material had m.p. 197°, $[\alpha]^{22}D$ +56°, lit.,[17] m.p. 197°, $[\alpha]D$ +58°.

3β-Acetoxyandrostan-16α,17α-diol.—3β-Acetoxy-Δ^{16}-androstene,[17] 55.6 mg., was treated with an excess of osmium tetroxide in 10 ml. of ether containing 0.1 ml. of pyridine. A flocculent tan precipitate immediately formed which darkened on standing. After 3 hours, 20 ml. of petroleum ether was added and the straw-colored supernatant fluid decanted. The solid was dissolved in 50 ml. of absolute ethanol. The solution was treated with a rapid stream of hydrogen sulfide until precipitation was complete. Filtration yielded a colorless solution which was evaporated to dryness under reduced pressure. The residue was crystallized from aqueous ethanol to yield 24.3 mg. (40%) of triol monoacetate, m.p. 149–151°, $[\alpha]^{22}D$ −0.089°. The analytical sample from petroleum ether had m.p. 153.5–154°, and had a strong internal hydrogen bond in the infrared.

Anal. Calcd. for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 72.03; H, 10.36.

Theoretical Calculations, Torsional Barriers.—The van der Waals interactions of 1,2-substituents are determined from the barrier to rotation about the C–C bond of an appropriately substituted ethane. This is convenient both because of the availability of these barriers in the literature and because several interactions are thus determined by a single calculation. The barriers employed in the present work are tabulated below. The barriers for use at the 17,13-position of the steroids are estimated. Thus, the barrier for rotation about the 2,3-bond of 2-methylbutane is desired for the 17,13-position in the 17-methylsteroids. The ratio of the barrier in 2-methylpropane to that of 2,2-dimethylpropane was assumed to be the same as that of the desired barrier to the barrier in 2,2-dimethylbutane. (Similarly, the barrier in 2-methylpropanol was estimated by increasing the barrier in ethanol in the ratio of the barriers in propane and 2-methylbutane.) The barriers for rotation against the carbonyl group for which the position of lowest potential is known to be that of eclipsing were assumed to be diminished from that of acetaldehyde. The barrier in α-methylpropionaldehyde may then be estimated as (V_0 ethane) (V_0 acetaldehyde)/(V_0 2-methylpropane).

1,3-Interactions.—The energy, E_{vw}, of the van der Waals interactions of a pair of functional groups is given by[29]

$$E_{vw} = \frac{-2.25\epsilon^* r^{*6}}{r^6} + 8.28 \times 10^5 \epsilon^* \exp. -r/0.0736r^*$$

where r is the distance between the interacting functions, r^* is the *effective* sum of the van der Waals radii of these groups and ϵ^* is a function of the types of interacting groups. The values of ϵ^* in kcal./mole where hydrogen is interacting with the second function are: hydrogen, 0.042; methyl, 0.117; hydroxyl, 0.103; bromine, 0.139. For methyl interacting with the second group; methyl, 0.326; hydroxyl, 0.286; bromine, 0.380. The values of ϵ^* have been chosen such that the usually accepted values for the energy of an axial methyl group (1.8 kcal./mole),[6] alcohol (0.8 kcal./mole)[6] and bromine (0.73 kcal./mole),[30] are twice the potential given by the above functions (two axial hydrogens interacting) when applied to the ideal chair form of cyclohexane.

Potential barriers to rotation (V_0 in kcal./mole)

Ethane[a]	2.800
Propane[b]	3.400
2-Methylpropane[c]	3.850
2,2-Dimethylpropane[c]	4.400
2-Methylbutane[d]	~3.760
2,2-Dimethylbutane[c]	4.300
Ethanol[e]	3.000
2-Methylpropanol[d]	~3.320
Bromoethane[f]	3.570
1-Bromo-2-methylpropane[d]	~3.950
Acetaldehyde[g]	1.150
α-Methylpropionaldehyde[d]	~0.850

[a] K. S. Pitzer, *Diss. Faraday Soc.*, **10**, 66 (1951). [b] K. S. Pitzer, *J. Chem. Phys.*, **12**, 310 (1944). [c] K. Ito, *J. Am. Chem. Soc.*, **75**, 2430 (1953). [d] See text for method of estimation. [e] S. C. Schumann and J. G. Aston, *J. Chem. Phys.*, **10**, 559 (1942). [f] D. R. Lide, *ibid.*, **30**, 37 (1958). [g] R. W. Kelb, C. C. Lin and E. B. Wilson, *ibid.*, **26**, 1695 (1957).

Bond lengths, Å.		Parameters employed	van der Waals radii, Å.	
C–C	1.54	—C–C–O 109.5°	H	1.20
C–H	1.10	—C–O–H 105° (adjusted	OH	1.86
C–Br	1.91	slightly for H-bonding)	CH_3	2.00
C–OH	1.43		Br	1.95
O–H	0.96			

(29) T. L. Hill, *J. Chem. Phys.*, **16**, 399 (1948).

(30) E. L. Eliel and R. G. Haber, *J. Am. Chem. Soc.*, **81**, 1249 (1959).

[CONTRIBUTION FROM THE JAMES BRYANT CONANT LABORATORY OF HARVARD UNIVERSITY, CAMBRIDGE 38, MASS.]

The Cleavage of *cis*- and *trans*-1,2-Dimethyl-1,2-cyclopentanediol by Chromic Acid

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Chromic acid in water oxidizes *cis*-1,2-dimethyl-1,2-cyclopentanediol to 2,6-heptanedione 17,000 times faster than the *trans* isomer; in 90% acetic acid, the factor is 800. These data suggest that the *cis*-diol (and open-chain diols by analogy) rapidly and reversibly form a cyclic ester with chromic acid; the rate-determining step of the oxidation process is then the decomposition of this ester with cleavage of the C–C bond. The *trans* isomer is presumably oxidized by a non-cyclic mechanism. The energetics of the fission of glycols is compared to that for the oxidation of secondary alcohols, and the selection of oxidants for cleavage *vs.* simple formation of ketone is discussed.

In a recent paper on the oxidation of pinacol to acetone,[1] one of us proposed a mechanism for the process in which a cyclic ester of chromic acid is formed, and then decomposes to cleavage products. The evidence in favor of this mechanism consisted chiefly of two facts: pinacol is oxidized much more rapidly than is its monomethyl ether, and the solvent isotope effect, k_{D_2O}/k_{H_2O} is 2.7. However, despite the advances which have recently been made[2] in the quantitative estimate of solvent deuterium isotope effects, the prediction for complex reactions involving several protonations is still uncertain. The present work was undertaken to investigate further the mechanism of the cleavage of glycols by chromic acid.

We have therefore measured the rates for the chromic acid oxidation of the two isomeric 1,2-

(1) Y. W. Chang and F. H. Westheimer, *J. Am. Chem. Soc.*, **82**, 1401 (1960).

(2) C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 42, 3207, 3214 (1961); C. G. Swain and R. F. W. Bader, *Tetrahedron*, **10**, 182 (1960); C. G. Swain, R. F. W. Bader and E. R. Thornton, *ibid.*, **10**, 200 (1960).

dimethyl-1,2-cyclopentanediols. The hydroxyl groups in these glycols are nearly in fixed positions, and a cyclic ester can be formed only from the *cis*-compound.

Experimental

Materials.[3]—**1,2-Dimethylcyclopentene** was prepared by a standard procedure from 2-methylcyclopentanone (Aldrich Chemical Co.; the material contained about 5% of impurities according to V.P.C.) and methylmagnesium iodide, the alcohol being dehydrated by iodine without prior isolation. The olefin was purified by distillation through an 18" spinning band Nester and Faust column and the fractions controlled by gas–liquid chromatography.

***cis*-2-Dimethyl-1,2-cyclopentanediol.**—1,2-Dimethylcyclopentene (6.4 g.) was added in portions to a solution of osmium tetroxide (17 g.) in ether (300 ml.), the reaction being catalyzed by pyridine (11 ml.). After 1 hour the dark deposit was collected (20.5 g.), dissolved in chloroform and decomposed by shaking it with a solution of mannitol (30 g.) in 10% KOH (300 ml.) in four portions during 24 hours. The combined water solutions were continuously extracted with chloroform. After chloroform and pyridine had been distilled off through a small column, a viscous residue remained, which, after distillation (90° at 9 mm.), gave the *cis*-glycol (6.10 g., 70% yield), m.p.[4] 19–22°. The product was purified further by three successive crystallizations from ethyl acetate (25-ml. portions) at −60° and a final distillation (86° at 8 mm.). In this way 2.5 g. of a very pure glycol melting[4] 25–25.2° have been obtained (lit.[5] gives 20.5–20.8°).

***trans*-1,2-Dimethyl-1,3-cyclopentanediol** was prepared from 1,2-dimethylcyclopentene and hydrogen peroxide by the method of Roebuck and Adkins.[6] Attempted purification of the crude product (m.p. 85–87°) by crystallization from petroleum ether and by sublimation was unsuccessful. According to a periodic acid assay, the material contained about 8% of an isomeric glycol, which was removed as follows: The crude glycol (3.6 g.) was allowed to stand overnight with a solution of periodic acid (0.6 g. of H_5IO_6) in water (20 ml.); the reaction mixture was neutralized by sodium bicarbonate, saturated with sodium sulfate and extracted with ethyl acetate. The (yellow) product obtained after distilling the solvent from the combined and dried (sodium sulfate) extracts was recrystallized from benzene–cyclohexane to give a product melting 105–107° (lit.[5] give 101.6°), but forming liquid crystals at a temperature about 20° below the melting point.

2,6-Heptanedione dioxime was prepared by reduction of 2,6-lutidine by sodium in methanol.[7,8] (Ethanol was found to be less suitable.) The distilled (148–150° at 1 mm.) very viscous product solidified after standing for several days; m.p. 71–83°. The solid dioxime was dissolved in ether (38 g. in 75 ml.), crystallized at −20°, washed with ether and dried; m.p. 81–85° (lit.[8] 83.4–84.6°).

2,6-Heptanedione was prepared from the purified dioxime by treatment with nitrous acid according to Overberger and co-workers.[8] The ether solution of the crude diketone was evaporated to dryness and the diketone distilled *in vacuo*. The product thus obtained melted[4] at 25–29° and showed several impurities by V.P.C.; it was further purified by crystallization from ether at −30°, yielding a product melting[4] at 31.8° (lit.[8] gives 32.6–33.4°), which gave a single peak by V.P.C.

2,6-Heptanedione bis-*p*-nitrophenylhydrazone was prepared in ethanol solution acidified by a few drops of acetic acid. On recrystallization from ethanol, the product formed fine yellow fibers melting at 175–176°. (The reported[9] m.p., 182–183°, could never be reached.)

Anal. Calcd. for $C_{19}H_{22}N_6O_4$: C, 57.18; H, 5.57; N, 21.09. Found: C, 57.18, 56.98; H, 5.61, 5.78; N, 20.79, 21.20.

2,6-Heptanedione bis-2,4-dinitrophenylhydrazone, prepared in the usual way, forms yellow crystals almost completely insoluble in standard solvents. It could be crystallized from pyridine to yield a product melting at 185–186° which did not change its properties on further purification, but, nevertheless, failed to give the correct analysis; the high carbon content suggested that some mono-2,4-dinitrophenylhydrazone might have been present.

Products. Oxidation of *cis*-1,2-Dimethyl-1,2-cyclopentanediol. (A) Isolation as Dinitrophenylhydrazone.—A solution of the glycol (37.8 mg.) in water (5 ml.) was mixed with a solution of $K_2Cr_2O_7$ (10 ml., 0.01 *M* in Cr), acidified with perchloric acid (1.0 *M*, 0.5 ml.). After the reduction of the chromic acid was completed (about 2 hours), 30 ml. of a saturated solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid was added. The collected and dried precipitate corresponded to 85% of the theoretical yield calculated for the bis-dinitrophenylhydrazone. Another experiment gave an 80% yield. Control experiments starting with the authentic 2,6-heptanedione gave 80 to 92% yields. The dinitrophenylhydrazone isolated from the oxidation experiments melted, after crystallization from dimethylformamide–benzene and from pyridine, at 183–185° and showed no melting point depression with the authentic sample.

(B) Isolation as *p*-Nitrophenylhydrazone.—The glycol (96.5 mg.) was dissolved in 45 mg. of $K_2Cr_2O_7$ (0.01 *M* in Cr) and acidified with perchloric acid (1.0 *M*, 2.0 ml.). After 1.5 hours the solution was diluted with ethanol (30 ml.) and *p*-nitrophenylhydrazine (245 mg. in 7 ml. of ethanol) was added. The collected precipitate corresponded to a 92% yield of the bis-*p*-nitrophenylhydrazone and melted at 170–172° (176.0–177.2° in capillary tube) and gave no melting point depression with the authentic analyzed sample. In another experiment a 93% yield was obtained. A control experiment starting with the authentic diketone and subjecting it for 4 hours to the action of perchloric acid of the same concentration as above gave a 96% yield of the bis-*p*-nitrophenylhydrazone. *cis*-1,2-Dimethyl-1,2-cyclopentanediol treated in the same way gave no precipitate.

Oxidation of *trans*-1,2-Dimethyl-1,2-cyclopentanediol. (A) In 90% Acetic Acid.—The glycol (51.7 mg.) was dissolved in 90% acetic acid (4 ml.), mixed with a solution of chromic anhydride in 90% acetic acid (0.1 *M*, 2 ml.) and acidified with sulfuric acid (6 ml. of 0.1 *M* in 90% acetic acid). After 1 hour, a solution of *p*-nitrophenylhydrazine (110 mg.) in ethanol (5 ml.) was added and the solution neutralized by the addition of a 15% sodium hydroxide solution (24 ml.). (The bis-*p*-nitrophenylhydrazone is soluble in acetic acid.) The derivative obtained in a 74% yield had an identical infrared spectrum as the authentic sample; the m.p. after a single crystallization from alcohol was 171.5–173°. A control experiment starting with the authentic diketone gave a 70% yield of the bis-*p*-nitrophenylhydrazone.

(B) In Water.—The glycol (48.4 mg.) and potassium dichromate (29.2 mg.) were dissolved in water (5 ml.) and perchloric acid added (60.4%; 1.0 ml.). After 11 hours, *p*-nitrophenylhydrazine (130 mg. in 5 ml. of ethanol) was added, and, after another hour, the reaction mixture was neutralized by the addition of a sodium acetate solution (3 *M*, 3.5 ml.). The collected precipitate corresponded to 93% of the theory for the bis-*p*-nitrophenylhydrazine and melted, after one crystallization from 40% alcohol and another from 95% alcohol, at 172.5–174.5°. The derivative gave no melting point depression and exhibited an identical infrared spectrum with the authentic sample. (The spectrum of the crude product and the unusually great losses during the first crystallization indicated, however, that the product formed in the oxidation of the *trans*-glycol in water is less homogeneous than that obtained in the previously described cases.) In a control experiment in which 2,6-heptanedione was treated for 12 hours with perchloric acid of the same concentration and then isolated in the same way as above, only 72% of the derivative (which, however, was considerably purer) was collected. *trans*-1,2-Dimethyl-1,2-cyclopentanediol subjected to the same treatment gave no precipitate

(3) Unless otherwise stated, all melting points were carried out on a Kofler type melting apparatus (Monoscope V, H. Bock, Frankfurt A. M.).

(4) The melting points were determined by an Anschütz thermometer immersed directly into the sample.

(5) V. C. Bulgrin and G. Dahlgren, Jr., *J. Am. Chem. Soc.*, **80**, 3883 (1958).

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

(7) A. C. Cope, H. L. Dryden, Jr., C. G. Overberger and A. A. D'Addieco, *J. Am. Chem. Soc.*, **73**, 3416 (1951).

(8) C. G. Overberger, T. B. Gibb, Jr., S. Chibnik, P.-T. Huang and J. J. Monagle, *ibid.*, **74**, 3290 (1952).

(9) C. Harries, *Ber.*, **47**, 784 (1914).

after the addition of *p*-nitrophenylhydrazine and sodium acetate.

Stability of *trans*-1,2-Dimethyl-1,2-cyclopentanediol in Acidic Solution.—The *trans*-glycol (71.2 mg.) dissolved in 3 *M* perchloric acid (5 ml.) and allowed to stand for 1 hour turned a deep yellow, but after the solution was neutralized with sodium hydroxide, extracted with ethyl acetate, and the extract evaporated, the diol was recovered nearly unchanged. The residue gave an infrared spectrum (in KBr) identical with that of the authentic glycol, and melted, after one recrystallization, at 106.5–108°, forming liquid crystals typical for this compound. In a similar way, it was shown that the *trans*-glycol is stable in a 0.1 *M* sulfuric acid solution in 90% acetic acid.

Kinetic Method.—The rates were determined spectrophotometrically at 350 mμ using 1-cm. quartz cells in a thermostated block. Measurements in very dilute solution of chromic acid were carried out at room temperature in 10-cm. cells.

Results

***cis*-1,2-Dimethyl-1,2-cyclopentanediol.**—The chromic acid oxidation of the *cis*-diol proceeds extremely rapidly; the rate is the greatest so far measured for the action of chromic acid on an organic compound. The principal reaction product, 2,6-heptanedione, is formed by fission; it is practically inert under the experimental conditions used for the oxidation of the glycol. Nevertheless, when the reaction is carried out with an excess of chromic acid, about twice as much oxidant is consumed as that required by stoichiometry. The reason for this has not yet been determined, but perhaps the intermediates of Cr^{IV} and Cr^{V}, which have been postulated[10] in chromic acid oxidations, attack other sites in the starting material or product. In this respect, the oxidation differs from that of isopropyl alcohol or pinacol, perhaps because these compounds offer, besides the first site of attack, only unreactive methyl groups.[11] The extent of the side reactions probably changes with changing relative concentrations of glycol and chromic acid, and may be responsible for the drift in the rate constants (Table I) observed with a variation in the initial concentration of chromic acid. Individual runs, however, (carried out with a large excess of glycol and acid) obey first-order kinetics to three half-lives. The oxidation of the *cis* glycol is first order in the substrate and in hydrogen ion. The fourth column of Table I gives the second-order rate constants found at each acidity; these figures can be directly compared with the second-order rate constants in Table II. The third-order rate constants in the fifth column have been calculated from those in the fourth column by dividing each entry by the corresponding concentration of hydrogen ion. In 90% acetic acid rather than water, the oxidation is faster by a factor of about 300.

***trans*-1,2-Dimethyl-1,2-cyclopentanediol.**—The *trans*-glycol is oxidized, either in water or 90% acetic acid, to a mixture of products in which 2,6-heptanedione predominates. To make sure that the product is actually formed from the *trans*-glycol, and not from some decomposition product, the diol was subject to the conditions under which the oxidation was carried out, and was recovered unchanged.

(10) *Cf.* W. Watanabe and F. H. Westheimer, *J. Chem. Phys.*, **17**, 61 (1949); F. H. Westheimer, *Chem. Revs.*, **45**, 419 (1949), and Errata, June, 1950.

(11) F. Mares and J. Roček, *Coll. Czech. Chem. Commun.*, **26**, 2370 (1961).

Kinetically, the reaction, like that for the *cis*-diol, is first order in the glycol and in chromic acid; in aqueous perchloric acid, 1.0–5.0 *M*, the logarithm of the rate constant is linear in H_0, with a slope of 1.45. The rate of the oxidation in 90% acetic acid is roughly 10,000 times higher than in water with the same concentration of mineral acid. This increase in rate on change of solvent is even higher than the ratio of 2,500, found by Cohen and Westheimer[12] for the oxidation of isopropyl alcohol in water and 86.5% acetic acid.

TABLE I

RATES OF OXIDATION OF *cis*-1,2-DIMETHYL-1,2-CYCLOPENTANEDIOL

Diol, *M*	Chromic acid, *M*	Perchloric acid, *M*	*k*, l./m. min.	10^{-3} *k*, (l./m.)^2 min.$^{-1}$
	(A) In water at 30°			
0.01	0.0005	0.005	8.63	1.73
.01	.0005	.01	17.4	1.74
.01	.0005	.02	35.5	1.77
.01	.0005	.04	64.6	1.62
.00075	.0005	.10	178	1.78
.000375	.0005	.10	168	1.68
.01	.0001	.01	21.2	2.12
.01	.0002	.01	21.1	2.11
.01	.0010	.01	13.7	1.37
.005	.0005	.01	16.0	1.60
.02	.0005	.01	17.5	1.75
.04	.0005	.01	15.6	1.56
	(B) In 90% acetic acid at room temperature			
		CH_3CO_2Na, *M*		
0.00254	0.0001	0.01	3.4	
.00313	.0001	0.001	15.3	
.00341	.0001	...	138	
		H_2SO_4, *M*		
0.00125	0.00005	0.001	502	
0.000272	0.00005	0.004	1640[a]	

[a] 25.1°.

TABLE II

RATES OF OXIDATION OF *trans*-1,2-DIMETHYL-1,2-CYCLOPENTANEDIOL AT 30°

Diol, *M*	Chromic acid, *M*	Perchloric acid, *M*	*k*, l./m. min.
	(A) In water		
0.01	0.0005	3.0	3.4
.01	.001	3.0	2.8
.01	.002	3.0	2.0
.01	.004	3.0	1.8
.005	.0005	3.0	3.0
.04	.0005	3.0	3.8
.0130	.0005	0.01	10^{-3}
.01	.0005	1.0	0.11
.01	.0005	5.0	90
		Sulfuric acid, *M*	
0.0151	0.0008	2.5	1.32
.0244	.0008	2.5	1.18
.0343	.0005	3.0	2.9
	(B) In 90% acetic acid		
0.01	0.0005	0.01	9.3
.01	.001	.01	9.3
.01	.002	.01	7.7
.01	.004	.01	7.6
.01	.01	.01	8.2
.0558	.0005	.004	1.96[a]

[a] Room temperature (23.7°).

(12) M. Cohen and F. H. Westheimer, *J. Am. Chem. Soc.*, **74**, 4387 (1952).

TABLE III

SOLVENT ISOTOPE EFFECT IN THE OXIDATION OF *trans*-1,2-DIMETHYL-1,2-CYCLOPENTANEDIOL AND ISOPROPYL ALCOHOL AT 30° IN 2.5 *M* ACID SOLUTION

Alcohol, *M*	Acid	CrO_3, *M*	*k*, l./m. min.	k_{D_2O}/k_{H_2O}
Diol, 0.0151	H_2SO_4	0.0008	1.32	
Diol, .0244	H_2SO_4	.0008	1.18	2.0
Diol, .0255	D_2SO_4	.0008	2.35	
Diol, .0292	D_2SO_4	.0008	2.55	
i-PrOH, 0.0103	H_2SO_4	.0005	2.49	2.3
i-PrOH, .00529	D_2SO_4	.0005	5.78	

they are predominantly oxidized to hydroxy ketones or hydroxy aldehydes without cleavage; some fission products, however, have been obtained even in the oxidation of ethylene glycol. As the hydroxycarbonyl compounds cannot be considered as intermediates in the glycol fission the two processes—the oxidation of a single hydroxyl group and the fission of the glycol molecule to two carbonyl compounds—must be regarded as concurrent. The rates for the glycol fission reactions can therefore be computed from the over-all reaction rates (based on chromic acid consumption) and the yields of

TABLE IV

EFFECT OF STRUCTURE ON THE RELATIVE RATES OF OXIDATION OF GLYCOLS, $R^1R^2C(OH)-C(OH)R^3R^4$, WITH CHROMIC ACID AND ON THE ENTHALPIES OF OXIDATION AND OF CLEAVAGE

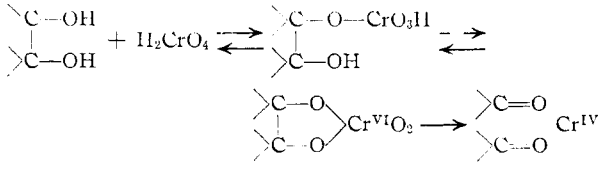
R^1	R^2	R^3	R^4	ΔH, oxidation to hydroxaldehyde or hydroxyketone[a] Klages	Franklin	ΔH, fission,[a] kcal./mole Klages	Franklin	CrO_3 fission rel. rates[b]
H	H	H	H	−51.7	−51.2	−30.9	−30.0	10^{-5}
CH_3	H	H	H	−54.4[c]	−53.9[c]	−34.2	−32.9	10^{-3}
				−51.6[d]	−51.1[d]			
CH_3	H	CH_3	H	−54.4	−53.9	−37.7	−35.7	10^{-2}
CH_3	CH_3	H	H	−51.7	−51.1	−36.0	−32.3	
CH_3	CH_3	CH_3	H	−54.4	−56.5	−39.4	−37.6	
CH_3	CH_3	CH_3	CH_3	....	....	−41.1	−40.0	1

[a] Calculated from the heats of combustion, using experimental figures for formaldehyde,[14] acetaldehyde[14] and acetone[15] and estimating the values for the rest of the compounds by Klages[16] and Franklin's[17] method using Wheland's[18] figures. The data refer to reaction of the glycols in the gas phase with elementary oxygen. [b] Estimated from rates and yields given by Chatterji and Mukherjee.[13] [c] Ketone. [d] Aldehyde.

Isotope Effects.—The solvent isotope effect, k_{D_2O}/k_{H_2O}, for the oxidation of the *trans*-glycol is 2.0; for isopropyl alcohol under the same conditions it is 2.3.

Discussion

Oxidation of *cis*-1,2-Dimethyl-1,2-cyclopentanediol.—The *cis*-glycol is oxidized 47 times as fast as its open-chain analog, pinacol, and much faster than the cyclic *trans* isomer (17,000 and 800 times faster in water and 90% acetic acid, respectively). This result is that predicted for oxidation *via* a cyclic ester as intermediate, and is therefore in agreement with the mechanism previously proposed for the oxidation of pinacol. In more detail, the mechanism can be represented as taking place by way of a cyclic ester, as



If the oxidation took place through a non-cyclic monoester of chromic acid, with assistance from the neighboring hydroxyl group, then the sharp distinction between the *cis*- and *trans*-glycols would be unexpected. To be more specific, a hydrogen-bonded structure would involve fusing a five- and seven-membered ring, and this fusion would not be strongly dependent on the stereochemistry of the ring junction.

Some information concerning the rate-controlling step may be obtained by considering the dependence of the rate of chromic acid cleavage on the structure of the glycol. When glycols containing primary or secondary hydroxyl groups react with chromic acid, fission products. Chatterji and Mukherjee[13] have measured both the total rates of oxidation of several aliphatic glycols and the percentages of cleavage which occur. From their data (and with the additional assumption that the percentage of cleavage for propylene glycol lies between those for ethylene and butylene glycols), the relative rates can be estimated for the fission of a series of glycols by chromic acid (Table IV). The rapid increase in rate with increase in alkyl substituents is paralleled by our finding that the cleavage of *cis*-1,2-dimethyl-1,2-cyclopentanediol proceeds more than 100 times as fast as the combined oxidation and cleavage of *cis*-1,2-cyclopentanediol.[19]

The dependence of rate on structure contrasts sharply with that for other reagents which cleave glycols. The rates for cleavage of diols by lead tetraacetate[20] first increase with the introduction of methyl groups, reach a maximum with *rac*-2,3-butanediol, and then decrease; the rate for pinacol is only about twice as high as that for propylene

(13) A. C. Chatterji and S. K. Mukherjee, *Z. physik. Chem.*, **208**, 281 (1958); **210**, 166 (1959).

(14) F. D. Rosini, D. D. Wagman, W. H. Evans, S. Levine and I. Jaffe, "Selected Values of Chemical Thermodynamic Properties," U. S. Government Printing Office, Washington, D. C., 1952.

(15) R. E. Pennington and K. A. Kobe, *J. Am. Chem. Soc.*, **79**, 300 (1957).

(16) F. Klages, *Chem. Ber.*, **82**, 358 (1949).

(17) J. L. Franklin, *Ind. Eng. Chem.*, **41**, 1070 (1949).

(18) G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, pp. 88 and 94.

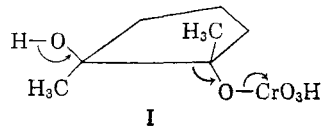
(19) The second-order rate constants (l. mole^{-1} min.$^{-1}$) for the chromic acid oxidation of four cyclic diols at 25° in 2.8 *M* sulfuric acid are: *cis*-1,2-cyclopentanediol, 208; *trans*-1,2-cyclopentanediol, 3.67; *cis*-1,2-cyclohexanediol, 104; *trans*-1,2-cyclohexanediol, 14.7. The rate constant for the oxidation of isopropyl alcohol under the same conditions is 3.47 l. mole^{-1} min.$^{-1}$; J. Krupička and J. Roček, unpublished results at the Československá akademie věd, Praha.

(20) R. Criegee, E. Hoger, G. Huber, P. Kruck, F. Martschceffel and K. Schellenberger, *Ann.*, **599**, 81 (1956).

glycol. In the cleavage of glycols with periodic acid, Bunton and co-workers[21] were able to separate the over-all rates into equilibrium and rate terms. They showed that the rate of decomposition of the cyclic intermediate increases with increasing substitution to a maximum for 2-methyl-1,2-propylene glycol, and then decreases with each additional methyl group. Furthermore, *cis*-1,2-dimethyl-1,2-cyclopentanediol reacts with periodic acid only 1/3000 as fast as does the parent compound, *cis*-1,2-cyclopentanediol.[5] Bunton[21] has shown that the rate-controlling step for the reaction with periodic acid of the more highly substituted glycols is the first step of the esterification, rather than the cleavage of cyclic esters. Since in chromic acid oxidation, the introduction of alkyl groups accelerates rather than retards the cleavage, the mechanism presumably differs from those for periodate and lead tetraacetate. A reasonable assumption ascribes the slow step to the actual cleavage, since alkyl groups could increase the rate by increasing the electron supply at the site of the oxidation. Additional support for this point of view can be obtained by comparing the reaction rates with the enthalpies for glycol fission (Table IV). Both rates and enthalpies[22] increase with increasing stability of the carbonyl product formed (*i.e.*, in the order: formaldehyde, acetaldehyde, acetone). This parallelism suggests that the structure of the transition state is quite near to that of the products, so that the rate-determining step is the decomposition of a cyclic ester, which is in rapid equilibrium with chromic acid and the glycol.

The more rapid rate of cleavage of the *cis* relative to the *trans*-glycol has been ascribed then to the formation, with the former, of a cyclic ester. Steric strain might also have been expected to accelerate the cleavage of the *cis*, relative to that of the *trans*-diol. This factor, however, if present at all, is of minor importance only. The difference between the heats of formation of *cis*- and *trans*-1,2-dimethylcyclopentanes[23] is only 1.7 kcal./mole, and the difference in energy between the two corresponding dihydroxy compounds must be even smaller, both because of methyl–hydroxyl repulsions in the *trans* isomer, and internal hydrogen bonding in the *cis*. Thus, strain energy is unlikely to be of major importance here.

Cleavage of *trans*-1,2-Dimethyl-1,2-cyclopentanediol.—The mechanism proposed for the *cis*-glycol obviously cannot obtain for the *trans*. Further, a different mechanism is indicated by the different response to change in solvent. Nevertheless, oxidation of the latter yields the same product (although of lower purity) as that from the former; the rate of oxidation of the *trans*-glycol is comparable to that for isopropyl alcohol and much greater than that for a simple tertiary alcohol; the glycol is oxidized almost instantaneously under experimental conditions where 1-methyl-1-cyclohexanol reacts only very slowly. A tentative mechanism is represented by I.



I

Alternately, a water molecule may assist in removing the proton from the hydroxyl group. The question of which step is rate controlling is left open. The solvent isotope effect is comparable to that for isopropyl alcohol under the same experimental conditions. This result could indicate either that the proton transfer from the OH group occurs after the rate-controlling step, or else that, in the complex oxidation process, the cleavage of this bond has only a minor influence on the over-all rate. The ambiguity throws some doubt on the use of the solvent isotope effect as a decisive tool for establishing mechanism in reactions where the transfer of a hydrogen atom is not the only process which occurs in the rate-controlling step.

Oxidation of Glycols which Contain α-Hydrogen Atoms.—A glycol of structure $R^1R^2C(OH)CH(OH)R^3$ can react with an oxidant either to produce an hydroxy aldehyde (or hydroxy ketone) or to cleave the central carbon–carbon bond; both processes have the same stoichiometry. Table IV shows that oxidation to the hydroxyaldehyde or ketone is energetically favored by 15 kcal./mole or more. When chromic acid oxidizes a glycol which contains an α-hydrogen atom, the energetically favored reaction predominates.[24] Chromic acid is therefore the "normal" oxidant; and the question must then be answered as to why periodic acid and lead tetraacetate and iodosobenzene diacetate fail to oxidize simple alcohols readily, or to oxidize appropriate glycols to α-hydroxycarbonyl compounds. No solution to this problem is yet available. But those oxidants (lead tetraacetate, periodic acid, iodosobenzene diacetate) where both the oxidant and its reduced product (lead diacetate, iodic acid, iodobenzene) are diamagnetic specifically cleave glycols. The effective oxidants for simple alcohols (chromic acid, permanganate) can function either as one-electron or as two-electron acceptors, and, furthermore, when they have accepted two electrons, the resulting ions are still paramagnetic. Whether this correlation is significant remains to be investigated. However, the reactions may be interpreted on the basis of a transition state which has been postulated for the chromic acid oxidation of hydrocarbons.[25] This transi-

(21) G. J. Buist and C. A. Bunton, *J. Chem. Soc.*, 1406 (1954); G. J. Buist, C. A. Bunton and J. H. Miles, *ibid.*, 4567, 4575 (1957).

(22) The enthalpies are those calculated for the oxidation of the alcohols or glycols to the carbonyl products with oxygen in the gas phase. This method ignores the heats of hydration of aldehydes and the heats of solvation, neither of which could be expected to make a major contribution to the stability of the incipient product in the transition state. We are comparing enthalpies of activation rather than free energies of activation because we believe that the entropy term included in the latter would manifest itself much more in the hypothetical reverse reaction than in the forward step.

(23) F. D. Rossini, K. S. Pitzer, R. L. Arnett, R. M. Braun and G. C. Pimantel, "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," Carnegie Press, Pittsburgh, Pa., 1953.

(24) The relative yields of different products obtained in oxidations with chromic acid must be interpreted with caution until the reactions have been carefully studied. The products obtained from oxidations with hexavalent chromium in some instances differ from those obtained by the action on the reactants of the compounds of tetravalent or pentavalent chromium produced during the reaction. See J. Hampton, A. Leo and F. H. Westheimer, *J. Am. Chem. Soc.*, **78**, 306 (1956); J. J. Cawley, Thesis, Harvard University, 1960.

(25) J. Roček, *Tetrahedron Letters*, 136 (1962).

tion state acquires its stabilization from resonance between structures each of which has two unpaired electrons: (1) a free-radical and Cr^{V}, and (2) a carbonium ion and Cr^{IV}.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY, NEW YORK 27, N. Y.]

Three-membered Rings. IV. Solvent Control for the Stereoselective Formation of Cyclopropanes Substituted at Two of the Ring Carbons

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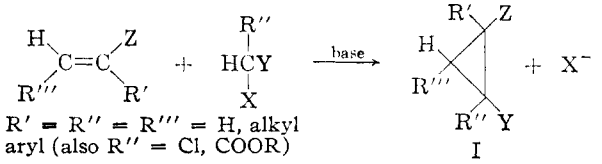
The interaction of α-substituted acrylic esters or acrylonitriles with α-halo-esters in the presence of base may be controlled by the solvent so as to allow the stereoselective formation of either *cis*- or *trans*-cyclopropane compounds. Reaction with no solvent or with hydrocarbon or ether solvents gives predominantly or exclusively the *cis* isomer; reaction in hexamethyl phosphoramide–benzene mixtures or in dimethylformamide gives predominantly the more stable isomer, usually the *trans* isomer. Ring closure of suitably substituted glutarate esters (and probably a number of related types of compounds) also is controlled by solvent in the same way.

The formation of polysubstituted cyclopropanes from α,β-unsaturated systems and α-halo-compounds in the presence of base is now well established.[1] It is also clear that under the experimental conditions normally



$R' = R'' = R''' = H$, alkyl aryl (also $R'' = Cl$, COOR)

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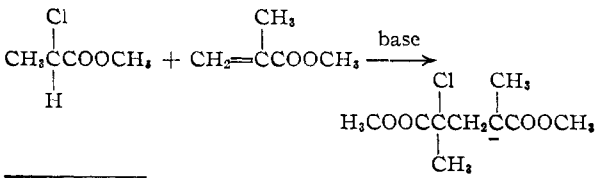
used, when $R''' = H$ the *cis* isomer (I, Y and Z *cis*) is the predominant or exclusive product.[1,b,e,g,h,j] This preference for *cis* isomer formation is to a large extent independent of the functional groups (Y,Z), substituents (R',R'') and the tempeature of the reaction.

This preference for *cis* isomers was quite surprising when first noted. Most other procedures leading to cyclopropanes from non-stereoisomeric starting materials usually produce the more stable *trans* isomers. To explain this *cis* selectivity a simple assumption was made that some sort of attractive interaction between the two functional groups is occurring at an intermediate step of the reaction. On the basis of the previous suggestion as to the general reaction path,[1a] the intermediate involved would be the anion produced by a Michael addition. Thus, as a specific example



Models of the anion suggest that in certain conformations the C–C–O of the anion can "wrap" around the carbon of the second carboxyl group. This would allow the charge of the anion to be distributed over the carbonyl of the second carboxyl group. Such charge distribution probably contributes very appreciably to stabilization of the intermediate anion in solvents of low dielectric constant, benzene, toluene, ethers and esters. Models also suggest that only slight, essentially unhindered rotation of the anionic group is necessary to result in displacement of the halogen and formation of the *cis*-cyclopropane isomer. Much greater, appreciably hindered rotation is required for a conformation leading to the *trans* isomer. Although this proposal is rather simple and presents some difficulties of interpretation, it does offer a working hypothesis: if the proposed interaction could be minimized, it should be possible to form *trans* isomers. To accomplish this, it seemed reasonable that in a medium of high dielectric constant and good solvating properties, external solvation of the anion would take place in preference to the proposed "internal solvation." With the attractive interaction removed, the transition states leading to the two possible isomers probably would have much of the character, the steric and electronic interactions, present in the products. Thus, the isomer ratios observed in the polar solvents should approach those expected on the basis of the relative stabilities of the stereoisomers. To test these ideas, a number of reactions were run in several solvents.[2] The results are summarized in Tables I and II.

It is quite obvious that solvents do have a marked effect on the isomer ratios, but usually an insignificant effect on the yields. The choice of polar solvents, dimethylformamide and hexamethylphosphoramide, was suggested by the work of Zaugg and co-workers[3]; also many of the commonly used polar solvents such as alcohols were not compatible with the reaction conditions. In the polar reaction

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(1) (a) L. L. McCoy, *J. Am. Chem. Soc.*, **80**, 6568 (1958); (b) L. L. McCoy, *J. Org. Chem.*, **25**, 2078 (1960); (c) L. L. McCoy, *J. Am. Chem. Soc.*, **82**, 6416 (1960); (d) R. Fraisse and R. Jacquier, *Bull. soc. chim. France*, 986 (1957); (e) M. Mousseron and R. Fraisse, *Compt. rend.*, **248**, 887 (1959); (f) M. Mousseron, R. Fraisse, R. Jacquier and G. Bonavent, *ibid.*, **248**, 1465 (1959); (g) M. Mousseron, R. Fraisse, R. Jacquier and G. Bonavent, *ibid.*, **248**, 2840 (1959); (h) R. Fraisse, *Bull. soc. chim. France*, 1102 (1959); (i) R. Fraisse and M. Guitard, *ibid.*, 418 (1960); (j) R. Fraisse and M. Guitard, *ibid.*, 788 (1960); (k) R. Fraisse and M. Guitard, *ibid.*, 200 (1961); (l) D. T. Warner and C. E. Morreal, *J. Am. Chem. Soc.*, **82**, 439 (1960); (m) O. Widman, *Ber.*, **51**, 533, 907 (1918).

(2) A preliminary report of this work has been published, ref. 1c.

(3) (a) H. E. Zaugg, B. W. Horrom and S. Borgwardt, *J. Am. Chem. Soc.*, **82**, 2895 (1960); (b) H. E. Zaugg, *ibid.*, **82**, 2903 (1960); (c) H. E. Zaugg, D. A. Dunningan, R. J. Michaels, L. R. Swett, T. S. Wang, A. H. Sommers and R. W. de Net, *J. Org. Chem.*, **26**, 644 (1961).