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Stereoselective C-Glycosidation of Glycals with Organoaluminum Reagents

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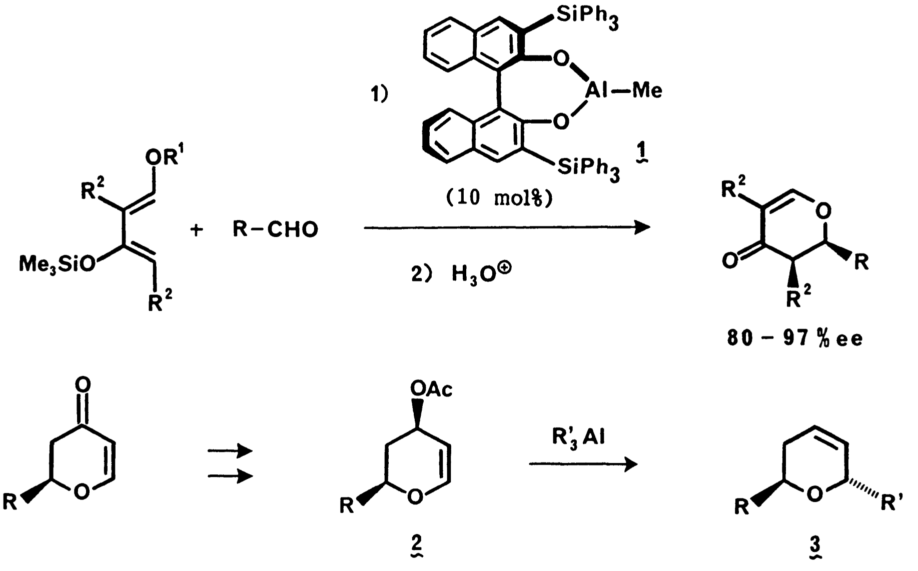
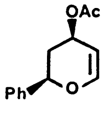
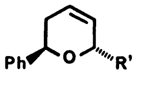
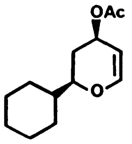
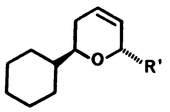
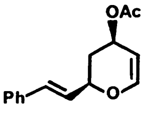
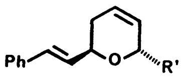
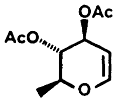
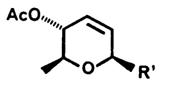
A new approach to the stereoselective synthesis of C-glycosides from glycals with various organoaluminum reagents has been demonstrated.

We have recently described the asymmetric hetero-Diels-Alder reaction of aldehyde and diene catalyzed by chiral organoaluminum reagent **1**, in which the dihydropyrones were produced with high enantiomeric purity.[1)] Since the resultant optically active dihydropyrones are readily transformed in a stereoselective way to glycals of the type **2**, it became of interest to investigate the C-glycosidation of glycal **2** in view of the high synthetic utility as chiral building blocks for the structural elaboration as already illustrated by the concise application to the synthesis of a variety of carbohydrates and polyether antibiotics.[2-6)] Here we wish to report a new method for the stereoselective C-glycosidation of glycals with organoaluminum reagents.



The requisite glycal **2** was readily obtainable by reduction of the dihydropyrones with $LiAlH_4$ in ether followed by acetylation with Ac_2O-Py. Treatment of the glycal **2** (R = Ph) in CH_2Cl_2 with trialkylaluminum, R'_3Al (4 equiv.) at -20 °C for 1 h led to the formation of C-glycoside **3** (R = Ph; R' = Me, Pr, i-Bu, C≡CBu) in 74-96% yield with high regio- and stereoselectivity. The trans stereochemistry of **3** (R = Ph) was confirmed by comparison with authentic samples.[3] Several other examples are listed in Table 1, in which the trans isomers predominated widely over the cis. In particular, alkynyl groups can be introduced with rigorous trans selectivity (Entry 4, 6, 7, and 9).

Table 1. Stereoselective C-glycosidation of glycals with trialkylaluminum[a]

Entry	Glycal	Trialkylaluminum	C-Glycoside[b]	Yield/% (trans/cis)[c]
1		Me_3Al		96 (96:4)
2		Pr_3Al		93 (87:13)
3		$i\text{-}Bu_3Al$		74 (94:6)
4		$Et_2AlC\equiv CBu$		85 (100:0)[d]
5		Me_3Al		91 (99:1)
6		$Me_2AlC\equiv CBu$		84 (100:0)[d]
7		$Me_2AlC\equiv CSiMe_3$		66 (100:0)[d]
8		Me_3Al		52 (91:9)
9		$Et_2AlC\equiv CBu$		55 (100:0)[d]
10		Me_3Al		74 (65:35)[e]
11		$Me_2AlC\equiv CBu$		80 (68:32)[e]

a) Reaction was carried out by treatment of glycal in CH_2Cl_2 with trialkylaluminum (4 equiv.) in hexane at -20–0 °C for 0.5-1 h. b) R' = alkynyl in the case of dialkylaluminum alkynide. The major trans isomers were depicted in the Table. c) Determined by GLC. d) The methylation or ethylation product **3** (R' = Me or Et) was also formed in 4-8% yield. e) The trans/cis refers to the relationship of the C_2-C_5 substituents in this particular case. See Ref. 5.

References

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