

# **$\alpha$ -C-Glycopyranosides from Lewis Acid Catalysed Condensations of Acetylated Glycals and Enol Silanes**

By ROBERT DAVID DAWE

(Guelph-Waterloo Centre for Graduate Work in Chemistry, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1)

and BERT FRASER-REID\*

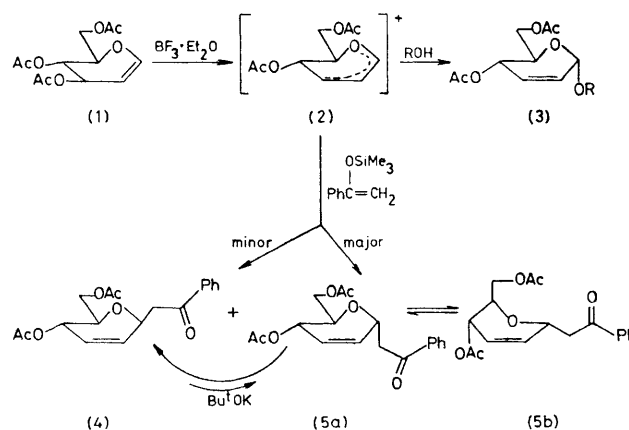
(Chemistry Department, University of Maryland, College Park, MD. 20742)

**Summary** Acetylated glycals undergo Lewis acid-catalysed condensations with enol silanes in virtually quantitative yields to form C-glycopyranosides in which the thermodynamically unfavourable  $\alpha$ -anomers<sup>1</sup> are formed predominantly.

THE development of routes to functionalized C-glycopyranosides is an area of interest in our laboratory and we have investigated methods based on enone photoalkylation,<sup>1</sup> sigmatropic rearrangements,<sup>2</sup> and Wittig olefinations<sup>2</sup> with varying degrees of success with respect to efficiency, yield, and stereoselectivity. We have sought improvements in these areas and, in view of recent reports,<sup>3-6</sup> we report herein some of our recent results.

Lewis acid-catalysed reactions at the anomeric centres of sugars are thought to involve the formation of glycosyl oxo-carbonium ions and these intermediates may be trapped with a variety of nucleophiles including activated arenes<sup>7</sup> and enol ethers.<sup>8</sup> The allyl-oxo-carbonium ion (2) has long been recognized as the intermediate in the Ferrier reaction<sup>9</sup> for preparation of *O*-glycosides (3) from acetylated glycals (1). We therefore sought to trap intermediate (2) for the preparation of unsaturated C-glycopyranosides (Scheme 1).

Results of the reactions of 1-trimethylsilyloxystyrene with 'triacetyl glucal'<sup>†</sup> (1) shown in the Table reveal an extremely high dependence upon the various reaction parameters. Thus overall yields were affected by changes in temperature (entries 1 and 2, 6 and 7), catalyst (entries 1 and 4, 8 and 9), and solvent (entries 1 and 5, 1 and 8). It was hoped that use of acetonitrile (entries 8 and 9) would have led to a substantial increase in the proportion of the  $\alpha$ -anomers since the intermediate nitrilium ion [C(1)-N<sup>+</sup>=CMe]<sup>10</sup> would be



SCHEME 1

obliged to adopt a  $\beta$ -orientation because of the reverse anomeric effect.<sup>11</sup> However the  $\alpha/\beta$  ratio is seen to be the same in entries 1 and 9, and in view of the ease of operation involved, we prefer the conditions of entry 1.

Compounds (4) and (5)<sup>‡</sup> were readily separated chromatographically. Previously,<sup>1,2</sup> we had found that C-glycopyranosides obeyed Hudson's rules of isorotation, and on this basis alone the assignment of structures to (4) and (5) would have been reversed. However, the  $\gamma$ -effect rule<sup>12</sup> of <sup>13</sup>C n.m.r. spectroscopy has been found to be a more discriminating tool for distinguishing between such epimers.<sup>2</sup> Accordingly the isomer in which C(5) is more shielded was assigned as (5).

TABLE. Lewis acid-catalysed reaction of (1) with CH<sub>2</sub>=C(OSiMe<sub>3</sub>)Ph

Entry	Solvent	Catalyst	T/°C	t/h	(5):(4)	% Yield
1 <sup>a</sup>	CH <sub>2</sub> Cl <sub>2</sub>	BF <sub>3</sub> ·Et <sub>2</sub> O	-40 to 0	0.5	4:1	99
2	"	"	-78	2.5	—	< 1
3	"	AlCl <sub>3</sub>	-40 to 0	1	7:3	92
4	"	CF <sub>3</sub> SO <sub>3</sub> SiMe <sub>3</sub> <sup>b</sup>	23	0.3	7:3	75
5	THF <sup>c</sup>	BF <sub>3</sub> ·Et <sub>2</sub> O	-40 to 23	5.0	—	< 1
6	"	AlCl <sub>3</sub>	-40 to 0	18	—	—
7	"	"	23	36	7:3	77
8	CH <sub>3</sub> CN	BF <sub>3</sub> ·Et <sub>2</sub> O	-45 to 0	0.75	—	< 1
9	"	AlCl <sub>3</sub>	-45 to 10	1	4:1	97

<sup>a</sup> A solution of compound (1) (1 mmol) and the enol silane (1.5 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (15 ml) was cooled to -40 °C under argon and practical grade BF<sub>3</sub>·Et<sub>2</sub>O (1.4 mmol) was added *via* a syringe. The mixture was allowed to warm to 0 °C when a bright yellow colour developed. This colour disappeared upon the usual work-up. <sup>b</sup> See reference 7. <sup>c</sup> Tetrahydrofuran.

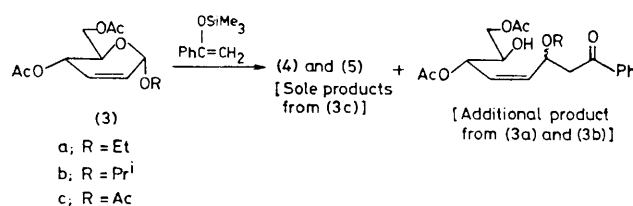
<sup>†</sup> 3,4,6-Tri-*O*-acetyl-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol.

<sup>‡</sup> For (4) [ $\alpha$ ]<sub>D</sub><sup>20</sup> + 111.3°; <sup>1</sup>H n.m.r.:  $\delta$  4.86 (*J*<sub>1,2</sub> 1.1 Hz, 1-H) and 3.79 (*J*<sub>4,5</sub> 8.7 Hz, 5-H); <sup>13</sup>C n.m.r.: 68.024 (C-5). For (5) [ $\alpha$ ]<sub>D</sub><sup>20</sup> 35.7°; <sup>1</sup>H n.m.r.:  $\delta$  4.95 (*J*<sub>1,2</sub> 2.3 Hz, 1-H) and 4.05 (*J*<sub>4,5</sub> 3.3 Hz, 5-H); <sup>13</sup>C n.m.r.: 73.293 (C-5). The value of *J*<sub>4,5</sub> for (4) indicates that this anomer is in the <sup>4</sup>C<sub>1</sub> conformation with the C(1) substituent equatorially oriented. This is to be expected since these molecules should not display an anomeric effect. The *J*<sub>4,5</sub> value for (5) suggests conformational mobility between <sup>4</sup>C<sub>1</sub> and <sup>1</sup>C<sub>4</sub> forms.

In our earlier study, it had been found that with C-glycopyranosides possessing an activated methylene group at the anomeric carbon, the  $\beta$ -anomers were thermodynamically favoured.<sup>2</sup> For the present study we established that the epimers (4) and (5) were not interconverted when placed separately in the reaction medium of entry 1. We then found that treatment of the major product (5) with potassium t-butoxide (strong base was found necessary) in benzene for six hours led to a predominance of the minor product (4). This equilibrium study therefore shows that these Lewis acid-catalysed condensations are kinetically controlled.

Other acetylated glycals have also been found to react with 1-trimethylsilyloxystyrene to give comparable products. However, with 2-acetoxy-analogues a complex mixture of intractable material was obtained. Reaction of (1) with 1-trimethylsilyloxycyclohexene gave the expected  $\alpha/\beta$  mixture in 95% isolated yield.

Alkyl hex-2-enopyranosides are also sources of allyl-oxocarbenium ions<sup>13</sup> and their potential for C-alkylation was therefore investigated. As indicated in Scheme 2 the



SCHEME 2

reaction of the alkyl glycosides (3a) or (3b) gave mixtures of acyclic as well as cyclic products, indicating that both C(1)-O bonds of these glycosides are amenable to cleavage. However with the *O*-acetyl analogue (3c), cleavage of the C(1)-O(5) bond was completely suppressed, cyclic compounds (4) and (5) being the only products.

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