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Preliminary communication

Synthesis of poly(isoprenyl) glycosides*

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It is now well established that phosphoric and pyrophosphoric esters of poly(isoprenols), notably dolichol and retinol, serve as intermediate carriers of the carbohydrate moiety for the glycosylation of polypeptides during the biosynthesis of asparagine-linked glycoproteins[1]. The role of undecaprenyl phosphate as a glycosyl-carrier lipid for the biosynthesis of bacterial, cell-surface polymers, *e.g.* peptidoglycan[2], lipopolysaccharide[2], and capsular polymers[2,3], was shown earlier. Therefore, a chemical synthesis of glycosylated poly(isoprenols) for use as substrates for studying the enzymology of glycosyltransferases should be extremely useful.

With the exception of the dolichols, most of the poly(isoprenols) have an allylic hydroxyl group. Because of the high reactivity of this center in the proximity of the phosphate (or pyrophosphate) group, the biologically synthesized intermediates are very unstable. It therefore appeared desirable to synthesize stable polyisoprenyl glycosides having the same anomeric configuration as the biologically active compounds, but without the intervening pyrophosphate linkage, in order to test their potential as substrates in study of glycosyltransferases. The first sugar residue in the asparagine-linked glycoproteins is 2-acetamido-2-deoxy-D-glucose; as a test case, therefore, the synthesis of allyl, geranyl, and farnesyl α-glycosides was initially attempted.

3,4,6-Tri-*O*-acetyl-2-(acylamido)-2-deoxy-α-D-aldopyranosyl halides (*e.g.*, **1**) react in nonpolar solvents with alcohols in the presence of heavy metal salts to give an oxazoline[4,5] (**2**), or oxazolidine[6] (**3**), which is then transformed into the β-D-aldopyranoside[7–15] (**4**) by the push–pull mechanism. Moreover, the Lees[16] prepared allyl α-glycosides by refluxing the sugar with allyl alcohol in the presence of an acid catalyst. In this method, an excess of the alcohol is needed, and the reaction takes place at a relatively high temperature, the boiling point of the solution in allyl alcohol. The biologically active poly(isoprenols) are available in only small amounts, and are rather unstable. Thus, it is not possible to prepare poly(isoprenyl) glycosides by this method.

We now report the synthesis of poly(isoprenyl) α-glycosides by protecting the amino group of a 2-amino sugar with a 2,4-dinitrophenyl group, and treating the derived

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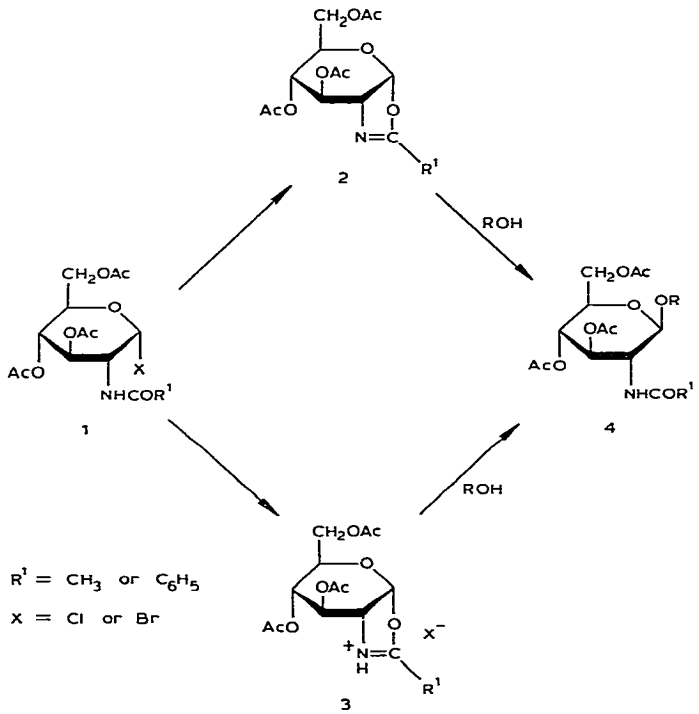
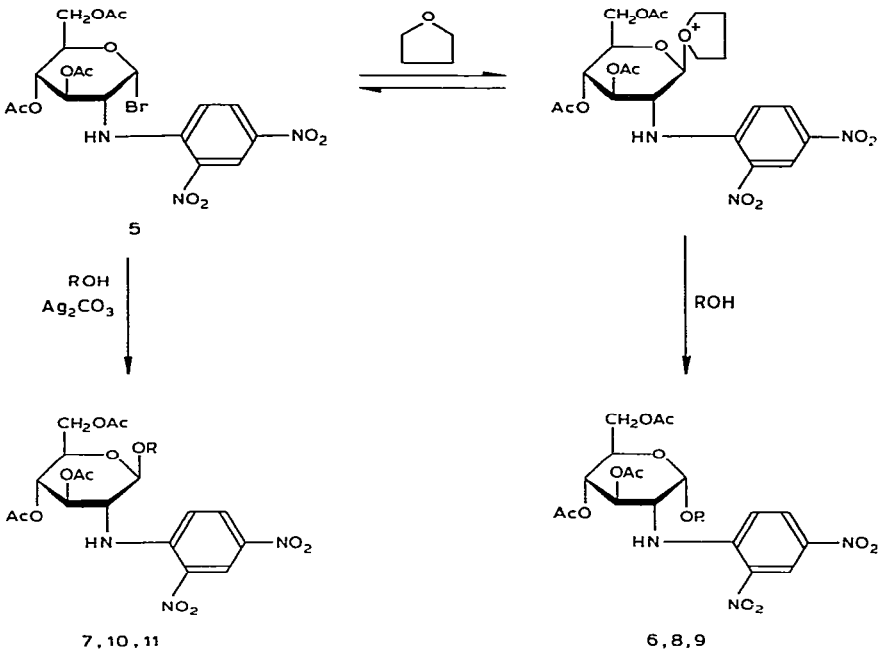


per-*O*-acetylaldosyl bromide with alcohols in 2 : 1 dichloromethane–oxolane (THF) in the presence of 2,6-lutidine as the acid acceptor.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-α-D-glucosyl bromide[17] (5.1 mmol) in the solvent (8 mL) was stirred with allyl alcohol (1.5 mmol) in the presence of 2,6-lutidine (2 mmol) for 40 h at room temperature, to give the allyl α-glycoside **6** as the major product; this was purified by chromatography on a column of Florisil, using 99 : 1 benzene–acetone as the eluant. The structure of **6** was established by its ^{1}H-n.m.r. spectrum, which showed a doublet at δ 5.15 ($J_{1,2}$ 4 Hz, equatorial H-1) for the anomeric proton, along with the usual, other signals. The corresponding β anomer (**7**) was prepared by a Koenigs–Knorr reaction in which **5** was stirred with allyl alcohol in the presence of Ag_2CO_3; compound **7** showed in its n.m.r. spectrum a doublet at δ 4.65 ($J_{1,2}$ 8 Hz, axial H-1) for the anomeric proton.

Similarly, **5** (1 mmol) reacts with geraniol (1.5 mmol) or farnesol (1.5 mmol) separately in 2 : 1 CH_2Cl_2–THF in the presence of 2,6-lutidine, to give geranyl (**8**) and farnesyl (**9**) 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-α-D-glucopyranoside, respectively. The structures were established by analogy, and on the basis of their ^{1}H-n.m.r. spectra, which showed doublets at δ 5.25 ($J_{1,2}$ 4 Hz) and 5.20 ($J_{1,2}$ 4 Hz), respectively, for the anomeric proton. Comparison was also made with the corresponding β-glycosides, *viz.* geranyl (**10**) and farnesyl (**11**) 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-β-D-glucopyranoside, prepared by the Koenigs–Knorr method. The formation of these α-glycosides is explicable on the basis of the mechanism given by Wulff *et al.*[17].



6 and 7 R = $-CH_2-CH=CH_2$

8 and 10 R = $Me_2C=CH(CH_2)_2CMe=CHCH_2$ — (geranyl)

9 and 11 R = $Me_2C=CH(CH_2)_2CMe=CH(CH_2)_2CMe=CHCH_2$ — (farnesyl)

These glycosides were also prepared by the method of Lloyd and Stacey[18], in which bromide **5** in dry chloroform was separately treated with allyl alcohol, geraniol, and farnesol, in the presence of pyridine as the acid acceptor, but, in this method, some other products were also obtained, although pure products could be obtained by preparative t.l.c.

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