Anal. Calcd. for $C_{10}H_{19}NO_3$: C, 59.70; H, 9.45; N, 6.96; neut. equiv., 201. Found: C, 59.97; H, 9.46; N, 6.70; neut. equiv., 195.

The ultraviolet absorption spectrum of an alcohol solution of the substance showed no appreciable absorption down to 220 mμ. The infrared absorption showed strong similarities to that of the oxime of 3,7-dimethyl-6-ketoöctanoic acid[18] in the OH, carbonyl and double bond regions and the substance was found to be amphoteric, being soluble in 5% hydrochloric acid and dilute sodium bicarbonate solutions. Interest in this compound hinges on the fact that its molecular formula and properties are those of an acyclic, saturated oximino acid indicating that a reduction took place in its formation and suggesting that the cyclopropane ring participated in the nitrosation reaction.

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[18] A. Baeyer and O. Manasse, *Ber.*, **27**, 1914 (1894).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Stereochemistry of the Addition of Hydrogen Bromide to 1,2-Dimethylcyclohexene

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It has been found that 1,2-dimethylcyclohexene adds hydrogen bromide to give *trans*-1,2-dimethylcyclohexyl bromide in acetic acid and in pentane. If the reaction in pentane is carried out by condensing an excess of hydrogen bromide in the reaction cell at −195° and then warming the heterogeneous mixture to −78°, some 20% *cis* bromide is produced. Addition to the isomeric olefins, 2,3-dimethylcyclohexene and 2-methylmethylenecyclohexane give, respectively, 13 and 35% *cis* bromide. From these results it is inferred that the addition of hydrogen bromide is not the microscopic reverse of the first-order elimination reactions of the bromides which are observed under different conditions. This conclusion is further strengthened by the fact that the solvolysis rates of the *cis* and *trans* bromides are virtually identical indicating that there is no participation of the *trans* hydrogen during the ionization of the *trans* bromide.

The relative antiquity of the reaction of hydrogen halides with olefins is indicated by the fact that Markownikoff formulated his famous rule concerning the structural specificity of the reaction in 1875.[1] Many years later Kharasch, Mayo and their co-workers elucidated in considerable detail the free radical mechanism of the abnormal addition of hydrogen bromide to unsymmetrical olefins.[2] Very recently Goering, Abell and Aycock have reported data which indicate a surprising stereospecificity for the radical reaction.[3]

It is surprising in a way that no careful study has been made of the mechanism of the more usual "ionic" reaction. The gross aspects are indicated by the mechanistic equivalent of Markownikoff's rule. However, questions of timing and stereochemistry have not been investigated with any care. Two cases are known in which the steric course of hydrogen bromide addition to an olefin has been determined. It is reported that both bromomaleic and bromofumaric acids give *meso*-dibromosuccinic acid[4] and that dibenzo[2,2,2]-bicycloöctatriene-2,3-dicarboxylic acid gives the *trans* adduct.[5] These examples are of limited general value because of the possibility of isomerization of the initial products and because the role of the neighboring carboxyl groups has not been clarified.

Because of the importance of the general reaction we have studied the steric course of the addition of hydrogen bromide to 1,2-dimethylcyclohexene and its isomers. This olefin is particularly appropriate for the study for several reasons. First, it is symmetrical so only two diastereomeric products can be formed unless unexpected skeletal rearrangements occur. Second, the bromides may be distinguished by the differences in their reactivity in the second-order elimination reaction. Third, the reaction is so rapid at low temperatures that it is highly improbable that the radical reaction can compete with polar processes. Lastly, the addition of hydrogen bromide to two isomeric olefins, 2,3-dimethylcyclohexene and 2-methylmethylenecyclohexane, gives mixtures of the same bromides as products.

Experimental

Preparation of 1,2-Dimethylcyclohexene and 2,3-Dimethylcyclohexene.—A mixture of the isomeric 1,2-dimethylcyclohexanols[6] was heated with a catalytic amount of iodine and the olefinic products were distilled from the reaction mixture as formed. The crude product was fractionated through a center-rod column operating at an efficiency of about 50 plates. In a typical run, 50 g. of crude product gave a trace of 2-methylmethylenecyclohexane, 7–8 g. of a product boiling at 129–131° from which about 5 g. of 2,3-dimethylcyclohexene could be isolated by refractionation, and about 40 g. of pure 1,2-dimethylcyclohexene. Physical constants are reported in Table I.

Oxidation of 2,3-Dimethylcyclohexene.—Since this olefin has apparently not been reported previously it was degraded to establish structure. Four grams of the olefin was stirred with 12 g. of potassium permanganate in 400 ml. of water. The reaction was allowed to proceed at ambient temperatures until the permanganate disappeared and the solution was boiled to coagulate the manganese dioxide and was then filtered. The filtrate was acidified with sulfuric acid and extracted with chloroform. The brown oil which remained after the removal of chloroform was not characterized but was stirred with an excess of aqueous sodium hypochlorite for 12 hours. At the end of this time the solution was brought to a boil, cooled, acidified and extracted with chloroform. The chloroform was removed by distillation and the residue was recrystallized from hexane giving 1.3 g. of pure α-methyladipic acid, m.p. 64°, and 1.2 g., m.p. 62–64°, over-all yield 53%, no melting point depression on admixture with authentic material.

2-Methylmethylenecyclohexane was prepared by Wallach[7] by decarboxylation of 2-methylcyclohexylideneacetic

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[1] S. Markownikoff, *Compt. rend.*, **81**, 670 (1875).

[2] For reviews see M. S. Kharasch, *J. Chem. Ed.*, **8**, 1703 (1931); F. R. Mayo and C. Walling, *Chem. Revs.*, **27**, 351 (1940).

[3] H. L. Goering, P. I. Abell and B. F. Aycock, THIS JOURNAL, **74**, 3588 (1952).

[4] G. W. Wheland, "Advanced Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 302, cites unpublished results by Mansfield, Kharasch and Mayo. Details are not available but it is implied that the reaction is ionic.

[5] W. R. Vaughan and K. Milton, THIS JOURNAL, **74**, 5623 (1952).

[6] Prepared by the method of G. Chiurdoglu, *Bull. soc. chim. Belg.*, **47**, 241 (1938).

[7] O. Wallach and E. Beschke, *Ann.*, **347**, 337 (1906).

acid. In our hands this reaction did not yield satisfactory results and it was found that the pyrolysis of both *cis*- and *trans*-1,2-dimethylcyclohexyl acetate gave substantial amounts of this olefin.[8] The pure compound was obtained by fractionation of pyrolysis mixtures and the physical constants are reported in Table I. In order to confirm the structure of the material it was oxidized with neutral permanganate to 2-methylcyclohexanone which was, in turn, characterized as the oxime and dinitrophenylhydrazone.

TABLE I

PHYSICAL CONSTANTS OF OLEFINS

Compound	B.p., °C. (745 mm.)	$n^{25}D$
1,2-Dimethylcyclohexene	136.2	1.4587
2,3-Dimethylcyclohexene	130.3–130.7	1.4534
2-Methylmethylenecyclohexane	124.5–124.8	1.4514

***cis*-1,2-Dimethylcyclohexyl Bromide.**—Mixtures of this bromide with the isomeric *trans* compound in which the amount of *cis* compound ranged from 50–70% were prepared by the reaction of hydrogen bromide with the *cis* alcohol in pentane at −78°. The results of this study will be reported in detail elsewhere.

***trans*-1,2-Dimethylcyclohexyl bromide** was prepared by the addition of hydrogen bromide to 1,2-dimethylcyclohexene as reported in this manuscript. The two bromides were not distilled because they showed a tendency to decompose on heating. The infrared spectra of residual material after removal of the solvent from a washed and dried pentane extract of reaction mixtures showed no evidence for the presence of starting materials when the bromides were made from the olefins, alcohols or acetates. Variation in the spectra could be fitted to a consistent two parameter treatment indicating the presence of only two constituents. Furthermore, dehydrohalogenation gave mixtures of the three above olefins in stoichiometric yield.

Procedures.—Reactions in pentane were carried out in a vacuum line similar to that described by Tolbert.[9] Before a run the system was evacuated overnight at a pressure of one micron. Hydrogen bromide from a tank was then introduced into the system and was condensed in a liquid nitrogen trap. It was purified by successive partial distillations after each of which the residue was pumped out of the system. Finally, the hydrogen bromide was transferred to a storage chamber and the system was pumped out. A flask containing pentane was then attached to the system and the pentane (Phillips Petroleum Company, Pure Grade) was distilled from phosphorus pentoxide into the reaction vessel which contained the olefin at −78°. The reaction was then carried out by admitting the hydrogen bromide to the reaction vessel which was stirred by means of a magnetic stirrer. In some cases the reaction vessel was cooled to −195° during the hydrogen bromide addition. In these experiments the reaction vessel was isolated from the system and the reaction mixture was warmed rapidly to −78°.

Reactions with hydrogen bromide in acetic acid were carried out with Eastman Kodak 30–32% reagent. Some experiments were carried out in the vacuum system but gave results no different from those obtained in open flasks. Short contact experiments were carried out by adding the olefin to the reagent in a separatory funnel which was then shaken briskly for the desired period of time. The reaction was then quenched by the immediate addition of pentane and then water. The pentane layer was separated, washed with aqueous base and water and dried over Drierite. The pentane was then removed by distillation and the residue was analyzed to determine relative amounts of the *cis* and *trans* isomers.

Analytical.—The study of the rates of bimolecular elimination from *cis*- and *trans*-1,2-dimethylcyclohexyl bromides is reported elsewhere.[8] In analytical procedures, a sample of mixed bromide was added to 0.3 *N* sodium hydroxide in 98% ethanol and the elimination reaction was allowed to proceed until a time calculated to be sufficient to consume 99% of the *trans* bromide.[7] The rate at which halide ion was subsequently produced was then carefully monitored and the amount of the slower reacting *cis* bromide was determined by extrapolation of a first order plot (manifold excess of base was used so its concentration was essentially invariant) to zero time.

The amounts of *cis* bromide in samples containing less than 20% of that isomer were determined by infrared analysis. Spectra were determined with a Baird Associates Recording Spectrophotometer using a 0.078-mm. cell. There was considerable overlapping between the characteristic bands for the *cis* compound (1080 and 971 cm.$^{-1}$) and neighboring bands for the *trans* compound. Therefore a series of synthetic mixtures were made up by diluting mixtures rich in the *cis* compound (as shown by kinetic analysis) with pure *trans* bromide. The *cis* content was then determined by graphical interpolation between points in the traces of the spectra of the samples of known composition. The results may be in error by as much as 1–2% in the absolute values for *cis* bromide in the reaction mixtures.

Results and Discussion

Addition in Acetic Acid.—The results of addition at room temperature (approximately 25°) are summarized in Table I. If any of the olefins is allowed to stand in contact with the reagent for one hour the composition reverts to the equilibrium mixture which contains 15% of the *cis* isomer. That this mixture is formed by the equilibration of initial products of a different composition is demonstrated by the results obtained with short contact times. In contact times of less than a minute 1,2-dimethylcyclohexene gives no appreciable amount of *cis* compound whereas the exomethylene isomer gives 35% *cis* and the third isomer, 2,3-dimethylcyclohexene gives 13% *cis*.

TABLE II

ADDITION OF HYDROGEN BROMIDE TO OLEFINS IN ACETIC ACID AND PENTANE

Olefin	Contact time, min.	Temp., °C.	*cis* Bromide formed, %
1,2-Dimethylcyclohexene	180	25	15
1,2-Dimethylcyclohexene	6	25	12
1,2-Dimethylcyclohexene	3	25	7
1,2-Dimethylcyclohexene	0.5	25	0
2-Methylmethylenecyclohexane	180	25	15
	0.6	25	35
2,3-Dimethylcyclohexene	180	25	15
2,3-Dimethylcyclohexene	0.6	25	13
1,2-Dimethylcyclohexene[a]	...	0	0
1,2-Dimethylcyclohexene	...	−78	0
1,2-Dimethylcyclohexene	...	−195 to −78	20

[a] Pentane solution.

These results indicated unequivocally that the addition of hydrogen bromide to these olefins cannot be exclusively by way of a carbonium ion intermediate of classical planar configuration. This conclusion is derived from two independent arguments. First, each of the three olefins would give the same carbonium ion so it would not be possible to account for the variation in the isomer ratio with substrate on the basis of such a mechanism.

The second argument relates to the solvolysis rates of the two bromides which have been found to be identical in several solvents.[8] While the rates have not been determined in acetic acid it is virtually certain that the equivalence of the rates would persist in this medium. This conclusion derives from the quantitative correlation solvolysis rates discovered by Winstein and Grunwald.[10] Since the rates are equal it follows that the stereo-

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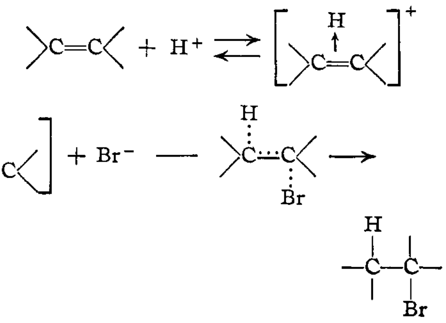
[8] T. D. Nevitt and G. S. Hammond, THIS JOURNAL, **76**, 4124 (1954).

[9] B. M. Tolbert, THIS JOURNAL, **69**, 1539 (1947).

[10] E. Grunwald and S. Winstein, *ibid.*, **70**, 846 (1948).

specific addition cannot be the microscopic reverse of first-order elimination. This means that if there are ionic intermediates in the reactions they are not identical. It is highly probable that the solvolytic reactions of the bromides proceed by way of a common intermediate carbonium ion which has the classical, planar configuration. The addition reaction must, therefore, avoid a path involving such an intermediate.

It seems inevitable that the rate determining step must involve the simultaneous formation of the C–H and C–Br bonds with hydrogen ion (or hydrogen bromide) and bromide ion (or hydrogen bromide) attacking opposite sides of the plane of the olefinic substrate. Such a process may be formulated as a completely concerted reaction or may equally well be regarded as involving the attack of bromide ion on a proton–olefin complex of the type frequently referred to by other investigators.[11] The following equations illustrate the process

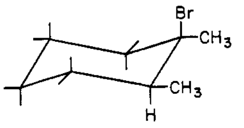


(1)

(2)

Transition state

Taft has previously presented evidence that reaction 1, if it occurs during the hydration of isobutene, must be rapid and reversible. In any event, the previous argument demonstrates that the proton bridge cannot be formed in the rate limiting step of the solvolysis reaction. This is a highly significant observation since the *trans* bromide seems to be almost uniquely constituted to permit hydrogen participation in the solvolysis reaction. It is almost certain that I represents the highly preferred conformation of the compound.[12] The hydrogen, bromine and the two intervening carbon atoms lie in a *trans*, coplanar configuration which should be optimum for participation. In view of the observed results it seems doubtful that proton bridges are ever formed in the rate controlling step of solvolysis reactions of saturated, tertiary bromides. Roberts and Yancey have already demonstrated that it is unlikely that the ethyl cation has a bridge structure.[13]



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Addition in Pentane.—The results shown in Table II again demonstrate a stereospecific *trans* process which may be reversed under special circumstances. At zero degrees and even at −78 degrees very clean *trans* addition can be effected. However, if a large amount of hydrogen bromide is condensed in the reaction vessel at the temperature of liquid nitrogen and the mixture is warmed rapidly to −78°, a fast reaction occurs to give 20% *cis* bromide.

The *trans* reaction is probably similar to that which occurs in acetic acid except that the molecularity in hydrogen bromide may be higher[14] as some of the acetic acid molecules of solvation are replaced by hydrogen bromide. The *cis* reaction is very likely a cyclic process involving an even larger number of hydrogen bromide molecules. It is obvious that such a process would probably involve a small activation energy since charge separation could be minimized but would be characterized by a large negative activation entropy. While the influences of increasing the hydrogen bromide concentration and decreasing temperature have not been separated, it is clear that the conditions which led to *cis* addition are compatible with the above considerations.

In summary, it seems probable that a stereospecific *trans* addition of hydrogen bromide to olefins may prove to be general for reactions carried out in non-polar solvents at ordinary temperatures. It is possible that further study will lead to the development of the *cis* reaction as a useful synthetic tool. It should also be noted that addition in acetic acid and other polar solvents may well go by a carbonium ion mechanism when hydrogen bromide activities are kept lower than was done in this study. In any event, the rapidity of solvolytic isomerization makes acetic acid appear to be an undesirable medium for stereospecific syntheses.

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[11] M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Clarendon Press, Oxford, 1949; R. Taft, THIS JOURNAL, **74**, 5372 (1952).

[12] Rough calculation shows that I should be stable by 3–4 kcal. per mole with respect to the alternative conformation in which bromine is equatorial and the two methyl groups polar.

[13] J. D. Roberts and Yancey, THIS JOURNAL, **74**, 5943 (1952).

[14] F. R. Mayo and M. C. Savoy, *ibid.*, **69**, 1348 (1949).