143. *The Hydroxylation of Cyclic Olefins by Iodine and Silver Acetate.*

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Hydroxylation of 1,2-dimethylcyclohexene by the Woodward procedure (iodine and silver acetate in wet acetic acid) is not stereospecific, but gives a mixture of *cis*- and *trans*-1,2-dimethylcyclohexane-1,2-diol. These compounds form a 1 : 1 molecular compound. By this method *cis*-diols were obtained from 1-methyl-cyclopentene and -cyclohexene, but not from 1,2-dimethylcyclopentene. Hydroxylation by iodine and silver acetate in dry acetic acid has also been examined.

The rates of oxidation of the cyclic diols by periodic acid and lead tetra-acetate have been measured.

Prévost converted olefins into *trans*-diols by the use of iodine and silver benzoate in dry, non-polar solvents, followed by alkaline hydrolysis. Woodward used iodine and silver acetate in wet acetic acid to convert olefins into *cis*-diols. These general methods are reviewed in ref. 1. They depend on the ability of a neighbouring carboxy-group to interact with a carbonium ion.[2] The intermediate (I) can open to give an ester of a *trans*- or a *cis*-diol. The mechanism of these reactions has been studied both stereochemically and by the use of O-18 as a tracer.[3]

For other purposes we required *cis*-1,2-dimethylcyclopentane- and -cyclohexane-1,2-diol,

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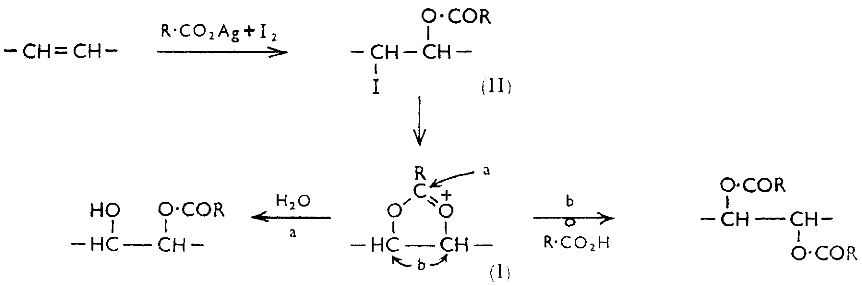
[1] Gunstone in "Advances in Organic Chemistry," ed. Raphael, Taylor, and Wynberg, Interscience Publ. Inc., New York, Vol. I, 1960, p. 117.

[2] Winstein and Buckles, *J. Amer. Chem. Soc.*, 1942, **64**, 2780, 2787; Winstein and Roberts, *ibid.*, 1953, **73**, 2297, and ref. cited therein.

[3] Wiberg and Saegebarth, *J. Amer. Chem. Soc.*, 1957, **79**, 6256.

and the Woodward procedure appeared to be a useful method for their preparation.[3] However, we found the method unsatisfactory for this purpose, although it is useful for the preparation of the less heavily substituted cyclic diols.[1,3] To assist in the analysis of the reaction products we measured the rates of glycol fission by periodic acid and lead tetra-acetate.



Results

Cyclohexenes.—The Woodward procedure, reaction between 1,2-dimethylcyclohexene and iodine and silver acetate in " wet " acetic acid (1·5% of water), gave after vacuum-distillation of the product and its recrystallisation a 1 : 1 molecular compound of the *cis*- and the *trans*-diol. Stereospecific *cis*-hydroxylation by this method had been reported previously.[3] Reaction in " dry " acetic acid gave no 1,2-diol.

We therefore studied the oxidation of 1-methylcyclohexene by the Woodward procedure and obtained the *cis*-1,2-diol. In agreement with other workers,[1,3] we also obtained the *cis*-diol from cyclohexene by the Woodward procedure and the *trans*-diol by using " dry " acetic acid.

Cyclopentenes.—The reaction between cyclopentene and iodine and silver acetate in " wet " acetic acid is reported to give the *cis*-diol in 48% yield.[3] By this method we converted 1-methylcyclopentene into the *cis*-diol in 20% yield, but obtained no diol from 1,2-dimethylcyclopentene.

Kinetics of Glycol Splitting.—We analysed the products by oxidation with periodic acid or lead tetra-acetate. Some reaction rates were in the literature, others we measured.

The second-order rate constants for the oxidation of many cyclic diols by lead tetra-acetate have been measured by Criegee and his co-workers,[4] who used acetic acid containing 0·5% of water as solvent. We include their values, interpolated to 25° where possible, for comparison in Table 1. The rate of the reaction is increased by small amounts of water.

TABLE 1.

Second-order rate constants, k_2 (l. mole^{-1} sec.$^{-1}$), for the oxidation of cyclic diols by lead tetra-acetate in acetic acid at 25°.

	Unsubst.		1-Me	1,2-Me$_2$						
	cis-	*trans*-	*cis*-	*cis*-			*trans*-			
Cyclopentane-1,2-*diols.*										
[H_2O] (%) ...	0·5	0·5	0·5	0·5				0·5		
10^3k_2	Very fast *	213 *†	Very fast	2·6 × 10^1 *†				141 *	145	
Cyclohexane-1,2-*diols.*										
[H_2O] (%) ...	0·5	0·5	0·5	0	0·5	2·0	0	0·5		2·0
10^3k_2	84 *†	3·73 *†	567	96	105 ‡	107	4·26	5·59 *	5 ‡	6·1

* Ref. 4. † At 20°. ‡ From kinetic analysis of a reaction product.

Second-order rate constants for periodate oxidation in water are given in Table 2 for several *cis*-1,2-diols. The reaction rates are compared at different pH values, but in regions where

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[4] Criegee, Höger, Huber, Krick, Marktscheffel, and Schellenberger, *Annalen*, 1956, **599**, 81; Criegee, *Angew. Chem.*, 1958, **70**, 173.

(except for *cis*-cyclohexane-1,2-diol [5]) the rate is little dependent upon pH,[6] the reactivity of *trans*-1,2-dimethylcyclohexane-1,2-diol is less than one-hundredth of that of the *cis*-diol, and *trans*-1,2-dimethylcyclopentane-1,2-diol is completely unreactive.

TABLE 2.

Second-order rate constants, k_2 (l. mole^{-1} sec.$^{-1}$), for the periodate oxidation of *cis*-1,2-diols.

Cyclopentanediols.

	Unsubst.	1-Me		1,2-Me$_2$		
Temp.	0°	0°		0°	25°	25°
pH	—	—	5·24	—	—	5·24
10^3k_2	1·77 × 10^4 *	2780 *	4200	4·8 *	10·5 *	17

Cyclohexanediols.

Temp.	0°	25°	0°		25°
pH	4·3	4·06	5·24	6·0	5·24
10^3k_2	2800 †	1·17 × 10^4 ‡	620	510	3·03

In the present work the buffers were: at pH 5·24, sodium acetate and perchloric acid, $\mu = 0{\cdot}01$ mole l.$^{-1}$; at pH 6·0, sodium dihydrogen phosphate, and sodium hydroxide, $\mu = 0{\cdot}01$ mole l.$^{-1}$.

* Unbuffered solutions at a region where the rates are insensitive to pH (ref. 6). † These values for cyclohexanediol are not directly comparable with the others because of mechanistic differences (ref. 5). ‡ Ref. 7.

DISCUSSION

Hydroxylation.—There are two requirements for *cis*-hydroxylation by the Woodward procedure in wet acetic acid: (1) The initial addition of iodine and acetic acid must be *trans* (anti-periplanar). (2) The acetylated iodohydrin (II) must be converted into the oxonium ion (I) with inversion of configuration, and this ion must be hydrolysed by attack upon the acetyl-carbon atom. The generality of *trans*-addition of, *e.g.*, halogen to a double bond has been ascribed to the existence of intermediate halogenium ions,[8] *e.g.*, (IIIa). But participation of the halogen at the carbonium ion centre adjacent to the point of initial attack will be less important when electron-releasing substituents are attached, because they can stabilise the carbonium ion structure (IIIb) and eclipsing between 1,2-substituents in the halogenium ion (IIIa) will destabilise this structure. The relative stabilities of the oxonium ion (I) and the carbonium ion (IV) will be similarly affected. The original evidence for the existence of oxonium ions in S_N1 reactions was obtained with secondary isomers.[2]

1-Methylcyclohexene is converted into the *cis*-diol by the Woodward procedure; this observation suggests that for 1,2-dimethylcyclohexene eclipsing and electron-release destabilise the bridged structures (IIIa) or (I), relative to the carbonium ions (IIIb) or (IV). The reactions for the cyclohexenes can be written as shown. The full lines represent reactions which lead to stereospecific *cis*-hydroxylation, and the broken lines represent non-stereospecific reaction paths.

The formation of *trans*-cyclohexanediols in dry acetic acid was not examined systematically, because there are other more convenient methods for their preparation. Only cyclohexene itself gave a significant yield of diol. The difficulty of forming oxonium ions (I) with the methyl-substituted olefins, or the difficulty of decomposing them, in dry acetic acid probably allows carbonium-ion rearrangements to occur more readily than substitution.

The poor yields from methylcyclopentenes may be associated with the difficulty of forming the iodonium or oxonium ions analogous to (IIIa) and (I), although *cis*-cyclopentanediols readily form ketals and borate complexes and are oxidised rapidly by periodic

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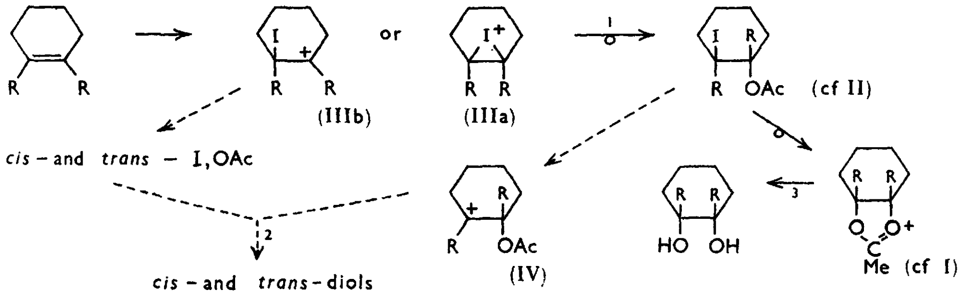
[5] Buist, Bunton, and Miles, *J.*, 1959, 743.
[6] Bulgrin and Dahlgren, *J. Amer. Chem. Soc.*, 1958, **80**, 3883.
[7] Honeyman and Shaw, *J.*, 1959, 2454.
[8] Roberts and Kimball, *J. Amer. Chem. Soc.*, 1937, **59**, 947.

acid and lead tetra-acetate by mechanisms which probably involve cyclic-ester intermediates. Winstein and his co-workers[2] have obtained evidence for oxonium ions in the acetolysis of dibromocyclopentane and related dibromides but note that a neighbouring group participates more actively in reactions of the corresponding open-chain or cyclohexane derivatives. Hydration of 1,2-dimethylcyclohexene is non-stereospecific, but *trans*-addition of halogen acids occurs although the products subsequently rearrange.[9]

Other heavily alkyl-substituted olefins are not hydroxylated by the Woodward procedure, *e.g.*, tetramethylethylene.[10]



Reagents: 1, AgOAc. 2, (i) Solvolysis, (ii) saponification. 3, (i) H_2O, (ii) saponification.

Oxidation by Periodate or Lead Tetra-acetate.—It is generally believed that oxidation of 1,2-diols by periodic acid proceeds through an intermediate cyclic ester. With lightly substituted acyclic diols this intermediate may be formed rapidly and to an appreciable extent, and break down slowly; the kinetic order is then between 1 and 2. A second-order rate law will be followed if (i) the intermediate is formed rapidly and reversibly, but in low concentration, or (ii) its formation is the rate-limiting step.[11] Some intermediate is built up during the oxidations of the cyclohexane-1,2-diols,[5] but not in those of the cyclopentane-1,2-diols.[6] Alkyl substituents should destabilise an intermediate by internal repulsions, and hinder its formation and assist its breakdown to products, and it seems that for the cyclopentane and the alkylated cyclic diols the rate of oxidation is that of formation of an intermediate. Where comparison is possible our rates of oxidation are slightly higher than those of Bulgrin and Dahlgren,[6] possibly because our solutions were buffered.

Lead tetra-acetate is a less specific reagent than periodic acid, and cleaves some 1,2-diols which are inert to periodic acid (those which do not readily form cyclic intermediates with periodic acid). The preferred mechanism of lead tetra-acetate oxidation probably involves a cyclic ester intermediate, but a second, less energetically favourable reaction path is available for tertiary diols which cannot form such an intermediate.[4,12]

Both 1,2-dimethylcyclohexanediols form a cyclic intermediate, and $k_{\text{cis}}/k_{\text{trans}} \simeq 20$ (Table 1), but *cis*-1,2-dimethylcyclopentanediol, which can form a cyclic intermediate, is *ca.* 200 times as reactive as the *trans*-isomer which cannot (cf. ref. 12).

Comparison of the reactivities of the *cis*-cyclohexanediols shows that one methyl group increases reactivity, and the second decreases it. Their inductive electron-release should assist attack of the hydroxyl groups on the lead atom, but they may sterically hinder this attack.

EXPERIMENTAL

Materials.—Cyclohexene and 1-methyl-cyclohexene and -cyclopentene were obtained by dehydration with formic acid of cyclohexanol and 1-methyl-cyclohexanol and -cyclopentanol,

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[9] Collins and Hammond, *J. Amer. Chem. Soc.*, 1960, **82**, 4323, and ref. cited therein.

[10] Gunstone and Morris, *J.*, 1957, 487.

[11] Bunton, *Ann. Reports*, 1959, **56**, 185.

[12] Criegee and Zogel, *Chem. Ber.*, 1951, **84**, 215; Angyal and Young, *J. Amer. Chem. Soc.*, 1959, **81**, 5251, 5467.

respectively. They were fractionally distilled through a helix-packed column. 1,2-Dimethylcyclohexene also was prepared by dehydration of 1,2-dimethylcyclohexanol with formic acid, which gave a cleaner product than sulphuric or phosphoric acid; after fractional distillation through a 4 ft. column packed with $\frac{1}{16}''$ Dixon gauze rings, it had b. p. 136·5°. 1,2-Dimethylcyclopentene was prepared by dehydration of 1,2-dimethylcyclopentanol with formic acid, and after fractionation through a helix-packed column had b. p. 104°. All the cycloalkenes gave single peaks when tested by gas–liquid chromatography through a Tween–Celite packed column. 1,2-Dimethylcyclopentanol was prepared from 2-methylcyclopentanone.[13]

" AnalaR " glacial acetic acid containing *ca.* 0·5% of water was used as " moist " acetic acid, and 1% of water was added to it to give " wet " acetic acid. The " dry " acetic acid was prepared by refluxing " AnalaR " material with potassium dichromate, then adding " AnalaR " acetic anhydride to remove the water, and was then fractionally distilled through a 4 ft. helix-packed column. It had b. p. 118° and m. p. 16·55° (corresponding to 99·95% acetic acid [14]).

Silver acetate was dried at 120° for 4 hr. and stored in a desiccator.

General Procedure.—Wiberg and Saegebarth's method [3] was in general followed in attempts to prepare *cis*-diols.

To a solution of olefin (0·05 mole) and dry silver acetate (0·125 mole) in stirred acetic acid (150 c.c.) powdered iodine (0·05 mole) was added during 1 hr. The iodine gradually reacted and after a further hr. the stirred mixture was heated for 3—4 hr. at 100°. The cooled solution was filtered, and the solid washed with ether. The combined liquids were concentrated to *ca.* 10 c.c. under reduced pressure at 50—60°, and added to 95% ethanol (50 c.c.). The filtered solution was then heated under reflux for 2 hr. with 40% aqueous sodium hydroxide (20 c.c.). After saponification the ethanol was evaporated and the residue extracted with chloroform. The extracts were washed with 40% aqueous sodium hydrogen sulphite and dried (Na_2SO_4). Evaporation of the chloroform gave the crude diol which was distilled in a vacuum. A similar procedure was followed for the attempted hydroxylations in " dry " acetic acid.

A summary of the methods of identification of the products follows.

Cyclohexene.—The *cis*-diol was obtained in 70% yield by the Woodward procedure; after recrystallisation from ethyl acetate at −60° it had m. p. 99° (lit.,[15] 98°). Its oxidation by periodic acid at 0° gave clean kinetics, confirming the absence of *trans*-diol. Hydroxylation in " dry " acetic acid gave the *trans*-diol in 65% yield. After recrystallisation from ethyl acetate it had m. p. 103—104° (lit.,[15] 103°). The m. p.s were depressed by addition of the other isomer.

1-*Methylcyclohexene.*—The *cis*-diol was obtained in 60% yield by the Woodward procedure. After recrystallisation from ethyl acetate it had m. p. 67° (lit.,[15] 68·5°), and gave clean kinetics on oxidation with periodic acid and lead tetra-acetate. It gave a borate complex, and a cyclic ketal with acetone, b. p. 182° (lit.,[15] 183—184°). Hydrolysis of this ketal gave pure *cis*-diol, m. p. 68·5°. Hydroxylation in " dry " acetic acid was unsuccessful.

1,2-*Dimethylcyclohexene.*—Hydroxylation *in* either " moist " or " wet " acetic acid, saponification, and vacuum-distillation, gave a mixture of the *cis*- and *trans*-diols in 50% yield. A similar yield was obtained if the initial reaction between the olefin and iodine and silver acetate was done in " dry " acetic acid, and the water then added. The product, on recrystallisation from hexane, gave a solid, m. p. 101°, whose m. p. was depressed by both the *cis*- and the *trans*-diol [Found: C, 66·6; H, 10·5; O, 22·4%; *M* (Rast), 282. Calc. for $C_{16}H_{32}O_4$: C, 66·7; H, 11·1; O, 22·2%; *M*, 288]. An identical product was obtained by crystallising a 1 : 1 mixture of the *cis*- and *trans*-diols from hexane at room temperature. The softening and clearing points (Table 3) were determined in small tubes, with stirring with a fine glass rod. The molecular compound has a maximum m. p. and gives two eutectics. Its infrared spectrum was different from those of the components and from a mechanical mixture of them. In particular the O–H stretching frequency (in Nujol or hexachlorobutadiene) was lower for the complex than for the other diols.

The composition of the reaction product before recrystallisation was obtained from its oxidation by lead tetra-acetate and periodic acid. The *trans*- is less reactive than the *cis*-diol with lead tetra-acetate (Table 1), and is almost completely unreactive towards periodic acid.

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[13] Brown and Garg, *J. Amer. Chem. Soc.*, 1961, **83**, 2951.

[14] Richmond and England, *Analyst*, 1926, **51**, 283.

[15] Raphael in " Chemistry of Carbon Compounds," ed. Rodd, Elsevier, Amsterdam, Vol. IIA, 1953, p. 163.

By using these two reagents, or by comparing curves of percentage reaction with lead tetra-acetate against time for the product with those for synthetic mixtures, we found that the crude product contained 55—65% of *cis*-diol. The relative amounts of the two diols did not appear to be very sensitive to the actual conditions of the hydroxylation.

One sample of the product was analysed kinetically by oxidation with lead tetra-acetate with $10^2[Pb(OAc)_4] = 4·14$M, and $10^3[\text{diol}] = 7·2$M. (Table 1). We analysed a plot of log [diol] against time,[16] and obtained rate constants for each diol in fair agreement with those determined directly (Table 1). This particular sample contained 57% of *cis*-diol.

TABLE 3.

Softening (approx.) and clearing points of mixtures of *cis*- and *trans*-1,2-dimethylcyclohexane-1,2-diol.

trans (%) ...	0	5·5	9·2	13·7	18·3	36·6	50	56	64	76·6	89·5	100
Clearing......	49°	42°	40°	70°	83°	97°	101°	101°	98°	95°	91°	92·5°
Softening ...		35°	—	—	38°	55°		95°	85°	82°	—	

We found no evidence for the formation of molecular compounds between either *cis*- or *trans*-1,2-dimethylcyclohexane-1,2-diol and either *cis*- or *trans*-cyclohexanediol, or between the last two compounds. However, *cis*- and *trans*-1,2,3,4-tetrahydronaphthalene-2,3-diol form a molecular compound.[17]

1-*Methylcyclopentene*.—The *cis*-diol was obtained in 20% yield by the Woodward procedure. Analysis with lead tetra-acetate and with periodic acid showed that no *trans*-diol was present. After recrystallisation from ethyl acetate the diol had m. p. 22° (lit.,[6] 23°).

Kinetics of Oxidation.—Standard methods were used for following the reaction of the diols with periodic acid and lead tetra-acetate.[4,5] Stoppered flasks were used, portions were removed at intervals and the periodic acid or lead tetra-acetate was estimated iodimetrically. The range of concentrations was: $10^3[\text{Diol}] = 1—10$M; $10^3[\text{Periodate}] = 2—7$M; $10^2[Pb(OAc)_4] = 1—5$M.

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[16] Frost and Pearson, " Kinetics and Mechanism," Wiley, New York, 1961, p. 162.

[17] Leroux, *Ann. Chim.* (*France*), 1910, **21**, 458.