

Silver Imidazolate-assisted Glycosidation. Part 5.* Synthesis of Carbohydrate Orthoesters

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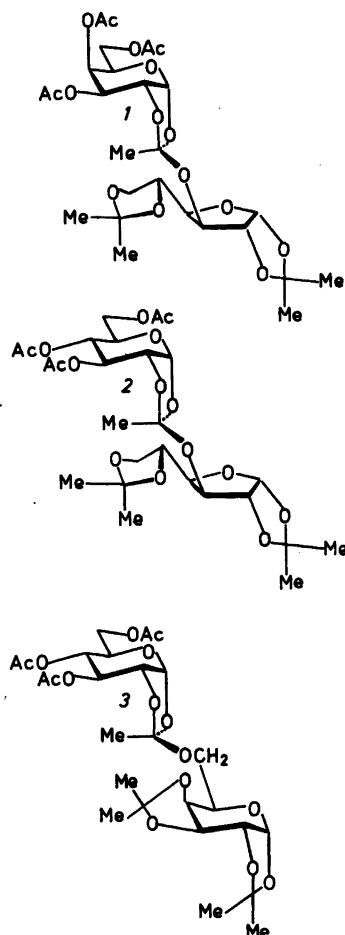
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The orthoester glycosidation method¹ is well-established in carbohydrate synthesis as a route to 1,2-*trans*-glycosides and several modifications of the original procedure have been described.² In all procedures, the crucial step is the conversion, under acidic catalysis of an orthoester into a glycoside. Common reaction systems include nitromethane as solvent and mercury(II) bromide as catalyst or, alternatively, 1,2-dichloromethane or chlorobenzene with 2,6-lutidinium or 2,4,6-collidinium perchlorate as catalysts.³ The conversion of orthoesters into 1,2-*trans*-glycosides is often highly stereospecific and we now report an efficient synthesis of complex orthoesters.

An acylglycosyl bromide, in dichloromethane at room temperature, is reacted with a protected carbohydrate containing a single free hydroxyl group in the presence of silver imidazolate⁴ and mercury(II) chloride to yield the corresponding orthoester. The addition of tetrabutylammonium chloride⁵ to the reaction mixture enhance the rate considerably, while the addition of tetrabutylammonium bromide has no such effect. Results are shown in Table 1.

Reducing the amount of silver imidazolate in the reaction mixture from 1.5 to 0.4–0.75 equivalents produces the corresponding 1,2-*trans*-glycoside in

yields of 75–92%. These yields tend to vary from one experiment to another and this approach to 1,2-*trans*-glycosides has been abandoned in favour of the



Scheme 1. Products obtained from 2,3,4,6-tetra-O-acetyl- α -D-hexopyranosyl bromides and diisopropylidene hexoses.

* Part 4 is Ref. 8.

Table 1. Reaction times, yields and physical constants of products.

Product	Reaction time	Yield %	α_D^{22} ($^\circ$, chloroform)	δ_{13C}	
				C(OR) ₃	C-1
1	7 days	63	36	121.6	97.4
1	3 h (Bu ₄ NCl present)	93			
2	24 h	93	-8 ^a	121.6	97.2
3	6 h	98	-21 ^b		

^a Ref. 7: -8°. ^b Ref. 7: -21°.

one described in part 6 of this series of papers. The experiments outlined in Table 1, however, show that complex orthoesters of carbohydrates are obtainable in high yields by the methodology described in the present paper.

Experimental. General methods were the same as those reported elsewhere.⁶

Orthoester synthesis. In a typical experiment, a mixture of 2,3,4,6-tetra-*O*-acetyl- α -D-glucopyranosyl bromide (616 mg, 1.5 mmol), 1,2:5,6-di-*O*-isopropylidene- α -D-glucopyranose (260 mg, 1.0 mmol), mercury(II) chloride (1.086 g, 4.0 mmol) and silver imidazolate (262 mg, 1.5 mmol) in dichloromethane (15 ml) containing 4 Å molecular sieves was stirred at room temperature for 24 h after which triethylamine (2 ml) was added. The mixture was stirred for an additional 30 min, filtered through a silica gel pad, concentrated and subjected to silica gel column chromatography (toluene-ethyl acetate, 1:1). Yields and physical constants for this (2) and the other two products are given in Table 1.

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