

solid (240 mg, 9% based on NMP,  $d_4^{25}$  mp 121.5–123°) was identified as N-methyl-2-pyrrolidonium tosylate 4 by spectral comparison and mixture melting point with authentic material.

*Anal.* Calcd for  $C_{12}H_{17}NO_4S$ : C, 53.11; H, 6.32; N, 5.15; O, 23.59; S, 11.82. Found: C, 52.58; H, 6.12; N, 5.11; O, 24.02; S, 12.12.

**Cleavage of 1 in Deuterated NMP.**—Ester 1 (31 mmoles) was dissolved in 3,3-dideuterio-N-methyl-2-pyrrolidone<sup>6</sup> (133 mmoles) and held at 150° for 20 min. An aliquot was then treated *via* glpc [175°, 6 ft  $\times$   $\frac{3}{8}$  in. column of silicone L-46 (20%) on Chromosorb W—no hydroxylic substrate was used to prevent exchange] and the eluted neopentyl alcohol was collected in carbon tetrachloride. Nmr analysis showed the neopentyl alcohol was hydroxyl deuterated (integration and correspondence of spectra with *bona fide* neopentyl alcohol O-D).

**Cleavage of (-)-2-Octyl ( $\pm$ )-*p*-Toluenesulfinate (2).**—A large-scale cleavage of ester 2 (45 g, 0.168 mole) in NMP (39.6 g, 0.40 mole) at 165° for 30 min was processed by preparative glpc (silicone oil-glycol column) to obtain sufficient alcohol for optical purity studies. (-)-2-Octanol (4.6 g,  $n_D^{25}$  1.4248, infrared spectrum correct, 21%) was collected, though the actual yield was considerably higher, and it showed  $[\alpha]_D^{25}$  -8.81° (97% retention based on original purity of alcohol used to make 2).

**Kinetic Study.**—Ester 1 (5 g, 22 mmoles) in NMP (50 ml) was heated at a constant temperature (see Table II). Aliquots (20  $\mu$ l) were taken every 3 min and analyzed for neopentyl alcohol by glpc on the silicone oil-glycol column. Its peak area was divided by that obtained from 20  $\mu$ l of a solution of 22 mmoles of neopentyl alcohol in 50 ml of NMP. In this way the percentage alcohol formed in a given time was obtained. The pseudo-first-order rate constant was then obtained by plotting  $\ln [100/(100 - \text{per cent alcohol})]$  vs. time and calculating the slope of the visually

(31) If all the sulfonic acid arose from sulfonic acid by eq 2 this yield would be 27% based on ester 1.

best straight-line fit. With the exception of the first points, good first-order kinetics were observed. An Arrhenius plot gave  $E^{act}$  which was taken to be, within  $\pm 10\%$  error,  $\Delta H^*$  also.  $\Delta S^*$  was then calculated from the Eyring equation. The data for the 120° run are given in Table III.

TABLE III  
KINETICS OF CLEAVAGE OF 1 IN NMP AT 120°

Time, sec	Peak area, cm <sup>2</sup> <sup>a</sup>	% alcohol (x)	Ln 100/(100 - x)	10 <sup>4</sup> k <sub>1</sub> , sec <sup>-1</sup>
180	0.16	3.5	0.040	... <sup>b</sup>
360	1.28	28.0	0.322	9.0
540	2.05	44.5	0.588	10.9
720	2.42	52.6	0.746	10.4
900	2.77	60.2	0.920	10.2

<sup>a</sup> 100% alcohol = 4.6 cm<sup>2</sup>. <sup>b</sup> Neglected.

**Registry No.**—1, 13146-08-2; 2, 13146-09-3; 3, 2943-42-2; 4, 13146-11-7; methyl *p*-toluenesulfinate, 672-78-6; cyclopropylcarbinyl *p*-toluenesulfinate, 13146-12-8; benzyl *p*-toluenesulfinate, 13146-13-9; neophyl *p*-toluenesulfinate, 13146-14-0; 3,3-dideuterio-N-methyl-2-pyrrolidone, 932-07-0.

**Acknowledgment.**—We wish to thank Abbott Laboratories, North Chicago, Ill., for technical assistance. Funds for this work were made available from Contract DA-31-124-ARO(D)-69 with the Army Research Office (Durham), to whom we express our gratitude.

## The Overoxidation of Carbohydrates with Sodium Metaperiodate<sup>1</sup>

B. G. HUDSON AND R. BARKER

Department of Biochemistry, The University of Iowa, Iowa City, Iowa

Received January 30, 1967

The periodate oxidation of 1,4-anhydroallitol (I), which serves as a model for the periodate oxidation of naturally occurring oligosaccharides, has been examined in the pH range 3–7.5. The overoxidation process which occurs has been shown to require the prior formation of 2,3-dihydro-6-formyl-3-hydroxy-1,4-dioxine (IV), which is hydroxylated by periodate to give a product which is further oxidized in a normal fashion. Compound IV has a strong absorption band in the ultraviolet ( $E_{278}^{M} = 2.49 \times 10^4$  at pH 8.5) which can be used as an index of the presence of this compound during the oxidation. The structure of IV in solution has been examined by nmr spectroscopy and its rate of formation and oxidation have been shown to be consistent with its being an important intermediate in the overoxidation of I.

Oxidation with sodium metaperiodate is one of the most useful tools for the exploration of the structures of carbohydrates and compounds containing oxidizable functions  $\alpha$  to each other. Normal oxidations involve adjacent hydroxyl, amino, carbonyl, or carboxyl functions in any combination, and the consumption of 1 molar equiv of periodate results in the cleavage of the carbon-carbon bond between the functional groups and the oxidation of each group to the next highest oxidation state. When only normal oxidation occurs, it is possible to deduce from the consumption of periodate and the quantities of the various oxidation products a great deal about the structure of the compound being oxidized. However, a number of structural features have been found which react with periodate in atypical ways leading to considerable am-

biguity in the interpretation of the results of periodate oxidations. Some of these structural features are readily discernible, and the abnormal oxidation associated with them can be taken into account. For example, sulfur-containing compounds can consume periodate with the formation of sulfoxides or sulfones with or without cleavage of carbon-carbon bonds.<sup>2,3</sup> The presence of sulfur is readily detected, and its presence requires that consideration be given to its consumption of oxidant. Other structural features are not associated with such an obvious marker and can severely limit the utility of the periodate method. The most important of these is the active methylene group which is produced as a result of normal oxidations of a variety of carbohydrates and which is almost always produced in the oxidation of naturally occurring

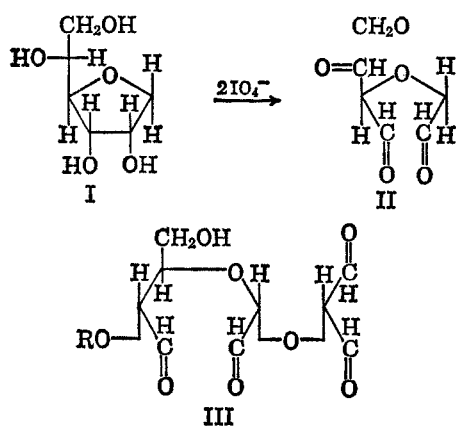
(1) Supported in part by Public Health Service Research Grant GM 11963, Public Health Service Fellowship GM 30,071 (to B. G. H.), and Public Health Service Research Career Program Award GM 24,808 (to R. B.) from the Institute of General Medical Sciences.

(2) (a) J. Okui, *J. Pharm. Soc. Japan*, **75**, 1262 (1955); (b) L. Hough and M. I. Taha, *J. Chem. Soc.*, 3994 (1957).

(3) Y. C. Lee and R. Montgomery, *Arch. Biochem. Biophys.*, **95**, 263 (1961).

di-,<sup>4-6</sup> oligo-, and polysaccharides.<sup>7-9</sup> Although methods have been devised to limit the rate of oxidation of this type of structure,<sup>8</sup> and corrections have been applied to discount oxidant consumption owing to its occurrence, it still constitutes a serious drawback to the application of the method to the elucidation of oligosaccharide structures. There is a great deal of current interest in the structures of oligosaccharides, of glycoproteins, and of the naturally occurring polysaccharides, and periodate oxidation is utilized<sup>3,10-12</sup> despite the ambiguities owing to overoxidation. Overoxidations by periodate have also been observed in attempts to establish the nucleotide sequence of polyribonucleotides,<sup>13</sup> by certain alditol phosphates,<sup>14</sup> and by adenosine 5'-aldehyde.<sup>15</sup> We decided, therefore, to examine the overoxidation reaction in a model system resembling that produced in oligosaccharide oxidations with a view to elucidating the course of the reaction and the factors which influence its rate.

The oxidation of the model compound, 1,4-anhydroallitol (I), has been examined because it is easily prepared and rapidly consumes 2 molar equiv of periodate in a normal fashion (I → II) to produce a tri-aldehyde (II) which is analogous to the polyaldehyde (III) formed in the oxidation of many polysaccharides.



It has been previously observed<sup>16</sup> that the overoxidation of I is accompanied by the production of a material which absorbs very strongly in the ultraviolet, and it was suggested that the compound giving rise to this absorption is an obligatory intermediate in the oxidation and has the structure IV. This manuscript describes the isolation of the absorbing compound, its characterization and properties, and its relationship to the overoxidation process.

### Experimental Section

Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Ultraviolet absorbancy measurements were

- (4) J. Courtois and M. Ramet, *Bull. Soc. Chim. Biol.*, **29**, 240 (1947).
- (5) M. L. Wolfrom, A. Thompson, A. N. O'Neill, and T. T. Galkowski, *J. Am. Chem. Soc.*, **74**, 1062 (1952).
- (6) F. S. H. Head and G. Hughes, *J. Chem. Soc.*, 603 (1954).
- (7) T. G. Halsall, E. L. Hirst, and J. K. N. Jones, *ibid.*, 1427 (1947).
- (8) A. L. Potter and W. Z. Hassid, *J. Am. Chem. Soc.*, **70**, 3489 (1948).
- (9) R. W. Jeanloz and E. Forchielli, *J. Biol. Chem.*, **190**, 537 (1951).
- (10) R. Montgomery and S. Nag, *Biochem. Biophys. Acta*, **74**, 300 (1963).
- (11) J. L. Simkin, H. S. Seshadri, and E. R. Skinner, *Nature*, **202**, 702, 4933 (1964).
- (12) A. K. Chatterjee, G. J. Durant, H. Hendrickson, Y. C. Lee, and R. Montgomery, *Biochem. Biophys. Res. Commun.*, **4**, 425 (1961).
- (13) H. C. Neu and L. A. Heppel, *J. Biol. Chem.*, **239**, 2927 (1964).
- (14) R. Barker, unpublished observation.
- (15) H. P. C. Hogenkamp, J. M. Ladd, and H. A. Barker, *J. Biol. Chem.*, **237**, 1950 (1962).

made using a Beckman D.U. monochromator with a Gilford attachment; spectra were obtained on a Cary Model 14 spectrophotometer. Infrared spectra were obtained using a Perkin-Elmer Model 21 spectrophotometer and nmr spectra were obtained using a Varian A-60 spectrometer. Chemical shifts are relative to tetramethylsilane as an external standard. Melting points are corrected.

Allitol was prepared from D-allono 1,4-lactone<sup>17</sup> by reduction with sodium borohydride using a modification of the procedure described by Wolfrom and Wood.<sup>18</sup>

To 30.3 g of D-allono 1,4-lactone in 250 ml of water at 4° was added 8 g of sodium borohydride in 50 ml of 0.001 *N* sodium hydroxide at 4°. After 48 hr at 4° the mixture was acidified with 30 ml of glacial acetic acid and, after the release of hydrogen had subsided, was passed over a column containing 200 ml of Dowex-50-X8 (H<sup>+</sup>) resin. The eluate was concentrated to dryness *in vacuo* at 75°. The residue was dissolved in 100 ml of methanol and concentrated to dryness *in vacuo* at 60°; this procedure was repeated five times to yield 30 g of clear syrup. The syrup was dissolved in 100 ml of methanol with warming; after cooling and seeding 19.5 g of crystalline allitol was obtained. The material had a melting point of 149–150°; the reported melting point of allitol is 150–151°. An additional 4 g of pure material was obtained by the addition of ethyl acetate to the mother liquor.

1,4-Anhydro-DL-allitol (I) was prepared by the acid-catalyzed anhydritization of allitol. A solution of 10 g of allitol in 250 ml of 4 *N* hydrochloric acid was refluxed for 50 hr. The solution was concentrated to a small volume *in vacuo* at 75° and the residue was concentrated six times from 100-ml portions of water. Traces of acid were removed by passing an aqueous solution of the product through a column 100 ml of Dowex-3 (OH<sup>-</sup>) resin and concentrating the eluate to dryness *in vacuo* at 75°. 1,4-Anhydro-DL-allitol (8.7 g, 96%) was obtained as a syrup which deposited crystals from solution in 125 ml of methanol-ethyl acetate (30:95, yield 7.4 g), mp 82°.

*Anal.* Calcd for C<sub>6</sub>H<sub>12</sub>O<sub>5</sub> (164.16): C, 43.90; H, 7.37. Found: C, 44.12; H, 7.46.

2,3-Dihydro-6-formyl-3-hydroxy-1,4-dioxine (IV).—To 200 ml of 0.166 *M* periodic acid at 0° was added 1.968 g (12 mmoles) of 1,4-anhydro-DL-allitol. After 8 min during which 2 molar equiv of periodate was consumed, the reaction mixture was passed over a column of 50 ml of Dowex-3 (CH<sub>3</sub>COO<sup>-</sup>) resin to remove periodic acid and iodic acid and the column was eluted with 200 ml of water. The eluate and washings were heated at 100° for 2 min. This treatment caused the absorbance at 270 mμ of a 500-fold dilution of the solution to increase from 0.04 to 0.530. Concentration of the heated eluate *in vacuo* at 50° yielded 1.299 g of white crystals. Recrystallization of 1.114 g of the material from 6 ml of water gave 0.53 g of material which was recrystallized from 2 ml of water to give 0.505 g, mp 140.5–141.5°. Further recrystallizations did not change this value. Small crops of material could be obtained by concentration of the various mother liquors.

*Anal.* Calcd for C<sub>5</sub>H<sub>8</sub>O<sub>4</sub> (130.09): C, 46.16; H, 4.62. Found: C, 46.12; H, 4.66.

The p*K*<sub>a</sub> of IV was determined spectrophotometrically. Aliquots (50 μl) of a solution of the compound (3.08 mg in 10 ml of water) were diluted to 5 ml with 0.1 ml with 0.1 *N* sulfuric acid (pH 1.0), 0.05 *M* acetate buffers of pH values 4.8, 5.51, and 7.10, and 0.05 *M* sodium bicarbonate (pH 8.34). The absorption spectrum of each solution was determined. The p*K*<sub>a</sub> was calculated using the Henderson-Hasselbach equation and the absorptions at pH 1.0 and 8.34 were calculated as being due to the acid and salt forms, respectively.

Periodate oxidations, with the exception of the oxidation carried out in the isolation of IV, were performed with sodium metaperiodate. Utilization of oxidant was followed by the method of Malaprade.<sup>20</sup> The iodine released from a suitable aliquot of the reaction mixture on addition of 1 ml each of 2 *N* sulfuric acid and 20% aqueous potassium iodide was titrated with 0.005 *N* sodium thiosulfate to a starch end point.

Oxidation of IV.—With the exception of those oxidations performed at pH 8.5 solutions were prepared by dissolving 13 mg

- (16) R. Barker, *J. Org. Chem.*, **29**, 869 (1964).
- (17) J. W. Pratt and N. K. Richtmyer, *J. Am. Chem. Soc.*, **77**, 1906 (1955).
- (18) M. L. Wolfrom and H. B. Wood, Jr., *ibid.*, **73**, 2933 (1951).
- (19) M. Steiger and T. Reichstein, *Helv. Chim. Acta*, **19**, 184 (1936).
- (20) L. Malaprade, *Compt. Rend.*, **186**, 382 (1928); *Bull. Soc. Chim. France*, [4] **43**, 683 (1928).

(0.1 mole) of the isolated compound in 50 ml of buffer at  $28 \pm 0.1^\circ$  and adding 2 ml of 0.326 *M* sodium metaperiodate. A sample was placed in a quartz cell having a 1-mm light path and the absorbance at 270  $m\mu$  at  $28 \pm 0.1^\circ$  recorded with time. At suitable times 0.5-ml aliquots were removed and the amount of oxidant was determined. For oxidations performed at pH 8.5 the concentrations of compound and periodate used were one-half those used at other pH values.

The products of the oxidation and their relative rate of formation were determined in an unbuffered oxidation.

**A.**—Formic acid was determined by addition of 1 ml of ethylene glycol to 3-ml aliquots of the reaction mixture withdrawn at suitable times. After 30 min the sample was titrated with 0.006 *N* sodium hydroxide to pH 7.5 using a universal indicator.<sup>21</sup> In the initial period of the oxidation in which IV is still present, the amount of sodium hydroxide required in the titration is not a correct measure of the formic acid produced since the compound itself behaves as an acid. The amount of sodium hydroxide required to titrate the compound present was calculated from the absorbance and this amount was subtracted from the amount of sodium hydroxide required in the titration to give the amount of formic acid produced.

**B.**—Formaldehyde was determined with chromotropic acid by an adaptation of the method of Frisell, *et al.*<sup>22</sup> To a 0.1-ml aliquot of the reaction mixture withdrawn at a suitable time were added 0.1 ml of water, 0.3 ml of 0.15 *M* sodium bisulfite, and 5 ml of chromotropic acid reagent, and the mixture was heated at  $100^\circ$  for 30 min. After cooling, 0.5 ml of a half-saturated, aqueous solution of thiourea was added and the absorbance was measured at 570  $m\mu$ . The amount of formaldehyde present was interpolated from a standard curve obtained using formaldehyde generated from hexamethylenetetramine by heating at  $100^\circ$  in 2 *N* sulfuric acid for 15 min.

**Interrupted Oxidation of 1,4-Anhydro-DL-allitol.**—To 41 mg (0.25 mmole) of 1,4-anhydro-DL-allitol in 2 ml of water at  $4^\circ$  was added 1.7 ml of 0.326 *M* sodium metaperiodate at  $4^\circ$  and the mixture was diluted to 5 ml with water and maintained at  $4^\circ$ . Aliquots (50  $\mu$ l) were withdrawn at intervals and the amount of oxidant utilized was determined. After 1 hr in which 1.90 molar equiv of periodate was utilized, 4 ml of the mixture was diluted to 100 ml with 0.5 *M* acetate buffer (pH 4.72) at  $28 \pm 0.1^\circ$ . A sample was placed in a 1-mm quartz cell maintained at  $28 \pm 0.1^\circ$  and the increase in absorbance at 270  $m\mu$  was recorded. At 450 min after dilution 2 ml of 0.326 *M* sodium metaperiodate was added to 50 ml of the solution. The utilization of oxidant and absorbance was measured as described above for the oxidation of the isolated compound.

The effect of pH on the rate of appearance of the absorbing substance was determined by making the dilution with buffer having the desired pH and recording the increase in absorbance at 270  $m\mu$ .

**Uninterrupted oxidations of 1,4-anhydro-DL-allitol and maltose** utilized 25 mg of 1,4-anhydro-DL-allitol or 36 mg of maltose dissolved in 80 ml of the appropriate buffer at  $28 \pm 0.1^\circ$ . To this solution was added 3 ml of 0.428 *M* sodium metaperiodate and the mixture was diluted to 100 ml with buffer and maintained at  $28 \pm 0.1^\circ$ . A sample was placed in a 1-mm quartz cell maintained at  $28 \pm 0.1^\circ$  and the absorbance at 270  $m\mu$  was recorded with time. Aliquots (0.5 ml) were withdrawn at suitable times and the amount of oxidant utilized determined.

## Results and Discussion

The rate of the overoxidation of I depends upon the pH of the medium. At low pH values overoxidation is slow, whereas normal oxidation is rapid. Therefore, the oxidation of I by periodic acid (pH approximately 1.5) was utilized to prepare II. When excess periodic and iodic acids were removed from the reaction mixture using a weakly basic anion-exchange resin, a solution was obtained which had virtually no absorption through the ultraviolet region. Prolonged storage of this solution at room temperature or heating to  $100^\circ$  for 2 min caused an ultraviolet absorbance ( $\lambda_{\max}$  272

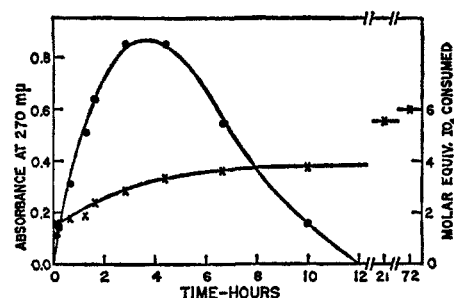
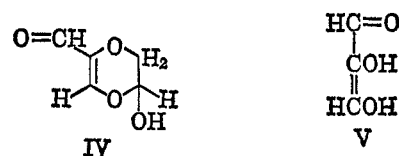


Figure 1.—Uninterrupted oxidation of 1,4-anhydro-DL-allitol in unbuffered solution:  $\times$ , periodate consumption, 0.003 *M* allitol and 0.02 *M* sodium metaperiodate;  $\bullet$ , absorbance of a 25-fold dilution of the oxidation mixture.

$m\mu$ ) to develop. The rate of periodate consumption in this solution was increased markedly when compared to that observed to occur during the overoxidation of 1,4-anhydro-DL-allitol I (Figure 1).

The crystalline compound which was isolated in approximately 50% yield from the heated solution of II was shown to be 2,3-dihydro-6-formyl-3-hydroxy-1,4-dioxine (IV) by elemental analysis, infrared, ultraviolet, and nmr spectroscopy, and molecular weight determination.

**Characterization of IV (2,3-Dihydro-6-formyl-3-hydroxy-1,4-dioxine).**—The compound has a strong absorbance peak in the ultraviolet region which has  $\lambda_{\max}$  267  $m\mu$  and  $E_{267}^M$   $1.26 \times 10^4$  at pH 1.0, and  $\lambda_{\max}$  278  $m\mu$  and  $E_{278}^M$   $2.49 \times 10^4$  at pH 8.4. An intense absorption band between 200 and 250  $m\mu$  is characteristic of  $\alpha,\beta$ -unsaturated carbonyl compounds,<sup>23,24</sup> and the presence of hydroxyl groups in the  $\alpha$  or  $\beta$  positions has been shown to cause a shift to higher wavelengths. For example, triose reductone (V) has  $\lambda_{\max}$  269  $m\mu$  in



acid and  $\lambda_{\max}$  287 in alkaline medium.<sup>25</sup> The two ring oxygens of IV would be expected to produce a similar shift to longer wavelengths.

The infrared spectrum shows strong absorptions at 3220 and 1640  $\text{cm}^{-1}$ . The first is characteristic of a hydroxyl group and the second of a carbonyl group. The carbonyl absorption is very broad (160  $\text{cm}^{-1}$  wide at one-half the peak height) and shifted to lower frequency, indicating the presence of a conjugated system.<sup>26</sup>

The nmr spectrum of IV is quite simple, but the splittings observed and the peak shapes are strongly dependent on the solvent used. In dimethyl sulfoxide- $d_6$  containing a small proportion of water (HDO and  $\text{D}_2\text{O}$ ) absorptions owing to the methylene and methinyl protons show splittings characteristic of an ABX system which would be expected on the basis of IV having a half-chair (IVa) or a boat (IVb) conformation.

(23) L. K. Evans and A. E. Gilliam, *J. Chem. Soc.*, 815 (1941); 565 (1943).

(24) R. B. Woodward, *J. Am. Chem. Soc.*, **63**, 1123 (1941); **64**, 72, 76 (1942).

(25) H. V. Evler and C. Martins, *Svensk Kem. Tidskr.*, **45**, 73 (1933); *Ann.*, **505**, 73 (1933).

(26) R. N. Jones and C. Sandorfy in "Technique of Organic Chemistry," Vol. IX, W. West, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p 481.

(21) Fisher Scientific Co., Chicago, Ill.

(22) W. R. Frisell, L. A. Meech, and C. G. Mackenzie, *J. Biol. Chem.*, **207**, 709 (1954).

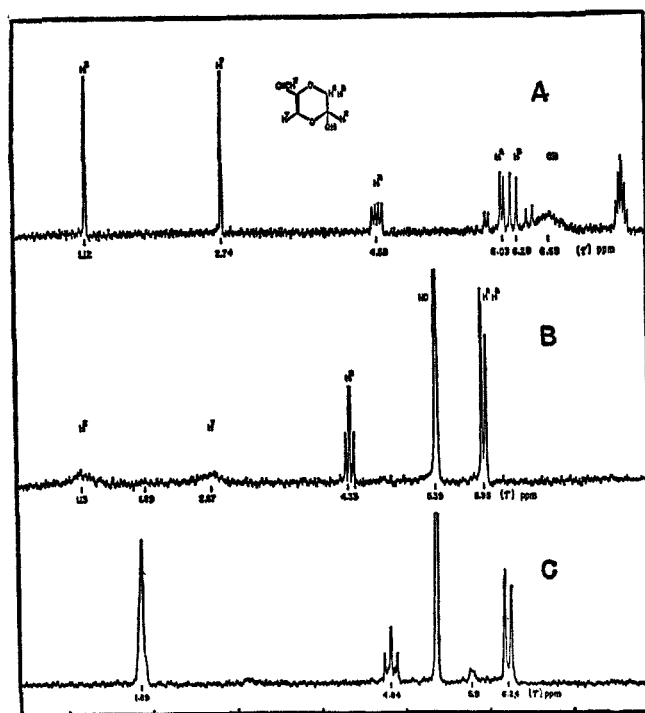
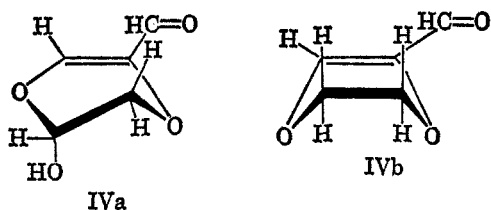


Figure 2.—The nmr spectra of compound IV. Chemical shifts are given in parts per million relative to tetramethylsilane as an external standard. All spectra were obtained at ambient temperature (approximately 40°): A, in dimethyl sulfoxide- $d_6$ ; B, in  $D_2O$ ; C, in  $D_2O$  containing 1 molar equiv of sodium bicarbonate.



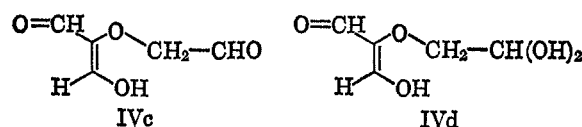
From the spectrum, values of  $J_{AX} = 5.1$  cps,  $J_{BX} = 1.9$  cps,  $J_{AB} = 12.1$  cps, and  $\Delta\nu_{AB} = 16.8$  cps were calculated.<sup>27</sup> The chemical shift of  $H^A$  and  $H^B$  are  $\tau$  6.16 and 6.39, respectively.

The anomeric configuration at C-2 has not been deduced from the calculated values of the coupling constants. When the angles between vicinal protons are calculated using the coupling constants and the Karplus equation<sup>28</sup> or the modifications of it which have been suggested,<sup>29,30</sup> values are obtained which do not meet the requirement that the sums of or the difference between the two angles be approximately equal to 120°. The discrepancy, which is never less than 20°, may reflect the influence of the unsaturated ring system on the values of the coupling constants or on the angle between the geminal protons at C-1.

The nmr spectrum of IV in  $D_2O$  is shown in Figure 2B. There are small differences in the chemical shifts of the vinylic ( $H^Y$ ), aldehydic ( $H^Z$ ), and methylenic protons ( $H^A$ ,  $H^B$ ), and a slightly greater difference in the chemical shift for the anomeric proton ( $H^X$ ). The

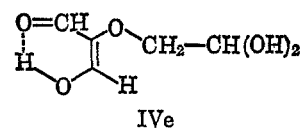
most noticeable effect of the solvent change is on the splitting of the methylene and the methinyl groups which now appear as a typical  $A_2X$  spectrum.

There are several possible explanations for this change. First, the solvent might preferentially affect the chemical shift of the A methylenic proton, moving it to lower field so that  $\Delta\nu_{AB}$  becomes much smaller than  $J_{AB}$ . Second, the change in solvent may increase the flexibility of the ring resulting in an averaging of the environments of the A and B protons. Third, the rate of anomerization may be increased in the protic solvent, producing a similar effect. Fourth, the compound may exist predominantly in an acyclic form in aqueous solution. In this form the methylenic protons are equivalent. Consideration of whether or not this acyclic form (IVc) predominates in aqueous solution



is pertinent to consideration of the mechanism of over-oxidation.

The chemical shift of the anomeric proton ( $H^X$ ) in dimethyl sulfoxide is  $\tau$  4.58 and the compound is in one of the cyclic forms of IV in this solvent. In  $D_2O$  the triplet from the same proton is at  $\tau$  4.33 in contrast to the signal from the aldehydic proton which is in the region of 1.12 in both solvents. The small change in chemical shift of the absorption due to  $H^X$  can be explained only if the aldehyde containing  $H^X$  in IVc is predominantly hydrated in aqueous solution, as shown in IVd. If the open-chain hydrate is the predominant species, the conjugated system would stabilize by hydrogen-bond formation so that IVe would represent the form in solution. The absorption of the hydrogen-bonded OH group would be expected to fall at very low field ( $\tau = -5.4$  for the enol hydrogen of 2,3-pentanedione), although rapid exchange with protons of the solvent would result in an average absorption for the solvent protons which would be only slightly displaced to lower field. The possibility that the compound has the structure IVd or IVe in aqueous solution cannot be



discounted entirely, although it requires an unusual number of coincidentally identical chemical shifts for protons in the ring form (present in dimethyl sulfoxide) and in the acyclic form.

The nmr spectrum of IV in dimethyl sulfoxide at 60° is almost identical with that obtained in  $D_2O$  solution. The spectrum due to  $H^A$ ,  $H^B$ , and  $H^X$  is a typical  $A_2X$  type with a triplet at  $\tau$  4.55 and a doublet at 6.03. Presumably the temperature increase accelerates the interconversion of ring forms, which may indicate that in  $D_2O$  solution the ring forms are rapidly interchanging. If the dimethyl sulfoxide solution is maintained at 60° for a short time, the effect of the temperature increase is completely reversible; however, prolonged storage at this temperature leads to irreversible changes in the

(27) R. H. Bible, "Interpretation of NMR Spectra," Plenum Press, New York, N. Y., 1965, p 86.

(28) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

(29) R. U. Lemieux, J. D. Stevens, and R. R. Fraser, *Can. J. Chem.*, **40**, 1955 (1962).

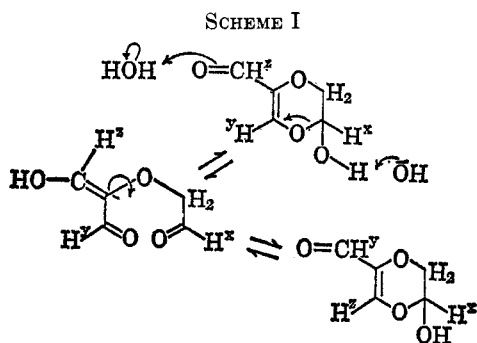
(30) R. J. Abraham, L. D. Hall, L. Hough, and K. A. McLaughlan, *Chem. Ind. (London)*, 213 (1962); *J. Chem. Soc.*, 3699 (1962).

spectrum indicating that the compound reacts with this solvent.

The effect of pH on the properties of IV is of interest since the overoxidation process is markedly influenced by pH. The compound is a weak acid with a  $pK_a' = 5.6$ . The nmr spectra in  $D_2O$  containing increasing proportions of sodium bicarbonate show that two distinct processes occur upon the addition of base. With the addition of 0.08 molar equiv of bicarbonate, the absorptions owing to the aldehydic and vinyl protons coalesce into a single absorption at  $\tau$  1.90 and a very small triplet and doublet appear at 4.90 and 6.24, respectively. With increasing "pH" the signal at  $\tau$  1.9 becomes sharper, and the absorptions at 4.90 and 6.24 increase at the expense of those at lower field. The spectrum in the presence of 1 molar equiv of bicarbonate is shown in Figure 2C.

The only effect of the addition of acid ( $H_2SO_4$ ) to an aqueous solution of IV is to sharpen the signals due to the aldehydic and vinylic protons.

The spectral changes observed can be rationalized as arising from an increased rate of exchange of the vinylic and aldehydic protons with increasing pH as shown in Scheme I and from an increase in the shielding of  $H^A$ ,  $H^B$ , and  $H^X$  in the anion. The rate at which



the vinyl and aldehydic protons exchange their roles is proportional to the amount of base present and is relatively rapid at low concentrations. Even in acidic aqueous medium, exchange occurs since the aldehydic and vinyl proton signals are much broader in  $D_2O$  to which  $H_2SO_4$  has been added to give a "pH" value of 1.0 than in dimethyl sulfoxide.

Prolonged storage in alkali or exposure to high pH causes the nmr spectrum to change to a single sharp absorption at  $\tau$  1.5 and to two very broad signals centered at 4.80 and 5.80. The change is accompanied by an increase in the number of protons in the solvent peak and probably indicates that polymerization has occurred.

**The Role of IV in the Overoxidation of 1,4-Anhydroallitol.**—To establish that IV (or one of the forms derivable from it in solution) is an obligatory intermediate in the overoxidation process it is necessary to show that IV is produced in the oxidation and to show that its properties are compatible with its being such an intermediate.

To establish that IV is produced in the oxidation of 1,4-anhydroallitol (I) the latter was oxidized with 2.2 molar equiv of periodate at  $0^\circ$ , after 1 hr in which 1.9 molar equiv of oxidant was consumed the reaction mixture was diluted 25-fold with acetate buffer pH 4.72 at  $28^\circ$ . The absorbance at  $270 m\mu$  of the diluted

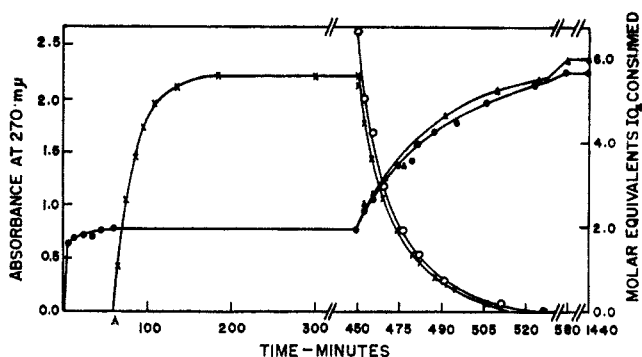


Figure 3.—Interrupted periodate oxidation of 1,4-anhydro-DL-allitol (X, absorbance, and ●, periodate consumption), and periodate oxidation of isolated compound IV (O, absorbance, and ▲, periodate consumption) at pH 4.72 and  $28 \pm 0.1^\circ$ . The initial solution was 0.05 M in 1,4-anhydro-DL-allitol and 0.11 M in sodium metaperiodate and was unbuffered at  $4^\circ$ . At A, a 25-fold dilution was made with 0.5 M acetate buffer, pH 4.72. At 450 min, 2 ml of 0.326 M sodium metaperiodate was added per 50 ml of the diluted reaction mixture. The oxidation is compared with that of a solution of IV in the same buffer at a concentration equal to the theoretical concentration of IV in the reaction mixture (see text).

solution was followed at  $28^\circ$ . The absorbance reached a maximum value after 140 min. At 140 and 390 min, the ultraviolet absorption spectrum of the solution was compared with that of an equimolar solution of IV in the same buffer; the peak shapes were identical. The extinction coefficient at  $270 m\mu$  calculated on the basis that all of the 1,4-anhydroallitol had been converted to the absorbing substance during this incubation was  $1.10 \times 10^4$ , whereas that of IV in this buffer is  $1.36 \times 10^4$ . The discrepancy appears to be due to the oxidation of a portion of the absorbing substance by the small excess of periodate used. If a similar amount of periodate is added to a solution of IV of the same molarity, the absorbance decreases within 60 min to a value which gives an apparent molar extinction coefficient of  $1.17 \times 10^4$ .

The periodate consumption of the solution of the absorbing substance described above was compared with that of a solution of IV having a similar initial absorbance. The rates and stoichiometries of the two oxidations are essentially identical (Figure 3) as are the products formed. In both cases the character of the absorption spectrum remains the same throughout the oxidation indicating that at this pH value (4.72) no other absorbing substance accumulates.

The absorbing substance in the oxidation mixture behaves as a weak acid with  $pK_a' = 5.5$  obtained by titration with sodium hydroxide.<sup>16</sup> Compound IV has  $pK_a' = 5.84$  obtained by spectrophotometric measurement made at various pH values. The discrepancy could be due to differences in the purity of the two preparations. The ultraviolet spectra of the two compounds are identical in alkaline medium and both show similar shifts in  $\lambda_{max}$  and extinction coefficient.

It is concluded from these studies that the absorbing substance produced in the interrupted oxidation of 1,4-anhydroallitol is compound IV.

Is IV produced during the overoxidation of I, and is it an important intermediate in this process? During the uninterrupted oxidation of I there is a steady increase in absorbance at  $270 m\mu$  during the first part of

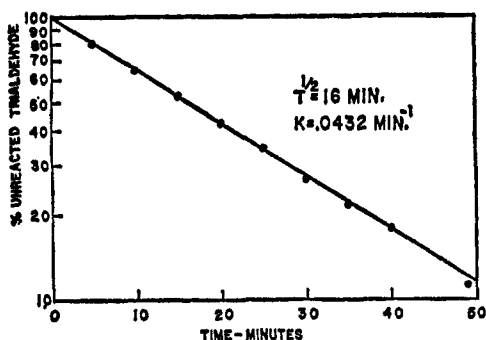


Figure 4.—First-order plot for the appearance of IV in the interrupted periodate oxidation of 1,4-anhydro-DL-allitol in 0.5 *M* acetate buffer (pH 4.72) at 28°.

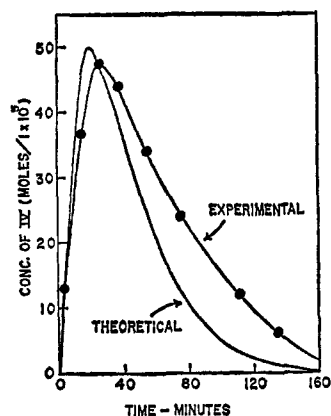


Figure 5.—A plot of the concentration of IV throughout the course of the periodate oxidation of 1,4-anhydro-DL-allitol (I) compared to the theoretical curve obtained using  $k_1 = 0.0432 \text{ min}^{-1}$  and  $k_2 = 0.0570 \text{ min}^{-1}$  in the expression  $IV = [II]_0 k_1 / k_2 - k_1 (e^{-k_1 t} - e^{-k_2 t}) / (k_2 - k_1)$  where  $[II]_0$ , the concentration of tri-aldehyde, is taken as the initial concentration of 1,4-anhydro-DL-allitol (I), pH 4.72,  $T = 28 \pm 0.1^\circ$ , initial concentration of I,  $2 \times 10^{-3} \text{ M}$ , initial concentration of periodate,  $1.6 \times 10^{-2} \text{ M}$ .

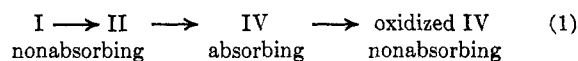
the overoxidation (Figure 1). The ultraviolet spectrum of this absorbing substance is identical with that of IV, and there is no doubt that the absorption is due largely to compound IV.

If IV is an important or obligatory intermediate in the oxidation process, then the factors which influence its formation and oxidation must influence the uninterrupted oxidation process in a similar fashion, and the rates of formation and oxidation of IV under any set of conditions must be sufficient to account for the over-all rates observed.

The rate of formation of IV at pH 4.72 and 28° is first order to over 90% completion (Figure 4). The first-order rate constant varies with pH; at pH values of 8.5, 6.0, 4.72, and 3.9 at 28° the constants are 1.0, 0.15, 0.0432, and 0.00472  $\text{min}^{-1}$ , respectively. The rate of formation of IV is also dependent on temperature; at pH 3.9 the rearrangement requires more than 36 hr at 28°, but is complete in 5 min at 100°.

The rate of oxidation of IV by periodate is also greatly influenced by pH; in part this reflects the effect of pH on the hydrolysis of esters produced during the oxidation, but it also reflects an effect of pH on the first step in the overoxidation process. The determination of a rate constant for the reaction of IV with periodate is difficult. The initial reaction must be at least bimolecular, and observations of rate based on periodate consumption are complicated by the fact that at least

three oxidations occur which involve products of the first reaction. However, the initial rate of oxidation of IV can be observed spectrophotometrically if the assumption is made that there are no strongly absorbing products formed in this step. From this measurement a "first-order rate constant" can be calculated. At pH 4.72 this "constant" is 0.057  $\text{min}^{-1}$ , and at pH 8.5 it has the value 0.231  $\text{min}^{-1}$ . Using the "constant" obtained at pH 4.72 it is possible to determine approximately what proportion of the uninterrupted overoxidation proceeds through the intermediate IV, since the variation in the concentration of IV and of periodate can be measured throughout the reaction. That the proportion is high is most easily demonstrated by assuming that the reaction proceeds only through the intermediate IV as shown in eq 1. The variation



in absorbance of the reaction mixture with time can be calculated using the constants  $k_1 = 0.0432 \text{ min}^{-1}$  and  $k_2 = 0.0570 \text{ min}^{-1}$  and the expression given by Frost and Pearson for an intermediate in a sequence of first-order reactions.<sup>31</sup> The theoretical curve, so obtained and the experimental data are shown in Figure 5. The assumption was made that the concentration of II at  $t = 0$  is equal to the initial concentration of 1,4-anhydroallitol (I), although this cannot be the case since the 2 molar equiv of periodate necessary to produce II are not consumed instantaneously. The effect of the slow generation of II would be to displace the theoretical curve to the right which would improve its fit with the experimental points. The near-coincidence of the theoretical curve and the experimental points demonstrates that IV must be an important if not an obligatory intermediate in the overoxidation process.

The contention that IV is the predominant intermediate in the overoxidation process is further supported by the finding that the amount of it which accumulates during the oxidation process is decreased when the concentration of oxidant is increased, but the initial rate of its formation is essentially unaffected (Figure 6). This finding is consistent with IV being an intermediate in the oxidation process and is not consistent with its being in equilibrium with a form which is involved in the oxidation. We conclude, therefore, that IV is, or gives rise to, the compound which is involved in the overoxidation step.

The effect of pH on the uninterrupted oxidation of 1,4-anhydroallitol (I) is shown in Figure 7. As the pH is increased, the rate of overoxidation increases, and the amount of IV which accumulates decreases. Since both the rate of formation of IV and the rate of its oxidation by periodate increase with pH, this is the expected result.

The stimulation in the rate of oxidation of IV produced by an increase in pH appears to be due to an increase in the concentration of a reactive species of the compound IV, namely the anion. Over the pH range 3.63 to 6.36 the predominant species of periodate present in solution is the monoanion  $\text{H}_4\text{IO}_6^-$ <sup>32</sup> and its

(31) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1961, p 166.

(32) C. E. Crouthamel, A. M. Hayes, and D. S. Martin, *J. Am. Chem. Soc.*, **73**, 82 (1951).

concentration is essentially constant over this range. The concentration of the dianion,  $\text{H}_3\text{IO}_6^{2-}$ , increases from one part in 100,000 to one part in 100 over the same range and accounts for one-half of the oxidant at pH 8.36. The rate of oxidation of IV increases by a factor of 6 as the pH is changed from 4 to 6, and there is very little increase in rate when the pH is increased from 6 to 8.5, clearly indicating that the dianion is not the reactive species of oxidant. Since the concentration of monoanion remains constant in the pH range over which a stimulation of rate is observed, the stimulation must be due to an increase in the amount, or rate of formation, of a reactive species of the substrate (IV).

The rate of oxidation is increased approximately five-fold when the pH of the medium is increased from 4.0 to 4.7. The concentration of the anionic form of an acid having  $\text{p}K_a' = 5.84$  increases by a factor of 4.75 with this pH change implying that an anionic form of IV ( $\text{p}K_a' = 5.84$ ) is the reactive species. In the higher pH ranges the rate differences are more difficult to interpret because of changes in the species of oxidant in solution. However, if  $\text{H}_4\text{IO}_6^-$  is assumed to be the principal oxidant, the effect of pH on rate of oxidation is approximately consistent with the monoanion of IV being the preferred substrate.

The effect of pH changes can also be explained as due to a marked increase in the rate of anomerization, which would be catalyzed by base, giving rise to a form which is more susceptible to oxidation for steric reasons.

It is not possible to deduce unequivocally from this data whether a cyclic or an acyclic form is being oxidized. However, it has previously been established<sup>33</sup> that cyclic 1,3-diketones are much more rapidly oxidized than their acyclic counterparts, some of which do not appear to be oxidizable. The effect of pH on the rate of oxidation of these cyclic diketones also indicates that an anionic form or a form, the formation of which is base catalyzed, may be reacting, and in these cases ring opening cannot occur.

There is a small salt effect on the rate of oxidation of IV by periodate. Both the initial and subsequent steps appear to be affected. The time required to reach one-half completion of periodate consumption in unbuffered medium is decreased from 340 to 230 min by the addition of 0.25 M sodium chloride. Variation of the buffer concentration from 0.05 to 0.25 M at pH 4.7 decreases the half-time for the reaction from 30 to 25 min. Further increases in buffer concentration have no effect. This type of salt effect on periodate oxidations has been observed previously<sup>34</sup> and is to be expected on the basis that ionic species are involved in the process.

On the basis of the preceding results and discussion, a proposal can be made regarding the events involved in the overoxidation of 1,4-anhydroallitol (I). In Scheme II the first-formed trialdehyde is in rapid equilibrium with hydrates and hemialdals, and compound IV is formed either by a dehydration of one of these ring forms, or as seems more probable in view of the catalysis of its formation by base, through an intermediate enol form. The oxidation of IV then

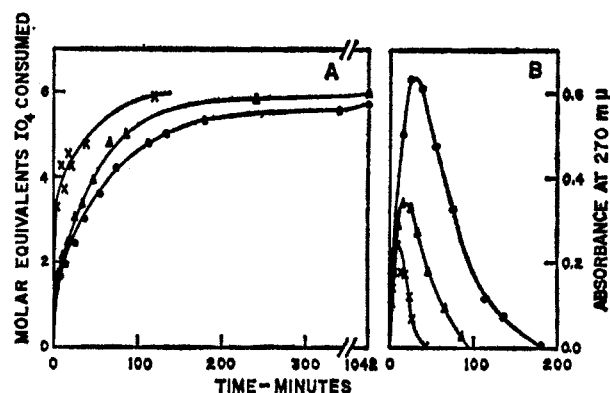


Figure 6.—Periodate oxidation of 1,4-anhydro-DL-allitol in 0.5 M acetate buffer (pH 4.72) at 28° at various concentrations of periodate: ●, 0.0128 M; ▲, 0.0256 M; and ×, 0.0512 M.

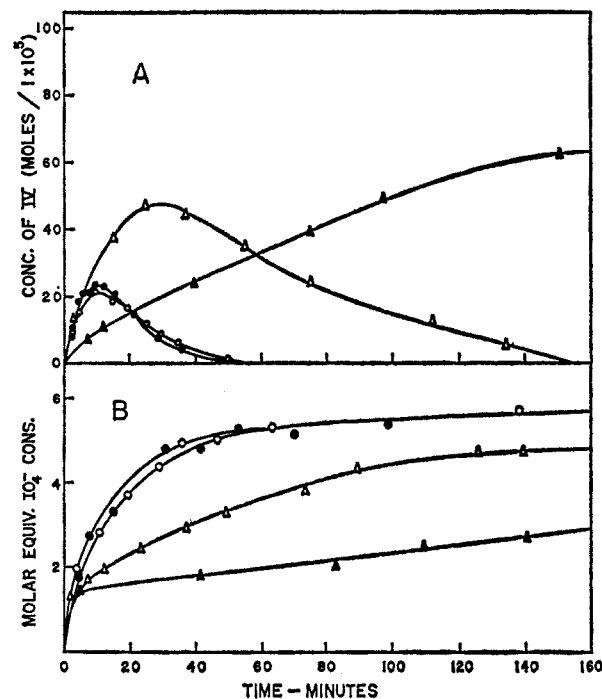


Figure 7.—Uninterrupted periodate oxidation of 1,4-anhydro-DL-allitol at various pH values at 28°: graph A, appearance of absorbing substance; graph B, periodate consumption; ●, ○, △, and ▲, oxidation at pH values of 8.5, 6.0, 4.72, and 4 (unbuffered solution), respectively.

proceeds most readily through the anion IVf which reacts with the monoanionic form of the oxidant  $\text{H}_4\text{IO}_6^-$  to produce the mesoxaldehyde derivative VI. This compound can be oxidized by normal oxidations in a variety of ways, and in all probability more than one pathway is followed. Studies by Huebner, *et al.*,<sup>35</sup> and by Cantley, *et al.*,<sup>36</sup> on systems of this general type have indicated the probability of this being the case. All of the intermediates produced are esters, and the rate of their hydrolysis, which would control the rate of oxidation of the products of hydrolysis, would be increased by an increase in pH.

The formation of the mesoxaldehyde derivative VI from IVf requires comment. The oxidation of compounds related to malondialdehyde has been proposed to proceed through the enol form (VII) by a mechanism

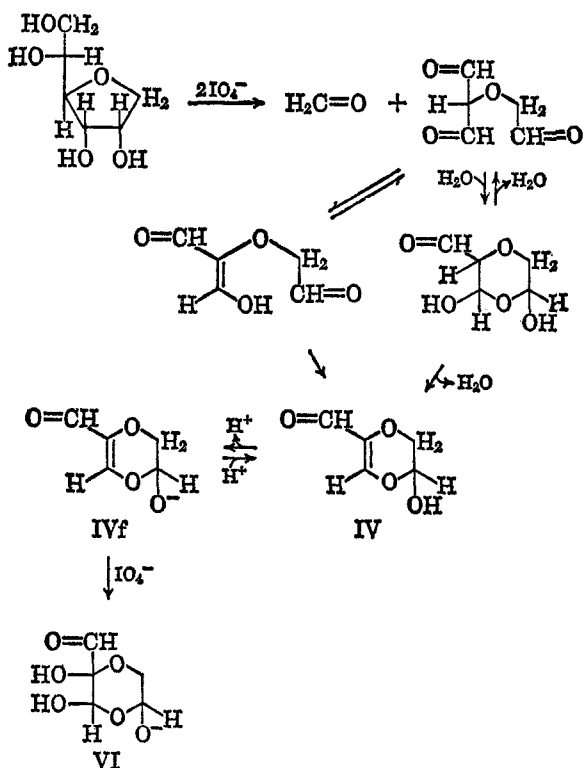
(33) M. L. Wolfrom and J. M. Bobbitt, *J. Am. Chem. Soc.*, **78**, 2489 (1956).

(34) J. E. Taylor, B. Soldano, and G. A. Hall, *ibid.*, **77**, 2656 (1955).

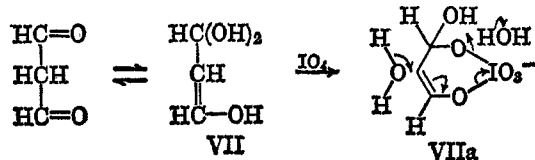
(35) C. F. Huebner, S. R. Ames, and E. C. Bubl, *ibid.*, **68**, 1621 (1946).

(36) M. Cantley, L. Hough, and A. O. Pittet, *J. Chem. Soc.*, 2527 (1963)

SCHEME II

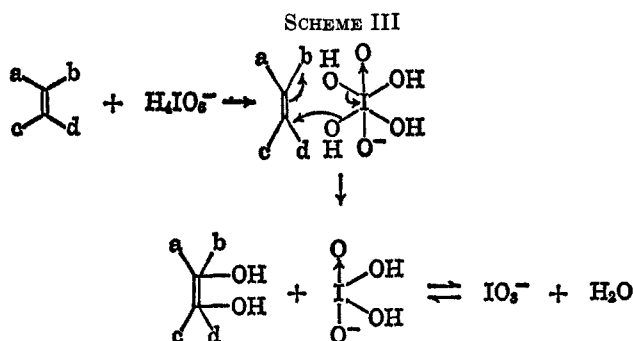


involving a six-membered cyclic complex VIIa, and, from a study of a variety of structural analogs of malondialdehyde, Bose, *et al.*,<sup>37</sup> concluded that the minimum requirement for complex formation and oxidation is the presence of 1,3-hydroxyls, one of which must be



derived from an enol. This structure is not present in IV.

The hydroxylation of a double bond by periodate is known to occur in the oxidation of 2-hydroxy-3-methoxycyclopenten-1-one,<sup>38</sup> and can be presumed to occur in the oxidation of indoles.<sup>39</sup> The oxidation of compounds containing "active" methylene groupings can also be explained on the basis of hydroxylation of a double bond generated by enolization as represented in Scheme III.



(37) J. L. Bose, A. B. Foster, and R. W. Stephens, *J. Chem. Soc.*, 3314 (1959).

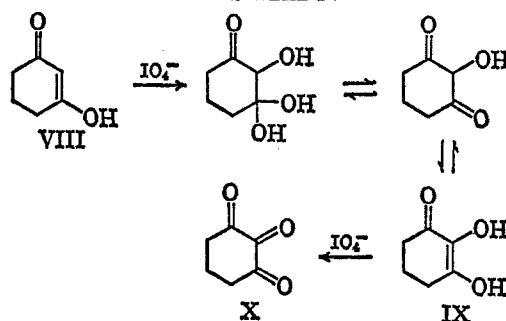
(38) G. Hesse and H. Mix, *Chem. Ber.*, **92**, 2427 (1959).

(39) L. J. Dolby and D. L. Booth, *J. Am. Chem. Soc.*, **88**, 1049 (1966).

The rate of this hydroxylation must depend upon the character of the substituents a, b, c, and d and would be expected to be strongly enhanced by electron-withdrawing groups if the periodate anion acts as a nucleophilic reagent. All of the periodate oxidations which are known to occur at double bonds appear to involve conjugated systems and it may be that conjugation is a prerequisite of oxidation (*i.e.*, hydroxylation).

Periodate may function in this fashion in the oxidation of cyclic 1,3-diketones<sup>38</sup> which exist to some extent in the enol form (VIII).<sup>40</sup> The product of hydroxylation

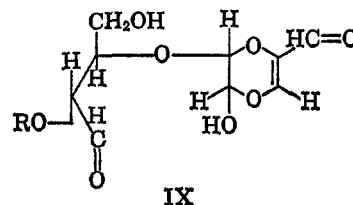
SCHEME IV



tion of the double bond can exist in several forms, one of which (IX) can react in a similar manner to produce the trione (X), which appears to be an intermediate in the complete oxidation of VIII.<sup>38</sup> This second step may also occur in a normal fashion as proposed by Bose, *et al.*<sup>37</sup>

All of the cases in which oxidation of active methylene groups occurs can be rationalized as involving an intermediate which is analogous to IV.

In the oxidation of polysaccharides, polyaldehydes resembling III can rearrange to form derivatives of IV such as XI. That such intermediates exist has been shown by examining the oxidation of maltose. At pH values of 8.5 and 6.0 as the oxidation proceeds an increase in absorbance at 270  $m\mu$  occurs which passes through a maximum in the first 20 min of the reaction.



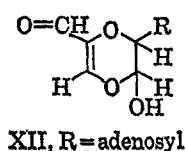
At pH 4.7 there is no increase in absorbance during the reaction. However, the presence in small amounts of absorbing material would merely slow the apparent rate of decrease in absorbance owing to consumption of periodate. These results are understandable in view of the fact that formate ester groups, which are quite stable at pH 4.7, are formed in the first normal oxidation steps and must be hydrolyzed before a rearranged product such as XI can form. If these hydrolyses are rate limiting at pH 4.7, then it would be impossible to accumulate a rapidly oxidized rearranged product.

The accumulation of a strongly absorbing compound has also been observed in the overoxidation of adenosine 5'-aldehyde.<sup>15</sup> The product of the normal oxidation

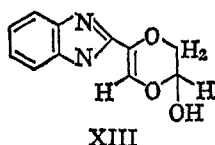
(40) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p. 376.



of adenosine 5'-aldehyde differs from the trialdehyde II only in that one of the methylene hydrogens is replaced by an adenosyl moiety. In this case the intermediate XII would form.



Similar intermediates would form in the overoxidation of hexofuranosides<sup>41</sup> in which R would be an oxygen-aglycone group. The overoxidation of anhydropentose benzimidazole derivatives<sup>42</sup> could also occur via a similar intermediate (XIII) in which the imidazole ring plays the role of the aldehydic group in IV.

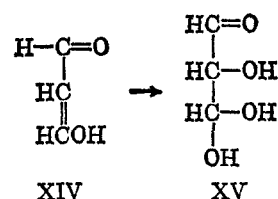


The overoxidation of 2-deoxy-D-erythro-pentose (2-deoxyribose) is also accompanied by an increase in

(41) T. G. Halsall, E. L. Hirst, and J. K. N. Jones, *J. Chem. Soc.*, 1427 (1947).

(42) C. F. Huebner, R. Lohmar, R. L. Dimler, S. Moore, and K. P. Link, *J. Biol. Chem.*, **150**, 503 (1945).

absorbance. In this case malondialdehyde is formed and the absorbance is probably due to the enol form of the compound (XIV) which can be hydroxylated to give the hydrated hydroxymalonaldehyde (XV).



### Summary

It has been shown that 2,3-dihydro-6-formyl-3-hydroxy-1,4-dioxine (IV) is an intermediate in the overoxidation of 1,4-anhydroallitol. The effect of pH on the rate of overoxidation has been explained in terms of its effect on the rate of formation and rate of oxidation of IV. It appears probable that the oxidation involves the monoanions of the oxidant and the substrate.

The overoxidation of maltose, 2-deoxy-D-erythro-pentose, adenosine 5'-aldehyde, anhydropentose benzimidazole derivatives, and hexofuranosides can proceed via analogous intermediates.

**Registry No.**—I, 10334-28-8; IV, 10334-29-9; sodium metaperiodate, 7790-28-5.

## Photochemistry of Nitroso Compounds in Solutions. VII.<sup>1</sup> Photoaddition of Nitrosamines to Various Olefins

Y. L. CHOW, CARLOS COLON, AND S. C. CHEN

*Department of Chemistry, Simon Fraser University, Burnaby, British Columbia, Canada*

Received December 27, 1966

The photoaddition of N-nitrosodimethylamine and N-nitrosopiperidine to various model olefins was shown to take place smoothly in the presence of an acid. The primary photoadduct was shown to be an  $\alpha$ -t-aminonitrosoalkane which underwent various secondary reactions. For the nitrosoalkane derived from monosubstituted and symmetrically disubstituted olefins the secondary process was dimerization to a *trans*-nitroso dimer or tautomerization to an  $\alpha$ -t-amino oxime. The nitrosoalkane derived from unsymmetrically di- or more substituted olefins readily underwent a cleavage reaction to give a ketoxime and an iminium salt. The orientation of the addition was exclusively in one direction wherein the amino moiety attached itself to the least-substituted carbon atom. Steric hindrance was shown to retard the photoaddition.

In the previous report one of us demonstrated that, in the presence of a dilute acidic medium, N-nitrosodialkylamines readily undergo a light-catalyzed addition across the carbon-carbon double bond of cyclohexene to yield  $\alpha$ -t-aminocyclohexanone oximes.<sup>2</sup> This photoaddition to cyclohexene has been shown to be a general reaction when both alkyl groups are secondary but not tertiary.

In the meantime, two addition reactions of N-chloramine to olefins under different conditions have been reported. The first one is the addition of a chloramine through dialkylamino radical generated by a redox metal ion couple, such as  $\text{Cu}^+-\text{Cu}^{2+}$  or  $\text{Fe}^{2+}-\text{Fe}^{3+}$  systems.<sup>3</sup> The second is the addition through a

dialkylaminium radical, a Hofmann-Löffler rearrangement intermediate, generated in a strongly acidic medium, e.g., 4 M  $\text{H}_2\text{SO}_4$ -AcOH.<sup>4</sup> Although there exists good evidence that the intermediates involved are quite different, the limited results available now do not permit a conclusion to be drawn with regard to the nature of these two addition reactions. For the interest of practical applications, it was desirable to explore the scope and limitation of the photoaddition of the N-nitrosodialkylamines. It was hoped that such a study would furnish a clue to the probable reaction mechanism and further provide a comparison of these three addition reactions.

In order to shed some light on the nature of this photoaddition, work was undertaken to clarify the question of orientation reactivity and stereochemistry of the reaction. In this report the photoaddition of

(1) For paper VI, see Y. L. Chow and A. C. H. Lee, *Can. J. Chem.*, **45**, 311 (1967).

(2) Y. L. Chow, *Can. J. Chem.*, **43**, 2711 (1965).

(3) (a) F. Minisci and R. Galli, *Tetrahedron Letters*, 167 (1964); 3197 (1964). (b) F. Minisci and R. Galli, *Chim. Ind. (Milan)*, **45**, 1400 (1963); **46**, 546 (1964).

(4) R. S. Neale, *J. Am. Chem. Soc.*, **86**, 5440 (1964); R. S. Neale, *Tetrahedron Letters*, 483 (1966).