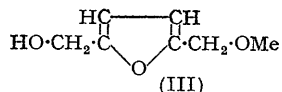
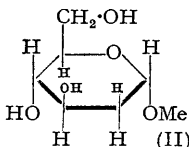
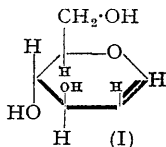


689. *Deoxy-sugars. Part XXIV.* Conversion of D-Glucal into Furan Derivatives.*

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D-Glucal on treatment with methanolic hydrogen chloride affords $\alpha\beta$ -methyl-2-deoxy-D-glucoside and other substances amongst which 2-hydroxymethyl-5-methoxymethylfuran was identified. Some properties and derivatives of this compound are described.

DURING previous investigations on deoxy-sugars (Overend, Shafizadeh, and Stacey, *J.*, 1951, 992) it was noted that treatment of D-galactal with methanolic hydrogen chloride afforded mainly α - and β -methyl-2-deoxy-D-galactosides, the yield of which decreased with increase of acid concentration. The reaction was complex since the optically active glycosidic products were invariably accompanied by an unidentified optically inactive liquid which absorbed bromine and possessed a methoxyl residue. We have found that a similar reaction takes place when D-glucal is treated with 2% methanolic hydrogen chloride. From this reaction α -methyl-2-deoxy-D-glucopyranoside (II) may be isolated as previously reported by Hughes, Overend, and Stacey (*J.*, 1949, 2846); a residual liquid product obtained from the reaction afforded on fractionation one component as a homogeneous, mobile, and colourless syrup, which closely resembled in the above properties the unidentified product obtained from D-galactal. This compound having empirical formula of $C_7H_{10}O_3$ was identified as 2-hydroxymethyl-5-methoxymethylfuran (III) on the following evidence. The ultra-violet absorption spectrum was closely similar to that of furfuryl alcohol, showing a maximum absorption at 216 $m\mu$ which indicates the presence of a pair of conjugated double bonds (cf. Braude, *Ann. Reports*, 1945, 42, 105). A crystalline 3 : 5-dinitrobenzoate was a useful characteristic derivative.



Hydrogenation using Raney nickel at room temperature resulted in absorption of 2 mols. of hydrogen and converted the liquid into tetrahydro-2-hydroxymethyl-5-methoxymethylfuran, the properties of which were in agreement with those recorded by Wiggins and Wood (*J.*, 1950, 1566) for a product obtained by treatment of 1 : 2 : 5 : 6-diepoxyhexane with sodium methoxide. This was a liquid and the above workers did not record the isolation of any crystalline derivative, so that further investigations were necessary to confirm its identity.

It was conveniently characterised by conversion into its *p*-nitrobenzoate. With alkaline potassium permanganate it afforded a potassium monocarboxylate which was converted into a liquid methyl ester and then into a crystalline amide, by standard methods. Oxidation of the tetrahydro-alcohol with hot dilute nitric acid afforded oxalic acid and unidentified products. Finally, methylation by the liquid ammonia technique afforded tetrahydro-2 : 5-bismethoxymethylfuran having the same constants as the product prepared by Wiggins and Wood (*loc. cit.*) from tetrahydro-2 : 5-bishydroxymethylfuran.

These observations prove the nature of the hydrogenated product and thus the skeleton orientation of (III). Further, the conjugated double bonds which had been demonstrated by the absorption spectrum must be as in (III) since any other assignment would furnish an optically active compound.

2-Hydroxymethyl-5-methoxymethylfuran was found to be a very labile compound which was rapidly decomposed with charring by hot mineral acids. The hydrogenated product was, however, recovered unchanged after treatment with hot N-hydrochloric acid.

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Acid treatment of tetramethyl 1 : 2-glucoseen (Wolfrom, Wallace, and Metcalf, *J. Amer. Chem. Soc.*, 1942, **64**, 265) and tetramethyl fructofuranose (Haworth, Hirst, and Nicholson, *J.*, 1927, 1513) affords 5-methoxymethylfurfuraldehyde, which is closely related to (III). Although under controlled conditions the aldehyde is smoothly oxidised to 5-methoxymethylfuroic acid without the double bonds in the furan ring being affected, attempted oxidation of (III) produced only degradation products and unchanged starting material, evidently owing to the greater resistance of the hydroxymethyl group to the oxidising agent (permanganate).

Formation of 2 : 5-disubstituted furans from hexoses and their oxidation products is a well-known feature of carbohydrate chemistry (cf. Newth, *Adv. Carbohydrate Chem.*, 1951, **6**, 83). The mechanism of some of these transformations has been discussed by Isbell (*J. Res. Nat. Bur. Stand.*, 1944, **32**, 45) who attached special importance to enolisation during these reactions. The conversion of D-glucal into 2-hydroxymethyl-5-methoxymethylfuran is a similar reaction which emphasises the effect of the double bond in these transformations. Recently we have found that treatment of D-glucal with 5% sulphuric acid forms a dehydration product which contains a pair of conjugated double bonds as shown by its ultra-violet absorption spectrum and yet is optically active. This liquid compound which is a by-product in the preparations of 2-deoxyglucose and 2-deoxygalactose from the glycols will form the subject of a later communication. Various interesting liquid products from the acid treatment of arabinol and 2-deoxyglucose are also being examined.

EXPERIMENTAL

D-Glucal.—Triacetyl D-glucal (cf. Fischer, *Ber.*, 1914, **47**, 196) (64 g.) was dissolved in dry methanol (1 l.), and sodium (160 mg.) was added. The solution was kept at room temperature for 2 days, treated with carbon dioxide, and evaporated under diminished pressure. The dry residue was extracted with hot ethyl acetate. The combined extracts were concentrated, affording D-glucal (25 g.), m. p. 57—59°, $[\alpha]_D^{20} = -8.0^\circ$ (c, 1.88 in water).

Treatment of D-Glucal with Methanolic Hydrogen Chloride.—D-Glucal (45 g.) was treated with 2% methanolic hydrogen chloride (250 c.c.) at room temperature. After 18 hours the dark brown mixture was neutralised with silver carbonate, and the filtered solution was evaporated to a syrup which was repeatedly extracted with ether. The remaining syrupy residue on extraction with hot ethyl acetate afforded a solid product, which after several recrystallisations from the same solvent furnished α -methyl-2-deoxy-D-glucopyranoside (1.86 g.), m. p. 92—93°, $[\alpha]_D^{20} = +145^\circ$ (c, 0.8 in methanol) [cf. Hughes, Overend, and Stacey (*loc. cit.*) who give m. p. 90—92° and $[\alpha]_D^{20} = +135^\circ$ (in water)]. The above ethereal extract on evaporation under reduced pressure afforded a liquid which was fractionally distilled under diminished pressure. Further fractionation of the main distillate afforded 2-hydroxymethyl-5-methoxymethylfuran (14.3 g.) as a homogeneous mobile liquid, b. p. 90° (bath-temp.), 47° (column-temp.)/0.3 mm., $n_D^{17} = 1.479$ (Found : C, 59.1; H, 7.4; OMe, 21.6%; M, 147. C₇H₁₀O₃ requires C, 59.2; H, 7.0; OMe, 21.8%; M, 142). The product was highly unsaturated, absorbed bromine, and decolorised potassium permanganate solution. It had no optical activity and was soluble in water, alcohol, ether, and benzene. When brominated in chloroform solution it decomposed with much charring.

The 3 : 5-dinitrobenzoate (prepared in pyridine at 0° during 20 hours) crystallised from methanol as pale yellow plates, m. p. 90°, $[\alpha]_D = \pm 0^\circ$ (Found : C, 49.9; H, 3.8; N, 8.3. C₁₄H₁₂O₈N₂ requires C, 50.0; H, 3.6; N, 8.3%).

Hydrogenation of 2-Hydroxymethyl-5-methoxymethylfuran.—2-Hydroxymethyl-5-methoxymethylfuran (4.71 g.) in aqueous methanol (50 c.c.) was shaken at room temperature in an atmosphere of hydrogen at a slight over-pressure, with Raney nickel (1.2 g.). After 2 days, absorption of hydrogen (1.41 l.) was complete. The solution was then filtered and evaporated to a syrup from which tetrahydro-2-hydroxymethyl-5-methoxymethylfuran (4.37 g.) was obtained as a colourless, mobile syrup, b. p. 130—140° (bath-temp.)/12 mm., $n_D^{18} = 1.457$ (Found : OMe, 21.5. Calc. for C₇H₁₄O₃ : OMe, 21.2%). Wiggins and Wood (*loc. cit.*) give b. p. 159—164° (bath-temp.)/15 mm., $n_D^{18} = 1.4511$. In pyridine (room temp., 16 hours; then at 0°, 3 days) it gave a p-nitrobenzoate, m. p. 59.5° (from ether) (Found : C, 57.1; H, 5.4; N, 4.8. C₁₄H₁₇O₆N requires C, 56.9; H, 5.8; N, 4.7%).

Oxidation of Tetrahydro-2-hydroxymethyl-5-methoxymethylfuran.—(a) *With potassium permanganate.* Tetrahydro-2-hydroxymethyl-5-methoxymethylfuran (0.790 g.) was added to a

solution of potassium permanganate (1.58 g.) and potassium hydroxide (0.61 g.) in water (60 c.c.). After 18 hours at room temperature the brown mixture was neutralised with carbon dioxide and the filtered solution evaporated to dryness under diminished pressure. The residue was washed with ether to remove any unchanged material and then extracted with dry methanol. The extract was concentrated (10 c.c.) and then heated under reflux for 5 hours with excess of methyl iodide (10 c.c.). The solvents were evaporated and the residue extracted with warm ether. The residue of this extraction was re-treated with methanol and methyl iodide and the above procedure repeated. The combined ethereal extracts were evaporated to a syrup from which the crude methyl ester was obtained (0.27 g.) as a colourless syrup, b. p. 140° (bath-temp.)/12 mm., n_D^{25} 1.444. This product (0.200 g.) was dissolved in absolute methanol, and the solution saturated with ammonia and set aside for 18 hours at room temperature. Evaporation of the solvent gave a solid residue which on recrystallisation from ether afforded *tetrahydro-5-methoxymethylfuran-2-carboxamide* (0.12 g.), m. p. $99-102^{\circ}$ (Found: C, 52.2; H, 8.1; N, 8.6. $C_7H_{13}O_3N$ requires C, 52.8; H, 8.2; N, 8.8%).

(b) *With nitric acid.* Tetrahydro-2-hydroxymethyl-5-methoxymethylfuran (2.01 g.) in nitric acid (d 1.15; 30 c.c.) was heated at 100° for 2 hours. When the vigorous evolution of nitric fumes ceased, the solution was diluted with water and evaporated under diminished pressure. This procedure was repeated several times until most of the nitric acid had been evaporated; a mixture of syrup and crystals was obtained. This was filtered through a sintered-glass crucible, and washed with ether. Recrystallisation from moist ether afforded oxalic acid dihydrate (0.41 g.), m. p. 99° .

Methylation of Tetrahydro-2-hydroxymethyl-5-methoxymethylfuran.—The monomethoxy-compound (1.215 g.) was added to dry liquid ammonia (100 c.c.), and sodium (0.4 g.) was added in small pieces. The mixture was mechanically stirred under dry conditions for 2 hours and then methyl iodide (1.07 c.c.) was added. This procedure was repeated three times. When the liquid ammonia had evaporated the residue was extracted with chloroform. The extract was dried ($MgSO_4$) and the solvent removed under diminished pressure. From the crude product tetrahydro-2 : 5-bismethoxymethylfuran (0.74 g.) was obtained as a colourless mobile liquid, b. p. $90-94^{\circ}$ (bath-temp.), 75° (column-temp.)/12 mm., n_D^{21} 1.4368 (Found: C, 60.1; H, 10.4; OMe, 38.4. Calc. for $C_8H_{16}O_3$: C, 60.0; H, 10.0; OMe, 38.7%). Wiggins and Wood (*loc. cit.*) give b. p. $90-95^{\circ}$ (bath-temp.)/12 mm., $n_D^{19.5}$ 1.4369.

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