

NATIONAL BUREAU OF STANDARDS REPORT

10 060

Progress Report
on
CRYSTALLINE DIMETHACRYLATE MONOMERS



U.S. DEPARTMENT OF COMMERCE
NATIONAL BUREAU OF STANDARDS

NATIONAL BUREAU OF STANDARDS

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CRYSTALLINE DIMETHACRYLATE MONOMERS

by

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(Abstract)

CRYSTALLINE DIMETHACRYLATE MONOMERS

Certain dimethacrylate monomers can be prepared and purified by recrystallization. Upon mixing, the crystals liquify by forming a ternary eutectic. The colorless oily liquid is suitable for use in composite formulations.

Previously, BIS-GMA¹ (a dimethacrylate monomer, the reaction product of an epoxy resin and methacrylic acid or of 4,4'-isopropylidenediphenol and glycidyl methacrylate)² was developed for use as a binder for reinforcing fillers. This dimethacrylate monomer, shown in Figure 1, has had widespread use in current commercial dental composite restorative materials. However, BIS-GMA is not completely color-stable and is too viscous for use without being thinned with methyl methacrylate or other comonomers of low viscosity. Furthermore, it cannot be purified by distillation or by crystallization since it is a mixture of high-molecular-weight optical isomers.

This report describes the synthesis and properties of three dimethacrylate monomers that were synthesized in order to reduce the viscosity, improve the color and storage stability and possibly other properties associated with the resin that forms the binder of composite restorative materials. The monomers, with melting points slightly above room temperature, form a liquid when combined in

ternary eutectic proportions. Their purification by recrystallization provides a means of attaining desired purity and of facilitating production control.

This paper does not deal with properties of the polymer or composite materials prepared from these monomers. It encompasses only the synthesis of the monomers and the formulation of a liquid eutectic monomer based on them.

Materials and Methods*

The three monomers, bis(2-methacryloxyethyl)isophthalate, (MEI); bis(2-methacryloxyethyl)terephthalate, (MET), and bis(2-methacryloxyethyl)phthalate (MEP) were condensation products of 2-hydroxyethyl methacrylate (HEMA) and the corresponding acid chlorides of the phthalic acid position isomers. Most of the compounds that were used are listed in Table 1. They were used as received.

*Certain commercial materials and equipment are identified in this paper to specify adequately the experimental procedure. In no instance does such identification imply recommendation or endorsement by the National Bureau of Standards or that the material or equipment identified is necessarily the best available for the purpose.

SYNTHESIS OF MEI.—The synthesis was carried out in a three-neck round-bottom flask placed in a cooling bath, equipped with stirrer, thermometer, dried nitrogen inlet, and a dropping funnel. BHT (butylated hydroxytoluene; 2,6-di-t-butyl-4-methyl phenol) and di-t-butyl sulfide, each equivalent to 0.1% of the theoretical yield of monomer were placed in the flask. To this was added 194 ml of pyridine (2.4 mols) and 305 ml of HEMA (2.4 mols) with stirring. Dried nitrogen was used as the reaction atmosphere and the cooling bath maintained the temperature within the range of 10-35°C throughout the reaction. Isophthaloyl chloride (203 gm; 1 mol), dissolved in 112 gm of acetone, was added dropwise to the stirred reagents in the reaction vessel. As the reaction proceeded, a white precipitate (pyridinium chloride) formed. The acid chloride solution was added over a four-hour period. The mixture after standing overnight without stirring was vacuum filtered to remove crystals of pyridinium chloride. The residue on the filter was rinsed with additional acetone and then discarded.



A clear yellow filtrate containing the monomer product was obtained.*

The filtrate was diluted with 300 ml of chloroform and washed three times in a separatory funnel using 500 ml of distilled water for each wash. The resin phase was evaporated down under vacuum to remove chloroform and water to approximately constant weight. A yellow liquid with a refractive index of $n_D^{23.5^\circ\text{C}} = 1.5087$ was obtained. The yield of this impure monomer was slightly over 90% of the theoretical. To this was added additional BHT and di-t-butyl sulfide (0.1% of each). The monomer was diluted with an equal volume of methanol and then cooled, with stirring, to a low temperature utilizing a dry ice bath. At a low temperature (about -20°C) the crystals formed spontaneously

* It might be possible to crystallize the monomer directly from this acetone solution by stirring and cooling it to a low temperature (e.g. -20°C or below) with the aid of a dry-ice (solid carbon dioxide) bath, although this was not attempted.



and developed rapidly. This slurry of crystalline monomer was then suction filtered, the crystals of monomer being retained on the filter paper.*

The crystals obtained were redissolved in warm methanol and recrystallized three times.

SYNTHESIS OF MET.—This compound was synthesized in essentially the same manner as MEI, with the following exceptions. Since the terephthaloyl chloride is less soluble in acetone, a larger quantity of acetone was required as a solvent and the mixture was warmed slightly.

SYNTHESIS OF MEP.—This monomer was synthesized in essentially the same manner as were MEI and MET, with the exception that no acetone was used in the synthesis since the phthaloyl chloride is liquid at room temperature and could therefore be added dropwise to the reaction flask.

* The filtrate can then be concentrated and cooled again to obtain additional crystalline monomer and this process repeated to obtain maximum yield of crystalline product.



DETERMINATION OF EUTECTIC COMPOSITION.—After the individual melting points of the three recrystallized monomers had been determined, the mixed melting point (first sign of melting) was determined for the binary systems MEI-MET, MEI-MEP and MET-MEP. The proportions of the binary eutectics were calculated from the theoretical³ relationship: $X_1 = \frac{100(T_2 - T_e)}{T_1 + T_2 - 2T_e}$ where X_1 is the mole percent of lower-melting component, T_1 is the melting point of the lower-melting component, T_2 is the melting point of the higher-melting component, and T_e is the eutectic temperature (first sign of melting of the mixture).

The three binary diagrams were then incorporated into a triangular ternary diagram to help predict the composition of the ternary eutectic. The approximate ternary eutectic composition was determined by trial and error,³ starting from the composition corresponding to the intersection of the lines normal to the sides of the triangle at the theoretical binary eutectic compositions.



Stabilizers and a polymerization accelerator⁴⁻⁸ as given in Table 2 were added to the approximate ternary eutectic mixture. This formulation (Table 2) was sent to an independent commercial laboratory for preliminary toxicity evaluation.

Results

After the MEI was recrystallized three times from methanol, it was a colorless white solid having a melting point of 42.3-43.3°C. After melting, the metastable liquid had a refractive index of $n_D^{22.4^\circ\text{C}} = 1.5116$.

After the MET was recrystallized four times as previously described, the white crystalline monomer had a melting point of 50-53°C, and the refractive index of the metastable liquid (measured immediately after melting) was $n_D^{22.3^\circ\text{C}} = 1.5135$. The yield after the first crystallization was greater than 55%.

After four recrystallizations, the colorless white crystals of MEP had a melting point of 39-40°C and the refractive index of the metastable liquid

(measured immediately after melting of some of these crystals) was $n_D^{22.3^\circ\text{C}} = 1.5095$. The yield was approximately 80% of theoretical at the time of the first crystallization.

The following data are only theoretical for the binary and approximate for the ternary systems but are presented since they might be useful in practical applications. Binary eutectics:

36% MET - 64% MEI, 31°C

45% MEI - 55% MEP, 26°C

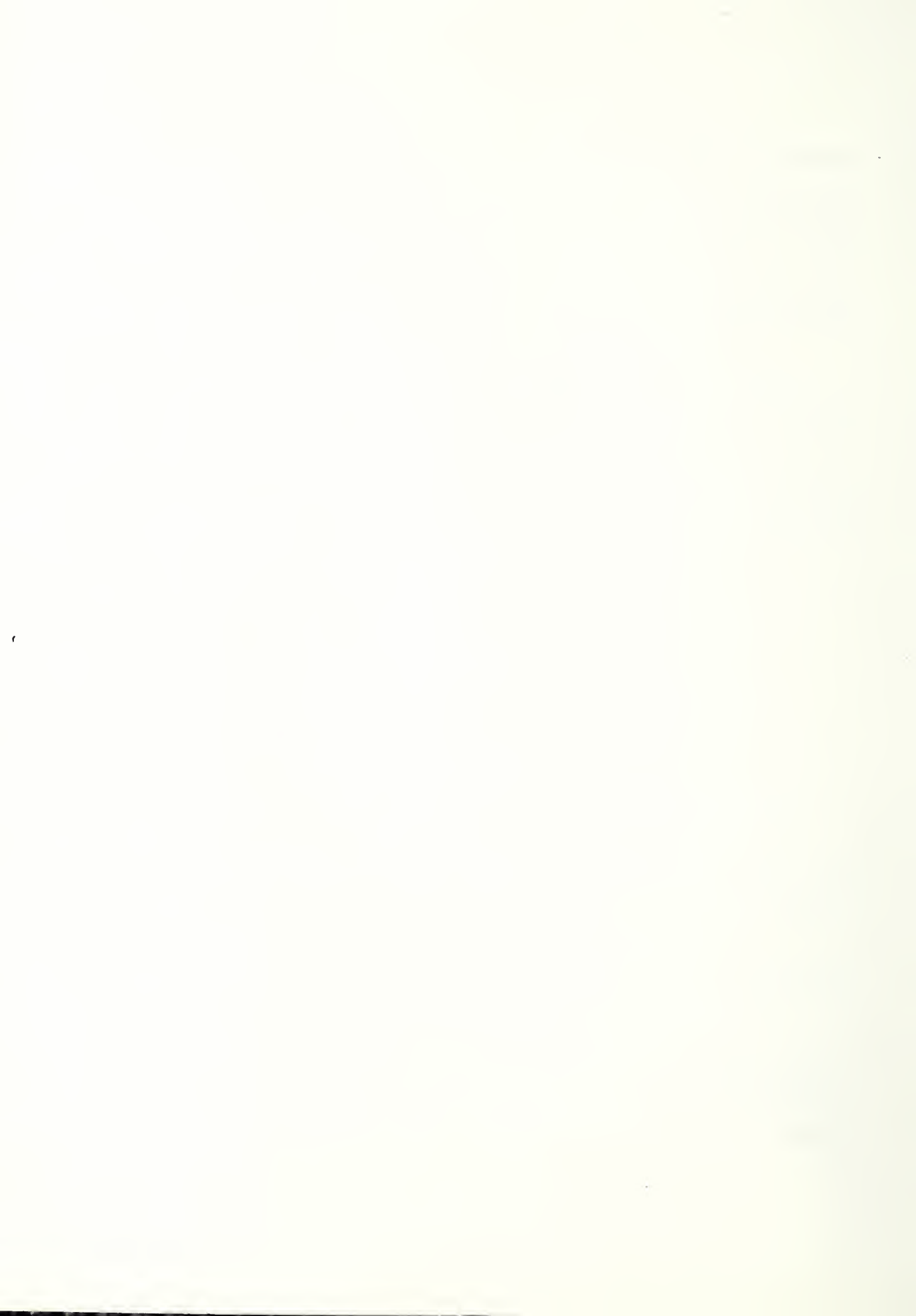
68% MEP - 32% MET, 29.5°C

Ternary eutectic:

47% MEI, 38% MEP, and 15% MET, ($< 23^\circ\text{C}$)

This ternary mixture is a colorless oily liquid at room temperature; it solidified under refrigeration (about 5°C).

TOXICITY.—The summaries of the toxicity results (on the formulation given in Table 2) are as follows: The monomer formulation was evaluated for acute oral toxicity by gastric intubation to groups of two adult male albino



rats at graded dosage levels of 1.0, 3.16, 10.0, and 31.6 ml/kg of body weight. The acute oral median lethal dose of the material for albino rats was 31.6 ml/kg of body weight; therefore, it is considered to be relatively harmless by the oral route.

The test material was also evaluated for acute eye irritation by a single application of 0.1 ml of the test material into one eye of each of three albino rabbits. No irritation was produced in one eye, and only slight conjunctival redness was produced in two eyes which subsided by 72 hours or day 4. The test material is considered to be essentially nonirritating to rabbit eyes.

Discussion

A considerable advantage of the ternary eutectic mixture prepared from the three dimethacrylate crystalline monomers as a binder for reinforcing fillers lies in the fact that its viscosity permits its use without the addition of thinners or diluents which may contribute undesirable properties. Having molecular weights of 390, the monomers of the liquid are nonvolatile and require no volatile additives. Their structural formulas are shown in Figure 2. Compared

with BIS-GMA it is reasonable to expect that the introduction of electron-withdrawing substituents into the aromatic ring will result in improved resistance to oxidation and subsequent color formation. Electron-withdrawing substituents deactivate aromatic nuclei thereby diminishing oxidation. Electron-donors, such as the alkyl and ether groups on the BIS-GMA rings, have the opposite effect.

Information on MEI was not found in the literature. A compound corresponding to MEP has been described.⁹ The acid-catalyzed condensation product of methacrylic acid, ethylene glycol, and phthalic acid, and of ethylene glycol monomethacrylate and phthalic anhydride was reported.^{10, 11} Both were reported to have $n_D^{20} = 1.500$ and $D_4^{20} = 1.18$; no mention was made of crystallization.

Crystalline products melting between 30 and 53°C have been reported to result from the reaction of bis-β-hydroxyethyl terephthalate with the acid chloride of methacrylic acid.¹²

A correction of a previous report¹³ should be made. It was stated that a liquid mixture of MEI and MET did not crystallize on standing at room temperature. This binary

mixture did crystallize at a later date, having been metastable for a considerable period of time.

Although the work reported here is part of a larger program encompassing the development of an esthetic adhesive restorative material,¹⁴ there is no reason to believe that the monomer system reported here has adhesive characteristics. To obtain adhesion, appropriate coupling agents that have been referred to previously,¹⁴ are indicated.

Properties of composite materials utilizing the formulation given in Table 2, are being investigated.

Conclusions

Improved purity of nonvolatile monomers can be achieved readily when the molecular characteristics are such as to facilitate recrystallization. The bis(2-methacryloxyethyl) esters of phthalic, isophthalic and terephthalic acids have melting points slightly above room temperature and they form a ternary eutectic mixture

that is liquid at room temperature. This colorless slightly viscous liquid appears to be suitable for formulation as the binder for composite materials for use in industry and in dentistry.

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TABLE 1

Materials Used in the Monomer Synthesis

Material	Grade	Source
Acetone	Reag. ACS	Allied Chem.
Chloroform	Reag. ACS	Allied Chem.
2-Hydroxyethyl methacrylate (HEMA)	96%	Rohm & Haas
Isophthaloyl chloride	98% min.	Hooker Chemical Corp.
Methanol	ACS	Fisher Sci. Co.
Phthaloyl chloride	Pract.	Matheson, Coleman & Bell
Pyridine	Reag.	Baker Chemical Co.
Terephthaloyl chloride	98% min.	Hooker Chemical Corp.

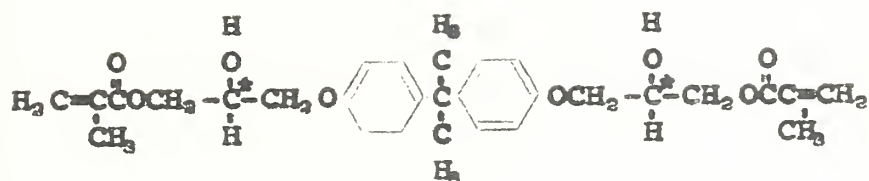
TABLE 2

A Liquid Monomer Formulation Based on the Ternary Eutectic
of Three Crystallizable Dimethacrylates

Weight %	Ingredients	Function	Source
45.6	Bis(2-methacryloxyethyl)isophthalate, (MEI)	Dimethacrylate	Synthesized
36.8	Bis(2-methacryloxyethyl)phthalate, (MEP)	Dimethacrylate	Synthesized
14.54	Bis(2-methacryloxyethyl)terephthalate, (MET)	Dimethacrylate	Synthesized
2.18	Permasorb MA [®]	Ultraviolet absorber	National Starch & Chem. Corp.
0.54*	N,N-dimethyl-3,5-dimethylaniline	Polymerization accelerator	Synthesized†
0.20	Tenox [®] BHT	Antioxidant stabilizer	Eastman Chem. Products, Inc.
0.14	Di- <u>tert</u> -butylsulfide	Antioxidant stabilizer	K & K Labs., Inc.

* The concentration of the amine accelerator is adjusted somewhat, depending on the application, to obtain the desired hardening time.

† In response to interest in this compound,⁵ Dr. Charles W. Taylor (3M Co.) synthesized the amine by a method⁶⁻⁸ utilizing relatively inexpensive starting materials and kindly furnished us a sample. This was the source of the accelerator used in the formulation described here. The material is now commercially available from Eastman Chem. Products, Inc.

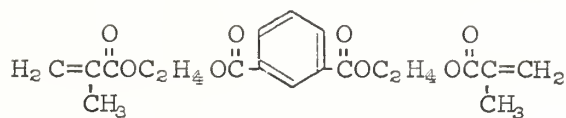


BIS-GMA

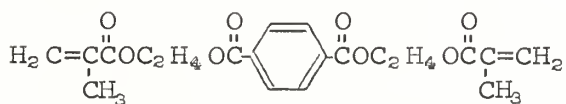


MMA

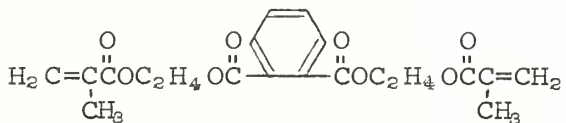
Fig. 1—Assumed structural formula of BIS-GMA^{1,2}. The asterisks indicate asymmetric carbon atoms that result in a number of stereoisomers. Methyl methacrylate (MMA) is shown for comparison.



MEI



MET



MEP

Fig. 2—Structural formulas of three dimethacrylate monomers. Bis(2-methacryloxyethyl)isophthalate, (MEI); bis(2-methacryloxyethyl)terephthalate, (MET), and bis(2-methacryloxyethyl)phthalate, (MEP) were each readily purified by crystallization.

