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Preliminary communication

A novel, reductive ring-opening of carbohydrate benzylidene acetals, with unusual regioselectivity

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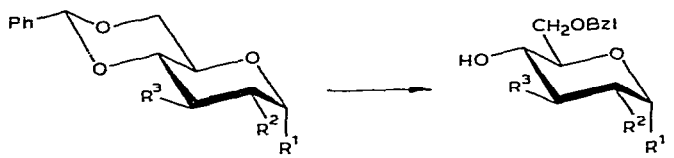
Reductive ring-opening of benzylidene acetals can be effected with lithium aluminium hydride–aluminium chloride[1]: When applied to 4,6-*O*-benzylidenehexopyranosides having benzyl substituents at O-3, 4-benzyl ethers with HO-6 free were obtained in high yield[2].

Horne and Jordan[3] have described the reduction of dimethyl acetals and ketals to methyl ethers, using sodium cyanoborohydride–HCl (gas)–methanol. We now report that the application of this method to 4,6-*O*-benzylidenehexopyranosides in an inert solvent yields 6-benzyl ethers with HO-4 free. Since these substances normally are obtained by multistep synthesis, the present method represents a useful addition to protection-group strategy in carbohydrate synthesis. The examples given below include hexopyranosides containing *O*-benzoyl, *O*-benzyl, and *N*-acetyl protecting-groups.



R^1	R^2	R^3
OMe	OBzl	OBzl
OMe	OBz	OBz
OBzl	NHAc	OBzl

A solution of the benzylidene acetal (1 mmol) and sodium cyanoborohydride (9 mmol) in dry tetrahydrofuran (15 ml) containing[4] powdered 3 Å molecular sieves was cooled to 0°. Hydrogen chloride in diethyl ether was added until the solution was acidic (pH paper, gas evolution). After 10 min at 0°, when t.l.c. indicated complete reaction, the mixture was poured into ice–water, and the product was extracted with dichloromethane. The extract was washed with saturated, aqueous sodium hydrogencarbonate, dried over sodium sulfate, filtered, dried, and concentrated *in vacuo*. The

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products were purified by chromatography[5] on silica gel. The results are given in Table I. The identity of the products was demonstrated by the use of trichloroacetyl isocyanate in ^{1}H-n.m.r. spectroscopy[6]. In the derivatives obtained, the signal for H-4 was shifted downfield to a unique position, and the identity of the signal was shown by appropriate, homonuclear spin-decoupling.

In preliminary experiments, reductive cleavage of 4,6-*O*-prop-2-enylidene acetals gave the corresponding 6-allyl ethers. This and other aspects of $NaCNBH_3$–HCl-promoted acetal cleavage in the carbohydrate series will be reported elsewhere.

TABLE I

PRODUCTS OBTAINED BY REDUCTIVE CLEAVAGE OF ACETALS

Starting material	*Product*[a]	*Yield (%)*	$[\alpha]_D$ *(degrees)*	*M.p. (degrees)*
Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside[7]	Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranoside[8]	81	+13[c]	
Methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside[9]	Methyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-α-D-glucopyranoside[b]	95	+113	
Benzyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[10]	Benzyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside[10,11]	60	+100[d]	144–145[e]

[a] The ^{1}H- and ^{13}C-n.m.r. spectra were in agreement with those published. [b] A satisfactory elemental analysis was obtained for this compound. [c] Lit.[8] +11°. [d] Lit.[10] +114°. [e] Lit.[10] 144–145.5°.

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