

## Novel Carbocyclization of a D-Glucose-derived Alkene

Derek Horton and James P. Roski

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210, USA

Cyclopentadiene reacts with a D-glucose-derived hex-3-ene derivative to give norbornene derivatives attached at the 2,3-position of a 1,6-anhydrohexose skeleton; although the bicyclic enone isolevoglucosenone is a plausible intermediate in this reaction, the products actually appear to arise through initial cycloaddition to a rearranged acyclic sugar derivative with subsequent generation of the anhydro ring.

The alkene **1**, 3-deoxy-1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-erythro-hex-3-enofuranose, obtainable in 84% yield by base-catalysed elimination [KOBU<sup>t</sup> (3 equiv.)] in THF (tetrahydrofuran) during 2 h at 0 °C from a 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucopyranose 3-toluene-*p*-sulfonate precursor,<sup>1</sup> reacts with cyclopentadiene (2 equiv.) under catalysis by ZnCl<sub>2</sub> (1 mol dm<sup>-3</sup>) in diethyl ether (0.5 equiv.) in benzene during 1 h at 45 °C to afford 34% of a dextrorotatory product **2**, C<sub>11</sub>H<sub>12</sub>O<sub>3</sub>, having m.p. 94–95 °C, [ $\alpha$ ]<sub>D</sub> +121 (CHCl<sub>3</sub>). Accompanying **2** is 16% of an isomeric, laevorotatory product **3**, m.p. 107–108 °C, [ $\alpha$ ]<sub>D</sub> –199, along with 3% of an additional isomer **4**, m.p. 107–108 °C, [ $\alpha$ ]<sub>D</sub> +178, plus a very low proportion of a fourth isomer **5**.

The evidence, notably of <sup>13</sup>C NMR spectroscopy, demonstrated that all four products may be formally considered as the four possible stereoisomeric Diels–Alder adducts of cyclopentadiene to the 2,3-double bond of 'isolevoglucosenone' (1,6-anhydro-2,3-dideoxy- $\beta$ -D-glycero-hex-2-enopyranos-4-ulose, **6**), as illustrated by the data shown (Fig. 1)

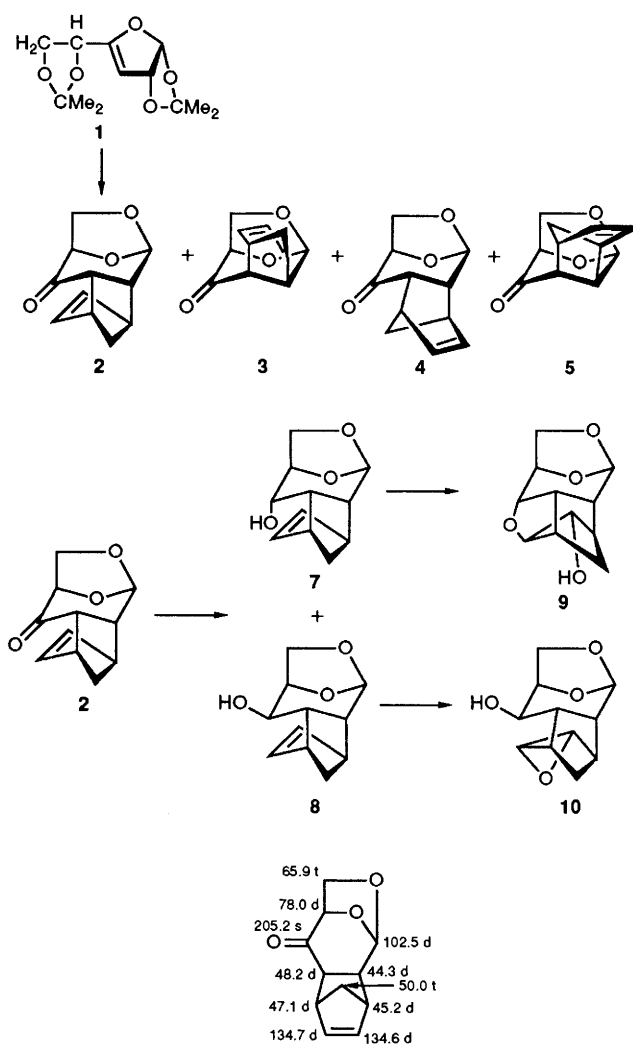


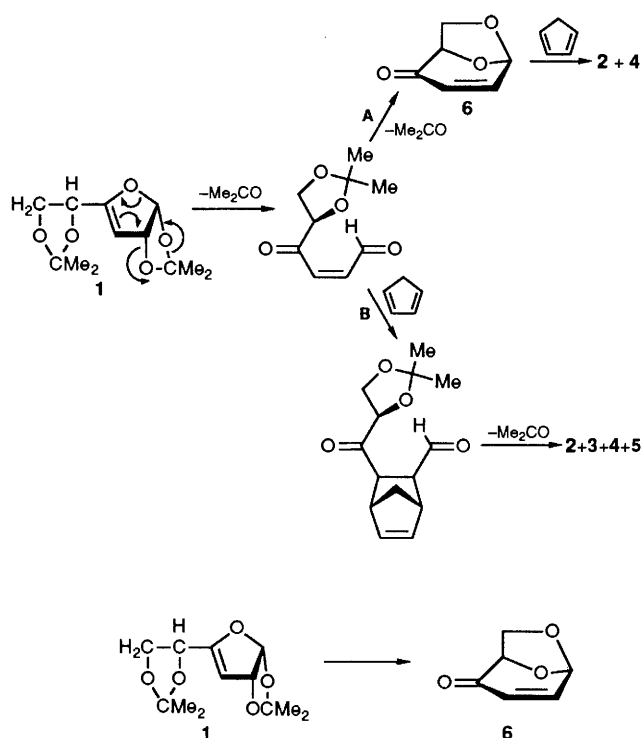
Fig. 1 <sup>13</sup>C NMR data for compound **2**

for the preponderant product **2**. The stereoisomeric identity of **2** was established as 'down-endo' by borohydride reduction to the 4-epimeric alcohols **7** (axial, 43%, m.p. 90–92 °C, [ $\alpha$ ]<sub>D</sub> –61.1 in CHCl<sub>3</sub>) and **8** (equatorial, 45%, m.p. 111–113 °C, [ $\alpha$ ]<sub>D</sub> +18.8 in CHCl<sub>3</sub>), converted by *m*-chloroperoxybenzoic acid into the polycyclic alcohol **9**, m.p. 143–144 °C, [ $\alpha$ ]<sub>D</sub> –104 in CHCl<sub>3</sub>, and the oxirane **10**, m.p. 154–156 °C, [ $\alpha$ ]<sub>D</sub> +11° in CHCl<sub>3</sub>, respectively; this confirms the structural attribution for **2**, which was also supported by <sup>1</sup>H NMR data and by a crystal structure analysis of alcohol **9**.

Adduct **3** was determined to be the 'up-endo' isomer and **4** the 'down-exo' isomer from NMR coupling and NOE data, which provide clear differentiation between the facial addition modes (*J*<sub>1,2</sub>: for **2**, 0; **3**, 4.3; **4**, 0 and **5**, 4.3 Hz, respectively).

Formation of the products observed in this reaction may be rationalized as resulting from net deacetonation of **1**, migration of the double bond to the 2,3-position with generation of carbonyl functionality at C-4 and C-1, together with cycloaddition to the 2,3 double bond and internal acetal formation between C-1 and O-5 and O-6. Two plausible sequences may be formulated involving electrophilic catalysis initiated at O-2 and proceed either (a) by initial formation of 'isolevoglucosenone' **6** which subsequently reacts with cyclopentadiene, or alternatively (b) Diels–Alder addition at the stage of an acyclic sugar derivative and subsequent closure of the anhydro ring.

The observed formation of topside adduct **3** militates against pathway (a) from steric considerations and by the behaviour of the 2-keto-3-ene isomer ('levoglucosenone') of **6** under similar conditions.<sup>2</sup> A sample of 'isolevoglucosenone' **6**, prepared by a multi-step sequence,<sup>3</sup> when allowed to react in



benzene at 47 °C with cyclopentadiene (2 equiv.) under  $ZnCl_2$  catalysis (0.5 equiv.), afforded uniquely in net 82% yield the two products (**2** and **4**, in 4:1 ratio) of lower-face addition, further supporting pathway (*b*).

The highly reactive enone **6**, having a multiplicity of useful selective reaction modes, is a potentially valuable chiral synthon, but its established syntheses<sup>3,4</sup> require multiple steps and proceed in only low to moderate yield. A convenient one-step access to **6** from alkene **1** was established by treating a solution of **1** in ether-pentane (3:2) with  $AlCl_3$  (0.5 equiv.) for 10 min at 0 °C, to yield 30–32% (flash chromatography) of **6**,  $[\alpha]_D +412$  ( $CHCl_3$ ). The chiral, strained enone **6** thus

readily available in four simple steps from D-glucose constitutes an attractive chiral synthon for a wide variety of targets.

*Received, 23rd December 1991; Com. 1106434G*

### References

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