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STEREOCHEMISTRY OF HYDROGEN BROMIDE ADDITION TO OLEFINS

by

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INTRODUCTION

The noncatalyzed addition of hydrogen halides to olefins has received little study. There is an amazing lack of knowledge, experimental evidence and agreement on a mechanism for this seemingly simple reaction run under evidently simple conditions. The stereochemistry of this reaction is known only through conjecture, and the kinetic studies on this reaction are far from complete.

The reason for this state of affairs becomes apparent on reviewing the literature. From the studies that have been made, the reaction appears to be exceedingly complex. Changes of experimental conditions materially affect results. In work with hydrogen bromide, both radical and ionic reactions frequently occur at the same time. Small amounts of impurities can catalyze the ionic addition of both hydrogen bromide and hydrogen chloride. Unfortunately, simple systems, amenable to kinetic studies, magnify the various side reactions.

The stereochemistry of hydrogen halide addition was investigated with compounds containing functional groups which are now known to affect materially the course of many reactions. This leaves considerable doubt as to the general applicability of these studies and perhaps explains some of the conflicting conclusions that can be drawn from them.

Furthermore, olefins used to study this reaction seem to have been chosen because of their ready availability. There has been no investigation undertaken on an olefin specifically designed to obviate many of the difficulties described above. It was the object of this investigation to synthesize a suitable system for a study of the hydrobromination of olefins and to study the stereochemistry of the reaction.

HISTORICAL REVIEW

The Addition of Hydrogen Bromide to Olefins

Very early it was realized that hydrogen halides add to unsymmetrical olefins in a structurally specific way. This was the basis for the well known empirical rule of addition to multiple bonds formulated by Markownikoff in 1875[1]. The rule states that the positive portion of the adding reagent will be found on the carbon atom richest in hydrogen. For example, isobutylene would be expected to produce t-butyl chloride rather than isobutyl chloride when treated with hydrochloric acid. Many years later Kharasch reviewed data on the orientation of olefin additions[2]. In order to clarify certain contradictory data, he and his students undertook a reinvestigation of hydrogen halide additions. In brief they found two types of hydrogen bromide addition, a normal or Markownikoff addition involving ionic intermediates and an abnormal, peroxide catalyzed, addition involving free radical intermediates.

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

[2] M. S. Kharasch, J. Chem. Education, 8, 1725 (1931).

The peroxide catalyzed reaction is in general faster and is never observed with hydrogen chloride under ordinary conditions. The subject of peroxide catalyzed additions has been treated fully elsewhere and will not be discussed further here[3].

Evidence concerning the stereochemistry of the ionic addition of hydrogen bromide to olefins is meager. Goering has shown that the free radical addition of hydrogen bromide to 1-bromocyclohexene and 1-methylcyclohexene occurs in a trans manner, giving cis 1,2-dibromocyclohexene and cis 1-bromo-2-methylcyclohexene[4].

Addition of hydrogen halides to triple bonds invariably leads to trans olefins. The trans olefin was obtained when hydrogen chloride was added to methylpropiolic acid in water[5]. In an ionic solvent, hydrogen bromide added to acetylene dicarboxylic acid to give bromofumaric acid[6]. Hydrogen chloride adds in a similar manner[7].

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[3] F. R. Mayo and C. Walling, Chem. Revs., 27, 351 (1940).

[4] H. L. Goering, P. I. Abell and B. F. Aycock, J. Am. Chem. Soc., 74, 3588 (1952).

[5] R. Friederich, Ann., 219, 322 (1883).

[6] A. Michael and C. M. Browne, Ber., 19, 1378 (1886); 20, 550 (1887); J. prakt. Chem., (2) 35, 257 (1887); A. Michael, ibid., 46, 224 (1892).

[7] W. Lossen, Ann., 348, 261 (1906).

Two examples are available of the addition of hydrogen bromide to olefins. The addition of hydrogen bromide to bromofumaric acid and bromomaleic acid gives, in each case, the dibromomeso acid[8]. The reaction between hydrogen bromide and dibenzo(2,2,2)bicyclooctatriene-2,3-dicarboxylic acid in glacial acetic acid results in trans addition[9].

There are several objections to drawing any conclusions about the ionic addition reaction from the results described above. First, all of the above reactions were conducted in hydroxylic solvents and the reaction may take a different path resulting in different products in nonpolar solvents. The work done with acetylenes does not necessarily apply to olefins. The possibility of isomerization of the acid prior to the addition of the hydrogen halide exists. Finally, all of the above cases involve compounds with a carboxyl group adjacent to the multiple bond. The carboxyl group has been shown to participate in some substitution reactions and the same type of intermediate is possible in the addition reaction[10].

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[8] G. W. Wheland, "Advanced Organic Chemistry", 2nd ed., John Wiley and Sons, Inc., New York, 1948, p. 302; Kharasch, Mansfield and Mayo, unpublished results.

[9] W. Vaughan and K. Milton, J. Am. Chem. Soc., 74, 5623 (1952).

[10] See page 17, this thesis.

About 1910 Maass became interested in studying addition complexes of various acids with alcohol, ether, etc. Evidence for or against complex formation was based on the melting point curves of various mixtures of acid and the complexing compound. As an outgrowth of this work the addition of hydrogen halides to olefins was studied[11-17].

Maass found that essentially no reaction takes place between hydrogen chloride or hydrogen bromide and olefins in the vapor phase in the absence of catalysts[14]. These results have been confirmed by other workers who found that data taken from the thermal decomposition of t-butyl chloride showed that the activation energy for addition in the vapor phase is unfavorably high[18]. Recent work indicates that

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[11] O. Maass, J. Am. Chem. Soc., 34, 1273 (1912).

[12] O. Maass and J. Russell, ibid., 40, 1561 (1918); 43, 1227 (1921).

[13] O. Maass and R. H. Wright, ibid., 43, 1098 (1928); 46, 2664 (1924).

[14] O. Maass and C. Siverts, ibid., 47, 2883 (1925).

[15] C. C. Coffin, H. C. Sutherland and O. Maass, Can. J. Research, 2, 267 (1930).

[16] C. H. Holder and O. Maass, ibid., 3, 526 (1930).

[17] C. C. Coffin and O. Maass, ibid., 16B, 453 (1938).

[18] G. B. Kistiakowsky and C. H. Stauffer, J. Am. Chem. Soc., 59, 165 (1937).

the addition of hydrogen bromide to olefins occurs in the vapor phase[19]. In a study of the kinetics of the decomposition of isopropyl bromide, considerable evidence was found that the reaction shown below occurs.

$$C_3H_6 + HBr \longrightarrow C_3H_7Br$$

A marked falling off of the rate of decomposition was observed at high initial pressures and in runs containing added propene.

No reaction occurs between hydrogen chloride and olefins of the types $RHC{=}CH_2$, $R_2C{=}CH_2$, $RHC{=}CRH$, and $R_2C{=}CHR$ at -78^{o} in toluene[20]. The addition reaction in the liquid phase occurs readily even at -70^{o} with hydrogen bromide and certain olefins. Leendertse found that olefins of the type, $-CH{=}CR_2$, reacted at this temperature to give very pure tertiary bromides. Olefins of the type, $RHC{=}CRH$, for example cyclohexene, did not react under similar conditions[21].

Maass and co-workers measured the melting point of hydrogen halide-olefin or acetylene mixtures. They found

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[19] A. Maccoll and P. T. Thomas, J. Chem. Physics, 19, 977 (1951).

[20] H. C. Brown and J. D. Brady, J. Am. Chem. Soc., 74, 3572 (1952).

[21] J. J. Leendertse, Rec. trav. chim., 57, 759 (1938); J. J. Leendertse, A. J. Tulleners and H. I. Waterman, ibid., 52, 515 (1933); 53, 715 (1934).

that unsymmetrical unsaturated hydrocarbons formed one to one complexes with hydrogen bromide or chloride. Complex formation at these low temperatures was very rapid, and it was complete before any appreciable amount of addition reaction had occurred. The symmetrical compounds, ethylene and acetylene, gave no evidence for complex formation[13,15]. Recently, this interaction between hydrogen chloride and olefins has been used as a measure of the basic strength of olefins[20].

When Maass allowed the hydrogen bromide-propylene complex to warm in the absence of solvent, addition took place. Hexyl bromide was also formed. In order to account for all the propene they also assumed some polymer formation[14]. Mayo and Savoy were able to isolate only a trace of hexyl bromide and reported no polymer formation when the reaction was run under similar conditions[22]. Maass found that an equimolar mixture of hydrogen bromide, hydrogen chloride and propene reacted almost as fast as a two to one mixture of hydrogen bromide and propene. Although, under the same conditions, hydrogen chloride does not react with propene.

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[22] F. R. Mayo and M. C. Savoy, J. Am. Chem. Soc., 69, 1348 (1947).

According to Maass, the amount of reaction in a given time is roughly proportional to the stability of the hydrogen halide-olefin complex. Thus, he proposed these compounds as intermediates in this reaction. However, the demonstration of the existence of these compounds cannot be regarded as conclusive evidence of their participation in this reaction as intermediates. Further work tended to support this proposal of Maass. Some of the reaction rates Maass had run had a negative temperature coefficient. This fits nicely with the fact that complex formation is favored by lowering the temperature. Mayo and Katz found that cooling a reaction mixture containing hydrogen chloride, isobutylene and pentane gave the reaction a remarkable temporary acceleration[23]. After rapid cooling and slow warming to the former reaction temperature, increases in rate from 100 to 1000 fold were observed. If the mixtures were warmed rapidly the rate was only doubled. They gave two alternative explanations for this behavior.

The decomposition of the complex may be slow enough so that when the mixture is warmed an artificially high concentration of complex allows the reaction to proceed at an artificially high rate. Or, at some intermediate temperature,

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[23] F. R. Mayo and J. J. Katz, J. Am. Chem. Soc., 69, 1339 (1947).

conditions might be favorable for a rapid chain mechanism, involving carbonium ions, to proceed. Other examples of this phenomenon are the polymerization of isobutylene by boron trichloride which proceeds more rapidly at very low temperatures than it does at 0°[24]. The polymerization of styrene by stannic chloride also has a very low activation energy[25].

O'Connor, Baldinger, Vogt and Hennion have studied, qualitatively, the rates of addition of hydrogen chloride and hydrogen bromide to 3-hexene and cyclohexene in several solvents. They were unable to obtain satisfactory kinetics[26]. The reaction proceeded rapidly in hydrocarbon solvents, while such solvents as ether and dioxane slowed the reaction considerably, presumably by lowering the _effective concentration_ of the halogen hydride through complex formation. These results were confirmed by additional experiments with α-pinene[27].

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[24] R. M. Thomas, W. I. Sparks, P. K. Frolich, M. Otto and M. Mueller-Cunradi, _ibid._, _62_, 276 (1940).

[25] G. Williams, _J. Chem. Soc._, 1946 (1938); 775 (1940).

[26] S. O'Connor, S. Fedelis, R. Baldinger, L. Vogt and G. F. Hennion, _J. Am. Chem. Soc._, _61_, 1454 (1939).

[27] G. F. Hennion and C. F. Irwin, _ibid._, _63_, 860 (1941).

Mayo and Savoy attempted to correlate previous work in this field and attempted to obtain rates for this reaction[22]. This investigation was interrupted by the war and apparently the authors do not intend to complete it. The first attempt to study this reaction was made with propylene and hydrogen bromide. The reaction was run in n-pentane and was followed dilatometrically. Briefly the following facts were obtained. Preliminary experiments showed that in the absence of any solvent hydrogen bromide reacts with propylene in the presence or absence of air to give isopropyl bromide and a trace of hexyl bromide. The presence of peroxides caused abnormal addition to take place. When the reaction mixture was diluted with n-pentane, the normal mode of addition was suppressed, the reaction giving nearly completely n-propyl bromide even though air and peroxides were carefully excluded. Similar abnormal addition was observed frequently even in the presence of inhibitors. In runs containing inhibitor that gave isopropyl bromide, the normal product, the reaction was roughly third order in hydrogen bromide and first order in propylene. The results were not very satisfactory since the presence of the inhibitors often caused two phases to appear in the reaction mixture. For this reason work on this particular reaction was discontinued.

Two supplementary experiments run with hydrogen bromide and propylene are of interest. Mayo and Savoy found that in ether an almost instantaneous reaction occurred giving both the normal and the abnormal product. This leaves the earlier work of Hennion and co-workers, discussed briefly above, open to some question since they found an opposite order of reactivity of hydrogen halides with 3-hexene or cyclohexene in ether and in hydrocarbon solvents[26,27]. Since Hennion's runs were made with symmetrical olefins it is impossible to determine if abnormal addition had occurred. Hennion felt that because inhibitors did not affect the rate and because the rates were slowest in ether where peroxide formation was most probable, normal addition had occurred. (Also, peroxide catalysis has never been observed in nitrobenzene, in which Hennion observed intermediate rates.)

The main result of this investigation by Mayo and Savoy was to show how sensitive to promotion of the abnormal chain mechanism the addition of hydrogen bromide to simple olefins becomes on dilution. As a further result of this work, it was shown that advantage could be taken of this effect to prepare β-bromostyrene from styrene, 1,2-dibromobutane from 2-bromobutane, and 2-bromo-3-methylbutane from trimethylethylene, compounds otherwise difficult to prepare[28].

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[28] C. Walling, M. S. Kharasch and F. R. Mayo, *J. Am. Chem. Soc.* 61, 1711, 2693 (1939).

Mayo and Katz worked with the hydrogen chloride-isobutylene system in the hope of obviating some of the difficulties which occurred when hydrogen bromide was used[23]. The kinetics here, too, were not very satisfactory. They found that such diverse substances as alcohols, phosphorous pentoxide, and mercury (chloride) catalyze the ionic reaction, so that the reaction becomes first order in hydrogen bromide. Again their kinetic studies showed evidence for a fourth order reaction. Some evidence was obtained for complex formation. Assuming "reasonable values" for the equilibrium constant for complex formation smoothed out the fourth order rate constants.

To summarize, there are at least three alternative mechanisms by which this reaction may be accomplished in nonaqueous solvents. First, there is the possibility of some chain reaction process occurring at some temperature below 0°. Second, there is the process suggested by Maass and apparently favored by Katz and Mayo involving the reaction of a hydrogen halide-olefin complex.

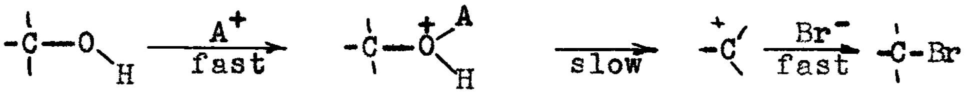
The third alternative put forward by Mayo and Katz involves the association of the complex with an indefinite number of hydrogen chloride molecules "much as in indefinite number of water molecules is associated with the S_N1 hydrolysis of t-butyl chloride". Thus the apparent activation energy might decrease as the temperature is lowered and more hydrogen halide becomes associated with the complex.

These reaction mechanisms are not complete enough to predict the stereochemistry of the reaction. Conversely, knowledge of the stereochemistry may help elucidate the reaction mechanism.

The Reaction of Hydrogen Bromide With Alcohols

Hydrogen bromide and alcohols react to form alkyl bromides. This reaction is well known and there are numerous examples of it in the literature. No attempt will be made here to review this literature critically. A discussion of the reaction paths this reaction can take is given below.

In polar solvents an S_N1* reaction is favored. The main feature of this reaction path is the formation of an intermediate carbonium ion, thus destroying the assymmetry of the original alcohol and resulting in extensive racemization. A widely accepted concept of the course of this reaction is shown below[29].



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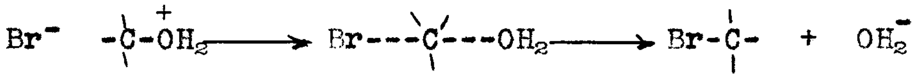
*Substitution, nucleophilic, first order.

[29] E. D. Hughes, *Trans. Faraday Soc.*, 37, 604, 612 (1941).

The driving force for this reaction is considered to be the solvation of the leaving group. Either the solvent or an electrophilic solute solvates the leaving group by means of simple electrostatic interaction or by the formation of a coordinate bond. The reaction is first order in alcohol and it is independent of the concentration of the bromide ion.

Nonpolar solvents favor the inversion of the configuration of the original alcohol. This type of reaction is called S_N2 or a Walden inversion[30]. The reaction is first order in alcohol and bromide ion. The mechanism of this reaction can be diagramed as shown below:



$$Br^- \quad -C-\overset{+}{O}H_2 \longrightarrow Br---C---OH_2 \longrightarrow Br-C- \quad + \quad OH_2^-$$

The driving force for this reaction is provided by the entering group. The carbon atom at the reaction site undergoes nucleophilic attack by the entering group, the new bond is made as the old bond is broken, and the configuration of the carbon atom is inverted[31].

There is a growing body of evidence to show that the difference between the S_N1 process and the S_N2 process is one of degree rather than one of kind. Swain has found

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[30] P. Walden, <u>Ber.</u>, <u>28</u>, 1287 (1895).

[31] L. P. Hammett, "Physical Organic Chemistry", McGraw-Hill Book Co., New York, 1940, p. 181.

that in the benzene solutions both the carbonium ion process and the bimolecular displacement reaction of alkyl halides are termolecular processes[32]. There is no apparent reason why the concerted termolecular process does not hold in solvents such as water and alcohol. If this is the case, then these processes may involve the electrophic solvolysis of the leaving group and the nucleophilic attack or solvolysis of the carbon atom at the reaction site. If the entering group participates in this process, inversion of the carbon atom occurs. The observed kinetic order of the reaction is a measure of the degree of participation of the solvent in the reaction. It should be pointed out that there is no direct experimental evidence that the reaction of hydrogen bromide with alcohols ever exhibits termolecular kinetics.

Under rather special circumstances more or less complete retention of configuration is observed. Two such reactions are known. The neighboring group displacement reaction occurs in systems where there is a neighboring group with an unshared pair of electrons. Evidence for the mechanism of this reaction is fairly complete. Often intermediate products are isolable[33]. The first step of the reaction

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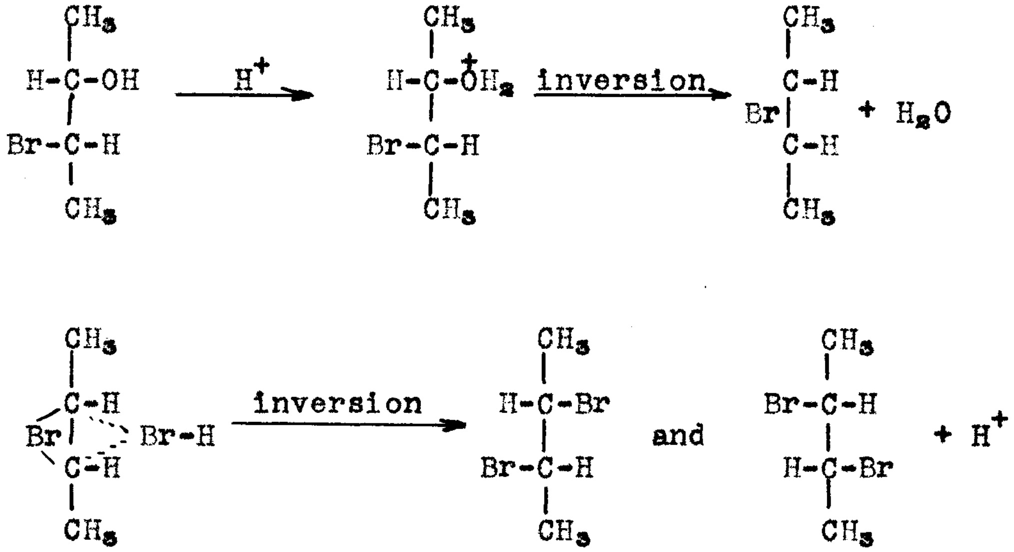
[32] C. G. Swain, J. Am. Chem. Soc., 70, 1119 (1948); C. G. Swain and C. Eddy, Ibid., 70, 2989 (1948).

[33] E. R. Alexander, "Ionic Organic Reactions", John Wiley and Sons, Inc., New York, 1950, p. 102.

consists of an intramolecular S_N2 reaction effected by the unshared electron pair of the neighboring group. The ring formed is opened by the attacking reagent in a second S_N2 reaction. The net result of the two inversions is a retention of configuration. An example of this reaction is the conversion of threo 3-bromo-2-butanol (I) to dl 2,3-dibromobutane (II) with complete stereospecificity in that no meso dibromide is produced[34].



Hydrogen bromide reacts in one other way to give retention of configuration. Apparently only two examples of this reaction were known previous to the studies presented

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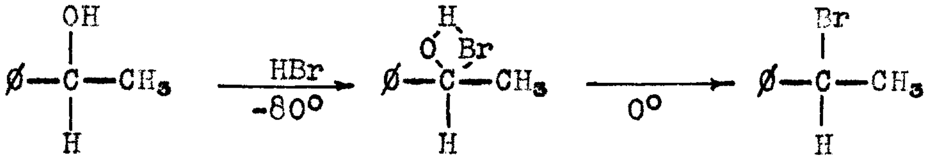
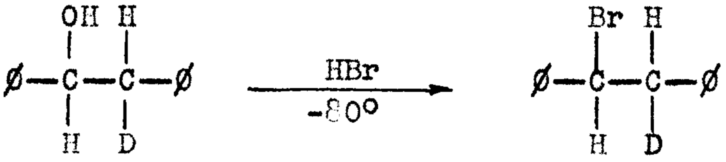
[34] S. Winstein and H. J. Lucas, J. Am. Chem. Soc., 61, 1576 (1939).

in this thesis. Both involved phenyl alkyl carbinols. Unless the reaction is carried out at low temperatures about -70°, partial inversion of configuration occurs. This reaction was discovered by Levine and Rothen[35]. The reaction was carried out by coating the bottom of a flask with a thin layer of *d* or *l* methyl phenyl carbinol and allowing gaseous hydrogen bromide, B. P. -67°, to diffuse into the flask. An addition complex forms. On warming, the addition complex decomposes into the alkyl bromide and water.



d series

No details are available on the other known example of this reaction except that it was run at -80° in pentane[36].



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[35] P. A. Levine and A. Rothen, *J. Biol. Chem.*, *127*, 237 (1939).

[36] D. B. Kellom and D. Y. Curtin, *Abstracts of the 122nd Meeting of the American Chemical Society*, p. 23M, 1952.

The *erythro* 2-deutero-1,2-diphenylethanol (III) gave predominantly *erythro* 2-deutero-1,2-diphenylethyl bromide (IV). Greater than 87 % retention of configuration was achieved.

In this present study it was necessary to explore the generality of the low temperature reaction of hydrogen bromide and alcohols.

Elimination Reactions

The elimination of the elements of hydrogen bromide can occur kinetically in two different ways. The reaction rate can be dependent only on the concentration of the alkyl bromide, the E1 reaction, or the reaction rate can exhibit a first order dependence on both the concentration of the alkyl bromide and the concentration of a base[37]. In the unimolecular

$$\begin{array}{llll} & CR_2\text{-}CR_2\text{-}X \longrightarrow & HCR_2\text{-}\overset{+}{C}R_2 + :X & \\ & & & E1 \\ Y: & HCR_2\text{-}\overset{+}{C}R_2 \longrightarrow & \overset{+}{Y}H + CR_2{=}CR_2 & \\ & & & \\ Y: & + HCR_2\text{-}CR_2X \longrightarrow & \overset{+}{Y}H + CR_2{=}CR_2 + :X & E2 \end{array}$$

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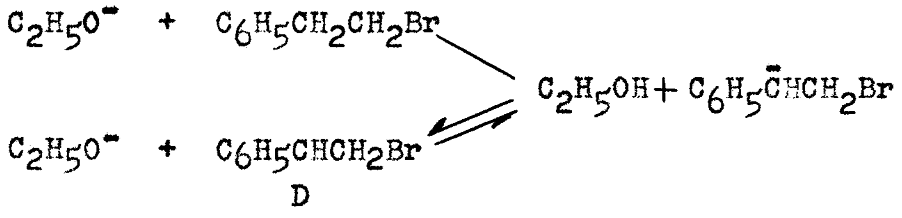
[37] E. D. Hughes and C. K. Ingold, *Trans. Faraday Soc.*, *37*, 657 (1941).

elimination, the reactive intermediate is formed in the same way as that for unimolecular substitution. The carbonium ion then loses a β-hydrogen.

The bimolecular elimination reaction is initiated by the extraction of a β-hydrogen by a nucleophilic agent. The halogen may or may not be removed at the same time. The term, E2 reaction, is reserved for the former case[38].

Evidence that the removal of the proton and the negative group is a simultaneous process has been obtained by an experiment by Skell and Hauser[39]. An E2 reaction was carried out on α-phenylethyl bromide in a solution of C_2H_5OD containing sodium ethylate. The reaction was allowed to run until approximately half complete. The mixture was worked up and the α-phenylethyl bromide was found to contain no deuterium. In this case, the equilibrium shown below must not exist.



$$\begin{array}{lcl} C_2H_5O^- + C_6H_5CH_2CH_2Br & \searrow & \\ & & C_2H_5OH + C_6H_5\overset{-}{C}HCH_2Br \\ C_2H_5O^- + C_6H_5\underset{D}{C}HCH_2Br & \leftrightharpoons & \end{array}$$

---

[38] E. D. Hughes, *Quart. Revs.*, *5*, 261 (1951).

[39] P. S. Skell and C. R. Hauser, *J. Am. Chem. Soc.*, *67*, 1661 (1945).

It then follows that the carbanion must lose bromide ion much faster than it can pick up deuterium. If deuterium exchange could occur it would be extremely rapid.

In both E1 and E2 processes elimination of alkyl halides proceeds to form the most highly branched olefin (within the restrictions on the E2 process discussed below)[40]. This observation has been termed the Saytzeff rule. Another way of stating this rule is that the olefin formed will be the olefin most stabilized by hyperconjugation because the more hyperconjugation, the lower the activation energy for the process. For example, one would predict that the dehydrohalogenation of secondary butyl bromide would produce 2-butene and not 1-butene, since one can write six hyperconjugation structures for the former product but only two for the latter. Because this treatment successfully predicts the products for a large number of reactions, the transition state for the loss of the proton must have a structure very similar to that of the olefinic product.

The E2 reaction has an important stereospecificity. This was first demonstrated by Hückel and his co-workers[41].

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[40] E. D. Hughes and C. K. Ingold, <u>Trans. Faraday Soc.</u>, <u>37</u>, 680 (1941).

[41] W. Hückel, W. Tappe and G. Legutke, <u>Ann.</u>, <u>543</u>, 191 (1940).

Several alkyl chlorides were allowed to react under both E1 and E2 conditions. The results of this study are given in Table I. It can be seen that although the E1 reaction gives as major products the most stable olefin, the E2 reaction gives predominantly products that cannot be predicted on the basis of the Saytzeff rule. On further examination, it can be seen that the products formed are those in which the eliminated halide and proton are trans to each other. Hückel suggested that the electrostatic repulsion between the base extracting the proton and the negative leaving group favors trans elimination.

Cristol and his co-workers have added much to our knowledge of the E2 reaction. They first investigated the rate of dehydrochlorination in aqueous ethanol with sodium hydroxide of the four isomeric 1,2,3,4,5,6-hexachlorocyclohexanes[42]. The β-isomer, which cannot undergo trans elimination (all adjacent chlorine and hydrogen atoms are cis to each other) reacted at a rate some 7000-24000 times slower than the other three isomers in which trans elimination is possible. A difference of 9.6-12.5 Kcal. was found in the activation energy of the β-isomer relative to the other three isomers. Rough calculations show that the electrostatic repulsion between the base extracting the

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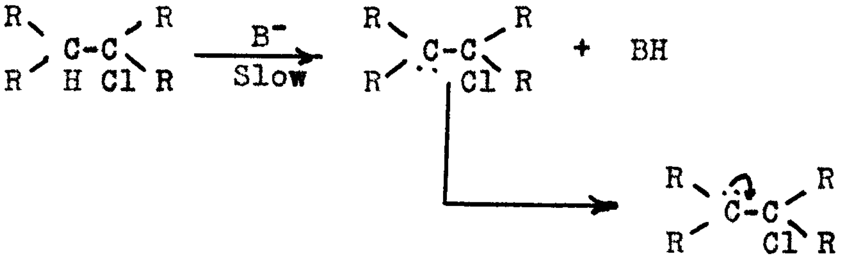
[42] S. J. Cristol, N. L. Hause and J. S. Meek, J. Am. Chem. Soc., 73, 674-9 (1951).

Table I

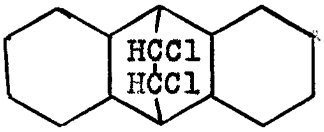
Comparison of Products of E_1 and E_2 Reactions

Reactant	E_1 Products ($B^- = CO_3^=$)	E_2 Products ($B^- = OCH_3^-$)
1-Menthyl chloride	Δ_3-(70%)- Δ_2-(30%) Menthene	Δ 2-Menthene (100%)
1-Menthyl tosylate		
trans α-Decalyl tosylate	$\Delta_{1,2}$-(75%) + *trans* $\Delta_{1,2}$-(25%)-Octalin	$\Delta_{1,9}$-(10%) - *trans* $\Delta_{1,2}$-(90%) Octalin
cis α-Decalyl tosylate	$\Delta_{1,9}$-(75%) + *cis* $\Delta_{1,2}$-(25%) Octalin	$\Delta_{1,9}$ Octalin (100%)
trans β-Decalyl tosylate	*trans* $\Delta_{2,3}$(80%) *trans* $\Delta_{1,2}$(20%) Octalin	*trans* $\Delta_{1,2}$ Octalin (100%)

proton and the negative leaving group could account for only a small part of the additional activation energy necessary in the _cis_ elimination. The superiority of the _trans_ process seems best explained on the basis of different mechanisms for the _cis_ and _trans_ eliminations. It seems very likely that the _trans_ elimination is a one stage concerted process. It was proposed that _cis_ elimination is a multiple stage process involving the formation of a transient carbanion and its possible inversion:



In a subsequent study Cristol and his co-workers obtained kinetic data on the dehydrochlorination in ethanolic alkali of the _cis_-_trans_ isomers of 11,12-dichloro-9,10-ethanoanthracene (I)[43].



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[43] S. J. Cristol and N. L. Hause, _J. Am. Chem. Soc._, _74_, 2193 (1952).

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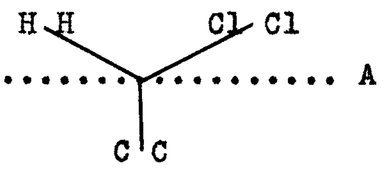
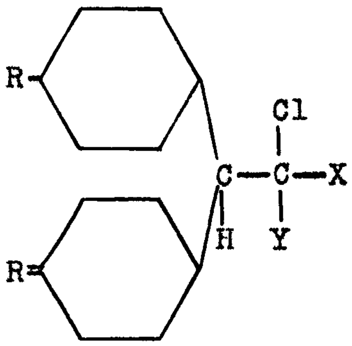
In the *cis* isomer, the *trans* hydrogen and chlorine atoms are each removed about 35° out of the plane *A* as shown in the diagram below drawn perpendicular to the C_{11} and C_{12} carbon atoms:



In the *trans* isomer, *trans* elimination is impossible. The *trans* dichloride (*cis* hydrogen and chloride atoms) unexpectedly reacted seven to nine times faster than the *cis* dichloride (*trans* hydrogen and chlorine atoms). This difference in rate was found to be due to a favorable entropy of activation and to the relatively high reaction temperature (about 100°). The energy of activation favored the *trans* elimination by about 4 Kcal. per mole. This difference in activation energies between the *cis* and *trans* processes is about 8 Kcal. less than the difference in activation energies observed in the case of the hexachlorocyclohexanes. This can mean that the preferred orientation of the transition state is probably planar for facile *trans* elimination.

The results of a kinetic investigation of the dehydrochlorination of various 2,2-diarylchloroethanes



X = H or Cl

Y = H or Cl

R = CH_3O, CH_3, H, F, Cl, Br.

seemed best explained by the model of the transition state described above[44]. It was found that if X and Y are both chlorine atoms, DDT, the reaction rate constant for dehydrochlorination, is 2.4 to 4.3 times as great as in compounds where X is a chlorine and Y is a hydrogen, DDD. And, in turn, the reaction rate constants for DDD are 5 to 6 times as great as the second order rate constants for DDM, in which X and Y are both hydrogens. The activation energy of the reaction is about 1.6 Kcal. less in DDT than in DDD and DDM, and accounts for most of the rate difference. The decrease in the reactivity of the DDM compounds over the DDD compounds is due entirely to a decrease in entropy of activation. Briefly, these results are explained best if we assume, as before, that both the carbon-hydrogen bond and the carbon-chlorine bond are broken in the rate determining step. As the number of chlorine atoms β to the hydrogen to

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[44] S. J. Cristol, N. L. Hause, A. J. Quant, H. W. Miller, K. R. Eiler and J. S. Meek, *J. Am. Chem. Soc.*, *74*, 3333 (1952).

be removed is increased, the strength of the hydrogen carbon bond is decreased by a negative inductive effect. This lowers the activation energy. However, increasing the number of chlorine atoms strengthens the carbon-chlorine bond, increasing the activation energy. Apparently in DDM and DDD these two effects are balanced, resulting in about the same energy of activation for the dehydrochlorination compounds. In DDT the inductive effect predominates, lowering the activation energy for dehydrochlorination. This is consistent with the facts that the ionization constants of the chloroacetic acids increase as the number of chlorine atoms is increased and that although the carbon-chlorine bond strength is increased in going from methyl chloride to methylene chloride, it is not strengthened appreciably in going from methylene chloride to chloroform.

In still another investigation Cristol and Begoon found that trans elimination was the superior process in the dehydrohalogenation of the chlorofumarate, chloromaleate, bromomaleate, and bromofumarate ions with sodium hydroxide in water and aqueous ethanol[45]. Simple calculations would predict larger electrostatic repulsions (and hence higher activation energies) for the halofumarates than for the

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[45] S. J. Cristol and A. Begoon, J. Am. Chem. Soc., 74, 5025 (1952).

halomaleates. This study shows "that the effect of electrostatic repulsion upon the energy of activation for elimination reactions is not of major importance" in solvents such as water and aqueous ethanol.

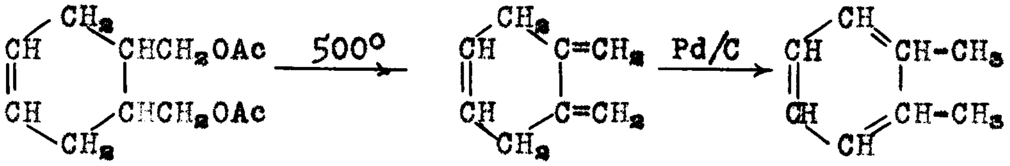
The E2 process, as the result of Cristol's work, is now fairly clear. Two mechanisms operate. The rate-wise superior trans process is a one stage concerted process. A planar transition state is preferred. A proton is removed by a base, a multiple bond is formed and the halide ion is lost. The activation energy of the process is a reflection of the ionic bond strengths of the hydrogen-carbon and the halogen-carbon bonds involved. The cis process is a two stage process. The rate determining step is the removal of the proton and the formation of a carbanion ion. The activation energy in the cis process reflects only the carbon-hydrogen bond strength.

In the course of this work, the E2 reaction was used in proving some structures and as a kinetic analytical method.

Acetate Pyrolysis

The acid catalyzed dehydration sometimes results in the rearrangement of the carbon skeleton. The amount of rearrangement is dependent on the structure of the alcohol and can occur to the exclusion of the formation of the unrearranged product.

It is possible to dehydrate alcohols without any structural change occurring. Two methods are available. The method of Tschugaef involves the distillation of the methyl xanthate of the alcohol. Xanthate formation is at best inconvenient and Tschugaef's method has been gradually superseded by a procedure in which a carboxylate ester of the alcohol is passed through a glass packed tube heated at 400-600°. The acetate is generally used. Other esters frequently utilized include benzoates, stearates, and ethyl carbonates[46]. A self-explanatory example of the utility of this method is shown below[47].



The stereochemical course of both xanthate and acetate decomposition with compounds containing a β-hydrogen atom

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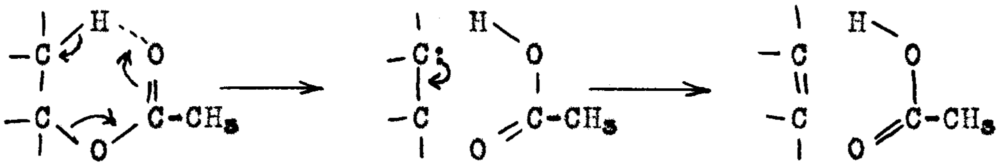
[46] G. L. O'Connor and H. R. Nace, <u>J. Am. Chem. Soc.</u>, <u>74</u>, 5454 (1952).

[47] W. Bailey and J. Rosenberg, "Abstracts of the 13th International Congress of Pure and Applied Chemistry", p. 422 (1951).

has been extensively studied and both give predominantly cis elimination[41,48,49,50,51,52,53,54]. That is, loss of a proton trans to the negative leaving group observed in the E2 elimination does not occur. An examination of the products of both xanthate and acetate decomposition indicates that a frontal attack is preferred. A cyclic mechanism has been proposed for this reaction[49].



Alexander and Mudrack studied the decomposition of cis and trans 2-phenylcyclohexyl acetates[51]. They found that

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[48] C. D. Hurd and F. Blunck, J. Am. Chem. Soc., 60, 2421 (1938).

[49] P. G. Stevens and J. H. Richmond, ibid., 63, 3132 (1941).

[50] D. J. Cram, ibid., 71, 5883 (1949).

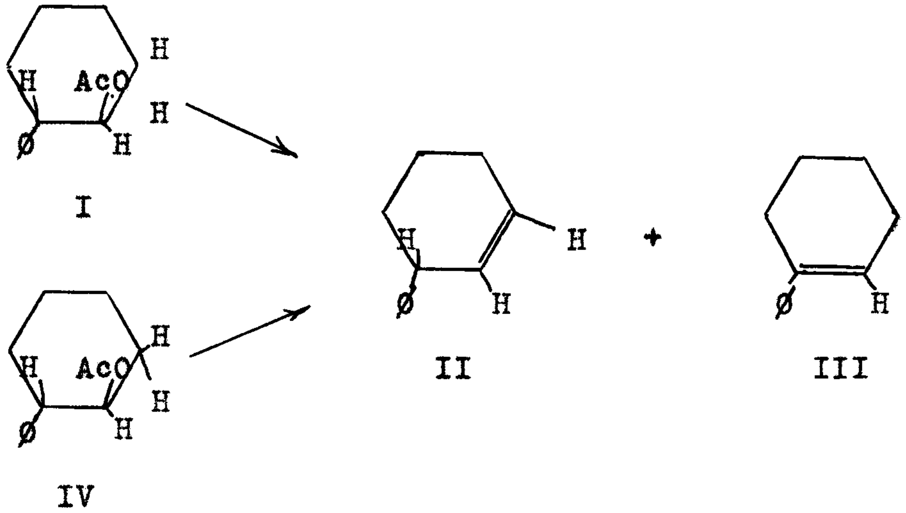
[51] D. H. Barton, J. Chem. Soc., 2174 (1949).

[52] E. Alexander and A. Mudrak, J. Am. Chem. Soc., 72, 1810 (1950).

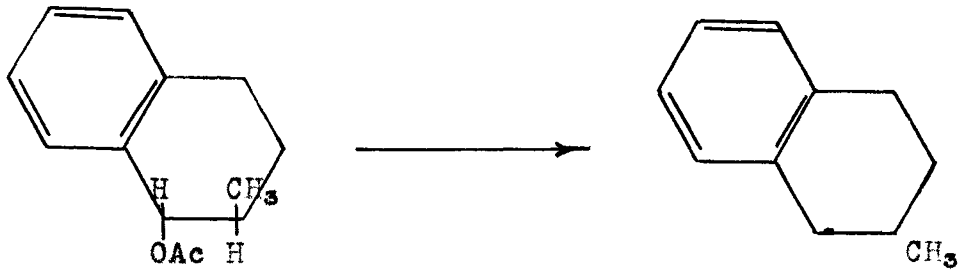
[53] E. Alexander and A. Mudrak, ibid., 72, 3194 (1950).

[54] W. Bailey and C. King, "Abstracts of the 122nd Meeting of the American Chemical Society", p. 3M (1952).

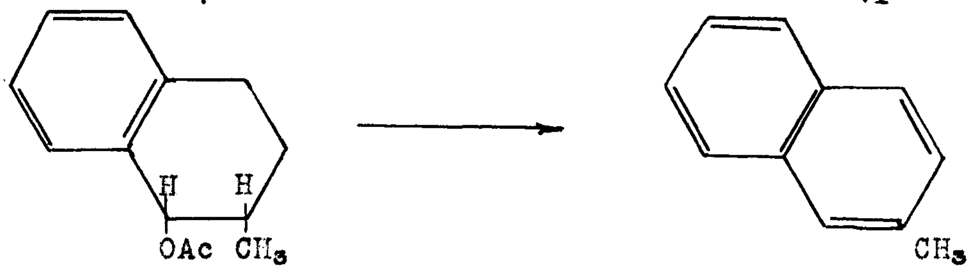
the *cis* acetate (I) gave 93 % of the 3-phenylcyclohexene (II), the product of *cis* elimination, and 7 % of 1-phenylcyclohexene (III). The *trans* acetate (IV), in which *cis* elimination can lead to either of the phenylcyclohexenes, gave 14 % of II and 86 % of III.



In another paper Alexander and Mudrak describe the results of the pyrolysis of *cis* and *trans* 2-methyltetralyl acetate[53]. It was found that the *cis* acetate, in which *cis* elimination is impossible, was more stable than the *trans* acetate. The *trans* acetate (V) gave the expected 2-methyl-3,4-dihydronaphthalene (VI). The *cis* acetate, when run under comparable conditions, did not give enough product for characterization. At higher temperatures, the *cis* acetate gave 2-methylnaphthalene (VIII). Since *cis* elimination is impossible for the *cis* acetate, 2-methylnaphthalene was formed by another reaction path.

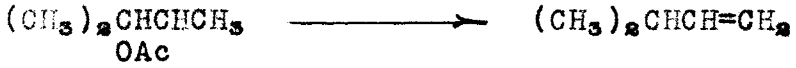


V VI



VII VIII

Most elimination reactions proceed to give an olefin having the largest number of alkyl groups as the principle product[55]. The second order elimination reaction involving an onium salt gives, as the principle product, the olefin containing the least number of alkyl groups (the Hoffman rule)[37]. The Tschugaef reaction has not been studied in this respect. A rather recent study indicates that the pyrolysis of esters follows the Hoffman rule[54]. The following reactions were run at 500°. Only one product was detected in each case.



$$\underset{\text{OAc}}{(CH_3)_2CHCHCH_3} \longrightarrow (CH_3)_2CHCH{=}CH_2$$

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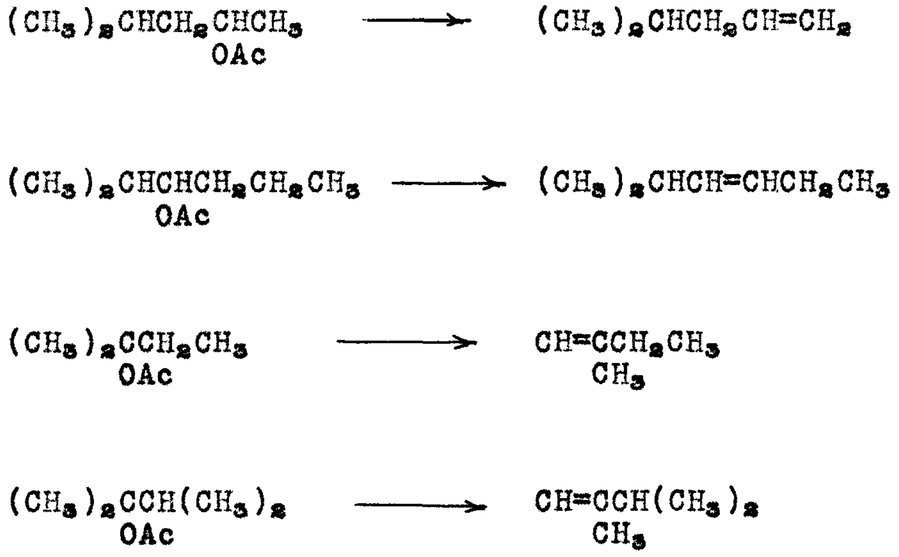
[55] p. 21, this thesis.



$$(CH_3)_2CHCH_2\underset{OAc}{CH}CH_3 \longrightarrow (CH_3)_2CHCH_2CH{=}CH_2$$

$$(CH_3)_2CH\underset{OAc}{CH}CH_2CH_2CH_3 \longrightarrow (CH_3)_2CHCH{=}CHCH_2CH_3$$

$$(CH_3)_2\underset{OAc}{C}CH_2CH_3 \longrightarrow CH{=}\underset{CH_3}{C}CH_2CH_3$$

$$(CH_3)_2\underset{OAc}{C}CH(CH_3)_2 \longrightarrow CH{=}\underset{CH_3}{C}CH(CH_3)_2$$

From this study it appears that the pyrolysis of acetates follows a highly selective path.

In the course of the present investigation this reaction was utilized as a tool for the proof of structure of certain substances and further observations were made as to the structural specificity of the reaction.

EXPERIMENTAL*

The Preparation of the Isomeric 1,2-Dimethylcyclohexanols, 1-Methylcyclohexanol and Their Derivatives

The preparation of 2-methylcyclohexanone

This preparation is essentially that of Signaigo and Crammer[56]. Five hundred grams of Eastman practical grade 2-methylcyclohexanol (4.4 moles) was mixed with a solution of one mole of sodium dichromate in 1.2 liters of water in a four liter beaker equipped with an efficient stirrer. The mixture was stirred rapidly and a mixture of 784 grams (8 moles) of sulfuric acid, one mole of sodium dichromate and 1.2 liters of water was added slowly to the reaction medium. The temperature of the reaction mixture soon reached 70° and the rate of addition was regulated to maintain this temperature. This addition took 3-4 hours. After the addition was complete the stirring was continued for an additional hour. The crude ketone was separated from the reaction medium using a four liter separatory funnel and

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*All melting points and boiling points in this section are uncorrected. Unless otherwise noted, the reagents were reagent grade and were used without further purification.

[56] F. K. Signaigo and P. L. Crammer, J. Am. Chem. Soc., 55, 3326-32 (1933).

the aqueous layer was extracted with several portions of chloroform. The crude ketone and the chloroform extracts were combined and washed with water and then with a 10 % sodium bicarbonate solution. The chloroform solution was dried over potassium carbonate. The solvent was removed and the ketone was distilled. The boiling point was 164.8-5.0°. Since the original alcohol has approximately the same boiling point (165-6°), the ketone always contains some 2-methylcyclohexanol as an impurity.

For certain preparations an alcohol free product was prepared. The alcohol was removed by precipitating the 2-methylcyclohexanone with sodium bisulfite, collecting the addition product in a large Buchner funnel, and washing the addition product well with ether. The ketone was regenerated by dissolving the addition product in a 10 % sodium carbonate solution. The ketone was taken up on benzene, dried and distilled.

Oxidation of the alcohol with chromic anhydride in acetic acid gave lower yields of the ketone than the method described above. An unidentified acid was produced in considerable amounts by the chromic anhydride oxidation.

A modification of the procedure described above involves the separation of the crude ketone from the reaction mixture by steam distillation.

The preparation of the 1,2-dimethylcyclohexanols and their separation

These compounds have been prepared and purified by Chiurdoglu[57]. The Grignard reaction between 2-methylcyclohexanone and methyl magnesium halide was carried out in the usual manner. Care must be taken to keep the reaction mixture at the reflux temperature of ether because the addition product solidifies on cooling and makes proper stirring of the solution impossible. Hydrolysis of the reaction mixture was best carried out with a saturated solution of ammonium chloride. The reaction mixture was then worked up in the usual manner. The yield is about 90 %.

A small amount of unreacted ketone always remained. This ketone cannot be removed by shaking the mixture with sodium bisulfite. In one experiment the crude alcohol was stirred for 24 hours with a saturated sodium bisulfite solution. An examination of the infrared spectra of the crude alcohol in a 0.1 millimeter cell still showed the presence of a ketone. The ketone could be removed quantitatively by warming the crude alcohol with p-nitrophenylhydrazine for several hours followed by distillation.

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[57] G. Chiurdoglu, P. Barchewitz and R. Freymann, Bull. soc. chim. Belg., 47, 453 (1938).

Alcohols purified in this manner tended to color on standing about a week, although their physical constants did not change. This color did not form in several months if the alcohols were stored in a deep freeze. Alcohols purified by fractional distillation and containing a small amount of ketone remained clear indefinitely. The pure alcohols can be distilled at their boiling points.

Fractionation of the isomeric alcohols at pressures of 25-45 millimeters through a center rod column operating at an efficiency of about 50 theoretical plates afforded a good separation. Less than a milliliter of mixed alcohols was usually obtained. Center cuts were used unless otherwise mentioned. The ratio of <u>trans</u> dimethyl alcohol to <u>cis</u> dimethyl alcohol was greater than 10:1. In an effort to obtain a larger supply of the <u>cis</u> alcohol the Grignard reagent was replaced in the preparation by methyl lithium. No noticeable change in the <u>cis</u>-<u>trans</u> ratio could be observed. The purity of these alcohols can be ascertained most readily by the determination of their melting points, since their cryroscoptic constants are rather large. A table of the physical constants of these compounds is given below.

Table II

Physical Constants of the Isomeric 1,2-Dimethylcyclohexanols

	B. P.		M. P.		$n_D^{25^\circ}$	
	a	b	a	b	a	b
cis 1,2-dimethylcyclohexanol	95.7°(53 mm)	82.8°(25 mm)	23.2°	24°	1.4628	1.4648
trans 1,2-dimethylcyclohexanol	86.8°(52 mm)	74.0°(25 mm)	13.2°	13°	1.4588	1.4613

[a] This thesis.

[b] G. Chiurdoglu, *Bull. soc. chim. Belg.*, *47*, 249 (1938); *ibid.*, *50*, 20 (1941).

The preparation of 1-methylcyclohexanol

This compound was prepared by the reaction of cyclohexanone and methyl magnesium halide. The preparation is similar to the preparation of the 1,2-dimethylcyclohexanols. Sodium bisulfite will remove any unreacted cyclohexanone. The compound, prepared in this manner, is quite pure and fractionation is probably unnecessary. The alcohol was fractionated through a center rod column. A 90 % yield of 1-methylcyclohexanol, B. P. 68° (24 mm), n_D^{25} 1.4582, Lit. B. P. 56.5 (10 mm), n_D 1.45874, was obtained[58].

The preparation of the acetates of 1-methylcyclohexanol and the 1,2-dimethylcyclohexanols

The following adaptation of conventional methods was found especially useful in the preparation of these acetates in yields of 90 % or better. About 0.05 mole of the alcohol was mixed with 30 milliliters of dimethylaniline and cooled in an ice bath. About 0.1 mole of acetyl chloride was added to this mixture in several portions with stirring.

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[58] K. Auwers, R. Hinterseber and W. Treppman, <u>Ann.</u>, <u>410</u>, 274 (1915).

The mixture was allowed to stand at room temperature for about an hour and heated on the steam bath for 3-4 hours. The reaction mixture was then cooled and poured into ice water containing about 10 % hydrochloric acid and covered with about 25 milliliters of pentane. The pentane was separated and extracted with 10 % hydrochloric acid in ice water until all the aniline was removed. The acetate in pentane was dried over potassium carbonate and distilled. Physical constants for the acetates are shown below.

Table III

Physical Constants of Some Alkylcyclohexyl Acetates

Cyclohexyl acetate	B. P.	n_D^{25}
cis 1,2-dimethyl-	84° (18 mm)	1.4440
trans 1,2-dimethyl-	78° (20 mm)	1.4401
1-methyl	74° (20 mm)	1.4435

In one experiment, the reaction mixture was heated on the steam bath for about 18 hours. The yield of acetate dropped to 50 %. An additional 35 % of the product was a mixture of olefins and acetate.

Other methods tried gave low yields and considerable amounts of unreacted alcohol. Heating the product on the steam bath is necessary, since very low yields of acetate were obtained on letting the reaction mixture stand for several days at room temperature.

The purity of the acetates was ascertained by an examination of their infrared spectra. Several strong lines present in the *cis*-dimethyl acetate were absent in the *trans*-dimethyl acetate and *vice versa*. The acetates were converted back to the alcohols by reduction with lithium aluminum hydride. The infrared spectra of the alcohols used as starting materials for the preparation of the acetates were identical with the alcohols obtained from the reduction of the acetates with lithium aluminum hydride.

Attempts to prepare 1-methylcyclohexyl p-toluenesulfonate

Considerable effort was given to the preparation of this tertiary tosylate from the alcohol and tosyl chloride. At no time was any product isolated.

The preparation was first attempted using sodium hydroxide or pyridine as the esterifying agent. The reaction temperature was varied from 50° to -20°. At high temperatures and short reaction times polymerization occurred. At lower temperatures and reaction times up to two weeks only the reactants could be recovered.

The reaction was also attempted using the alcoholate of sodium or potassium and tosyl chloride. The reaction of a tertiary alcohol and sodium or sodium hydride was too slow to be of any use. The alcoholate of potassium could be formed using potassium and refluxing in benzene or by the use of sodium-potassium alloy at room temperature. This reaction is slow and about a 100 % excess alcohol is necessary for the reaction time of about 8 hours. Again, either the reaction of the alcoholate with tosyl chloride did not occur to any extent at low temperatures and long reaction times, or at higher temperatures decomposition products rendered recovery of the reaction product, if formed, impossible.

There is no recorded preparation of a tertiary tosylate in the chemical literature. From the experience gained in the above attempts, the preparation of a tertiary tosylate is thought to be possible although the preparation of these compounds will probably demand exacting technique and carefully controlled conditions.

The Preparation of the Dimethylcyclohexenes and Proof of Their Structure

The preparation of 1,2-dimethylcyclohexene and 2,3-dimethylcyclohexene

These compounds were prepared by distilling crude 1,2-dimethylcyclohexanol from a few grams of iodine[56]. The crude dimethylcyclohexenes were washed thoroughly with concentrated sodium hydroxide and dried over Drierite. The olefins were fractionated from barium oxide with a center-rod column operating at an efficiency of about 50 plates. In a typical run, 50 grams of crude product gave a trace of 1-methylene-2-methylcyclohexane, 7-8 grams of a product boiling from 129-131 and yielding about 5 grams of 2,3-dimethylcyclohexene, and about 40 grams of pure 1,2-dimethylcyclohexene boiling sharply at 136.2° (n_D^{25} 1.4587).

The 1,2-dimethylcyclohexene has been prepared by many investigators. The weighted average of several values is B. P. 135.4-9, n_D^{25} 1.4590[59].

The 2,3-dimethylcyclohexene was isolated from the fractional distillation of the mixture of olefins boiling from 129-131°. The distillation was carried out in a

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[59] G. Egloff, "Physical Constants of Hydrocarbons, Vol. II," Reinhold Publishing Corporation, N. Y., 1940.

center rod column operating at an efficiency of about 70 plates. From about thirty grams of the mixture 6 grams of pure 2,3-dimethylcyclohexene was recovered. An additional 12 grams of material of better than 90 % purity was obtained. The criterion of purity was the comparison of the infrared spectra of successive samples with synthetic samples. The 2,3-dimethylhexane, B. P. 130.3-0.71, n_D^{25} 1.4534, could not be found in the literature.

The preparation of α-methyladipic acid from 2,3-dimethylcyclohexene

This acid was prepared from 2,3-dimethylcyclohexene by oxidation in aqueous permanganate to the keto-acid and then by treatment of the keto-acid with sodium hypochlorite.

Four grams of 2,3-dimethylcyclohexene was treated with 12 grams of potassium permanganate in 400 milliliters of water and stirred at ambient temperatures until the color of the permanganate disappeared. The solution was boiled to coagulate the manganese dioxide formed and filtered. The cooled solution was acidified with sulfuric acid and extracted with chloroform. The chloroform solution was dried and the chloroform was removed leaving a brown oil.

No attempt was made to identify the oil. The oil was oxidized with sodium hypochlorite by stirring the oil with an excess of sodium hypochlorite for 12 hours. At the end of this time the solution was brought to a boil, cooled and acidified. The solution was extracted with chloroform, dried and the chloroform removed. Recrystallization from hexane gave 1.3 grams of pure α-methyladipic acid, M. P. 64°, and 1.2 grams of crude α-methyladipic acid M. P. 62-64°. Total yield was 3.0 grams, 53 %. This product did not depress the melting point of α-methyladipic acid prepared by the permanganate oxidation of 3-methylcyclohexene[60].

The preparation of 1-methylene-2-methylcyclohexane

This compound has been prepared previously by Wallach[61]. A Reformansky reaction was run with ethyl bromoacetate on 2-methylcyclohexanone followed by dehydration of the resulting hydroxy-ester, saponification of the ester and pyrolysis of the resulting unsaturated acid.

Following Wallach's procedure the unsaturated acid was prepared. Simple distillation did not cause the unsaturated acid to decarboxylate.

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[60] L. Bouveault and R. Locquin, Bull. soc. chim., 3, 436 (1908).

[61] O. Wallach and E. Beshke, Ann., 347, 338 (1906).

The compound was then prepared by the pyrolysis of trans 1,2-dimethylcyclohexyl acetate. The method is described in a following section. An 80 % yield of 2-methylenemethylcyclohexane, B. P. 124.5-4.8°, n_D^{25} 1.4514, Lit. B. P. 122-125°, n_D^{22} 1.4516, was obtained on fractionation of the olefin mixture.

The compound was identified by its oxidation in neutral permanganate to 2-methylcyclohexanone. The yield was 65 %. The 2-methylcyclohexanone was characterized by its oxime M. P. 42-3°, Lit. M. P. 43°, and 2,4-dinitrophenylhydrazone, M. P. 137-8°, Lit. M. P. 137[62].

The Pyrolysis of the Isomeric 1,2-Dimethylcyclohexyl Acetates and 1-Methylcyclohexyl Acetate

The apparatus

The pyrolysis furnace consisted of a Fischer micro combustion furnace mounted vertically. The ends of the furnace were enlarged slightly to accommodate a 10 milliliter pyrex tube packed with 1/16 inch pyrex helices and fitted with ground glass joints. A plug of glass wool was used to

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[62] R. Shriner and R. Fuson, "The Systematic Identification of Organic Compounds," 2nd ed., John Wiley and Sons, Inc., New York, p. 221, 1940.

keep the helices in place. A dropping funnel with a by-pass (so that the nitrogen pressure was constant in the dropping funnel and the pyrolysis tube) was connected to the top of the pyrolysis tube. The bottom of the pyrolysis tube extended beyond the ground glass joint into a two-necked flask immersed in a salt ice bath. The second neck of the flask was provided with a nitrogen outlet. During a run, nitrogen was passed through the pyrolysis tube at a very slow rate. The temperature was measured with a 500° thermometer placed in the combustion furnace.

The procedure

The acetate pyrolysis was carried out in the conventional manner[48]. The acetate was added to the pyrolysis tube at a rate of 2-3 drops per minute. One pass through the pyrolysis tube was used. The pyrolysis products were collected in pentane over aqueous sodium bicarbonate. At the end of the run the pentane layer was separated and extracted with sodium bicarbonate. The pentane layer was dried over potassium carbonate. The pentane solvent was removed and the infrared spectrum of the residue was examined. Operating with one gram samples of the acetates, practically quantitative recovery of pyrolysis products was obtained. From 97-99 % of the acetate was converted to olefins.

The acetic acid olefin mixture obtained from trans acetate did not rearrange when passed through the pyrolysis tube a second time. The 2,3-dimethylcyclohexene and acetic acid passed through the pyrolysis tube unchanged.

The olefins on treatment with hydrogen and palladium on charcoal gave predominantly cis-1,2-dimethylcyclohexane and some of the trans compound. No 1,1-dimethylcyclohexane could be found by examination of the infrared spectra.

The analysis

The analysis of the pyrolysis products was accomplished with the aid of a Baird Associates Model B Infrared Spectrophotometer. The infrared spectra of the pyrolysis products were compared to those of synthetic mixtures. A cell of 0.073 mm was used throughout this work. The results of the analysis are shown in Table IV.

The Reaction of Hydrogen Bromide and Alcohols and Acetates

Reagents

Hydrogen bromide (Matheson, 99.9 %, bromine free) was condensed in the vacuum line and distilled twice before it was used.

Table IV

The Composition of the Olefins Obtained from the Acetate Pyrolysis

Cyclohexyl Acetate	Percent Olefins		
	1,2-dimethyl-cyclohexene	2,3-dimethyl-cyclohexene	2-methyl-methylene-cyclohexane
trans 1,2-dimethyl	0	7±3	93±5
trans 1,2-dimethyl	0	12±3	88±5
cis 1,2-dimethyl	4±3	5±3	91±5
cis 1,2-dimethyl	9±3	5±3	86±5
	methylene-cyclohexane	1-methyl-cyclohexene	
1-methylcyclo	86±5	14±5	
1-methylcyclo	87±5	13±5	

Normal pentane (Phillips, 99 %, 1 % isopentane) was dried over phosphorous pentoxide and distilled in the vacuum line from phosphorous pentoxide.

Acetic acid (Baker and Adamson, reagent grade) was used without further purification.

cis and trans 1,2-Dimethylcyclohexanol were prepared as described above.

cis and trans 1,2-Dimethylcyclohexyl acetate were prepared as described above.

The vacuum line

The vacuum line used for the reaction of hydrogen bromide with alcohols is shown in Figure 1. The apparatus was suggested by the vacuum line used by Tolbert[63]. Some examples of the use of this line will be described below.

Before the line was to be used, the entire system was evacuated overnight at a pressure of about 1 micron. At the start of a reaction hydrogen bromide was introduced into the system and purified in the following fashion. The stopcocks leading to the storage bulb A and the reaction flasks, C, D, E, F and G, to the traps and pumps and to the vacuum gage were closed. A tank of hydrogen bromide

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[63] B. M. Tolbert, J. Am. Chem. Soc., 69, 1530 (1947).

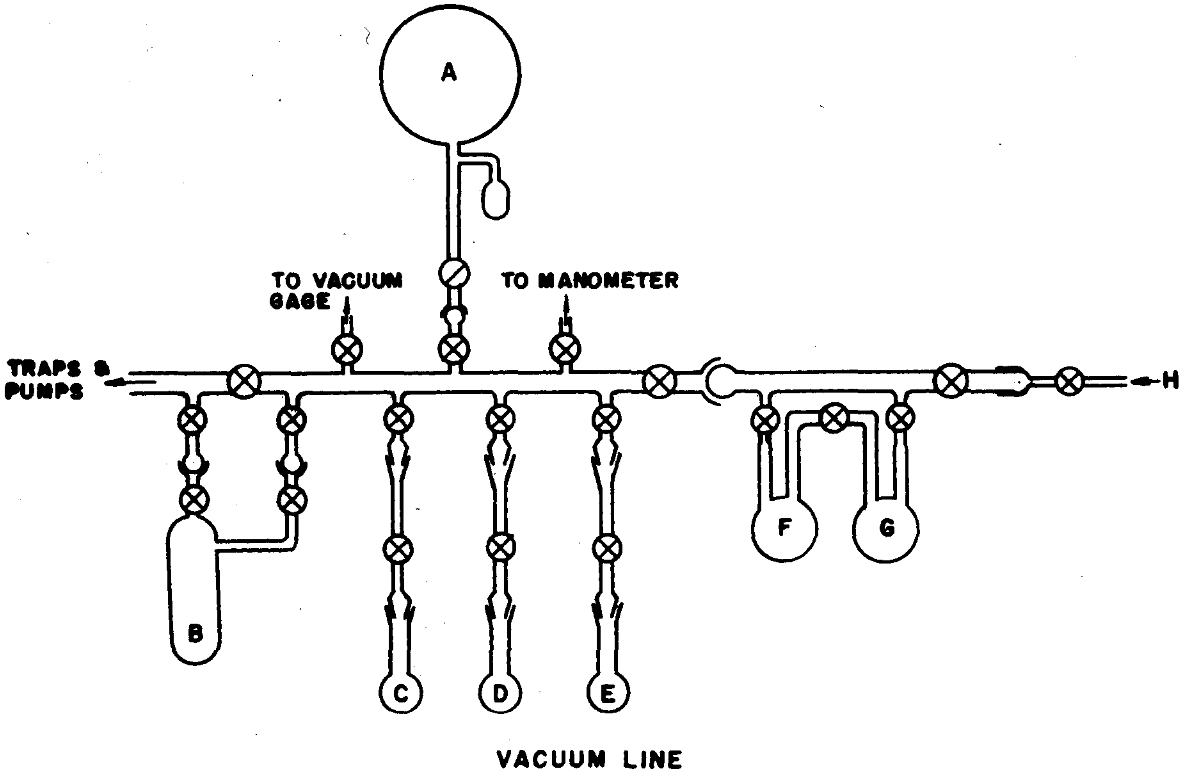


Figure 1

Vacuum Line

was attached at the inlet H with a short piece of Tygon tubing. The stopcock leading to the pumps and traps was opened and the line and the connection to the tank of hydrogen bromide was evacuated. The stopcock leading to the pumps and traps was closed, and the stopcocks leading to F and G were opened. F and G were immersed in liquid nitrogen. Hydrogen bromide was allowed to flow into the system and condensed in F and G. After sufficient hydrogen bromide had condensed, the tank of hydrogen bromide and the stopcocks at H were closed. The stopcock to the traps and pumps was opened and the system pumped out briefly. The hydrogen bromide collected in G was distilled into F. G was closed off from the rest of the system and the entire system including F was evacuated for about ten minutes. The pumps and traps were again closed off and G was opened to the rest of the system. The contents of G were distilled stepwise into F by filling A until the pressure of the system rose to nearly 760 millimeters, closing off G and then condensing the contents of A into F. F was then closed, G was opened and the process continued. Since A holds about 2.2 liters, the hydrogen bromide could be measured into F by approximately tenths of moles. Some residual hydrogen bromide was always left in G. This served to trap any water that may have been present. When as much hydrogen bromide as was needed was moved to F, F was closed off and the remaining hydrogen bromide in C was pumped into the removable trap B. As hydrogen bromide was needed for a reaction it was moved from F to A and thence to the reaction flask. At the end of a series of reactions some hydrogen bromide was left in F to trap any water or bromine present. At any point excess hydrogen bromide could be disposed of by pumping it into the removable trap B.

Other reactants could be handled and purified using similar techniques. Pentane, for example, was purified by distillation from phosphorous pentoxide from E onto phosphorous pentoxide in D and finally into C. Because C could be removed from the line several reaction flasks could be filled from D.

Analysis

The yields from the reaction were essentially quantitative. Infrared spectra were run on all products, in 0.07 millimeter cells. Evidence for olefin formation or for the presence of unreacted alcohol could not be found in the infrared spectra.

In the case of the cis-trans bromides, analysis was carried out by an examination of the E2 kinetics if the amount of cis bromide was more than 20 %. A qualitative estimate of the isomer ratio of the reaction products, if the amount of cis bromide was less than 20 %, could be made by comparing the infrared spectra with synthetic mixtures.

A summary of these reactions is given in Table V. Details of the individual reactions are given below.

Reactions in acetic acid

1-Methylcyclohexanol, 1 gram, was mixed with 20 milliliters of glacial acetic acid. The flask was attached to the vacuum line, cooled in dry ice, evacuated to the vapor pressure of acetic acid at -75° and allowed to warm to near room temperature. As the mixture started to melt, a bulb containing 2.1 liters of gaseous hydrogen bromide at approximately 1 atmosphere was opened. The pressure dropped sharply. The flask was cooled in liquid nitrogen, the residual hydrogen bromide condensed on the neck of the reaction flask, the bulb originally containing the hydrogen bromide was closed off and the contents of the flask allowed to warm to room temperature. This was accomplished quickly and the acetic acid-alcohol mixture soon melted again and absorbed most of the remaining hydrogen bromide. The mixture on melting was stirred for a few minutes and allowed to stand for about two hours at 25°. On occasion, the reaction mixture was worked up after shorter intervals and the reaction was found to be complete. After two hours the

Table V

The Reaction of Hydrogen Bromide and <u>cis</u> and <u>trans</u> 1,2-Dimethylcyclohexanyl Alcohols, Acetates and Bromides

Reaction Medium	Temp.	Minute Reaction	Reactant	<u>cis</u> Bromide[a]
acetic acid	25°	3	<u>trans</u> alcohol	8
" "	"	6	" "	12
" "	"	60	" "	16
" "	"	60	" "	16
" "	"	120	" "	15
" "	"	120	" "	16
" "	"	3	<u>cis</u> "	28
" "	"	60	" "	24
" "	"	60	" "	20
" "	"	180	" "	16
" "	"	60	<u>trans</u> acetate	16
" "	"	60	<u>cis</u> "[a]	17
" "	"	60	<u>trans</u> bromide	17
" "	"	60	<u>cis</u> "[b]	23
" "	"	60	" "[c]	19
pentane	0°	60	<u>trans</u> alcohol	23
"	"	60	" "	20
"	"	60	<u>cis</u> "	36
"	"	60	" "	25
"	-78°[d]	60	<u>trans</u> "	26
"	-78°	60	" "	24
"	-78°[d]	60	<u>cis</u> "	71
"	"	60	" "	65
"	-78°	60	" "	54
"	"	60	" "	62
"	"	60	" "	48
"	"	60	" "	52

[a] Estimated error, ±2 %.

[b] <u>trans</u> (64 %) and <u>cis</u> (36 %) 1,2-Dimethylcyclohexyl bromide.

[c] <u>trans</u> (75 %) and <u>cis</u> (25 %) 1,2-Dimethylcyclohexyl bromide.

[d] Reaction mixture was frozen in liquid nitrogen and warmed to -78° during the reaction time.

reaction mixture was poured into a separatory funnel containing 30 milliliters of pentane and 20 milliliters of water. The heterogeneous mixture was shaken and the aqueous layer was separated. The pentane solution was washed twice with 10 milliliter portions of water and once with 5 milliliters of sodium bicarbonate. The pentane solution was then dried over Drierite for about 15 minutes and the pentane was removed at 20 milliliters on the vacuum line.

In some runs and in large scale preparations, 30-32 % hydrogen bromide in acetic acid (Eastman, reagent grade) was used. Three to four times the calculated amount of this reagent was added. The rest of the procedure is the same as described above. Both procedures gave the same results.

One gram samples of <u>cis</u> and <u>trans</u> 1,2-dimethylcyclohexanol and <u>cis</u> and <u>trans</u> 1,2-dimethylcyclohexyl acetates and bromides were treated with hydrogen bromide in acetic acid by the method described above.

Reactions in pentane near 0°

The 0° bath was prepared from chipped ice and water. In a typical run <u>cis</u> 1,2-dimethylcyclohexanol, 1 gram, was placed in a 25 milliliter flask on the vacuum line. Ten milliliters of pentane was distilled from phosphorous pentoxide into the flask containing the alcohol. The solution of pentane and alcohol was placed in a bath at the desired temperature. The solution of alcohol and pentane was stirred and allowed to absorb hydrogen bromide gas. The initial pressure in the system was about 600 milliliters. The pressure of the hydrogen bromide decreased and within ten minutes became constant. The reaction mixture was stirred for about 45 minutes. At the end of the reaction time, the bromide was recovered by the method described in the last section.

One gram samples of trans 1,2-dimethylcyclohexyl alcohol were treated in the same manner.

Reactions in pentane near -78°

The solution was maintained at about -78° by means of a powdered dry ice bath. One gram samples were run in the same manner described above except for the following modifications. When the hydrogen bromide was released in the system the pressure dropped rapidly to about 100 millimeters and a solid addition compound formed. At the end of the 45 minute reaction time the excess hydrogen bromide was distilled from the solution. The solution was then worked up in the usual way. In some runs the hydrogen bromide was condensed in the reaction mixture at -180° and warmed quickly to -80°.

The Solvolysis of Some Alkylcyclohexyl Bromides

Reagents

Methyl ethyl ketone (Eastman Kodak, reagent grade) was dried over Drierite for two days and distilled through a short column.

Lithium perchlorate ($LiClO_4 \cdot 3H_2O$--G. F. Smith Co.) was dehydrated in vacuo for 12 hours at 130°. An aqueous solution was made up to 2.5 N by dissolving the dehydrated lithium perchlorate in the requisite amount of redistilled water.

Triethyl amine (Eastman Kodak, reagent grade) was dried over sodium and distilled. A center cut, B. P. 88°, was used. An approximately 0.01 N solution was prepared in toluene or benzene and standardized against a standard hydrochloric acid solution before and after each run. The normality of this solution remained fairly constant for several months.

Toluene (Merck, reagent grade) was dried over sodium and distilled through a short column.

Benzene (Mallinckrodt, reagent grade) was dried over sodium and distilled through a short column.

Brom phenol blue (Harleco) was dissolved in methyl ethyl ketone to make a 0.2 % solution.

Hydrochloric acid was used to prepare a standard aqueous acid solution, approximately 0.03 N. It was standardized periodically against standard barium hydroxide.

Barium hydroxide was used as a standard aqueous base, approximately 0.04 N. The base was standardized periodically with potassium acid phthalate.

1-Methylcyclohexyl bromide, cis-1,2-dimethylcyclohexyl bromide and trans 1,2-dimethylcyclohexyl bromide have been described elsewhere.

The kinetic method

The method used to follow the solvolysis of the alkylcyclohexyl bromides consisted of placing about 0.2 milliliters of the bromide in a solution of water and methyl ethyl ketone. A measured portion of this solution was removed from the reaction mixture, placed in methyl ethyl ketone (to quench the reaction) and the hydrogen bromide liberated was titrated with a standard solution of triethyl amine in benzene or toluene. The amount of alkyl bromide was found by titrating a known amount of solution at "infinite time".

The following procedure was used. The solvolysis mixture was prepared by mixing together 200 milliliters of methyl ethyl ketone, 10 milliliters of 2.5 N lithium perchlorate solution and 40 milliliters of water. The total volume of this solution is 245.0±0.5 milliliters at 25° and the final normality of the lithium perchlorate is 0.0980. The solvolysis medium was allowed to adjust itself to the temperature of the constant temperature bath for at least one hour. At this time, ten milliliters of solution was removed and titrated in the manner described below. This was taken as the blank and was invariably zero.

About 190 milligrams (1 millimole) of the alkylcyclohexyl bromide was pipetted into the reaction flask with vigorous swirling. Zero time was taken as the time when about half the bromide was introduced. The flasks were quickly returned to the constant temperature bath. The temperature of the bath was 25.3°. The temperature remained constant to ±0.02°. After about 60 minutes, 10 milliliters was pipetted from the reaction flask to a beaker containing about 50 milliliters of methyl ethyl ketone, and titrated with previously standardized 0.01 N triethyl amine. One drop of 0.2 % solution of brom phenol blue was used as an indicator. The endpoint is quite sharp. The indicator changes from yellow to green to deep blue. The appearance of the green color was taken as the endpoint. Similar titrations were run at intervals of 30 to 90 minutes over the first part of the run. The reaction was generally allowed to proceed overnight and titrations were continued the next day.

Occasionally, the alkylcyclohexyl bromides were weighed into the solvolysis mixture. More often, the amount of bromide was determined by allowing the reaction to stand at room temperature for 3 or 4 days, when the solvolysis was essentially complete, and then determining a final titer.

Calculations

The unimolecular rate constants were calculated from the integrated form of the rate equation,

$$k = \frac{1}{t} \ln \frac{a-x}{a}$$

where $\underline{a}$ is the initial concentration of the alkylcyclohexyl bromide and $\underline{x}$ is the concentration of hydrogen bromide liberated after time $\underline{t}$. A typical rate run is shown in Table VI. Table VII shows the values obtained for the unimolecular rate constants.

Table VI

The Solvolysis of trans 1,2-Dimethylcyclohexyl Bromide in 55.4 Mole Percent Water in Methyl Ethyl Ketone at 25.3° and Constant Ionic Strength

Vol. of Titrant*	Time (min.)	10^4k (min^{-1})
0.95	73	207
1.97	167	207
2.90	264	219
3.52	350	208
4.49	506	212
5.21	682	215
6.43	1329	203
6.54	1490	215
6.72	1938	216
6.81		
		Average.........211

---

*Initial normality of the bromide.....0.00729
Normality of the titrant.............0.0106$_5$

Table VII

The Solvolyses of Alkylcyclohexyl Bromides at 25.3°

Cyclohexyl Bromide	Initial Normality of Bromide	$k \times 10^4$ (min^{-1})	% Total Reaction
trans 1,2-Dimethyl	0.00488	207	98
" "	0.00729	211	97
" "	0.00563	209	93
" "	0.00541	209	97
" "	0.00397	206	94
" "	0.00795	205	98
	Average....	208	
cis 1,2-Dimethyl[*]	0.00541	209	98
" "	0.00643	214	93
" "	0.00613	216	98
" "	0.00492	208	94
	Average....	212	
1-Methyl	0.00540	194	95
"	0.00648	197	92
"	0.00674	199	94
"	0.00716	194	89
	Average....	196	

---

[*] A mixture of *cis* and *trans* compound containing 71 % *cis*.

The Elimination Reactions of Some Alkylcyclohexyl Bromides

Reagents

Ethanol (reagent grade) was distilled from sodium hydroxide after refluxing over sodium hydroxide for about 10 hours. Water was added to the ethanol to make a solution 98 weight percent ethanol, $n_D^{25^\circ}$ 1.35999, d. 0.79106.

Methanol (Baker and Adamson reagent grade) was used without further purification.

Sodium methylate and sodium hydroxide were prepared by dissolving freshly cut sodium in methanol or 98 weight percent ethanol. The solution was made up fresh before use and standardized against standard hydrochloric acid.

Cyclohexane (Eastman reagent grade) was distilled from sodium shavings.

Lithium perchlorate has been described elsewhere.

Silver nitrate (Baker and Adamson reagent grade) was dissolved in distilled water to make a 0.05 normal solution. The solution was standardized periodically against sodium bromide.

Potassium thiocyanate (Baker and Adamson reagent grade) was dissolved in distilled water to make a 0.05 normal solution and compared with the standard silver nitrate solution before each run.

Ferric ammonium sulfate (Baker and Adamson reagent grade) was dissolved in 3 normal nitric acid to make a saturated solution.

Nitric acid (Baker and Adamson reagent grade) was mixed with distilled water to give a 3 normal solution.

Triethyl amine in benzene has been described elsewhere.

cis 1,2-Dimethylcyclohexyl bromide and trans 1,2-dimethylcyclohexyl bromide have been described elsewhere.

The kinetic method

Procedure I was used to detect the solvolysis rates of the *cis* and *trans* 1,2-dimethylcyclohexyl bromides in 98 weight percent ethanol or methanol. The method was essentially the same as that described on page 59. Lithium perchlorate was added to give the desired ionic strength. The infinite titer was determined by allowing an aliquot to stand about 24 hours with 4 to 5 times its volume of water.

Procedure II was used to determine the E2 rates of the *cis* and *trans* 1,2-dimethylcyclohexyl bromide. Exactly 100 milliliters of previously standardized sodium hydroxide in 98 weight percent ethanol or sodium methylate in methanol was pipetted into the reaction flask and allowed to stand in the constant temperature bath at 25.3°. The constant temperature bath has been described on page 60. After allowing the temperature of the solution to adjust itself to that of the bath about 0.4 milliliter of bromide was quickly pipetted into the reaction flask. Five milliliter aliquots were removed from the reaction flask from time to time. The reaction was quenched by allowing the contents of the pipette to mix with about 25 milliliters of cyclohexane. The mixture in the cyclohexane was extracted twice with 20 milliliter portions of 3 normal nitric acid. The water extracts were titrated for bromide by the Volhard method[63a]. The original concentration of the bromide was determined by mixing a five milliliter sample of the reaction mixture into 4 to 5 times its volume of water and allowing the mixture to stand for 24 hours. A final titer was then determined.

Calculations

The unimolecular rate constants were calculated from the integrated form of the rate equation,

$$k = \frac{1}{t} \ln \frac{a-x}{a} \qquad (1)$$

where a is the original concentration of the alkylcyclohexyl bromide and x is the concentration of hydrogen bromide

[63a] Willard & Furman

liberated after time t. Table VIII shows a typical rate determination. Table IX shows the effect of varying the ionic strength of the solvolysis rate. Table X shows the solvolysis rates obtained.

The pseudounimolecular rate constants, k', were calculated from the equation above. The second order rate constants, k_2, were then calculated from the equation shown below, where B is the average concentration of the base during time t.

$$k' = k_2 [B] + k_1 \qquad (2)$$

Since samples of cis 1,2-dimethylcyclohexyl bromide free from trans 1,2-dimethylcyclohexyl bromide were unobtainable, advantage was taken of the fact that the cis 1,2-dimethylcyclohexyl bromide reacted at a rate slower than the trans 1,2-dimethylcyclohexyl bromide. Rates on the cis compound were determined after more than 99 % of the trans compound had reacted. Typical rate runs are shown in Table XI. The effect of varying the base concentration is shown in Table XII. The second order rates obtained are shown in Table XIII.

Table VIII

The Solvolysis of trans 1,2-Dimethylcyclohexyl Bromide in 98 Weight Percent Aqueous Ethanol at 25.3° and Constant Ionic Strength

Vol. of Titrant*	Time (min.)	10^5k (min^{-1})
.46	126	46
.68	260	47
1.00	380	47
1.20	465	47
1.61	630	46
2.17	1225	45
2.43	1845	46
2.53	2020	47
6.22		
	Average.......	$46._5$

---

*Initial normality of the bromide..........0.179
Normality of the titrant.................0.0289

Table IX

The Effect of Varying the Ionic Strength on the Solvolysis of trans-1,2-Dimethylcyclohexyl Bromide in 98 Weight Percent Aqueous Ethanol at 25.3°

Normality $LiClO_4$	Initial Normality Bromide	10^5k (min^{-1})
0.000	0.0083	36
0.059	0.0084	41
0.118	0.0073	47
0.177	0.0091	53
0.236	0.0088	58

Table X

The Solvolysis of cis and trans 1,2-Dimethylcyclohexyl Bromide

1,2-Dimethyl-Cyclohexyl Bromide	Initial Normality of Bromide	10^5k_1 (min^{-1})	% Total Reaction Followed
trans	0.179	$46._5$	40
"	0.248	$45._2$	26
"	0.193	$44._7$	32
	Average......	$45._5$	
"	0.0189	307[a]	55
"	0.0249	312[a]	62
"	0.0256	302[a]	34
	Average.....	307[a]	
cis[b]	0.213	44.5	82
"	0.184	$44._8$	79
"	0.255	$46._3$	88
	Average......	$45._2$	

---

[a] Solvolysis run in methanol.

[b] A mixture of cis and trans compound containing 62 % cis.

Table XI

The Second Order Elimination Reaction of *trans* 1,2-Dimethylcyclohexyl Bromide in 98 Weight Percent Aqueous Ethanol, 0.520 Normal in Sodium Hydroxide at 25.3°

Vol. of Titrant*	Time (min.)	10^4k (min^{-1})
0.78	32	93
0.94	41	90
1.07	52	84
1.33	66 1/2	88
1.49	75	90
1.74	96 1/2	88
1.86	108	88
1.98_5	124	85
2.14	138	88
2.31	164	87
		Average.......88

*Normality of the titrant..............0.0475
Initial normality of the bromide......0.0304

Table XII

The Effect of the Variation of the Base Concentration On the Elimination Reaction of <u>cis</u> and <u>trans</u> 1,2-Dimethylcyclohexyl Bromide in Ethanol and Methanol at 25.3°

Reaction Medium	1,2-Dimethyl-cyclohexyl Bromide	Normality of Base	First Order Rate Constant (min^{-1})	Second Order Rate Constant (min^{-1})*
sodium methylate/methanol	<u>trans</u>	0.0000	0.0036	-----
" " "	"	0.0151	0.0042	-----
" " "	"	0.0303	0.0046	0.032
" " "	"	0.0605	0.0054	0.030
" " "	"	0.158	0.0067	0.020
sodium hydroxide/ethanol	"	0.0000	0.00045	-----
" " "	"	0.0395	0.0012	0.020
" " "	"	0.0790	0.0016	0.015
" " "	"	0.345	0.0052	0.014
" " "	"	0.520	0.0088	0.015
" " "	<u>cis</u>	0.0000	0.00045	-----
" " "	"	0.345	0.00098	0.0012
" " "	"	0.520	0.00146	0.0013

*Calculated from equation 2, page 67.

Table XIII

Second Order Rate Constants for the Elimination
Reaction Between cis and trans
1,2-Dimethylcyclohexyl Bromide
in 0.520 Normal Sodium Hydroxide
in 98 Weight Percent Ethanol
at 25.3°

1,2-Dimethyl-Cyclohexyl Bromide	Initial Normality of Bromide	k'(min^{-1}) (a)	$k_2(min^{-1})$ (b)
trans	0.0304	0.0088	0.0155
"	0.0294	0.0090	0.0160
"	0.0230	0.0084	0.0149
		Average....	0.0155
cis	0.0236	0.00144	0.00126
"	0.0302	0.00146	0.00130
"	0.0307	0.00149	0.00135
		Average....	0.00130

[a] Pseudo first order rate constant.

[b] Second order rate constant. The first order rate constant in this medium is estimated to be 0.00080.

Product analysis

It was of interest to obtain a knowledge of the products obtained from the alkylcyclohexyl bromides when treated with various bases. The results of this investigation are shown in Table XIV. These results are of a qualitative nature (with the exception of the reaction of trans 1,2-dimethylcyclohexyl bromide with sodium hydroxide in ethanol) and must be considered as unconfirmed results. The procedures used are given below. The contents of these mixtures were determined by comparing their infrared spectra with the infrared spectra of synthetic mixtures by the method described on page 48.

Pyridine, 2-picoline and 2,6-lutidine were used to prepare olefins from trans 1,2-dimethylcyclohexyl bromide. A 2 gram sample of the bromide was treated with 30 milliliters of either pyridine and collidine for about 4 days at room temperature. At this time the mixture was heated at 60° for 3 hours. The mixture was cooled to room temperature and carefully washed into a separatory funnel with 60 milliliters of pentane and 30 milliliters of water. The solution was washed free of organic base with dilute sulfuric acid. The pentane solution was dried and the pentane removed in the usual manner. The residual oil was dried over a few grains of potassium carbonate. The yield of product was

Table XIV

Product Analysis of the Reaction of cis and trans 1,2-Dimethylcyclohexyl Bromide with Various Bases at 25°

1,2-Dimethylcyclohexyl Bromide	Base	Products: 1,2-Dimethylcyclohexene	Products: 2,3-Dimethylcyclohexene	Products: 2-methylenecyclohexene
trans	2,6-lutidine[a]	100	0	0
"	2-picoline	100	0	0
"	pyridine	100	0	0
"	$LiAlH_4$	100	0	0
"	"	100	0	0
"	sodium methylate	100	0	0
"	sodium methylate	100	0	0
"	sodium ethylate	100	0	0
"	sodium ethylate	100	0	0
cis[b]	sodium ethylate	87±5	0	13±5
" [c]	sodium ethylate	50±5	0	50±5
trans	ethanol-water	96±3	0	4±3

---

[a] Reaction incomplete after four days.

[b] Mixture of cis and trans bromides containing 22 % cis.

[c] Mixture of cis and trans bromides containing 63 % cis.

better than 95 %. An infrared spectrum was taken of the mixture and the mixture of olefins was hydrogenated at atmospheric pressure in ethyl alcohol with palladium on charcoal as a hydrogenation catalyst. The product from the reaction of lutidine contained large amounts of unreacted bromide and was not hydrogenated. The saturated hydrocarbons were taken up in pentane washed with water and passed through a small column packed with alumina to remove the last traces of ethyl alcohol. The pentane was removed and an infrared spectrum taken. The infrared spectra revealed no rearranged products and was identical with the spectra of pure <u>cis</u> 1,2-dimethylcyclohexane. The <u>trans</u> isomer could not be detected.

<u>Sodium methylate</u> in absolute methyl alcohol was used to prepare olefins from the <u>trans</u> 1,2-dimethylcyclohexyl bromide. A 2 gram sample of the bromide was mixed with a 2 normal solution of sodium methylate and allowed to stand for three days. The solution was then mixed with an equal volume of pentane and washed thoroughly with water and dried. The pentane solution containing the olefins was then chromatographed to remove the last traces of methyl alcohol and the pentane was removed. The yields were better than 95 %. An infrared spectrum was taken of the products. The products were hydrogenated, as described above, and yielded <u>cis</u> 1,2-dimethylcyclohexane (infrared spectra).

Lithium aluminum hydride in ether gave olefins from *trans* 1,2-dimethylcyclohexyl bromide. The alkyl bromide was treated with three times the calculated amount of a saturated ether solution of lithium aluminum hydride in the usual manner. The mixture was allowed to stand at room temperature for three days and hydrolized with sodium potassium tartrate solution. The olefins were taken up in pentane, dried and the pentane removed. The yield was about 85 %. An infrared spectrum of the mixture was taken. The olefin mixture was hydrogenated, as described above, and took up the theoretical amount of hydrogen yielding *cis* 1,2-dimethylcyclohexane.

The solvolysis products of *trans* 1,2-dimethylcyclohexylbromide in a 60 % by volume methyl alcohol solution were examined. After the mixture of 2 grams of alkyl bromide and 50 milliliters of the alcohol-water mixture were allowed to stand for 2 days, the mixture was extracted with pentane, washed with water, dried, passed through a chromatography column and the pentane removed. An infrared spectrum was taken of the products. The products were hydrogenated to *cis* 1,2-dimethylcyclohexane as described above.

Addition of Hydrogen Bromide to 1,2-Dimethylcyclohexene and other Olefins

The olefins and other reagents and the vacuum line have been previously described. The methods used were described on pages 50-57. The results are shown in Table XV. Some observations are recorded below.

Reactions in acetic acid

The 1,2-dimethylcyclohexene, 2,3-dimethylcyclohexene and 2-methylenemethylcyclohexane were treated with hydrogen bromide in acetic acid. The reaction was exothermic and rapid. The solution was colored an intense red at the end of a run. This color formed almost immediately with the 2,3-dimethylcyclohexene. The red color could be removed by extracting with water.

Reactions in pentane near 0° and -78°

The 1,2-dimethylcyclohexene reacted readily even at -78°. Apparently the reaction is complete in about 10 minutes. The reaction mixture remained colorless throughout the reaction at both temperatures.

Table XV

Reaction Products of Hydrogen Bromide Addition to 1,2-Dimethylcyclohexene

Solvent	Temp.	Reaction Time (Min.)	Percent *cis* 1,2-Dimethylcyclohexyl Bromide
acetic acid	25°	60	16
" "	"	60	17
" "	"	3	7
" "	"	60	14[a]
" "	"	3	12[a]
" "	"	60	16[b]
" "	"	3	28[b]
ether	"	30	0
pentane	0°	30	1
"	"	30	2
"	"	30	1[c]
"	"	30	5[c]
"	-78°	30	33[d]
"	"	30	22[d]
"	"	30	19[d]
"	"	30	0
"	"	30	1
"	"	30	0
"	"	30	3[c]
"	"	30	0[c]

[a] Addition to 3,4-Dimethylcyclohexene.

[b] Addition to 2-Methylenemethylcyclohexene.

[c] Care to operate in a clean vacuum line was neglected in these runs.

[d] Reaction mixture was frozen in liquid nitrogen and warmed to -78° during the reaction time.

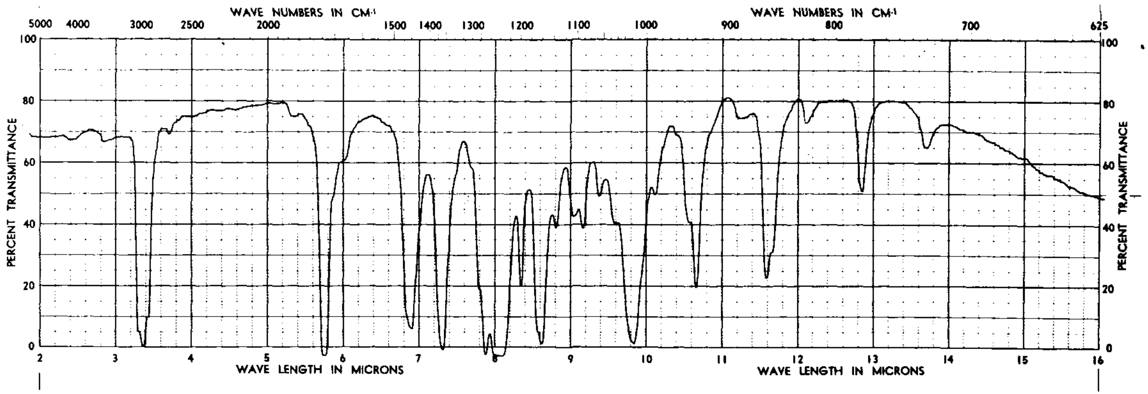
Some Infrared Spectra

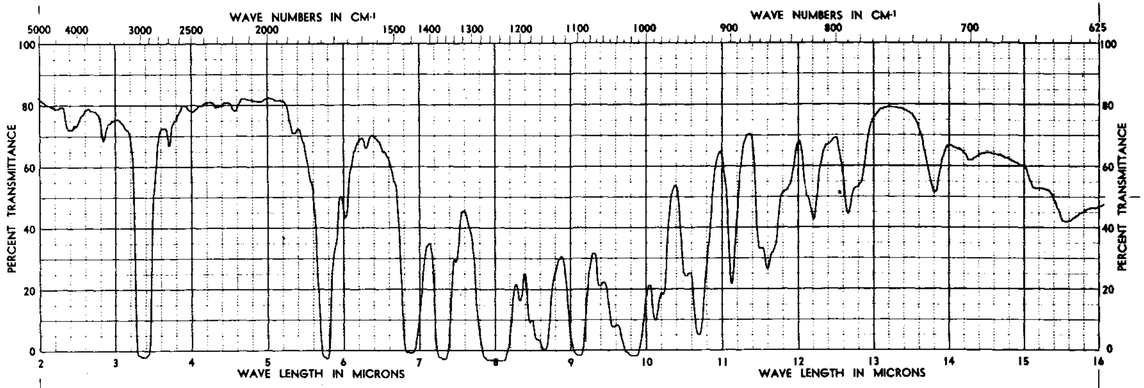
The infrared spectra for several compounds described previously are shown on the following pages. The spectra were obtained on a Baird Associates Model B infrared spectrophotometer. Bands useful in the identification of these compounds are evident. The infrared spectra for the *cis* and *trans* 1,2-dimethylcyclohexanols have been recorded elsewhere[57].

Plate 1. trans 1,2-Dimethylcyclohexyl acetate in a capillary cell.

Plate 2. cis 1,2-Dimethylcyclohexyl acetate in a capillary cell.

Plate 3. 1-Methylcyclohexyl acetate in a capillary cell.


WAVE NUMBERS IN CM-1
5000
4000
3000
2500
2000
1500
1400
1300
1200
1100
1000
900
800
700
625
PERCENT TRANSMITTANCE
0
20
40
60
80
100
WAVE LENGTH IN MICRONS
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16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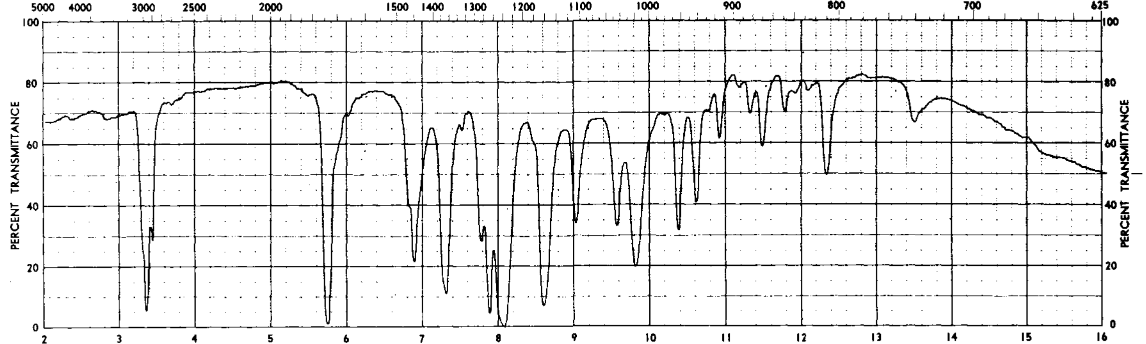
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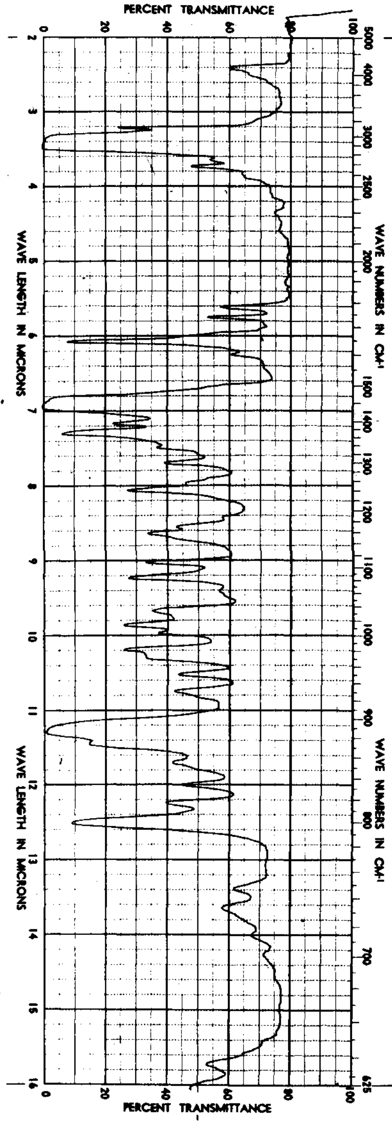
Plate 4. 1,2-Dimethylcyclohexene. Cell length: 0.072 mm. Note the faint band at 6.02 microns characteristic of symmetrical olefins. The 7.40 band is useful in the identification of this compound.

Plate 5. 2,3-Dimethylcyclohexene. Cell length: 0.072 mm. Characteristic bands are marked.

Plate 6. 2-Methylenemethylcyclohexane. Cell length: 0.072 mm. This compound is contaminated with 1 % trans acetate (Figure 2) and about 2 % 2,3-dimethylcyclohexene (Figure 6).

Plate 7. Olefin mixture from pyrolysis of cis 1,2-dimethylcyclohexyl acetate. Cell length: 0.072 mm.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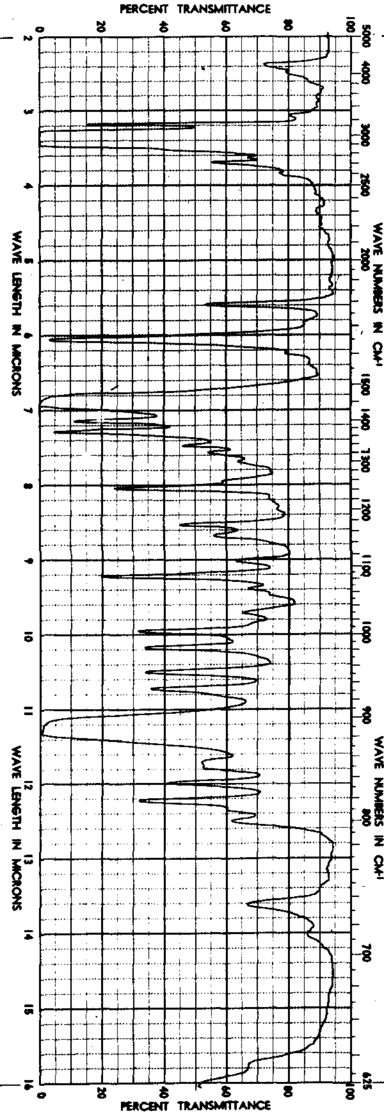
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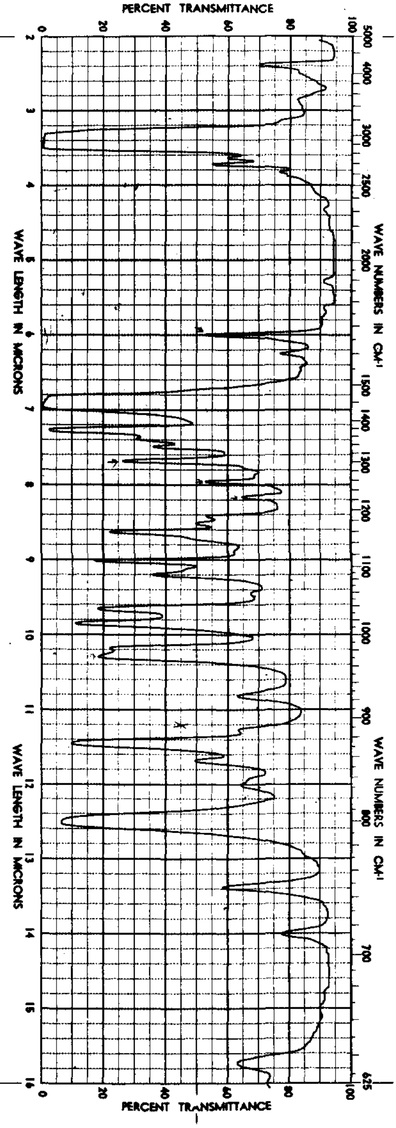
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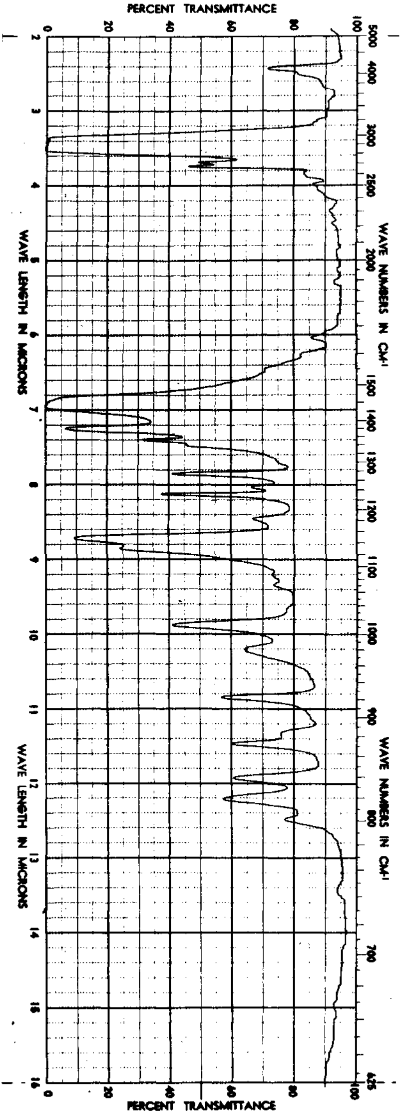
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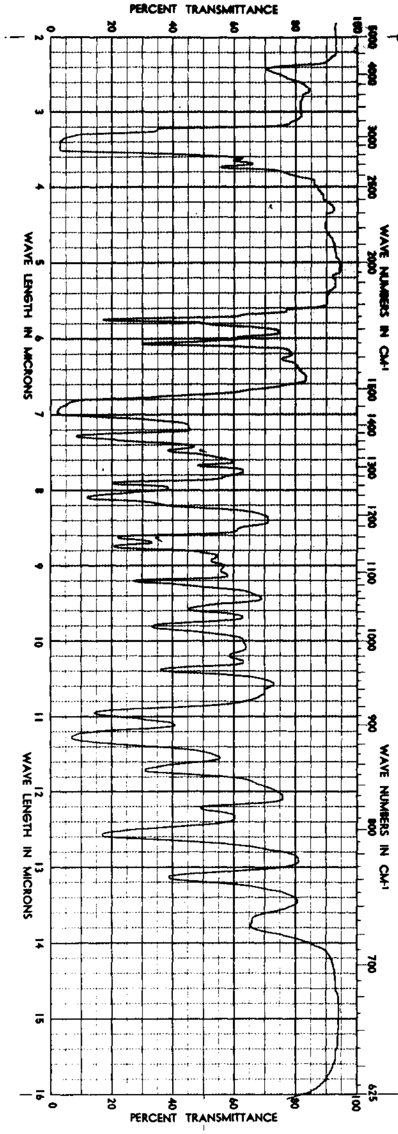
Plate 8. 1-Methylcyclohexene. Cell length: 0.072 mm.

Plate 9. Methylenecyclohexane. Cell length: 0.072 mm.

Plate 10. Olefins from pyrolysis of 1-methylcyclohexyl acetate. Cell length: 0.072 mm.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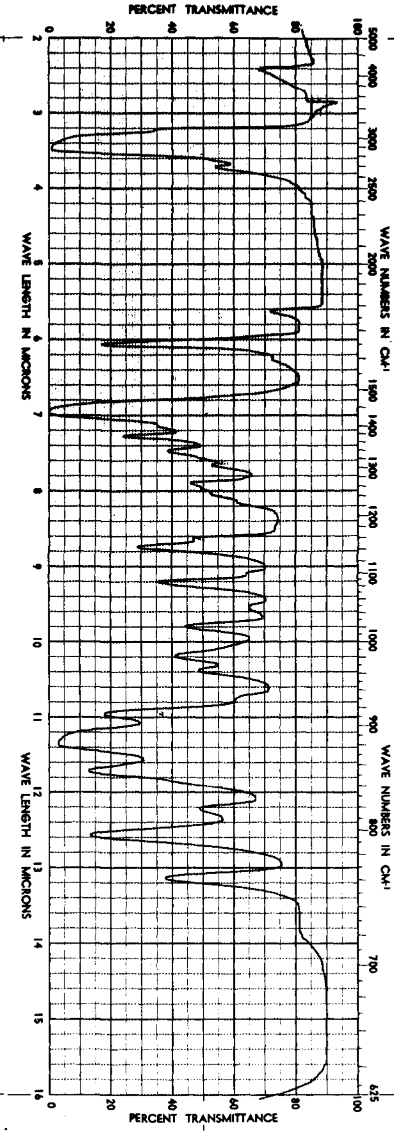
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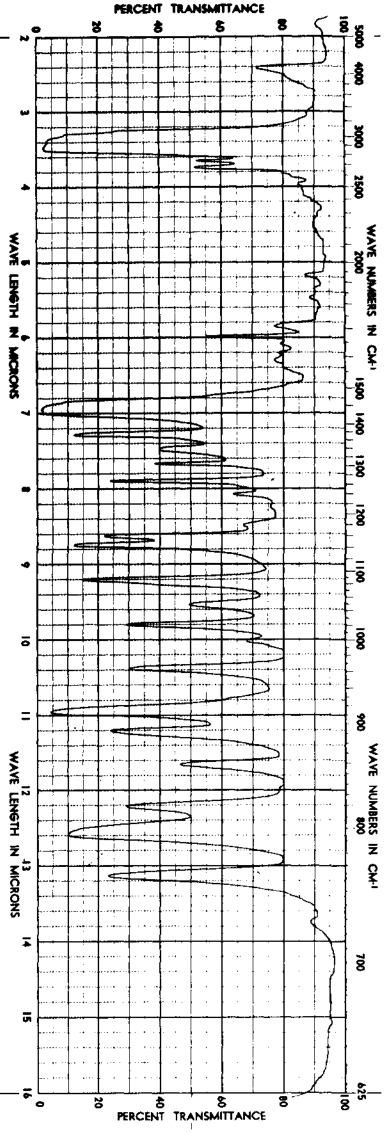
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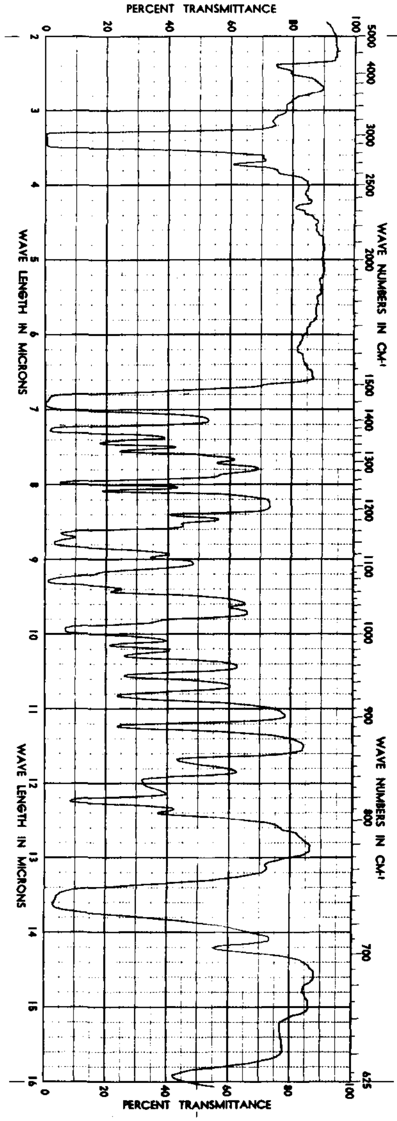
Plate 11[*]. _trans_ 1,2-Dimethylcyclohexyl bromide. Cell length: 0.072 mm.

Plate 12[*]. 85 % _trans_ and 15 % _cis_ dimethylcyclohexyl bromide. Cell length: 0.072 mm.

Plate 13[*]. 72 % _trans_ and 28 % _cis_ dimethylcyclohexyl bromide. Cell length: 0.072 mm.

Plate 14[*]. 30 % _trans_ and 70 % _cis_ dimethylcyclohexyl bromide. Cell length: 0.072 mm.

[*] Note how bands at 7.75, 930, 943 and 10.30 microns increase as the amount of _cis_ bromide increases.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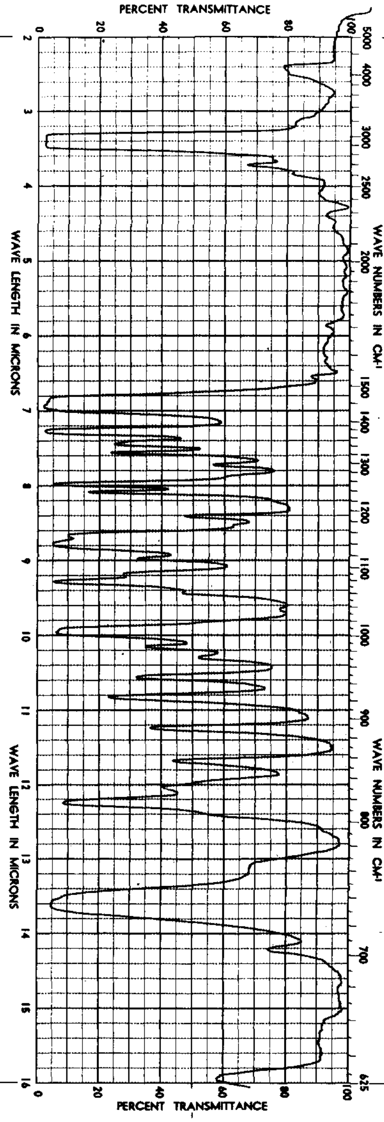
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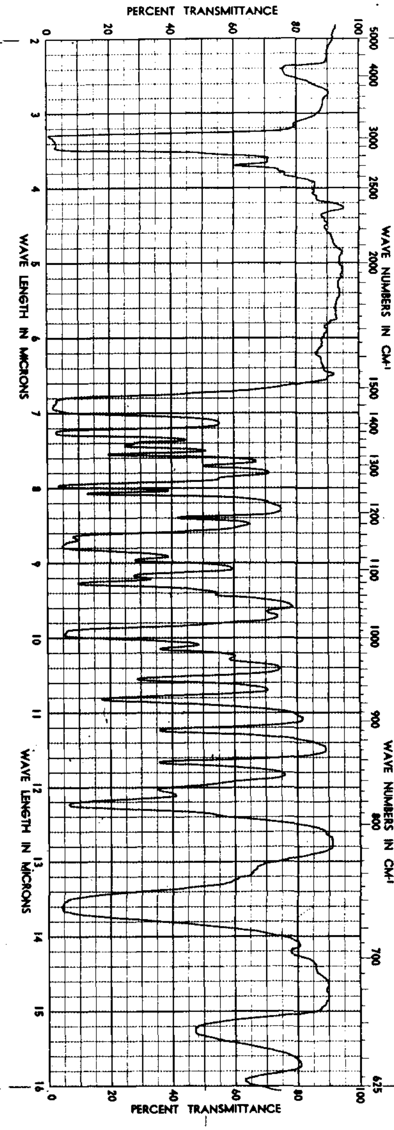
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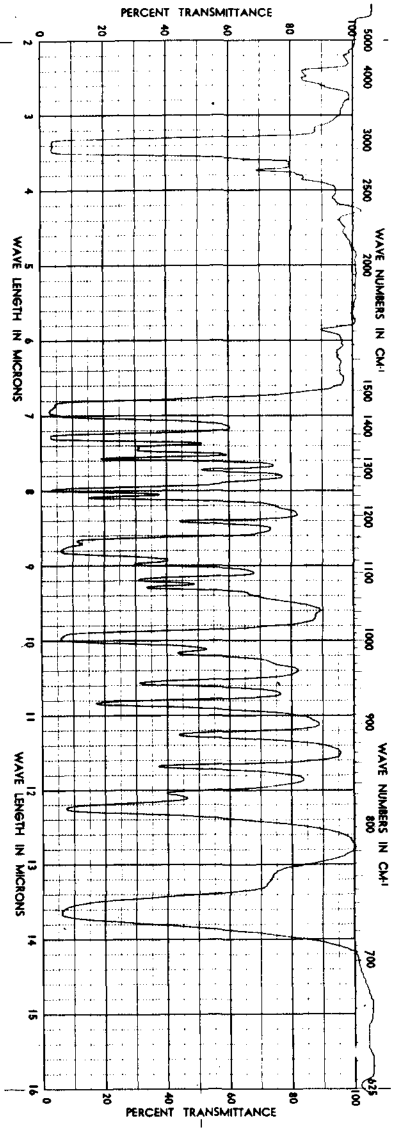
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DISCUSSION

Acetate Pyrolysis

The evidence of the configuration of the cis and trans 1,2-dimethylcyclohexanol is reasonable but not conclusive. The assignment of configuration has been made on the basis of infrared absorption spectra, relative rates of hydrogenation and the reaction between lithium aluminum hydride and and 1,2-dimethyl-1,2-epoxycyclohexane[57,64,65]. Since some of the conclusions of this thesis depend on the accuracy of the assignments of the configuration of these alcohols, an additional, more conclusive determination of their structure was undertaken. Hence, the pyrolysis of the acetates of these alcohols was carried out.

The stereospecificity of acetate pyrolysis has been discussed above[66]. In this reaction, the cis elements of acetic acid are lost. On pyrolysis, the trans 1,2-dimethylcyclohexyl acetate (I) can give either 2-methylenemethylcyclohexene (II) or 2,3-dimethylcyclohexene but not

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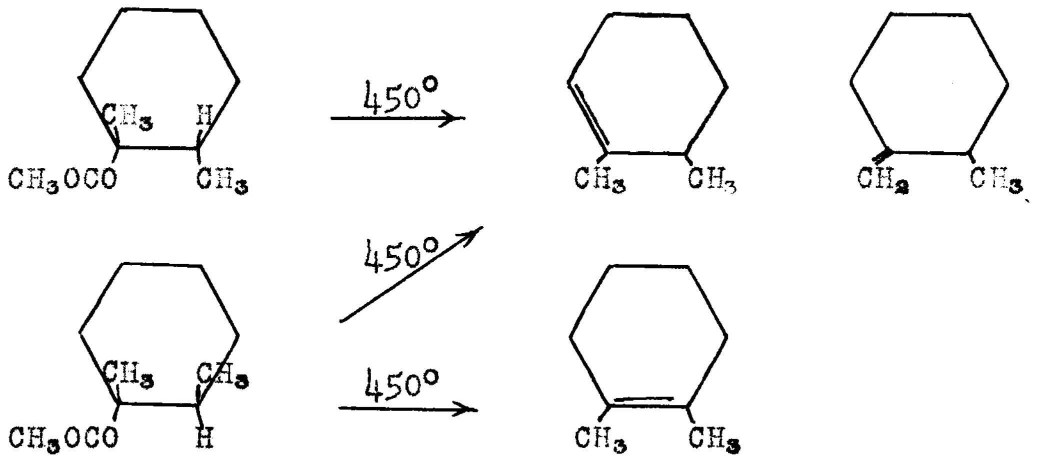
[64] G. Chiurdoglu, Bull. soc. chim. Belg., 44, 531 (1935).

[65] L. W. Trevoy and W. G. Brown, J. Am. Chem. Soc., 71, 675 (1949).

[66] Page 29, this thesis.

1,2-dimethylcyclohexene (IV) if *cis* elimination occurs. The *cis* 1,2-dimethylcyclohexyl acetate (V) can give all three olefins on pyrolysis.



The 1,2-dimethylcyclohexyl acetates were prepared from the pure *cis* and *trans* dimethylcyclohexanols by treatment with acetyl chloride in dimethyl aniline. The acetates could be reduced with lithium aluminum hydride to the original alcohol with no loss in configuration. Hence, the alcohols must have been converted to the acetate with no loss in configuration.*

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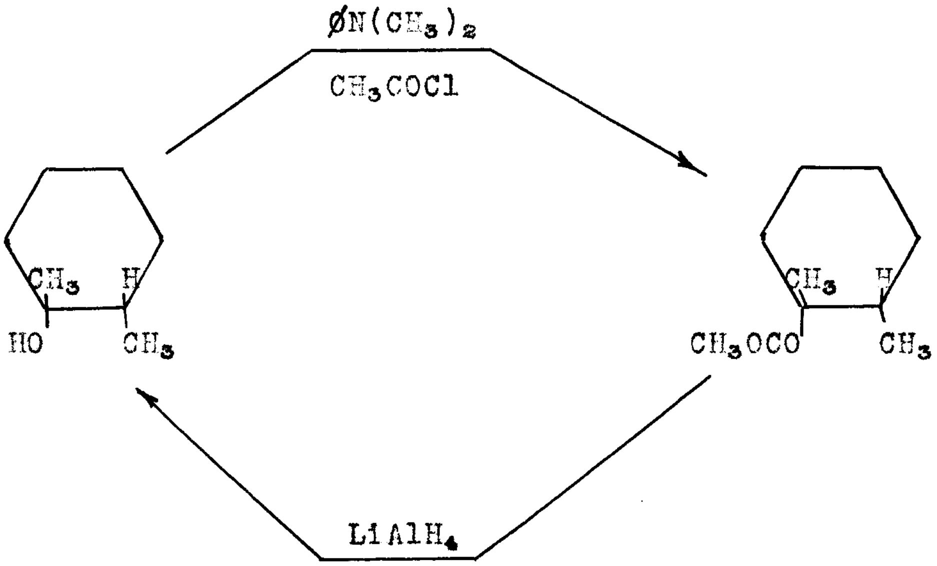
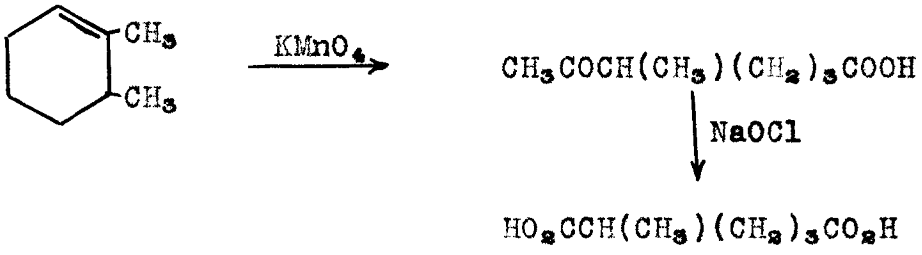
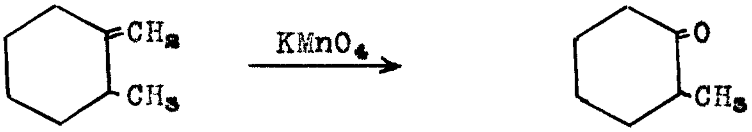
*The cleavage with lithium aluminum hydride must have resulted in acyl-oxygen cleavage and hence retention in configuration since alkyl-oxygen fission would have resulted in a hydrocarbon and not an alcohol in this medium.



A knowledge of the olefinic products of the reaction was also necessary. The 1,2-dimethylcyclohexene is well known[59]. Apparently 2,3-dimethylcyclohexene has never been reported. It was obtained as a by-product from the preparation of 1,2-dimethylcyclohexene. This olefin was identified by oxidation, in two steps, to the known α-methyladipic acid (VI). The 2-methylenecyclohexene had been prepared previously[61]. Its structure was checked by oxidizing it to the known 2-methylcyclohexanone (VII).



VI

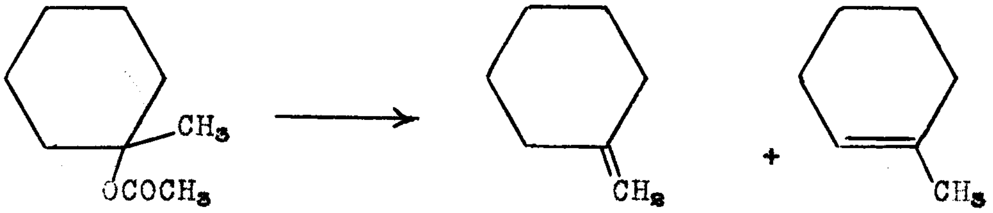


VII

The results of the pyrolysis of the isomeric 1,2-dimethylcyclohexanyl acetates are shown in Table IV. Both isomers gave predominantly 2-methylenemethylcyclohexane and some 2,3-dimethylcyclohexene. The cis acetate gave substantial amounts of 1,2-dimethylcyclohexene which was absent in the pyrolysis products of the trans acetate. In order to prove that no isomerization had occurred during the pyrolysis, two experiments were performed. The olefinic products of the pyrolysis of cis 1,2-dimethylcyclohexyl acetate were mixed with acetic acid and passed through the pyrolysis tube again. The ratio of the olefins present did not change. A sample of olefin rich in 3,4-dimethylcyclohexene was treated in the same manner with no isomerization occurring.

From the results discussed above, it is apparent that the configurations of the alcohols have been assigned correctly.

Recently it has been reported that pyrolysis of acyclic acetates results exclusively in the formation of olefins having the smallest number of alkyl groups[54]. In the cyclic compounds described above, although the olefin with the smallest number of alkyl groups predominated, considerable amounts of the other isomers were formed. In order to further check these results, the pyrolysis of 1-methylcyclohexyl acetate (VIII) was carried out. The products obtained again were mixtures, with the exocyclic olefin, methylenecyclohexane predominating.



It is not altogether clear why simple aliphatic acetates lead to the formation of olefins having the smallest number of alkyl groups. A few generalizations may be made regarding this reaction. The preferred transition state for thermal eliminations of this type is that the four centers of importance in the reaction should lie in one plane[67,68]. A primary hydrogen is more susceptible to nucleophilic attack by the carbonyl oxygen than secondary or tertiary[69]. Steric interaction between the acetate group and the rest of the molecule favors the formation of olefins with the smallest number of alkyl groups. Attainment of a planar transition state presents no difficulties with simple aliphatic acetates. Therefore the course of the reaction is determined by the latter two factors.

Cyclic compounds present clarifying data. The configurations of these compounds can be known with more certainty. An analysis of the conformations of some substituted cyclohexanes is given in the following section. It will be sufficient here to point out that imposing a planar transition state for this process makes cis elimination to form an endocyclic olefin possible only in the "boat" form of the cyclohexane molecule. The preferred exocyclic compound can arise from the "chair" form of the molecule. The chair form of the cyclohexane molecule is about 5 kilocalories more stable than the "boat" form[70].

---

[67] O. H. R. Barton, J. Chem. Soc., 2174 (1949).

[68] S. Glasstone, H. Erying and K. W. Laidler, "Theory of Rate Processes", D. Van Nostrand Co., Inc., New York, 1941, p. 90.

[69] J. Morton, Doctorial Dissertation, Iowa State College, 1952.

[70] R. B. Turner, J. Am. Chem. Soc., 74, 2118 (1952).

It therefore seems probable that a higher activation energy is necessary to obtain the endocyclic olefin.

It is not obvious why exclusive formation of olefins having the smallest number of alkyl groups is not observed in the case of cyclic compounds. The arguments set forth above are, in fact, stronger for cyclic compounds than for the aliphatic compounds which show an even higher structural specificity in the pyrolysis reaction.

Elimination Reactions

The elimination reactions of the isomeric 1,2-dimethylcyclohexyl bromides were studied in order to establish their configurations and to obtain a method of analysis for mixtures of the two bromides. In a previous section the stereospecificity of the E2 reaction has been discussed. The E2 reaction involves the simultaneous elimination of an atom or group and a trans β hydrogen. A planar transition state is at least preferred.

It is apparent that cis 1,2-dimethylcyclohexyl bromide cannot give 1,2-dimethylcyclohexene, whereas the formation of this olefin is possible with the trans isomer. Initial experiments showed that 1,2-dimethylcyclohexyl bromide, from the reaction of hydrogen bromide in acetic acid, gave nearly pure 1,2-dimethylcyclohexene when treated with sodium methylate in methanol. Since this olefin could arise from either the cis or trans 1,2-dimethylcyclohexyl bromide under E1 conditions it became necessary to establish the kinetic order of the reaction. The rate expression for the elimination in sodium methylate was found to be:

$$\frac{dBr}{dt} = 0.004 \left[T\right] + 0.03 \left[NaOCH_3\right] \left[T\right]$$

T = 1,2-dimethylcyclohexyl bromide*

From the rate equation it can be seen that a considerable portion of the reaction goes by the E1 path. The high base concentrations necessary to obtain a relatively pure second order reaction is prohibitive. Following reaction rates in this medium in order to analyze mixtures of cis and trans bromides would be unnecessarily difficult.

Lowering the ionizing power of the medium should decrease the E1 rate[37]. Accordingly, the reaction rates

---

*The bromide used here will be shown to be a mixture containing 15 % of the cis bromide and 85 % of the trans in a section below. These rate constants hold within experimental error for the pure trans bromide. There are two reasons for this. At the low base concentrations studied the E1 reaction accounts for a large part of the rate and the E1 rates for the two isomeric bromides are nearly equal. The E2 rate constants were determined over the first 15 % of each run. Over this part of the reaction the slower E2 rate of the cis compound contributes little to the over-all rate.

were obtained in ethyl alcohol-sodium hydroxide mixtures. In this medium, the E2 reaction was roughly 100 times as fast as the E1 reaction in 3 normal base. Again the primary reaction product was 1,2-dimethylcyclohexene. Hence, the reaction product was 1,2-dimethylcyclohexanol and hydrogen bromide in acetic acid must have given trans 1,2-dimethylcyclohexyl bromide as the major product.

The pure trans 1,2-dimethylcyclohexyl bromide gave only 1,2-dimethylcyclohexene when treated with sodium hydroxide in ethanol. The rate equation is given below.

$$\frac{dBr}{dt} = 0.00045\,[T] + 0.0155\,[T]\,[OH]$$

A sample of pure cis 1,2-dimethylcyclohexyl bromide was unavailable. Mixtures of cis and trans bromides gave mixtures of the three olefins; 1,2-dimethylcyclohexene, 2,3-dimethylcyclohexene and 2-methylenemethylcyclohexane. The amount of 2,3-dimethylcyclohexene and 2-methylenemethylcyclohexane formed corresponded roughly to the amount of the cis isomer present. Quantitative conversion of the cis 1,2-dimethylcyclohexyl bromide to olefins along the E2 reaction path is difficult on the basis of the rate equation shown below because of the high concentration of base needed.

$$\frac{dBr}{dt} = 0.00045\,[T] + 0.00130\,[T]\,[OH]$$

The configuration of the bromides were thus established by the criterion of <u>trans</u> elimination in the E2 reaction.

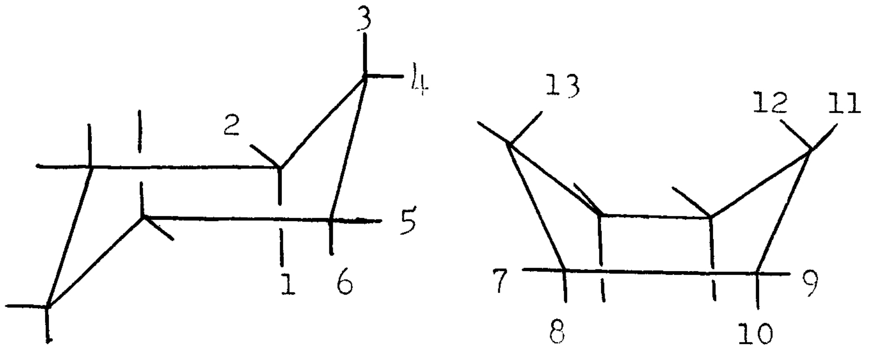
Hughes and Ingold have stated that electromeric effects control the course of the E2 reaction[37]. The products are predicted on the basis of the Saytzeff rule. The olefinic products of certain of the elimination reactions of the 1,2-dimethylcyclohexyl bromides do not conform to this rule. In order to show this it will be necessary to examine the conformations of these molecules*. Cristol has postulated that a planar transition state is necessary for facile second order elimination[43]. The conformations to be considered are shown in Table XVI, together with the possible products if a planar intermediate is essential. In this analysis it is assumed that original geometry of the cyclohexyl bromide influences the geometry of the transition state.

---

*"The word 'conformation' is used to denote those arrangements in space of atoms of a molecule which are free from strain (other than that imposed by valence requirements) and yet are not superimposable on each other." D. H. R. Barton, J. Chem. Soc., 1027 (1953).

Table XVI

Conformations of cis and trans 1,2-Dimethylcyclohexyl Bromide



		Position		Product		
Conformation	Bromide Isomer	Methyl groups	Bromine group	(a)	(b)	(c)
a	trans	3,6	4			X
b	"	4,5	3	X	X	X
c	"	7,10	8			X
d	"	7,10	9			X
e	"	10,12	9			X
f	"	10,12	11			X
g	"	9,11	12		X	X
h	"	9,11	10			X
i	cis	3,5	4			X
j	"	3,5	6		X	X
k	"	8,10	7			X
l	"	7,9	8			X
m	"	10,11	9			X
n	"	10,11	12		X	X
o	"	9,12	10			X
p	"	9,12	11			X

[a] 1,2-dimethylcyclohexene

[b] 2,3-dimethylcyclohexene

[c] 2-methylenemethylcyclohexane

Some of the structures shown in Table XVI are so strained that they can be discounted. In particular it is not likely that any atom larger than hydrogen can be at position 12. The introduction of an atom larger than hydrogen at position 12 caused the molecule to shift into a different conformation due to interference from the hydrogen at position 13. By the same reasoning it is unlikely that nucleophillic attack on a hydrogen at position 12 is possible. We will therefore neglect conformations e, f, g, h, m, n, o and p.

Smaller differences in strain can be postulated for the remaining conformations. Although it is difficult to make a case for the removal of any of the remaining conformations from consideration it is instructive to discuss the relative stabilities of the remaining conformations. Other factors being equal conformations having the chair form are in general more stable than those having the boat form[71]. Also conformations having groups or bulky atoms at both 4 and 5 and either 3 or 6 are more stable than compounds having groups at 3 and 6 and either 4 or 5*. In general large groups are most stable at positions 4 and 5[72].

---

[71] D. H. R. Barton, Experientia, 6, 316 (1950).

*This postulate neglects electrostatic interaction between groups. For example, 1,2-difluorocyclohexane probably exists almost exclusively in the 3,6 conformation.

[72] E. Bose, ibid., 8, 458 (1952); A. J. Birch, Ann. Reports, 48, 192 (1951).

A more quantitative estimate of the relative stabilities of the four conformations can be made. If we take the value, 1.0 Kcal/mole, for the steric interaction between a methyl group and a neighboring hydrogen and 0.4 Kcal. for the steric interaction between a bromine atom and a neighboring hydrogen we obtain the following energies for interaction. Conformation b (trans isomer) has a steric interaction of 3.0 Kcal. Conformations i and j (cis isomers) have intermediate values of 4.0 and 4.5 Kcal. respectively. Conformation a, the least favorable conformation, has a steric interaction of 5.5 Kcal.

The value, 1.0 Kcal., for methyl-hydrogen interaction gives the best agreement between observed and calculated entropies for a number of alkylcyclohexanes (gaseous state)[70]. The value of 0.5 for hydrogen-bromine interaction is estimated. It is apparent from a study of the models of n-butane and n-propyl bromide that the steric interaction is much less in the case of n-propyl bromide. Values from 0.2 to 0.7 would not effect the argument.

Considering trans 1,2-dimethylcyclohexyl bromide, it can be seen that conformation b is the most stable. This conformation allows for the formation of 1,2-dimethylcyclohexene, the product predicted on the basis of the Saytzeff rule.

The cis 1,2-dimethylcyclohexyl bromide gave a mixture of 3,4-dimethylcyclohexene and 2-methylenemethylcyclohexane.

Only 3,4-dimethylcyclohexene would be predicted on the basis of the Saytzeff rule. Let us consider conformations i and j. Conformations k and l are less stable and lead to the same product as conformation i and arguments about conformation i are similar to arguments about conformations k and l.

In considering conformations i and j it can be seen from the above discussion that conformation i is favored. Since the formation of 2,3-dimethylcyclohexene occurs it must arise from the less stable j conformation. The difference in stability of the two conformations, estimated at about Kcal., explains in part the formation of 2-methylenemethylcyclohexane in violation of the Saytzeff rule. A further examination of conformation j shows that nucleophillic attack on the *trans* hydrogen is sterically more favorable on the methyl group. This same methyl group shields the *trans* hydrogen on the ring. Also, the bulk of the two *cis* methyl groups may render attainment of a strictly planar transition state for the formation of 2,3-dimethylcyclohexene difficult.

These steric effects must more than counterbalance the electromeric effect favorable to the formation of 2,3-dimethylcyclohexene. That is, qualitatively, the energy lost through the steric effect in the transition state leading to 2,3-dimethylcyclohexene is greater than the energy gained by hyperconjugation in the transition state.

Both steric effects and electromeric effects are reflected in the E2 rates. The E2 rate of the trans 1,2-dimethylcyclohexyl bromide is ten times the E2 rate of the cis 1,2-dimethylcyclohexyl bromide at 25°. Intermediates from the trans bromide leading to the formation of 1,2-dimethylcyclohexene are more stabilized by hyperconjugation and hence have a lower energy of activation than the intermediates leading to the formation of 2,3-dimethylcyclohexene and 2-methylenemethylcyclohexane. There is little steric inhibition of the elimination reaction of the trans bromide, while steric effects control the products of the elimination reaction of the cis bromide. On the other hand, the E1 (solvolysis) rates of the two bromides are equal over a range of conditions. Here the rate controlling step is the cleavage of the bromine-carbon bond which is subjected to similar effects in both isomers.

Some investigators believe that the directive effects in elimination reactions are primarily controlled by steric effects[73]. It was of interest to vary the steric requirements of the attacking base in the reaction with trans 1,2-dimethylcyclohexyl bromide. The 1,2-dimethylcyclohexene

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[73] H. C. Brown and Ichiro Moritani, Abstracts of the 122nd Meeting of the American Chemical Society, 1952, p. 2M.

was obtained as the exclusive product of the E2 reaction when the series of bases--sodium methylate, sodium ethylate and lithium aluminum hydride--was used.* In the series, pyridine, 2-picoline and 2,6-lutidine, only 1,2-dimethylcyclohexene could be detected. The rate of reaction decreased as the steric requirements of the base were increased. The reaction with pyridine seemed complete in one day. The reaction with 2-picoline was complete in 2-3 days. And the reaction with 2,6-lutidine was only half complete in four days. When the reaction was forced by refluxing the mixtures 2-methylenemethylcyclohexane and 2,3-dimethylcyclohexene appeared in the reaction product. These results are shown in Table XIV.

The Reactions of Hydrogen Bromide and Alcohols

The cis and trans 1,2-dimethylcyclohexyl bromides are products of the addition of 1,2-dimethylcyclohexene and hydrogen bromide. It was necessary to prepare these compounds by some independent means and obtain their properties in order to study the addition reaction.

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*It is of interest to note that the E2 reaction occurs to the exclusion of the S_N2 process when lithium aluminum hydride is used as the base in this reaction.

The 1,2-dimethylcyclohexyl bromides were prepared by the reaction of hydrogen bromide and the mixed 1,2-dimethylcyclohexanols. The mixture of bromides obtained from this reaction was found to be predominantly trans 1,2-dimethylcyclohexyl bromide. The necessity for the preparation of the cis 1,2-dimethylcyclohexyl bromide led to investigation of the reactions of the pure isomeric alcohols with a variety of reagents. The most comprehensive study was made on the reaction of the pure isomeric alcohols with hydrogen bromide. These reactions will be discussed in some detail below. Some other attempted reactions will be described briefly first.

An unsuccessful attempt was made to prepare the bromides by reacting the alcohols with phosphorous tribromide. The tertiary alcohols failed to react in several days at room temperature. Unidentified phosphorous esters were recovered. Such esters can form from the reaction of alkyl bromides and phosphorous acid. However, since phosphorous acid is insoluble in this solvent the bromides very probably were never formed.

Another approach involving the synthesis of the bromides by way of the reaction of sodium bromide with the tosylates of the 1,2-dimethylcyclohexanols was unsuccessful. The synthesis of these tertiary tosylates could not be accomplished.

A summary of the reactions of hydrogen bromide with the 1,2-dimethylcyclohexanols and some related compounds is shown in Table V, page 55. It can be seen that cis 1,2-dimethylcyclohexyl bromide was obtained in amounts varying from 15 % to over 70 % depending on the reaction medium. The lowest yield of cis bromide was obtained in acetic acid with the trans alcohol. The highest percentages of cis bromide were obtained in pentane at low temperatures with the cis alcohol.

The data indicate that in acetic acid the ratio of cis to trans 1,2-dimethylcyclohexyl bromide reaches an equilibrium value of about 1:5, 16 % cis bromide. The reaction of hydrogen bromide in acetic acid for one hour with trans 1,2-dimethylcyclohexyl alcohol, cis and trans 1,2-dimethylcyclohexyl acetate and trans 1,2-dimethylcyclohexyl bromide gave this equilibrium mixture. The cis alcohol gave this equilibrium mixture after a reaction time of three hours. It was shown in the previous section that the stability of the most stable trans conformation relative to the most stable cis conformation is about 1.0 Kcal./mole. The free energy change for the reaction, cis to trans bromide, derived from the equilibrium concentrations of the isomeric bromides in acetic acid amounts to 1.1 Kcal./mole. This good agreement between the two values is probably fortuitous. The correlation does show that this equilibrium value is reasonable.

If the reaction product of cis 1,2-dimethylcyclohexanol is worked up after a reaction time of one hour the reaction mixture contained a somewhat larger proportion of cis 1,2-dimethylcyclohexyl bromide than the equilibrium value. Further experiments showed that when a sample of 1,2-dimethylcyclohexyl bromide containing 36 % cis bromide was placed in the reaction medium with hydrogen bromide the amount of cis bromide present was decreased to about 23 % after an hour. A sample of trans bromide attained the equilibrium value in one hour. Experiments in which trans alcohol was allowed to remain in contact with acetic acid-hydrogen bromide for a considerably shorter time, 3 and 6 minutes, showed more trans bromide than found in equilibrated bromide mixtures.

The reactions in acetic acid are shown in Figure 2. Both the S_Ni and S_N1 processes operate in this solvent. The expected reaction path is the S_N1 process since this reaction is favored by tertiary compounds and polar solvents. The intermediate carbonium in the S_N1 reaction can react to form a bromide of either configuration. The intermediate carbonium ion can also react with the solvent to form either isomeric acetate. Since, as shown in Figure 2, the acetates are in equilibrium with the carbonium ion, this makes no difference in the fate of the original alcohol.

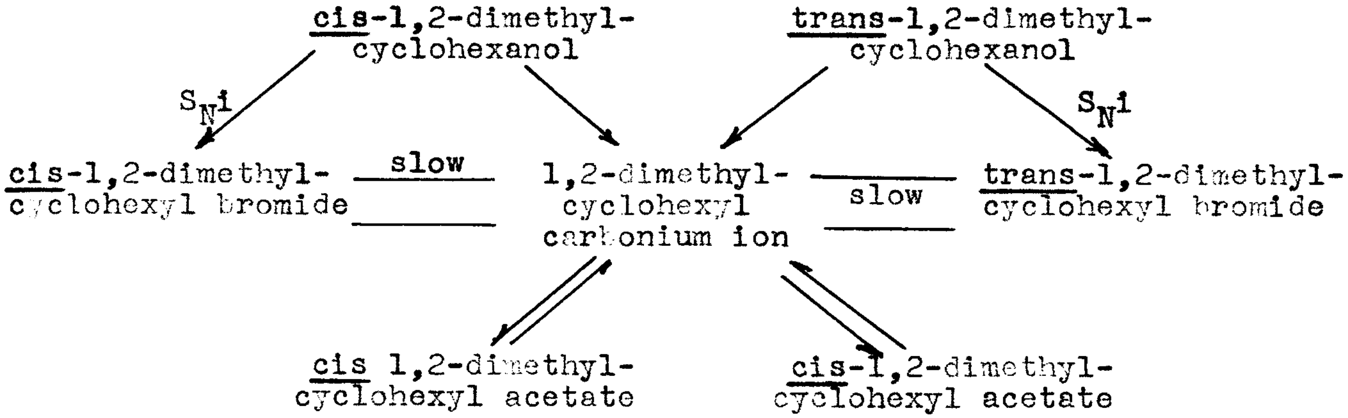


Figure 2

Reactions of Hydrogen Bromide in Acetic Acid at 25° with *cis* and *trans* 1,2-Dimethylcyclohexanols and Their Derivatives

Alkyl-oxygen fission was observed in the formation of the 1,2-dimethylcyclohexyl bromides from the 1,2-dimethylcyclohexyl acetates. This reaction must have occurred to a considerable extent since the alternative reaction path, acyl-oxygen fission, in the case of the *cis* acetate, leads to the formation of *cis* 1,2-dimethylcyclohexanol as an intermediate. The *cis* alcohol gave a different product ratio than was observed with the *cis* acetates and hence could not have been an intermediate. This is believed to be the first unambiguous demonstration of this cleavage leading to the formation of an unrearranged halide.

The reaction which results in retention of configuration noted with *cis* and *trans* 1,2-dimethylcyclohexanol must proceed along a different reaction path. Since the *cis* bromide, in excess of 16 %, is slowly converted to the *trans* bromide, the amount of *cis* 1,2-dimethylcyclohexyl bromide initially produced is somewhat greater than the product ratio indicates. By similar reasoning it can be seen that initial yields in experiments which give less than 16 % *cis* bromide must have been altered by the equilibration process. Retention of configuration must have occurred in both cases. Because the isomeric 1,2-dimethylcyclohexyl bromides proceed to equilibrium concentrations fairly rapidly and because the determination of amount of *trans* bromide in excess of the equilibrium concentration is not highly accurate, it is impossible to calculate precisely the amount of reaction going by the S_Ni path. A qualitative estimate based on the bromide ratio in reactions run for three minutes indicate that about one fourth of the product obtained from <u>cis</u> alcohol is formed through an S_Ni mechanism and that roughly half the bromide obtained from the <u>trans</u> alcohol is formed by this mechanism.

In pentane the products of the hydrobromination of 1,2-dimethylcyclohexanol have no chance to equilibrate. The products can be recovered in the same ratio as they were formed. The S_N1 reaction should not be of as much importance in this medium since it is much slower than the competitive S_N2 or S_Ni processes in nonpolar solvents. The S_N2 and S_Ni reactions are less affected by a change of solvent because of the greater charge separation in their transition states[29]. However, the S_N1 process is favored in reaction of tertiary compounds and so cannot be neglected.

It can be seen that groups in the polar position on the cyclohexane ring are more susceptible to bimolecular displacements than groups in the equatorial position. Backside attack in the latter compounds is strongly hindered by the bulk of the cyclohexane ring. Conformations of the isomeric <u>cis</u> and <u>trans</u> dimethylcyclohexanols which have hydroxyl groups in the polar position should be preferred.

The geometry of the transition state of the S_N2 reaction is much better known than that of the S_Ni reaction. The steric requirements of a cyclic transition state, commonly proposed for the $S_{N}i$ reaction, would seem to give preference to displacement of substituents in the equatorial position.

Thus far the attainment of the transition state has been considered by examining the stability of the reactants. It is possible that the stability of the products influences the transition state, as is the case in the $S_{N}1$ reaction. Unfortunately, the nature of the $S_{N}2$ reaction makes consideration of both reactants and products necessary and our knowledge of the $S_{N}i$ reaction is insufficient to predict whether consideration of reactants or products or both are necessary.

From the data in Table V, we can obtain some knowledge of the reactions taking place. The *trans* 1,2-dimethylcyclohexanol gave about 25 % of the *cis* bromide at 0° and -78°. The *cis* bromide can form by way of the $S_{N}2$ process or the $S_{N}1$ process. The remaining 75 % *trans* bromide is formed by way of $S_{N}i$ and $S_{N}1$ reactions. The $S_{N}1$ reaction will contribute predominantly to the final concentration of the *trans* bromide if the equilibrium between the *cis* and *trans* forms is the same in pentane as it was in acetic acid. Since in any case the $S_{N}1$ reaction would not be expected to predominate in this solvent most of the observed *cis* bromide was formed by way of the $S_{N}2$ reaction. A conformational examination of the products and the reactants of this reaction shows that the reactant, *trans* 1,2-dimethylcyclohexanol contains a hydroxyl group in the polar position in its most stable conformation and the product, *cis* 1,2-dimethylcyclohexyl bromide contains the bromine atom in the polar position. Although in the latter conformation is not the most stable for the *cis* bromide it is not energetically far removed from the most stable conformation. It is impossible to tell what percentage of the *trans* bromide formed in this reaction was formed by the S_Ni reaction and what percentage was formed by the S_N1 reaction. However, as stated above, it seems unlikely that the S_N1 reaction would predominate in this medium.

In pentane at 0° the *cis* 1,2-dimethylcyclohexanol gives about 30 % *cis* 1,2-dimethylcyclohexyl bromide. At -78° yields of *cis* bromide approaching 70 % were realized. Using the same reasoning outlined above it can be seen that most of the *cis* bromide formed as a result of an S_Ni reaction, the S_N1 reaction giving predominantly the *trans* bromide.

Comparing the results of the reactions of both *cis* and *trans* 1,2-dimethylcyclohexanols with hydrogen bromide in pentane at -78° it can be seen that the S_Ni reaction proceeds to about 70 % with both alcohols. Most of the remainder of the reaction follows the S_N2 path. The possibility of the S_N1 reaction cannot be excluded.

The situation of the reactions in pentane at 0° is less clear. A conformational analysis of the cis and trans products and reactants shows no important energy difference that would favor one mode of reaction over another. From this analysis there is every reason to suppose the ratio kS_Ni/kS_N2 should be approximately the same for both isomers. If this is the case then in pentane at 0° about 30 % of the reaction goes by the S_Ni path, 25 % by the S_N2 path and the remainder by a different mechanism presumably somewhat the analogous to the S_N1 path. Yet it is difficult to rationalize so large a portion of the reaction proceeding by a carbonium ion mechanism in this medium.

The most striking fact achieved by the investigation of the reactions of the 1,2-dimethylcyclohexanols with hydrogen bromide is the generality of the S_Ni mechanism in polar and nonpolar solvents over a range of temperatures. Although the S_Ni reaction seems to be fairly common in the case of chlorosulfite esters and similar compounds only two examples of this mechanism operating with hydrogen bromide have been described prior to this investigation and these both involved secondary benzyl alcohols.

The Addition of Hydrogen Bromide to 1,2-Dimethylcyclohexene

The 1,2-dimethylcyclohexene was chosen as the olefin with which to study the addition to hydrogen bromide to a double bond. It had some obvious advantages. It was readily available. Being cyclic, cis-trans isomerization of the olefin, which has led to certain ambiguities in other studies, is impossible. The 1,2-dimethylcyclohexene contains no groups or atoms containing unshared electron pairs, rendering the possibility of neighboring group reactions remote. The olefin, being tetrasubstituted, will undergo extremely rapid ionic reactions, and hence will obviate the difficulties arising from competitive free radical processes.

This olefin also had certain disadvantages, the most unfortunate being the lack of knowledge of its structural isomers, and the bromide products. Another disadvantage is that the cyclohexyl system is not rigid and therefore several conformations of each molecule must be considered in any discussion of reaction mechanisms. Also, the product being a tertiary bromide isomerizes or solvolyzes rapidly in polar solvents.

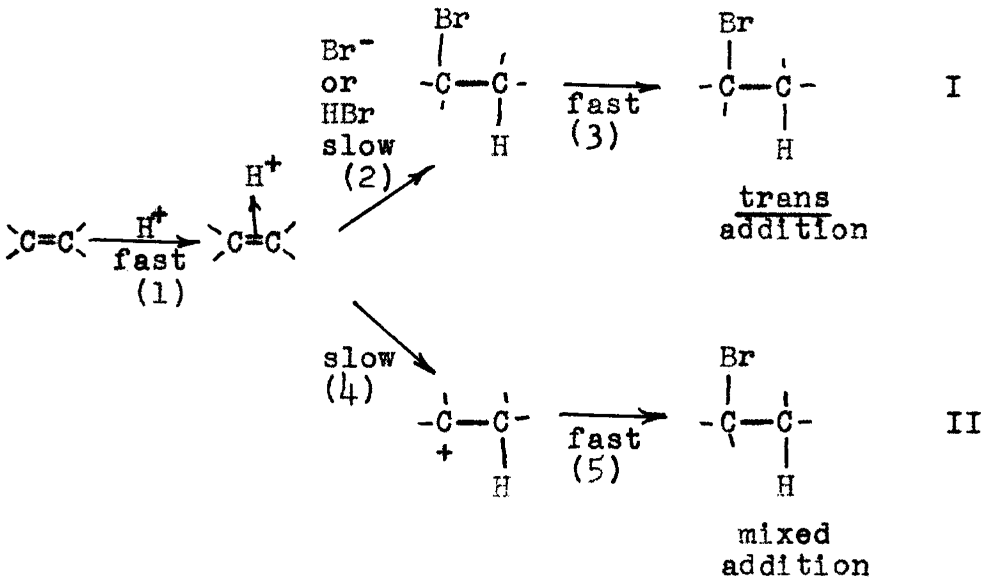
The proof of structure of the compounds used in this study has been discussed in a previous section.

The results to be discussed are shown in Table XV. The addition reactions were run first in acetic acid. The equilibration of the reaction products, the 1,2-dimethylcyclohexyl bromides in this solvent, was discussed in the previous section. The equilibrium ration of *cis* to *trans* 1,2-dimethylcyclohexyl bromide was 16 % *cis*.

The isomeric olefins, 1,2-dimethylcyclohexene, 2,3-dimethylcyclohexene and 2-methylenemethylcyclohexane were treated with 32 % hydrogen bromide in acetic acid to give 1,2-dimethylcyclohexyl bromide 7 %, 12 % and 28 % in *cis* 1,2-dimethylcyclohexyl bromide respectively when the reaction was terminated after 3 minutes. Equilibrium concentrations were obtained when the reaction time was increased to one hour. Since the bromides isomerize in this medium to the equilibrium concentration, 16 % *cis*, the initial concentrations of *cis* bromide in each case above are somewhat further from 16 % than the percent of recovered *cis* bromide indicates.

The reaction of 1,2-dimethylcyclohexene with hydrogen bromide in pentane at 0° and at -78° gave almost exclusively the *trans* bromide. When hydrogen bromide and the olefin were frozen in liquid air to obtain higher concentrations of hydrogen bromide, about 25 % *cis* 1,2-dimethylcyclohexyl bromide was formed. Since the reaction mixture was warmed rapidly to -78°, the observed *cis* addition is thought to be a function of the hydrogen bromide concentration and not due to the lower temperature during the first part of the reaction. The temperature and the concentration effects were not separated by this investigation.

A postulation of two modes of addition of hydrogen bromide to olefins is useful for purposes of discussion[74]. These are shown in the equations below.



The first step in either reaction path is the protonation of the double bond. This kind of carbonium ion has been called a π complex, and can be considered as an

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[74] C. C. Price, "Mechanisms of Reactions at the Carbon-Carbon Double Bond," Interscience Publishers, Inc., New York, 1946, p. 40.

interaction between a proton and the electrons in the orbitals of an olefin[75]. This fast equilibration is considered not to change the stereochemistry of the double bond. Similar complexes of silver ion with the cis and trans 2-butenes or 2-pentenes are formed without isomerization of the olefins[76].

If trans addition is observed, a concerted attack of bromide ion on the more electropositive carbon atom is indicated. The geometry of the reactive intermediate species resembles the product of Reaction II shown above.

If stereospecific trans addition is not observed and a mixture of the cis and trans forms is produced, then the reaction must proceed through an intermediate in which the steric integrity of the olefin is lost. The postulated protonated double bond formed rearranges to a classical carbonium ion. This is believed to be a discrete step and requires a certain activation energy[77]. This, then, is the rate determining step. The planar carbonium ion is quickly destroyed by bromide ion, and either cis or trans 1,2-dimethylcyclohexyl bromide is produced.

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[75] M. J. S. Dewar, J. Chem. Soc., 406 (1946).

[76] H. J. Lucas, R. J. Moore and D. Pressman, J. Am. Chem. Soc., 65, 227 (1943); S. Winstein and H. J. Lucas, ibid., 59, 45 (1937).

[77] M. J. S. Dewar, Bull. soc. chim. France, C75 (1951).

The reaction of hydrogen bromide and 1,2-dimethylcyclohexene in acetic acid showed some stereospecificity. More <u>trans</u> bromide was formed than that obtained at equilibrium. Therefore, part of the reaction must go by Mechanism I shown above. Since the reaction product is not pure <u>trans</u> bromide, the <u>cis</u> bromide observed in the reaction product was formed by way of Mechanism II or by partial equilibration of the <u>trans</u> bromide.

The reaction of hydrogen bromide with 2,3-dimethylcyclohexene and 2-methylenemethylcyclohexane gave product ratios differing from each other and also from 1,2-dimethylcyclohexene. Had the three isomeric olefins given similar product ratios it would have seemed probable that they had proceeded through a common intermediate carbonium ion as indicated in Mechanism II. Since different product ratios were observed in the hydrogen bromide addition in acetic acid with the three olefins, it is apparent that three different reaction intermediates are involved. These intermediates are the three different proton-olefin complexes which undergo attack by bromide ion, in the rate determining step, to give three different product ratios.

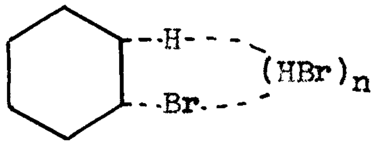
The data obtained from the elimination reactions of the isomeric bromides support this view. The rate of the E1 reaction is nearly equal for the <u>cis</u> and <u>trans</u> 1,2-dimethylcyclohexyl bromides, while their E2 rates differ by a factor of 100. The E1 reaction can be seen to follow the reverse of the path shown in Reactions 1, 4 and 5, with step 5 being slow and rate determining and Reactions 1 and 4 being fast and practically irreversible. Because of the equality of rates it is likely that the E1 reaction of both isomeric bromides involves similar, if not the same, carbonium ions. Further, this is the carbonium ion postulated as an intermediate in the addition reaction. In the case of the E1 reaction as well as the case of hydrogen bromide addition under discussion this carbonium ion decomposes to give most stable products in a nonstereospecific manner.

On the other hand the E2 reaction follows a path which is the reverse of Reactions 1, 2 and 3. The rate determining step is the Reaction 3. As evidenced by the reaction rates, a different intermediate is involved depending on which olefin is formed. Conversely, it seems unlikely the intermediates from three different olefins would decompose to give a similar mixture of bromides.

The addition of hydrogen bromide, at low concentrations in pentane, to 1,2-dimethylcyclohexene results in only one product, trans 1,2-dimethylcyclohexyl bromide. The reaction may proceed by direct attack of bromide ion on the proton-olefin complex as shown in Mechanism I. It is interesting that Menion found a large difference in rate of addition in hydrocarbon solvents and in ether inasmuch as both give the same products[27]. As far as the similarity of products shows a similarity of mechanism, Henion's conclusion that the difference in rates results from competition with the donor solvent for halogen acid is reasonable.

Our discussion thus far has not taken into account the fourth order rates observed for the addition of hydrogen bromide and hydrogen chloride to olefins in hexane reported by Mayo and co-workers[22,23]. The several possibilities for the high order kinetics suggested by Mayo include; the reaction of a 1:1 hydrogen halide-olefin complex with the dimer hydrogen halide, the reaction of a 2:1 complex with a single molecule of hydrogen bromide, the reaction of a 1:1 complex with an indefinite number of hydrogen halide molecules, and some kind of chain transfer reaction. None of these possibilities can be eliminated on the basis of the results reported in this thesis. Mechanism I described above can account for only two molecules of hydrogen bromide, but can readily be adapted to account for any of Mayo's possibilities. There remains the possibility that the olefins studied by Mayo add hydrogen bromide by a mechanism different than 1,2-dimethylcyclohexene. This is regarded as unlikely, however.

The anomolous <u>cis</u> addition encountered at low temperatures must proceed by a reaction path different than any described above. From the data presented, it appears that high concentrations of hydrogen bromide favor this reaction. An intermediate similar to the species postulated for the S_Ni reaction may occur. This intermediate is shown below, where n ranges from 0 to 3. The low temperature favors the



restricted orientation necessary as does the manyfold excess of hydrogen bromide.

SUMMARY

The structure assigned to the isomeric *cis* and *trans* 1,2-dimethylcyclohexyl alcohols was substantiated by the results of the pyrolysis of their acetates. The pyrolysis of tertiary cyclohexyl alcohols gave least substituted olefins, following the Hofmann rule.

The isomeric *cis* and *trans* 1,2-dimethylcyclohexyl bromides were prepared and their structure was proven by product and rate studies of their elimination reactions. The second order elimination reactions of the *cis* and *trans* 1,2-dimethylcyclohexyl bromides demonstrate that the planarity of the transition state is more important than electromeric effects in determining the olefinic reaction product. This difference in products was reflected in the rates. The products of the elimination reaction of *trans* 1,2-dimethylcyclohexyl bromide with pyridine, 2-picoline and 2,6-lutidine are controlled by the steric requirements of the base.

A study was made of the reaction of the isomeric *cis* and *trans* 1,2-dimethylcyclohexanols and the corresponding acetates with hydrogen bromide in order to obtain a method of preparation for *cis* 1,2-dimethylcyclohexyl bromide. The reaction in acetic acid gave products indicating some

retention of configuration occurred. Retention of configuration was also observed in pentane at 0° and -78°. The reaction of cis 1,2-dimethylcyclohexanol and hydrogen bromide at -78° constituted a preparative method for cis 1,2-dimethylcyclohexyl bromide.

The addition of hydrogen bromide to 1,2-dimethylcyclohexene in acetic acid was found to proceed by both a classical carbonium ion mechanism to give cis and trans addition and by a process which gave trans addition. In pentane at 0° trans addition occurred. The stereochemistry of the addition reaction at -78° can be controlled by the concentration of hydrogen bromide. Low concentrations of hydrogen bromide give trans addition while massive hydrogen bromide concentrations give mixed cis and trans addition.

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