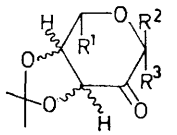
Synthesis of Vicinal Monoamino-dideoxysugars

By PETER M. COLLINS,* W. GEORGE OVEREND,* and VERONICA M. RACZ
(*Department of Chemistry, Birkbeck College, University of London, Malet Street, London* WC1E 7HX)

Summary Sequential treatment of methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose (I) with aqueous NaOH and phenylhydrazine results in elimination of acetone and formation of 2-*S*-methoxytetrahydropyran-3,4-dione 4-phenylhydrazone (III), which has been converted into a 3-amino-3,4-dideoxypentose; and similarly, a 3-amino-3,4,6-trideoxyhexose has been obtained starting with methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosidulose (II).

METHYL glycosiduloses have been used extensively as intermediates in the modification of sugars. Such modification is at the site of the hydroxy-group in a methyl glycoside at which oxidation has been effected to produce the glycosidulose. Now we report a sequence of reactions which results in modification at C(3) and C(4) of a methyl glycopyranosid-2-ulose derivative.



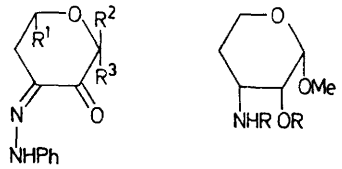
(I) $R^1 = R^2 = H$, $R^3 = OMe$, Configuration at C(3)–C(4) L-*erythro*

(II) $R^1 = Me$, $R^2 = OMe$, $R^3 = H$, Configuration at C(3)–C(4) D-*erythro*

The ulosides used here, methyl 3,4-*O*-isopropylidene-β-L-*erythro*-pentopyranosidulose (I) and methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosidulose (II) [respectively m.p. 98—99° and 73—74°; $[\alpha]_D$ + 230° (*c* 0·5)† and −106° (*c* 1·5)] were prepared in good yields by methods already described.[1,2] Three products were formed when compound (I) (5 mmol) in hot EtOH (5 ml) was treated with aq. NaOH (0·5 ml of 2·5M, 0·5 min) and then with phenylhydrazine (5 mmol; 2 min). The major product (72%) was 2-*S*-methoxytetrahydropyran-3,4-dione 4-phenyl hydrazone (III) (m.p. 157—158·5°, $[\alpha]_D$ − 138° (*c* 1), δ (100 MHz, $CDCl_3$) 4·76 (s, H-2), 2·71 (octet, $J_{5e,5a}$ 16·5, $J_{5e,6a}$ 4·0, $J_{5e,6e}$ 2·5 Hz), 3·07 (octet, $J_{5a,6a}$ 11·0, $J_{5a,6e}$ 6·0 Hz), 3·90 (octet, $J_{6e,6a}$ 11·0 Hz), 4·21 (sextet, H-6a), 3·51 (s, OMe), 7·0–7·3 (m, Ar, NH); *m/e* 234 (70%, M^+), 204 (20%, $M^+ - CH_2O$), 203 (30%, $M^+ - MeO$), 174 (60%, $M^+ - HCO_2Me$ confirmed by *m** 129·4), 173 (100%, $M^+ - HCO_2Me - H$, confirmed by *m** 172·0).

After compound (III) had separated by crystallisation the minor products, isolated after column chromatography, were identified as the phenylhydrazone of the parent uloside [10% as syrup, $[\alpha]_D$ +350° (*c* 0·5)] and 3,4-*O*-isopropylidene-L-*erythro*-pentosazone (2%, m.p. 186–187°). The sole product obtained after reaction without initial treatment with NaOH, for 24 h, at ambient temperature is the phenylhydrazone of (I) (quantitative yield).

When compound (III) is reduced (glacial HOAc, PtO_2/H_2, room temp), methyl 3-acetamido-2-*O*-acetyl-3,4-dideoxy-α-D-*erythro*-pentopyranoside (V) (80%, m.p. 90–91°) is obtained after acetylation. This compound is obtained in lower yield (20%) by sequential reduction (i, $NaBH_4$; ii, PtO_2/H_2) and acetylation. The intermediate methyl 4-deoxy-α-D-*glycero*-pentopyranosid-3-ulose phenylhydrazone (68%) had m.p. 156°, $[\alpha]_D$ + 165° (*c* 1·0, EtOH). Deacetylation of (V) with boiling M-NaOH afforded syrupy methyl 3-amino-3,4-dideoxy-α-D-*erythro*-pentopyranoside (VI) (80%) which gave a crystalline *N*-salicylidene derivative, m.p. 144°, $[\alpha]_D$ + 41° (*c* 1·5). The free amino-sugar [isolated as the hydrochloride, m.p. 123—124°, $[\alpha]_D$ + 24° equilib. (*c* 1·03, H_2O)] was obtained from the glycoside (VI) by treatment with 15% aq. HCl or, better, from the *N*-salicylidene derivative by treatment with M-HCl.



(III) $R^1 = R^2 = H$, $R^3 = OMe$ (V) R = Ac

(IV) $R^1 = Me$, $R^2 = OMe$, $R^3 = H$ (VI) R = H

When compound (II) in EtOH was treated sequentially with 2M NaOH and phenylhydrazine it yielded as major product, methyl 4,6-dideoxy-α-L-*glycero*-hexopyranosid-2,3-diulose 3-phenylhydrazone (IV), m.p. 143°, $[\alpha]_D$ +320° (*c* 0·5). Reduction of (IV) afforded an aminoglycoside isolated either as its *N*-salicylidene derivative [m.p. 131—132°, $[\alpha]_D$ −41° (*c* 0·5)] or as the syrupy *O*,*N*-diacetyl compound, $[\alpha]_D$ −47° (*c* 3·5). Both compounds could be converted into 3-amino-3,4,6-trideoxy-L-*ribo*-hexose hydrochloride (70%), m.p. 92—94°, $[\alpha]_D$ −18° equilib. (*c* 3, H_2O).

The configurations of the aminodideoxyglycosides were assigned on the basis of n.m.r., c.d., and *X*-ray crystallographic analysis[3] and details will be given elsewhere.

This reaction sequence provides a convenient route for the preparation of modified sugars containing the $-CH_2CHNH_2-$ system such as occurs in amino-sugar components[4,5] of some antibiotics.

(*Received, 23rd December* 1974; *Com.* 1561.)

† Unless stated otherwise all optical rotations were measured on solutions in chloroform. Satisfactory elemental analyses and spectra (mass, n.m.r., i.r. and u.v.) were obtained for all new compounds.

[1] J. S. Burton, W. G. Overend, and N. R. Williams, *J. Chem. Soc.*, 1965, 3433.
[2] P. M. Collins and W. G. Overend, *J. Chem. Soc.*, 1965, 1912.
[3] R. A. Palmer and H. Palmer, personal communication.
[4] J. Cleophax, S. D. Gero, J. Leboul, and A. Forchioni, *J.C.S. Chem. Comm.*, 1973, 710.
[5] K. F. Koch and I. A. Rhoades, *Antimicrobial Agents Chemotherapy*, 1970, 309.