ABSTRACT

Title of Thesis : Synthesis and characterization of a novel blocked isocyanate adhesive based on diphenylmethane- 4, 4' - diisocyanate

Yangming Lin, Master of Science in Chemical Engineering, 1988

Thesis directed by : Professor David S. Kristol

The dental adhesive monomers based on diphenylmethane - 4,4'- diisocyanate (MDI) were prepared and studied in this research. The diisocyanate, MDI, was first reacted with hydroxyethyl methacrylate (HEMA) to form an intermediate adduct. This adduct had an active isocyanate end group. It was then bonded with o-chlorophenol (OCP), a blocking agent , to produce a blocked isocyanate monomer.

The new blocked isocyanate (HEMA-MDI-OCP) was found to have an average value of more than 1200 psi in tensile tests measuring its adhesion to dentin slices.

SYNTHESIS AND CHARACTERIZATION

OF

A NOVEL BLOCKED ISOCYANATE DENTAL ADHESIVE BASED

ON

DIPHENYLMETHANE - 4, 4' - DIISOCYANATE

BY

YANGMING LIN

Thesis submitted to the Faculty of the Graduate School of
the New Jersey Institute of Technology in partial fulfillment of
the requirement for the degree of
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APPROVAL SHEET

Title of Thesis: Synthesis and Characterization of A Novel Blocked Isocyanate Dental Adhesive Based on Diphenylmethane -4, 4' - Diisocyanate

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INTRODUCTION

1.1 Development of dental adhesives in NJIT

Isocyanate based dental adhesives have been developed by various researchers during the last two decades. In the field of dental material, it is also known as urethane dental adhesives.

W. H.Snyder and D. S. Kristol in N J I T have led a research team to study the isocyanate dental adhesives for a long period. In their previous work, the toluene -2,4-diisocyanate (TDI) was used as the major raw material.

The synthetic method and physical test approach for TDI based adhesives have been well developed [1-6].There are two series of TDI-based monomers under study. One is simply to bond hydroxyethyl methacrylate (HEMA) and blocking agents with the single TDI molecule. The other uses the pentaerythritol as a backbone in which four molecules of TDI were first attached to the pentaerythritol. Subsequently, equal amounts of HEMA and blocking agents were combined with those TDI branches. These adhesives are initially obtained in the form of monomers.

From the experimental data, in vitro, the tensile bonding strength tests showed remarkably good results[3,4]. In fact, these are much better than those of commercial dental adhesives. Additionally, a toxicity test in vivo was also done[7]. It further confirms that these monomers are acceptable for animals.

As a result, isocyanate adhesives are believed to have great potential for the adhesion of dentin.

1.2 Review of isocyanate dental adhesives

It has been recognized that isocyanate should be capable of modifying dentin surfaces. This is due to the fact that they can react with hydroxyl, amino and carboxyl groups to form urethanes.

Many researchers [8-11] believed that modifying the original isocyanates was necessary because these functional groups have poor tissue tolerance and generally low on viscosity. Therefore, for dental applications, isocyanates are usually converted to prepolymers by reacting a polyfunctional isocyanate with a polyol so that the ratio of isocyanate to hydroxy is high. That is, they still need an excess amount of isocyanate. However, when they are used as a complete restoration, their bulk tensile strengths were relatively poor.

In the mean time, Kristol et. al.,[13] found, however, that the isocyanate end groups in most available dental adhesives was so unstable that they would react with saliva water which may cause the degradation of adhesion in vivo. For avoiding this problem and designing multifunctional adhesives, they proposed to apply the blocking - deblocking concept of isocyanates to the adhesion between synthesized monomers and natural tissue (dentin).

Based upon this concept, a series of studies were carried out as discussed above in which diisocyanate was initially bonded with a methacrylate group on one end. To mask the other active isocyanate group, certain blocking agents were used to obtain the blocked isocyanate. This blocked isocyanate, when used as an adhesive, would partial ly deblock and would then react with the active hydroxyl group of amino acids of dentin to form a strong bonding. In addition, the methacrylate group of the same monomer could copolymerize with the added methyl methacrylate (MMA).

1.3 **Present studies**

It is obvious that all of the previous studies were based upon TDI. On the other hand, another widely used isocyanate, MDI (Diphenylmethane- 4,4'- diisocyanate), exbhibits stronger adhesion strength, for the adhesion of

bovine enamel, than other common diisocyanate, such as TDI, HDI etc.[14] This interesting result of MDI has hence stimulated the present study for its application to dental adhesives.

Similar to TDI, MDI is a bifunctional isocyanate. In its molecule, two isocyanate groups are positioned opposite ends of on both benzene rings, whereas, those groups on TDI are at meta positions.

Unlike TDI, comparatively little information has been published regarding the dental adhesives derived from MDI. However, this present research tries to develop an adhesive based upon MDI rather than TDI in the restorative material. The adhesion principle , of course, follows the blocking-deblocking mechanism mentioned above.

For synthesis, excess amounts of purified MDI reacted with HEMA initially to get an intermediate, MDI-HEMA adduct. The blocking agent, o-chloro phenol, was then used to mask the adduct. Thus, a monomeric adhesive consists of MDI, HEMA and blocking agent was synthesized.

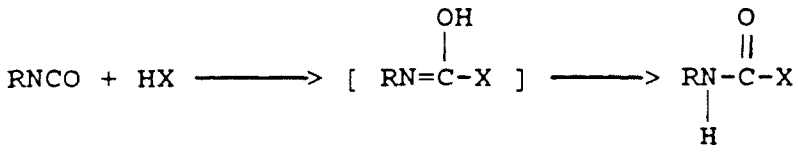
This synthesized compound was analyzed by infrared spectroscopy, elemental analysis and nuclear magnetic resonance spectra. It was also characterized with the melting points. For evaluation of this adhesive, bonding

strength tests were run in order to compare this new monomer to the strengths of other adhesives.

II. BACKGROUND REVIEW

2.1 Reactions of isocyanate

The concerned reactions of isocyanates in this research are those which involve compounds containing an active hydrogen.



Where the hydrogen becomes attached to the nitrogen of the isocyanate, and the remainder of the active hydrogen compound becomes bonded to the carbonyl carbon.

Generally the reaction proceeds readily at ordinary temperature or, after moderate heating, without the use of catalysts. It is known that isocyanates are very hydroscopic and easily hydrolyzed by water with varying degree of rapidity which gives the corresponding disubstituted urea.

$$RNCO + H_2O \longrightarrow RNHCOOH \longrightarrow RNH_2 + CO_2$$

$$RNH_2 + RNCO \longrightarrow RNHCONHR$$

Therefore, extreme care must be exercised in handling isocyanate and its derivatives so that undesirable side reactions can be avoided.

Some compounds such as certain amino acids containing a hydrogen atom attached to a nitrogen atom will react with isocyanates as shown below.

$$RNCO + HNR'R'' \longrightarrow RNHCONR'R''$$

Usually, the most basic nitrogen compounds are the most reactive ones unless steric hindrance is excessive. Amine react to give substituted urea [21], amides give acyl ureas [22], and ureas give biurets [23, 24].

$$RNCO + R'_2NH \longrightarrow RNHCONR'_2$$

$$RNCO + R'CONH_2 \longrightarrow RNHCONHCOR'$$

$$RNCO + H_2NCONH_2 \longrightarrow RNHCONHCONH_2$$

Similarly, other compounds containing hydrogen atoms attached to oxygen react with isocyanates too. All types of alcohols- primary, secondary, tertiary, and polyhydric react to give carbamates [25, 26].

$$RNCO + R'OH \longrightarrow RNHCOOR'$$

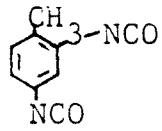
Phenols, including polyhydric phenols, react especially in the presence of catalyst [27].

$$RNCO + Ar\text{-}OH \xrightarrow{\text{catalyst}} RNHCOOAr$$

The reactions of diisocyanates are usually more complicated than are those of monoisocyanates. The reactivity of a diisocyanate initially is similar to that of a monoisocyanate substituted by an activating group, in this case the second isocyanate group. As soon as one isocyanate group has reacted with a hydroxyl, the remaining isocyanate group has a reactivity similar to that of a monoisocyanate replaced by a urethane group.

$$OCN\text{-}R\text{-}NCO + R'OH \longrightarrow OCN\text{-}R\text{-}NHCOOR'$$

Previous work used 2,4 tolylene diisocyanate (2,4-TDI) [1-6],



we chose to use methylene diphenyl diisocyanate (MDI), a molecule in which two isocyanates are on different aromatic rings, in equivalent positions, well separated by a methylene group, and the reaction of one NCO group does not affect the reactivity of the second appreciably [30, 31]. Furthermore, the para location of the isocyanate groups mean freebdom from steric hindrance. In this respect, MDI differs significantly from 2,4- and 2,6-TDI, in which:

(a) the para isocyanate group in TDI is more reactive than the ortho isocyanate group

(b)the reaction of one isocyanate group diminishes the

reactivity of the other

In addition, Bailey et al., [32] found that a sharp decrease in the rate of reaction of TDI at approximately 50 % reaction. Meanwhile MDI showed only a slight decrease in rate as the reaction proceeded. These are shown as figures 1 and 2.

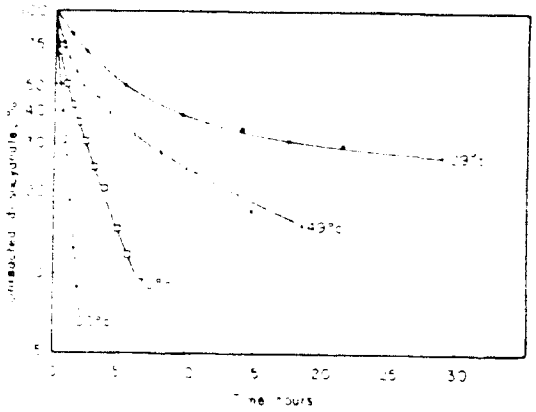


Fig. 1 Reaction of 2,4-toluene diisocyanate with diethylene glycol adipate polyester, in chlorobenzene [32]

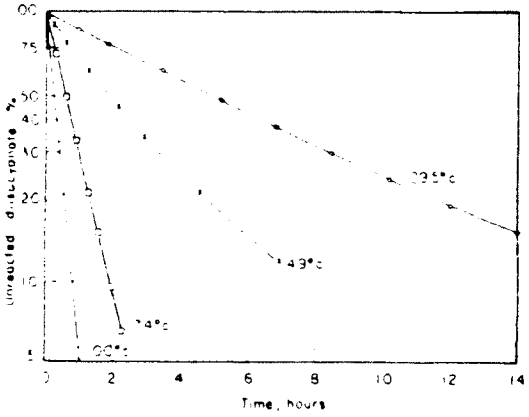
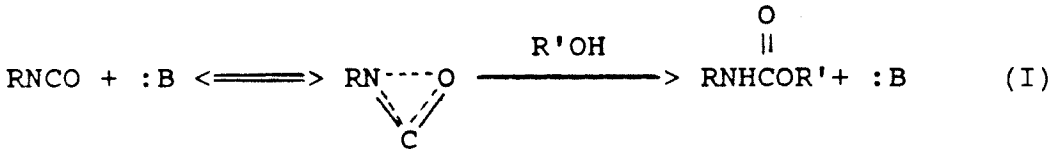


Fig. 2 Reaction of 4,4'-diphenylmethane diisocyanate with diethylene glycol adipate polyester in chlorobenzene [32]

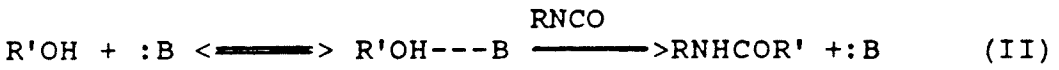
2.2 Catalytic reaction of isocyanates

Practically, catalysts have been widely used in the isocyanate-hydroxyl reaction to give desired yield. Usually, two kinds of catalysts are available. One is the tertiary amines which are effective in proportion to their base strengths except triethylenediamine. Organometallic compounds are another group of catalysts that are used especially to control the relative rates of isocyanates with the secondary hydroxyl of polyethers and water.

The mechanism of the base-catalyzed reaction of isocyanates with alcohols is still under investigation. The two mechanisms [33] under discussion are the nucleophilic catalysis activating the isocyanate (I) and a general base catalysis activating the alcohol (II).



(I)

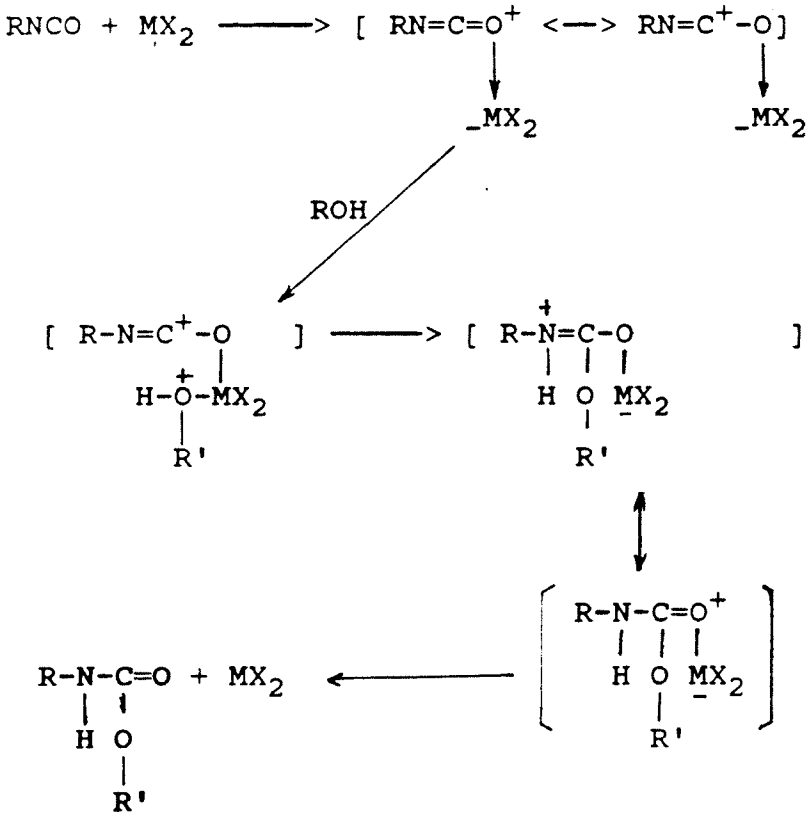


(II)

In most cases, mechanism I is still widely accepted for the reaction of isocyanates with alcohols. The catalytic

activity of tertiary amines is the result of the free electron pair of the nitrogen. If crowding or steric hindrance, caused by branched or bulky substituents, exists about the amine nitrogen, the availability of the free electron pair is reduced. Also, electron-donating substituents enhance catalytic activity.

However, the metal compounds can catalyze the isocyanate reaction more satisfactorily. Bamford et. al., [33] proposed a reaction mechanism for metal catalysts:



Where the hydroxyl group enters on the metal side of the complex and attaches in close proximity to the isocyanate nitrogen, can explain the remarkable catalytic actions of the metals.

Besides these a synergistic effect by combining amine and tin catalysts were also found [34, 35, 36]. For example, the reaction of phenyl isocyanate with butanol, synergistic effects were found with combination of tertiary amines and tin catalysts as shown below [29].

Table I. Reaction Rates And Catalysts

Catalyst	Mol%	$k * 10^4$, l/mol.s
triethylamine	0.88	2.4
di-n-butyltin diacetate	0.0015	20
triethylamine/ di-n-butyltin diacetate	0.99/ 0.00098	88

2.3 Blocked Isocyanate

Blocked isocyanates are adducts which can decompose back to isocyanates and nucleophiles. They have been used in certain applications, such as coatings, enamels, and adhesives etc. Usually, the reaction proceeds as a reversible reaction. For example, the TDI-trimethylol propane adduct reacts with a phenol [40] :

$$C_2H_5C(CH_2OCONH\text{-}Ar\text{-}NCO)_3 + 3\ C_6H_5\text{-}OH$$
$$\Longleftrightarrow C_2H_5(CH_2OCONH\text{-}Ar\text{-}NHCOOC_6H_5O)_3$$
$$\text{[carbamate]}$$

The free isocyanate would be regenerated when heat (up to 150^0C) is applied; deblocked isocyanate then is capable of reacting with the active hydrogen-containing component.

Both aromatic and aliphatic isocyanates can be blocked by a variety of blocking agents. These include phenols, oximes, lactams, alcohols, and hydroxamic acid esters etc. In fact, the extent of the deblocking or dissociation depends upon the nature of isocyanate as well as blocking agent. Aromatic isocyanate and active hydrogen-containing aromatics have a greater deblocking tendency than aliphatic ones [13].

As an example, HEMA is an alcohol and has little to no tendency to dissociate at ambient conditions once it has

been bonded to an isocyanate. In the case of a diisocyanate, it is possible to react one isocyanate with a mole of HEMA, followed by treatment with a phenol, which then yields a final adduct which is a blocked isocyanate.

A series of blocking reactions has been well reviewed by Wicks [28]. It is interesting that synergistic effect of catalysts can also influence the deblocking of the blocked isocyanates.

For example, the catalyst pair consisting of organotin compounds and tertiary amines is able to lower both the deblocking temperature and time as compared to the uncatalyzed systems [40].

Besides, some other potential metal compounds have been developed and claimed to be effective deblocking catalysts [31, 37, 38, 39].

2.4 Mechanism for Dentin Adhesion

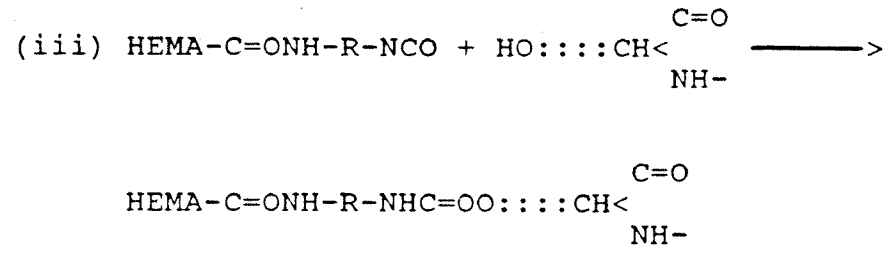
Approximately fifty percent (by volume) of an organic matrix, mainly collagen, is contained in the dry dentine composite [43]. The collagen is in intimate association with a complementary inorganic phase which is represented mainly by apatitic calcium phosphate. Because many amino groups are present in the collagen , as shown in Table I, they can provide potential bonding sites for reaction with isocyanate.

Because the blocked monomer may deblock and reform a free isocyanate, it can then react with available amino or hydroxyl groups in the collagen to produce a urea or urethane. The well-known reactions of organic isocyanates with active hydrogen compounds are therefore applicable to the dentin bonding.

(i) HEMA-C=ONH-R-NHCOOAr <⟹> HEMA-C=ONH-R-NCO + ArOH

(ii) HEMA-C=ONH-R-NCO + NH_2::::CH< (C=O, NH-) ⟶

HEMA-C=ONH-R-NH-C=ONH:::::CH< (C=O-, NH-)



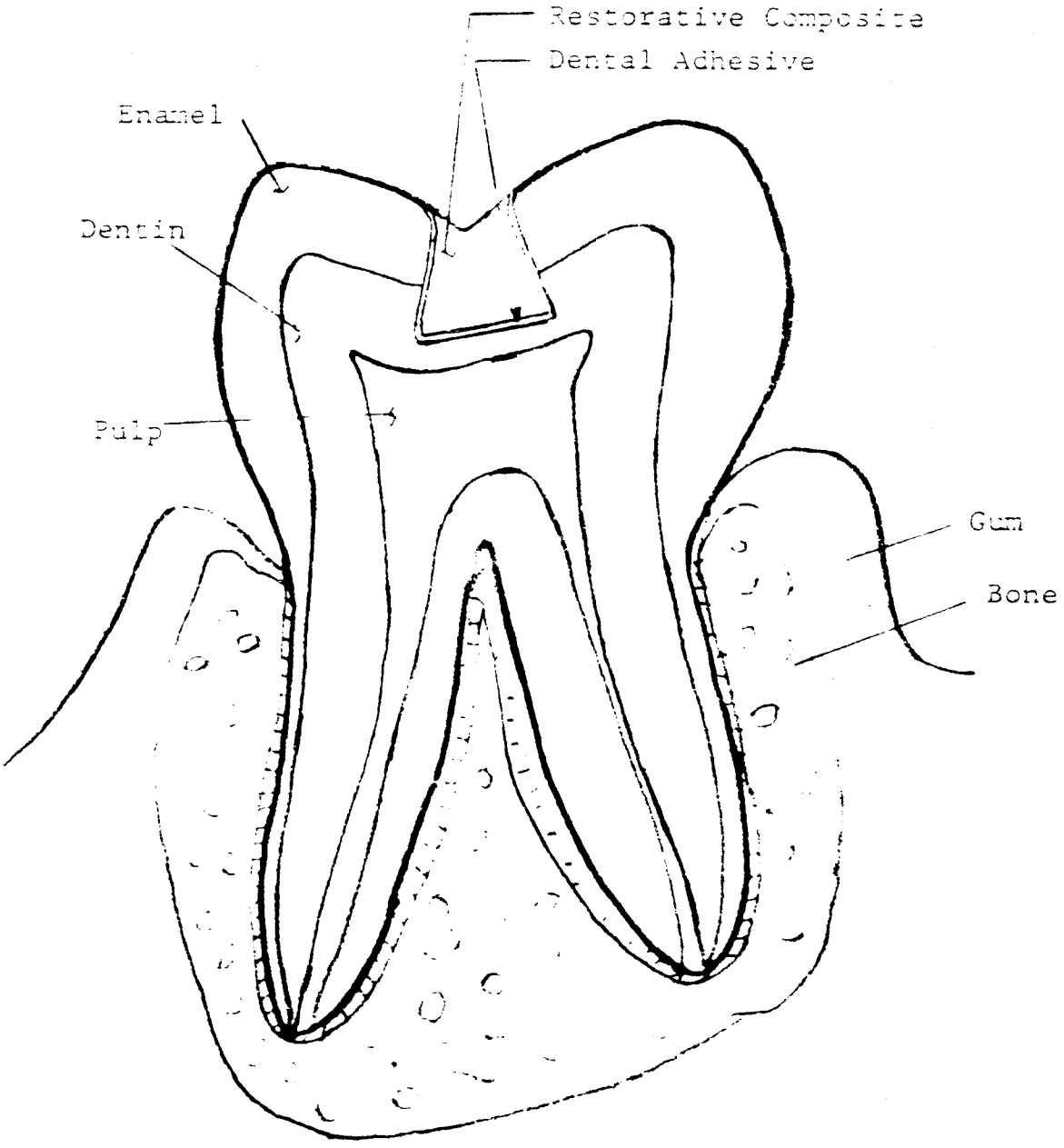
Thus, it is reasonable to suggest that the adhesion to dentine may be accomplished by using blocked isocyanate adducts.

Table II

Key Amino Acid Residues in Human Bone Collagen Potentially Reactive with Isocyanate[43]

Amino Acid	Structure of Residue	%
Arginine	$H_2NC(=NH)-NH-(CH_2)_3-$	8.80
Lysine	$H_2N(CH_2)_4-$	4.40
Serine	$HO-CH_2-$	4.06
Hydroxy-proline	$HO-CH(-CH_2-)-CH_2-$	14.10
Aspartic Acid	$HO-C(=O)-CH_2-$	6.70
Glutamic Acid	$HO-C(=O)-CH_2CH_2-$	11.40

Figure 3 Application of Dental Adhesive



2.5 Radical Copolymerization of Methacrylates

Since there is a methacrylate end group presents in the synthesized monomer, the polymerization of dental material can simultaneously be accompanied with the copolymerization of MMA and synthesized monomers. For discussion, they are arbitrarily assigned to be monomers A and B respectively.

In the free radical copolymerization of two monomers, A and B, the four propagation steps possible are,

$$A^* + A \xrightarrow{k_{11}} A^*$$

$$A^* + B \xrightarrow{k_{12}} B^*$$

$$B^* + A \xrightarrow{k_{21}} A^*$$

$$B^* + B \xrightarrow{k_{22}} B^*$$

where A* and B* are growing polymer chains with A and B, respectively at the active growing ends.

The polymer compositions given by the reactivity ratios:

$$r_1 = k_{11} / k_{12}$$

$$r_2 = k_{22} / k_{21}$$

These ratios of rate constants provide an excellent indication of monomer distribution in the polymer. If r_1 and r_2 are less than 1, the polymers tend to alternate. If r_1 is greater than 1 and r_2 is less than 1, A predominates in the polymer.

Table III summarizes monomer distributions for equimolar concentrations of monomers and varying reactivity ratios. To prevent forming a polymer with a wide distribution of compositions, it is necessary that the more reactive monomer be added during the course of the polymerization.

Some available reactivity ratios for MMA (A) and other comonomers (B) are shown in Table IV [45]. The last column shows the relative reactivities of various monomers with MMA radicals.

$$1/r_1 = k_{12} / k_{11}$$

As defined, the inverse of the monomer reactivity ratio gives the ratio of the rate of reaction of a radical with another monomer to its rate of reaction with its own monomer. It is interesting to note that these values do not differ very much for homologues derivatives.

Table III Monomer Distribution in A Copolymer [42]

Reactivity Ratios	Monomer Distribution in Chain A	B
$r_1>>1$, $r_2>>1$	long blocks	long blocks
$r_1>>1$, $r_2<<1$	long blocks	very short blocks
$r_1<<1$, $r_2>>1$	very short blocks	long blocks
$r_1<<1$, $r_2<<1$	very short blocks	very short blocks
$r_1= 1 = r_2$	random length	random length

Table IV Monomer reactivity ratios, A=MMA [45]

B	r_1	r_2	Temp.^{0} C	$1/r_1$
Methacrylic Acid				
Benzyl ester	0.78	1.38	60	1.28
Butyl ester	0.79	1.27	60	1.27
Cyclohexyl ester	0.86	1.15	60	1.16
Ethyl ester	0.92	1.08	60	1.09
Isobutyl ester	0.91	1.09	60	1.10
Isopropyl ester	0.89	1.20	60	1.12
Phenethyl ester	1.09	1.33	60	0.91
Carbamic Acid				
Isopropenyl-2,3-epoxypropyl ester	1.70	0.12	60	0.59
Vinyl-,2,3-epoxy propyl ester	2.75	0.10	60	0.36

2.6 Shrinkage and autoacceleration of MMA during polymerization

A large volume reduction, about 21 % [41] will take place during the cure of methacrylates. This also lead the problem of residual stress which may cause mechanical failure of bulk polymer.

In addition, at conversions above 20%, the reaction becomes autoaccelerated. During this phase, the rapid increase in viscosity and liberation of heat can raise the internal temperature and elevate the reaction rate unless measures are taken to dissipate the heat.

In extreme cases, a violent runaway polymerization, such as low molecular weight, equilibrium of polymerization and depolymerization, can occur.

Meanwhile, the effects of shrinkage and autoacceleration can be controlled by interrupting the polymerization to form a syrup containing 25 to 50% polymer[45]. Syrups can then be stored safely with little change until they are used.

Alternatively, it can also prepared as one utilized in this project. That is dissolving 20 - 30% wt. of finely divided PMMA in the MMA monomer solution to form prepared syrups for subsequent use.

The amounts of shrinkage and heat production thus drop during the second stage of cure or copolymerization in accordance with the polymer content.

Using syrups also shortens the cure time, decreases the tendency of leakage, and greatly reduces the chance of danger runaway. These results obviously show the importance of prepared PMMA-MMA syrups.

EXPERIMENTAL

Melting points were determined on a MEL-TEMP melting point apparatus. NMR spectra were recorded on a 60 MHz, Varian EM-360 spectrometer (tetramethylsilane, internal standard in d-DMSO). Infrared spectra of solids (KBr) were run on a Perkin-Elmer 1310 instrument. Elemental analyses were performed by ORS, New York, NY.

Diphenylmethane diisocyanate was donated by BASF Co., and was purified prior to use. Both methylene chloride and N-methyl-2-pyrrolidone were purchased from Thiokol-Alpha Products. They were distilled before synthesis. 2-Hydroxyethyl methacrylate was received from Aldrich and was vacuum distilled. Dibutyltin dilaurate was used as received from Thiokol-Alpha Products.

1. Synthesis of MDI-HEMA adduct

In a 500 mL., three-necked, round-bottomed flask equipped with a mechanical stirrer and a condenser and nitrogen inlet were placed 25.02 g (0.10 mole) of diphenylmethane diisocyanate (MDI) (163-166^{0}C / 0.3 torr). 200mL. of methylene chloride (40^{0}C, 760 torr) were filled into flask. With rapid stirring MDI would dissolve in the solvent.

A solution of 3.25 g (0.025 mole) of 2-hydroxyethyl methacrylate (HEMA) (67^{0}C/ 3.5 torr) and 0.05ml of

dibutyltin dilaurate in 30 ml. of methylene chloride was added dropwise through an addition funnel into the reaction flask, as shown in the Appendix A. At room temperature the mixture was stirred continuously for 20 hours.

The bulk solution was then filtered and some suspended solid was obtained - fraction I, which appears to consist mainly of di-HEMA substituted byproduct.

The filtrate was further concentrated under a gradually increasing vacuum, from 15 to 10 torr, by using a rotary evaporator. This yielded a second white solid, designated fraction II, which appears to be the desired MDI-HEMA adduct. Fraction II was collected by vacuum filtration and stored in a vacuum dessicator.

Subsequent removal of methylene chloride, down to 4 torr, produced a sticky solid, designated fraction III, which appears to be a mixture of fraction I, II, and unreacted MDI.

The yield of fraction II, MDI-HEMA adduct, is 35-45 %.

2. Preparation of blocked monomer

A dry nitrogen filled, 100-ml, single-necked, round-bottomed flask was charged with 50 ml of dry distilled N-methylpyrrolidone (NMP), 5 g (0.013 mole) of MDI-HEMA adduct, 6.77 g (0.053 mole) of o-chlorophenol, and 0.05ml of dibutyltin dilaurate (DBTDL).

The flask was then placed in a heating mantle over a magnetic stirrer, as shown in Appendix B. Raised the reaction temperature gradually up to 35-40^{0}C and let the bulk solution be stirred with a teflon-clad magnetic stirring bar.

The extent of reaction was monitored by following the disappearance of the isocyanate by infrared spectrum. After all the isocyanate was depleted, the reaction solution was filtered into a dry flask with a magnetic stirring bar. Nitromethane, 100 mL , freshly distilled, was charged dropwise into the solution through an addition funnel under nitrogen, as shown in Appendix C.

As soon as about half amount of nitromethane was added, a solid suspension would be found in the bulk solution. The remainder of the nitromethane was added, causing more precipitation. The precipitated solid was filtered and washed with dry acetone twice. It was then dried at vacuum dessicator at 35^{0}C for 24 hours. Average product yield is about 40 %.

3. Adhesive Test

Prepared dentine slices, methyl methacrylate - polymethyl methacrylate syrup and aluminum coupon as developed previously.[3]

Weighed 150 mg of monomer and dissolve it in a solvent

mixture: N-methyl pyrrolidone - acetone (3ml: 2ml). Tooth slices were washed with dimethoxy ethane, air dried, and treated with the monomer solution for 5 minutes. Then, placed tooth slices on a drying stand for about 3-5 minutes.

Dipped tooth slices in the (PMMA-MMA + N,N-DMPT + Benzoyl peroxide)mixture and placed them in between the coupon surfaces in jig. A 2-Kg weight was placed over the jig and let stand for one hour.

After an hour the rubber sleeves were removed from aluminum coupons which were placed then into a 0.99% saline solution for 24 hours.

The sandwiched coupons were tested in tension for the breaking strength of adhesive monomer. This was done on Instron model 4201. Among the samples one was a blank control consisting of PMMA/MMA alone.

RESULT AND DISCUSSION

1. Results-characterization

(a) MDI-HEMA adduct

Infrared spectra in KBr and NMR spectra in 10% solution in d-DMSO have been carried out and are listed and analyzed in APPENDIX E. Elemental analysis was also included in it.

The product begins to decompose gradually at 200^0C and does not melt.

(b) o-chlorophenol-MDI-HEMA

Infrared spectra in KBr and NMR spectra in 10% solution in d-DMSO have been carried out and are listed and analyzed in APPENDIX F. Elemental analysis was also included in it.

However, some deviation still remains in the elemental analysis. This may be caused by some impurities. Because these compounds cannot be recrystallized due to their decomposition at high temperature, purification can be performed only by precipitation. This necessarily leads to some impurities to be included in the major product.

The product begins to decompose gradually at 210^0C and does not melt.

2. The bonding test results are listed as shown in APPENDIX H. Table V compares the bonding strength for various isocyanate-based adhesives.

From the relative values of tensile tests, the MDI based dental adhesive exhibits very good results. Even though less amount of MDI adhesives was used, its average bonding strength approaches closely that of chloro-TDI-HEMA-Pentaerythritol, and exceeds several other TDI-based adhesives.

Table V: Comparison of Bonding Strength for Various Isocyanate-based Dental Adhesives

Adhesive	Avg. Bonding Strength
Chlorophenol-MDI-HEMA	1268 psi
Eugenol-TDI-HEMA-PENTA.	864 *
Eugenol-TDI-HHMA-PENTA.	518 *
Chlorophenol-TDI-HEMA-PENTA.	1426 *
Chlorophenol-TDI-HHMA-PENTA.	585 *

* Data summarized from reference [3].

The theoretical number of available isocyanate groups for deblocking in TDI/ Pentaerythritol based adhesive monomer is two, whereas only one is available in the MDI

based monomer.

This may account for partially the difference of the result. In fact, the para positioned isocyanate of MDI is sterically more reactive than the ortho one of TDI for bonding to dentin after deblocking.

However, other factors should also be considered when bonding data are compared. These include the freshness of dentin slices, concentration of monomer, the solvent used, tester, and cross-head speed. A brief list is made below.

ADHESIVE	CONCENTRATION	TESTER	CROSSHEAD SPEED
MDI based	30 mg/ml	INSTRON 4201	0.51 mm/min
TDI based	667 mg/ml	SCOTT/CRE 500	1.0 mm/min

The dentin slices used in this test was obtained from precut tooth slices which were stored in saline solution. In order to meet the clinical requirements another solvent may have to be substituted for N-methyl pyrrolidone.

2. The role of solvent for homogeneous reaction is to provide a nonreactive medium in which all reactants are soluble. Active hydrogen solvents obviously can not be used for the present reactions. In the preparation of MDI-HEMA adduct, methylene chloride was chosen as the reaction medium. However, certain solvents such as toluene and benzene are also applicable, as shown in the Table VI.

Table VI Reaction Medium Suitable for Synthesis

Reaction	Solvent
MDI / HEMA	Benzene, chlorobenzene, toluene, methylene chloride.
Blocking of MDI-HEMA adduct	Dimethyl sulfoxide, N-Methyl-2- pyrrolidone

The MDI-HEMA adduct was found to be insoluble in common ether such as tetrahydrofuran, dioxane and dimethoxy ethane, although they are good solvents for TDI derivatives. Instead, some solvents which have higher solubility parameters were found suitable for the blocking reaction. These include N-methyl-2- pyrrolidone (NMP), and dimethyl sulfoxide (DMSO).

However, the hygroscopicity and the high boiling point of these polar solvents should be considered carefully. Due to this property of some solvents, the undesirable water might be carried which in turn may lead to bulk gelation

during the blocking reaction of isocyanate.

For obtaining purified product, it is betterto use a solvent which has a low boiling point so that solvent can be removed easily. This is not a problem for the first stage reaction (MDI / HEMA / methylene chloride), but solvent such as NMP which remained in the blocking product was difficult to separate unless warming (to 35^0C) was applied under vacuum for a considerable period.

In addition, dry acetone may be utilized for the final washing of blocked monomers to remove high boiling point solvent.

It was also observed that MDI-HEMA adduct did not dissolve in pyrridine, acetyl acetone, acetonitrile, acetophenone, and 2-methoxy ethyl ether at below 60^0C. Therefore, they were not considered as the solvent for the homogeneous blocking reaction.

3. During the blocking reaction, there was sometimes observed the occurrence of gel. Usually, it appeared as a yellow syrup and was found insoluble in solvents. The gel actually corresponds to the formation of an infinite network in which polymer molecules have been bonded to each other to form a macroscopic molecule.

Many factors in the chemical process may cause this undesirable gelation. It may be visualized in the following manners:

(a) The presence of water in reagent

Lyman [46] found an interesting example : adding 0.4% mole of water to the reaction of MDI with ethylene glycol in DMSO caused a series of reactions,

$$Ar\text{-}NCO + H_2O \longrightarrow ArNH_2 + CO_2$$

$$Ar\text{-}NH_2 + Ar\text{-}NCO \longrightarrow AR\text{-}NH\text{-}C{=}O\text{-}NHAr$$

$$Ar\text{-}NH\text{-}C{=}O\text{-}NHAr + Ar\text{-}NCO \longrightarrow Ar\text{-}N(C{=}O\text{-}NHAr)\text{-}C{=}O\text{-}NHAr \longrightarrow \ldots\ldots$$

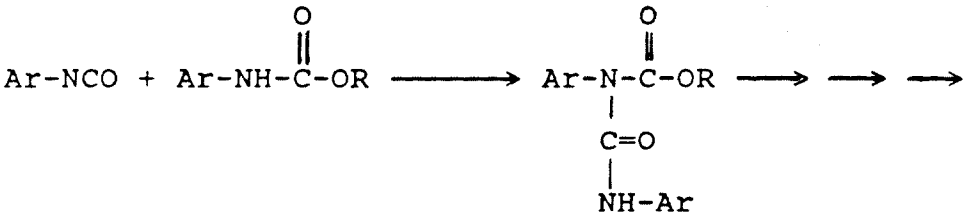
The urea thus formed could act as a potential crosslinking site by reacting with the isocyanate to form a biuret. Morton et al., [47] also reported that relative rate of reaction of isocyanate with a urea is much faster than that with a urethane.

In the present study the moisture might enter the system by the contaminated solvent and poorly sealed system parts. Therefore, to avoid undesirable water attacking a highly drying reagent and a proper inert gas blanket are required inevitably.

(b) Elevated temperature

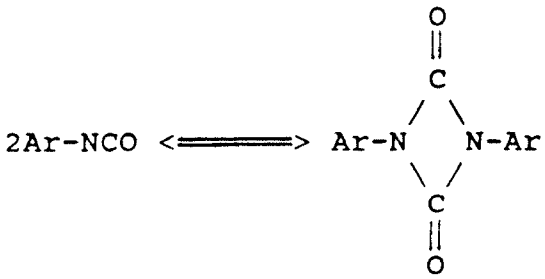
At elevated temperature, the reaction between an isocyanate and a urethane group may also produce an allophanate. It may further lead to branching or

crossing[46].

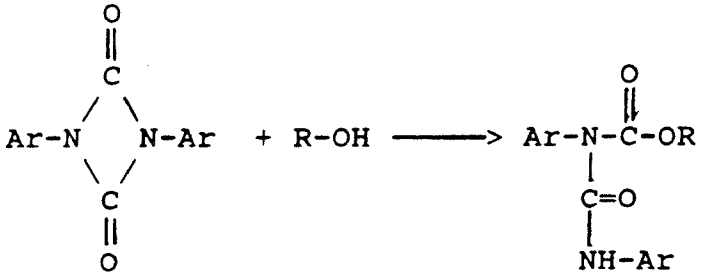


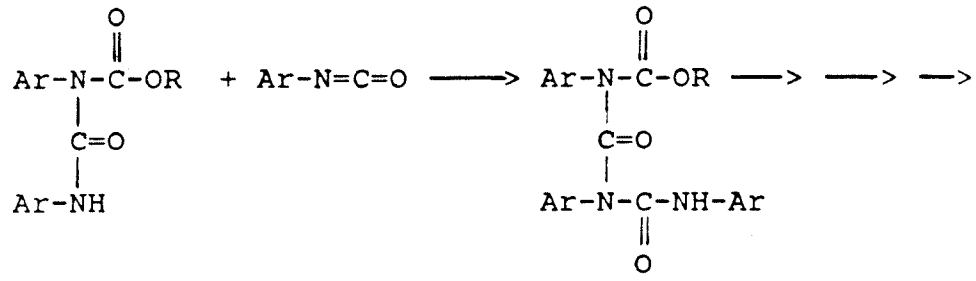
(c) Isocyanate dimer

Even at low temperature the dimerization of aromatic isocyanates is easily found in the presence of acidic or basic catalysts[46]. The formation proceeds



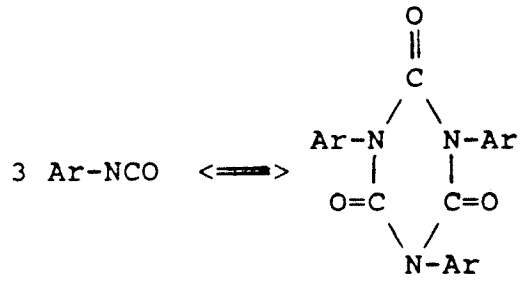
The dimer can introduce potential branching or crosslinking sites into the molecule chain,





(d) Isocyanate trimer

At less extent than dimer, the isocyanate trimer is formed at high temperature, especially in the presence of acidic and basic catalysts.[46] A representative structure is



This structure is very stable to both hydrolytic and thermal attack. However, it would further react with active hydrogen and then lead to crosslinking as well as upset the reactant balance. Kogon[49] suggested that trimer such as triphenylisocyanurate can be formed via the reaction of dimer and allophanate.

Considering these side reactions, the gel should be avoided by using dry and purified reaction medium, and by keeping reaction mass under the cover of inert gas stream such as dry nitrogen, argon etc. during the reaction period.

One of the most important parameter to control is the reaction temperature below 45^0 C. In this way, not much solvent will be lost due to vaporization and the dimer will not form easily. Addition of some amounts of solvent after isocyanate has been depleted about fifty percent is also highly recommended; this added solvent appears to reduce gel formation.

Small amounts of inhibitors such hydroquinones may also be added as soon as the reaction has proceeded more than halfway.

4. The raw MDI rock as received from the supplier has a white-yellow color. To prevent decomposition it should be stored below 0^0C under dry inert gas. While the MDI is used as a reactant, it may alternatively be purified by recrysta llization in addition to the traditional vacuum distillation (163-166 ^{0}C / 0.3 torr).

In fact, both methods were utilized during this research period. The former is introduced as follows:

The raw MDI rock is crushed and weighed. It is then dissolved in twice weight of dry, distilled n-hexane under reflux. To the hot solution, a little bit of decolorizing

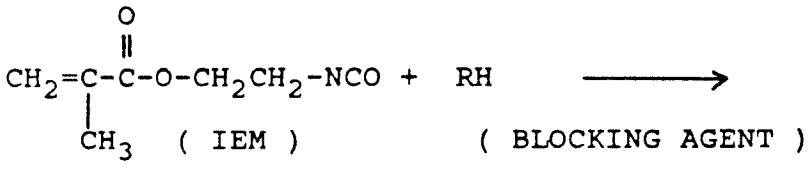
charcoal is added carefully. The solution is then filtered hot into cold hexane (below 5^0 C). MDI will be precipitated immediately as white crystal. These precipitates are collected by filtering and are vacuum dried.

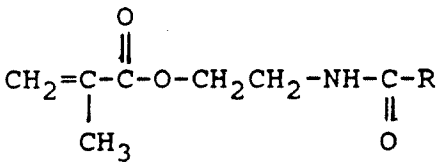
Following the procedure of recrystallization the separation of the MDI as an oil can be prevented [50], and the compound is obtained as a pure, white crystalline solid, m.p. 42^0C.

5. Blocking agent is one of the most critical species in this research. Conventional phenols such as o-methoxyphenol, o-chlorophenol, p-cresol and eugenol have been used.[1-6] Through the past studies, o-chlorophenol and o-methoxyphenol exhibited very good results.

In fact, some other phenols are also applicable to the blocking-deblocking system. They include 2,4-dimethylphenol, 2,4-di-t-butylphenol, methyl p-hydroxybenzoate and methyl salicylate.

A recent study [51] for the isocyanatoethyl methacrylate (IEM) [53,54,55], CAS no. 030674-80-7, has shown the thermal deblocking temperature for common blocking agents falls within 110-200^{0}C, as shown in Appendix D.





Among which the lowest deblocking temperatures demonstrated for isocyanate derivatives were in the phenols and imidazole. Instead, alcohols, lactums, and oximes gave the

most stable formulations.

Since MDI-HEMA adduct, an aromatic isocyanate, has a somewhat analogous structure to the aliphatic IEM, it is believed that phenol blocking agents should behave a similar sequences. Moreover, one may expect somewhat lower splitting temperatures when aromatic isocyanates are substituted for the aliphatic diisocyanate.

For instance, in the system:

$$R\text{-}NH\text{-}C{=}O\text{-}X + H\text{-}Y \Longleftrightarrow R\text{-}NHC{=}O\text{-}Y + H\text{-}X$$

reaction toward the right (at a given temperature) will be more favored when R is aromatic, rather than aliphatic, when X changes in the sequence OAr > OR, and when Y changes in the sequence RNH > ArNH > RO > ArO [52]. As a result, the proposed amino-isocyanate reaction seems to be reached more easily.

6. During the blocking reaction, it was found that reaction proceeded very slow even in the presence of organotin catalyst [2,4,51]. This can be understood by the fact of the steric hindrance of HEMA substitution and the acidicity of phenols.

Due to its resonance stabilization, phenols are more acidic or less basicity than the aliphatic alcohol. Usually they react more slowly with isocyanates than do the alcohols. Saunder et al., [52] described that, at temperature 50-75^{0}C,

that reaction of most isocyanates with phenols is really slow.

$$RNCO + Ar\text{-}OH \longrightarrow RNHCOOAr$$

In the present system blocking agents, such as o-chlorophenol and o-methoxyphenol possess other groups on the phenol nucleus, their reaction with isocyanates will thus be retarded.

$$\xrightarrow{\quad} \underset{\text{increasing electronegativity (acid strength)}}{R_3C\text{-}H \quad R_2N\text{-}H \quad RO\text{-}H \quad F\text{-}H}$$

$$\Longrightarrow \underset{\text{increasing electronegativity}}{Li \quad Be \quad B \quad C \quad N \quad O \quad F}$$

The low reaction progress apparently because electronegative groups have reduced the basicity of the hydroxyl group still more.

On the other hand, certain catalysts such as tertiary amine or aluminum chloride was suggested to promote the reaction [52]. As an example dimethylaniline shows a significant catalytic effect. Its coordination sequence has been proposed as below.

$$Ar\text{-}OH + ArN(CH_3)_2 \Longleftrightarrow ArO^- + ArNH^+(CH_3)_2$$

$$RNCO + ArO^- \Longleftrightarrow [\ RN{=}C\text{-}O\ ]^-$$

$$\Big|$$

$$OAr$$

$$\Big\downarrow \ ArNH^+(CH_3)_2$$

$$RNHCOOAr \quad + \quad ArN(CH_3)_2$$

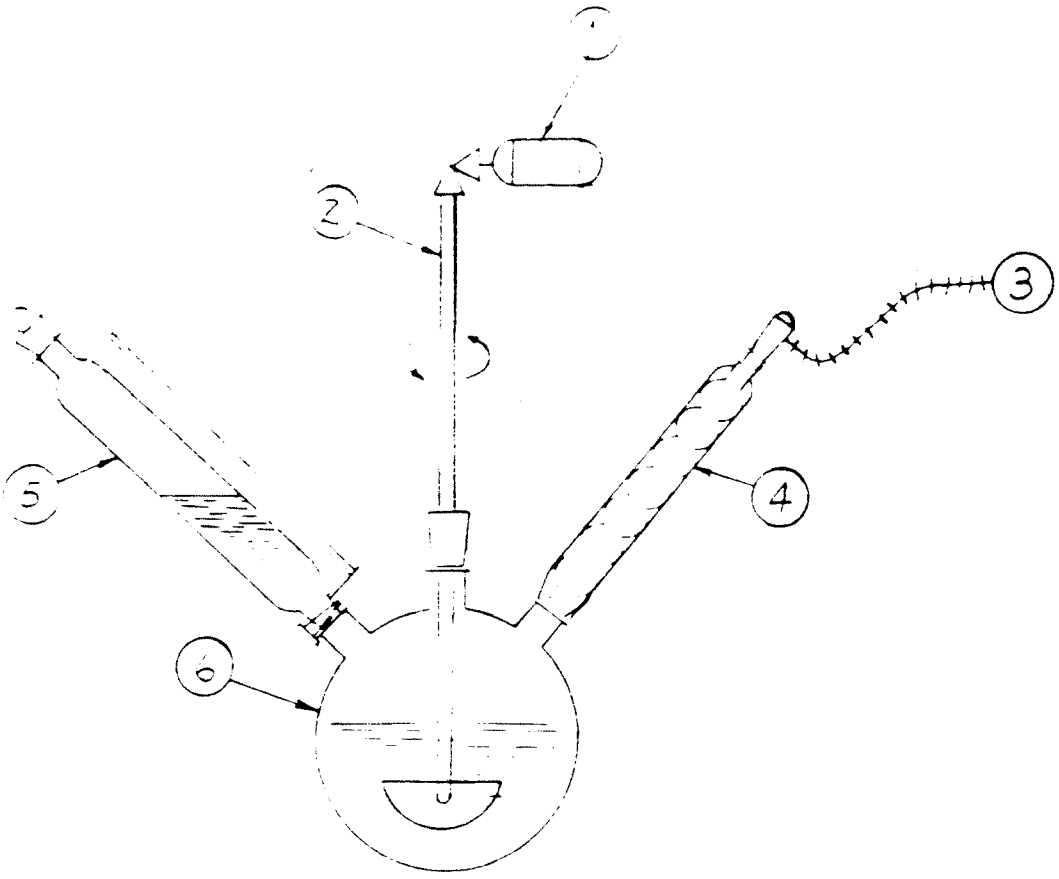
Currently, the kinetic comparison between organotin and tertiary amine for isocyanate reaction is not available. Therefore, for shortening the reaction time, some amines such as triethyl amine and dimethyl aniline may be studied to see if reaction rate can be accelerated effectively.

V. CONCLUSION

1. The method of synthesis for MDI-based adhesive has been developed as detailed in the text. Moreover, the bonding test of the monomeric adhesive also shows a very impressive result. Therefore, MDI derivative has a great potential when it is applied to the dental adhesion. It is believed the goal of this research has been reached.

2. Further studies such as new blocking agents, optimization of blocking reaction, investigation of deblocking requirements, and copolymerization of monomers are recommended in order to improve the adhesion system more effectively.

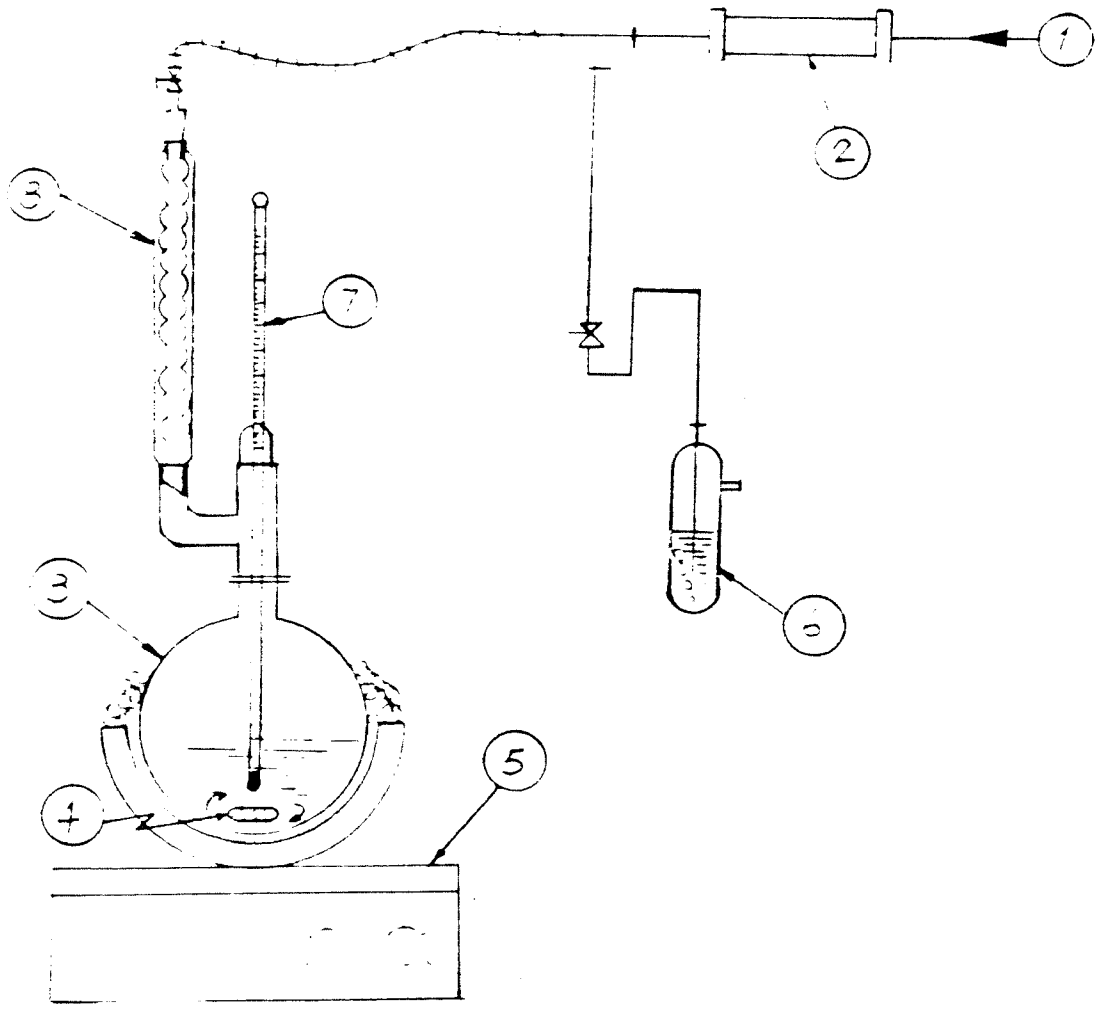
APPENDIX A: Apparatus for Synthesis of MDI-HEMA Adduct



1: AC motor; 2: agitator; 3: dry nitrogen; 4: condenser

5: addition funnel; 6: three-necked baffled flask

APPENDIX B: Apparatus for Preparation of Blocked Monomer

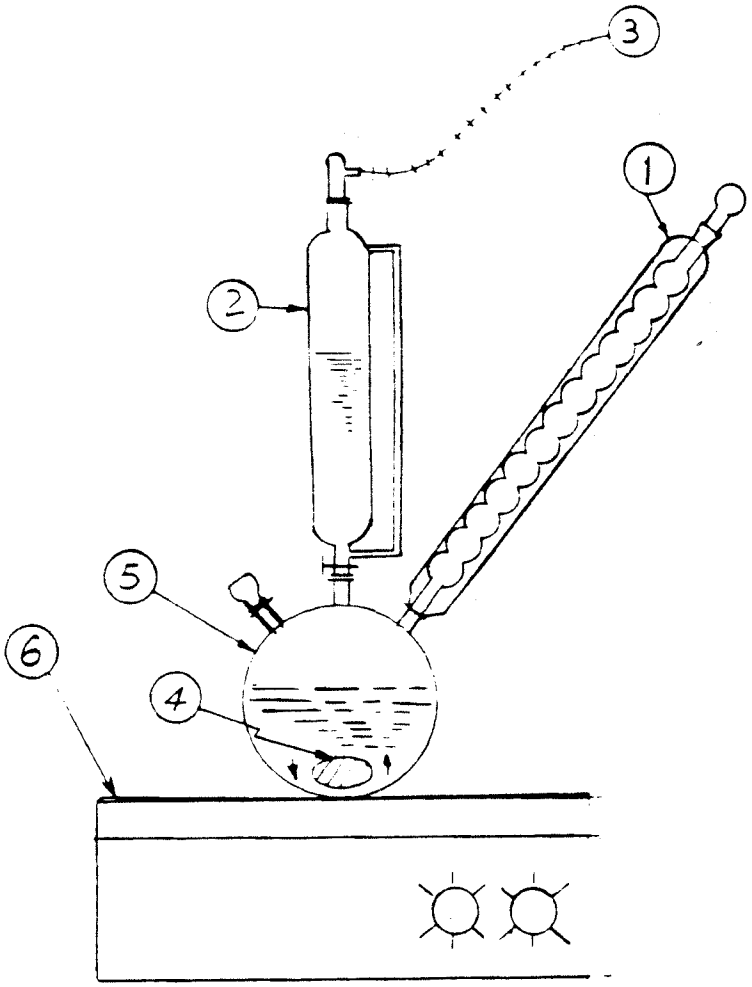


1:nitrogen; 2: drying tube; 3: one-necked flask;

4: teflon-clad magnetic bar; 5: magnetic stirrer

6: oil seal; 7: thermometer; 8: condenser

APPENDIX C: Apparatus for Precipitating Blocked Monomer

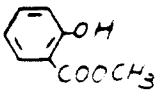
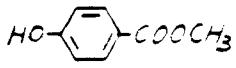
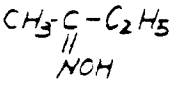
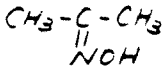
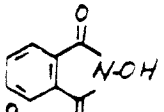
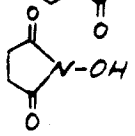
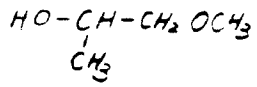
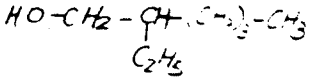
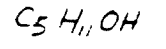
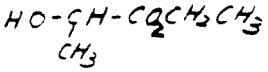
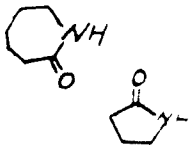
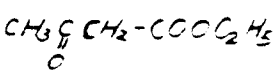


1: condenser; 2: addition funnel; 3: dry nitrogen

4: teflon-clad magnetic bar; 5: three-necked flask;

6: magnetic stirrer

APPENDIX D: Deblocking Temperature of Isocyanatoethyl Methacrylate Masked with Various Blocking Agents [51]

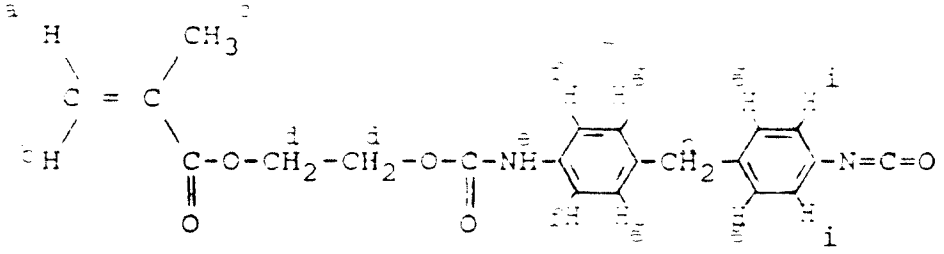
Group	Derivative	Temperature, ^{0}C	Structure
Phenol	Methyl Salicylate	110-120	
	Methyl p-Hydroxy Benzoate	130	
Imidazole	Imidazole	110-130	
Oxime	Methyl Ethyl Ketoxime	140-150	
	Acetone Oxime	130-140	
N-Hydroxy-mides	N-hydroxyphthalimide	170-175	
	N-hydroxysuccinimide	160	
Alchols	Methoxy Propanol	175-200	
	2-Ethyl Hexanol	>200	
	Pentol	200	
	Ethyl Lactate	200	
Lactams	6-Caprolactum	175-200	
	Pyrrolidinone	250	
Other	ethyl Acetoacetate	>175	

APPENDIX E: Spectrum and Elemental Analysis for HEMA-MDI Adduct

1. **Infrared Analysis**

C-H stretching	3010 (w) cm^{-1}
	2990 (w)
C-H bending	
methyl	1410 (m)
alkene	850 (w)
C-C aromatic	1510-1530 (s)
ester stretching	
C=O	1710 (s)
amide C=O stretching	1640 (s)
N-H stretching	3330 (s)
C-N vibration, aromatic	1230 (s)
N=C=O	2260 (s)

2. NMR spectrum analysis



a = 5.55 ppm, b = 5.70, c = 2.05, d = 4.30, e = 7.85

f = 6.70-6.80, g = 6.70-6.80, h = 3.90, i = 6.70-6.80

APPENDIX E (continued)

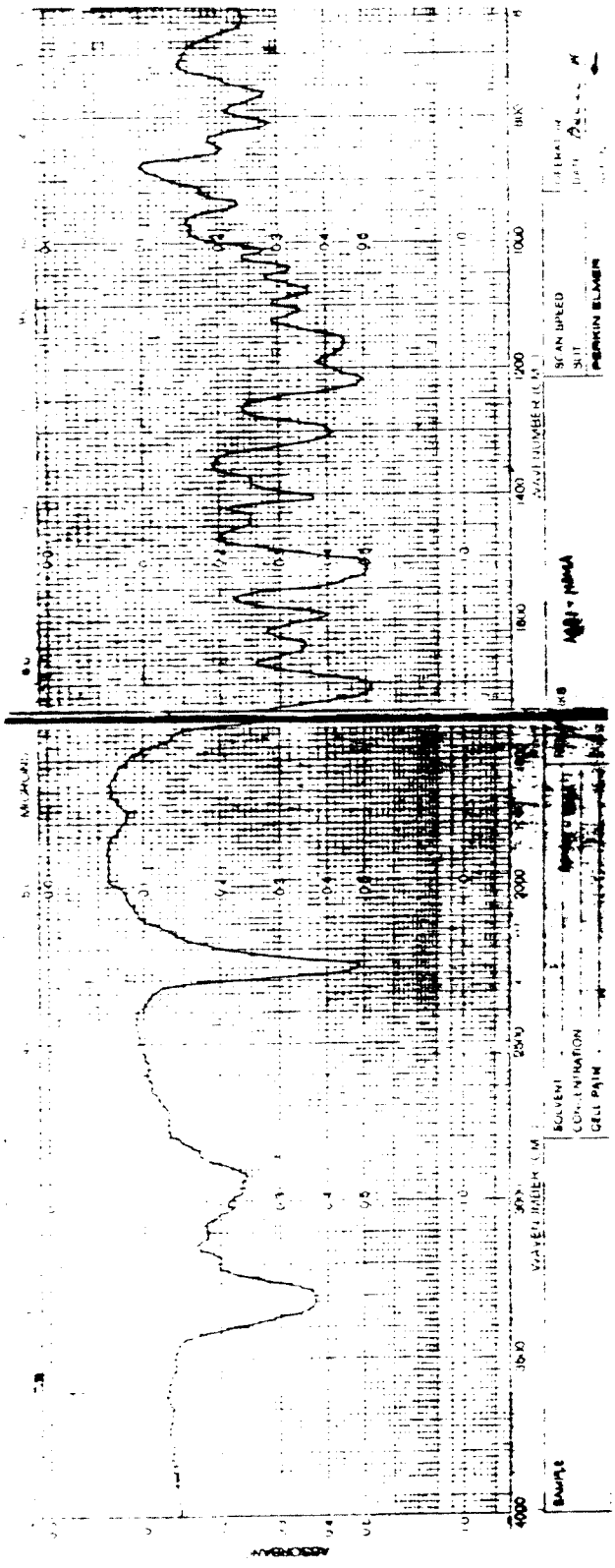
3. **Elemental analysis**

MDI-HEMA adduct

	Calculated	Found
C:	66.3%	67.5%
H:	5.30	5.64
N:	7.40	7.93

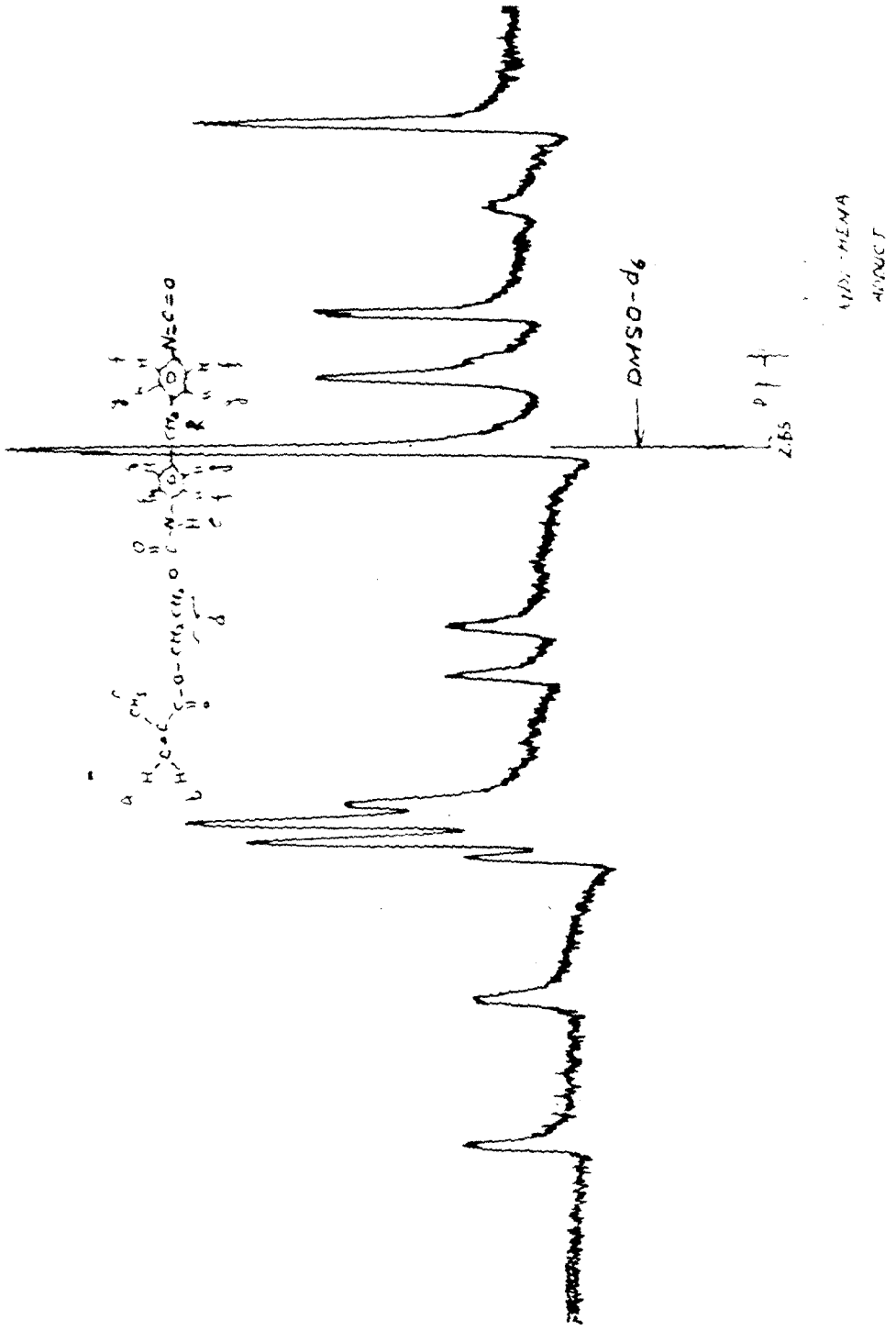
APPENDIX E (continued)

Infrared Spectrum of MDI-HEMA Adduct



APPENDIX E (continued)

NMR Spectrum of MDI-HEMA Adduct



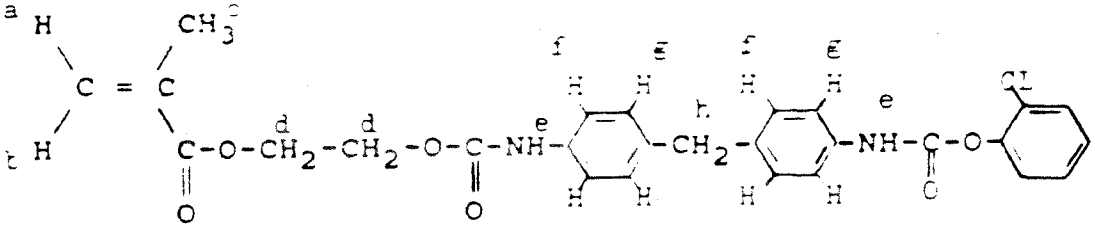
APPENDIX F: Spectrum and Elemental Analysis for o-chlorophenol-HEMA-MDI adduct

1. **Infrared Analysis**

C-H stretching	3050 (w) cm^{-1}	
	2970 (w)	
C-H bending		
alkene	850 (w)	
	1410 (w)	
alkane,		
$-CH_2-$	1440-1460 (w)	
$-CH_3$	1410 (m)	
C-C aromatic	1510 (s)	
multiple bond stretching	1460 (w)	
ester stretching		
C=O	1720 (s)	
amide		
C=O stretching	1660 (s)	
N-H stretching	3330 (s)	
C-O stretching	1305 (s)	
C-N vibration, aromatic	1230 (s)	

APPENDIX F (continued)

2. NMR spectrum analysis



a = ? ppm, b = 6.25, c = 1.90, d = ?, e = 7.80
f = 6.55-6.65, g = 6.55-6.65, h = 3.55

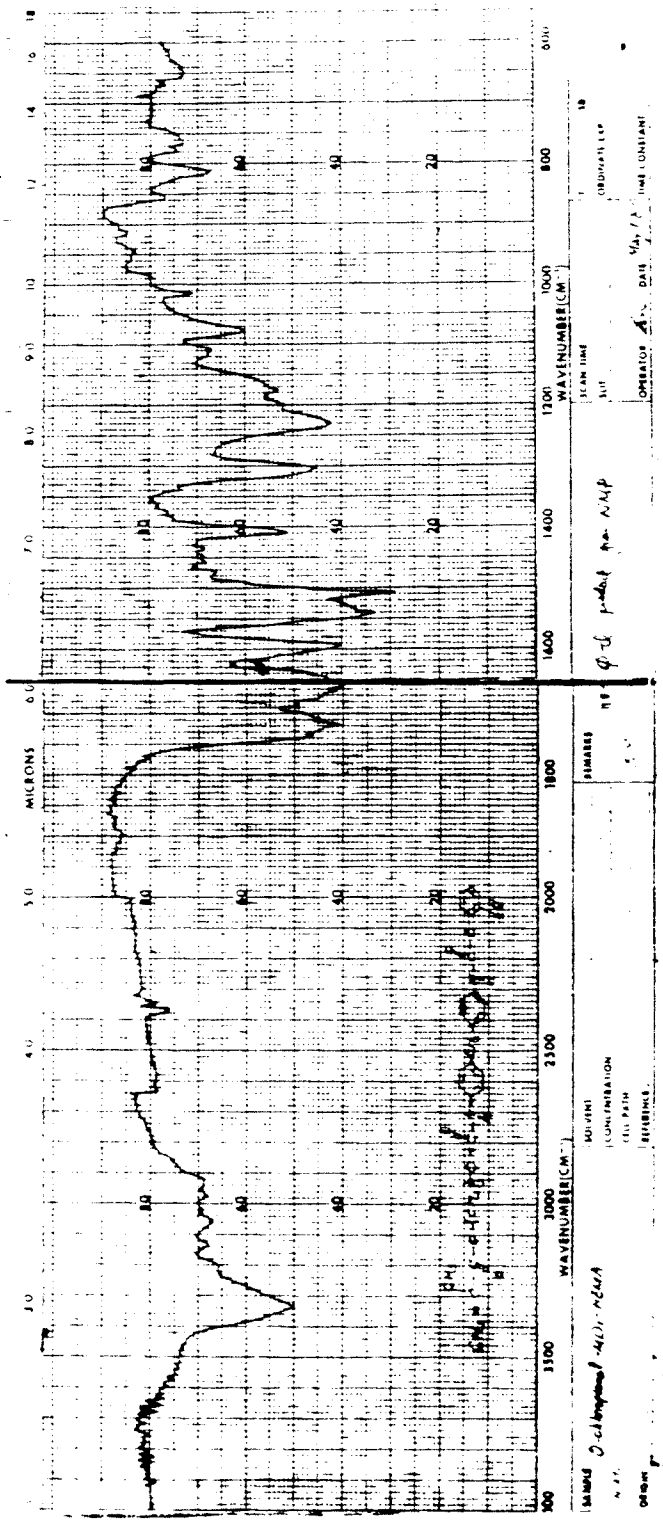
3. Elemental analysis

o-chlorophenol-MDI-HEMA

	Calculated	Found
C:	63.7 %	66.2 %
H:	4.95	5.81
N:	5.53	9.27
cl:	6.97	5.06

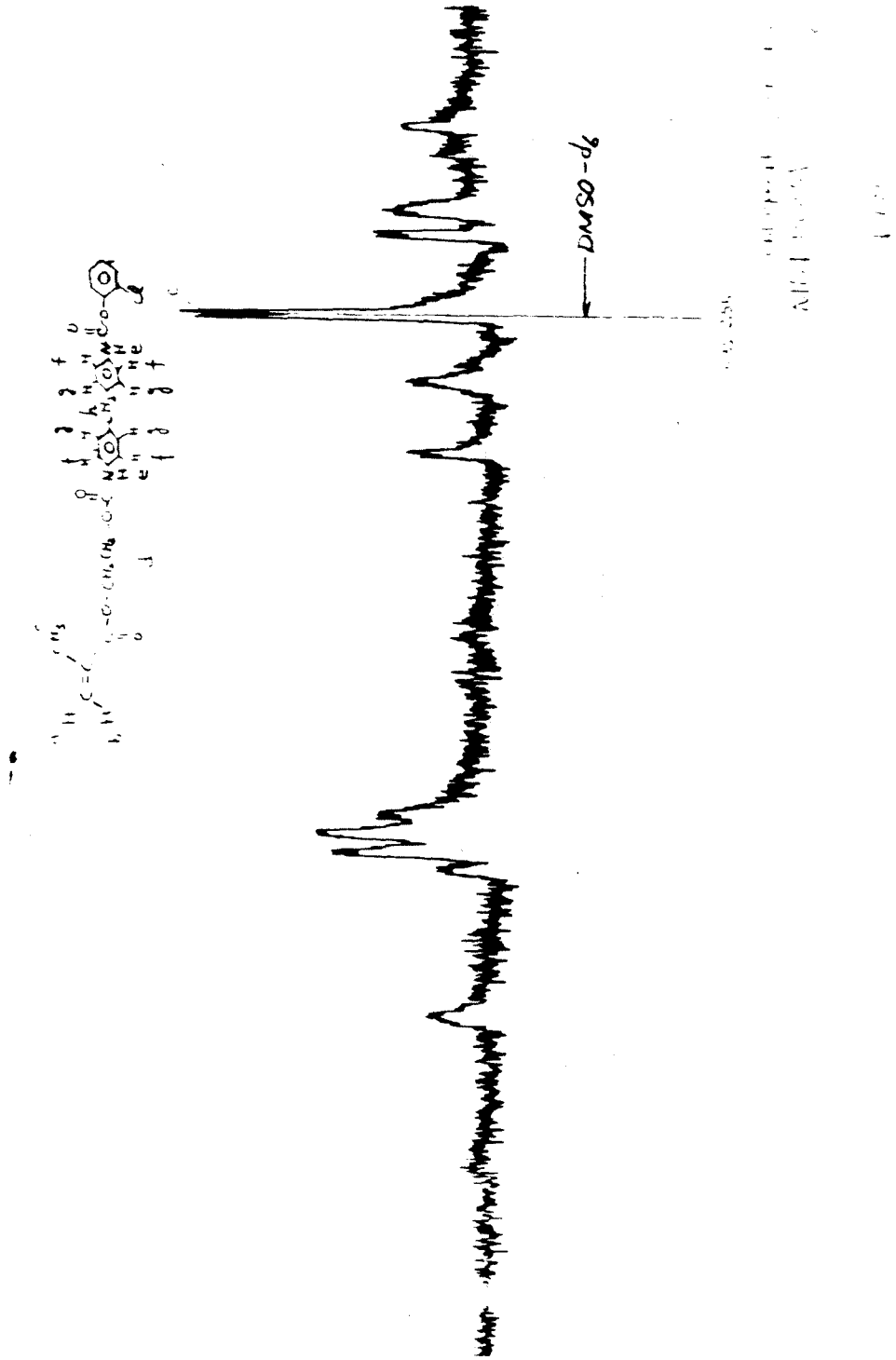
APPENDIX F (continued)

Infrared Spectrum of o-chlorophenol-MDI-HEMA



APPENDIX F (continued)

NMR Spectrum of o-chlorophenol-MDI-HEMA



APPENDIX G : Bonding test result for o-chlorophenol-MDI-HEMA

	Sample #		Bonding strength	
Batch 1	1	(control)	369	psi
	2		644	
	3		1445	
	4		1737	
	5		743	
	6		658	
Batch 2	7	(control)	52	
	8		1657	
	9		2261	
	10		1158	
	11		2076	
	12		898	
Batch 3	13	(control)	0	(failed prior to testing)
	14		1501	
	15		1207	
	16		412	
	17		1356	

---

n (sample) = 14

Avg = 1268 psi

std. dev. = 557 psi

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