

**S-(ω -HYDROXYALKYL) ESTERS OF
THIOACRYLIC AND THIOMETHACRYLIC
ACIDS**

BACKGROUND OF THE INVENTION

The government has certain rights in this invention pursuant to Research Grant No. NIDR DE 09696.

This invention relates in general to compositions of matter and, more particularly, to thiomethacrylic and thioacrylic acid ester compounds, methods of preparation of such compounds and polymers made therefrom.

Dental composites are typically applied in a multi-step process designed to provide a secure adhesive bond and seal at the interface of the dental adhesive and tooth surface. As an example, when the restorative is a cavity filling, the decayed tooth material is cut away and an etching composition such as citric acid is applied to the tooth surface. The etching composition serves to remove debris remaining from the cutting process and causes demineralization of a thin layer of underlying dentin to facilitate the wetting and penetration of the subsequently applied dental adhesive. A conditioner such as 2-hydroxyethylmethacrylate (HEMA) is also commonly applied to the dentin prior to or concurrently with application of the dental adhesive to enhance the wetting, penetration and bonding of the dental adhesive to the dentin.

The dental adhesive must be capable of wetting the prepared dentin surface as well as bonding with the organic composite resin which is commonly used to fill the hollow area in the portion of the tooth that has been cut away. The dental adhesive must also possess a sufficient shear bond strength to withstand the shrinkage experienced by many dental composite resins, such as those based on bis-GMA (2,2'-bis[4-(2-hydroxy-3-methacryloyloxypropoxy)]phenyl propane). The adhesive is typically a vinyl monomer mixture which undergoes chemical or photo-initiated polymerization. The composite resin may include the same or different monomer material as used for the dental adhesive, as well as suitable filler material.

HEMA homopolymers and copolymers have also been used extensively as biomaterials in diagnostic and therapeutic devices and for implants. These polymer materials are known as hydrogels because of their hydrophilicity and insolubility in water. The high water content, soft and rubbery consistency and low interfacial tension of HEMA polymers closely resemble those same properties found in living tissues. Because of these similarities, HEMA polymers have been used as diagnostic devices such as catheters, electrode catheters, carriers for enzyme immunoassay, gel-entrapped enzyme electrode probes, cell culture substrates, and electrophoresis gels. HEMA polymers have also been used in therapeutic applications as absorbent coatings for blood perfusion, hemodialysis membranes, blood oxygenators, degradable therapeutic systems, drug-delivery systems, and medicated and soft contact lenses. Implant uses of HEMA polymers includes intraocular lenses, artificial corneas, soft tissue substitutes, burn dressings, transdermal drug-delivery patches. Other uses are known, including as separation membranes.

Despite these widely varying uses of HEMA polymers, it would be desirable in certain applications to achieve a faster rate of vinyl polymerization of the HEMA monomer. Another problem presented by the use of HEMA as a dental restorative conditioner and in other tissue applications is the difficulty in determining the degree of penetration of HEMA

into the underlying dentin or tissue. Radioactive labelling procedures can be used to determine the degree of penetration of HEMA, but it would be desirable to use alternate procedures which do not require the use of radioactive markers. For example, compounds containing sulfur atoms can be localized in tissue samples using energy-dispersive spectroscopy and auger spectroscopy.

Alkyl thiolacrylates are known and methods of preparation have been reported. Although alkyl thiol esters have been obtained by the treatment of a mercaptan with an acid chloride, the use of acryloyl chloride in this process has been generally unsuitable because the mercaptan is added to the carbon-carbon double bond at the same time as the formation of the ester. Instead of directly forming the thiol esters, Marvel et al. in *Journal of Polymer Science*, Vol. XIX, pages 59-71 (1956), described the process of preparing saturated alkyl thioesters by first reacting mercaptan with α,β -dibromopropionyl chloride to form the thiol ester, followed by the elimination of the bromine atoms by the addition of sodium iodide.

Braude, in *J. Organic Chem.*, Vol. 22, pages 1675-78 (1957), reported that the thioesters could be prepared by contacting methacryloyl chloride with the lead salt of the mercaptan. Sumrell et al. later disclosed that methacryloyl chloride could be directly reacted with methyl mercaptan in the presence of sodium hydroxide at a temperature below 10° C. to form methyl thiolmethacrylate. *J. Amer. Chem. Soc.*, Vol. 80, pages 2509-13 (1958). Otsu et al. have also reported on the copolymerization of several alkyl thioacrylates with styrene in *Die Makromolekulare Chemie*, Vol. 119, pages 140-146 (1968).

SUMMARY OF THE INVENTION

It is an object of this invention to provide a compound which has properties comparable to HEMA but contains a thiol group which can be localized using energy-dispersive spectroscopy so that the degree of wetting and penetration of the compound into the substrate to which it is applied can be determined without the use of radioactive labelling procedures.

It is also an object of this invention to provide a compound which can be polymerized to form homopolymer or copolymer materials for use in a wide variety of biomaterial applications.

As a corollary to the preceding object, it is another object of this invention to provide a compound which has a faster rate of vinyl polymerization in comparison to HEMA so that the compound can be used in place of HEMA, including in those applications where the faster rate of polymerization is more suitable.

In one aspect, the invention provides novel compounds of the general formula I:



wherein:

R is hydrogen or methyl; and
n is 1, 2 or 3.

In another aspect, the invention is directed to a method of preparing compounds of formula I, said method comprising serially carrying out the following steps:

(a) contacting an ω -mercaptoalkanol with an oxy-block-