1,6-Anhydro-4-deoxy-4-diazo-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranose, A Stable Diazo-sugar from a Keto-sugar Precursor

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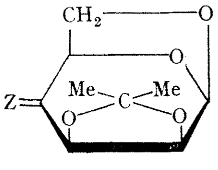
Summary The keto-sugar derivative 1,6-anhydro-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranos-4-ulose (I) has been converted by way of the sodium salt of its 2,4,5-trichlorobenzenesulphonylhydrazone into 1,6-anhydro-4-deoxy-4-diazo-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranose (IV); this diazo-sugar can be sublimed without decomposition and derivatives of this type are of potential value in synthesis of branched-chain and other modified sugars.

IN the carbohydrate field, chain-terminal diazo-derivatives (diazomethyl ketones, RCO·CHN_2) have been prepared by the action of diazomethane on fully acetylated aldonyl chlorides, and afford a convenient route from aldoses to higher ketoses.[1] With the advent of good preparative methods for fully protected keto-derivatives of carbohydrates[2,3] it was of interest to explore the Bamford–Stevens route[4] as a possible method for introducing a non-terminal diazomethyl group ($R^1R^2CN_2$) into a carbohydrate chain. We describe the conversion of a 4-keto-sugar derivative, 1,6-anhydro-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranos-4-ulose,[2] (I), in good yield into the corresponding 4-diazo-derivative (IV), a stable, yellow, crystalline compound.

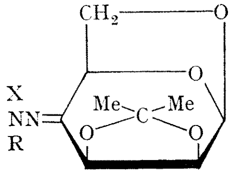
The ketone[2] (I) (500 mg.) was added to a hot solution of

2,4,5-trichlorobenzenesulphonic acid hydrazide (560 mg.) in methanol (3 ml.) and ethyl acetate (sufficient for dissolution of the hydrazide). The solution was kept for 1 hr. at 30° and 18 hr. at 0°, and then evaporated. Crystallization of the residue from ethanol gave the 2,4,5-trichlorobenzenesulphonylhydrazone (II), yield 510 mg. (44%), m.p. 187—189° (decomp.), $[\alpha]^{20}_{D}$ $-$ 42·6 ± 1° (*c* 3·5, chloroform); λ_{max} (KBr) 6·42 μm. (C=N); n.m.r. data [100 MHz., $(CD_3)_2CO$: τ $-$0·11 (1H singlet, disappeared on deuteriation, NH), 1·79, 2·05 (1H singlets, aryl protons), 8·49, 8·62 (3H singlets, CMe_2). A suspension of (II) (200 mg.) in hexane was heated under reflux for 1·5 hr. with an excess of oil-free sodium hydride, and the solvent was evaporated. The flask containing the resultant salt (III) was fitted with a vacuum adaptor and a cold-finger condenser. Pyrolysis[4] of the residue for 3 hr. at 120° and 0·1 Torr gave a yellow solid on the condenser, yield 68 mg. (73%). Recrystallization of the solid from ethyl ether gave the diazo-derivative (IV) as fine, yellow needles, m.p. 107—108° (decomp.), $[\alpha]^{20}_{D}$ *ca.* 0° (*c* 0·6, diethyl ether), λ_{max} (hexane) 4·82, 5·06 μm. ($=N_2$)[5]; n.m.r. data (100 MHz, C_6D_6, first-order spectrum, assignments also verified by spin-decoupling): τ 4·69 (1H doublet, $J_{1,2}$ 2·7 Hz, 1-H), 5·54 (1H quartet, $J_{2,3}$ 6·5, $J_{3,5}$ 0·9 Hz, 3-H), 5·83 (1H broadened doublet, $J_{5,6exo}$ 5·0 Hz, 5-H), 6·22 (1H doublet, $J_{6exo,6endo}$ 6·8 Hz, $J_{5,6endo}$ 0 Hz,*endo*-6-H), 6·38 (1H quartet, 2-H), 6·66 (1H quartet, *exo*-6-H), 8·39, 8·82 (3H singlets, CMe_2). The diazo-derivative (IV) in diethyl ether showed a positive Cotton effect in its o.r.d. spectrum (max. at 488 nm., zero at 442 nm.) and a positive c.d. curve centred at 455 nm.; these observations contrast with those for the starting ketone (I), which exhibits[2] a negative c.d. curve and a negative Cotton effect in its o.r.d. spectrum.

The diazo-derivative (IV), and analogues prepared from other conveniently accessible keto-sugars[2,3] such as 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose [3-diazo-derivative, $\lambda_{max}(Et_2O)$ 4·72 μm, *m/e* 270, 255, 242, and 227] and 1,6-anhydro-3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranos-2-ulose should prove useful in synthesis of a wide range of novel sugar derivatives of chemotherapeutic interest, especially in the field of modified nucleosides as potential carcinolytes. By carbenoid-type reactions induced photolytically or thermolytically, the diazo-derivatives offer routes to spiro-alkyl derivatives (by reaction with alkenes), and to unsaturated sugars of the enol-ether type (by a hydride shift). Insertion reactions and various reactions with polar species may be useful for introducing unusual elements and novel functionality (including *gem*-dialkyl groups) at the site of the original keto-group. Carbohydrate diazo derivatives of this type also offer possibilities for studying the stereochemical course of carbenoid reactions in an environment of rigidly controlled molecular geometry.



(I) Z=O
(IV) Z=N_2



(II) R=H; (III) R=Na
[X=2,4,5-trichlorobenzenesulphonyl]

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[1] M. L. Wolfrom, D. I. Weisblat, W. H. Zophy, and S. W. Waisbrot, *J. Amer. Chem. Soc.*, 1941, **63**, 201.

[2] D. Horton and J. S. Jewell, *Carbohydrate Res.*, 1966, **2**, 251; 1967, **5**, 149; D. Horton and E. K. Just, *ibid.*, 1969, **9**, 129.

[3] P. J. Beynon, P. M. Collins, and W. G. Overend, *Proc. Chem. Soc.*, 1964, 342; W. Sowa and G. H. S. Thomas, *Canad. J. Chem.*, 1966, **44**, 836; *cf.* J. S. Brimacombe, *Angew. Chem.*, 1969, **81**, 415.

[4] W. R. Bamford and T. S. Stevens, *J. Chem. Soc.*, 1952, 4735; L. F. Friedman and H. Shechter, *J. Amer. Chem. Soc.*, 1959, **81**, 5512; H. Shechter, personal communication.

[5] P. Yates, B. L. Shapiro, N. Yoda, and J. Fugger, *J. Amer. Chem. Soc.*, 1957, **79**, 5756.