Preliminary communication

Relative reactivity of the hydroxyl groups in methyl 4,6-*O*-benzylidene-D-glycopyranosides (*trans*-fused series) towards tosyl chloride in pyridine

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Although interest in the selective sulphonylation of secondary hydroxyl groups in carbohydrate derivatives is of long-standing, few systematic studies have been reported[1]. Explanations of selective reaction have depended, therefore, on a limited number of examples of different types of compounds.

We have now studied the reaction of all eight possible methyl 4,6-*O*-benzylidene-D-glycopyranosides having *trans*-fused ring systems, with one equivalent of tosyl chloride in pyridine at room temperature. The reaction mixtures were examined by t.l.c. and the products separated by p.l.c. Seven of the required starting materials were known, and methyl 4,6-*O*-benzylidene-β-D-allopyranoside was synthesised by standard procedures from the known[2] methyl β-D-allopyranoside.

Three compounds in the series, namely α-D-*gluco*[3,4], β-D-*gluco*[5,6], and α-D-*manno*[7] ★★ have been the subject of selective tosylation studies. The results from the five newly-studied compounds are given in Table I; in Table II the results for all eight compounds are presented together with other relevant data, such as hydrogen-bonding possibilities.

Previous workers[1] have regarded hydrogen bonding as the factor which dictates the pattern of reaction. For example, the difference between the behaviour of the α- and β-D-*gluco* compounds has been attributed to the fact that intramolecular, hydrogen-bond formation between HO-2 and MeO-1 is favoured in the α-D anomer where these are *cis* groups. However, as has already been pointed out[9], intramolecular hydrogen-bonding is not likely to be important in pyridine, unless such bonding is specially involved in the transition state.

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★★A result similar to that reported in ref. 7 was obtained with the ethylidene analogue[8].

TABLE I

PARTIAL TOSYLATION OF METHYL 4,6-*O*-BENZYLIDENE-α-D-GLYCOPYRANOSIDES IN PYRIDINE AT ROOM TEMPERATURE

Compound	*Reaction time*	*Products (%)*			
		Diol	*2-Ester*	*3-Ester*	*Diester*
α-allo	24 h	[a]	23 [b]		
β-allo	8 days	[a]	17 [c]		
α-altro	18 h	50	26 [d]	17 [e]	7 [f]
β-altro	17 h	70	13 [g]		
β-manno	20 h	[a]		32 [h]	

[a] Diol not isolated: t.l.c. plates showed only diol plus the single mono-ester shown; p.l.c. isolation gave a single compound. [b] Known compound[11]. [c] Structure assigned on n.m.r. evidence. [d] Known compound[12]. [e] Gave the corresponding 2,3-anhydro-mannoside on mild treatment with alkali. [f] Known compound[13]. [g] Gave the corresponding 2,3-anhydro-alloside on mild treatment with alkali. [h] Structure assigned on the basis of the non-reaction of the debenzylidenated compound with periodate.

Consideration of the data in Table II shows that, for each of the four compounds where there is a choice between an axial and an equatorial hydroxyl group, it is the equatorial group that is selectively sulphonylated in agreement with the well-established principles of conformational analysis. For the compounds that contain two *ax* hydroxyl groups (*altro*) or two *eq* groups (*gluco*), it appears that the pattern of selectivity can be correlated with the presence of a *cis* HO-2--MeO-1 hydrogen bond, as present in the α-D-*gluco* and β-D-*altro* compounds. In Table II, the possibilities for hydrogen bonding between HO-3 and RO-4 are also shown, but these do not correlate with the observed selectivity.

Thus, from this stereochemical series of compounds, it appears that selectivity is controlled by preferential equatorial reaction and, if that is not possible, by hydrogen bonding. These findings are in keeping with a recent paper on the selective tosylation of 1,2-*O*-cyclohexylidene-*myo*-inositol (four *eq*-OH) in which the mono-ester formed was at the only hydroxyl group having a neighbouring OR group in an axial position[10].

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TABLE II

SUMMARY OF SELECTIVE TOSYLATION DATA FOR METHYL 4,6-*O*-BENZYLIDENE-D-GLYCOSIDES (*trans*-FUSED SERIES)

Compound	*Mono-esters formed*		Eq-*OH*	Eq-ax *H-bond*		Eq-eq *H-bond*	
	O-2	*O-3*		*HO-2/O-1*	*HO-3/O-4*	*HO-2/O-1*	*HO-3/O-4*
α-*allo*	X		HO-2	X	X		
β-*allo*	X		HO-2		X	X	
α-*altro*	X	X			X		
β-*altro*	X			X	X		
α-*gluco*	X		HO-2, HO-3	X			X
β-*gluco*	X	X	HO-2, HO-3			X	X
α-*manno*		X	HO-3				X
β-*manno*-		X	HO-3	X			X

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