Appendix

The only integrals different from zero which arise when developing eq. 3 are those of the form

$$\int \xi \, \mathrm{sp}_\xi \, d\tau = \frac{5}{2\sqrt{3}} \frac{1}{\delta}, \text{ atomic units, } \xi = x, y, z$$

and it is easily found that the coordinates for the charge centroids are

$$C_1 = \bar{x}_1 = -A \cos^2 \alpha \sin^2 \beta \sin \gamma \cos \gamma$$
$$\bar{y}_1 = A \sin \alpha \cos \alpha \sin \beta \cos \gamma$$
$$\bar{z}_1 = -A \cos^2 \alpha \sin \beta \cos \beta \cos \gamma$$
$$C_2 = \bar{x}_2 = -A \sin^2 \alpha \sin^2 \beta \sin \gamma \cos \gamma$$
$$\bar{y}_2 = -A \sin \alpha \cos \alpha \sin \beta \cos \gamma$$
$$\bar{z}_2 = -A \sin^2 \alpha \sin \beta \cos \beta \cos \gamma$$
$$C_3 = \bar{x}_3 = -A \cos^2 \beta \sin \gamma \cos \gamma$$
$$\bar{y}_3 = 0$$
$$\bar{z}_3 = A \sin \beta \cos \beta \cos \gamma$$
$$C_4 = \bar{x}_4 = A \sin \gamma \cos \gamma$$
$$\bar{y}_4 = 0$$
$$\bar{z}_4 = 0$$

where

$$A = 5a_0/\sqrt{3}\delta \qquad a_0 = 0.5292 \times 10^{-8} \text{ cm.}$$

PITTSBURGH, PENNA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WYOMING]

The Effect of Methyl Substitution on the Periodate Oxidation of *cis*- and *trans*-Cyclopentanediol-1,2[1]

BY VERNON C. BULGRIN AND GEORGE DAHLGREN, JR.

RECEIVED MARCH 3, 1958

The mechanism of the periodate oxidation of *cis*- and *trans*-cyclopentane-diol-1,2 and methylated derivatives is shown to be similar to that for pinacol. The reaction proceeds through apparently bimolecular non-catalyzed and acid-catalyzed paths. The effect of methyl substitution on the rate of the reaction, and the inertness of the *trans*-1,2-dimethyl compound toward oxidation by periodate support the postulate of a cyclic intermediate, the formation of which is rate determining.

Introduction

The periodic acid cleavage of vicinal glycols has been shown to proceed through either of two mechanisms. The first of these involves the formation of an intermediate complex between the oxidant and the reductant, the rate-determining step being the disproportionation of the intermediate. Such a mechanism results in pseudo first-order kinetics if glycol is present in sufficient excess. The second of the two involves no kinetically detectable amount of intermediate, is second order and involves, contrary to the first, a hydrogen ion catalyzed path as well as the non-catalyzed path. Duke and Bulgrin[2,3] were able to assign the former reaction scheme to the periodate oxidation of ethylene and methylated ethylene glycols, with the exception of pinacol. The reactive periodate species was shown to be a monovalent periodate ion, presumably IO_4^-; equilibrium and rate constants were determined for the formation and disproportionation, respectively, of the intermediate. Pinacol was found to follow the second scheme, both uncatalyzed and hydrogen ion catalyzed second-order paths being available. It was suggested that in the case of pinacol, the reaction is second order because the complex-forming step has become rate determining.

Bulgrin[4] studied the rates of cleavage of *cis*- and *trans*-cyclopentane-diol-1,2 by periodate and found the reaction to be second order but was unable to demonstrate hydrogen ion catalysis at 0°.

The question of the nature of the intermediate has not been answered fully. Criegee[5] and Price[6,7] have suggested a cyclic complex between glycol and a periodate species. Such an intermediate would be consistent with the specificity of periodate for cleavage of vicinal glycols. In forming the complex, a tetrahedral IO_4^- ion may coördinate a glycol molecule in the same way it coördinates two water molecules to form the octahedral $H_4IO_6^-$ ion.

Levesley[8] and Cordner and Pausacker[9] have concluded that the oxidation of vicinal glycols by lead tetraacetate probably does not involve a cyclic intermediate; Cordner suggests a monoesterification type mechanism. Criegee,[10] in his study of the lead tetraacetate oxidation of glycols, was unable to assign a single mechanism to cover all cases.

Wiberg and Saegebarth[11] state that a monoesterification type mechanism in the periodate oxidation of glycols does not agree with the experimentally observed rule that *cis*-compounds react faster than *trans*- and conclude that the intermediate is cyclic.

Buist and Bunton[12] have presented data, including some spectroscopic data, from which they conclude that the intermediate is not only cyclic but is necessary for the reaction to take place.

A kinetic study of the periodate oxidation of methylated *cis*- and *trans*-cyclopentanediol-1,2 was undertaken in order to help clarify the nature of the intermediate and to determine the extent of steric effects on the reaction.

---

[1] This work was supported in large part by a Frederick Gardner Cottrell Grant from the Research Corporation.

[2] F. R. Duke, THIS JOURNAL, **69**, 3054 (1947).

[3] F. R. Duke and V. C. Bulgrin, *ibid.*, **76**, 3803 (1954).

[4] V. C. Bulgrin, *J. Phys. Chem.*, **61**, 702 (1957).

[5] R. Criegee, *Sitzber. Ges. Beforder. ges. Naturw. Marburg*, **69**, 25 (1934).

[6] C. C. Price and M. J. Knell, THIS JOURNAL, **64**, 552 (1942).

[7] C. C. Price and T. J. Kroll, *ibid.*, **60**, 2727 (1938).

[8] P. Levesley, W. A. Waters and A. N. Wright, *J. Chem. Soc.*, 840 (1956).

[9] J. P. Cordner and K. H. Pausacker, *ibid.*, 102 (1953).

[10] R. Criegee, E. Hoerger, G. Huber, P. Kruck, F. Marktscheffel and H. Shellenberger, *Ann. Chim. Justus Liebigs*, **599**, 81 (1956).

[11] K. B. Wiberg and K. A. Saegebarth, THIS JOURNAL, **79**, 2822 (1957).

[12] (a) G. J. Buist, C. A. Bunton and J. H. Miles, *J. Chem. Soc.*, 4567 (1953); (b) G. J. Buist, C. A. Bunton and J. H. Miles, *ibid.*, 4575 (1957); (c) G. J. Buist and C. A. Bunton, *ibid.*, 4580 (1957).

Experimental

All fractionations, except where otherwise noted, were performed in a Todd Scientific Co. Precise Fractionation Assembly packed with either glass helices or a monel spiral.

All hydrogen ion activities were measured with a Beckman Model G *p*H meter.

Preparation of the Glycols.—*cis*- and *trans*-cyclopentanediol-1,2 were prepared as described in a previous paper.[4]

1-Methylcyclopentene was prepared from cyclopentanone in 67% yield by a method similar to that described by Signaigo and Cramer,[13] using methylmagnesium bromide and dehydration of the resulting alcohol with phosphoric acid. The material had a refractive index $n^{20}\text{D}$ of 1.4320 and boiled at 67.0° at 588 mm. when fractionated.

2-Carbethoxycyclopentanone was prepared in 62% yield from diethyl adipate by a method similar to that reported by Pinkney.[14] Sodium metal dispersed in anhydrous toluene was the condensing agent. The ketone was distilled and the sodio salt prepared by means of a similar sodium dispersion; methylation was accomplished by addition of methyl iodide. (Attempts to methylate the sodio salt in the flask in which ring closure had been achieved resulted in ring opening to give, ultimately, large quantities of adipic acid.) Toluene was removed by distillation and the 2-methyl-2-carbethoxycyclopentanone decarboxylated with concentrated hydrochloric acid. The resulting 2-methylcyclopentanone (64% yield based upon 2-carbethoxycyclopentanone) boiled at 40–45° (uncor.) at 20 mm.

1,2-Dimethylcyclopentene was prepared from 2-methylcyclopentanone by the procedure used for 1-methylcyclopentene. Upon distillation, a fraction boiling in the range 95.1–95.8° (uncor.) at 594 mm. and having a refractive index $n^{25}\text{D}$ of 1.4383 was collected. Gas chromatographic analysis showed the substance to be 95.7% pure, the single impurity, 4.3%, presumably being 2,3-dimethylcyclopentene. A second preparation, in which the toluene was not completely removed in the first stages of the procedure, gave a material which boiled at 95.8° (uncor.) at 589 mm.; gas chromatographic analysis showed the composition to be 70.6% 1,2-dimethylcyclopentene, 0.4% 2,3-dimethylcyclopentene and 29.0% toluene.

trans-1-Methylcyclopentanediol-1,2 was made from 1-methylcyclopentene by the method of Adkins and Roebuck.[15] A fraction (60% of the theoretical amount) boiling at 111.0° (uncor.) at 10 mm. was collected. The melting point, determined from cooling curves, was 62.5° (uncor.).

cis-1-Methylcyclopentanediol-1,2 was prepared from 1-methylcyclopentene by the method of Bartlett and Bavley,[16] using an aqueous-acetone solution of $KMnO_4$. The temperature of the reaction mixture was kept below −40°. Upon recovery from the reaction mixture by extraction with ether the glycol was vacuum distilled; a fraction (17% of the theoretical amount) boiling at 98.0° (uncor.) at 10 mm. was collected. The melting point was found to be 23.0–23.5° (uncor.) by means of heating curves and 22.7° (uncor.) by means of a cooling curve.

trans-1,2-Dimethylcyclopentanediol-1,2 was prepared from 1,2-dimethylcyclopentene by a method similar to that for the preparation of the *trans*-1-methyl compound. The material was extracted from the reaction mixture with hot (45–50°) ethyl acetate. The solution was dried with anhydrous calcium sulfate and the ethyl acetate removed by distillation; the brown solid residue was taken up in ethyl ether and the insoluble impurities removed by filtration. After evaporation of the ether, the glycol was purified by sublimation at 55–60° at 590 mm. to give long white needles. Resublimation of a small amount of the product through a large quantity of anhydrous calcium sulfate gave a product melting sharply at 101.6° (uncor.). (Purification of the crude glycol by three successive recrystallizations from ethyl ether gave a much lower yield of less pure product.)

cis-1,2-Dimethylcyclopentanediol-1,2 was prepared from 1,2-dimethylcyclopentene in very low yields by three different modifications of the $KMnO_4$ procedure. The small amounts of product obtained boiled at 105–107° (uncor.) at 20 mm. A much higher yield (85%) of a much purer product was obtained by treating a solution of the hydrocarbon in anhydrous ethyl ether with equivalent amounts of osmium tetraoxide (Varlacoid Chemical Co.) and anhydrous pyridine. The osmiate–pyridine complex was decomposed by shaking its chloroform solution with several portions of a water solution containing excess mannitol and 10% KOH, until the chloroform layer became nearly colorless. The water layers were extracted continuously for 10 hr. with hot chloroform, the chloroform extracts were combined and the solvent removed by evaporation. Distillation in a micro apparatus with a short Vigreux column gave a colorless liquid boiling at 108.0–108.2° (uncor.) at 20 mm. and having a refractive index $n^{22}\text{D}$ of 1.4715. A melting range of 20.5–20.8° was determined by stirring a small sample of the material in a test tube immersed in a water-bath, the temperature of which was gradually lowered.

Analysis of the Glycols.—Five of the glycols were analyzed by allowing aqueous solutions to stand with excess periodic acid for various times and determining the excess periodic acid in the usual manner, using standard solutions of sodium arsenite and iodine, the titration mixtures being buffered with excess sodium bicarbonate. Analysis of the data showed these per cent. purities.

cis-cyclopentanediol-1,2	97.5 ± 0.2
trans-cyclopentanediol-1,2	99.3
cis-1-methylcyclopentanediol-1,2	97.3
trans-1-methylcyclopentanediol-1,2	100.0
cis-1,2-dimethylcyclopentanediol-1,2	99.0

trans-1,2-Dimethylcyclopentanediol-1,2 was found to be inert toward oxidation by periodate in acid solution. When allowed to stand at room temperature in aqueous solution with excess periodic acid, the once-sublimed material was 4.0% oxidized in 27 minutes and 4.4% oxidized in 3 days. It was concluded that the oxidizable material was 2,3-dimethylcyclopentanediol-1,2, arising from the 4.3% 2,3-dimethylcyclopentene impurity in the hydrocarbon from which the glycol was prepared. Lead tetraacetate oxidation of the once-sublimed glycol showed a purity (oxidizable glycols) of 89%. Upon drying over P_2O_5 at 100 mm. for two days, this material had a melting range of 100.7–101.6° (uncor.) and was 99.0% oxidized by lead tetraacetate, indicating the non-oxidizable impurity in the once-sublimed material to be water.

Rate Determinations.—The reaction rate was studied by a method outlined previously,[3] using a large excess of potassium iodide in saturated sodium bicarbonate solution, containing a measured excess of sodium arsenite, as a quenching solution, and titrating the excess arsenite with standard iodine solution. All rate constants so determined were reproducible to within 3%, usually to within 1 or 2%.

Ionic strength was held constant at 0.20 by the addition of the proper amount of sodium nitrate to the reaction mixtures. The *p*H of the reaction mixture was adjusted by addition of the proper amounts of sodium hydroxide or perchloric acid. It had been determined previously that in the *p*H range 1–6, the *p*H of such reaction mixtures varied by less than 0.1 unit during the observed part of the reaction.

Results and Discussion

Of the six glycols studied, five were found to exhibit similar behavior except for magnitudes of rate constants. The sixth, *trans*-1,2-dimethylcyclopentanediol-1,2, was found to be inert toward oxidation by periodic acid at room temperature over a period of three days.

Two paths were found to be available for the reaction. The first of these is an uncatalyzed (by hydrogen ion) path involving the reaction scheme

$$IO_4^- + G \xrightarrow{k_2} \text{products}$$

and following the kinetic expression

$$\frac{-\,d[P]_T}{dt} = k_2[IO_4^-][G] = k_2'[P]_T[G]$$

where $[IO_4^-]$ and $[G]$ = concentration of negative periodate ion and glycol, respectively; $[P]_T$ =

---

(13) F. K. Signaigo and P. L. Cramer, THIS JOURNAL, **55**, 3326 (1933).

(14) P. S. Pinkney, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 116.

(15) A. Roebuck and H. Adkins, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 217.

(16) P. D. Bartlett and A. Bavley, THIS JOURNAL, **60**, 2416 (1938).

total periodate concentration as determined by analysis.

$$k_2' = k_2/f \qquad (1)$$

$$f = 1 + \frac{1}{K_D} + \frac{A_{H^+}\gamma_{IO_4^-}}{K_1 K_D \gamma_{H_5IO_6}} \qquad (2)$$

$\gamma_{IO_4^-}$ and $\gamma_{H_5IO_6}$ are the respective activity coefficients; A_{H^+} = activity of hydrogen ion, determined from *p*H measurements; K_1 and K_D are defined by the equilibria

$$H_5IO_6 \overset{K_1}{\rightleftharpoons} H^+ + H_4IO_6^-$$

$$H_4IO_6^- \overset{K_D}{\rightleftharpoons} IO_4^- + 2H_2O$$

The factor *f* corrects for the availability of IO_4^- ion and indicates that the uncatalyzed reaction rate should fall off rapidly below *p*H values of about 3. Such *p*H behavior has been shown to be the case quantitatively for glycols not undergoing hydrogen ion catalysis.[3]

The second path differs only in the observed hydrogen ion catalysis and becomes important at *p*H values below about 3. Typical plots of observed second-order rate constants *versus* *p*H are shown in Figs. 1 and 2. All five of the oxidizable glycols behaved in a similar manner. The calculated curves shown are based upon the previously defined expression for K_2', using the rate data obtained in the *p*H region 4-5, where the third term in the expression for *f* is negligible.

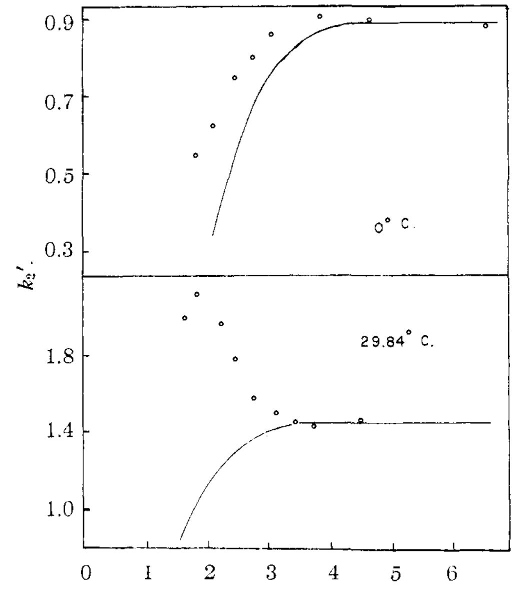


Fig. 1.—*trans*-1-Methylcyclopentanediol-1,2, variation of pseudo second-order rate constants with *p*H: curve shown is calculated from equation 1, *i.e.*, assuming no hydrogen ion catalysis.

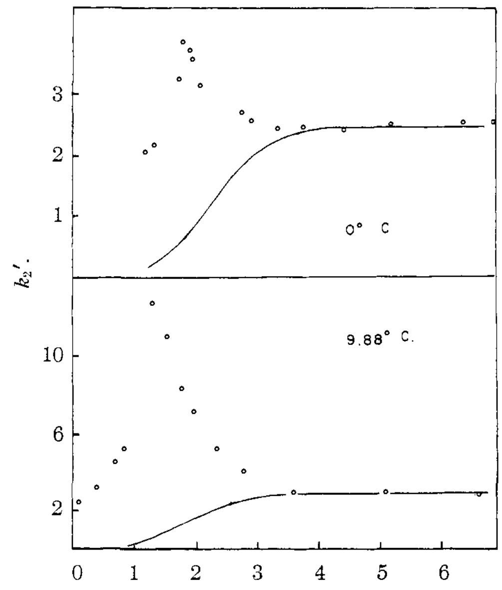


Fig. 2.—*cis*-1,2-Dimethylcyclopentanediol-1,2, variation of pseudo second-order rate constants with *p*H: curve shown is calculated from equation 1, *i.e.*, assuming no hydrogen ion catalysis.

For the *p*H range 4-5 ,where the rate of reaction is independent of *p*H, second-order rate constants k_2' were obtained from equal concentrations of periodate and glycol and for various excess amounts of glycol; good agreement (within 3%) in the constants was obtained for each glycol. For large excesses of glycol, the reaction becomes pseudo first order, with the pseudo first-order rate constant k_1' equal to k_2'[G]. Typical plots[17] of the reciprocal of k_1' *versus* the reciprocal of [G] are shown in Fig. 3; extrapolation of the straight lines to the origin substantiates second-order kinetics over the entire concentration range.[18] From the slopes of

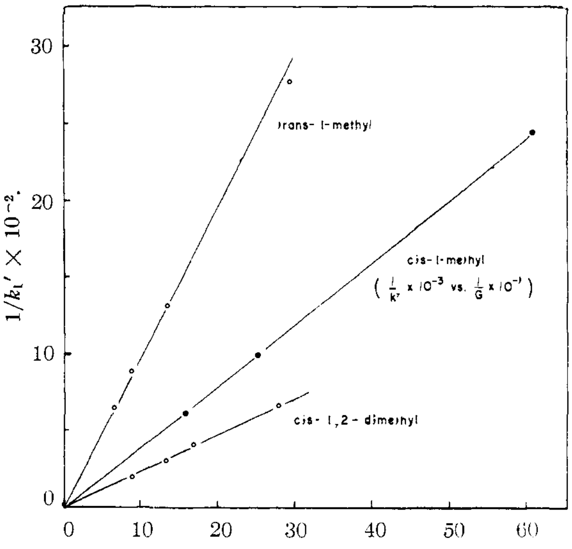


Fig. 3.—Typical plots of the reciprocal of the pseudo first-order rate constants *versus* the reciprocal of the average glycol concentrations at 0°.

---

[17] For the purpose of the plots, the average glycol concentration during the observed portion of the reaction was used. Maximum variation in the glycol concentration during the observed part of a given run can be shown to be less than 10% in all cases, usually less than 5%.

[18] Because of the rapidity of the reaction, a plot of this type could not be made for *cis*-cyclopentanediol-1,2.

these plots, second-order rate constants k_2' were calculated and found to agree within 3% with the constants determined from the second-order runs.

Assuming the observed hydrogen ion catalysis to be first order and that the observed second-order rate constant k_2' may be represented by

$$k_2' = \frac{k_2 + k_H[H^+]}{f}$$

where k_2 is the rate constant for the uncatalyzed reaction, calculated from the data for the *p*H range 4–5, and k_H is the rate constant for the hydrogen ion catalyzed reaction, it can be shown that a plot of log $(fk_2' - k_2)$ *versus* *p*H in the region where hydrogen ion catalysis takes place would give a straight line with slope of −1 and intercept equal to log (k_H/γ_{H^+}). Typical plots are shown in Fig. 4; the straight lines are drawn with slopes of −1.

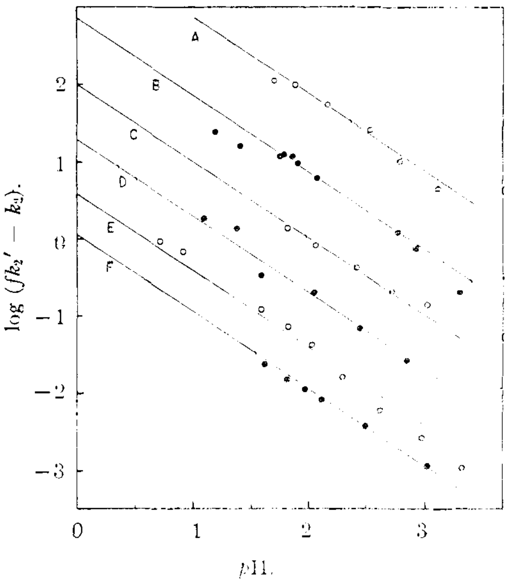


Fig. 4.—Typical plots illustrating first order hydrogen ion catalysis; slopes of lines are −1, intercepts are −log k_H/γ_{H^+}: A, *cis*-cyclopentanediol-1,2, 25.06°; B, *cis*-1-methylcyclopentanediol-1,2, 0°; C, *trans*-cyclopentanediol-1,2, 0°; D, *cis*-1,2-dimethylcyclopentanediol-1,2, 29.82°; E, *cis*-1,2-dimethylcyclopentanediol-1,2, 0°; F, *trans*-1-methylcyclopentanediol-1,2, 15.10°.

Tables I and II give the experimentally determined values of k_2 and k_H for the rate expression

$$\frac{-d[P]_T}{dt} = (k_2 + k_H[H^+])[IO_4^-][G]$$

Table III gives the calculated activation energies and entropies for the uncatalyzed reaction. Plots of log k_2 *vs.* the reciprocal of the absolute temperature gave good straight lines for all of the glycols. The thermodynamic functions for pinacol, reported previously,[3] are included. Pinacol was the only glycol in a series of methylated ethylene glycols for which no kinetically determinable intermediate complex could be demonstrated. The mechanism of the pinacol oxidation is similar to that for the cyclopentanediol series.

TABLE I

RATE CONSTANTS FOR THE UNCATALYZED REACTION

Glycol	k_2(l. mole^{-1} sec.$^{-1}$) 0.00°	T°
cis-Cyclopentanediol-1,2	17.7	21.6 (15.06) 23.1 (25.06)
trans-Cyclopentanediol-1,2	1.01	1.29 (19.73) 1.48 (29.84)
cis-1-Methylcyclopentanediol-1,2	2.78	3.15 (9.88) 3.76 (25.03)
trans-1-Methylcyclopentanediol-1,2	0.0112	0.0161 (9.88) .0187 (15.01) .0255 (25.05)
cis-1,2-Dimethylcyclopentanediol-1,2	0.0048	.0081 (15.24) .0128 (29.82)
trans-1,2-Dimethylcyclopentanediol-1,2		Not oxidized

TABLE II

RATE CONSTANTS FOR THE HYDROGEN ION CATALYZED REACTION

Glycol	k_H (l.^{2} mole^{-2} sec.$^{-1}$) 0.00°	T°
cis-Cyclopentanediol-1,2	3000	6000 (25.06)
trans-Cyclopentanediol-1,2	90	100 (29.84)
cis-1-Methylcyclopentanediol-1,2	700	1000 (9.88)
trans-1-Methylcyclopentanediol-1,2	0.8	0.9 (15.10)
cis-1,2-Dimethylcyclopentanediol-1,2	3	20 (29.82)
trans-1,2-Dimethylcyclopentanediol-1,2		Not oxidized

TABLE III

THERMODYNAMIC FUNCTIONS OF ACTIVATION FOR THE UNCATALYZED REACTION, $G + IO_4^- \xrightarrow{k_2}$ PRODUCTS

Glycol	$\Delta H^{\ddagger}$ (kcal./mole)	$\Delta F^{\ddagger}$ (kcal./mole)	$\Delta S^{\ddagger}$ (cal./deg./mole)
cis-Cyclopentanediol-1,2	1.2 ± 0.3	14.4 ± 0.0	−48
trans-Cyclopentanediol-1,2-	1.5 ± .1	15.9	−53
cis-1-Methylcyclopentanediol-1,2	1.4 ± .1	15.4	−51
trans-1-Methylcyclopentanediol-1,2	4.8 ± .2	18.4	−50
cis-1,2-Dimethylcyclopentanediol-1,2	4.8 ± .1	19.1	−52
trans-1,2-Dimethylcyclopentanediol-1,2	Not cleaved by periodate		
Pinacol[3]	7.2 ± 0.2	19.5	−45

That no kinetically detectable amount of an intermediate exists for any of these glycols may be explained on the basis of a small (less than unity) equilibrium constant for its formation or, preferably, that the formation of the intermediate has become rate determining.

The following observations support the postulate that the intermediate is cyclic. First, the presence of an intermediate, the disproportionation of which is rate-determining, has been demonstrated only for those glycols having a substantial degree of free rotation about the bond between the hydroxyl bearing carbon atoms.[2,3] Among this group are ethylene glycol and its methylated derivatives, with the exception of pinacol. In general, the equilibrium constants for the formation of the intermediate decrease with increasing methyl substitution from propylene glycol to trimethylethylene glycol, becoming quite small in the case of the latter compound. Buist[12] has presented evidence which indicates that for trimethylethylene glycol the rates of formation and disproportionation of the intermediate may be comparable. For pinacol,[3] where rotation is expected to be highly hindered, resulting in a more favorable *trans*-configuration for the hydroxyl groups, and for all of the cyclopentanediols studied in this work, no intermediate could be demonstrated from rate data, presumably because the formation of such an intermediate has become slow compared to its disproportionation.

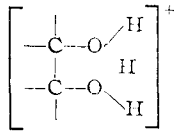
Second, *trans*-1,2-dimethylcyclopentanediol-1,2, a glycol which from steric considerations might not be expected to form a cyclic intermediate at all, is not oxidized by periodate.

Third, *cis*-1,2-dimethylcyclopentanediol-1,2 is cleaved more slowly than *trans*-1-methylcyclopentanediol-1,2. This last observation is not surprising if the intermediate is considered to be cyclic; from models, it appears that two methyl groups for the *cis*-compound may offer more hindrance to the formation of an octahedrally coördinated complex with periodate ion than one methyl group for the *trans*-compound. Presumably, the optimum oxygen–oxygen distance for the formation of such a complex is intermediate to that for the *cis*- and the *trans*-compounds.

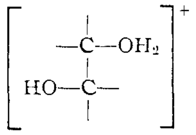
Finally, cyclic structures have been postulated for several stable complexes of glycols, notably those with boric acid and with sodium molybdate.

It is observed that methyl substitution increases the ratio k_H/k_2 at 0° for the *cis*-compounds of the cyclopentanediol series, from 170 for the unmethylated glycol to 625 for the dimethylated glycol; methyl substitution has little effect on the ratio for the *trans*-isomers. These facts suggest the observed hydrogen ion catalysis may involve a prior equilibrium to give a protonated glycol species, the latter reacting more rapidly with IO_4^- ion than does the glycol itself. *cis*-Glycols could form a protonated species such as (I) whereas *trans*-glycols would be limited to cations of type II.

I



II



The rate constants for the two paths, given in Tables I and II, together with the fact that *trans*-1,2-dimethylcyclopentanediol-1,2 does not cleave at any *p*H in the acid region, suggest that the two paths are substantially the same, differing only in the role of hydrogen ion, and that the same type intermediate is involved in both.

LARAMIE, WYOMING

[CONTRIBUTION FROM THE LABORATORY OF CELLULAR PHYSIOLOGY AND METABOLISM, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH]

The Distribution of Fatty Acids between *n*-Heptane and Aqueous Phosphate Buffer

BY DEWITT S. GOODMAN

RECEIVED JANUARY 2, 1958

A study has been made of the distribution of eight fatty acids between *n*-heptane and aqueous phosphate buffer at *p*H 7.45, ionic strength 0.16 and 23°. The fatty acids studied included octanoic, decanoic, lauric, myristic, palmitic, stearic oleic and linoleic acids. C^{14}-Carboxyl labeled acids were used for assay, enabling accurate measurements to be made at extremely low concentrations and over a range of several orders of magnitude in each case. The data obtained with octanoic, decanoic, lauric and myristic acids are consistent with the assumption of a monomer–dimer equilibrium in the organic phase, without association in the aqueous phase. The association (dimerization) constants for these four fatty acids in heptane saturated with water have been calculated from these data and are, respectively, 5.8, 6.9, 7.0 and 9.3×10^3. These constants are compared with others available in the literature. With these 4 fatty acids the partition ratio for the monomeric forms in the two phases has been found to increase geometrically with chain length, the increase being approximately 17-fold for each two carbon increment. In contrast, the data obtained with the four highest fatty acids studied are markedly different and are not susceptible to quantitative interpretation at the present time.

In 1891 Nernst successfully accounted for the distribution of benzoic acid between water and benzene by assuming the existence of dimers in the benzene phase.[1] Since then the association of carboxylic acids has been the subject of numerous investigations by a variety of methods. Vapor density measurements by Fenton and Garner[2] and by Coolidge,[3] demonstrated the existence of fatty acid dimers in the gaseous state. X-Ray studies of the solid[4] and liquid[5] states have indicated that in these states fatty acid molecules are paired. Molecular weight and distribution measurements have shown that fatty acids are present as dimers when in solution.[6,7] Most of the quantitative studies available have dealt, however, with carboxylic acids other than the fatty acids.[8] Notable exceptions are the investigations of Pohl, Hobbs and

---

[1] W. Nernst, *Z. physik. Chem.*, **8**, 110 (1891).

[2] T. M. Fenton and W. E. Garner, *J. Chem. Soc.*, 694 (1930).

[3] A. S. Coolidge, THIS JOURNAL, **50**, 2166 (1928).

[4] A. Muller, *Proc. Roy. Soc.* (*London*), **154A**, 624 (1936).

[5] R. M. Morrow, *Phys. Rev.*, **31**, 10 (1928).

[6] M. Trautz and R. Moschel, *Z. anorg. Chem.*, **155**, 13 (1926).

[7] W. Herz and H. Fischer, *Ber.*, **38**, 1138 (1905).

[8] The term "fatty acid" is herein used to refer to the straight or branched chain aliphatic carboxylic acids.