

AN IMPROVED SYNTHESIS OF ETHYL α -HYDROXYMETHYLACRYLATE, A UNIQUE ISOMERIC ANALOG OF HEMA

Joseph M. Antonucci¹, Jeffrey W. Stansbury¹ and Bruce O. Fowler²

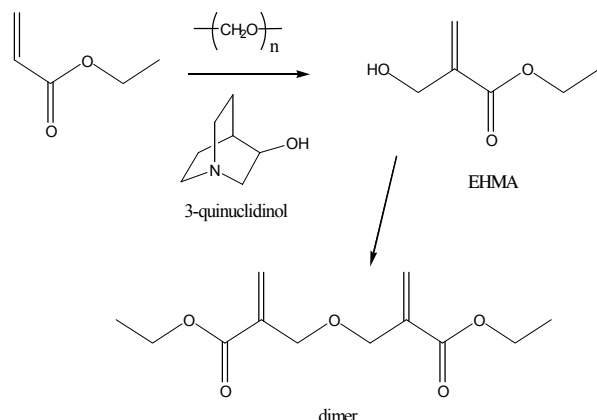
¹Polymers Division, National Institute of Standards and Technology, Gaithersburg, MD 20899, USA. ²National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD 20892, USA.

Introduction

HEMA (2-hydroxyethyl methacrylate), a hydrophilic, surface active monomer is widely used in dental adhesives, resin-modified glass ionomer cements and, in its polymeric forms, in numerous biomedical applications. Poly(HEMA), or PHEMA, was the first synthetic hydrogel intended for use as a biomaterial.¹ Some of the traditional uses of HEMA polymers and copolymers include soft contact lenses, vascular grafts, soft tissue substitutes, and hydrogels for controlled-release delivery systems. HEMA also has found use in the formulation of photocurable bioactive composites with remineralization potential.² Recently, a unique isomeric analog of HEMA, ethyl α -hydroxymethylacrylate (EHMA), was synthesized.³⁻⁶ This study describes a facile high yield synthetic method for the preparation of highly pure EHMA and compares the bulk polymerizability of EHMA with HEMA.

Experimental*

Synthesis (Scheme A) and Characterization of EHMA. In a stoppered flask equipped for magnetic stirring was placed 10 mmol ethyl acrylate, 10 mmol paraformaldehyde, 1.25 mmol 3-quinuclidinol, 2.5 g dimethyl sulfoxide and 0.85 g of distilled water. The mixture was heated at 100 °C for 30 min and, after cooling to room temperature, extracted with dilute aqueous hydrochloric acid to remove the quinuclidinol. Vacuum distillation of the crude product yielded mass fractions of 75 % to 80 % EHMA. The purified EHMA was characterized by FT-IR and ¹H/¹³C NMR spectroscopies. As shown below, some dimer product also forms but this can be minimized by controlling the reaction conditions; the dimer also can be isolated by vacuum distillation. EHMA has low water solubility (mass fraction of about 10 %) whereas HEMA is miscible with water in all proportions.



Scheme A. Synthesis of EHMA from ethyl acrylate.

Polymerization of EHMA. Previous studies have described the polymerization of EHMA with conventional free radical initiators, e.g. benzoyl peroxide.⁴ In this study we investigated the visible light photopolymerization of EHMA alone and with Bis-GMA activated with CGI 1700 (CIBA) at a mass fraction of 3 % as the photoinitiator. Comparative photopolymerizations were conducted with HEMA. Homopolymerizations of EHMA and HEMA and their copolymerization with Bis-GMA were analyzed by photo-DSC (conditions: 30 °C, nitrogen purge, 150 W Xe source, irradiation intensity of 4.3 mW/cm²). Final homopolymer and copolymer conversions also were obtained as follows: Polymer films approximately 20 : m in thickness of each monomer system were formed between glass slides by

visible light irradiation for 60 s per side in a Triad 2000 unit (Dentsply) followed by postcuring at 37 °C for 24 h.

Results and Discussion

EHMA formation is rapid relative to that of the dimer. The addition of DMSO provides homogenous reaction mixtures that reduce reaction times and result in high conversions of the acrylate to EHMA with minimal dimer formation. The presence of water in the reaction media also favorably influences the EHMA-dimer equilibrium since water is liberated in the dimerization. As a measure of the relative rates of polymerization, the maximum heat flow values were 7.6 W/g for HEMA and 3.2 W/g for EHMA (relative standard uncertainty, 3 %). However, essentially identical degree of conversion values were obtained for the homopolymerizations, with HEMA at 73.5 % and EHMA at 72.6 % (relative standard uncertainty, 3 %). Copolymerizations of Bis-GMA/HEMA and Bis-GMA/EHMA (65:35, mass ratios) in the photo-DSC under the same conditions previously described gave heat flow maxima of 15.9 W/g and 12.9 W/g, respectively. The degree of conversion in these copolymer systems was calculated as 63.4 % for Bis-GMA/HEMA and 59.9 % for Bis-GMA/EHMA. Under different polymerization conditions (Triad 2000), triplicate FT-IR measurements of conversion for each type of monomer system gave the following results: HEMA \approx EHMA \approx 97 % (Figures 1 and 2); Bis-GMA/HEMA, 86.2 % and Bis-GMA/EHMA, 89.9 % (standard uncertainty, 0.9 %).

Computer modeling (Scheme B) indicated that EHMA forms a more stable intramolecular hydrogen bond compared with HEMA. This appears to be validated by analysis of the carbonyl absorption in the infrared spectra of the isomers (Figures 3 and 4). Three different IR wavenumber carbonyl stretching bands are possible for each monomer corresponding to free $\text{C}=\text{O}$ and intramolecular and intermolecular hydrogen bonded $\text{C}=\text{O}$, designated as $\text{C}=\text{O}\cdots\text{HO}$ -. Second derivative IR (Figure 4) and peak fit spectra show three bands for EHMA (1726, 1712, and 1697) cm^{-1} (standard uncertainty, 1 cm^{-1}). The 1726 cm^{-1} band derives from free carbonyl and the latter two, plausibly, from intramolecular and intermolecular hydrogen bonded carbonyl, respectively. HEMA has two second derivative and peak fitted bands at 1721 cm^{-1} and 1705 cm^{-1} . These bands, respectively, derive from free carbonyl and, plausibly, intermolecular hydrogen bonded carbonyl; a third band for possible intramolecular hydrogen bonded carbonyl was not clearly detected which suggests minimal bonding of this type in HEMA. Second derivative FT-IR spectra of EHMA (not shown) show two vinyl bands at 1645 cm^{-1} and 1635 cm^{-1} . This indicates two types of vinyl groups, which plausibly arise from the presence and absence of intramolecular hydrogen bonding.

Conclusion

EHMA has decreased water solubility compared with HEMA, probably due to strong intramolecular hydrogen bonding interactions. The rate of homopolymerization of EHMA was somewhat less than that of HEMA, whereas their rates of copolymerization with Bis-GMA were virtually the same. Significantly, the final conversion values of EHMA and HEMA polymers and copolymers were essentially equivalent. Modeling studies predict that neat EHMA should exhibit considerably more intramolecular hydrogen bonding than HEMA; FT-IR results appear to confirm this prediction. Unlike HEMA and PHEMA, which yield ethylene glycol on hydrolytic degradation, EHMA and PEHMA would yield ethyl alcohol. Overall, these results suggest that EHMA has the potential to serve as an alternative to HEMA in dental and biomedical applications.

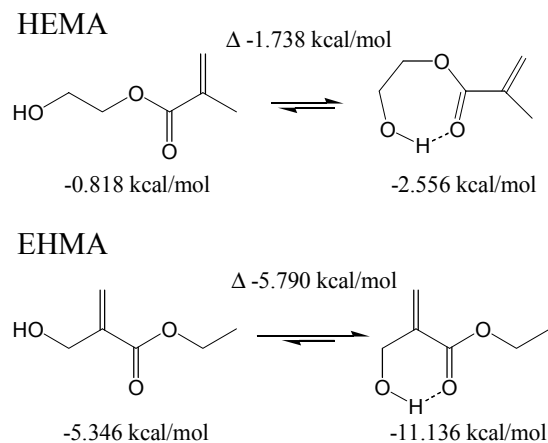
Acknowledgement. This work supported by NIST-NIDCR IA Y1-DE-7006-0. We are grateful for gifts of HEMA and Bis-GMA from Esstech, and of CGI 1700 from CIBA.

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

References

- (1) Wichterle, O.; Lim, D., *Nature (London)* 1960, 185, 118.
- (2) Skrtic, D.; Hailer, A.W.; Takagi, S.; Antonucci, J.M.; Eanes, E.D., *J Dent Res* 1996, 75, 1679.
- (3) Hoffmann, H.M.; Rabe, J., *J Org Chem* 1985, 50, 3849.

- (4) Mathias, L.J.; Kusefoglu, S.H.; Kress, A.O., *Macromolecules* 1987, 20, 2326.
 (5) Stansbury, J.W., *J Dent Res* 1990, 69, 844.
 (6) Antonucci, J.M.; Stansbury, J.W.; Cheng, G.W., In: *Polymers of Biological and Biomedical Significance*, Shalaby, S.W.; Ikada, Y.; Langer, R.; Williams, J. (eds.), ACS Symposium Series 540, American Chemical Society, Washington, DC, 1994, pp. 191-201.



Scheme B. Computer modeling showing the minimized energies for the linear and cyclic structures of HEMA vs EHMA. The strong preference of EHMA to engage in intramolecular hydrogen bonding via a six-membered ring is indicated.

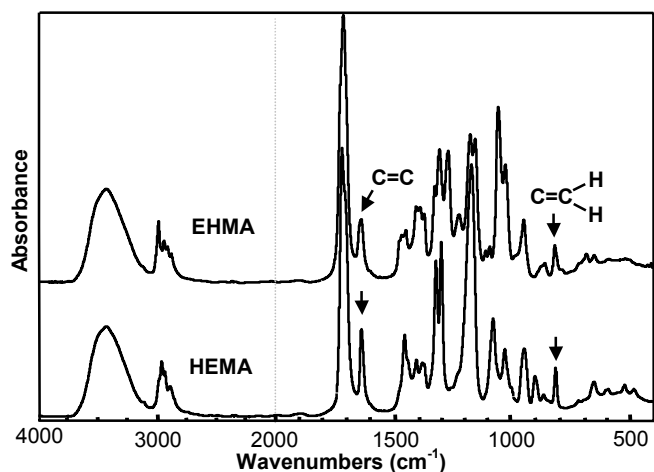


Figure 1. Comparison of FT-IR spectra of EHMA vs HEMA from 4000 cm^{-1} to 500 cm^{-1} .

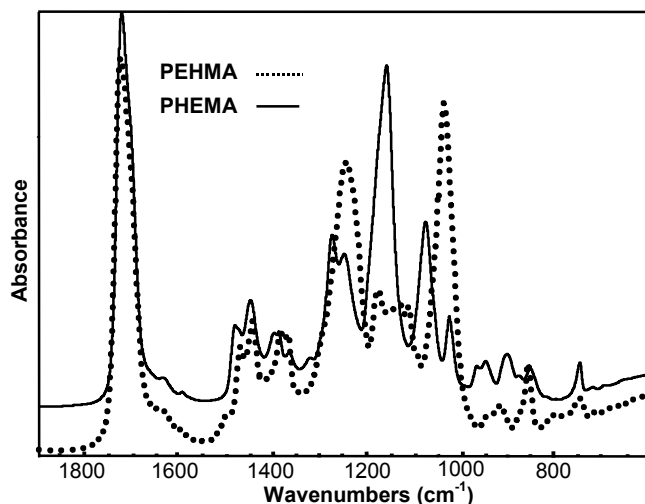


Figure 2. FT-IR spectra of PEHMA and PHEMA showing virtually no vinyl absorption bands.

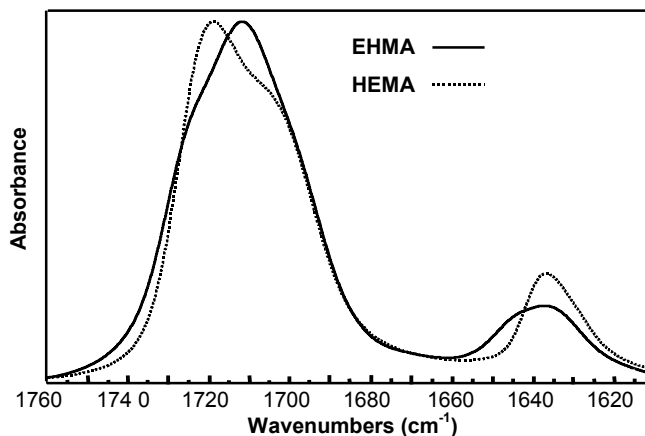


Figure 3. Expanded FT-IR spectra showing carbonyl and vinyl absorption bands of EHMA and HEMA. Note that both carbonyl bands have unresolved structure, and the vinyl band of EHMA is a doublet (see text).

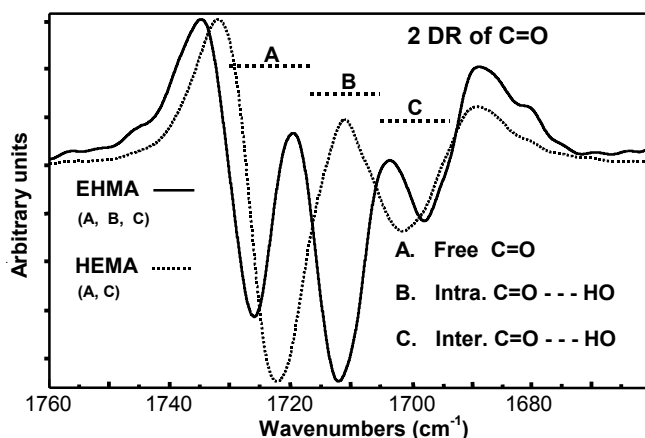


Figure 4. Second derivative FT-IR spectra of carbonyl bands of EHMA and HEMA. EHMA has three bands, A, B, and C; HEMA has two bands, A and C. The expected vibrational origins of the bands A, B, and C are denoted.