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Preliminary communication

Preparation of a glycosyl chloride suitable for synthesis of *N*-glycoprotein "core" pentasaccharide*

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The "core" region of the saccharide chains of the *N*-glycoproteins contains a β-D-(1→4)-linked D-mannosyl residue. β-D-Mannosides may be synthesized by two principal routes, involving (*a*) initial synthesis of a β-D-glucoside by a stereospecific Koenigs–Knorr reaction employing a 2-*O*-acyl-α-D-glucosyl halide, followed by *O*-deacylation, oxidation, and highly stereoselective reduction at C-2 to effect epimerization[1], or (*b*) stereoselective glycosidation utilizing a D-mannosyl halide having a nonparticipating group at C-2, the degree of selectivity being dependent on the use of a freshly prepared silver catalyst, and careful choice of an "aglycon" having the appropriate configuration[2,3]

In this laboratory, the first approach has been employed[4,5] in two successful syntheses of the "core" trisaccharide **1**. To extend this method to the pentasaccharide **2**, it was necessary to synthesize a glycosyl donor having an acyl group at O-2, "temporary"

β-D-Man*p*-(1→4)-β-D-Glc*p*NAc-(1→4)-Glc*p*NAc
1

α-D-Man*p*-(1→3)-[α-D-Man*p*-(1→6)]-β-D-Man*p*-(1→4)-β-D-Glc*p*NAc-(1→4)-Glc*p*NAc
2

protecting groups[6] at O-3 and O-6, and a "persistent" protecting group at O-4. Furthermore, the groups at O-3 and O-6 should be independently removable, so that an isotopically labeled α-D-mannopyranosyl group may be specifically introduced into one of these two positions. This is necessary in order that the synthetic oligosaccharides may function as precursors of exogenous, glycosyl acceptors in biosynthetic experiments[7]. To

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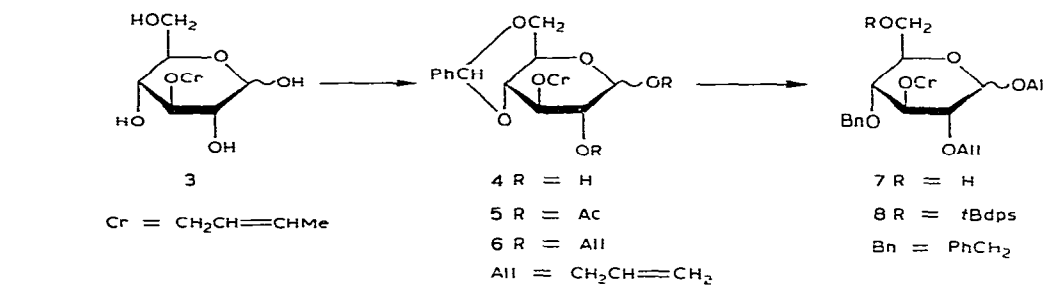
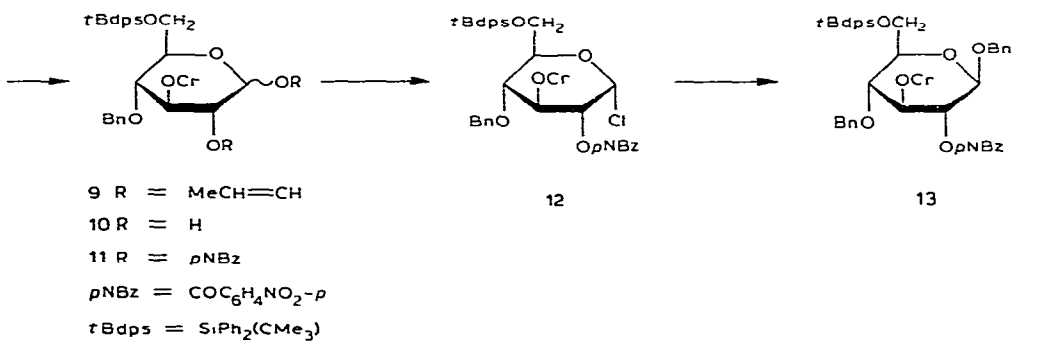
fulfil these requirements, we have synthesized 4-*O*-benzyl-3-*O*-(2-butenyl)-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-(*p*-nitrobenzoyl)-α-D-glucopyranosyl chloride (**12**).

3-*O*-(2-Butenyl)-D-glucose[8] (**3**) was converted into the 4,6-*O*-benzylidene derivative **4**, m.p. 247° (dec.), $[\alpha]_D^{26}$ +19° (*c* 0.5, chloroform). In an attempt to convert **4** into the 4-*O*-benzyl-6-hydroxy derivative, it was treated with lithium aluminum hydride–aluminum chloride[9], but t.l.c. examination of the reaction mixture (Merck precoated plates; anisaldehyde spray-reagent) indicated formation of an intractable mixture. Therefore, **4** was acetylated to give **5**, which, on treatment with allyl bromide in the presence of a weak base (silver oxide), gave the amorphous 1,2-di-*O*-allyl compound **6** in 70% yield; R_F 0.60 (2:1, v/v, hexane–ethyl acetate), $[\alpha]_D^{23}$ +44° (*c* 0.52, chloroform). In contrast to the result obtained with **4**, reductive ring-opening of the benzylidene group of **6** yielded the desired 4-*O*-benzyl derivative **7** (90%), R_F 0.45 (1:1, v/v, hexane–ethyl acetate), $[\alpha]_D^{23}$ +96° (*c* 0.28, chloroform).

Conversion of **7** into the 6-(*tert*-butyldiphenylsilyl) ether **8** was effected by treatment with *tert*-butylchlorodiphenylsilane and imidazole[10], and **8** was isolated as a syrup (90%), R_F 0.62 (3:1, v/v, hexane–ethyl acetate), $[\alpha]_D^{28}$ +59° (*c* 0.21, chloroform). For the removal of the allyl substituents from **8**, isomerization to the 1,2-di-*O*-(1-propenyl) compound **9** was achieved by treatment with tris(triphenylphosphine)-rhodium(II) chloride[11], after which, hydrolysis with mercuric chloride[12] gave the diol **10**





in 60% yield, as a mixture of anomers, R_F 0.74, 0.79 (10:1, v/v, chloroform–methanol), $[\alpha]_D^{24}$ +39° (*c* 0.2, chloroform). In order to facilitate formation of the glycosyl chloride, compound **10** was converted into the 1,2-di-*O*-(*p*-nitrobenzoyl) derivative **11** (80%), which was, surprisingly, noncrystalline; it had R_F 0.56, 0.62 (2:1, v/v, hexane–ethyl acetate), $[\alpha]_D^{25}$ +34° (*c* 0.18, chloroform). By treatment with hydrogen chloride in dry diethyl ether, compound **11** was converted into the desired glycosyl chloride **12** (70%), R_F 0.69 (4:1, v/v, hexane–ethyl acetate), $[\alpha]_D^{23}$ +46° (*c* 0.5, chloroform), characterized by conversion, in 68% yield, into benzyl 4-*O*-benzyl-3-*O*-(2-butenyl)-6-*O*-(*tert*-butyldiphenylsilyl)-2-*O*-(*p*-nitrobenzoyl)-β-D-glucopyranoside (**13**). The ^{1}H-n.m.r. spectrum of **13** showed no evidence for contamination of the product by the α-D anomer. The synthetic intermediates **4**, **5**, **6**, **7**, **8**, **9**, **10**, and **11** gave the expected ^{1}H-n.m.r. spectra and elemental analyses.

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