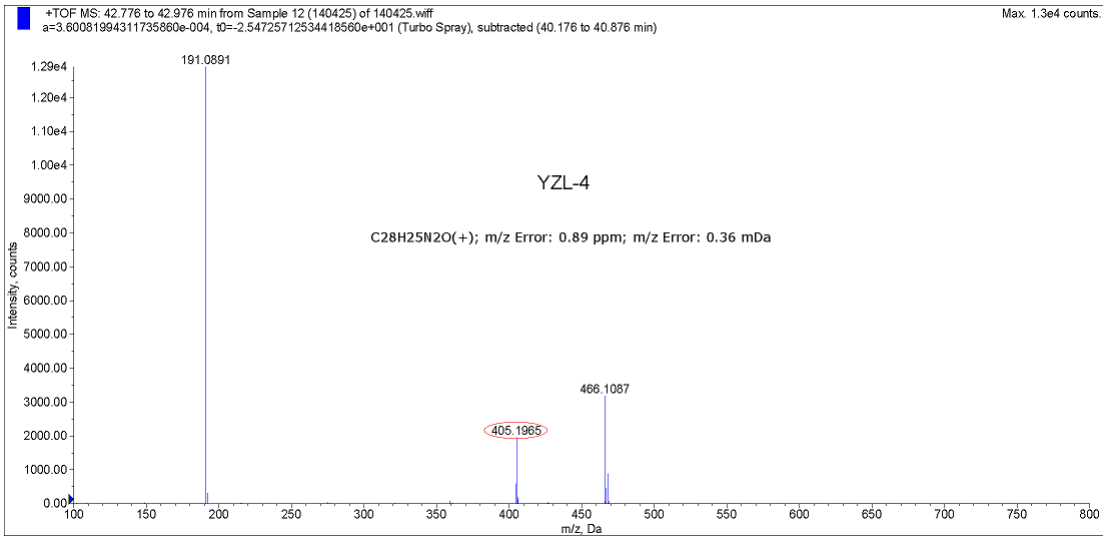


Fig. S22 The HR-MS spectroscopy of **5**

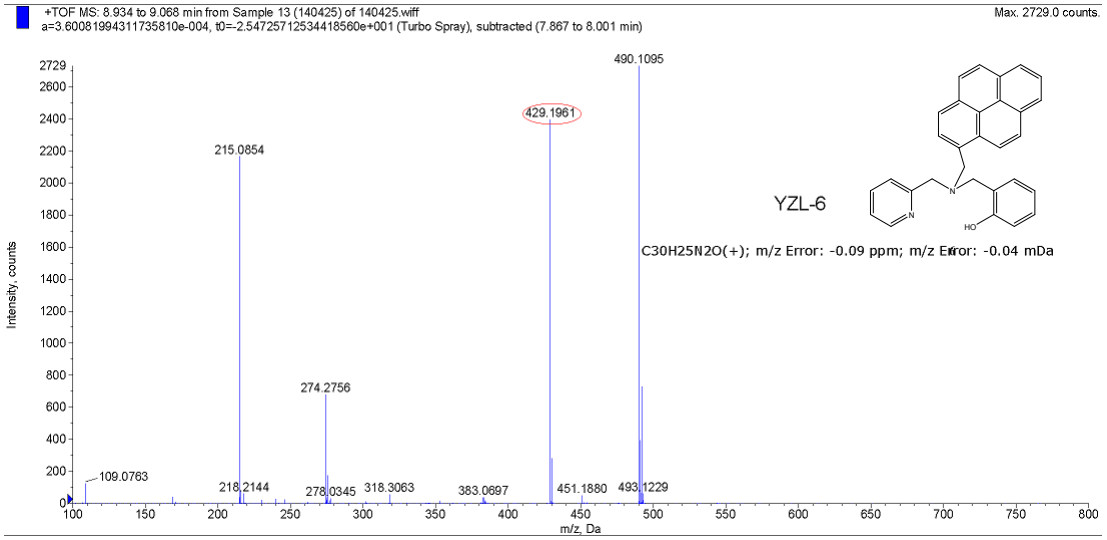


Fig. S23 The HR-MS spectroscopy of **6**

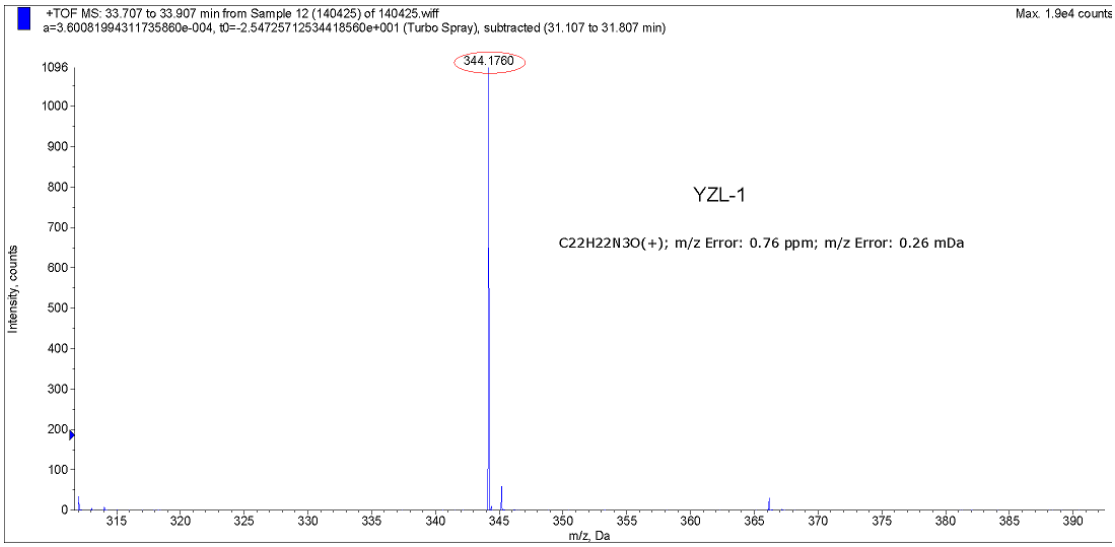


Fig. S24 The HR-MS spectroscopy of **7**

FT-IR spectroscopy data

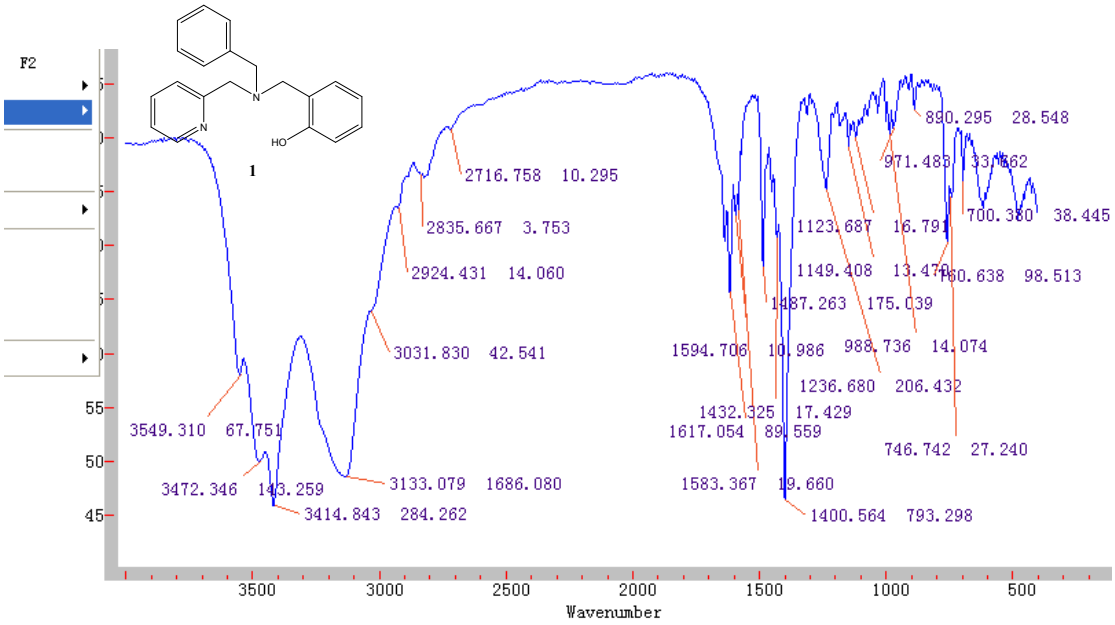


Fig. 25 The FT-IR spectroscopy of **1**

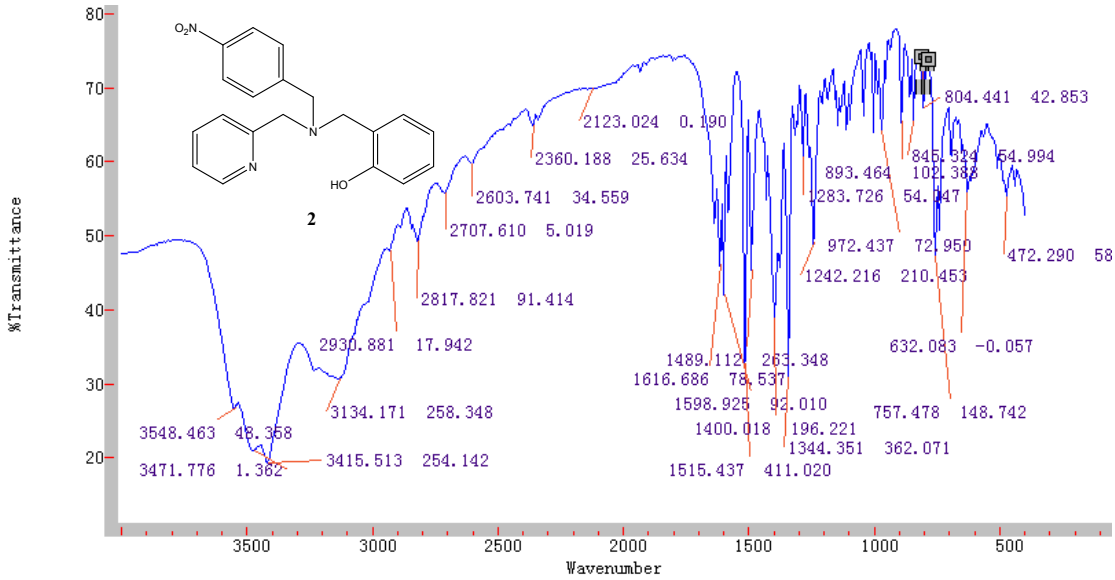


Fig. 26 The FT-IR spectroscopy of **2**

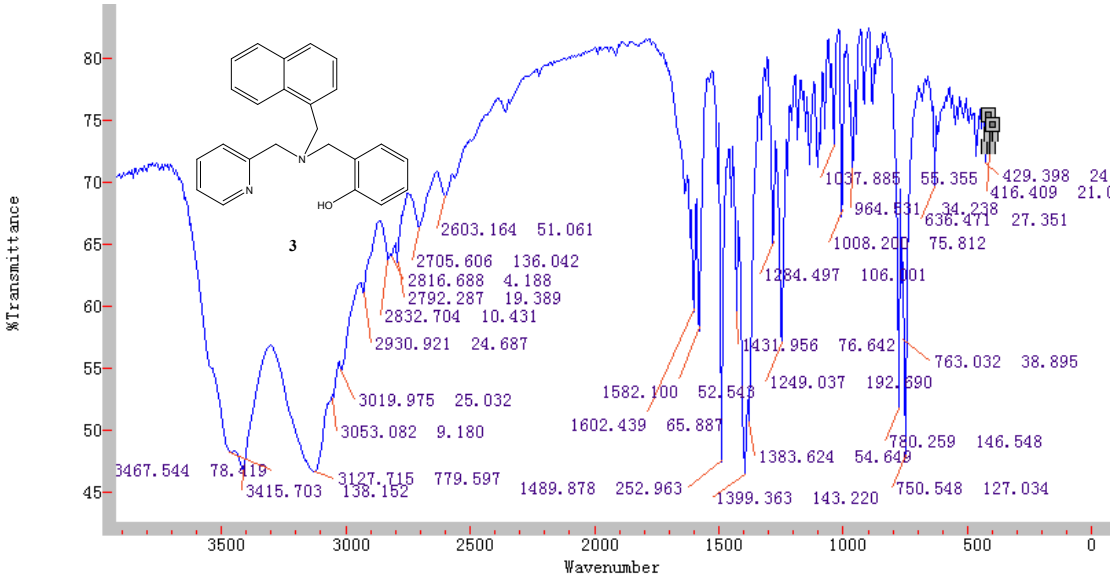


Fig. 27 The FT-IR spectroscopy of **3**

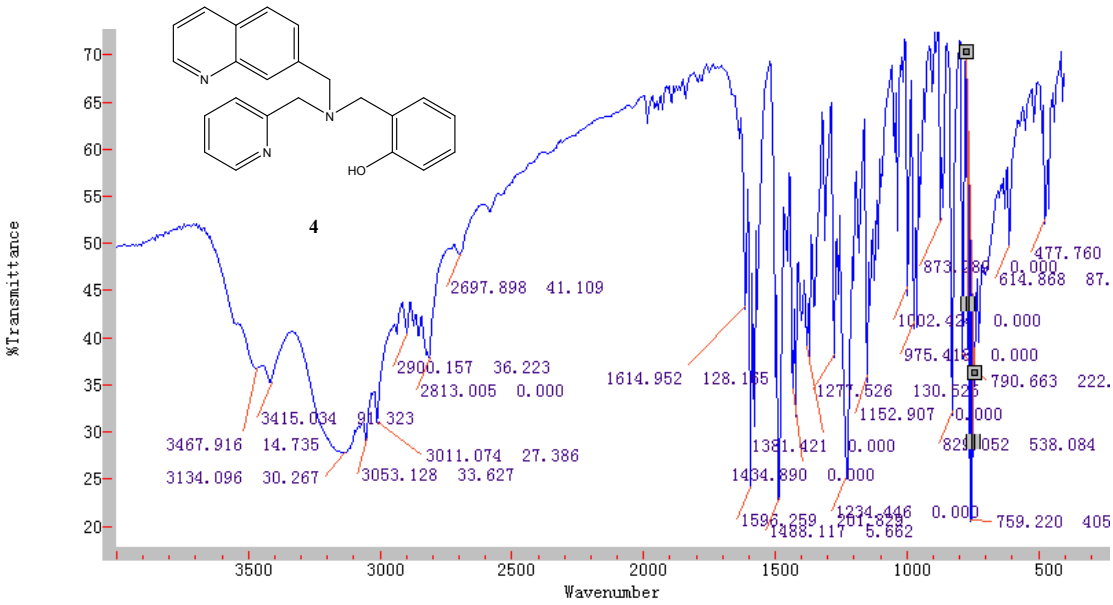


Fig. 28 The FT-IR spectroscopy of **4**

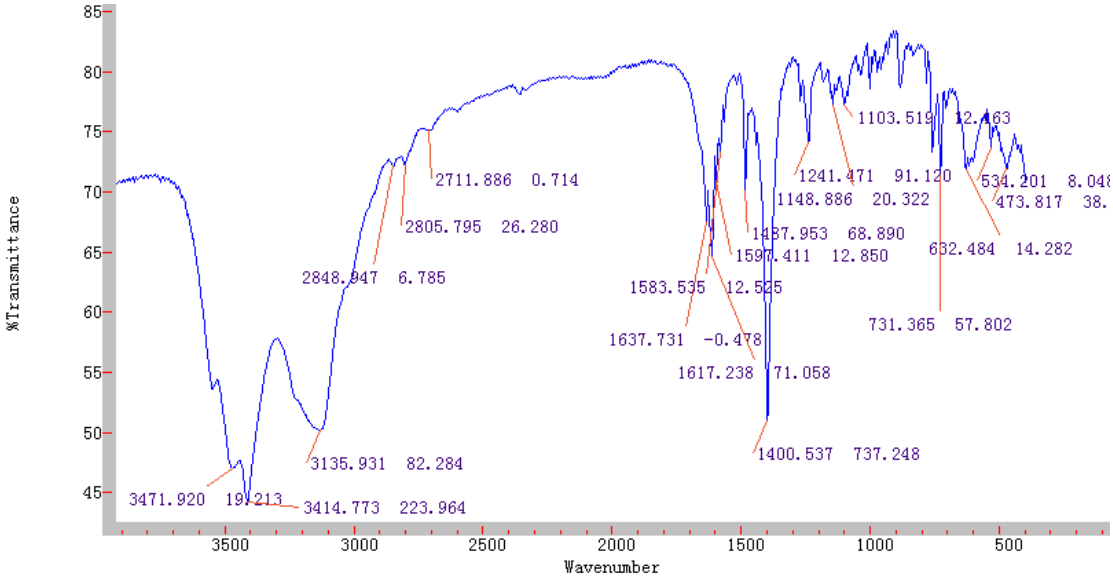


Fig. 29 The FT-IR spectroscopy of **5**

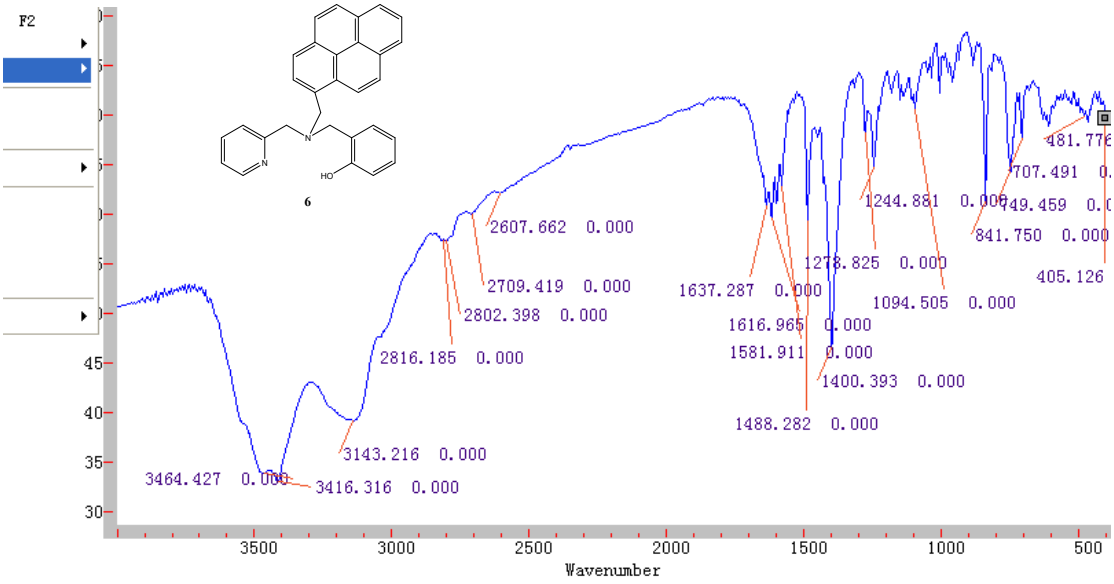


Fig. 30 The FT-IR spectroscopy of **6**

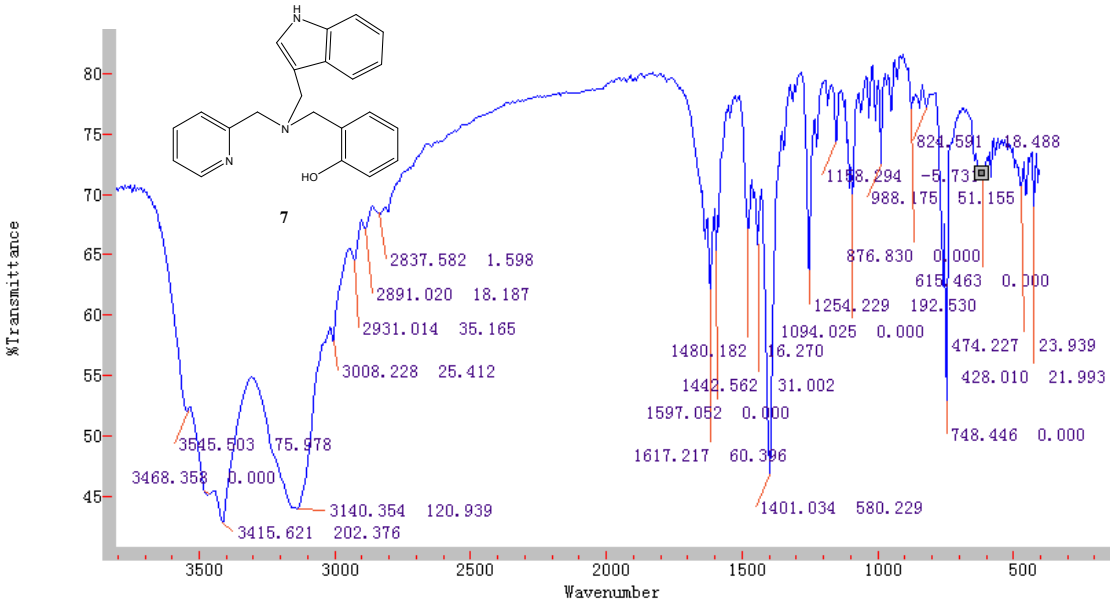


Fig. 31 The FT-IR spectroscopy of **7**