New Synthetic Route to 2′,3′-Unsaturated Pyranosyl Thymine from the Corresponding O^2,2′-Cyclonucleoside

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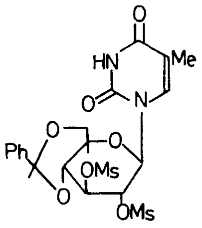
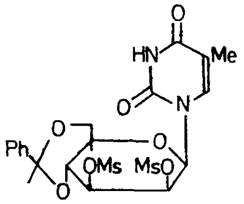
Summary Treatment of the O^2,2′-cyclonucleoside (**3**) with NaI–Zn gives the corresponding 2′,3′-unsaturated nucleoside (**4**) in fair yield.

In view of their physiological significance, nucleoside derivatives having double bonds between C-2 and C-3 of the sugar residues have received special attention.[1] Nucleosides of this type are also useful intermediates for the synthesis of many biologically important compounds. We describe here that 2′,3′-unsaturated pyranosyl thymine can be formed from the O^2,2′-cyclonucleoside precursor.

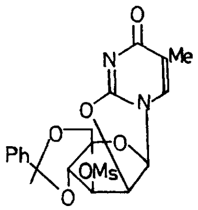
Compound (**1**) was prepared by the nitromethane–mercuric cyanide method.[2] Treatment of (**1**) with sodium benzoate (1 equiv.) in *NN*-dimethylformamide (DMF) at 120° for 1 h gave a new crystalline product (**3**) in quantitative yield, m.p. 249·5—251° (decomp.); $[\alpha]_D^{18}$ — 176° (*c*, 1·0 Me_2SO); λ_{max} (EtOH) 253 nm, λ_{min} (EtOH) 222 nm; δ $[(CD_3)_2SO]$ 7·90 (1H, s), 7·42 (5H, s, ArH), 6·15 (1H, d, $J_{1',2'}$ 3·0 Hz, H-1′), 5·80 (1H, s, H-7′), 5·3—5·7 (2H), 3·75—4·35 (4H), 3·30 (3H, s, $MeSO_2$), and 1·85 (3H, s, Me); *m/e* 436 (M^+).‡ Reaction of (**3**) with a 20-fold excess of NaI–Zn[3] in refluxing DMF for 2 h led to the disappearance of starting material (R_f 0·25) and the formation of one



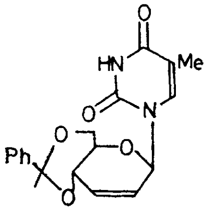
(1)



(2)



(3)



(4)

Ms = $MeSO_2$

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‡ Satisfactory analytical data were obtained.

major (less polar) product (R_f 0·6) and two minor (polar) products (R_f 0·2, 0·05) by t.l.c. (Merck, Kieselgel GF 60); (benzene–ethanol, 5:1). The less polar product in chloroform solution was precipitated by addition of 50% aq. EtOH. After this procedure had been performed twice, the homogeneous crystalloid material (**4**) was obtained in 44% yield, m.p. 242·5—243·5° (decomp.) (from Me_2CO or MeCN–EtOH), $[\alpha]_D^{18°}$ + 85·3° (*c*, 0·75 MeCN); λ_{max} (EtOH) 262 nm, λ_{min} (EtOH) 233 nm; δ [$(CD_3)_2SO$] 7·45 (5H, ArH), 7·18 (1H, s), 6·65 (1H, d, $J_{1',2'}$ 2·2 Hz, H-1′), 6·50 (1H, d, $J_{2',3'}$ 10·5 Hz, H-3′), 5·76 (1H, q, $J_{1',2'}$ 2·2, $J_{2',3'}$ 10·5 Hz, H-2′), 5·72 (1H, s, H-7′), 3·8—4·7 (4H) and 1·90 (3H, s, Me);[4] *m/e* 342 (M^+).‡ NaI and Zn were both essential in this reaction. This is the first example of the conversion of a O^2,2′-cyclonucleoside into the corresponding unsaturated nucleoside.§

Albano *et al.*[5] have reported the reaction of the disulphonic group of a cyclic sugar system with NaI–Zn in refluxing DMF, which was originally used in the conversion of an acyclic disulphonated cyclitol into the unsaturated compound by Tipson and Cohen.[6] Under the same conditions, the reaction of (**1**) gave a mixture of (**3**) and (**4**) in poor yield (10%). This result indicates that the reaction conditions might not be basic enough to cyclise (**1**) into (**3**). Moreover, treatment of (**2**) (δ 6·16, d, $J_{1',2'}$ 0·7 Hz, H-1′),[7] which is a 2′-epimer of (**1**) having the same configuration as (**3**), gave no unsaturated product under the same conditions. Thus application of the Tipson–Cohen reaction to disulphonic esters of pyranosyl nucleosides was unsuccessful¶ for the synthesis of 2′,3′-unsaturated nucleosides since these sulphonated nucleosides are unstable and rapidly change into unidentified compounds under these conditions. However, the formation of a double bond between C-2 and C-3 of the sugar unit of pyranosyl thymine is conveniently performed by using O^2,2′-cyclo type nucleosides as precursors.

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§ Horwitz *et al.* reported the introduction of 2′,3′-unsaturation into the furanosyl unit of pyrimidine nucleosides from 2′-deoxy-O^2,3′-cyclonucleosides by base-catalysed elimination (J. P. Horwitz, J. Chua, M. A. Da Rooge, M. Noel, and I. L. Klundt, *J. Org. Chem.*, 1966, **3**, 205).

¶ Recently Anzai *et al.* reported application of this reaction to disulphonated furanosyl nucleosides which are impossible to cyclise between the base and the sugar part (K. Anzai, and M. Matsui, *Agric. Biol. Chem.* (*Japan*), 1973, **37**, 345).

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