Extension of Sugar Chains through Acetylenic Intermediates

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WE report herein examples of the extension of sugar chains by ethynylation of *aldehydo*-sugar derivatives. The versatility of the terminal acetylene function for a variety of synthetic transformations makes the acetylenic sugar derivatives attractive as intermediates for synthesis of deoxy-sugars, unsaturated sugars of various types, amino-sugars, alditols,[1] and other unusual carbohydrate derivatives, such as occur in many antibiotics. The examples illustrate chain extension of sugars, at the ω-carbon through dialdoses, and at C-1 through *aldehydo*-aldoses.[2] Degradative methods for configurational assignment are presented.

1,2 : 3,4-Di-*O*-isopropylidene-α-D-galactopyranose was oxidized with the dimethyl sulphoxide–*NN'*-dicyclohexylcarbodi-imide–pyridinium phosphate reagent[3] to give 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose, yield 58%, b.p. < 140° (bath, 0·15 mm.), τ 0·24 (1-proton singlet, H-6), λ_{max}^{film} 3·70, 5·75μ, Schiff positive. Ethynylation of the latter with ethynylmagnesium bromide in tetrahydrofuran gave 7,8-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-D-*glycero*(and L-*glycero*)-α-D-*galacto*-oct-7-ynopyranose, yield 85%, τ 7·45 (1-proton, $C{\equiv}CH$), λ_{max}^{KBr} 2·89, 3·07, 4·72 μ, containing the 6-epimers in about 2 : 1 proportion (t.l.c.). The preponderant epimer had m.p. 130–131° (from ligroin), τ 7·43 (1-proton doublet, $J_{6,8}$ 2 c./sec., H-8). Hydrogenation of the latter over Lindlar catalyst gave the corresponding 7,8-olefin, m.p. 106—108°, τ 3·6—4·9 (4-proton multiplet, H-1, $CH{=}CH_2$). These 8-carbon sugar derivatives are of interest for synthesis of structures related to lincomycin.

Ethynylation of 1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose[4] (I) gave 6,7-dideoxy-1,2-*O*-isopropylidene-α-D-*gluco*(and β-L-*ido*)-hept-6-ynofuranose (II), λ_{max}^{film} 3·10, 4·75 μ; diacetate b.p. 105° (bath, 0·18 mm), λ_{max}^{film} 3·10, 4·75, 5·75 μ,

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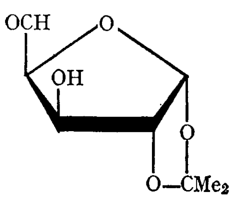
[1] R. Lespieau, *Adv. Carbohydrate Chem.*, 1946, **2**, 107; *cf.* I. Iwai and K. Tomita, *Chem. Pharm. Bull.* (Japan), 1963, **11**, 184.

[2] Analyses and spectra were consistent with the given formulations. N.m.r. data refer to deuterochloroform solutions or pure liquids, with tetramethylsilane as internal standard.

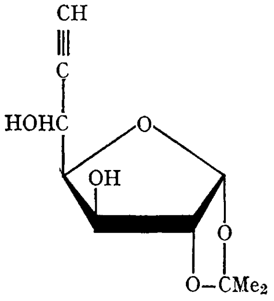
[3] K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, 1963, **85**, 3027.

[4] K. Iwadare, *Bull. Chem. Soc. Japan*, 1941, **16**, 40.

τ 7·3 (1-proton, C≡CH). Benzoylation of (II) gave a mixture of 5-epimeric 3,5-dibenzoates from which the D-*gluco*-epimer was obtained by fractional crystallization, m.p. 191—193°, λ_{max}^{KBr} 3·07, 4·70, 5·80 μ, τ 7·55 (1-proton doublet, $J_{5,7}$ 2·5 c./sec., H-7). Reduction of the latter over Lindlar catalyst gave the corresponding 6,7-olefin (III), yield 70%, m.p. 143—145°, τ 3·9—4·9 (5-proton multiplet, H-1,3,5,6,6′). Ozonolysis of this olefin, followed by reduction with hydrogen over Adams' catalyst, borohydride reduction, and acid hydrolysis, gave a glucose (papergram). This reaction sequence establishes the configuration of the precursors.



(I)



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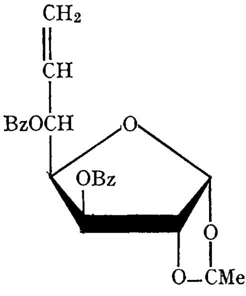

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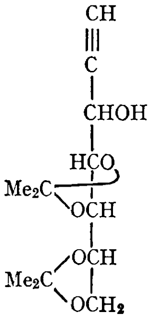

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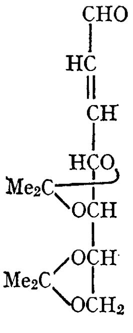
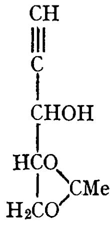


(V)



(VI)

2,3:4,5-Di-*O*-isopropylidene-*aldehydo*-L-arabinose[5] was ethynylated to give 4,5:6,7-di-*O*-isopropylidene-L-*gluco*(and L-*manno*)-3,4,5,6,7-pentahydroxyhept-1-yne (IV), yield 85%, λ_{max}^{film} 2·92, 3·06, 4·74 μ, τ 7·52 (1-proton, C≡CH) resolvable by thin-layer or (better) gas–liquid chromatography to give a 3:2 mixture of a fast-moving isomer, m.p. 67—69°, $[\alpha]_D^{22}$–6·5° (*c* 3, chloroform), and a slower-moving isomer, syrup, $[\alpha]_D^{22}$ + 24° (*c* 2·4, chloroform). The isomers were hydrogenated over Lindlar catalyst to the corresponding olefins, subjected to ozonolysis, hydrogenated over Adams' catalyst, and hydrolyzed with 1% sulphuric acid for 3 hr. at 100°. The product from the crystalline, lævorotatory isomer was a glucose (papergram), that from the dextrorotatory isomer was a mannose; this sequence establishes the configurations of the two isomers of (IV) and their derivatives. Acetylation of (IV) gave the mixed, 3-epimeric 3-acetates, b.p. 150° (bath, 0·15 mm.), λ_{max}^{film} 3·10, 4·73, 5·73 μ, τ 7·47 (C≡CH), which on treatment with an equivalent of bis(1,2-dimethylpropyl)borane[6] in diglyme, followed by hydrogen peroxide, gave *trans*-2,3-dideoxy-4,5:6,7-di-*O*-isopropylidene-*aldehydo*-L-*arabino*-hept-2-enose (V), b.p. 65° (bath, 0·03 mm), λ_{max}^{film} 3·70, 5·92, 6·08 μ, τ 0·38 (1-proton doublet, $J_{1,2}$ 7 c./sec., H-1), 3·68 (1-proton octet, $J_{2,3}$ 16 c./sec., J_{24} 1·5 c./sec.,

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[5] H. Zinner, E. Wittenburg, and G. Rembarz, *Chem. Ber.*, 1959, **92**, 1614.
[6] H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, 1961, **83**, 3834.

H-2), 3·15 (1-proton quartet, $J_{3,4}$ 4 c./sec., H-3), Schiff-positive.

Ethynylation of 2,3-*O*-isopropylidene-*aldehydo*-D-glyceraldehyde (τ 0·3, CHO) gave 4,5-*O*-isopropylidene-D-*erythro*(and D-*threo*)-3,4,5-trihydroxypent-1-yne (VI), b.p. 59—60° (bath, 0·15 mm.), $\lambda_{\max}^{\text{film}}$ 3·10, 4·75 μ, τ 7·49 (1 proton, C≡CH). Acetylation of (VI) gave the corresponding 3-acetates, yield 60%, b.p. 38—39° (0·015 mm.), resolvable by preparative gas–liquid chromatography into the separate 3-epimers, obtained in 3 : 2 proportion. The preponderant epimer, eluted first, in 90% epimeric purity, had $[\alpha]_D^{30}$ − 41° (*c* 0·7, chloroform), τ 7·52 (1-proton doublet, $J_{1,3}$ 2·2 c./sec., H-1), 7·89 (3-proton singlet, OAc), 4·60 (1-proton quartet, $J_{3,4}$ 6·8 c./sec., H-3), the other epimer (90% epimeric purity) had $[\alpha]_D^{30}$ + 50° (*c* 1, chloroform), τ 7·48 (1-proton doublet, $J_{1,3}$ 2·2 c./sec., H-1), 7·88 (3-proton singlet, OAc), 4·57 (1-proton quartet, $J_{3,4}$ 3·8 c./sec., H-3). Treatment of the mixed acetates of (VI) with an excess of bis(1,2-dimethylpropyl)borane,[6] followed by hydrogen peroxide, gave *trans*-2,3-dideoxy-4,5-*O*-isopropylidene-*aldehydo*-D-*glycero*-pent-2-enose, distilled oil, Schiff positive, τ 0·55 (1-proton doublet, $J_{1,2}$ 7 c./sec., H-1), 3·80 (1-proton octet, $J_{2,3}$ 16 c./sec., $J_{2,4}$ 1 c./sec., H-2), 3·30 (1-proton quarter, $J_{3,4}$ 4·5 c./sec., H-3). This product, substance (V), and similar α,β-unsaturated *aldehydo*-sugars, may be useful intermediates in synthesis.

(*Received, August 23rd*, 1965; *Com.* 529.)