

## A 4-Oxacyclohexanone-1,5-Lactone Photoisomerization with 1,2:4,6-Di-*O*-alkylidene- $\alpha$ -*D*-hexopyranos-3-ulose Derivatives

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Five 4-oxacyclohexanones (1)–(5) derived from 1,2:4,6-di-*O*-alkylidene glucose have been shown to photoisomerize to the 2,3:4,6-di-*O*-alkylidene-aldono-1,5-lactones (7)–(11) respectively.

The photoreactions of 3-oxacyclohexanone derivatives prepared from carbohydrates have been found<sup>1</sup> to be influenced by the nature and position of the numerous alkoxy substituents present on the ring. The photoisomerization of sugar derivatives possessing the less studied 4-oxacyclohexanone structure we describe here, compared with earlier reported<sup>2</sup> reactions on closely related compounds, indicates that their photochemistry is also dependent on the protecting groups.

U.v.-irradiation of the 4-oxacyclohexanone, 4,6-*O*-ethylidene-1,2-*O*-isopropylidene- $\alpha$ -*D*-ribo-hexopyranos-3-ulose (1) in acetonitrile† solution gave one non-polar product which

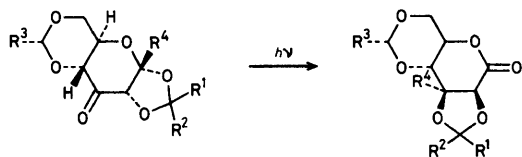
was isolated in 45% yield by flash chromatography<sup>3</sup> and shown to be 4,6-*O*-ethylidene-2,3-*O*-isopropylidene-*D*-mannono-1,5-lactone (7), m.p. 115 °C,  $[\alpha]_D^{25} +43^\circ$  (*c* 1.0, in CHCl<sub>3</sub>),  $\delta_C$  (CDCl<sub>3</sub>) 168.5, identical to the lactone produced by oxidation of 4,6-*O*-ethylidene-2,3-*O*-isopropylidene-*D*-mannopyranose with dimethyl sulphoxide and acetic anhydride.<sup>4</sup>

The diacetalated 3-uloses (2) and (3) and the methyl and ethyl 1,2-orthoacetates (4) and (5) were similarly photoisomerized to the lactones (8),(9),(10), and (11) respectively.

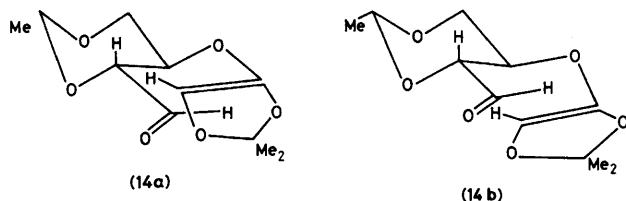
Ketones (1) and (3) were also isomerized in irradiated benzene solutions although the conversion of (1) into (7) was less clean under these conditions. However in the presence of trifluoroacetic acid (0.01 M) its transformation into (7) was improved.

Some insight into this unusual transformation was gained by irradiating compound (6), the C-1 deuteriated analogue of (1),

† Irradiations were carried out on 1–5% solutions in quartz tubes with a 450 W Hanovia medium pressure Hg lamp. New compounds were characterized by elemental analysis and/or mass spectroscopy and by <sup>1</sup>H and <sup>13</sup>C n.m.r. spectroscopy.



- (1)  $R^1 = R^2 = R^3 = \text{Me}, R^4 = \text{H}$   
 (2)  $R^1 = R^2 = \text{Me}, R^3 = \text{Ph}, R^4 = \text{H}$   
 (3)  $R^1 = \text{Et}, R^3 = \text{Ph}, R^2 = R^4 = \text{H}$   
 (4)  $R^1 = \text{OMe}, R^2 = \text{Me}, R^3 = \text{Ph}, R^4 = \text{H}$   
 (5)  $R^1 = \text{OEt}, R^2 = \text{Me}, R^3 = \text{Ph}, R^4 = \text{H}$   
 (6)  $R^1 = R^2 = R^3 = \text{Me}, R^4 = \text{D}$   
 (7)  $R^1 = R^2 = R^3 = \text{Me}, R^4 = \text{H}$   
 (8)  $R^1 = R^2 = \text{Me}, R^3 = \text{Ph}, R^4 = \text{H}$   
 (9)  $R^1 = \text{Et}, R^3 = \text{Ph}, R^2 = R^4 = \text{H}$   
 (10)  $R^1 = \text{OMe}, R^2 = \text{Me}, R^3 = \text{Ph}, R^4 = \text{H}$   
 (11)  $R^1 = \text{OEt}, R^2 = \text{Me}, R^3 = \text{Ph}, R^4 = \text{H}$   
 (12)  $R^1 = R^2 = R^3 = \text{Me}, R^4 = \text{D}$



in acetonitrile which yielded the lactone (12) deuteriated at C-3. This deuterium transfer was intramolecular since irradiation of equal amounts of the 4,6-*O*-ethylidene[1-<sup>2</sup>H]ketone (6) and the 4,6-*O*-benzylidene-ketone (2) in acetonitrile gave the 4,6-*O*-ethylidene[3-<sup>2</sup>H]lactone (12) and the 4,6-*O*-benzylidene-lactone (8). Products arising by intermolecular hydrogen or deuterium abstraction from C-1, a reaction known<sup>5</sup> to occur with simple 2-alkoxytetrahydropyran derivatives, were not observed.

A mechanism in keeping with these results and established phototransformations is set out in Scheme 1. Formation of enal (14) from the biradical (13) produced by  $\alpha$ -cleavage<sup>6</sup> nicely accounts for the transfer of hydrogen from C-1 to C-3. The mode of subsequent C-2-C-3 bond formation is more obscure. Intramolecular Paterno-Buchi<sup>7</sup> generation of an oxetane could afford a 2,6-dioxabicyclo[3.1.1]heptane system [*i.e.* (16)] which contains the required bond. Although unsubstituted structures of this type have not been synthesised,<sup>‡</sup> carbohydrate analogues<sup>8</sup> and a 7,7-difluoro derivative have,<sup>9</sup> and they show a susceptibility to acid catalysed nucleophilic oxetane ring opening similar, although greatly attenuated, to that for the oxetane ring in thromboxane A<sub>2</sub>.<sup>10</sup> Thus (16) could afford the lactone (7) via (15).

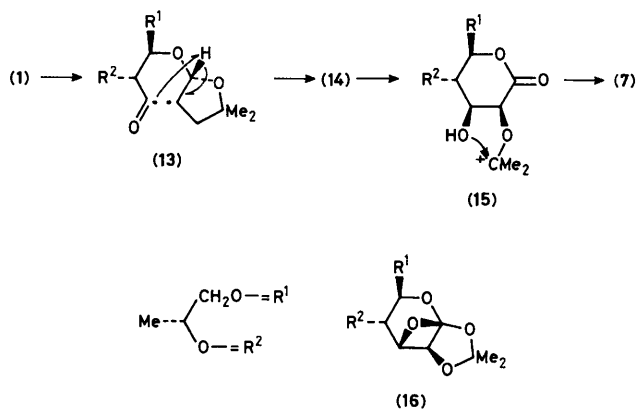
However a shortcoming with this mechanism is the orientation assumed in the oxetane ring formation which is difficult to justify. § Furthermore, the enal (14) would reach a detectable concentration during this process, but n.m.r. spectroscopic examination of a solution of (1) in CD<sub>3</sub>CN under u.v. irradiation revealed no aldehyde (14).

Consequently, it is proposed that (14) is rapidly transformed into (15) by intramolecular nucleophilic attack at the carbonyl group by the terminal carbon of the electron rich double bond. ¶ Subsequent ring closure converts (15) into the

‡ Added in proof. After this manuscript was submitted, an example of this ring system without electronegative substituents was reported, S. S. Bhagwat, P. R. Hamann, and W. C. Still, *Tetrahedron Lett.*, 1985, 1955.

§ Formation of a 2,6-dioxabicyclo[3.2.0]heptane system is at least as attractive as the one proposed.

¶ Addition of methanol to 3-(isopropenyloxy)propanal with concomitant ring closure to give 4-hydroxy-2-methoxy-2-methyltetrahydropyran (see ref. 11) could be related to this reaction.



Scheme 1

lactone (7). It is significant that irradiation of (1) in aqueous acetonitrile gave the 4,6-*O*-ethylidene-D-mannono-1,5-lactone. Since it was found that the isopropylidene group in (7) is not hydrolysed under these aqueous reaction conditions it would appear that (15) is trapped by water to give a hemiacetal which then affords the partially deblocked lactone.

Conformational factors could account for the stereochemistry of the product. The approach of the double bond from above the carbonyl group in (14a) would yield the *allo*-compound, but this is restricted because of an interaction between the erstwhile H-3 and axial H-4 atoms. On the other hand the alternative conformation (14b) in which the double bond approaches the carbonyl from below, is not sterically unfavourable and yields (15) with a *manno*-configuration.

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