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Synthetic polymers based on carbohydrates: preparation, properties and applications

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SUMMARY: A series of (meth)acryl and maleinimide derivatives of acetylated mono- and disaccharides as well as macromonomers based one cellulose triacetate blocks were synthesized. After radical polymerisation the protecting groups were removed to yield glycopolymers. Hydrophilic silicone rubbers for medical uses were prepared by covalent incorporation of trimethylsilyl (TMS) protected sugar derivatives and subsequent removal of the TMS groups. Azido substituted sucrose was grafted photochemically onto polypropylene surfaces to enhance their wettability. Hydrogels prepared from sucrose methacrylates were reacted with succinic- and maleic acid anhydride to yield efficient adsorbers for bilirubin.

Introduction

The restriction of petrochemical resources on one hand and the growing productions on agricultural markets on the other hand lead to increasing activity in the use of renewable resources in organic syntheses. Carbohydrates as organic raw materials can open new perspectives on the way to biocompatible and biodegradable products. For example, the use of such raw materials for the preparation of polymers might provide organic materials with new properties. Although the economics of the development of a new plastic makes it unlikely that any entirely new polymer will supplant existing ones, the research on carbohydrate based monomers and polymers has attracted considerable attention in recent years, mainly with respect to very specialised applications in basic biochemical and biomedical research such as molecular recognition processes, drug delivery systems, affinity chromatography, cell culture systems. In these applications cost is not the prime consideration thus tolerating even more complicate syntheses of the monomers, which are a consequence of the polyfunctionality of the sugars.

Polymers consisting of a hydrophobic but chemically and biologically stable synthetic C-C backbone and a side chain of a natural hydrophilic saccharide are called "poly(vinylsaccharides)"

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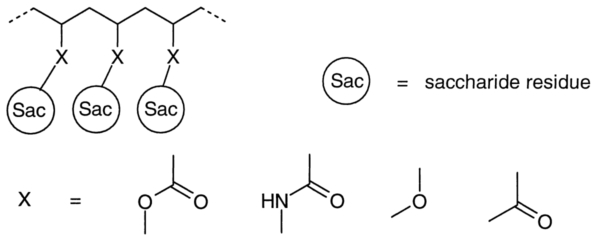
or "glycopolymers"[1], including linear as well as crosslinked types. The saccharide residue can be bonded to the C-C backbone by ester-, amide-, ether- or C-C-linkage (Scheme 1).

Scheme 1:



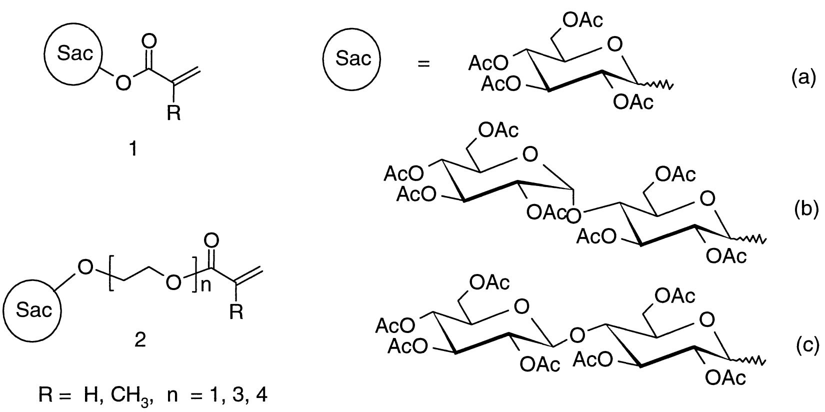
Several reviews dealing with various aspects of glycopolymers have appeared in the past few years[1-6]. In this paper we provide a short overview of our work on monomers and polymers containing saccharide residues.

Synthesis and polymerization of sugar monomers

The preparation of linear, water-soluble glycopolymers requires the synthesis specifically monofunctionalized polymerizable saccharides. Due to the polyfunctionality of sugars generally multistep syntheses including protecting-group chemistry are necessary to get sugar monomers. However, the removal of protecting groups is a crucial point: in deprotection at the monomer stage the lability of the polymerizable group may interfere with the deprotection procedure, whereas protecting group removal from polymers is not quantitatively in many cases. Nevertheless most glycopolymers were obtained by deprotection of the polymers.

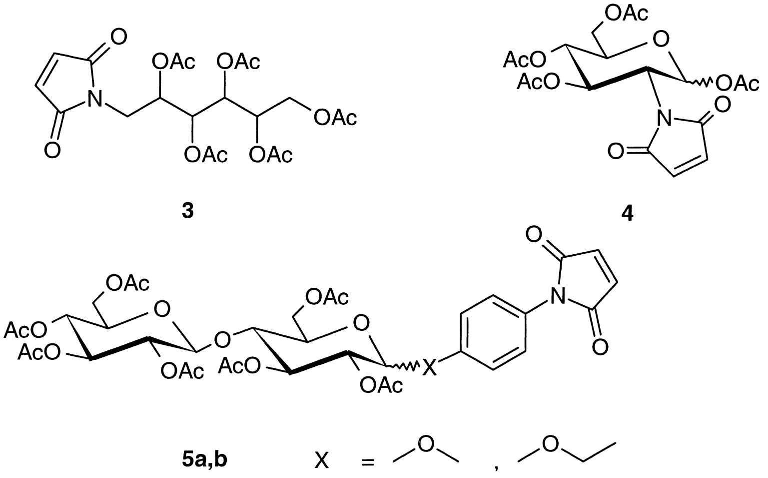
Starting from acetylated saccharides, glycosylhalides or glycols we have prepared a series of monofunctional (meth)acrylate derivatives of glucose, maltose and cellobiose (1a,bc, Scheme 2) by standard glycosidation or esterification methods. In order to get glycopolymers in which the saccharide residue is accessible to various biomolecules we synthesized also some monomers with hydrophilic spacers[7,8] (2a,b,c, Scheme 2).

Scheme 2:

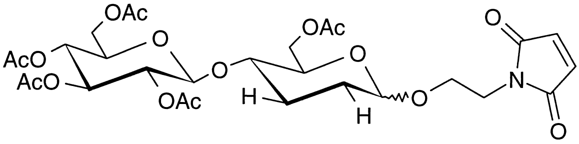


Additional polymerizable sugars were obtained by reaction of amino substituted saccharides with maleic anhydride (3-5, Scheme 3) or with reactive maleinimide derivatives [8,9] (various combinations of X and Sac, Scheme 4).

Scheme 3:



Scheme 3 (continued) :



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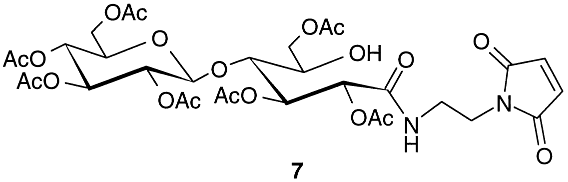

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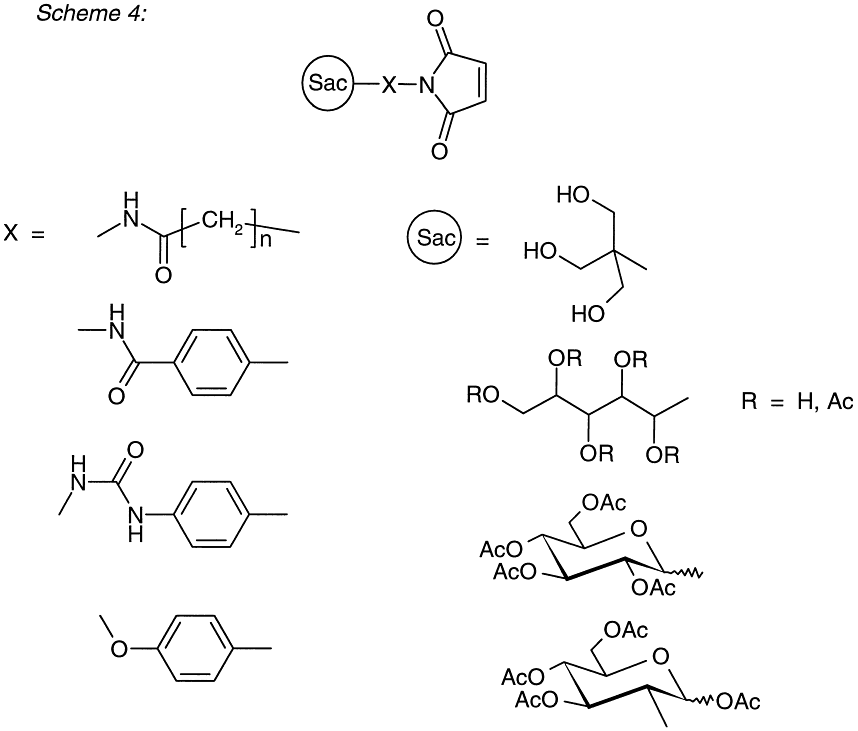
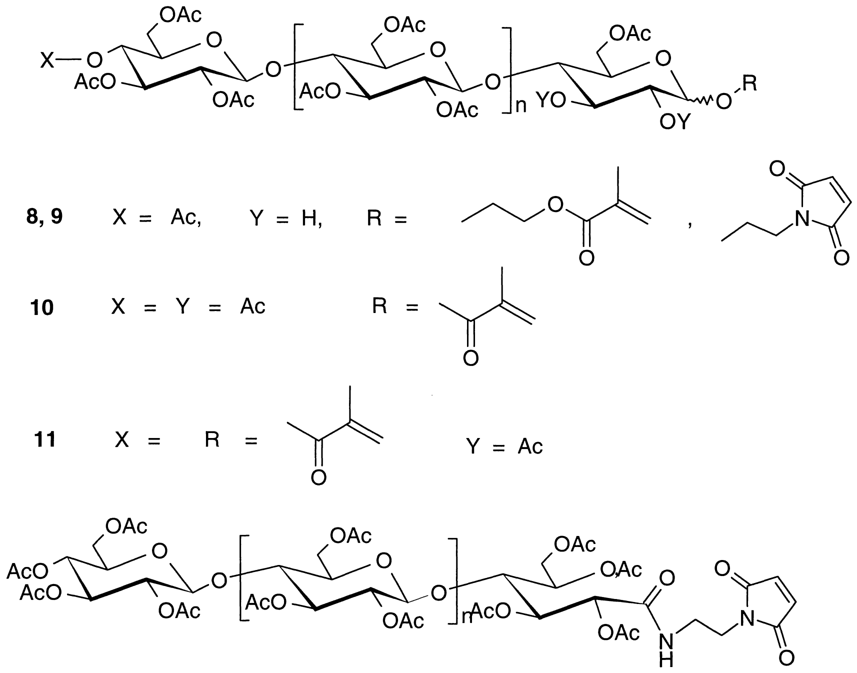
Scheme 4:



By similar reactions we prepared macromonomers based on cellulose triacetate (CTA) blocks [8)] (8-12, Scheme 5). The CTA blocks with molecular weights of 2500 were obtained by controlled acid degradation of commercial CTA.

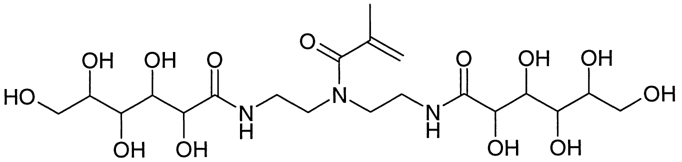
Scheme 5:



12

Without use of protecting groups a methacrylamide containing two sugar residues was obtained by reaction of 2 moles gluconolactone with diethylenetriamine and subsequent acylation of the secondary amino group with methacrylic acid anhydride [7)] (**13**, Scheme 6).

Scheme 6:



13

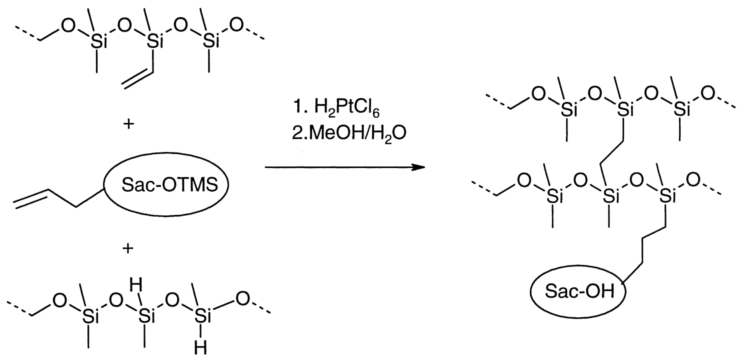
All acetylated sugar monomers were converted to polymers by radical polymerization and subsequently deacetylated with sodium methylate to give water soluble glycopolymers. Molecular weights and polydispersities were determined by GPC.

Carbohydrate modified polysiloxanes

Whereas numerous combinations of synthetic polymer backbones and saccharides have been reported in the literature, polysiloxanes have been scarcely considered, although such hydrophobic/hydrophilic hybrid polymers are expected to exhibit interesting properties useful in many applications, for example as biocompatible materials, surfactants, resins etc. In previous work we described hydrophilic polysiloxanes containing glucose and sucrose residues [10, 11]. Linear polysiloxanes containing carbohydrate residues were reported also recently by Stadler et al. [12,13].

Since silicone rubbers are characterised by extremely hydrophobic surfaces which may be a drawback in various medical applications such as surgical implants or contact lenses, we incorporated sugars into silicones to get "hydrophilic silicones" exhibiting better wettability and biocompatibility. For this purpose allylethers of polyols and sugars containing trimethylsilyl (TMS)-protected hydroxyl groups were synthesized and used as additives in the preparation of silicone rubbers by crosslinking of commercial H-Si- and vinyl-Si-polysiloxanes. The resulting hydrophobic silicone rubbers were converted into hydrophilic types with covalently bonded polyol-residues by hydrolysis to split off the TMS-groups (Scheme 7).

Scheme 7:



Contact angle and mechanical measurements of the modified silicone films demonstrated increased wettability dependent on the content of hydroxyl groups without significant loss of mechanical strength.

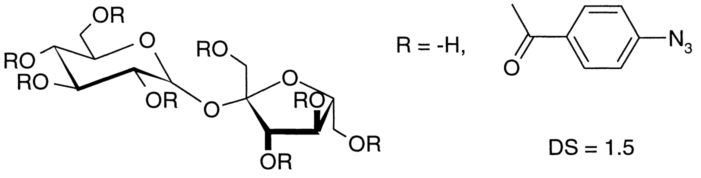
Photochemical modification of polymer surfaces with carbohydrate derivatives

Considerable interest has been drawn to hydrophobic-hydrophilic properties of polymer surfaces, since they are essential in many applications such as for adhesion, antistatic properties, dyeability, printability and biocompatibility of polymers. Advantageously, surface modification of existing polymeric materials can improve the materials' interaction with the environment while the mechanical (bulk) properties remain essentially unchanged.

In order to impart hydrophilic properties to the surface of hydrophobic polymers, various techniques for surface modification have been used, including plasma treatment, surface grafting, chemical modification, surface-modifying agents, ion beam treatment, adsorption and polymerisation of amphiphiles [14,15)]. Whereas by methods such as flame-, plasma-, ion beam-treatment or chemical modification functional groups are formed on the surface rather unspecifically, defined molecules or polymers can be fixed by surface grafting or adsorption. For durable modifications it is essential that the modifying agent is bound covalently onto the polymer surface, requiring polymers and/or surface modifiers with appropriated reactive groups.

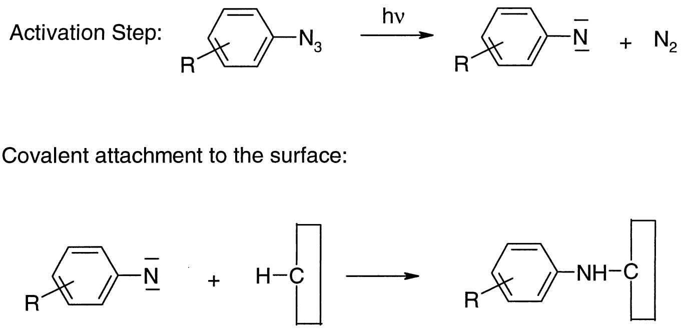
For the hydrophilic surface modification of standard polymers such as polyolefines we used the photochemical reactivity of aryl azides [16)]. For this purpose we have synthesized molecules containing photoactivable 4-azidobenzoyl groups and sugar moieties, e.g. partially substituted sucrose esters with 4-azidobenzoyl chloride (Scheme 8).

Scheme 8:



Upon UV irradiation an aryl azide splits off nitrogen and a nitrene as highly reactive intermediate is formed which can undergo various reaction pathways including insertion into C-H bonds on the surface of polymers (Scheme 9).

Scheme 9:



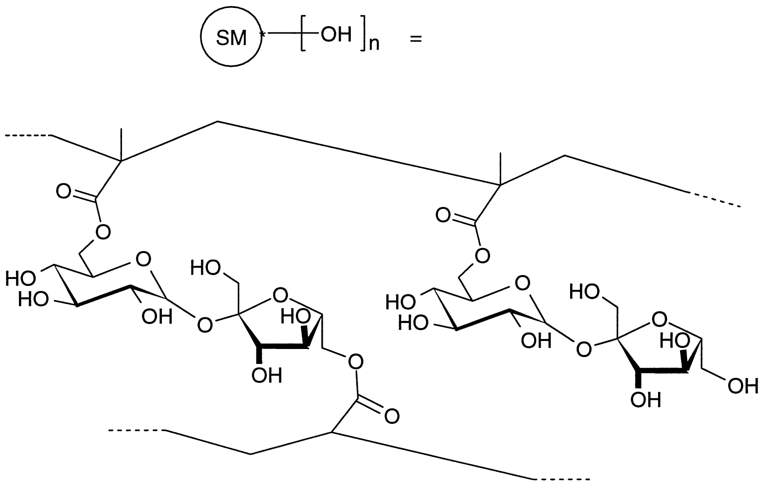
For example, polypropylene films and sheets were pre-treated with swelling agents (n-hexane, toluene) to enhance the diffusion of the azide into the polymer surface Then the polymer was immersed in acetone solutions containing the azide and after drying the materials were irradiated with a high pressure mercury lamp. Unreacted azide and by-products were then removed by rinsing with acetone.

The properties of the modified PP surfaces were investigated by contact angle measurements and by application of special test inks (Arcotec®), suitable for simple and quick evaluation of surface tension of polyolefines. The results demonstrated that the surface hydrophilicity of polypropylene is strongly increased by covalent attachment of sucrose residues (e.g. contact angle decrease from 90° to 55°). Due to their polyfunctionality, which enables also further derivatizations, photolysis of sucrose azides provides a useful route for surface modification of “difficult“ surfaces exhibiting no reactive centers such as polyolefines.

Hydrophilic carriers based on sucrose methacrylates

The polyfunctionality of saccharides and the preparation of monofunctional vinyl sugars from unprotected sugars creates a severe synthetic problem, especially with di- and oligosaccharides. Apart from the direct glycosidation of some unprotected monosaccharides with hydroxyethylmethacrylate, few enzymatic syntheses of disaccharide monomers have been reported in recent years [17)]. The easiest way should be the esterification of sugars with (meth)acrylic acid, but it was shown to be nearly impossible to get pure monofunctionalized acrylates, since this method yields always mixtures of substituted saccharides. However, this can be taken as an advantage for the synthesis of crosslinked gels. Transesterification of sucrose with methyl methacrylate yields mixtures of sucrosemethacrylates (SMs) with various degrees of substitution dependent on the molar ratio and reaction conditions[18)]. By suspension polymerization of these monomers spherical particles of SM-gels are obtainable, which can be modified by reactions of the hydroxyl groups (Scheme 10).

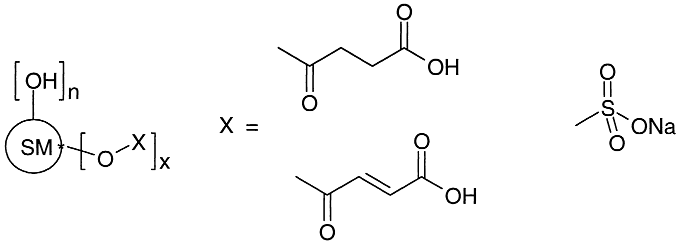
Scheme 10:



In previous work we reported the synthesis and some applications of such hydrogels based on sucrose methacrylates . Due to their hydrophilic nature these carriers exhibit fast kinetics in aqueous systems. For example SM-gels containing chelating groups [19], catalytic active moieties [20,21] and bactericides [22] have been synthesized and tested successfully.

Modified SM gels have shown also to be useful as adsorbents for extracorporeal blood purification. For this purpose the carriers were reacted with succinic anhydride, maleic acid anhydride and chlorosulfonic acid and the incorporated acid groups were converted to salts.

Scheme 11:



Thus anionic modified SM-gels were obtained which were shown to be biocompatible. *In vitro* tests demonstrated high efficiencies of these gels in the selective adsorption of blood components such as bilirubin.

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