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Influence of substituent on Equilibrium of benzoxazine synthesis from Mannich Base and formaldehyde

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N-substituted aminomethylphenol (Mannich base) and 3,4-dihydro-2H-3- substituted -1,3-benzoxazine (benzoxazine) were synthesized from substituted phenol (p-cresol, phenol, p-chlorophenol), substituted aniline (p-toluidine, aniline, p-chloroaniline) and formaldehyde to study influence of substituent on equilibrium of benzoxazine synthesis from Mannich base and formaldehyde. ^{1}H-NMR and charge of
10 nitrogen and oxygen atoms illustrate effect of substituent on reactivity of Mannich base, while oxazine ring stability is characterized by Differential scanning calorimetry (DSC) and C-O bond order. Equilibrium constants are tested from 50 $^{\circ}$C to 80 $^{\circ}$C. Results show that substituent attached to phenol or aniline has same impact on reactivity of Mannich base, however it has opposite influence on oxazine ring stability and equilibrium constant. Comparing with the phenol-aniline system, electron-donating methyl
15 on phenol or aniline will increase the charge of nitrogen and oxygen atoms in Mannich base. When the methyl group locates at para position of phenol, oxazine ring stability increases, and the equilibrium constant climbs; when the methyl group locates at the para position of aniline, oxazine ring stability decreases, the benzoxazine hydrolysis tends to happen, equilibrium constant is significantly low.

Introduction

20 3,4-Dihydro-2H-3-substituted-1,3-benzoxazine (benzoxazine) is readily prepared by condensation of phenolic derivative, formaldehyde and primary amine. The compound can be polymerized to polybenzoxazine, which has attracted industrial and academic attention as high performance thermosetting
25 polymer because of its excellent mechanical properties, high heat resistance, and low dielectric constant etc. [1, 2] Large varieties of phenolic derivative and primary amine allow benzoxazine considerable molecule-design flexibility. Substituents such as aldehyde [3], hydroxymethyl [4,5] and silane [6,7] have been introduced
30 into the compound as required. The ring-opening polymerization mechanism [8-11] and influence of structures on polymerization [12,13] were researched. However, the structures affect benzoxazine synthesis, which is important but rarely discussed.

The structures of phenolic derivative and primary amine have a
35 great effect on synthesis of benzoxazine monomer. In condensation of substituted phenol with primary amine and formaldehyde, the products could be benzoxazine, N-substituted aminomethylphenol (Mannich base) and N, N'- bis (2-hydroxybenzyl) amine, the type and yield of product were
40 influenced by substituents on phenol and the structure of amine. [14-16] Both electron density at the free ortho position of phenols and the reactivity of phenolic hydroxyl played an important role. [17,18] Influence of electronic effects from bridging groups of bisphenols on benzoxazine synthesis was investigated,[12] results
45 showed that electron-donating groups resulted in high yield of product while electron-withdrawing groups were not conducive to benzoxazine synthesis. Effect of primary amine structures is more complicated. In synthesis of naphthoxazine from 2-naphthol, primary aromatic amines and formaldehyde, different substituent
50 on amine led to different yield. [19] For most amine, the reaction should be carried out under neutral or basic condition, while for weak amine (pKa<3) to synthesize benzoxazines, the reaction must be operated in the strongly acidic condition (pH=1.2). [20] More detailed and systematic research is lacking.
55 Chemical equilibrium and influence of reactant structure are meaningful to benzoxazine synthesis. However, reaction of phenolic derivative with primary amine and formaldehyde is too complex to study equilibrium of oxazine ring formation directly from the three reactants. Mannich base, the product of reaction of
60 phenol, primary amine and formaldehyde in a mole ratio of 1:1:1, is considered as the intermediate in benzoxazine synthesis. [18] The compound reacts with formaldehyde to form benzoxazine and no by-product is generated. In previous work, kinetic of reaction between 2-phenylaminomethylphenol (phenol-aniline based
65 Mannich base) and formaldehyde to benzoxazine was investigated, results showed that the reaction ran rapidly, the reverse reaction is hydrolysis of benzoxazine to Mannich base [21]

In this paper, p-substituted phenol and p-substituted aniline were used to synthesize Mannich base, influence of substituent on
70 chemical equilibrium of benzoxazine synthesis from Mannich base and formaldehyde was investigated. pKa of phenol and primary amine [22], structures of Mannich base and reaction are shown in Scheme 1. Substituents on phenol or aniline have the same effect on reactivity of phenolic hydroxyl and secondary

amine in Mannich base, but have the opposite effect on the stability of oxazine ring. Influence of substituent on equilibrium constant of reaction between Mannich base and formaldehyde to benzoxazine agree with that on the stability of oxazine ring. For the electron-donating methyl group on para position of phenol, the charge of nitrogen and oxygen atoms increase, the C-O bond order and stability of oxazine ring increase, the reverse reaction hydrolysis of benzoxazine becomes difficult, and the equilibrium constant is higher. However, for methyl at para of aniline, the charge of nitrogen and oxygen increase, but the stability of oxazine ring drops, hydrolysis of benzoxazine is easy and the reverse reaction is favored, the equilibrium constant is significantly low.
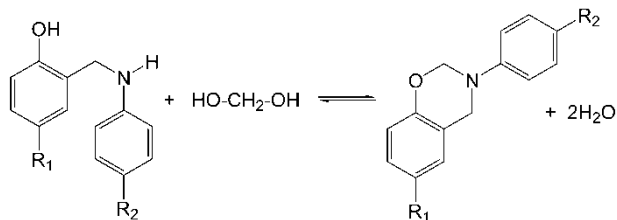
Mannich base	Benzoxazine	R_1	pKa of phenol	R_2	pKa of amine
MB(H-H)	BOZ(H-H)	H	10.00	H	4.62
MB(CH₃-H)	BOZ(CH₃-H)	CH_3	10.26	H	4.62
MB(Cl-H)	BOZ(Cl-H)	Cl	9.38	H	4.62
MB(H-CH₃)	BOZ(H-CH₃)	H	10.00	CH_3	5.00
MB(H-Cl)	BOZ(H-Cl)	H	10.00	Cl	3.93

Scheme 1 Reaction between Mannich base and formaldehyde to benzoxazine and Abbr. of compounds.

Experimental section

Materials

Phenol (≥99%, ACS) and aniline (≥99%, ACS) were purchased from Aladdin chemistry Co. Ltd. p-Cresol (≥98%, AR), p-chlorophenol (≥99%, AR) and dioxane (≥99.5%, AR) were from the Chengdu Kelong Chemical Reagents Corp. p-Toluidine (≥99%, AR) and p-chloroaniline (≥98%, CP) were from the Shanghai Tingxin Chemical Factory. Paraformaldehyde (≥98%, CP) was from Ercros Industrial S.A. Spain. All reagents were used as received.

Characterization and computation

Fourier transform infrared (FTIR) spectroscopies were characterized on a Nicolet Magna 650 instrument with a resolution of 4 cm^{-1} by KBr pellets. ^{1}H NMR spectroscopies were obtained on a Bruker TD-65536 NMR (400 MHz) using deuterated dimethyl sulfoxide (DMSO-d6) with tetramethylsilane as solvent. Differential scanning calorimetry (DSC) was performed on TA Instruments Q20 under nitrogen atmosphere. Melting points (mp) of compounds and nonisothermal DSC thermograms of benzoxazine monomers were characterized at a heating rate of 10 ^{o}C /min. Isothermal DSC thermograms of benzoxazine monomers were tested at 210 ^{o}C. Enthalpy of combustion was tested by burning samples in a SHR – 15B Oxygen Bomb Calorimeter (Nanjing Sangli Electronic

Equipment Factory). Molecular simulation was performed using Dmol^3 program in Materials Studio 4.0(Accelrys, USA). Charge of atom is partitioned by Hirshfeld method.

Synthesis of Mannich base

0.5 mol of substituted phenol and 0.5 mol of substituted aniline were dissolved in toluene at 70 ^{o}C to form a homogeneous solution. 0.5 mol of paraformaldehyde was added into the solution. The mixture was stirred for 5h, a transplant solution was obtained. The solution was cooled to room temperature and filtered. Yellow powder was obtained and then recrystallized in ethanol and acetone respectively. The product was obtained as white powder.

2-phenylaminomethy-phenol (MB (H-H))[23]
Yield: 40%. Mp: 115.7 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 9.49 (s, 1H, Ar-OH), 6.5 - 7.2 (9H, Ar-H), 5.97 (t, 1H, NH), 4.19 (d, 2H, Ar-CH$_2$-N). FTIR (KBr, cm^{-1}): 3415 (OH, stretch), 3266 (NH, stretch), 1251 (C-N, stretch).

4-methyl-2-phenylaminomethy-phenol (MB (CH₃-H))[24]
Yield: 64%. Mp: 101.8 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 9.25 (s, 1H, Ar-OH), 6.5 - 7.1 (8H, Ar-H), 5.94 (t, 1H, NH), 4.14 (d, 2H, Ar-CH$_2$-N), 2.14 (s,Ar-CH$_3$,3H). FTIR (KBr, cm^{-1}): 3424 (OH, stretch), 3276 (NH, stretch), 1259 (C-N, stretch).

4-chloro-2-phenylaminomethy-phenol (MB (Cl-H))
Yield: 64%. Mp: 113.1 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 9.86 (s, 1H, Ar-OH), 6.1 - 7.2 (8H, Ar) 6.10 (t, 1H, NH), 4.18 (d, 2H, Ar-CH$_2$-N). FTIR (KBr, cm^{-1}): 3418 (OH, stretch), 3268 (NH, stretch), 1253 (C-N, stretch).

2- (4-tolylamino-methyl)-phenol (MB (H-CH₃))[25]
Yield: 80%. Mp.: 118.4 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 9.43 (s, 1H, Ar-OH), 6.4 - 7.1 (8H, Ar), 5.70 (t, 1H, NH), 4.16 (d, 2H, Ar-CH2-N), 2.12 (s, Ar-CH$_3$, 3H). FTIR (KBr, cm^{-1}): 3414 (OH, stretch), 3260 (NH, stretch), 1249 (C-N, stretch).

2- (4-chlorophenylamino-methyl)-phenol (MB (H-Cl))[26]
Yield: 64%. Mp.: 125.3 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 9.54 (s, 1H, Ar-OH), 6.5 - 7.2 (8H, Ar) 6.24 (t, 1H, NH), 4.15 (d, 2H, Ar-CH2-N). FTIR (KBr, cm^{-1}): 3415 (OH, stretch), 3257 (NH, stretch), 1250 (C-N, stretch).

Synthesis of benzoxazine

Benzoxazine was prepared by condensation of phenol, primary amine and formaldehyde in solution as reported[3] and recrystallized in acetone twice. White crystal was obtained.

3, 4-dihydro-3-phenyl -2H -1,3-benzoxazine (BOZ (H-H))
Mp: 58.0 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 6.7 - 7.3 (9H, Ar-H), 5.44 (s, 2H, O-CH$_2$-N), 4.66 (s, 2H, N-CH$_2$-Ar). FTIR (KBr, cm^{-1}): 1225 (Ar-O-CH$_2$), 938 (oxazine ring).

3, 4-dihydro-3-phenyl -6-methyl-2H -1,3-benzoxazine (BOZ (CH₃-H))
Mp: 55.7 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 6.6 - 7.3 (8H, Ar), 5.40 (s, 2H, O-CH$_2$-N), 4.61 (s, 2H, N-CH$_2$-Ar) , 2.19 (s, Ar-CH3, 3H). FTIR (KBr, cm^{-1}): 1222 (Ar-O-CH$_2$), 943 (oxazine ring).

3, 4-dihydro-3-phenyl -6-chloro-2H -1,3-benzoxazine (BOZ (Cl-H))
Mp: 62.7 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 6.7-7.3 (8H, Ar), 5.47 (s, 2H, O-CH$_2$-N), 4.67 (s, 2H, N-CH$_2$-Ar). FTIR (KBr, cm^{-1}): 1226 (Ar-O-CH$_2$), 943 (oxazine ring).

3, 4-dihydro-3- (4-methylphenyl) -2H -1,3-benzoxazine (BOZ (H-CH₃))

Mp: 84.1 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ = 6.7-7.1 (8H, Ar), 5.40 (s, 2H, O-CH$_2$-N), 4.60 (s, 2H, N-CH$_2$-Ar),
5 2.18 (s, Ar-CH$_3$, 3H). FTIR (KBr, cm^{-1}): 1223 (Ar-O-CH$_2$), 940 (oxazine ring).

3, 4-dihydro-3- (4-chlorophenyl) -2H -1,3-benzoxazine (BOZ (H-Cl))

Mp: 62.2 ^{o}C (DSC). ^{1}H NMR (400 MHz, DMSO-d6, ppm): δ =
10 6.7-7.3 (8H, Ar), 5.44 (s, 2H, O-CH$_2$-N), 4.65 (s, 2H, N-CH$_2$-Ar). FTIR (KBr, cm^{-1}): 1222 (Ar-O-CH$_2$), 945 (oxazine ring).

Reaction between Mannich base and formaldehyde

The aqueous formaldehyde solution was prepared by dissolving paraformaldehyde in water and titrated to determine the
15 concentration as reported. [21] Mannich base was dissolved in dioxane as calculated. Aqueous formaldehyde solution and extra water were added. Concentrations of Mannich base and formaldehyde were 0.7 mol/kg and concentration of total water including both in the formaldehyde solution and in the extra was
20 about 4.54 mol/kg. The reaction time at 50 ^{o}C, 60 ^{o}C, 70 ^{o}C and 80 ^{o}C is 6 h, 4 h, 4 h and 2 h respectively, which was fixed by Fig. S1. All systems were homogeneous in the process of reaction.

The reaction solution was dropped into NMR tubes, excessive n-propylamine was added immediately to consume remaining
25 formaldehyde. The samples were tested by ^{1}H-NMR to measure of benzoxazine formation.

Results and Discussion

Influence of substituent on reactivity of Mannich base

30 In order to study influence of substituent on equilibrium of reaction between Mannich base and formaldehyde to benzoxazine, p-substituted phenol (phenol, p-cresol and p-chlorophenol) with aniline system and p-substituted aniline (aniline, p-toluidine and p-chloroaniline) with phenol system were chosen to synthesize
35 Mannich base and benzoxazine, the structures and Abbr. of compounds are shown in Scheme 1.

^{1}H NMR data of Mannich bases are listed in Table 1. Compared with MB(H-H), signals assigned to -OH and -NH on Mannich base with the electron-donating methyl group (MB(CH$_3$-H) and
40 MB(H-CH$_3$)) move to high field, which indicates that charges of oxygen and nitrogen increase. For compounds substituted by electron-withdrawing chlorine atom, charges of these atoms decrease. Results of ^{1}H NMR show that substituent on phenol and aniline has the same effect on reactivity of Mannich base.
45 Additionally, substituent on phenol shows stronger influence on oxygen atoms, as substituent on aniline affects nitrogen atoms substantially.

Table 1 ^{1}H-NMR data of Mannich base

Mannich base	$\delta_{N\text{-}H}$ (ppm)	$\delta_{O\text{-}H}$ (ppm)
MB(H-H)	5.97	9.49
MB(CH$_3$-H)	5.94	9.25
MB(Cl-H)	6.10	9.86
MB(H-CH$_3$)	5.70	9.43
MB(H-Cl)	6.24	9.54

50

Influence of substituent on stability of oxazine ring

Thermal ring-opening polymerization of benzoxazine monomers has been investigated widely. [12, 13] After heating, C-O bond on oxazine ring cleavages, followed by polymerization. With
55 increasing C-O bond strength, oxazine ring obtains higher stability, reaction will become more difficult to happen. Non-isothermal and isothermal DSC analysis were used for monitoring benzoxazine ring-opening reaction to reveal the effect of substituent on stability of oxazine ring. DSC thermograms are
60 shown in Fig. 1 and Fig. 2, and summary data are listed in Table 2.

According to Fig. 1A and Fig. 2A, the initial and peak temperature for thermal polymerization of benzoxazine increase after the electron - donating methyl group is introduced in phenol,
65 in isothermal DSC, BOZ(CH$_3$-H) shows a longer induction period than BOZ(H-H), which proves the higher stability of oxazine ring; on the other side, BOZ(Cl-H) presents lower curing temperature as well as shorter induction period, resulting from the decrease of ring stability after hydrogen on para position of
70 phenol being substituted by electron-withdrawing chlorine atom. If the substituent appears on the para position of aniline, it has opposite effect, as shown in Fig. 1B and Fig. 2B. Oxazine ring of BOZ(H-CH$_3$) has lower stability, while stability of BOZ(H-Cl) is higher. Substituent on aniline has less impact, comparing with its
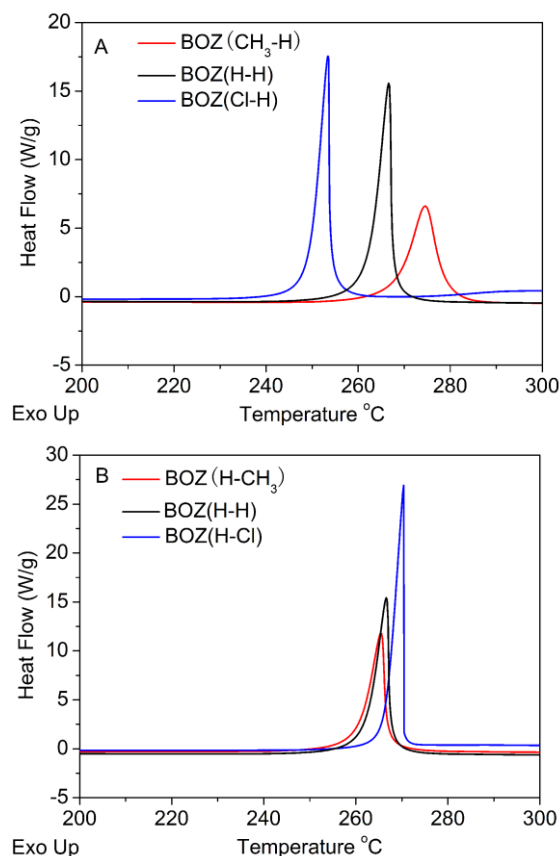75 presence on phenol.

Fig. 1 Non-isothermal DSC thermograms of benzoxazine at a heating rate of 10 ^{o}C/min. A. substituted phenol – aniline system; B. phenol - substituted aniline system
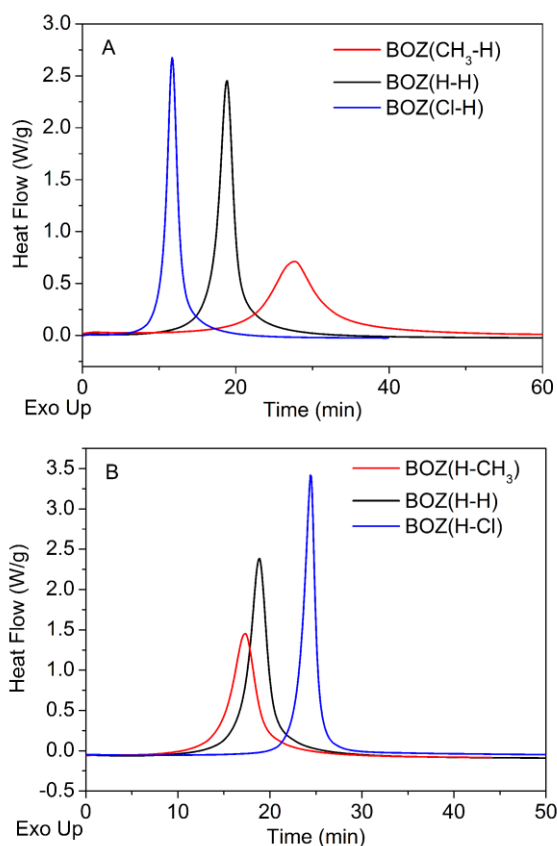
Fig. 2 Isothermal DSC thermogram of benzoxazine at 210 °C. A. substituted phenol – aniline system; B. phenol - substituted aniline system

Table 2 DSC data of benzoxazine

Benzoxazine	Non-isothermal DSC		Isothermal DSC		ΔH(kJ/mol)
	T_{onset} (oC)	T_{peak} (oC)	t_{onset} (min)	t_{peak} (min)	
BOZ(H-H)	262.1	266.7	16.9	18.9	86.7
BOZ(CH3-H)	268.0	274.5	22.3	27.7	81.1
BOZ(Cl-H)	249.3	253.4	10.4	11.7	92.2
BOZ(H-CH3)	260.5	265.5	14.7	17.4	88.9
BOZ(H-Cl)	266.3	270.4	23.0	24.4	85.1

Molecular Simulation

In order to elucidate the effect of substituent on reactivity of Mannich base and stability of oxazine ring, charge of oxygen atom and nitrogen atom on Mannich base and bond order of C-O on oxazine ring were computed by Materials Studio 4.0, results are shown in Table 3.

Table 3 Results of molecular simulation

Mannich base	Charge of atom		Benzoxazine	Mayer Bond Order of C-O
	O	N		
MB(H-H)	-0.185	-0.118	BOZ(H-H)	0.961
MB(CH3-H)	-0.187	-0.118	BOZ(CH3-H)	0.962
MB(Cl-H)	-0.181	-0.116	BOZ(Cl-H)	0.949
MB(H-CH3)	-0.185	-0.120	BOZ(H-CH3)	0.945
MB(H-Cl)	-0.183	-0.115	BOZ(H-Cl)	0.962

Results in Table 3 show, Mannich bases containing electron-donating methyl group, MB(CH3-H) and MB(H-CH3), have increased charge density on oxygen and nitrogen atoms, however, in Mannich bases with electron-withdrawing chlorine atom, MB(Cl-H) and MB(H-Cl), charges on oxygen and nitrogen atoms decrease. The results are consistent with chemical shift in ^{1}H-NMR.

Bond order reflects the relative strength of covalent bonds. C-O bond order shows the oxazine ring stability in this case. When para position on phenol is substituted by methyl, C-O bond order increases, revealing the increasing stability of oxazine ring, but bond order drops down after phenol being substituted by chlorine atom. Substituent shows an opposite effect if being introduced in aniline. The results of bond order agree with the benzoxazine DSC analysis.

Influence of substituent on equilibrium of reaction between Mannich base and formaldehyde

To investigate the effect of substituent on reaction equilibrium, Mannich bases with different substituents react with formaldehyde in dioxane at 70 °C for 4 h, the ^{1}H-NMR spectra are shown in Fig. 3. Benzoxazine is indentified by signals around 5.4 ppm and 4.6 ppm, which are assigned to O-CH$_2$-N and N-CH$_2$-Ar on oxazine ring. Moreover, signal at about 4.2 ppm assigned to Ar-CH$_2$-N on remaining Mannich base. It is obviously in Fig. 3A, while the para position of phenol is occupied by electron-donating methyl group, reaction degree climbs up, however, it drops if the substituent is electron-withdrawing chlorine, Mannich base is massive preserved. Substituent on para position of aniline has opposite influence, as shown in Fig. 3B, reaction degree between MB(H-CH$_3$) and formaldehyde is lower than that between MB(H-H) and formaldehyde, while reaction degree in MB(H-Cl) system is the highest.
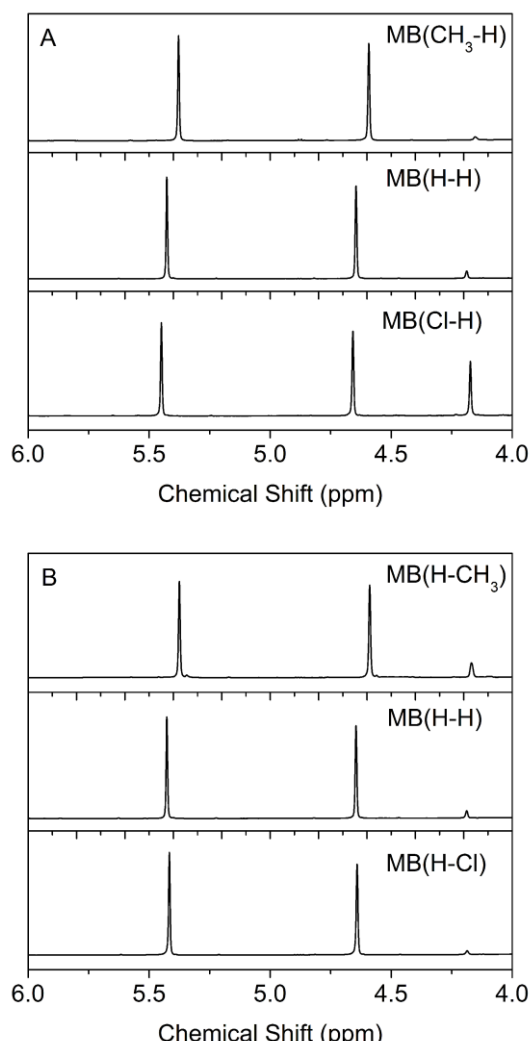
Fig. 3 ^{1}H-NMR spectra of reaction solution of Mannich base and formaldehyde at 70 ºC for 4h. A. substituted phenol system; B. substituted aniline system

5 After reaction between Mannich base and formaldehyde, only the product benzoxazine and remained Mannich base can be observed. Accordingly, eq(1) is used to calculate benzoxazine concentration [BOZ], thereby, the remained Mannich base concentration [MB] and formaldehyde concentration[F], as well 10 as water concentration [H_2O].

$$[BOZ] = \frac{I_{\delta=5.44}}{I_{\delta=5.44} + I_{\delta=4.18}} \cdot [MB]_0 \qquad eq(1)$$

$$[MB] = [MB]_0 - [BOZ]$$

$$[F] = [F]_0 - [BOZ]$$

$$[H_2O] = [H_2O]_0 + [BOZ]$$

$[MB]_0$, $[F]_0$ and $[H_2O]_0$ denote initial concentration of Mannich base, formaldehyde and water, respectively.

Based on the chemical property of formaldehyde, formaldehyde 15 molecules are minute in aqueous solution, they exist mostly in form of methylene glycol or poly(methoxyl) glycol, while the concentration is low, formaldehyde mainly appears in form of methylene glycol [27,28], therefore, the reaction equation and

equilibrium constant can be expressed as follows.

$$MB + HOCH_2OH = BOZ + 2H_2O$$

20
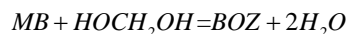
$$K = \frac{[BOZ] \cdot [H_2O]^2}{[MB] \cdot [F]}$$

The equilibrium constants of reaction between Mannich bases with different substituents and formaldehyde from 50 to 80 ºC are listed in Table 4. Fig. 4 shows the plot lnK vs. 1/T. When formaldehyde reacts with Mannich base with methyl on para 25 position of phenol, the equilibrium constant is remarkably bigger than that it reacts with MB(H-H), and the MB(Cl-H) system holds the smallest equilibrium constant. At 50 ºC, reaction between MB(H-H) and formaldehyde has an equilibrium constant 3540, while it is 6653 in MB(CH$_3$-H) system, and it drops 30 substantially to 129 when para position is occupied by chlorine atom. On the other hand, while the substituent locates on aniline, it has opposite influence on equilibrium constant, for example, at 50 ºC, reaction between MB(H-CH$_3$) and formaldehyde has an equilibrium constant 936, while it is 7621 in MB(H-Cl) system.

35

Table 4 Equilibrium constant and enthalpy of reaction between substituted Mannich base and formaldehyde

Mannich base	Temp. (ºC)	Yeild (%)	K (mol/kg)	ΔrxnH (kJ/mol)
MB(H-H)	50	90	3540 ±43	-15.84[*] (-27.0)[**]
	60	89	3095 ±108	
	70	89	2760 ±51	
	80	87	2105 ±89	
MB(CH$_3$-H)	50	93	6653 ±188	-10.21 (-22.6)
	60	92	5763 ±26	
	70	92	5210 ±85	
	80	92	4827 ±11	
MB(Cl-H)	50	60	129 ±1	-12.40
	60	57	111 ±6	
	70	56	102 ±4	
	80	54	86 ±2	
MB(H-CH$_3$)	50	82	936 ±39	-11.89 (-22.4)
	60	81	821 ±78	
	70	80	773 ±12	
	80	79	624 ±11	
MB(H-Cl)	50	93	7621 ±556	-13.21
	60	93	6249 ±334	
	70	92	5672 ±253	
	80	91	4970 ±303	

* calculated by equilibrium constant

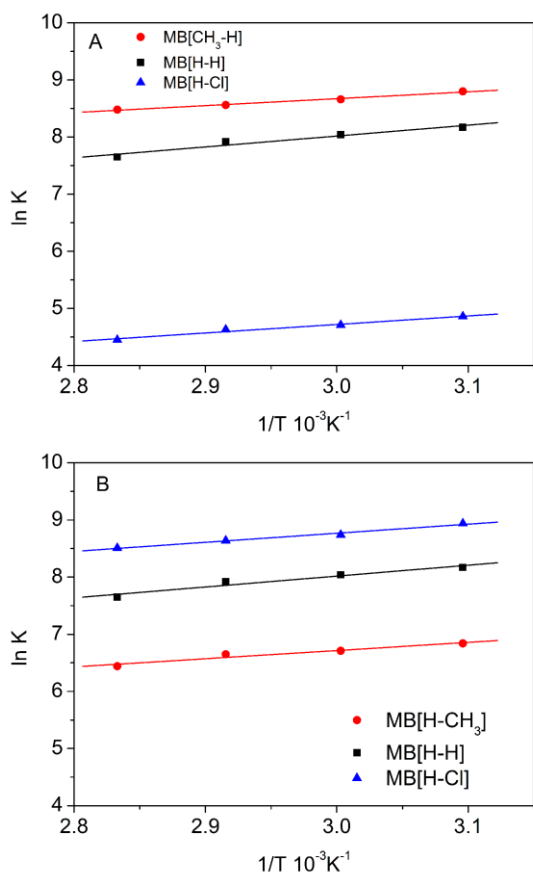** calculated by enthalpy of combustion

Fig. 4 Plot ln K versus 1/T. A. substituted phenol-aniline; B. phenol-substituted aniline

Reaction equilibrium constant is determined by the structures of the reactants and products, which affect forward and reverse reaction, respectively. Substituent on Mannich base will affect the reactivity of secondary amine and phenolic hydroxyl group. According to the results of ^{1}H NMR and molecular simulation, while substituents are attached to phenol or aniline, it shows the same trend of influence on charge density of nitrogen and oxygen atoms on Mannich base. In benzoxazine, from DSC outcome and C-O bond order, when substituent locates at para position on phenol or aniline, it has reverse impact on C-O bond strength, as well as ring stability. In comparison with MB(H-H), when electron-donating methyl group is attached on the para position of phenol, the reaction of MB(CH$_3$-H) and formaldehyde to benzoxazine and water has larger equilibrium constant, oppositely, the electron-withdrawing chlorine atom will cause the drop in equilibrium constant. By comparison, substituents on para position of aniline also play an opposite role on equilibrium constant, they cause a decrease of equilibrium constant in MB(H-CH$_3$) system and an increase in MB(H-Cl) system. The summary data are plotted in Fig. 5. Trend of equilibrium constant agrees with the change of oxazine ring stability.
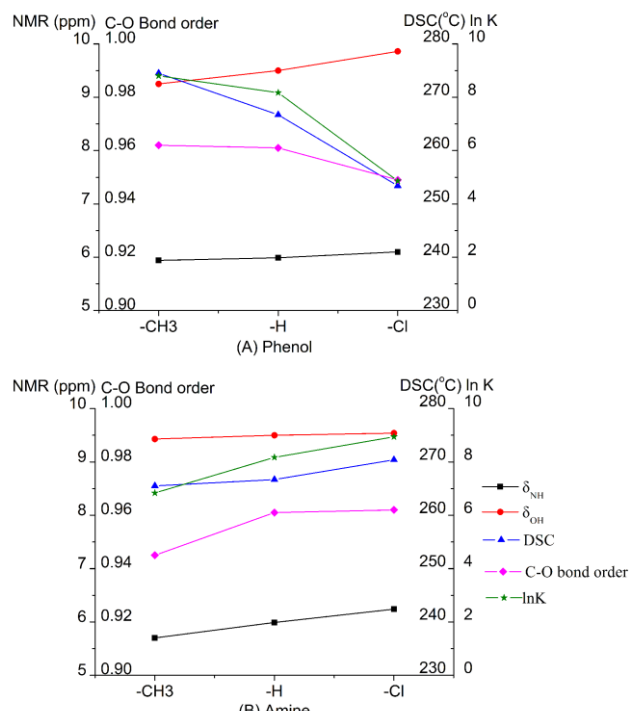

Fig. 5 Summary of ^{1}H-NMR, DSC, Bond order and Equilibrium Constant

Previous study[21] shows, in the forward reaction between Mannich base and formaldehyde, dehydration of methylene glycol to formaldehyde molecule is the rate-determining step, while reaction between Mannich base and formaldehyde molecule to benzoxazine is significantly faster. Therefore, effect of Mannich base reactivity on the whole reaction is far less than the reverse reaction, which is benzoxazine hydrolysis. While the electron-donating group is attached on para position of phenol, C-O bond strength and ring stability increase, hydrolysis is reluctant to happen, also, the equilibrium constant of reaction between Mannich base and formaldehyde to benzoxazine increases. However, if the electron-donating group located at the para position on aniline, C-O bond strength and ring stability will drop, and the hydrolysis will happen more easily, degree of reverse reaction increases, leading to low equilibrium constant.

The reaction yield(Y) of Mannich base and formaldehyde to benzoxazine can be calculated by eq(2), result is shown in Table 4. The theoretical yield can also be expressed by eq(3), showing it is a function of equilibrium constant, formaldehyde remnant and water concentration. During the benzoxazine synthesis, multiple methods can be adopted to increase yield, for example, excessive formaldehyde, low water concentration, or hydrophobic solvent such as toluene, chloroform et al. On the other hand, in electron-withdrawing group substituted phenol or electron-donating group substituted amine system, with decreased ring stability and equilibrium constant, higher formaldehyde quantity should be used in order to achieve higher benzoxazine yield.

$$Y = \frac{[BOZ]}{[MB]_0} \quad eq(2)$$

$$Y = \frac{K[F]}{[H_2O]^2 + K[F]} \quad eq(3)$$

In Table 4 and Fig. 4, it's obvious that equilibrium constant climbs as temperature drops in each system. According to Van't Hoff equation, assume the enthalpy of reaction($\triangle$rxnH) holds constant, it can be hence calculated, results are listed in Table 4. Reactions between Mannich base with different substituents and formaldehyde exhibit close enthalpy of reaction, ranged from -10 kJ/mol to -16 kJ/mol, it shows the reaction is exothermic.

Enthalpy of combustion, formation and reaction

Enthalpy of formation ($\triangle_f$H) is fundamental thermodynamic data of organic chemistry. In this paper, enthalpies of combustion ($\triangle$cH) corresponding to Mannich base as well as benzoxazine are tested, accordingly, enthalpy of formation $\triangle_f$H is calculated, detailed data are shown in Table 5. Results of chlorine containing compounds are not given because of incomplete combustion.

BOZ(CH$_3$-H) and BOZ(H-CH$_3$) are isomers, former has an enthalpy of formation -27.5 kJ/mol, which is much smaller than latter with 20.8 kJ/mol, which proves the former isomer has more stable structure.

Table 5 Enthalpy of combustion and formation of Mannich base and benzoxazine

	$\triangle$cH(J/g)	$\triangle$cH(kJ/mol)	$\triangle_f$H(kJ/mol)
MB(H-H)	34598.2	6885.0	-88.2
BOZ(H-H)	34923.8	7368.9	2.2
MB(CH$_3$-H)	35353.4	7530.3	-122.2
BOZ(CH$_3$-H)	35638.0	8018.6	-27.5
MB(H-CH$_3$)	35579.1	7578.3	-74.2
BOZ(H-CH$_3$)	35852.5	8066.8	20.8

Enthalpy of reaction ($\triangle$rxnH) can be calculated from $\triangle_f$H of reactants and products. Formaldehyde is treated as methylene glycol, its enthalpy of formation in aqueous solution is 108617 cal/mol(-454.2kJ/mol) [29], $\triangle_f$H of Mannich base and benzoxazine in solution is treated as in solid state. $\triangle$rxnH is calculated as the following equation, results are given in Table 4.

$$\Delta_{rxn}H = \Delta_f H(BOZ,s) + 2\Delta_f H^{\theta}(H_2O,l) \\ - \Delta_f H(MB,s) - \Delta_f H^{\theta}(HOCH_2OH,aq)$$

Enthalpy of reaction calculated from enthalpy of formation is about -20 kJ/mol, it further proves the reaction between Mannich base and formaldehyde to benzoxazine is exothermic. The enthalpy calculated by equilibrium constant and by enthalpy of formation is close, which shows the reliability of two methods.

Conclusions

Mannich base and benzoxazine with substituent on para position of phenol or amine is synthesized. Influence of substituent on the reaction equilibrium from Mannich base and formaldehyde to benzoxazine is investigated. Substituent attached to phenol or aniline has same impact on reactivity of Mannich base, however it has opposite influence on oxazine ring stability and equilibrium constant. Comparing with the phenol-aniline system, electron-

donating methyl on phenol or aniline will increase the charge of nitrogen and oxygen atoms in Mannich base. While the methyl group locates at para position of phenol, C-O bond strength in oxazine ring increases, ring stability increases, and the equilibrium constant climbs; while the methyl group locates at the para position of aniline, oxazine ring stability decreases, the benzoxazine hydrolysis are tend to happen, equilibrium constant is significantly low.

Notes and references

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