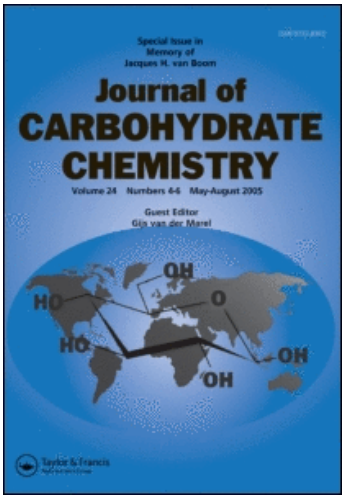

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COMMUNICATION

GLYCOSIDES OF MONOALLYL DIETHYLENE GLYCOL. A NEW TYPE OF SPACER GROUP FOR SYNTHETIC OLIGOSACCHARIDES

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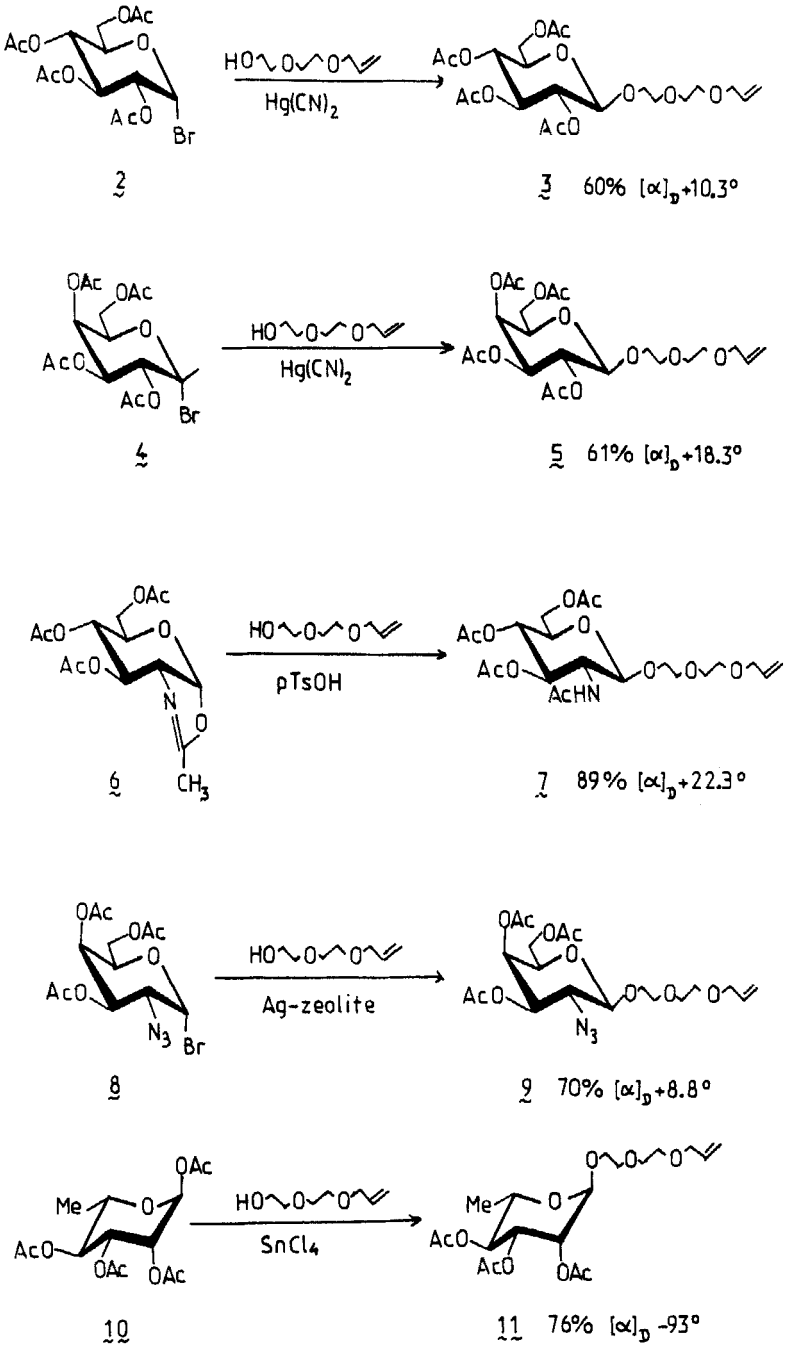
The preparation of spacer-armed synthetic oligosaccharides, which can be coupled to either proteins or polymers for use respectively as immunogens or immunoadsorbants for affinity chromatography, is today an important field in chemistry. The methoxycarbonyloctyl glycosides developed by Lemieux and coworkers[1] are frequently used and remain the most popular. Other glycosides with amide,[2] thioether,[3] and ether[4] type spacer groups have also been employed. Recently, an alternative to coupling to proteins appeared when copolymerization of allyl glycosides with acrylamide provided excellent immunogens.[5]

In an attempt to combine the possibilities afforded by these two approaches in the same spacer molecule, we would like to report in this communication the use of 3,6-dioxa-Δ-8-nonanol-1 (monoallyl diethylene glycol, **1**, Scheme 1) in the synthesis of spacer-armed glycosides. One of the most important advantages of this compound is its easy preparation from diethylene glycol and either allyl chloride or bromide under phase-transfer conditions (benzyltriethylammonium chloride - dichloromethane - 1 N NaOH) in a yield of 20-30%. ^{1}H NMR data δ 5.88



Scheme 1

(m, 1H, -CH=), 5.20 (m, 2H, CH_2=), 4.18 (s, 1H, OH), 3.92 (m, 2H, CH_2 allyl), 3.59 (s, 8H, CH_2O).

Glycosylation of monoallyldiethylene glycol (**1**) was evaluated by different methods for different compounds. Tetra-O-acetyl-α-D-glucopyranosyl bromide (**2**) and tetra-O-acetyl-α-D-galactopyranosyl bromide (**4**) were found to react with alcohol **1** in the presence of mercuric cyanide (dichloromethane, room temperature, 24 h) to give the corresponding β-D-glycosides **3** and **5** in good yields. The corresponding glycoside of N-acetyl-2-deoxy-D-glucosamine (**7**) was better prepared from the oxazoline **6**[6] and the alcohol **1** in the presence of p-toluenesulfonic acid (dichloroethane, 80 °C, 12 h). The β-D-galactosaminide **9** was prepared from 3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl bromide (**8**)[7] and silver zeolite in toluene (room temperature, 48 h). The α-L-rhamnoside **11** was prepared from tetra-O-acetyl-α-L-rhamnopyranose (**10**) and the alcohol **1** in the presence of tin tetrachloride. Yields and optical rotations for all the monosaccharides are presented in Scheme 1.[8] The ^{13}C NMR spectra (Table 1) for all these compounds showed similar characteristic signals at intervals of 134-135 and 117-118 ppm for the two allylic carbons and five signals in the regions 68-72 ppm corresponding to $-CH_2O$-protons. These signals may be distinguished from the skeletal carbons of the sugar by the effect of the two attached protons on INEPT spectra.

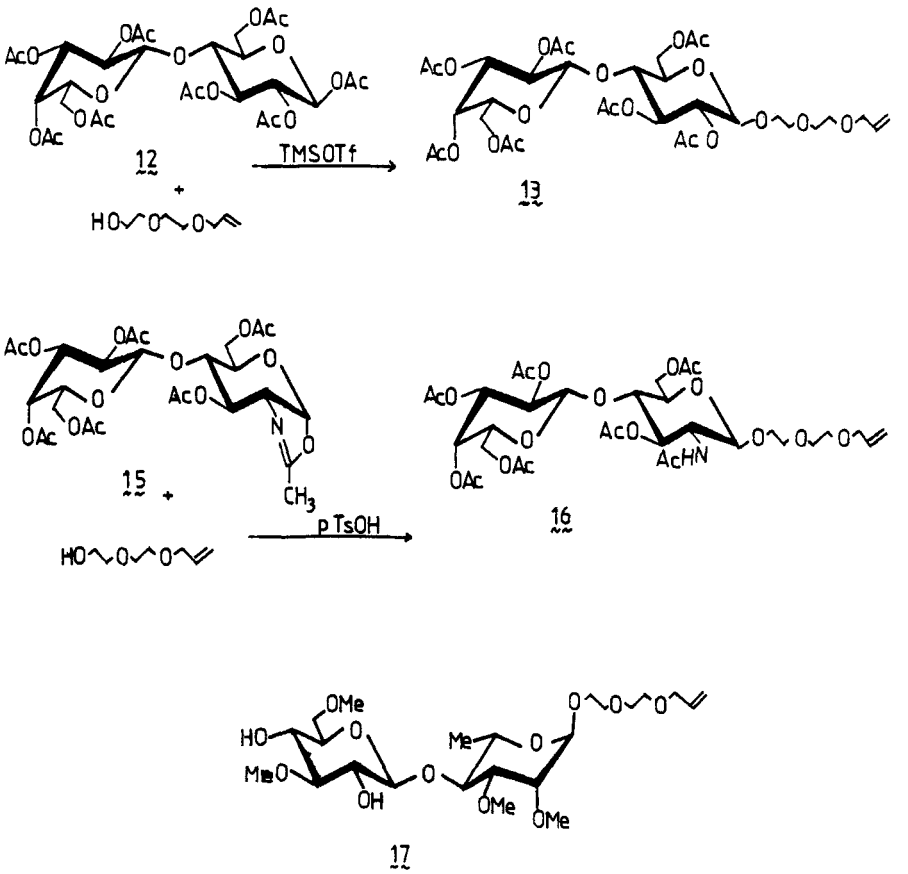
Deprotected glycosides were copolymerized with acrylamide under the same conditions described for allyl glycosides.[5] On the other hand, the allylic double bond was easily transformed into an aldehyde by passing a calculated quantity of ozone through a solution of the compound in methanol at -25 °C. The resulting aldehyde, without purification, was then coupled to bovine serum albumin (BSA) by reductive amination with sodium cyanoborohydride.[9]

The success demonstrated with the monosaccharides encouraged us to apply the procedure to the synthesis of oligosaccharides. The β-

Table 1. ^{13}C NMR Spectral Data for Monosaccharide Derivatives

Compound	C-1	C-2	C-3	C-4	C-5	C-6	$-CH_2O-$	=CH	$=CH_2$	CH_2O(All)
3	100.9	71.5	73.0*	68.6	71.9*	62.1	70.5, 69.5, 70.8, 69.0	134.8	117.0	72.2
5	101.4	69.0	70.7	67.2	71.0	61.4	70.7, 69.5, 70.4, 69.0	134.8	117.0	72.2
7	102.0	54.0	73.6	68.9	71.8	62.4	70.6, 69.2, 71.9, 68.5	134.4	118.1	72.2
11	102.8	61.2	71.3*	66.7	71.0*	61.4	70.8, 69.4, 71.0, 69.8	135.0	116.9	72.4
13	97.6	70.0*	69.2*	66.4	71.3	17.4	70.8, 69.5, 70.2, 67.2	134.9	116.9	72.2

* These assignments may be exchanged.



Scheme 2

octaacetate of lactose (**12**) reacts (Scheme 2) with alcohol **1** in the presence of trimethylsilyl triflate (dichloromethane, room temperature, 45 min) to give the β-lactoside **13** in a yield of 71% ($[\alpha]_D$ = -25.3°). The ^{13}C NMR spectrum of **13** agreed well with the proposed structure. The anomeric carbons appeared at δ 100.8 (C-1) and 101.1 (C-1'), respectively. The β-acetate of lactosamine (**14**)[10] was transformed into the oxazoline **15** by the action of trimethylsilyl triflate.[11] Treatment of this oxazoline with the alcohol **1** in dichloroethane, in the presence of p-toluenesulphonic acid (80 °C, 12 h) gave the β-lactosaminide **16**

($[\alpha]_D = -17^o$) in a 45% overall yield from the acetate. The anomeric carbons appeared in the ^{13}C NMR spectrum at δ101.8 (C-1) and 101.0 (C-1').

After compounds **13** and **16** were deacetylated using sodium methoxide in methanol, the disaccharides were copolymerized with acrylamide under the conditions previously described[5] to give products with molecular weights in the range of 50 - 100 kDa that contained 25-30% of carbohydrate as determined by the phenol-sulfuric method. Oxidation of deacetylated **13** and **16** with ozone (methanol, -25 ^oC) quantitatively gave the corresponding aldehyde. Coupling with BSA was accomplished by reductive amination with sodium cyanoborohydride (phosphate buffer, pH 7.4, 3 days, 37 ^oC). Several proportions of the three components were studied in a series of reactions, and a molar ratio of aldehyde-cyanoborohydride-$BSANH_2$ 3.5:50:1 gave good results. Neoglycoproteins were obtained which contained from 9 to 15 mols of hapten/mol of BSA.

Additional complex antigens were also obtained, a fact which demonstrates the flexibility of this strategy. Thus starting from the α-L-rhamnoside **11**, a sequence of reactions previously reported[12] for allyl α-L-rhamnoside was performed leading to disaccharide derivative **17**. The acetylated compound showed in the ^{13}C NMR spectrum signals corresponding to anomeric carbons at δ96.9 (C-1) and 101.0 (C-1'); four signals corresponding to methoxy carbons at δ57.1, 58.5, 58.9, and 59.6 and other signals which agreed well with the proposed structure.[8] A comparative study of both the copolymer and the neoglycoprotein obtained from **17** and their ability to bind specific antibodies to *Mycobacterium leprae* are now in progress.

Finally, we should point out that with the use of the benzyl group in the protection of hydroxyls, the main incompatibility of this strategy may be overcome by either of two routes: (1) The sequence of epoxidation, removal of the benzyl group by hydrogenation, and then opening of the epoxide with allyl alcohol, or (2) coupling directly with

polyvinyl alcohol. Optimal conditions for these two procedures are now under investigation.

In conclusion, glycosides of monoallyl diethylene glycol are useful alternative compounds for the preparation of neoglycoproteins and copolymers. The utility of the two types of antigens for oligosaccharides reported herein, as well as other oligosaccharides that are currently in preparation, will be published elsewhere.

REFERENCES

1. R. U. Lemieux, D. R. Bundle, and D. A. Baker, J. Am. Chem. Soc., **97**, 4076 - 4083 (1975).
2. H. Paulsen, J. C. Jacquinet, and W. Rust, Carbohydr. Res., **104**, 191 - 219 (1985).
3. J. Dahmen, T. Frejd, G. Gronberg, T. Lave, G. Magnusson, and G. Noori, Carbohydr. Res., **118**, 292 - 301 (1983).
4. P. H. Amvam-Zollo and P. Sinaÿ, Carbohydr. Res., **150**, 199 - 212 (1986).
5. A. Y. Chernyak, A. B. Levinsky, B. A. Dmitriev, and N. K. Kochetkov, Carbohydr. Res., **128**, 269 - 282 (1984).
6. R. U. Lemieux and H. Driguez, J. Am. Chem. Soc., **97**, 4063 (1975).
7. R. U. Lemieux and R. M. Ratcliffe, Can. J. Chem. **57**, 1244 - 1251 (1979).
8. All new compounds gave ^{1}H and ^{13}C NMR and/or high resolution FAB-mass spectra in accordance with the proposed structure. FAB-MS data show m/z (M+1) = 477.6 for **3**, 478.0 for **7**, 764.9 for 13, and 511.4 for **17**.
9. R. T. Lee and Y. C. Lee, Biochemistry, **19**, 156 (1980).
10. J. Alais and A. Veyrieres, Carbohydr. Res., **93**, 164 (1981).
11. S. Nakabayashi, C. D. Warren, and R. W. Jeanloz, Carbohydr. Res., **150**, C7 - C10.
12. J. R. Mariño-Albernas, V. Verez-Bencomo, L. Gonzales, and C. S. Perez, Carbohydr. Res., **166**, 197 - 206 (1987).