Tetrahedron Letters No.45, pp.3981-3983, 1969. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF BRANCHED-CHAIN NITRO AND AMINO SUGARS VIA THE NITROMETHANE SYNTHESIS

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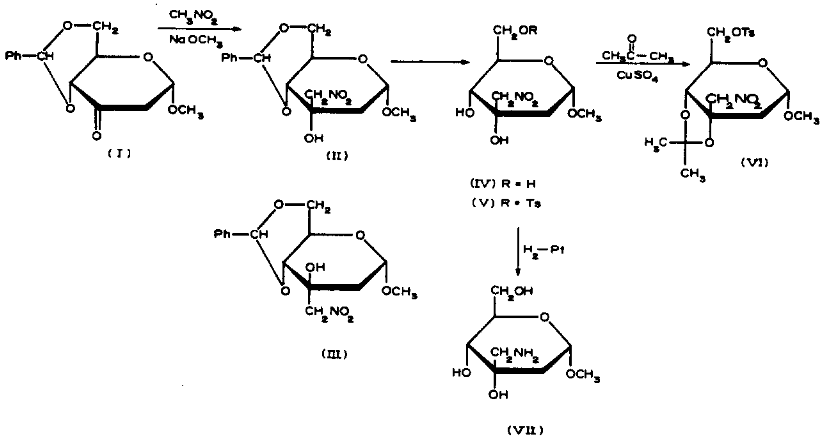
(Received in USA 3 July 1969; received in UK for publication 25 August 1969)

Numerous reports have described the condensation of aldoses and the cyclization of dialdehydes with nitromethane to afford nitro carbohydrates (1,2). The latter are of significance because of their utilization as intermediates in the synthesis of amino sugars *via* the Nef (3) or Schmidt-Rutz (1,4) reaction. In addition, there is a recent report of the occurrence of nitro sugars in some antibiotics (5). Surprisingly, to the best knowledge of the authors, there is no published report of the condensation of endocyclic 3-keto derivatives with nitromethane.

In this communication we wish to report the conversion of several ketoses into branched-chain nitro and amino sugars. The following is an example of the procedure used at present. An amount of 1.35 g of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose I (6) was condensed with nitromethane (35 ml) in the presence of 1 N sodium methoxide (5.3 ml) at room temperature for 16 h. The product was deionized over IR 120 (H^+) resin, then evaporated to dryness, and the residue fractionally crystallized from ethyl acetate-petroleum ether (b.p. 30-60°) to yield methyl 4,6-*O*-benzylidene-2-deoxy-3-*C*-nitromethyl-α-D-*ribo*-hexopyranoside II (63%), m.p. 192-194°, $[\alpha]_D^{22}$ +88° (*c* 2, chloroform). After the mother liquor was evaporated to dryness, the residue was crystallized from ethanol-water to give the D-*arabino* isomer III (22%), m.p. 117-118° $[\alpha]_D$ +69° (*c* 2, chloroform).

The structures of II and III were assigned on the basis of the following facts. Debenzylidenation of II with Dowex 50W-X8 resin under reflux for 1 h afforded IV, m.p. 105-106°, $[\alpha]_D^{22}$ +85° (*c* 2, ethanol). The latter, after conversion into the monotosylate V, $[\alpha]_D^{22}$ +158° (*c* 2, chloroform), was allowed to react with acetone in the presence of anhydrous copper sulfate to yield VI, $[\alpha]_D^{22}$ +83° (*c* 2, chloroform). Under similar reaction conditions debenzylidenated III failed to yield an appreciable amount of the monoisopropylidene derivative. Therefore, II must have the *ribo* and III the *arabino* configuration. It is interesting to note that in the nuclear magnetic resonance (first order n.m.r. taken at 60 Mc in $CDCl_3$ with internal TMS standard) spectrum of III the axial C-2 hydrogen signals occur as a quartet at τ 8.05 and show a typical large spin coupling to the equatorial C-2 hydrogen ($J_{2a,2e}$ $\sim$ 14 Hz) and a larger than expected $J_{2a,1e}$ equal to 4.3 Hz. To account for the latter large coupling it is suggested that the axial C-2 hydrogen is long-range coupled with the axial nitromethyl group on C-3 of III. The equatorial C-2 hydrogen at τ 7.6 shows the expected $J_{2e,2a}$ of 14 Hz, and in addition, the small $J_{2e,1e}$ of about 1 Hz. On the other hand, the C-2 hydrogens of II give rise to a triplet centred at about τ 7.8 having a width of about 11 Hz. In the latter case, it is suggested that the equatorial nitromethyl group on C-3 is not long-range coupled with the hydrogens on C-2 thus giving a narrow band of signals.



On the other hand, condensation of 1,2:5,6-di-*O*-isopropylidene-α-*D*-*ribo*-hexofuranos-3-ulose (7) with nitromethane followed by crystallization of the product from petroleum ether (b.p. 60-100°) yielded stereoselectively 1,2:5,6-di-*O*-isopropylidene-3-*C*-nitromethyl-α-*D*-allofuranose, m.p. 138-140°, $[\alpha]_D^{22}$ +31° (*c* 2, chloroform). Selective hydrolysis of the latter with 0.1 N sulfuric acid in methanol for 3 h at room temperature afforded 1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-*D*-allofuranose, m.p. 96-97°, $[\alpha]_D^{22}$ +71° (*c* 3, water). Sodium metaperiodate oxidation of the latter followed by sodium borohydride reduction of the *aldehydo*-derivative yielded 1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-*D*-ribofuranose, m.p. 77-78°, $[\alpha]_D^{22}$ +28° (*c* 2, chloroform). 5-*O*-Benzyl-1,2-*O*-isopropylidene-α-*D*-*erythro*-pentofuranos-3-ulose (8) was also converted exclusively into 5-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-nitromethyl-α-*D*-ribofuranose, m.p. 103-104°, $[\alpha]_D^{22}$ +41° (*c* 2, chloroform). Structures were assigned on the basis of the n.m.r. spectral measurements and on mechanistic considerations. Previous workers (9) have found that 3-keto-hexoses possessing a ketone group adjacent to the bridgehead of two fused

5-membered rings generally react with nucleophilic reagents to give products with the "allo" configuration.

Hydrogenation of the nitro sugars was achieved using platinum in the presence of dilute hydrochloric acid or 10% palladium on charcoal to yield amino sugars. For example, IV on hydrogenation afforded methyl 2-deoxy-3-*C*-aminomethyl-α-*D*-*ribo*-hexopyranoside as a syrup, $[\alpha]_D^{22}$ +79° (*c* 2, water) R_f (*D*-glucosamine) 1.1 (5:3:5:1 pyridine-water-ethyl acetate-acetic acid).

ACKNOWLEDGEMENT

This work was supported by the Canadian Research Council of Canada.

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