

Novel Syntheses of Halogeno- and Deoxy-sugars

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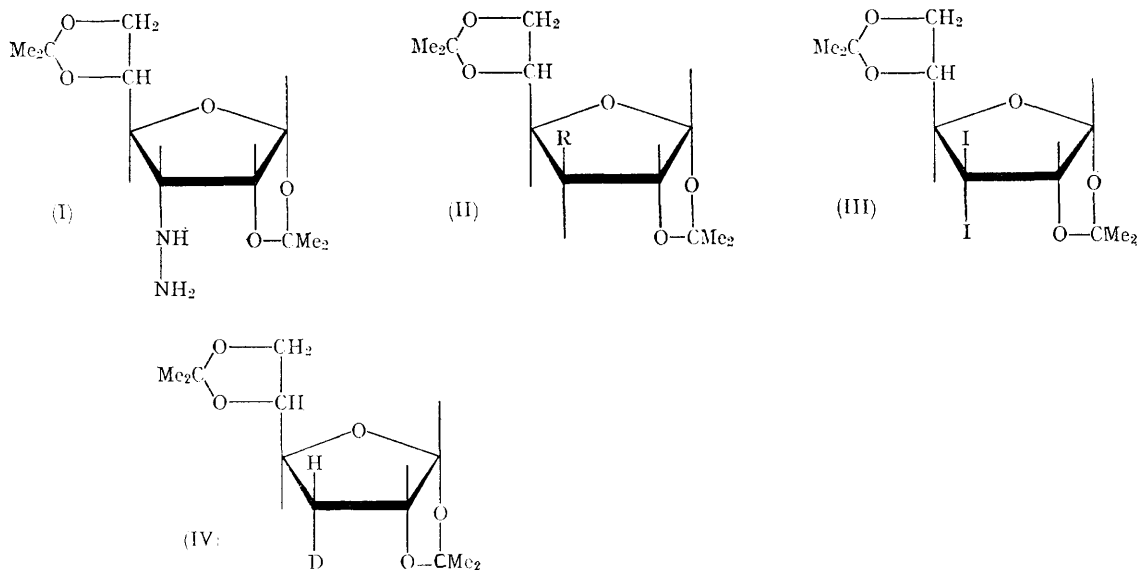
THE isolation of a number of biologically important compounds containing deoxy-sugars has stimulated further interest in the synthesis of the latter. Although a variety of routes to deoxy-sugars are available, we describe here a novel approach to these compounds, using a reaction which may have advantages in particular cases and which should also have wider synthetic use.

When a number of alkylhydrazines were oxidised by iodine (2 mol.) in aqueous potassium iodide the corresponding alkyl iodide was formed. For example, the cyclohexylhydrazine afforded cyclohexyl iodide in 57% yield. Applied to the readily available 3-deoxy-3-hydrazino-1,2:5,6-di-*O*-isopropylidene-D-allofuranose (I),¹ the reaction gave the oily *gluco*-iodide (II; R = I), λ_{\max} 255 m μ

¹ R. U. Lemieux and P. Chu, *J. Amer. Chem. Soc.*, 1958, **80**, 4745; B. Coxon and L. Hough, *J. Chem. Soc.*, 1961, 1643.

(ϵ , 500) together with the crystalline *gem*-di-iodide (III), m.p. 113°, λ_{\max} 288 $m\mu$ (ϵ , 1250). The surprising formation of the latter substance may be accounted for by tautomerisation of the di-imide intermediate to the hydrazone followed by further reaction with the halogen (*cf.* Barton *et al.*²). The proportion of di-iodide was reduced when *N*-iodosuccinimide in chloroform was used as the reagent and with iodine itself in the same solvent the yield of (II; R = I) was essentially quantitative. No evidence for the presence of the *allo*-iodide in the products has been found. Both the mono- and di-iodide were completely converted into 3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-glucufuranose (II; R = H), b.p. 76—82°/0.1 mm.,³ by hydrogenation over Raney nickel. With *N*-bromosuccinimide as halogenating agent the bromide (II; R = Br) was formed in good yield, but reaction with *N*-chlorosuccinimide was less satisfactory, although (II; R = Cl) was a major product.

long-known,⁴⁻⁶ does not appear to have been used preparatively. Ferricyanide or periodate⁶ oxidation of the *allo*-hydrazine (I), at room temperature in alkaline aqueous medium, gave the 3-deoxy-compound (II; R = H) (30—40%). When carried out in deuterium oxide, this reaction gave the *allo*-monodeutero-compound (IV) (isotopic purity >94%). The configuration of this compound and those of the halogeno-sugars were established by n.m.r. spectroscopy. The high stereospecificity of the reaction is noteworthy and suggests that it may prove useful for deuterium labelling in other systems. The complete retention of configuration observed is in contrast to the partial inversion found⁶ in the corresponding oxidation at 100° of (+)-2-phenyl-2-butyldiazine to 2-phenylbutane. In view of this we are making a further study of the stereochemical course of the periodate oxidation and of the reactions leading to the halogeno-sugars, where complete inversion was observed.



The oxidative conversion of mono-alkylhydrazines into the corresponding alkane, although

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² D. H. R. Barton, R. E. O'Brien, and S. Sternhell, *J. Chem. Soc.*, 1962, 470.

³ E. J. Hedgley, W. G. Overend, and R. A. C. Rennie, *J. Chem. Soc.*, 1963, 4701.

⁴ N. Kishner, *J. Russ. Phys. Chem.*, 1899, **31**, 1033; 1910, **42**, 1198; 1911, **43**, 577. (*Chem. Zentr.*, 1900, I, 957; 1911, I, 221; 1911, II, 362).

⁵ L. Cambi and E. D. Paglia, *Atti Accad. Naz. Lincei, Rend., Classe Sci. Fis., Mat., Nat.*, 1963, **35**, 425; (*Chem. Abs.*, 1964, **61**, 5501).

⁶ D. J. Cram and J. S. Bradshaw, *J. Amer. Chem. Soc.*, 1963, **85**, 1108.