538. *Reaction of Some Alkyl Iodides with Periodate.*

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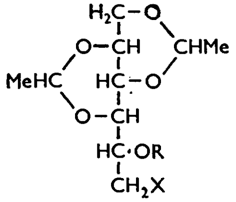
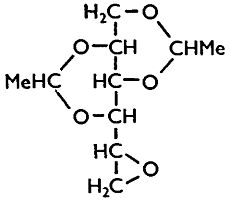
Alkyl iodides are slowly attacked by periodate. Three mols. of oxidant are consumed in the ultimate conversion of the iodine into iodate ion with concomitant formation of hydrogen ions. Elemental iodine is an intermediate in the reaction. Alkyl chlorides and bromides are much less susceptible to attack although reaction is facilitated by vicinal carbonyl groups.

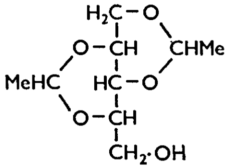
PERIODATE is known to cleave 1,2-glycols and related compounds.[1] However, other types of oxidation reaction have been recognized,[1,2] for example, the so-called over-oxidation [3] in which a methylene group is hydroxylated so that further cleavage becomes possible. Whilst studying α-halogenoacetaldehydes [4] we observed that alkyl iodides themselves are attacked by periodate. The reaction was first met with 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) but may be general for alkyl iodides.



(I), X = I, R = H. (II), X = Br, R = H.
(III), X = Cl, R = H. (IV), X = I, R = Ac.
(V), X = I, R = CO·Cl$_3$. (VI), X = OH, R = H.



(VII)



(VIII)

Reaction of 1,3-2,4-di-*O*-ethylidene-D-glucitol [5] (VI) with 1 mol. of toluene-*p*-sulphonyl

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[1] See Bobbitt, *Adv. Carbohydrate Chem.*, 1956, **11**, 9.
[2] Greville and Northcote, *J.*, 1952, 1945.
[3] See, *e.g.*, Wolfrom and Bobbitt, *J. Amer. Chem. Soc.*, 1956, **78**, 2489.
[4] Bose, Foster, and Stephens, unpublished work.
[5] Appel, *J.*, 1935, 425; Bourne and Wiggins, *J.*, 1948, 1933.

chloride and then with acetic anhydride (both in pyridine) gave a 5-*O*-acetyl-6-*O*-toluene-*p*-sulphonyl derivative which was converted[6] into 5,6-anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol (VII) by sodium methoxide. The same compound was less conveniently obtained by preparation of 1,3-2,4-di-*O*-ethylidene-6-*O*-toluene-*p*-sulphonyl-D-glucitol and its treatment with sodium methoxide.[7] The epoxide ring in compound (VII) was opened by methylmagnesium iodide,[6] to yield 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I). A better method of preparing the iodo-compound (I) involved treating the epoxide (VII) with hydriodic acid in aqueous tetrahydrofuran[8] at −10°. Under similar conditions the epoxide was converted into 6-bromo-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (II) by hydrobromic acid and into 6-chloro-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (III) by hydrochloric acid.

By comparison with the behaviour of similar compounds,[6,9] the epoxide derivative (VII) would be expected to yield 6-substituted products in these reactions. Attempts to prove this for the iodo-compound (I) by acidic hydrolysis of the ethylidene residues were unsuccessful. Under conditions (0·1N-sulphuric acid at 95° in an open vessel) where the ethylidene residues were removed from 1,3-2,4-di-*O*-ethylidene-D-glucitol (VI) in 3 hr. the alkyl iodide group in compound (I) was extensively, if not completely, hydrolysed. The iodo-compound (I) was reduced to 6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol by lithium aluminium hydride or by Raney nickel and hydrogen in the presence of sodium hydrogen carbonate; the deoxy-group in this compound is at position 6 because the deoxyhexitol produced by acidic hydrolysis reduces approximately 4 mol. of periodate. Similarly 6-bromo- and 6-chloro-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol each yielded a product on acidic hydrolysis which reduced approximately 4 mol. of periodate, confirming the 6-position of the halogen atoms. The alkyl chloride group of compound (III) remained intact during the acidic hydrolysis but the alkyl bromide group in the bromide (II) underwent *ca.* 11% of hydrolysis.

Acid-hydrolysis of alkylidene derivatives is usually performed in open vessels,[10] and, in the case of 1,3-2,4-di-*O*-ethylidene-D-glucitol, went smoothly to completion with no obvious break which would indicate a different rate of hydrolysis of the ethylidene residues. In sealed tubes, however, an equilibrium was rapidly established after the release of *ca.* 1·2 mol. of acetaldehyde, leaving a hexitol derivative (presumably[10] essentially 2,4-*O*-ethylidene-D-glucitol) which consumed 1·39 mol. of periodate. Work in sealed tubes may thus have some value for graded acid-hydrolysis of polyalkylidene carbohydrates.

When aqueous 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) containing sodium metaperiodate was stored at room temperature, 4 mols. of oxidant were slowly consumed ($t_{\frac{1}{2}}$ *ca.*, 100 hr.; see Figure). Acid-hydrolysis of the carbohydrate product gave xylose (identified by chromatography), and reduction with sodium borohydride gave 1,3-2,4-di-*O*-ethylidene-D-xylitol identical with the product of sequential periodate oxidation and borohydride reduction of 1,3-2,4-di-*O*-ethylidene-D-glucitol (VI). (A racemic mixture would result from the reaction of xylitol with acetaldehyde.[10]) In a separate experiment, when 3·84 mol. of periodate had been consumed (after 593 hr.) by the 6-iodo-compound (I), 1·13 equiv. of hydrogen ion and 0·61 mol. of formaldehyde had been liberated. It is possible that, owing to the prolonged reaction and the presence of iodine, some oxidation of formaldehyde to formic acid occurred (cf. Davidson[11]). The reaction of the 6-iodo-compound (I) with periodate appeared not to be due to acid-hydrolysis of the alkyl iodide group (the pH of the periodate solutions used was 4·5) followed by oxidation of iodide ion. Thus iodide ion was not formed when aqueous solutions of the

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[6] Cf. Foster and Overend, *J.*, 1951, 1132.

[7] Puskas and von Vargha, *Ber.*, 1943, **76**, 862.

[8] Cf. Lucas and Garner, *J. Amer. Chem. Soc.*, 1950, **72**, 2145.

[9] Wiggins and Wood, *J.*, 1950, 1566.

[10] See Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.

[11] Davidson, *J. Textile Inst.*, 1941, T117.

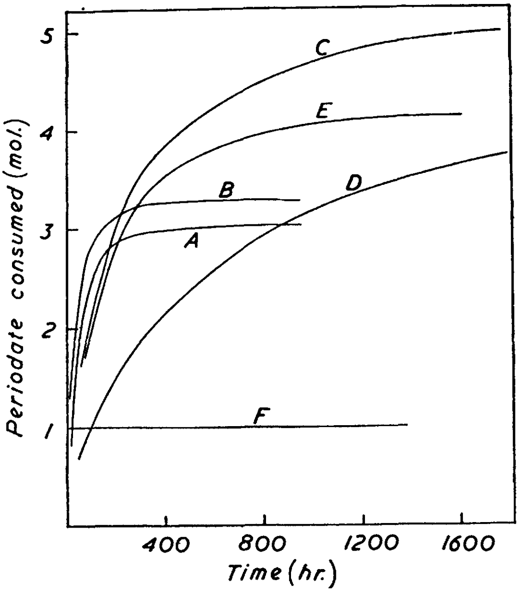
6-iodo-compound (I), acidified severally to pH 4·5 and 2·5, were stored for long periods. 1,3-2,4-Di-*O*-ethylidene-D-glucitol rapidly consumed 1 mol. of periodate at pH 4·5, but no further reaction occurred; the ethylidene residues were stable under these conditions.

These observations indicate the probable stoicheiometry of the reaction of 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) with periodate as:

$$R{\cdot}CH(OH){\cdot}CH_2I + 4IO_4^- \longrightarrow R{\cdot}CHO + H{\cdot}CHO + 5IO_3^- + H^+ \quad . \quad . \quad . \quad . \quad (1)$$

$$I^- + 3IO_4^- \longrightarrow 4IO_3^- \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Mellor[12] records a complex reaction between periodate and iodide, but Willard and Greathouse[13] consider equation (2) to operate when excess of periodate and iodide react at 70—80°. Tolstikov[14] reports that the reaction proceeds in the pH range 4·3—7·0 and that iodate ions are amongst the products. Mixing aqueous solutions of sodium metaperiodate and sodium iodide caused rapid precipitation of iodine which then slowly disappeared; approximately three mols. of periodate were ultimately consumed with no change in pH of the medium. Willard and Greathouse's observations are thus confirmed. The 6-iodo-compound (I) (and each of the alkyl iodides studied) reacted with periodate, liberating iodine but to an extent never exceeding its solubility, so that the initial reaction of periodate with the alkyl iodide must be slow and essentially independent of subsequent reactions.



Oxidation of alkyl iodides with periodate at room temperature. The solutions (100 *ml.*) *contained approx.* 0·68 *mmole of alkyl iodide and* 6·25 *mmoles of sodium periodate. A, methyl iodide; B, ethyl iodide; C, iodoacetic acid; D, β-iodopropionic acid; E,* 6-*deoxy*-1,3-2,4-*di*-O-*ethylidene*-6-*iodo*-D-*glucitol; F,* 1,3-2,4-*di*-O-*ethylidene*-D-*glucitol.*

Methyl and ethyl iodide consume approximately 3 mol. of periodate (see Figure) with liberation of hydrogen ion. Iodoacetic acid reacted slowly (reaction incomplete after 2000 hr.) with the apparent consumption of 4 mol. of oxidant (see Figure) and liberation of formaldehyde and hydrogen ion. It seems probable that glycollic acid initially formed is itself slowly attacked by periodate. β-Iodopropionic acid consumed 5—6 mol. of periodate, liberating both hydrogen ion and formaldehyde. β-Hydroxypropionic acid,

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[12] Mellor, " A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Longmans, London, 1922, Vol. II, p. 407.

[13] Willard and Greathouse, *J. Amer. Chem. Soc.*, 1938, **60**, 2869.

[14] Tolstikov, *Sbornik Statei po obshchei Khim., Akad. Nauk S.S.S.R.*, 1953, **2**, 1249; *Chem. Abs.*, 1955, **49**, 2921.

presumably an initial product of the reaction, is, surprisingly, slowly oxidised by periodate (0·25 mol. of oxidant consumed at pH 5·1 in 75 days at room temperature). This and related reactions will be discussed in detail in a separate paper.

The mechanism whereby alkyl iodides are attacked by periodate is not readily apparent. Conductivity measurements[15] indicate that alkyl halides are ionized to a limited extent so that, in the presence of periodate, oxidation to iodine and bromine would be expected and, since the ionization equilibria would be disturbed, would proceed to completion. Were this in fact the situation then any reagent capable of reacting rapidly with halide ions should also disturb the ionization equilibria and the rate of the reaction should be largely independent of the attacking species. This is not the case. Thus, with aqueous methyl iodide silver ions reacted completely within a few hours (cf. Gand[15,16] and Dostrovsky and Hughes[17]), periodate ions within a few days, iodate ions in presence of acid extremely slowly and cupric ions in neutral solution not detectably. It is possible that the reaction may proceed by the attack of periodate on the alkyl iodide in the form of an ion-pair.[18]

Under the conditions where the 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (I) reacted with periodate the 6-bromo- and the 6-chloro-analogue were essentially unaffected. Similarly 1,2-dibromoethane was not attacked by periodate but ethyl bromoacetate, bromoacetaldehyde,[4] and chloroacetaldehyde[4] were. Although reaction of alkyl halides with periodate is slow compared with the usual rates of periodate oxidation, it should be borne in mind when the periodate oxidation of halogenated carbohydrates is contemplated. Moreover, a knowledge of the stoicheiometry of the reactions could be of value in certain structural studies.

Although 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol with acetic anhydride in pyridine readily gave a 5-acetate and with trichloroacetyl chloride a 5-trichloroacetate, toluene-*p*-sulphonylation could not be effected. Recovery of unchanged starting material from the last reactions suggested that there might be some steric hindrance but scale models revealed no obvious shielding of the hydroxyl group and apparently similar compounds give toluene-*p*-sulphonates.[19] It is of interest that Stork and White[20] have recorded that *trans*-6-alkyl-2-*cyclo*hexen-1-ols readily gave acetates but did not give toluene-*p*-sulphonates.

EXPERIMENTAL

The consumption of periodate was determined essentially by Jackson's method.[21]

6-Deoxy-6-halogeno-derivatives of 1,3-2,4-*Di-*O*-ethylidene-*D*-glucitol.*—(*a*) 5,6-Anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol[7,22] (0·43 g.) was added to boiling ethereal methylmagnesium iodide (3 ml.) [prepared from ether (275 ml.), magnesium (16·4 g.) and methyl iodide (93 g.)], and the mixture was boiled under reflux for 4 hr. After cooling to −10° the complex was decomposed with 2N-hydrochloric acid. To the separated ether layer were added two chloroform extracts of the aqueous layer, and the combined solutions were washed with aqueous sodium hydrogen carbonate (twice), then water (twice), dried ($MgSO_4$), and evaporated. Recrystallization of the residue (0·14 g., 20%) four times from benzene–light petroleum (b. p. 60—80°) gave *6-deoxy-*1,3-2,4-*di-*O*-ethylidene-*6-*iodo-*D*-glucitol*, m. p. 151°, $[\alpha]_D^{21}$ −3·8° (*c* 4·5 in $CHCl_3$) (Found: C, 35·4; H, 5·1; I, 36·2. $C_{10}H_{17}O_5I$ requires C, 34·9; H, 5·0; I, 36·9%). The poor yield is probably due to the low solubility of the anhydro-compound in ether.

(*b*) A stirred solution of 5,6-anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol (6 g.) in tetrahydrofuran (100 ml.) at −15° was treated with 56% hydriodic acid (3·88 ml., 1·04 mol.), so that the temperature did not rise above 0°. The solution was then stored at −5°, and the consumption

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[15] Gand, *Ann. Fac. sci. Marseille*, 1939, **12**, 134; *Chem. Abs.*, 1941, **35**, 681.

[16] Gand, *Bull. Soc. chim. France*, 1945, **12**, 303.

[17] Dostrovsky and Hughes, *J.*, 1946, 169.

[18] Winstein, 14th Congr., Internat. Union Pure Appl. Chem., *Experientia*, 1957, Suppl. 2, p. 149.

[19] Foster and Overend, *J.*, 1951, 3452.

[20] Stork and White, *J. Amer. Chem. Soc.*, 1956, **78**, 4609.

[21] Jackson, " Organic Reactions," 1944, Vol. II, p. 361.

[22] Wiggins, *J.*, 1946, 388.

of acid followed by titration of aliquot parts with standard sodium hydroxide solution; reaction was essentially complete in 10 hr. After 43 hr. sodium thiosulphate and potassium carbonate were added to remove free iodine and excess of acid, followed by sufficient water to form two phases. The organic layer was separated and evaporated and the residue extracted several times with chloroform. The combined extracts were dried ($MgSO_4$) and concentrated to yield a residue (8·13 g., 86%) having m. p. 145—146° which was not changed by recrystallization from benzene–light petroleum (b. p. 60—80°). The yields of 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol in a series of experiments were in the range 45—86% and the m. p.s of various preparations, although sharp in each case, varied within the range 144—153°.

By essentially the same procedure, 5,6-anhydro-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·2 g.) in tetrahydrofuran (12 ml.) with 45·5% hydrobromic acid (0·123 ml., 1·1 mol.) gave 6-*bromo*-6-*deoxy*-1,3-2,4-*di*-O-*ethylidene*-D-*glucitol* (0·27 g., 98%) which after recrystallization from benzene–light petroleum (b. p. 60—80°) had m. p. 141—143°, $[\alpha]_D^{21}$ −4·1° (*c* 4·4 in $CHCl_3$) (Found: C, 40·1; H, 5·7; Br, 26·3. $C_{10}H_{17}O_5Br$ requires C, 40·4; H, 5·8; Br, 26·9%).

Treatment of a solution of the anhydro-compound (0·2 g.) in tetrahydrofuran (10 ml.) with 10·4N-hydrochloric acid (0·107 ml., 1·2 mol.) essentially as above gave 6-*chloro*-6-*deoxy*-1,3-2,4-*di*-O-*ethylidene*-D-*glucitol* (0·08 g., 38%, after recrystallization from benzene–light petroleum), m. p. 156—158°, $[\alpha]_D^{21}$ +0·3° (*c* 3·3 in $CHCl_3$) (Found: C, 47·7; H, 6·7; Cl, 14·0. $C_{10}H_{17}O_5Cl$ requires C, 47·5; H, 6·8; Cl, 14·0%). Yields of *ca.* 70% were obtained in subsequent preparations.

The halogeno-compounds were all soluble in water, and in certain of the preparations, irrespective of the halogen being introduced, a small amount of a water-insoluble, halogen-free compound was obtained, which, after recrystallization from ethanol, had m. p. 168—169° (Found: C, 53·25; H, 5·8%); the molecular weight (Rast in camphor [23]) (455 ± 60) suggested some type of dimerization.

6-Deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol with acetic anhydride and pyridine gave a 5-*acetate*, m. p. 128—129°, $[\alpha]_D^{21}$ −35·7° (*c* 4·4 in $CHCl_3$) (Found: C, 37·5; H, 5·0; I, 32·6. $C_{12}H_{19}O_6I$ requires C, 37·3; H, 5·0; I, 32·9%), and with trichloroacetyl chloride in pyridine gave a 5-*trichloroacetate*, m. p. 130·5—131·5°, $[\alpha]_D^{21}$ −38·3° (*c* 6·1 in $CHCl_3$) (Found: C, 29·3; H, 3·1; I, 25·7. $C_{12}H_{16}O_6Cl_3I$ requires C, 29·4; H, 3·3; I, 25·9%).

Acid-hydrolysis of 1,3-2,4-*Di*-O-*ethylidene*-D-*glucitol*.—(a) *In a sealed tube.* 1,3-2,4-Di-*O*-ethylidene-D-glucitol (2 g.) was dissolved in a small volume of water, 5N-sulphuric acid (10 ml.) was added, and the volume adjusted to 50 ml. Aliquot parts (4 ml.) were sealed in ampoules and immersed in boiling water. At suitable intervals ampoules were cooled to −10°, and a portion (1 ml.) of the contents diluted with water to 10 ml. Vicinal glycol groups were determined by periodate oxidation, and acetaldehyde essentially by Dyer's method.[24] Equilibrium was established in <10 min., 1·2 mol. of acetaldehyde being liberated, and the remaining carbohydrate consumed 1·39 mol. of periodate.

(b) *In an open vessel.* Hydrolyses at 95° involved (1) a 0·16% solution of 1,3-2,4-di-*O*-ethylidene-D-glucitol in N-sulphuric acid and (2) a 5·3% solution in 0·1N-sulphuric acid, with the following results:

(1)	Time (min.)	0	5	10	15		
	IO_4 consumption (mol.)	1·04	4·42	4·99	5·05		
(2)	Time (min.)	0	22	44	50	120	160
	IO_4 consumption (mol.)	1·10 *	2·42	3·42	4·00	4·65	4·92

* This portion stored at room temperature for 3·5 hr. before analysis.

Reduction of 6-*Deoxy*-1,3-2,4-*di*-O-*ethylidene*-6-*iodo*-D-*glucitol*.—(*a*) To a solution of lithium aluminium hydride (0·83 g., 4 mol.) in dry ether (20 ml.), 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (2 g.) was added and the mixture boiled for 6·5 hr. Excess of hydride was destroyed with ethyl acetate, water was added, and the aqueous solution was extracted with ethyl acetate and then chloroform. The combined extracts were evaporated, the residue was extracted with chloroform and the dried ($MgSO_4$) extracts were evaporated. Recrystallization

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[23] Linstead, Elvidge, and Whalley, "Modern Techniques of Organic Chemistry," Butterworths, London, 1955, p. 145.

[24] Dyer, "Methods of Biochemical Analysis," Interscience, New York, 1956, Vol. III, p. 129.

of the residue (0·56 g., 44%) from ethanol–light petroleum (b. p. 60—80°) gave 6-*deoxy*-1,3-2,4-*di*-O-*ethylidene*-D-*glucitol*, m. p. 178—179°, $[\alpha]_D^{21}$ $-8·9°$ (*c* 1·5 in $CHCl_3$) (Found: C, 55·4; H, 8·4. $C_{10}H_{18}O_5$ requires C, 55·1; H, 8·3%).

(*b*) Raney nickel (*ca.* 0·1 g.; W-2), platinum oxide (*ca.* 10 mg.), and saturated aqueous sodium hydrogen carbonate (4 ml.) were added to a solution of 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (1 g.) in ethanol (6 ml.). The mixture was shaken in hydrogen at a slight overpressure; hydrogen consumption (70 ml., 1 mol.) was complete within 3 hr. The filtered solution was evaporated and the residue extracted several times with ethyl acetate. Evaporation of the extracts and recrystallization of the residue from ethanol–light petroleum (b. p. 60—80°) gave 6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·2 g., 41%), m. p. 173—174°.

Acid-hydrolysis and Periodate Oxidation of 6-*Deoxy*-1,3-2,4-*di*-O-*ethylidene*-D-*glucitol and its* 6-*Bromo- and* 6-*Chloro-derivatives.*—6-Bromo-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·1017 g., 0·342 mmole), 6-chloro-6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·08645 g., 0·342 mmole), and 6-deoxy-1,3-2,4-di-*O*-ethylidene-D-glucitol (0·0746 g., 0·342 mmole) were severally dissolved in 0·2N-sulphuric acid (5 ml.), and the solutions heated at 95° for 3 hr. The consumptions of periodate were: 6-bromo-6-deoxy-compound 3·96 mol.; 6-chloro-6-deoxy-compound 3·97 mol.; 6-deoxy-compound 4·12 mol. The value for the bromo-compound is corrected for a small amount (11·3%) of hydrolysis of the alkyl bromide.

Action of Periodate on 6-*Deoxy*-1,3-2,4-*di*-O-*ethylidene*-6-*iodo*-D-*glucitol.*—(*a*) To a solution of the iodo-compound (0·2352 g., 0·684 mmole) in water was added 0·25M-sodium metaperiodate (25 ml., 8·8 mmoles), and the volume adjusted to 100 ml. A similar solution containing 1,3-2,4-di-*O*-ethylidene-D-glucitol (0·16 g., 0·684 mmole) was prepared for comparison. The solutions were stored at room temperature in the dark and the following consumption of periodate observed:

Time (hr.)	25	48	93	144	281	619	955	1296
IO_4 consumption (mol.) ...	0·62	1·17	1·70	2·38	3·20	3·83	4·03	4·13

After 2·5 hr. 1,3-2,4-di-*O*-ethylidene-D-glucitol had consumed 1·02 mol. of periodate; no further uptake occurred during the next 1000 hr.

During the oxidation of the iodo-compound, free iodine was produced although its concentration never exceeded its solubility and it had disappeared after 950 hr. This was observed in all oxidations of the iodides in aqueous solution by sodium metaperiodate.

After 355 hr. an aliquot part (5 ml.) of the reaction solution containing the iodo-compound was treated with ethylene glycol (1 ml.) for 5 min., then 0·5N-sulphuric acid (2 ml.) was added and the solution boiled for 3 hr. The hydrolysate was neutralized with barium carbonate, then filtered, and the filtrate concentrated to small bulk. Analysis of the concentrate by paper chromatography on Whatman No. 4 paper with a formic acid–acetic acid–water–ethyl acetate (1 : 3 : 4 : 8) solvent system and detection with aniline hydrogen phthalate [25] revealed a single reducing component with properties identical with those of D-xylose.

(*b*) An aqueous solution of sodium metaperiodate and 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol identical with that described in (*a*) was stored in the dark at room temperature. The consumption of periodate was followed, as were the liberation of hydrogen ion (by Dyer's method [24]) and the production of formaldehyde (by the chromotropic acid method [26]). After 593 hr. 3·84 mol. of periodate had been consumed ($t_{\frac{1}{2}}$ oxidation 140 hr.), 1·13 equiv. of H^+ and 0·61 mol. of formaldehyde being liberated. Reaction was still proceeding after 2000 hr. The pH values of solutions of the iodo-compound (50 mg.) in water (25 ml.) were adjusted to 4·5 and 2·5 by dilute sulphuric acid, and the mixtures were stored at room temperature. Iodide ions were not released during 750 hr.

1,3-2,4-*Di*-O-*ethylidene*-D-*xylitol.*—(*a*) A solution of 1,3-2,4-di-*O*-ethylidene-D-glucitol (3 g.) and sodium metaperiodate (5·37 g., 2 mol.) in water (60 ml.) was stored at room temperature for 20 min. and then continuously extracted with benzene for 20 hr. Evaporation of the extract gave a syrupy residue (1·83 g.) which was dissolved in water (20 ml.) and treated with sodium borohydride (0·52 g.) for 5 hr. at room temperature. Excess of hydride was decomposed with dilute acetic acid, and the solution basified with sodium hydrogen carbonate and continuously extracted with benzene for 20 hr. Evaporation of the extract and recrystallization

[25] Partridge, *Nature*, 1949, **164**, 443.

[26] O'Dea and Gibbons, *Biochem. J.*, 1953, **55**, 580.

of the residue (1·5 g.) from ethanol gave 1,3-2,4-*di*-O-*ethylidene*-D-*xylitol*, m. p. 161—162°, $[\alpha]_D^{21}$ +5·6° (*c* 4·5 in $CHCl_3$) (Found: C, 52·8; H, 7·9. $C_9H_{16}O_5$ requires C, 52·9; H, 7·9%).

(*b*) An aqueous solution (1 l.) containing 6-deoxy-1,3-2,4-di-*O*-ethylidene-6-iodo-D-glucitol (2·352 g.) and sodium metaperiodate (13·35 g.) was stored at room temperature for 29 days. Reaction was then complete. 200 ml. of the solution were continuously extracted with benzene for 4 days. Concentration of the extract gave a syrupy residue (0·276 g.) which on reduction with sodium borohydride as described in (*a*) gave 1,3-2,4-di-*O*-ethylidene-D-xylitol, m. p. and mixed m. p. 154—156°.

Comparison of Reaction of Sodium Metaperiodate with the 6-*Iodo*-, 6-*Bromo*-, *and* 6-*Chloro-derivatives of* 6-*Deoxy*-1,3-2,4-*di*-O-*ethylidene*-D-*glucitol.*—Aqueous solutions (100 ml.) containing 0·684 mmole of halogeno-derivative and sodium metaperiodate (equivalent to 25 ml. of a 0·25M-solution) were stored at 25—26° in the dark. The consumptions of periodate were:

Time (hr.)		20	63	119	164	239	354
IO_4 reduced (mol.) :	iodide	1·1	2·21	3·14	3·55	3·94	4·25
	bromide	—	—	0·04	—	—	0·05
	chloride	—	—	0·05	—	—	0·06

Action of Sodium Metaperiodate on Sodium Iodide.—To a solution of sodium iodide (0·051 g., 0·342 mmole) in water, 0·25M-sodium metaperiodate (11 ml.) was added and the volume adjusted to 50 ml. Iodine was immediately precipitated. After 7 days the mixture was free from insoluble iodine and the consumption of periodate was followed thereafter:

Time (days)	7	8	10	12
Consumption (mol.)	2·84	2·87	2·92	2·93

The pH of the mixture was initially and finally 4·4.

Action of Sodium Metaperiodate on Some Alkyl Halides.—Solutions of methyl iodide (0·1008 g., 0·710 mmole), ethyl iodide (0·1022 g., 0·655 mmole), iodoacetic acid (0·1275 g., 0·684 mmole), and β-iodopropionic acid (0·1371 g., 0·684 mmole) severally in water (100 ml.) containing sodium metaperiodate (equivalent to 25 ml. of 0·25M-solution) were stored at room temperature in the dark. The consumption of periodate was followed, with the results shown in the Figure. The hydrogen ion and formaldehyde production were determined by the methods previously noted and the following results were obtained:

	H^+ (equiv.) after 1048 hr.	CH_2O (mol.) after 1390 hr.	CH_2O (mol.) after 2611 hr.
MeI	0·73	—	—
EtI	0·71	—	—
$CH_2I{\cdot}CO_2H$	1·16	0·35	0·48
$CH_2I{\cdot}CH_2{\cdot}CO_2H$	1·5	0·52	0·65

Under similar conditions 1,2-dibromoethane did not react with periodate but ethyl bromoacetate reacted slowly with the formation of bromine.

Reaction of Methyl Iodide with Ag^+, Cu^{++}, *and* IO_3^-.—To a saturated (0·082M) aqueous solution (50 ml.) of methyl iodide the following aqueous solutions were severally added: 0·95N-silver nitrate (25 ml.), N-copper sulphate (25 ml.), and N-potassium iodate (25 ml.). No reaction of methyl iodide was apparent in the presence of Cu^{++} after several weeks; an immediate slight colour was formed in the iodate solution and slowly intensified as iodine was released; there was an immediate precipitate of silver iodide[4] in the presence of Ag^+, essentially complete within 2 hr.

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