

occurring through the  $\pi$ -electrons of the nitrogen-nitrogen double bond.

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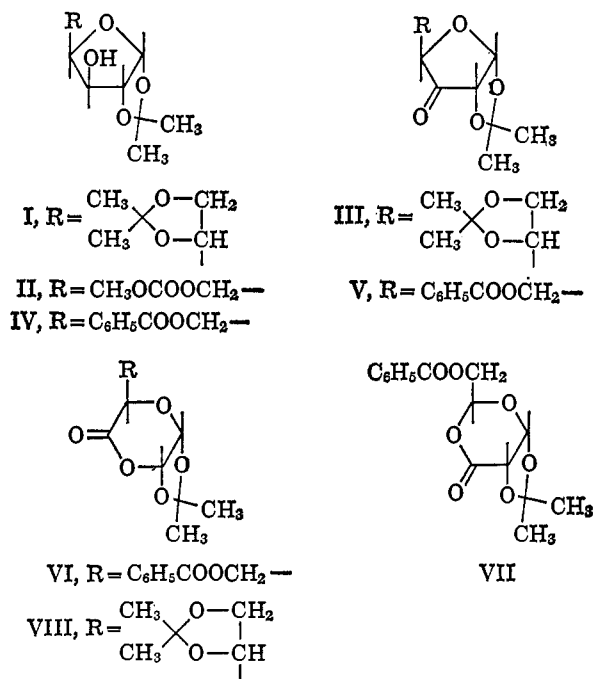
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## An Oxygen Insertion Reaction of Osuloses

Sir:

As a starting point for further synthetic work we were interested in preparing a suitably constituted 3-ketofuranose. To this end, both 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucufuranose (I) and 5-carbomethoxy-1,2-*O*-isopropylidene- $\alpha$ -D-xylofuranose (II) were sub-



jected to several oxidizing conditions in an attempt to convert the free 3-hydroxyl to a keto function. However, none of the oxidizing agents, which included chromium trioxide in pyridine, acetone, and acetic acid, aluminum isopropoxide in acetone, potassium permanganate in acetone, and lead tetraacetate in benzene, gave a useful amount of the desired product. Either complex mixtures or unreacted starting materials were obtained. During the course of this work a new method for oxidizing hindered hydroxyl groups in carbohydrate derivatives using ruthenium tetroxide<sup>1</sup> was reported,<sup>2</sup> whereby 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucufuranose was converted into 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-ribo-3-hexulofuranose (III). Another group recently reported<sup>3</sup> that an oxidation of 5-*O*-benzoyl-1,2-*O*-isopropylidene- $\alpha$ -D-xylofuranose (IV) with chromium trioxide in *t*-butyl alcohol gave 5-*O*-benzoyl-1,2-*O*-isopropylidene- $\alpha$ -D-erythro-3-pentulofuranose (V). We have applied the ruthenium tetroxide procedure to the oxidation of IV [ $\lambda_{\text{max}}^{\text{Nujol}}$  2.8 (hydroxyl)

(1) Prepared from ruthenium dioxide obtained from Englehard Industries, Newark, N. J. For other oxidations using ruthenium tetroxide see L. M. Berkowitz and P. N. Rylander, *J. Am. Chem. Soc.*, **80**, 6682 (1958).

(2) P. J. Beynon, P. M. Collins, and W. G. Overend, *Proc. Chem. Soc.*, 342 (1964).

(3) K. Oka and H. Wada, *Yakagaku Zasshi*, **83**, 890 (1963); *Chem. Abstr.*, **60**, 1825 (1964).

and 5.82  $\mu$  (benzoate);  $\tau^{\text{CDCl}_3}$  4.03 (C-1 proton, doublet;  $J_{1,2} = 3.5$  c.p.s.), 5.42 (C-2 proton, doublet;  $J_{2,1} = 3.5$  c.p.s.), and 5.44  $\pm$  0.42 p.p.m. (C-3, 4, 5 protons, multiplet)] and have also isolated V [ $\lambda_{\text{max}}^{\text{Nujol}}$  5.62 (cyclic ketone) and 5.77  $\mu$  (benzoate);  $\lambda_{\text{max}}^{\text{CHCl}_3}$  5.62 (cyclic ketone) and 5.81  $\mu$  (benzoate);  $\tau^{\text{CDCl}_3}$  3.87 (C-1 proton, doublet;  $J_{1,2} = 4.5$  c.p.s.) and 5.44  $\pm$  0.28 p.p.m. (C-2, 4, 5 protons, multiplet)]. The course of reaction was followed by t.l.c. (silica;  $\text{CHCl}_3$ -EtOAc, 4:1) and it was noted that, as the oxidation proceeded in the presence of excess ruthenium tetroxide, an increasing amount of an unexpected product was being formed. After 24 hr. this product, now the major product, was isolated and its elemental analysis and infrared and n.m.r. spectra indicated that it was the product of oxygen insertion, 1,2-*O*-isopropylidene-6-*O*-benzoyl-3-oxa- $\alpha$ -D-erythro-4-hexulopyranose (VI) [m.p. 111–112°;  $[\alpha]_D +81^\circ$  (c 1.03,  $\text{CHCl}_3$ );  $\lambda_{\text{max}}^{\text{Nujol}}$  5.70 (lactone) and 5.80  $\mu$  (benzoate);  $\tau^{\text{CDCl}_3}$  4.08 (C-1 proton, doublet;  $J_{1,2} = 3.8$  c.p.s.), 4.32 (C-2 proton doublet;  $J_{2,1} = 3.8$  c.p.s.), and 5.23  $\pm$  0.19 p.p.m. (C-5, 6 protons, multiplet)]. That the inserted oxygen is in the 3-position as in VI and not in the 4-position as in the isomeric VII is indicated by n.m.r. spectra. The position of the C-5 proton resonance in VI is essentially unchanged compared to that of the C-4 proton in V, whereas the C-2 proton resonance of VI shows a large downfield chemical shift compared to that of the C-2 proton in V.

Overend's<sup>2</sup> oxidation of 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-glucufuranose (I) [ $\tau^{\text{CDCl}_3}$  4.07 (C-1 proton, doublet;  $J_{1,2} = 3.8$  c.p.s.), 5.48 (C-2 proton, doublet;  $J_{2,1} = 3.8$  c.p.s.), and 5.81  $\pm$  0.26 p.p.m. (C-3, 4, 5, 6 protons, multiplet)] with ruthenium tetroxide was repeated. After a few hours the product III, as reported<sup>2</sup> previously, was produced, while after 48 hr. the product of oxygen insertion, 1,2:6,7-di-*O*-isopropylidene-3-oxa- $\alpha$ -D-ribo-4-heptulopyranose (VIII) [m.p. 62–64°;  $[\alpha]_D +86^\circ$  (c 0.5,  $\text{CHCl}_3$ );  $\lambda_{\text{max}}^{\text{Nujol}}$  5.68  $\mu$  (lactone);  $\tau^{\text{CDCl}_3}$  4.12 (C-1 proton, doublet;  $J_{1,2} = 3.7$  c.p.s.), 4.29 (C-2 proton, doublet;  $J_{2,1} = 3.7$  c.p.s.), and 5.64  $\pm$  0.34 p.p.m. (C-5, 6, 7 protons, multiplet)] was obtained.

The products VI and VIII<sup>4</sup> represent a new class of carbohydrate derivatives, and the oxygen insertion reaction is a new reaction<sup>5</sup> of ruthenium tetroxide.

(4) All compounds reported have given satisfactory elemental microanalyses.

(5) H. Nakata, *Tetrahedron*, **19**, 1959 (1963), has reported the conversion of  $\beta$ -cholestanol into 4-oxo-A-homo-5 $\alpha$ -cholestan-3-one in acetic acid solution containing excess lead tetraacetate and catalytic amounts of ruthenium tetroxide. It seems likely that in this case, as Nakata suggested, the oxygen insertion results from a Baeyer-Villiger reaction involving peracetic acid.

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## A Total Synthesis of *dl*- $\Delta^1$ -Tetrahydrocannabinol, the Active Constituent of Hashish<sup>1</sup>

Sir:

We wish to report that we have completed the first total synthesis<sup>2</sup> of *dl*-cannabidiol<sup>3</sup> (Ia) and *dl*- $\Delta^1$ -3,4-

(1) Hashish. VI. For Part V see H. Budzikiewicz, R. T. Aplin, D. A. Lightner, C. Djerassi, R. Mechoulam, and Y. Gaoni, *Tetrahedron*, in press.