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Part I. Characterization and polymerization of quinuclidinium-carboxylate inner salt. Part II. Alternating copolymerization of 2-substituted-2-oxazoline and epoxide

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Part I

Characterization and Polymerization of Quinuclidinium-Carboxylate Inner Salt

Part II

Alternating Copolymerization of 2-Substituted-2-Oxazoline and Epoxide

By

Caixia Lu

A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, the City University of New York.

1990

This manuscript has been read and accepted for the Graduate Faculty in Chemistry in satisfaction of the dissertation requirements for the degree of Doctor of Philosophy.

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Date

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ABSTRACT

Part I: CHARACTERIZATION AND POLYMERIZATION OF 1-[(4-CARBOXYPHENYL)METHYL]-QUINUCLIDINIUM INNER SALT

Part II: ALTERNATING COPOLYMERIZATION OF 2-SUBSTITUTED-2-OXAZOLINES AND EPOXIDES

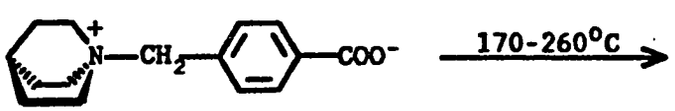
by

Caixia Lu

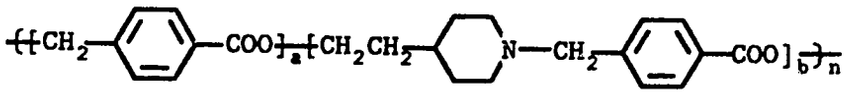
Adviser: Professor George Odian

Part I:

Zwitterion I, 1-[(4-carboxyphenyl)methyl]-quinuclidium inner salt, prepared from quinuclidine and 4-(chloromethyl)-benzoic acid as a monohydrate, was stable at room temperature. The monohydrate lost its water of hydration at 90°C under vacuum to form a stable anhydrous zwitterion. Bulk polymerizations of both the hydrate and the anhydrous zwitterion were studied at 170-260°C. Polymers with structure II were produced with number average molecular weight in the range 4,000 to 16,000 g/mole. ^{1}H, ^{13}C, 2-D COSY NMR and FT-IR spectroscopies were used for the identification of structures I and II. The molecular weight of polymer II was determined by VPO and thermal properties of the polymer were evaluated by DSC and TGA.



I



II

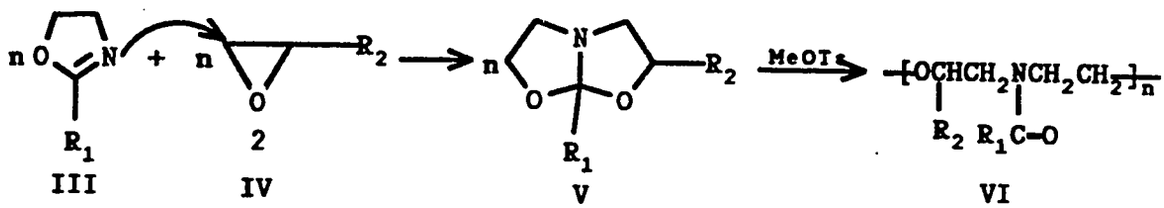
Part II:

The alternating copolymerizations of 2-substituted-2-oxazolines and styrene oxide have been studied for the first time. The 2-substituted-2-oxazolines employed were 2-methyl-2-oxazoline (MeOXA), 2-*t*-butyl-oxazoline (*t*-BuOXA), and 2-phenyl-2-oxazoline (PhOXA).

In order to synthesize the alternating copolymer of oxazoline and styrene oxide, poly[2-phenyl-4-alkanoyl-1-oxa-4-azahexanediyl] (VI), two different approaches have been used:

Approach 1--Directly copolymerize the 2-oxazoline and styrene oxide. In this approach, both homopolymerization of styrene oxide and copolymerization of oxazoline and styrene oxide were involved.

Approach 2--Synthesize a bicyclic amide acetal (V) from the oxazoline and styrene oxide first, then homopolymerize the bicylic compound using methyl tosylate as a cationic initiator to produce the desired alternating copolymer (VI):



III IV V VI

The synthesis of bicyclic amide acetals and some of its reactions have been also studied in detail.

NMR and IR spectroscopies were used for characterization of the prepared compounds and VPO was used to determine the molecular weights of the polymers.

ACKNOWLEDGMENTS

Graduate school has been both a rewarding educational experience as well as a boring and frustrating one. Five and a half years of graduate study was a rather long and difficult period of my life, especially, as a foreign student. No matter what, I'm glad that I finally made it and I owe it to my family, to my professors and to my friends.

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To my father, mother, sister and brother, I would like to let you know that without you, my success would have no real meaning.

I would also like to say to my friends, Rose P., Fang S., Libaniel R. and Dominick C., thank you guys for all the good and bad times that we have shared together. You made my stay here enjoyable and memorable.

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I am grateful to the College of Staten Island of the City University of New York for the teaching assistantships and other financial support.

I would like to gratefully acknowledge that compound I was first synthesized in our laboratories by Dr. Patharija Gunatillake.

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Part I

Characterization and Polymerization of Quinuclidinium-Carboxylate Inner Salt

Chapter 1 INTRODUCTION TO ZWITTERIONIC POLYMERIZATION

1-1 Background

Zwitterionic polymerization is a polymerization in which two kinds of monomers interact with each other to generate a zwitterion or zwitterionic intermediate leading to the production of an alternating copolymer. The zwitterion or zwitterionic intermediate is responsible for both initiation and propagation process, therefore, one of the advantages of zwitterionic polymerization is that it is not necessary to employ a catalyst (initiator) to initiate the copolymerization.

The two kinds of monomers employed are a nucleophilic monomer (M_N) and an electrophilic one (M_E). The general scheme is given as follows:

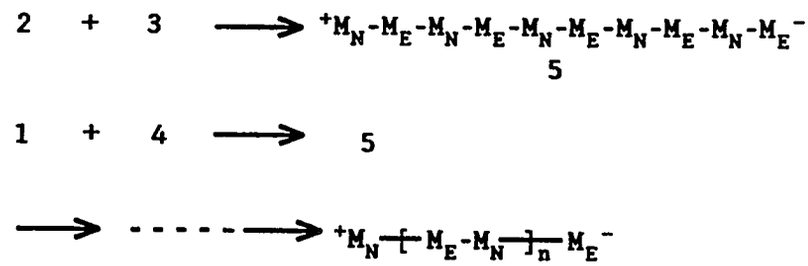
$$M_N + M_E \longrightarrow {}^{+}M_N\text{-}M_E^{-} \quad (1)$$

$$1 + 1 \longrightarrow {}^{+}M_N\text{-}M_E\text{-}M_N\text{-}M_E^{-} \quad (2)$$

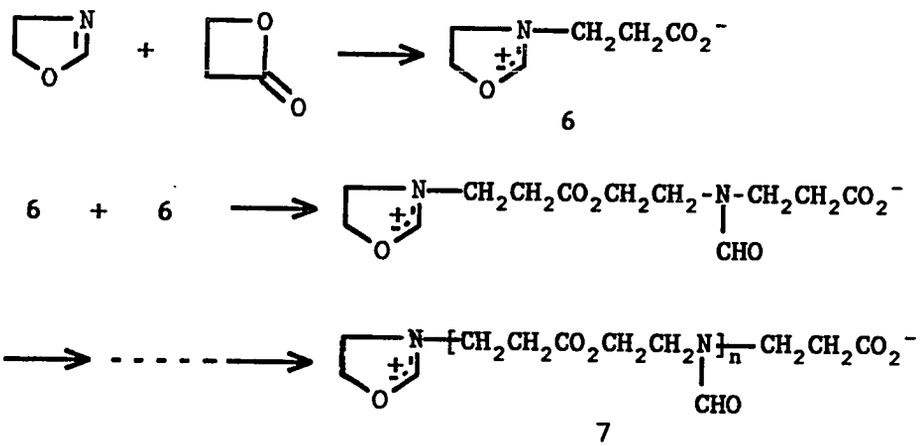
$$1 + 2 \longrightarrow {}^{+}M_N\text{-}M_E\text{-}M_N\text{-}M_E\text{-}M_N\text{-}M_E^{-} \quad (3)$$

$$2 + 2 \longrightarrow {}^{+}M_N\text{-}M_E\text{-}M_N\text{-}M_E\text{-}M_N\text{-}M_E\text{-}M_N\text{-}M_E^{-} \quad (4)$$

$$1 + 3 \longrightarrow 4$$



The pioneering work of zwitterionic copolymerization was reported by Saegusa at al[1] in 1972, which involved the formation of an alternating copolymer from 2-oxazoline and β-propiolactone 7:



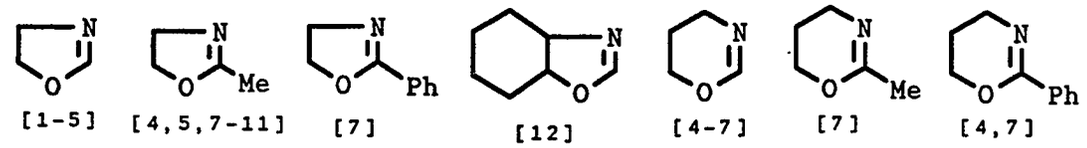
Many different nucleophilic monomer pairs have been studied for zwitterionic polymerization ever since. Saegusa's work in this area can be divided into three parts.

(1) Copolymerization involving ammonium-type zwitterions

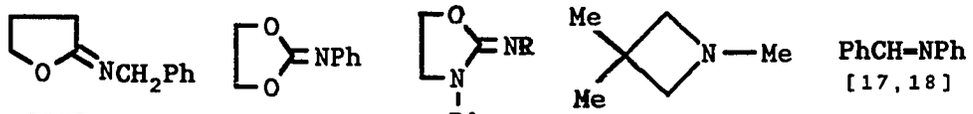
The zwitterionic pairs in which the M_N monomers generate ammonium sites are listed in Table 1-1.

Table 1-1 M_N and M_E monomer pairs in which M_N monomers generate ammonium sites

M_N monomers



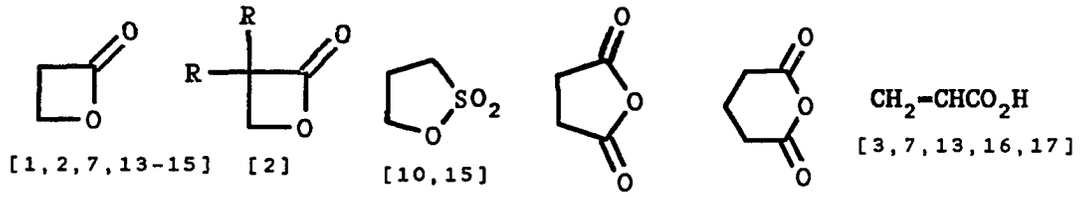
[1-5] [4,5,7-11] [7] [12] [4-7] [7] [4,7]



[13] [14] [15] [16]

PhCH=NPh
[17,18]

M_E monomers



[1,2,7,13-15] [2] [10,15] [6,7] [6]

CH_2=CHCO$_2$H
[3,7,13,16,17]

CH_2=CCO$_2$H
[8]

CH_2=CCO$_2$H (X-Cl,Br)
[2]

CH_2=CHCO$_2$R (R-CH_2CH_2OH, $CH_2CH_2CH_2OH$)
[4,12]

CH_2=CHCONH$_2$
[5]

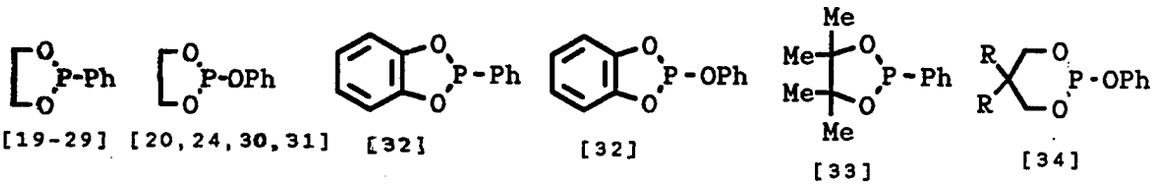
CH_2=CHSO$_2$NH$_2$
[11]

(2) Copolymerization involving phosphonium-type zwitterions

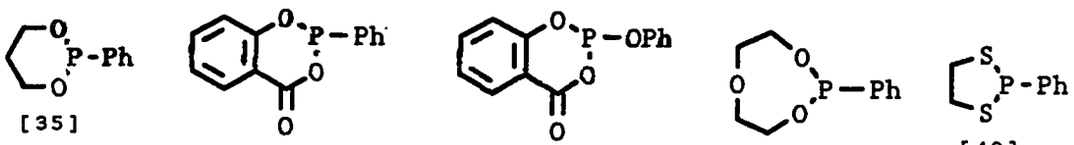
The trivalent phosphorus monomers can generate phosphonium sites by reacting with various M_E monomers. The monomer pairs which involve the phosphonium sites are summarized in Table 1-2.

Table 1-2 M_N and M_E monomer pairs in which M_N monomers generate phosphonium sites

M_N monomers



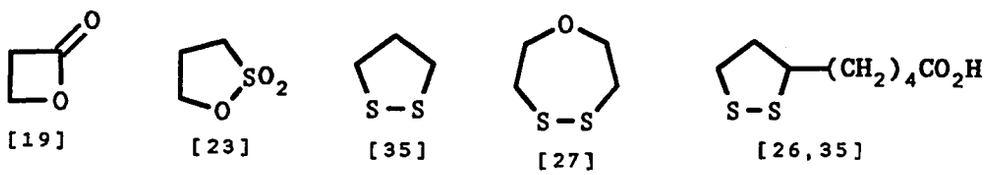
[19-29] [20,24,30,31] [32] [32] [33] [34]



[35] [26,35-39] [36,37] [25] [40]

$(PhO)_2PPh$ [32] $(PhO)_3P$ [32]

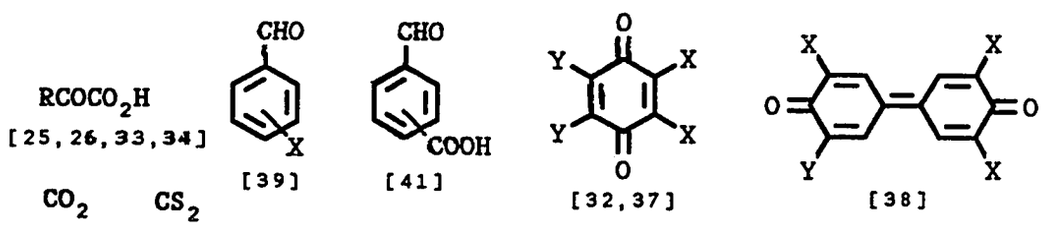
M_E monomers



[19] [23] [35] [27] [26,35]

$CH_2=CHCO_2H$ [19,26,40] $CH_2=CCO_2H$ [24,36] $RCH=CHCO_2H$ [36] $CH_2=CHCO_2CH_2CH_2CO_2H$ [20]

$CH_2=CHCO_2CH_2CH_2OH$ [21] $CH_2=CHCOX$ [22] $CH_2=CHCO_2NH_2$ [19] $CH_2=CHSO_2NH_2$ [24]



$RCOCO_2H$ [25,26,33,34] [39] [41] [32,37] [38]

CO_2 [28] CS_2 [29]

(3) Other copolymerizations involving zwitterions

These zwitterionic copolymerizations involve oxonium or

sulfonium zwitterions generated from cyclic ether or cyclic sulfide, respectively:

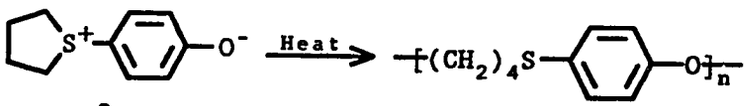
[42, 43, 44]

[45]

Tomalia and coworkers[46] studied the polymerization of acrylic acid with 2-alkyl-2-oxazolines, 2-thiazolines, and 2-imidazolines.

Overviewing these publications, two conclusions stand out: the molecular weights of the copolymers are uniformly very low (<1,000-3,000) and the copolymer structures as well as polymerization mechanisms are poorly understood.

Schmidt and coworkers prepared and separated a sulfonium phenolate type zwitterion monomer 8. Heating this monomer gave polymer 9[47]:

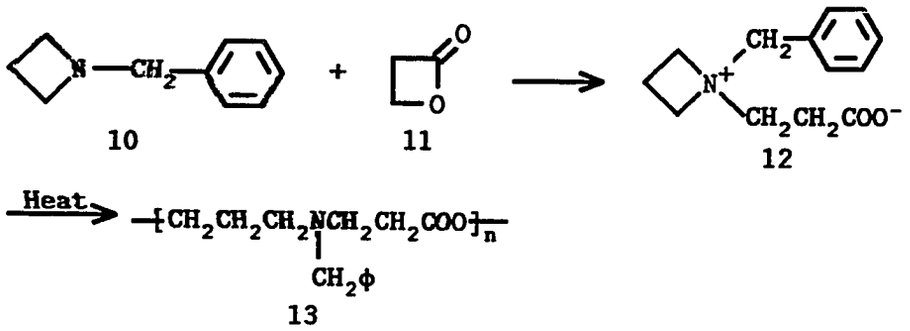


8 9

This system is very different from any of the other zwitterion systems reported in two aspects: (1) the zwitterion is stable enough to be isolated, and (2) the molecular weight of the polymer prepared is much higher than other zwitterion polymerization systems. Although this was probably the most significant work in the field, it had gone

almost unnoticed by other workers. Other than Schmidt's work, the following research has also been done on the this type of polymerization:

(1) 3-(N-benzylazetidino)propionate system[49]:

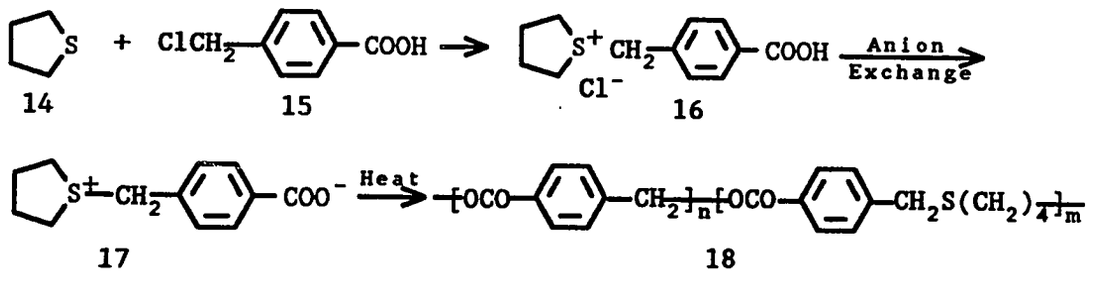


10 11 12

13

The molecular weight of the produced polymer 13 was about 6,000.

(2) 1-[4-hydroxy-3-(2-hydroxyethoxy)phenyl]-thiophenium hydroxide system[48.a]:



14 15 16 17 18

The molecular weight of polymer 18 was 5,000-41,000 which varied with polymerization conditions. This work was done by our group.

The common characteristics of this type of zwitterion is that both the positive and negative charge centers are

reasonably stable.

Other than the above one, the following studies have also been done by our group in recent years[48]:

(1) 2-methyl-2-oxazoline with acrylic acid[48.b]

(2) Tetrahydrothiophenium-arene systems derived from 2-(2-hydroxyethoxy)phenol and α-naphthol[48.c]

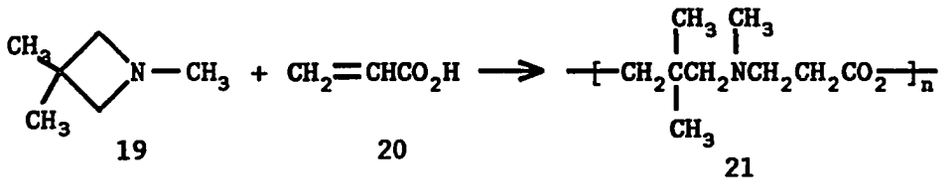
(3) 2-Methyl-2-oxazoline with methacrylic acid[48.d]

(4) 2-Mercaptoalkyl-2-oxazoline system derived from 2-isopropenyl-2-oxazoline and 1,2-ethanedithiol[48.e]

1-2 Zwitterionic Polymerization Employing Cyclic Amine

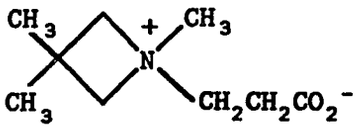
Since the interest of our research is related to cyclic amines, therefore, the publications related to the zwitterionic polymerization which involved cyclic amines as electrophilic monomers are reviewed in detail except the 3-(N-benzylazetidino)-propionate system mentioned earlier:

(1) 1,3,3-trimethylazetidine 19 with acrylic acid 20[16]

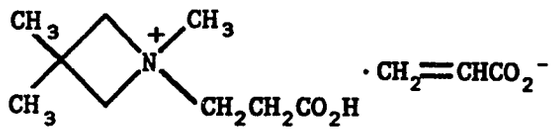


19 20 21

22 as an intermediate was supported by the isolation of azetidinium acrylate 23 as a white crystalline solid after reaction at 10°C in diethyl ether overnight.



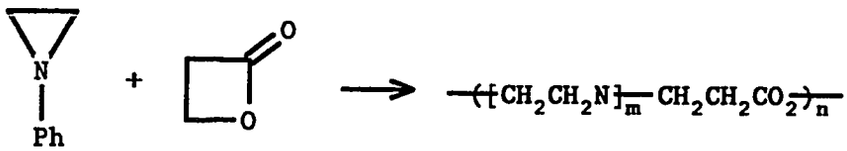
22



23

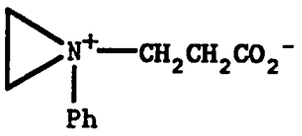
(2) N-phenylazetidine 24 with β-propiolactone 25[49]

Copolymerization of N-phenylazetidine with β-propiolactone took place at 0°C in acetonitrile without any catalyst to give copolymer 26:



24 25 26

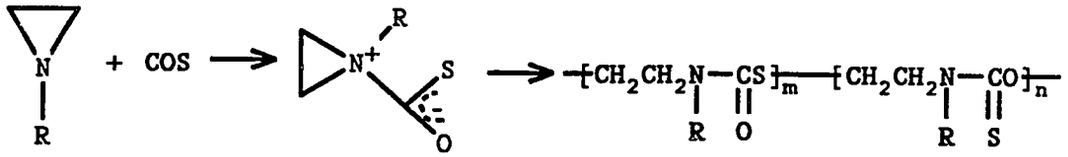
The monomer reactivity ratios were r_1=7.5 (M_1=24) and r_2=0.15 (M_2=25), therefore, copolymer 26 normally should not be an alternating one unless zwitterion 27 was formed as an intermediate.



27

(3) Aziridine 28 with carbonyl sulfide 29[50]

Copolymerization of aziridine 28 and carbonyl sulfide 29 produced alternating polymer 31:

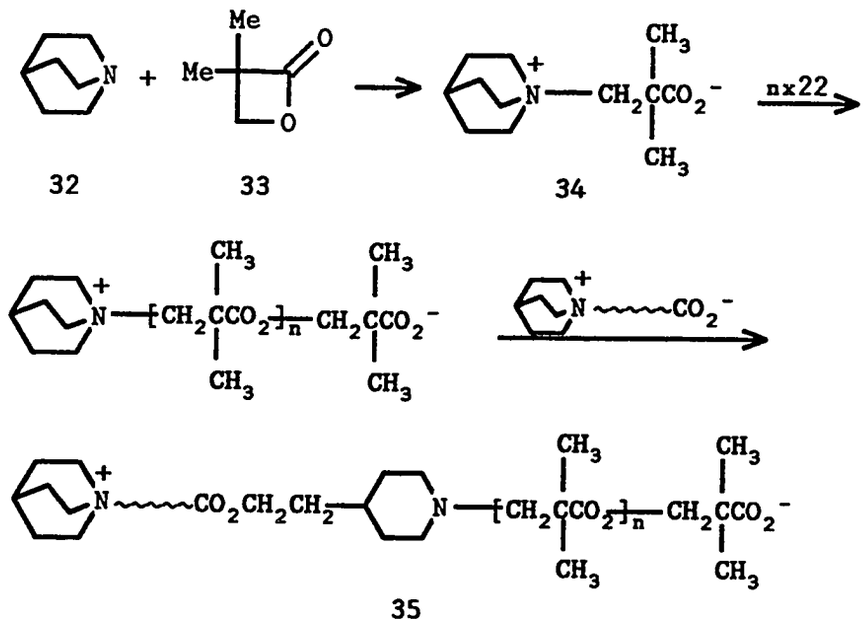


28 29 30 31

The involvement of genetic zwitterion 30 explains the formation of alternating polymer 31 with two different repeating units.

(4) Quinuclidine 32 with pivalolactone 33[51]

When quinuclidine 32 was used as initiator to induce the anionic polymerization of pivalolactone 33, it was observed that more than one molecule of initiator 32 was incorporated into one polymer molecule. This was explained by the formation of zwitterion intermediate 34 which participated in the propagation of the polymer chain:

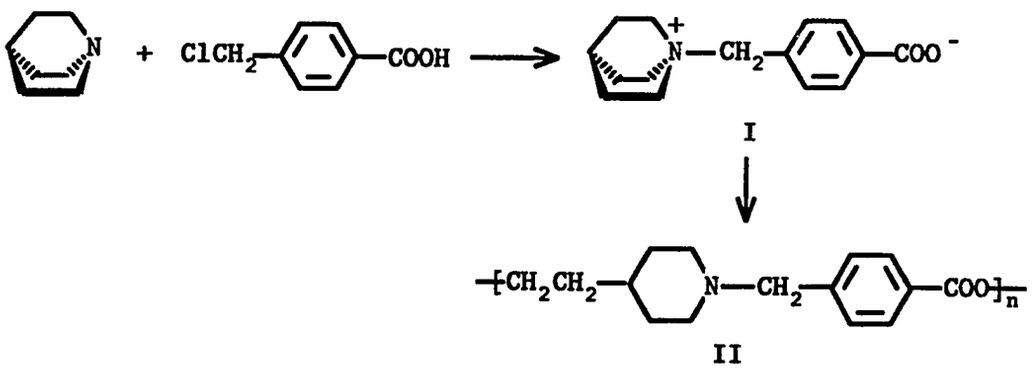


32 33 34

35

1-3 Our Proposed Research

According to the literature, the cyclic amines used for zwitterionic polymerization are those ring systems which are not very stable, such as three-, four-, and (2,2,2)-bicyclic six-membered-rings. In our research, the cyclic amine--quinuclidine was chosen as the nucleophilic monomer and 4-(chloromethyl)-benzoic acid the electrophilic monomer. Quinuclidine and 4-(chloromethyl)-benzoic acid were proposed to react with each other to form zwitterion I, 1-[(4-carboxyphenyl)methyl]-quinuclidium inner salt, and then zwitterion I would polymerize through a zwitterionic mechanism to produce an alternating copolymer II as shown below:



I

II

Since the positive charge center as well as the negative charge center is stable, this system should be one of the few systems in which the zwitterion intermediate can be separated and polymerized to produce a polymer with high molecular weight.

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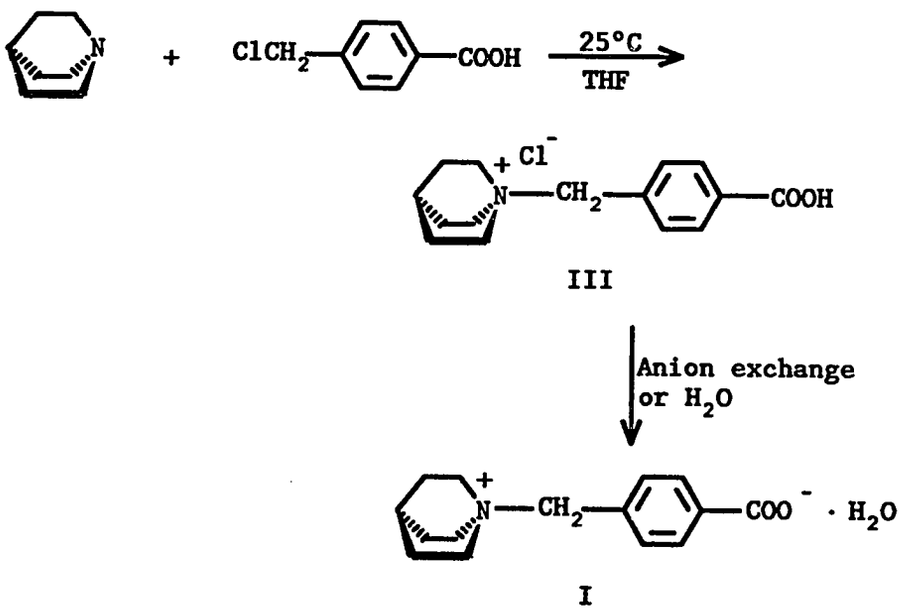
Chapter 2 PREPARATION AND CHARACTERIZATION OF 1-[(4-CARBOXYPHENYL)METHYL]QUINUCLIDINIUM INNER SALT

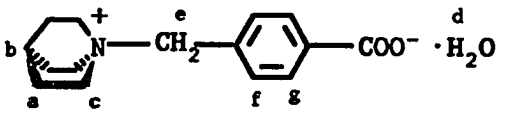
2-1 Preparation and Characterization of 1-[(4-Carboxyphenyl) methyl]Quinuclidinium Inner Salt (I)

1-[(4-Carboxyphenyl)methyl]quinuclidinium inner salt(I) was prepared from 4-(chloromethyl)benzoic acid and quinuclidine through a two-step process as shown below:



In the first step, 1-[(4-carboxyphenyl)methyl]quinuclidinium hydrochloride inner salt III was formed, Cl^- was then exchanged with OH^- of the anionic strong base resin in the second step to produce the hydrate of zwitterion I. The ^1H and ^{13}C NMR spectra of the final product were taken for

the characterization of the structure, which are shown in Figures 2-1 and 2-2 respectively.



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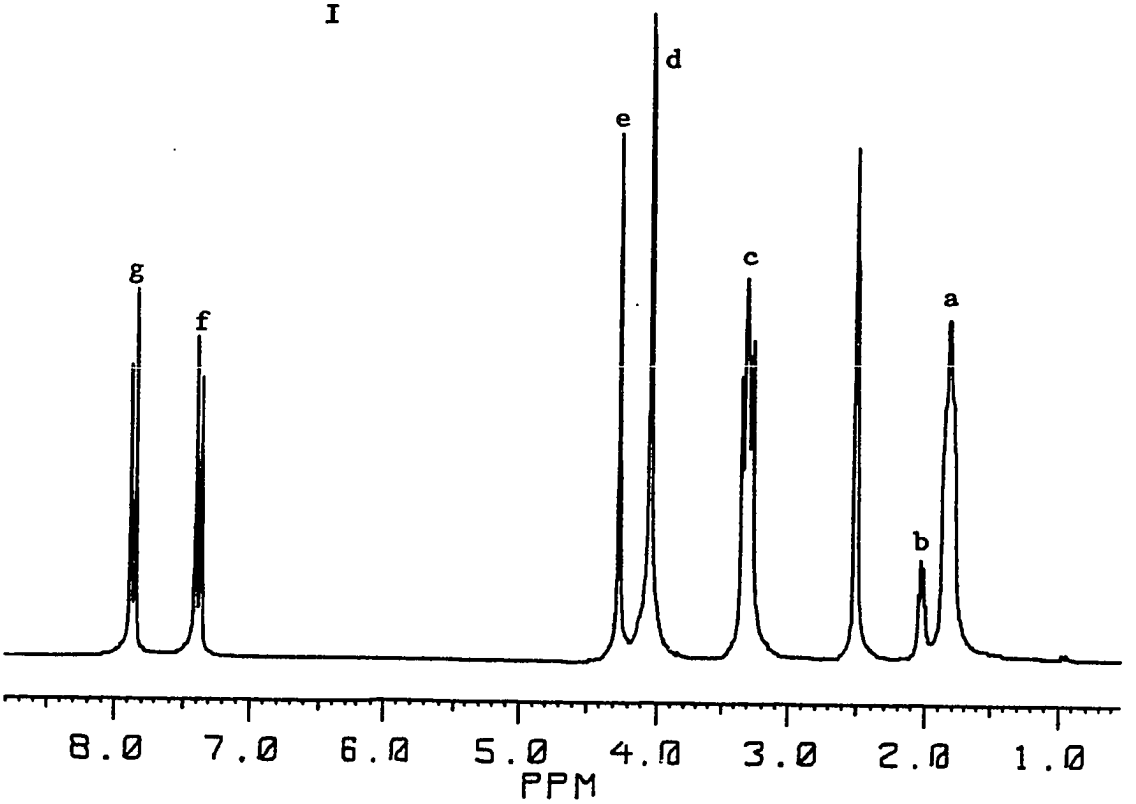
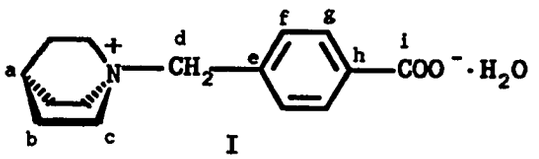


Figure 2-1 200.1-MHz ^1H NMR spectrum of 1-[(4-carboxyphenyl)methyl]-quinuclidium inner salt (I) hydrate: conc.: 6%, solvent: DMSO-D_6/D_2O (20:1 v:v), temp.: 40°C.

The assignment of the ^1H NMR spectrum is as follows (Figure 2-1): multiplet at 1.80 ppm (6H): methylene protons H_a, multiplet at 2.00 ppm (1H): proton H_b, multiplet at 2.49 ppm: DMSO-D_6 solvent peak, triplet (J_{ac}=9.5 Hz) at 3.39 ppm (6H): methylene protons H_c, singlet at 4.02 ppm (2H):

protons of water, which is contributed by the zwitterion hydrate and solvents (D_2O and DMSO-D_6), peak at 4.25 ppm (2H): methylene protons H_e, doublet (J_{gf}=11.3 Hz) at 7.36 ppm (2H): aromatic protons H_f, and doublet (J_{fg}=11.3 Hz) at 7.86 ppm (2H): aromatic proton H_g.



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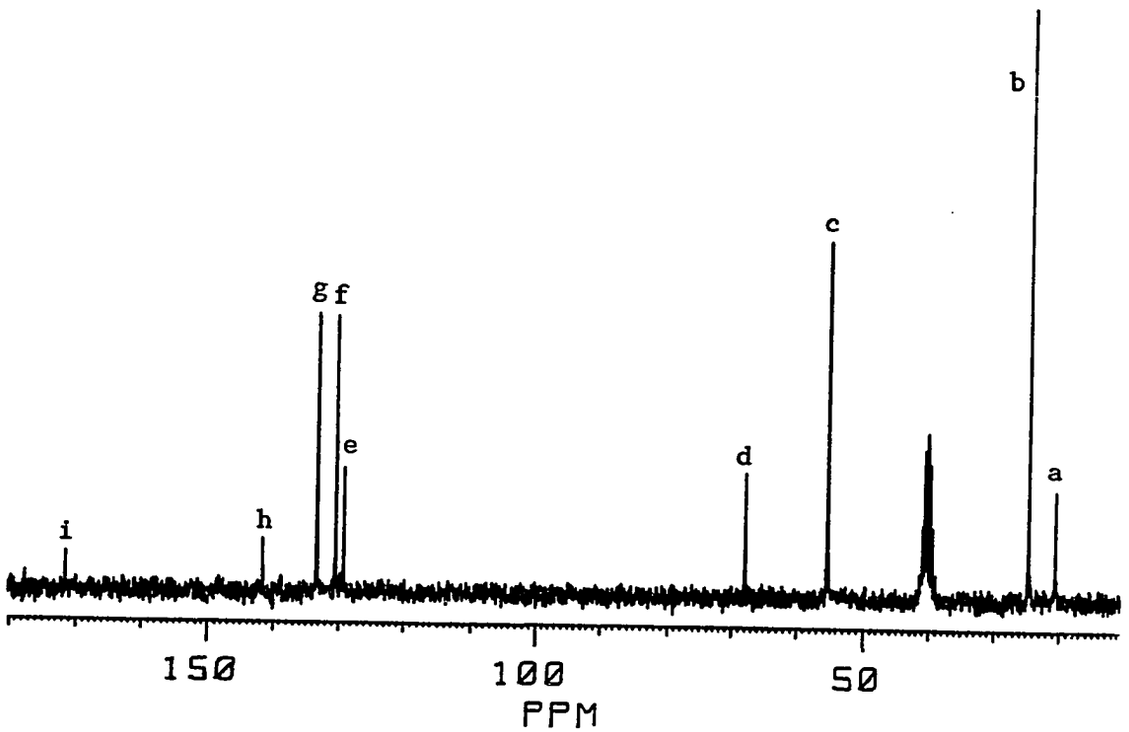


Figure 2-2 50.3-MHz ^{13}C NMR spectrum of 1-[(4-carboxyphenyl)methyl]-quinuclidium inner salt (I) hydrate: the same sample as Figure 2-1.

The assignment of the ^{13}C NMR spectrum is as follows (Figure 2-2): peak at 20.1 ppm: tertiary carbon C_a, peak at

24.1 ppm: methylene carbons C_b, multiplet at 39.5 ppm: DMSO solvent peak, peak at 55.0 ppm: methylene carbon C_c, peak at 67.6 ppm: methylene carbon C_d, peak at 129.0 ppm: aromatic quaternary carbon C_e, peak at 130.2 ppm: aromatic carbon C_f, peak at 133.0 ppm: aromatic carbon C_g, peak at 141.4 ppm: aromatic quaternary carbon C_h, peak at 171.2 ppm: carbonyl carbon C_i.

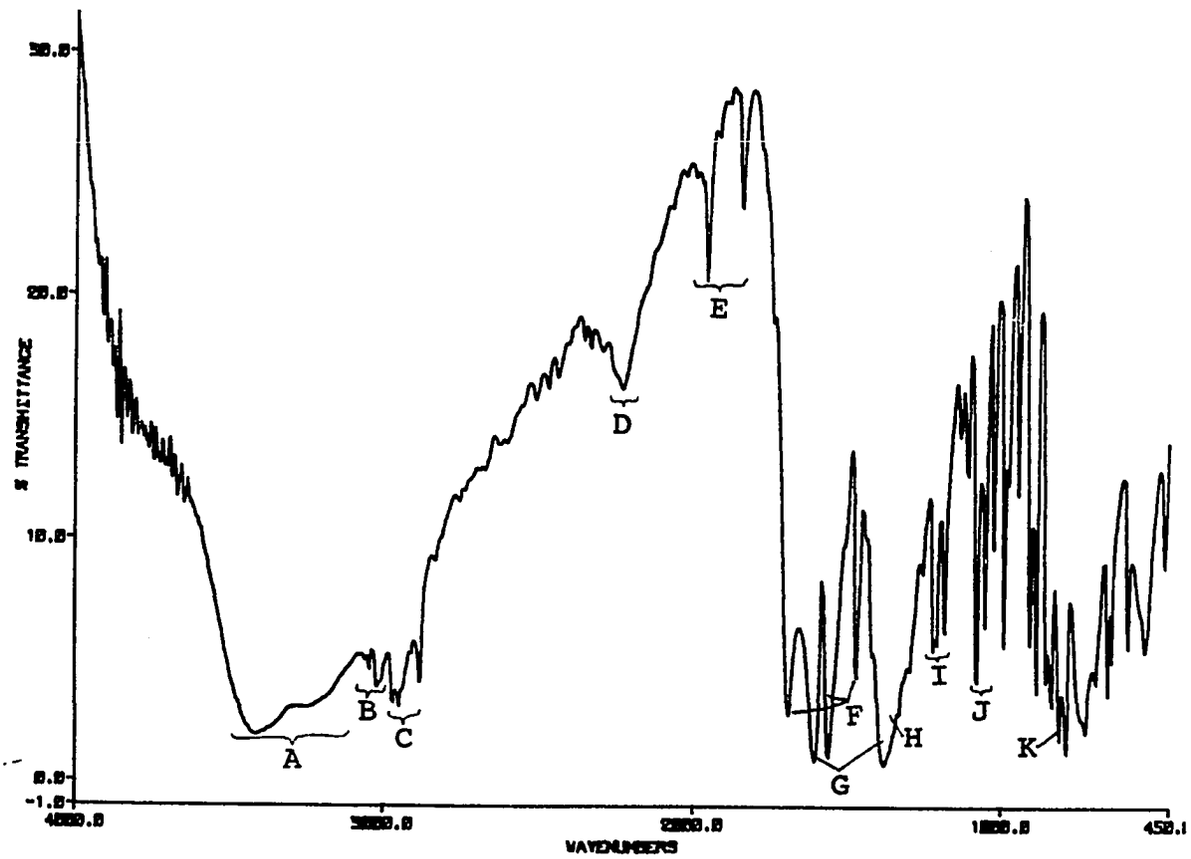


Figure 2-3 FT-IR spectrum of zwitterion hydrate I, KBr pellet.

The FT-IR spectrum (Figure 2-3) of the hydrate of zwitterion I was taken to supply additional information: A. υ_{O-H} of hydration water: 3600-3100 cm^{-1}, B. υ_{C-H} of aromatic

ring: 3070 and 3055 cm^{-1}, C. υ_{C-H} of methylene: 2947, 2904 and 2877 cm^{-1}, D. υ_{C-N} of amine salt: 2225 cm^{-1}, E. combination bands of aromatic ring: 1994 and 1840 cm^{-1}, F. υ_{C-C} of the benzene ring: 1685, 1600 and 1558 cm^{-1}, G. carboxylate ion, $\upsilon_{as(O-C-O)}$: 1605 cm^{-1} and $\upsilon_{s(O-C-O)}$: 1415 cm^{-1}, H. δ_{CH2} of methylene: 1420-1327 cm^{-1}, I. ω_{CH2} of methylene: 1215 and 1170 cm^{-1}, J. υ_{C-N} of amine salt: 1072 and 1018 cm^{-1}, K. $\delta_{C-H(out\ plane)}$ of benzene ring: 806 cm^{-1}.

The ^1H NMR spectrum of the product of reaction between quinuclidine and 4-(chloromethyl)benzoic acid, before anion exchange was carried out, is shown in Figure 2-4.

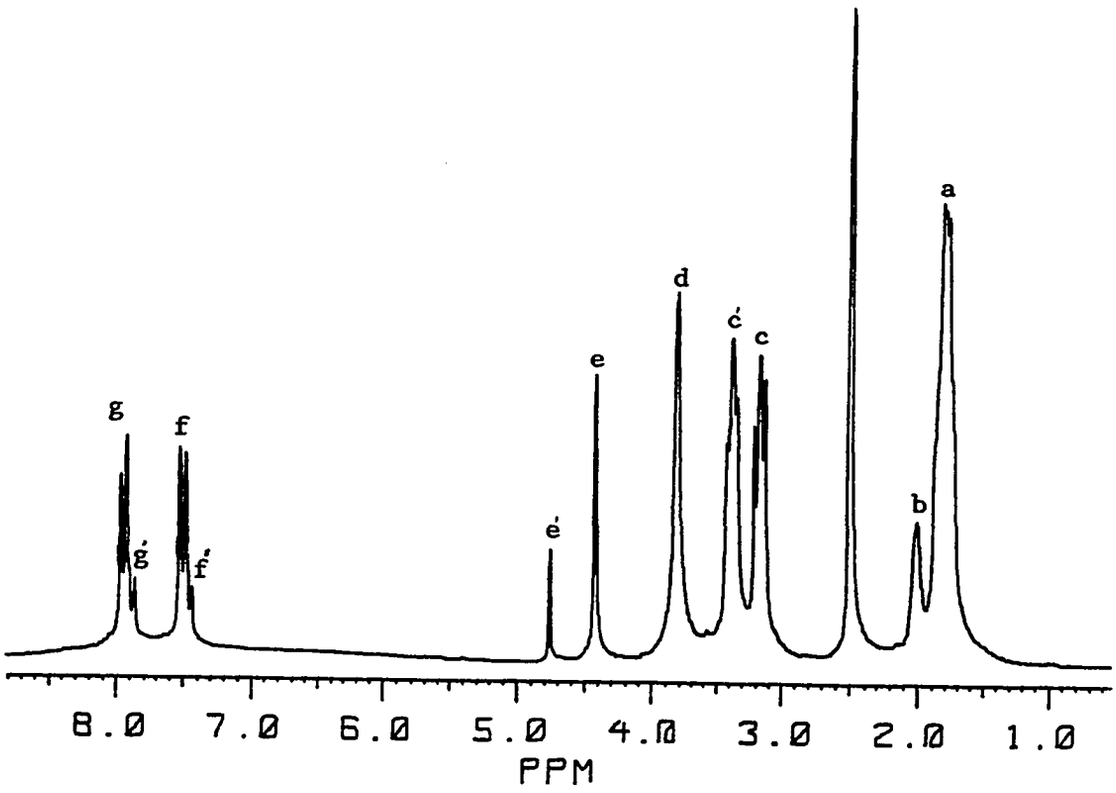
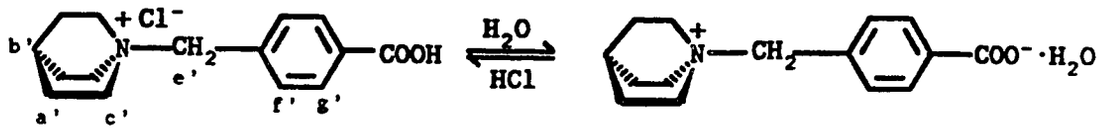


Figure 2-4 200.1-MHz ^1H NMR spectrum of the reaction product of quinuclidine and 4-(chloromethyl)benzoic acid: conc.: 4%, solvent: DMSO-D_6, temp.: 50°C.

Comparing Figure 2-1 with Figure 2-4, it is obvious that the product before anion exchange already contained the zwitterion hydrate I; the product actually was a mixture of I and III. In other words, the hydrochloride salt III can readily react with water which was present in the reaction system to form the hydrate I:



III I

Experimental result also proved that the reaction of III and water was a reversible reaction: by dissolving the crude product mixture in methanol/water (v:v 3:1), then drying the solution, the amount of the hydrate increased according to the ^1H NMR spectra. Therefore, the anionic exchange step was necessary in order to prepare pure I.

In Figure 2-4: peaks (a, b, c, d, e, f and g) belong to the zwitterion hydrate and can be assigned in the same way as for the spectrum in Figure 2-1; notice that the water peak shifted to lower field, from 4.02 ppm to 3.79 ppm. Because of the structure similarity between III and I, most peaks of III are either completely or partially overlapped with the corresponding peak of I, except proton $H_{c'}$ and $H_{e'}$. Signals f′ and g′ are methylene protons $H_{f'}$'s and $H_{g'}$'s respectively, and signals c′ and e′ are methylene protons $H_{c'}$'s and $H_{e'}$'s as indicated in the structure of III. There

is no signal in range 10-13 ppm for the proton of a carboxylic acid, this might be due to the proton exchanging.

One might think that after Cl^- is exchanged with OH^-, the anion exchange product would be a hydroxide inner salt IV instead of a hydrate. Theoretically speaking, since OH^- is a much stronger base than $R\text{-}COO^-$, the equilibrium shown below should shift to the right to form the hydrate I.

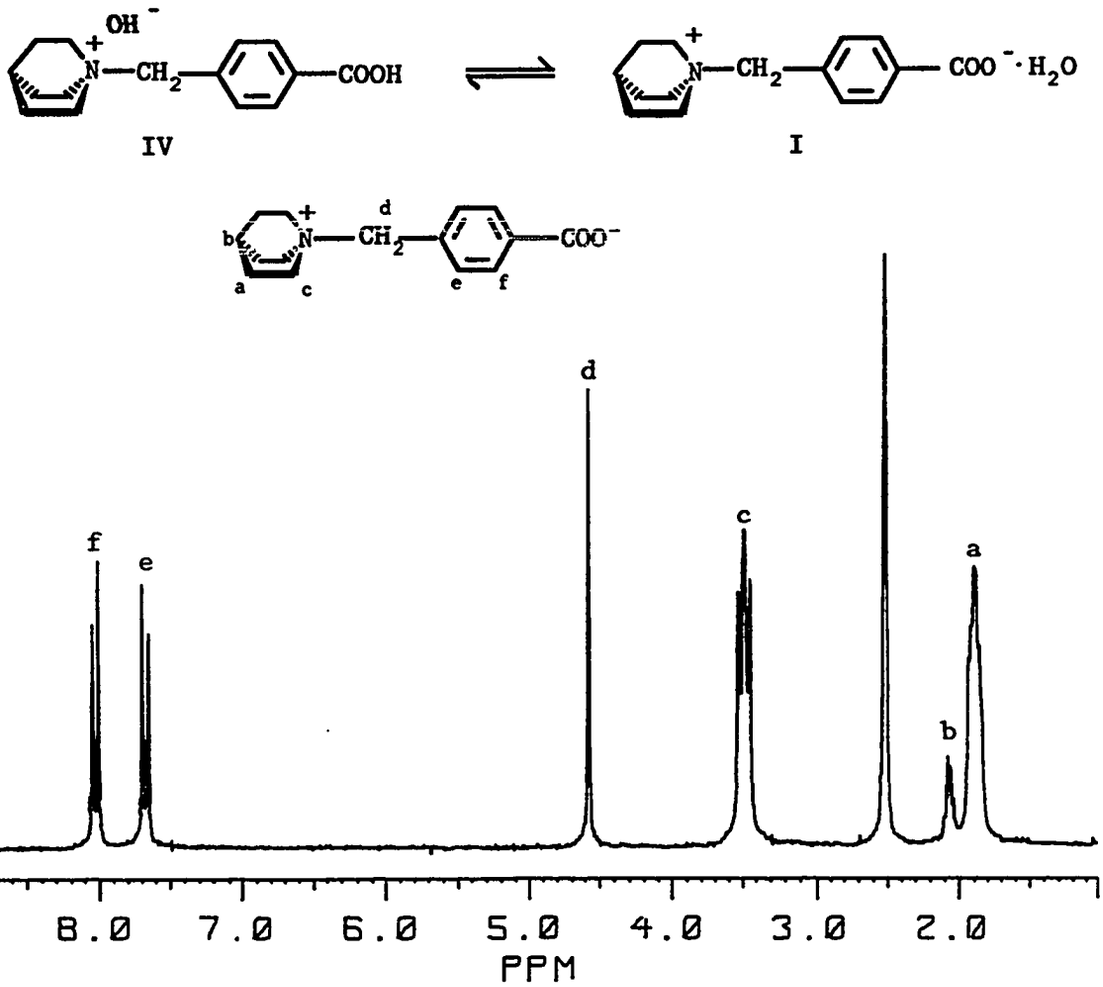


Figure 2-5 200.1-MHz ^1H NMR spectrum of 1-[(4-carboxyphenyl)methyl]-quinuclidium inner salt, anhydrous: conc.: 4%, solvent: DMSO-D_6, temp.: 40°C.

The experimental results also support the theory: by heating the anion exchanged product under vacuum, an *anhydrous* zwitterion I was obtained. The ^1H NMR spectrum of the *anhydrous* zwitterion I is shown in Figure 2-5. The only difference between Figure 2-1 and 2-5 is that the water peak is missing in the latter.

2-2 Determination of the Amount of the Water of Hydration

The amount of the water of hydration was determined by Karl-Fisher titration and TGA. The results of Karl-Fisher titration is listed in Table 2-1 and the TGA diagram is shown in Figure 2-6.

Table 2-1 The Karl-Fisher titration results

Compound	Water (%)
Hydrate I	6.55
Anhydrous I	.36
Calculated Value of Hydrate Containing One Mole of H_2O	6.82

Based on the Karl-Fisher titration results, it is concluded that the zwitterion hydrate I contained one mole of water and could be dehydrated as high as 95%. The thermogravimetric analysis (Figure 2-6) supported the Karl-Fisher titration result: the zwitterion hydrate started to lose water at 60°C, and lost all the water of hydration (6.8%) at the temperature ≤175°C which varies from sample to

sample. It also showed that the anhydrous I was stable but started to decompose when temperature reached 200°C.

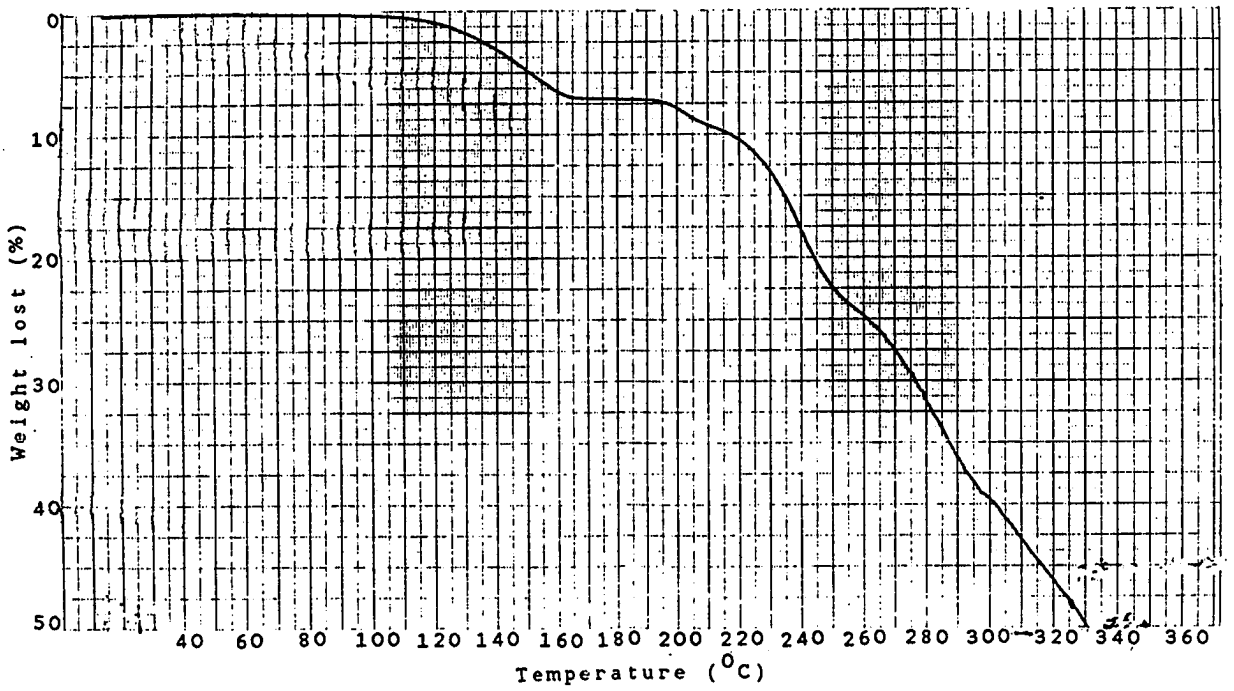
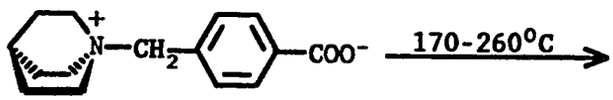


Figure 2-6 TGA diagram of zwitterion hydrate II.

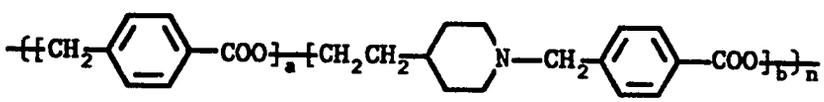
Chapter 3 PREPARATION AND CHARACTERIZATION OF POLYMER II

Since both anhydrous zwitterion I and its hydrate could be prepared and were very stable, bulk and solution polymerization were carried out on both of them. The solution polymerization was difficult to perform due to the fact that there was no solvent that could dissolve both zwitterion I and the produced polymer. The polymers prepared from both bulk and solution basically had the same structure according to the analysis of the NMR spectra, but the polymer prepared from bulk polymerization gave a simpler ^1H NMR spectrum. Since the bulk polymerization was easier to perform and had a yield as high as 99%, while the solution polymerization had a yield of less than 10%, our study concentrated mostly on the bulk polymerization.

The bulk polymerization was carried out for both anhydrous and hydrate forms of I between 170-260°C, which produced the same type of polymer—polymer II as shown in the following equation:



I



II

As the temperature increased, the time needed to complete the polymerization decreased tremendously and the color of the polymer became darker, from a very light yellow to brownish color. Typical ^{1}H and ^{13}C NMR spectra of polymer II are shown in Figures 3-1 and 3-3, respectively.

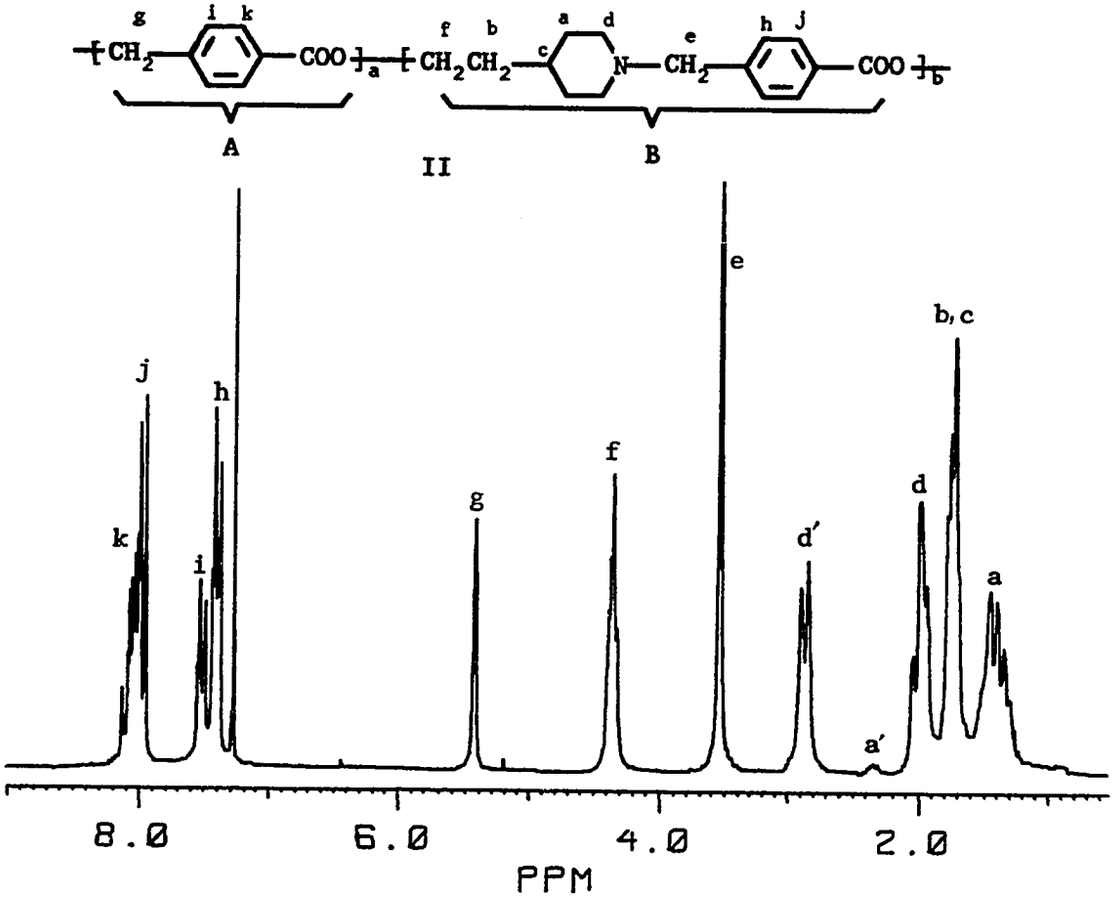


Figure 3-1 200.1-MHz ^{1}H NMR spectrum of polymer II: Conc.: 3%, solvent: $CDCl_3$, temp.: 25°C.

The assignment of the ^{1}H NMR spectrum (Figure 3-1): multiplet (a) at 1.22-1.56 ppm: methylene protons(H_a's), multiplet (b,c) at 1.56-1.85 ppm: methylene protons(H_b's)

overlapped with tertiary proton (H_c), multiplet (d) at 1.85-2.09 ppm and doublet (d') at 2.87 ppm: methylene protons (H_d) at axial and equatorial position, singlet (e) at 3.52 ppm: methylene protons (H_e), multiplet (f) at 4.35 ppm: methylene protons (H_f), singlet (g) at 5.41 ppm: methylene protons (H_g), singlet at 7.27 ppm: solvent peak, multiplets at 7.32-7.58 and 7.89-8.15 ppm: aromatic protons, the peaks with higher intensities (h and j) corresponding to protons (H_h's and H_j's), and the peaks with lower intensities (i and k) corresponding to protons H_i and H_k. Peak (a') is contributed by the ending group which is discussed in Chapter 4. Since protons H_e's and H_g's are the same type of methylene protons which belong to repeating units A and B respectively, the ratio of A:B can be measured by comparing the integration of peaks e and g.

Due to the overlapping of the proton signals in the ^1H NMR spectrum, a 2-D COSY experiment (Figure 3-2) was run to confirm the assignment of the ^1H NMR spectrum. The assignment of the cross peaks in Figure 3-2: peak (a,c): coupling between H_a and H_c, peak (c,d): coupling between H_c and H_d, peak (a,d): coupling between H_a and H_d, peak (d,d'): coupling between H_d and H_d, peak (d',c): coupling between H_d and H_c, peak (a,d): coupling between H_a and H_d, peak (f,b): coupling between H_f and H_b, peak (g,i): long range coupling between H_g and H_i, peak (e,h): long range coupling between H_e and H_h, peak (h,j) or (i,k): coupling between H_h and H_j or H_i and H_k.

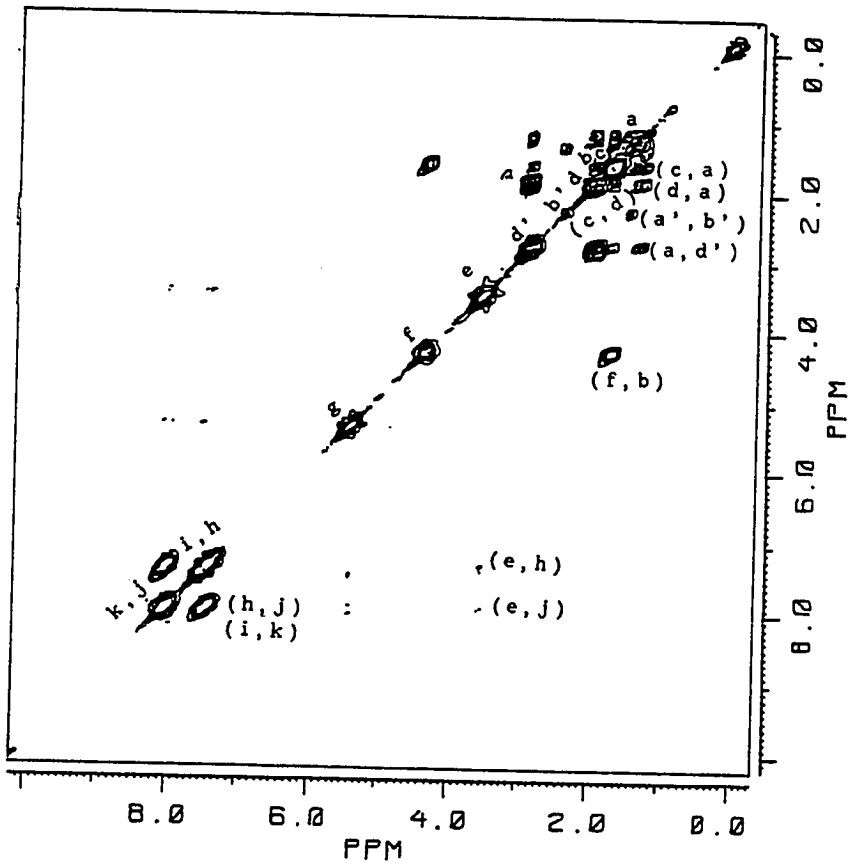
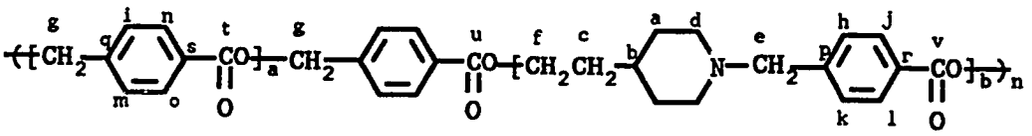


Figure 3-2 2D-COSY experiment of polymer II, solvent:$CDCl_3$, conc.: 7%, temp.: 300°C.

The 2-D COSY NMR spectrum (Figure 3-2) agrees with the assignments of the ^1H NMR spectrum. As a matter of fact, some of the assignments of Figure 3-1 depend on the 2-D COSY to a certain degree.

The ^{13}C NMR spectrum (Figure 3-3) provided more information about the polymer chain linkage which the ^1H and COSY spectra can not give. This will be discussed in greater detail in Chapter 4. The assignment of the ^{13}C NMR spectrum (Figure 3-3): peak (a) at 32.05 ppm: methylene

carbons, C_a, peak (b) at 32.68 ppm: tertiary carbon, C_b, peak (c) at 35.11 ppm: methylene carbon, C_c, peak (d) at 53.63 ppm: methylene carbons, C_d, peak (e) at 62.71 ppm: methylene carbon, C_e, peak (f) at 62.85 ppm: methylene carbon C_f, and peak (e) and (f) is partially overlapped, peak (g) at 65.63 ppm: methylene carbon C_g, peak (h) at 127.43 ppm: aromatic carbon C_h, peak (i) at 128.27 ppm: aromatic carbon C_i, peak (k) at 128.73 ppm: aromatic carbon C_k, peak (j) at 128.87 ppm: aromatic proton C_j, peak (l)



II

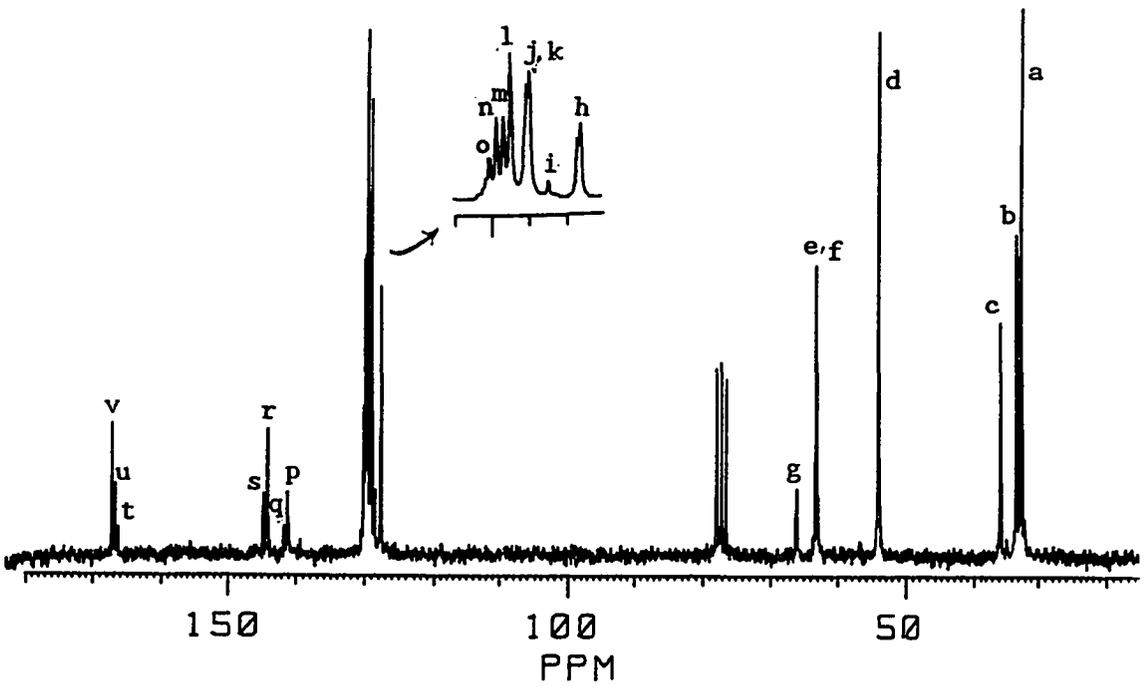


Figure 3-3 50.3-MHz ^{13}C NMR spectrum of polymer II: conc: 7%, solvent: $CDCl_3$, temp.: 25°C.

at 129.28 ppm: aromatic carbon C_l, peak (m) at 129.48 ppm: carbon C_m, peak (n) at 129.84 ppm: aromatic carbon C_n, peak (o) at 129.94 ppm: aromatic carbon C_o, peaks (p) and (p') at 140.83 and 141.01 ppm respectively: quarternary aromatic carbon C_p, peak (q) at 141.46 ppm: quarternary aromatic carbon C_q, peak (r) at 144.00 ppm: quarternary aromatic carbon C_r, peak (s) at 144.51 ppm: quarternary aromatic carbon C_s, peak (t) at 165.62 ppm: carbonyl carbon C_t, peak (u) at 165.98 ppm: carbonyl carbon C_u, peak (v) at 166.36 ppm: carbonyl carbon C_v.

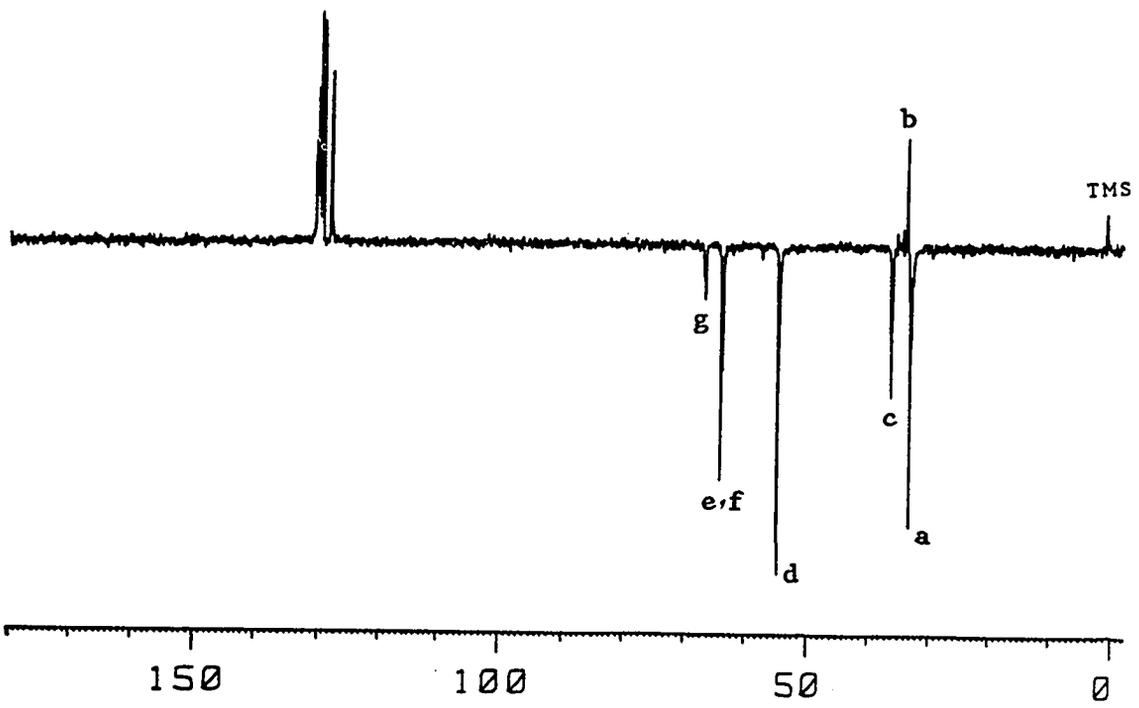


Figure 3-4 DEPT spectrum of polymer II: Conc: 7%, solvent: $CDCl_3$, temp.: 25°C.

A DEPT spectrum (Figure 3-4) of the polymer was taken

in order to help the assignment of the carbon spectrum as well as to determine the multiplicities of the carbons. In Figure 3-4, the methylene carbons, C_a, C_c, C_d, C_e, C_f, and C_g gave signals with negative intensities, the methine carbon C_b and the unsubstituted aromatic carbons, C_h, C_i, C_j, C_k, C_l, C_m, C_n, and C_o had positive intensities. The carbons which do not give signals in the DEPT spectrum are the quaternary aromatic carbons, C_p, C_q, C_r and C_s, and the carbonyl carbons, C_t, C_u and C_v.

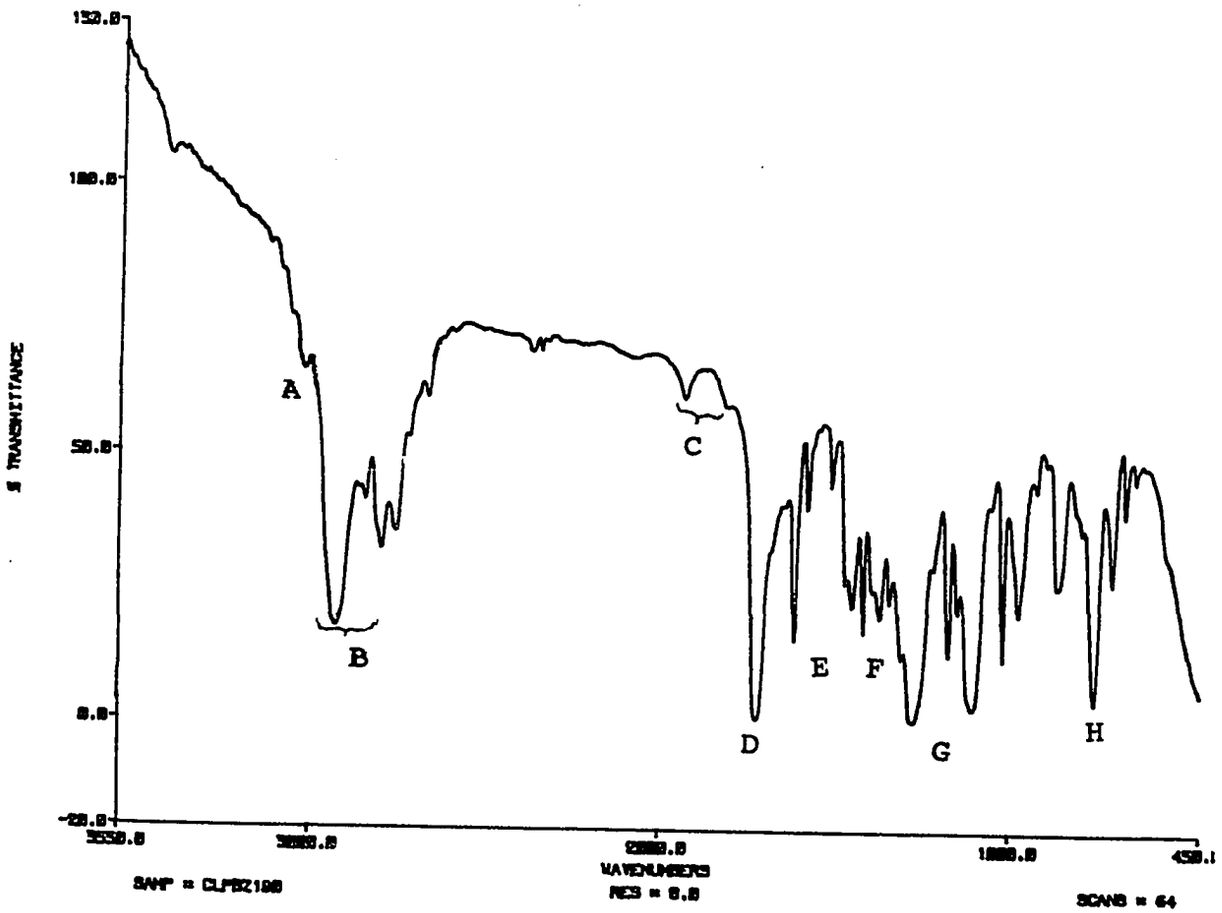


Figure 3-5 FT-IR spectrum of polymer II: the sample was prepared as a thin film deposited on a NaCl plate at 25°C.

Since polymer II has been prepared for the first time, a FT-IR spectrum (Figure 3-5) was taken to obtain more information.

The assignment of the IR spectrum (Figure 3-5): A. υ_{C-H} of aromatic ring: 3016.7 cm^{-1}, B. υ_{C-H} of methylene or methine group: 2924, 2847, 2797, and 2762 cm^{-1}, C. combination bands of aromatic ring: 1933 and 1813 cm^{-1}, D. $\upsilon_{C=O}$ of carbonyl group: 1720 cm^{-1}, E. υ_{C-C} of benzene ring: 1623, 1578, and 1506 cm^{-1}, F. δ_{C-H} of methylene group: 1466, 1447, and 1416 cm^{-1}, G. $\upsilon_{as(C-O-C)}$ and $\upsilon_{s(C-O-C)}$ of ester: 1265 and 1123 cm^{-1} respectively, and H. $\delta_{C-H(out\ plane)}$ of benzene ring: 864 cm^{-1}.

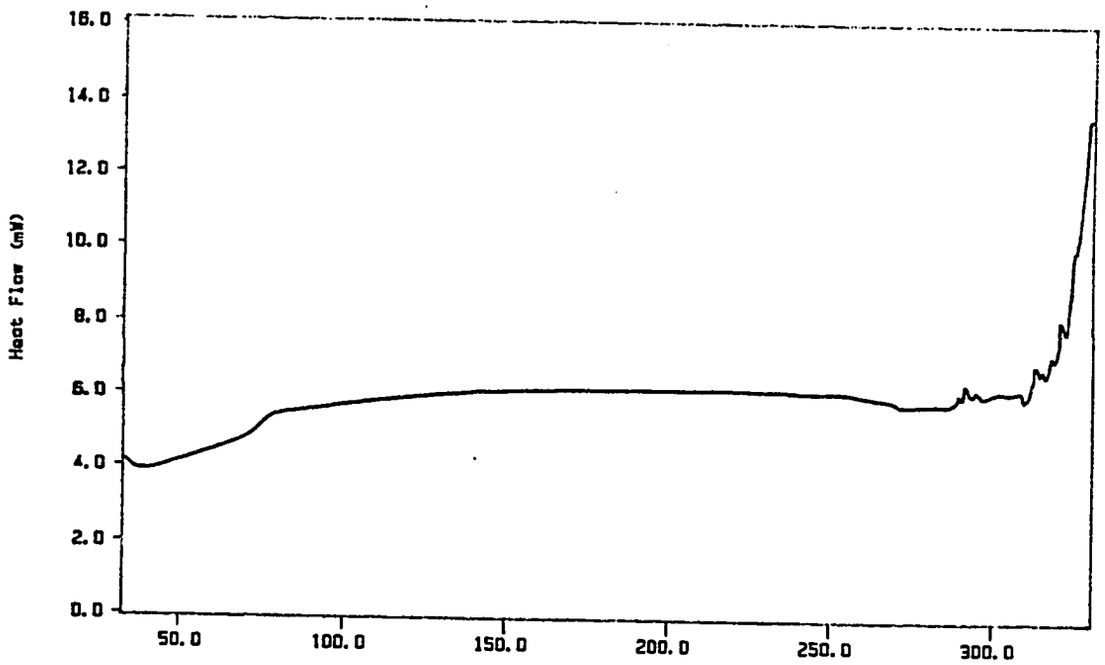


Figure 3-6 DSC diagram of polymer II: amount of sample used: 7 mg

The thermal properties of the polymer were evaluated by DSC (Figure 3-6) and TGA (Figure 3-7). The DSC diagram (Figure 3-6) of polymer II showed that the T_g of the polymer was 73°C and decomposed at 300°C; TGA data indicated that polymer was reasonably stable since the weigth lost of the polymer is less than 2% when the temperature reached 300°C.

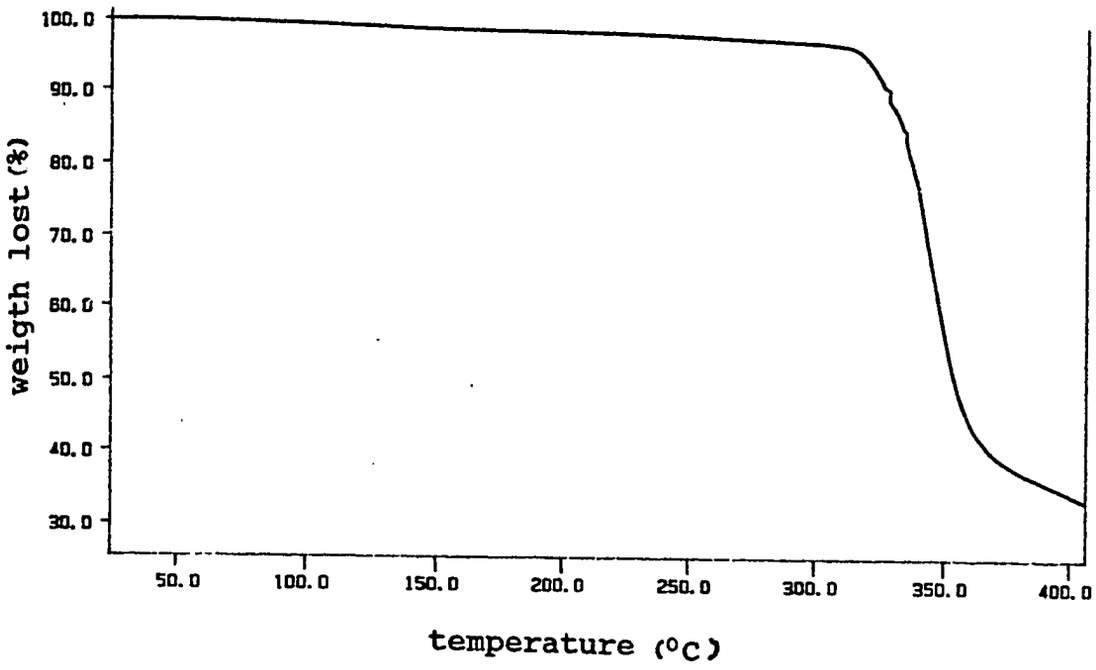


Figure 3-7 TGA diagram of polymer II: sample weight: 5.8 mg

The elemental analysis results of the polymers with different A:B ratios are consistant with the theoretical value regardless of any error that might be involved in the measurement of A:B ratios by ^1H NMR analysis.

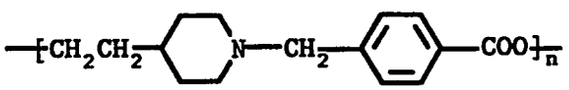
Table 3-1 Elemental analysis results of polymer II with various A:B ratios

Polymer II A:B	Theoretical			Experimental		
	C%	H%	N%	C%	H%	N%
17.4:82.6	73.26	7.46	5.12	72.57	7.80	5.62
32.6:67.4	73.07	7.11	4.52	71.85	6.87	4.24
68.8:31.2	72.46	6.00	2.59	71.69	6.33	3.28

Chapter 4 MECHANISTIC STUDY OF THE POLYMERIZATION OF 1-[(4-CARBOXYPHENYL)METHYL]QUINUCLIDINIUM INNER SALT

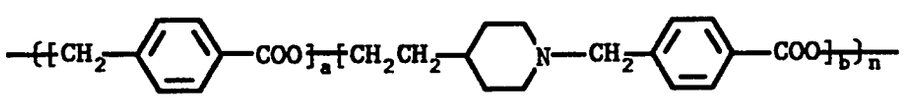
It is obvious that the polymerization of 1-[(4-carboxyphenyl)]quinuclidinium inner salt is not a conventional zwitterionic polymerization, since the produced polymer contains A and B as repeating units, instead of having only A as the repeating unit:

The structure of the conventional polymer:



B

The structure of produced polymer:



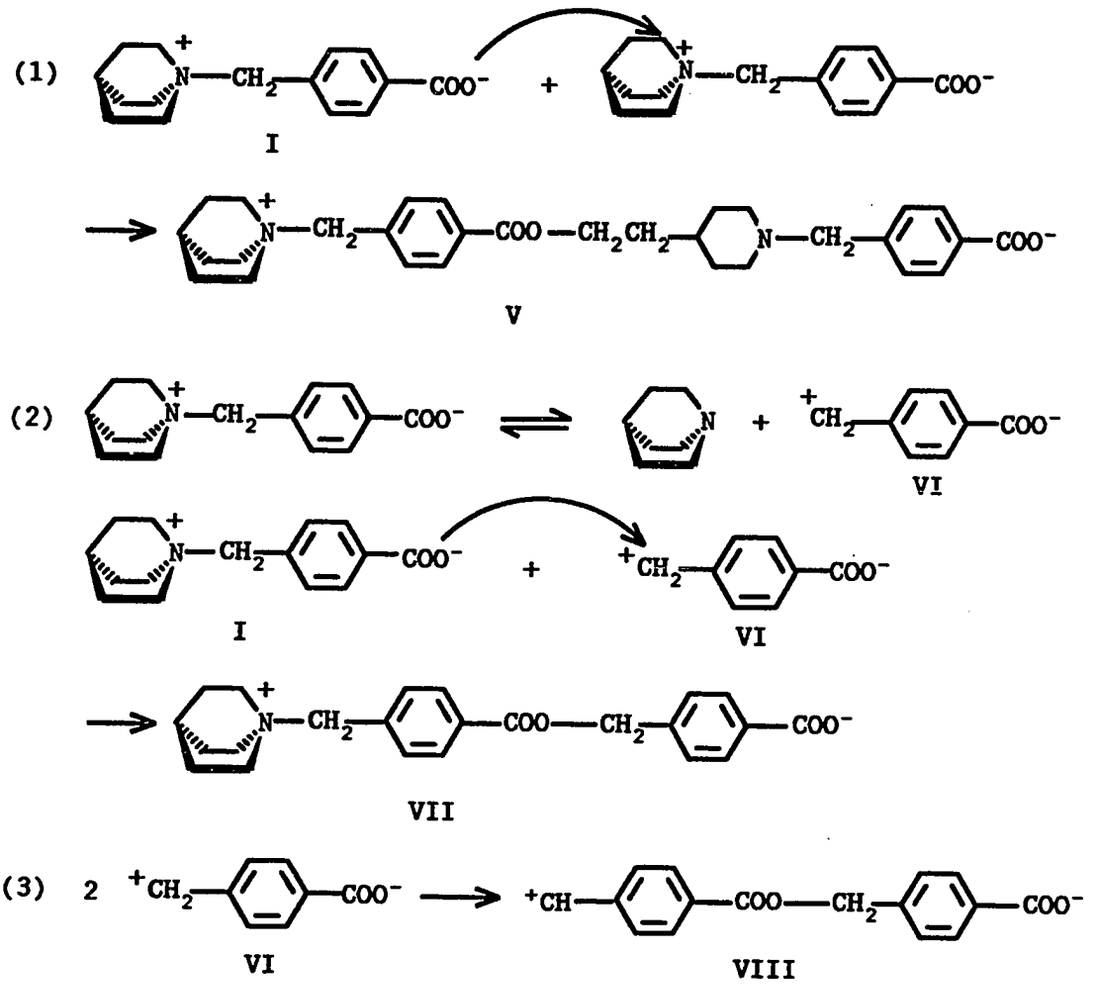
A B

4-1 The Mechanism of Initiation

During the bulk polymerization process, as soon as the sealed polymerization tube containing zwitterion I, hydrate or anhydride, was heated at the selected temperature, a sublimate was formed on the top of the polymerization tube. This sublimate was identified as quinuclidine by ^1H NMR spectroscopy. For the hydrate, there was also water condensed on the top of the tube. Based on the experimental observations and the structure of polymer II confirmed by

NMR analysis, an initiation mechanism can be proposed as following:

Initiation:



The first type of initiation, (1), is conventional for zwitterionic polymerization. The second and third types of initiation, (2) and (3), are more likely to occur. First, the formation of the sublimate of quinuclidine was formed in the very early stage of the polymerization; second, the reaction between I and VI or VI and VI are much easier than the reaction between the two zwitterions I, since VI has a

much greater reactivity than I. Due to the increase of the distance between the positive and negtive charge centers, both the positive and negative charge centers of V are more reactive that of I. As a result, propagation should occur easier than the first type of initiation, (1).

4-2 The Mechanism of Propagation

Due to the decomposition of the zwitterion I, the propagation reaction should involve the reaction of the growing species with zwitterion I, $^{+}B^{-}$ as well as the p-carboxylatebenzyl carbocation, $^{+}A^{-}$.

Propagation:

$$^{+}BB^{-} \underset{V}{} + \underset{I}{^{+}B^{-}} \longrightarrow {}^{+}BBB^{-}$$

$$^{+}BBB^{-} + \underset{VI}{^{+}A^{-}} \longrightarrow {}^{+}BBBA^{-}$$

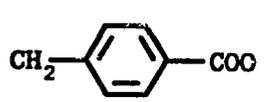
$$^{+}BBBA^{-} + {}^{+}B^{-} \longrightarrow {}^{+}BBBAB^{-}$$

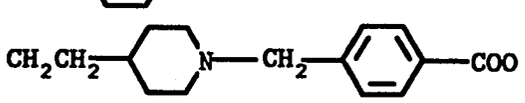
$$\underset{VII}{^{-}BA^{+}} + {}^{+}A^{-} \longrightarrow {}^{-}BAA^{+}$$

$$^{-}BAA^{+} + {}^{+}BB^{-} \longrightarrow {}^{-}BAABB^{+}$$

$$^{+}BBBA^{-} + {}^{+}A^{-} \longrightarrow {}^{+}BBBAA^{-}$$

$$\text{------>} \; {}^{+}BABBBABAABABABBAAABBABBB^{-}$$

A: 

B: 

Among these growing species, —BB^{-} or —AB^{-} type growing species are more reactive than —AA^{-} or —BA^{-} because of the induction effect of -COO- in -A- which

decreases the electron density of the nucleophile oxygen in $-COO^-$. Whenever there is a $—A^+$, it should react with a more reactive growing species, $—BB^-$ or $—AB^-$ rather than $—AA^-$ and $—BA^-$. However, since $—A^+$ is very reactive and can react with either $—AA^-$ or $—BA^-$ growing species, the result should be a random polymer chain containing A and B as small blocks.

The ^{13}C NMR spectra (Figure 4-1) of polymer II with different A:B ratios support the random polymer chain structure. The A:B ratios were measured by corresponding ^1H NMR spectra as decribed in page 27.

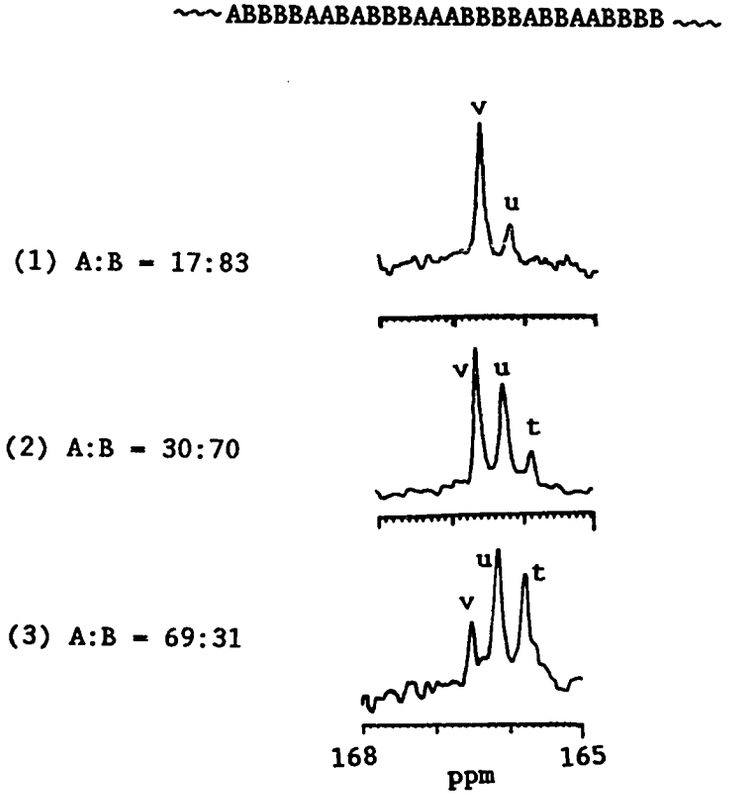


Figure 4-1 50.3-MHz ^{13}C NMR spectra of polymer II with different A:B ratios: carbonyl carbon region, 165-168 ppm.

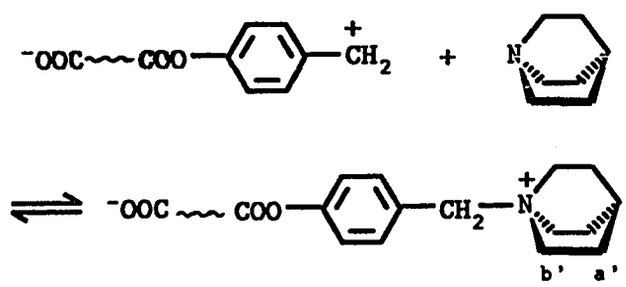
In the 165-168 ppm region of the ^{13}C NMR spectra of polymer II, three different carbonyl carbon signals are observed (Figure 3-3). They are assigned as: (a) carbonyl carbon in B-blocks (peak v), (b) carbonyl carbon of A which is next to the B-block (peak u), and (c) carbonyl carbon of A-block (peak t). The intensity variation of the peaks is in agreement with the A:B ratio.

In Figure 4-1, for the polymer with A:B ratio of 17:83, there is little probability of forming the A-block and peak t of A-block was not observed. As the A:B ratio increased, the probability of forming an A-block increased as evidenced by an increase in the intensity of peak t.

4-3 The Mechanism of Termination

The mechanism of termination is proposed as an equilibrium reaction between the benzyl carbocation and quinuclidine; in other words, there is no real termination.

Termination:



In the ^{1}H NMR spectrum of polymer II (Figure 3-1), the small peak b′ at 2.27-2.42 ppm was considered as the

contribution of the end-group. The 2-D COSY spectrum (Figure 3-2) showed that peak b′ was coupled with only the peak at 1.45 ppm H_a, which were overlapped with peak a for protons H_a. It was also observed that the ^1H NMR spectra of polymer samples with different molecular weight had various intensities for peak b′; the intensity decreased as the molecular weight increased.

Further experiments helped confirm the assignment of the end group. The ^1H NMR spectrum showed no change after reacting the polymer with D_2O. Acetylation was carried out for polymer II by reacting it with acetyl chloride. Again, there was no charge in the ^1H NMR spectrum. Both experiments proved that the end group does not contain a active proton, i.e., it is not a hydroxy group.

The termination reaction also suggested that some sublimate of quinuclidine may come from the decomposition of the growing species.

4-4 Reaction Condition and Polymer Structure

This study also showed that reaction time, pressure, temperature and time affected the polymer structure, i.e. the A:B ratio, reaction rate, and molecular weight.

Table 4-1 contains information on structure and number average molecular weight of polymers prepared at different conditions. The A:B ratio was measured by comparing the relative intensity of peaks e and g as demonstrated in Figure 3-1 and the number average molecular weight was

determined by VPO.

Table 4-1 compositions of polymer II prepared at different condition from zwitterion I

	Reaction condition		Polymer Composition Repeating Units Ratio A:B		Number Average Molecular Weight	
	Temp. (°C)	Time (hr.)	In Vacuum[1]	In Nitrogen[2]	In Vacuum	In Nitrogen
Anhydrous	180	27	31.5:68.5	23.9:76.1	9.3×10^3	—
	190	23	32.6:67.4	26.3:73.7	8.8×10^3	7.1×10^3
	205	12	33.1:66.9	28.0:72.0	10.2×10^3	—
	220	9	43.4:56.6	31.5:68.5	8.0×10^3	7.0×10^3
Hydrate	180	72	17.4:82.6	—	4.3×10^3	—
	202	24	22.7:77.3	—	6.0×10^3	—
	240	0.317	26.8:73.2	—	—	—
	240	0.633	27.1:72.9	—	5.3×10^3	—
	240	0.95	28.6:71.4	—	6.4×10^3	—
	180[3]	48	68.8:31.2	—	16.6×10^3	—

[1] The sample was sealed in a vacuum of 0.1 mmHg

[2] The sample was sealed in nitrogen

[3] The sample was polymerized by continuously pumping a vacuum of 0.1 mmHg

From the results listed in Table 4-1, the following conclusions can be drawn: (a) although the polymerization of the hydrate of zwitterion I gives the same type of polymer as the anhydrous zwitterion, the molecular weights and the A:B ratios of the polymers prepared from the hydrate are lower than those of the polymers prepared from the anhydrous zwitterion; (b) the polymers prepared from the sample sealed

under nitrogen have lower molecular weight and A:B ratio than the polymers prepared from the sample sealed under vacuum; (c) as the temperature increased, the A:B ratio decreased for both polymers prepared from anhydrous material and the hydrate; (d) the molecular weight of the polymer prepared at 180°C under continuous vacuum is the highest; and (e) the molecular weight and A:B ratio increased as the reaction time increased (see polymerization of hydrate at 240°C).

All those conclusions strongly support the proposed polymerization mechanism. The molecular weight is affected by the termination of the polymer chain, in this case, the equilibrium of the growing species and quinuclidine. The higher the concentration of quinuclidine, the lower the molecular weight, since quinuclidine terminates the growing chain. The A:B ratio of the polymer also depends on the concentration of quinuclidine in the reaction mixture. In both the proposed initiation reaction (equation (2)) and termination reaction, quinuclidine is involved in the equilibria, it is obvious that as the concentration of quinuclidine decreases in the reaction mixture, the population of repeating unit A will increase. As a conclusion, the A:B ratio increases as the concentration of quinuclidine in the reaction mixture decreases. As the vacuum increases, the ease of sublimation increases, the concentration of quinuclidine in the reaction mixture decreases, the molecular weight and A:B ratio increase.

Agreeing with these conclusions, the polymers prepared in vacuum did had a higher molecular weight and A:B ratio than the one prepared in nitrogen. This also explains why the polymer prepared from the anhydrous zwitterion I had a higher molecular weight and A:B ratio than the one prepared from the hydrate of I, since the water of hydration vaporizes at the polymerization temperature and decreases the vacuum.

The termination mechanism also explains the increase of the A:B ratio and molecular weight with reaction time. As the reaction time increase, the quinuclidine from the reaction mixture sublimes and condenses on the top of the polymerization tube continuously. This process decreases the amount of quinuclidine in the reaction mixture, therefore, both the A:B ratio and molecular weight increases.

Chapter 5 EXPERIMENTAL PART

5-1 Synthesis of 1-[(4-Carboxyphenyl)methyl]quinuclidinium Inner Salt (I)

All the reagents were used as received. 4-Chloromethylbenzoic acid, 9.0 g (0.0528 mol), was dissolved in 45 ml of THF in an Erlenmeyer flask and cooled in an ice-water bath. Quinuclidine, 6.1 g (0.0532 mol), dissolved in 25 ml of THF in an addition funnel, was added dropwise into the 4-chloromethylbenzoic acid solution with stirring at 5°C. The reaction mixture yield a white precipitate after stirring at ambient temperature overnight. The white precipitate was filtered and then washed with two 25 ml portions of THF followed by 25 ml of Et_2O. After drying under a N_2 flow for 2 hrs, 13.4 g of the white precipitate was obtained, which was a mixture of I and III.

The white precipitate (5.7 g) was dissolved in 25 ml of methanol in a beaker, then an activated anion exchange resin (Dowex 1x2-200, strongly basic form) was slowly added into the solution until the pH reached 10.5. The solution with the resin was filtered and the resin was washed with three 20 ml portions of methanol. The filtrate was concentrated to 30 ml and added into 400 ml of Et_2O dropwise to give a white precipitate. The precipitate was filtered and washed with two 20 ml portions of Et_2O and dried under N_2 flow for 4 hrs, then dried in a rotary evaporator at 15 mmHg of

pressure at 40°C for 15 hrs. This precipitate weighed 3.3 g was the hydrate of zwitterion I.

After heating the hydrate of zwitterion I at 90-100°C under a vacuum of 0.1 mmHg for 40 hrs, the anhydrous zwitterion I was obtained, which was a white fine powder.

The procedure for the activation of Dowex 1x2 200 anion-exchange resin was as follows: 3M NaOH was added into the resin and the resin was soaked for one minute. The resin was then collected by vacuum filtration and washed with distilled water until the filtrate became neutral. After it was washed with methanol to remove the water, the resin was ready for use.

5-2 Determination of Water of Hydration of 1-[(4-Carboxyphenyl)methyl]Quinuclidinium Inner Salt (I)

The amount of water of hydration was determined by Karl- Fischer Titration. The Karl-Fischer reagent consists of I_2, pyridine, and SO_2 in a 1:10:3 mole ratio, dissolved in methanol or ethylene glycol monomethyl ether. Karl-Fischer reagent reacts with H_2O according to following reactions:

$$C_5H_5N \cdot I_2 + C_5H_5N \cdot SO_2 + C_5H_5N + H_2O \longrightarrow 2\ C_5H_6N^+I^- + C_5H_5N^+SO_3^-$$

$$C_5H_5N^+SO_3^- + CH_3OH \longrightarrow C_5H_6N^+CH_3OSO_3^-$$

The most commom procedure is to titrate a known volume of stardardized Karl-Fischer reagent with a solution of the

unknown in methanol. The reagent is first standardized with a methanol solution containing a known amount of water.

The amount of sample used for the titration was approximately 250 mg. The water contents for both the hydrated and the anhydrous 1-[(4-Carboxyphenyl)methyl]-quinuclidinium inner salt (I) were determined as 6.55% and 0.36% respectively as listed in Table 2-1.

5-3 Zwitterionic Polymerization of 1-[(4-Carboxyphenyl)-methyl]Quinuclidinium Inner Salt

The zwitterionic polymerization was carried out for both hydrated and anhydrous zwitterion I. The procedure was rather simple: The hydrate or anhydride sample (0.4-0.5 g) was added into a polymerization tube, then sealed in N_2 or under a vacuum of 0.1 mmHg or continuously evacuated at 0.1 mmHg pressure without sealing the tube. The polymerization tube was kept in an oil bath at a selected temperature for a specified period to allow the polymerization to occur. The temperature varied from 170 to 240^{o}C. When the polymerization was completed, a semitransparent strong plastic-like material colored from white to yellow was formed.

Since the zwitterion polymerized before it melted, some of the starting material powder (less than 1%) was always left unreacted. To purify the polymer, 10 ml of methylene chloride was used to dissolve the polymer. The zwitterion was not dissolved by methylene chloride and was removed

either by centrifugation or filtration. The clear filtrate was added to in 100 ml of Et_2O to precipitate the polymer. The polymer precipitated out as a fabric- or plastic-like material.

5-4 The Acetylation of Polymer II

Polymer II (0.1 g), pyridine (0.1 ml) and acetyl chloride (0.15 ml) were dissolved in 3.0, 0.5 and 1.0 ml methylene chloride respectively. The pyridine solution was slowly added to the polymer solution with stirring at ambient temperature followed by addition of the acetyl chloride solution was added. The reaction mixture became brownish in color and the polymer precipitated out as a brown viscous material.

The polymer precipitate was dissolved in 4 ml of a mixed solvent of 1:1 water/acetone (v:v) and added to 20 ml of 3M NaOH to afford a white-yellow solid. The precipitate was washed with distilled water, then vacuum dried.

5-5 The Measurement of Molecular Weight

Since the polymer had a relatively low molecular weight and dissolved in various solvents, such as toluene, methylene chloride, chloroform, tetrachloroethane and 1,2,4-trichlorobenzene, a UIC 070 Vapor Pressure Osmometer was used to measure the molecular weight. Chloroform was chosen as solvent because of its high sensitivity, the concentration of the polymer solution used for the

measurement was 3-10%, and the measurement was carried out at 40°C. The results are listed in Table 4-1.

The molecular weight measurement was also performed by GPC using a Water 150-C ALC/GPC. This method was not applicable to our system, since there is a rather strong interaction between the polymer and the gel of the GPC column which prevents polymer flow.

5-6 Thermal Analysis

5-6.1 The Thermal Gravimetric Analysis (TGA)

TGA was performed on the hydrate of zwitterion I to determine the amount of water of hydration and stability of zwitterion I. A Dupont 990 Thermal Analyzer coupled to a 950 Thermogravimetric Analyzer module was used for the measurement. The hydrate of zwitterion I (10.0-15.0 mg) was weighed in an aluminum pan in the TGA module, heated to 240°C at a rate of 10°C/min. under a nitrogen atmosphere with a flow rate of 50 ml/min. The amount of water of hydration was measured as 6.8% which corresponded to 1.0 mole of water of hydration.

5-6.2 Differential Scanning Calorimetry (DSC)

DSC was carried out with a Dupont 990 coupled with a 910 Differential Scanning Calorimeter. DSC was performed on the hydrate of zwitterion I as well as polymer II. Zwitterion I (8 to 10 mg) or polymer II (15 to 20 mg) was heated from 25 to 340°C under a N_2 flow (flow rate of 50

ml/min.).

5-7 Nuclear Magnetic Resonance Spectroscopy

5-7.1 ^{1}H and C^{13} NMR Spectroscopy

Spectra were obtained on an IBM WP 200SY FT-NMR spectrometer using a 5-mm dual $^{13}C/H^{1}$ probe. All ^{1}H spectra were obtained at 200.1 MHz and ^{13}C spectra at 50.3 MHz.

5-7.2 Distortionless Enhancement by Polarization Transfer (DEPT) Spectroscopy

The spectrum was taken by using the following standard pulse sequence:

^{1}H: D_1—90^{0}—1/2J—180—$1/2J_{C-H}$—P_0—$1/2J_{C-H}$—BB

^{13}C:————————90^{0}————180^{0}————FID

where D_1 is the relaxation delay, P_0 is a pulse width whose value depends on the desired multiplicities selection. In our experiment, a D_1 of 2 sec. and $P_0=135^{0}$ was used. When $P_0=135^{0}$, the signals of positive intensity are for the carbons bonded to an odd number of protons, the signals of negative intensity are for the carbons bonded to even number of protons, and the carbons which do not bonded to any protons have zero intensity. J_{C-H} is the one bond J scalar coupling constant between carbon and hydrogen; J_{C-H} of 135 Hz was used for the experiment.

5-7.3 ^{1}H-^{1}H Correlated Spectroscopy (COSY)

The COSY spectrum was obtained by the use of the

standard pulse sequence:

^1H: D_1——90^0——D_0——90^0——FID

D_1 is the relaxation delay between each experiment and D_0 is the delay between the two 90^0 pulses. The frequency axes F_1 and F_2 contain the ^1H chemical shift values while the 1-D spectrum appears along the diagonal. Smaller off-diagonal cross peaks arise from coupling between the protons. A total of 256 experiments of 1K data points were collected, the number of scans was 16, the sweep width was 2500Hz, and the relaxation delay was 3 seconds.

5-8 Infrared Spectroscopy (IR)

IR spectra were recorded on a Bio-Rad Digilab FTS-40 spectrometer. Depending on the the sample type, a KBr pellet or NaCl plate holding a thin film of sample deposite was used in order to obtain the IR spectra.

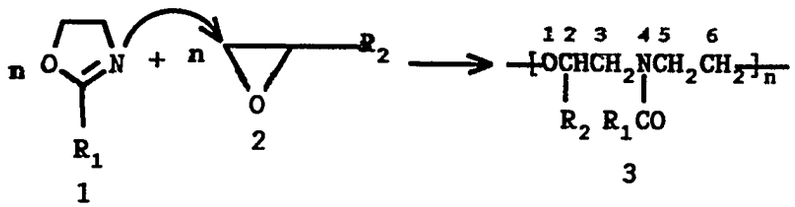
Part II

Alternating Copolymerization of

2-Substituted-2-Oxazoline and Epoxide

Chapter 6 INTRODUCTION

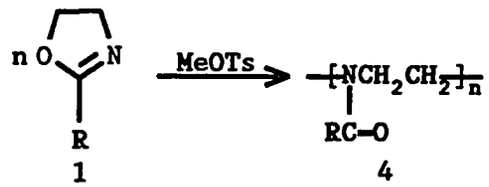
Copolymerization of 2-substituted-2-oxazolines and epoxides have been investigated in our laboratory in an effort to produce the alternating copolymer 3, poly[2-alkyl-4-alkanoyl-1-oxa-4-azahexanediyl].



Copolymer 3 is of considerable interest. When R_2=H, hydrolysis of the carbonyl group would yield a copolymer of ethylene oxide and ethylene imine (whose homopolymers are both water soluble) which may show interesting thermal and solubility behavior. The unhydrolyzed polymer should show interesting surfactant properties, if one employs a long hydrocarbon chain for the R group.

6-1 Background

Homopolymerizations of 2-substituted-2-oxazolines and epoxides have been achieved. The homopolymerization of 2-substituted-2-oxazoline was accomplished through cationic ring-opening polymerization[1]:



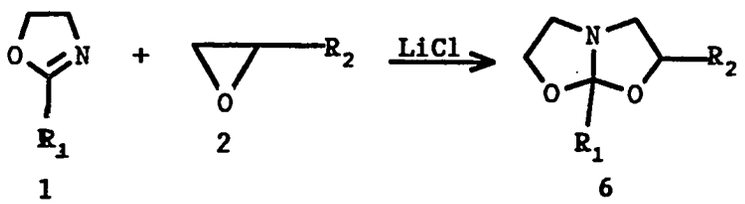
1 4

Epoxide have been polymerized by using anionic initiators[2]:

2 5

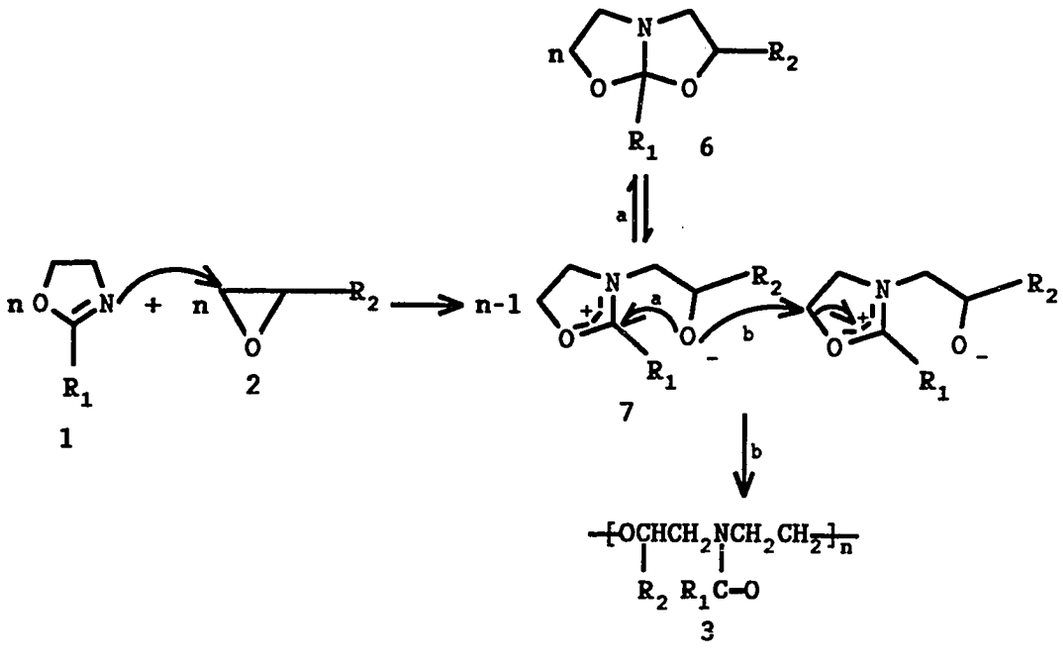
Cationic initiators also polymerize epoxides.

Feinauer and Seeliger reported the reaction of various 2-substituted-2-oxazolines with ethylene oxide and monosubstituted ethylene oxides to form a bicyclic compound 6, tetrahydro-2,7$_a$-substituted-7$_a$H-oxazolo[2,3-b]oxazole, by the following reaction[3]:



1 2 6

The yield of the bicyclic compound was in the range 17.0-69.2% depending on R_1 and R_2. A brown viscous distillation residue was also obtained. If the brown residue is the alternating copolymer of the oxazoline and epoxide, one can postulate that reaction proceeds through the zwitterion intermediate 7:

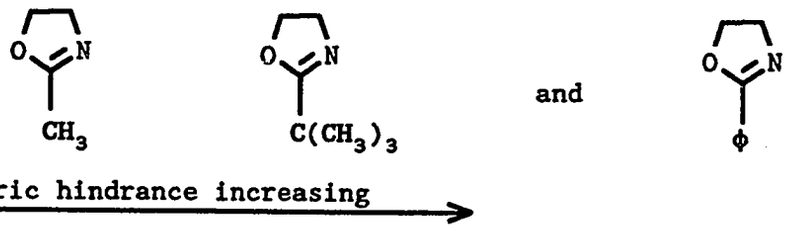


Zwitterion intermediate 7 either undergoes ring closure to form the bicyclic compound 6 or reacts with itself to form the alternating copolymer 3 in a competitive reaction. The formation of the polymer gives an explanation for the low yield of bicyclic compound in many of the experiments.

Our interest centered on preparing copolymer 3, not the bicyclic compound 6. The approach to minimizing formation of the bicyclic compound involved increasing the sizes of R_1 and R_2, especially R_1, which would increase the steric hindrance for cyclization. Polymerization would then become the major reaction since R_1 and R_2 impose less steric hindrance on polymerization (path (b)) than cyclization (path (a)).

In our experiments, the 2-substituted-2-oxazolines used

were:

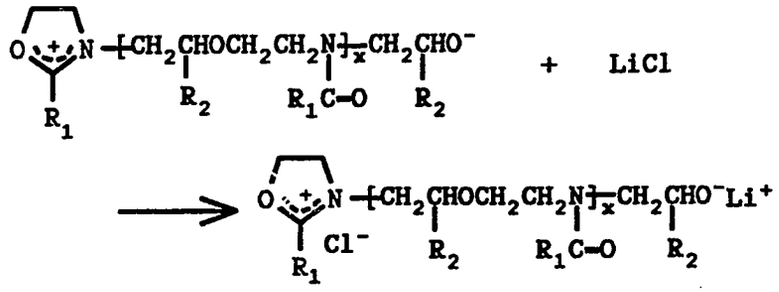


2-Phenyl-2-oxazoline was used in order to compare the reactivity between alkyl and aromatic substituted oxazoline.

The epoxides used were:

The reason for using these two epoxides was to compare the reaction activity between alkyl and aromatic substituted epoxides. There was also a different steric hindrance involved in the two epoxides.

One of the disadvantages of previous zwitterion polymerizations is the inability to obtain high molecular weight polymers. This is perhaps due to the increasing charge separation between the positive and negative ends of a growing zwitterion and, also the initial zwitterion may not be stable enough. One way to overcome this is to use a salt such as LiCl to help stabilize the zwitterions ionic charge:



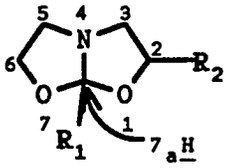
Since both of 2-substituted-2-oxazoline and epoxide can undergo homopolymerization as mentioned previously, it is quiet possible that homopolymerzation of either oxazoline or epoxide will occur during the zwitterion polymerization process. This would affect the formation of the alternating polymer structure. The oxazoline and epoxide may form a stable bicyclic amide acetal 6 in the early stage. This would result in too short a lifetime for the zwitterion intermediate 7 to undergo self-reaction to form the alternating polymer 3. There is a good possibility for anionic polymerization of the epoxide since the oxazoline is a base. The bicyclic amide acetal 6 formed at the early stage of the reaction can react to each other to open one or both of the ring to form a polymer.

In order to obtain a alternating copolymer, it may be necessary to separate the bicyclic compound first followed homopolymerization with a catalyst or initiator to force both rings of 6 to open to produce the polymer 3.

6-2 The Background of Synthesis and reactions of tetrahydro-2,7,-substituted-7,H-oxazolo[2,3-b]oxazole

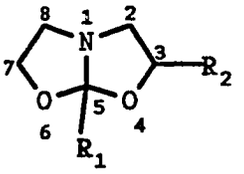
The IUPAC nomenclature of compound 6 is tetrahydro-

2,7$_a$H-substituted-oxazolo[2,3-b]oxazole:



6

Originally, it was named as 4,6-dioxa-1-azabicyclo[3,3,0]-octane. For convenience it will be referred to as 3,5-substituted-bicyclic amide acetal[4] in this dissertation:



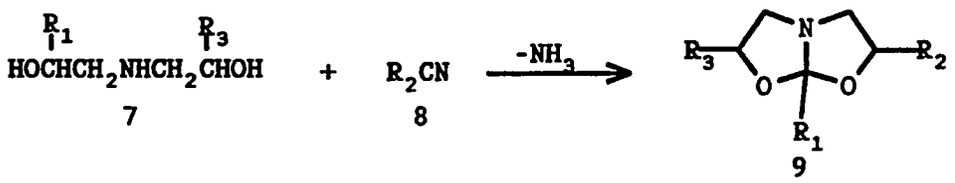
6

6-2.1 Synthesis of bicyclic amide acetals

Two approaches have been used to prepare the bicyclic amide acetals:

(1) Cycloaddition of epoxides to 2-oxazolines as mentioned earlier[3,5].

(2) Reaction of iminodiethanols with aliphatic nitriles in the presence of a catalystic amount of the sodium alcoholate derived from the iminodiethanol reactant[6].



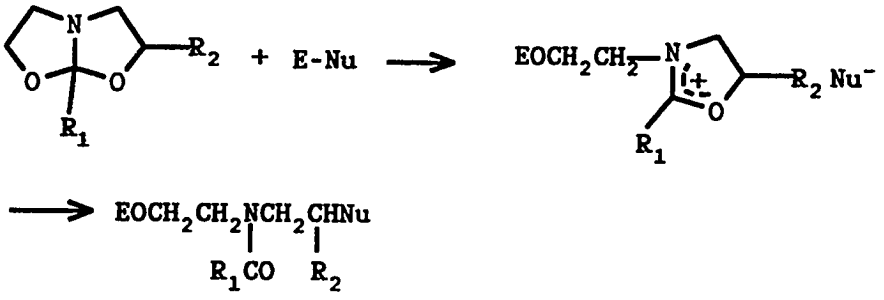
7 8 9

The literature indicates that both approaches give a diastereisomeric mixtures. Separation of the enantiomers has not been attempted.

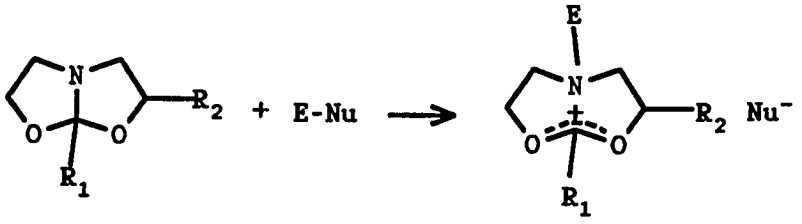
6-2.2 Reactions of bicyclic amide acetals

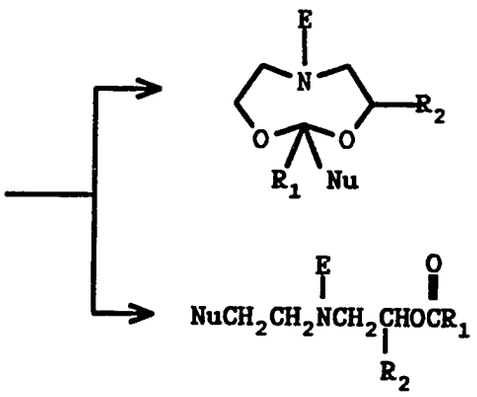
The amide acetals are very reactive compounds in reactions with carboxylic acids, phenols, amines, aldehydes and alkylating agents[5]. The reactions proceed either with C—O or C—N cleavage.

(1) Reactions that proceed with C—O cleavage:



(2) Reactions that proceed with C—N cleavage:



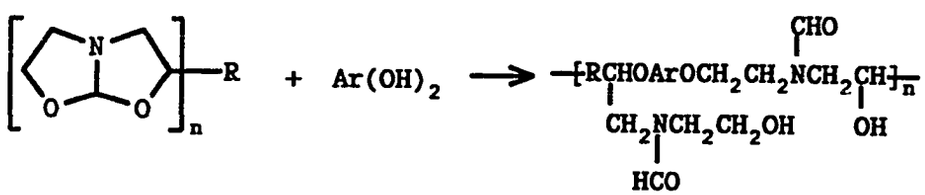


6-2.3 Polymerizations that Employed Bicyclic Amide Acetals

Recently, bicyclic amide acetals were used as monomers in copolymerizations.

(1) Bicyclic amide acetals react with maleimide or maleimide derivatives to give a polymeric material[7]. The polymeric products have been found to be insoluble in most common solvents indicating a cross-linked structure, although no definite structure has been assigned to these compounds.

(2) Bis(bicyclic amide acetals) react with bis- or poly-phenolic compounds to produce poly(ether amide)[8]:



(3) Bicyclic amide acetals react with saturated carboxylic acid anhydrides to give linear, low molecular weight polymers[9].

(4) Bicyclic amide acetals react with maleic anhydride

polymers to cause cross-linking[10].

These are patented results with little information about the structures of the polymers produced, their characterizations or mechanistic studies of the polymerizations.

6-3 Our Research Agenda

In our research, two approaches are used to prepare the alternating copolymer: (1) directly copolymerization of 2-substituted-2-oxazline and epoxide using LiCl as a catalyst (Chapter 9); and (2) preparing 3,5-substituted-bicyclic amide acetals followed by their homopolymerization (Chapter 9 and 10) with or without an initiator.

Because our work concerned the copolymerizations between epoxides and oxazolines, epoxides and 2-oxazolines were used to synthesize the bicyclic amide acetals.

Our major interest was in the complete characterization of monomers and polymers prepared as well as mechanistic studies of the reactions involved.

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[1] T. Seagusa and S. Kobayashi, Makromol. Chem., Macromol. Symp. 1, 23 (1986).

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[8] A. B. Geol, U.S. Patent 4,639,505 (1987).

[9] R. Feinauer, Angew. Chem. Int. Ed. 6, 178 (1967).

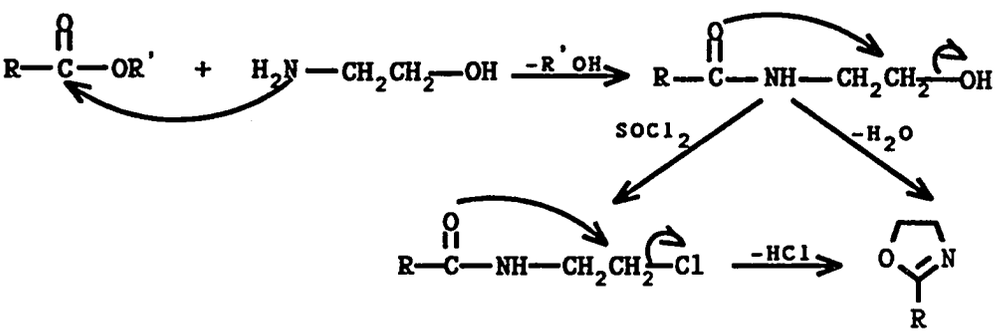
[10] A. B. Geol, U.S. Patent 4,539,376 (1985)

Chapter 7 SYNTHESIS OF 2-SUBSTITUTED-2-OXAZOLINE

Of the three 2-substituted-2-oxazolines which were used in our research, 2-methyl-, 2-*t*-butyl-, and 2-phenyl-oxazolines, only 2-methyl-2-oxazoline was commercially available, the other two had to be synthesized.

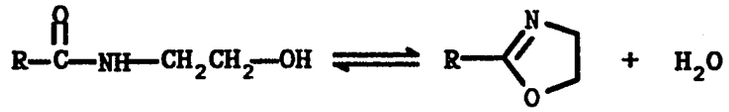
7-1 Background of Oxazoline Synthesis

Synthesis of 2-substituted-2-oxazoline is very important considering its vast application in organic synthesis[1]. Many different methods have been developed for preparing various 2-oxazolines[2,3]. Most syntheses of oxazolines are based on N-(2-hydroxyalkyl)amide, which is readily prepared by treatment of carboxylic acids, acid chlorides or their esters with the amino alcohols. Usually the N-(2-hydroxyalkyl)amide is treated with reagents such as $SOCl_2$, RSOCl, $COCl_2$, or $PO(OR)_2Cl$ in order to replace the hydroxyl group by a group X which can be eliminated more readily.



Obviously the simplest way of preparing an oxazoline is

thermal cyclization of N-(2-hydroxyalkyl)-amides directly, but the yields are low. The low yields may be due to an unfavorable equilibrium for cyclization[4]:

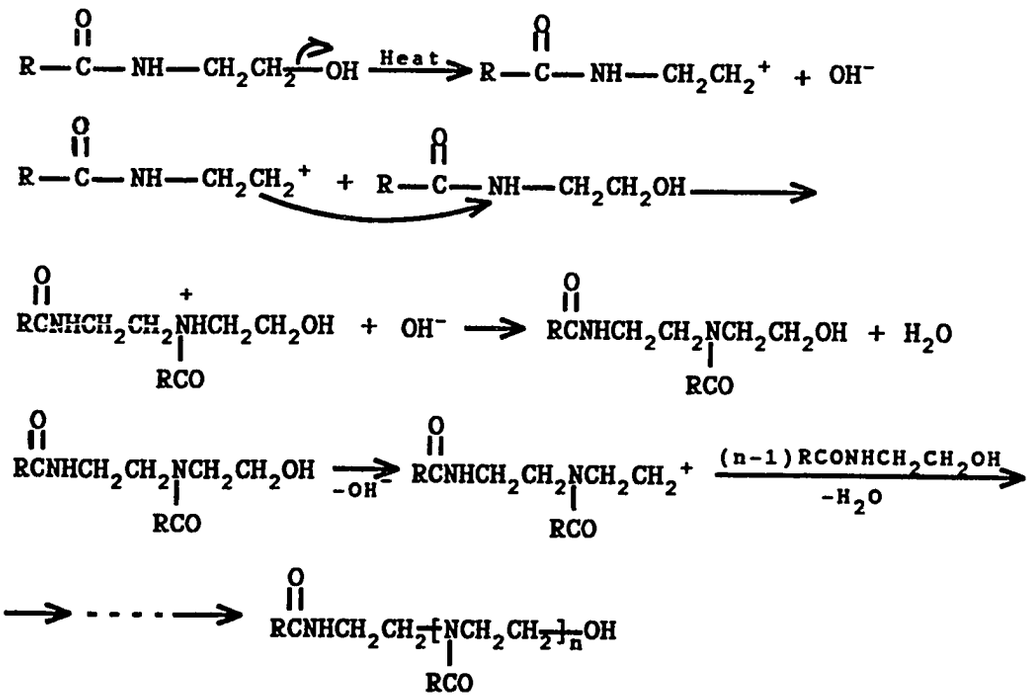


This equilibrium normally lies well to the left, but it shifts towards the right at high temperatures, and is established so rapidly on alumina that side reactions cannot interfere. It was also reported that dehydration could be carried out in the gas phase to drive the equilibrium to the right side[3]. Although the conversion is increased, the reaction conditions are much more complicated in the gas phase and thermal stability of the oxazoline is dubious.

According to published results, 2-substituted-2-oxazolines such as 2-methyl- and 2-ethyl-oxazolines were obtained in yields of 22.5-25.9%[5], using the corresponding carboxylic acid and ethanol amine . In the thermal cyclization step, the distillate amounted to about 75% of the N-(2-hydroxylalkyl)amide which was one of the reasons for the low yields. The synthesis of *t*-BuOXA has also been reported by the same method[6]. However, when we tried to synthesize *t*-BuOXA in the same manner, the yield was as low as 10%, and 30% of the starting material was converted to a brown viscous material during the thermal cyclization step. There were two facts which lowered the yield: (1) the

formation of the viscous material; (2) some *t*-BuOXA cannot be recovered from water because of its high solubility in water.

The formation of the viscous material indicated that some kind of polymerization occured during distillation at the high temperature. It is mentioned in the introduction that oxazolines can be polymerized through a cationic polymerization mechanism, therefore, a cationic species may involved in the thermal polymerization during distillation. The polymerization is postulated as cationic polymerization as given in the following scheme:



If this occurs, an anionic inhibitor, such as sodium hydroxide, should terminate the polymerization, and it did prevent the formation of the viscous material in our

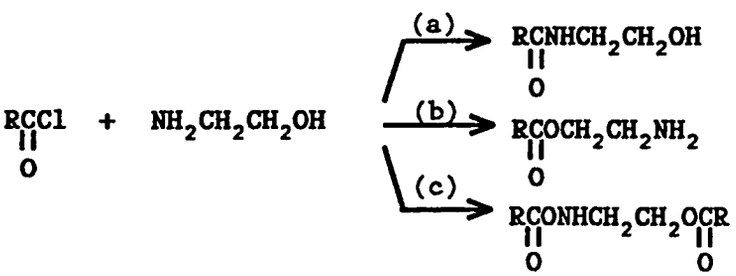
experiments.

7-2 Synthesis of *t*-BuOXA

In our research, synthesis of *t*-BuOXA has been achieved by using ethanolamine and trimethylacetyl chloride as starting materials through a two-step reaction: (1) preparing trimethylacetyl-2-amino ethanol from the condensation reaction of trimethylacetyl chloride and ethanolamine; (2) dehydration of trimethylacetyl-2-amino ethanol to produce *t*-BuOXA by using sodium hydroxide as a catalyst.

7-2.1 Condensation Reaction of Trimethylacetyl Chloride and Ethanolamine

Theoretically speaking, condensation of an acid chloride with ethanolamine can occur in three different ways: at the NH-end or OH-end or by reaction at both NH- and OH-ends of ethanolamine:



Since the NH-end is a better nucleophile than OH-end reaction (a) should predominate.

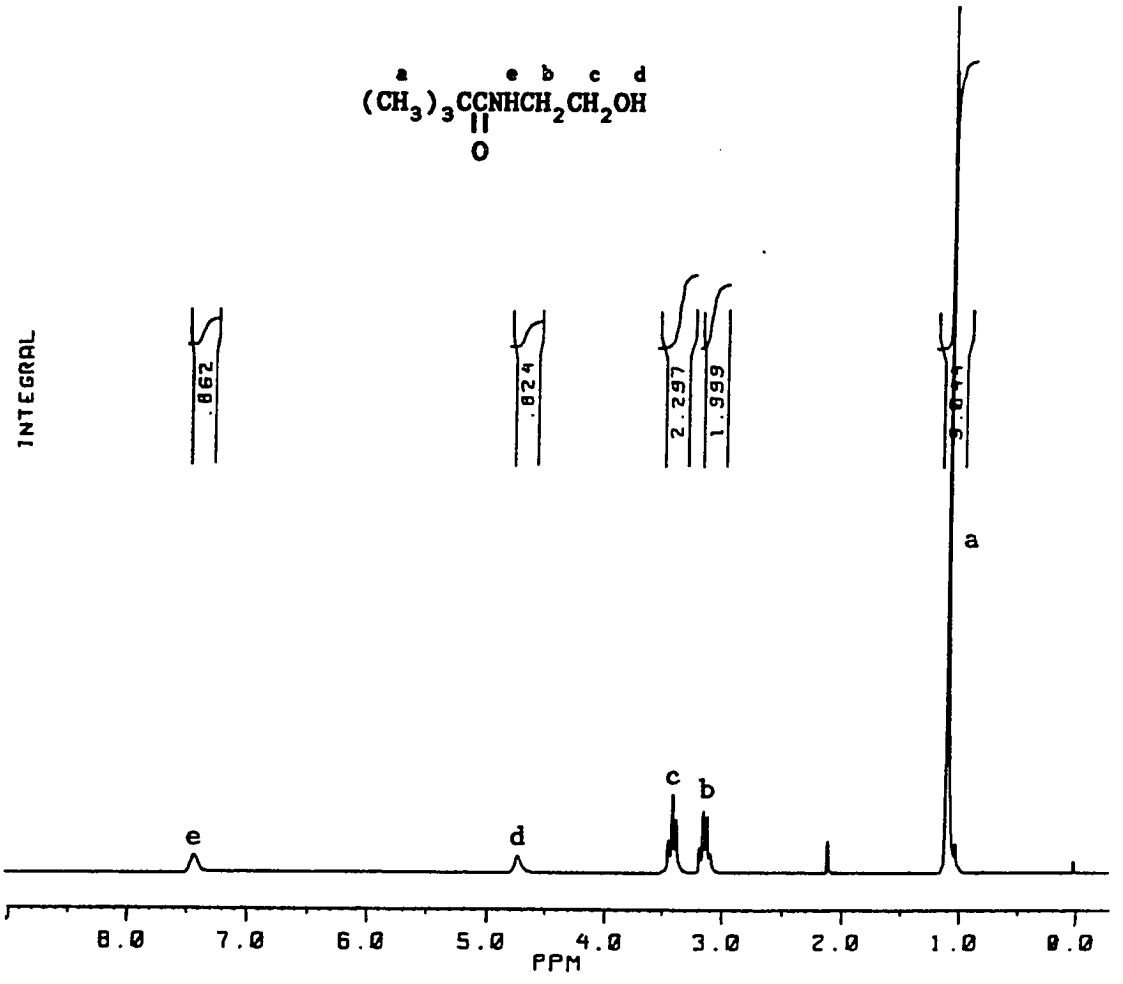


Figure 7-1 200.1-MHz ^{1}H NMR spectrum of trimethylacetyl-2-amino ethanol in DMSO-D_6 at 25°C.

It was observed in our experiments that when the condensation reaction of ethanolamine and trimethylacetyl chloride was carried out under mild conditions, i.e., at low temperature (<25°C) and using dilute solutions (3M) of reactants, only trimethylacetyl-2-amino ethanol was formed through path (a) with a yield of 83%. Figure 7-1 and 7-2 are the ^{1}H and ^{13}C NMR spectra respectively for this

compound.

The assignments for the ^{1}H NMR spectrum (Figure 7-1) are: singlet at 1.12 ppm (3H): methyl protons H_a, quartet (J_{cb}=5.8 Hz, J_{eb}=5.8 Hz) at 3.15 ppm (2H): methylene protons H_b, triplet (J_{bc}=5.8 Hz) at 3.40 ppm (2H): methylene protons H_c, broad singlet at 4.75 ppm (1H): hydroxy proton H_d, broad singlet at 7.44 ppm (1H): amide proton H_e.

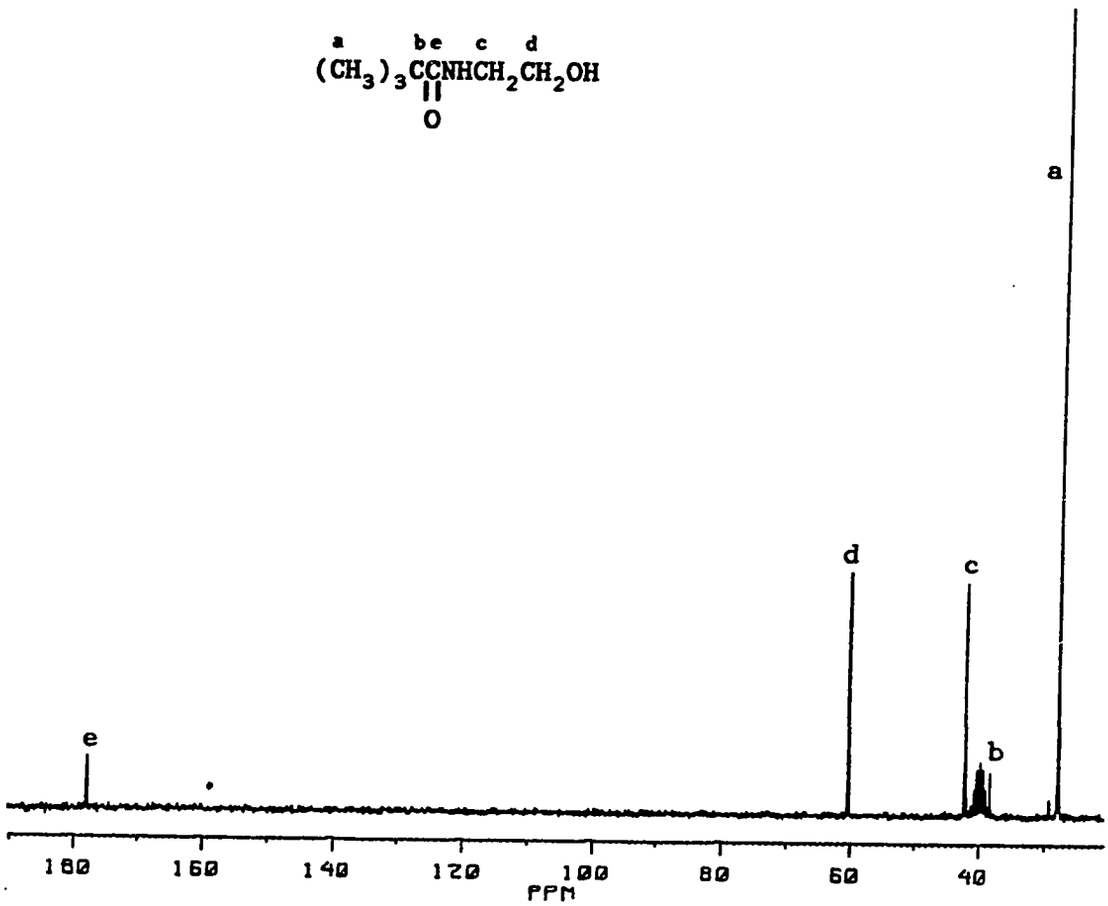


Figure 7-2 50.3-MHz ^{13}C NMR spectrum of trimethylacetyl-2-amino ethanol in DMSO-D_6 at 25°C.

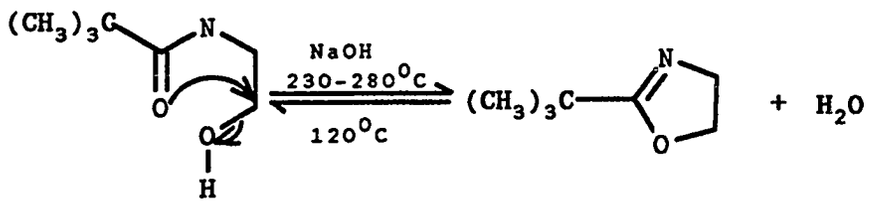
The assignment for the ^{13}C NMR spectrum (Figure 7-2)

The assignment for the ^{13}C NMR spectrum (Figure 7-2) are as follows: peak at 28.0 ppm: the methyl carbons C_a, peak at 38.3 ppm: tertiary carbon C_b, peak at 42.5 ppm: methylene carbon C_c, peak at 60.6 ppm: methylene carbon C_d, peak at 178.1 ppm: carbonyl carbon C_e.

When trimethylacetyl chloride and ethanolamine were directly mixed at above 30°C, the condensation selectivity decreased and a mixture of products were obtained based on ^1H NMR analysis. The mixture is probably formed by paths (a), (b), and (c) (page 65), no further experiments have been done to separate the mixture.

7-2.2 Cyclization of Trimethylacetyl-2-Amino Ethanol

The cyclization of trimethylacetyl-2-amino ethanol was found to proceed in a reversible manner:



At low temperature (120°C), the equilibrium lies well towards the left. When the trimethylacetyl-2-amino ethanol is heated above 230°C, by distilling *t*-BuOXA and water out of the system, the equilibrium can be driven towards cyclization. When trimethylacetyl-2-amino ethanol was thermal decomposed, only 70% (by weight) was distilled out and the other 30% became a dark brown viscous material. The

polymerization of *t*-BuOXA at high temperature. As soon as NaOH was introduced into the system, there was no formation of the viscous material, the equilibrium could be driven to the right side by removing water and *t*-BuOXA, and conversion of the cyclization reaction was close to 100%. No further experiment has been done on how NaOH inhibited the formation of the viscous material, since our interest was increasing the yield of *t*-BuOXA. Figures 7-3 and 7-4 are the ^{1}H and ^{13}C NMR spectra of *t*-BuOXA respectively.

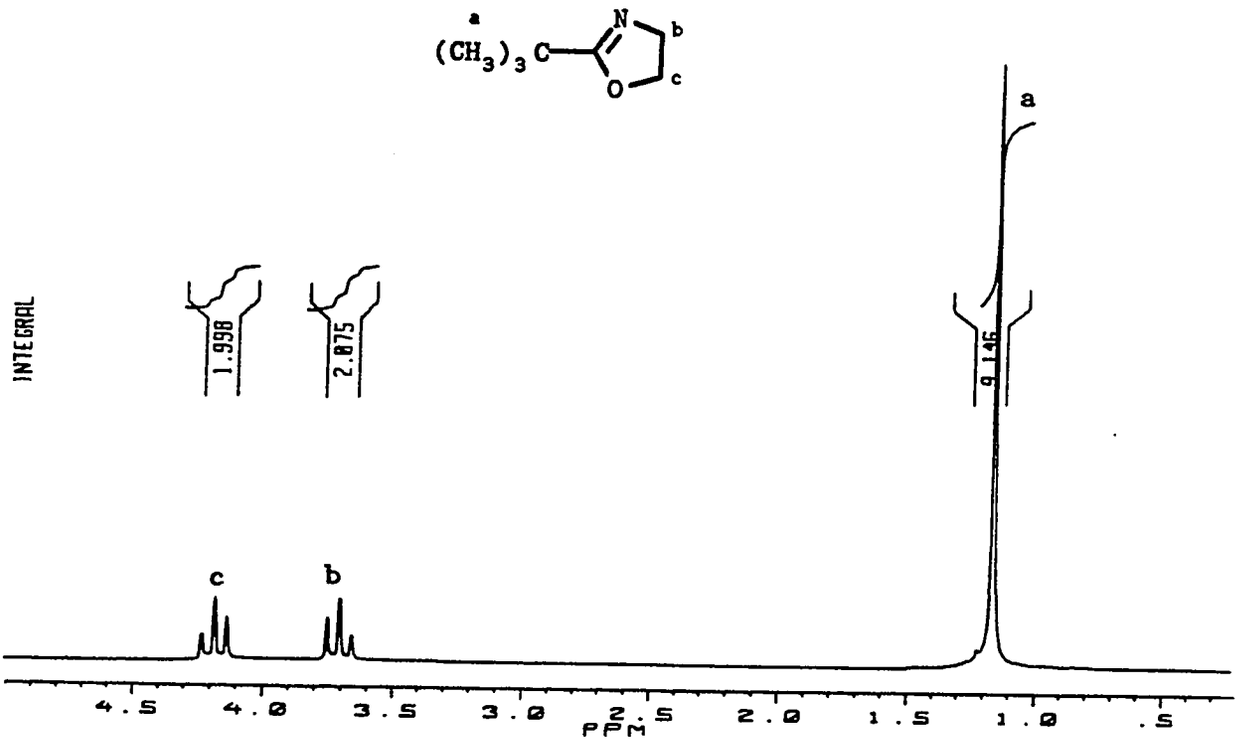


Figure 7-3 200.1-MHz ^{1}H NMR spectrum of *t*-BuOXA in DMSO-D_6 at 25°C.

The assignments for the ^{1}H NMR spectrum (Figure 7-3) are as follows: singlet at 1.17 ppm (9H): methyl protons H_a,

triplet (J_{cb}=10.0 Hz) at 3.71 ppm (2H): methylene protons H_b, and triplet (J_{bc}=10.0 Hz) at 4.18 ppm (2H): methylene protons H_c.

The assignments for the ^{13}C NMR spectrum (Figure7-4) are as follows: peak at 28.0 ppm: methyl carbons C_a, peak at 43.1 ppm: tertiary carbon C_b, peak at 54.4 ppm: methylene carbon C_c, peak at 67.1 ppm: methylene carbon C_d, and peak at 173.0 ppm: carbon C_e.

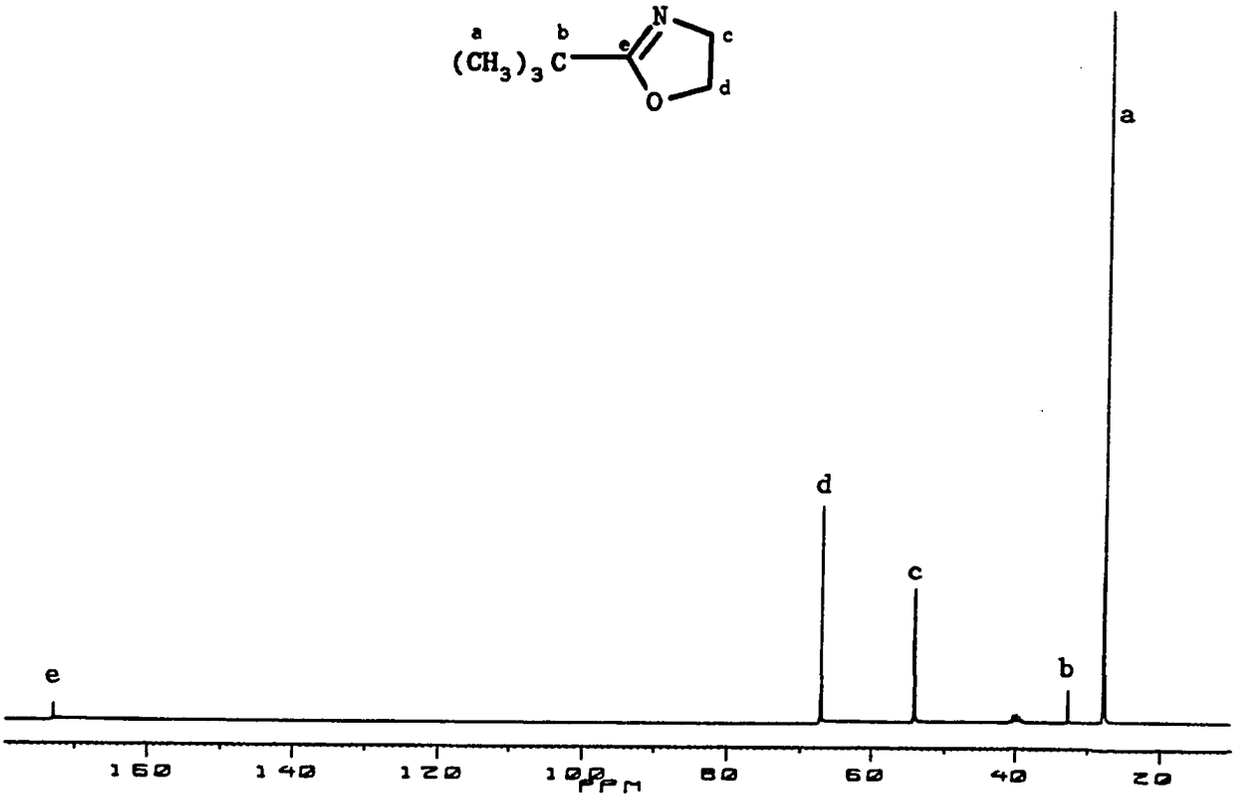


Figure 7-4 50.3-MHz ^{13}C NMR spectrum of *t*-BuOXA in DMSO-D_6 at 25°C.

Elemental analysis supported the structure of both trimethyl acetyl-2-amino ethanol(A) and *t*-BuOXA(B), see Table 7-1.

Table 7-1 Elemental analysis results of trimethylacetyl-2-amino ethanol (A) and t-BuOXA (B)

Compound	Theoretical			Experimental		
	C%	H%	N%	C%	H%	N%
(A)	57.93	10.34	9.66	57.95	10.56	9.72
(B)	66.14	10.24	11.02	66.10	10.52	11.17

7-2.3 Experimental Part

Preparation of trimethylacetyl-2-amino ethanol[7]: Trimethylacetyl chloride (1.62 mole) dissolved in 400 ml of toluene was added to a solution of ethanolamine (1.68 mole) in 300 ml of distilled water to form an emulsion. The emulsion was stirred and cooled in an ice-water bath, then 18% aqueous solution of sodium hydroxide (1.68 mole) was gradually added in the emulsion. The reaction mixture was stirred intensely with a magnetic bar for four hours at 10°C to allow the reaction to come to complete. When the stirring was stopped, the emulsion separated to two layers; the top clear toluene layer was discarded and the water was evaporated from the cloudy water-layer portion, leaving a white paste. The white paste was dissolved in 400 ml of acetone and filtrated to remove the indissoluble NaCl. The filtrate was cooled in an acetone/dry ice bath to allow crystallization to occur. After 4 hours, a white crystalline product was formed. The crystal was collected by vacuum filtration, and dried under vacuum. The white crystal was trimethylacetyl-2-amino ethanol with a purity of

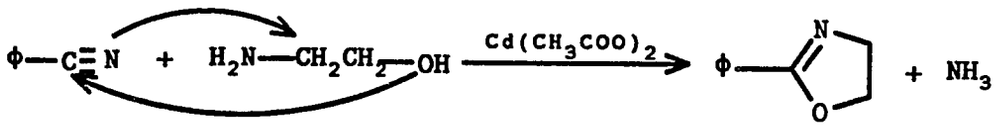
crystal was trimethylacetyl-2-amino ethanol with a purity of 99% and a melting point of 38°C. The product was 195.0 g, i.e., the yield was 83%.

Preparation of *t*-BuOXA: trimethylacetyl-2-amino ethanol (195 g) was mixed with sodium hydroxide (5.0 g) and then placed in the flask of a distillation set-up. The flask was heated to 250-270°C to cause distillation of *t*-BuOXA and water. More than 90% of the flask contents distilled over. KOH (60 g) was addedd to the crude product to break down the liquid into two layers, the top layer was *t*-BuOXA and the bottom layer was mixture of water, *t*-BuOXA, and KOH. The *t*-BuOXA layer was dried with another 5 g of KOH and then distilled from CaH_2 to yield 85g colorless liquid. The yield was 50%, b.p. 141-142°C (literature 141-142°C)[3], density 0.934 g/ml, and the purity 99% according to ^1H NMR spectroscopy. Due to the loss of *t*-BuOXA into the bottom aqueous layer in the separation step, the yield was not as high as expected.

The synthetic method described here could also be used as a synthetic approach for other 2-alkyl-2-oxazolines.

7-3 Synthesis of 2-Phenyl-2-Oxazoline

The synthesis of 2-phenyl-2-oxazoline is based on the method of Witte and Seeliger[8]:



Experimental procedure: Benzonitrile (102.1 ml,1.0 mole), ethanolamine (78.5 ml, 1.3 mole), and $Cd(CH_3COO)_2$ (6.66 g, 0.0250 mole) are added to a two-neck flask fitted with a reflux condenser. The top of the condenser was connected to a hydrochloric acid reservoir which trapped the NH_3 released from the reaction. Upon refluxing the reaction mixture at 110-120°C for 25 hrs, the colorless reaction mixture changed to a dark red color. Distillation yielded a colorless crude product at 124-127°C/15 mmHg. The yield was 80% (the reported yield was 85%).

The crude product was purified by fractional distillation from potassium hydroxide, and the pure product had a purity of more than 99% according to ^1H NMR analysis.

7-4 Purification of 2-methyl-2-oxazoline

The commercially available 2-methyl-2-oxazoline was purified by fractional distillation from potassium hydroxide. The pure 2-methyl-2-oxazoline was colorless and had a purity of >99% based on ^1H NMR analysis.

REFERENCE:

[1] S. Kobayashi and T. Seagusa, Ring-Opening Polymerization, 2, Chapter 11, Elservier Applied Science, Essex, England (1984).

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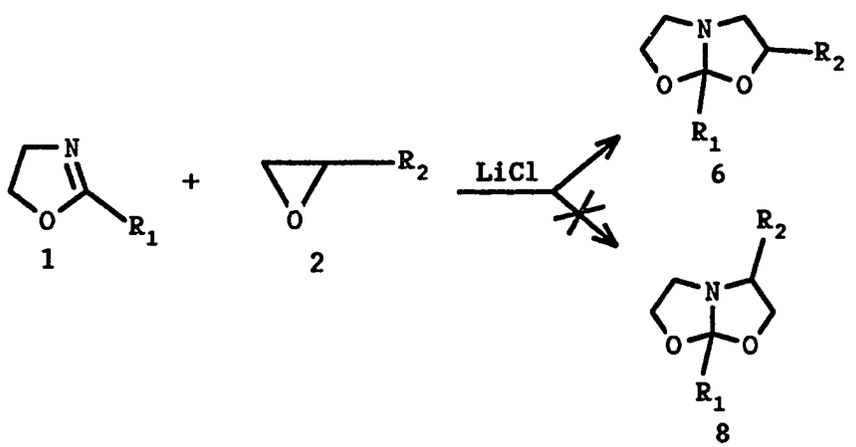
CHAPTER 8 INVESTIGATION OF THE REACTION BETWEEN 2-SUBSTITUTED-2-OXAZOLINES AND STYRENE OXIDE

8-1 INTRODUCTION:

As we mentioned in Chapter 6, there are two approaches for the preparation of bicyclic amide acetals and our approach is Approach 1—synthesis of bicyclic amide acetals by cycloaddition of epoxides to 2-oxazolines. In Feinauer and Seeliger's papers[1,2], it was claimed that the bicyclic amide acetals were formed according to the reaction:



The following statements were made in their papers: (1) only 6 was formed because of steric hindrance of R_2 which prevented the α-ring-opening of the epoxide ring; (2) compound 6 is a diastereomeric mixture of the cis and trans forms; and (3) LiCl was used as a catalyst. What was not covered were: (1) there was lack of proof about why the α-ring-opening reaction did not occur, (2) the separation of

the cis and trans forms was never achieved, (3) the NMR spectral assignments were dubious, and (4) the role of LiCl as a catalyst was not discussed.

In our research, 2-methyl-, 2-*t*-butyl- and 2-phenyl-2-oxazolines were reacted with styrene oxide and propylene oxide to prepare the bicyclic amide acetals. The influences of the catalyst(LiCl) and the substituent(R_1) of oxazoline on the ring-opening reaction of styrene oxide have been studied in detail, the separation of cis and trans forms has been achieved and complete NMR spectral assignments have been made for the prepared bicyclic amide acetals.

8-2 The Reaction of Cycloaddition of Epoxide to Oxazoline

The following pairs of reactants have been studied for preparing the corresponding bicyclic amide acetals under various reaction conditions using LiCl as a catalyst:

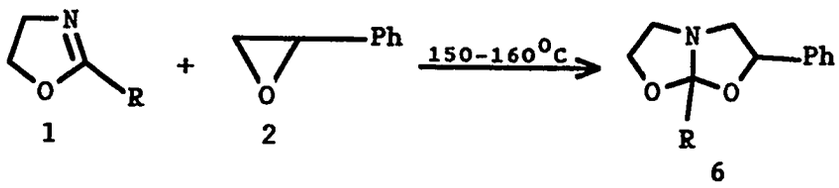
(1) 2-methyl-2-oxazoline and styrene oxide
(2) 2-*t*-butyl-2-oxazoline and styrene oxide
(3) 2-phenyl-2-oxazoline and styrene oxide
(4) 2-methyl-2-oxazoline and propylene oxide
(5) 2-*t*-butyl-2-oxazoline and propylene oxide
(6) 2-phenyl-2-oxazoline and propylene oxide

Among the six pairs, the cyclization reaction between the first three pairs occurred readily and gave a reasonable yield, but the reactions between the oxazolines and propylene oxide proceeded only to a limited degree, less than 10%. Since styrene oxide was more reactive than

propylene oxide, our subsequent work was carried out with the first three pairs.

8-2.1 Preparation and Characterization of Bicyclic Amide Acetals

The bicyclic amide acetals 6 were prepared by the following reaction:

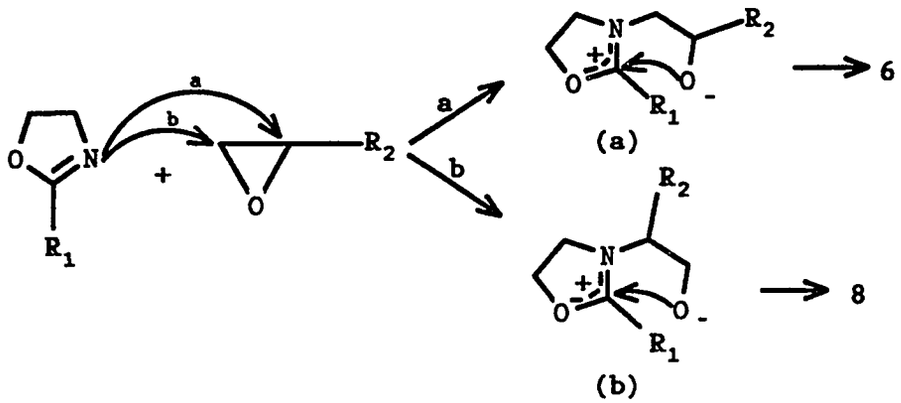


R = CH_3, $(CH_3)_3C$, and C_6H_5

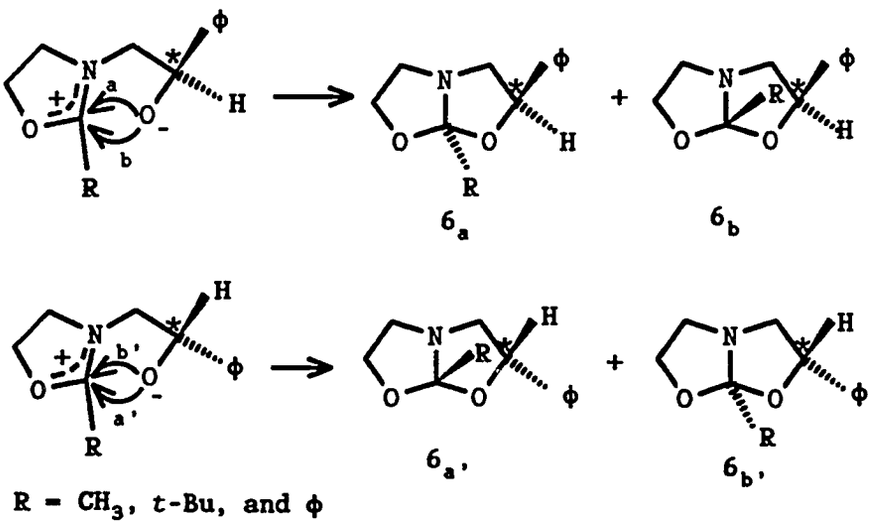
The crude products were obtained from the vacuum distillation of the reaction mixture, and the pure products 6 were obtained by crystallization of the crude products from ether at -40°C. By comparing and identifying the ^1H and ^{13}C NMR spectra (Figures 8-1, 8-2, 8-3, and 8-4) of the crude product and the pure product, it was confirmed that the crude product was a mixture of the bicyclic isomers, 6 and 8, while the recrystallized product contained only 6 as a mixture of cis and trans forms. 8 is the minor product and will be discussed later. The crude product containing 6 and 8 indicated that both α- and β-ring openings had occurred. This disagreed with what was reported in Feinauer and Seeliger's paper[1]. The results also showed that 6 was the major product, i.e., β-ring opening of the epoxide was

predominant, which is consistent with the literature on ring opening reactions of styrene oxide[3,4].

Based on the experimental results, the following reaction mechanism is proposed:



There are two ways for intermediate (a) to close the ring as shown below and because of the chiral center in the styrene oxide, four isomers can be formed:



R = CH_3, *t*-Bu, and ϕ

Since the trans-isomers 6_a and $6_{a'}$ or the cis-isomers 6_b and $6_{b'}$ are each a pair of enantiomers, and the chemical

shifts for enantiomers are the same, only two sets of chemical shifts should be observed for trans and cis isomers. Since the formation of the trans isomer involves less steric hindrance than the cis isomer, the trans isomer should be the major product. The ^{1}H NMR spectrum strongly support the expection. The ^{1}H and ^{13}C NMR spectra of recrystallized 5-methyl-3-phenyl-bicyclic amide acetal are shown as an example in Figure 8-1 and 8-2. Since the cis-methyl is above the benzene ring while trans-methyl is far away from the benzene ring of the bicyclic compound, the methyl group of the cis-isomer should have a lower chemical shift than the trans-isomer, which is exactly what is observed in the ^{1}H NMR (Figure 8-1), i.e., the methyl signal with lower intensity is at higher field. Two sets of peaks with different intensities can be observed for the trans- (higher intensities) and cis- (lower intensities) isomers, respectively, and some of the peaks are partially or completely overlapped which are understandable, since the trans- and cis-isomers are very similar structurally.

The assignments for the ^{1}H NMR spectrum (Figure 8-1) are as follows: singlet (a′) at 1.51 ppm: methyl protons of cis-isomer, $H_{a'}$, singlet (a) at 1.60 ppm: methyl protons of trans-isomer, H_a, triplet (b′) at 2.64 ppm: $H_{b'}$, the triplet is caused by the coupling of $H_{b'}$ with $H_{d'}$ and $H_{f'}$, triplet (b) at 2.84 ppm: H_b, the triplet is caused by the coupling of H_b with H_d and H_f, multiplet (c,c′) at 2.90-3.25 ppm: partially overlapped multiplet of H_c and $H_{c'}$, the multiplets

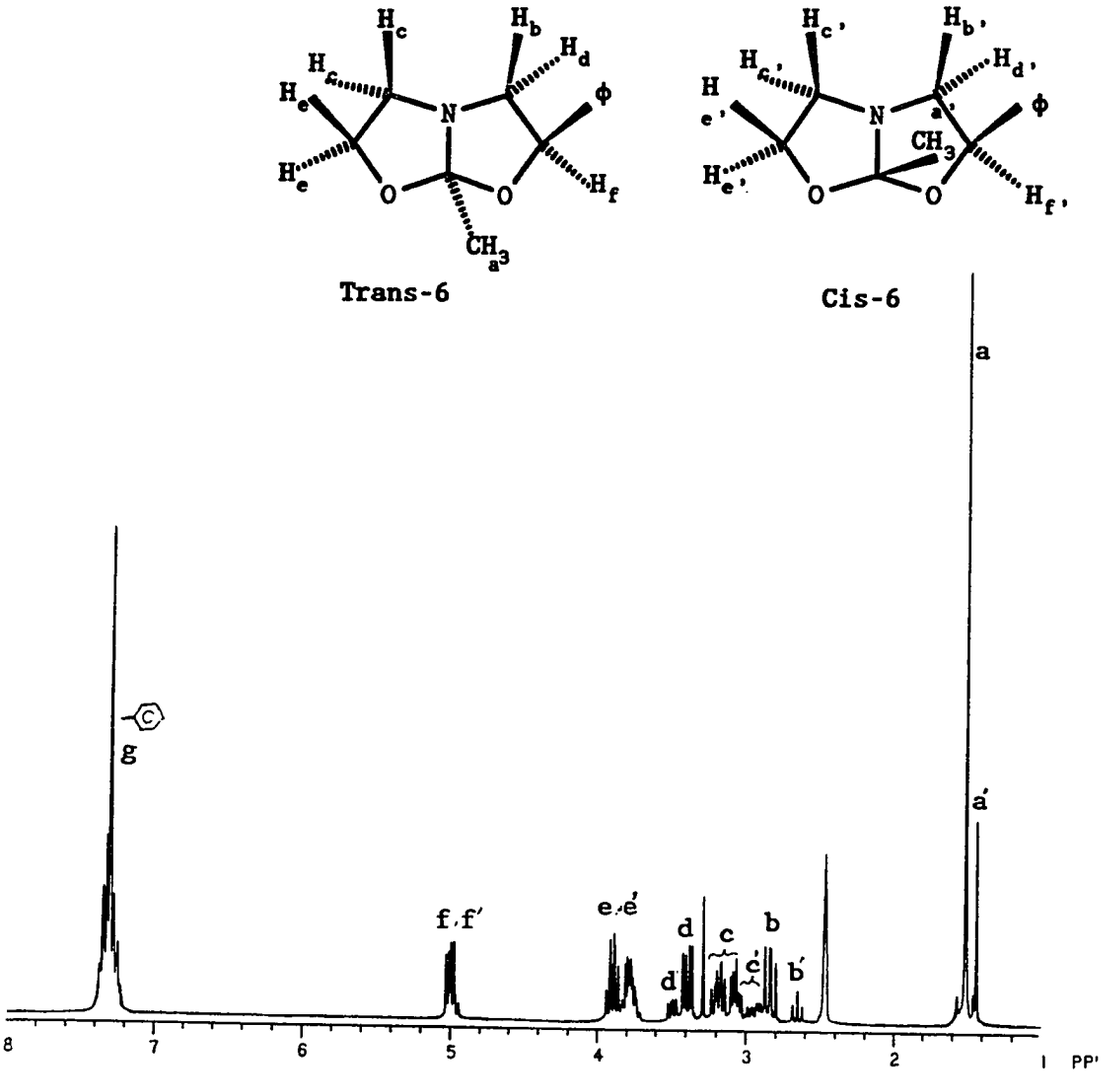


Figure 8-1 300-MHz ^1H NMR spectrum of 5-methyl-3-phenyl-bicyclic amide acetal in DMSO-D_6 at 25°C.

are caused by thecoupling between two H_c or $H_{c'}$ themselves and H_c with H_e or $H_{c'}$ with $H_{e'}$, quartet (d) at 3.38 ppm: H_d, the quartet is caused by the coupling of H_d with H_b and H_f, quartet (d') at 3.49 ppm: $H_{d'}$, the quartet is caused by the coupling of $H_{d'}$ with $H_{b'}$ and $H_{f'}$, multiplet (e,e') at

3.37-4.00 ppm: completely overlapped multiplet of H_e and $H_{e'}$, the multiplets are caused by the coupling between H_e or $H_{e'}$ themselves and H_e with H_c or $H_{e'}$ with $H_{c'}$, multiplet (f,f') at 4.80-5.10 ppm: partially overlapped quartets of H_f and $H_{f'}$, the quartets are caused by coupling of H_f with H_b and H_d or $H_{f'}$ with $H_{b'}$ and $H_{d'}$, multiplet (g) at 7.12-7.45 ppm: phenyl protons.

One might notice the large difference of chemical shifts between H_b and H_d or $H_{b'}$ and $H_{d'}$. This is explained by ring current effect since H_b or $H_{b'}$ is above the benzene ring while H_d or $H_{d'}$ is on the side of the ring. The chemical shift of the one which is above the ring (H_b or $H_{b'}$) moves upfield and the one which is on the side of the ring (H_d or $H_{d'}$) moves downfield.

The assignments for the ^{13}C NMR spectrum (Figure 8-2 (B)) are as follows: 25.0 ppm (a,a'): completely overlapped methyl carbons of trans- and cis-isomers, C_a and $C_{a'}$, 52.0 ppm peak (b'): cis-$C_{b'}$, 53.2 ppm peak (b): trans-C_b, 60.0 ppm peak (c'): cis-$C_{c'}$, 61.7 ppm peak (c): trans-C_c, 63.0 ppm peak (d'): cis-$C_{d'}$, 65.3 ppm peak (d): trans-C_d, 78.0 ppm peak (e,e'): completely overlapped trans-C_e and cis-$C_{e'}$, 123.3 ppm peak (f,f'): partially overlapped trans-C_f and cis-$C_{f'}$, 126.2 ppm peak (g,g'): slightly overlapped trans-C_g and cis-C_g, 127.7 ppm peak (h,h'): completely overlapped trans-C_h and cis-$C_{h'}$, 128.4 ppm peak (i,i'): completely overlapped trans-C_i and cis-$C_{i'}$, 140.3 ppm peak (j,j'): partially overlapped trans-C_j and cis-$C_{j'}$.

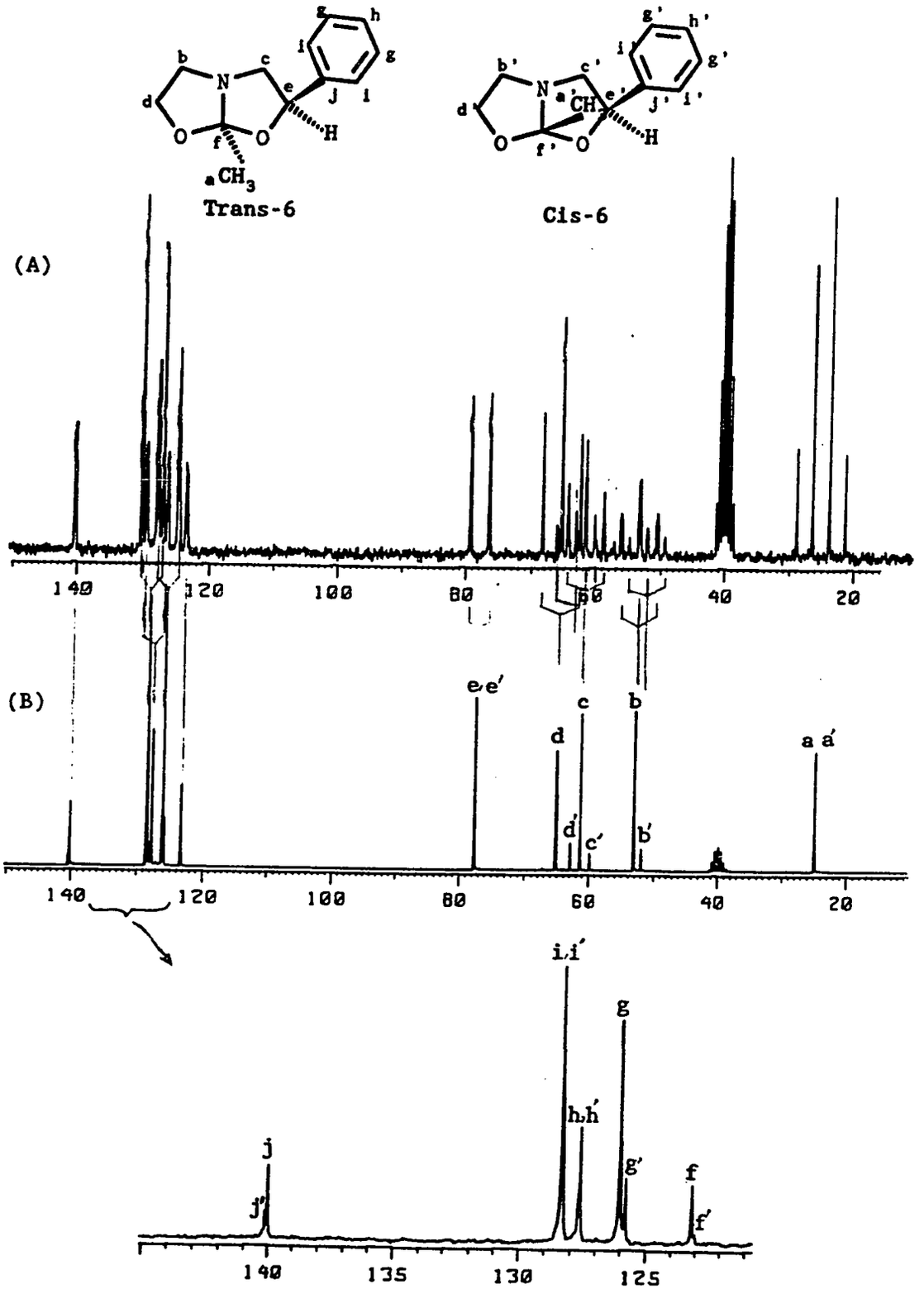
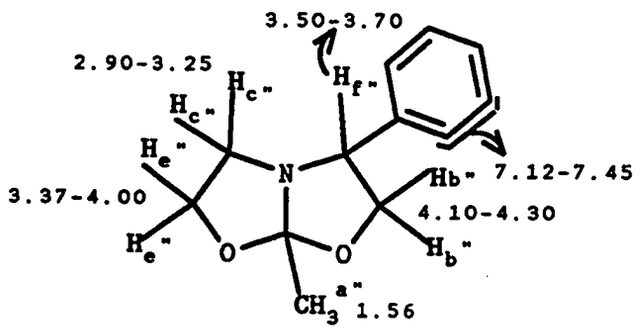


Figure 8-2 50.3-MHz ^{13}C NMR spectrum of 5-methyl-3-phenyl-3-bicyclic amide acetal in DMSO-D_6 at 25°C.

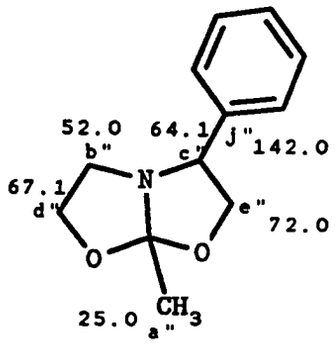
Figure 8-2 (A) is the coupled ^{13}C NMR spectrum, which is consistent with the assignment of Figure 8-2 (B): the peaks due to the carbons bonded to three protons are split into quartets (a and a′), the peaks due to carbons bonded to two protons are split into triplets (b, b′, c, c′, d, and d′), the peaks due to carbons bonded to one proton are split into doublets (e or e′, g, g′, h or h′,i′, and i), and the peaks due to carbons not bonded to any proton are not split (f, f′, j, and j′).

Although the pure trans form of 6 can be obtained by the recrystallization of the mixture of cis and trans form of 6, the pure cis form of 6 and pure isomer 8 have not been separated due to their low percentage (discussed later) in the crude product. The assignment of the NMR spectra for isomer 8 was achieved by comparing the ^{1}H and ^{13}C NMR spectra of the recrystallized product (Figure 8-1 and 8-2) and the crude product (Figure 8-3 and 8-4). The spectra of the crude product showed an extra set of chemical shifts and some of them are partially or completely overlapped with isomer-6. This extra set of chemical shifts is believed to be contributed by isomer 8 and can be assigned as follows:

^{1}H:



^{13}C:



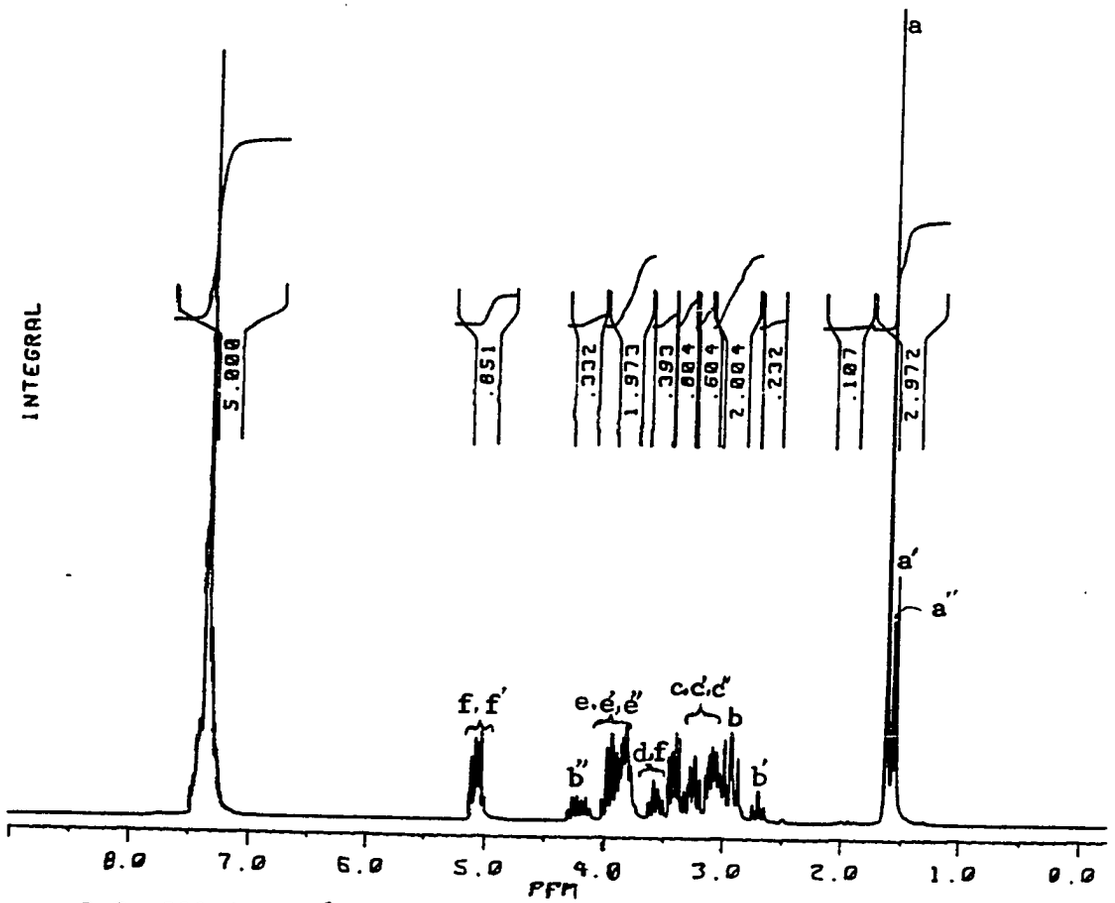


Figure 8-3 200.1-MHz ^1H NMR spectrum of the crude product of MeOXA and styrene oxide pair in DMSO-D_6 at 25°C.

The assignment for the ^1H NMR spectrum of Figure 8-3 are as follows: 1.56 ppm singlet (a"): the methyl protons, $H_{a"}$, which is partially overlapped with methyl protons of isomer 6; $H_{c"}$ and $H_{e"}$ are completely overlapped with corresponding protons (H_c and H_e) of isomer 6 at 2.90 ppm and 3.37-4.00 ppm respectively; quartet at 3.50-3.70 ppm: $H_{f"}$, which is partially overlapped with the $H_{d'}$ of isomer 6; sextet at 4.10-4.30 ppm: $H_{b"}$, which is completely separated from isomer 6; phenyl protons are completely overlapped with that of isomer 6 at 7.12-7.45 ppm.

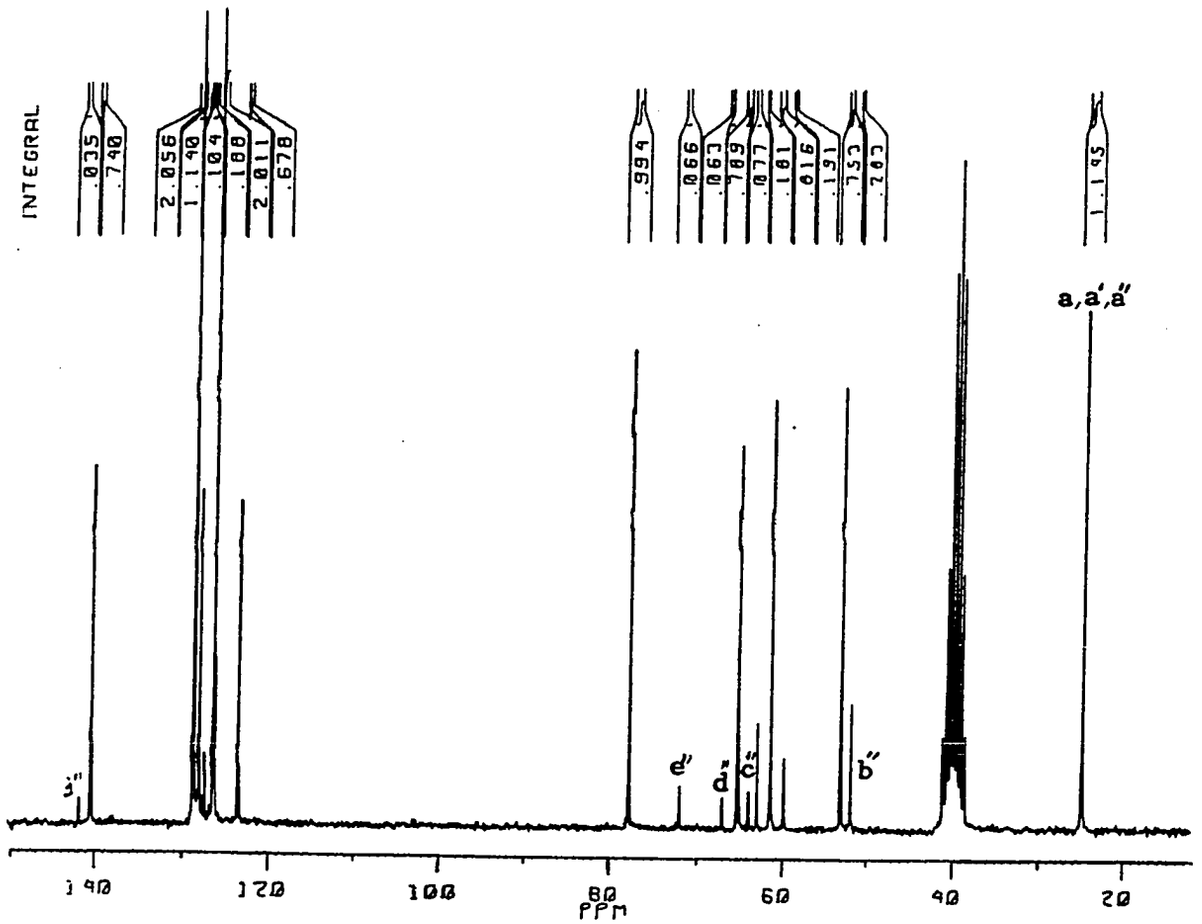


Figure 8-4 50.3-MHz ^{13}C NMR spectrum of the crude product of MeOXA and styrene oxide pair in DMSO-D_6 at 25°C.

The assignments for the ^{13}C NMR spectrum (Figure 8-4) are as follows: 25.0 ppm: methyl carbon, $C_{a''}$, which is completely overlapped with isomer 6; 52.0 ppm: $C_{b''}$, which is overlapped with $C_{b'}$ of isomer 6; 64.1 ppm: $C_{c''}$; 67.1 ppm: $C_{d''}$; 72.0 ppm: $C_{e''}$; 142.0 ppm: $C_{j''}$; and the rest of the carbons are overlapped with the corresponding carbons of isomer 6.

An IR spectrum (Figure 8-5) of pure 5-methyl-3-phenyl-bicyclic amide acetal was also taken to supply additional information about the structure. A. υ_{C-H} of phenyl group:

3083 and 3052 cm^{-1}, B. υ_{C-H} of the methylene or methine groups: 2989, 2935 and 2882 cm^{-1}, C. overtone or combination band pattern for monosubstituted phenyl: 1955, 1862, 1813 and 1730 cm^{-1}, D. υ_{C-C} of benzene ring: 1604 1482 and 1454 cm^{-1}, E. υ_{C-O} or υ_{C-N} : 1157, 1111 and 1022 cm^{-1}, and F. δ_{C-H} of monosubstituted phenyl: 756 and 698 cm^{-1}.

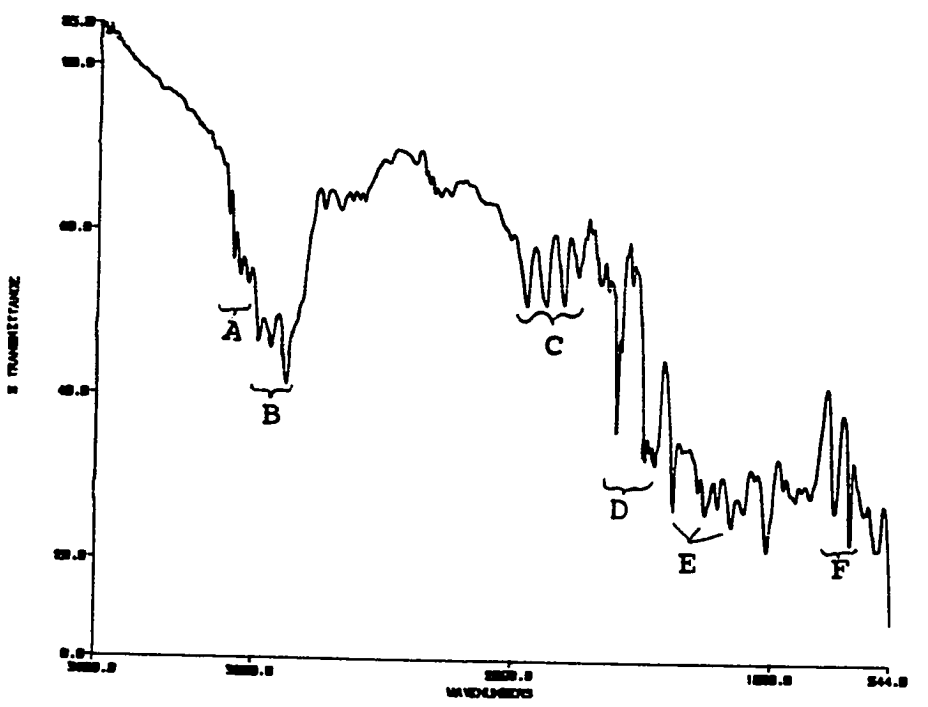
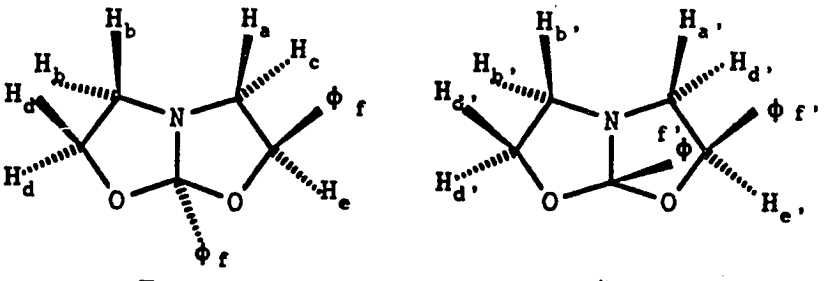


Figure 8-5 FT-IR spectrum of 5-methyl-3-phenyl-bicyclic amide actal: the sample was melted between NaCl plates

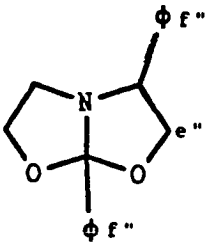
The NMR and IR spectra of the products of 2-*t*-butyl- and 2-phenyl-2-oxazolines with styrene oxide are very similar to those of the 2-methyl-2-oxazoline with styrene oxide system as shown in Figure 8-6 to 8-11. The assignments of these spectra are also very similar and will not be discussed here.

assignment of these spectra will not be discussed here.



Trans- Cis-

3,5-diphenyl-bicyclic amide acetal



2,5-diphenyl-bicyclic amide acetal

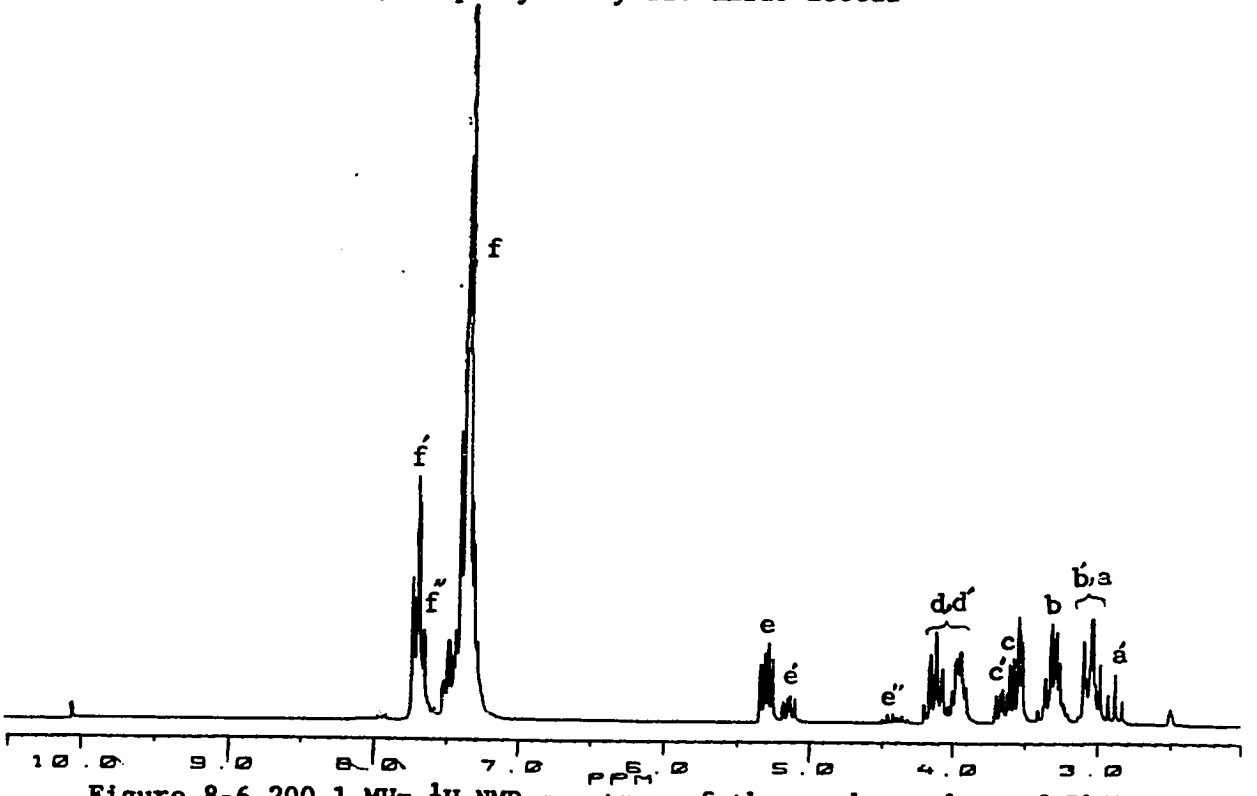
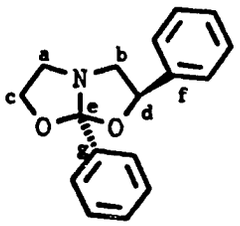
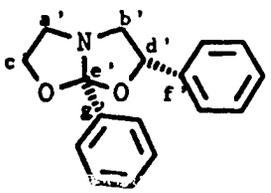


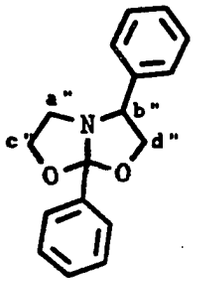
Figure 8-6 200.1-MHz ^{1}H NMR spectrum of the crude product of PhOXA and styrene oxide pair in DMSO-D_6 at 25^{o}C.





Trans- Cis-

3,5-diphenyl-bicyclic amide acetal



2,5-diphenyl-bicyclic amide acetal

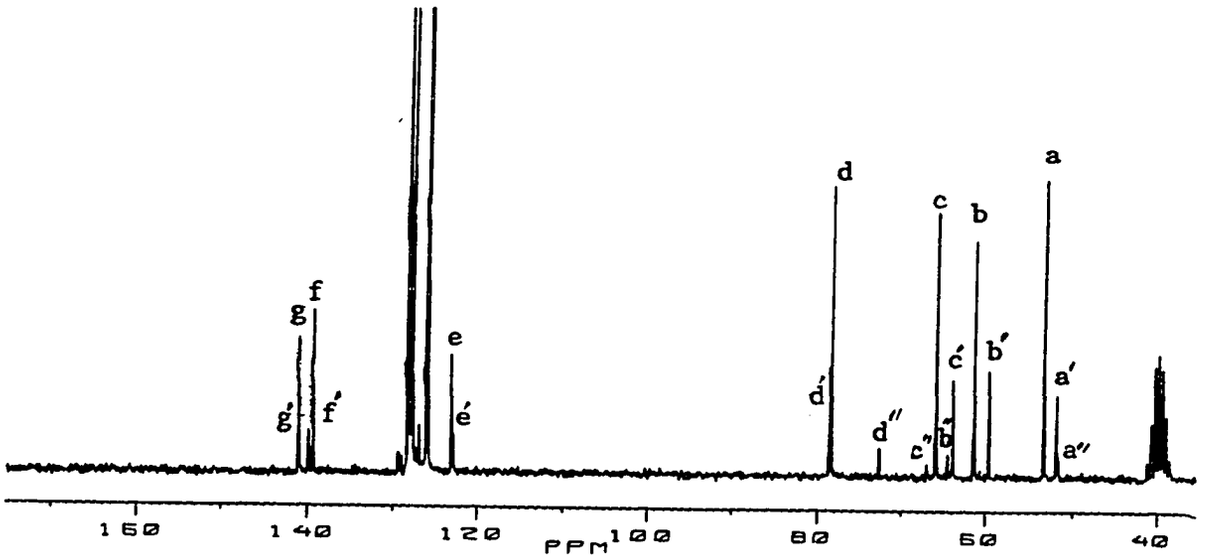
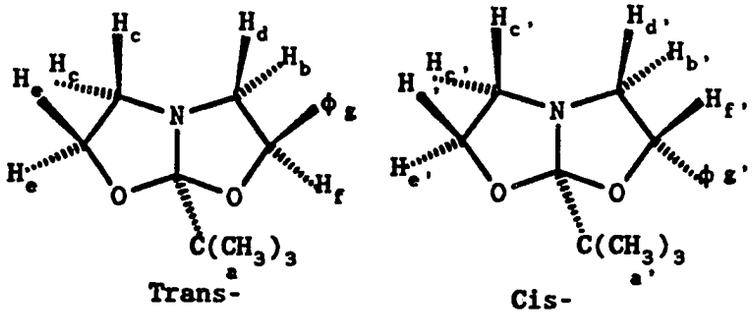
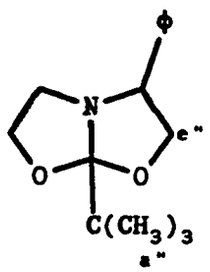


Figure 8-7 50.3-MHz ^{13}C NMR spectrum of the crude product of PhOXA and styrene oxide pair in DMSO-D_6 at 25°C.



5-*t*-butyl-3-phenyl-bicyclic amide acetal



5-*t*-butyl-2-phenyl-bicyclic amide acetal

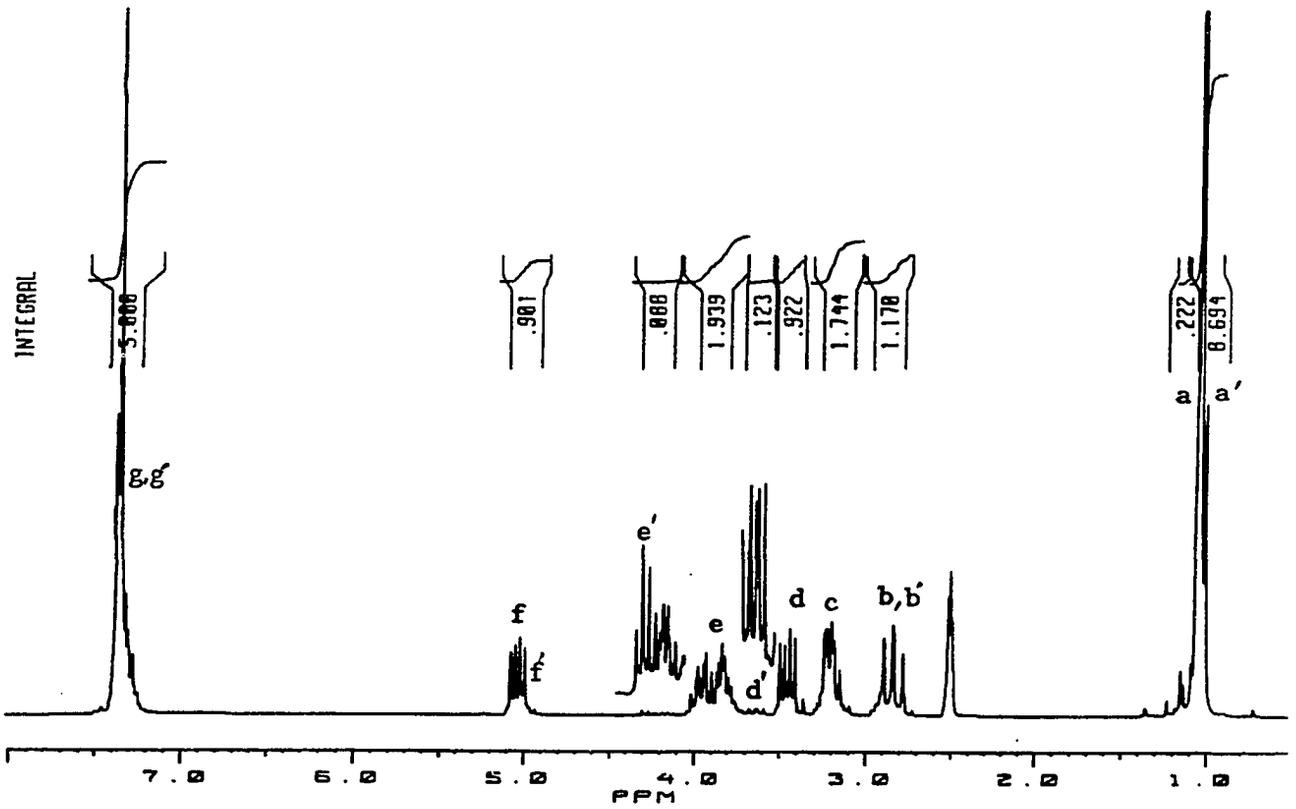
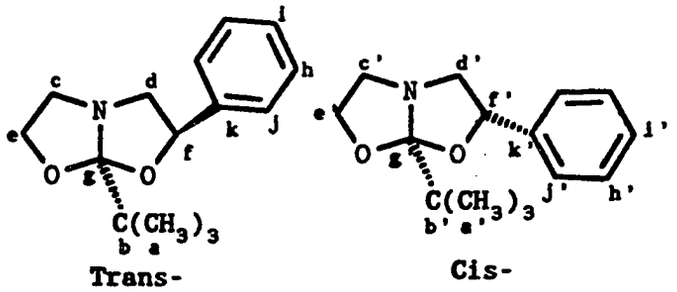
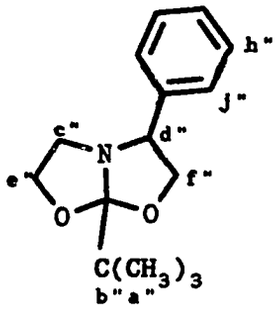


Figure 8-8 200.1-MHz ^{1}H NMR spectrum of the crude product of *t*-BuOXA and styrene oxide pair in DMSO-D_6 at 25^{o}C.



5-*t*-butyl-3-phenyl-bicyclic amide acetal



5-*t*-butyl-2-phenyl-bicyclic amide acetal

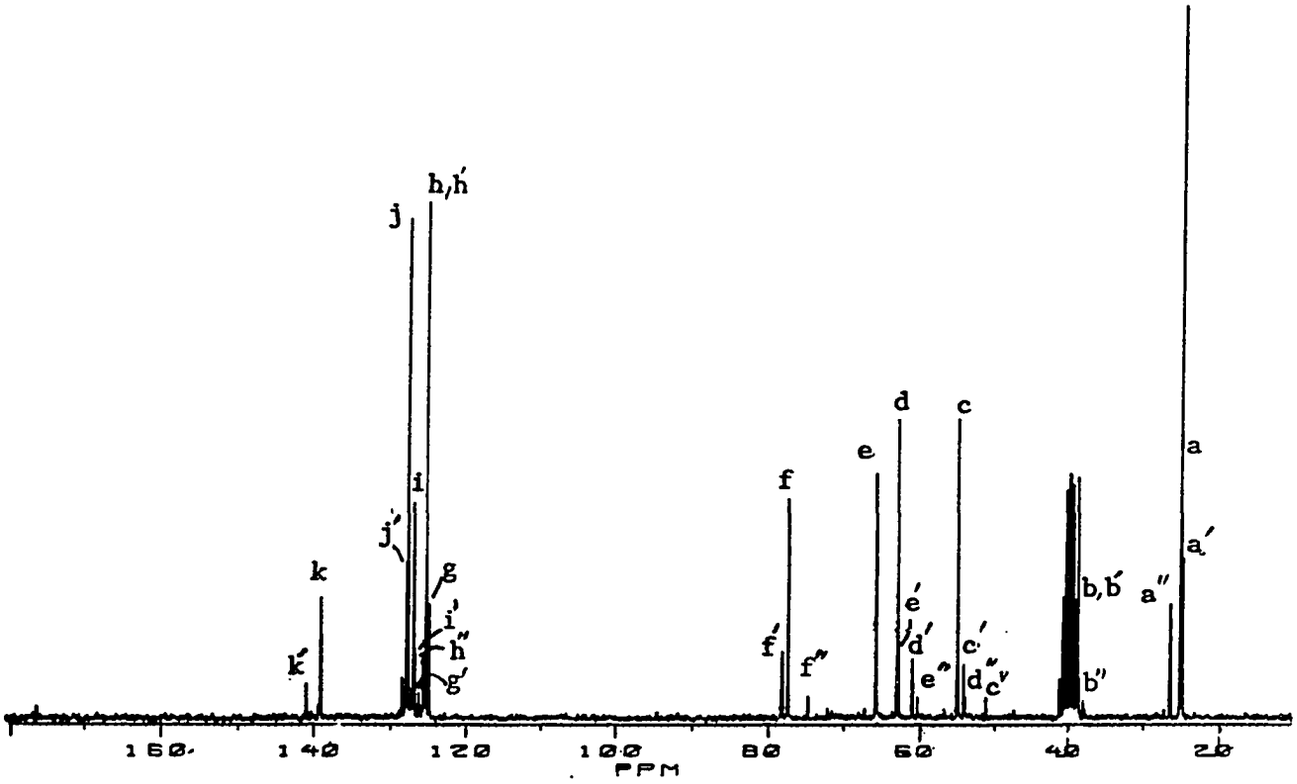


Figure 8-9 50.3-MHz ^{13}C NMR spectrum of the crude product of *t*-BuOXA and styrene oxide pair in DMSO-D_6 at 25°C.

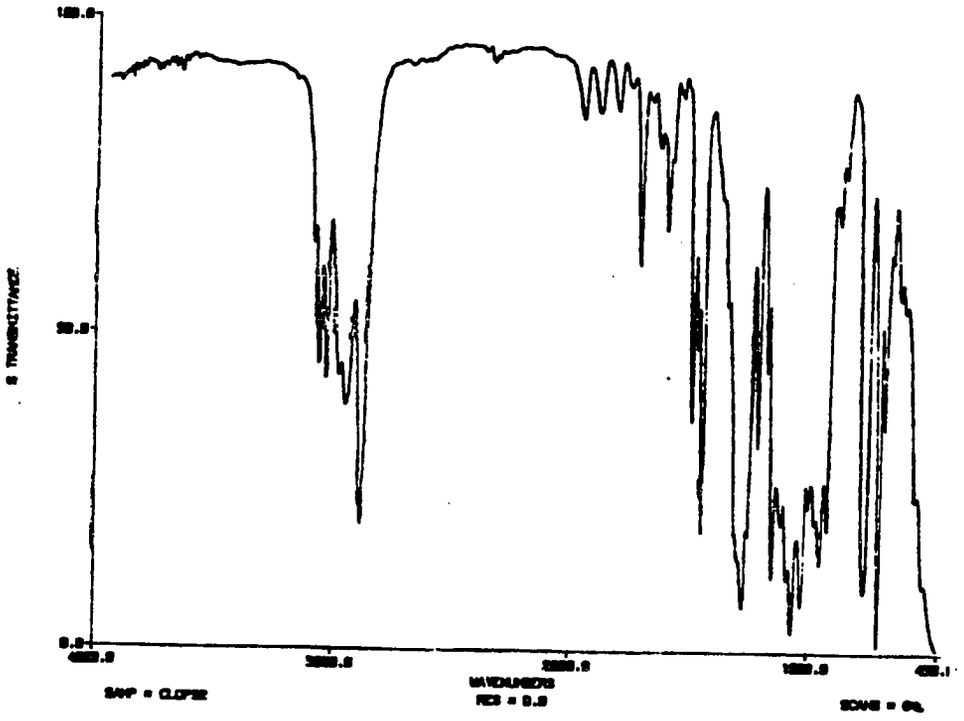


Figure 8-10 FT-IR spectrum of the crude product of PhOXA and styrene oxide pair: sample fluid between NaCl plates.

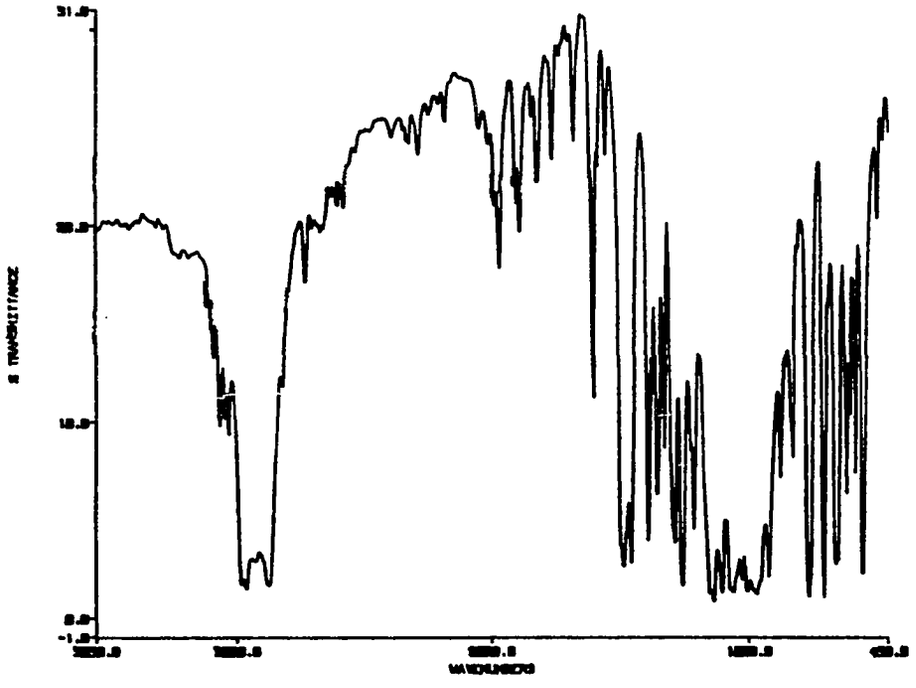


Figure 8-11 FT-IR spectrum of pure 5-*t*-butyl-3-phenyl-bicyclic amide acetal, KBr pellet

If the extra set of chemical shifts was contributed by isomer 8 as assumed, the elemental analysis results should match with the theoretical values of 6 or 8 for either the crystalline or the crude products. The elemental analysis results of the crude and crystalline products were consistent with the proposed structures, as shown in Table 8-1.

Table 8-1 Elemental analysis results of the 3,5-substituted-bicyclic amide acetal

Bicyclic acetal amide of		5-Methyl-3-phenyl-	5-*t*-Butyl-3-phenyl-	3,5-Diphenyl-
C%	Theoretical	70.24	72.87	76.40
	Experimental	70.27	72.92	76.40
H%	Theoretical	7.32	8.50	6.37
	Experimental	7.42	8.55	6.43
N%	Theoretical	6.83	5.67	5.24
	Experimental	6.85	5.63	5.20

5-Methyl- and 5-*t*-butyl-3-phenyl bicyclic amide acetals were the crystalline products and 3,5-diphenyl bicyclic acetal amide was the crude product

8-2.2 Factors which Affecting the Cycloaddition of Styrene Oxide to the Oxazolines

Our study showed that the cycloaddition of styrene oxide to oxazoline was affected by the size of the substituent on the oxazoline and whether the catalyst LiCl

was used. These factors affected both the direction of the ring-opening and ring-closing.

For the 2-methyl-2-oxazoline and styrene oxide pair, when LiCl was used, the time and temperature needed to complete the reaction were shorter and lower than without using LiCl. However, the results also showed that LiCl could assist polymerization of both styrene oxide and the bicyclic amide acetal, which resulted in a low yield in the preparation of the bicyclic amide acetal. When LiCl was used, the yield of bicyclic compound was 54% and about 33% of starting material became polymeric material. Without LiCl, the yield increased to 65%, and the formation of the polymeric material was about 12%. For 2-*t*-butyl-2-oxazoline with styrene oxide and 2-phenyl-2-oxazoline with styrene oxide pairs, in the presence of the LiCl, the formation of polymeric materials was faster than the formation of the bicyclic compounds. This made it essentially impossible to prepare the bicyclic amide acetals from these two pairs using LiCl as a catalyst. However, directly heating the corresponding oxazoline and styrene oxide mixtures at 150-160^{o}C, yielded the bicyclic amide acetals as the major products in yields of 60-70%. There were two factors which lowered the yield: (1) the conversion to bicyclic amide acetal was not very high, and (2) the formation of the polymeric material occurred as a side reaction.

By measuring the relative peak intensities of isomers 6

and 8 in the ^1H NMR spectra of the crude products, the percentage of cis and trans forms of 6 and 8 can be measured. The measurements were done by comparing the relative intensities of the following signals: (1) 2-methyl-2-oxazoline and styrene oxide pair: peak (f,f') of 6 and peak (b") of 8 in Figure 8-3, (2) 2-phenyl-2-oxazoline and styrene oxide pair: peak (e,e') of 6 and peak (e") of 8 in Figure 8-6, and (3) 2-*t*-butyl-2-oxazoline and styrene oxide pair: peak (f,f') of 6 and peak (e") of 8 in Figure 8-8.

Based on ^1H NMR spectroscopy, the formation of 8 is about 4-15% depending on (1) the size of R_1 group: as the size increases, the percentage slightly decreases; and (2) catalyst LiCl: using LiCl give a higher percentage than without using it; see Table 8-2.

Table 8-2 The effects of LiCl and R_1 on the formation of 6 and 8

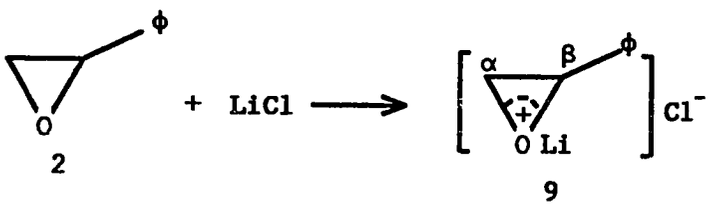
2-Substituted-2-oxazoline Styrene oxide (1:1 mole ratio)	Percentage(%)	
	6	8
2-Methyl-, with LiCl	85	15
2-Methyl-, without LiCl	93	7
2-Phenyl-, without LiCl	94	6
2-*t*-butyl-, without LiCl	96	4

The samples were the crude products

From the previous proposed mechanism, an intermediate

was formed in the first step. Since LiCl can stabilize the intermediate, this increases both the rate of the formation of the bicyclic acetal amide and the chance for the intermediate to react with other monomers instead of undergoing the ring closing reaction. Therefore, LiCl can help the formation of polymeric material.

There may be an interaction between LiCl and styrene oxide as shown below:



2 9

In 9, the β-carbon is carrying more of a positive charge than the α-carbon does, the chance of β-carbon being attacked by oxazoline to form the intermediate (b) is increased in the presence of LiCl. Therefore, the formation of 8 is increased when LiCl was used as shown in Table 8-2.

The percentages of the cis- and trans-isomers were measured by comparing the following signals of the crude products: (1) 5-methyl-3-phenyl-bicyclic amide acetal: peak (b') belonging to the cis-isomer and peak (f,f') belonging to both the cis- and trans-isomers of Figure 8-3, (2) 3,5-diphenyl-bicyclic amide acetal: peak (e) belonging to the trans-isomer and peak (e') belonging to the cis-isomer of Figure 8-6, and (3) 5-*t*-butyl-3-phenyl-bicyclic amide

acetal: peak (d) belonging to the trans-isomer and peak (d') belonging to the cis-isomer of Figure 8-8.

Table 8-3 The effect of LiCl and R on the formation of cis- and trans-isomers

2-Substituted-2-oxazoline reacting with styrene oxide (1:1 mole ratio)	Cis-isomer (%)	Trans-isomer (%)
2-Methyl, with LiCl	30	70
2-Methyl, without LiCl	27	73
2-Phenyl, without LiCl	26	74
2-t-Butyl-, without LiCl	10	90

The samples used for the measurement were the crude products

During the ring closing process of intermediate (a), due to the special steric hindrance between R and phenyl groups, the cis-isomers should be less stable and not as easy to form as the trans-isomers. According to the ^1H NMR spectra, the formation of trans-isomers is about 70-90% and cis-isomers are 10-30% depending on reaction conditions and the size of the R group: (1) when LiCl is used, since it can stabilize the intermediate (a), the selectivity of the ring closing direction should be decreased. As a result the percentage of cis-isomer is slightly higher than without using LiCl; (2) as the size of R increases, the steric hindrance between R and the phenyl group increases, resulting in an increase in the percentage of trans-isomers

(Table 8-3).

Table 8-4 The effect of R on cyclization

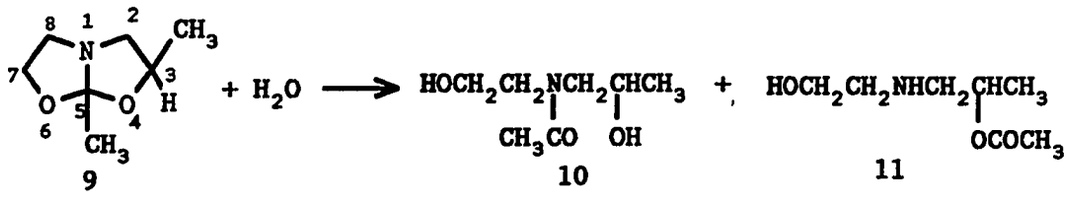
2-Substituted-2-oxazoline reacting with styrene oxide (1:1 mole ratio)	Reaction time	Reaction temperature	Conversion
2-Methyl-	17 hrs.	150-160°C	73%
2-Phenyl-	48 hrs.	153°C	70%
2-t-Butyl-	144 hrs.	157-163°C	70%

The reactions were performed under N_2 by directly mixing the corresponding reactants.

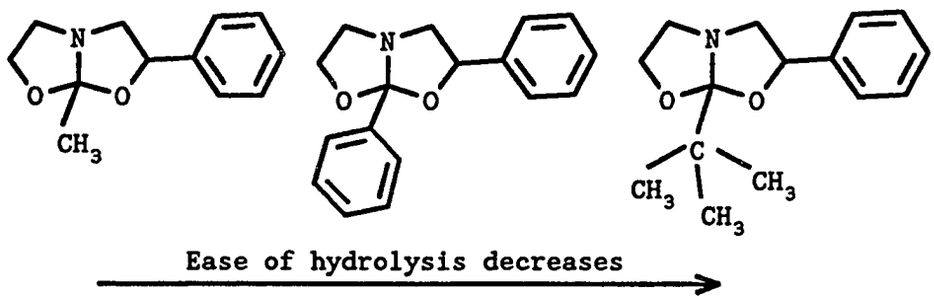
The ease of cyclization also depended on the size of R. Cyclization was easier when the R group was smaller, (see Table 8-4). The larger the size of the R group on the oxazoline, the longer it took to reach the same conversion when the reaction temperature was about the same.

8-3 Hydrolysis of the Bicyclic Amide Acetals

According to Feinaur and Henckel[5], the hydrolysis of 3,5-dimethyl-bicyclic amide acetal(9) under mild conditions (allowing to stand with water) yields the C—O cleavage product 10 to the extent of 90-95% and the C—N cleavage product 11 to the extent of 5-10%:

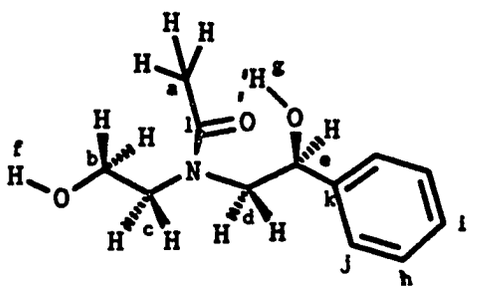


Hydrolysis was carried out for the bicyclic amide acetal amides involved in our study: 5-methyl-3-phenyl-, 5-*t*-butyl-3-phenyl, and 3,5-diphenyl-bicyclic amide acetals. The ease of the hydrolysis depended on the type of the substituents, i.e., the substituent on the no. 5 carbon in our case. The experimental results showed that as the size of the substituent on carbon-5 increases, the hydrolysis became more difficult.

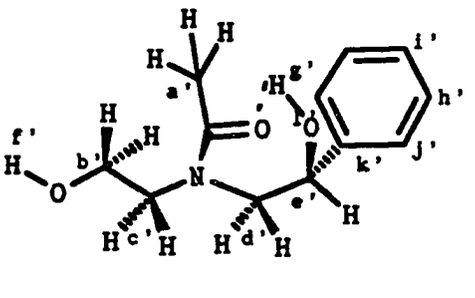


At room temperature, 5-methyl-3-phenyl bicyclic amide acetal dissolved in water and reacted with water in a few minutes; 3,5-diphenyl bicyclic acetal amide did not dissolve in water but dissolved in water/acetone (v:v 1:10), and completely hydrolyzed after one day; 5-*t*-butyl-3-phenyl bicyclic also did not dissolve in water but in water/acetone (v:v 1:9), and only 5% underwent hydrolysis after two days. Since carbon-3 is a chiral center and the bicyclic acetal

acetal (Figure 8-12 and 8-14) show that there are two sets of chemical shifts, which may be attributed to a racimic mixture of the (R)- and (S)-isomers 13.



13-(R)



13-(S)

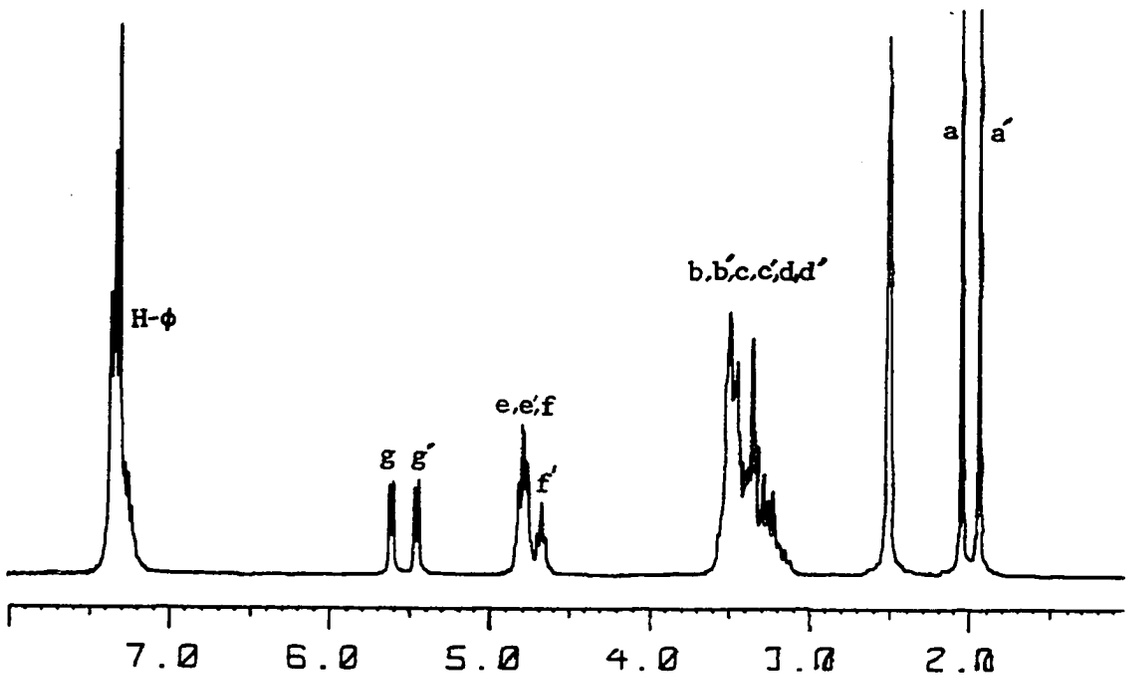


Figure 8-12 200.1-MHz ^{1}H NMR spectrum of the hydrolysis product of 5-methyl-3-phenyl-bicyclic amide acetal in DMSO-D_6 at 25°C

Analysis of the ^{1}H NMR spectrum (Figure 8-12) is as follows: 1.93 ppm (singlet): (S)-methyl protons, $H_{a'}$, 2.05

ppm (singlet): (R)-methyl protons, H_a, 3.10-3.62 ppm (multiplet): (R) and (S)-methylene protons: H_b, H_b', H_c, H_c', H_d, and H_d', 4.65 ppm (triplet): (S)-H_f', 4.72-4.87 ppm (multiplet): H_e, H_e', H_f, and H_f', 5.95 ppm (doublet): (S)-H_g', 6.11 ppm (doublet): (R)-H_g, 7.15-7.96 ppm (multiplet): (R) and (S)-phenyl protons.

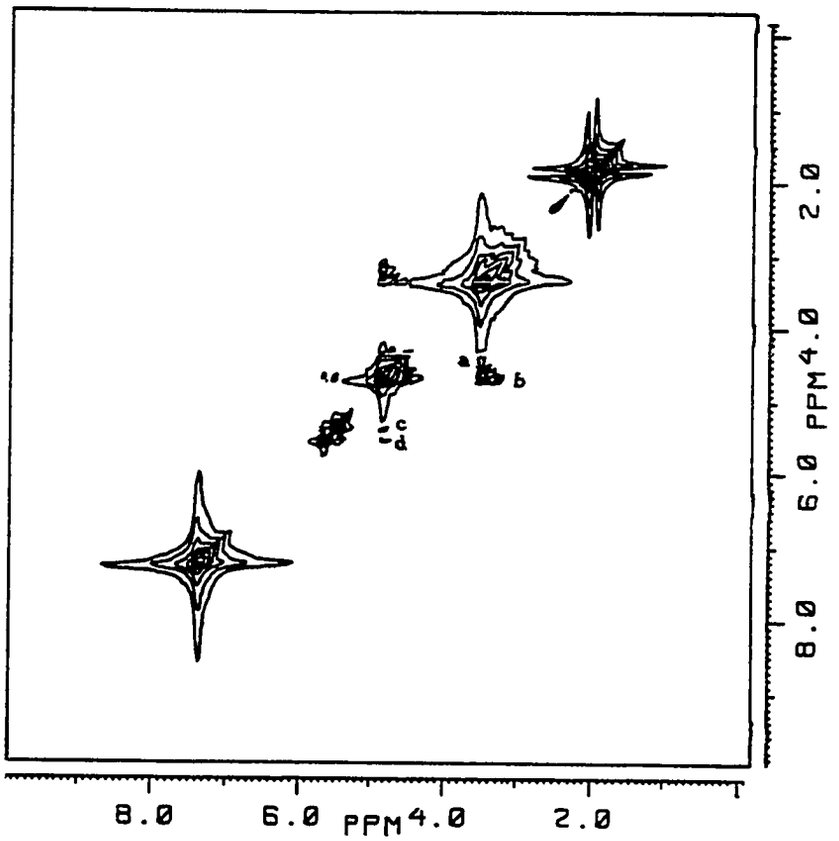


Figure 8-13 COSY spectrum of the hydrolysis product of 5-methyl-3-phenyl-bicyclic amide acetal in DMSO-D_6 at 25°C.

A COSY experiment (Figure 8-13) was run to confirm the assignments of the ^1H NMR spectrum. The following correlations were observed: peak (a): coupling between H_b' and H_f', peak (b): coupling between H_e and H_d, or H_e' and

$H_{d'}$, or H_f and H_b, peak (c): coupling between $H_{e'}$ and $H_{g'}$, peak (d): coupling between H_e and H_g.

Analysis of the ^{13}C NMR spectrum (Figure 8-14) is as follows: 21.0 ppm: (R)-C_a and (S)-$C_{a'}$, overlapped, 49.0 ppm: (S)-$C_{c'}$, 52 ppm: (R)-C_c, 54.5 ppm: (S)-$C_{d'}$, 57.5 ppm: (R)-C_d, 59.2 ppm: (R)-C_b and (S)-$C_{b'}$, partially overlapped, 71.0 ppm: (R)-C_e and (S)-$C_{e'}$, overlapped, 126.0 ppm: (R)-C_h and (S)-$C_{h'}$, partially overlapped, 127.2 ppm: (R)-C_i and (S)-$C_{i'}$, partially overlapped, 128.5 ppm: (R)-C_j and (S)-$C_{j'}$, partially overlapped, 143.5 ppm: (R)-C_k, 144.0 ppm: (S)-$C_{k'}$, 170.7 ppm: (R)-C_l and (S)-$C_{l'}$, partially overlapped.

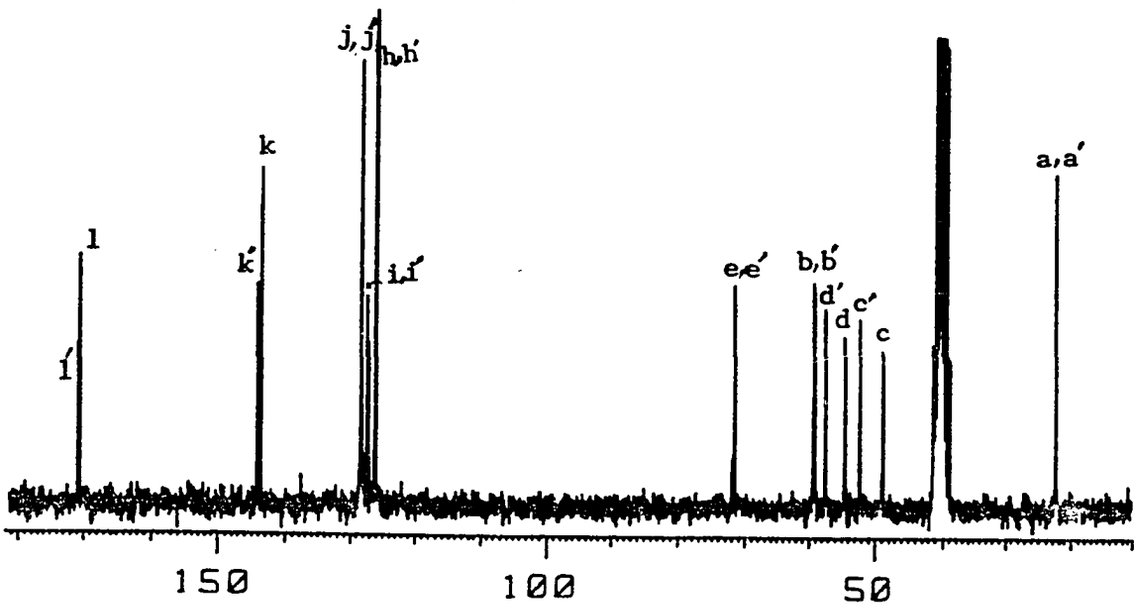
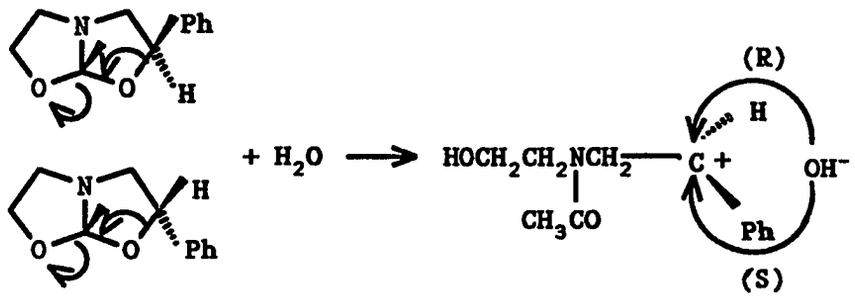
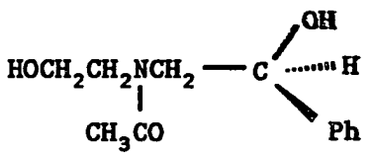


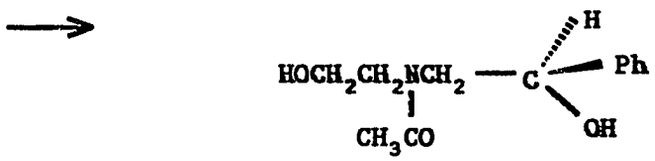
Figure 8-14 50.3-MHz ^{13}C NMR spectrum of the hydrolysis product of 5-methyl-3-phenyl-bicyclic amide acetal in DMSO-D_6 at 25°C.

Based on the experimental results, the following hydrolysis mechanism is proposed:





13-(R) 50%



13-(S) 50%

This mechanism does not agree with what was proposed by Feinauer and Henckel[2], since there was no formation of the C-N product as they claimed.

The ^{13}C NMR spectrum of hydrolysis products (14) of 3,5-diphenyl-bicyclic amide acetal shown in Figure 8-15 also supports the above mechanism. The ^{1}H NMR spectrum of the hydrolysis product is not shown here because of its poor resolution; the reason for that is not clear.

Identification of the ^{13}C NMR spectrum (Figure 8-15) is as follows: 47.8 ppm peak (a): (R)-C_a, 52.2 ppm peak(a'):

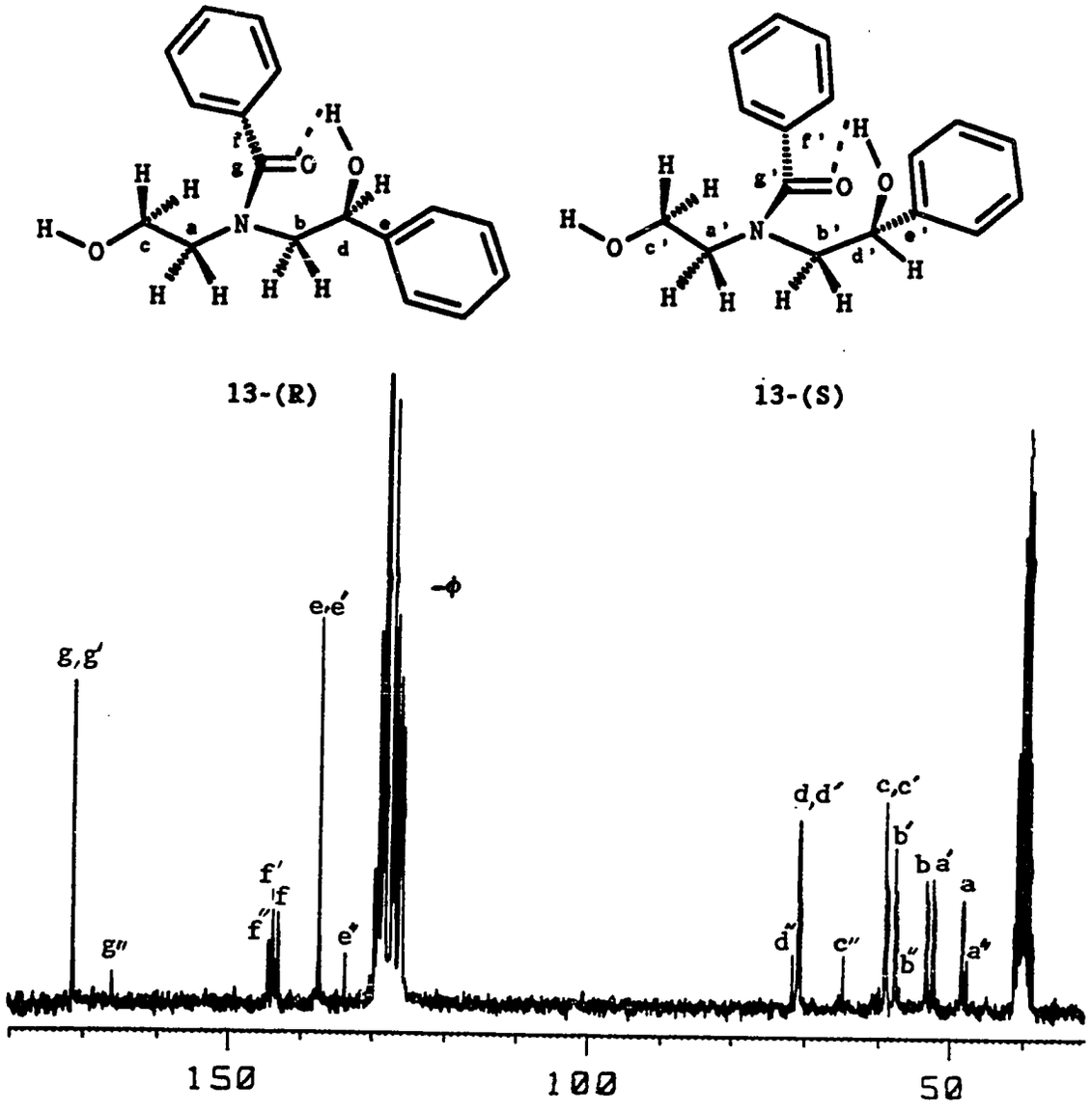
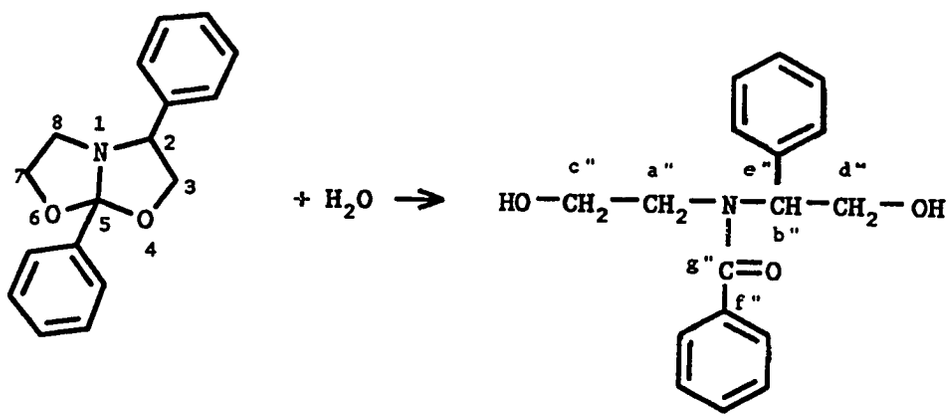


Figure 8-15 50.3-MHz ^{13}C NMR spectrum of the hydrolysis product of 3,5-diphenyl-bicyclic amide acetal in DMSO-D_6 at 25°C.

(S)-$C_{a'}$, 53.2 ppm peak (b): (R)-C_b, 58.0 ppm peak (b′): (S)-$C_{b'}$, 59.1 ppm peak (c, c′): (R)-C_c and (S)-$C_{c'}$, which are partially overlapped, 70.9 ppm peak (d, d′): (R)-C_d and (S)-$C_{d'}$, which are partially overlapped, peaks in the range 126-129.5 ppm: phenyl carbons of both (R) and (S)-isomer, the assignments for the individual peak has not been

achieved, 157.1 ppm peak (e, e'): (R)-C_e and (S)-$C_{e'}$, which are completely overlapped, 142.9 ppm peak (f): (R)-C_f, 143.5 ppm peak (f'): (S)-$C_{f'}$, 171.0 ppm peak (g, g'): (R)-C_g and (S)-$C_{g'}$, which are completely overlapped.

It is noticed that there is a set of peaks with very low intensities (labled by double prime ") in Figure 8-15. As mentioned earlier in this chapter, the 3,5-diphenyl bicyclic amide acetal prepared is not pure, actually it contains about 6% of 2,5-diphenyl bicyclic amide acetal. This set of peaks is believed to be contributed by the hydrolysis product (14) of 2,5-diphenyl bicyclic amide acetal:



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Assignment for the extra set of peaks in Figure 8-15 is as follows: peak(a") at 47.9 ppm: $C_{a"}$, peak(b") at 57.8 ppm: $C_{b"}$, peak(c") at 65.00 ppm: $C_{c"}$, peak(d") at 71.7 ppm: $C_{d"}$, peak(e") at 133.0 ppm: $C_{e"}$, peak(f") at 144.1 ppm: $C_{f"}$, peak(g') at 165.6 ppm: $C_{g"}$; all of the phenyl carbons rather than the quaternary carbons ($C_{e"}$ and $C_{g"}$) are in the range

125.5-130.0 ppm and were not identified individually.

8-4 EXPERIMENTAL PART

8-4.1 Preparation of 5-Methyl-3-Phenyl-Bicyclic Amide Acetal:

Two methods have been developed depending on the presence or absence of a LiCl catalyst.

A. Styrene oxide (100 ml, 0.88 mole), 2-methyl-2-oxazoline (75 ml, 0.88 mole), and LiCl (1.5 g, 0.035 mole) were mixed in a 250 ml three-neck-flask under a N_2 atmosphere. The mixture was refluxed at 120°C for 4 hrs. Then the reaction mixture were distilled under vacuum (0.05 mmHg), a colorless oily crude product (97 g) was obtained at 100-110°C, and approximately 60 g of a brown viscous material was left in the flask.

B. Styrene oxide (121.8 ml, 1.07 mole) and 2-methyl-2-oxazoline (91.0 ml, 1.07 mole) were mixed in a flask under N_2. The mixture was refluxed at 150-160°C for 46.0 hrs under N_2, then distilled as described above. A crude product (143 g) was obtained, and a brown viscous material (25 g) was left in the flask.

8-4.2 Purification of 5-Methyl-3-Phenyl-Bicyclic Amide Acetal:

The crude product (10 g) was dissolved in 120 ml of ether at room temperature, and cooled in an acetone/dry-ice bath to allow crystallization to occur. After 4-6 hrs,

white needle shaped crystals formed. The ether solution above the crystal was decanted while it was kept cool, and then another 100 ml of ether was added for recrystallization. The crude product prepared without LiCl needed to be recrystallized twice and the product prepared with LiCl needed three recrystallizations to reach a purity of 99%. The white crystals were dried under vacuum at room temperature which had a melting of 32.0-34.0°C. The recovery upon recrystallization was 35% when LiCl was used and 60% when LiCl was not involved.

8-4.3 Preparation of 5-*t*-Butyl-3-Phenyl-Bicyclic Amide Acetal:

2-*t*-BuOXA (90 ml, 0.66 mole) and styrene oxide (6 ml, 0.66 mole) were refluxed under N_2 at 157-163°C for 7 days. The reaction mixture was distilled under vacuum (0.05 mmHg) and the crude product was collected at 113-120°C to give 110 g of a colorless oily liquid; a brown-black viscous material (15 g) was left in the flask.

8-4.4 Purification of 5-t-butyl-3-phenyl-bicyclic amide acetal:

The crude product (10 g) was dissolved in 100 g of ether at room temperature, then cooled in an acetone/dry ice bath. White crystals were formed after 2-4 hrs, the solution above the crystals was decanted off and 90 ml of fresh ether was added to dissolve the crystals. The

solution was cooled to allow recrystallization. After the solution above the crystals was decanted off, the white crystals were vacuum dried at room temperature. The purity of the crystals were >99% with a m.p. of 82.5-83.0°C and the recovery upon recrystallization was 78.8%.

8-4.5 Preparation of 3,5-Diphenyl-Bicyclic Amide Acetal:

2-Phenyl-2-oxazoline (90 ml, 0.74 mole) and styrene oxide (89 ml, 0.78 mole) were mixed and refluxed at 150-160°C for 3.5 days in a N_2 atmosphere. The reaction mixture was then distilled under vacuum (0.05 mmHg), 127 g of crude product came out at 155-163°C which was a yellow viscous liquid. Meanwhile there was 45 g brown tar left in the flask.

Purification of the crude product in order to obtain the pure 3,5-diphenyl--bicyclic amide acetal has been tried using different approaches, such as fraction distillation and crystallization, but a pure product was not obtained.

8-4.6 Hydrolysis of the Bicyclic Amide Acetals

A. Hydrolysis of 5-methyl-3-phenyl-bicyclic amide acetal: pure 5-methyl-3-phenyl-bicyclic amide acetal (1.0 g) was dissolved in 1.0 ml of distilled water to give a clear solution. After the excess water was taken away by vacuum, a colorless viscous product was obtained.

B. Hydrolysis of 5-*t*-butyl-3-phenyl- and 3,5-diphenyl-bicyclic amide acetals: the pure 5-*t*-butyl-3-phenyl- or

crude 3,5-diphenyl-bicyclic amide acetal (1.0 g) was dissolved in 20 ml of acetone to afford a clear solution, and distilled water was added to the solution just before it became cloudy. After the solution was stirred at ambient temperature for two day, water and acetone was pulled off by vacuum to give the hydrolysis product.

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[1] R. Feinaur and W. Seelinger, Justus Liebigs Ann. Chem. 698, 174 (1966) (Ger.)

[2] R. Feinauer, Synthesis 16 (1971).

[3] W. Reeve and J. Christoffel, Am. Chem. Soc. 72, 1480 (1950)

[4] Z. Jedlinski, J. Kasperczyl, and A. Dworak, Makromol. Chem. 183, 587 (1982)

[5] R. Feinauer and E. Henckel, Liebigs Ann. Chem. 716, 135 (1968)

Chapter 9 COPOLYMERIZATION OF 2-METHYL-2-OXAZOLINES AND STYRENE OXIDE

9-1 Introduction

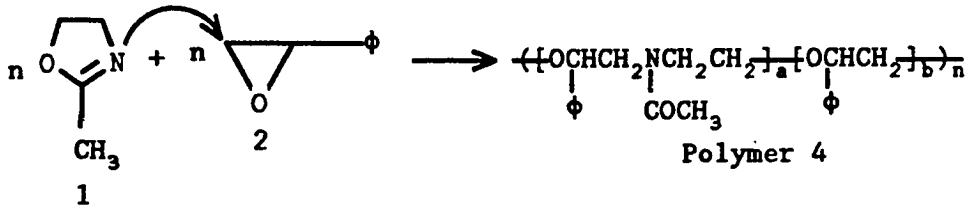
As mentioned in Chapter 6, it was planned to prepare copolymer 3 in two different ways: (1) directly copolymerize oxazolines and styrene oxide; and (2) prepare the bicyclic amide acetal first, then homopolymerize it. Both direct copolymerization of styrene oxide and oxazoline and homopolymerization of the bicyclic amide acetal can produce a polymeric material, but characterization of the polymer structure by NMR spectroscopy turned out to be very difficult. It seemed that the polymers obtained from both approaches did not have the same repeating unit as copolymer 3.

9-2 Copolymerization of 2-Methyl-2-Oxazoline and Styrene Oxide Using LiCl as a Catalyst

Since a polymer was obtained as a by-product during the preparation of 3,5-substituted-bicyclic amide acetals from oxazolines and styrene oxide, direct copolymerization of the oxazolines and styrene oxide was performed in order to synthesize the desired polymer--polymer 3.

By reacting 2-methyl-2-oxazoline with styrene oxide in the presence of LiCl for a longer period of time and at the same or higher temperature than those used for preparing the bicyclic compound, a very viscous material was formed.

After dissolving this material in methylene chloride and then precipitating in ethyl ether, a yellow powder of polymer was obtained.



The ^{1}H and ^{13}C NMR spectra (Figures 9-1 and 9-2) of the polymer (polymer 4) were taken for the identification of its structure.

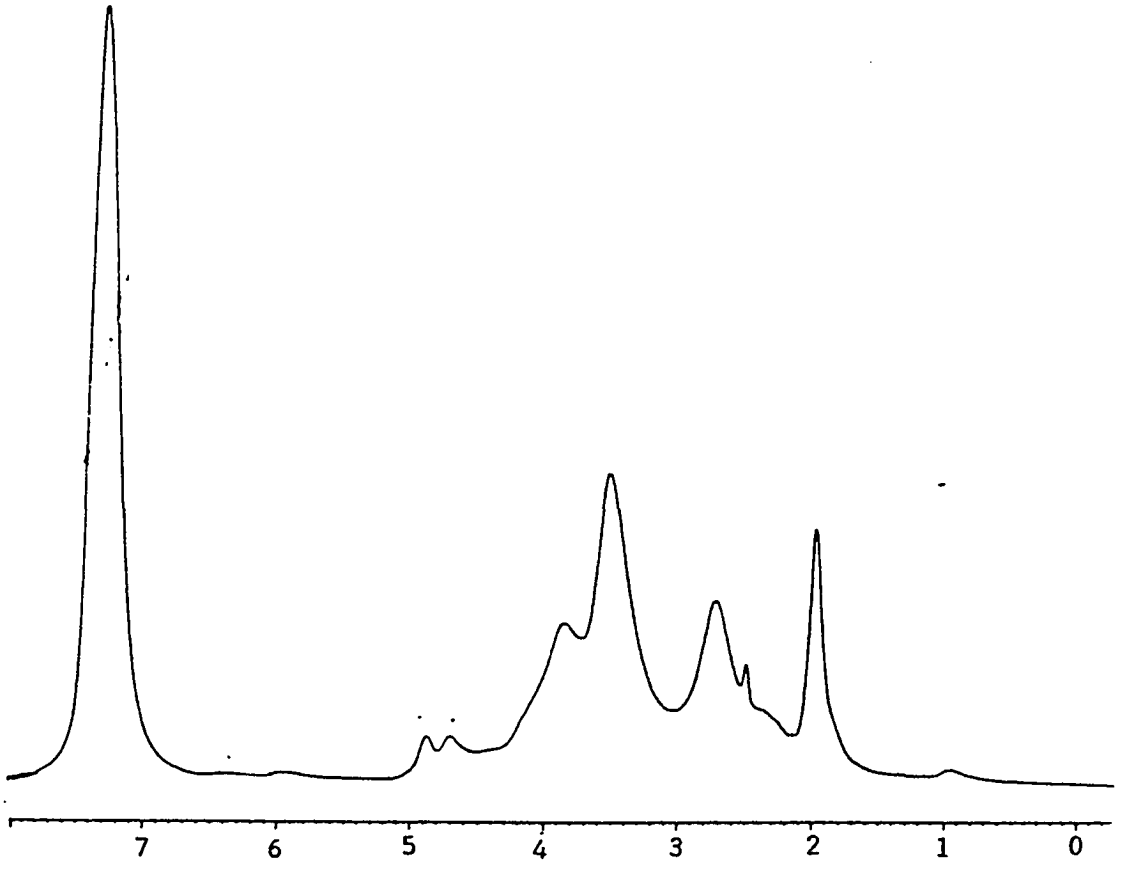


Figure 9-1 200.1-HMz ^{1}H NMR spectrum of polymer 4 in DMSO-D_6 at 25°C.

The resolution of the ^{1}H NMR spectrum (Figure 9-1) is very poor, the only information provided by it is that an acetyl methyl and a phenyl group are present in the polymer with a chemical shift of 1.9 and 7.3 ppm respectively.

In the ^{13}C NMR spectrum (Figure 9-2), two peaks at 59 and 71 ppm have very high intensities in the 40 to 85 ppm region, the methylene and methine carbon absorption region. Experimental results showed that the disappearance of styrene oxide was faster than oxazoline, and some oxazoline stayed unreacted at the end of the reaction. It was also observed that as the polymerization time increased, the relative intensities of these peaks decreased compared with other peaks in the region (Figure 9-2). Combining those facts, we concluded that during copolymerization of styrene oxide and oxazoline, three reactions occurred simultaneously in the early stages: (1) styrene oxide and oxazoline reacted with each other to form bicyclic amide acetal which was the major reaction, (2) the newly formed bicyclic compound reacted with itself to form polymer, and (3) styrene oxide reacts with itself or the polymer propagation species of the bicyclic compound to become a part of polymer.

If the peak at 71 ppm is assigned as the methine carbon and the peak at 59 ppm as the methylene carbon of styrene oxide repeating unit in the polymer chain, all the observations can be explained:

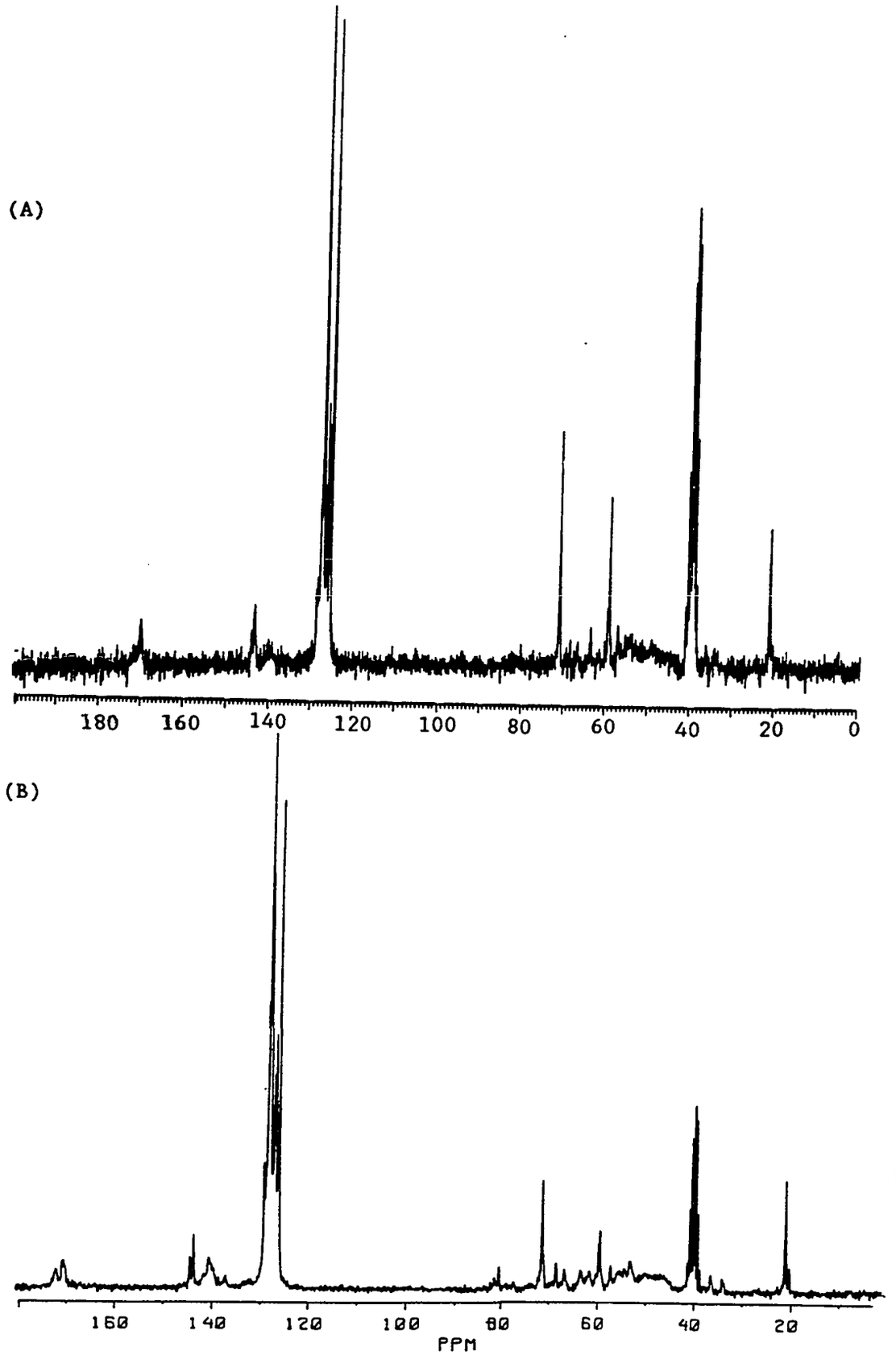


Figure 9-2 50.3-HMz ^{13}C NMR spectrum of polymer 4 in DMSO-D_6 at 25°C: polymerization conditions: (A) 6 hr/120°C and (B) 10 hr/120°C.

(1) In the early stage of the polymerization process, the concentration of styrene oxide is high, and the polymer formed should have a higher population of styrene oxide repeating units in the polymer chain. As polymerization time increases, the concentration of styrene oxide decreases and the population of the styrene oxide repeating unit in the polymer chain will decrease. As a result, the relative intensities of the peaks at 71 and 59 ppm will decrease as the polymerization time is prolonged.

(2) Due to participation of styrene oxide to the homopolymerization, the disappearance of styrene oxide is faster than that of the oxazolines.

(3) The ^{13}C NMR spectrum (Figure 9-2) shows that there are signals for the methyl carbon at 21 ppm and for the carbonyl carbon at 170 ppm, i.e., a CH_3CO group exists in the polymer chain. This is from the homopolymerization of the bicyclic compound. There are many other signals in 40 to 85 ppm region and the assignments of those peak are not clear.

9-3 Homopolymerization of 3,5-Substituted-Bicyclic Amide Acetals Using LiCl as a Catalyst

Due to the homopolymerization of styrene oxide, direct copolymerization of styrene oxide and 2-methyl-2-oxazoline did not produce the desired alternating copolymer 3. To prevent the homopolymerization of styrene oxide, 5-methyl-3-phenyl-bicyclic amide acetal was prepared from styrene oxide and 2-methyl-2-oxazoline and used to synthesis the

polymer.

The polymerization was carried out in the temperature range 100--200°C with the polymerization being slower at lower reaction temperatures. A yellow to brownish colored brittle polymer was obtained. After purification of the polymer by dissolving it in methylene chloride and precipitating the solution in ether, a yellow powder--polymer 5 was obtained.

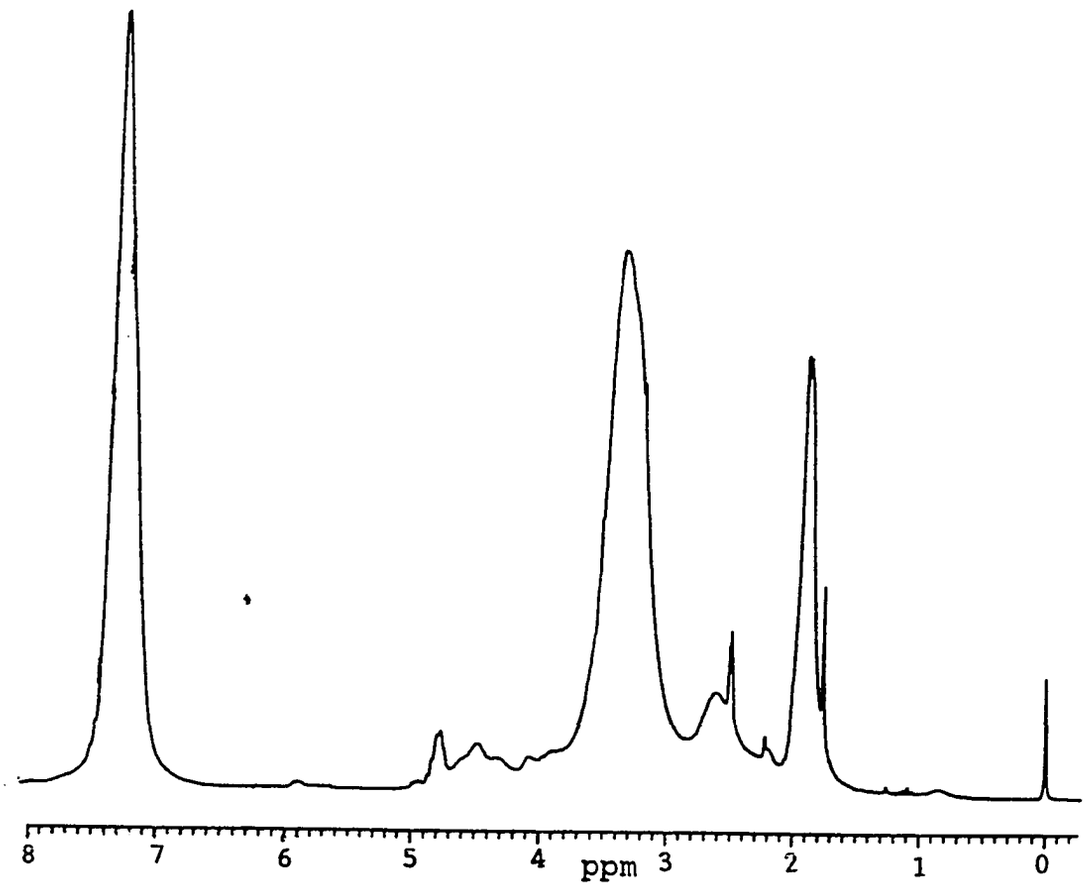


Figure 9-3 200.1-HMz ^{1}H NMR spectrum of polymer 5 in DMSO-D_6, at 25°C.

Figures 9-3 and 9-4 are the ^{1}H and ^{13}C NMR spectra of polymer 5. Again the resolution of the ^{1}H NMR spectrum is

very poor and only the methyl and phenyl group can be identified at 1.9 and 7.2 ppm respectively. The ^{13}C NMR spectrum is more complicated than expected, especially in the region of the methylene and methine carbons (40 to 100 ppm), where instead of having only four signals, there were more than eight signals.

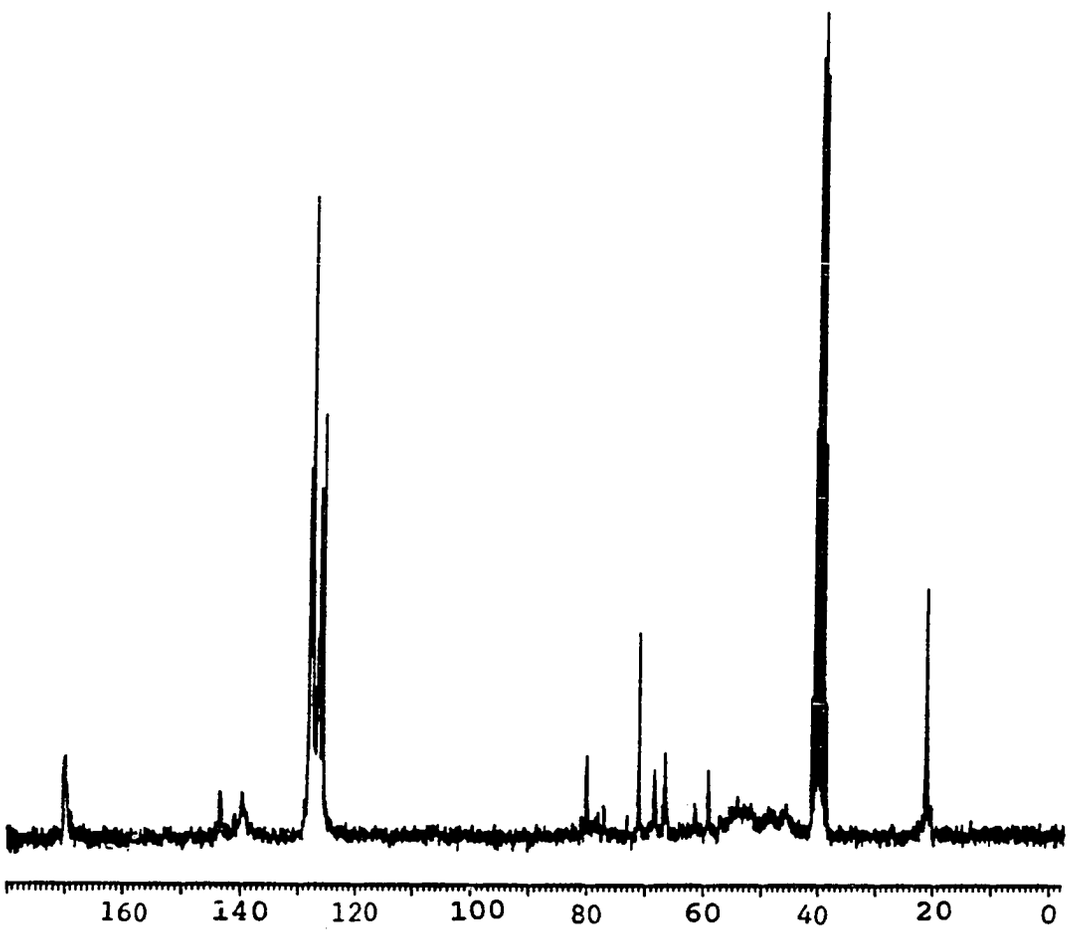
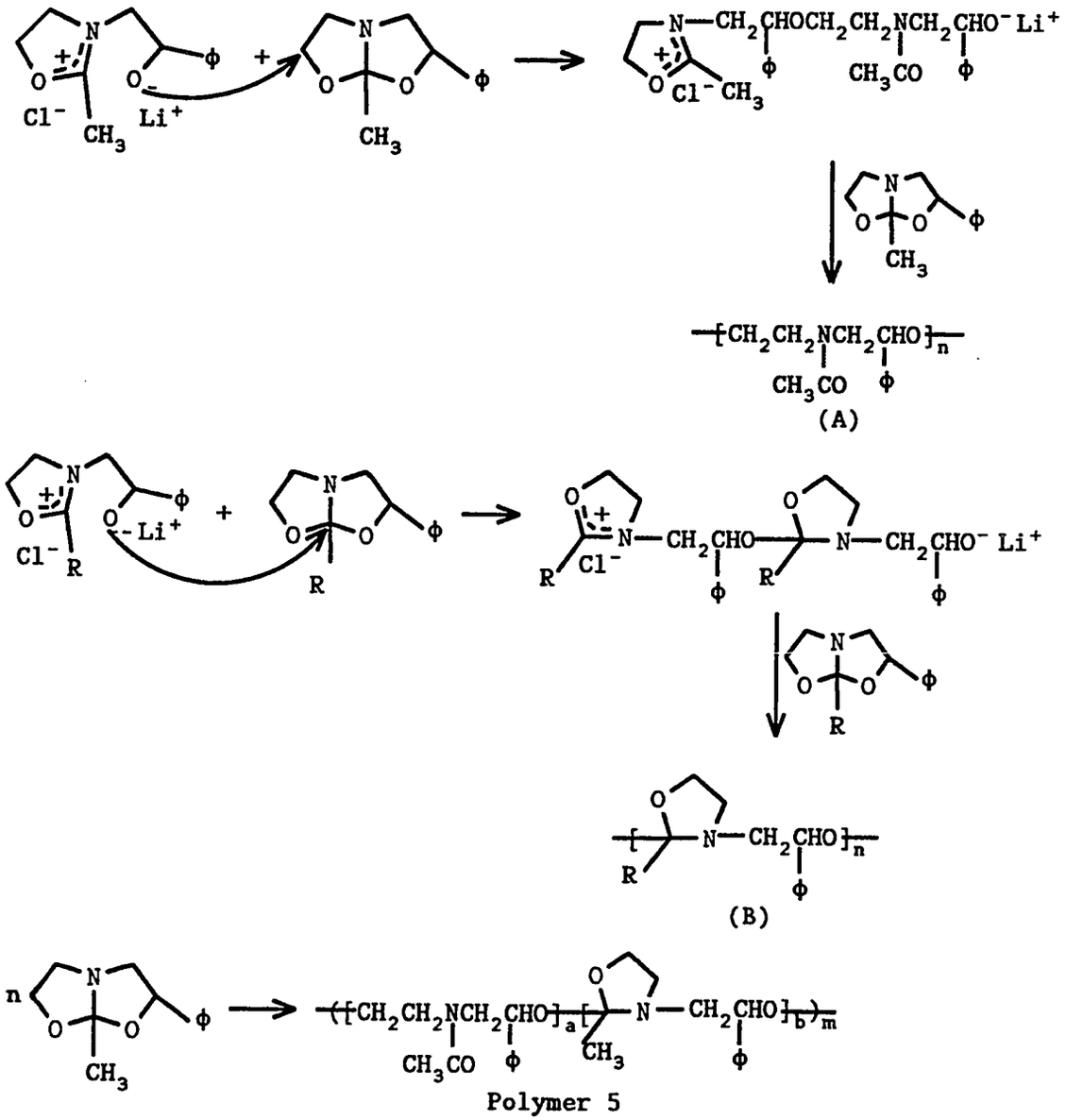


Figure 9-4 50.3-HMz ^{13}C NMR spectrum of polymer 5 in DMSO-D_6 at 25°C.

In order to understand the extra signals in the region, we proposed the following mechanism:



Polymer 5

In the proposed mechanism, two types of ring-opening reactions are involved: (1) both rings of the bicyclic amide acetal open simultaneously to produce the desired alternating repeating unit (A), and (2) only one of the rings of the bicyclic amide acetal opens to form a polymer with a repeating unit (B) containing a ring. Both types of ring-opening polymerization may occur at the same time to produce

a polymer containing both A and B as repeating units.

The ^{13}C NMR spectrum (Figure 9-4) supports the proposed mechanism to a certain extent. Signals at 21 and 170 ppm are carbons of methyl and carbonyl groups, i.e., there is a CH_3CO group in the polymer, which confirms the exists of the repeating unit A in the polymer. The signal at 139 ppm can be assigned as the tertiary carbon in the five member-ring of the repeating unit B and the signal at 80.5 ppm is assigned as the methine carbon of the repeating unit of B. The signals at 126-129 ppm are those phenyl carbons with one proton attached to it and the signal at 144 ppm is the quaternary carbon of the phenyl group. The signal at 71 ppm is the methine carbon in repeating unit A. The assignments of the other signals are not clear.

9-4 Experimental Part

9-4.1 Preparation and Purification of Polymer 4

Styrene oxide (2.000 ml, 0.0175 mole), 2-methyl-2-oxazoline (1.486 ml, 0.0175 mole), and lithium chloride (50 mg, 1.18×10^{-3} mole) were added in a polymerization tube with a magnetic stirrer, and the tube was sealed in a N_2 atmosphere. The tube was kept at 120°C for a selected period of time (normally 40 to 80 hrs) to allow the polymerization to occur. A very viscous material, yellow to brown in color, was formed. The viscous material was dissolved in 20 ml of methylene chloride to afford a slightly cloudy solution, the cloudyness was caused by the

lithium chloride which was removed by centrafugation. The clear solution was added 200 ml ether to give a yellow precipitate (polymer 4) which was filtered off, was washed with 20 ml of ether and dried under vacuum.

9-4.2 Preparation and Purification of Polymer 5

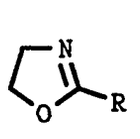
The pure 5-methyl-3-phenyl-bicyclic amide acetal (2.0 g, 9.76×10^{-3} mole) and lithium chloride (50 mg, 1.18×10^{-3} mole) were added into a polymerization tube containing a magnetic stirrer and the tube was sealed under a N_2 atmosphere. The polymerization tube was then kept at a constant temperature (100--190°C) until the reaction mixture became very viscous. It took 24 to 240 hrs depending on the reaction temperature with the reaction time needed decreasing with increasing temperature. The viscous reaction mixture, a brittle solid at 25°C, which was purified by using the same approach as for polymer 4 to yield a yellow powder (polymer 5).

CHAPTER 10 CATIONIC POLYMERIZATION OF 3,5-SUBSTITUTED BICYCLIC AMIDE ACETALS

10-1 Introduction

Since the polymerization of 5-methyl-3-phenyl-bicyclic amide acetal with LiCl as catalyst did not produce copolymer 3 but a polymeric mixture, LiCl was not strong enough to lead the polymerization in one direction. We attempted to use an initiator which would allow the polymerization to occur in the desired way.

First we had to decide what kind of initiator (anionic or cationic type) should be used. Obviously an anionic initiator can not be employed since copolymer 3 contains a carbonyl group which can react with an anionic initiator. Compare the structure of 2-substituted-2-oxazoline and 3,5-substituted-bicyclic amide acetal:



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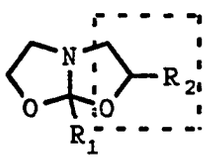
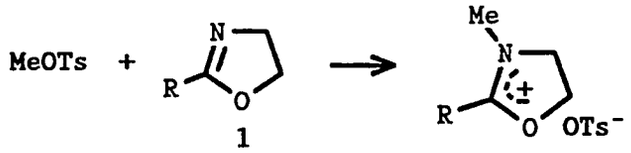


6

The difference between 6 and 1 is that the π-bond of 1 is substituted by what is shown in the dotted box of 6. According to Saegusa and Kobayashi[1] cationic ring-opening polymerization of 2-substituted-2-oxazoline gave poly(N-acylethylimine) with methyl tosylate (MeOTs) used as

the initiator. A polymerization mechanism was proposed as the following:



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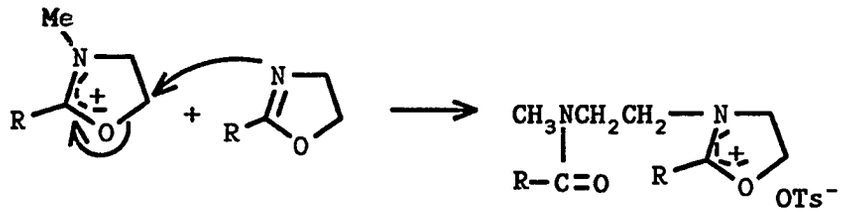
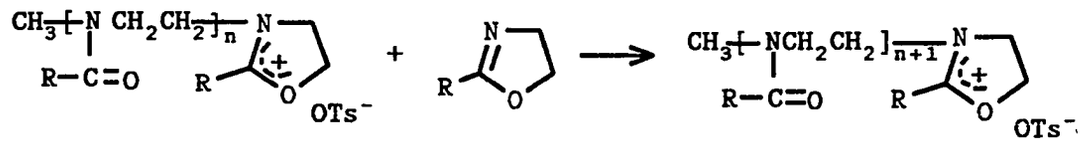
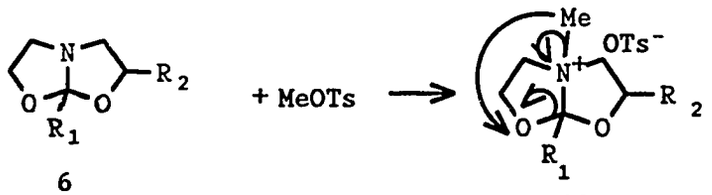


In general:



When MeOTs is used to initiate the cationic ring-opening polymerization of 6, the proposed polymerization mechanism is as the following:



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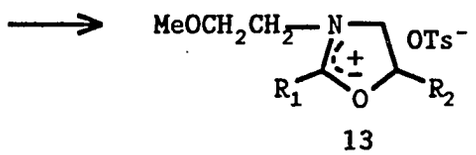

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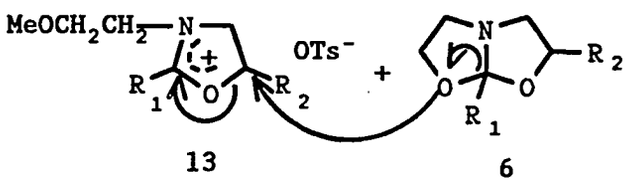

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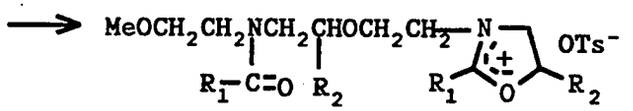

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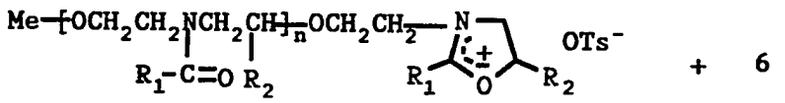
In general:



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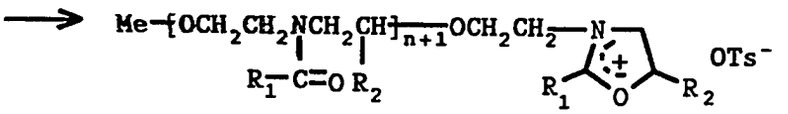
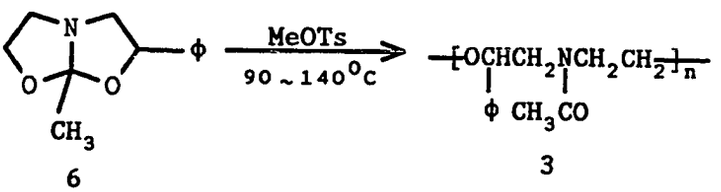


16

10-2 Cationic Polymerization of 5-Methyl-3-Phenyl-Bicyclic Acetal Amide

The cationic polymerization of 5-methyl-3-phenyl-bicyclic amide acetal using MeOTs as initiator was carried out as shown below:



6 3

The polymer prepared was very brittle and had a yellownish color. Both ^{1}H and ^{13}C NMR spectra (Figures 10-1 and 10-2) of the polymer were taken for characterization of the structure.

Unfortunately the resolution of the ^{1}H NMR spectrum (Figure 10-1) is again very poor, which does not allow the characterization of the structure of the polymer.

Assignments can be made for the spectrum as follows: singlet at 2.1 ppm: the methyl protons, singlet at 7.4 ppm: the phenyl protons, doublet at 7.8 ppm: the phenyl protons of -OTs. The assignment of peaks in the region 2.6-5.3 ppm is not clear.

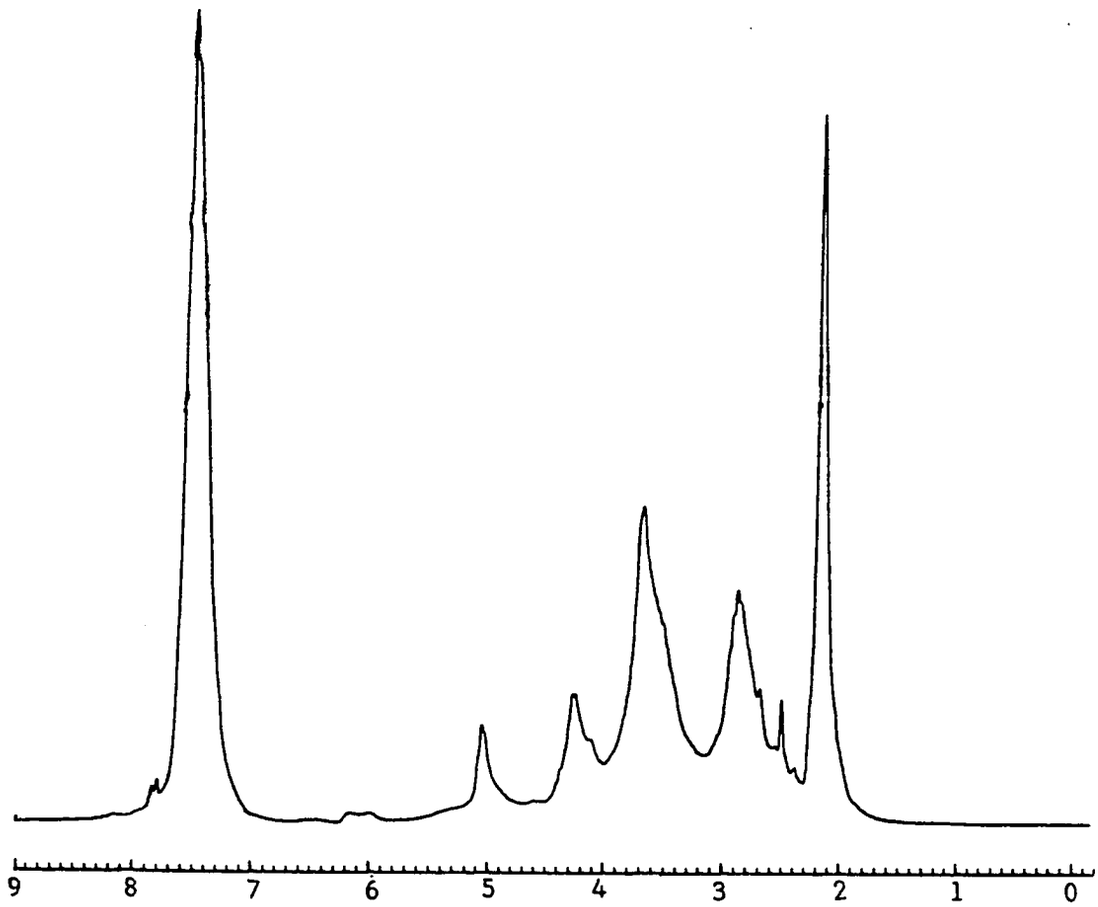
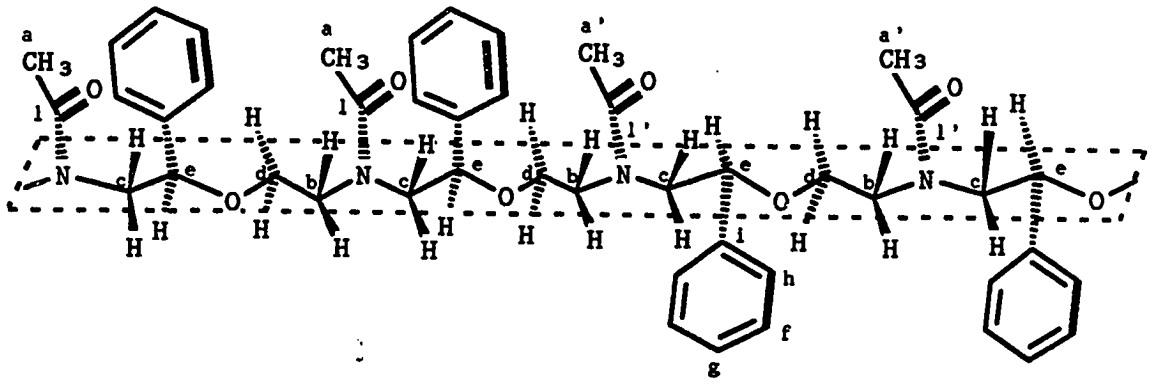


Figure 10-1 200.1-MHz ^{1}H NMR spectrum of polymer 3 in DMSO-D_6 at 100°C.

The ^{13}C NMR spectrum of the polymer was taken at 25°C and 100°C (Figures 10-2 and 10-4). It is very clear that the spectrum changes as the temperature changes. In the region 42--73 ppm there are 9 peaks at 25°C, and they merge

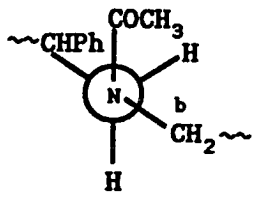
to 5 peaks at 100°C. The explanation for this is that the interchanging of the conformations of the polymer is affected by temperature. The gauche and anti conformations interchange slowly at 25°C, but the average of the two conformations is seen at 100°C due to the fast rotation of the polymer backbone. The spectrum is simpler at high temperature than at low temperature.

In order to assign the ^{13}C NMR spectrum, let's look into the detail of the conformations of polymer 3 first. The anti staggered arrangement of the polymer 3 is shown below:

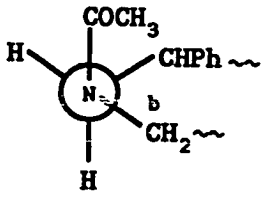


and the staggered Newman projections for different bonds are as follows:

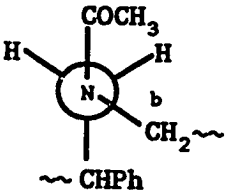
N—C^{c} Bond:



Anti (A)

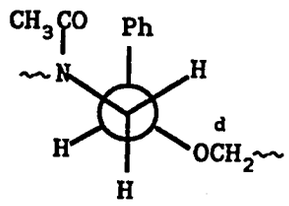


Gauche (B)

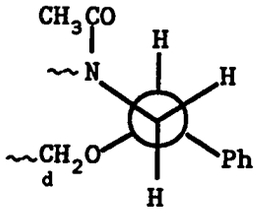


Gauche (C)

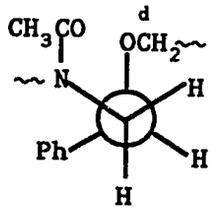
$C^c—C^e$ Bond:



Anti (D)

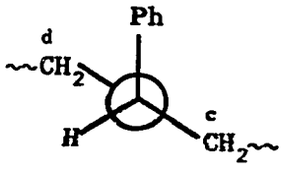


Gauche (E)

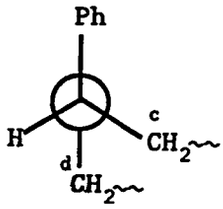


Gauche (F)

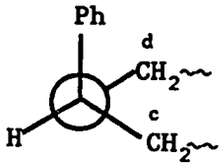
$C^e—O$ Bond:



Anti (G)

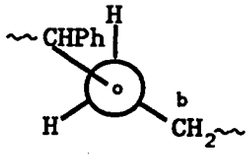


Gauche (H)

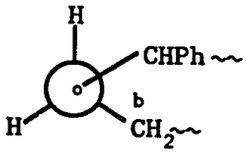


Gauche (I)

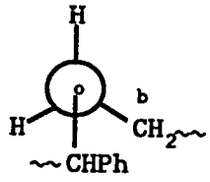
$O—C^d$ Bond:



Anti (J)

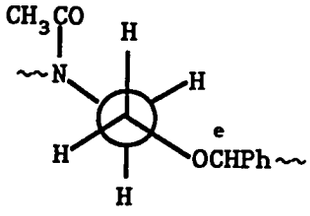


Gauche (K)

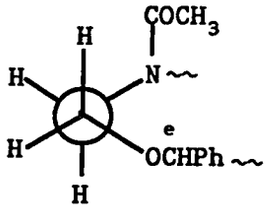


Gauche (L)

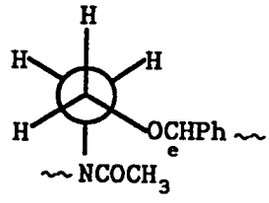
$C^d—C^b$ Bond:



Anti (M)

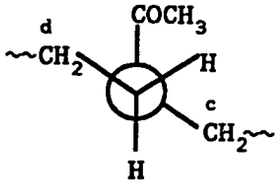


Gauche (N)

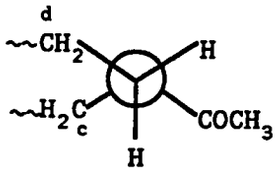


Gauche (O)

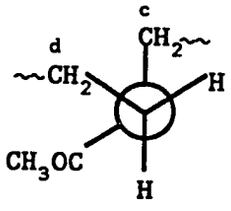
$C^b—N$ Bond:



Anti (P)



Gauche (Q)



Gauche (R)

The chemical environment of a carbon atom depends on the conformations of the polymer. For example, consider the Newman projections of N--C^c bond. The $^bCH_2$ of both gauche conformations (A and B) are in the same chemical environments (between H and CHPh), but the $^bCH_2$ in the anti conformation has a different one (between two H's). If both anti and gauche conformations can be distinguished, two C^b signals should be observed. One C^b signal would be observed if the difference between anti or gauche conformations cannot be distinguished. Using the same reasoning, the conclusions listed in Table 10-1 can be obtained.

When the anti and gauche conformations are distinguishable, according to Table 10-1, there should be two carbon signals for C^b, two for C^c, four for C^d, and two for C^e. The ^{13}C NMR spectrum at 25°C has nine signals in the region for these four carbons. The DEPT experiment (Figure 10-3) confirmed that the peak at 71.2 ppm is for C^e and the other eight signals are methylene carbons. The signal for C^e does not split into two as expected, the explanation is that C^e is shielded by the phenyl group and is no longer sensitive to the change of the conformation. C^b, C^c and C^d give eight signals which agree with the expectation of Table 10-1.

When the gauche conformation is the only conformation which exists, there should be five carbon signals, one each for C^b, C^c and C^e, and two for C^d. On the other hand, when the anti conformation is predominant, there should have two

types of C^d (as indicated in anti-staggered conformation of polymer 3, d and d'), one type each of C^b, C^c and C^e, i.e., five carbon signals in the region. At 100°C, if the difference between the anti and gauch conformations can no longer be distinguished, only five signals will be observed in the region, which matches the experimental results (Figure 10-4).

Table 10-1 The chemical environments of carbons in different conformations

Bond of Projection	Types of Carbon	Number of Signals of Carbon	
		Anti and Gauche Distinguishable	Anti and Gauche Undistinguishable
N--C^c	C^b gauche to CHPh (C,B) C^b anti to CHPh (A)	Two C^b's	One C^b's
C^c--C^e	$C^1OC^aH_3$ gauche to Ph (D,F) $C^1OC^aH_3$ anti to Ph (E)	Two C^a's Two C^1's	Two C^a's Two C^1's
C^e--O	C^d gauche to Ph (G,I) C^d anti to Ph (H)	Two C^d's	Two C^d's
O--C^d	C^b gauche to CHPh (K,L) C^b anti to CHPh (J) C^e gauche to C^bH_2 (K,L) C^e anti to C^bH_2 (J)	Two C^b's Two C^e's	One C^b One C^e
C^d--C^b	——	——	——
C^b--N	C^d gauche to $COCH_3$ (P,R) C^d anti to $COCH_3$ (Q) C^c gauche to C^dH_2 (R,Q) C^c anti to C^dH_2 (P)	Two C^d's Two C^c's	Two C^d's One C^c

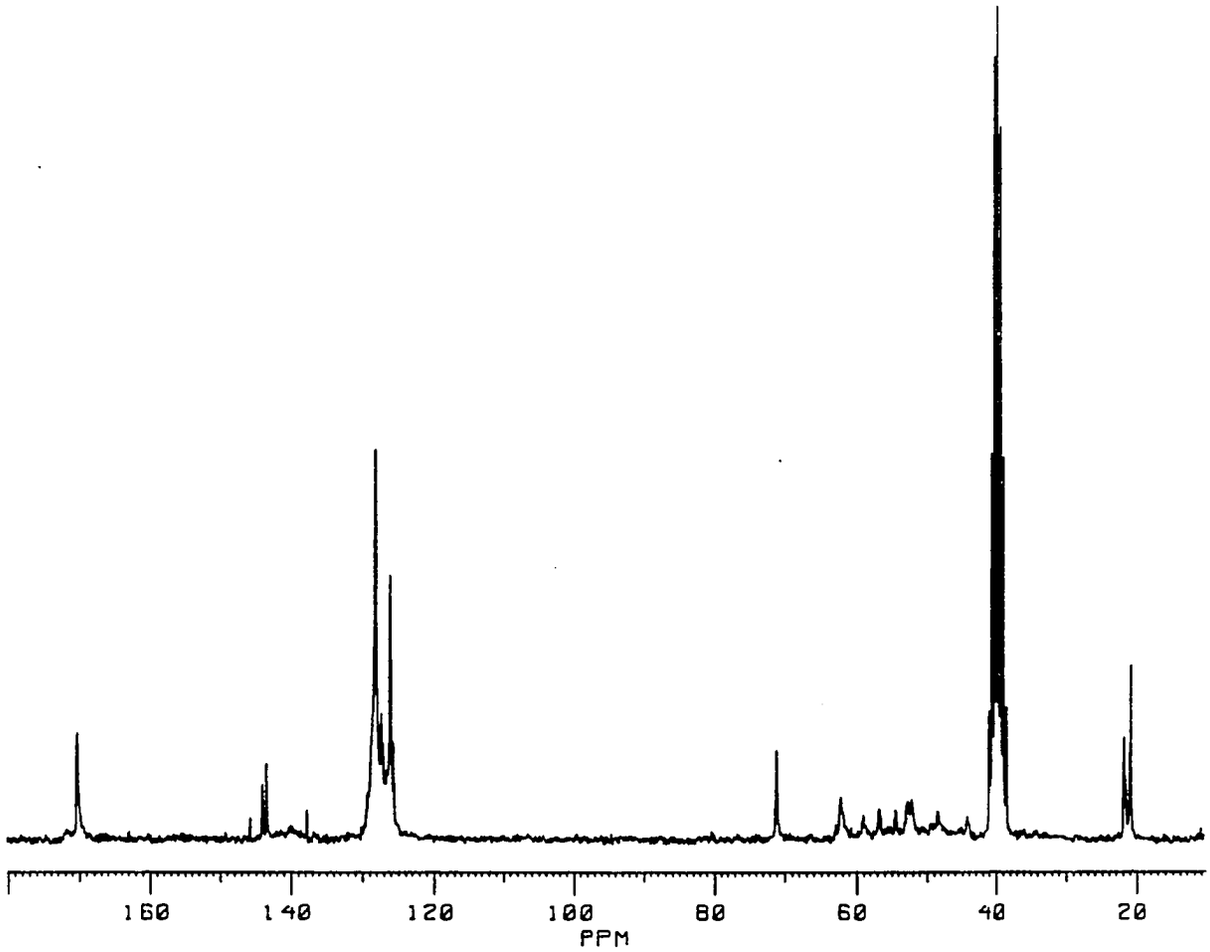


Figure 10-2 50.3-MHz ^{13}C NMR spectrum of polymer 3 in DMSO-D_6 at 25°C.

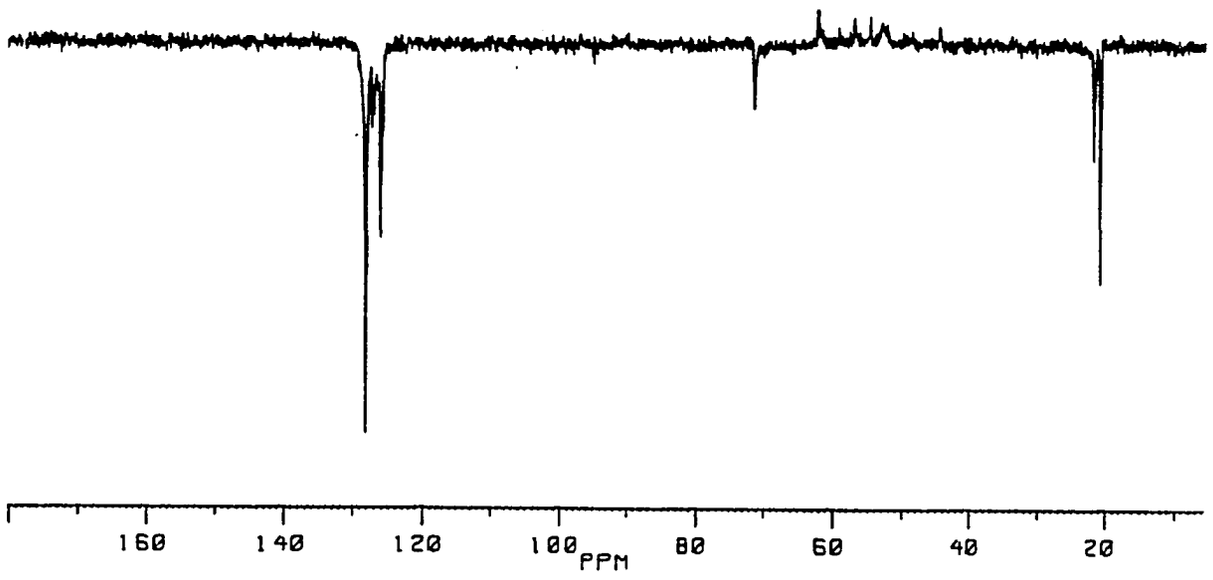


Figure 10-3 50.3-MHz DEPT spectrum of polymer 3 in DMSO-D_6 at 25°C.

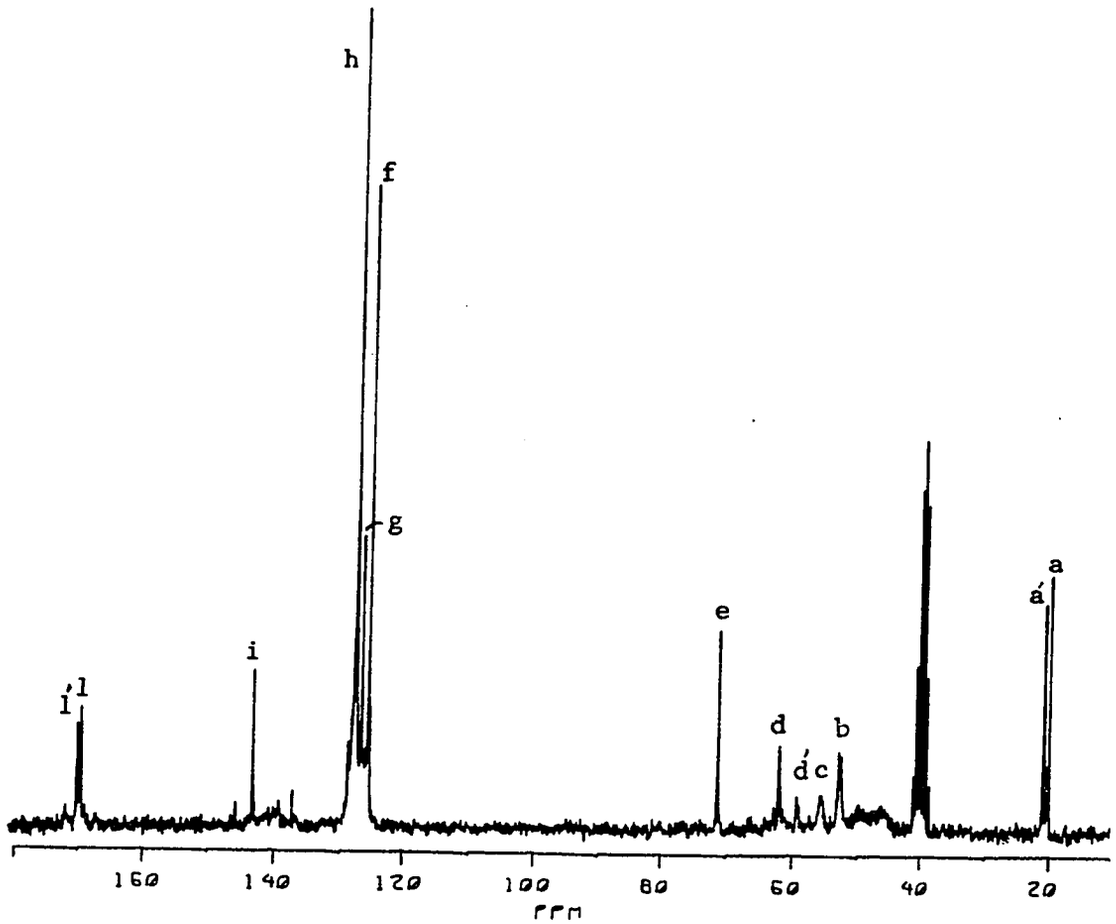


Figure 10-4 50.3-MHz ^{13}C NMR spectrum of polymer 3 in DMSO-D_6 at 100°C.

The assignment for the ^{13}C NMR spectrum is as follows: A. At 25°C (Figure 10-2): the two peaks at 20.5 and 21.8 ppm: methyl carbon (C^a and $C^{a'}$), the eight signals at 43-63 ppm: contributed by C^b, C^c and C^d (a ditailed assignment is not possible), peak at 71.1 ppm: methine carbon (C^e), peak at 126.0 ppm: phenyl carbon (C^f), peak at 127.5 ppm: phenyl carbon (C^g), peak at 128.0 ppm: phenyl carbon (C^h), peak at 143.5 and 144.3 ppm: phenyl carbon (C^i), peak at 170.2 ppm: carbonyl carbon (C^l). There are also signals contributed by -OTs as the ending group of the polymer: the signal for the methyl carbon of -OTs partially overlaps with that for the

methyl carbon of the polymer at 21.8 ppm, peak at 138.1 ppm: the tertiary carbon attached to methyl group, peak at 146 ppm: the tertiary carbon attached to $-SO_3$, and the other peaks for the phenyl carbons are completely or partially overlapped with those for the phenyl carbons in the polymer repeating unit.

B. The assignment of Figure 10-2 agrees with the DEPT experiment (Figure 10-3), i.e., the carbons attached to an even number of protons have positive intensities, the carbons attached to an odd number of protons have negative intensities, and the tertiary carbons have zero intensities.

C. At 100°C (Figure 10-4): peak at 20.0 ppm: $C^{a'}$, peak at 20.5 ppm: methyl carbon of -OTs, peak at 21.1 ppm: C^{a}, peak at 52.6 ppm: C^{b}, peak at 56.3 ppm: C^{c}, peak at 59.1 ppm: C^{d}, peak at 62.0 ppm: $C^{d'}$, peak at 71.2 ppm: C^{e},peak at 125.6 ppm: C^{f}, peak at 126.2 ppm: C^{g}, peak at 128.0 ppm: C^{h}, peak at 143.4 ppm: C^{i}, peak at 169.2 ppm: $C^{l'}$, peak at 170.0 ppm: C^{l}, peak 137.2 ppm: tertiary carbon of -OTs attached to methyl group, peak at 146.0 ppm: tertiary carbon of -OTs attached to $-SO_3$.

The elemental analysis results agree with the proposed structure of polymer 3, see Table 10-2.

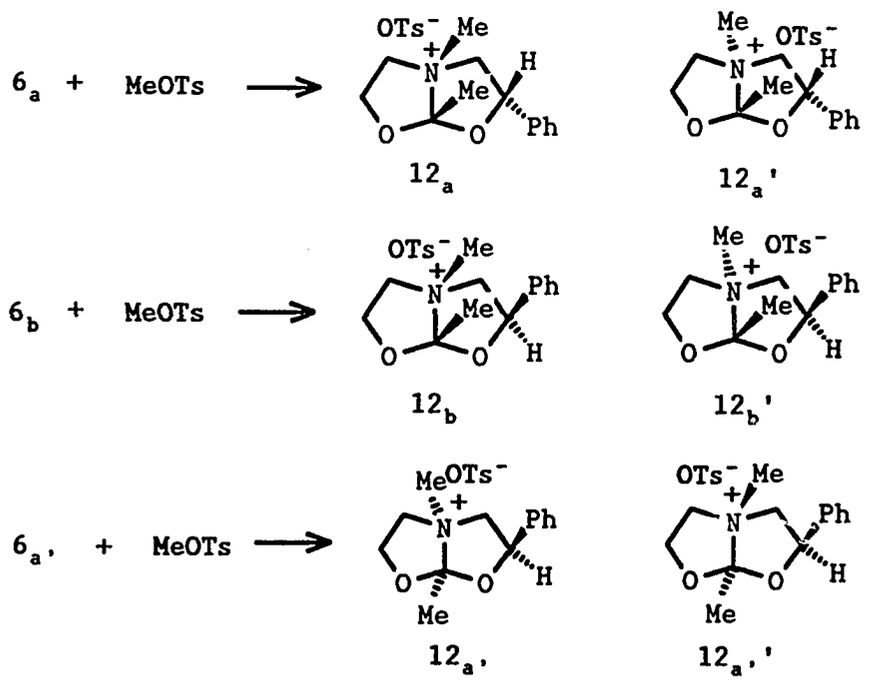
Table 10-2 Elemental analysis results of polymer 3

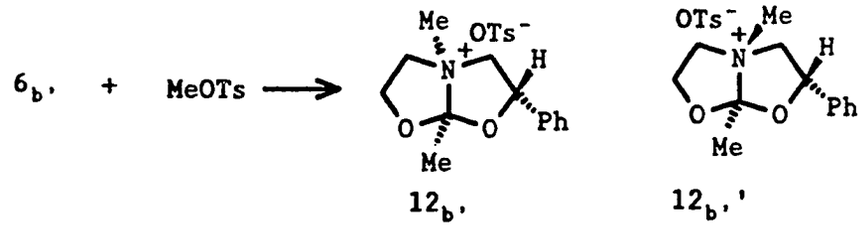
Element	C%	H%	N%
Theorietical Value	70.24	7.32	6.83
Experimental Value	70.20	7.47	6.37

10-3 Mechanistic study of the Cationic Ring Opening Polymerization of Bicyclic Amide Acetal

In the introduction to this chapter, a polymerization mechanism was proposed which involves the formation of compound 12. Compound 12 can be prepared and used as an initiator instead of MeOTs, which strongly supports the proposed polymerization mechanism. Both ^{1}H and ^{13}C NMR of compound 12 were taken for the purpose of characterization; see Figure 10-5 and 10-6.

Since the bicyclic compound, 5-methyl-3-phenyl-bicyclic amide acetal, as prepared, was an isomer-mixture as we discussed in Chapter 8, compound 12 would also be an isomer-mixture. Based on the four isomers of 6 (6_a, 6_b, $6_{a'}$, $6_{b'}$), eight isomers of 12 should be derived from 6:





But only configurations (12_a, 12_b, $12_{a'}$, $12_{b'}$) with the two methyls on the same side of the ring are possible. When the two methyls are on different sides of the ring, one of the five-membered-ring will be twisted, which is very unstable; therefore isomers, $(12_a)'$, $(12_{a'})$, $(12_b)'$ and $(12_{b'})'$ can not form. Two sets of chemical shifts should be observed for enantiomers (12_a, $12_{a'}$) and (12_b, $12_{b'}$).

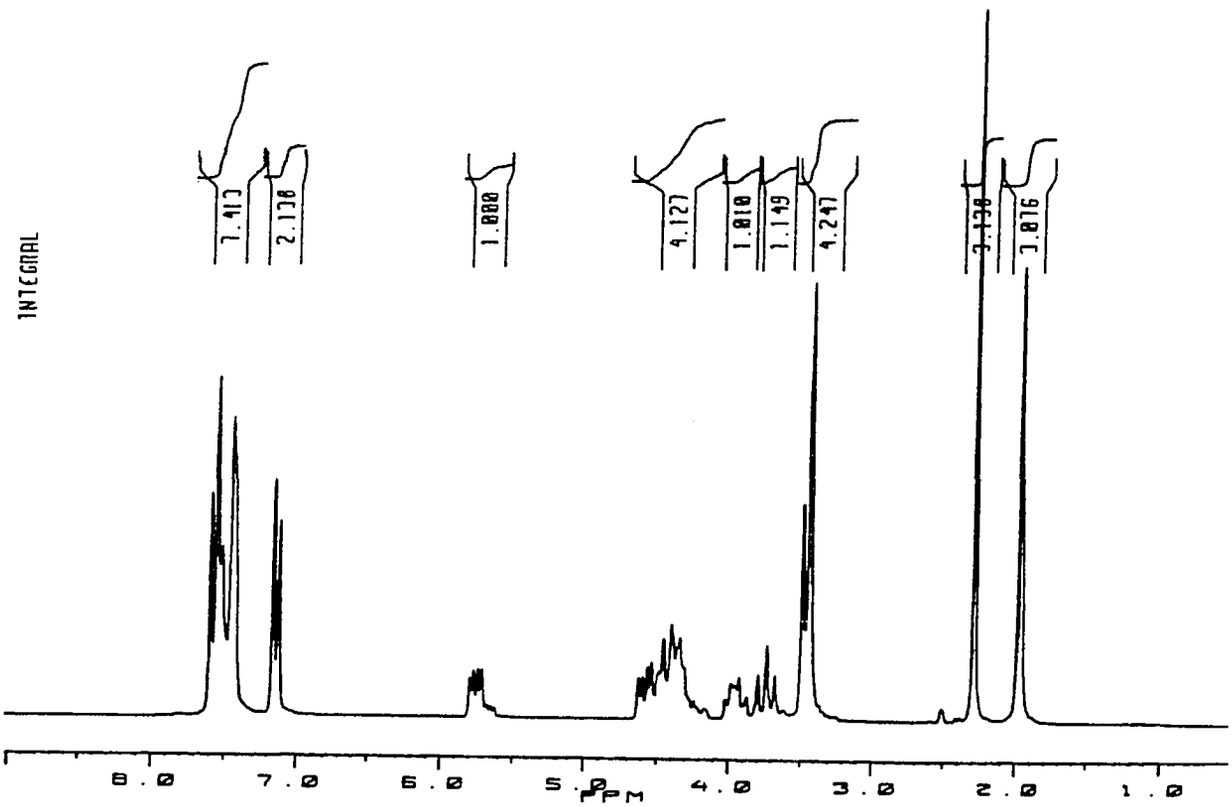
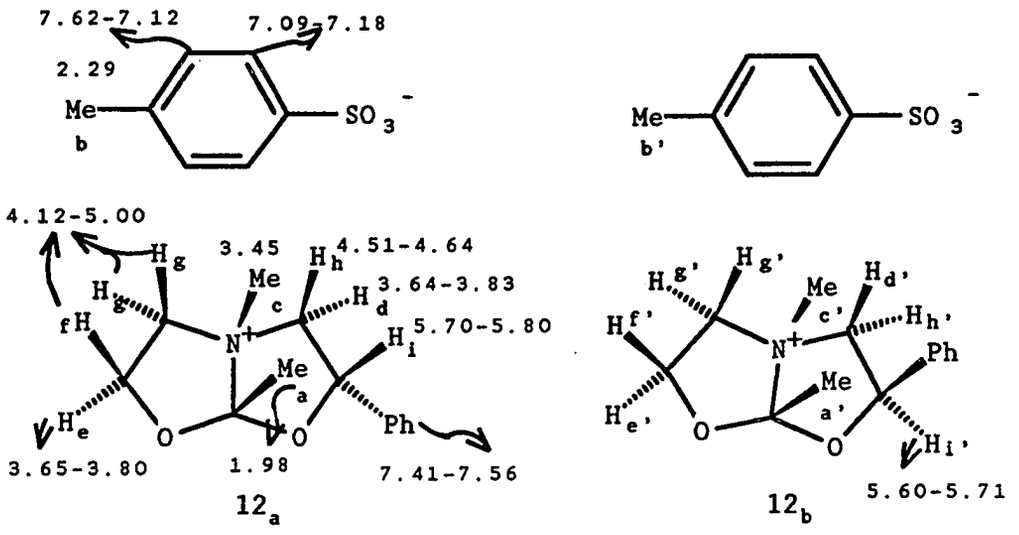
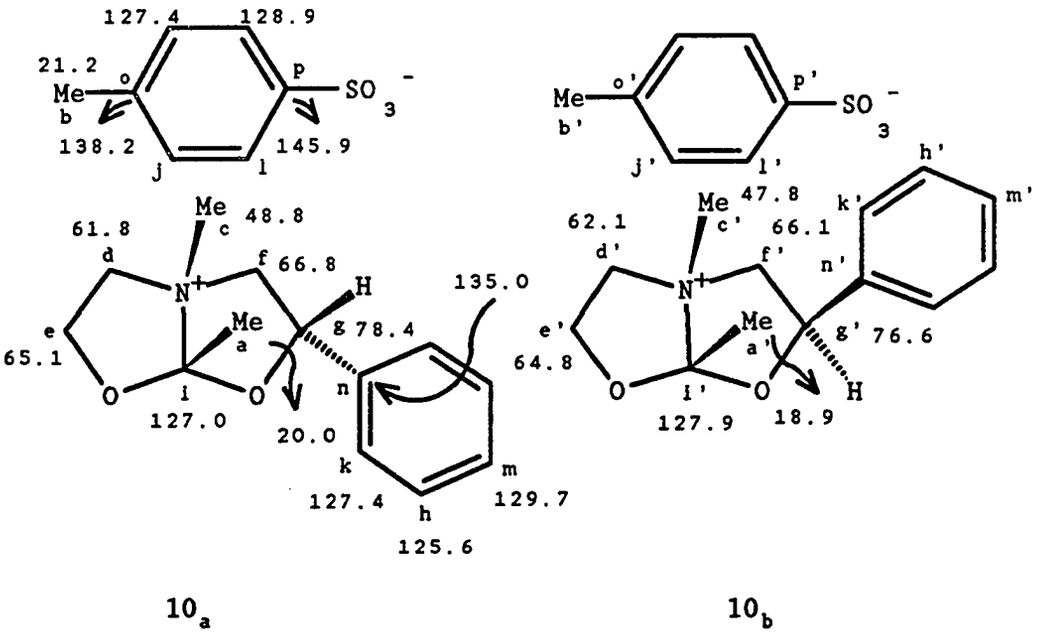


Figure 10-5 200.1-MHz ^{1}H NMR spectrum of compound 12 in DMSO-D_6 at 25°C.

The assignment for the ^{1}H NMR spectrum (Figure 10-5) is indicated as follows:



Assignment for the ^{13}C NMR spectrum (Figure 10-6) is as shown below:



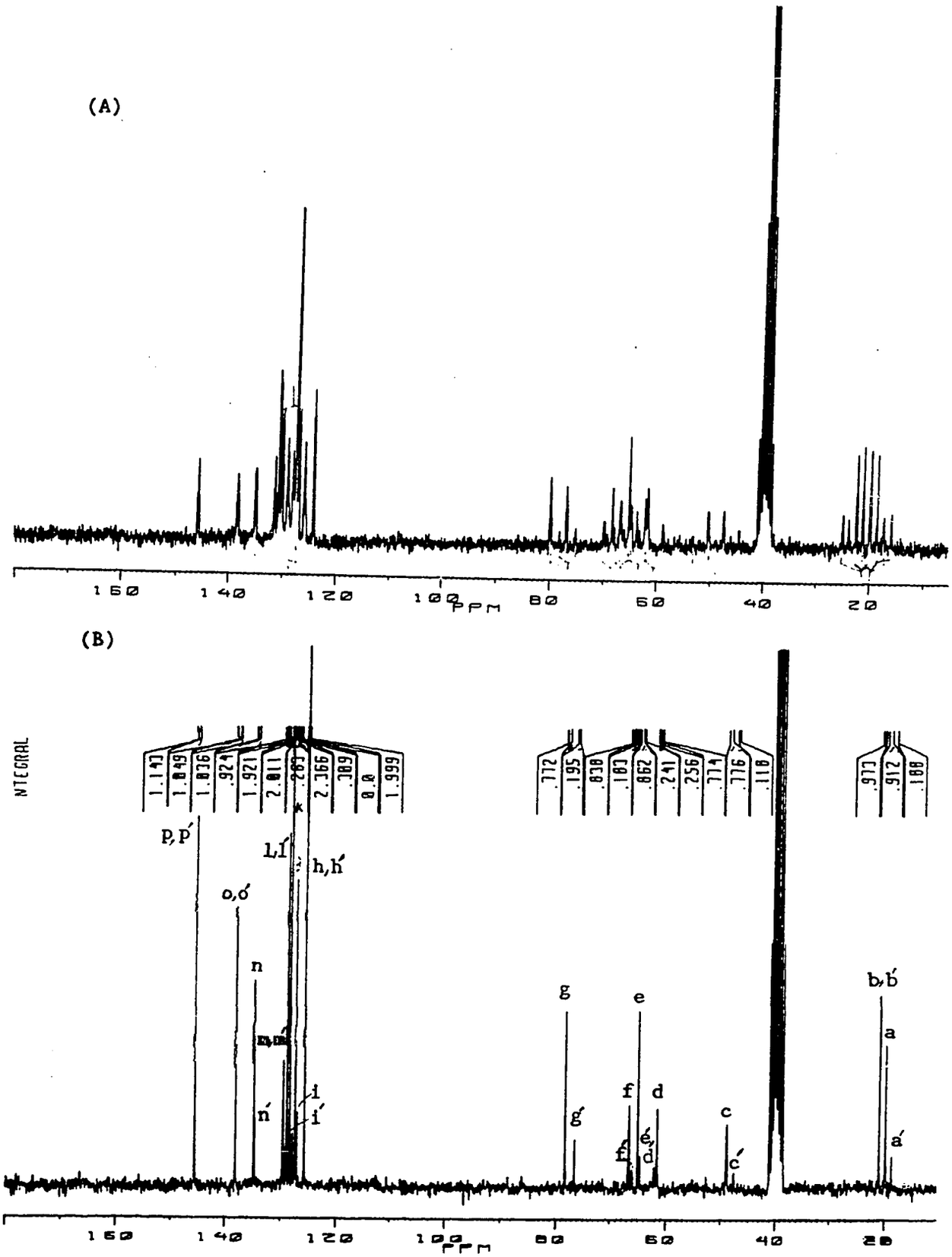


Figure 10-6 50.3-MHz ^{13}C NMR spectrum of compound 12 in DMSO-D_6 at 25°C: (A) coupling and (B) decoupling

The effects of initiator on molecular weight was studied by using different amount of MeOTs. The number average molecular weight of polymer 3 has been determined by VPO and the results are listed in Table 10-3.

Table 10-3 The effect of initiator (MeOTs) on the molecular weight

Mole Ratio of Monomer:MeOTs	Polymerization Condition	Number Average Molecular Weight	Average Number Repeating Unit per Polymer
41.84	120°C/21 hrs	2.43×10^3 g/mole	11.9
22.00	120°C/21 hrs	2.58×10^3 g/mole	12.6
11.21	120°C/21 hrs	1.94×10^3 g/mole	9.5

Analyzing the data listed in Table 10-3, we can reach the following conclusions: (1) Under the experimental conditions, the maximum number average molecular weight is approximately 2.5×10^3 g/mole; (2) the number average molecular weight is very slightly affected by the amount of MeOTs.

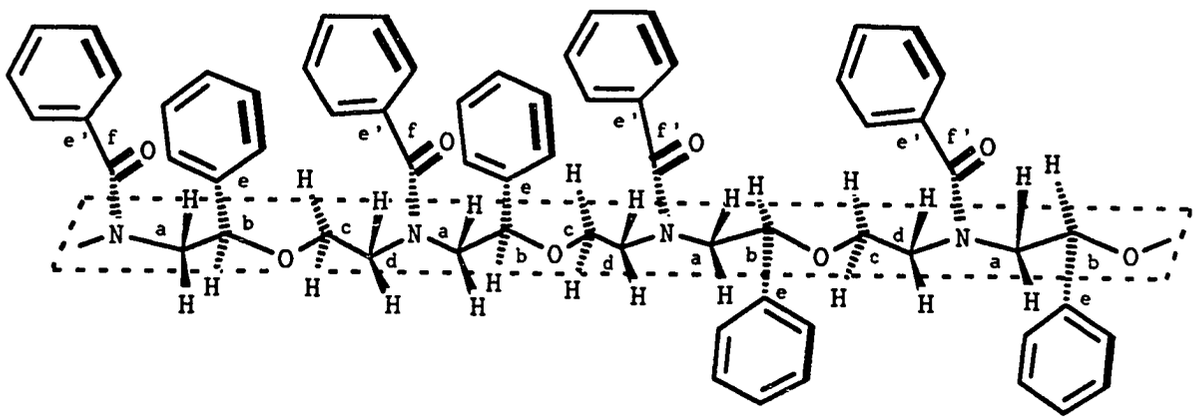
When the monomer:MeOTs ratio is high (>13), the molecular weight is independent of the amount of MeOTs. This indicates that there is a self-termination reaction involved in the polymerization which limits the molecular weight.

10-4 Polymerization of Other Bicyclic Amide Acetals

The polymerization of 3,5-diphenyl-bicyclic amide acetal and 5-*t*-butyl-3-phenyl-bicyclic amide acetal were

also carried out. The 5-*t*-butyl-3-phenyl-bicyclic amide acetal did not produce a polymer as did 5-methyl-3-phenyl-bicyclic amide acetal. The reason for this may be that the *t*-butyl group is too bulky which prevents two monomers from getting close enough to each other to react.

When MeOTs was used as initiator to polymerize 3,5-diphenyl-bicyclic amide acetal, a brittle polymer 3′ was formed with a brownish color. The ^{13}C NMR spectrum is shown in Figure 10-5 which is very similar to the one of polymer 3 (Figure 10-4). The anti-staggered arrangement of polymer 3′ is shown as follows.



The similarity between the ^{13}C NMR spectra of polymer 3 and 3′ is obvious, which is expected. Assignment for the ^{13}C NMR spectrum (Figure 10-7) is as follows: Peak at 20.5 ppm: the methyl carbon of OTs^-; peak at 50.9 ppm: C_a; peak at 58.2 ppm: C_d; peak at 62.6 ppm: C_b; peak at 70.6: C_c; peaks at 125.4-130 ppm: phenyl carbons except the quaternary carbon (C_f or $C_{f'}$); peak at 133.0 ppm: C_e; peak at 136.9

ppm: $C_{e'}$; peaks at 137.4 and 145.7 ppm: the quaternary carbons of OTs^-; peak at 165.4 ppm: C_f; peak at 170.8 ppm: $C_{f'}$.

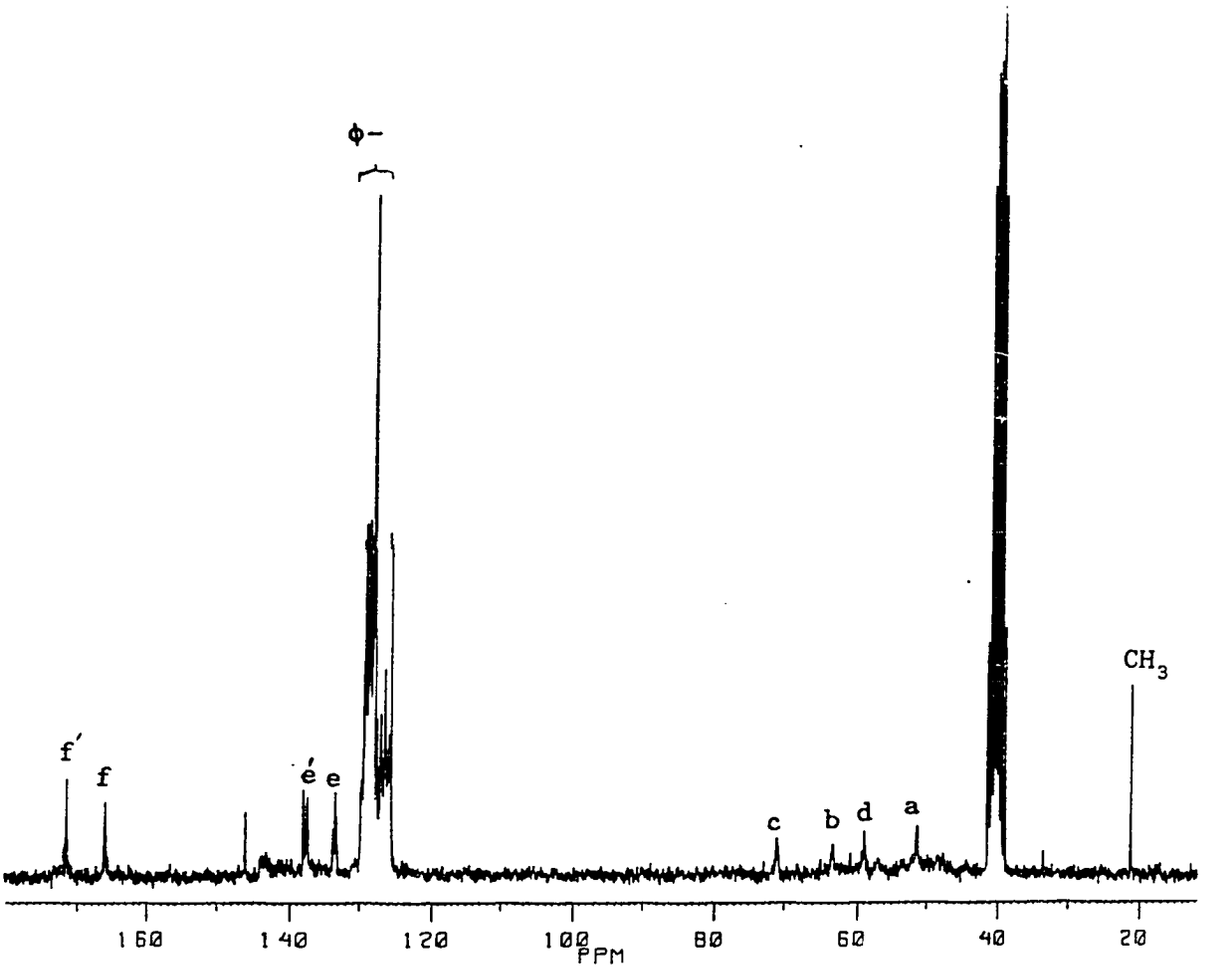


Figure 10-7 50.3-MHz ^{13}C NMR spectrum of polymer 3' in DMSO-D_6 at 40°C.

10-5 Experimental Part

10-5.1 Synthesis of Polymer 3

5-Methyl-3-phenyl-bicyclic amide acetal (2.000 g, 9.76×10^{-3} mole) and methyl tosylate (10 to 100 μl) were added into a polymerization tube with a magnetic stirrer and sealed under a 0.05 mmHg vacuum. The tube was then kept at

120°C for 48 hrs to produce a light yellow brittle polymer. The polymer was purified by dissolving in methylene chloride and precipitating in ether to afford a light yellow powder (polymer 3) with a yield of 70%.

Polymer 3 was also prepared by using 200 mg of compound 12 as initiator under exactly the same conditions as when methyl tosylate was used.

10-5.2 Synthesis of Compound 12

Pure 5-methyl-3-phenyl-bicyclic amide acetal (1.140 g, 5.554×10^{-3} mole) and methyl tosylate (1.034 g, 5.554×1^{-3} mole) were mixed in a N_2 atomosphere at ambient temperature. The reaction mixture was solidified to give a transparent solid after 6 hours. The solid was dissolved in 20 ml of methylene chloride and then was precipitated in ether. The precipitate formed was compound 12 which can be used as a initiator. The yield was 90%.

10-5.3 Synthesis of Polymer 3'

Crude 3,5-diphenyl-bicyclic amide acetal (2 g, 7.49×10^{-3} mole) and methyl tosylate (50 ul) were sealed in a polymerization tube under a vacuum of 0.05 mmHg. The polymerization tube was then kept at 80°C for 50 hrs to yield a brownish brittle polymer. The polymer was purified in the same way as polymer 3 except the solvent used for precipitation was hexane/ether (v:v 3:1). The yield was 63%.

REFERENCE

[1] T. Saegusa and S. Kobayashi: Makromol. Chem., Macromol. Symp. 1, 23 (1986).