Abstract: The purpose of the current study was to synthesize a methacrylate monomer with a thiohydantoin structure. In a flask, (2-thiohydantoin-4-yl) propionic acid, 10-hydroxydecy methacrylate, 4-dimethylaminopyridine, and tetrahydrofuran (THF) were placed in a nitrogen atmosphere. A THF solution of N,N'-dicyclohexylearbodiimide was added and stirred at room temperature. Ethyl acetate and n-hexane were then added to the reaction mixture. The reacted slurry was purified by chromatography with silica gel and hexane-ethyl acetate gradient elution solvent. The structure of the compound was assigned with proton nuclear magnetic resonance spectrum analysis, infrared spectroscopy, and high-resolution mass spectral analysis. The colorless viscous liquid obtained in yield of 49% was characterized as 10-methacryloyloxydec-2-thiohydantoin-4-yl)propionate (MDTHP) or 10-methacryloyloxydecyl-(2-thiohydantoin-4-yl)propionate (2-THPDM). The MDTHP was soluble to acetone, isopropanol, and methyl methacrylate up to 2.6%.

Keywords: adhesive, bonding, noble metal alloy, thiol, thione

Introduction

Vinyl and methacrylic monomers with mercapto, thiooxo, or sulfide groups have been used for priming copper and noble metals. A triazine thiol, 6-(4-vinylbenzyl-η-propyl) amino-1,3,5-triazine-2,4-dithiol (VBATDT or VTD) [1], was used as a coating agent for copper plating. A thiophosphine, 10-methacryloyloxydecyl dihydroxipropophosphate (M10PS, MDTP) (Kojima et al., J J Dent Mater 6 Spec 10, 112, 1987) [2]; a disulfide, methacryloyloxydecyl 6,8-dithiooctanoate (MDDT) [3,4]; and a thiouracil, 6-methacryloyloxyhexyl 2-thiouacil-5-carboxylate (MTU-6) [5], have been reported as functional methacrylates. These monomers are dissolved in solvents and are being used as single liquid priming agents capable of bonding dental noble metal alloys [6-12].

Thiohydantoin is one of the five-membered heterocyclic compounds with thione structure. However, characteristics of thiodyantoin derivatives with polymerizable functional groups have not been reported. This report describes the synthesis of a thiohydantoin compound with a methacryloyloxydecyl group.

Materials and Methods

Reagents

Reagents, N,N'-dicyclohexylearbodiimide (DCC) and 4-dimethylaminopyridine (DMAP), were commercially obtained and purified by recrystallization. Ethyl acetate, n-hexane, tetrahydrofuran (THF), and 1,10-decane diol were purified by distillation. Reagent grade 2,6-di-tert-butyl-4-methylphenol, i.e., 3,5-di-tert-butyl-4-hydroxytoluene (BHT); aceton; isopropanol; and methyl methacrylate (MMA) were used without further purification. VBATDT was synthesized according to the method described by Mori and Nakamura [1].

10-hydroxydecy methacrylate (HDMA)

Methacryloyl chloride was synthesized by reacting glacial methacrylic acid and thionyl chloride in the presence of cuprous chloride [13]. Methacryloyl chloride was then reacted with 1,10-decane diol with equivalent molar ratio in THF. Pyridine was used as the de-hydrochloric acid agent. The mixture of HDMA and 1,10-decanediol dimethylacrylate was separated through column chromatography [14].

(2-thiohydantoin-4-yl)propionic acid (THPA)

A thiohydantoin derivative, THPA, was synthesized according to the method described by Szabo and Karabinos [15] and Duggan et al. [16].

Synthesis and characterization of a methacrylate with thiohydantoin structure

In a 300-mL four-necked flask, 4.45 g (23.6 mmol) THPA, 6.88 g (28.4 mmol) HDMA, 0.58 g (4.73 mmol) DMAP, 7.0 mg BHT, and 90 mL THF were placed in a nitrogen atmosphere. A solution of 5.82 g (24.8 mmol) DCC in 30 mL THF was dropped from a funnel and stirred for 4.5 h at room temperature. Next, 150 mL ethyl acetate and 30 mL n-hexane were added to the reaction mixture and stirred for 10 min.

The white slurry was filtrated through a pad of Hyflo Super Cel (Fujifilm Wako Pure Chemical Corp., Osaka, Japan), and the filtrate was condensed under reduced pressure. The oily product was purified twice by chromatography with 100 g silica gel (SNAP KP-Sil Cartridge, Biotage Japan Ltd., Tokyo, Japan) and hexane-ethyl acetate (5-100%) gradient elution solvent.

The structure of the compound was assigned with proton nuclear magnetic resonance (‘H-NMR) spectrum analysis (270 MHz, JEOL Excalibur 270, JEOL Ltd., Akishima, Japan) in CDCl3. Chemical shifts (δ) were expressed in parts per million and are internally referenced with tetramethylsilane. Infrared (IR) spectroscopy (Nicolet Magna 560, Thermo Fisher, Yokohama, Japan) was used to analyze the functional groups of the synthesized compound. The exact mass of the synthesized compound was determined by high-resolution mass spectral (HRMS) analysis (Shimadzu Shimadzu 2050).
Results

The colorless viscous liquid obtained from the condensation of 23.6 mmol THPA and 28.4 mmol HDMA was 4.79 g in yield of 49%. Figures 1, 2 and Table 1 summarize the results of analysis of the synthesized compound. From the results of $^1$H-NMR spectrum analysis, IR spectroscopy, and HRMS analysis, the compound was characterized as 10-methacryloyloxydecyl-(2-thiohydantoin-4-yl)propionate (MDTHP) or 10-((3-(5-oxo-2-thioxo-4-imidazolidinyl)propanoyl)oxy)decyl methacrylate (2-THPDM).

Table 1 Assignment of the monomer synthesized

| Chemical sift (ppm) | Integral value | Assignment* |
|--------------------|----------------|-------------|
| 8.44 1H            | N               | singlet, broad |
| 7.53 1H            | N               | singlet, broad |
| 6.10 1H            | Ho              | multiplet    |
| 5.55 1H            | Ho              | multiplet    |
| 4.26 1H            | He              | doublet of doublet |
| 4.14 2H            | Hm or Hd        | triplet      |
| 4.10 2H            | Ha              | triplet      |
| 2.34-2.21 1H       | Hb              | multiplet    |
| 2.17-2.01 1H       | Hb              | multiplet    |
| 1.95 3H            | Hn              | multiplet    |
| 1.72-1.60 4H       | H(e, l)         | multiplet    |
| 1.43-1.26 12H      | H(f, g, h, i, j, k) | multiplet |

IR (ATR) HRMS (ESI) C$_{20}$H$_{33}$N$_2$O$_5$S

| Wave number (cm$^{-1}$) | Assignment | Calculated | Found      |
|-------------------------|------------|------------|------------|
| 3,293                   | C(=O)NH    | 413.211    | 413.2111   |
| 2,919                   | CH         |            |            |
| 2,832                   | CH         |            |            |
| 1,734                   | C=O        |            |            |
| 1,713                   | C(=O)O     |            |            |
| 1,705                   | NH=O       |            |            |

*Proton assignment in Fig. 1

Table 2 Solubility of MDTHP and VBATDT to solvents

| Solvent     | 2.6% MDTHP | 0.65% MDTHP | 2.6% VBATDT | 0.65% VBATDT |
|-------------|------------|-------------|-------------|--------------|
| Acetone     | +          | +           | +           | +            |
| Isopropanol | +          | +           | –           | –            |
| MMA         | +          | +           | –           | –            |

+, soluble; –, insoluble

Discussion

Several thiols, thiones, and sulfides have been used for the surface modification of copper and noble metals. Because of the chain transfer reactions in polymerizable solvents or monomer liquids, it has been difficult to synthesize monomers with both mercapto and methacryloyl groups. The VBATDT reported by Mori and Nakamura [1] exhibited a thione structure after recrystallization from diethyl ether and $n$-hexane. However, a thioxo group of the VBATDT disappeared after absorption to copper or noble metals possibly because this group tautomerized into a mercapto group to form a bond between sulfur and metal elements. Based on the findings, organic sulfur compounds with methacryloyl groups have been synthesized. Among them, MTU-6 and MDDT have effectively enhanced the bonding performance of noble metals and alloys [4,7-12].

Thiohydantoin is a five-numbered cyclic compound with a thioxo
group. In order to improve hydrophobicity, 10-hydroxydecyl methacrylate was used for the esterification of THPA. The synthesized monomer was not able to distill or recrystallize owing to the number of methylene groups incorporated into the monomer structure. The monomer was therefore purified with solvent extraction followed by column chromatography. As shown in Table 1 and Fig. 1, the monomer was purified with a yield of 49%. However, care was taken during the elimination of the solvent to avoid polymerization of the purified monomer. This oily compound was soluble in acetone, isopropanol, and MMA up to 2.6%; this concentration was sufficient for it to be used as a priming agent, with desirable characteristics compared with VBATDT.

Although the bonding performance of this compound to metals and alloys has not been evaluated, this monomer may be potentially applicable as a functional adhesive monomer for bonding between acrylic resin-based materials and noble metals and alloys.

Acknowledgments
This study was supported in part by a grant from Sun Medical Co., Ltd. (2017 and 2018).

Conflict of interest
Hideo Matsumura, Takashi Yamamoto, and Shigeru Mio applied for a patent: Sulfur-containing polymerizable monomer and use of thereof. International Laid-Open Patent Publication, No. WO2020/032268 A1, Sun Medical Co., Ltd., February 13, 2020.

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