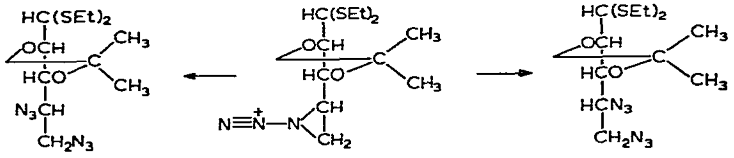
Preliminary communication

Sugars containing nitrogen in the ring

4,5-DIACETAMIDO-4,5-DIDEOXY-L-XYLOPYRANOSE AND THE ANOMERIC 4-ACETAMIDO-4,5-DIDEOXY-D-XYLOFURANOSES

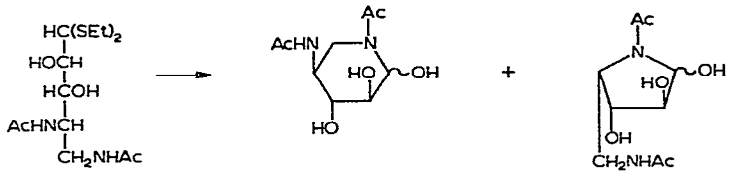
Previous reports from these laboratories described the synthesis of sugars containing nitrogen as a ring atom in six[1]- and five[2]-membered derivatives. Related substances have also been reported by other investigators[3–5].

We now wish to report the synthesis of the title compounds, which can exist as cyclic structures with nitrogen as the hetero atom, or as acyclic modifications. Acetonation of 5-azido-5-deoxy-D-arabinose diethyl dithioacetal[1] afforded the 2,3-*O*-isopropylidene derivative, $[\alpha]^{24}_{\mathrm{D}}$ +61° (*c* 1.16, in chloroform)[6] which was subsequently converted to the 4-*O*-methylsulfonyl derivative, $[\alpha]^{24}_{\mathrm{D}}$ +54° (*c* 0.32, in chloroform). Treatment of the latter with sodium azide in *N*,*N*-dimethylformamide afforded predominantly 4,5-diazido-4,5-dideoxy-2,3-*O*-isopropylidene-L-xylose diethyl dithioacetal (I), isolated as a pure liquid, $[\alpha]^{24}_{\mathrm{D}}$ +110° (*c* 0.145, in chloroform). A second product formed in an approximate ratio of 1:60 with respect to I was also isolated, and assigned structure II by infrared spectral and optical rotational data, $[\alpha]^{24}_{\mathrm{D}}$ + 65° (*c* 0.31, in chloroform). Such a product, corresponding to an overall retention of configuration at C-4, could be formed by neighboring-group participation by the C-5 azide function as in the intermediate "azidonium" ion[7] III. Preferred attack at the primary carbon atom in III would explain the predominance of I. Reduction of I with lithium aluminum hydride, followed by *N*-acetylation, afforded the corresponding 4,5-diacetamido derivative, m.p. 112–114° which, on hydrolysis, gave 4,5-diacetamido-4,5-dideoxy-L-xylose diethyl dithioacetal (IV) as colorless crystals, m.p. 136–137°. The mass spectrum[8,9] of this product was compatible with its structure. Demercaptalation[10] of IV afforded a mixture of the pyranose V and furanose VI products. Compound V, which was the major product (R_F 0.28) was obtained as a colorless homogeneous sirup, $[\alpha]^{24}_{\mathrm{D}}$ +30° (*c* 0.8, in methanol) or a hygroscopic solid. Infrared spectral data: $\lambda^{\mathrm{KBr}}_{\mathrm{max}}$ 1640 cm^{-1}, amide I; 1560 cm^{-1}, amide II; n.m.r.



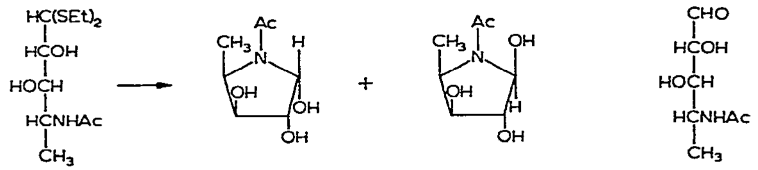
(I) (III) (II)

spectral data: (D_2O) τ 7.83, 7.80 (ring acetyl); τ 7.98 (C-4 acetyl); τ 4.43, $J \simeq 3$ c.p.s.; τ 4.00, $J \simeq 3$ c.p.s. (C-1 hydrogen). Isomerization studies in acid and base showed partial conversion of V to VI. The formation of variable proportions of VI and of the acyclic modification (n.m.r.), causing some tailing of the furanose spot, was enhanced by longer reaction times and mode of isolation. Compound VI (R_F 0.48) showed a singlet at τ 8.05 (C-5 acetyl) and a doublet at τ 9.80 (ring acetyl).



(IV) (V) (VI)

In an effort to further validate the participating character of the azido group, the displacement was studied in a derivative where the terminal azide group was replaced by hydrogen. Thus, treatment of 5-deoxy-2,3-*O*-isopropylidene-4-*O*-(*p*-nitrobenzenesulfonyl)-L-arabinose diethyl dithioacetal, $[\alpha]^{24}_{D}$ $-34°$ (*c* 1.5, chloroform) with sodium azide in *N*,*N*-dimethylformamide gave 4-azido-4,5-dideoxy-2,3-*O*-isopropylidene-D-xylose diethyl dithioacetal as the sole product, $[\alpha]^{24}_{D}$ $-109°$ (*c* 1.13, in chloroform). Reduction of this product, followed by *N*-acetylation, gave the crystalline 4-acetamido derivative, m.p. 90–91°; $[\alpha]^{24}_{D}$ $-27°$ (*c* 1, chloroform). Removal of the acetal group afforded crystalline 4-acetamido-4,5-dideoxy-D-xylose diethyl dithioacetal (VII), m.p. 103–105°; $[\alpha]^{24}_{D}$ $+16°$ (*c* 1, methanol).



(VII) (VIII) (IX) (X)

Demercaptalation[10] of (VII) afforded a sirup (90%), $[\alpha]^{24}_{D}$ $+11.2°$ (at equil., *c* 4.6, methanol) which formed a double spot on paper chromatograms. Isolation of the respective components afforded the homogeneous products R_F 0.65 (*n*-BuOH–EtOH–H_2O, 3:1:1) and R_F 0.72 as colorless sirups in an approximate ratio of. 1:1[11]. Their identification as anomers was established by chemical, i.r., and n.m.r, studies. For the R_F 0.65 component: τ 4.72 (C-1 hydrogen); τ 7.82, 7.85, 7.88 7.92 (acetyl hydrogens); τ 8.88, 8.97 (C-5 hydrogens, main peaks). A peak at τ 8.03 (acetyl hydrogens) due to the acyclic form X was also detected indicating the presence of X in the original mixture. The ratio was approximately 1:12. The spectrum of the R_F 0.72 component showed peaks at τ 4.84 (C-1 hydrogen); τ 7.82, 7.85, 7.88, 7.92

(acetyl hydrogens); τ 8.86, 8.80, 8.75 (C-5 hydrogens, main peaks). Exposure of the respective deuterium oxide solutions of the anomers to hydrogen chloride vapor afforded identical spectra in each case, indicating rapid equilibration. The same crystalline benzylphenylhydrazone, m.p. 106–107° was obtained from either anomer.

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Research Laboratories,
Parke, Davis & Co., Ann Arbor, Mich.
(U.S.A.)

STEPHEN HANESSIAN

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11 A tentative assignment of α- and β-configurations to VIII and IX respectively could be made based on the presence of a relatively symmetrical multiplet for the C-1 hydrogen signal in IX (higher τ value) compared to an apparent split multiplet ($J \simeq$ 4–5 c.p.s.) in the spectrum of VIII (lower τ value). The lack of resolution of the anomeric hydrogen signals at 24° is due to the presence in solution of several rotational isomers[4]. Optical rotational data obtained from VIII and IX are not unambiguously discriminating.

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