Addition Reactions of a 2,3-Unsaturated Sugar

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DERIVATIVES of unsaturated sugars are useful models for the study of addition reactions to carbon–carbon double bonds, as precise stereochemical information on the products is readily obtained. With suitable derivatives it is possible to vary the nature and orientation of substituents in the vicinity of the double bond, and to control the flexibility of the molecule by use of various cyclic and bridged-ring systems. Products of such addition reactions are frequently useful for synthesis of rare and modified sugars. Recently reports[1] have described the addition of the elements of "BrF" and "IF" to 3,4,6-tri-*O*-acetyl-D-glucal, a 1,2-unsaturated derivative that has a strongly polarized double bond which is part of a cyclic enol–anhydride system. We describe the addition of various electrophiles to the *cis*-alkene system of methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside[2] (I). This alkene is probably somewhat polarized because the combined inductive effects on one allylic carbon atom (C-1) exceed those on the other (C-4).

Attempts to brominate (I) in an inert solvent led to complex, unstable mixtures.[3] Treatment of 3 g. of (I) in dry methanol with an excess of bromine at room temperature in the presence of $BaCO_3$ and a soluble inorganic salt gave 3·45 g. (70%) of a crystalline dibromide,† m.p. 79—81°, $[\alpha]_D^{20}$ + 72·5° (*c* 1, chloroform). This was formulated as methyl 4,6-*O*-benzylidene-2,3-dibromo-2,3-dideoxy-α-D-altropyranoside (II) on the basis of n.m.r. spectroscopic data,‡ which agreed with data[4] on related derivatives. In C_6D_6 the adduct (II) showed narrow multiplets at τ 5·31, 5·67, and 5·50, assigned to H-1, H-2, and H-3, respectively. The observed $J_{2,3}$ and $J_{3,4}$ couplings were 2—4 Hz, and small (*ca.* 1 Hz) $J_{1,2}$ and $J_{1,3}$ couplings were observed.

The dibromide (II) was refluxed in xylene with an excess of potassium t-butoxide, to yield crystalline methyl 4,6-*O*-benzylidene-2-bromo-2,3-dideoxy-α-D-*threo*-hex-3-enopyranoside (III) (90%) m.p. 187—189°, $[\alpha]_D^{20}$ + 77 ± 1° (*c* 1, chloroform). The structure was indicated by n.m.r.spectroscopy in $CDCl_3$: τ 5·18 (brs, $J_{1,2}$ < 1 Hz, H-1), τ 5·86 (H-2), τ 3·58 ($J_{2,3}$ *ca.* 1 Hz, H-3). No product of 1,2-elimination (*cis*) was evident under these severe reaction conditions, probably because the presence of two oxygen atoms at C-1 inhibits removal of H-1 as a proton.

A solution of (I) in carbon tetrachloride was kept for 14 hr. at 4° with an excess of acetyl hypobromite in carbon tetrachloride. The major product had m.p. 171—173°, $[\alpha]_D^{20}$ + 89 ± 1° (*c* 1, chloroform) and was identified by n.m.r. spectroscopy in C_6D_6 as methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-bromo-2-deoxy-α-D-glucopyranoside (IV); it showed the H-1, H-2, and H-3 signals at τ 5·50, 6·28, and 4·13, respectively, with couplings $J_{1,2}$ 3·5, $J_{2,3}$ 11, and $J_{3,4}$ 9·5 Hz. A second, isomeric adduct, isolated in addition to (IV) and formed to a greater extent at lower temperatures of reaction, had m.p. 101—103° and was formulated as methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-bromo-3-deoxy-α-D-altropyranoside (V); in C_6D_6 it showed the H-1, H-2, and H-3 signals at τ 5·44, 4·59, and 5·75, respectively, with $J_{1,2}$ < 1, $J_{2,3}$ *ca.* 2·5, and $J_{3,4}$ *ca.* 3·5 Hz.

Treatment of (I) with methanolic mercuric acetate for 5 days at room temperature gave a crystalline MeO–HgOAc adduct, m.p. 179—180°.

The alkene (I) was inert toward carbene-type reagents and gave back unchanged starting material when treated under forcing conditions with ethoxycarbonylcarbene [from ethyl diazoacetate at 110° in the presence of copper(II) sulphate], and with dichlorocarbene (from ethyl trichloroacetate and strong, non-aqueous base). However, under the Simmons–Smith[5] conditions it was possible to prepare a crystalline cyclopropyl derivative (VI), m.p. 126—128°, whose structure was confirmed by mass-spectrometric and n.m.r. data; the configuration shown is supported by a mechanistic rationale[6] based on the directive influence of O-1 and O-3, and by the $J_{1,2}$ coupling (5 Hz). Degradative studies are in progress to furnish independent verification of the configuration of (VI) and the other adducts described.

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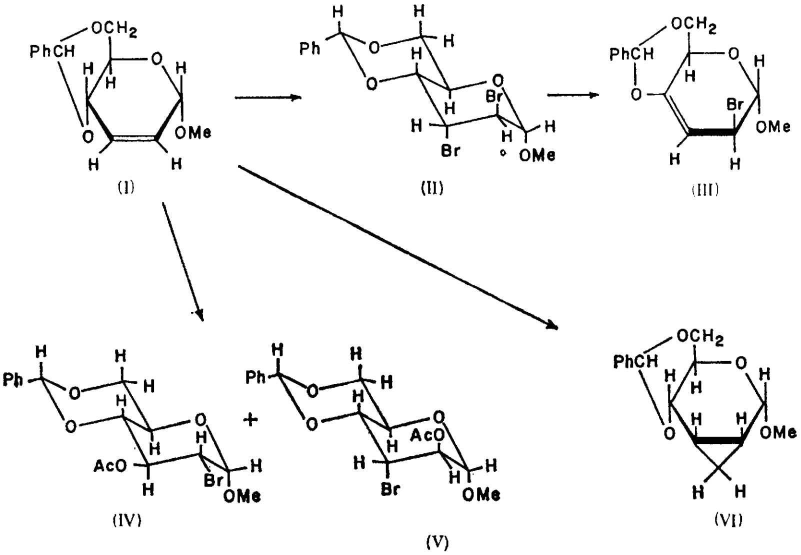
† All products described gave satisfactory elemental analyses, were homogeneous by t.l.c., and gave i.r. and n.m.r. spectra in agreement with the structures assigned. Spin-decoupling was used to verify the H-1, H-2, and H-3 assignments in the adducts (II)—(V).

‡ N.m.r. spectra were measured at 100 MHz with a Varian HA-100 n.m.r. spectrometer and chemical shifts refer to an internal standard of tetramethylsilane.



The results indicate that addition reactions to alkenes such as (I) can be effected with a high degree of stereoselectivity, and thus have potential in synthetic carbohydrate chemistry. The reaction leading to (II) is undoubtedly ionic, while the additions leading to (IV) and (V) are probably free-radical processes.

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