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Note

A new approach to the synthesis of oligosaccharides

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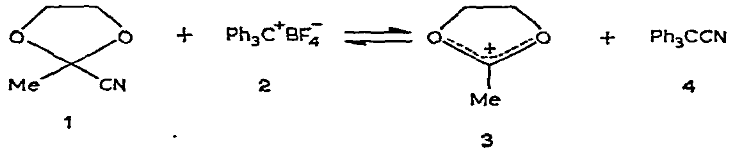
Acyloxonium ions involving C-1 and C-2 of an aldose moiety in a five-membered ring are usually assumed to be intermediates in oligosaccharide syntheses by the Koenigs–Knorr and orthoester methods[1,2]. Such acyloxonium ions may also be generated in many other ways[3]. One such reaction in simple, non-carbohydrate systems[4] is the abstraction of cyanide ion from the pyruvonitrile cyclic acetal **1** by triphenylcarbonium tetrafluoroborate (**2**) in acetonitrile to give the acyloxonium ion **3**, the equilibrium being shifted to the right by crystallization of triphenylacetonitrile **4**. Before this and related reactions can be used for glycoside synthesis, two problems must be solved; these involve displacement of the equilibrium towards the desired acyloxonium ion, and removal of the strong acid (*e.g.*, HBF_4) formed in the reaction of the acyloxonium salt with alcohols.

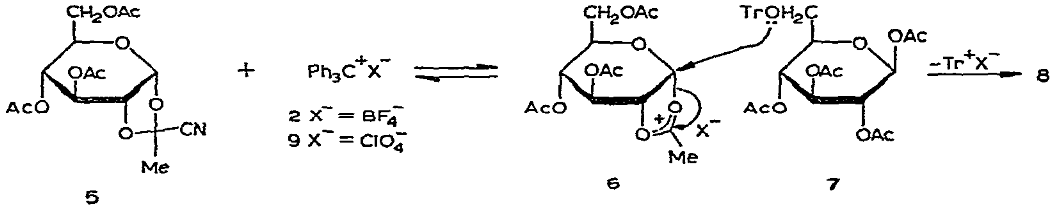
We now describe an approach which avoids both difficulties, and which is based on Meerwein's data[4] cited above and on the glycosylation of trityl ethers with glycosyl halides[5].

The nitrile **5**[6] reacts with a catalytic amount of triphenylcarbonium ion to give the acyloxonium ion **6** and triphenylacetonitrile (**4**). The subsequent, irreversible reaction of **6** with the trityl ether **7**, which provides the appropriate equilibrium shift, leads to the disaccharide derivative **8** (gentiobiose octa-acetate) with regeneration of the triphenylcarbonium ion. Thus, the latter ion catalyses the reaction, and gentiobiose octa-acetate **8** was synthesised from **5** and **7**.

The interaction of equimolar amounts of **5** and **7** was studied by using dichloromethane as solvent, 0.05 and 0.10 mole of the tetrafluoroborate **2** or perchlorate **9** as catalyst, reaction temperatures of 0, 20, or 40°, and reaction times of 2–48 h.

The reaction is solvent dependent; *e.g.*, no reaction occurred in acetonitrile. The nature of the counter ion (BF_4^- or ClO_4^-) does not significantly affect the reaction. The yield of **8** did not depend noticeably on the reaction temperature and duration, although the results are slightly better when the reaction is carried out at 42° for a few hours. Treatment of the reaction mixture with dry methanol at room temperature results in the rapid and complete detritylation of any unreacted **7**.





The condensation of **5** and **7** under optimal conditions in the presence of either fluoroborate **2** or perchlorate **9** gave **8** in yields of 42 and 64%, respectively.

The principle of oligosaccharide synthesis described herein, based on carbonium ion-catalysed generation of an acyloxonium ion, may be of more general application.

EXPERIMENTAL

All operations were carried out by using the high-vacuum technique (h.v.) described earlier[7]. Acetonitrile and dichloromethane was distilled from calcium hydride before use. The nitrile **5** was prepared by the method of Coxon and Fletcher[6], the trityl ether **7** by the method of Helferich *et al.*[8], and the triphenylcarbonium salts by the method of Dauben *et al.*[9]. T.l.c. was performed on alumina[10], using chloroform–acetone (4:1). M.p.s. were determined with a Kofler apparatus, and optical rotations with a Perkin–Elmer 141 polarimeter. Evaporation of solutions was performed *in vacuo* at 40°.

β-Gentiobiose octa-acetate **8**. — (*a*) *Analytical experiments.* In the limbs of a tuning fork-shaped tube (⅄) were separately placed a solution of the nitrile **5** (0.10 mmole) and the trityl ether **7** (0.10 mmole) in benzene, and a solution of the salt **2** or **9** (0.005 or 0.01 mmole) in nitromethane. The solutions were freeze-dried and the residues were thoroughly dried *in vacuo* (h.v.). Solvent (1 ml) was then distilled (h.v.) into the tube, the tube was sealed (h.v.), and the contents were mixed. After storage under the appropriate conditions, the tube was opened, dry methanol (0.5 ml) was added, followed, after 20–30 min at room temperature, by 2 drops of pyridine. The mixture was concentrated, and the residue was washed with hexane, dried, and analysed by t.l.c. Octa-acetate **8** (major), unreacted **5** (minor), glucose tetra-acetate (from **7**, minor), and non-carbohydrate trityl derivatives were found in all reactions in dichloromethane. After prolonged reaction, a side product having an R_F value less than that of **8** was also observed. No octa-acetate **8** was observed for the reactions in acetonitrile.

(*b*) *Preparative experiments*. The nitrile **5** (0.50 mmole) and trityl ether **7** (0.50 mmole) were allowed to react as described above in dichloromethane (3.5 ml) in the presence of the salt **2** or **9** (0.025 mmole) at 45° for 80 min. The tubes were opened, dry methanol (2.5 ml) was added, followed after 30 min by a few drops of pyridine. The mixture was concentrated, and the residue was washed thrice with hexane (5, 2, and 1 ml), dried, and crystallized from ethanol (5 ml). Gentiobiose octaacetate **8** was thus obtained (0.14 g, 42%, using **2**; and 0.22 g, 64%, using **9**), having m.p. 193–196° alone and in admixture with authentic material, and $[\alpha]_D$ $-4.5°$ (*c* 3.6, chloroform); lit.[11] m.p. 196°, $[\alpha]_D$ $-5.35°$ (chloroform).

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