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Silver Imidazolate-assisted Glycosidations. Part 6. Synthesis of 1,2-*trans*-Linked Disaccharides

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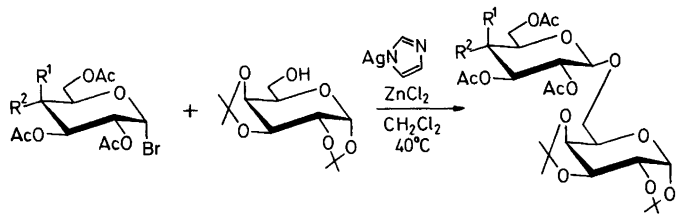
The use of silver imidazolate and zinc chloride as a promoting system for the synthesis of 1,2-*trans*-linked disaccharides in the D-glucopyranose and D-galactopyranose series is described.

Syntheses of 1,2-*trans*-linked di- and oligosaccharides [1,2] are generally based upon the original work of Koenigs and Knorr [3] or upon the orthoester glycosylation method.[4,5] In the former type of approach silver triflate has been shown to be a most efficient glycosidation promotor.[6–8]

In our continued exploration of the use of silver imidazolate–Lewis acid promoted glycosidation reactions [9] we now report on the use of silver imidazolate and zinc chloride as a useful promoting system for the synthesis of 1,2-*trans*-linked glycosides. In disaccharide syntheses the molar proportions of 2,3,4,6-tetra-*O*-acetyl-α-D-hexopyranosyl bromide–aglycone–zinc chloride–silver imidazolate was 1.5:1: ~6:0.75 in dichloromethane containing molecular sieves. Using this procedure four disaccharides, *3*, *4*, *5* and *6* were made. The yields of the β-1,6-linked disaccharides *3* and *4* were 90 and 87 %, respectively, those of *5* and *6* were 30 and 37 %, respectively, demonstrating the expected lowering of yield with lowering aglycone reactivity. In the reaction mixture containing *5* a by-product with higher mobility than that of *5*, presumably a product of acetal migration,[10] was observed on TLC with ^{13}C NMR parameters identical to those of 6-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose.[10] In these reactions it is essential that not more than 0.75 mol equivalents of silver imidazolate is used, in order to avoid the formation of orthoesters.

EXPERIMENTAL

General methods were the same as those reported elsewhere.[11] Silver imidazolate was prepared as previously described. Commercial dry zinc chloride was fused by heating in a Pyrex tube until vigorous boiling ceased and the melt was poured into tetrachloromethane. The pellets of dry zinc chloride thus formed may be stored under carbon tetrachloride for up to two weeks. Before use, the pellets were transferred into a mortar under dichloromethane, crushed to a fine powder, weighed, and transformed rapidly into the reaction vessel. Twice the required amount of zinc chloride was weighed out to compensate for adhering solvent.



1 R^1=H R^2=OAc
2 R^1=OAc R^2=H

3 R^1=H R^2=OAc (90%)
4 R^1=OAc R^2=H (87%)

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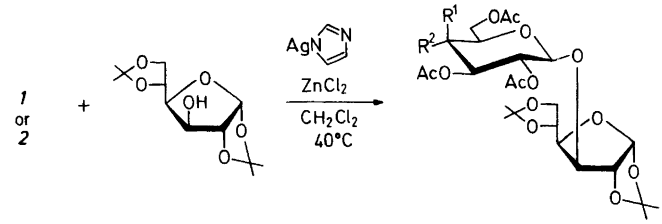

5 R^1=H R^2=OAc (30%)
6 R^1=OAc R^2=H (37%)

Glycosylation procedure. 6-O-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (3). A mixture of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (*1*) (616 mg, 1.5 mmol), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (260 mg, 1.0 mmol), silver imidazolate (131 mg, 0.75 mmol) and zinc chloride (about 820 mg, ~6 mmol) in dichloromethane (15 ml) containing 4 Å molecular sieves was stirred in the dark at 40 °C for 14 h. The mixture was filtered, the solids were washed with toluene (75 ml) and the combined filtrate and washings poured into saturated aqueous sodium carbonate (250 ml) and toluene (250 ml). The mixture was stirred for 30 min and then separated. The organic phase was washed with aqueous sodium hydrogencarbonate and then water, dried ($MgSO_4$), filtered, concentrated and subjected to silica gel column chromatography (toluene–ethyl acetate 2:1) to yield *3* (530 mg, 90 %), $[\alpha]_D^{22}$ −53° (*c* 1.0, chloroform) [lit. [3] $[\alpha]_D$ −55° (chloroform)], $\delta_{^{13}C}$ ($CDCl_3$, from internal TMS): 96.0 (C-1), 101.7 (C-1'), 108.4 and 109.1 [2 × *C* $(OR)_2$].

6-O-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (4). After a reaction time of 14 h and work-up including silica gel column chromatography (toluene–ethyl acetate 5:2), an 87% yield of *4* was obtained. $[\alpha]_D^{22}$ −44° (*c* 1.0, chloroform) [lit.[3] −47° (chloroform)], $\delta_{^{13}C}$ ($CDCl_3$): 96.4 (C-1), 101.4 (C-1'), 108.6 and 109.3 [2 × *C* $(OR)_2$].

3-O-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (5). After a reaction time of 72 h and work-up, including silica gel column chromatography (toluene –ethyl acetate 1:1) a 30 % yield of *5* was obtained, m.p. 131–133 °C (from diethyl ether–light petroleum), $[\alpha]_D^{22}$ −20° (*c* 1, chloroform) [lit.[5] m.p. 130–132 °C, $[\alpha]_D$ −21° (chloroform)]. $\delta_{^{13}C}$ ($CDCl_3$): 101.1 (C-1'), 105.0 (C-1), 108.8 and 112.2 [2 × *C*$(OR)_2$].

3-O-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (6). After a reaction time of 48 h and work-up [including silica gel column chromatography (toluene–ethyl acetate 2:1)], a 37% yield of *6* was obtained, m.p. 157 °C (from chloroform–light petroleum), $[\alpha]_D^{22}$ −9° (*c* 1, chloroform). Anal. $C_{26}H_{38}O_{15}$: C, H. $\delta_{^{13}C}$ ($CDCl_3$): 100.0 (C-1') 105.0 (C-1), 108.7 and 112.1 [2 × *C* $(OR)_2$].

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