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SYNTHESIS AND APPLICATIONS OF PSEUDOPOLYSACCHARIDES[1)]

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Immobilised carbohydrates are widely used in many areas of chemistry and biochemistry[2-5)]. A common method of synthesis is the attaching of monosaccharides via the glycosidic group to a suitably functionalised solid support. We wish to report here on a complementary approach where reducing carbohydrates are coupled through a chemically and enzymatically inert ether-linkage to polyvinylalcohol or biopolymers. The resulting soluble pseudopolysaccharides are of high actual interest both in the realm of solid-phase glycoside synthesis[6)] and as potential carriers of drugs[7)]. Furthermore, they may serve as a useful probe in the study of protein-carbohydrate-interactions[8)].

Starting with the D-galactose-6-O-allylethers[9)] 6, 9, and 10, the hitherto unknown 6-O-(R,S)-epoxypropyl-derivatives 3, 11, and 12 were prepared in excellent yield[10)] by mild oxidation using m-chloroperbenzoic acid (MCPBA) in dichloromethane (30-40°, 24-72 h)[11)]. Spectroscopic data and elemental analysis of the crystalline oxiranes thus obtained are in perfect accord with the proposed structures (Tab. I).

Ring-opening of the ω-oxirano sugars 3 and 12 with nucleophiles (OCH_3^-, $i\text{-}C_3H_7O^-$, and $n\text{-}C_4H_9O^-$) leads as expected[12,13)] nearly exclusively to the primary ethers. Thiirane 4, prepared by treatment of 3 with thiourea under these conditions mainly undergoes elimination.

Base-catalysed addition of polyvinylalcohol ($\bar{M}$~20 000 and~70 000 D) in DMSO with traces of KOH (45°, 18-36 h) gives in 70% yield the polyvinylether 5 ($[\alpha]_D^{20}$ = -28°, c=0,5 in $CHCl_3$), which is separated from unchanged monomer by gelfiltration on Sephadex LH 20. Subsequent hydrolysis of the lyophilised product (0,1 N HCl, 50°, 4 h) affords the pseudopolysaccharide 8 ($[\alpha]_D^{25}$ = -3°, c=0,5 in H_2O); easily soluble in water, pyridine, DMSO etc.. The degree of substitution as judged from elemental analysis and from the pmr-spectrum of 5 is between 23% and 60% depending on the reaction conditions. - In the same way, the benzylgalactoside 12 is grafted onto polyvinylalcohol affording the polyvinylether 13. Upon removal of the benzyl blocking groups by catalytic

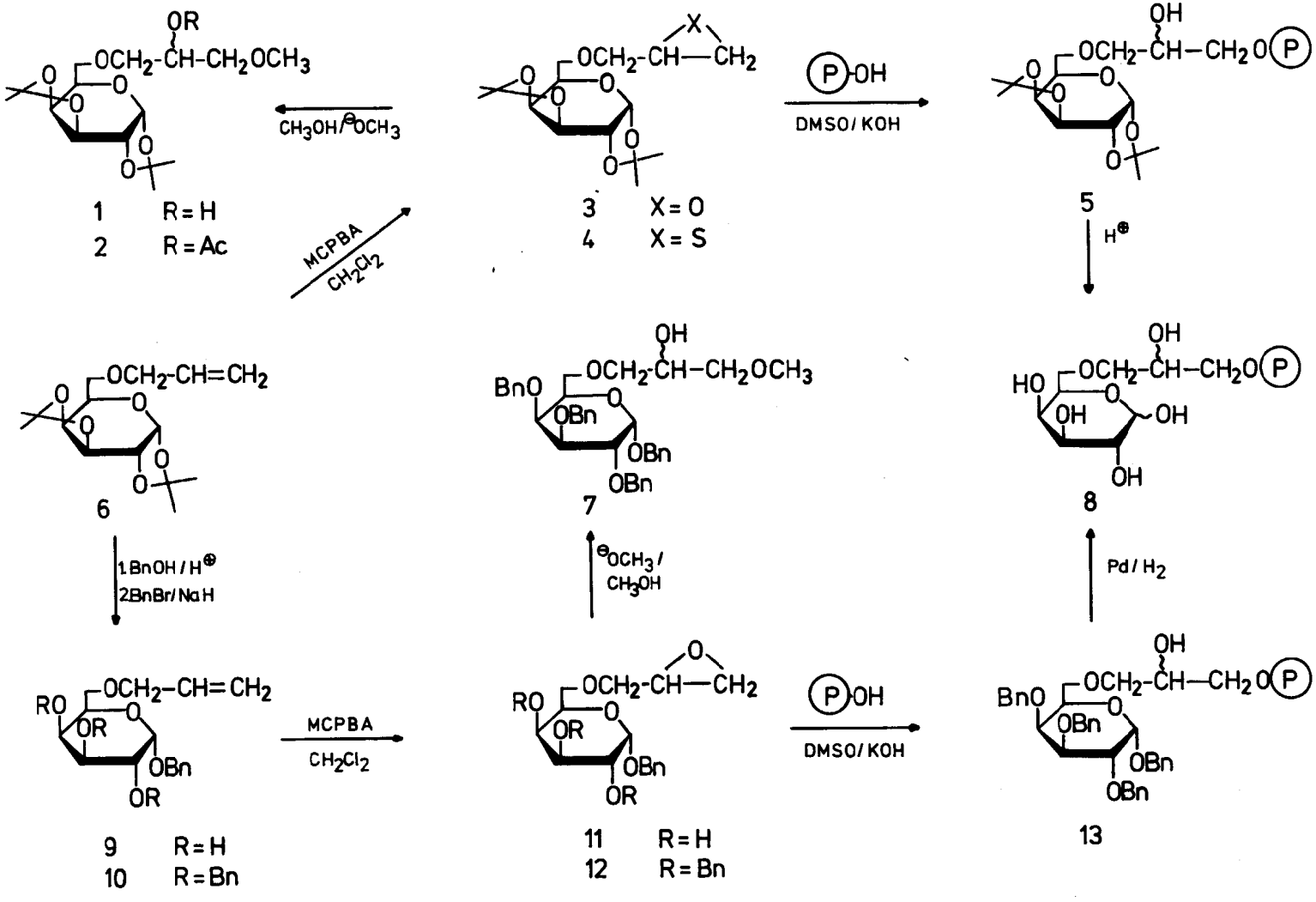
OR
OCH2-CH-CH2OCH3
CH3OH/⊖OCH3
MCPBA
CH2Cl2
1 R=H
2 R=Ac
X
OCH2-CH—CH2
3 X=O
4 X=S
P-OH
DMSO/KOH
OH
OCH2-CH-CH2O(P)
5
H⊕
OCH2-CH=CH2
6
1.BnOH/H⊕
2.BnBr/NaH
OH
OCH2-CH-CH2OCH3
BnO
OBn
7
⊖OCH3/
CH3OH
HO
OH
8
Pd/H2
RO
OR
9 R=H
10 R=Bn
MCPBA
CH2Cl2
11 R=H
12 R=Bn
13

Table I

Compound	m. p. /yield[a]	$[\alpha]_D^{20}$	MS(m/e)	^{13}C-nmr(δ, ppm)[f]	
				C-8	C-9
1	81%	- 63°[b]	349(MH^+), 331(MH^+-H_2O)[e]	---	---
2	79%	- 56°[b]	390(M^+), 335(M^+-CH_2OCH_3), 330(M^+-CH_3COOH)[d]	---	---
3	73-74°, 91%	- 67°[c]	316(M^+), 301(M^+-CH_3)[d]	50, 8 176, 7 Hz	44, 3 175, 8 Hz
4	96%	- 66°[b]	333(MH^+), 318(MH^+-CH_3) 301(MH^+-S)[e]	32, 0 163, 0 Hz	23, 8 160, 1 Hz
7	78%	+ 47°[c]	502(M^+-$OCH_2C_6H_5$)[d]	---	---
11	112°, 83%	+120°[b]	327(MH^+), 309(M^+-H_2O)[e]	50, 3 174, 8 Hz	44, 2 176, 4 Hz
12	70-72°, 90%	+ 82°[c]	597(M^+) 490(M^+-$OCH_2C_6H_5$)[d]	50, 6 176, 4 Hz	44, 2 176, 0 Hz
14	63%	- 90°[c]	336(M^+), 321(M^+-CH_3), 229(M^+-$OCH_2C_6H_5$)[d]	50, 7(C7) 177, 0 Hz	44, 2(C8) 175, 4 Hz

a final step, b in $CHCl_3$, c in CH_2Cl_2, d electron impact, e field desorption, f chemical shift and geminal coupling constant of secondary and primary oxirano- (3, 11, 12, 14) and thiirano-(4) carbon atoms, respectively; $CDCl_3$ as solvent.

hydrogenation (Pd/C at atmospheric pressure in CH_3OH/H_2O, 4:1), polymers are obtained which display the same structural features as 8, though they have a lower degree of substitution.

The carbohydrate portion of these pseudopolysaccharides retains the typical reactivity of monosaccharides with respect to acetalation, esterification and glycoside formation which is of major importance as to their use in template directed syntheses[6]. On the other hand, the polymers behave as polysaccharides during interaction with biopolymers where they induce transformations of the secondary structure. A striking example is our CD-study of the interaction between 5 or 8 and poly-L-lysine[14]. In CH_3OH/H_2O-mixtures we observed, even at low concentrations of methanol, a considerable stabilisation of the polyamine in the α-helical form which can not be effected by polyvinylalcohol alone. A comparably high proportion of ordered regions in the polyamine is usually only found upon chemical substitution of the ε-amino group in the polypeptide; e. g. by reaction with reducing monosaccharides[15-17] or aromatic aldehydes[18]. It can also

be induced by grafting of 5 directly onto poly-L-lysine[19]. These results confirm our early suggestion that the biologically important helix-coil transition in poly-L-lysine can be induced by non-covalent bonding between macromolecules[15].
The material accumulated up to now has encouraged us to extend our efforts to the synthesis of oxirano-derivatives of biologically active carbohydrates (antibiotics, sialic acids). Grafting of these sugars onto (bio)polymers will provide substances which in their versatility go beyond the initial objective of our study.

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