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SYNTHESIS, CHARACTERIZATION, REACTION MECHANISM AND KINETICS OF 3,4-DIHYDRO-2H-1,3-BENZOXAZINE AND ITS POLYMER

by

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Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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SYNTHESIS, CHARACTERIZATION, REACTION MECHANISM AND KINETICS OF 3,4-DIHYDRO-2H-1,3-BENZOXAZINE AND ITS POLYMER

ABSTRACT

by

JINGPING LIU

A method for the synthesis of 3,4-dihydro-3-pentafluorophenyl-2H-1,3-benzoazine in a high yield derived from pentafluoroaniline is described. The synthesized compounds are characterized by Fourier-Transfer Infrared spectroscopy (FTIR), proton nuclear magnetic resonance spectroscopy (1H NMR), size exclusion chromatography (SEC) and normal-phase high performance liquid chromatography (HPLC). The synthesis of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoazine by the condensation of pentafluoroaniline with formaldehyde and bisphenol-A is monitored in 1,4-dioxane solution at 75°C by attenuated total reflection Fourier transform infrared (ATR-FTIR) technique using a liquid cell. It is found that the pH value of the reaction medium is the controlling factor in term of the yield. A strongly acidic condition is necessary for the synthesis of similar compounds from other very weak amines having a pKa lower than 3. In the presence of trace amount of HCl, the synthesis of benzoazine includes a two step reaction. The formation of 1,3,5-tripentafluorophenylperhydro-1,3,5-triazine are involved in the first step of the reaction, which can be completed almost immediately after the addition of acid. The reaction between the acid-promoted cleavage of the perhydrotriazine and derivative of bisphenol-A and formaldehyde is the rate limiting reaction.
The methods to synthesize 3,4-dihydro-1,3-benzoxazine by thermal reaction of paraformaldehyde, phenol and amine in the absence of solvent are developed. The reaction of solventless synthesis of 3,4-dihydro-2H-3-(4-methyl)phenyl-1,3-benzoxazine has been monitored by means of normal phase HPLC, FTIR and proton NMR at different reaction temperature in a closed and an open system respectively. The thermal transitions involved in this heterogeneous system resulted from both physical phase changes and chemical reactions are described in detail by differential thermal analysis (DTA). The role of the decomposition of paraformaldehyde in the whole reaction has been emphasized. The pressure, temperature and stoichiometric effects are also discussed. It has been found that the reaction kinetics and mechanism strongly depend on the reaction temperature. Within 50-75°C, the overall reaction rate is controlled by the decomposition rate of paraformaldehyde. Pseudo-stoichiometric effect plays an important role in this temperature range. At 100°C, the overall reaction rate is a function of the concentrations of paraformaldehyde, toluidine and bisphenol-A. Reaction mechanisms in both cases are proposed.

A new type of polymer, the repeat unit of which is composed by 3,4-dihydro-2H-1,3-benzoxazine, has been synthesized by reaction between methylene-bis-(2,6-dimethylaniline), formaldehyde and bisphenol-A in the organic solvent contained certain amount of triethylamine and water. The polymer structure is characterized by means of FTIR, NMR. Molecular weight and its distribution is measured by SEC. Several factors affecting on molecular weight of the polymer such as solvent, catalyst, cocatalyst, temperature and reactant ratio have been discussed in detail. It has been found Lewis base, water and temperature have great effect on the molecular weight and molecular weight distribution, and solvent and reactant ratio have certain influence on the benzoxazine ring content on the polymer backbone.
....to my parents
....to my husband, Chicheng

and

my daughter, Kelly
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CHAPTER 1
BACKGROUND AND MOTIVATION
LITERATURE REVIEW OF SYNTHESIS OF 3,4-DIHYDRO-2H-1,3-BENZOXAZINE
Introduction

Benzoazidine is a single benzene ring fused to another six-membered heterocycle containing one oxygen atom and a single nitrogen atom. There are a number of possible isomeric benzoazines depending upon the relative position of the two heteroatoms and the degrees of oxidation of this oxazine ring system. 3,4-Dihydro-2H-1,3-benzoazine is one kind of hydrogenated derivatives of benzoazine\(^1\). When the benzene ring is replaced by naphthalene, the corresponding oxazine become naphthoxazine.

\[
\begin{align*}
\text{2H-1,3-benzoazine} & \quad \text{3,4-dihydro-2H-1,3-benzoazine} \\
\end{align*}
\]

Interest in oxazines and their benzo derivatives dates back well into the early part of the last century because some derivatives exhibit color. Monocyclic oxazine function as bases and as very useful synthetic intermediates, particularly for the construction of carbonyl derivatives and as starting materials for many complex heterocyclic systems\(^1\). Some benzoazines and their salts have been shown to possess interesting pharmacological properties, such as having antidepressant activity\(^2\), useful as insecticides\(^3\) and antiarrhythmics\(^4\). As a specific kind of hydrogenated benzoazines, 3-substituted-3,4-dihydro-2H-1,3-benzoazine was studied mainly as alternative product of Mannich reaction in the middle of this century\(^5\)-\(^8\). Few applications of this compound had been reported in polymer area until it was identified as an intermediates of the amine-catalyzed phenolic resin\(^9\). Comparative study of curing of phenol-formaldehyde resin with hexamethylenetetramine(HMTA) and benzoazine by thermal analysis methods: thermogravimetry(TG), differential thermogravimetry(DTG), differential thermal analysis(DTA) and pyrolysis gas
chromatography (GC) was done\(^\text{10}\). During curing with 3,3'-ethylene-bis(3,4-dihydro-2H-1,3-benzoxazine) at low temperature, ammonia was not evolved and weight loss of the cured blends was significantly lower than in curing with HMTA. In recently decade, this type of benzoxazine was found as a new type of precursor of phenolic resin\(^\text{11-15}\). Some of polybenzoxazine materials have excellent physical, mechanical properties\(^\text{16-17}\) and processability\(^\text{18}\). However, most of recent work emphasized the polymerization of well-established 3-substituted-3,4-dihydro-2H-1,3-benzoxazine by ring-opening reaction. Because of few applications of this type of benzoxazines in the past, the studies on these compounds have not been actively pursued. The well-established 3,4-dihydro-2H-1,3-benzoxazines are few. Many areas such as characterization of the compounds, reaction mechanism and kinetic are seldom touched before. With the development of benzoxazine polymers, various types of benzoxazine compounds have recently been explored. Thus, chemistry of 3,4-dihydro-2H-1,3-benzoxazine synthesis needs to be developed correspondingly. In the following chapters, some hitherto unknown benzoxazines and benzoxazine polymers are synthesized and characterized by FTIR, proton NMR and chromatography. The reaction mechanisms are proposed. A new solventless synthesis method is developed and its reaction kinetics is investigated. In this chapter, previous works related to the synthesis of 3,4-dihydro-2H-1,3-benzoxazine is summarized.

**Synthesis methods**

Most of 3-substituted-3,4-dihydro-2H-1,3-benzoxazines resulted from the reaction of p-substituted phenols with formaldehyde and a primary amine in a molar ratio of 1:2:1, respectively\(^\text{6,7}\). This reaction may be considered as variant of the Mannich reaction. Reaction is best carried out by first condensing the primary amine with formaldehyde to form the \(N, N\)-dimethylolamine[1] which is then allowed to react
with the phenol. Alternatively when a p-substituted phenol, formaldehyde, and a primary amine were allowed to react in a molar ratio of 1:1:1, p-aminomethylphenols, i.e. Mannich base[2], were formed. These compounds condensed with formaldehyde in the presence of base to yield the 3,4-dihydro-2H-1,3-benzoxazine[3]. Difunctional benzoxazines were prepared in a similar way from various combinations of difunctional primary amines and monofunctional phenols or difunctional phenols as well as polyhydric phenols with monofunctional primary amines. When naphthols were used instead of phenols, 3,4-dihydro-2H-1,3-naphthoxazines were obtained. Another way to prepare naphthoxazines was the condensation of 1-(p-toluidinomethyl)-2-naphthol with formaldehyde in refluxing ethyl acetate. But 1-(p-toluidinomethyl)-2-naphthol is not the normal intermediate in the direct synthesis.

The following is the general synthesis procedure.
2 HCHO + R'NH₂ → R'N\textsubscript{CH₂OH} + R\textsubscript{CH₂OH} [1]

\[ \text{KOH} \xrightarrow{\text{H}^+} \text{OH} \]

\[ + \text{HCOH} \xrightarrow{- \text{HCOH}} \]

R: CH₃, C(CH₃)₃, C₆H₅, NHCOCH₃, Br, Cl, OH
C(CH₃)C₆H₅OH, COC₆H₅OH, C₆H₅OH,
R': CH₃, C(CH₃)₃, C₆H₁₂, G₆H₅CH₂, C₆H₅(CH₃)CH, C₆H₅,
HO(CH₂)₂, CH₂=CHCH₂

scheme 1
The alternating method to synthesize 3,4-dihydro-2H-1,3-benzoxazine was developed by Aversa et al. They first synthesized N-(2-hydroxy-3,5-dimethylbenzyl)-\(\beta\)-aminopropanoic acid[4] via the Mannich reaction between 2,4-dimethylphenol, aqueous formaldehyde and 3-aminopropanoic acid in ethanol. This amino acid was allowed to react in 96% sulfuric acid at room temperature. After neutralization, 3-(2-hydroxy-3,5-dimethyl)benzyl-3,4-dihydro-6,8-dimethyl-2H-1,3-benzoxazine[5] was obtained. The reaction mechanism was proposed as scheme 2.

\[
\begin{align*}
\text{CH}_3\text{N} & \xrightarrow{\text{H}^+} \text{N}^+\text{H}_2^+ \text{OH} \\
\text{CH}_3\text{OH} & \xrightarrow{-\text{H}_2\text{O}} \text{CH}_3\text{N}^+\text{H}_2^+ \text{OH} \\
\text{Ar} = & \text{CH}_3\text{OH} \\
\text{CH}_3 & \xrightarrow{\text{ArCH}_2^+} \text{N}^+\text{H}_2^+ \text{CH}_2^+ \\
\text{CH}_3 & \xrightarrow{-\text{H}^+} \text{N}^+\text{H}_2^+ \text{CH}_2^+ \\
\end{align*}
\]

[4]

[5]

Scheme 2

In this method, the alkylating agent arises from acid-induced deamination of the phenolic Mannich base. Thus, the variety of substituent on N-3 position of benzoxazine ring is limited.

The benzoxazine[5] can also be obtained by heating the mixture of 2,4-xylenol and hexamethylenetetramine (3.4:1 mole) at 135°C for 2 hr in air[25].

Holly and Cope synthesized bis-(3,4-dihydro-2H-1,3-benzoxazine-3-yl)methylene[6] by the reaction of one mole 2-hydroxybenzylamine with two moles formaldehyde[26]. This benzoxazine can be further reacted with phenol to form 3,4-dihydro-3-(2-hydroxy)benzyl-2H-1,3-benzoxazine[7][27].
Some 3,4-dihydro-2H-1,3-benzoxazine with substituents on C-2 or C-4 were also synthesized although their applications in polymer area have not been found yet. 2,2-Bibenz-1,3-oxazine[8] was obtained by the reactions of salicylamines(o-hydroxybenzylamine) with glyoxal or α-diketones in methanol at a temperature lower than 20°C (scheme 4)²⁸.
3-Phenyl-2-(o-hydroxyphenyl)-4-cyanodihydro-1,3-benzoazine [9] has been prepared by condensation of aniline, potassium cyanide and salicylaldehyde. The reaction proceeds as follows (scheme 5) \(^{29}\).

\[
\begin{align*}
\text{CHO} & + \text{NH}_2 & + \text{KCN} & \rightarrow & \text{OH} \\
\text{NCN} & & & & \text{[9]} \\
\end{align*}
\]

scheme 5

A number of 3,4-dihydro-2H-1,3-benzoazines bearing carbonyl group on C-4 \([10-13]\) have been synthesized from salicylamide \([7,30-31]\).

\[
\begin{align*}
\text{RCHO} & \quad \text{[10]} \\
\text{CH}_2=\text{CHOCOCH}_3 & \quad \text{[11]} \\
\text{COCl}_2 & \quad \text{[12]} \\
\text{O} & \quad \text{[13]} \\
\end{align*}
\]

scheme 6

Structure [13] can be made by the base catalyzed ring expansion of 2-substituted 2H-1,2-benzisoxazolin-3-one during the alkylation of 3-hydroxy-1,2-benzisoxazole also \(^{32}\).
3-Substituted-3,4-dihydro-2H-1,3-benzoxazine-2,4-dione[14] was prepared by the following reaction: 

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{C-} & \quad \text{O} \\
\text{OCH}_3 & \quad \text{N=SCH}_3
\end{align*}
\] + \begin{align*}
\text{N} = \text{C-} & \quad \text{N} = \text{C-} \\
\text{H} & \quad \text{H} \\
\text{H} & \quad \text{H}
\end{align*}
\rightarrow \begin{align*}
\text{O} & \quad \text{O} \\
\text{N} & \quad \text{N} \\
\text{N} & \quad \text{N}
\end{align*}

\[180^\circ\text{C} \quad \text{H}^+ \quad \text{H}_2\text{O}
\]

scheme 7

**Reaction conditions and side reactions.**

Phenolic Mannich bases derived from primary amines have shown the importance of several reaction variables on the course of the condensation. This included the nature and position of substituents on the phenol, reaction ratios, temperature, and the basicity of the amine. Besides the benzoxazine, the other by-products found were bis(2-hydroxybenzyl)amine[15], Mannich base (free base) depending upon the condensation conditions and the specific reactants employed. No benzodipyrrole[16] were produced during reaction: 

\[15\] [16]
Effects of Phenol structure

Substituent ortho to the phenolic hydroxyl group plays an important role in determining the course of the reaction. In the reaction of 2,4-di-t-butyl-5-methyl-phenol with N, N-dimethylolmethylamine, the only product isolated was N, N-bis-(3,5-di-t-butyl-2-hydroxy-6-methylbenzyl)-methylamine even when the reaction ratio employed (1:1) was that calculated for ben佐zaine formation. In contrast, only ben佐zaine was isolated when p-t-butyl-phenol or p-bromophenol reacted with N, N-dimethylolcyclohexylamine even when molar ratio of phenol to amine was 2:1. Phenols having bulky alkyl substituents on one of the ortho position were much more effective than isopropyl or methyl in reducing the reactivity of the phenolic hydroxyl group. i.e. the size of the ortho substituents on the phenol limits the conformation of hydroxyl group so that the hydroxyl group cannot move totally free in favor of the formation of ben佐zaine ring\textsuperscript{34}.

Varying the electrophilic character of substituents on the ortho position of phenol can affect both the course of the condensation and the stability of the ben佐zaines, also. If an N-methylol Mannich base is considered as an intermediate, the competitive reactions then involve either ring closure with the phenolic hydroxyl (ben佐zaine formation), or an electrophilic attack on the ortho position of another molecule of the phenol to yield a bis-(hydroxybenzyl)amine. Any lowering of the electron density at the free ortho position would, accordingly, be expected to be unfavorable to the latter reaction. Varying the electrophilic character of substituents on the para position of phenol did not lead to significantly different results.

The reaction of polyhydroxybenzenes with various N, N-dimethylolamines derived from representative primary aliphatic and alicyclic amines produced monomeric heteroxylic products. From phloroglucinol, formaldehyde and benzylamine in dioxane
solution, catechol, 3,4,6,7,8,10,11,12-octahydro-3,7,11-tribenzyl-2H-benzo[1,2-e-3,4 e']tri-m-oxazine was obtained in yield about 48%35.

1-Naphthol had different reaction course from 2-naphthol because 1-naphthol has more active hydrogen (both 2 and 4 position as well as hydroxy group)22.

Effects of Amines

The effect of the basicity of amines was more complicated. Generally, from strong amines, such as methylamine, corresponding Mannich base and bis(hydroxybenzyl)amine were isolated; the mild amine, like cyclohexylamine, resulted in Mannich base only and the weak amine, such as benzylamine, led to the isolation of Mannich base in high yield along with some benzoxazine. Phenol was 2,4-dichlorophenol here36.

There are two isomers, symmetrical[17] and unsymmetrical[18] benzoxazine, derived from hydroquinone. Only benzylamine and 2-phenyl-propylamine, which are less basic than other aliphatic amines, can result in isomer [18]. This indicates the importance of the basic strength of the amine in determining the course of related condensations. However, from allylamine and 2-aminoethanol, the basicities of which are comparable to the benylamine, only isomer [17] can be isolated37.

\[
\begin{align*}
\text{isomer}[17] & \quad \text{isomer}[18]
\end{align*}
\]

The reaction of representative primary aromatic amines with formaldehyde and selected naphthol compounds were studied. It seems that basicity of the amines has
certain effect on the temperature to form naphthoxazine. Condensation of 2-naphthol with formaldehyde and p-toluidine in a 1:2:1 molar ratio at 50°C in methanol solution resulted in a 91% yield of 2,3-dihydro-2-p-tolyl-1H-naphth[1,2-e]-m-oxazine[19b]. Replacement of p-toluidine with aniline, p-aminobenzoic acid, p-bromoaniline or o-toluidine resulted in analogous products[19c,f,e].

\[
\begin{align*}
\text{R} & : \text{CH}_3 \\
\text{b} & : \text{p C}_6\text{H}_5\text{CH}_3 \\
\text{c} & : \text{C}_6\text{H}_5 \\
\text{d} & : \text{m C}_6\text{H}_5\text{CH}_3 \\
\text{e} & : \text{p C}_6\text{H}_5\text{Br} \\
\text{f} & : \text{p C}_6\text{H}_5\text{COOH}
\end{align*}
\]

Difunctional amines like p-phenylenediamine, reacted almost immediately in the cold with four moles of formaldehyde and two moles of 2-naphthol to form 2,2'-p-phenylene-bis-(2,3-dihydro-1H-naphth[1,2-e]-m-oxazine)[20]. With o-nitroaniline, however, the only product was 1-(o-nitroanilinomethyl)-2-naphthol[21]. In hot dioxane, the corresponding naphthoxazine was obtained in low yield (27%) along with the linear Mannich base (17%). Much higher yields can be obtained when m- or p-nitroanilines were employed. The tendency of o-nitroaniline to behave as a secondary amine in the condensation may be due to the favorable situation for chelation in this compound. Refluxing in dioxane was also required to effect naphthoxazine formation with the feebly basic s-tribromoaniline\(^2\).
No Mannich base has been isolated directly from the 2-naphthol reacted with formaldehyde and primary amines because the Mannich base obtained from acidic hydrolysis of corresponding oxazine can only stabilize as crystal or in solution as hydrochlorides and undergo self-condensation with great ease to form the bridge structure, i.e., N, N-bis(2-hydroxy-1-naphthylmethyl)alkylamine[22] or the benzoxazine after neutralization. The stronger or weaker the amines are, the less stable the bases, which would form mainly either N, N-bis(2-hydroxy-1-naphthylmethyl)alkylamines for strong amines or the naphthoxazine along with bis(2-hydroxy-1-naphthyl)methane for weak amines. Bulky aliphatic substituents on the nitrogen of the amine would be expected to discourage either intermolecular hydrogen bonding or the addition of the Mannich base[38].

Effects of Aldehyde Structure

Condensation of 2-naphthol with acetaldehyde ammonia resulted in a high yield of 1,2-dihydro-1,3-dimethyl-3H-naphth-[1,2-e]-m-oxazine[23]. Aromatic aldehydes
were reported to yield the corresponding Schiff base[24], while naphthoxazines were obtained when aliphatic aldehydes were employed.

A higher yield of oxazine can be obtained using benzene than in ethanol\(^{39}\).

**Temperature, time and reactant ratio**

The ratio of the two benzoazaine isomers derived from hydroquinone mentioned above affected by the reaction conditions also: isomer [17] decreases with the decreased reflux time while the amount of isomer [18] remains constant; long time and low temperature favor isomer [17] but will decrease the amount of isomer [18]; Two step reaction, i.e., amine reacted with formaldehyde first, increase the yield of isomer [17] but has no effect on isomer [18]. Steric factors do not benefit the formation of isomer [18]\(^{36}\).

Temperature was found to be an important factor in determining the course of the reaction. 2-Naphthol with formaldehyde and methylamine in a molar ratio of 1:2:1, respectively, was found to result in high yield of 2,3-dihydro-2-methyl-1H-naphthalene[1,2-e]-m-oxazine(19a) in methanol solution at 60°C; when the molar ratio was 2:2:1, high yield of N,N-bis-(2-hydroxy-1-naphthylmethyl)-methylamine(bridge) was formed at 25°C. However, the only product was corresponding naphthoxazine when benzylamine was used. Low temperature (0°C) favors the formation of the bridge structure while high temperature(60°C) was favorable for the closure of oxazine ring when methylamine was used. For cyclohexylamine, the products depended on the molar ratio as well as temperature.
Reactivity of 3,4-dihydro-2H-1,3-benzoxazine

Reaction of benzoxazine with aqueous hydrochloric acid resulted in the elimination of formaldehyde and formation of isomeric hydrochloride salts in high yield. The hydrochloride salt was treated with aqueous sodium bicarbonate and formed free base. The benzoxazine was quite stable toward hot aqueous alkali,1,6,7. For some benzoxazines, such as [6], the ring can be opened even in the presence of phenol22. In an acidic condition, naphthoxazines yielded formaldehyde, the other product was a red resinous substance. Hydrochlorides of naphthoxazines from aromatic amines were unstable, while the related naphthoxazines from aliphatic amines formed highly stable hydrochloride salts39. The stability of the benzoxazine in alcohols was found to depend upon the particular phenol and primary amine used in the synthesis. The benzoxazines derived from a strongly basic amine and a less acidic phenol were more stable in the hot alcohols34.

Substituents on the benzoxazine ring have certain effect on the ring stability. Structures bearing carbonyl groups are generally more sensitive to base-catalyzed hydrolysis. The substituent on C-2 can shift the ring(benzoxazine)-chain(Schiff base) equilibrium if there is no substituent on N-340.

In the presence of compounds with active hydrogen such as phenol, naphthol, indoles, carbazole, imides and aliphatic nitro compounds, the ring opening reaction of benzoxazine occurred to form the Mannich bridge structure. This new type of aminoalkylation always happen at the ortho position. A possible explanation for these results may be related to the free ortho position which puts the latter in a favorable position for reaction as a result of intermolecular hydrogen bonding in the initial step.

Significantly higher yield was found if ortho aminoalkylation products were obtained in the reaction with a given phenolic compound when the benzoxazine was
derived from phenol having an ortho substituent. In another word, the ring is easier to open when there is a substituent on the C-8 position of benzoxazine. The presence of more than one reactive ortho position in the initial product may lead to another aminoalkylation reaction. That is why the polymerization can happen. Benzoxazines derived from methylamine were found to be much more reactive than those from benzylamine while those from cyclohexylamine were of intermediate reactivity. Only starting materials were isolated when the analogous benzoxazine derived from cyclohexylamine was employed. A possible correlation exists between the aminoalkylation aptitude of the benzoxazine and the basic strength of the amine used in the synthesis of the benzoxazine.

Electron density at the active sites on the ring of the phenolic substrate also appeared to be important: 2-naphthol, which is known to have a high electron density at position 1, was readily aminoalkylated by 1,3-benzoxazines. 2,4-Dichlorophenol was not aminoalkylated under any of the conditions. The benzoxazines derived from phenol with dihalogen substituents were among the most active aminoalkylation agents.

Condensation of phenols with formaldehyde and primary amines is shown to yield N, N-bis-(hydroxybenzyl)-amines (bridge structure) directly in certain instances, such as in a molar ratio of 2:2:1 respectively.

For N-methylnaphthoxazine, reaction with phenol or the aminomethylation of the phenol did not occur, but instead, high yields of N, N-bis(2-hydroxy-1-naphthylmethyl)methylamine were obtain. It is presumed that the phenol brought about ring opening of the naphthoxazine to form the corresponding Mannich base which then underwent self condensation to form N, N-bis(2-hydroxy-1-naphthylmethyl)methylamine. For naphthoxazines derived from benzylamine, aniline or p-toluidine, no aminoalkylation was observed and the starting materials were recovered in high yield.
Polydihydrobenzoxazine prepared from aromatic amine with $pK_b > 7$ with polyamines are more stable than those from aliphatic amines with $pK_b < 7$ at room temperature. The polydihydrobenzoxazines cure more completely at lower temperature and are less subject to side reactions than those derived from more basic amines with $pK_b < 7^{43}$.

Dihydro-benzoxazine polymers and prepolymer heated both alone and with epoxy resins provide gel times of several hours at $T > 100^0C^{44}$. 
References


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CHAPTER 2

SYNTHESIS AND CHARACTERIZATION OF 3,4-
DIHYDRO-3-FLUOROPHENYL-2H-1,3-BENZOXAZINE
INTRODUCTION

Phenolic polymers are char-forming, high-temperature-resistant materials. Structurally, they can be altered to improve their resistance to higher temperatures by adding greater stiffness to the polymer chains. Such methods include introducing polar and bulky substituent into the polymer, minimizing the amount of readily oxidizable hydrogen atoms, and increasing the number of highly stable structural units. Some polymers which contain fluorine in aromatic systems are reported to exhibit stability up to 1000 °C [1]. Also, the introduction of fluorine into the polymer is expected to decrease the friction coefficient and refractive index. The oxygen index increases from about 33 for unsubstituted phenolic materials to about 75 for meta-halogen substituted phenolic materials [2]. Unfortunately, the lack of molecular design flexibility imposed by traditional phenolic chemistry makes it impossible to introduce more than two halogen atoms into each aromatic ring in phenolic materials [3].

More than forty years ago, Burke et al synthesized 3, 4-dihydro-2H-1,3-benzoxazine by means of a modified Mannich reaction through the condensation of a p-substituted phenol with formaldehyde and primary amine [4]. During the past decade, polybenzoxazines have shown the possibility of becoming a new type of precursor in producing phenolic materials[5-9]. The method of synthesis also increases the molecular design flexibility for phenolic resin. Since then, various amines have been used for polybenzoxazine synthesis including both aliphatic and aromatic monoamines and diamines [4, 10-13]. Higginbottom found the specific composition of the phenol and amine used to form the poly(dihydrobenzoxazine) can significantly affect the yield and the potential for side reaction. The resulting poly(dihydrobenzoxazines) are also different in their properties depending on whether they are formed from a strongly basic or a weakly basic amine. Dihydrobenzoxazines derived from weakly basic amine (pK_a<7) show greater stability and are more resistant to side reactions and aging.
effects. These weakly basic amine products will react as fast or faster and often more completely than the strongly basic amine products with the polyamine components[7]. Burke, Hammer and Weatherbee pointed out the importance of the basic strength of the amine in determining the course of related condensation reaction[10]. Almost all amines that have been applied to the synthesis of dihydrobenzoxazine have rather strong basicity except the corresponding naphthoxazine was obtained in low yield when nitroaniline reacted with formaldehyde and naphthol in hot dioxane[25]. The pKₐ values of these amines are within the range 3-13, while the pKₐ values of polyhalogenated amines are usually below 3 (table 1).

The Mannich reaction involves the condensation of a hydrogen-active molecule with formaldehyde and amine. The reactive hydrogen atom to be substituted by an aminomethylene group can belong to a very wide series of different H-active compounds such as phenol. On the other hand, the amine moiety gives the molecule typical basic properties and the capacity to speed up base-catalyzed reaction [14]. Phenolic Mannich bases derived from primary amines have shown the importance of several reaction variables on the course of the condensation. These included the nature and position of substituents on the phenol, stoichiometry, temperature, and the basicity of the amine[6]. Thus, the basicity of the amine is the predominant factor in this particular reaction. To date, there is no report on the use of very weak amines (pKₐ < 3) in the synthesis of 3, 4-dihydro-2H-1, 3-benzoazaine.

This chapter intends to present the synthesis of previously unknown 3, 4-dihydro-3-fluorophenyl-2H-1,3-benzoazines by the reactions of formaldehyde and bisphenol-A with penta-, tri-, di-, and mono-fluoroaniline, under neutral or acidic conditions. The tetrafluoro-substituted aromatic amine, 4, 4'-diaminoctafluorobiphenyl, as well as another weak amine with a strong electron withdrawing substituent, 4-cyanoaniline (pKₐ = 1.7) are also used. The structures of
the resulting synthetic compounds are characterized by means of nuclear magnetic resonance spectroscopy (NMR), Fourier transform infrared spectroscopy (FT-IR), Raman spectroscopy, size exclusion chromatography (SEC) and high performance liquid chromatography (HPLC). The major factors affecting the benzoxazine yields are also discussed.

EXPERIMENTAL

Materials: Bisphenol-A, 4, 4'-thiodiphenol, 4,4'-dihydroxybenzophenone and the fluorine-containing amines were purchased from Aldrich Chemical Company; Aminobenzonitrile, 4,4'-dihydroxybiphenyl and bis-4-hydroxyphenylsulfone were produced by Fluka Company. Solvents, formaldehyde and aniline were supplied by Fisher Scientific Company. All the chemicals were used without further purification.

Synthesis

A synthesis scheme from monoamine, bisphenol-A and formaldehyde is illustrated below:
2RNH₂ + 4CH₂O + OH⁻ → \[\text{Resin I, R} \quad \text{Resin III, R} \quad \text{Resin IV, R} \quad \text{Resin V, R} \quad \text{Resins VI, VII & VIII, R is} \]

A. Synthesis of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine (resin I)

i) Procedure I

1.85 gram (0.01 mole) 98% pentafluoroaniline (PFA) was dissolved in 5 ml of either 1,4-dioxane or ethyl ether and was added dropwise to 1.62 gram (0.02 mole) aqueous 37% formaldehyde in a three-necked flask which was cooled in an ice bath. The mixture was stirred magnetically for about 1 hour before adding 1.16 gram (0.005 mole) bisphenol-A in 5 ml of 1,4-dioxane or ethyl ether. The pH value of the solution was kept between 0.6 and 1.5 by adding trace amounts of hydrochloric acid. A pH meter was used to control the amount of HCl added. The mixture was heated to around
55°C for 5 hours. The solvent was then evaporated by a rotary evaporator under reduced pressure. A light yellow viscous liquid was obtained.

ii) Procedure II

1.20 gram (0.04 mole) paraformaldehyde was added to the mixture of 3.70 gram (0.02 mole) 98% pentafluorooaniline in 1 ml distilled water and 5 ml 1,4-dioxane. The temperature was raised to 50°C and the mixture was continuously stirred for 3 hours until the paraformaldehyde was dissolved. Then, 2.32 grams (0.01 mole) bisphenol-A in 5 ml dioxane was added. The pH value of the solution was controlled to a value of 1.2 by adding trace amounts of hydrochloric acid. The temperature was kept at 55-60 °C for 5 hours. Then the solvent was evaporated under reduced pressure

B. Synthesis of 4,4'-di[3,4-dihydro-6-methyl-2H-1,3-benzoxazine-3-yl]-octafluorobiphenyl or [octafluoro-1',1''-biphenyl]-4', 4''-di-3,4-dihydro-6-methyl-2H-1,3-benzoxazine (resin II)

The synthesis scheme is shown below:

\[
2\text{HO-CH}_3 + 4\text{CH}_2\text{O} + \text{H}_2\text{N-CH}_2\text{NH}_2 \xrightarrow{\text{H}^+} \text{CH}_3\text{O-CH}_3 + 4\text{H}_2\text{O}
\]

1.82 gram (0.005 mole) 4,4'-diaminoctafluorobiphenyl dissolved in 5 ml 1,4-dioxane was added dropwise to 1.62 gram (0.02 mole) aqueous 37% formaldehyde in a
three-necked flask which was cooled in an ice bath. The mixture was stirred magnetically for about 1 hour before adding 1.08 gram (0.01 mole) 4-methyl phenol in 5 ml of 1,4-dioxane. The pH value of solution was controlled to about 1.2 by dropping trace hydrochloric acid and about 0.5 ml deionized water. A pH meter is used to control the amount of HCl added. The temperature was raised and the mixture was heated to 55°C for 5 hours. The solvent was then evaporated by a rotary evaporator under reduced pressure. The paste-like product was washed with acetonitrile or methanol several times. A white powder was obtained. The washings were cooled in a refrigerator, then the white powder precipitant was filtered. The remaining solution was evaporated by rotary evaporator. A yellow liquid was obtained. The white powder was 4,4′-di[3,4-dihydro-6-methyl-2H-1,3-benzoazine-3-yl]-octafluorobiphenyl and 4-hydroxyl-4′-[3,4-dihydro-6-methyl-2H-1,3-benzoazine-3-yl]-octafluorobiphenyl, whereas the yellow liquid consisted mostly of dimer.

C. Synthesis of 3,4-dihydro-2H-3-[2,3,4-trifluoro]phenyl-1,3-benzoazine (resin III)

1.47 gram (0.01 mole) 2,3,4-trifluoroaniline in 5 ml 1,4-dioxane was added dropwise to 1.62 gram (0.02 mole) aqueous 37% formaldehyde in a three-necked flask which was cooled in an ice bath. The mixture was stirred magnetically for about 1 hour before adding 1.16 gram (0.005 mole) bisphenol-A in 5 ml of 1,4-dioxane. The solution pH was controlled to about 1.2 by adding trace hydrochloric acid and about 0.5 ml deionized water. A pH meter was used to control the amount of HCl added. The temperature was raised and the mixture was heated to 55°C for 5 hours. The solvent was then evaporated by a rotary evaporator under a reduced pressure.

D. Synthesis of 3,4-dihydro-2H-3-[2,6-difluoro]phenyl-1,3-benzoazine (resin IV)

1.29 gram (0.01 mole) 2,6-difluoroaniline in 5 ml 1,4-dioxane was added dropwise to 1.62 gram (0.02 mole) aqueous 37% formaldehyde in a three-necked flask
synthesis of resin III

E. Synthesis of 3,4-dihydro-2H-3-[4-cyano]phenyl-1,3-benzoxazine (resin V)

1.18 gram (0.01 mole) 4-cyanoaniline in 5 ml 1,4-dioxane was added dropwise to 1.62 gram (0.02 mole) aqueous 37% formaldehyde in a three-necked flask which was cooled in an ice bath. The rest of the procedure was the same as for the synthesis of resin III. The product was dissolved in chloroform, then the solution was filtered and the solvent was evaporated. The yellow paste was 3,4-dihydro-2H-3-[4-cyano]phenyl-1,3-benzoxazine resin.

F. Synthesis of 3,4-dihydro-2H-3-[2-fluoro]phenyl-1,3-benzoxazine (resin VI)

1.11 gram (0.01 mole) 2-fluoroaniline in 5 ml 1,4-dioxane was added dropwise to 1.62 gram (0.02 mole) aqueous 37% formaldehyde in a three-necked flask which was cooled in an ice bath. The mixture was stirred magnetically for one hour before adding 1.16 gram (0.005 mole) bisphenol-A in 5 ml 1,4-dioxane. The temperature was raised and the mixture was heated at 55°C for 5 hours. The solvent was then evaporated by a rotary evaporator under reduced pressure.

Characterization

The Fourier transform infrared (FT-IR) spectrophotometer used was a Bomem Michelson MB110 FT-IR spectrophotometer which was equipped with a medium band-pass mercury-cadmium-telluride (MCT) detector with the specific detectivity, $D^*$, of $1 \times 10^{10}$ cmHz$^{1/2}$W$^{-1}$. All spectra were recorded at a resolution of 4 cm$^{-1}$ and displayed in the absorbance mode. Coaddition of one hundred scans was sufficient to obtain good signal-to-noise (S/N) ratio spectra.

The Raman instrument used was a Bomem DA3 FT-Raman spectrometer. It was equipped with an InGaAs detector, the specific detectivity, $D^*$, was $1 \times 10^{14}$
cmHz$^{1/2}$W$^{-1}$. A 5W Nd:YAG laser (yttrium-aluminum-garnet) was used at 1.064 nm as the excitation source. The spectral resolution was 4 cm$^{-1}$ with typical coaddition of 500 scans.

The NMR spectrometer used was a Varian XL-200 NMR spectrometer with a proton frequency of 200 MHz. Deuterochloroform or deuteracetone with 1% tetramethylsilane (TMS) was used as a solvent. Coaddition of 16 scans yielded sufficient S/N ratio spectrum.

Size exclusion chromatography (SEC) was performed with a Waters GPC chromatograph equipped with a Waters 510 HPLC pump, U6K Universal Injector, Waters 440 UV Detector fixed at 254 nm, and Waters 410 Refractive Index Detector. Three columns, μ- styrigel™ 1000 nm, 100 nm and 50 nm, were connected in series and used with HPLC grade tetrahydrofuran (THF) as the eluent. The flow rate was 1 ml/min throughout the experiment.

High performance liquid chromatography (HPLC) was similarly done with a Waters 510 HPLC pump, U6K Universal Injector, Waters 484 Tunable UV Detector fixed at 254 nm except that the column used was a Waters Partisol 5, a silica gel column, and chloroform/ethyl acetate mixture with 2-to-1 volume ratio as the eluent. The flow ratio linearly varied from 0.5 ml/min to 2 ml/min.

RESULTS AND DISCUSSION

Figure 1 shows the SEC trace of the synthesized compound from bisphenol-A/PFA/formalin reaction (resin I). There is only one strong narrow peak at 28.0 min with a shorter retention time than either PFA (30.5 min) or bisphenol-A (29.6 min). The small peaks at 31 min and 34 min result from peroxide, water or other impurities in
THF. This provides evidence that the products have very similar hydrodynamic volumes, i.e., the distribution of molecular weights is small.

A better separation can be obtained from HPLC as shown in Figure 2. In HPLC with silica gel columns, the stronger the base, the stronger the interaction with the acidic adsorbent, and the longer the amine takes to elute [24]. Therefore, basic amines usually have longer retention time than acidic phenol, e.g., toluidine has a longer retention time than bisphenol-A. However, pentafluoroaniline has a shorter retention time than bisphenol-A since the five fluorines considerably decrease the strength of the interaction between the unshared pair of electrons on the nitrogen and the Si-OH groups. The formation of benzoxazine further weakens the interaction between both hydroxyl and amino functional groups and the silica gel surface. Since the species with more pentafluorophenyl or benzoxazine rings has better solubility in chloroform, their retention times should be shorter. Therefore, the 1st peak results from dimer or other oligomers of benzoxazine; the 2nd peak involves 6,6'-isopropyl-di-3,4-dihydro-3-pentafluorophenyl-2H-1,3-benzoxazine, which will be abbreviated dibenzoxazine; the 3rd peak is the intermediates, which will be discussed in a later publication; the 4th peak is 2-[4-hydroxyl phenyl]-2-[3,4-dihydro-2H-3-pentaflourophenyl-1,3-benzoxazine-6yl]-propane, which is abbreviated monobenzoxazine; the 5th peak arises from PFA, and the 6th peak is bisphenol-A. When the pH value of reaction media is below 2, there are almost no unreacted reactants left; the dibenzoxazine and monobenzoxazine are the major products. The yields of dibenzoxazine and monobenzoxazine were approximately 50-60% and 20-10%, respectively, depending on the pH value. In the solution with pH=1.2, the yield of benzoxazine rings can reach about 90%. Thus, this condition is used as optimized condition.

Proton NMR is a useful tool to identify the benzoxazine structure [5,15-16]. The $^1$H NMR spectrum of synthesized compound 3,4-dihydro-2H-3-
pentfluorophenyl-benzoxazine is presented in figure 3. The assignment of each resonance is also shown. There are two characteristic singlet at 4.5 and 5.2 ppm arising from the two methylene groups in the benzoxazine molecule. It is quite obvious that the singlet resonance at 6.8 ppm comes from the 5-position hydrogen (labelled e) in the benzoxazine ring since there is no spin-spin coupling. Another two doublets around 6.7 ppm and 7.1 ppm arise from the 7- and 8- position aromatic hydrogens (labelled d and f) in benzoxazine ring, respectively. The peak at 3.7 ppm comes from 1,4-dioxane. For 4,4'-di[3,4-dihydro-6-methyl-2H-1,3-benzoxazine-3-yl]-octafluorobiphenyl, the characteristic two singlets of the methylene groups in benzoxazine ring shift down-field slightly since the electronic environment around the methylene groups varies with different amines and phenols(Figure 4(a)). Similar resonances for other benzoxazines can be found in the proton NMR spectra of other synthetic compounds (Figure 4(b)-(d)).

Hydroxyl and amino groups are identified with difficulty in the ¹H NMR spectra but they are easily observed by IR spectra. However, few articles have appeared in the literature on the identification of benzoxazine by means of IR spectroscopy [22]. It is difficult to give vibrational frequency assignments to such a complex molecule without detailed structural analysis. However, some characteristic frequencies which are relative to the benzoxazine ring formation or vibrations can be experimentally observed. Figure 5 shows the infrared spectra of the synthesized compound which is 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine according to the proton NMR spectrum and its original reactants. As expected for a benzoxazine structure, the antisymmetric and symmetric stretching bands of the primary amine group at 3517 cm⁻¹ and 3419 cm⁻¹ as well as the NH₂ deformation mode at 1610 cm⁻¹ totally disappeared. The NH₂ twisting and wagging in pentafluroaniline assigned at 1097 cm⁻¹ and 685 cm⁻¹ are too weak to be observed. Long and Steete calculated
Vibrational frequency and atomic displacement in the model compounds C₆F₅X (X=H,D,F,Cl,Br and I)[26,27]. Paniran et al.[17] and Green et al.[18] gave the vibrational frequency assignments of C₆F₅X molecules (X= halogen, NH₂, CN and CH₃). They found that there are a few frequencies of benzene ring modes affected by the X substituent in the series. Although all the ring vibration modes of benzene derivatives are more or less coupled with the stretching and bending modes of substituents, it has been proven that if either the force constant of carbon-substituent bonds or the mass of the substituent is large enough, the coupling between C-substituent in plane bending with the in-plane skeletal vibration of benzene nucleus is absent or very feeble. Some bands moving to the higher frequencies should be less like a ring mode and more like carbon-substituent stretching; the others reappeared with increasing purity of ring vibration at lower frequencies than those of the corresponding C₆H₆ ring[19, 20]. For Cᵥ symmetry of C₆F₅X molecule, the in-plane symmetric vibrations include the six radial skeletal vibrational modes and five other symmetry vibrations. Three modes have essentially constant frequencies throughout. The frequencies are about 1672, 1523 and 1480 cm⁻¹ in C₆F₅NH₂, respectively. This unusually high frequency above 1600 cm⁻¹ is due to the fluoro substituents which introduce significant changes in the electronic distribution of the ring. The 1523 cm⁻¹ band is attributed to the C-F stretching from the ring in-phase stretching mode. The frequencies of three other modes change notably when the mass of the X substituent increases. One is at 946 cm⁻¹, which is predominantly the C-N stretching mode. The second mass sensitive mode is essentially a ring deformation which is around 436 cm⁻¹. The third mass sensitive mode is a C-F deformation meta to the X substituent, which ranges from 320 to 239 cm⁻¹. The in-plane antisymmetric vibrations involve ten tangential skeletal vibrational modes. There are four ring modes whose frequencies are essentially constant despite the mass variation of the X substituent. The ranges of these
frequencies are 1649-1654, 1510-1513, 1246-1268, and 433-443 cm⁻¹. Another three frequencies of tangential vibration modes vary only slightly with the change of X substituent, the ranges of which are around 1173, 722 and 322 cm⁻¹ in pentafluoroaniline. Among these ten tangential skeletal vibrational modes, only two modes show marked mass sensitivity. One of these is the C-X deformation mode whose frequency varied from 1305 cm⁻¹ in C₆F₅H to 285 cm⁻¹ in C₆F₅NH₂. The other is a C-F deformation mode, the frequency of which in C₆F₅NH₂ is 198 cm⁻¹ [17,18,26,27]. The 1010-1004 cm⁻¹ in PFA involves Fermi resonance of three vibrational modes. One is ring breathing at 559 cm⁻¹. Another is the in-plane ring quadrant asymmetric bending at 443 cm⁻¹, which are constant with different X-substituent. The third mode is one of the in-plane ring semicircle stretching around 1020 cm⁻¹, which is affected by the variation of X substituent. In summary, within the 4000-500 cm⁻¹ range, the frequency changes of benzene ring modes at 946, 1173, 1035 and 1010-1004 cm⁻¹ can be observed for C₆F₅NH₂ when there are changes in substitution on the NH₂-group. When this primary amino group reacts with formaldehyde and forms a tertiary amino group, which becomes part of the benzoxyazidine ring, the N-CH₂ free rotation has been hindered. Thus the substituent mass, X, cannot be regarded as only the nitrogen atom. Instead, the whole benzoxyazidine ring is equivalent to the mass of the substituent X. Therefore, the frequencies or the intensities of the band which relate to the C-X vibration may change. These bands shift and split into the 990 cm⁻¹ and 977 cm⁻¹ doublet. The 946 cm⁻¹ band, which is mass sensitive, shifts to higher wavenumber around 966 cm⁻¹ after the two hydrogen atoms in the amine group have been replaced by methylene. Also, the intensity of the 1173 cm⁻¹ band is significantly reduced in the synthesized compound. Although the lowest frequency out-of-plane ring mode appears to be very sensitive to the substituent X, four
of six out-of-plane ring modes are located below 500 cm$^{-1}$ as are the other mass sensitive in-plane ring modes, which are all beyond our mid-IR range. Another two out of plane ring modes are too weak to be observed in our experiment.

Within the 4000-500 cm$^{-1}$ range, it is difficult to observe significant changes caused by the variation on -X from the ring mode of C$_6$F$_5$X except for the range, 1010-940 cm$^{-1}$. Therefore, it is reasonable to assume that the frequencies involving pentafluorophenyl, C$_6$F$_5$-, vibrational modes in pentafluoroaniline are almost the same as in the benzoxazine. In order to aid the band assignment, the IR and Raman spectra of the reaction mixture with different amounts of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine from PFA/bisphenol-A/formalin reaction are shown in Figure 6 and Figure 7, respectively. The distinct frequencies arising from the benzoxazine ring can be observed. The 3400 and 1179 cm$^{-1}$ arising from the OH stretching mode and the C-O stretching mode coupled with the OH deformation mode, respectively, disappear. At the same time, two new bands at 1234 cm$^{-1}$ and 1023 cm$^{-1}$ increase in intensities. These bands are regarded as antisymmetric and symmetric C-O-C stretching, respectively. The band occurred around 1500 cm$^{-1}$ in benzene described as a CH deformation coupled with a ring stretching motion is at 1512 cm$^{-1}$ in bisphenol-A. The frequency of this band has a strong dependence on the relative position of the substituents because of the forced coupling of the C-H deformation modes with C-substituent stretch. It is strongly infrared active but weak in Raman. The 1512 cm$^{-1}$ band in bisphenol-A shifts to 1503 cm$^{-1}$ in the synthesized compound. The intensity of the out-of-plane wag of two adjacent hydrogens at 829 cm$^{-1}$ in bisphenol-A decreases greatly in both Raman and IR in synthesized compound which contained benzoxazine with higher yield. In the Raman spectra, as the amount of benzoxazine increases, the 760 cm$^{-1}$ band arising from the benzoxazine ring breathing combining
with one of the in-plane C=C bending modes of 1,2,4-trisubstituted benzene ring increases greatly. The 760 cm\(^{-1}\) band can be observed in IR but it is relatively weak. The 647 cm\(^{-1}\) band, which is due to the 2,4-disubstitued benzene ring mode, decreases at the same time. There are several weak bands within the 1470-1364 cm\(^{-1}\) region, which can arise from methyl and methylene deformation as well as some ring modes. Because ring modes in this region are usually weak in Raman spectrum, these bands probably come from methyl and methylene groups since there are some strong bands in this range in Raman.

Accordingly, the 1502, 1234, 1023 and 760 cm\(^{-1}\) bands are unique in the spectra of the compound with high yield fluorinated benzoxazine. The assignment of these bands is in agreement with Dunkers and Ishida's assignment on the model compounds of 3,4-dihydro-2H-1,3-benzoxazine derived from aliphatic amine\(^{[22]}\). Therefore, it is reasonable to assign these bands to the vibrations related to the benzoxazine group, which allow characterization of the 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazines. These bands can also be observed in other 3,4-dihydro-2H-3-fluorophenyl-benzoxazines synthesized from a bisphenol-A/formalin/fluoranilnine system, such as resin IV and resin III (Figure 8 and Figure 9). With the increase of the length or size of the substituent on nitrogen, the intensity of the band at 760 cm\(^{-1}\) decreases\(^{[22]}\). Therefore, for resin II, the 760 cm\(^{-1}\) band is weak in both Raman and IR spectra.

In a neutral solution, aniline can react with formaldehyde and bisphenol-A to give 3,4-dihydro-2H-1,3-benzoxazine\(^{[5]}\). However, when 2-fluoroaniline, or 2,6-difluoroaniline, or 2,3,4-trifluoroaniline are used, the yield of benzoxazine significantly decreases with the increase of the number of the fluorine substituents on aromatic ring (table 1). Even more drastic effect has been observed with 2,3,4,5,6-pentafluoroaniline
where no benzoazaine ring was formed by the synthesis procedure described by Burke[4,10-12] and Ning[5]. The only oxazine obtained was naphtoxazine when PFA, 2,6-dihydroxynaphthalene and formalin refluxed in hot dioxane for six hours. Only after several months storage, has a small amount of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoazaine been found as illustrated in table 2. However, elevated temperature was not an efficient method to accelerate the rate of the formation of the benzoazaine in this case. Instead, there was large amount of paraformaldehyde produced when the temperature was raised to 92°C. In table 3, there is a small amount of benzoazaine produced under neutral or weak basic condition, but no benzoazaine is formed at pH=11 even after two-month storage at room temperature. This phenomenon is contrary to the conclusion derived by Burke, i.e., 3-substituted-3,4-dihydro-2H-1,3-benzoazaines were quite stable toward hot aqueous alkali but not stable in acid[4]. Furthermore, when 2,3,4,5,6-pentafluorobenzil is used, the yield of the benzoazaine ring is a function of the pH value of the reaction medium. Only under strongly acidic conditions (pH<2.5), can 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoazaine be obtained in high yield. In Figure 10, the contents of benzoazaine are characterized by both ¹H NMR and HPLC. From ¹H NMR, the yields are calculated from equation 1. For pure dibenzoazaine, the ratio should be 2; For the pure monobenzoazaine, this ratio should be 1.

\[
\text{Mole fraction} = \frac{3I_{\delta_{5.1}}}{I_{\delta_{1.6}}} \tag{1}
\]

where, \(I\) = integrated intensity; \(\delta_{5.1}\) = the ¹H NMR peak at 5.1 ppm which arises from methylene hydrogens at benzoazaine; \(\delta_{1.6}\) = the ¹H NMR peak at 5.1 ppm which arises from methylene hydrogen at 2,2-diphenylpropyl.

Another curve is obtained from HPLC by the following calculation, which represents the relative content of benzoazaine.

\[
\text{Relative content} = \frac{A_{6.2} + A_{5.5}}{\Sigma A_i} \tag{2}
\]
A is peak area, the subscript refers to the elution time in minutes of each peak. The peak with retention time at 6.2 min is assigned as dibenzoazine and the peak at 5.5 min involves the monobenzoazine. The curve fitting has been done before calculation. Because the UV extinction coefficients of every species in our product are not the same, some deviation in the HPLC results is expected. Both curves in Fig. 10 show the same tendency, that is, the yield of benzoazine strongly depends on the pH value of reaction medium. For other fluoro-substituted aromatic amines with low basicity (pKₐ<3), the strong acidic reaction medium is also necessary to improve benzoazine yields (table 1). With the number of fluorine substituents on the benzene ring increasing, the basicity of the amine decreases. This acid effect becomes more perceivable. This rule can also be applied to weak amines with other kinds of electron withdrawing substituents, the pKₐ of which is below 3, such as aminobenzonitrile. For monofluoroaniline, which pKₐ is higher than 3, the yield of benzoazine decreases when pH changes from neutral to strong acid.

As seen in Figure 10, the benzoazine yield reaches a maximum when the pH of the reaction medium is around 1.2. It seems that there is an optimum condition related to the basicity of weak amine and the acidity of the reaction medium. Each combination of reactants requires a different pH or acidity for maximum yield. For pentafluoroaniline, this condition is pH=1.2. In the acidic medium, the intensity of the ¹H NMR peak at 4.2 ppm and the 1st peak in HPLC increased when the pH decreased from 2 to 0.6. This probably results from the by-products, such as bridge structure (CH₂-N-CH₂). Figure 11 shows the SEC curves of both the original resin II and its purified product. After purification, the peak at 27 min in SEC and peak at 4.2 ppm in proton NMR spectrum disappeared, indicating that the purified product contains little dimer or other oligomers. Thus, the content of dimer or other oligomers in the synthetic resins can be observed in SEC. The SEC chromatograms of other resins are shown in
Figure 12. The major peaks around 28 min arise from benzoxazine, and the shoulders or small peaks at lower retention time are caused by dimer and other oligomers. From Figure 12, it can be viewed that the shoulders of the major peaks become more observable when the pKa values of the amines increase since the acidity of the reaction medium (pH=1.2) is the optimized condition only for pentafluoroaniline.

The concentration of reactants has slight effect on the gross benzoxazine yield. High concentration favors the formation of benzoxazine as shown in table 4.

The other important factor to affect the benzoxazine formation is the dielectric constant, which is usually parallel to the solubility parameter of the solvent (table 5). The yield of benzoxazine in both 1,4-dioxane and ethyl ether is relatively high. The values of their dielectric constants (ε) are low; ε=2.2 for 1,4-dioxane and ε=4.2 for ethyl ether. The yield in methanol is poor. The dielectric constant of methanol is high (ε=32.7).

The influence of functional substituents on the orientation of the Mannich reaction in the case of phenols is complex. When an aliphatic amine is used in the synthesis, the p-phenol with relatively strong acidity facilitates the ring-closing formation of benzoxazine since the opposite ring-opening reaction of benzoxazine happens more easily for the phenols with weaker acidity[5, 12]. However, this is not suitable for a very weak amine such as pentafluoroaniline. The acidity and solubility of p-phenol play important roles in the synthesis of 3-pentafluorophenyl-1,3-benzoxazine. The pK_a of p-phenols increases in the following order: 4, 4'-dihydroxyphenylsulfone < 4, 4'-dihydroxybenzophenone <4, 4'-thiodiphenol <bisphenol-A. When they react with PFA and formalin in the reaction medium with the pH value around 1, there is almost no benzoxazine formed for dihydroxyphenylsulfone and 4, 4'-dihydroxybenzophenone. However, in thiodiphenol /PFA/formalin system, benzoxazine has been found from ^1H NMR as well as certain amount of by-products.
and intermediates. In addition, the reaction conditions play an important role. Poor solubility of 4, 4-dihydroxydiphenyl, whose pK\textsubscript{a1} is about 9.5, in dioxane also contributes to the poor yield. Table 6 lists the yields of different p-phenols reacted with PFA and formaldehyde. The same phenomenon has also been found for the synthesis of 4,4'-diaminoctafluorobiphenol/formaldehyde/p-phenol resins. When p-fluorophenol is used instead of 4-methyl-phenol, the yield of benzoxazine decreases to 17% because the pK\textsubscript{a} of p-fluorophenol is about 9.8 while pK\textsubscript{a} of 4-methyl-phenol is around 10.3. The electrophiles formed from amine and formaldehyde are so weak that only the phenols with relatively high electron density on the aromatic ring can be attacked by this electrophile. Thus, benzoxazine can be formed by using 4-methylphenol, thiodiphenol or bisphenol-A because -CH\textsubscript{3}, -S-, -C(CH\textsubscript{3})\textsubscript{2}- are weak electron-donor substituents while O=S=O and C=O are electron-withdrawing groups.

**CONCLUSIONS**

3,4-Dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine can be synthesized in high yields by the condensation of 2,3,4,5,6-pentafluoroaniline, formaldehyde and bisphenol-A only when the pH of the reaction medium is below 2.5. A strongly acidic reaction media is a necessary condition to synthesize 3,4-dihydro-2H-1,3-benzoxazine from those amines having a pK\textsubscript{a} lower than 3. 3,4-Dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine can be characterized by the resonance at 4.5, 5.1 and 6.8 ppm from \textsuperscript{1}H NMR spectra and the 1502, 1234, 1023 cm\textsuperscript{-1} bands in IR spectra as well as the 760 cm\textsuperscript{-1} band in the Raman spectra. Solvents with low dielectric constants aid in improving the yield of benzoxazine and para-substituted phenols with electron-withdrawing substituents do not favor the formation of benzoxazine.
Reference


Table 1: The effect of pKa of amine and pH on the percent yield of benzoxazine

<table>
<thead>
<tr>
<th>amine</th>
<th>pKa of amine</th>
<th>in neutral</th>
<th>pH=1.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>aniline</td>
<td>4.58**</td>
<td>75%</td>
<td>-------</td>
</tr>
<tr>
<td>resin VI</td>
<td>2-fluoroaniline</td>
<td>3.2**</td>
<td>28%</td>
</tr>
<tr>
<td>resin IV</td>
<td>2,6-difluoroaniline</td>
<td>~ 2**</td>
<td>25%</td>
</tr>
<tr>
<td>resin V</td>
<td>4-aminobenzonitrile</td>
<td>1.74**</td>
<td>------</td>
</tr>
<tr>
<td>resin III</td>
<td>2,3,4-trifluoroaniline</td>
<td>------</td>
<td>15%</td>
</tr>
<tr>
<td>resin II*</td>
<td>4,4’-diaminoctafluorobiphenyl</td>
<td>------</td>
<td>~ 0</td>
</tr>
<tr>
<td>resin I</td>
<td>2,3,4,5,6-pentafluoroaniline</td>
<td>-2.2***</td>
<td>~ 0</td>
</tr>
</tbody>
</table>

* resin II is obtained by condensation of 4-methylphenol with formalin and the amine, the pKa refers to the pKa1 of the phenol.
** pKa data from reference 21
*** pKa data from reference 17
Table 2: Time effect on the yield of benzoxazine in resin I

<table>
<thead>
<tr>
<th>pH</th>
<th>7.8</th>
<th>9.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>time (month)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>yield(%)</td>
<td>-0</td>
<td>12</td>
</tr>
</tbody>
</table>

Table 3: Yield of benzoxazine in resin I after two-month storage

<table>
<thead>
<tr>
<th>pH</th>
<th>11</th>
<th>9.9</th>
<th>9.5</th>
<th>8.9</th>
<th>8.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>yield(%)</td>
<td>0.0</td>
<td>17</td>
<td>22</td>
<td>18</td>
<td>39</td>
</tr>
</tbody>
</table>
Table 4: Concentration effect on the yield of benzoaxazine

<table>
<thead>
<tr>
<th>conc. of solute (%)</th>
<th>18</th>
<th>24</th>
<th>37</th>
</tr>
</thead>
<tbody>
<tr>
<td>yield(%)</td>
<td>86</td>
<td>88</td>
<td>90</td>
</tr>
</tbody>
</table>

Table 5: Solvent effect on the yield of dibenzoaxazine

<table>
<thead>
<tr>
<th></th>
<th>in dioxane</th>
<th>in ethyl ether</th>
<th>in methanol</th>
</tr>
</thead>
<tbody>
<tr>
<td>ε</td>
<td>ε=2.2</td>
<td>ε=4.2</td>
<td>ε=32.7</td>
</tr>
<tr>
<td>yield(%)*</td>
<td>80</td>
<td>70</td>
<td>20</td>
</tr>
</tbody>
</table>

*yield calculated from equation (1)*

Table 6: The effect of pKa of p-phenol on the yield of benzoaxazine in PFA/formalin/p-phenol resins

<table>
<thead>
<tr>
<th>p-phenol</th>
<th>pKa₁*</th>
<th>yield of benzoaxazine(%)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>bisphenol-A</td>
<td>~10</td>
<td>80</td>
</tr>
<tr>
<td>4, 4'-thiodiphenol</td>
<td>~9.5</td>
<td>50</td>
</tr>
<tr>
<td>4, 4'-dihydroxybenzophenone</td>
<td>~8.0</td>
<td>~0</td>
</tr>
<tr>
<td>4, 4'-dihydroxyphenylsulfone</td>
<td>~7.8</td>
<td>~0</td>
</tr>
</tbody>
</table>

* pKa₁* from reference 23

** yield calculated from the ratio: \( \frac{I_d5.1ppm}{I_d6.9ppm+I_d6.7ppm} \times 100\% \)
Figure 2.1 SEC chromatograms of PFA/bisphenol-A/formaldehyde resin (resin I)
Figure 2.2 Absorption HPLC of PFA/bisphenol-A/formaldehyde resin (resin I)
Figure 2. $^1$H NMR spectrum of PFA/bisphenol-A/formaldehyde resin (resin I)
Figure 2.4 $^1$H NMR spectra of the various resins.

(a) 4-cyanoaniline/bisphenol-A/formaldehyde resin (resin V);
Figure 2.4  (b) 4,4'-diaminoctafluorobiphenyl/4-methylaniline/formaldehyde resin (resin II).
Figure 2.4  (c) 2,3,4-trifluoroaniline/bisphenol-A/formaldehyde (resin III);
Figure 2.4  (d) 2,6-difluoroaniline/bisphenol-A/formaldehyde resin (resin IV);
Figure 2.5  Infrared spectra of resin I and its reactants.
Figure 2.6 Infrared spectra of resin I reaction mixture with different yield of benzoxazine.
Figure 2.7  Raman spectra of resin I reaction mixture with different yield of benzoxazine.
Figure 2.8  Infrared spectra of other fluorobenzoxazines
Figure 2.9  Raman spectra of other fluorobenzoxazines
Figure 2.10 The relationship between yield of fluorobenzoxazine in resin I and pH of reaction medium.
Figure 2.11  SEC chromatograms of resin II
Figure 2.12  SEC chromatograms of fluorobenzoxazine resins
CHAPTER 3
REACTION MECHANISM OF 3,4-DIHYDRO-2H-3-PENTAFLUOROPHENYL-1,3-BENZOXAZINE FORMATION
INTRODUCTION

Benzoazines are an attractive class of monomers for new phenolic resins due to their ring opening mechanism rather than the condensation reactions of traditional phenolic resins. Most shortcomings associated with the traditional phenolic resin chemistry have been overcome by using the benzoazine as a precursor [1-4].

3-substituted-3,4-dihydro-2H-1,3-benzoazine results from the reaction of p-substituted phenols with formaldehyde and a primary amine in a molar ratio of 1:2:1, respectively [5]. The chemical structure of the benzoazine is shown below.

\[
\begin{array}{c}
\text{R} \\
\text{N} \\
\text{R'}
\end{array}
\]

The synthesis reaction is a multiple Mannich aminomethylation of phenol on two specific positions. One is ortho to the hydroxyl group of aromatic ring, and the other is on the hydroxyl group. Phenolic Mannich bases derived from primary amines have demonstrated the importance of several reaction variables on the course of the condensation. This included the nature and position of substituents on the phenol, reaction ratios, temperature and the basicity of the amine [1-2, 6-8].

For relatively strong amines, which have pK\text{a} values in the range 3~13, the reaction was best carried out by first condensing the primary amine with formaldehyde to form the N,N-dihydroxymethylamine which was then allowed to react with the phenol. Alternatively, when a p-substituted phenol, formaldehyde, and a primary amine are simultaneously allowed to react in a molar ratio of 1:1:1, aminomethylphenols were formed. These compounds condensed with formaldehyde in the presence of base to
yield the 3-substituted-3,4-dihydro-2H-1,3-benzoxazine [1-2, 5-7]. The benzoxazine was quite stable toward hot aqueous alkali and readily formed hydrochloride salt [8]. However, a strongly acidic reaction medium is necessary to synthesize 3,4-dihydro-2H-1,3-benzoxazine from the amines having pKₐ values below 3. For example, 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine has been synthesized in high yield by the condensation of 2,3,4,5,6-pentafluoroaniline, formaldehyde and bisphenol-A only when the pH value of the reaction system is below 2.5 [9]. Although the chemistry of Mannich reaction has been the subject of investigation by an increasing number of researchers [10-12], few papers deal with this specific Mannich reaction, by which the 3,4-dihydro-2H-benzoxazine is synthesized.

Hellmann and Opitz have shown that the course of the Mannich condensation follows the following sequence: addition of the amine to formaldehyde to form an N-hydroxymethyl group (>N-CH₂-OH) or related derivative which then reacts with a labile hydrogen compound (HR) to produce a Mannich base (>N-CH₂-R). A hydroxymethyl derivative of the labile hydrogen compound (R-CH₂-OH) could not be the intermediate in Mannich reaction since such a pathway could only lead to a methylene-bis derivative of the labile hydrogen compound (R-CH₂-R) and not to a Mannich base. In other words, formaldehyde interacts with the amine as the initial step in the Mannich condensation [13]. However, it is well-known that the reactions between formaldehyde and aromatic amines are varied and complex. It is often difficult to obtain reproducible results after isolation, and the formation of some compounds appears to be capricious even under standardized conditions [14,15]. Neither the initial "aldol" ArNHCH₂OH nor the schiff base ArN=CH₂ has been isolated from the products of aromatic amine and formaldehyde although they are regarded as the initial products [28, 29]. The products initially formed in the condensation of formaldehyde
and ammonia or primary amines undergo a series of transformations by participating with the remaining N-H bonds, leading to a mixture of various compounds, the nature of which mainly depends upon reaction conditions such as the ratio of reactants, pH, and temperature. When an aromatic amine is involved, the situation becomes even more complex. In neutral or weakly acid solution, carbon-nitrogen bonds only forms, but in acid solution (pH<3), both carbon-carbon and carbon-nitrogen bonds are formed, and the reaction involves the benzene ring [16]. In some cases, by-products may be formed by side-reactions. Such processes may occur to the exclusion of the normal Mannich reaction, completely destroying the normal products such as formation of methylene-bis derivatives of the active hydrogen compound (R-CH2-R) or methylene-bis-amines (>N-CH2-N<) or similar compounds [11].

In the mechanistic study of the classic Mannich reaction, Thompson pointed out that N-hydroxymethylamine, N-methoxymethylamine, and methylenediamine could all be formed in the course of the Mannich reaction, depending upon the reactants and the conditions employed [12]. Generally, N-hydroxymethylamines exist only at lower temperature; N,N-methylenediamines are formed exclusively when formaldehyde and amines are allowed to react without cooling; nitrogen hemi-acetals are converted to O,N-acetals (methoxymethylamine) with alcohols or to N,N-acetals with amines (N,N-methylenediamine) without added catalyst. These two kinds of acetals are very acid sensitive and follow a well-defined reaction course in acid hydrolysis [15]. Liebermann and Wagner found that N,N'-methylenediamine is the intermediate formed in Mannich reaction prior to formation of the aminomethyl carbonium ion [17]. Alexander and Underhill found that acidic hydrogen compound was in the enol form rather than in the ionized form when N-hydroxymethylamine was suggested to react with the acidic hydrogen compound [18].
In this chapter, we discuss the mechanism of the condensation reaction of pentafluoroaniline and formaldehyde in both basic and acidic reaction media by means of Fourier transform infrared spectroscopy (FT-IR), nuclear magnetic resonance spectroscopy (NMR) and high performance liquid chromatography (HPLC). A new reaction mechanism for the formation of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoazine is proposed and studied by means of attenuated total reflection Fourier transform infrared (ATR-FTIR) using a liquid cell.

**Experimental**

**Materials**

2,3,4,5,6-Pentafluoroaniline (98%) was purchased from Aldrich Chemical Company. Bisphenol-A was produced by Shell Company. 1,4-Dioxane and formaldehyde (37% aqueous solution) were supplied by Fisher Scientific Company. All the chemicals were used without further purification.

**Sample preparation**

N-hydroxymethyl-pentafluoroaniline dominant products:

1.6 Gram (0.02 mole) aqueous 37% (w/w) formaldehyde in 5 ml 1,4-dioxane or 0.6 gram (0.02 mole) paraformaldehyde which had been heated and stirred in 1 ml distilled water until the solution became transparent, was cooled in an ice bath. A basic catalyst was added until the expected pH value was achieved. Triethylamine, pyridine, and sodium carbonate were used as basic catalysts. Then 1.8 gram (0.01 mole) pentafluoroaniline in 5 ml 1,4-dioxane was added gradually, continuing agitation for about 1 hour. Subsequently, the solvent was evaporated in vacuum below 50°C. The reaction can also be carried out in methanol, ethyl ether or other solvent.

1, 3, 5-tripentafluorophenylperhydro-1, 3, 5-triazine dominant products:
1.6 Gram (0.02 mole) Aqueous 37% (w/w) formaldehyde in 5 ml 1,4-dioxane was added to 1.8 gram (0.01 mole) pentafluoroaniline in 5 ml dioxane. About 1 ml acetic acid was added and the solution was continuously stirred for one hour at an elevated temperature. After the reaction was completed, the solvent was evaporated under vacuum. The product was then dissolved in ethyl ether and shaken with excess sodium sulfite in order to remove the unreacted formaldehyde and water. The ether was subsequently evaporated by means of rotary evaporator at room temperature.

**Liquid sample for ATR-FTIR**

1.8 Gram (0.01 mole) 98% Pentafluoroaniline dissolved in 1 ml 1,4-dioxane was added to 1.6 gram (0.02 mole) aqueous 37% (w/w) formaldehyde solution in a three neck flask at room temperature. The mixture was stirred magnetically for about 1 hour before adding 1.1 gram (0.005 mole) bisphenol-A in 3 ml dioxane. The solution was then heated to 75°C and kept at this temperature during the reaction. 0.5 ml solution was sampled and designated as the sample at t=0 min. Trace amount of 37% HCl aqueous solution was dropped into the system. The sampling was done at 1, 5, 10, 30, 60, 119, 187 and 234 minutes after the addition of acid and the sample was kept at room temperature. The ATR spectrum was taken for each sample within 30 minutes after the sampling. There was no detectable difference between the sample that was examined immediately after sampling and the sample that was kept at room temperature for 1 hour, indicating slow reaction at this temperature.

**Characterization**

The synthesized compounds were characterized by Fourier transform infrared spectroscopy (FT-IR), nuclear magnetic resonance spectroscopy (NMR), size exclusion chromatography (SEC), and high performance liquid chromatography (HPLC).
The FTIR instrument used was a Bomem Michelson MB FT-IR spectrophotometer which is equipped with a liquid nitrogen cooled, medium band-pass, mercury-cadmium-teuicide (MCT) detector with the specific detectivity, $D^*$, of $1 \times 10^{10}$ cmHz$^{1/2}$W$^{-1}$. All spectra were recorded at a resolution of 4 cm$^{-1}$ and displayed in the absorbance mode. Coaddition of 50 scans was sufficient to obtain good signal-to-noise (S/N) ratio spectra for transmission IR.

For ATR-FTIR, a germanium trapezoid with dimensions of 52x20x2 mm with an end face angle of 60 degrees was obtained from Harrick Scientific Co. and was used as an internal reflection element (IRE). This IRE was used in an internal reflection attachment from Wilks Scientific Corporation. Coaddition of 200 scans yielded sufficient S/N ratio for quantitative analysis.

The NMR spectrometer used was a Varian XL-200 NMR spectrometer. Deuteriochloroform or deuteroacetone with 1% tetramethylsilane (TMS) was used as a solvent. Coaddition of 16 scans yielded a sufficient S/N ratio spectrum.

HPLC was done with Waters 510 HPLC pump, U6K Universal Injector, and Waters 484 Tunable UV Detector fixed at 254 nm. The column used was Waters Partisil 5 with a partially silanized silica column. Chloroform / ethyl acetate mixture with 2-to-1 volume ratio was used as the eluent. The flow rate was changed from 0.5 ml / min. to 2 ml / min linearly.

RESULTS AND DISCUSSION

In a neutral solution, aniline can react with formaldehyde and bisphenol-A to afford 3,4-dihydro-2H-1,3-benozxazine[3,4]. However, when 2-fluoroaniline or 2,6-difluoroaniline is used, the yield of benoxazine significantly decreases with the increase of the number of the fluorine substituents on aromatic ring. Even more drastic effect has been observed with 2,3,4,5,6-pentafluoroaniline where no benzoxazine ring
was formed by the same procedure unless after storage for few months [9]. Rising reaction temperature cannot accelerate this reaction rate. Instead, the intermediates are decomposed to liberate formaldehyde, which then condenses into polyformaldehyde. Only when the pH value of the reaction medium is below 2.5 can the benzoxazine be obtained in high yield for a pentafluoroaniline, formaldehyde, and bisphenol-A system. This result is in contradiction with the phenomena found before, i.e., 3,4-dihydro-2H-1,3-benzoxazines would hydrolyze under such strongly acidic conditions [8]. Also, the formaldehyde would polymerize or react with phenol to form methylene bridges (Ar-CH₂-Ar) quite easily [19,20]. Thus, for a very weak amine such as pentafluoroaniline, the mechanism of Mannich reaction is somewhat unique.

In Mannich reaction, if the nucleophilicity of the carbanion derived from the labile hydrogen compound is greater than that of the amine, the reaction between the labile hydrogen compound and formaldehyde would be favored over the reaction between amine and formaldehyde. Under such conditions, a symmetrical methylene derivative of the labile hydrogen compound results[11]. This is not the situation for the strong amine/phenol/formaldehyde system since the amino group is a much stronger nucleophile than phenol. Sometimes, a basic medium is used in order to yield carbanions with greater nucleophilicity than phenol, which can react with N-hydroxymethylamine more easily. However, the introduction of fluorine substituents onto the benzene ring of an aromatic amine greatly decreases the nucleophilicity of the amino group because fluorine is the most electronegative element. Therefore, it is understandable that the formation of Mannich base using pentafluoroaniline or other very weak amines would be more difficult than that from relatively strong amines.

In basic conditions, the condensation of pentafluoroaniline and formaldehyde yields a mixture of products, and the amount of each component varies with the concentration and pH value of reaction system. The composition also varies from batch
to batch. Figure 1 shows the typical FT-IR and proton NMR spectra of this mixture, from which the N-hydroxymethylamine can be easily identified by its -OH and C-O stretching bands at 3350 cm\(^{-1}\) and 1053 cm\(^{-1}\), respectively, in the IR spectrum. In the NMR spectrum, there are two doublets and two broad shoulders which combine into one peak after addition of deuterated water due to the exchange between the hydrogens on amino or hydroxyl groups and the deuterium from D\(_2\)O in the solution. When the basicity of the reaction medium increases, the 3450 cm\(^{-1}\) band decreases and 3350 cm\(^{-1}\) band increases in intensity, which means that the amount of -OH group increases and -NH group decreases (figure 2). The intermediates, usually regarded as N-hydroxymethylamine, or N,N-dihydroxymethylamine in Burke's reaction[5-8], which are stable in neutral and basic solutions, are too inert to be electrophiles for the substitution reaction on phenol. The stability of these amino alcohols increases with the increase of the solution basicity when triethylamine content increases from 0.5% to 80%, i.e., pH varied from 8.4 to 11[9].

In the presence of a mild acid such as acetic acid, the products from the reaction between pentafluoroaniline and formalin seem quite simple and reproducible. Figure 3 shows that there is little absorbance within the region around 3600-3300 cm\(^{-1}\), which means there are few amino and hydroxyl groups in this compound. The spectrum is extremely simple implying that the structure is somewhat symmetric. Furthermore, there is no absorbance around C-O stretching vibration from IR spectrum. There is only one broad peak around 4.6 ppm in proton NMR spectrum, which is slightly lower than the chemical shift arising from CH\(_2\)-O and in the range related to the proton resonance of N-CH\(_2\)-N. As we know, the proton magnetic resonance spectra of aromatic polyfluoro-compounds show protons in side-chains coupled with the fluorines ortho to the side chain and only with these fluorines. All these couplings are through space and not through the bonds. Thus, if the conformation of the molecule allows the proton to
approach the ortho fluorines, coupling will take place [21]. When there are two ortho-
fluorines, the side chain protons show triplet or quadruplet. If the structure is
perhydrotiazine from pentafluoroaniline, there would be four fluorines ortho to the
methylene group and the ring structure restrains the rotation of the methylene group.
Therefore, the peak from the protons of methylene should be very broad. According
to the analysis above, the component obtained from mildly acidic condition is probably
1,3,5-tripentafluorophenylperhydro-1,3,5-triazine. In summary, the
hydroxymethylamine and perhydrotiazine can be formed by the condensation of
pentafluoroaniline and formaldehyde depending on the pH value. Under basic
conditions, N-hydroxymethylamines are the dominant products. In mildly and strongly
acidic media, perhydrotiazine is the major reaction product.

In the previous study[9], a good separation of 3,4-dihydro-2H-3-
pentafluorophenyl-1,3-benzoxazine resin by HPLC was obtained. Here the same
conditions are used for analyzing the intermediates. In a dilute solution (18%wt) in an
ice bath, the majority of pentafluoroaniline(retention time = 6.5 min) remains unreacted
after stirring for one hour(figure 4). The component at 5.8 min increases when the pH
decreases from neutral to 2. Because the competition between the solute molecules and
the solvent molecules for an active site on the surface of silica gel column provides the
driving force and selectivity for separations, the stronger the hydrogen bonding or
dipole interaction between the specific functional groups of the eluate and the silanol
group on the silica gel surface, the longer the retention time is. It is obvious that the
formation of perhydrotiazine weakens the interaction between the amino group and the
silanol group, thus it should have shorter retention time than the amine. Therefore, the
peak at 5.8 min is regarded as the perhydrotiazine of pentafluoroaniline. With the
acidity increasing continuously to pH =1.2, this peak decreases and, at the same time,
another new peak at 6.0 min appears. It is already found that the perhydrotiazine can
be hydrolyzed in the presence of a strong acid to form minimum ion and carbonium ion or their salt forms [16]. When the pH is greater than 2, perhydrotriazine cannot be hydrolyzed. The yields of both dibenzoxazine and monobenzoxazine are very low [9] and a significant amount of unreacted phenol and perhydrotriazine remains in the resin as indicated in figure 5 and figure 6.

For the reaction with a higher concentration, i.e., 37% by weight of reactant content, the reaction paths are shown in figure 7 by means of HPLC. Similar components exist but the perhydrotriazine is produced at a low temperature and the yield is also higher than in dilute dioxane solution. In addition, the majority of pentafluoroaniline is reacted.

Since some species can only be stable in solution, an ATR-liquid cell attachment for FTIR is used in order to monitor the true reaction paths. The reproducibility of this experiment is found to be quite good. The vibrational modes involving the radical skeletal vibrations of benzene ring that couple with carbon-substituent stretching are regarded as sensitive bands to the mass and electronic state change upon substitution [22]. Thus, the region around 1070–920 cm\(^{-1}\) is chosen as the frequency range to monitor the reaction. Also in this region, there are characteristic bands at 1023 and 966 cm\(^{-1}\) for benzoxazine[9, 23], 990 cm\(^{-1}\) for both perhydrotriazine and benzoxyazine, and 1010–998 cm\(^{-1}\) Fermi doublet and 950 cm\(^{-1}\) for pentafluoroaniline[24]. Another interesting region is around 1500-1530 cm\(^{-1}\), in which there are bands arising from bisphenol-A at 1513 cm\(^{-1}\) and from pentafluorophenyl at 1523 cm\(^{-1}\) [22, 25]. Both benzoxazine and perhydrotriazine give rise to a band at 1503 cm\(^{-1}\). The formalin solution shows a well resolved band at 1150 cm\(^{-1}\) and a broad band around 1220–1200 cm\(^{-1}\).

Figures 8 and 9 are the ATR-FTIR spectra of pentafluoroaniline reacting with formalin in 1,4-dioxane solution (37% by weight of reactant contents). In neutral
conditions, there is a relatively strong band at 950 cm\(^{-1}\) and a doublet at 1010–998 cm\(^{-1}\) superimposed with a weak band at 990 cm\(^{-1}\), indicating that only a small amount of pentafluoroaniline can react with formaldehyde to form perhydrotiazine. However, in the presence of trace amounts of hydrogen chloride, the 1010 and 998 cm\(^{-1}\) doublet and the 950 cm\(^{-1}\) band decrease quickly. At the same time, the bands at 1503 and 990 cm\(^{-1}\) due to perhydrotiazine appear and their intensities become greater with the increase of the temperature. In this experiment, neither aminocarboxonium ion nor iminium ion can be observed. Since the hydrolysis of perhydrotiazine is an equilibrium procedure, it has a greater tendency to form perhydrotiazine rather than ionic forms in 1,4-dioxane because of dioxane's low dielectric constant. It is well-known that the solvents with low dielectric constants are poor ionizing media [26]. In the addition of bisphenol-A, there is little effect on the reaction course between amine and formaldehyde. The perhydrotiazine forms first in the presence of acid (figures 10 & 11). But when the temperature increases, the band at 990 cm\(^{-1}\) decreases and new bands at 1023 and 966 cm\(^{-1}\) appear. As shown in figure 12, the bands at 1010, 998 and 950 cm\(^{-1}\) which arise from pentafluoroaniline decrease almost immediately after adding the acid. At the same time, the 990 cm\(^{-1}\) band increases drastically within 1 minute because perhydrotiazine forms quickly after adding acid (figure 13). This indicates that the first step of the reaction completes within the first minute in the presence of acid.

The above result provides the evidence that the synthesis of benzoxazine is a two step reaction. The first step involves the condensation of an amine with formaldehyde to form a perhydrotiazine. The condensation mechanism between formaldehyde and pentafluoroaniline in both acidic and basic media is proposed as follows.
In an aqueous medium, a very fast acid and base catalyzed hydration reaction of formaldehyde to methylene glycol occurs, the equilibrium constant of this reaction is about $10^{14}$[15]. Thus, methylene glycol is found in aqueous solutions as the key monomeric species. The methylene glycol could form hydroxymethylene carbonium ion, which is the hydroxylation agent, when pH value is below 2.6 [15]. This is consistent with our observation from IR spectra using the liquid cell. No carbonyl group vibrations can be observed, which is supposed to appear around 1740–1720 cm$^{-1}$ for most aliphatic aldehydes [25]. Instead, there are a broad band around 1200–1220 cm$^{-1}$ and a band at 1150 cm$^{-1}$, which represent the O–H deformation and C–O
antisymmetric vibration from methylene glycol, respectively:

\[
\begin{align*}
\text{n O}=\text{CH}_2 & + \text{n H}_2\text{O} \rightarrow \text{HO}\{\text{CH}_2-\text{O}\}_n\text{H} \\
n=1,2,3 & \\
\text{methylene glycol} & \\
\text{H}^+ + \text{HOCH}_2\{\text{CH}_2-\text{O}\}_n\text{H} & \rightarrow \uparrow\text{CH}_2\text{O-CH}_2-\text{OH} + \text{H}_2\text{O} \\
n=0,1,2 & \\
\text{hydroxymethylene} & \\
\text{carbonium ion} &
\end{align*}
\]

In figure 14, the 1150 cm\(^{-1}\) band almost disappeared within 5 minutes after the addition of acid. One explanation for this sudden decrease is that the formation of perhydrotriazine will consume half the amount of formaldehyde within 5 minutes. If the subsequent reaction were carried out in such a way that the acid promoted cleavage of perhydrotriazine reacted with another half amount of formaldehyde and bisphenol-A to form benzoazine, the concentration of formaldehyde should keep decreasing in the same way as the increase of benzoxazine. However, in fact, the amount of methylene glycol is almost constant after 5 minutes.

The following reaction between bisphenol-A and formaldehyde in the strong acidic pH range occurs as an electrophilic substitution. It has been known that the addition of the carbonium ion from hydroxymethylene glycol to bisphenol-A can form the transition structure in an acidic medium, which will form methylolphenol and release a hydrogen cation very quickly[19, 20]. In the strongly acidic solution, the methylolphenol is not stable and has a tendency to become a benzylic carbonium ion, which is also an electrophile as an aminocarbonium ion. In our reaction, the 1513 cm\(^{-1}\) band arising from the bisphenol-A ring C=C stretching disappears within 5 minutes after addition of acid. Usually, this band is very strong for p-substituted phenols. Only when there are strong electron-withdrawing substituents in the molecule, does this vibrational mode become very weak. The electron densities on the benzene ring of both
methylolphenol and the benzylic carbonium ion are lower than that of the free phenol. Thus, the intensity at 1513 cm\(^{-1}\) decreases when the following reactions happen.

\[
\begin{align*}
\text{OH} & \quad + \text{CH}_2\text{-O-H} \quad \text{slow} \quad \left[ \begin{array}{c}
\text{OH} \\
\text{R}
\end{array} \right] \quad \text{fast} \quad + \text{H}^+ \\
\text{transition structure} & \quad \text{methylol-phenol}
\end{align*}
\]

\[
\begin{align*}
\text{OH} & \quad \text{CH}_2\text{OH} \quad + \text{H}^+ \quad \text{benzylic carbonium ion} \\
\text{R} & \quad \text{R}
\end{align*}
\]

In order to study the second step of the reaction, the reaction rate of each species is determined by monitoring the change of the intensity of each band in the IR spectra as a function of the reaction time at 75°C. A curve resolving technique is carefully applied to obtain the absorbance contribution of each band. The bands at 1523 cm\(^{-1}\) from pentafluorophenyl and 1046 cm\(^{-1}\) from 1,4-dioxane are chosen as internal standard bands. The ratio of the intensities of these two bands is constant during the whole reaction period.

Since both perhydrotriazine and benzoxazine have absorptions at 990 cm\(^{-1}\), the two competitive reactions result in the decrease of the 990 cm\(^{-1}\) band with the consumption or hydrolysis of perhydrotriazine at the beginning of second step of the reaction and the increase with the formation of benzoxazine (figure 13). The
concentration of perhydrotriazine, \( C_2 \), should be proportional to the absorbance at 990 cm\(^{-1} \) in the following way according to Beer's law.

\[
C_2 = \frac{(A_{990} - \frac{\alpha_1}{\alpha_1} A_{1023})}{A_{1522}}
\]  

Here, "\( A_{990} \)" is the absorbance at 990 cm\(^{-1} \); "\( A_{1023} \)" is the absorbance at 1023 cm\(^{-1} \). "\( A_{1522} \)" is the absorbance of the reference band at 1522 cm\(^{-1} \). "\( \alpha_1 \)" is the specific absorptivity of benzoazidine at 990 cm\(^{-1} \); "\( \alpha_1' \)" is the specific absorptivity of the perhydrotriazine at 990 cm\(^{-1} \).

By using equation (1), an approximate relationship between the concentration of perhydrotriazine and the reaction time is shown in figure 16. We can find that the perhydrotriazine decreases with the reaction time at 75°C. The perhydrotriazine would not decrease in the absence of bisphenol-A (figure 9), indicating that the hydrolysis of the perhydrotriazine equilibrium occurs and the ionization tendency is quite weaker than the formation of perhydrotriazine. Formation of benzoazidine consumes the ionic species and the hydrolysis equilibrium shifts to the right side.

Actually, there would be two competing electrophiles in the solution. One is the aminocarbonium ion from perhydrotriazine, the other is the benzylic carbonium ion. Both these electrophiles could attack the ortho position of the phenol and form either aminomethylenebenzophenol or dihydroxydiphenylmethane depending on reaction condition and the competition between the nucleophilicity of these two carbonium ions. Therefore, there are three possible mechanisms in terms of the second step reaction. One mechanism is the benzylic carbonium ion attacking the perhydrotriazine. The second possible mechanism is the hydrolyzed perhydrotriazine acting as an electrophile and attacking the phenol, which further reacts with another formaldehyde to form benzoazidine. The third one is that aminocarbonium ion attacks the methylolphenol.
According to the general synthesis of Novolac phenolic resin, the methylolphenols formed from bisphenol-A and formalin are unstable under strong acidic condition, and it can transfer into benzylic carbonium ion. The subsequent formation rate of dihydroxydiphenylmethane was found to be as fast as the formation of benzylic carbonium ion. The rate is proportional to the hydrogen ion concentration[20]. If this is the case in our synthesis, we would obtain a certain amount of dihydroxydiphenylmethane, i.e., bridge structure (Ar-CH2-Ar) as well as benzoaxazine. Furthermore, the formation of benzoaxazine would happen not only in the medium with the pH< 2.5 but also at pH=3.0, since benzylic carbonium can be formed in methanol with pH=3. However, the benzoaxazine is indeed the major product in this condition. Few bridge structures have been found. The benzoaxazine can only form when pH below 2.5[9], which happens to be the aforementioned condition of hydrolysis of the perhydrotriazine. Therefore, benzylic carbonium is not the intermediate of the formation of benzoaxazine, and the equilibrium of benzylic carbonium and methylolphenol shifted to left side.

If the second mechanism is true, the reaction rate of the formation of benzoaxazine should be the function of the concentration of free bisphenol-A and methylene glycol as well as the concentration of aminocarbonium ion. In figure 17, the bands at 1023 cm\(^{-1}\) and 966 cm\(^{-1}\) which arise from benzoaxazine do not exist in the first minute, then increase quickly in the following ten minutes. After which, they continue to increase gradually. There seems a delay between maximum benzoaxazine formation and the maximum decrease of the concentration of reactants. In other words, the concentrations of pentafluoroaniline, formaldehyde and bisphenol-A are almost constant during the formation of benzoaxazine (figures 12, 14 & 15). That means the second step reaction is almost zero order with respect to the reactants. However, the concentrations of the intermediates decrease in the similar tendency as the increase of
Another intermediate mentioned before in figure 10, another intermediate is the hydroxymethylene derived from bisphenol-A and formaldehyde. The change at 1177 cm\(^{-1}\) indeed can give some information about this intermediate. As shown in figure 15, the band at 1513 cm\(^{-1}\), which represents the free bisphenol-A, is absent in the second step reaction. However, the band at 1177 cm\(^{-1}\) which represents the C-O stretching interacting with the OH deformation decreases in the second step reaction in figure 18. As we know, 4-monosubstituted and 2,4-disubstituted phenols have a very similar strong absorption within 1160–1174 cm\(^{-1}\), which is insensitive to the variance of the substituents [27]. Therefore, it is reasonable to assume that the variation of the intensity of this vibrational mode mostly comes from the methylolphenol. According to the above observation, the second step reaction is a function of the concentration of these two intermediates, perhydrotriazine and methylolphenol.

Thus, when very weak amine such as pentafluoroaniline participates the Mannich reaction with formaldehyde and phenol in an acidic medium, hydroxymethyl derivative of the labile hydrogen compound (here is methylolphenol) can be another intermediate.

Combining the analysis above, the mechanisms for the second step reaction are summarized as follows.
Considering the step cleavage of perhydrotriazine, aminocarbonium ion can also be produced as follows.
Accordingly, acid can increase the reactivity of perhydrotriazine, but it can also reduce the reactivity of phenol with respect to the electrophilic substitution on the benzene ring. Acid can also increase the probability of the formation of benzylic carbonium ion.

When the pH is less than 2, the reactivity of phenol becomes more important, but the benzoxyzinyl is an electron-donating substituent, which increases the electron density on the aromatic ring. Hence, it is easier to continue the electrophilic substitution on the phenyl ring of the monobenzoxazine than that of bisphenol-A. In figure 19, the
content of monobenzoxazine decreases rapidly when pH value is below about 1.5 because of some monobenzoxazine converts into dibenzoxazine and others begin to form a Mannich base bridge structure (Ar-CH₂-N-CH₂-Ar) (5.3 min, 4.4 ppm) at the same time (figure 20).

When pH is less than 1.1, unreacted perhydrotriazine increases (figure 5), indicating that the reactivity of hydrogen on phenol has become the control factor of the synthesis.

Consequently, there are at least two limitations to the formation of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine via the condensation of p-substituted phenol with formaldehyde and 2,3,4,5,6-pentafluoroaniline, or other weak aromatic amines with strong electron-withdrawing o,p-substituents. One limitation arises from nucleophilicity of the amine. The intermediates derived from the amine and formaldehyde should be active enough. Another limitation depends on the properties of phenol under the first limitation, including the acidity and the solubility of phenol, which determines the hydrogen activity on phenyl ring and its accessibility to the intermediates, respectively. For this reason, 4, 4'-dihydroxyphenylsulfone, whose $K_a$ is thousand times that of bisphenol-A, can hardly form benzoxazine with pentafluoroaniline/formaldehyde [9]. On the contrary, lower electronic density on the ortho position of phenol, resulted from the electron-withdrawing substituents, can improve the yield of 3,4-dihydro-2H-1,3-benzoxazine when benzyamine is used [8].

**Conclusion**

Under basic conditions, the major products from the reaction of formaldehyde and 2,3,4,5,6-pentafluoroaniline are hydroxymethylpentafluoroanilines. In the presence of mild acid, the exclusive products of the above reaction is 1,3,5-
Under strong acid conditions, an equilibrium between the hydrolysis and formation of this substance is established. In pH=1.2 reaction media, the synthesis of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine includes a two step reaction. The first step reaction involves the formations of perhydrotriazine and derivative of bisphenol-A and formaldehyde, which can be completed almost immediately after addition of acid. The second step reaction are rate controlling reaction involving an acid-promoted cleavage of the perhydrotriazine and its reaction with the derivative of bisphenol-A and formaldehyde.
Reference
Figure 3.1  (a) $^1$H NMR spectrum of the products of the reaction between pentafluoroaniline and formaldehyde under basic condition (b) IR spectrum of products from the reaction of pentafluoroaniline and formalin under basic condition.
Figure 3.2  IR spectra of the products of the reaction between pentafluoroaniline and formaldehyde under different basic conditions.
Figure 3.3  (a) $^1$H NMR spectrum of product of reaction between pentafluoroaniline and formaldehyde under acidic condition (b) IR spectrum of the product of the reaction between pentafluoroaniline and formaldehyde under acidic condition.
Figure 3.4  HPLC results of the products from the reaction between pentafluoroaniline and formaldehyde (solute con.18% wt).
Figure 3.5  Content of perhydrotriazine as a function of pH value of the reaction medium. (Reaction condition: 50°C/6 hours in 1,4-dioxane)
Figure 3.6  Content of unreacted bisphenol-A as a function of pH value of the reaction medium.
Figure 3.7 HPLC graphics of the products from the reaction between pentafluoroaniline and formaldehyde (37%wt).
Figure 3.8  ATR-IR spectra of the products from the reaction between pentafluoroaniline and formaldehyde in dioxane.
Figure 3.9  ATR-IR spectra of the products from the reaction between pentafluoroaniline and formaldehyde in dioxane
Figure 3.10  ATR-IR spectra of the solutions sampled during the synthesis procedure (range 1080–920 cm⁻¹).
Figure 3.11  ATR-IR spectra of the solutions sampled during the synthesis procedure (range 1600–1400 cm$^{-1}$).
Figure 3.12  The amount of pentafluoroaniline as a function of reaction time at 75°C.
Figure 3.13  Relative intensity of the band at 990 cm$^{-1}$ as a function of the reaction time at 75$^\circ$C.
Figure 3.14 The relative intensity of the band at 1150 cm$^{-1}$ due to formalin as a function of the reaction time at 75$^\circ$C.
Figure 3.15  Concentration of bisphenol-A as a function of reaction time at 750°C.
Figure 3. 16  Relative concentration of perhydrotriazine as a function of reaction time at 75°C in second step reaction.
Figure 3.17  The concentration of benzoazine as a function of reaction time at 75°C.
Figure 3.18  Relative intensity of C-O stretching band at 1177 cm⁻¹ as a function of reaction time.
Figure 3.19 Contents of mono- & di-benzoxazine as a function of pH value of the reaction medium.
Figure 3.20  Content of bridge structure as a function of pH value of the reaction medium
CHAPTER 4
THERMAL BEHAVIORS IN SOLVENTLESS SYNTHESIS OF
3,4-DIHYDRO-2H-1,3-BENZOXAZINE MONOMER
Introduction

Assorted 3-substituted-3,4-dihydro-2H-1,3-benzoazines have been synthesized by the condensation of primary amines, formaldehyde and p-substituted phenols in a 1:2:1 molar ratio since the 1940's[1-10]. In order to obtain homogeneous reaction media, some organic solvents such as 1,4-dioxane, toluene or alcohol were employed. Generally, the solvent governs the movement and energy of reacting species. A reaction may suffer a several-million-fold change in rate when the solvent is changed[11]. Usually, a reaction solvent cannot be regarded as just an inert reaction medium. Rather, the solvent is an entity that actively contributes to the enthalpy and entropy terms of reaction through solute-solvent interactions. Therefore, few reactions are carried out in the hydrocarbon solvents since electrostatic interactions between solute molecules and the solvents hardly occur at all. The solutes often exist as dimers or higher associates[12]. However, the yield of 3-cyclohexyl-3,4-dihydro-2H-1,3-benzoazine derived from cyclohexylamine, formaldehyde, and phenol in hydrocarbon solvents such as cyclohexane and xylene was higher than in the solvents with strong dissolving abilities like tetrahydrofuran(electron-donor solvent), 1-butanol (hydroxyl solvent) and acetonitrile(dipolar aprotic solvent)[13]. In other words, the yield increased with the decrease of the solubility parameter of the solvent. For the synthesis of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoazine, the yield also increased with the decreased dielectric constant, which often runs parallel to the dissolving power of solvent, and the increase of the concentration of the reactants[11]. This phenomenon implies that the less the interaction between the solvent and solutes, the more favorable the formation of benzoazine.

In another aspect, the usage of organic solvent during the synthesis not only increases the cost of the products but also causes environmental problem. Furthermore,
the solvent residue in the synthetic precursor leads to potential problem for the further processing.

It is well-known that pure monomeric formaldehyde can exist only for a limited time at ordinary and low temperature. Commercially available formaldehyde is usually either in methylene glycol forms which dissolved in polar or aqueous solution or in polymeric forms[14]. When the polymeric form, usually paraformaldehyde, was applied to the reaction for benzoxazine synthesis, the hydrolysis of paraformaldehyde in aqueous solution was generally the first step. Thus, the forms of formaldehyde employed in the reaction are quite different in the traditional methods from that in the solventless synthesis although the formation of benzoxazine by using the same reactants can be carried out both in the solution and without solvent. The mechanism is changed completely and the kinetics are greatly altered. So far, only Kopf and Wagner have prepared the benzoxazine in the absence of solvent by heating hexamethylenetetramine and 2,4-xylenol[15]. Solventless synthesis of benzoxazine by using paraformaldehyde has not been reported.

Solventless synthesis of benzoxazine resin involves heterogeneous reactions. Unlike a homogeneous reaction system, in which chemical reaction is the major issue, heterogeneous reactions usually involve one or several physical processes, such as absorption, diffusion, phase change, dissolution, or precipitation as well as chemical reactions. Sometimes, the physical processes play a very important role in controlling the chemical reaction mechanism and kinetics[16]. So far, the studies on heterogeneous reactions focus on heterogeneous catalysis, and electrochemical reactions. Few papers deal with the heterogeneous solventless reaction.

In this chapter, the synthesis methods of 3,4-dihydro-2H-1,3-benzoxazine monomer are developed by the thermal reaction of paraformaldehyde with phenols and
amines in the absence of solvent. The thermal behaviors during the reaction procedure are analyzed and the pressure effect on reaction behavior is also discussed.

**Experimental**

**Materials:**

Bisphenol-A (BPA) was purchased from Shell Company; para-toluidine (TO), aniline, cyclohexamine, and other amines were purchased from Aldrich Chemical Company; paraformaldehyde (PF) (99%) was produced by Fluka Company. All the chemicals were used without further purification.

**Synthesis of 3,4-dihydro-3(4-methylphenyl)-2H-1,3-benzoxazine (B-T)**

**Pre-mixing method**

- Open System

0.21 g (0.002 mole) P-toluidine, 0.23 g (0.001 mole) bisphenol-A and 0.12 g (0.004 mole) paraformaldehyde were weighed and put into a mortar. The sample was ground and mixed with a pestle. For best mixing results, the ground sample can be put into a vial and mixed by a bead miller for several hours. The oven was pre-heated to 75°C or 110°C for one hour and the temperature was calibrated. Then, the vial containing the sample was opened and put into the preheated oven. The vial was kept at 75°C for 1 hour or 110°C for 20 minutes, and then cooled in an ice bath. A two-layer solid was obtained. The upper layer was clear and yellow, the lower layer was a white opaque paste that contained the product. Recrystallization of the product in ethyl ether yielded 0.2 g white powder. Evaporation of the solvent of the mother liquor produced a yellow viscous liquid. The recrystallization can also take place in ethyl acetate or tetrahydrofuran or acetone.

- Closed System
I. 0.21 g (0.001 mole) P-toluidine, 0.23 g (0.002 mole) bisphenol-A and 0.12 g (0.004 mole) paraformaldehyde were put into a mortar. The sample was ground and mixed with a pestle. The sample was put into a capillary. Then the open end of the capillary was sealed and put into an oven, which had been pre-heated to 75°C for one hour. The capillary was kept at 75°C for 1 hour, and then cooled in an ice bath.

II. The autoclave made in-house was heated to a certain temperature and kept at that temperature for half an hour. The temperature was then calibrated by Model 2000 temperature controller made by Cole-Parmer Instrument Company. A 2.07 g mixture of p-toluidine, bisphenol-A, and paraformaldehyde in a molar ratio of 2:1:4 was put in an aluminum dish and wrapped with aluminum foil. The sample was then put into the autoclave. The autoclave was evacuated. After the vacuum valve was closed, high-pressure dry nitrogen gas was filled into the autoclave until the gauge pressure reached the required value. The autoclave was kept under this temperature and pressure for 20 min. The temperatures chosen were 65°C and 105°C. The gauge pressures were 0, 20, 50, 70 and 120 psi.

*Melt method*

A distillation apparatus was set up for the experiment. 2.14 g (0.02 mole) p-Toluidine, 2.28 g (0.01 mole) bisphenol-A, and 1.20 g (0.04 mole) paraformaldehyde were put into the flask, which was pre-heated in an oil bath at 110°C. The mixture was then stirred with magnetic stirrer for 20 minutes at this temperature. Within the first minute, the mixture melted and became a light brown transparent liquid. After the liquid was heated for about 20 minutes, the mixture turned light yellow and opaque. Then the flask containing the mixture was cooled in an ice bath. Recrystallization of the product in ethyl ether yielded a white powder. After evaporation of the solvent of the mother liquor, a yellow viscous liquid was obtained.
Synthesis of 3,4-dihydro-3-phenyl-2H-1,3-benzoxazine (B-a)

1.86g (0.02mole) aniline, 2.28g (0.01mole) bisphenol-A, and 1.20g (0.04mole) paraformaldehyde were put into the Erlenmeyer flask, which was then heated on a hot plate. The solid dissolved in the aniline at about 50°C. The mixture was stirred with magnetic stirrer for 10 minutes at 110–120°C and turned into a clear yellow liquid. The liquid was then poured into an aluminum dish and cooled. A yellow solid was obtained.

Synthesis of 3,4-dihydro-3-methyl-2H-1,3-benzoxazine (B-m)

1.5ml (0.02mole) 40% aqueous methylamine, 2.28g (0.01mole) bisphenol-A and 1.20g (0.04mole) paraformaldehyde were put into the Erlenmeyer flask, which was then heated on a hot plate. The mixture was stirred with magnetic stirrer for 10 minutes at 110°C and turned into a white opaque paste. The paste was poured into an aluminum dish and cooled. A white solid was obtained.

Synthesis of 3,4-dihydro-3-cyclohexyl-2H-1,3-benzoxazine (P-c)

1.4 ml (0.01mole) cyclohexylamine, 0.94g (0.01mole) phenol and 0.60g (0.02mole) paraformaldehyde were put into the Erlenmeyer flask, which was then heated on a hot plate. The solid dissolved in cyclohexylamine at about 45°C. The mixture was stirred with a magnetic stirrer for 10 minutes at 110°C and turned into a clear yellow liquid. Then the liquid was poured into a vial and cooled down. A yellow liquid was obtained.

Characterization

The reactants and their mixture were characterized by differential thermal analysis (DTA). The composition of the synthesized products under different condition
was characterized by high performance liquid chromatography (HPLC), nuclear magnetic resonance spectroscopy (NMR), and size exclusion chromatography (SEC).

The DTA instrument used was a METTLER FP900 Thermosystem which includes a FP84 microscope hot stage with a PT100 DTA/DSC sensor and a FP90 central processor. The sample was placed in an aluminum crucible and covered under pressure. The heating rate was 10°C/min. The temperature range was 30-280°C. The observation of the physical change was carried out with a Mel-TemII melting point meter. The sample was put into capillary. The heat rate is controlled at about 20°C/min.

HPLC was done with a Waters 510 HPLC pump, U6K Universal Injector, and Waters 484 Tunable UV Detector fixed at 254 nm. The column used was a Waters Partisil 5 with a partially silanized silica column. A chloroform-ethyl acetate mixture with 2-to-1 volume ratio was used as the eluent. The flow rate was 1 ml/min.

SEC was done with a Waters 510 HPLC pump, U6K Universal Injector, and Waters 410 Refractive Index detector and Waters 440 UV detector fixed at 254 nm. Three columns, m-strage™, 1000 nm, 100 nm, and 50 nm, were connected in series and used with HPLC grade tetrahydrofuran (THF) as the eluent. The flow rate was 1 ml/min.

The NMR spectrometer used was a Varian XL-200 NMR spectrometer. Deuterochloroform or deuteroacetone was used as a solvent. 1% tetramethylsilane (TMS) in the solvent was used as a standard. Coaddition of 32 scans yielded a sufficient S/N ratio spectrum.

Results and discussion

Comparison between the solution and solventless synthesis of benzoxazine

Table 1 shows the benzoxazine yields of three resins synthesized in 1,4-dioxane and without the solvent. The yields obtained from both methods have no significant
differences. However, the reaction time shortens significantly in the solventless procedure. From the $^1$H NMR spectra of as-synthesized B-a resins in figure 1, a species at 4.9 ppm (N-methylolamine) is observed in solution-synthesized sample while the peaks at 4.25 (Mannich base) and 4.35 ppm (bridge structure) are higher in solventless-synthesized sample. From their HPLC chromatograms in figure 2, the compositions of the resins are quite different. There are relatively large amount of unreacted aniline (5.8 min), bisphenol-A (4.6 min), intermediates and by-products as well as the benzoxazine monomer (3.5 min) in the solution-synthesized sample. More oligomers (3.2 min) are in the solventless synthesized sample. In brief, the number of reaction by-products are reduced in solventless synthesis. In figure 3, there is no great difference between the two samples when cyclohexylamine was used.

Phase transition involved in the solventless synthesis

Since the heterogeneity of the solventless reactions arises mostly from the thermal instability and uncertain melting behavior of paraformaldehyde, the understanding of the thermal transitions of paraformaldehyde and the effect factors is quite important.

Paraformaldehyde is defined as a mixture of polyoxymethylene glycols containing 93 to 99 % formaldehyde. Figure 4 shows the DTA thermograms of paraformaldehyde. For the pure paraformaldehyde, a broad endothermic peak appears at 145°C. The sample pan was also found empty and no melting behavior can be observed during heating from room temperature to 180°C in the atmosphere. It is obvious that this peak corresponds to the decomposition of paraformaldehyde. As we know, the partial pressure of formaldehyde over paraformaldehyde is in reality the decomposition pressure of the polyoxymethylene glycols of which it is composed. The decomposition pressure follows the Lacy equation in temperature range 10-58°C[14b]. The extrapolated equation is shown below
\[
\log P_{\text{CH}_2\text{O}} = 9.941 - 2905/T
\]

\(P_{\text{CH}_2\text{O}}\): Formaldehyde vapor partial pressure (mmHg) over paraformaldehyde.

According to this equation, the paraformaldehyde would evaporate spontaneously when \(T > 138^\circ\text{C}\) in atmosphere. In the DTA thermogram of paraformaldehyde, the decomposition peak is indeed shown in the temperature range very close to this value. Below this temperature, the equilibrium between decomposition of paraformaldehyde and polymerization of monomeric formaldehyde vapor would be established in a closed system. At an ordinary temperature, paraformaldehyde gradually vaporizes, and on long exposure to the atmosphere complete volatilization eventually takes place in an open system. This depolymerization is greatly accelerated by heat. The weight loss percentages of paraformaldehyde at different temperatures in an open system are shown in figure 5. At \(59^\circ\text{C}\), after 20 min, the weight loss percentage of paraformaldehyde is a constant. The concentration of gaseous formaldehyde is very small at this temperature. Apparently, it seems that the equilibrium between decomposition and polymerization of monomeric formaldehyde is established. This is probably because the diffusion rate of gaseous formaldehyde in the air is much slower than that of polymerization. Thus, the diffusion of gaseous formaldehyde into the air can be neglected. The system reaches an apparent equilibrium within the observation period. In the higher temperature range but below its spontaneous degradation temperature, no equilibrium can be observed within our experimental periods. When paraformaldehyde mixes with water in a molar ratio of 1:1, a small peak appears at around 100 - 110^\circ\text{C} besides the decomposition peak in figure 4. It indicates that some paraformaldehyde hydrolyzes in this temperature.

It has been found that dilute alkalis and acids markedly accelerate the rate of decomposition. Under an alkaline condition, the hydroxyl end groups are attacked and degradation proceeds in a step-wise fashion with successive splitting of formaldehyde.
units from the ends of the linear molecules. Under an acidic condition, the oxygen linkage within the chains may also be attacked, with splitting of the large molecules into smaller fragments[14a]. A weak base, amine, and a weak acid, phenol, are present in our solventless reaction system. The question is whether and how the amine and phenol affect the rate of decomposition of paraformaldehyde in the solventless reaction system.

As shown in figure 6, pure bisphenol-A has a sharp melting peak at 158°C. In the presence of toluidine, the melting point of bisphenol-A decreases to 78°C because the strong hydrogen bonding between amino groups and phenolic hydroxyl groups weakens the H-bonding between the phenolic groups. However, in the range of 30-270°C, there are two endothermic peaks in the DTA thermogram of the mixture of bisphenol-A and paraformaldehyde in a molar ratio of 1:4 (figure 7a). One is at 117°C, at which the mixture is molten and turned into a clear liquid. The other is around 158°C, at which the bubbles were produced in the molten liquid. The infrared spectrum of this molten liquid obtained after this DTA test is similar to the spectrum of bisphenol-A. This phenomenon can be explained partially by Walker's statement: "In the absence of added catalysts, anhydrous formaldehyde and paraformaldehyde dissolve in molten phenol without apparent reaction to give clear, colorless solution which smells strongly of formaldehyde"[14c]. An increase in the content of bisphenol-A in this mixture to 1:1 produces three endothermic peaks in the DTA thermogram (figure 7b). Comparing with the graph (a) in figure 7, the peak around 114°C is relatively stronger; the peak at 158°C is relatively weaker and a new peak appears at 134°C. Observations found during this heating procedure included the partial melting of the white powder at 114°C and complete melting by 130°C, followed by the appearance of bubbles at higher temperature. This indicated that bisphenol-A induces paraformaldehyde to melt readily around 114-117°C even before bisphenol-A melts, and it has a little effect on the decomposition temperature of paraformaldehyde, i.e., the decomposition temperature
increases slightly. This is probably because formaldehyde is trapped by bisphenol-A, so that the evaporation becomes more difficult. In the presence of paraformaldehyde, the melting point of bisphenol-A also decreases. The decrease depends on the content of paraformaldehyde in the mixture. In 1:1 molar ratio, the melting point is around 134°C. In 1:4 molar ratio of bisphenol-A to paraformaldehyde, the melting point decreases to 117°C.

However, toluidine does not induce paraformaldehyde melting. Similarly, paraformaldehyde has no effect on the melting behavior of toluidine. In the DTA thermogram of the mixture of toluidine and paraformaldehyde (figure 8), toluidine melts always at 44°C as it does in its pure form in spite of the changes of the molar ratio between toluidine and paraformaldehyde. However, the other peaks are quite sensitive to this ratio. There are two exothermic peaks at 79 and 89°C when the ratio is 1:2, and one exothermic peak at 86°C or 96°C when the ratio is changed from 1:1 to 3:1. These peaks are related to the reaction of toluidine and monomeric formaldehyde. The reactions that occur between formaldehyde and aromatic amine are varied and complex. One mole toluidine can react with either half or one or two moles of formaldehyde to form different products [17]. If this temperature shift were only caused by different stoichiometric reactions between toluidine and paraformaldehyde, the endothermic peak at 140°C would have disappeared since all the paraformaldehyde would have reacted, i.e., no endothermic peak around 140°C. However, a large amount of paraformaldehyde remains as shown in figure 8a and b. As mentioned before, within this reaction temperature range, there is an apparent equilibrium between decomposition of paraformaldehyde and polymerization of monomeric formaldehyde. Thus, when the paraformaldehyde content is relatively high, the equilibrium concentration of free formaldehyde in vapor over the mixture is also high. In other words, a certain
concentration of monomeric formaldehyde needed to initialize the reaction can be obtained at lower temperature for the mixture which contained large amount of paraformaldehyde. Therefore, when the ratio of paraformaldehyde over toluidine increases from 1/3 to 1 to 2, the peak temperature shifts from 96 to 86 to 79°C. At a higher temperature, the equilibrium concentration is hardly reached within our experimental time. The concentration of monomeric formaldehyde depends only on the degradation rate which is only a function of the temperature. It is independent of the concentration of paraformaldehyde at around 100°C as shown in figure 5, in which a zero order decomposition can be observed. The mixture contains a small amount of paraformaldehyde evaporated more completely under the same temperature and time conditions. Therefore, the remaining paraformaldehyde would decrease with the decrease of the PF/TO ratio. It is well-known that the activation energy of reaction between amine and formaldehyde is quite low, which can happen quickly even in an ice bath[18]. The decomposition rate of paraformaldehyde is slow and strongly depends on the temperature. Thus, the consumption rate of monomeric formaldehyde is much faster than the rate of its production. As the result, the reaction stops quickly because there is no enough monomeric formaldehyde to continue the reaction. If there is a large excess amount of paraformaldehyde, the reaction can start again when enough formaldehyde is produced or accumulated with the increase of temperature or reaction time. Therefore, the second peak at 89°C can be observed in the DTA thermogram of the sample with highest paraformaldehyde ratio. Actually, this cycle can be repeated until all the paraformaldehyde has been consumed. Indeed, we can observe the third exothermic peak in the DTA thermogram of the sample with ratio=2 (figure 8a) and the starting of the second exothermic peak in the DTA thermogram of the sample with the ratio=1 (figure 8b). However, when temperature increases up to 134°C, at which the decomposition rate increases so quickly that the rate of formaldehyde production is
faster than that of monomeric formaldehyde consumption, an endothermic peak corresponds to the decomposition of paraformaldehyde eventually. This indicates that the reaction between p-toluidine and monomeric formaldehyde is independent of the initial ratio of toluidine and paraformaldehyde as long as there is enough paraformaldehyde, but depends on the temperature and time. From these DTA thermograms and the visual melting observations, it seems that p-toluidine cannot directly react with paraformaldehyde. But at low temperature, toluidine can react with the gaseous formaldehyde and catalyse the decomposition of paraformaldehyde. Since it takes time for paraformaldehyde to decompose at regular reaction temperatures, the consumption rate of toluidine is expected to be much slower in solventless synthesis than in solution synthesis. Thus, the first reaction step is less noticeable than that in the solution and the opportunity of side reactions caused by the products from the reaction in the first step are reduced. However, since the lifetime of free toluidine is longer than that in solvent synthesis, the oxidation of toluidine could become a new side reaction.

When three reactants, bisphenol-A, paraformaldehyde and p-toluidine, are stoichiometrically mixed and heated, a homogeneous phase can be obtained until the temperature reaches about 140°C. The interaction between bisphenol-A and paraformaldehyde has been interfered by the presence of toluidine. In its DTA thermogram (figure 9), an endothermic peak at 44°C appears first, which corresponds to the melting point of toluidine. Then, bisphenol-A start to melt around 66°C as the base line starts to rise. However, before this melting behavior reaches its maximum, an exothermic peak at 88°C appears. Besides the reaction between toluidine and formaldehyde, this peak may also reflect the formation of benzoazole rings. For the same reason mentioned above, this reaction stops before it consumes all the reactants since the concentration of one of the reactants, monomeric formaldehyde, is controlled by the thermal decomposition of paraformaldehyde, the rate of which is too low to
produce enough formaldehyde to finish the reaction at this temperature and within such a short time. Therefore, a large amount of unreacted paraformaldehyde is left and decomposes spontaneously at higher temperatures, which is shown as a large endothermic peak at 140°C. When the sample is heated to 110°C and held at this temperature for a while, the peak arising from the decomposition of paraformaldehyde decreases with increasing isothermal time, and disappears eventually (figure.9c). The peak around 120°C may be caused by the melting of the paraformaldehyde due to the hydrogen bonding between phenolic hydroxyl groups and the oxymethylene or the glycol end groups. This peak is absent in the DTA thermogram of the mixture of toluidine and paraformaldehyde as expected. The bezoxazine crystal also has a melting point at 119°C (figure 10 a). However, there is no melting peak for the as-synthesized resin(figure 10 b). Benzoxazine ring opening reactions happen in the temperature range 225 to 251°C, depending on the purity of the benzoxazine(figure10).

**Pressure Effect**

As mentioned in the previous section of this chapter, the solventless synthesis involves the gaseous phase reaction, i.e., monomeric formaldehyde from the degradation of paraformaldehyde. It has been known that pure, dry formaldehyde gas shows no visible polymerization at temperatures of 80°C and 100°C. At ordinary temperatures, the dry gas polymerizes slowly, building up a white film of polyoxymethylene on the walls of the containing vessel. Kinetic studies indicate that this transformation takes the form of a surface reaction[14d]. A unimolecular reaction happens at high pressures and a polymolecular one at pressures below 200 mmHg. In the presence of water vapor and other polar impurities, formaldehyde gas is stable only at pressures 2 to 3 mmHg at ordinary temperatures[19]. This means that in a closed system, the equilibrium constant between decomposition and polymerization would
decrease with the increase of pressure. Therefore, a lower equilibrium concentration of monomeric formaldehyde in the reaction system results under high pressure. The rates of the reactions that require monomeric formaldehyde as a reactant, such as the formation of benzoxazine ring from Mannich base C-CH$_2$-NH-R and formaldehyde, decrease. The lifetime and contents of intermediates and reactants increase. The by-products, such as methylene-bis-toluidine (4.1 min), perhydrotriazine (3.8 min) and Mannich base (3.6 min) also would increase as marked by the star in figure 11. In our autoclave, the total pressure is increased by filling the nitrogen gas in a vessel with constant volume. According to Dalton's law, the partial pressure of formaldehyde would not change. The overall pressure can only affect the equilibrium concentration and has no influence on the rate of the decomposition and the rate to reach the equilibrium, which depends on the partial pressure of formaldehyde. The partial pressure is only a function of temperature. As mentioned before, the time to reach the equilibrium state is in the same magnitude as the consumption rate of formaldehyde by the reaction at 65°C. Therefore, the pressure effect is less important. With the increase of temperature, the tendency of paraformaldehyde degradation increases. Both decomposition rate and equilibrium constant would also increase. Comparing figure 11 with figure 12, the pressure effect on the composition of the synthesized compound at 105°C becomes less significant than that at 65°C.

In the closed system, the amount of perhydrotriazine is higher as shown in figure 13. In the open system, there is more Mannich base than that in the closed system (figure 14). In figure 15, it is found that when temperature increases to the point close to its spontaneous decomposition temperature, the yields of benzoxazine in the closed system, which is equivalent to apply the pressure on the reaction vessel, are higher than that in the open system. There are relatively large amounts of high molecular weight species in the open system (figure 16). At temperature above 120°C,
the rate of formaldehyde production is much faster than its consumption. The decomposition becomes irreversible and unreacted formaldehyde evaporates in the air. In addition, toluidine quickly evaporates in this temperature range. As a result, the stoichiometric ratio of the reactants is no longer ideal for the formation of benzoxazine in the open system. In figure 17, there are no noticeable changes in terms of the composition with the temperature increases in the closed system.

Conclusion

In the absence of solvent, 3,4,-dihydro-2H-1,3-benzoxazine can be formed within minutes in the temperature range around 100-120°C. The yields show little difference from that obtained in solution synthesis. The thermal controlling reaction between toluidine and formaldehyde, and the H-bonding between bisphenol-A and paraformaldehyde are two major advantages over solution synthesis for improving the yield of benzoxazine. In the lower temperature range, longer time is needed to fulfill the reaction requirement. In the higher temperature range, the reaction needs to be carried out in a closed system or under slight pressure for the best results. Between 100-120°C, the pressure effect is insignificant. Below or above this temperature, pressure has an effect on the composition of the products.

Solventless reaction in bisphenol-A/paraformaldehyde/toluidine system mostly involves gas-solid(formaldehyde/paraformaldehyde) gas-liquid (formaldehyde/toluidine /molten bisphenol-A), liquid-solid (molten bisphenol-A/ paraformaldehyde ) interactions. The thermal decomposition of paraformaldehyde plays a key role in solventless reaction.


Table 1. Yield of the benzoazaine (calculated from proton NMR)

<table>
<thead>
<tr>
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<th>B-t</th>
<th>B-a</th>
<th>P-c</th>
</tr>
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<tbody>
<tr>
<td>in dioxane*</td>
<td>0.75</td>
<td>0.80</td>
<td>0.62***</td>
</tr>
<tr>
<td>solventless**</td>
<td>0.75</td>
<td>0.83</td>
<td>0.57***</td>
</tr>
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</table>

* refluxed for 6 hour.
** 110°C/10 min
*** the yield calculated from HPLC graph.
Figure 4.1 Proton NMR spectra of benzoazole resin synthesized from bisphenol-A and aniline. (a) synthesized in 1,4-dioxane solution. (b) synthesized without solvent.
Figure 4.2  HPLC chromatograms of benzoazine resin synthesized from bisphenol-A and aniline. (a) synthesized in 1,4-dioxane solution. (b) synthesized without solvent.
Figure 4.3  HPLC chromatograms of benzoxazine resin synthesized from phenol and cyclohexylamine. (a) synthesized in 1,4-dioxane solution. (b) synthesized without solvent.
Figure 4.4  DTA thermograms of paraformaldehyde. (a) mixed with water in a molar ratio of 1:1. (b) pure.
Figure 4.5 The conversion of paraformaldehyde during the isothermal decomposition at different temperatures in the open system. (a) 150°C. (b) 120°C. (c) 100°C. (d) 59°C.
Figure 4.6  The DTA thermograms of bisphenol-A and the mixture of bisphenol-A and toluidine. (a) bisphenol-A. (b) mixed with toluidine in a molar ratio of 1:2.
Figure 4.7  DTA thermograms of the mixture of bisphenol-A and paraformaldehyde in different molar ratio. (a) BPA:PF=1:4. (b) BPA:PF=1:1.
Figure 4.8  DTA thermograms of the mixture of paraformaldehyde/toluidine in
different ratios. (a) PF:TO=2:1. (b) PF:TO=1:1. (c) PF:TO=1:3.
Figure 4.9  DTA thermograms of the mixture of bisphenol-A, toluidine and paraformaldehyde (1:2:4) (a) 30-270°C. (b) 30-110°C/110°C-20min/110-270°C  (c) 30-110°C/110°C-60min/110-270°C
Figure 4.10 The DTA thermograms of B-T benzoxazine resin. (a) as-synthesized. (b) recrystallized.
Figure 4.11 HPLC chromatograms (CHCl₃ and ethyl acetate as eluent) of B-T resin synthesized under different pressure at 65°C. (a) 0 psi (b) 20 psi (c) 45 psi (d) 120 psi.
Figure 4.12  HPLC chromatograms (CHCl3 and ethyl acetat as eluent) of B-T resin synthesized under different pressure at 105°C. (a) 0 psi. (b) 20psi. (c) 50psi (d) 70 psi. (e) 120psi.
Figure 4.13  HPLC chromatograms of B-T resin obtained in the closed system at lower temperatures. (a) 75°C. (b) 85°C. (c) 100°C. (d) 110°C.
Figure 4.14  HPLC chromatograms of B-T resin obtained in the open system at lower temperatures. (a) 75°C. (b) 85°C. (c) 100°C. (d) 110°C.
Figure 4.15 The relationship between benzoxazine yield of B-T resin and the reaction temperatures. (a) open system. (b) closed system.
Figure 4.16  The SEC chromatograms of B-T resin obtained in open system at higher temperatures. (a) 120°C. (b) 140°C. (c) 150°C.
Figure 4.17  The SEC chromatograms of B-T resin obtained in the closed system at higher temperatures. (a) 120°C. (b) 140°C. (c) 150°C
CHAPTER 5
MECHANISM AND KINETICS OF SOLVENTLESS
SYNTHESIS OF 3,4-DIHYDRO-2H-3-(4-METHYL)PHENYL-
1,3-BENZOXAZINE MONOMER
Introduction

Many 3-substituted-3,4-dihydro-2H-1,3-benzoxazines have been synthesized in organic solution by the condensation of primary amine, formaldehyde and p-substituted phenol in a 1:2:1 ratio since the late 1940s[1-10]. Recently, we developed a fast, economical approach to synthesize benzoxazines in the absence of solvent[11]. In this solventless reaction system, the thermal decomposition of paraformaldehyde plays a very important role in determining the formation of benzoxazine and the side products, all of which were much more sensitive to temperature and reaction time than that in solution synthesis. A narrow temperature range for obtaining high-yield benzoxazine has been found in an open reaction system. Furthermore, the solventless system is a heterogeneous system, in which gas-liquid, liquid-solid, and gas-solid interaction are involved[11]. For those reactions that are strictly heterogeneous, i.e., those involving different phases, their variety is greater than that of a homogeneous reaction. Despite their diversity, the reaction rate depends not only on the chemical nature of the phases present, but also on their physical state and on the diffusion coefficients of all the substances present through all the others, as well as on the exact nature of the physical contact.[12] Thus, it is quite possible that the mechanism and kinetics involved in our solventless reaction differ greatly from that in the solution which is a homogenous system. Although many types of heterogeneous reactions are possible through various combinations of solid, liquid, and gas phase, the various types of heterogeneous reactions have not yet all undergone even a qualitative study because of the great variety and diversity of their kinetic behavior. The kinetics of gaseous reactions which proceed at the surfaces of solid catalysts have been investigated more extensively than others[13]. No study has yet been reported on the kinetics and mechanism of solventless synthesis of benzoxazine. The overall reaction kinetics of the Mannich
reaction of ethylmalonic acid with formaldehyde and dimethylamine is second order in terms of intermediates and third order in terms of the reactants[14].

In general, the kinetic models are either phenomenological or mechanistic based on the elementary reaction. In this paper, the major elementary processes during 3,4-dihydro-2H-3-(4'-methyl)phenyl-1,3-benzoxazine formation are studied by high performance liquid chromatography (HPLC) and Fourier transform infrared spectroscopy (FTIR) at three different temperatures (59, 75 and 100°C). Reaction mechanisms are proposed. Proton nuclear magnetic resonance ($^1$H NMR) spectra are also used to interpret the reaction intermediates during the solventless synthesis at 50°C. The solubility of paraformaldehyde in non-polar solvents, such as chloroform and ether, is used as the measure of the reactivity of paraformaldehyde.

**Experimental**

**Materials:**

Bisphenol-A was purchased from Shell Company; para-Toluidine was supplied by Aldrich Chemical Company; paraformaldehyde (99%) was produced by Fluka Company. All the chemicals were used without further purification.

**Sample preparation for kinetic study**

4.2g (0.04 mole) Toluidine, 4.6g (0.02 mole) bisphenol-A, and 2.4g (0.08 mole) paraformaldehyde were weighed and put into a mortar. The sample was ground and mixed with a pestle. The ground sample was put into a vial and mixed by a bead miller for several hours. The well-mixed sample was divided into many parts. For the open system, each part was put into a small vial. For the closed system, each part was put into a capillary and the open end of the capillary was sealed. The oven was pre-heated to a chosen temperature for one hour and the temperature was calibrated with a thermocouple. Then, all the vials and capillaries containing the sample were put into the
From then on, a vial and a capillary were taken out from the oven at certain time intervals and the reaction was quenched in an ice bath immediately. After reaction, every capillary was broken carefully and put into a clean vial in which 2-3 ml chloroform was added. The vials were shaken until the samples were dissolved. Then, the vials were put into the centrifuge for about 20 minutes. The yellow solution and the white powder were separated. The solvent in solution was removed by vacuum distillation. The white powder was washed by chloroform and dried at room temperature in a vacuum oven. The white powder was unreacted paraformaldehyde, which has been confirmed by its IR spectrum. The temperatures chosen for kinetic studies were 59, 75 and 100°C.

To perform the kinetic analysis, analytical equations that express the conversion in terms of time were derived by applying curve fitting to the experimental data. The analytical expressions and their differentials were used for determining the reaction order.

Characterization

HPLC was done with a Waters 510 HPLC pump, U6K Universal Injector, and Waters 484 Tunable UV Detector fixed at 254 nm. The column used was a Waters Partisil 5 with a partially silanized silica column. A chloroform / ethyl acetate mixture with 2-to-1 volume ratio was used as the eluent. The flow rate was 1 ml/min.

The FT-IR instrument used was a Bomen Michelson MB FT-IR spectrophotometer which is equipped with a liquid nitrogen cooled, medium band-pass, mercury-cadmium-telluride (MCT) detector with the specific detectivity, D*, of $1 \times 10^{10}$ cmHz$^{1/2}$W$^{-1}$. All spectra were recorded at a resolution of 4 cm$^{-1}$ and displayed in the absorbance mode. Coaddition of 200 scans was sufficient to obtain good signal-to-noise (S/N) ratio spectra for transmission IR.
The NMR spectrometer, a Varian XL-200, NMR was used with a proton frequency of 200 Hz. Deuterochloroform with 1% tetramethylsilane(TMS) was used as a solvent. Coaddition of 32 scans yielded sufficient S/N ratio spectrum.

**Results and discussion**

Since the formaldehyde polymers hardly dissolve in nonpolar organic solvent, the solubility of paraformaldehyde is used as a measurement of its reactivity[15]. The amount of unreacted paraformaldehyde in solventless reaction of toluidine/bisphenol-A/paraformaldehyde system is plotted vs. the reaction time at 59°C in curve (a) in figure 1. This curve fits an exponential equation. At 75°C, a similar relationship between the conversion of paraformaldehyde and reaction time is found as shown in curve (b) in figure 1. However, the concentration of paraformaldehyde no longer follows the exponential relationship with respect to the reaction time when the reaction temperature elevates to 85°C and 100°C as shown in curves (c) and (d).

In figure 2, the relative benozxazine contents are calculated from the HPLC chromatograms. The analytical equations that express the conversion in terms of time is derived by applying a third-order polynomial fit to the experimental data. The differentials of these analytical equations obtained at 59°C is found to have a linear relationship in terms of the concentration of unreacted paraformaldehyde as shown in figure 3. This means that the overall reaction rate of the formation of benzoaxazine in the solventless system also follows first order kinetics at this relative low reaction temperature.

It is known that the apparent equilibrium between gaseous formaldehyde and paraformaldehyde can be established at a low temperature during the reaction period although the rate of thermal decomposition of pure paraformaldehyde is very slow[11]. For example, it takes 15 minutes to reach this apparent equilibrium at 59°C. In the
presence of toluidine and bisphenol-A, the concentration of monomeric formaldehyde is reduced continuously due to the reaction. Therefore, the equilibrium is destroyed and shifts to the decomposition direction. Because the rate of formaldehyde production is much slower than that of consumption, the rebuilding of equilibrium is always under way until the end of the reaction. As a result, the rate of thermal-induced decomposition of paraformaldehyde appears to be slower than the rate of its consumption in the solventless synthesis and no equilibrium can be observed during the reaction. In this case, paraformaldehyde degrades in the following manner.

\[ \text{HO(\text{CH}_2\text{O})_n\text{H}} \xrightarrow{k_n} \text{CH}_2\text{O} + \text{HO-(\text{CH}_2\text{O})_{n-1}\text{H}} \]

\[ \text{HO-(\text{CH}_2\text{O})_{n-1}\text{H}} \xrightarrow{k_{n-1}} \text{CH}_2\text{O} + \text{HO-(\text{CH}_2\text{O})_{n-2}\text{H}} \]

\[ \text{HO(\text{CH}_2\text{O})_3\text{H}} \xrightarrow{k_1} \text{CH}_2\text{O} + \text{HO(\text{CH}_2\text{O})_2\text{H}} \]

\[ \text{HO(\text{CH}_2\text{O})_2\text{H}} \xrightarrow{k_2} \text{CH}_2\text{O} + \text{HOCH}_2\text{OH} \]

\[ \text{HOCH}_2\text{OH} \xrightarrow{k_1} \text{CH}_2\text{O} + \text{H}_2\text{O} \]

The rate of production of monomeric formaldehyde can be express as following:

\[ \frac{d[F]}{dt} = \sum_{i=1}^{n} k_i [PF]^i \quad (1) \]

Here, \([F]\): mole concentration of monomeric formaldehyde produced;

\([PF]\): paraformaldehyde mole concentration;

\(k_i\): reaction constant of decomposition;

\(i\): degree of polymerization of paraformaldehyde.

Assuming that the decomposition constant of paraformaldehyde is independent of its degree of polymerization, i.e., \(k_1=k_2=k_3=\ldots=k_n=k\), (1) can be rewritten as:

\[ \frac{d[F]}{dt} = k \sum_{i=1}^{n} [PF]^i \quad (2) \]
Since, \( \frac{d[P\!F]_i}{dt} = k_{i+1}[P\!F]_{i+1} - k_i[P\!F]_i \), \( i = 2, \ldots, n-1 \) \hspace{1cm} (3)

In steady state \( \frac{d[P\!F]_i}{dt} \to 0 \), then, \([P\!F]_i = [P\!F]_n \) \hspace{1cm} (4)

and \( [P\!F]_n = \frac{2[P\!F]_u}{n(n+1)M_F} \) \hspace{1cm} (5)

Combining (2), (4) and (5), we have

\( \frac{d[F]_1}{dt} = k_n[P\!F]_n = \frac{2k[P\!F]_u}{(n+1)M_F} \) \hspace{1cm} (6)

Here, \( M_F \) is the molecular weight of monomeric formaldehyde. \([P\!F]_u \) is the concentration of unreacted paraformaldehyde, which is proportional to the insoluble part of the reactant mixture in nonpolar solvent.

According to the equation (6), the decomposition rate of paraformaldehyde follows first order kinetics with respect to paraformaldehyde concentration, which is in accordance with the experimental result mentioned before in figure 1. In figure 3, the reaction rate of the formation of benzoxazine is proportional to the paraformaldehyde concentration at the low temperature 59°C. This means that the step degradation of paraformaldehyde is the controlling step of the overall reaction.

After the decomposition of paraformaldehyde, the succeeding reactions involve heterogeneous reactions. From the previous study, toluidine is molten, monomeric formaldehyde is gaseous, and bisphenol-A is still solid at 59°C and 75°C. Formaldehyde cannot react with bisphenol-A in the absence of catalyst, but it can be physically adsorbed on the surface of bisphenol-A particles. This interaction is weakened in the presence of toluidine. Formaldehyde gas is entrapped and chemically bonded with molten toluidine[11]. It is known that heterogeneity of the reaction medium does not require the phenomenon to display the kinetic characteristics of a heterogeneous reaction[12]. Despite its apparently heterogeneous characteristic, the process may be treated as if it were a homogeneous reaction except if the interface plays
a significant role in the process. Since the reactants has been well mixed before heated and the particle size of paraformaldehyde is less than 1μm as observed from microscopy, the distribution of monomeric formaldehyde in the reaction system can be regarded as homogeneous in the macro scale. However, in this case, the real concentrations of formaldehyde and bisphenol-A are lower than their stoichiometric ratio because only the decomposed paraformaldehyde and the surface part of bisphenol-A are available for the reaction. In other words, besides the differences between the reaction constants of every step, the alteration of the stoichiometry would change the reaction rate greatly. We can call this effect a pseudo-stoichiometric effect, which is unique for solventless synthesis of benzoxazine. Thus, besides the slow degradation of paraformaldehyde, the reactive dissolution of bisphenol-A should have some effects on the consecutive reactions at this temperature. In the previous chapter, we observed the cessation of the reaction between toluidine and formaldehyde due to the lack of monomeric formaldehyde. This is a typical case for pseudo-stoichiometric effect.

In figure 4, at 59°C, the toluidine disappears at a different rate from that at which paraformaldehyde is consumed. It does not follow nth-order kinetics. The concentration of toluidine decreases very quickly in the first 15 minutes, then it declines successively but slowly. The consumption rate of bisphenol-A, differs from those of toluidine and paraformaldehyde, and is quite slow in the early stage of the reaction. When the reaction temperature was elevated to 75°C as shown in figure 5, the rate of consumption of paraformaldehyde is similar as that at 59°C. However, the reaction rates of toluidine and bisphenol-A are much faster than those at 59°C. It is well known that if the reaction mechanism involves more than one step, it is possible for one reactant to disappear at a rate quite different from that at which other reactants are consumed or at which products are formed. As mentioned above, the first step is the decomposition of paraformaldehyde. After that, several possible reaction might occur,
which include the formation of N-methyloltoluidine (>NCH₂OH)(I) aminal(methylene-bis-toluidine)(Φ-HN-CH₂-NH-Φ) (II), perhydrotriazine(>N-CH₂-)₃(III), Mannich base(Φ-HN-CH₂-Φ')(IV) and methylolphenol(Φ'-CH₂OH), depending on the reaction condition. It has been found that formation of methylolphenol is very difficult without base and solvent[11]. Eventually, benzoaxazine(V) is formed from the further reactions of these intermediates.

From proton NMR spectra shown in figure 6 (a) and (b), four new peaks can be seen after 5 minutes at 50°C. Two peaks at 4.5 ppm and 5.3 ppm are due to the two methylene groups in the benzoaxazine ring, respectively. 1,3,5-Tris(p-tolyl)-perhydro-1,3,5-triazine(perhydrotriazine) has a peak at 4.7 ppm[16]. The peak at 4.6 ppm is probably caused by aminal. N-methyloltoluidine, which should be around 4.9 ppm, can not be observed from NMR during the synthesis. This is probably because N-methyloltoluidine is somewhat unstable in the absence of solvent and at elevated temperature, it quickly converts into aminal by condensing with another toluidine or forms perhydrotriazine by a self-condensation reaction. The possible reactions of formation of intermediates are as follows (reaction 1-3)

\[ \text{NH}_2 \quad + \quad \text{CH}_2\text{O} \quad \xrightarrow{(1) \quad k'} \quad \text{HNCH}_2\text{OH} \quad + \quad \text{H}_2\text{O} \]

\[ \text{HNCH}_2\text{OH} \quad \xrightarrow{(2)} \quad \text{HNCH}_2\text{CH}_3 \quad + \quad 3\text{H}_2\text{O} \]
Because of the poor contact of methyloltoluidine with bisphenol-A, the Mannich base (4.2 ppm) is difficult to be formed directly from the reaction between N-methyloltoluidine and bisphenol-A when it competes with the reaction (2) and (3). It can be formed later by the reaction between aminal and bisphenol-A, which is shown as reaction (5) in the following scheme.
Accordingly, the formation of aminal and perhydrotriazine becomes quite exclusive at the beginning. Therefore, only these two species are detected in the NMR spectrum at this reaction time.

Benzoxazine(V) appears at the very beginning of the reaction before the Mannich base. There are two explanations. One is that the rate of reaction between the Mannich base and formaldehyde (reaction 6) is much faster than the formation of the Mannich base (reaction 5) at the beginning of the reaction so that the lifetime of the Mannich base is too short to be detected. However, the concentration of the other reactant of reaction 5, bisphenol-A, is almost constant in the early stage of the reaction at 59°C as shown in figure 4. This indicates that rate of reaction (5) hardly occurs. Therefore, this explanation may not be proper. The other possibility is that reaction (6) is not the major approach to form benzoxazine so that the Mannich base is not the major intermediate. Instead, perhydrotriazine is the real intermediate in the solventless synthesis of benzoxazine at the beginning of the reaction at this low temperature. After 10 minutes, some Mannich base appears along with some oligomers at 4.3 ppm. With increased time, the amount of benzoxazine increased and aminal decreased, while the amount of perhydrotriazine decreases at the beginning and remains almost constant after 10 minutes as shown in figure 7.

The IR and HPLC experiments give the same results. The in-phase out-of-plane C-H bending vibrations of substituted aromatics vary with the change of the substitution position[17], which are 830 cm\(^{-1}\) and 810 cm\(^{-1}\) for bisphenol-A and toluidine, respectively. Two benzene ring vibrations around 560-400 cm\(^{-1}\) which involve out-of-plane ring bending by quadrants are also sensitive to the substitution position. For para substitution, it gives rise to about at 552-446 cm\(^{-1}\) and shifts to lower frequency region around 476-428 cm\(^{-1}\) for 1,2,4-trisubstitution[17]. After reaction, 1,4-disubstituted bisphenol-A would become 1,2,4-trisubstituted resulting
from either benzoazine or Mannich base. The band in 819 cm\(^{-1}\) arises from 1,2,4-trisubstitution in-phase out-of-plane C-H bending vibration. The appearance of this band indicates that the electrophilic substitution on bisphenol-A takes place. In figure 8, the absorbances of 830 cm\(^{-1}\) and 565-550 cm\(^{-1}\) decrease quickly within 20 min. maintaining almost constancy afterward. Comparing with figure 4, the tendencies of the change of these two bands in figure 8 are consistent with the conversion of toluidine in terms of the reaction time calculated from HPLC. The intensity change of band in 819 cm\(^{-1}\) during reaction is also consistent with the decrease of bisphenol-A from HPLC results. The rate of toluidine consumption almost ceases after 20 minutes although there are still about one-third toluidine unreacted. This means that the insufficiency of monomeric formaldehyde becomes critical, i.e., the pseudo-stoichiometric effect. In the HPLC chromatograms of the samples obtained during the reaction at 59° C (figure 9), a peak at 3.8 min corresponds to perhydrotriazine and aminal. Another peak with retention time at 3.6 min arises besides the bisphenol-A (4.6 min) and toluidine (6.4 min). This peak involves Mannich base. The changes of perhydrotriazine and aminal (3.8 min) contents have the same tendency as shown in NMR although the maximum point shifts because of differences in the reaction temperature. In the latter stage of the reaction, with the increase of Mannich base, reaction (6) begins to compete with reaction (1) in terms of the consumption of monomeric formaldehyde. In figure 4, toluidine consumption almost ceases but paraformaldehyde continues to decrease. This implies that reaction (6) is dominant. It can be observed in figure 10 that Mannich base turns into benzoazine gradually with the slow release of formaldehyde from paraformaldehyde. Therefore, Mannich base is also the intermediate to form benzoazine in the late stage of the solventless reaction.

The absorbances of vibration bands at 820, 830 and 565-550 cm\(^{-1}\) shown in figure 11 vary with reaction time at 75° C in the similar ways as those at 59° C. In
figure 12, a linear relationship between the concentration of toluidine and the reaction rate of ortho substitution on phenolic benzene ring has been found during the first 20 minutes of the reaction. This indicates that the reaction rate of toluidine determines the rate of substitution on the phenolic benzene ring. In other words, the rate of the reaction between toluidine and formaldehyde is slower than its consecutive substitution reaction and almost the same as its previous step, the production of formaldehyde.

Consequently, reaction (1) is also the controlling step due to the pseudostochiometry of formaldehyde. This phenomenon is quite unusual since, in solution reaction, amine and formaldehyde react almost immediately after mixing, which is usually regarded as the fastest step.

At 100°C, both toluidine and bisphenol-A are molten, but paraformaldehyde is still solid. For a well-premixed mixture of reactants, paraformaldehyde particles homogeneously distribute in the liquid of toluidine and bisphenol-A. In this case, the reaction system can be treated as homogeneous system as in solution and the pseudostochiometry effect need not be considered.

Since paraformaldehyde decomposition rate is very fast at this temperature compared to the succeeding reactions[11], it is no longer the controlling step of the overall reaction rate for benzoxazine formation. Three reactants are consumed in the same manner as shown in figure 13, which means the rate of formation of benzoxazine depends on the concentration of three reactants.

It has been found that the hydrogen bonding greatly affect the physical state of the reactants in the absence of solvents. The melting point depressions of paraformaldehyde and bisphenol-A have been observed in their mixture, while toluidine cannot induce paraformaldehyde melting[11], which indicates that the hydrogen
bonding between the bisphenol-A and paraformaldehyde does exist. This interaction can be described as follows.

\[
\begin{align*}
\text{CH}_2\text{O}(\text{CH}_2\text{O})_n\text{H} \\
\text{R} + \text{OH(\text{CH}_2\text{O})_n-1\text{H}} & \xrightarrow{K} & \text{R} 
\end{align*}
\]

From figure 14, Mannich base increase to its maximum amount at the beginning of the reaction, then decreases. At the same time, benoxazine content increase quickly also(figure 2). The amount of aminal and perhydrotriazine are low(figure 15). At this temperature, benoxazine ring would open to form the oligomers as shown in figure 16.

As a result, the following mechanism is proposed for the solventless synthesis of 3,4-dihydro-3-(4-methyl)phenyl-1,3-benoxazine at 100°C.
According to the above reaction mechanism, third-order kinetic relationships

with respect to the starting materials indeed exist:

\[ K = \frac{[C_{IV}]}{[C_{BPA}][C_{PF}]} \]  

(7)

\[ \frac{dC}{dt} = k[C_{IV}][C_{TO}] = Kk[C_{BPA}][C_{PF}][C_{TO}] \]  

(8)

For a 3rd-order reaction kinetics in terms of the starting materials, the following relationship should be obeyed:

\[ \frac{dC}{dt} = kK(a - x)(b - x)(c - 2x) \]  

(9)

If \( a = b = \frac{c}{2} \), equation (11) can be rewritten as follows:

\[ \frac{dC}{dt} = 2kK(a - x)^3 = 2kK(b - x)^3 = \frac{kK}{4}(c - 2x)^3 \]  

(10)

After integration of (12),

\[ Kkt = \frac{1}{(a - x)^2} - \frac{1}{a^2} = \frac{1}{(b - x)^2} - \frac{1}{b^2} = \frac{1}{16(c - 2x)^2} - \frac{1}{16c^2} \]  

(11)

Since,
\[
\frac{a-x}{a} = \frac{C_{BPA}}{C_{BPA}}, \quad \frac{b-x}{b} = \frac{C_{TO}}{C_{TO}}.
\]

Then, \(kKt = \frac{1}{a^2} [\left(\frac{C_{BPA}}{C_{BPA}}\right)^2 - 1] = \frac{1}{b^2} [\left(\frac{C_{TO}}{C_{TO}}\right)^2 - 1]\) \hspace{1cm} (12)

here,

\(C\): the relative concentration of the components calculated from HPLC results. The subscripts refer to the reactants

\(k\): reaction constant

\(a, b, c\): the initial molar concentrations of the reactants

\(x\): the change in concentration of the reactants

From figure 17, a linear relationship between the right term in expression (12) and reaction time is obtained. Therefore, the rate of benzoxazine formation at 100°C is apparent third-order. Therefore, the controlling step is the formation of Mannich base at this reaction temperature.

The yields of benzoxazine in the open system differ from that in the closed system in the reaction temperature range 50-150°C[11]. But the rate of substitution on bisphenol-A in the open system is almost the same as that in the closed system in the early stage of the reaction although reaction in the closed system ceases a little earlier than in the open system (figure 18). The activation energy in the closed system is similar to that in the open system within 50-110°C(figure 19).

**Conclusion**

At low temperature, 590°C, pseudo-stoichiometry of monomeric formaldehyde has a great effect on the overall reaction rate, which follows apparently first order kinetics in terms of the paraformaldehyde concentration. The decomposition of paraformaldehyde is the controlling step. The perhydrotriazine is
the major intermediate in the formation of benzoxazine in the early stage of the reaction.

At 75°C, the reaction between toluidine and monomeric formaldehyde is the rate controlling reaction.

At the high reaction temperature, 100°C, the overall reaction rate is controlled by the formation of Mannich base, which follows third-order kinetics with respect to the concentration of paraformaldehyde, bisphenol-A and toluidine. Mannich base is the intermediate in the formation of benzoxazine.

The reaction rates and activation energy are similar for both closed and open reaction systems.
Figure 5.1  The relationship between the content of paraformaldehyde and the reaction time (a) 59°C (b) 75°C (c) 85°C (d) 100°C
Figure 5.2  Relationship between benzoxazine content and reaction time at different temperature
Figure 5.3 Reaction order determination at 59°C. Rate of benzoxazine formation vs. paraformaldehyde content.
Figure 5.4  The relationship between the reaction time and the normalized reactant concentrations at 59°C. TO: toluidine BPA: bisphenol-A. PF: paraformaldehyde
Figure 5.5  The relationship between the normalized reactant concentrations and the reaction time at 75°C
Figure 5.6  $^1$H NMR spectra of reaction system at different reaction time at 50°C
Figure 5.7  The relationship between the reaction time and the contents of intermediates and benzoaxazine calculated from proton NMR at 50°C. (a) benzoaxazine (b) perhydrotriazine (c) aminal
Figure 5.8  Relative intensity of IR band vs. reaction time at 590°C
Figure 5.9  HPLC chromatograms of reaction system
Figure 5. 10  Contents of intermediates and product vs reaction time at 59°C (a) perhydrotriazine and aminal (b) Mannich base (c) benzoazine
Figure 5.11 The relationship between the absorbance of the vibration bands involved the substitution on bisphenol-A and the reaction time at 75°C
Figure 5.12  Slow step determination after decomposition of paraformaldehyde at 75°C. Rate of substitution reaction vs. the content of toluidine.
Figure 5.13  The relationship between the reaction time and the normalized reactant contents at 100°C. TO: toluidine BPA: bisphenol-A PF: paraformaldehyde
Figure 5.14  Content of Mannich base vs. reaction time at different temperature
Figure 5.15  Contents of perhydrotriazine plus aminal vs. reaction time at different temperature
Figure 5.16  Content of oligomer during solventless synthesis at 100°C
Figure 5.17  Reaction order determination at 100°C
Figure 5.18  Relative intensity of IR bands vs. reaction time in open and closed system.
Figure 5.19  Reciprocal temperature vs content of toluidine at constant reaction time
CHAPTER 6
SYNTHESIS AND CHARACTERIZATION OF NOVEL
POLYMERS CONTAINING 3,4-DIHYDRO-2H-1,3-
BENZOXAZINE GROUPS
Introduction

As a new type of novel phenolic polymer precursors, a number of mono- and difunctional 3,4-dihydro-2H-1,3-benzoxazine monomers have been synthesized by the condensation of primary amine, formaldehyde and phenol[1-5]. The benzoxazine monomer can be polymerized thermally by a ring-opening reaction with or without catalyst to form a crosslinked network[6-8]. The polymer obtained in this way is called polybenzoxazine. The shrinkage of polybenzoxazine polymerized from difunctional benzoxazine monomer is near zero while most thermosetting polymers usually shrink 2% to 6% upon polymerization because the covalent bonds are shorter than the intermolecular distance of the monomers[9]. It seems that the benzoxazine ring has smaller hydrodynamic volume than its corresponding structure after ring opening. Thus, for linear benzoxazine-based polymer, i.e., the repeat unit contains benzoxazines ring, expansion is expected after thermal treatment. In polybenzoxazine polymer, the main chain contains a linear Mannich base structure(-CH2-N-CH2-), resulting from the opened benzoxazine rings. The potential energy of this bridge structure is higher (+0.001kcal/mole) than that before ring opening (-0.0245kcal/mole)[10], which implies that the stablility of a polymer containing benzoxazine rings in the main chain may be close to or rival that of polybenzoxazine.

For the synthesis of traditional phenolic resins, the existence of intramolecular hydrogen bonding hinders the chain propagation so that high molecular weight polymer is difficult to achieve[11]. However, introducing benzoxazine rings into the backbone of the phenolic polymer can eliminate the intramolecular hydrogen bonding, and linear high molecular weight polymer can be obtained. As a functional group, benzoxazine rings possess some interesting properties, such as colorlessness and good solubility in non-polar solvents. The benzoxazine-based polymer is expected to keep some of these
properties. However, no polymers containing the benzoazine group in the main chain have been synthesized or reported to date.

Although the chemistry of monofunctional and difunctional benzoazine has been developed for many years, the need for very high conversions to synthesize high polymer places several stringent requirements on any reaction to be used for polymerization: a favorable equilibrium, the absence of cyclization, and lack of other side reactions. These stringent requirements are met by a relatively small fraction of the reactions. For condensation polymerization, high molecular weight polymer can only be obtained at very high conversion of the reactants[12].

Polymers that contain nitrogen atoms in their chain backbone are called Mannich base polymers. Mannich base polymers come into use mainly as binders in electrophoretic coatings, flocculants in waste-water treatment, additives with various protective functions for lubricating oils, polymeric antioxidants for plastics, ion-exchange resins, polymeric complexing agents, and surface active agents[13-14]. When the Mannich reaction is carried out between a 'substrate' containing at least two active hydrogen atoms and a bis-secondary amine(or a primary amine). It is also possible for the amino group and the active hydrogen to be present on the same monomeric molecule, a polycondensation takes place and a polymeric derivative is produced. Polymers have been synthesized by Mannich polymerization, i.e., the addition-condensation polymerization between polyfunctional active hydrogen compounds, formaldehyde and primary monoamines and secondary diamines[15-17]. The common problem is that the molecular weight of linear polymers is quite low(Mn<3000) because the reactants can react in a number of ways. Additionally, multiple functional groups produce a crosslinked polymer which is difficult to characterize. The choice of the right conditions for a Mannich reaction is critical for achieving high yields with the minimum of side reactions.
According to the definition, polybenzoxazine and polymers containing benzoxazine rings in the main chain belong to the Mannich base polymer family. However, in a benzoxazine ring, two Mannich base structures exist. One is the C-Mannich base(C=C-CH2-N<), the other is the O-Mannich base(O-CH2-N<). In other words, the formation of a benzoxazine ring requires that two different Mannich reactions happen on the different sites of one substrate. In a previous study of benzoxazine monomer synthesis, the yield of benzoxazine varied from 54% to 92% with different amines and phenols[18-20]. The yield also strongly depended on the pH of the reaction system. For a relatively strong amine, neutral or basic conditions are favored[21]. High yield benzoxazine can be obtained only at certain acidic conditions when weak amines are used[22].

In this chapter, a polymer containing 3,4-dihydro-2H-benzoxazine in the main chain is synthesized by the reaction of 4,4'-methylene-bis-(2,6-dimethylaniline)(MBDMA), formaldehyde(F) and bisphenol-A(BPA). The effects of the reaction conditions such as reactant ratio, solvent, temperature, water, and catalyst on the molecular weight have been investigated by size exclusion chromatography(SEC). Fourier transform infrared spectroscopy (FTIR) and proton nuclear magnetic resonance spectroscopy (1H NMR) are used to observe the structure of the polymer. The rate of polymerization has been studied by means of FTIR and SEC.

**Experimental**

**Materials:**

Bisphenol-A was purchased from Shell Company. 4,4'-Methylene-bis(2,6-dimethylaniline) was purchased by the Aldrich Chemical Company. Formaldehyde(37%wt aqueous solution) and triethylamine were produced by the
Fisher Scientific. Paraformaldehyde was purchased from the Fluka Chemical Company. All solvents such as chloroform, 1,4-dioxane, dimethylsulfone, tetrahydrofuran and acetone were also obtained from the Fisher Scientific. All the chemicals were used without further purification.

Synthesis

The reaction is shown in scheme 1. A 20 ml 1,4-dioxane solution of 5.0876 g (0.02 mole) methylene-bis-(2,6-dimethylaniline) was prepared in a 150 ml three-neck flask. Added to this solution at room temperature were 2.4024 g (0.08 mole) paraformaldehyde and 6 ml distilled water. The mixture was continuously stirred for half an hour, and 5ml triethylamine was added. After 20 minutes, 4.5658 g (0.02 mole) bisphenol-A in 20 ml 1,4-dioxane was added. The temperature was then raised to 85°C and kept at this temperature until the solution became turbid. Then the solvent was evaporated under reduced pressure. The polymer was washed with acetone several times and dried in the air for several hours.

Fractionation of polymer

A 20 ml chloroform solution of a 2 g of crude polymer that was synthesized in dioxane, 23%(wt) triethylamine, and 6%(wt) water for 12 hours was prepared and kept in a test tube for several days at room temperature. Acetone was added to the polymer solution and the test tube was shaken until the solution became cloudy. The tube was then centrifuged for about half hour. The clear liquid phase was separated from the precipitate by filtration. The precipitate was washed with acetone several times and dried in air for several hours.

Characterization
Size exclusion chromatography (SEC) was done with a Waters 510 HPLC pump, U6K Universal Injector, Waters 440 UV Detector fixed at 254 nm and Waters 410 Refractive Index Detector. Three columns, μ-styragel™ 1000 nm, 100 nm and 50 nm, are connected in series and used with HPLC grade chloroform as the eluent. The flow rate is 1 ml/min. The column temperature was kept at 35°C. Twelve polystyrene standard samples with different molecular weights and narrow molecular weight distributions(polydispersity=1.06) were used for calibration. Further calibration was done with one difunctional benzoxazine sample and one difunctional amine.

The Fourier transform infrared (FT-IR) spectrophotometer used was a Bomem Michelson MB 110 FT-IR spectrophotometer which is equipped with a liquid nitrogen cooled, medium band-pass, mercury-cadmium-telluride (MCT) detector with a specific detectivity, D*, of 1x10^{10} cmHz^{1/2}W^{-1}. All spectra were recorded at a resolution of 4 cm^{-1} and displayed in the absorbance mode. Coaddition of 200 scans was sufficient to obtain good signal-to-noise (S/N) ratio spectra for transmission IR. One of the vibrational modes of benzene skeletal stretching coupled with CH deformation around 1500 cm^{-1} was chosen for quantitative study of the reaction. The frequency of this band for bisphenol-A was at 1511 cm^{-1} and it was at 1500 cm^{-1} for benzoxazine. The 1484 cm^{-1} band of toluidine was utilized as reference band. The deconvolution has been carried out by commercial software, SpectIR™, by New Methods Research Inc. The peak height is used as the measurement of the amount of functional groups, which has been found to have good reproducibility.

The nuclear magnetic resonance (NMR) spectrometer used was a Varian XL-200 NMR spectrometer with a proton frequency of 200 Hz. Deuterochloroform with 1% tetramethylsilane (TMS) was used as a solvent. Coaddition of 32 scans yielded a sufficient S/N ratio spectrum. The peaks at 5.0 ppm, 2.2 ppm and 1.6 ppm, which arose from methylene or methyl groups on benzoxazine, moieties of 4,4'-methylene-
bis(2,6-dimethylaniline) and bisphenol-A, respectively, were integrated. The ratios of the peaks at 5.0 ppm to the peak at 2.2 ppm, $x_4 = \frac{I_{5.0}}{6xI_{2.2}}$, or to the peak at 1.6 ppm, $x_p = \frac{I_{5.0}}{3xI_{1.6}}$, were used to characterize the polymer structure and calculate the degree of polymerization, $n$.

For a polymer with very high molecular weight, $\lim_{n \to \infty} x_a = \lim_{n \to \infty} x_p = 2$.

If $x_a = x_p = x < 2$, it means that amine and phenol have an equivalent chance to be an end group.

Thus, $n = \frac{x - 1}{2 - x}$

If $x_a > x_p = x$, it indicates that majority of the end groups are phenol. Similarly, if $x_p > x_a = x$, most of the end group are amines.

Thus, $n = \frac{x}{2 - x}$

Results and discussion

Solvent Effect

Under the same conditions used for the synthesis of monomeric difunctional benzoxazine in 1,4-dioxane, the polymer containing the benzoxazine group precipitated from solution with low molecular weight as shown in figure 1(a). The average degree of polymerization was only 1.5 according to Table 1. Similar phenomena happened when the reaction was carried out in other polar solvents, such as dimethylsulfoxide (DMSO) and tetrahydrofuran (THF)(figure 1 d, b). We already know that there are two kinds of aminomethylation reactions required to form a benzoxazine ring. One is the electrophilic substitution on the benzene ring of the phenol to form a carbon-Mannich base(C-CH$_2$-N<), which is responsible for the chain propagation. The other is the formation of an oxygen-Mannich base(O-CH$_2$-N<), by which benzoxazine closes its ring. Here, the ratio of $A_{1511}/A_{1484}$ is used to characterize the first reaction as well as
the molecular weight or the degree of polymerization. $A_{1500}/A_{1484}$ is used to represent the benzoxazine content. According to the IR and NMR data listed in table 1, the chemical structures of the precipitates from dioxane and THF are almost the same. Most end groups of the precipitates in these two batches are from amine moiety since $x_a < x_p$. This indicates that once one end of the amine attaches on the polymer, its reactivity for further reaction is lower than that of phenol connected on the polymer. Thus, the succeeding reaction of the amino group on the polymer becomes the controlling step for further chain propagation. In the solvent mixture of THF and chloroform, both phenol and amino groups on the polymer have almost equal reactivity since $x_a = x_p$. It seems that the reactivity of the end group is improved slightly when the solubility of the reaction medium decreases. As the result, the molecular weight of the precipitate from the THF/chloroform mixture increases slightly (figure 1 c). The dissolving power of DMSO is the strongest among the solvents used in these four batches, and the benzoxazine content of the precipitate from DMSO is the lowest (table 1). The retention time of the sample from DMSO is the highest, indicating the lowest molecular weight (figure 1 d). This indicates that the dissolving power of the solvent has a certain effect on benzoxazine formation and chain propagation. The phenomenon can be explained as the following. It has been observed that the yield of benzoxazine is higher in a solvent with a low solubility parameter while the amount of the Mannich bridge structure, i.e., the ring-opened structure, is higher in polar solvent [23]. The solubility parameter of benzoxazine is lower than the corresponding chain structure. Once the benzoxazine ring is formed, the solubility of the molecule in polar solvent decreases greatly due to the weakening of the interactions between the solvent and the molecule so that the precipitation occurs. The higher the solubility parameter of the solvent, the lower the content of benzoxazine allowed in the precipitation. If benzoxazine ring formation is faster than the chain propagation, the polymer containing benzoxazine in its main chain
would precipitate with very low degree of polymerization. We already found that the Mannich base formation was the controlling step in the synthesis of difunctional benzoxazine[24]. In other words, the ring formation is indeed faster than the electrophilic substitution on the ortho position of phenol. Thus, reducing the dissolving power of the reaction medium seems to improve molecular weight of the precipitation. For this reason, molecular weight of polymer containing benzoxazine in the main chain increases with a decrease in the dissolving power of the solvent as mentioned above. However, this improvement is limited by a kinetic factors. In non-polar solvents or without solvent, the reaction system is heterogeneous due to the poor solubility of the reactants in a non-polar solvent and the high melting point of the amine. From the kinetic point of view, the equivalence of the end groups in the reactants and in the polymer, which is the basic assumption for traditional condensation polymerizations, is no longer appropriate. Therefore, the accessibility of the molecule containing benzoxazine rings to the reactants decreases because the reactants cannot dissolve in non-polar solvents very well. The worst thing is that side reactions have more of a chance to occur because the reactants and the polymer are in different phases. In fact, two batches were carried out in chloroform and without solvent respectively. Both reactions failed to produce benzoxazine-based polymer. In the homogeneous system, the rates of the reaction decreases with the decreases in solubility of the reaction medium. In the mixed solvent of THF and chloroform (1:1 vol.), both the rate of the benzoxazine formation and the equilibrium content of benzoxazine were lower than in dioxane as shown in figure 2. The consumption rate of bisphenol-A was less solvent-dependent (figure 3). There is a contradiction in the synthesis of the polymer containing benzoxazine in the main chain: the final product prefers nonpolar solvent while the process needs a polar medium to form the products.
To solve this problem, the chain propagation should happen before the ring formation when polar solvent is used. However, the Mannich base structure (C=C-CH₂-NH-C=C) is less stable than benzoxazine at elevated temperature[25]. The formation of benzoxazine rings still happen even when the ratio of reactants is stoichiometric for the formation of the Mannich base, i.e., mole ratio of the reactants BPA:MBDMA:F = 1:1:2.

From the above result, the improvement of the reaction rate of carbon-Mannich base formation becomes critical in order to obtain the high molecular weight benzoxazine polymer.

A kinetic study of the Mannich reaction was first carried out by Alexander and Underhill in a dimethylamine/ ethylmalonic acid/formaldehyde system [26]. They found that the maximum reaction rate occurred when the pH was around 3~4. When a weak amine with a pKa<3 was used, aminomethylation on the ortho position of bisphenol-A took place only when pH<2.5[22]. Recently, higher reaction rates were observed where the molar ratio of amine/formaldehyde was 2:1 in 3-pentadecylphenol/di-n-propylamine/formaldehyde system[27]. Excess of amine beyond a 2:1 ratio resulted in the reduction of the rate due to the increased phenoxide ion formation and decreased hydrogen bonding of phenol and aminal(methylene-bis-amine). Excess formaldehyde in relation to amine caused a rate reduction attributable to decreased aminal formation. Under acidic conditions, formation of an iminium salt from an aminol (methylolamine) might be expected. However, no reaction occurred, and a Mannich base was not detected. Since phenols are acidic and capable of existing as free phenol or phenolate ion and, since the reactive intermediate of amine conceivably might react as a neutral molecule or as a positively charged molecule, a maximum rate ought to be observed at some definite pH if two neutral (phenol plus amine) or two charged ions (phenolate ion plus positively charged amine derivative) interact. The observed rate versus pH profile
provided a maximum supporting this mechanism[28] Burchhalter et al. found that the reaction rate of N, N'-methylene-bismorpholine / 2,4-dimethylphenol / formaldehyde system reached its maximum point when the pH is between 9.6 and 10.2[29]. In summary, whether aminomethylation happens in acidic or in basic medium depends on the relative reactivity of amine and substrate. If the substrate is strong nucleophile such as an organic acid, the electrophilicity of the products from amine and formaldehyde become determining factor, acidic medium is necessary for the formation of Mannich base. If the nucleophilicity of the substrate is relatively weak, such as phenol, reaction should be carried out in basic media in order to improve the electron density on the benzene ring. Therefore, in order to synthesize high molecular weight benoxazine-based polymer, basic conditions are probably required.

Catalytic Effect

When triethylamine (TEA) is introduced into the reaction system, the pH reaches the range in which the maximum rate of aminomethylation reaction achieved in the N, N'-methylene-bismorpholine / 2,4-dimethylphenol / formaldehyde system. In figure 4, the precipitate from the system with 3%(wt) triethylamine contains some higher molecular weight components. From Table 2, it can be found that the solubility of the products decreases, which implies that the molecular weight increases, with the increased amount of triethylamine. When triethylamine is less than 8%, precipitation results in the cessation of the chain growth. This indicates that benoxazine ring formation is still faster than the chain propagation. When triethylamine is up to 13%, the chain propagation rate becomes faster than that of ring formation. Eventually, crosslinking happens and the polymer becomes an insoluble gel even in sulfuric acid when the amount of triethylamine increases to 23%. The IR data indicates that oligomer with higher benoxazine ring content stays in the liquid phase with the increase of
triethylamine so that less unreacted bisphenol-A is left in the liquid phase. In figure 5, both the rate of ring formation and conversion of bisphenol-A, which implies the chain extension, increase. The increment of the latter is greater. Therefore, enhancement of chain growth rate and improvement of solubility of benzoxazine in the reaction medium are a consequence when triethylamine is added, which results in high molecular weight polymer. Ideally, we can adjust the amount of triethylamine to control the molecular weight.

A similar trend, i.e. the molecular weight increases with the increased amount of triethylamine, is shown in figure 6 when the solvent changes, but the degree of this catalytic effect is different. In the presence of 3% triethylamine, precipitation does not occur when the reaction is carried out in a dioxane/chloroform mixture (5:4 vol.). Thus, the reaction products can stay in the solution longer and a higher molecular weight polymer can be obtained. This is also shown in the decrease of bisphenol-A content (table 3). However, the benzoxazine ring content decreases with the increased reaction time, also. From table 3, the rates of both ring formation and bisphenol-A consumption increase in the presence of triethylamine in both reaction media. The increment for the reactions in the mixed solvent is higher. When the amount of triethylamine increases to 8%, the solvent effect is almost eliminated.

It is well known that high molecular weight polymer can be obtained only at high conversion of the reactants (>99%) for linear condensation polymerization reactions. Also, the reactivity of the functional group is independent of molecular weight. However, in this condensation polymerization, conversion of the bisphenol-A is only about 90% when an insoluble polymer gel forms, and the relationship between conversion of bisphenol-A and molecular weight follows the pattern of traditional step polymerization (figure 7). The molecular weight distribution is very broad as shown in
It seems that higher molecular weight species tend to react with each other, and some reactants remain unreacted by the end of the synthesis.

Water effect

Another interesting phenomenon is shown in figure 9. In the absence of water, an increase in the amount of base catalyst does not affect the molecular weight growth rate. This means that water plays an important role in the reaction. Similar conclusions can be drawn when comparison is made between the rates of molecular weight growth with and without the water under the same basic condition (23% triethylamine) as shown in figure 10. When the amount of water increases, the growth of molecular weight is faster, especially in the later stage of the reaction. However, precipitation occurs within 16 hours when the amount of water increases to 12% (wt). There is a maximum point for this water-enhancement effect when the amount of triethylamine in the reaction system is relatively low (3% wt) as shown in figure 11 (a). It seems that water also makes the polymer precipitate early because the mixture of water and organic solvent becomes more polar so that the solubility of polymer containing benzoxazine rings in this mixture is poorer.

From figure 12, it can be observed that the water has little effect on the reaction rates of benzoxazine ring formation and the consumption of bisphenol-A. However, the molecular weight increases quickly in the presence of water (figure 10). In other words, molecular weight is higher in the presence of water at the same reaction time or conversion. This means that water makes small species more active. As the result, the polydispersity index of molecular weight should become smaller in the presence of water. Figure 11(b) and 13 confirms this hypothesis: the polydispersity index of polymer synthesized without water is higher than that in the presence of certain amount of water. For the same reasons, the gel can dissolve in sulfuric acid when the reaction
is carried out in dioxane with 8% water and 23% triethylamine, while in the presence of the same amount of the triethylamine, the gel cannot dissolve in sulfuric acid when the amount of water is below 6%. Here, water can prevent crosslinking.

Thompson[25] has pointed out, "The water present can both serve as a solvent and/or lead to reversal of the Mannich reaction in basic media. Aqueous formaldehyde may also be used for acidic media condensation, again providing some reversibility difficulties in certain cases." Tychoponlos[30] found that the rate of the Mannich reaction of phenols and ketones with secondary amines is greatly increased in aqueous media compared with alcoholic or hydrocarbon solvents. The enhanced rates of Mannich reactions carried out in partly aqueous solutions were ascribed to the involvement of an extended cyclic transition state. The water effect on the synthesis of polymer containing benzoazaine in the main chain seems more complex than the single Mannich reaction. It plays a contradictory role in the synthesis of benzoazaine-based polymer. It is both a precipitation agent, which stops the chain growth, and a cocatalyst, which accelerates the rate at which high molecular weight species are formed in basic media.

Temperature Effect

In figure 14, two batches are carried out at two temperatures, 44°C and 88°C. Acceleration of the bisphenol-A consumption rate is more detectable than that of the formation of benzoazaine ring at the elevated temperature. At 44°C, no precipitation takes place even for a 95 hour reaction while gelation occurs within 15 hours at 88°C. This indicates that elevating the temperature can effectively improve the chain propagation rate, although benzoazaine formation is less sensitive to the temperature alteration.
Reactant Ratio Effect

For a condensation polymerization, the reactant ratio usually needs to follow the strict stoichiometric ratio. Otherwise, excess amounts of one reactant would act as terminating groups. However, amount of formaldehyde can be altered during the synthesis of polymer containing benzoxazine in the main chain.

When an excess amount of a formaldehyde aqueous solution is added, two consequences come into view. The relative content of benzoxazine increases as well as the decrease of concentration of bisphenol-A (Table 5). The molecular weight increases also as shown in figure 15. The more formalin, the earlier the precipitation occurs. Since formalin contains 63% water, the water effect is also involved when excess formalin was used. In order to separate the water effect, additional paraformaldehyde is added to the reaction system. From table 5, it can be seen that the changes of the contents of benzoxazine and bisphenol-A are caused by excess formaldehyde. In basic media, excess formaldehyde has similar effect on the formation of benzoxazine ring but there seems to be no effect on the consumption of bisphenol-A. In the presence of triethylamine, there is no significant change of the molecular weight with the increase of formaldehyde as shown in figure 16.

Fractional Precipitation

Since the solubility of the polymer containing benzoxazine in the main chain in chloroform decreases with increased molecular weight, addition of precipitant, acetone, makes the high molecular weight fraction precipitate. By addition of acetone as precipitant into polymer/chloroform solution, high molecular weight polymer can be obtained (figure 17). Table 6 indicates that the number average molecular weight of the polymer containing benzoxazine can reach above ten thousand.
Conclusion

For the first time, a polymer containing 3,4-dihydro-2H-1,3-benzoxazine in the main chain has been synthesized by addition-condensation reaction of methylene-bis-(2,6-dimethylaniline), formaldehyde and bisphenol-A. The molecular weight of this novel polymer depends strongly on the amount of organic base such as triethylamine, the amount of water and polarity of the solvent. Chain propagation of the polymer can be accelerated by adding triethylamine and elevating the reaction temperature. The rate of benzoxazine ring formation can be adjusted by changing the solvent and using excess formaldehyde. Water plays an important role during the synthesis. It is a cocatalyst and precipitation agent. It also can narrow the molecular weight distribution and prevent crosslinking.
References


23. J. Liu, S. Stevenson and H. Ishida, research report(1992)


Table 6.1 Solvent effect on the structure of the precipitate

<table>
<thead>
<tr>
<th>solvent</th>
<th>IR</th>
<th>NMR</th>
</tr>
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<tr>
<td></td>
<td>$I_1_{500}/I_{1484}$</td>
<td>$I_1_{511}/I_{1484}$</td>
</tr>
<tr>
<td>dioxane</td>
<td>92</td>
<td>10</td>
</tr>
<tr>
<td>THF</td>
<td>90</td>
<td>16</td>
</tr>
<tr>
<td>THF/CH$_3$Cl</td>
<td>87</td>
<td>11</td>
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<tr>
<td>DMSO</td>
<td>68</td>
<td>15</td>
</tr>
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Table 5.2 Effect of basic catalyst

<table>
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<tr>
<th>amount of TEA (%wt)</th>
<th>pH</th>
<th>polymer appearance</th>
<th>solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.4</td>
<td>white powder</td>
<td>insoluble in acetone, soluble in THF and CHCl$_3$</td>
</tr>
<tr>
<td>3</td>
<td>10.1</td>
<td>white powder</td>
<td>insoluble in acetone and THF, soluble in both CHCl$_3$ and H$_2$SO$_4$</td>
</tr>
<tr>
<td>8</td>
<td>10.4</td>
<td>white powder</td>
<td>partially soluble in CHCl$_3$, soluble in H$_2$SO$_4$</td>
</tr>
<tr>
<td>13</td>
<td>10.6</td>
<td>light yellow gel, tough</td>
<td>insoluble in CHCl$_3$, soluble in H$_2$SO$_4$</td>
</tr>
<tr>
<td>23</td>
<td>10.6</td>
<td>light yellow gel, tough</td>
<td>insoluble in both CHCl$_3$ and H$_2$SO$_4$</td>
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Table 6.3 Catalyst effect on relative contents of bisphenol-A and benzoazine in different solvent

<table>
<thead>
<tr>
<th>TEA(%)</th>
<th>solvent</th>
<th>$I_{1500}/I_{1484}$</th>
<th>$I_{1511}/I_{1484}$</th>
</tr>
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<tr>
<td>0</td>
<td>dioxane</td>
<td>92 (66)</td>
<td>10 (50)</td>
</tr>
<tr>
<td></td>
<td>dioxane/chloroform</td>
<td>- (59)</td>
<td>- (52)</td>
</tr>
<tr>
<td>3</td>
<td>dioxane</td>
<td>84 (75)</td>
<td>10 (33)</td>
</tr>
<tr>
<td></td>
<td>dioxane/chloroform</td>
<td>- (85)</td>
<td>- (22)</td>
</tr>
<tr>
<td>8</td>
<td>dioxane</td>
<td>85</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>dioxane/chloroform</td>
<td>80</td>
<td>16</td>
</tr>
<tr>
<td>13</td>
<td>dioxane</td>
<td>- (80)</td>
<td>- (30)</td>
</tr>
<tr>
<td></td>
<td>dioxane/chloroform</td>
<td>81</td>
<td>20</td>
</tr>
<tr>
<td>23</td>
<td>dioxane</td>
<td>- (90)</td>
<td>- (33)</td>
</tr>
</tbody>
</table>

*the values in the brackets are from liquid phase. others are from precipitate.

Table 6.4 Time effect on the relative contents of bisphenol-A and benzoazine in the presence of 3% triethylamine in dioxane/chloroform

<table>
<thead>
<tr>
<th>time(hr)</th>
<th>23</th>
<th>47</th>
<th>78</th>
<th>88</th>
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<tr>
<td>$I_{1500}/I_{1484}$</td>
<td>85</td>
<td>67</td>
<td>64</td>
<td>63</td>
</tr>
<tr>
<td>$I_{1511}/I_{1484}$</td>
<td>22</td>
<td>19</td>
<td>18</td>
<td>13</td>
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</table>
Table 6.5 Reaction ratio effect

<table>
<thead>
<tr>
<th>reactant ratio* (BPA/MBDMA/F)</th>
<th>cloud point (hour)</th>
<th>(I_{1500}/I_{1484})</th>
<th>(I_{1511}/I_{1484})</th>
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</thead>
<tbody>
<tr>
<td>without 1:1:4:2(PF)</td>
<td>-</td>
<td>88</td>
<td>31</td>
</tr>
<tr>
<td>basic 1:1:8</td>
<td>&lt;16</td>
<td>84</td>
<td>31</td>
</tr>
<tr>
<td>catalyst 1:1:10</td>
<td>4</td>
<td>85</td>
<td>30</td>
</tr>
<tr>
<td>23% 1:1:2</td>
<td>no</td>
<td></td>
<td></td>
</tr>
<tr>
<td>23% triethyl-amine 1:1:4</td>
<td>12</td>
<td>73</td>
<td>38</td>
</tr>
<tr>
<td>1:1:6</td>
<td>-</td>
<td>79</td>
<td>38</td>
</tr>
<tr>
<td>1:1:8</td>
<td>7</td>
<td>85</td>
<td>36</td>
</tr>
</tbody>
</table>

*BPA: bisphenol-A
MBDMA: methylene-bis-(2,6-dimethylaniline)
F: formaldehyde aqueous solution
PF: paraformaldehyde

Table 6.6 Molecular weight of polymer

<table>
<thead>
<tr>
<th>polymer</th>
<th>(M_n)</th>
<th>(M_w)</th>
<th>PDI</th>
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<tr>
<td>as-synthesized</td>
<td>3200</td>
<td>349000</td>
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<tr>
<td>fraction</td>
<td>12200</td>
<td>296000</td>
<td>24.3</td>
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Scheme 6.1 Reaction scheme for 3,4-dihydro-2H-1,3-benzoxazine based polymer synthesis.
Figure 6.1  SEC chromatograms of precipitates from different solvents. (a) from 1,4-dioxane (b) from tetrahydrofuran (THF) (c) from a mixture of tetrahydrofuran and chloroform (1:1 vol) (d) from dimethylsulfoxide (DMSO)
Figure 6.2  Solvent effect on the reaction rate of benzoxazine formation. Relative contents of benzoxazine calculated from FTIR spectra vs. reaction time. (a) in a mixture of tetrahydrofuran and chloroform. (b) in 1,4-dioxane
Figure 6.3 Solvent effect on the consumption rate of bisphenol-A: relative contents of bisphenol-A calculated from FTIR spectra vs. reaction time. (a) in mixture of tetrahydrofuran and chloroform (b) in 1,4-dioxane
Figure 6.4    SEC chromatograms of two batches of polymer synthesized with and without triethylamine (TEA) in 1,4-dioxane (a) 0% TEA (b) 3% TEA
Figure 6.5  Catalytic effect on the reaction rates: relative contents of bisphenol-A (BPA) and benzoxazine (B) calculated from FTIR spectra vs. reaction time. (a) BPA, 23% TEA (b) BPA, 0% TEA (c) B, 0% TEA (d) B, 23% TEA
Figure 6.5   SEC chromatograms of two batches of polymer synthesized in a mixture of 1,4-dioxane and chloroform (5:4 vol) (a) 3% TEA (b) 8% TEA
Figure 6.7  The relationship between number average molecular weight, molecular weight distribution and conversion of bisphenol-A calculated from SEC chromatograms. (a) number average molecular weight (Mn) (b) polydispersity index(PDI) reaction. media: 23% TEA and 6% water in 1,4-dioxane.
Figure 6.8  SEC chromatograms of the reaction system at different reaction times
Figure 6.9  Number average molecular weight of the polymers obtained in the absence of water vs. reaction time (a) 3% TEA (b) 23% TEA
Figure 6.10  Number average molecular weight of the polymers obtained in the presence of 23% triethylamine and different amount of water vs. reaction time (a) 12% (b) 6% (c) 0%
Figure 6.11  Number average molecular weight and molecular weight distribution of polymer obtained in the presence of 3% triethylamine vs. water content in the reaction media (a) Mn (b) PDI
Figure 6.12 Water effect on the reaction rates of the functional groups: relative contents of bisphenol-A (BPA) and benzoxazine (B) calculated from FTIR spectra vs reaction time. (a) BPA, 6% water (b) B, 6% water (c) BPA, 0% water (d) B, 0% water
Figure 6.13  Polydispersity index (PDI) vs reaction time in the presence of 23% triethylamine and different amounts of water (a) 0% (b) 6%
Figure 6.14 Temperature effect on the reaction rates of the functional groups: relative contents of bisphenol-A (BPA) and benzoxazine (B) calculated from FTIR spectra vs reaction time. (a) B, 88°C (b) BPA, 88°C (c) B, 44°C (d) BPA, 44°C
Figure 6.15 SEC chromatograms of polymers synthesized without basic catalyst in different reactant ratio. BPA/MBDMA/F (a) 1:1:10 (b) 1:1:8 (c) 1:1:4
Figure 6.16 SEC chromatograms of polymers synthesized with 23% triethylamine at different reactant ratios. BPA/MBDMA/F (a) 1:1:2 (b) 1:1:4 (c) 1:1:8
Figure 6.17  SEC chromatograms of as-synthesized polymer and its fractions (a) as-synthesized (b)fraction
3,4-Dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine can be synthesized in high yields by the condensation of 2,3,4,5,6-pentafluoroaniline, formaldehyde and bisphenol-A only when pH of the reaction system is below 2.5. A strongly acidic reaction media is a necessary condition to synthesize 3,4-dihydro-2H-1,3-benzoxazine from those amines having a pKₐ lower than 3. 3,4-Dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine can be characterized by the resonance at 4.5, 5.1 and 6.8 ppm from ¹H NMR spectra and the 1502, 1234, 1023 cm⁻¹ bands in IR as well as the 760 cm⁻¹ band in the Raman spectrum. Solvents with low dielectric constants aid in improving the yield of benzoxazine; para-substituted phenols with electron-withdrawing substituents do not favor the formation of benzoxazine.

Under basic conditions, the major products from the reaction of formaldehyde and 2,3,4,5,6-pentafluoroaniline are hydroxymethypentafluoroanilines. In the presence of mild acid, the exclusive products of the above reaction is 1,3,5-tripentafluorophenylperhydro-1,3,5-triazine. Under strong acidic conditions, an equilibrium between the hydrolysis and formation of this substance is established. In pH=1.2 reaction media, the synthesis of 3,4-dihydro-2H-3-pentafluorophenyl-1,3-benzoxazine includes a two step reaction. The first step reaction involves the formations of perhydrotriazine and methylolphenol, which can be completed almost immediately after addition of acid. The second step reaction are rate controlling reaction involving the equilibrium of an acid-promoted cleavage of the perhydrotriazine and its reaction with methylolphenol.

In the absence of solvent, 3,4-dihydro-2H-1,3-benzoxazine can be formed within minutes in the temperature range around 100-120°C. The yields shows little difference from that obtained in solution synthesis. The thermal controlling reaction between toluidine and formaldehyde, and the H-bonding between bisphenol-A and
paraformaldehyde are two major advantages over solution synthesis for improving the yield of benzoazine. In the lower temperature range, longer time is needed to fulfill the reaction requirement. In the higher temperature range, reaction needs to carry out in a close system or under slightly high pressure for the best results. Between 100-120°C, pressure effect is insignificant. Below or up this temperature, pressure has certain effect on the composition of the products.

Solventless reaction in bisphenol-A/paraformaldehyde/toluidine system mostly involves gas-solid(formaldehyde/paraformaldehyde) gas-liquid (formaldehyde/toluidine/molten bisphenol-A), liquid-solid (molten bisphenol-A/paraformaldehyde) interactions. The thermal decomposition of paraformaldehyde play a key role in the reaction. In low temperature range 59-75°C, pseudo-stoichiometry of monomeric formaldehyde has great effect on the overall reaction rate. The decomposition of paraformaldehyde is the controlling step. The perhydrotriazine is the major intermediate to form the benzoazine in the early stage of the reaction.

At high reaction temperature 100°C, overall reaction rate is controlled by the formation of Mannich base, which follows third-order kinetics with respect to the concentration of paraformaldehyde, bisphenol-A and toluidine. Mannich base is the intermediate to form the benzoazine. The reaction rate and activation energy are similar in both close and open system.

For the first time, 3,4-dihydro-2H-1,3-benzoazine base polymer is synthesized by addition-condensation reaction of methylene-bis-(2,6-dimethylaniline), formaldehyde and bisphenol-A. Molecular weight of this novel polymer depends strongly on the amount of organic base as triethylamine, water and alternation of the solvent. Chain propagation of the polymer can be accelerated by triethylamine and elevating temperature. The rate of benzoazine ring formation can be adjusted by change solvent and reactant ratio. Water play an important role during the synthesis. It
is assistant catalyst and precipitation agent. It also can narrow the molecular weight distribution and prevent crosslinking.


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