Tetrahedron Letters No.38, pp. 2725-2727, 1964. Pergamon Press Ltd.
Printed in Great Britain.

NUCLEOSIDES. VIII. SYNTHESIS OF 2',3'-UNSATURATED PYRIMIDINE NUCLEOSIDES FROM OXETANE DERIVATIVES

J. P. Horwitz, J. Chua, M. A. Da Rooge and M. Noel

Rollin H. Stevens Memorial Laboratory, Detroit Institute of Cancer Research, Detroit, Michigan 48201, U.S.A.

(Received 27 July 1964)

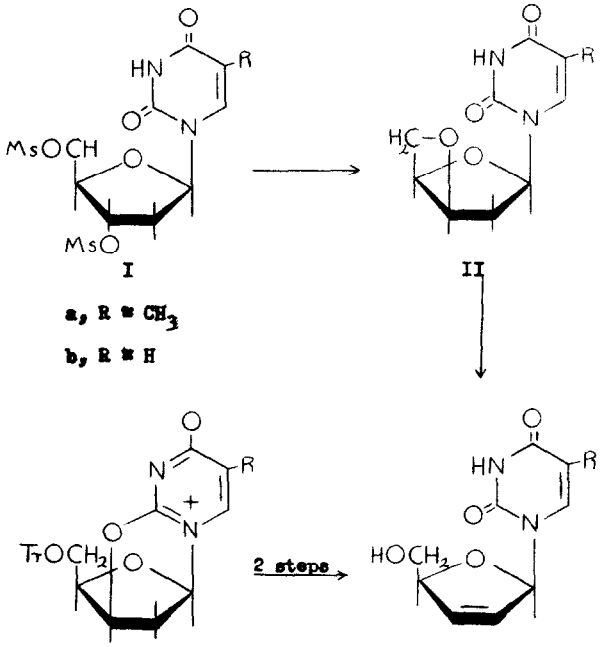
Unsaturated nucleosides are of current interest (1) as possible intermediates in the biosynthesis of purine and pyrimidine deoxyribonucleotides from the corresponding ribonucleotides. A recent communication (2) from this laboratory described the introduction of a 2',3'-double bond into a pyrimidine nucleoside by the action of potassium t-butoxide on a 2'-deoxy-2,3'-anhydronucleoside in dimethyl sulfoxide (DMSO). We wish now to report a base-induced elimination reaction in which an oxetane ring comprises the leaving group* and which results in the formation of 2',3'-unsaturated nucleosides in high yield.

Treatment of 1-(2'-deoxy-3',5'-epoxy-β-D-threo-pentofuranosyl) thymine (IIa) (3) with two equivalents of potassium t-butoxide in DMSO at room temperature for 2 hr. gave a solid (79% yield), m.p. 165-166°, $[\alpha]_D^{25}$ - 42° with properties consistent with 1-(2',3'-dideoxy-2'-ene-β-D-glycero-pentofuranosyl)thymine (IIIa) (Found: C, 53.4; H, 5.4; N, 12.3)**. An

* R. E. Gramera, T. R. Ingle and P. Whistler [J. Org. Chem. 29, 878, 1083 (1964)] have recently reported a sodium methoxide-catalyzed elimination reaction of a secondary tosyloxy group in a D-glucofuranose structure which leads to exocyclic olefin-bond formation. One of two reaction paths proposed by these authors includes the formation of an oxetane ring intermediate, which, unfortunately, could not be trapped.

** An attempt to effect the same elimination reaction with sodium methoxide was unsuccessful.

identical product was obtained from the action of the same base-solvent system on 2,3'-anhydro-1-(2'-deoxy-5'-O-trityl-β-D-lyxosyl)thymine (IV) (3) followed by detritylation of the protected olefin. Catalytic (10% Pd-C) reduction of IIIa, obtained by either route, gave the known 3'-deoxythymidine (4,5).



I II

a, R = CH_3

b, R = H

IV III

The same conditions of elimination applied to 1-(2'-deoxy-3',5'-epoxy-β-D-threo-pentofuranosyl)uracil (IIb), m.p. 208-210°, $[\alpha]_D^{25}$ - 125° (Found: C, 51.4; H, 4.7; N, 13.3) gave the previously described 1-(2',3'-dideoxy-2'-ene-β-D-glycero-pentofuranosyl)uracil (IIIb) (2) in 76% yield. The oxetane derivative, IIb, was obtained by the action of aqueous sodium hydroxide on 3',5'-di-O-mesyl-2'-deoxyuridine (Ib), m.p. 145-146.5°, $[\alpha]_D^{25}$ + 16°, (Found: C, 34.4; H, 4.3; N, 7.2), according to the procedure

described previously (3) for the synthesis of IIa from Ia. Catalytic reduction of IIIb gave 2',3'-dideoxyuridine (4).

Acknowledgment.--This investigation was supported in part by Public Health Service Research Grants No. CA-02903 and No. CY-5943 from the National Cancer Institute and in part by an institutional grant to the Detroit Institute of Cancer Research from the United Foundation of Greater Detroit allocated through the Michigan Cancer Foundation.

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