Seven-membered Ring Sugars: Factors Influencing the Formation of Branched-chain 3-Deoxy-3-nitro-septanosides

By MARTIN E. BUTCHER and J. BARRY LEE

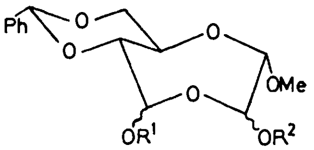
(*The Hatfield Polytechnic, Bayfordbury Research Laboratories, Lower Hatfield Road, Herts* SG13 8LD)

Summary Nitro-compounds have been condensed with the periodate-oxidised product of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside; the type of product obtained depends upon the solvent system used, the catalyst, and the size of nitro-compound.

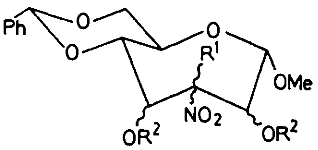
THE formation of a 3-deoxy-3-nitro-septanoside by the reaction of nitromethane with the periodate oxidation product (I) of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside has been reported.[1] In view of the interest in branched-chain amino-sugars,[2] in particular in the antibiotic field, we have investigated the synthesis of some branched-chain seven-membered ring sugars resulting from corresponding condensations with higher analogues of nitromethane. We report some interesting effects which govern the formation of dioxepan structures or of branched-chain sugars.

Nitroethane condensed smoothly, in MeOH–NaOMe with the hydrated dialdehyde (I) to give, as a single isomer, the crystalline septanoside (IV) in 38% yield, m.p. 219—221 °C. The ^{1}H n.m.r. spectrum of the 2,4-di-*O*-acetyl derivative (V) shows clearly 2-H and 1-H as doublets ($J_{1,2}$ 7 Hz) and 4-H and 5-H as doublets ($J_{4,5}$ 9 Hz) suggesting that the acetoxy-groups lie equatorially. This is consistent with either the D-*glycero*-α-D-*ido* or the D-*glycero*-α-D-*talo* configuration. Increasing the size of R in the nitro-precursors (RCH_2NO_2), however, led to a competing reaction which gave the methoxy-dioxepan (II) or (III). This dialdehyde (I) is known[3] to react with some alcohols at elevated temperatures to form alkoxy-dioxepans but their formation at 0 °C has not been reported.

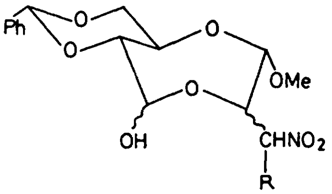
When pyridine, or in some cases DMF, was used as solvent with 1 equiv. of NaOMe as base, ready condensation of either nitromethane or nitroethane occurred to give the corresponding 3-deoxy-3-nitro-septanosides (VI) and (IV) respectively and, in the case of nitroethane, an improved



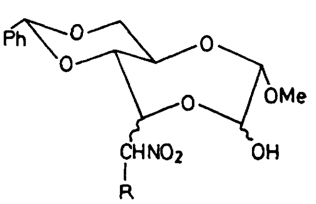
(I); $R^1 = R^2 = H$
(II); $R^1 = H$, $R^2 = Me$
(III); $R^1 = Me$, $R^2 = H$



(IV); $R^1 = Me$, $R^2 = H$
(V); $R^1 = Me$, $R^2 = Ac$
(VI); $R^1 = R^2 = H$
(VII); $R^1 = Et$, $R^2 = H$



(VIII); R = Et
(IX); R = cyclohex-1-enyl
(X); R = Ph



(XI); R = Me
(XII); R = Et
(XIII); R = H

yield (60%) was obtained. In contrast 1-nitropropane reacted under the same conditions to give a mixture of products, the major product being the expected septanoside (VII), m.p. 188—190 °C, with a minor amount of a second crystalline substance shown to be the dioxepan (VIII). The i.r. spectrum of this compound shows nitro, hydroxy, and aromatic absorbances; acetylation gave only a mono-acetoxy-derivative, the ^{1}H n.m.r. spectrum of which shows only one acetyl methyl resonance at τ 7·85. The proton on the acetoxy-bearing carbon gives a doublet at τ 4·35 and is coupled (J 8 Hz) to 9′-H rather than 6-H, showing that the nitropropyl side chain must be at position 7. Lichtenthaler[4] has reported the cyclisation of 1-nitropropane with glutaraldehyde but only 1-ethyl-1-nitro-cyclohexanediol was formed. However, analogous products, *i.e.* dioxans, in the six-membered sugar series have been reported[5] when either ethyl nitroacetate or phenylnitromethane are cyclised with D-methoxy-D-hydroxymethyl-diglycolic aldehyde. However no change-over point as we report here has been observed previously. The reaction of sodium salts of larger nitroanalogues with the dialdehyde (I) in pyridine, for example 1-nitromethylcyclohexene and phenylnitromethane, led exclusively to the formation of the corresponding crystalline 7-substituted dioxepans (IX) and (X). Clearly some relief of steric strain is obtained by formation of the dioxepan structures over the normal 3-deoxy-3-nitro-septanoside when the nitro-precursor is large.

When the alkoxide catalyst was replaced by 40% aqueous KOH, again with pyridine as solvent, reaction at 0 °C of nitroethane with compound (I) gave two isomers, m.p. 151—153 and 159—161 °C, of the 9-substituted dioxepan (XI), which were separated by preparative t.l.c. in 42% overall yield. These isomers had identical i.r. spectra. The ^{1}H n.m.r. spectrum of the predominant isomer shows the methyl signal at τ 8·4 as a doublet (J 7 Hz) thus showing that the methyl group is in a side chain rather than attached directly to a ring, as in compound (IV) where it appears as a singlet. Only a mono-acetyl derivative could be formed, the ^{1}H n.m.r. spectrum of which shows the proton on the acetoxy-bearing carbon atom at τ 4·42 as a doublet coupled to 6-H (J 7 Hz), showing that the side chain is at position 9. There was insufficient of the minor isomer for a detailed ^{1}H n.m.r. study. The reaction of 1-nitropropane under the same conditions also gave two isomers of the corresponding 9-(1-nitropropyl)-dioxepan (XII), but nitromethane gave a mixture of the 9-nitromethyldioxepan (XIII) and the more usual 3-deoxy-3-nitro-septanoside (VI). The reason for this change in product when the base catalyst is changed, is unclear.

Satisfactory microanalytical data were obtained for all compounds reported here.

(*Received*, 27*th June* 1974; *Com.* 761.)

---

[1] M. L. Wolfrom, U.G. Nayak, and T. Radford, *Proc. Nat. Acad. Sci. U.S.A.*, 1967, **58**, 1848.

[2] F. W. Lichtenthaler, *Fortschr. Chem. Forsch.*, 1970, **14**, 556.

[3] R. D. Guthrie and J. Honeyman, *J. Chem. Soc.*, 1959, 2441; R. D. Guthrie, *Adv. Carbohydrate Chem.*, 1961, **16**, 112.

[4] F. W. Lichtenthaler, H. Leinert, and R. Scheidegger, *Chem. Ber.*, 1968, **101**, 1819.

[5] S. Zen, A. Yasuda, H. Hashimoto, and Y. Takeda, *Nippon Kagaku Zasshi*, 1969, 90, 110.