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The Mechanism of the Prins Reaction. IV. Evidence against Acetoxonium Ion Intermediates[1]

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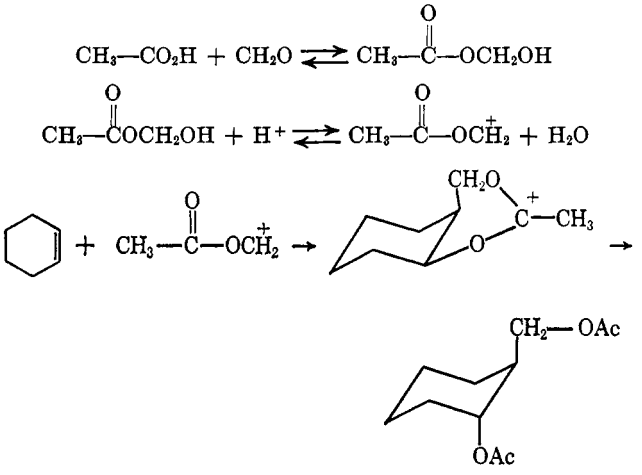
The acetolysis of *trans*-2-acetoxymethylcyclohexyl brosylate gives predominantly *cis*-2-acetoxymethylcyclohexyl acetate in the presence of added acetate ion or added strong acid. Acetolysis of *trans*-2-acetoxymethylcyclohexyl brosylate-carbonyl-O^{18} yields *cis*-diacetate containing nearly all of the O^{18}. Saponification of the labeled diacetate yields *cis*-2-hydroxymethylcyclohexanol containing about 80% of the label indicating that the six-membered acetoxonium ion is an important intermediate. Kinetic studies show that *cis*- and *trans*-2-acetoxymethylcyclohexyl brosylate solvolyze at nearly the same rate, although product studies indicate no acetoxonium ion formation with the *cis* isomer. We conclude that the acetolysis of *trans*-2-acetoxymethylcyclohexyl brosylate proceeds in part by a "normal" solvolytic pathway. The fact that the acetoxonium ion yields mainly *cis*-2-acetoxymethylcyclohexyl acetate whereas the Prins reaction of cyclohexene in acetic acid affords the *trans* isomer argues strongly against acetoxonium ion intermediates in the Prins reaction.

In a previous report we suggested that the Prins reaction in acetic acid might involve intermediate acetoxonium ions.[3] It is the purpose of the present



study to determine if this mechanism is an important pathway for the Prins reaction in acetic acid. Solvolysis studies clearly indicated the reality of such six-membered cyclic acetoxonium ions and we wish to present the results of further studies on the formation and reactions of these ions. Our previous studies of the products from the acetolysis of *trans*-2-acetoxymethylcyclohexyl brosylate led us to the erroneous conclusion that added strong acid influenced the kinetic distribution of products. It is now clear that the diacetate of *cis*-2-hydroxymethylcyclohexanol is destroyed by *p*-bromobenzenesulfonic acid in acetic acid under the solvolysis conditions used in our previous studies and the product distributions we reported did not measure the kinetic distributions of *cis*- and *trans*-2-hydroxymethylcyclohexanol derivatives. Previous control experiments on the stability of the products to strong acid in acetic acid employed *p*-toluenesulfonic acid which we find to be much less effective than *p*-bromobenzenesulfonic acid in catalyzing the destruction of the solvolysis products.

The products from the acetolysis of *trans*-2-acetoxycyclohexyl brosylate are summarized in Table I. The reactions were carried out for 4–10 half-lives and the products were stable to these conditions.

TABLE I

PRODUCTS OF ACETOLYSIS OF *trans*-2-ACETOXYMETHYLCYCLOHEXYL BROSYLATE

Solvent[a]	Olefin,[b] %	2-Acetoxymethylcyclohexyl acetate, % *cis*	*trans*
HOAc–1.2 *M* KOAc	20	80	...
HOAc	29	62	9
HOAc–3% H_2O	22	78	...

[a] All solvolyses were carried out at 100°. [b] The olefin was 3-acetoxymethylcyclohexene contaminated with *ca.* 5% of 1-acetoxymethylcyclohexene.

Other investigators[4] have reported that the acetolysis of *trans*-2-acetoxymethylcyclohexyl tosylate in the presence of potassium acetate gives a mixture of the

(1) Supported by the Petroleum Research Fund of the American Chemical Society, Grant No. 915-A 4.

(2) Alfred P. Sloan Research Fellow.

(3) L. J. Dolby, C. N. Lieske, D. R. Rosencrantz, and M. J. Schwarz, *J. Am. Chem. Soc.*, **85**, 47 (1963).

(4) Ö. Kovács, G. Schneider, and L. Láng, *Proc. Chem. Soc.*, **374** (1963).

TABLE II

RATES OF SOLVOLYSIS OF THE 2-ACETOXYMETHYLCYCLOHEXYL BROSYLATES

Isomer	KOAc ($\times 10^2$ *M*)	ROBs ($\times 10^2$ *M*)[a]	Temp., °K.	$k_1 \times 10^4$, sec.$^{-1}$	ΔH^*, kcal./mole	ΔS^*, e.u.
trans	...	1.047	351.90	0.81 ± 0.04	26.7 ± 0.7	-1.6 ± 1.8
	...	1.047	367.51	4.64 ± 0.18		
	...	1.047	382.51	19.8 ± 1.2		
	...	1.047	382.55	18.2 ± 1.0		
	1.969	0.9182	351.90	0.57 ± 0.01	26.2 ± 0.3	-3.7 ± 0.8
	1.969	0.9182	351.92	0.59 ± 0.06		
	1.969	0.9182	367.46	3.02 ± 0.03		
	1.969	0.9182	367.51	3.34 ± 0.04		
	1.969	0.9182	382.51	12.8 ± 0.4		
	1.969	0.9182	382.55	12.8 ± 0.4		
cis	...	0.8115	351.90	1.13 ± 0.02	24.9 ± 1.2	-6.4 ± 3.3
	...	0.8115	351.92	0.95 ± 0.02		
	...	0.8115	367.51	4.34 ± 0.27		
	...	0.8115	382.51	17.4 ± 0.8		
	...	0.8115	382.55	22.0 ± 1.0		
	2.941	1.200	351.90	0.79 ± 0.02	26.7 ± 0.1	-1.6 ± 0.2
	2.941	1.200	351.92	0.80 ± 0.01		
	2.941	1.200	367.51	4.22 ± 0.08		
	2.941	1.200	382.51	18.6 ± 1.1		
	2.941	1.200	382.55	18.5 ± 1.3		

[a] 2-Acetoxymethylcyclohexyl brosylate, substrate (initial concentration).

cis- and *trans*-2-acetoxymethylcyclohexyl acetates, but we find that none of the *trans*-diacetate is formed from *trans*-2-acetoxymethylcyclohexyl brosylate using high concentrations of potassium acetate. Since the *cis*-diacetate is the major substitution product under all of the acetolysis conditions, whereas the Prins reaction yields the *trans* isomer, it is doubtful that acetoxonium ion intermediates are involved in the Prins reaction of cyclohexene. Although the evidence presented previously strongly indicated the intervention of the acetoxonium ion in the acetolysis of *trans*-2-acetoxymethylcyclohexyl acetate, the fact that the major product is the *cis*-diacetate, which could also arise by simple displacement with inversion, made it desirable to examine the acetolysis in more detail.

In an effort to determine the importance of internal assistance by neighboring acetate in the transition state, we examined the rate of acetolysis of both *cis*- and *trans*-2-acetoxymethylcyclohexyl brosylate. The rate data are presented in Table II.

The observation that both *cis*- and *trans*-2-acetoxymethylcyclohexyl brosylate solvolyze at very nearly the same rate is not easy to interpret. If both brosylates solvolyze normally, the *cis* isomer might be expected to be much faster than the *trans* isomer. For example, *cis*-2-methylcyclohexyl tosylate solvolyzes faster than the *trans* isomer in methanol at 50° by a factor of 90[5] and neomenthyl tosylate undergoes acetolysis faster than menthyl tosylate by a factor of 85 at 50°.[6] Although the conformation with an axial tosylate group must be a major one for *cis*-2-methylcyclohexyl tosylate and neomenthyl tosylate is an axial tosylate, the rate differences between these *cis*- and *trans*-2-alkylcyclohexyl tosylates is much larger than might be expected. Axial cyclohexyl arenesulfonates, which are not substituted in the 2-position, solvolyze two to four times as fast as their equatorial epimers in the absence of neighboring-group effects.[7] Although the reasons for the unusual reactivity of *cis*-2-alkylcyclohexyl tosylates are not clear, it is reasonable to believe that *cis*-2-acetoxymethylcyclohexyl brosylate should solvolyze faster than the *trans* isomer except for internal assistance by neighboring acetate in the *trans* isomer. Kovács and co-workers report that *cis*-2-acetoxycyclohexylcarbinyl tosylate solvolyzes faster than the *trans* isomer by a factor of 100 in acetic acid at 100°.[4] Rate enhancement is quite clear in this case and both *cis*-2-acetoxycyclohexylcarbinyl tosylate and *trans*-2-acetoxymethylcyclohexyl brosylate afford the same six-membered acetoxonium ion. It is worth noting that the primary tosylate, *cis*-2-acetoxycyclohexylcarbinyl tosylate, is reported to solvolyze faster than the secondary tosylate, *trans*-2-acetoxymethylcyclohexyl tosylate, by a factor of 15.[4] The ethanolysis of this pair of tosylates affords the same ortho ester derived from the acetoxonium ion, but the primary tosylate gives a much higher yield (71%) of ortho ester[4] than is obtained from the secondary tosylate (22.5%)[4] or the secondary brosylate (19%).[3]

The products from the solvolysis of *cis*-2-acetoxymethylcyclohexyl brosylate in acetic acid containing potassium acetate at 100° are shown in Table III.

TABLE III

PRODUCTS OF ACETOLYSIS OF *cis*-2-ACETOXYMETHYLCYCLOHEXYL BROSYLATE

	%
1-Acetoxymethylcyclohexene	70
3-Acetoxymethylcyclohexene	18
trans-2-Acetoxymethylcyclohexyl acetate	6
1-Acetoxymethylcyclohexyl acetate	6

The products were identified from their retention times on vapor phase chromatography and by comparison of the infrared spectra of collected samples with those of authentic samples. The products were not

(5) W. Hückel, R. Bross, O. Fechtig, H. Feltkamp, S. Geiger, M. Hanach, M. Heinzel, A. Hubele, J. Kurz, M. Maier, D. Maucher, G. Näher, R. Neidlein, and R. Rashingkar, *Ann.*, **624**, 204 (1959).

(6) H. L. Goering and R. Reeves, *J. Am. Chem. Soc.*, **78**, 4932 (1956).

(7) S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955); (b) S. Winstein, E. Grunwald and L. Ingraham, *ibid.*, **70**, 821 (1948).

stable under the reaction conditions in the absence of added potassium acetate. The product distribution strongly suggests that there is no acetoxonium ion intermediate in this case. The yield of elimination products is 80% in contrast to the 20% of elimination with *trans*-2-acetoxymethylcyclohexyl brosylate. Moreover, the substitution products show rearrangement which is not characteristic of acetoxonium ions. Hence we conclude that assistance by neighboring acetate does not take place in the acetolysis of *cis*-2-acetoxymethylcyclohexyl brosylate.

The acetolysis of *trans*-2-acetoxymethylcyclohexyl brosylate labeled at the carbonyl group with O^{18} has been examined in an effort to clarify the details of the acetoxonium ion formation and subsequent reaction in this system. The required labeled brosylate was prepared by acetylating *trans*-2-hydroxymethylcyclohexyl brosylate with acetyl-O^{18} chloride. The labeled brosylate was solvolyzed in acetic acid with and without added acetate ion, and the diacetates were isolated by vapor phase chromatography and analyzed for O^{18} content. Acetolysis in acetic acid without added acetate ion afforded a mixture of *cis*- and *trans*-2-acetoxymethylcyclohexyl acetate which could not be separated in adequate amounts for isolation, but the mixture was analyzed for excess O^{18}. Solvolysis in the presence of added acetate ion afforded only the *cis*-diacetate which yielded only *cis*-2-hydroxymethylcyclohexanol upon saponification. The *cis*-2-hydroxymethylcyclohexanol obtained from the acetolysis in the presence of added acetate ion was purified by vapor phase chromatography and analyzed directly, but the acetate mixture from acetolysis in the absence of added potassium acetate afforded a mixture of *cis*- and *trans*-2-hydroxymethylcyclohexanol which we could not separate chromatographically. Separation was achieved by converting the diol mixture to the corresponding acetonides which could easily be separated by vapor phase chromatography, and the acetonides were then analyzed for excess O^{18}. Samples used for O^{18} analyses gave satisfactory analytical data for carbon, hydrogen, and oxygen. The results of these tracer studies are summarized in Table IV.

TABLE IV

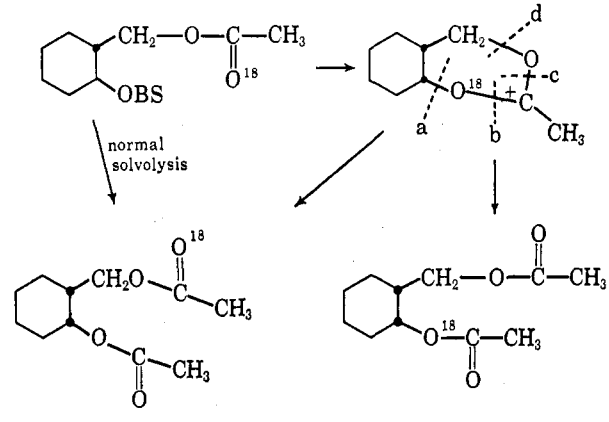
LABELED PRODUCTS FROM THE ACETOLYSIS OF *trans*-2-ACETOXYMETHYLCYCLOHEXYL BROSYLATE-CARBONYL-O^{18}

Solvent	Products	% of excess O^{18} in *trans*-2-acetoxymethylcyclohexyl brosylate
HOAc–KOAc	*cis*-2-Acetoxymethylcyclohexyl acetate	95
	cis-2-Hydroxymethylcyclohexanol	76
Dry HOAc	*cis*- and *trans*-2-acetoxymethylcyclohexyl acetates (85:15)	94
	Acetonide of *cis*-diol	82
	Acetonide of *trans*-diol	3

The two samples of labeled brosylate contained about 2.5% excess O^{18} in the carbonyl oxygen. The O^{18} analyses of the product acetates indicate that very little if any of the label is lost prior to acetolysis. The data recorded for the acetolysis in acetic acid containing potassium acetate is for a single experiment in which the solvolysis was carried out for 2 hr. at 100° (*ca.* 4 half-lives). To examine the possible loss of O^{18} from the products under these conditions a second acetolysis was continued for 14 hr. The *cis*-diacetate from this experiment contained 84% of the original excess O^{18} and the *cis*-2-hydroxymethylcyclohexanol obtained by saponification of this diacetate contained 72% of the original label. These results indicate that the loss of alkyl O^{18} after the substitution reaction is negligible.

The O^{18} incorporation into the *cis*-diol product under both solvolysis conditions indicates that about 80% of this product is certainly formed from the six-membered acetoxonium ion. At least two possibilities may be considered for the formation of the *cis*-diacetate labeled only at the carbonyl oxygen. The carbonyl-labeled *cis*-diacetate may be formed by normal solvolytic displacement with inversion or it could arise from a displacement with retention of configuration at the secondary carbon of the acetoxonium ion. The possible paths leading to carbonyl and alkyl oxygen-18 *cis*-diacetate are summarized in Scheme I.

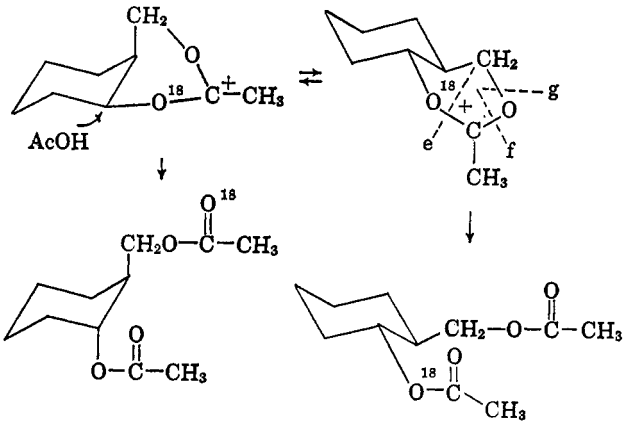
SCHEME I



Fission of bond a and substitution with retention of configuration would give rise to carbonyl-labeled *cis*-diacetate, whereas fission of bonds b, c, or d would give alkyl oxygen-labeled *cis*-diacetate. The available kinetic and tracer studies do not allow a clear choice between the two paths for the formation of carbonyl-labeled *cis*-diacetate. Although it is attractive to propose that the alkyl oxygen-labeled *cis*-diacetate is formed mainly by a displacement on the primary carbon of the acetoxonium ion, the data do not exclude other possibilities.

It is interesting to note that the *trans*-diol product resulting from acetolysis in the absence of added acetate ion also contains a small amount of O^{18}. Duplicate O^{18} analyses from two experiments gave values ranging from 1.9 to 3.6% for the fraction of isotopic oxygen incorporated into the *trans*-diol. The O^{18} analyses were performed on the *trans*-acetonide in this case. That the excess O^{18} was not the result of contamination by the *cis*-acetonide was shown by vapor phase chromatography of the samples used for analysis. It was previously suggested that the *trans*-diacetate might arise from the acetoxonium ion by displacement with inversion at the secondary carbon or by isomerization

SCHEME II



to the *trans*-acetoxonium ion followed by cleavage of bonds e, f, or g[3] (see Scheme II).

The intervention of the *trans*-acetoxonium ion could account for formation of labeled *trans*-diol, but in any case the path resulting in labeled *trans*-diol is a very minor one.

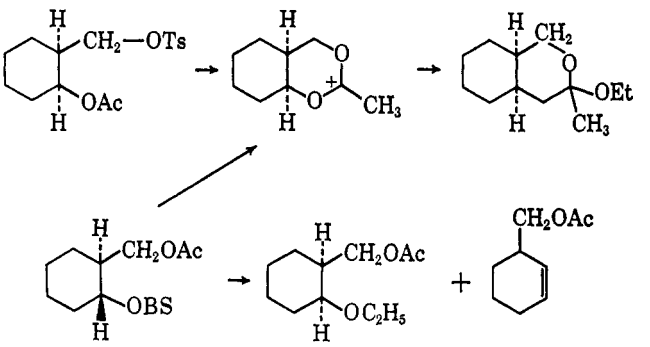
The remaining uncertainties regarding the formation and reactions of the six-membered acetoxonium ion from the solvolysis of *trans*-2-acetoxymethylcyclohexyl brosylate center on the mode of formation of the *cis*-diacetate. One possibility is that the internally assisted pathway is only about four times faster than the normal solvolytic process. This is consistent with the extent of O^{18} labeling in the *cis*-diol product, and the kinetic studies do not give a quantitative estimate of rate enhancement.

Although the evidence is not completely decisive, we conclude that the solvolysis proceeds in part by a "normal" solvolytic pathway. This hypothesis easily accounts for the low fraction of O^{18} in the *cis*-diol. It might also be expected that the normal solvolytic displacement would be more important in high concentrations of acetate ion and this appears to be the case since the *cis*-diol obtained from acetolysis in the presence of acetate ion contained slightly less O^{18} than *cis*-diol from acetolysis in pure acetic acid. Another observation which indicates that two mechanisms are operating is that the ethanolysis of *trans*-2-acetoxymethylcyclohexyl tosylate or brosylate affords the ortho ester in only 20% yields, and the major products are the expected olefin and the ether resulting from normal displacement with inversion.[3] This result cannot be ascribed to poor trapping of the acetoxonium ion by ethanol because ethanolysis of *cis*-2-acetoxycyclohexylcarbinyl tosylate yields the same ortho ester in 70% yield.[4] It must be concluded that acetoxonium ion formation accounts for not more than 30% of the ethanolysis reaction. (See Scheme III.)

Since acetic acid is less nucleophilic than ethanol, it is expected that the internally assisted pathway would be more important in acetic acid than in ethanol. This appears to be the case since the ratio of the assisted rate to normal ethanolysis is *ca.* 1:3 and the corresponding rate ratio in acetic acid would be 2:1 or 3:2 depending on the extent of olefin formation from the acetoxonium ion.

It is worthwhile to compare briefly the results and conclusions of the present study with those of earlier investigations of acetoxonium ion intermediates. It

SCHEME III



appears that the driving force for formation of six-membered acetoxonium ion intermediates is much less than that for the five-membered cyclic acetoxonium ions. *trans*-2-Acetoxycyclohexyl tosylate solvolyzes nearly 700 times as fast as the *cis* isomer,[8,9] whereas *cis*- and *trans*-2-acetoxymethylcyclohexyl brosylates solvolyze at about the same rate. In both cases the *cis* isomer gives inversion of configuration[9] and there is no evidence for participation by neighboring acetate. We conclude that the ethanolysis of *trans*-2-acetoxymethylcyclohexyl brosylate proceeds by two paths, since only 20% of the ortho ester is obtained and the rest of the material is the normal ethanolysis products. In contrast, the ethanolysis of *trans*-2-acetoxycyclohexyl tosylate affords only the ortho ester and its hydrolysis products.[10,11] Finally, it appears that the acetolysis of *trans*-2-acetoxymethylcyclohexyl brosylate also proceeds by two pathways. The foregoing hypothesis is consistent with the results of the oxygen-18 studies which are substantially different from the results of a similar study of five-membered cyclic acetoxonium ions in the reaction of silver benzoate with *erythro*-1-benzoyloxy-2-bromo-1,2-diphenylethane.[12]

Experimental Section[13]

trans-2-Acetoxymethylcyclohexyl Brosylate.—To a stirred solution of 20.0 g. of *trans*-2-hydroxymethylcyclohexanol in dry pyridine (100 ml.) at 0° was added dropwise 13.3 g. of acetyl chloride. Stirring was continued for 4 hr. at room temperature; then the reaction mixture was cooled in an ice bath and *p*-bromobenzenesulfonyl chloride (45 g.) was added. The reaction mixture was stirred for 20 hr. at room temperature and then it was diluted with ice–water and acidified with phosphoric acid. The resulting mixture was extracted with chloroform and the chloroform extracts were washed with 10% phosphoric acid, sodium carbonate solution, and water. Evaporation of the

(8) S. Winstein, C. Hanson, and E. Grunwald, *J. Am. Chem. Soc.*, **70**, 812 (1948).

(9) S. Winstein, R. Grunwald, R. E. Buckles, and C. Hanson, *ibid.*, **70**, 816 (1948).

(10) S. Winstein, H. Hess, and R. Buckles, *ibid.*, **64**, 2796 (1942).

(11) S. Winstein and R. Buckles, *ibid.*, **65**, 613 (1943).

(12) K. B. Wiberg and K. Saegebarth, *ibid.*, **79**, 6256 (1957).

(13) All melting points and boiling points are uncorrected; distillations were carried out, unless otherwise stated, using a 70-cm. modified Podbielniak tantalum-spiral column. Microanalyses are by Berkeley Analytical Laboratories, Berkeley, Calif., Pascher and Pascher Microanalytical Laboratory, Bonn, Germany, and Josef Nemeth, Urbana, Ill. Infrared spectra were determined, in carbon disulfide solution, with a Beckman IR-7 infrared spectrophotometer. Proton magnetic resonance spectra were determined in carbon tetrachloride solution with tetramethylsilane as internal standard with a Varian A-60 spectrometer. Gas chromatographic analyses employed an Aerograph Model A-90-P gas chromatograph with helium as the carrier gas. It is assumed that the area under the effluent peaks is directly proportional to the mole fraction of the component eluted. The acetic acid used in these studies was first refluxed with potassium permanganate (10% by weight), then distilled onto triacetyl borate (30% by weight), and then refluxed for 24 hr. and distilled.

chloroform afforded the crude acetate brosylate (28 g.) which was crystallized from chloroform–petroleum ether (b.p. 30–60°) to yield 25 g. (42%) of *trans*-2-acetoxymethylcyclohexyl brosylate, m.p. 91–92° (lit.[3] m.p. 91.5–93°).

***trans*-2-Hydroxymethylcyclohexyl brosylate** was prepared as described previously.[3]

Acetic Acid-O^{18}.—To 10 ml. of water-O^{18} (5.88 atom % excess) in a distilling flask with a side arm was added dropwise acetyl chloride (40 ml.), with cooling. Distillation of the residue afforded 28.5 g. of acetic acid-O^{18} boiling at 114–115°.

Acetyl Chloride-O^{18}.—To cooled acetic acid-O^{18} (12.0 g.) was added dropwise 6.5 g. of phosphorus trichloride. The mixture was heated at 45° for 1 hr., and the residue was distilled through a short column to give acetyl chloride-O^{18} (9.0 g., 57%), b.p. 50–51°, which was used directly in the next step.

***trans*-2-Acetoxymethylcyclohexyl Brosylate-carbonyl-O^{18}.**—To a stirred solution of *trans*-2-hydroxymethylcyclohexyl brosylate (10 g.) in 50 ml. of chloroform was added dropwise acetyl chloride-O^{18} (2.5 g.) and stirring was continued overnight. Evaporation of the chloroform afforded the labeled acetate brosylate (9.0 g., 80%), m.p. 92–93° after crystallization from ether–petroleum ether. Duplicate isotopic oxygen analyses indicated 2.87 and 2.80% excess oxygen-18, calculated as one labeled oxygen. Analyses of a second preparation showed 2.66 and 2.67% excess oxygen-18. The O^{18} analyses were carried out as described by Doering and Dorfman and modified by Denney and Greenbaum.[14]

Anal. Calcd. for $C_{15}H_{19}BrO_5S$: C, 46.04; H, 4.89; O, 20.46. Found for run 1: C, 46.21; H, 4.99; O, 20.64. Found for run 2: C, 46.56; H, 4.91.

***cis*-2-Acetoxymethylcyclohexyl brosylate** was prepared as described for *trans*-2-acetoxymethylcyclohexyl brosylate. From 10.5 g. of *cis*-2-hydroxymethylcyclohexanol there was obtained 9.0 g. (28%) of the acetate brosylate. The analytical sample melted at 98–99° after several crystallizations from methylene chloride–hexane.

Anal. Calcd. for $C_{15}H_{19}BrO_5S$: C, 46.04; H, 4.89; S, 8.20. Found: C, 46.07; H, 5.06; S, 0.08.

1-Hydroxycyclohexylcarboxylic acid was prepared by the method of Bucherer.[15] It was obtained as colorless plates melting at 106–107° (lit.[15] m.p. 106–107°).

1-Hydroxymethylcyclohexanol was prepared from 1-hydroxycyclohexylcarboxylic acid by lithium aluminum hydride reduction. It was obtained in 67% yield and melted at 75–76° (lit.[16] m.p. 75–75.5°).

1-Acetoxymethylcyclohexyl acetate was obtained by the method of Nazarov and Kuznetzov[17] from 1-hydroxymethylcyclohexanol. It was purified by vapor phase chromatography on a didecyl phthalate column. The analytical sample had $n^{25}D$ 1.4525 (lit.[17] $n^{20}D$ 1.4538).

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.83, 61.95; H, 8.42, 8.53.

Acetonides of *cis*- and *trans*-2-Hydroxymethylcyclohexanols.—The respective 1,3-diols were treated with 2 equiv. of 2,2-dimethoxypropane, an excess of acetone, and a trace of *p*-toluenesulfonic acid and allowed to stand at room temperature for 48 hr. These were isolated by quenching in sodium carbonate solution and extracting with ether. The residues were purified by vapor phase chromatography on 5 ft. × 0.25 in. 15% didecyl phthalate column at 150° and gas flow of 50 cc./min. The *cis* isomer, $n^{25}D$ 1.4566, had a retention time of 13.5 min. and the *trans* isomer, $n^{25}D$ 1.4588 (lit.[18] $n^{25}D$ 1.4602), had a retention time of 15.5 min.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.65; O, 18.79. Found for the *cis*-acetonide: C, 70.49; H, 10.57; O, 18.54. Found for the *trans*-acetonide: C, 70.31; H, 10.56; O, 18.69.

Reaction of *cis*-2-Acetoxymethylcyclohexyl Acetate with Acetic Acid–*p*-Toluenesulfonic Acid.—*cis*-2-Acetoxymethylcyclohexyl acetate (0.1055 g.) and anhydrous acetic acid (5 ml.) 0.089 *M* in *p*-toluenesulfonic acid were heated at reflux for 24 hr. This was worked up as usual and analysis of the residue by gas chromatography on the Carbowax column (*vide infra*) indicated 9% olefinic acetate, 89% *cis*-2-acetoxylmethylcyclohexyl acetate, and 2% decomposition products. Collection of effluent peaks from multiple injections afforded 0.0487 g. of the diacetate. A control reaction was carried out with 0.0992 g. of the diacetate except that this was not heated at reflux but rather just worked up after solution in the acetic acid mixture. The yield of diacetate obtained was 0.0578 g. In each case pure *cis*-2-acetoxymethylcyclohexyl acetate was recovered as determined from its infrared spectrum.

Reaction of *cis*-2-Acetoxymethylcyclohexyl Acetate in Acetic Acid–*p*-Bromobenzenesulfonic Acid.—*cis*-2-Acetoxymethylcyclohexyl acetate (0.119 g.) and 5 ml. of anhydrous acetic acid 0.065 *M* in *p*-bromobenzenesulfonic acid were heated at reflux for 24 hr. The reaction mixture contained 9% olefinic acetate, 64% diacetate, and 27% decomposition products. *cis*-2-Acetoxymethylcyclohexyl acetate (0.023 g.) was obtained by collection of multiple injections. A similar reaction starting with 0.118 g. of diacetate, but not including the 24-hr. reflux period, yielded after work-up 0.0755 g. of the diacetate.

Control Reaction. *cis*-2-Acetoxymethylcyclohexyl Acetate in the Prins Reaction.—Glacial acetic acid (11.5 ml.), paraformaldehyde (3.0 g.), and 0.1 ml. of concentrated sulfuric acid were stirred and heated at 50° for 15 min. To this was then added 0.34 g. of *cis*-2-acetoxymethylcyclohexyl acetate and this was heated at 50° for 30 min. and then at 70° for 2 hr. This was worked up in the usual manner and the residue was analyzed on the Carbowax column. The trace showed the presence of unsaturated acetate, unidentified decomposition products observed in the solvolyses, and *cis*-2-acetoxymethylcyclohexyl acetate as determined from its retention time and its infrared spectrum.

Acetolysis of *trans*-2-Acetoxymethylcyclohexyl Brosylate in Acetic Acid with Added Acid.—*trans*-2-Acetoxymethylcyclohexyl brosylate (0.216 g.) was treated with 3 ml. of a 0.0887 *M* *p*-toluenesulfonic acid in anhydrous acetic acid and heated at 100° for 2 hr. This was worked up in the usual manner and the diacetate fraction was analyzed utilizing comparison of the infrared spectra with those of known mixtures. It contained 88% *cis*-2-acetoxymethylcyclohexyl acetate and 12% of the *trans* isomer. A similar experiment containing 0.232 g. of the acetate brosylate was treated with 3 ml. of the same acetic acid solution and heated at reflux for 40 min. The analysis of the diacetate fraction indicated 82% *cis*-2-acetoxymethylcyclohexyl acetate and 18% of the *trans* isomer.

Solvolysis of *trans*-2-Acetoxymethylcyclohexyl Brosylate in Acetic Acid with Added Water.—The results of the solvolysis under four different conditions of *trans*-2-acetoxymethylcyclohexyl brosylate are presented in Table V. The yield of reaction products was determined by vapor phase chromatography and the per cent composition of the diacetate fractions was obtained by comparison with infrared spectrum of known mixtures. These analyses are accurate to ±2%. The indicated mixtures were heated at 100° for 2 hr. and worked up in the usual fashion.

TABLE V

ACETOLYSIS OF *trans*-2-ACETOXYMETHYLCYCLOHEXYL BROSYLATE

Substrate, g.	HOAc, g.	H_2O, g.	Olefin	% CH_2OAc, OAc	% CH_2OAc, OAc
0.301	4.73	...	29	62	9
0.293	4.45	0.13	22	78	..
0.342	4.41	0.25	23	77	...
0.296	4.65	0.48	24	76	...

Acetolysis of *trans*-2-Acetoxymethylcyclohexyl Brosylate in Acetic Acid with Added Acetate Ion.—A solution of 18 ml. of anhydrous acetic acid, 0.9 ml. of acetic anhydride, 1.8 g. of dry potassium acetate, and 3.0 g. of *trans*-2-acetoxymethylcyclohexyl brosylate was heated at 100° for 12 hr. The diacetate fraction was separated by preparative vapor phase chromatography on Carbowax 20 M. Analytical vapor phase chromatography of the diacetate fraction indicated it to be pure *cis*-2-acetoxymethylcyclohexyl acetate. This analysis was performed on a Perkin-Elmer 800 gas chromatograph utilizing a 1/16 in. × 150 ft. diethylene glycol succinate column at a temperature of 135° and nitrogen flow rate of 10 cc./min. This column effected

(14) W. von E. Doering and E. Dorfman, *J. Am. Chem. Soc.*, **75**, 5595 (1953); D. B. Denney and M. A. Greenbaum, *ibid.*, **79**, 979 (1957).

(15) H. Bucherer, *Ber.*, **27**, 1230 (1894).

(16) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 181 (1939).

(17) I. N. Nazarov and N. V. Kuznetzov, *Zh. Obshch. Khim.*, **29**, 767 (1959).

(18) E. E. Smissman and R. A. Mode, *J. Am. Chem. Soc.*, **79**, 3447 (1957).

separation of *cis*- and *trans*-2-acetoxymethylcyclohexyl acetate with retention times of 23 and 25 min., respectively.

Acetolysis of *cis*-2-Acetoxymethylcyclohexyl Brosylate in Anhydrous Acetic Acid.—*cis*-2-Acetoxymethylcyclohexyl brosylate (0.62 g.) was placed in a 25-ml. round-bottom flask and dried *in vacuo* over phosphorus pentoxide for 48 hr. Anhydrous acetic acid (10 ml.) was distilled onto the brosylate and the mixture was heated at 100° for 2 hr. The reaction was worked up in the usual manner. The reaction products were analyzed by vapor phase chromatography over a 3.5 ft. × 0.25 in. 20% Carbowax 20 M on 60–80-mesh firebrick column at 170° and gas flow of 50 cc./min. The trace showed nine peaks. The two main effluent peaks were collected from multiple injections, one at 3 min. and the other at 9 min. The peak at 9 min. was identified as *trans*-2-acetoxymethylcyclohexyl acetate by comparison of its retention time and infrared spectrum with that of an authentic sample. The earlier peak was subjected to analysis on a 5 ft. × 0.25 in. 15% didecyl phthalate on 60–80-mesh firebrick column at 150° and 50-cc./min. gas flow. Two compounds were obtained: the first eluted, 12 min., was shown to be 3-acetoxymethylcyclohexene and the latter peak, 13.5 min., was shown to be 1-acetoxymethylcyclohexene. These were identified from their retention times and infrared spectra. Yields in the acetolysis were 8% *trans*-2-acetoxymethylcyclohexyl acetate, 40% 3-acetoxymethylcyclohexene, 22% 1-acetoxymethylcyclohexene, and 30% unidentified products.

Acetolysis of *cis*-2-Acetoxymethylcyclohexyl Brosylate in Anhydrous Acetic Acid with Added Acetate Ion.—*cis*-2-Acetoxymethylcyclohexyl brosylate (0.47 g.) and 1.08 g. of potassium acetate were placed in a 10-ml. flask and dried under vacuum over phosphorus pentoxide for 48 hr. Anhydrous acetic acid (7.0 ml.) was distilled onto the brosylate and the resulting solution was heated at 100° for 2 hr. The reaction mixture was processed in the usual manner and the products were examined by vapor phase chromatography on the Carbowax column. Three peaks were observed: the earliest, 3 min., was a mixture of 3-acetoxymethylcyclohexene (18%) and 1-acetoxymethylcyclohexene (70%),[19] the next peak at 7 min. was 1-acetoxymethylcyclohexyl acetate (6%), and the last, at 9 min., was *trans*-2-acetoxymethylcyclohexyl acetate (6%). These were determined by comparison of retention times and infrared spectra with those of authentic samples.

Acetolysis of *trans*-2-Acetoxymethylcyclohexyl Brosylate-carbonyl-O^{18} in Anhydrous Acetic Acid.—*trans*-2-Acetoxymethylcyclohexyl brosylate-carbonyl-O^{18} (5.03 g., 2.67 and 2.66 atom % excess O^{18}) was placed in a 100-ml. flask, dried, and then heated at 100° for 2 hr. in 72 ml. of dry acetic acid and 3 ml. of acetic anhydride. The reaction was worked up as usual and the residue was distilled at reduced pressure; fraction I, b.p. 55–60° (.5 mm.), contained 3-acetoxymethylcyclohexene (0.300 g.), and the second and third fractions, b.p. *ca.* 77° (0.5 mm.), were combined to afford 0.870 g. of the diacetate-O^{18} mixture. The diacetate fraction was further purified by vapor phase chromatography on the Carbowax column to give 0.550 g. of pure diacetate-O^{18}.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47; O, 29.87. Found: C, 61.37; H, 8.55; O, 29.41; O^{18}, 2.56, 2.53 atom % excess.

Separation of *cis*- and *trans*-2-Acetoxymethylcyclohexyl Acetates-O^{18}.—The diacetate-O^{18} (0.490 g.) mixture was treated with sodium hydroxide (0.20 g.) in methanol (30 ml.), and this solution was allowed to stand at 25° for 48 hr. after which the methanol was partially removed at reduced pressure and the residue was continuously extracted with ether. The ether extract was dried and evaporated, after which the residue was treated with 2,2-dimethoxypropane (10 ml.), 20 ml. of acetone, and a trace of *p*-toluenesulfonic acid. The reaction mixture was stored for 48 hr. at room temperature and processed as previously described. The *cis*- and *trans*-acetonides were separated by vapor phase chromatography on the didecyl phthalate column and identified by comparison with authentic samples. The acetonide mixture contained 86% of the *cis* isomer and 14% of the *trans* isomer. A second experiment was carried out as just described except that the total crude product was saponified and converted to acetonides.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.65. Found for the *cis*-acetonide: C, 70.29; H, 10.53; O^{18}, 2.17, 2.21 atom % excess. Found for the *trans*-acetonide, run I: C, 70.08; H, 10.75; O^{18}, 0.096, 0.052 atom % excess. Found for the *trans*-acetonide, run II: C, 70.31; H, 10.56; O^{18}, 0.10, 0.08 atom % excess.

Acetolysis of *trans*-2-Acetoxymethylcyclohexyl Brosylate-carbonyl-O^{18} in Anhydrous Acetic Acid with Added Acetate.—*trans*-2-Acetoxymethylcyclohexyl brosylate-carbonyl-O^{18} (2.64 g., 2.67 and 2.66% excess O^{18}) and 1.54 g. of potassium acetate were placed in a 50-ml. flask and desiccated under vacuum over phosphorus pentoxide for 48 hr. Anhydrous acetic acid (37 ml.) was then distilled onto this and the reaction flask was heated at 100° for 2 hr. This was worked up in the usual manner. Vapor phase chromatography of the residue afforded pure *cis*-2-acetoxymethylcyclohexyl acetate-O^{18} as determined by its infrared spectrum compared with that of an authentic sample. A second sample of the acetate brosylate was solvolyzed for 14 hr. and processed as just described.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found for run I: C, 61.35; H, 8.47; O^{18}, 2.58, 2.55 atom % excess. Found for run II: C, 61.54; H, 8.56; O^{18}, 2.23, 2.26 atom % excess.

The remainder of the diacetate was saponified and worked up in the usual manner. The residue was crystallized from ether three times and sublimed once to afford crystalline *cis*-2-hydroxymethylcyclohexanol melting at 50–51° (lit.[3] m.p. 47–47.5°).

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.58; H, 10.84; O, 24.58. Found for run I: C, 64.06; H, 11.05; O, 25.10; O^{18}, 2.07, 2.02 atom % excess. Found for run II: C, 64.40; H, 10.81; O, 24.35; O^{18}, 1.89, 1.95 atom % excess.

Titrations.—Procedures used were basically those described by Winstein, Grunwald, and Ingraham.[20]

Analyses were performed with a standard acetate solution of approximately 0.02 *N* and a standard acid solution of the same order of normality. A known amount of reagent grade sodium carbonate was diluted in a volumetric flask with acetic acid to afford the standard acetate solution. A known amount of 70% perchloric acid was diluted with acetic acid in a similar fashion and titrated with the standard base. Brom phenol blue was the indicator employed. Kinetic points were obtained from titrations of 4-ml. portions of the solvolysis solutions. The titrations were performed with a 10-ml. buret graduated in 0.02-ml. increments. The precision of the titrations was 0.5%.

Rate Measurements.—Solutions 0.01 to 0.02 *M* in the compounds to be solvolyzed were made up in the following manner. A weighed portion of material was placed in a 500-ml. erlenmeyer flask with a ground-glass joint. The flask and its contents were thoroughly dried under vacuum over phosphorus pentoxide. The flask was then fitted with a condensor and drying tube and anhydrous acetic acid was distilled directly into it. The flask was then fitted to a continuously filling pipet protected from atmospheric moisture.

Ampoules were then filled from this and immediately sealed. In each case 60 ampoules were prepared in order to have two complete runs at three different temperatures.

The results were calculated on an IBM 1620 computer utilizing a rate program which calculates first-order rate constants and activation parameters from time, concentration, and temperature data, assuming variance in concentration data only.[21] In some instances the reaction followed a good linear first-order rate constant through three half-lives and then at later stages followed second-order kinetics. In these instances the initial rates were utilized to calculate activation parameters.

(19) The mixture was analyzed on the didecyl phthalate column.

(20) S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Am. Chem. Soc.*, **70**, 821 (1948).

(21) We are indebted to Mr. C. E. Klopfenstein and Mr. C. L. Wilkins for making their Fortran program available to us.