490. *Periodate Oxidation. Part I. Structure and Some Reactions of Periodate-oxidised Methyl* 4 : 6-O-*Benzylidene*-α-D-*glucoside.*

By R. D. GUTHRIE and JOHN HONEYMAN.

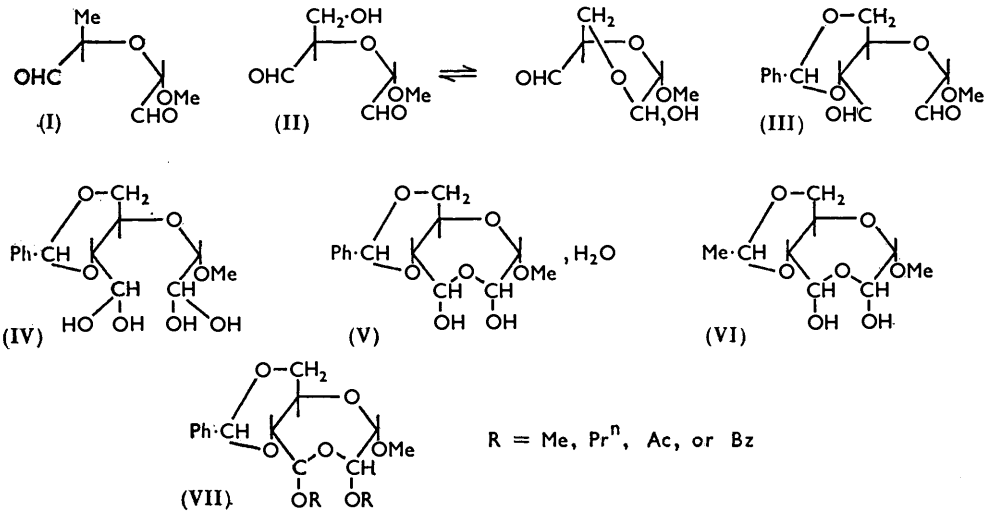
The product from the periodate oxidation of methyl 4 : 6-*O*-benzylidene-α-D-glucoside has been shown to exist in the hemialdal form (V), and this structure and its formation are discussed. In water an equilibrium exists between the open-chain dialdehyde (III) and the hemialdal form; in alcohols equilibria exist between the dialdehyde (III) and the hemialdal mono-*O*-alkyl derivatives (*e.g.*, VIII). Reaction of periodate-oxidised methyl 4 : 6-*O*-benzylidene-α-D-glucoside with phenylhydrazine yields a 1-oxa-4 : 5-diaza*cyclo*octane derivative (XI or XII).

THE " dialdehydes " from periodate oxidation fall into two classes: those with no alcoholic group in the molecule, *e.g.*, (I) from methyl α-D-rhamnoside, and those having a free hydroxyl group which may allow the formation of cyclic hemiacetals, *e.g.*, (II) from methyl α-D-glucoside.[1] The present paper concerns the dialdehyde (III) which is best prepared

[1] Cadotte, Dutton, Goldstein, Lewis, Smith, and Van Cleve, *J. Amer. Chem. Soc.*, 1957, **79**, 691.

from methyl 4 : 6-*O*-benzylidene-α-D-glucoside although other sources include the corresponding D-mannoside [2] and the 3-amino-3-deoxy-α-D-altroside.[2]

This crystalline periodate-oxidation product has been shown to have the composition of a " dialdehyde dihydrate." [3,4] Rowen, Reeves, and Forziatti,[3] who found that the infrared spectrum had no carbonyl, but strong hydroxyl, absorption bands, suggested that the compound was the dihydrated dialdehyde (IV). We have now confirmed the



elementary analysis and infrared spectrum but conclude that a more likely structure is that of a hemialdal * hydrate (V) with only one of the molecules of water covalently bound in the molecule. This was based in part on the many cases in the literature of the isolation of " dialdehyde monohydrates " from compounds of this class.[5,6,7] It is also significant that the product (VI) from methyl 4 : 6-*O*-ethylidene-α-D-glucoside, obtained as a crystalline " dialdehyde monohydrate," also had hydroxyl, but no carbonyl, infrared absorption. Both these compounds reduced Fehling's solution, but did not restore the colour to Schiff's reagent, behaviour consistent with the presence of the –O·CH(OH)– group; in this respect the compounds resemble reducing sugars. The product from methyl 4 : 6-*O*-benzylidene-α-D-glucoside showed the complex mutarotation in pyridine expected for a compound of the type illustrated. The hemialdal hydrate is insoluble in most common organic solvents, but is readily soluble in pyridine, dimethyl sulphoxide, and *NN*-dimethylformamide.

Structures (V) and (VI) are similar to those suggested by other workers [1,7,8] for analogous periodate oxidation products.

Recrystallisation of the hemialdal hydrate (V) from nitromethane gave a product whose analysis corresponded to the hemialdal and whose infrared spectrum had hydroxyl but no carbonyl absorption. The spectrum of the hydrate has a small absorption in the

* By " hemialdal " we denote a compound containing the group –CH(OH)·O·CH(OH)– (cf. Barry and Mitchell, *J.*, 1953, 3631).

[2] Honeyman and Shaw, *J.*, 1959, 2454.
[3] Rowen, Reeves, and Forziatti, *J. Amer. Chem. Soc.*, 1951, **73**, 4484.
[4] Baddiley, Buchanan, and Szabo, *J.*, 1954, 3826.
[5] Jackson and Hudson, *J. Amer. Chem. Soc.*, 1937, **59**, 994; Maclay, Hann, and Hudson, *ibid.*, 1939, **61**, 1660.
[6] Carter, Clark, Dickson, Loo, Skell, and Strong, *Science*, 1946, **103**, 540.
[7] Garcia Gonzalez, Aparicio, and Roncero, *Anales real Soc. espaň. Fís. Quím.*, 1948, **44**, *B*, 243; Garcia Gonzalez, Aparicio, and Rizo, *ibid.*, 1956, **52**, *B*, 717; Schreier, Stohl, and Hardegger, *Helv. Chim. Acta*, 1954, **37**, 574.
[8] Goldstein, Lewis, and Smith, *J. Amer. Chem. Soc.*, 1958, **80**, 939.

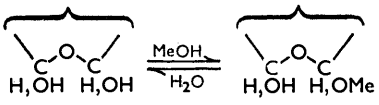
region 1640—1610 cm.$^{-1}$, usually assigned to water of crystallisation, whereas the anhydrous hemialdal has not. The hemialdal showed complex mutarotation in pyridine. Smith and his co-workers [9] have also prepared the anhydrous hemialdal but by different methods.

Acetylation or benzoylation of the hemialdal or its hydrate gave a crystalline diester (VII; R = Ac or Bz), which had no aldehydic carbonyl absorption in the infrared spectrum. Methylation or propylation by Purdie's method gave the corresponding crystalline hemialdal diglycosides (VII; R = Me or *n*-Pr). Formation of these derivatives is good evidence that structure (V) is correct for the " dialdehyde dihydrate." The same conclusion was reached independently by Smith and his co-workers who prepared a di-*p*-nitrobenzoate of the hemialdal as well as the fully methylated derivative (VII; R = Me),[10] with physical constants [11] in agreement with those of the sample we obtained.

An attempt was made to prepare sulphonates of the hemialdal, but only unchanged compound was isolated on pouring the product into water. The action of sulphonyl chlorides on sugar derivatives with a free reducing centre can lead to the formation of the corresponding chloride [12] which can be hydrolysed by pouring the reaction solution into water.

Neither the conformation of the seven-membered ring nor the position of the two hydroxyl groups with respect to the ring is known; if it is assumed that the dialdehyde is formed first and that hemialdal formation then occurs, the bulkier hydroxyl groups will take up positions in the plane of the ring, with the hydrogen atoms " axial ". Smith has suggested that periodate oxidation of methyl α-L-rhamnoside gives a product which has a six-membered ring and will have the hydroxyl groups of the hemialdal group equatorial.[8]

When the hemialdal or its hydrate was boiled with methanol, and the resulting solution concentrated and cooled, a new white crystalline compound was obtained. The infrared spectrum had a single absorption in the hydroxyl region, and none in the carbonyl region. This compound is one of the eight possible hemialdal monomethyl glycosides (VIII), with a methoxyl group on $C_{(2)}$, as shown, or on $C_{(3)}$.[13]



(VIII)

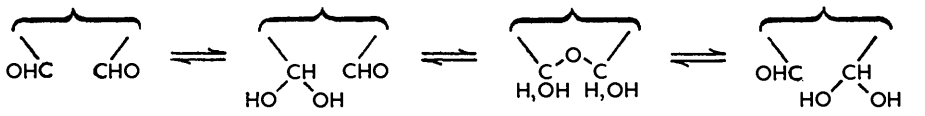
Reaction of the hemialdal hydrate with ethyl, propyl, or benzyl alcohol yielded the corresponding crystalline hemialdal monoglycoside, all of which gave the hemialdal hydrate on recrystallisation from water. The hemialdal monobenzyl glycoside could be recrystallised unchanged from ethanol. The mother liquor from preparation of the monobenzyl glycoside gave a very small amount of a second monobenzyl glycoside.

Hemialdal formation from similar dialdehydes has been postulated by several groups of workers,[1,7,8,14] but no mechanism of formation has been suggested except by Aparicio and Molini,[15] published during our studies, for the products from the oxidation of various 2-(1 : 4-anhydrotetrahydroxybutyl)furan derivatives.

The most probable mechanism for formation of the hemialdal group is by hydration of one aldehyde group followed by a normal lactol ring closure between one of the hydroxyl groups so formed and the other aldehyde group, as shown. Such a system allows for equilibrium between the true dialdehyde and the hemialdal form in solution. This has been extended to include the formation of the hemialdal monoglycosides by the reaction of the hemialdal with alcohols.[13] Hemiacetal formation could occur on one aldehyde

[9] Goldstein, Lewis, and Smith, *Chem. and Ind.*, 1958, 595.
[10] *Idem*, American Chemical Society, Abstracts of Meeting, September, 1957.
[11] Smith, personal communication.
[12] Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 125.
[13] Guthrie and Honeyman, *Chem. and Ind.*, 1958, 388.
[14] Barry and Mitchell, *J.*, 1953, 3631.
[15] Aparicio and Molini, *Anales real Soc. españ. Fís. Quím.*, 1956, **52**, *B*, 723.

group, followed by ring closure, as above, to give the eight isomeric monoglycosides. These equilibria explain the fact that crystallisation of the hemialdal monoglycosides from water yielded the hemialdal hydrate, whereas the hemialdal dimethyl glycoside (VII; R = Me), with which no such equilibrium is possible, is unaffected by boiling water. The compounds can be recrystallised from a different alcohol from that from which they were prepared without removal of the alkoxy-group or its replacement by the alkoxy-group of

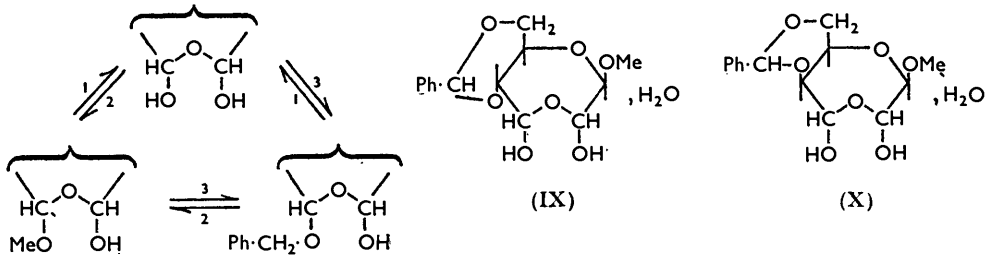


the new alcohol. For example, the hemialdal monobenzyl glycoside can be recrystallised from ethanol. Smith assumed that this meant that the alcohol bound into the hemialdal monoglycoside was " an integral part of the molecule." [9] It has been shown, however, that boiling the hemialdal monobenzyl glycoside under reflux with methanol for 30 min. gave the monomethyl glycoside, and boiling this under reflux for 30 min. with benzyl alcohol gave the hemialdal monobenzyl glycoside. The reaction sequence shown below was therefore established, which is good evidence for the existence of equilibria.

It is expected that the reactions of the hemialdal in solution will bear out these equilibria, derivatives of the hemialdal and the free dialdehyde being formed in different reactions, by analogy with reducing sugars.

As already mentioned the product of periodate oxidation of methyl 4 : 6-*O*-ethylidene-α-D-glucoside has the composition of a " dialdehyde monohydrate," showing hydroxyl but not carbonyl absorption in the infrared spectrum. Formation of a tri-*O*-methyl derivative with Purdie's reagents confirmed that this compound has structure (VI).

The products of periodate oxidation of methyl 4 : 6-*O*-benzylidene-β-D-glucoside, and of methyl 4 : 6-*O*-benzylidene-β-D-galactoside were isolated as " dialdehyde dihydrates," [2] showing hydroxyl but not carbonyl absorption in the infrared spectra. By analogy with the compound prepared above, structures (IX) and (X) are suggested.



(IX) (X)

1, H_2O 2, MeOH 3, $Ph{\cdot}CH_2{\cdot}OH$

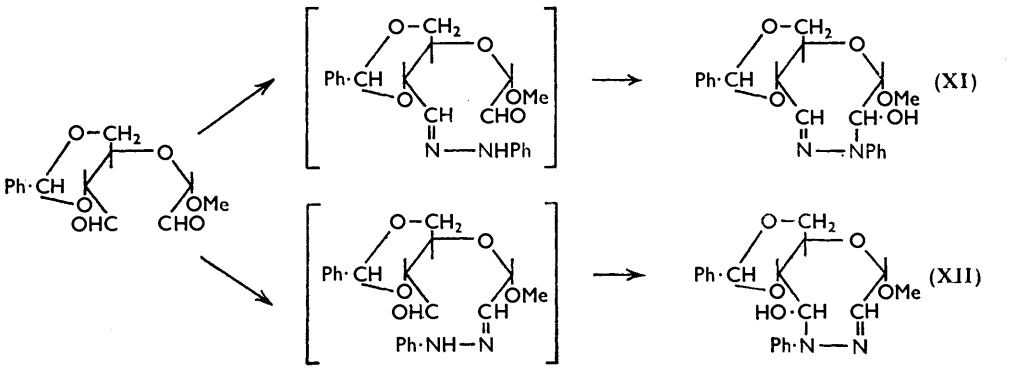
These findings have been used to explain the anomalous reaction with methanol [16] of oxycellulose prepared by use of nitrogen dioxide and oxycellulose prepared by use of periodate.

The reaction of a hot aqueous solution of the hemialdal hydrate with phenylhydrazine or of the hemialdal monomethyl glycoside with phenylhydrazine in methanol gave a yellow crystalline product, $C_{20}H_{22}O_5N_2$, corresponding to reaction of one molecule of the free dialdehyde and one molecule of phenylhydrazine with the elimination of one molecule of water. The infrared spectrum had hydroxyl absorption and only weak absorption in the C=N region at about 6·2 μ. The product, which did not form a formazan, reduced Fehling's solution less rapidly than did D-mannose phenylhydrazone. Benzoylation or methylation of the product showed that it had one hydroxyl-group. The infrared

[16] Nevell, *Chem. and Ind.*, 1958, 389.

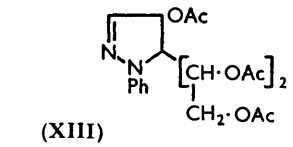
spectra of both derivatives showed no NH or OH absorption and again there was weak absorption in the C=N region.

Hydrolysis of the phenylhydrazine derivative with aqueous ethanolic acetic acid in the presence of phenylhydrazine gave a good yield of glyoxal bisphenylhydrazone, which was also obtained directly from the hemialdal hydrate under the same conditions.

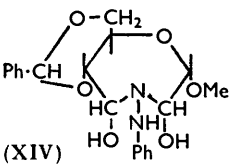


Structures (XI) and (XII) are consistent with the observed facts; both are derivatives of 1-oxa-4 : 5-diaza*cyclo*octane. The yellow colour is probably due to the C=N–N–Ph group in a ring. No eight-membered ring analogues were noted in the literature but the five-membered pyrazolines are well-known. 1-Phenyl-Δ^2-pyrazolines are yellow,[17] and the product (XIII) from the acetylation of D-mannose phenylhydrazone which is believed to be a 1-phenyl-Δ^2-pyrazoline is also orange-yellow.[18] The latter compound did not form a formazan.[19]

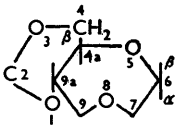
The ultraviolet maxima of 1-phenyl-Δ^2-pyrazolines [17] and of (XIII) are greater than those of the phenylhydrazine derivative and at slightly higher wavelengths; the increased ring size may cause the C=N–N–Ph chromophore to be less planar than in a five-membered ring, such as the 1-phenyl-Δ^2-pyrazolines. A decrease in $\lambda_{max.}$ and in $\varepsilon_{max.}$ due to steric effects have been observed.[20] The condensation of one molecule of a phenylhydrazine with each " dialdehyde " unit of an oxycarbohydrate has been reported on several occasions,[21-24] but no detailed study has been made of the structures of these products.



(XIII)



(XIV)



(XV)

Mester and Moczar [24] have stated with no detail, " . . . periodate-oxidised methyl 4 : 6-*O*-benzylidene-α-D-glucoside . . . in which there is no possibility of cyclic hemiacetal formation will not yield formazan (after reaction with phenylhydrazine). . . . This observation permits a ' hemialdal ' structure for this compound." The structure suggested is

[17] Duffin and Kendall, *J.*, 1954, 408.
[18] Wolfrom and Blair, *J. Amer. Chem. Soc.*, 1946, **68**, 2110; 1947, **69**, 3153.
[19] Mester and Major, *ibid.*, 1955, **77**, 4297.
[20] Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890; Huisgen *et al.*, *Annalen*, 1954, **586**, 1, 30; 1957, **610**, 57.
[21] Akiya, Okui, and Suzuki, *J. Pharm. Soc. Japan*, 1952, **72**, 785, 891.
[22] Barry and Mitchell, *J.*, 1954, 4020.
[23] Mester, *J. Amer. Chem. Soc.*, 1955, **77**, 5452; Mester and Moczar, *Chem. and Ind.*, 1957, 761.
[24] Mester and Moczar, *ibid.*, p. 764.

presumably (XIV), which is ruled out by the present work for it contains two hydroxyl groups and has the composition $C_{20}H_{24}O_6N_2$. Structures similar to (XIV) were suggested by Barry [22] for the products of condensation of phenylhydrazine with some oxypolysaccarides.

Nomenclature —These products of periodate oxidation cannot be named according to existing rules of carbohydrate nomenclature, and they are therefore described systematically as derivatives of *trans-m*-dioxano[5,4-*e*][1 : 4]-dioxepan (XV), where the prefix *trans* refers to the ring fusion. The stereochemistry of substituents in the dioxepan ring will be defined arbitrarily. $C_{(4)}$ [$C_{(6)}$ in the original sugar] being used as reference (β). Such a system enables the same symbol to be retained for the original glycosidic centre, now numbered $C_{(6)}$. The stereochemistry at $C_{(2)}$, $C_{(7)}$, and $C_{(9)}$ is not specified; thus (IX) is 7 : 9-dihydroxy-6β-methoxy-2-phenyl-*trans-m*-dioxano[5,4-*e*][1 : 4]-dioxepan hydrate.

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. Alumina was type H, 100/200 mesh, supplied by Peter Spence Ltd. 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.

7 : 9-*Dihydroxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan.*—Methyl 4 : 6-*O*-benzylidene-α-D-glucoside was oxidised with sodium periodate in aqueous solution.[4] The crystalline 7 : 9-dihydroxy-6α-methoxy-2-phenyl-*trans-m*-dioxano[5,4-*e*][1 : 4]-dioxepan hydrate (V) was washed with water and light petroleum, and recrystallised from water, aqueous acetone, or aqueous *NN*-dimethylformamide to yield the hemialdal hydrate, m. p. 143—144° (yield 65—80%) (Found: C, 53·0; H, 6·5. Calc. for $C_{14}H_{18}O_7,H_2O$: C, 53·2; H, 6·3%). The product reduced Fehling's solution, did not restore the colour to Schiff's reagent, and formed a grey precipitate with Tollens's reagent.

The product showed no absorption in the carbonyl region of the infrared spectrum, but had strong absorptions in the hydroxyl region at 3430 (shoulder), 3360, and 3260 cm.$^{-1}$, and a weak absorption at 1640—1610 cm.$^{-1}$, assigned to water of crystallisation. The mutarotation in pyridine was complex: $[\alpha]_D^{17}$ +60·8° (8 min.) ⟶ +64·0° (17 min.) ⟶ +61·3° (100 min.) ⟶ +62·4° (17 hr., constant) (*c* 4·0). The water of crystallisation was not lost at 87°/0·2 mm. for 24 hr., and higher temperatures caused excessive charring. In a water determination (Karl Fischer), made in *NN*-dimethylformamide, the product behaved as a dialdehyde dihydrate (Found: H_2O, 12·2. Calc. for $C_{14}H_{16}O_6,2H_2O$: H_2O, 11·4%).

Recrystallisation of the hemialdal hydrate (V) from nitromethane gave anhydrous 7 : 9-*dihydroxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan*, m. p. 144—145°, $[\alpha]_D^{18}$ +62·5° (13 min.) ⟶ +64·0° (3 hr.) ⟶ +63·0° (24 hr., constant) (*c* 4·0 in pyridine) (Found: C, 56·7; H, 5·9. $C_{14}H_{18}O_7$ requires C, 56·4; H, 6·1%). The infrared spectrum showed no absorption in the carbonyl region, but strong absorption in the hydroxyl region at 3410 and 3270 cm.$^{-1}$. Crystallisation of the hemialdal from water yielded its hydrate.

Esterification.—A solution of the hemialdal hydrate (V) (2 g.) in pyridine (20 ml.) and acetic anhydride (5 ml.) was kept at 0° for 17 hr. Pouring the product into ice-water gave a white precipitate (1·95 g., 81%). Two recrystallisations of the dried material from ethyl acetate–light petroleum and two from ethanol gave needles of 7 : 9-*diacetoxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* (VII; R = Ac), m. p. 177—179°, $[\alpha]_D^{20}$ +84·7° (*c* 1·81 in chloroform) (Found: C, 56·5; H, 5·8; OMe, 9·3. $C_{18}H_{22}O_9$ requires C, 56·5; H, 5·8; OMe, 8·1%).

A solution of benzoyl chloride (3 ml.) in pyridine (5 ml.) was added dropwise to one of the hemialdal hydrate (V) (2 g.) in pyridine (15 ml.) at 0°. Excess of benzoyl chloride was decomposed with water after 30 min., and after a further 15 min. the reaction solution was poured into ice–water. The precipitate was washed with water and dried. Four crystallisations from ethanol gave needles of 7 : 9-*dibenzoyloxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* (VII; R = Bz), m. p. 177—178°, $[\alpha]_D^{18}$ +5·9° (*c* 1·77 in chloroform) (Found: C, 66·0; H, 5·4. $C_{28}H_{26}O_9$ requires C, 66·4; H, 5·2%).

The same products were obtained by esterification of the anhydrous hemialdal.

Etherification.—After dry silver oxide (2 g.) had been added gradually (1·5 hr.) to a suspension of the hemialdal hydrate (V) (0·6 g.) in boiling methyl iodide (10 ml.), the mixture was boiled under reflux for a further 13 hr. Silver compounds were removed, the solvent was evaporated, and the residue was crystallised from ethanol (0·5 g., 76%) and then thrice from methanol, giving 6α : 7 : 9-*trimethoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* (VII; R = Me), m. p. 194° (sublimed), $[\alpha]_D^{17}$ +117° (*c* 0·71 in chloroform), $[\alpha]_D^{18}$ +60·7° (*c* 0·56 in pyridine), $[\alpha]_D^{19}$ +104° (*c* 0·2 in methanol) [Found: C, 59·1; H, 7·0; OMe, 26·4%; *M*, 338 (ebullioscopic in benzene). $C_{16}H_{22}O_7$ requires C, 58·9; H, 6·8; OMe, 28·5%; *M*, 326]. The product did not reduce Tollens's reagent or Fehling's solution, and was unchanged (95%) after 15 min. in boiling water. Smith [11] reported m. p. 191°, $[\alpha]_D$ +60·0° (in pyridine).

The same product was obtained on methylation of the hemialdal.

Silver oxide (3 g.) was added in portions during 1·5 hr. to a suspension of the hemialdal hydrate (V) (1 g.) in boiling *n*-propyl iodide (5 ml.) and chloroform (8 ml.); boiling under reflux was continued for a further 24 hr. Filtration, concentration and crystallisation from light petroleum (0·6 g., 48%) and then from *n*-heptane gave 6α-*methoxy*-2-*phenyl*-7 : 9-*di*-n-*propoxy*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* (VII; R = *n*-Pr), m. p. 139·5—141°, $[\alpha]_D^{21}$ +35·3° (*c* 1·02 in pyridine) (Found: C, 62·7; H, 7·8. $C_{20}H_{30}O_7$ requires C, 62·8; H, 7·9%).

Reaction of the Hemialdal with Alcohols.—The hemialdal hydrate (V) (2 g.) was boiled under reflux with methanol (50 ml.) until solution was complete. The solution was concentrated to about 4 ml. and stored at 0°; 7-(or 9)-*hydroxy*-6α : 9(or 7)-*dimethoxy*-2-*phenyl*-trans-m-*dioxano*-[5,4-e][1 : 4]-*dioxepan* (VIII) was then deposited (1·36 g.), m. p. 145—146°, $[\alpha]_D^{17}$ +79·3° (6 min.) ⟶ +84·6° (23 hr., constant) (*c* 3·27 in pyridine) (Found: C, 57·8; H, 6·4; OMe, 19·9. $C_{15}H_{20}O_7$ requires C, 57·7; H, 6·5; OMe, 19·8%). The product reduced Fehling's solution and could be recrystallised unchanged from ethanol–light petroleum, but was converted by boiling water into the hemialdal hydrate.

The same product was obtained from the hemialdal and methanol.

Methylation gave 6α : 7 : 9-trimethoxy-2-phenyl-*trans-m*-dioxano[5,4-*e*][1 : 4]-dioxepan (as VII), m. p. 193°.

Acetylation of the di-*O*-methyl compound (VIII) gave, after two recrystallisations from ethanol, the 7(or 9)-*acetoxy*-6α : 9(or 7)-*dimethoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan*, as needles, m. p. 204° (sublimed), $[\alpha]_D^{20}$ +74·0° (*c* 0·3 in chloroform) (Found: C, 57·5; H, 6·4; OMe, 19·1. $C_{17}H_{22}O_8$ requires C, 57·6; H, 6·2; OMe, 17·5%).

Reaction of the hemialdal hydrate (V) with ethanol, as for methanol, yielded 7(or 9)-*ethoxy*-9(or 7)-*hydroxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan*, m. p. 144—145° (Found: C, 59·1; H, 6·1. $C_{16}H_{22}O_7$ requires C, 58·9; H, 6·8%). The product was also obtained by repeated recrystallisation of the hemialdal hydrate from mixtures of ethanol with light petroleum, *NN*-dimethylformamide, or dimethyl sulphoxide. Recrystallisation of the product from water gave the hemialdal hydrate.

Reaction of the hemialdal hydrate (V) with *n*-propanol in the same way yielded 7(or 9)-*hydroxy*-6α-*methoxy*-2-*phenyl*-9(or 7)-*propoxy*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan*, m. p. 139—142° (Found: C, 59·5; H, 7·1. $C_{17}H_{24}O_7$ requires C, 60·0; H, 7·1%). The product, which reduced Fehling's solution, gave the hemialdal hydrate on recrystallisation from water.

The hemialdal hydrate (V) (2 g.) was boiled under reflux in benzyl alcohol (40 ml.) and *n*-heptane (10 ml.) for 30 min. The solution was cooled, diluted with ether (200 ml.), and stored at −20° overnight to give 7(or 9)-*benzyloxy*-9(or 7)-*hydroxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* as needles (from ethanol), m. p. 163—165°, $[\alpha]_D^{17}$ −2·3° (10 min.) ⟶ −9·0° (24 hr.) (*c* 1·8 in pyridine) (Found: C, 64·7; H, 6·5. $C_{21}H_{24}O_7$ requires C, 64·9; H, 6·2%). The product could be recrystallised unchanged from methanol or ethanol, but boiling under reflux with methanol for 30 min., followed by concentration gave the hemialdal monomethyl glycoside. Similarly the monobenzyl glycoside could be prepared by boiling the monomethyl glycoside under reflux with benzyl alcohol. Recrystallisation from water gave the hemialdal hydrate.

Acetylation of the product gave, after two recrystallisations from ethanol–*n*-heptane, 9(or 7)-*acetoxy*-7(or 9)-*benzyloxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan*, m. p. 174—175°, $[\alpha]_D^{21}$ +38·6° (*c* 1·6 in chloroform) (Found: C, 64·3; H, 6·3. $C_{23}H_{26}O_8$ requires C, 64·2; H, 6·1%).

Concentration of the mother liquor from the preparation of the monobenzyl glycoside, and

storage at 0° for several days gave a very small amount of 9(or 7)-*benzyloxy*-7(or 9)-*hydroxy*-6α-*methoxy*-2-*phenyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan*, m. p. 161—163°, $[\alpha]_D^{21}$ +28·3° (*c* 1·29 in pyridine), also shown to be different from the above isomer by infrared spectrometry (Found: C, 64·6; H, 6·1%).

Reaction with Phenylhydrazine.—The hemialdal hydrate (V) (2 g.) was boiled under reflux with aqueous acetic acid (10%; 20 ml.) and ethanol (35 ml.) containing phenylhydrazine (4·5 ml.) for 1·5 hr. The yellow solid which separated when the solution was cooled in ice was recrystallised from aqueous ethanol, yielding pale yellow plates of glyoxal bisphenylhydrazone (1·05 g., 70%), m. p. 165—166° (decomp.).

Phenylhydrazine (1 ml.) was added to a solution of the hemialdal hydrate (V) (2 g.) in water (500 ml.) at about 80°. Rapid cooling and shaking precipitated a yellow solid (1·8 g., 75%), m. p. 142—156°, which was washed with water and dried *in vacuo* (P_2O_5). Chromatography of this material on alumina, elution with benzene, and recrystallisation twice from *n*-heptane yielded the 1-*oxa*-4 : 5-*diaza*cyclo*octane derivative* (XI or XII), m. p. 182—183°, $[\alpha]_D^{20}$ +8·6° (*c* 1·81 in chloroform) (Found: C, 64·8; H, 6·0; N, 7·1. $C_{20}H_{22}O_5N_2$ requires C, 64·9; H, 6·0; N, 7·6%). The product reduced Fehling's solution and did not form a formazan when a solution in ethanol–pyridine was added to an aqueous benzenediazonium chloride solution. The product had the absorption expected for OH or NH groups and a weak absorption at 1610 cm.$^{-1}$; the ultraviolet spectrum had $\lambda_{max.}$ 266 mμ, $\varepsilon_{max.}$ 9640, in ethanol.

The same product was obtained by adding phenylhydrazine hydrochloride and excess of sodium acetate to a hot solution of the hemialdal hydrate (V) in water. It also resulted from heating the hemialdal monomethyl glycoside (VIII) with phenylhydrazine in refluxing methanol, concentrating the solution, and chromatographing the residue. Hydrolysis of the solid in the presence of phenylhydrazine, using the method above, yielded, after two recrystallisations from aqueous ethanol, glyoxal bisphenylhydrazone (74%), m. p. 162—164° (decomp.).

Benzoyl chloride (1 ml.) in pyridine (2 ml.) was added to a solution of the phenylhydrazine derivative (XI or XII) (1·5 g.) in pyridine (30 ml.) at 0°, and the mixture kept at 0° for 20 min. Water was then added, and after a further 10 min. the solution was poured into water. Chloroform extraction, concentration, and crystallisation from aqueous ethanol gave pale yellow needles (0·55 g., 45%) of the *benzoate* of the 1-oxa-4 : 5-diaza*cyclo*octane derivative, m. p. 123—124°, $[\alpha]_D^{21}$ +158° (*c* 1·2 in chloroform) (Found: C, 68·8; H, 5·7; N, 5·6; Bz, 23·3, 22·1. $C_{27}H_{26}O_6N_2$ requires C, 68·3; H, 5·5; N, 5·9; Bz, 22·2%). The product did not form a formazan, and the infrared spectrum had absorption expected for an ester but no absorption typical of OH and NH groups, and also weak absorptions at 1602 and 1500 cm.$^{-1}$. The ultraviolet spectrum had $\lambda_{max.}$ 230 and 270 mμ (ε 18,820 and 17,250 respectively) in ethanol.

Methylation of the phenylhydrazine derivative (XI or XII) with Purdie's reagents for 15 hr. gave, on removal of the silver compounds, concentration of the filtrate, and two crystallisations from aqueous ethanol, a small amount of the *methylated derivative*, m. p. 118—121° (Found: OMe, 15·0. $C_{21}H_{24}O_5N_2$ requires OMe, 16·1%). The infrared spectrum showed no absorption due to OH or NH groups and had a weak absorption at 1610 cm.$^{-1}$.

7 : 9-*Dihydroxy*-6α-*methoxy*-2-*methyl*-trans-m-*dioxano*[5,4-e][1 : 4]-*dioxepan* (VI).—This compound, prepared by the oxidation of methyl 4 : 6-*O*-ethylidene-α-D-glucoside, had m. p. 130—131°, $[\alpha]_D^{20}$ +8·8° (in water), $[\alpha]_D^{16}$ +97·6° (20 min.) ⟶ +91·0 (24 hr.) (*c* 2·72 in pyridine). It (0·5 g.) was methylated with Purdie's reagents during 17 hr. Removal of the silver compounds, concentration of the filtrate, and two crystallisations from light petroleum containing one drop of ethanol gave the 6α : 7 : 9-*trimethoxy*-2-*methyl*-trans-m-*dioxano*[5,4-e]-[1 : 4]-*dioxepan*, m. p. 178°, $[\alpha]_D^{22}$ +85·8° (*c* 0·17 in pyridine) (Found: C, 50·4; H, 7·9; OMe, 34·4. $C_{11}H_{20}O_7$ requires C, 50·0; H, 7·6; OMe, 35·3%). The infrared spectrum had no hydroxyl or carbonyl absorption.

The authors thank the Department of Scientific and Industrial Research for a maintenance award to R. D. G.

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

[*Received, October 23rd*, 1958.]