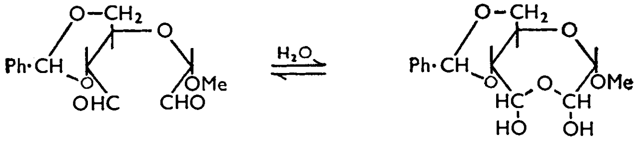
491. *Periodate Oxidation. Part II.*[1] *The Action of Amines on the Product of Periodate Oxidation of Methyl* 4 : 6-O-*Benzylidene*-α-D-*glucoside.*

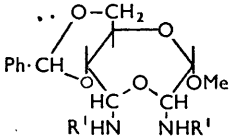
By R. D. GUTHRIE, JOHN HONEYMAN, and MARGARET A. PARSONS.

The action of some amines on the product of periodate oxidation of methyl 4 : 6-*O*-benzylidene-α-D-glucoside has led to the isolation of derivatives either of the open-chain dialdehyde (I) or of the hemialdal form (II). This result provides further evidence for the suggested [1,2] equilibria of this compound.

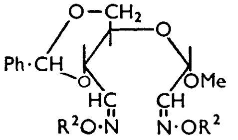
IN solutions of the product of periodate oxidation of methyl 4 : 6-*O*-benzylidene-α-D-glucoside an equilibrium is considered to exist between the open-chain dialdehyde (I) and the hemialdal form (II).[1,2]



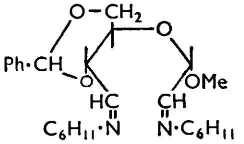
(I) (II)



(III)

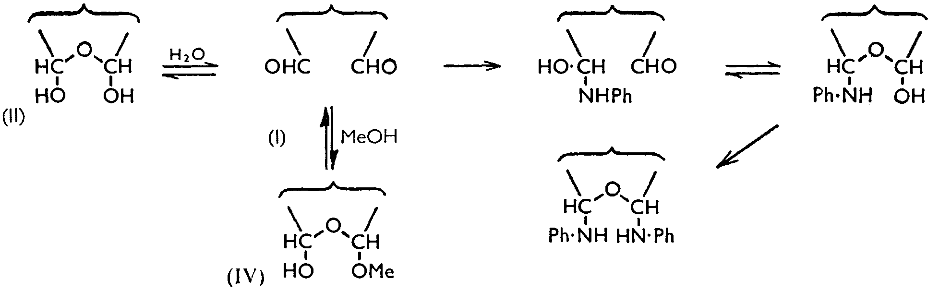


(V)



(VI)

The product of periodate oxidation of methyl 4 : 6-*O*-benzylidene-α-D-glucoside, isolated as the hemialdal monohydrate, is found to react readily, under mild conditions, with several amines; with aniline, *o*-toluidine, *p*-xylidine, or benzylamine condensation occurs giving cyclic derivatives (III), analogous to the *N*-substituted aldosylamines obtained similarly from aldoses.[3] Compound (III; $R^1 = Ph$) is also obtained by treating 7(or 9)-hydroxy-6α : 9(or 7)-dimethoxy-2-phenyl-*trans*-*m*-dioxano[5,4-*e*][1 : 4]-dioxepan [1] (IV) with aniline; therefore (III; $R^1 = Ph$) is probably formed *via* the dialdehyde (I) present in the equilibrium mixture from both (II) and (IV), as shown. The melting points of these cyclic derivatives varied with the rate of heating and the melting was generally preceded or accompanied by browning and decomposition; in this respect they resemble *N*-glycosylamines.[3]



---

[1] Part I, preceding paper.

[2] Guthrie and Honeyman, *Chem. and Ind.*, 1958, 388.

[3] Ellis and Honeyman, *Adv. Carbohydrate Chem.*, 1955, **10**, 95.

Reaction of the hemialdal monohydrate with hydroxylamine and with *cyclo*hexylamine yielded the dialdehyde dioxime (V; $R^2 = H$) and the dialdehyde bis-*N*-*cyclo*hexylaldimine (VI), respectively. The latter compound was also obtained by reaction of the dioxanodioxepan (IV) with *cyclo*hexylamine. The dioxime, which showed a weak complexing power towards copper and nickel, was further characterised as the bis-*O*-acetyloxime (V; $R^2 = Ac$) and the bis-*O*-methyloxime (V; $R^2 = Me$). The isolation of these open-chain derivatives provides further support for the equilibrium suggested for the parent compound.

EXPERIMENTAL

Light petroleum is the fraction, b. p. 60—80°. All solutions were concentrated *in vacuo*; those in chloroform or ether were previously dried with inorganic desiccants. The identity of compounds was proved where necessary by mixed m. p. determination and infrared spectrometry; all compounds had infrared spectra consistent with the assigned structures.

Reaction of 7 : 9-*Dihydroxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan Hydrate with Amines*.—(*a*) *With hydroxylamine.* The hemialdal hydrate (2 g.), sodium acetate (2 g.), and hydroxylamine hydrochloride (1 g.) in water (150 ml.) were kept at about 70° for 12 min. On cooling, a gel separated which was extracted with chloroform. Concentration of the extracts and two crystallisations from light petroleum gave (1·2 g., 59% after first crystallisation) 2 : 4-O-*benzylidene*-3-O-(D-1-*methoxy*-2-*oxoethyl*)-D-*erythrose dioxime* (V; $R^2 = H$) as needles, m. p. 99—101°, $[\alpha]_D^{18}$ $-11·9°$ (*c* 1·85 in chloroform) (Found: C, 54·0; H, 6·4; N, 9·2. $C_{14}H_{18}O_6N_2$ requires C, 54·2; H, 5·9; N, 9·0%).

Acetylation of the dioxime with acetic anhydride in pyridine at 0° gave, after recrystallisations from aqueous ethanol, 2 : 4-O-*benzylidene*-3-O-(1-*methoxy*-2-*oxoethyl*)-D-*erythrose bis*-O-*acetyloxime* (V; $R^2 = Ac$), m. p. 122·5—124°, $[\alpha]_D^{21}$ $-22·8°$ (*c* 1·58 in chloroform) (Found: C, 55·0; H, 5·7; N, 7·0. $C_{18}H_{22}O_8N_2$ requires C, 54·8; H, 5·6; N, 7·1%).

Methylation of the dioxime with Purdie's reagents for 1 hr. gave, after recrystallisations from aqueous ethanol, needles of 2 : 4-O-*benzylidene*-3-O-(1-*methoxy*-2-*oxoethyl*)-D-*erythrose bis*-O-*methyloxime* (V; $R^2 = Me$) (58%), m. p. 112—113°, $[\alpha]_D^{18}$ $-15·9°$ (*c* 0·9 in chloroform) (Found: N, 7·9. $C_{16}H_{22}O_6N_2$ requires N, 8·3%).

The addition of dilute aqueous cupric sulphate to a warm aqueous solution of the dioxime gave a clear solution, but the addition of one drop of ammonia solution produced a flocculent pale green precipitate, which on addition of more ammonia dissolved to give a dark-blue solution. Similar formation of a complex was observed with nickel nitrate.

(*b*) *With* cyclo*hexylamine.* The hemialdal hydrate (5 g.) was added to a boiling solution of *cyclo*hexylamine (50 ml.) in water (450 ml.), boiling was continued for 2 min., and the mixture then cooled. The product was collected, washed with water, dried, and recrystallised from *n*-heptane, yielding needles (5 g., 72%), m. p. 119—122°. Further recrystallisations gave 2 : 4-O-*benzylidene*-3-O-(1-*methoxy*-2-*oxoethyl*)-D-*erythrose bis*-N-cyclo*hexylaldimine* (VI), m. p. 115—117°, $[\alpha]_D^{17}$ $+11·0°$ (*c* 1·2 in chloroform), $[\alpha]_D^{21}$ $-28·6°$ (*c* 0·5 in pyridine) (Found: C, 70·8; H, 8·6; N, 6·0. $C_{26}H_{38}O_4N_2$ requires C, 70·6; H, 8·7; N, 6·3%). The same product was obtained by use of *cyclo*hexylammonium chloride and sodium acetate, or when a solution of the hemialdal hydrate (1 g.) in *cyclo*hexylamine (5 ml.) was heated at 95° for 15 min., cooled, and poured into ice–water (150 ml.).

The hemialdal hydrate (1 g.) was dissolved in boiling methanol (25 ml.), and *cyclo*hexylamine (2 ml.) was then added. After the solution had been boiled under reflux for a further 15 min. it was concentrated and cooled. The resulting solid, on recrystallisation from *n*-heptane, gave the bis-*N*-*cyclo*hexylaldimine (VI), (1·1 g., 80%), m. p. 114—116°.

(*c*) *With* o-*toluidine.* *o*-Toluidine (8·5 ml.) and the hemialdal hydrate (3 g.) were warmed at 98° for 15 min. Water (150 ml.) was added to the cooled solution followed by acetic acid (50 ml.). The solid was washed by decantation with saturated sodium hydrogen carbonate solution and with water; two crystallisations from acetone gave needles of 6α-*methoxy*-2-*phenyl*-7 : 9-*di*-o-*toluidino*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* (III; $R^1 = o\text{-Me}{\cdot}C_6H_4$), m. p. 138—140° (decomp.), $[\alpha]_D^{21}$ $+6·3°$ (*c* 0·5 in pyridine) (Found: C, 70·1; H, 6·4; N, 6·0. $C_{28}H_{32}O_5N_2$ requires C, 70·6; H, 6·8; N, 5·9%).

(*d*) *With* p-*xylidine.* Reaction of *p*-xylidine (20 ml.) and the hemialdal hydrate (4·6 g.) by method (*c*) gave needles of 6α-*methoxy*-2-*phenyl*-7 : 9-*di*-p-*xylidino*-trans-m-*dioxano*[5,4-e]-[1 : 4]-*dioxepan* (III; $R^1 = 2:5\text{-}Me_2C_6H_3$) (5·9 g., 80%), m. p. 155—156° (decomp.), $[\alpha]_D^{21}$ +108° (*c* 0·5 in pyridine) (Found: C, 71·4; H, 7·1; N, 5·3. $C_{30}H_{36}O_5N_2$ requires C, 71·4; H, 7·2; N, 5·6%).

(*e*) *With aniline.* Reaction of aniline (20 ml.) and the hemialdal hydrate (5 g.) by the same method gave needles of 7 : 9-*dianilino*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e]-[1 : 4]-*dioxepan* (III; $R^1 = Ph$) (5·2 g., 72%), m. p. 165—167° (decomp.), $[\alpha]_D^{21}$ +29·2° (*c* 0·5 in pyridine) (Found: C, 69·5; H, 6·3; N, 6·2. $C_{26}H_{28}O_5N_2$ requires C, 69·6; H, 6·3; N, 6·3%). The product could also be recrystallised from aqueous *NN*-dimethylformamide.

The hemialdal hydrate (1 g.) was added to a boiling solution of anilinium chloride (2·5 g.) and sodium acetate (5 g.) in water (100 ml.). Boiling was continued for 4 min. and the flocculent solid was collected and crystallised to yield the dianilino-derivative (56%), m. p. 162—165° (decomp.), also obtained by warming aniline with 7(or 9)-hydroxy-6α : 9(or 7)-dimethoxy-2-phenyl-*trans-m*-dioxano[5,4-*e*][1 : 4]-dioxepan [1] (IV) at 80°. It was also obtained by refluxing the hemialdal hydrate in methanol, and then adding aniline to the resulting dioxanodioxepan (IV), followed by concentration and chromatography of the product on alumina, elution with benzene, and crystallisation of the product from aqueous acetone.

(*f*) *With benzylamine.* Reaction of the hemialdal hydrate and benzylamine by method (*c*) gave a pale yellow product which was washed with water and dried *in vacuo* (P_2O_5). The first crop of crystals obtained by triturating this product with light petroleum could not be recrystallised, but further crops were combined and recrystallised from light petroleum, giving needles of 7 : 9-*bisbenzylamino*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* (III; $R^1 = PhCH_2$), m. p. 95—96°, $[\alpha]_D^{21}$ +35·4° (*c* 0·5 in pyridine) (Found: C, 70·5; H, 6·3; N, 5·9. $C_{28}H_{32}O_5N_2$ requires C, 70·6; H, 6·8; N, 5·9%). This product was also obtained by treating the hemialdal hydrate with aqueous benzylamine under the conditions described in (*b*).

The authors thank Dr. H. Spedding for helpful discussion and the Department of Scientific and Industrial Research for a maintenance award (to R. D. G.). Part of this work was sponsored by the Office, Chief of Research and Development, U.S. Department of Army, through the European Office.

KING'S COLLEGE, UNIVERSITY OF LONDON, STRAND, W.C.2.
SHIRLEY INSTITUTE, MANCHESTER, 20.

[*Received, November 21st*, 1958.]