Novel Carbocyclization of a D-Glucose-derived Alkene

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Cyclopentadiene reacts with a D-glucose-derived hex-3-enose 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-α-D-*erythro*-hex-3-enofuranose, obtainable in 84% yield by base-catalysed elimination [KOBu^t (3 equiv.) in THF (tetrahydrofuran) during 2 h at 0 °C] from a 1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose 3-toluene-*p*-sulfonate precursor,[1] reacts with cyclopentadiene (2 equiv.) under catalysis by $ZnCl_2$ (1 mol dm^{-3}) in diethyl ether (0.5 equiv.) in benzene during 1 h at 45 °C to afford 34% of a dextrorotatory product **2**, $C_{11}H_{12}O_3$, having m.p. 94–95 °C, $[\alpha]_D$ +121 ($CHCl_3$). Accompanying **2** is 16% of an isomeric, laevorotatory product **3**, m.p. 107–108 °C, $[\alpha]_D$ −199, along with 3% of an additional isomer **4**, m.p. 107–108 °C, $[\alpha]_D$ +178, plus a very low proportion of a fourth isomer **5**.

The evidence, notably of ^{13}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-β-D-*glycero*-hex-2-enopyranos-4-ulose, **6**), as illustrated by the data shown (Fig. 1)

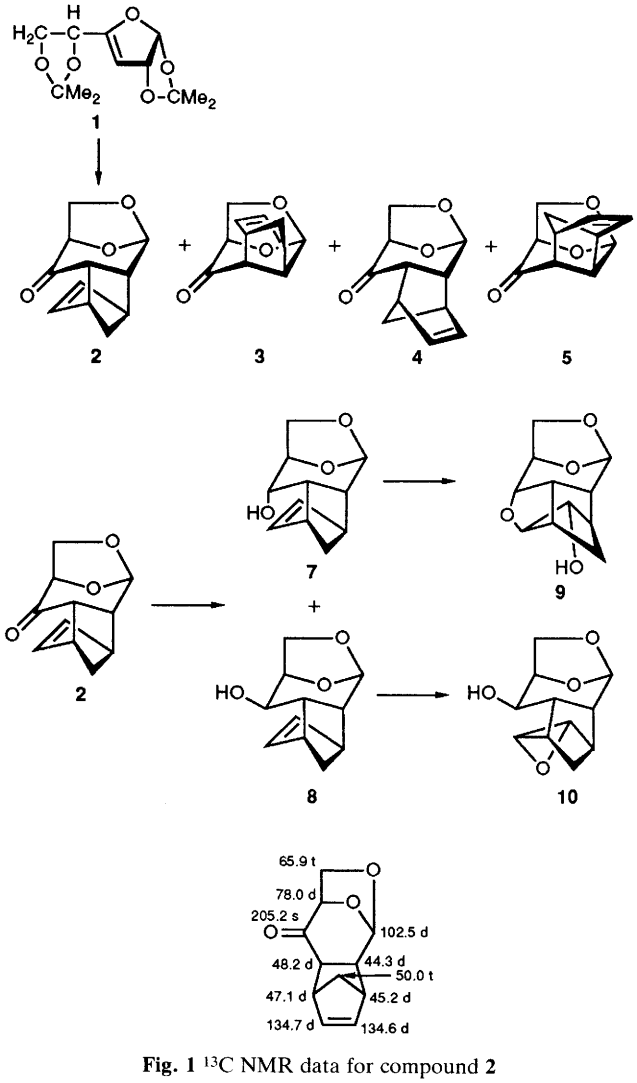


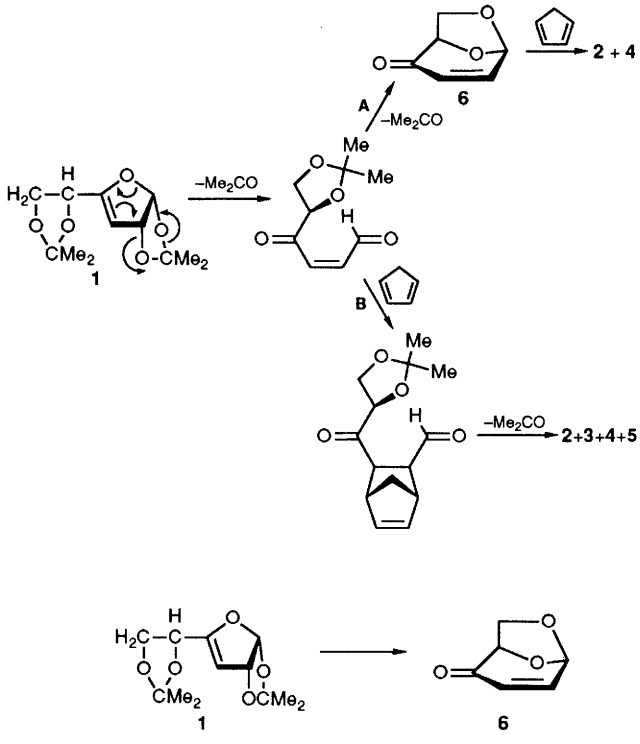
Fig. 1 ^{13}C NMR data for compound **2**

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, $[\alpha]_D$ −61.1 in $CHCl_3$) and **8** (equatorial, 45%, m.p. 111–113 °C, $[\alpha]_D$ +18.8 in $CHCl_3$), converted by *m*-chloroperoxybenzoic acid into the polycyclic alcohol **9**, m.p. 143–144 °C, $[\alpha]_D$ −104 in $CHCl_3$, and the oxirane **10**, m.p. 154–156 °C, $[\alpha]_D$ +11° in $CHCl_3$, respectively; this confirms the structural attribution for **2**, which was also supported by ^1H 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 ($J_{1,2}$: 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.[2] A sample of 'isolevoglucosenone' **6**, prepared by a multi-step sequence,[3] 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[3,4] 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.

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