Studies on the Synthesis of a Methacrylate-Based Dental Restorative Resin

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SYNOPSIS

The synthesis of bisphenol A–glycidyl methacrylate (BIS–GMA), the resin component in most dental composite restorative materials, catalyzed by different tertiary amine accelerators such as N,N'-dimethyl-p-toluidine (DMPT), N,N'-dimethylamino phenethyl alcohol (DMAPEA), and N,N'-dimethylamino ethyl methacrylate (DMAEMA) is reported in this work. The effect of varying concentrations of accelerators and the reaction conditions of the synthesis as a function of time is studied in detail. The kinetics of the reaction between epoxide and carboxyl group during the formation of BIS–GMA is monitored using infrared (IR) and chemical techniques. The reaction is found to follow first-order and zero-order kinetics with respect to epoxide and acid, respectively. The degree of epoxide and acid conversion has been calculated as a function of time. The percentages of various isomers, formed under different reaction conditions have been reported. Characterization procedures for BIS–GMA have been developed.

INTRODUCTION

A resin based on a polyepoxy precursor has been reported to be used as the matrix for the commonly used composite dental restoratives.[1,2] This resin, 2,2-bis[4-(2-hydroxy-3-methacryloyloxypropoxy)]-phenyl propane or bisphenol A–Glycidyl methacrylate (BIS–GMA), is a reaction product of methacrylic acid and diglycidyl ether of bisphenol A (DGEBA). It is believed that the backbone of the molecule provides superior toughness and other desirable properties[3] for the final composite. The purity and other characteristics of BIS–GMA play a prominent role in its end applications. Hence synthesis conditions and characterization of BIS–GMA are of utmost importance. Very little information is available regarding the synthesis[4] of BIS–GMA and characterization of BIS–GMA extracted from commercial composites.[5–8]

The addition esterification reaction of DGEBA and methacrylic acid is catalyzed by tertiary amine to produce BIS–GMA. The mechanism of the re-

action is complex and is not fully elucidated.[9] Hence, it would be of great interest and value to study the kinetics and mechanism of the reaction.

Hence the objective of this study was designed as follows:

1. To study the effect of amine accelerator in BIS–GMA synthesis
2. To determine the order of the BIS–GMA synthesis kinetically
3. To characterize BIS–GMA spectroscopically and compare with those described in other studies[5–8]
4. To identify and quantify the various isomers formed during BIS–GMA synthesis chromatographically

EXPERIMENTAL

Materials

Diglycidyl ether of bisphenol A (DGEBA) (Ciba Geigy, India) was used after analyzing its structure by IR spectrum (917 cm^{-1}, terminal epoxy, 1020–1040 cm^{-1}, aliphatic ether, 1220–1240 cm^{-1}, aro-

matic ether, and 3400–3450 cm⁻¹, hydroxyl group) and checking its purity by various analyses such as epoxy equivalent weight (179 eq/100 g), hydroxy value (0.1474 eq/100 g), hydrolyzable chlorine content (0.2810%), and a sharp peak (100%) obtained in high performance liquid chromatography (HPLC) without any traces of impurity. Methacrylic acid (AR, Cambrian, Croydon) was purified as per reported procedure.[10] N,N'-dimethyl-p-toluidine (DMPT) (E. Merck, Schuchardt, Germany) (bp 211°C) and 2-dimethylaminoethyl methacrylate (DMAEMA) (E. Merck) (bp 182–183°C) were purified by distillation. 4-(Dimethylaminophenethyl alcohol) (DMAPEA) (Aldrich, U.S.A.) was used without further purification.

METHODS

Synthesis of BIS–GMA Resin[6]

The reaction of DGEBA and methacrylic acid (1 : 2.1, weight ratio) was carried out in nitrogen atmosphere using various amounts of tertiary amine (DMPT, DMAEMA, and DMAPEA) catalyst in absence of solvent at 60°C until the reaction was complete. The addition esterification reaction was monitored by following the disappearance of absorption peak at 917 cm⁻¹ (10.9 μm wavelength) characteristic of terminal epoxide group using IR spectroscopy. The reaction product was purified by acid–alkali treatment and stabilized with 60 ppm of inhibitor (hydroquinone).

For the kinetic investigation, infrared spectroscopy technique was used for the determination of residual epoxide content and acid concentration was determined by chemical analysis. A Perkin-Elmer Model 597 grating infrared double beam spectrophotometer was used. Samples withdrawn at different intervals of time were coated as a thin film between two disks of sodium chloride and placed in the sample beam. The intensities of the terminal epoxide absorbance peak at 917 cm⁻¹ and aliphatic ether absorbance peak at 1040 cm⁻¹ were measured using a standard baseline method.[11] The characteristic peak at 917 cm⁻¹ originates from the terminal epoxide groups and its intensity varies drastically during the addition esterification. The epoxide concentration and the degree of conversion were obtained by the following equations:

relative ratio of epoxide

$$= \frac{\text{absorbance intensity of epoxide}}{\text{absorbance intensity of ether}}$$

epoxide concentration (%)

$$= 100 \times \frac{\text{relative ratio of epoxide at time } t}{\text{relative ratio of epoxide at zero time}}$$

Degree of conversion (%)

$$= 100\% - \text{epoxide concentration (%)}$$

Regression analysis[12] was carried out for epoxide and acid concentration data applying the least square fit method for both zero-order and first-order kinetics.

NMR spectra of the BIS–GMA, synthesized at various conditions, were recorded in a Varian EM 360, 60 MHz NMR spectrometer in CDCl₃ using TMS as the internal standard.

UV spectra of the acid–amine solutions,[13] extracted from synthesized BIS–GMA samples, were obtained using a Shimadzu, UV–visible spectrophotometer, Model UV 240, and the absorption maxima near 260 nm were recorded.

Refractive indices of the synthesized samples were determined at 25°C using an Atago Abbe refractometer, Type 3T.

The isomer[7,8] formation in the BIS–GMA reaction was analyzed by means of HPLC (Model 6000 A, Water Associates, U.S.A. with absorbance detector) and the components were separated under the conditions specified in Table I.

RESULTS AND DISCUSSION

The reaction between epoxide and carboxyl groups is usually employed in the preparation of highly crosslinked elastomers and different network structured polyepoxides.[9] The functional groups present in these reactants can participate in some competing side reactions[9,14,15] such as etherifications, condensation, esterification, and hydrolysis. Generally, onium salts, tertiary amines, and phosphines are effective catalysts for the acid–epoxide reaction which proceeds at only moderately elevated temperatures.[16]

**Table I Analytical HPLC,
Chromatographic Conditions**

Column: 0.39 × 30 cm, Porosil
Particle size: 10 μm
Flow rate: 2 mL/min
Chart speed: 1 cm/min
Detector: UV 254 nm
Mobile phase: methylene chloride : ethyl acetate,
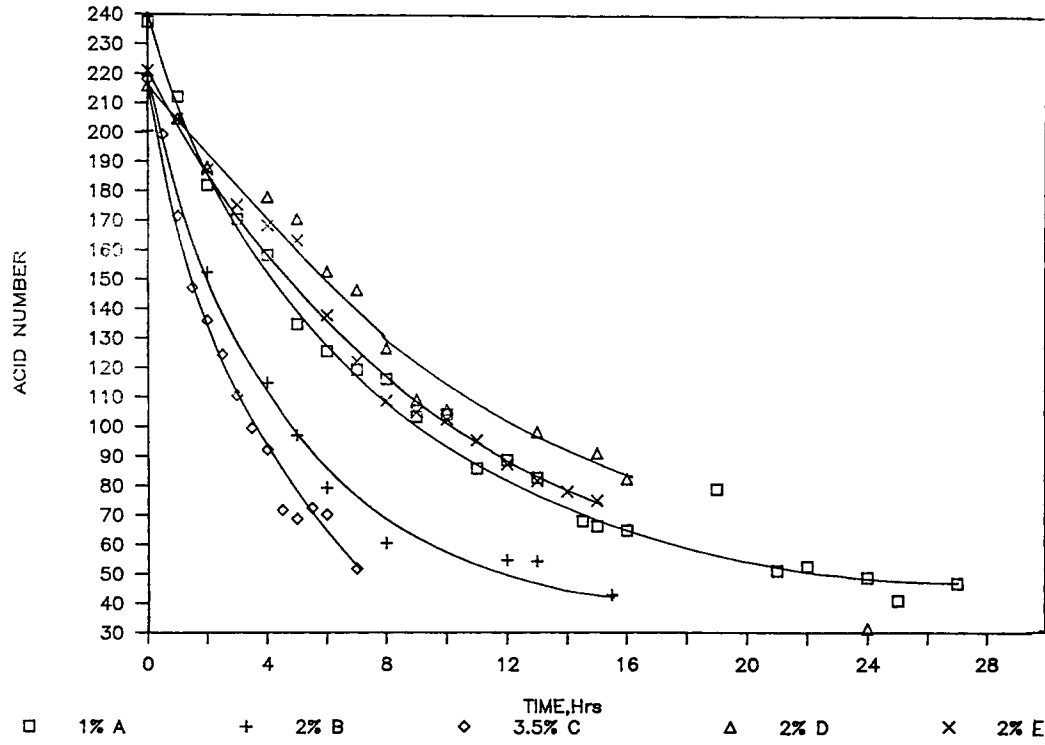   80 : 20 (v/v)

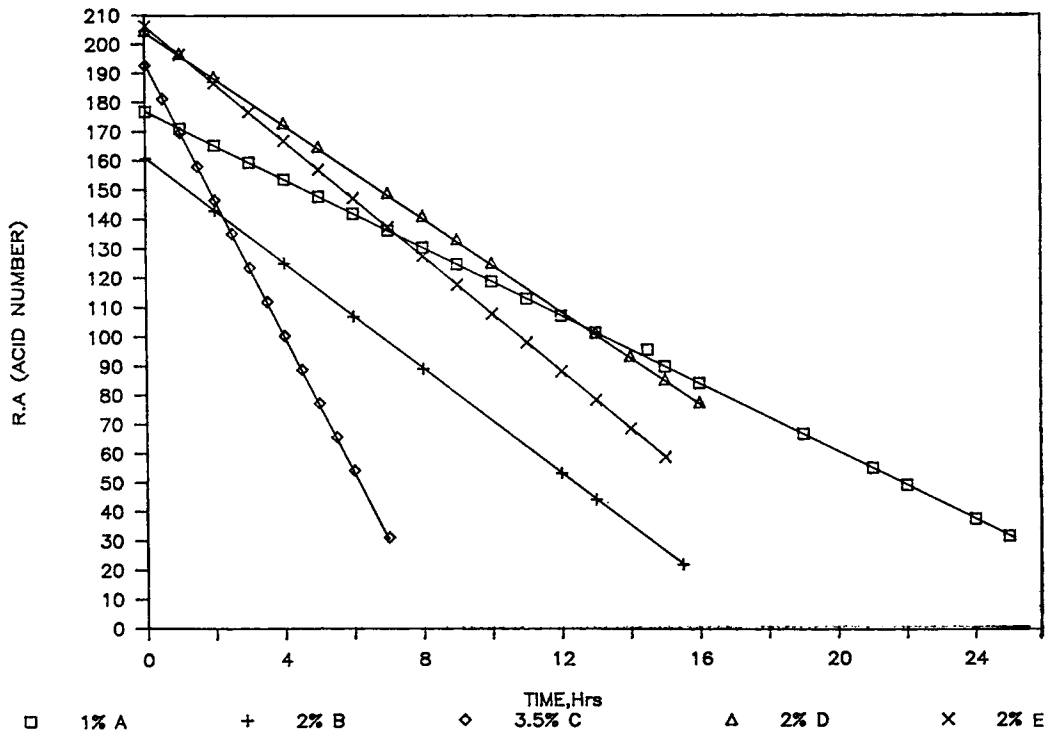**Figure 1**   Acid conversion in BIS–GMA: (A–C) DMPT; (D, E) DMAEMA and DMAPEA.

Figure 2   Zeroth-order kinetic plot of BIS–GMA from acid conversion plot (A–E).

Some homopolymerization will occur in the uncatalyzed reaction.[14] It has been found that tertiary amines are used as catalysts in these types of reactions, which not only affect the rate of reaction, but also largely or wholly suppress the undesirable side reactions.[14]

Kinetics and Mechanism

Generally, this reaction depends on several factors such as type of catalyst, amount of catalyst, ratio of reactants, and temperature.[9] In order to get pure and linear unsaturated vinyl resin, BIS–GMA (2,2 bis [4(2-hydroxy-3-methacryloyloxy propoxy)] phenyl propane) adduct from DGEBA and methacrylic acid, the kinetic study was carried out under controlled synthesis conditions. The kinetics of the reaction of DGEBA and methacrylic acid, catalyzed with three different tertiary amines (namely, DMPT, DMAEMA, and DMAPEA) was studied in the absence of solvent at 60°C (higher temperature leads to undesirable side reactions[9]) under inert atmosphere. The concentrations of DGEBA and methacrylic acid were in the ratio of 1 : 2.1. The catalyst concentration varied from 0.75 to 3.5% (weight ratio). Acid conversion in BIS–GMA was

plotted against the function of time (Fig. 1). The gradual decrease in acid number indicates the smooth addition esterification. The straight lines in the Figure 2 are least square fit regression plots,[12] obtained from acid conversion plots.

The coefficient of correlation, rate constant, and standard deviations are presented along with similar data obtained, using first order kinetics (Table II). On the basis of the correlation coefficient, the linear relationship of acid number versus time appears to be the better fit. This obviously reveals that the reaction follows zero-order kinetics with respect to acid (i.e., independent of acid concentration, which is high in the reaction).

In addition, the epoxide conversion in BIS–GMA evaluated from IR data (Figures 3–5) also proved the smooth addition esterification. Figure 6 revealed the first-order nature of BIS–GMA reaction with respect to epoxide concentration. One hundred percent epoxide conversion and 85% acid conversion were observed (Figs. 7 and 8) in all synthesis conditions, and the time taken for 100% epoxide conversion is found to be directly dependent on the catalyst concentration (Fig. 9).

The mechanism of the reaction between epoxide and carboxyl group is complicated and has not yet been fully elucidated.[9] There are different concep-

Table II   Results of Regression Analysis

Code No. and Cat. Concn (%) (DMPT)	Conversion	Zero-Order Kinetics		First-Order Kinetics	
		Correlation Coefficient[c]	Rate Constant (s^{-1})	Correlation Coefficient[c]	Rate Constant (mol/s)
KM2 1	Acid	0.9098106 (23.57807)	0.001611	0.7973842 (0.3359611)	0.0000135
KM6 2	Acid	0.8990238 (24.64172)	0.0024978	0.8345211 (0.2365081)	0.0000191
KM11 3.5	Acid	0.959188 (15.26688)	0.0064142	0.8525357 (0.3316015)	0.0000713
KM20[a] 2	Acid	0.9769224 (10.61955)	0.0027379	0.9072449 (0.279998)	0.0000361
KM21[b] 2	Acid	0.9793264 (10.75023)	0.0022149	0.9068448 (0.3149232)	0.0000369
KM1 0.75	Epoxide	0.9767404 (10.38878)	0.0006194	0.9987321 (0.06011762)	0.0000236
KM2 1	Epoxide	0.9863069 (6.322319)	0.0006179	0.9955778 (0.04800929)	0.0000155

[a] DMAPEA catalyst.
[b] DMAEMA catalyst.
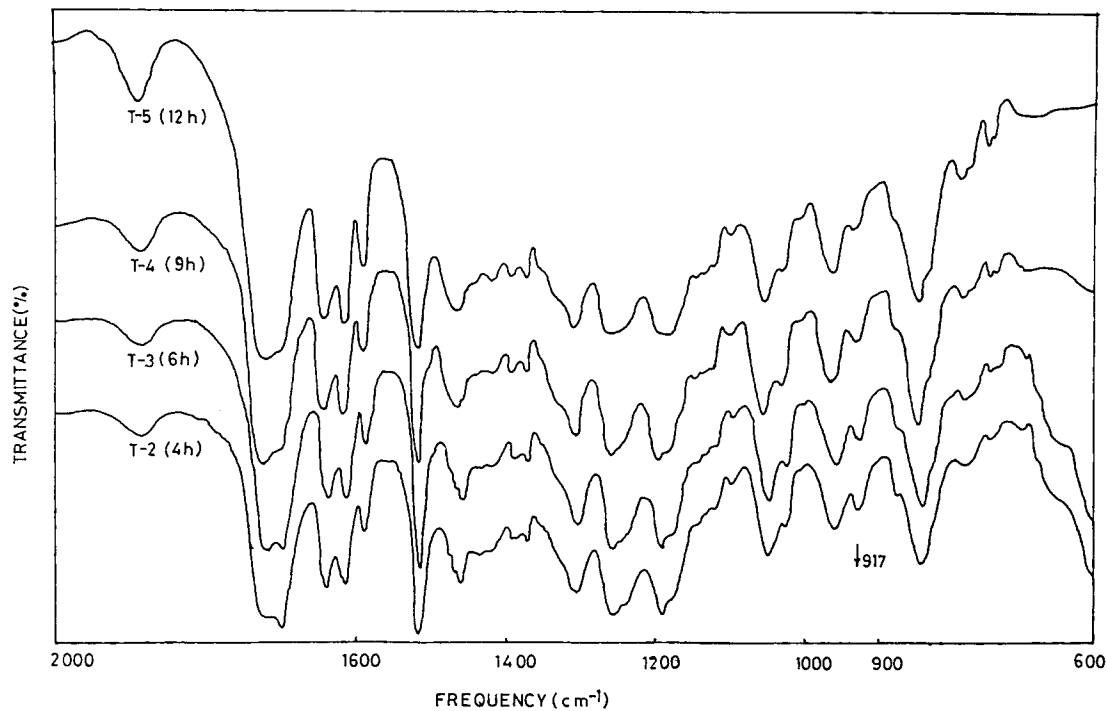[c] The number in parentheses represents standard deviation.

Figure 3   Monitoring of BIS–GMA synthesis as a function of time.

tions of the initiation step in the literature.[15,17] From the results obtained, the absence of induction period[15] (Figs. 1 and 2) and the zero-order kinetic nature of acid conversion indicate that the initiation step involves the acid–amine adduct, where the acid is proton donor.[15,17]

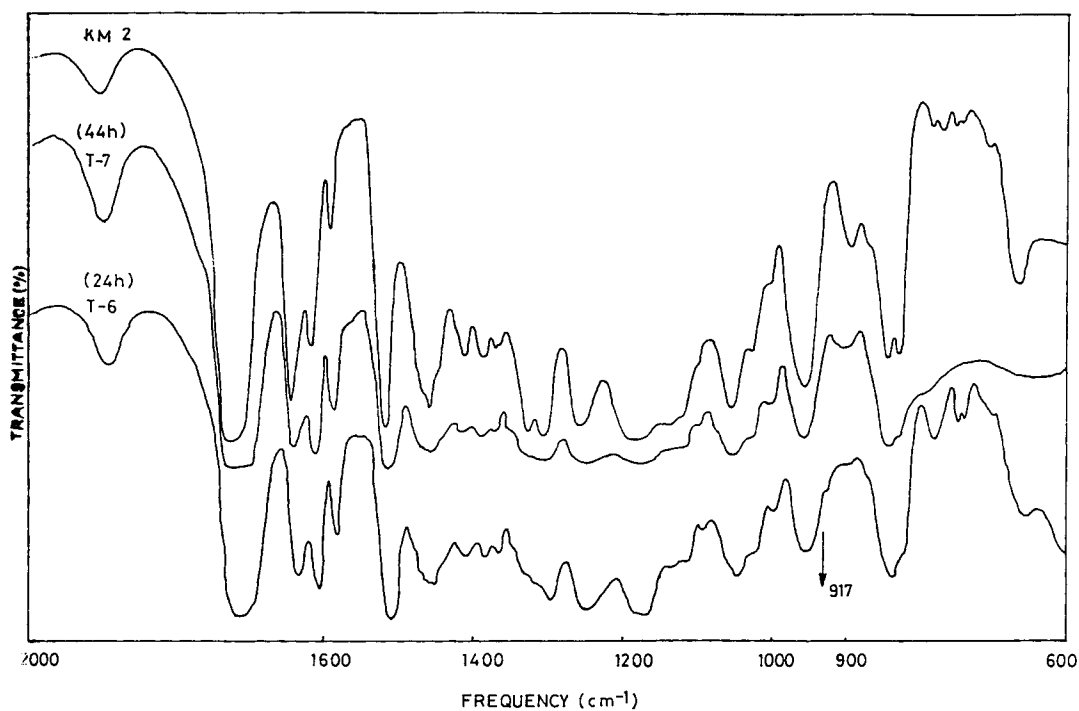The following reaction mechanism may be consistent with the facts described above:

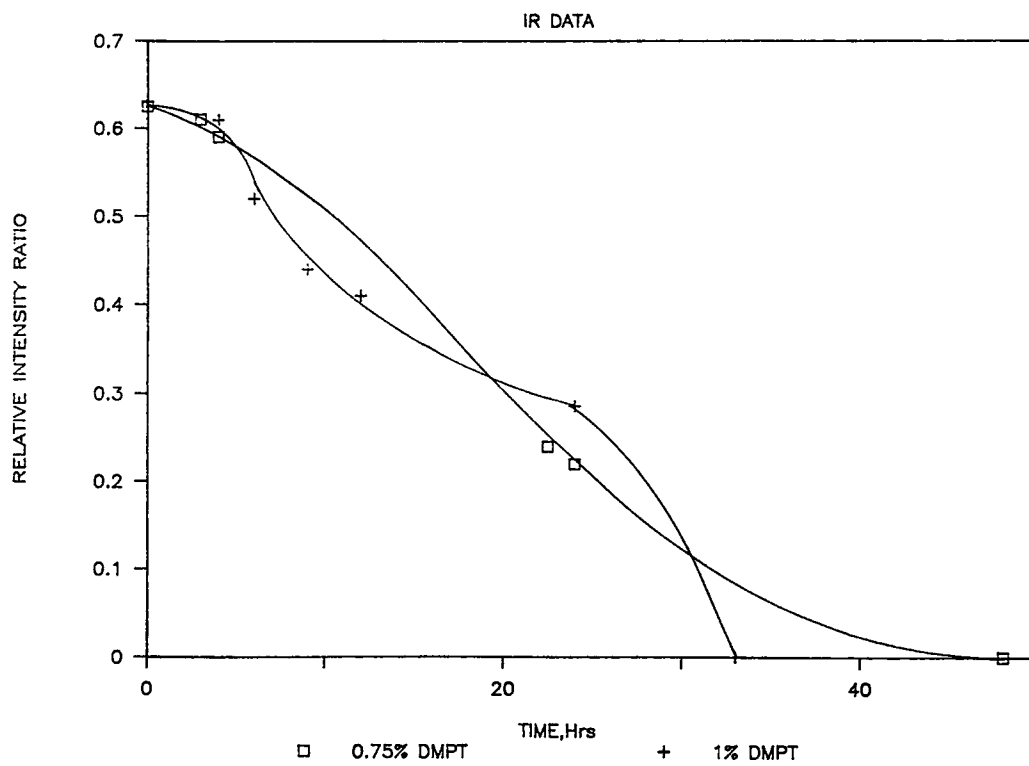**Figure 4**   Monitoring of BIS–GMA synthesis as a function of time.

IR DATA

Figure 5   Epoxide conversion in BIS–GMA.

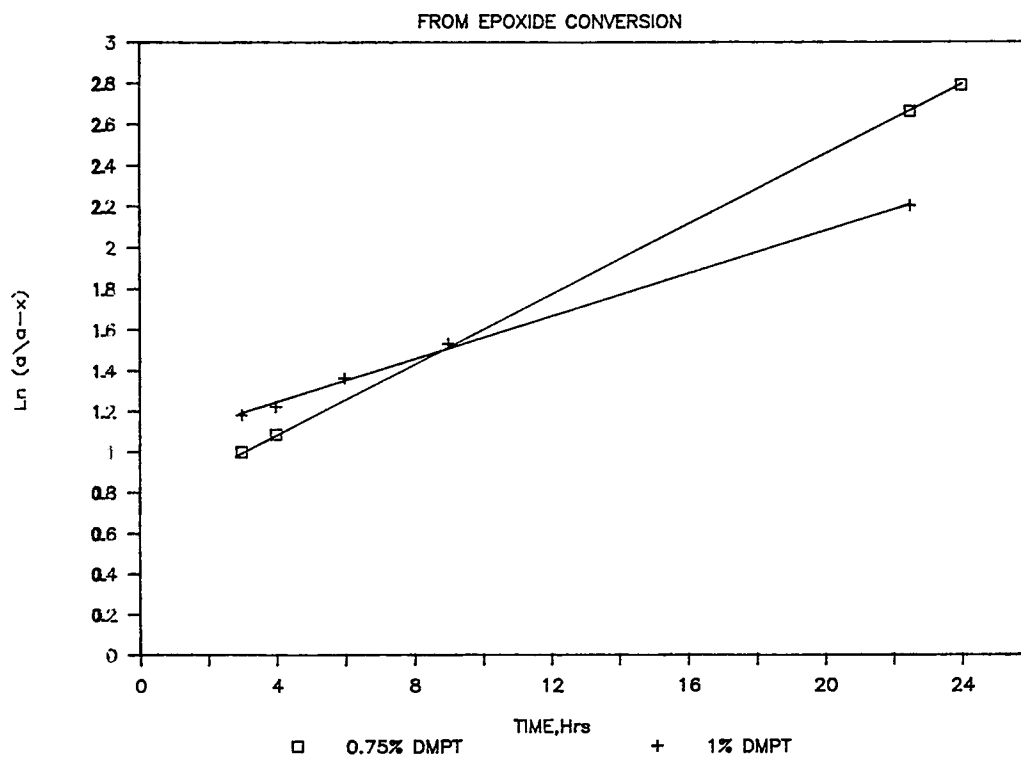FROM EPOXIDE CONVERSION

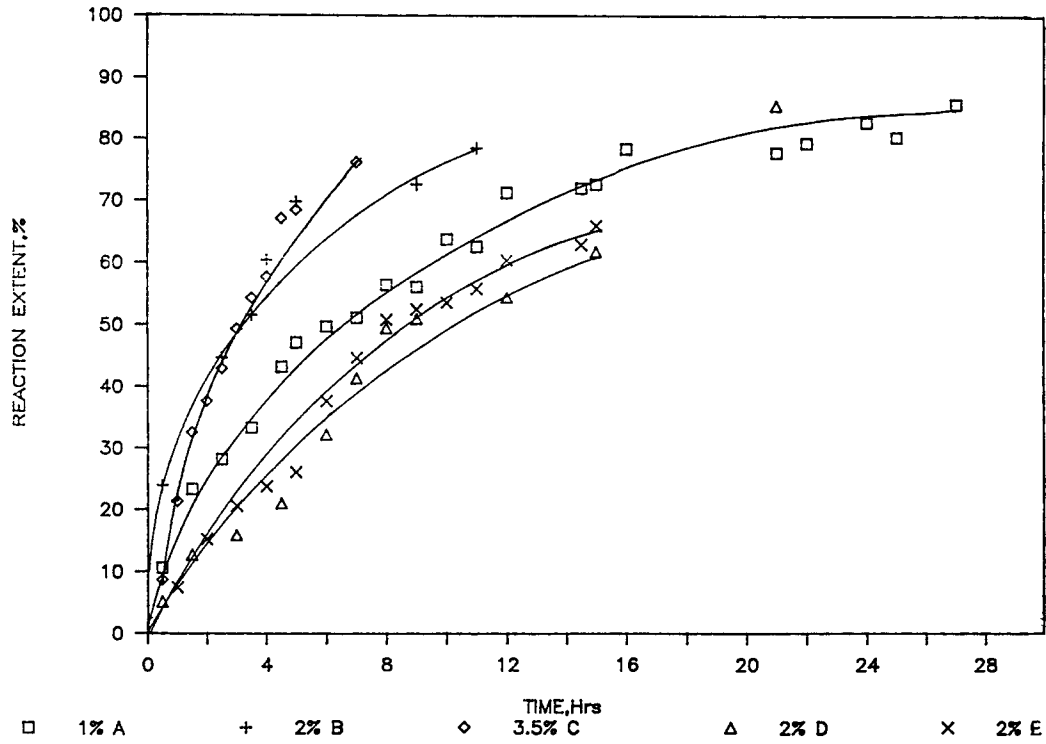**Figure 6**   First-order kinetic plot of BIS–GMA.

Figure 7   Degree of acid conversion in BIS–GMA: (A–C) DMPT; (D, E) DMAEMA and DMAPEA.
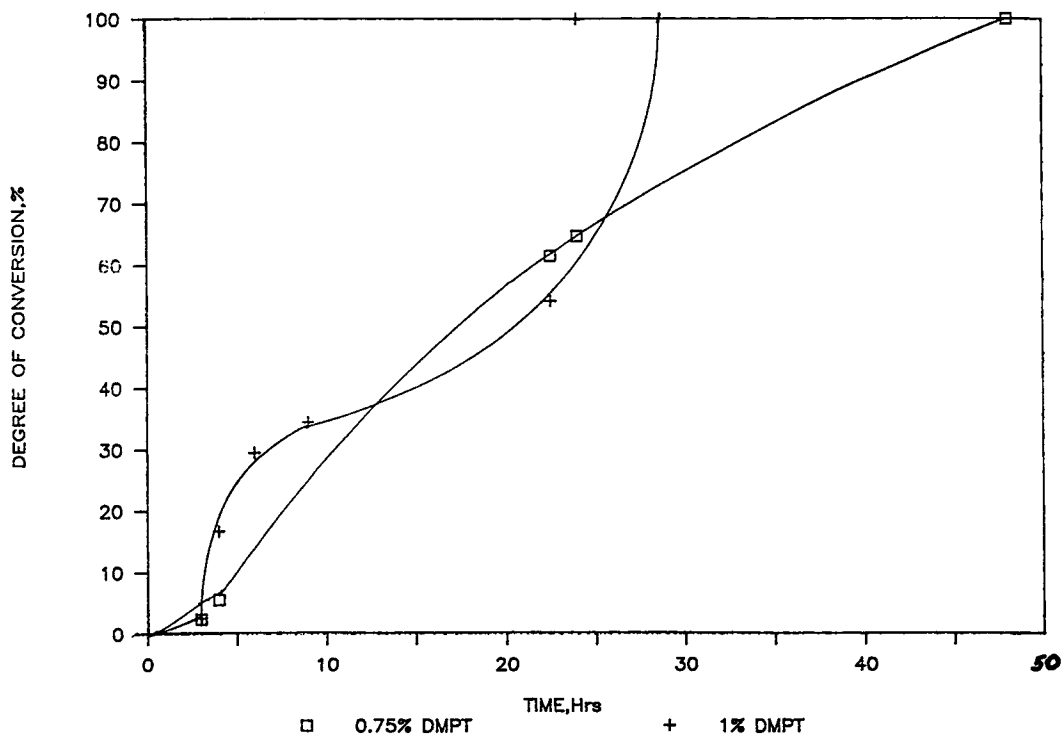

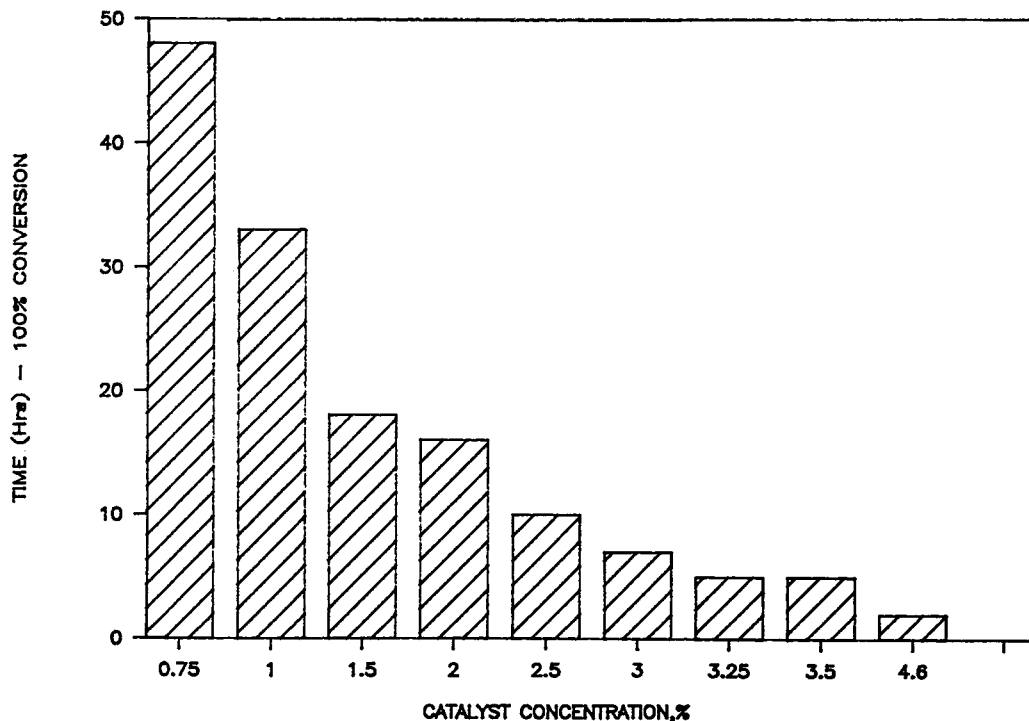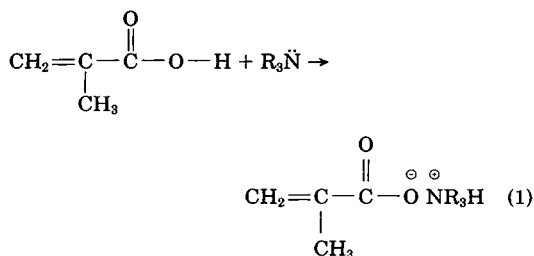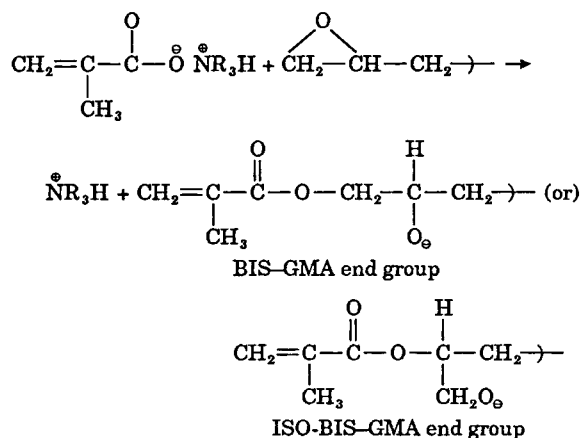**Figure 8**   Degree of epoxide conversion in BIS–GMA IR method.

Figure 9   100% conversion of oligomer catalyst (DMPT) concentration effect.

1. Initiation: activation of acid by amine

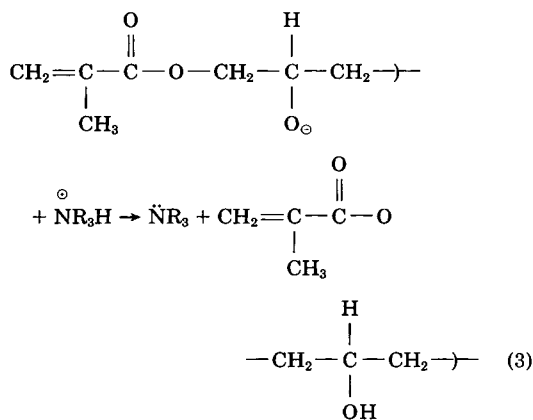$$CH_2=\underset{\underset{CH_3}{|}}{C}-\underset{\underset{}{\overset{\overset{O}{||}}{}}}{C}-O-H + R_3\ddot{N} \rightarrow$$

$$CH_2=\underset{\underset{CH_3}{|}}{C}-\underset{\underset{}{\overset{\overset{O}{||}}{}}}{C}-\overset{\ominus}{O}\,\overset{\oplus}{NR_3H} \quad (1)$$

The excess of acid over amine can shift the equilibrium strongly to the right.

2. Transfer:

$$CH_2=\underset{\underset{CH_3}{|}}{C}-\underset{\underset{}{\overset{\overset{O}{|}}{}}}{C}-\overset{\ominus}{O}\,\overset{\oplus}{NR_3H} + CH_2{-}CH{-}CH_2{-})- \rightarrow$$

$$\overset{\oplus}{NR_3H} + CH_2=\underset{\underset{CH_3}{|}}{C}-\underset{\underset{}{\overset{\overset{O}{||}}{}}}{C}-O-CH_2-\underset{\underset{O\ominus}{|}}{\overset{\overset{H}{|}}{C}}-CH_2{-})- \text{ (or)}$$

BIS–GMA end group

$$CH_2=\underset{\underset{CH_3}{|}}{C}-\underset{\underset{}{\overset{\overset{O}{||}}{}}}{C}-O-\underset{\underset{CH_2O\ominus}{|}}{\overset{\overset{H}{|}}{C}}-CH_2{-})-$$

ISO-BIS–GMA end group

The type of reaction is widely accepted in normal acid or anhydride reaction with epoxide.[14,15,17]

3. Deactivation: Reaction of alkoxide anion with the deactivated amine, regenerates the catalyst in the reaction

$$CH_2=\underset{\underset{CH_3}{|}}{C}-\underset{\underset{}{\overset{\overset{O}{||}}{}}}{C}-O-CH_2-\underset{\underset{O\ominus}{|}}{\overset{\overset{H}{|}}{C}}-CH_2{-})-$$

$$+ \overset{\ominus}{NR_3H} \rightarrow \ddot{N}R_3 + CH_2=\underset{\underset{CH_3}{|}}{C}-\underset{\underset{}{\overset{\overset{O}{||}}{}}}{C}-O$$

$$-CH_2-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-CH_2{-})- \quad (3)$$

The regenerated catalyst (tertiary amine) in the deactivation step was also identified by UV spectrum obtained by using acid solution of BIS–GMA[13] (Fig. 10).

The effect of various catalysts on the BIS–GMA synthesis was studied by comparing three different amines namely DMPT, DMAEMA, and DMAPEA.
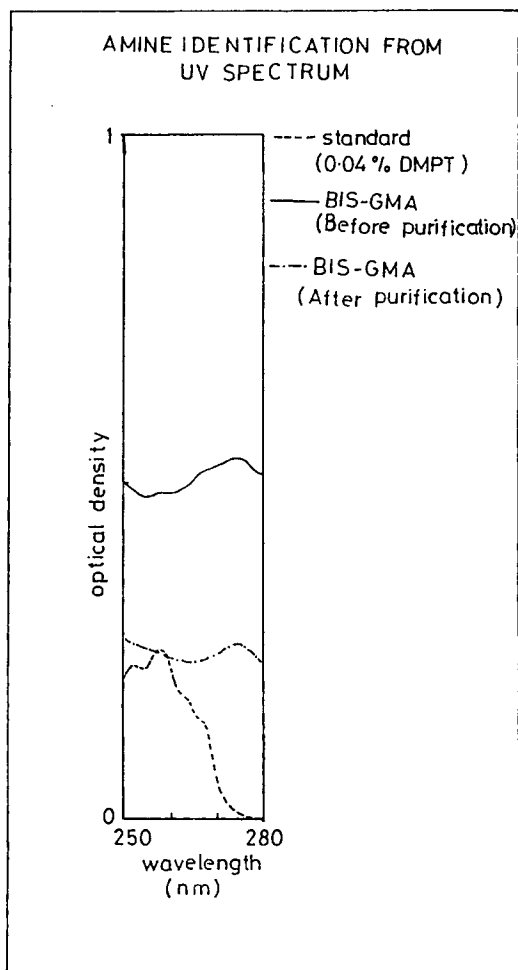
AMINE IDENTIFICATION FROM
UV SPECTRUM

---- standard
(0·04 % DMPT)

——— BIS-GMA
(Before purification)

—·—· BIS-GMA
(After purification)

optical density

250   280
wavelength
(nm)

Figure 10 Amine identification from UV spectrum.

Among these, DMAPEA is reportedly the most reactive one[18] which is evidenced in this work by the higher rate constant and the fastest rate for 100% epoxide conversion (Tables II and III).

Characterization of BIS–GMA

The yield of the purified product was about 50–80% (Table III). The color of BIS–GMA samples is in the range pale yellow to brown. The synthesized BIS–GMA samples were analyzed by techniques such as IR, NMR, and HPLC. Solubility and refractive indices were also observed.

The solubility nature of BIS–GMA is tested in various polar and nonpolar solvents. It is found to be highly soluble in polar solvents like $CHCl_3$, CH_2Cl_2, DMF, DMSO, and DMAc, partially soluble in nonpolar solvents like benzene, toluene, xylene, and CCl_4 and insoluble in water.

Table III shows refractive indices of different batches of BIS–GMA. They were found to lie in the range of 1.544–1.559.

The IR spectra of BIS–GMA conversion in Figures 3 and 4 show the formation of addition esterification product as a function of time with gradual disappearance of the terminal epoxide absorption at 917 cm^{-1}. The other characteristic absorption peaks at 939 cm^{-1} ($C=CH_2$, Bending), 1639 cm^{-1} ($C=CH_2$, stretching), 1665 cm^{-1} (carbonyl), and 3400 cm^{-1} (hydroxyl) are also observed.

The BIS–GMA product has been identified as a mixture of isomers of similar chemical nature,[7,8]

Table III Catalyst Concentration Effect in BIS–GMA Synthesis

Code No.	Catalyst[a] Concn (%)	Time Taken for 100% Conversion (h)	Refractive Index (25°C)	Yield (%)
KM1	0.75	48	1.5582	58
KM2	1	33	1.5484	53
KM3	1.5	18	1.5512	50
KM5	2	16	1.5496	54
KM8	2.5	10	1.5510	60
KM9	3	7	1.5484	58
KM10	3.25	5	1.5446	50
KM11	3.5	5	1.5518	56
KM12	4.6	2	1.5402	50
KM20	2[b]	15	1.5516	72
KM21	2[c]	23	1.5512	69

[a] DMPT catalyst.
[b] DMAPEA catalyst.
[c] DMAEMA catalyst.

**Table IV   NMR Identification Data of BIS–GMA Samples**

Group (No. of Protons)	Chemical Shift	Integration					
		KM2	KM3	KM5	KM6	KM7	KM12
CH_3 Ar—C—Ar (6)	1.6 (s)	2.2	2.4	3.0	2.15	3.0	2.2
C=C—CH_3 (6)	1.9 (s)	2.1	2.35	3.0	2.15	3.0	2.2
O—CH_2—CH—CH_2—O[a] OH (5)	3.9–4.5 (m)	3.2	3.3	4.4	3.6	5.2	4.0
C—CH_2—OH[b] (2)	3.5–3.7 (s)	0.5	0.8	0.7	—	—	—
Ar—O—CH_2[b] (2)	4.1–4.2 (d)	—	—	—	—	—	—
O—C—H[b] (1)	5.2–5.3 (s)	0.275	0.2	0.45	0.1	0.1	0.15
H—C=C—COO (trans) (2)	5.6 (s)	0.75	0.8	1.0	0.75	1.0	0.75
H—C=C—COO (cis) (2)	6.1 (s)	0.75	0.8	1.0	0.75	1.0	0.75
Aromatic C—H (4)	6.8 (d)	1.5	1.7	2.05	1.5	2.05	1.5
Aromatic C—H (4)	7.1–7.2 (d)	1.5	1.7	2.05	1.5	2.05	1.5
End group ratio: BIS–GMA : ISO-BIS–GMA[c]		70 : 30	75 : 25	70 : 30	80 : 20	80 : 20	80 : 20

[a] BIS–GMA end group.
[b] ISO-BIS–GMA end group.
[c] Calculated from the integration.

from NMR data. The characteristic peaks and its integration values are presented in the Table IV. The isomers are referred to as BIS–GMA and ISO-BIS-GMA in the literature.[7,8] The easiest way to detect the ISO-BIS-GMA isomer in the NMR spectrum is to observe a singlet at δ = 5.2 ppm, due to tertiary (—CH—) methine proton and a doublet at δ = 3.5–4.14 ppm, corresponding to the (—C—CH_2—OH and Ar—O—CH_2—) methylene protons. Sometimes this doublet peak overlaps with the methylene protons of BIS–GMA isomers. All other protons absorb at exactly the same position as the BIS–GMA isomer. It is obvious that these two isomer structures differ only by an interchange of the OH groups and the methacryl units [mechanism, eq. (2)]. From the integration data (Table IV), some 20–30% of the total number of end groups are present in the isomeric form, branched BIS–

GMA. The ratio of these two isomers, BIS–GMA and ISO-BIS–GMA (1st and 2nd) in the product depends on the reaction variables such as concentration of reagents, temperature, pH, reaction time, etc. This ratio is different in different preparations. Since both epoxy moieties of DGEBA react independently of each other, it is likely that the product is a mixture of three isomers as follows:
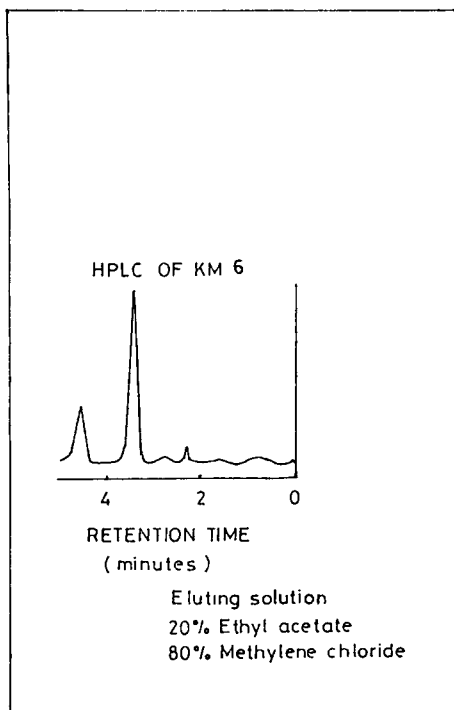
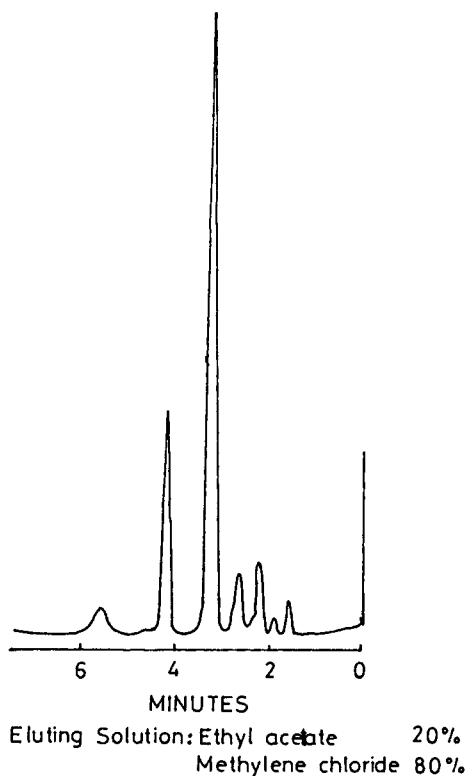a. Linear BIS–GMA—1st isomer:
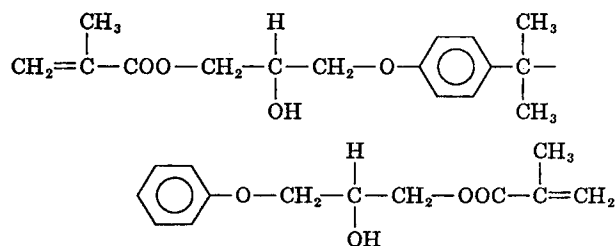
Figure 11   HPLC of KM6.

Figure 13   HPLC of KM13.

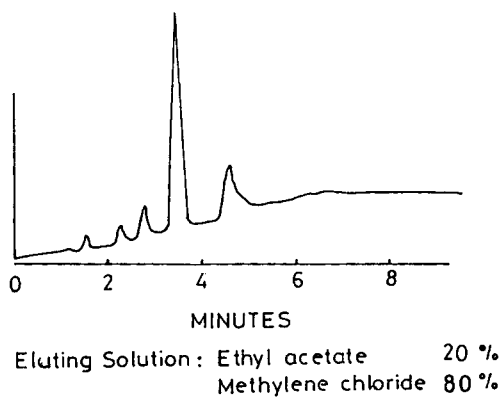b. Branched BIS–GMA (ISO-BIS–GMA)—
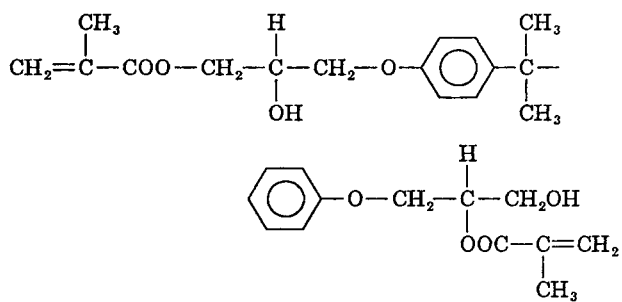2nd isomer:

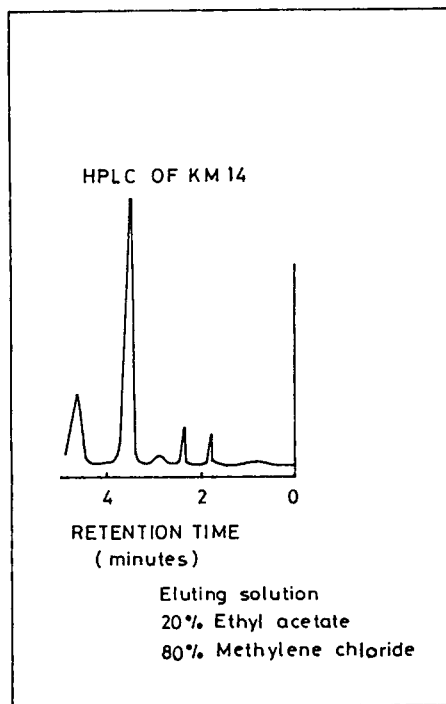**Figure 12**   HPLC of KM12.

Figure 14   HPLC of KM14.

Table V HPLC Data[a] of the BIS–GMA Samples[b]

Code No.	Amount of Catalyst (%)	1st Isomer (3.5 min)[c] (%)	2nd Isomer (4.5 min)[d] (%)	3rd Isomer (2.5 min)[e] (%)
KM6	2	73	23	5
KM12	4.6	67	20	8
KM13	3.5	60	20	7
KM14	4.6	65	17	9

[a] Peak height ratio.
[b] Synthesised at different conditions.
[c] BIS–GMA end group at both ends.
[d] ISO-BIS–GMA end group at one end.
[e] ISO-BIS–GMA end group at both ends.

c. Double branched BIS–GMA—3rd isomer:
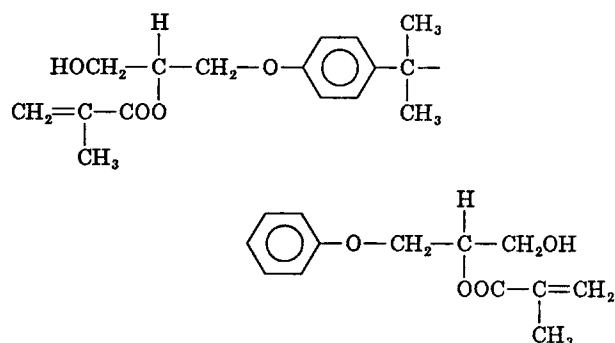
The presence of three isomers was confirmed by analytical HPLC data (Figs. 11–14 and Table V). The ratio of linear isomer (1st isomer) to a branched isomer (2nd isomer) is approximately 3 : 1, as published.[7,8] The 3rd isomer (double branched BIS–GMA) is also expected in the mixture in at least 2%,[8] but it was observed as 5–10% in the present study, which may be attributed to different synthetic conditions. From Table V it is obvious that the quantity of double branched isomer is higher with increasing accelerator amount. Traces of lower or higher molecular weight species were also obtained along with these three isomers as side products with higher amount of accelerator. Side products and double branched isomers were considerably minimized in KM6 with 2% accelerator.

CONCLUSION

Conclusions from this study are:

1. Based on the kinetic data obtained for the amine catalyzed reaction between epoxy and carboxyl groups, the reaction follows first-order and zero-order kinetics with respect to epoxide and acid, respectively.

2. A comparison of three different amine catalysts on the BIS–GMA synthesis reveals that their order of reactivity is

DMAPEA > DMPT > DMAEMA

as evidenced by their rate constant and the time taken for 100% epoxide conversion.

3. Characterization of the synthesized BIS–GMA reveals that it consists of a mixture of three isomers such as the linear, the branched BIS–GMA, and the double branched BIS–GMA. Ratio of the BIS–GMA end group to the ISO-BIS–GMA end group is approximately 3 : 1, as in the literature. In addition, it was found that the quantity of the double branched isomer increased with increase in accelerator amount.

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