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Syntheses and Properties of Novel Vinyl Monomers Bearing a Glycoside Residue

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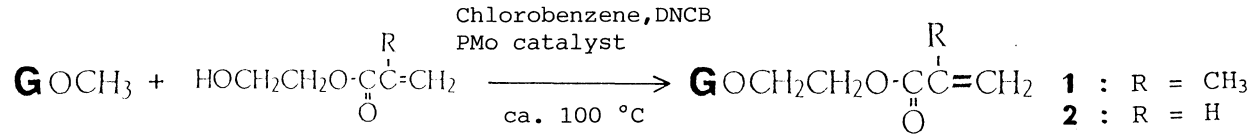
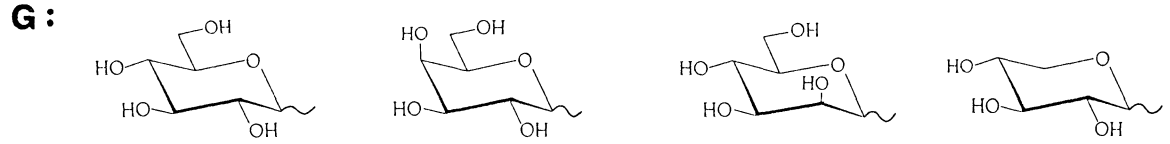
Novel acrylic monomers bearing a monosaccharide residue were synthesized in reactions of some methyl glycosides with 2-hydroxylethyl acrylate or methacrylate in the presence of heteropoly acid. All of them were highly soluble in water and readily polymerized by radical initiators.

Polymers bearing saccharide residues on their side chain have been prepared in order to investigate their applicabilities to highly water-holding substance[1-3] and pharmacological or biomedical materials.[4,5] These polymers are also of much interest in view of the cell biology, in which saccharide units play important roles in the intercellular recognition process.[6-10]

In our efforts to prepare such monomers that can be employed as the building blocks of functionalized polymers suitable for the above-mentioned materials, we have been synthesized several saccharide-bound monomers without any protective groups, as shown in Scheme 1.[11,12] One of the remarkable features of these monomers is that the acrylic ester moiety and the saccharide unit are bound together with a glycosidic linkage, which occurs quite frequently in nature. We now wish to report the novel syntheses of this sort of monomers and some of their chemical and physical properties.

Saccharide-bound ethyl acrylate or methacrylate monomers (**1** and **2**) were synthesized in the reactions of methyl glycoside with an excess amount of 2-hydroxyethyl methacrylate (2-HEMA) or 2-hydroxyethyl acrylate in the presence of heteropoly acid catalyst and polymerization inhibitor. Typical procedures for the preparation of glucosyloxyethyl methacrylate





Scheme 1.

(GEMA, **1a**) are described below. Methyl α-D-glucopyranoside (44.7 g, 0.23 mol) was suspended in a mixture of 2-HEMA (300 g, 2.30 mol) and chlorobenzene (60 g) containing phosphomolybdic acid (PMo, 4.5 g, 2.5 mmol), as a catalyst, and 2,4-dinitrochlorobenzene (DNCB, 4.5 g), as an inhibitor. Then, the suspension was heated to 112 °C and stirred for 3 h, with frequent monitoring with TLC over silica gel (chloroform:methanol=3:1). When the change was no longer observed on the TLC after ca. 3 h, the reaction mixture was cooled and then neutralized with sodium hydrogen carbonate. The yield of GEMA at this stage was determined by quantitative analysis on capillary gas chromatography.[13] The crude product obtained was purified by column chromatography over silica gel with a chloroform/methanol eluent.

The use of a hard acid like p-toluenesulfonic or sulfuric acid as a catalyst resulted in the predominant polymerization of 2-HEMA and/or GEMA; no appreciable amount of GEMA was obtained. Hence, the use of soft phosphomolybdic acid is highly recommended as the catalyst for the specific glycosidation in high yield.

Table 1. Preparation of glycoside monomers

Monomer	R	G[a)]	Molar[b)] ratio	Reaction conditions temp/°C	time/min	Conversion /mol%
1a	Me	Glucoside[c)]	10:1	112	180	64
1b	Me	Galactoside[c)]	10:1	110	60	72
1c	Me	Mannoside[c)]	10:1	105	30	67
1d	Me	Xyloside[d)]	10:1	105	30	76
2a	H	Glucoside[c)]	10:1	110	90	60
2b	H	Galactoside[c)]	10:1	107	50	75
2c	H	Mannoside[c)]	10:1	106	20	61
2d	H	Xyloside[d)]	10:1	105	20	80

a) Monomer produced was a mixture of pyranoside anomers and franoside anomers.
b) Hydroxyethyl acrylate:methyl glycoside ratio in the starting mixture.
c) α-Glycoside was used as a starting compound.
d) β-Glycoside was used as a starting compound.

Table 2. Properties of some glycoside monomers

Monomer	Anomer[a] ratio	Chemical shift[b] ppm	$[\alpha]_D^{20}$[c]	Coloring[d] reactions
1a	2:1	99.6, 103.8	75°	487.6 nm
1b	2:1	98.8, 103.4	71°	486.8 nm
1c	3:1	100.1, 100.3	30°	488.4 nm
1d	4:1	98.8, 103.3	63°	480.4 nm
2a	5:2	99.3, 103.4	76°	486.8 nm

a) Anomer ratios (α/β) of purified glycopyranoside monomer, determined by capillary gas chromatography.[13]
b) ^{13}C-NMR chemical shift from TMS in ppm of C_1 carbon in $CDCl_3$.
c) Specific rotation in methanol (c 3.0).
d) λ_{max} of sample solution after treatment with phenol-sulfuric acid mixture.

The structures of these glycoside monomers (**1a-d** and **2a-d**) rest on their ^{1}H and ^{13}C NMR and IR spectra, and also on the specific chemical reactivities toward phenol-sulfuric acid, orcinol-sulfuric acid, bromine, and mercaptan; see Table 2. They also showed optical activity originating from the saccharide unit; the specific rotations are shown in Table 2. As readily anticipated from the fact that the hydrophilic saccharide moiety occupies most of the molecular volume of each glycoside monomer as demonstrated by a CPK space-filling model examination, these monomers were highly soluble in polar solvents like water, alcohols, and ethers, but entirely insoluble in nonpolar benzene, toluene, and heptane.

The toxicity of GEMA was surveyed to some extent since GEMA is expected for the commercial use. Fortunately, GEMA showed very high biodegradability; this glucose-bound methacrylate was decomposed completely within 28 days by any soil microorganisms that had been collected from 10 different sites of Japan. Furthermore, in the Ames test, no mutagenic activity was found for five kinds of bacteria, including *Escherichia coli* and *Salmonella typhimurium*. The oral toxicity test according to the OECD guideline revealed that GEMA did not affect the survival rate of rats even at the very high dosage up to 16000 mg/kg.

These monomers readily polymerized in aqueous solution by radical initiators, such as potassium persulfate. The homopolymer of GEMA thus prepared had an average molecular weight of ca. 5×10^5, as determined by gel permeation chromatography. The GEMA polymer was soluble in water, DMF, and DMSO but insoluble in other organic solvents, such as methanol, acetone, ether, chloroform, toluene, and heptane. The saccharide contents

in the homopolymers of GEMA were reduced to ca. 1/5 in 6 days of digestion by soil bacteria in a buffered aqueous solution at 28 °C. Copolymerization of these monomers were also carried out with other vinyl monomers, such as alkyl acrylate and methacrylate, acrylonitrile, and styrene derivatives. The properties and possible applications of these homo- and co-polymers are under current investigations.

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13) After acetylation of the sample with 3:1 (v/v) mixture of pyridine and acetic anhydride, the amounts of monomers were determined by gas chromatography (capillary column: Ultra-I (cross-linked methylsilicone) 25 m x 0.2 mm i.d.; column temperature: 270 °C; detector: FID; carrier gas: He; internal standard: octyl β-D-thioglucopyranoside tetraacetate).

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