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Addition of hydrogen bromide to cyclohexadiene

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ADDITION OF HYDROGEN BROMIDE
TO CYCLOHEXADIENE

by

John Warkentin

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

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INTRODUCTION

The ionic addition of hydrogen bromide to cyclohexadiene can conceivably occur in four different ways. These four ways are: (1) 1,2-trans-addition; (2) 1,2-cis-addition; (3) 1,4-trans-addition, and (4) 1,4-cis-addition. Studies of 1,2-addition to simple olefins indicate a strong stereochemical preference for trans-addition. On the other hand, cis-1,4-addition appears to be considerably favored over trans-1,4-addition.

The product of mono-addition of hydrogen bromide to a conjugated diene is an allyl bromide. A tendency for allylic compounds to rearrange thermally, or to give rearranged products from various reactions, is well known.

A tracer study of the addition of hydrogen bromide to cyclohexadiene was undertaken to determine the geometry of the addition and to estimate the ease of rearrangement of the 3-bromocyclohexene produced.

HISTORICAL

Electrophilic Addition of Hydrogen Halides to
Mono Olefins

In 1875 Markownikoff¹ enunciated his well known rule concerning the direction of addition of unsymmetrical reagents to unsymmetrical olefins. The rule states that the positive (electrophilic) part of the reagent will add to the unsaturated carbon atom having the larger number of hydrogen atoms. Thus, propene reacts with hydrogen bromide to produce isopropyl bromide rather than n-propyl bromide.

Early work on the orientation of addition to olefins, however, brought forth conflicting results and it soon became evident that the reaction can be very complex. Kharasch and his students correlated most of the available data in their 1931 review of hydrogen halide additions². They found two mechanisms for hydrogen halide additions to olefins. The normal addition (predicted by Markownikoff's rule) involves ionic intermediates as indicated by the catalytic effect of light or peroxides. Free radical additions have been discussed by Mayo and Walling³ and will not be dealt with here.

The stereochemistry of ionic addition of hydrogen halides

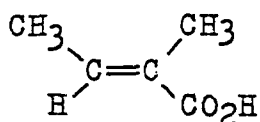
¹W. Markownikoff, Compt. rend., 81, 670 (1875).

²M. S. Kharasch and O. Reinmuth, J. Chem. Ed., 8, 1703 (1931).

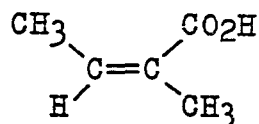
³F. R. Mayo and C. Walling, Chem. Revs., 27, 351 (1940).

to ethylenes received little attention in early investigations. Some additions to acetylenes were carried out and these always lead to trans olefins. For example Friedrich showed that the reaction of methylpropionic acid with hydrogen chloride in water yields β -chlorocrotonic acid⁴. This is the trans acid formed by trans-addition. Analogously Michael obtained chlorofumaric acid from the trans-addition of hydrogen chloride to acetylene dicarboxylic acid⁵.

More recently the stereochemistry of hydrogen halide addition to ethylenes has also received attention. Young, Dillon and Lucas found that tiglic acid and angelic acid gave different adducts with hydrogen iodide⁶. The addition prod-



tiglic acid



angelic acid

ucts from tiglic acid and angelic acid gave pure cis- and trans-2-butene respectively, when treated with sodium carbonate. If the decarboxylative elimination is trans as postulated by Grovenstein and Lee⁷, then the hydrogen iodide addi-

⁴R. Friederich, Ann., 219, 368 (1883).

⁵A. Michael, J. prakt. chem., 52, 289 (1885).

⁶W. G. Young, R. T. Dillon and H. J. Lucas, J. Am. Chem. Soc., 51, 2528 (1929).

⁷E. Grovenstein, Jr., and D. E. Lee, J. Am. Chem. Soc., 75, 2639 (1953).

tion must also have been trans. The formation of meso dibromosuccinic acid from bromomaleic acid and hydrogen bromide must also proceed by trans-addition⁸. A further example of stereospecific addition is due to Vaughan and Milton⁹ who showed that hydrogen bromide adds trans to dibenzo-(2,2,2)-bicyclooctatriene-2,3-dicarboxylic acid in acetic acid.

In all the examples cited above to illustrate stereospecific trans-addition, the olefin employed contained another functional group which could possibly have influenced the steric course of the addition. That neighboring groups like the carboxyl function can be involved in additions to olefins has been demonstrated. Tarbell and Bartlett¹⁰ obtained halo- β -lactone as the primary product from the halogenation of sodium dimethyl maleate or sodium dimethyl fumarate. Other examples of participation by neighboring groups in addition reactions have been provided by Winstein and co-workers^{11, 12}.

⁸M. S. Kharasch, J. V. Manfield and F. R. Mayo, Unpublished results in G. W. Wheland, "Advanced Organic Chemistry", p. 302, 2nd ed. John Wiley and Sons, New York (1949).

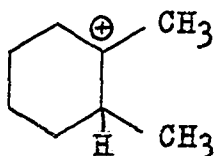
⁹W. R. Vaughan and K. M. Milton, J. Am. Chem. Soc., 74, 5623 (1952).

¹⁰D. S. Tarbell and P. D. Bartlett, J. Am. Chem. Soc., 59, 407 (1939).

¹¹S. Winstein and L. Goodman, J. Am. Chem. Soc., 76, 4368 (1954).

¹²L. Goodman and S. Winstein, J. Am. Chem. Soc., 79, 4788 (1957).

Additions of hydrogen bromide to olefins not complicated by the presence of other functional groups have been carried out recently by Hammond and his research group^{13, 14}. Hammond and Nevitt studied the stereochemistry of hydrogen bromide addition to the isomeric olefins 1,2-dimethylcyclohexene, 2,3-dimethyl-cyclohexene and 2-methylmethylenecyclohexane. In acetic acid the three olefins gave, respectively, 0, 13 and 35 per cent cis-1,2-dimethylcyclohexyl bromide. This work showed that the addition of hydrogen bromide is not the microscopic reverse of first-order elimination as had been previously supposed. Addition to the three olefins cannot go through a common cationic intermediate, since all three would be expected to form the same tertiary carbonium ion, namely



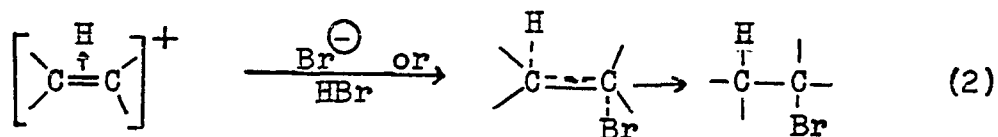
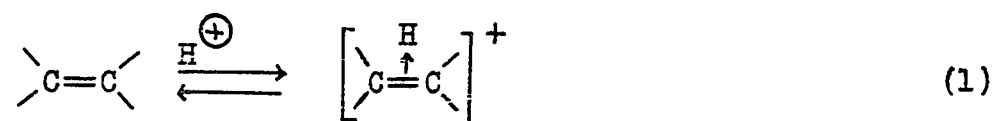
and would, therefore, give the same cis-trans isomer distribution in the products. Additional support for the thesis that a carbonium ion is not formed in the rate determining step of the addition was found in the fact that the isomeric cis- and trans-1,2-dimethylcyclohexyl bromides solvolyse at

¹³G. S. Hammond and T. D. Nevitt, J. Am. Chem. Soc., 76, 4121 (1954).

¹⁴T. D. Nevitt and G. S. Hammond, J. Am. Chem. Soc., 76, 4124 (1954).

the same rate. Since it is probable that the solvolysis reactions go through a common, planar carbonium ion, it follows that the addition reactions do not proceed via such an intermediate.

Hammond and Nevitt proposed the following scheme to account for their results.



Step 1 produces a π -complex¹⁵ between proton and olefin. It is interesting to note that silver ion complexes of the cis- and trans-2-butenes have been isolated without olefin isomerization^{16, 17}. The proton-olefin complex may react with bromide ion or hydrogen bromide from the side opposite the proton bridge to form trans-addition product. The authors also pointed out that the mechanism might be completely concerted with electrophile and nucleophile adding simultaneously to opposite sides of the double bond.

¹⁵M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Clarendon Press, Oxford (1949).

¹⁶H. J. Lucas, R. J. Moore and D. Pressman, J. Am. Chem. Soc., 65, 227 (1943).

¹⁷S. Winstein and H. J. Lucas, J. Am. Chem. Soc., 59, 45 (1937).

The kinetics of ionic addition of hydrogen halides to olefins is complex. Maass and his co-workers^{18, 19, 20} showed that the rate of addition of hydrogen chloride to propylene as well as the products of the addition varied with the ratio of reactants. A 1:1 mixture of the starting materials gave equimolar amounts of isopropyl chloride and hexyl chloride with one quarter of the hydrogen chloride remaining unreacted. With a 2:1 ratio of acid to olefin the reaction rate was accelerated 10-15 times and the yield of hexyl chloride was decreased. Moreover, hydrogen bromide reacted about 200 times faster than hydrogen chloride but the rate of reaction of the former could be accelerated by addition of the latter under conditions where hydrogen chloride did not react appreciably. These observations are in accord with a mechanism involving a high molecularity in hydrogen halide.

The rates of the hydrogen chloride addition to propylene¹⁸ and to the isomeric butylenes^{19, 20} show surprising temperature coefficients. In the temperature range 45 to 70° the coefficients are negative. Maass and co-workers proposed that in a non-polar solvent the addition involves the rearrangement of a 1:1 complex between olefin and hydrogen

¹⁸C. H. Holder and O. Maass, Can. J. Res., 16B, 453 (1938).

¹⁹C. C. Coffin, H. S. Sutherland and O. Maass, Can. J. Res., 2, 267 (1930).

²⁰C. C. Coffin and O. Maass, Can. J. Res., 3, 526 (1930).

halide. Such a reaction path would explain the observed temperature dependence of the rate, since the formation of a loose complex should be favored by low temperature.

The reaction order in olefin and in hydrogen halide has been investigated by Mayo and co-workers^{21, 22} for several systems. The ionic addition of hydrogen bromide to propylene in pentane solvent was found to be approximately first order in olefin and third order in hydrogen halide. Abnormal addition was difficult to suppress even when air and peroxides were carefully excluded. Addition of a hydroxylic solvent like ethanol greatly increased the rate, lowered the order in hydrogen halide and suppressed abnormal addition. Catalysts such as water, mercury chlorides and phosphorus pentoxide reduced the order in hydrogen halide to approximately first. The rate of addition was greatly accelerated by cooling the reactants to -80° and then warming them to 0° . Mayo, et al.^{21, 22} accounted for the overall fourth order kinetics by postulating the reaction of a 1:1 complex of hydrogen halide and olefin with dimeric hydrogen halide. The lower order observed in the presence of catalysts was explained in terms of replacement of some hydrogen halide units in molecular aggregates by molecules of catalyst.

²¹F. R. Mayo and M. G. Savoy, J. Am. Chem. Soc., 69, 1348 (1947).

²²F. R. Mayo and J. J. Katz, J. Am. Chem. Soc., 69, 1339 (1947).

Hammond and Nevitt also studied addition in a non-polar solvent along with the additions in acetic acid (see page 5). The reaction of hydrogen bromide with 1,2-dimethylcyclohexene in pentane solution produced pure trans-1,2-dimethylcyclohexyl bromide when carried out at 0° and -78°. When the reactants in pentane were combined at -196° and then rapidly warmed to -78° some 20 per cent cis bromide was formed. Hammond and Nevitt felt that the mechanism of addition in a non-polar solvent was similar to that in polar solvents (see page 6) except that the charge separation in the transition state would be eased through solvation by hydrogen halide molecules, or molecular aggregates of hydrogen halide. Such a mechanism would also account for the observed high reaction order in hydrogen halide when additions are carried out in non-polar media. The cis-addition was thought to be due to a cyclic mechanism involving large aggregates of hydrogen bromide.

Electrophilic Additions to Conjugated Dienes

Elucidation of the geometry of addition to conjugated dienes is complicated not only by the possibility of both 1,2- and 1,4-cis- and trans-addition but also by the possibility that some initially-formed products may undergo allylic rearrangement. The addition of halogens to conjugated systems, for example, is commonly regarded as a two step process; electrophilic attack by halogen or halonium ion

followed by nucleophilic attack by halide ion^{23, 24, 25, 26}. The electrophile coordinates with a terminal double bond, or else it attacks from a frontal position to form a coplanar, symmetrical transition state in which it is coordinated with both double bonds of the conjugated system. Addition through the former intermediate could be either cis or trans, while the latter mechanism should lead to cis-addition.

Mislow and Hellman²⁷ found that chlorination of butadiene in the dark at Dry Ice temperatures gave exclusively trans-1,4-dichloro-2-butene. They showed that the product could not have been formed by isomerization of initially-formed cis dichloride. Although Slobidin and Zabojev²⁸ reported, on the basis of Raman spectra, that the bromination of butadiene gives cis-1,4-dibromide, Mislow²⁹ has found

²³P. B. D. de la Mare, E. D. Hughes and C. K. Ingold, J. Chem. Soc., 17 (1948).

²⁴P. B. D. de la Mare, Quart. Revs. (London), 3, 126 (1949).

²⁵H. D. C. Waters, A. R. Caverhill and P. W. Robertson, J. Chem. Soc., 1168 (1947).

²⁶I. Roberts and G. E. Kimball, J. Am. Chem. Soc., 59, 947 (1937).

²⁷K. Mislow and H. M. Hellman, J. Am. Chem. Soc., 73, 244 (1951).

²⁸Ya. M. Slobodin and S. A. Zabojev, Zhur. Obsheei Khim., 22, 603 (1952).

²⁹K. Mislow, J. Am. Chem. Soc., 75, 2512 (1953).

evidence that bromine addition to butadiene is also trans. The trans assignment rested chiefly upon the reduction of the product to trans-2-butene with lithium aluminum hydride followed by addition of bromine to form meso-2,3-dibromobutane. Hence it is likely that butadiene does not add halogen by direct addition of a halogen molecule to the 1,4-positions via a "frontal" attack.

Cis-1,4-addition has also been demonstrated. Sweeting and Johnson³⁰ found that 2,3-dimethylbutadiene adds bromine to form a small amount of cis-1,4-dibromide although the latter was found to be thermodynamically unstable with respect to the trans isomer. The 9,10-chlorination of some anthracene derivatives has been shown to be cis in cases where the 9 and 10 positions are not sterically hindered³¹. Both cis- and trans-1,4-addition occur when cyclopentadiene adds bromine in chloroform solution at -10° to -15° ³².

Hydrochlorination of 2,3-dimethyl-1,3-butadiene in the presence of zinc chloride has been studied by Howard, et al.³³

³⁰O. J. Sweeting and J. R. Johnson, J. Am. Chem. Soc., 68, 1057 (1946).

³¹E. Bergmann and A. Weizmann, J. Am. Chem. Soc., 60, 1801 (1938).

³²J. Thiele, Ann., 314, 300 (1900).

³³F. L. Howard, T. W. Mears, A. Fookson, P. Pomerantz and D. B. Brooks, J. Research Nat'l. Bur. Standards, 38, 374 (1947).

and by Hatch and Journey³⁴. The results are not in agreement. Howard and co-workers reported a quantitative yield of 1-chloro-2,3-dimethyl-2-butene while Hatch and Journey obtained at most 15 per cent of this product; the remainder being 3-chloro-2,3-dimethyl-1-butene resulting from 1,2-addition. The latter workers found that the primary chloride undergoes facile rearrangement at room temperature to the tertiary chloride. Such isomerization may well account for the difference between the results found by the two groups.

In the course of this study deuterium bromide was added to cyclohexadiene in an attempt to determine the stereochemistry of the addition. Possible modes of reaction in this system include 1,2-cis- and trans-addition, as well as 1,4-cis- and trans-addition. Four isomeric deuterio-3-bromocyclohexenes could be formed by these modes of reaction. The possibility that these isomers might become equilibrated through allylic rearrangement had to be considered.

Allylic Rearrangement

Rearrangements in the reactions of allylic compounds are well known. General surveys of the subject have been made by Young³⁵ and by Prevost³⁶.

³⁴L. F. Hatch and G. E. Journey, J. Am. Chem. Soc., 75, 3712 (1953).

³⁵W. G. Young, J. Chem. Educ., 27, 357 (1950).

³⁶Ch. Prevost, Bull. Soc. Chim. France, C 1, 1951.

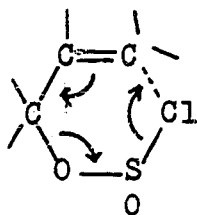
Nucleophilic displacement on an allylic system can occur by a variety of mechanisms. Under conditions favoring unimolecular reaction (S_N1) an allylic carbonium ion is formed, for which two extreme canonic structures may be written. A nucleophile may react at either end of the allylic system to give two structurally isomeric products, except in systems which ionize to form a symmetrical allylic ion. The S_N1 reaction resulting in allylic rearrangement is usually denoted by the symbol S_N1' .

Internal rearrangement of the type S_N1 is usually denoted by the symbol S_N1' . The net result of such a rearrangement is the migration of the allyl substituent to the "far end" of the allylic system. Rearrangement of this type in a system such as allyl bromide or 3-bromocyclohexene can be detected only by tracer methods.

The stereochemistry of the S_N1' rearrangement of allylic systems has been demonstrated. Goering and co-workers³⁷ showed that starting material, recovered from the incomplete acetolysis of optically active cis-5-methyl-2-cyclohexenyl chloride, had been extensively (26 per cent) converted into its enantiomer without geometric isomerization. The rearrangement is generally believed to proceed through an ion pair and is also called "internal return." The reaction of allyl alcohols with thionyl chloride may also give rearranged

³⁷H. L. Goering, T. D. Nevitt and E. F. Silversmith, J. Am. Chem. Soc., 77, 5026 (1955).

products. This reaction proceeds through an intermediate chlorosulfite^{38, 39} which may decompose to products either by way of an ion pair, or through a cyclic intermediate such as I. A cyclic intermediate somewhat like I may be involved in the thermal rearrangement of allyl halides⁴⁰.



I

Under conditions favoring bimolecular displacement, allylic systems may react to give both normal and rearranged products. Rearrangement occurs when the nucleophile attacks at the "far end" of the allyl system. The double bond is shifted toward the leaving group and the latter is expelled. This mechanism, denoted by the symbol S_N2' , was first demonstrated in the reaction of α -methylallyl chloride and α -ethylallyl chloride with diethylmalonate ions⁴¹. The

³⁸E. S. Lewis and C. E. Boozer, J. Am. Chem. Soc., 74, 308 (1952).

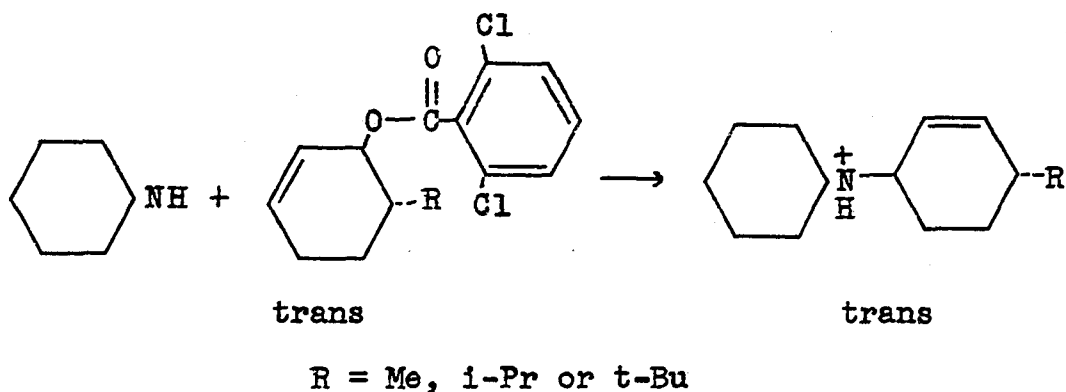
³⁹C. E. Boozer and E. S. Lewis, J. Am. Chem. Soc., 75, 3182 (1953).

⁴⁰E. L. Eliel in M. S. Newman, "Steric Effects in Organic Chemistry," p. 99, John Wiley and Sons, Inc., New York 1956.

⁴¹R. E. Kepner, S. Winstein and W. G. Young, J. Am. Chem. Soc., 71, 115 (1949).

product from Δ -methylallyl chloride was rearranged to the extent of 10 per cent while that from Δ -ethylallyl chloride was rearranged to the extent of 23 per cent. Steric hindrance to the normal S_N2 reaction was shown to be an important factor affecting the course of bimolecular nucleophilic displacement on allyl systems. The compounds 1-chloro-2-butene and 1-chloro-2-pentene, which are the primary isomers of the above compounds respectively, gave no rearranged products.

The stereochemistry of the S_N2' reaction has been elucidated. Stork and White⁴² showed that the incoming group in an S_N2' reaction approaches the allylic system from the side from which the leaving group is expelled. Other instances of stereospecific S_N2' reactions have been reported⁴³.



⁴²G. Stork and W. N. White, *J. Am. Chem. Soc.*, **75**, 4119 (1953).

⁴³A comprehensive review is given by E. L. Eliel in M. S. Newman, "Steric Effects in Organic Chemistry," pp. 95-98, John Wiley and Sons, Inc., New York 1956.

In the course of this study, acetate displacements were carried out on deuterio-3-bromocyclohexenes under conditions favorable to bimolecular displacement. The possibility that the products might be extensively rearranged, had to be considered.

Elimination Reactions

Elimination of the elements of hydrogen halide from an organic molecule can occur in two kinetically distinct ways. These two elimination paths are usually denoted by the symbols E_1 and E_2 ⁴⁴. A third elimination mechanism which is kinetically indistinguishable from E_2 elimination is of interest in allylic systems. This process, called 1,4-conjugate elimination⁴⁵, is sometimes denoted by the symbol E_2' .

The rate of the E_1 reaction depends only on the concentration of alkyl halide because the rate determining step is the breaking of the carbon-halogen bond to generate a carbonium ion and halide ion. The carbonium ion then loses a proton in a subsequent fast step to generate olefin.

The E_2 reaction proceeds through the removal of β -hydrogen by a base, accompanied or followed by loss of halide ion.

⁴⁴E. D. Hughes and C. K. Ingold, Trans. Faraday Soc., 37, 657 (1941).

⁴⁵S. J. Cristol, W. Barasch and C. H. Tieman, J. Am. Chem. Soc., 77, 583 (1955).

Evidence favoring concerted loss of hydrogen halide has been obtained by Skell and Hauser⁴⁶. Through the use of a deuterated solvent they were able to show that if a carbanion intermediate is involved in E₂ elimination, it loses halide ion faster than it can pick up hydroxylic deuterium from solvent. Equilibration of hydrogen between a hydroxylic molecule and a carbanion is expected to be extremely rapid. It follows that, in E₂ elimination from halides, the elements removed are lost simultaneously.

A guide to prediction of the direction of elimination from alkyl halides is embodied in the Saytzeff rule. The rule states that both the E₁ and E₂ processes proceed so as to form the most highly branched olefins as the predominant products. In other words, the direction of elimination is dominated by olefin stability, indicating that the transition state probably has much olefinic character.

While E₁ eliminations always follow Saytzeff's rule, Huckel and co-workers⁴⁷ have demonstrated that E₂ eliminations may deviate from that rule. They found that the products of E₂ elimination from menthyl chlorides could best be accounted for if the elements of hydrogen chloride were required to be trans in order for elimination to occur. The preference for

⁴⁶P. S. Skell and C. R. Hauser, J. Am. Chem. Soc., 67, 1661 (1945).

⁴⁷W. Huckel, W. Tappe and G. Legutke, Ann., 543, 191 (1940).

elimination from a trans configuration was attributed to minimized electrostatic repulsion between the entering base and the carbon-halogen dipole.

Much insight into the details of the E_2 reaction has been provided recently by Cristol, et al.⁴⁸ who studied E_2 eliminations from the four isomeric hexachlorocyclohexanes. Of these, the β -isomer is the only one which has all adjacent hydrogen and chlorine atoms cis to one another. Again a preference for trans-elimination was observed, for the β -isomer underwent elimination 7000 to 24000 times more slowly than the other three isomers. The authors suggested that, while trans-elimination is probably a concerted process, cis-elimination may be a multi-step process proceeding via the inversion of a first-formed carbanion.

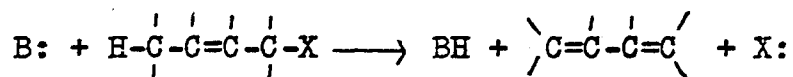
Although activation energies for cis-elimination are generally several kilocalories per mole higher than for trans-elimination, the entropy of activation is sometimes such as to make cis-elimination energetically more favorable, especially for reactions carried out at high temperature. For example, Cristol and Hause⁴⁹ found that trans-11,12-dichloro-9,10-ethanoanthracene eliminates the elements of hydrogen chloride seven to nine times faster in ethanolic alkali than the

⁴⁸S. J. Cristol, N. L. Hause and J. S. Meek, J. Am. Chem. Soc., 73, 674 (1951).

⁴⁹S. J. Cristol and N. L. Hause, J. Am. Chem. Soc., 74, 2193 (1952).

corresponding cis-dichloride. In this system neither of the isomers can achieve a trans, coplanar configuration of adjacent hydrogen and chlorine atoms. In the cis isomer both the hydrogen and the chlorine are out of coplanarity by about 35° . The trans isomer has adjacent hydrogen and chlorine atoms completely cis to one another, making trans-elimination impossible. Hence the fact that the trans-dichloride reacted faster must mean that the elimination went cis. Cristol and Hause explained the result in terms of a favorable entropy of activation for cis-elimination. The energy of activation actually favored trans-elimination by 4 kilocalories per mole. Other work by Cristol and co-workers⁵⁰ on dehydrohalogenations of halofumarate and halomaleate ions shows that facile trans-elimination can be expected in systems that can achieve a trans, coplanar configuration without undue strain.

Studies of bimolecular elimination have been extended to include 1,4-conjugative elimination of the type:

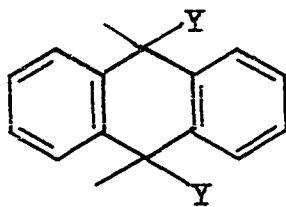


Cristol, et al.⁵¹ studied eliminations from the 9,10-posi-

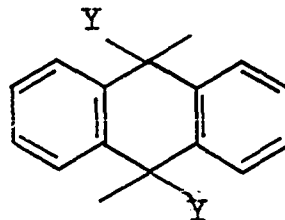
⁵⁰S. J. Cristol and A. Begoon, J. Am. Chem. Soc., 74, 5025 (1952).

⁵¹S. J. Cristol, W. Barasch and C. H. Tieman, J. Am. Chem. Soc., 77, 583 (1955).

tions of 9,10-dihydroanthracene derivatives. These compounds were chosen to eliminate competition from 1,2-elimination.



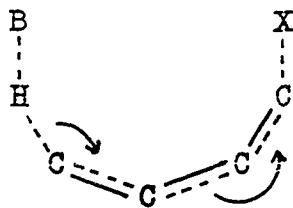
cis



trans

The dibenzoates and diacetates of cis- and trans-1,5-dichloro-9,10-anthradiol as well as the trans-monobenzoate were treated with sodium hydroxide in ethanol-dioxan. Under these conditions the dibenzoates and diacetates lost benzoic acid and acetic acid respectively, while the monobenzoate lost water. The authors showed that trans-monobenzoate and cis-monobenzoate are not intermediates in base-catalysed elimination from the dibenzoate and that the reaction was second order. The results indicated a remarkable preference for cis-elimination. At 22° the trans-dibenzoate lost benzoic acid about 1200 times as fast as the cis-dibenzoate; the latter being converted in high yield to cis-diol. In the diacetates cis-elimination was also favored by a large factor. Finally, base catalysed elimination of water from the isomeric diols and of hydrogen chloride from trans-1,8-dichloroanthracene-9,10-dichloride also indicated that 1,4-conjugate elimination from these systems has a high cis-stereospecificity. The authors pictured the reaction as a concerted cis process

involving inversions at carbons 1 and 3, as depicted below.



In the course of this work, second order eliminations were carried out on deuterio-3-bromocyclohexenes. Obviously, competitive 1,2- and 1,4-elimination could occur in this system.

Acetate Pyrolysis

The pyrolysis of acetates and other esters is now a well known method for the preparation of olefins⁵². The stereochemical course of the reaction has been studied extensively⁵². All of the results indicate a preference for cis-elimination. Curtin and Kellom⁵³ estimated that, in the pyrolysis of acetates, cis-elimination is favored over trans-elimination by a factor of about eight. Their conclusion was derived from a study of the pyrolyses of the acetates of erythro- and threo-2-deutero-1,2-diphenylethanol. For that

⁵²The references are too numerous to be cited here. See, for example, D. J. Cram, "Olefin-Forming Eliminations" in M. S. Newman, "Steric Effects in Organic Chemistry", pp. 305-314, John Wiley and Sons, Inc., New York 1956.

⁵³D. Y. Curtin and D. B. Kellom, J. Am. Chem. Soc., 75, 6011 (1953).

system, the authors estimated that the isotope effect, favoring the loss of hydrogen over the loss of deuterium, is about 2.8.

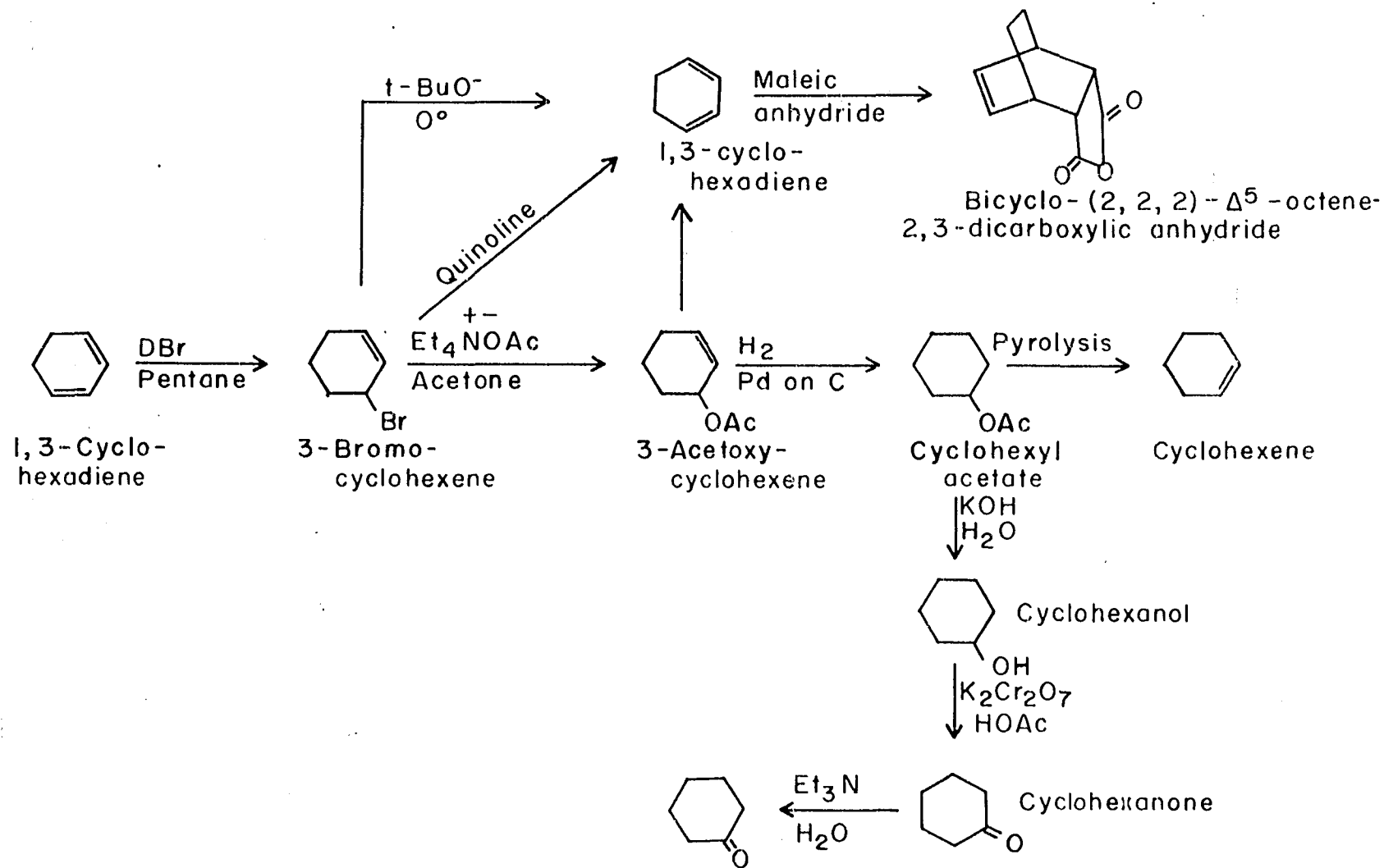
The temperatures for optimum yields of olefins from the pyrolysis of a large number of esters of cyclohexanol, have been determined by Smith and Wetzel⁵⁴. At temperatures lower than the optimum temperature, pyrolysis was incomplete, while at higher temperatures yields were lowered due to charring of the products.

In this work, some deuterated esters were pyrolysed. Predominant cis-elimination was assumed. Temperatures considerably higher than the optimum temperatures reported by Smith and Wetzel⁵⁴ were used to assure complete pyrolysis.

⁵⁴G. G. Smith and W. H. Wetzel, J. Am. Chem. Soc., 79, 875 (1957).

Figure 1. Schematic outline of the approach used in this work

Deuterium in the compounds has not been indicated in the formulae.



EXPERIMENTAL⁵⁵

Chemicals

Acetone

Commercial acetone was dried over anhydrous potassium carbonate for several days. It was dried further by decanting it onto anhydrous calcium sulfate. Distillation through a 6 inch Vigreux column gave acetone boiling at 55°.

Acetyl bromide

Acetyl bromide (Eastman White Label, Eastman Kodak Co.) was used without further purification.

Bromobenzene

Reagent grade bromobenzene (Allied Chemical and Dye Corporation) was washed with 10 per cent sodium hydroxide solution and with water. It was dried over calcium chloride and distilled through an Oldershaw column at an efficiency of 17 plates. The boiling point was 154° at 749 mm. mercury.

3-Bromocyclohexene

3-Bromocyclohexene, derived from the reaction of N-bromo-succinimide with cyclohexene, was distilled through a spinning band column. The fraction boiling in the range 54 to 59° at

⁵⁵All melting points and boiling points reported in this section are uncorrected.

13 to 15 mm. was redistilled from a Claisen flask to remove the yellow color. Colorless material boiling at 58° (14 mm.) was collected. The refractive index (n^{20}) was 1.5293 (lit.⁵⁶, b.p. 80 to 82° at 35 mm., n^{20} 1.5269).

2-Cyclohexenone

2-Cyclohexenone (Technical Grade, Aldrich Chemical Co.) was distilled through a Vigreux column. The fraction used boiled at 62 to 65° (14 mm.), n^{18} 1.4829.

Deuterium oxide

Deuterium oxide of purity greater than 99.5 per cent was obtained from Stuart Oxygen Company.

Kerosene

Commercial kerosene was stirred with concentrated sulfuric acid for several hours. The organic layer was separated and the treatment was repeated with fresh acid until the latter no longer became discolored after contact with the hydrocarbon mixture. The kerosene was then washed with water, dried over potassium hydroxide and distilled from a Claisen flask. The fraction boiling in the range 180 to 210° at 749 mm. was used.

⁵⁶J. D. Park, H. J. Gerjovich, W. R. Lycan, and J. R. Lacher, J. Am. Chem. Soc., 74, 2189 (1952).

Maleic anhydride

Maleic anhydride (Eastman White Label, Eastman Kodak Co.) melting at 55 to 56° was used directly.

Pentane

Technical Grade pentane (Matheson, Coleman and Bell) was distilled through a 1.5 foot, insulated Vigreux column. The boiling point was 34 to 35° at 750 mm.

Quinoline

Synthetic quinoline (Matheson, Coleman and Bell) was distilled from zinc dust. Colorless material boiling at 227° (735 mm.) was collected.

Thionyl bromide

Thionyl bromide was prepared according to the directions given in *Inorganic Syntheses*⁵⁷. The boiling point of the yellow product was 47 to 48° at 22 mm.

Preparation of Cyclohexadiene

A 500 ml. round-bottomed flask was fitted with a 6 inch Vigreux column fashioned after a Claisen distilling head. The column was equipped with a condenser, thermometer and

⁵⁷H. S. Booth, *Inorganic Syntheses*, 1, 113 (1939).

dropping funnel. Two hundred and fifty ml. of quinoline was heated to the reflux temperature in the flask and 100 g. (0.62 mole) of 3-bromocyclohexene was added dropwise. The diene that distilled out was dried over calcium chloride and redistilled through the same column. The yield of cyclohexadiene boiling at 79 to 80° (742 mm.) was 40.4 g. n^{20} 1.4733 (lit.^{58, 59}, n^{20} 1.4742 and 1.4739, respectively).

Ultraviolet Spectrum of Cyclohexadiene in Pentane

The ultraviolet absorption spectrum of cyclohexadiene in pentane was determined in the region 240 to 275 $m\mu$ with a Beckmann Model DU spectrophotometer and matched 1 cm. silica cells. The diene used boiled in the range 77 to 80° at 739 mm. and had a refractive index (n^{20}) of 1.4720. A plot of per cent transmittance versus wavelength is a smooth curve, for the region studied, with a minimum at 257 $m\mu$. At the latter wavelength the value $\log \epsilon = 3.70$ was obtained at a diene concentration of 5.490×10^{-5} mole per liter. This value of the extinction coefficient is somewhat lower than one reported in the literature. $\log \epsilon = 3.78$ at 257 $m\mu$ was estimated by interpolation of values listed by Henri and Pickett⁵⁹. A plot of per cent transmittance versus concen-

⁵⁸E. P. Carr and H. Stücklen, J. Chem. Phys., 6, 55 (1938).

⁵⁹V. Henri and L. W. Pickett, J. Chem. Phys., 7, 439 (1939).

tration for the concentrations 5.353×10^{-5} and 19.625×10^{-5} moles per liter, gave a good straight line indicating that the solution of cyclohexadiene in pentane obeys Beer's law over the concentration range in question.

Apparatus for Addition of Deuterium

Bromide to Cyclohexadiene

The apparatus for generating deuterium bromide consisted of a 300 ml. round-bottomed flask sealed to a 100 ml. dropping funnel. There were three outlets from the flask, spaced equally around the juncture of the flask with the dropping funnel. Two of these were small stopcocks and the third was a 6 inch condenser with inside diameter of 0.5 inches. One stopcock was connected, by means of Tygon tubing, to the top of the dropping funnel to permit equalization of the pressures in the flask and the funnel. The other was attached to a source of dry, oxygen-free nitrogen.

The opening at the top of the condenser led, through a drying tube (1 foot in length and 1 inch in diameter) filled with calcium chloride, to the gas inlet of a standard apparatus for catalytic hydrogenation at atmospheric pressure. The apparatus had three gas burettes of 500, 100 and 10 ml. capacity, respectively, which were filled with mineral oil along with the leveling bulb. A 500 ml. bulb was connected to the gas delivery tube by means of a "T" joint. The

purpose of the latter was to act as a ballast tank to minimize pressure changes arising from small surges of gas from the deuterium bromide generator. The outlet from the system was a sintered glass disk on a tube protruding through the narrow end of a standard taper male joint which was fitted to one of the necks of a painted 500 ml., three-necked round-bottomed flask. The remaining two necks of the flask held a stirrer and a condenser. The entire apparatus was, therefore, merely a system for generating a gas for measuring its volume and, finally, for bubbling it into a desired solution under a low but adjustable pressure. The apparatus was mounted in a well ventilated hood.

Typical Addition of Deuterium Bromide to Cyclohexadiene

In a typical run the apparatus described above was flushed with dry, oxygen-free nitrogen. The bulb of the deuterium bromide generator was then charged with acetyl bromide (49.2 g., 0.40 mole) while deuterium oxide (7.5 g., 0.375 mole) was placed into the dropping funnel. A solution of cyclohexadiene (15.0 g., 0.187 mole) in 300 ml. pentane was run into the painted reaction flask. Chloranil (0.015 g.) and 2,6-di-*t*-butyl-*p*-cresol (0.030 g.) were added and the stirrer was started to hasten dissolution of those inhibitors. The nitrogen was turned off, the stopcock to the reaction

flask was closed, and generation of deuterium bromide was begun by allowing deuterium oxide to drop into the acetyl bromide. As soon as the manometer indicated an increase in pressure in the system, a stopcock to the atmosphere was opened. This was done in order to displace most of the nitrogen from the system. When fumes of deuterium bromide were evolved from the outlet, the stopcock was closed and the burettes were filled with gas by lowering the leveling bulb. The deuterium bromide source was then isolated from the burettes by turning a stopcock. The burettes were opened to the reaction flask and deuterium bromide was forced through the fritted disk into the pentane solution, under a pressure of about 12 mm. of mercury above atmospheric, by manipulation of the leveling bulb. When 1165 ml. (0.052 mole) of deuterium bromide had been passed into the solution a 0.5 ml. aliquot of the latter was diluted with pentane and analysed for remaining cyclohexadiene by ultraviolet spectrophotometry. The amount of diene used up was calculated to be 0.052 mole, indicating one to one stoichiometry. After the reaction had reached about 50 per cent of completion, the decrease in remaining cyclohexadiene following addition of a known volume of deuterium bromide was generally from 10 to 25 per cent less than the amount calculated on the basis of a mole for mole reaction. This effect can be attributed to the escape of some deuterium bromide from the solution at low concentrations of cyclohexadiene, rather than to a change in the stoichiometry

of the reaction. No dibromocyclohexanes were obtained from any of the addition runs.

When the reaction was 95 per cent or more complete, the addition of deuterium bromide was stopped and nitrogen was bubbled through the solution to displace any dissolved deuterium bromide. The pentane was then stripped off under nitrogen, at a pressure of about 70 mm. and with the distillation flask at 0°. When all the pentane had distilled, the pressure was decreased to 0.2 mm. Distillation of 3-bromocyclohexene-d occurred slowly without the application of heat. Deutero-3-bromocyclohexene having refractive index (n^{20}) of 1.5262 (lit.,⁶⁰ n^{20} 1.5269) was obtained in 83 per cent yield.

Unreacted cyclohexadiene was isolated from a run carried to about 80 per cent of completion. The infrared spectrum of a solution of the diene in carbon tetrachloride (ca. 40 mg. per ml. in 1 mm. cells) showed no absorption bands due to carbon-deuterium vibrations.

The addition of deuterium bromide to cyclohexadiene was carried out at 0° and at -78°. For the run at -78°, the workup procedure described above was modified. When it was found that the large amount of deuterium bromide dissolved in the pentane at -78° could not be removed by bubbling nitrogen through it, the solution was distilled under vacuum with the

⁶⁰J. D. Park, H. J. Gerjovich, W. R. Lycan and J. R. Lacher, J. Am. Chem. Soc., 74, 2189 (1952).

flask at -50° . To protect the vacuum pump a pyrex tube, 12 inches in length and 1 inch in diameter, was filled with sodium hydroxide pellets and inserted into the vacuum line. The yield of crude 3-bromocyclohexene remaining in the distillation flask after the pentane had been stripped off was 96 per cent. Only a fraction of the product was distilled in order to obtain an analytical sample. The bulk of the bromide was stored at -78° until required.

Preparation of Tetraethylammonium Acetate

Tetraethylammonium acetate was prepared from tetraethylammonium bromide, silver oxide and acetic acid in the following way. Silver nitrate (580 g., 3.25 mole) was dissolved in a minimum amount of water and the solution was made basic by the addition of one liter of a solution containing 160 g. (3 mole) of sodium hydroxide. The precipitated silver oxide was filtered and washed with water until free of base. It was added in small portions to a solution of 630 g. (3 mole) of tetraethylammonium bromide in one liter of water. The precipitated silver halide was removed by filtration and the filtrate was tested for bromide ion. Addition of silver oxide was continued until the test for bromide became negative. Acetic acid was added to neutralize the solution of tetraethylammonium hydroxide. Water was evaporated from the solution by evacuating the flask, at the temperature of the steam

bath, with a water aspirator. The crude tetraethylammonium acetate which separated was recrystallized by dissolution in hot, anhydrous acetone followed by cooling with a Dry Ice-acetone mixture. White, crystalline material obtained in this way was free from bromide ion. When dried over phosphorus pentoxide it slowly liquified. Owen and Smith⁶¹ have shown that the solid form is the tetrahydrate while the liquid form is the monohydrate of tetraethylammonium acetate. Unless otherwise specified, the monohydrate was used in the reactions reported later.

Typical Acetate Displacement on 3-Bromocyclohexene

3-Bromocyclohexene (4.0 g., 25 mole) was refluxed on the steam bath for 11 hours with tetraethylammonium acetate monohydrate (9.9 g., 0.048 mole) in 170 ml. of anhydrous acetone. The precipitated tetraethylammonium bromide was filtered off and washed with acetone. To the acetone solution was added 200 ml. of ether and 150 ml. of water and the organic layer was separated. It was washed once with 10 per cent potassium carbonate solution and once with water. The solution was dried over anhydrous potassium carbonate. Distillation through a 6 inch, insulated, Vigreux column gave 3.2 g. (90%) of 3-acetoxycyclohexene, b.p. 79 to 83° at 25 mm.

⁶¹L. N. Owen and P. N. Smith, J. Chem. Soc., 4035 (1952).

Typical Hydrogenation of 3-Acetoxycyclohexene

A solution of 3-acetoxycyclohexene (3.1 g., 0.022 mole) in 65 ml. of cyclohexane was hydrogenated at atmospheric pressure in the presence of 1 g. of five per cent palladium-on-charcoal. The mixture took up 103 per cent of the calculated amount of hydrogen gas. When absorption of hydrogen ceased, the solution was filtered through paper to remove the catalyst. The latter was washed with a few ml. of cyclohexane. The solution was then washed with ten per cent aqueous potassium carbonate to remove any acetic acid which might have been formed by hydrogenolysis of the starting material⁶². The cyclohexane layer was dried with potassium carbonate and the solvent was distilled off, at atmospheric pressure, through a 6 inch Vigreux column. Distillation of the residue under reduced pressure gave 2.54 g. (82%) of cyclohexyl acetate boiling in the range 75 to 80° at 25 mm. The infrared spectrum of the product showed no absorption at 6.10 microns indicating that little or no unsaturated ester was present.

⁶²When the catalyst was platinum and the solvent was ethyl acetate, cyclohexenyl acetate took up more than the calculated volume of hydrogen. The reaction was stopped after 130 per cent of the theoretical amount of hydrogen had been absorbed. Distillation of the solution gave a substantial amount of acetic acid boiling in the range 118 to 130° and only 16 per cent of crude cyclohexyl acetate. Hydrogenolysis occurred to the extent of about 50 per cent when the reaction was carried out in tetrahydrofuran with palladium-on-charcoal catalyst. Apparently solvent polarity is a critical factor in catalytic hydrogenation of some allylic compounds.

Saponification of Cyclonexyl Acetate

Cyclohexyl acetate (4.0 g., 0.028 mole) was refluxed for 3.5 hours with 15 per cent aqueous potassium hydroxide solution. Some material was lost when bumping occurred near the end of the heating period. The solution was extracted with ether and the ether layer was washed once with water. It was dried, first over potassium carbonate, and then over calcium sulfate. Distillation through a 6 inch, Vigreux column gave 2.26 g. (80%) of cyclohexanol boiling near 70° at 20 mm. The refractive index of the product was 1.4601 at 25° (lit.,⁶³ 1.4656 at 22.6°).

In analogous runs with deuterated ester the cyclohexanol was not distilled, but rather, the crude material left after evaporation of the ether was oxidized directly to cyclohexanone as described below.

Oxidation of Cyclohexanol

Cyclohexanol was oxidized by cyclohexanone according to the procedure of Fieser⁶⁴. Sodium dichromate-dihydrate (3.0 g.) was dissolved in 5.5 ml. of glacial acetic acid and the

⁶³Handbook of Chemistry and Physics, p. 888, 39th ed., Chemical Rubber Publishing Company, Cleveland, Ohio (1958).

⁶⁴L. F. Fieser, "Experiments in Organic Chemistry," p. 94, 3rd ed., D. C. Heath and Co., New York (1955).

solution was cooled to about 10° . It was poured all at once into a 6 inch test tube containing a solution of cyclohexanol (3.0 g., 0.03 mole) in 5 ml. acetic acid at 10° . The mixture was stirred briefly with a thermometer. A maximum temperature of 52° was attained in 15 minutes. The mixture was allowed to stand at room temperature for 10 more hours, when water was added and the cyclohexanone was steam distilled until no more oil came over. Extraction of the distillate with ether, drying of the ether solution with potassium carbonate and distillation through a 6 inch, Vigreux column gave 1.5 g. (51%) of cyclohexanone boiling in the range 54 to 58° at 20 mm. Deuterocyclohexanones were subjected to equilibration with aqueous base prior to distillation.

Hydrogen-deuterium Exchange between Cyclohexanone and Deuterium Oxide

Cyclohexanone (1.52 g.) was allowed to stand at room temperature with 4 ml. of heavy water (approximately 60 per cent deuterium oxide) and 10 drops of triethylamine for 18 hours with occasional shaking. The milky suspension was then extracted with ether and the ether layer was dried with potassium carbonate. All the ether and most of the triethylamine were then distilled off at atmospheric pressure by heating the distilling flask to 100° with an oil bath. The residual cyclohexanone was analysed qualitatively for deuterium in the

infrared with a Perkin-Elmer Infracord spectrophotometer. The spectra of solutions containing 100 mg. cyclohexanone per ml. of carbontetrachloride showed a strong absorption band at 4.60 microns with a shoulder at 4.70 microns. Carbon-deuterium stretching vibrations are expected to appear in this region. It follows then that alpha hydrogen or deuterium of cyclohexanone exchanges with hydrogen or deuterium of water under the conditions described above.

Deuterium-hydrogen Exchange between Deuterio-cyclohexanone and Water

Deuterio-cyclohexanone was one of the products obtained from deuterio-3-bromocyclohexene as indicated in the general scheme in Figure 1. In order to determine how much of the deuterium was in the alpha positions of the cyclohexanone the latter was subjected to base-catalysed exchange with a large excess of water. The procedure was similar to the one outlined above. About 15 ml. of water was used for each gram of cyclohexanone and one drop of triethylamine was added for every 3 ml. of water. The equilibration conditions were again 18 hours at room temperature. Cyclohexanone was extracted with ether and the ether layer was washed with five per cent hydrochloric acid to remove triethylamine. The solution was dried with potassium carbonate and distilled through a 6 inch, insulated Vigreux column. Physical constants of

the samples of deuterocyclohexanone obtained from different addition runs are listed in Tables 2 and 3.

Preparation of Potassium Tertiary Butoxide

Tertiary butanol (Matheson, Coleman and Bell) was refluxed with sodium and distilled through a 1.5 foot Vigreux column. A middle fraction boiling at 81° was treated with potassium metal. The procedures for handling potassium and for the preparation of potassium tertiary butoxide described in *Organic Syntheses*⁶⁵, were followed. Excess butanol was removed from the product by triturating it twice with a few ml. of benzene and by decanting the benzene. The potassium tertiary butoxide was then dissolved in anhydrous, thiophene-free benzene.

Elimination of the Elements of Hydrogen

Bromide from 3-Bromocyclohexene

Samples of deuterio-3-bromocyclohexene, prepared by the addition of deuterium bromide to cyclohexadiene, were subjected to conditions which caused elimination, thus regenerating cyclohexadiene. Elimination with potassium tertiary-butoxide was chosen because of the rapid rate of the reaction at temperatures low enough to make facile allylic rearrangement of 3-bromocyclohexene improbable. In a typical run,

⁶⁵A. C. Cope, *Organic Syntheses*, 30, 19 (1950).

3-bromocyclohexene (5.0 g., 0.031 mole) at -78° was added, all at once, to 110 ml. of 0.297N potassium tertiary-butoxide in benzene at 20° . The mixture was shaken for 15 minutes and the liquid was decanted into a distilling flask from the potassium bromide which had settled out. Cyclohexadiene and benzene were distilled under reduced pressure at a maximum pot temperature of 50° . The distillate was immediately treated with maleic anhydride by a procedure analogous to the one described in the next section.

Elimination from one sample of deuterio-3-bromocyclohexene was carried out at the reflux temperature of quinoline. The bromide (4.1 g., 0.025 mole) was added dropwise to 25 ml. of refluxing quinoline in a 50 ml. distilling flask and the diene was removed by continuous distillation. When all the bromide had been added, 5 ml. of toluene was dropped into the quinoline to act as a "chaser". The distillate was diluted with 40 ml. of toluene prior to reaction with maleic anhydride, which is described below.

Preparation and Purification of Bicyclo-(2,2,2)-

Δ^5 -octene-2,3-dicarboxylic Anhydride

To the solution of cyclohexadiene in toluene obtained as indicated above, was added finely divided maleic anhydride (2.7 g., 0.027 mole). The mixture was swirled to dissolve the anhydride and was then heated at 100° with an oil bath for

about 5 hours. Skelly B was added to precipitate the adduct which was removed by filtration and recrystallized from hot Skelly B. The first crop of crystals, weighing 1.83 g., melted at 146.5 to 147° after being dried in a vacuum desiccator. A second crop of crystals, obtained by concentrating the mother liquor, weighed 1.63 g. and melted at 142 to 145°. The total yield was 90 per cent.

Benzene solutions of cyclohexadiene, obtained by elimination with potassium tertiary-butoxide as described above, were treated with maleic anhydride in an analogous manner. The yields of adduct obtained in this way were always lower (35 to 60 per cent) than yields obtained via elimination with quinoline, partly because the adduct had to be recrystallized from Skelly B three or four times before the melting point exceeded 140°. The nature of the impurities was not investigated. Small quantities of a water-soluble, white solid, melting at 245 to 255° with sublimation, were obtained twice.

Pyrolysis of 3-Acetoxycyclohexene

The pyrolysis was carried out in a Pyrex tube of 20 mm. diameter packed with one-eighth inch Pyrex helices. The packed section, which was 15 cm. long, was heated to 500° by one section of a three-unit electric macro combustion apparatus. Samples of the ester weighing from one to two grams were dropped into the top of the vertically-mounted pyrolysis

tube at the rate of one drop in 5 seconds. Oxygen-free nitrogen was passed into the top of the tube at the rate of one bubble in 2 seconds. The pyrolysis products were collected in a trap cooled by a Dry Ice-acetone bath. Toluene was added to the pyrolysis products and the solution was washed with dilute aqueous base to remove acetic acid. The toluene layer was dried over potassium carbonate before treatment with maleic anhydride by the procedure described in the previous section.

Pyrolysis of Cyclohexyl Acetate

Cyclohexyl acetate was pyrolysed in the apparatus and under the conditions described above except that the temperature was raised to 530°. A larger sample of ester was used to permit purification of cyclohexene by distillation. Instead of toluene, ether was used to dissolve the pyrolysis products. Acetic acid was removed from the solution by washing it with dilute base. The ether layer was dried with potassium carbonate and the ether was distilled slowly through a 6 inch, Vigreux column. Residual cyclohexene was transferred to single-unit micro distillation apparatus having a Vigreux column, 4 inches long and .25 inches in diameter, surrounded by a vacuum jacket. Physical constants of the cyclohexene are reported in Table 2.

Preparation of 1-Deutero- Δ^2 -Cyclohexenol

A solution of 2-cyclohexenone (6.53 g., 0.068 mole) in 50 ml. of ether was added dropwise, with stirring, to a slurry of lithium aluminum deuteride (0.76 g., 0.02 mole) in 50 ml. of ether. The mixture was refluxed overnight. Water and dilute hydrochloric acid were added cautiously to hydrolyse the mixture and to dissolve inorganic salts. The ether layer was separated and washed with aqueous base. It was dried, first over sodium sulfate and then over calcium sulfate. Distillation gave 5.0 g. of labelled cyclohexenol b.p. 55 to 58° at 8 mm.

Preparation of 1-Deutero-3-Bromocyclohexene

A cold solution of 1-deutero- Δ^2 -cyclohexenol (5.0 g., 0.05 mole) in 50 ml. of ether was added to thionyl bromide (11.0 g., 0.053 mole). The mixture was allowed to stand at 0° for 1 hour. Ether was removed by distillation at 15 mm. pressure without heating. A solid, which was probably the bromosulfite, settled out in the flask as the volume of liquid decreased. When the flask was heated to 50°, the solid decomposed and turned black. The yield of 1-deutero-3-bromocyclohexene boiling at 48° (8 mm.) was 3.2 g. The infrared spectrum showed a carbon-deuterium band at 4.50 microns, indicating that deuterium was in a vinyl position.

Preparation of Trans-2-Deuterocyclohexyl Bromide

Deuterium bromide, generated from 5.0 g. (0.25 mole) of heavy water and 50 g. (0.33 mole) of acetyl bromide, was passed into a solution of 30 g. (0.36 mole) of cyclohexene in 200 ml. of pentane. Chloranil (0.05 g.) and di-*t*-butyl-*p*-cresol (0.05 g.) were used as inhibitors. The apparatus and procedure were those described on Page 27. All the deuterium bromide was passed into the solution in 1 hour.

The pentane solution was washed thoroughly with aqueous sodium carbonate and it was dried over calcium chloride. Distillation gave unreacted cyclohexene plus 7.1 g. of deuterocyclohexyl bromide b.p. 47 to 50° at 15 mm. Infrared spectra of the recovered cyclohexene, obtained at concentrations as high as 200 mg. per ml. carbon tetrachloride, showed a very weak band at about 4.8 microns. Absorption due to allyl deuterium is expected in this region. It is probable, therefore, that a small percentage of the bromide contained more than one deuterium atom per molecule.

Preparation of Cis-2-Deuterocyclohexyl Acetate

Trans-2-deuterocyclohexyl bromide (5.76 g., 0.039 mole) was added to a solution of tetraethylammonium acetate monohydrate (16.5 g., 0.080 mole) in 100 ml. of anhydrous acetone. The mixture was refluxed for 15 hours and the precipitated tetraethylammonium bromide was removed by filtration. Ether

(150 ml.) and water (150 ml.) were added to the acetone solution and the organic layer was separated. It was washed thoroughly with water and dried over potassium carbonate. Distillation of the ether solution gave 0.6 g. of labelled acetate, boiling at 62° (16 mm.).

Unsuccessful Experiments

The following reactions were carried out before the scheme finally used in this work was attempted. They were designed to convert the labile deuterio-3-bromocyclohexene into a derivative suitable for unambiguous determination of the position of deuterium in the parent compound. These approaches were abandoned, generally because the yields of desired products were too low.

Catalytic hydrogenation of 3-bromocyclohexene

Attempts to hydrogenate 3-bromocyclohexene were made under a variety of conditions. The solvent, the catalyst, the temperature and the pressure of hydrogen were varied in search of suitable conditions for the reaction. Some hydrogenolysis was observed in all attempts. Fumes of hydrogen bromide were evolved when the reaction flask was opened.

At atmospheric pressure and 25° , a mixture of 3-bromocyclohexene (3.0 g., 0.0086 mole), 20 ml. of absolute methanol and platinum oxide (0.060 g.) was allowed to absorb two per cent more than the calculated amount of hydrogen.

The reaction mixture was filtered, diluted with water and extracted with ether. The ether layer was dried over potassium carbonate and distilled. A small amount of unidentified material, boiling in the range 65 to 100°, could have been cyclohexane arising from hydrogenolysis of 3-bromocyclohexene. A second fraction, boiling at 125 to 135°, was identified on the basis of its boiling point and pleasant odor as either cyclohexyl methyl ether or cyclohexenyl methyl ether or possibly a mixture of the two. It is apparent that 3-bromocyclohexene solvolyses fairly rapidly in absolute methanol.

In a second run the only change from the above conditions was the substitution of dioxan for methanol. The system took up the calculated volume of hydrogen in 5 days. Distillation of the filtered solution gave only 0.98 g. of high-boiling material (b.p. 66 to 70° at 25 mm.) having a refractive index of 1.5168 at 20°. The refractive index of 3-bromocyclohexene is about 1.5269⁶⁶ at 20° while that of cyclohexyl bromide is near 1.4937⁶⁷. These figures suggest that the product obtained was mostly the starting material, possibly containing some cyclohexyl bromide. No attempt was made to isolate cyclohexane, the expected ultimate product of hydrogenolysis,

⁶⁶J. D. Park, H. J. Gerjovich, W. R. Lycan, and J. R. Lacher, J. Am. Chem. Soc., 74, 2189 (1952).

⁶⁷Determined by the author using Reagent Grade cyclohexyl bromide (Matheson, Coleman and Bell).

from the dioxan solvent because the boiling points of the compounds are close together.

Similar results were obtained with five per cent palladium-on-charcoal catalyst in ethyl acetate at low temperature and under a high pressure of hydrogen. When 3-bromocyclohexene (5.0 g., 0.031 mole) in 80 ml. of ethyl acetate was shaken with 0.5 g. of the catalyst at -55° under 40 p. s. i. of hydrogen, no decrease in the pressure was observed in 80 minutes. Copious fumes of hydrogen bromide were evolved when the flask was opened. The solvent was stripped off under reduced pressure and the residue was distilled twice through a 6 inch Vigreux column. From the second distillation, 0.31 g. of starting material (b.p. 40° at 5 mm., n_{25}^{25} 1.5269) was collected.

Hydrogenation with a less active catalyst in the form of palladium supported on barium sulfate, was attempted next. The catalyst had been used several times by Mr. George Wenzinger. 3-Bromocyclohexene (10.0 g., 0.062 mole) in 50 ml. benzene was shaken with one gram of the catalyst for 9.5 hours under a hydrogen pressure of 28 p. s. i. The pressure was increased to 40 p. s. i. for 15 more hours. Distillation gave 7.0 g., b.p. 26 to 27° at 2 mm. The infrared spectrum of the liquid showed very weak absorption at 6.10 microns. It reduced permanganate rapidly, however, indicating that some easily oxidized function, such as an olefinic

linkage, was present. In addition the carbon-hydrogen band at about 3.32 microns which appears in the spectrum of 3-bromocyclohexene but not in that of cyclohexyl bromide, was present. It seems likely that the material isolated was mainly a mixture of 3-bromocyclohexene and cyclohexyl bromide.

No further attempt was made to hydrogenate 3-bromocyclohexene when it was found that 3-acetoxycyclohexene derived from it can be hydrogenated in good yield.

Ozonolysis of 3-bromocyclohexene

Ozone, generated by a Welsbach T-33 Ozonator was bubbled through a fritted disk into a solution of 3-bromocyclohexene (8.0 g., 0.049 mole) in 100 ml. of ethyl acetate. Gases not absorbed by the solution were bubbled through an aqueous solution of potassium iodide. The ozonolysis was judged complete when iodine was liberated in the potassium iodide solution.

Acetic acid (100 ml.) was added to the reaction mixture and the mixed solvent was concentrated by evaporation under reduced pressure at room temperature. Additional acetic acid (200 ml.) was added and evaporation of the solvent was continued until a suspension was obtained. This suspension was added over a period of 5 minutes to a solution of 24.2 g. of 30 per cent hydrogen peroxide, 1.0 ml. of concentrated sulfuric acid and 45 ml. of water. The resulting solution was allowed to stand at room temperature overnight before it was

heated to 100° for 0.5 hours. The gummy, yellow paste which had settled was separated and dissolved in dilute sodium hydroxide solution on the steam bath. A pleasant odor was given off by the hot solution indicating that neutral compounds were probably present. The latter were removed by ether extraction of the basic solution. The solution was then acidified and again extracted with ether. Evaporation of the ether left a viscous oil from which about 0.1 g. of a white solid (m.p. 175 to 185°) eventually crystallized. The melting point of α -bromoadipic acid is 131°⁶⁸. A search of the literature revealed that succinic acid is obtained from the ozonolysis of 3-chlorocyclohexene⁶⁹. The melting point of succinic acid is 185°⁷⁰. It is, therefore, likely that ozonolysis of 3-bromocyclohexene, followed by oxidation of the ozonide, also gives succinic acid. As the mechanism for ozonolysis of allylic compounds resulting in the loss of two carbon atoms has not been worked out, the reaction could not be used as part of a degradative scheme.

Osmium tetroxide-periodate oxidation of 3-bromocyclohexene

Oxidation of olefins to carbonyl compounds by periodate in the presence of a catalytic amounts of osmium tetroxide

⁶⁸W. H. Ince, J. Chem. Soc., 67, 159 (1895).

⁶⁹E. C. Kooyman and E. Farenhorst, Rec. Trav. Chim., 70, 867 (1951).

⁷⁰Handbook of Chemistry and Physics, 30th ed., Chemical Rubber Publishing Co., Cleveland, Ohio (1947).

has been reported in the literature^{71, 72}. For compounds giving aldehydes sensitive to self condensation, Pappo and co-workers⁷¹ carried out the reaction in a two-phased solvent consisting of equal volumes of ether and water. A slight modification of their procedure was used in an attempt to oxidize 3-bromocyclohexene to α -bromoadipaldehyde.

To 750 ml. of water and 300 ml. of ether in a 3 liter round-bottomed flask, was added 100 g. (0.62 mole) of 3-bromocyclohexene and 0.5 g. of osmium tetroxide. Potassium periodate (224 g., 0.975 mole) was then added in small portions, with stirring, over a period of 10 hours. The ether layer was separated and dried over potassium carbonate and calcium sulfate. It was then added dropwise to a slurry of lithium aluminum hydride (20 g., 0.53 mole) in ether in order to reduce the di-aldehyde, if any, to the corresponding diol. The mixture was refluxed for 20 hours after which it was hydrolysed by the addition of water and hydrochloric acid. Distillation of the dried ether layer gave 4.54 g., b.p. 40° at 2 mm. mercury.

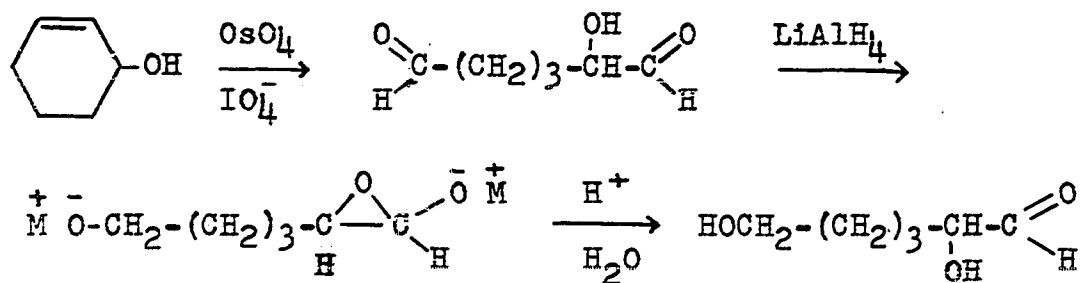
The infrared spectrum of the product showed a broad band at about 2.9 microns, a carbonyl band at 5.85 microns and a shoulder at 6.1 microns. A test for aldehydes with Tollen's

⁷¹R. Pappo, D. S. Allen, Jr. R. U. Lemieux and W. S. Johnson, J. Org. Chem., 21, 478 (1956).

⁷²P. Wieland, K. Heusler, H. Ueberwasser and A. Wettstein, Helv. Chim. Acta 41, 74 (1958).

Reagent was positive. The compound reacted with 2,4-dinitrophenylhydrazine and with semicarbazide hydrochloride in a few hours to form solids melting at 115 to 117° and 177°, respectively. Permanganate oxidation of 1 g. of the liquid gave 0.4 g., m.p. 90 to 95°, of an acid having a neutralization equivalent of 66.6. The melting point and neutral equivalent of glutaric acid are 97.5° and 66.0, respectively.

The infrared and other data seem to indicate that the product contained a hydroxyl group and an aldehyde function. It was found that 3-bromocyclohexene hydrolyses rapidly in water. Hence it is likely that the first step that occurred in the attempted oxidation was solvolysis of the halide, even in the presence of the ether phase. The observed product was, therefore, probably derived from 3-hydroxycyclohexene. Qualitative elemental analysis showed that the compound did not contain halogen, indicating that bromine was lost in some stage of the reaction sequence. The product may have been 2,6-dihydroxyhexanal formed in the manner suggested below.



Oxidation of the final product would yield glutaric acid. Furthermore, equilibrium between the free-aldehyde and the corresponding hemiacetal could account for the low intensity of the carbonyl band in the infrared and for the slow formation of the derivatives. A search of the literature failed to produce physical constants for 2,6-dihydronyhexanal or for any carbonyl derivatives of it.

Epoxidation of 3-bromocyclohexene

3-Bromocyclohexene (20.0 g., 0.123 mole) was stirred at 0° with 0.138 moles of perbenzoic acid⁷³ in 300 ml. of chloroform. The rate of consumption of peracid was followed by iodometric titration of aliquotes of the solution. The approximate per cent completion was 57 after 11 hours and 85 after 36 hours. After 42 hours the chloroform solution was washed three times with 35 ml. of 10 per cent sodium carbonate solution and once with 25 ml. of saturated sodium chloride solution. It was dried with sodium sulfate and the solvent was stripped off under reduced pressure. Distillation of the residue gave 14.0 g. of a fraction boiling in the range 43 to 53° at 3 mm. and 2.3 g. of a second fraction (b.p. 35° at 1 mm.). Infrared spectra of the two liquids were similar enough to justify the combination of the two fractions. The

⁷³H. Gilman and A. H. Blatt, eds., "Organic Syntheses, Collective Vol. 1," p. 431, John Wiley and Sons, Inc., New York (1941).

infrared spectra, run in a capillary cell, had a weak carbonyl band at 5.85 microns which was attributed to a ketonic impurity. Absorption bands at about 8.0, 8.6 and 11.6 microns have been assigned to the oxirane ring⁷⁴. These all appeared as sharp peaks. Patterson⁷⁵ has found that oxiranes have additional characteristic infrared absorption bands at 11.2 and 12.3 microns. The spectra under discussion here had a sharp band at 11.25 microns, but there was no trace of one at 12.3 microns.

Reaction of 3-bromocyclohexene epoxide with phenylmagnesium bromide

To an ether solution of the epoxide of 3-bromocyclohexene (14.2 g., 0.08 mole) was added dropwise 68.5 ml. of 1.24 N phenylmagnesium bromide in ether. The solution had to be heated during the addition to maintain a slow reflux rate. When about half the Grignard reagent had been added to the epoxide, a white precipitate appeared in the flask. When all the reagent had been added and the mixture had been refluxed for 12 hours, a liquid phase appeared in place of the precipitate. The mixture was hydrolysed with ammonium chloride solution and the ether layer was separated. It was dried with potassium carbonate prior to distillation of the ether. There

⁷⁴L. J. Bellamy, "The Infra-Red Spectra of Complex Molecules," 2nd ed., p. 118, John Wiley and Sons, Inc., New York (1958).

⁷⁵W. A. Patterson, Analyt. Chem., 26, 823 (1954).

was obtained 2.1 g. of unidentified forerun (b.p. 20° at 35 mm.) which probably contained ether and some benzene formed by hydrolysis of excess Grignard reagent. The residue in the distilling flask would not distill when the pot temperature was raised to 50° at 1.5 mm. mercury. It was a viscous brown oil weighing 13.8 g., which would not crystallize on standing. The whole sample was dissolved in 10 ml. of benzene and the solution was chromatographed on neutral alumina, using Skelly B as eluent. Biphenyl (0.51 g., m.p. 57 to 58° , mixed m.p. 56 to 57°) was obtained from the first 100 ml. of eluent. Further elution of the column gave 0.77 g. of a bromine-containing solid, melting at 128 to 131° , and 0.33 g. of purer material melting at 135 to 139° . Recrystallization of the latter afforded an analytical sample melting at 138 to 140° .

Anal. Calcd. for $C_{12}H_{15}Br$: C, 56.15; H, 5.89; Br, 31.3.

Found: C, 56.14; H, 6.04; Br, 29.5.

The analytical results indicate that the product may have been a 2-bromo-6-phenylcyclohexanol or a 2-phenyl-3-bromocyclohexanol. Either one or both of these compounds would be expected from the attack by phenyl Grignard reagent on the oxirane function of the substrate.

The infrared spectrum of the higher-melting fraction in carbon tetrachloride had the following peaks (units are in microns while s, m and w denote strong, medium and weak intensity, respectively): 2.82s, 3.30m, 3.38m, 3.48s, 3.55s,

5.22w, 5.62w, 5.95w, 6.30m, 6.75m, 6.98s, 7.31w, 7.50m, 7.70w, 7.86s, 8.29s, 8.57m, 8.99s, 9.32 (shoulder), 9.46s, 9.75m, and 10.72s.

Several liquid fractions were also obtained from the chromatographic column. Three of these, together weighing about 3.2 g. had very similar infrared spectra with a carbonyl band at 5.82 microns. A later fraction had only one strong band other than carbon-hydrogen bands in its infrared spectrum (carbon tetrachloride solution). The band was at 9.14 microns; the region where ethers absorb strongly.

The carbonyl compounds might have been α -bromocyclohexanone or α -phenylcyclohexanone. The former could conceivably be derived from an enolate salt formed by the action of magnesium halide, which is present in all Grignard reagents, on the epoxide. α -phenylcyclohexanone could be obtained via coupling between the epoxide of 3-bromocyclohexene and phenyl Grignard reagent, followed by opening of the epoxide as postulated for the formation of α -bromocyclohexanone.

The compound which showed absorption characteristics of ethers may have been formed by attack of the Grignard reagent on oxygen rather than on carbon of the oxirane function. One product to be expected from such reaction between the epoxide and the Grignard reagent under consideration, is phenyl- Δ^2 -cyclohexenyl ether. The infrared spectrum of the product did not have bands expected for an aromatic ring and it had only

a minute peak at 6.18 microns in the region where the double bond of an allyl ether should be detected. Hence the compound was probably not phenyl- Δ^2 -cyclohexenyl ether.

This approach to the analysis of deuterio-3-bromocyclohexene for the position of deuterium was dropped because of the complexity of the product mixture whose components were nearly all viscous oils.

Analysis for Deuterium

To analyse a compound for deuterium content a sample large enough to yield about 0.25 g. of water was burned in a combustion tube and the water was collected. The water was purified and analysed for deuterium oxide content (weight per cent) by a method involving the density. The number of deuterium atoms per molecule of organic precursor could then be calculated.

Combustion apparatus

The combustion train consisted of a three-unit, macro furnace with a Vycor combustion tube of 1.8 cm. diameter having a 24-40 standard joint at one end and a 14-35 joint at the other. A plug of silver wool was packed into the tube near the small opening to remove halogens from the products of combustion. After the silver wool there was a small plug of glass wool, followed by enough copper oxide to half fill

the tube. Oxygen from a cylinder was dried by bubbling it through concentrated sulfuric acid in two gas-washing bottles and by passing it through a three-foot, Pyrex tube of 1.5 inch diameter containing potassium hydroxide pellets, a plug of glass wool and anhydrous calcium sulfate, in that order. The receiver for combustion water was U-tube number 1 in Figure 2.

To prepare for a combustion the whole tube was heated to dull redness by turning on the furnace at 55 volts, and oxygen was passed into the tube at a rate of about one bubble per second. This was done in order to completely remove any materials from a previous combustion. The small and medium sections of the furnace were then turned off and allowed to cool. The receiving tube was attached and thoroughly flamed with a micro burner. When it had cooled, a mixture of Dry Ice and acetone in a Dewar flask was raised under the U-tube.

The sample to be burned was quickly introduced through the large opening of the combustion tube by momentarily disconnecting the oxygen inlet. Solids were introduced in a porcelain combustion boat which had been flamed with a Meeker burner and cooled in a desiccator. Liquids for combustion were stored in pyrex ampules. For a combustion the top of an ampule was cut with a file and the ampule was pushed tip first into the Vycor tube until it touched the copper oxide packing. The heat transferred to the sample by the copper

oxide was sufficient to vaporize volatile liquids slowly from the ampule. The center section of the furnace was turned on at a low voltage to vaporize higher boiling liquids at a reasonable rate. From previous work the author has found that rapid volatilization of a sample leads to "flash-backs" which may open the connection at the oxygen inlet or burst the combustion tube. For the combustion of solids the center section of the furnace was turned on at a fairly high setting to sublime or melt the material. Oxygen was passed into the tube at the rate of about one bubble per second throughout the duration of a combustion.

When the ampule or boat was empty, the water which had collected in the outlet joint of the tube was "swept" into the receiver by heating with a micro burner. The U-tube was removed from the combustion system and was closed with a standard taper stopper.

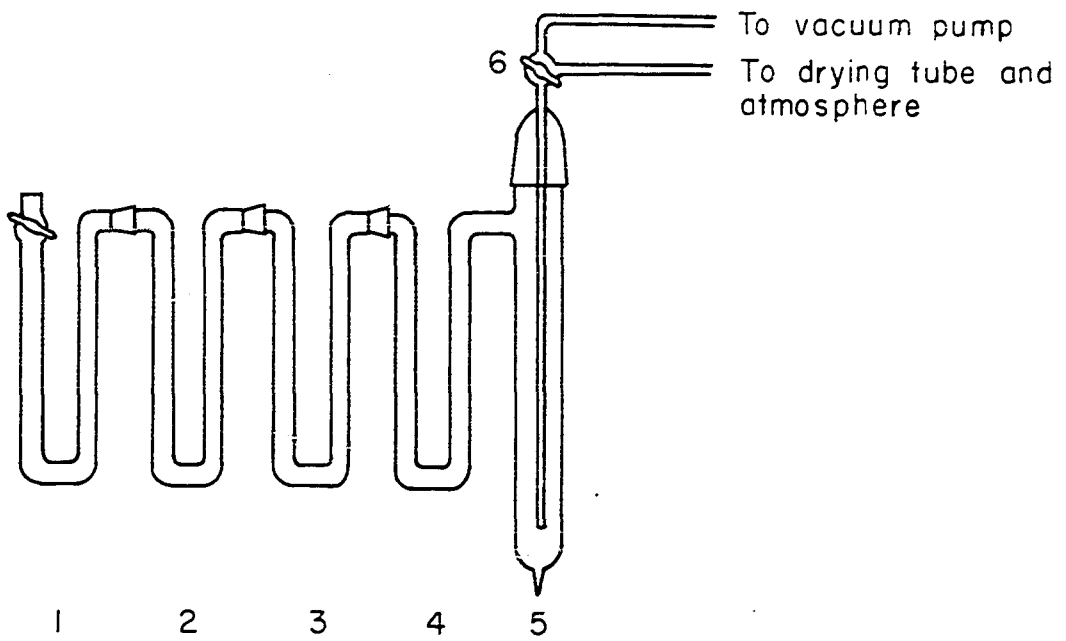
Purification of water samples

Water obtained from the oxidation process was purified by a modification of the method of Keston, Rittenberg and Schoenheimer⁷⁶. The purification apparatus is shown in Figure 2. It consisted of three Pyrex U-tubes with standard taper (14-35) joints numbered 2, 3 and 4, in the diagram. Tube 1 served as receiving tube during combustions and

⁷⁶A. S. Keston, D. Rittenberg and R. Schoenheimer, J. Biol. Chem., 122, 227 (1937).

contained the water sample to be purified. Before connecting this tube to the system the rest of the apparatus was evacuated to 0.15 mm. mercury and was thoroughly flamed with a micro burner. The two-way stopcock 6, in Figure 2, was turned to allow air to enter the system through a tube, 12 inches long and one inch in diameter, filled with Drierite. A plug of glass wool in the drying tube kept particles of drying agent from being swept into tube 5. Small amounts of calcium oxide and potassium permanganate were then dropped into tube 2 and tube 1 was connected. Tube 2 was surrounded by a Dry Ice-acetone freezing mixture and the stopcock 6 was returned to the vacuum position. The water sample was distilled into tube 2 by warming tube 1 with a beaker full of water. When the distillation was completed the system was restored to atmospheric pressure, tube 1 was removed, tube 2 was closed with a Pyrex stopper and the freezing bath was moved to tube 3. The water in tube 2 was then refluxed on the calcium oxide and permanganate for a moment. When the water had cooled the system was again evacuated to distill the sample into tube 3. The water was distilled twice more, so that it ended up in tube 5. It was transferred from the latter to a clean, dry serum vial equipped with self-sealing hypodermic stopper. The transfer was made with Pyrex tubing having a long capillary tip. Clean and dry tubing for this purpose was drawn out to a capillary just before use and a capillary was used

Figure 2. Apparatus for purification of water samples



only once.

Analysis of water samples for deuterium oxide content

Water samples obtained by the combustion of deuterated organic compounds were analysed by a method involving the density. The falling drop method described by Kirshenbaum⁷⁷ was employed. It involves the time of fall of a drop of the water through a given length of a water-insoluble medium of low viscosity.

The apparatus consisted of a Pyrex tube 62 cm. in length and 1.5 cm. in diameter. One end was closed and the other was a 19-38 ground glass joint. The tube was filled with a mixture of bromobenzene and kerosene of density 0.9988 at 26.2°, to within 5 cm. of the top and it was mounted vertically in a thermostat to within 4 cm. of the top. It was supported firmly so that no vibrations were transmitted to the tube. The temperature of the water in the thermostat was kept at about 26.2° and it was controlled to within $\pm 0.008^\circ$.

To obtain precision with the falling drop method it is necessary to reproduce the drop size as well as possible. Very complicated micropipettes for controlling drop size have been constructed⁷⁷. A simple micropipette that has been reported to give drop sizes reproducible to within 1 per cent,

⁷⁷I. Kirshenbaum, "Physical Properties and Analysis of Heavy Water," pp. 324-343, McGraw-Hill Book Co., Inc., New York (1951).

is that described by Wright⁷⁸. Such a pipette was made out of 0.5 mm. capillary tubing by drawing out a section to a fine capillary. The tip was rounded smoothly by grinding it with a carborundum stone. Two marks were scratched onto the capillary tubing at points above the tip.

The pipette was equipped with a screw arrangement⁷⁸ for accurately filling it to the top mark and for discharging the sample exactly to the lower mark. From the diameter of the capillary and the distance between the marks, the drop size was calculated to be about 5 cubic mm. The uniformity of the drop size can be inferred from the reproducibility of the falling time for drops of the same sample (Table 1).

With the micropipette dry and ready, a vial was opened and the pipette was rinsed twice with the sample to be analysed. It was then refilled and the tip was wiped carefully with hard filter paper. The pipette was held above the falling drop apparatus in such a way that the tip of the pipette just entered the solution. Water was discharged to the lower mark to form a drop clinging to the tip of the pipette. The drop was released by slowly raising the pipette out of the solution. The time required for it to fall

⁷⁸M. M. Wright, Trail Report 3 (SAM Report 100XR-216), [Substitute Alloy Materials] June 15, 1942. (Original not available for examination; cited by I. Kirshenbaum, "Physical Properties and Analysis of Heavy Water," p. 336, McGraw-Hill Book Co., Inc., New York 1951).

through a 20 cm. length of the solution was determined with a stopwatch graduated in tenths of a second. A cathetometer, accurate to $\pm .005$ mm. was focused at a point about 28 cm. from the bottom of the tube. When the drop passed the horizontal cross-hair of the instrument, the stopwatch was started and the cathetometer was lowered by exactly 20 cm. to obtain the second observation.

A calibration curve was obtained by allowing drops of standard protium oxide-deuterium oxide solutions to fall through the tube and by plotting weight per cent deuterium oxide against time of fall (sec.). The curve is shown in Figure 3. The curve for a second bromobenzene-kerosene solution is shown in Figure 4. Weight per cent deuterium oxide in the unknowns was read directly from large plots of the curves.

Figure 3. Calibration curve for Solution I in the falling-drop apparatus

Ordinate: weight per cent deuterium oxide

Abcissa: time in seconds

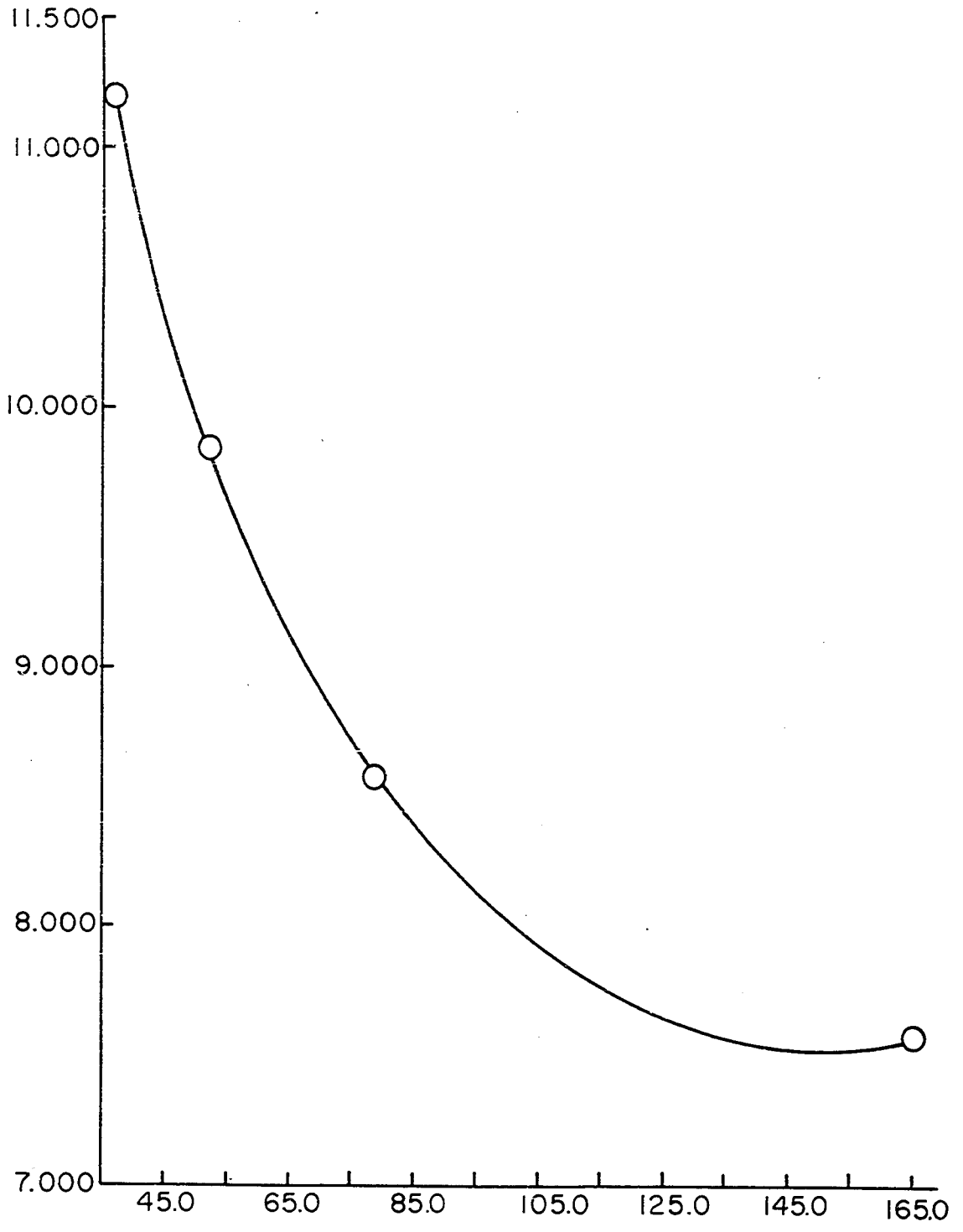
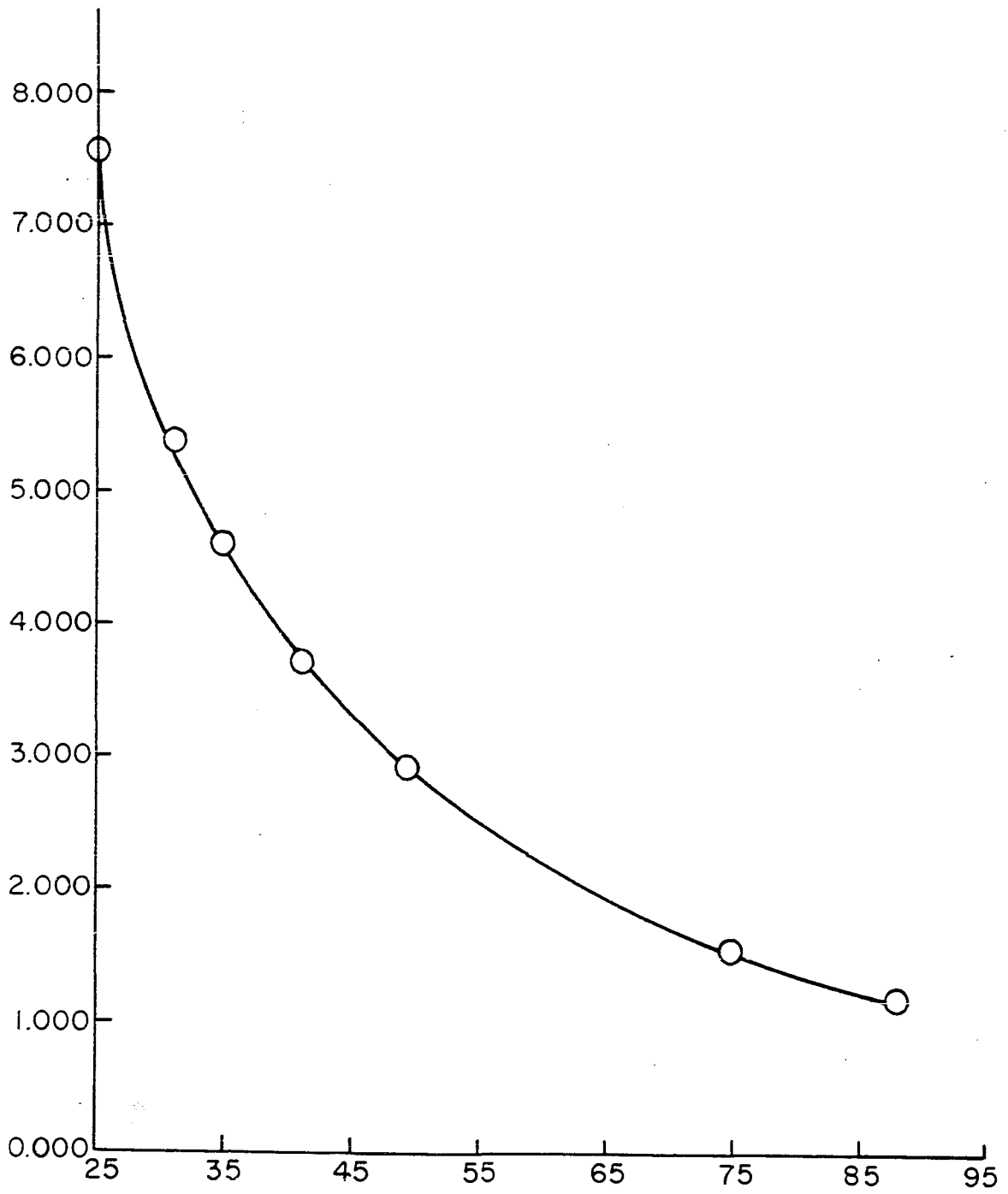


Figure 4. Calibration curve for Solution II in the falling-drop apparatus

Ordinate: weight per cent deuterium oxide

Abscissa: time in seconds



RESULTS

General Treatment of Data

Three drops of water from each combustion sample were timed in the falling-drop apparatus. The three figures thus obtained were averaged and the weight per cent deuterium oxide corresponding to the mean falling time was read from a large scale plot of the appropriate calibration curve. Where duplicate or triplicate combustions of the same compound had been carried out, the percentage figures obtained as indicated above, were again averaged. Data from calibration of the falling-drop apparatus are tabulated in Table 1 and plotted in Figure 3 and Figure 4. Time of fall data for the combustion waters are listed in Table 2 for samples originating from addition of deuterium bromide to cyclohexadiene at -78° . Data for the addition run carried out at 0° are tabulated in Table 3.

Mean per cent by weight deuterium oxide values for water samples were used to calculate the number of gram atoms of deuterium per mole of organic precursor by means of the

$$\text{equation } A = \frac{9NW}{10^3 - W}$$

where A = gram atoms of deuterium per mole of organic compound;

N = the number of hydrogen atoms in an undeuterated molecule of the compound;

W = the weight per cent deuterium oxide in the water of

combustion of the compound.

The above relationship can be derived by considering the weights of protium oxide and deuterium oxide produced by combustion of a partially deuterated organic compound.

Losses of deuterium accompanying a given reaction were obtained by simple subtraction of the deuterium contents of the product from that of the reactant. Percentage losses were obtained by dividing loss figures by initial deuterium content.

An estimate of the amount of cis-2-deuterium in the cyclohexyl acetate was obtained from the pyrolysis results in the following manner. Three species of cyclohexyl acetate had to be considered. The fraction of molecules having cis-2-deuterium was denoted by I; that of molecules having deuterium in positions other than the cis-2-position was denoted by II and the fraction of undeuterated molecules was labelled III. From the analysis of the acetate (0.72 gram atoms deuterium per mole) Equation 1 was obtained.

$$(1) \frac{I + II}{III} = \frac{0.72}{0.28} = 2.7$$

The rates of loss of hydrogen and deuterium during pyrolysis of the acetate are given by Equations 2 and 3, respectively,

$$(2) - \frac{dH}{dt} = k_H I + 2k_H II + 2k_H III$$

$$(3) - \frac{dD}{dT} = k_D I$$

where k_H = the rate constant for pyrolysis in which cis-2-hydrogen is lost;

k_D = the rate constant for pyrolysis in which cis-2-deuterium is lost;

and where the factors 2 take account of the fact that some molecules have two cis-2-hydrogens. Assuming an isotope effect ($\frac{k_H}{k_D}$) of 3 by analogy to the work of Curtin and Kellom⁷⁹, substituting $k_H = 3k_D$ into Equation 2, dividing by Equation 3 and substituting $III = \frac{I+II}{2.57}$ from Equation 1 one obtains Equation 4.

$$(4) \frac{dH}{dD} = \frac{5.33I + 8.33II}{I}$$

In the pyrolysis, the loss of 0.10 gram atoms of deuterium per mole must have been accompanied by the loss of 0.90 gram atoms of hydrogen per mole⁸⁰. This result gives Equation 5.

$$(5) \frac{dH}{dD} = \frac{0.90}{0.10} = 9.0$$

⁷⁹D. Y. Curtin and D. B. Kellom, J. Am. Chem. Soc., 75, 6011 (1953).

⁸⁰The critical assumptions in this treatment are that pyrolysis of the acetate shows 100 per cent cis-stereospecificity, that no molecules contained more than one deuterium atom, that the pyrolysis was carried to 100 per cent conversion and finally, that the assumed isotope effect is not greatly in error.

Substitution of Equation 5 into Equation 4 gives $\frac{I}{II} = 2.27$, which together with the relation $I + II = 0.72$, gives 68 per cent I and 32 per cent II. This result is clearly at variance with the result of the analysis of cyclohexanone, which indicates that only 46 per cent of the deuterated ester had deuterium in the 2-position (Table 2). This discrepancy is treated in the Discussion Section.

Estimates of the stereochemical distribution of 4-deuterium in 3-acetoxycyclohexene and in 3-bromocyclohexene were obtained more directly. With the assumption that the unsaturated acetate undergoes cis-1,2-elimination only and that eliminations from the bromide go 1,2-trans, the amount of cis-4-deuterium in the acetate and of trans-4-deuterium in the bromide could be obtained directly from the deuterium losses accompanying the eliminations. For example, the loss of 0.10 atoms deuterium per molecule accompanying pyrolysis of 3-acetoxycyclohexene indicates that $\frac{0.10}{0.72} \times 100 = 14$ per cent of the labelled acetate had cis-4-deuterium. The amounts of trans-4-deuterium in the bromides were calculated from elimination results in the same manner. The results are tabulated in Table 2. The limits of error listed in Tables 2 and 3, indicate only the precision of the analyses.

Table 1. Time of fall for drops of standard deuterium oxide-protium oxide mixtures

Weight per cent deuteri- um oxide	Solution I ^a		Weight per cent deuteri- um oxide	Solution II ^b	
	Time (sec.)	Mean ^b		Time (sec.)	Mean ^b
11.216	37.4	37.7 ± 0.2	7.575	25.5	25.1 ± 0.3
	38.0			25.0	
	37.7			24.8	
9.850	52.7	52.7 ± 0.3	5.410	31.6	31.8 ± 0.1
	53.0			31.8	
	53.5			32.0	
8.583	79.2	79.1 ± 0.4	4.604	35.1	35.3 ± 0.2
	78.2			35.3	
	80.1			35.6	
7.575	165.0	165.1 ± 2.1	3.734	41.2	41.1 ± 0.1
	168.3			40.9	
	162.0			41.2	
			2.814	50.8	49.9 ± 0.4
				49.9	
				50.2	
			1.535	74.7	74.4 ± 0.3
				74.5	
				74.0	

^aSolution numbers refer to different bromobenzene-kerosene mixtures used in the falling-drop apparatus.

^bIndicated errors are mean deviations.

Table 2. Data applying to addition of deuterium bromide to cyclohexadiene at -78°

	3-Bromo- cyclo- hexene	3-Acetoxy- cyclo- hexene	Cyclo- hexanone	Bicyclo-(2,2,2)- Δ^5 -octene- 2,3-dicarboxylic anhydride ^a			Cyclo- hexene
				A	B	C	
Physical constants	b.p. 59° at 15 mm. ^b n_{20}^{20} 1.5310	b.p. $83-83.5^{\circ}$ at 28 mm. ^b n_{25}^{25} 1.4561	b.p. $46.5-49^{\circ}$ at 15 mm. ^b	m.p. $142-145^{\circ}$	m.p. $146-147^{\circ}$	m.p. $142-146^{\circ}$	b.p. $79-81.5^{\circ}$ at 743 mm. ^b
Time of fall (sec.)	74.0^c	26.9	50.8	26.1	28.4	26.7	26.6
Sample I	73.7	27.2	50.6	26.2	28.7	26.7	26.6
	74.4	27.1	51.1	26.4	28.6	26.9	26.8
Mean	74.0 ± 0.2	27.1 ± 0.1	50.8 ± 0.2	26.2 ± 0.1	28.6 ± 0.1	26.8 ± 0.1	26.7 ± 0.1
Time of fall (sec.)	73.7^c	27.4	49.7	26.4	27.9	26.4	
Sample II	73.1	27.1	49.6	26.5	27.9	26.2	
	72.8	27.1	50.4	26.2	27.4	26.6	
Mean	73.2 ± 0.3	27.2 ± 0.1	49.9 ± 0.3	26.4 ± 0.1	27.7 ± 0.2	26.4 ± 0.01	

^aFrom cyclohexadiene and maleic anhydride. Source of cyclohexadiene; A potassium-t-butoxide and 3-bromocyclohexene; B quinoline and 3-bromocyclohexene; C pyrolysis of 3-acetoxycyclohexene.

^bInfrared spectrum identical with that of the pure compound except for minor details.

^cWater from the bromide was analysed with solution I in the falling-drop apparatus. All other water samples were analysed with solution II.

Table 2. (Continued)

	3-Bromo- cyclo- hexene	3-Acetoxy- cyclo- hexene	Cyclo- hexanone	Bicyclo-(2,2,2)- Δ^5 -octene- 2,3-dicarboxylic anhydride ^a			Cyclo- hexene
				A	B	C	
Time of fall (sec.)		27.7			27.9		
Sample III		27.3			28.2		
		27.2			28.2		
Mean		27.4 \pm 0.2			28.1 \pm 0.1		
Weight per cent deu- terium oxide in water	8.80 8.85	6.64 6.61 6.52	2.74 2.79	7.01 6.93	6.13 6.43 6.33	6.75 6.97	6.79
Mean per cent deu- terium oxide	8.82 \pm 0.03 $\bar{}$	6.59 \pm 0.05 $\bar{}$	2.77 \pm 0.03 $\bar{}$	6.97 \pm 0.04 $\bar{}$	6.30 \pm 0.11 $\bar{}$	6.86 \pm 0.11 $\bar{}$	6.79 \pm 0.03 $\bar{}$
Gram atoms deuterium per mole	0.721 \pm 0.002 $\bar{}$	0.716 \pm 0.005 $\bar{}$	0.390 ^d \pm 0.003 $\bar{}$	0.632 \pm 0.004 $\bar{}$	0.572 \pm 0.009 $\bar{}$	0.62 \pm 0.01 $\bar{}$	0.625 \pm 0.003 $\bar{}$
Per cent deuterium in 4-posi- tion ^e	46	46	*				

^dCorrected for a dilution factor. Deuterocyclohexanone was quantitatively diluted, prior to combustion, with unlabelled cyclohexanone boiling at 63° (30 mm.).

^eThe asterisk in the same row indicates from which analysis the result was calculated.

Table 2. (Continued)

	3-Bromo- cyclo- hexene	3-Acetoxy- cyclo- hexene	Cyclo hexanone	Bicyclo-(2,2,2)- Δ^5 -octene- 2,3-dicarboxylic anhydride ^a			Cyclo- hexene
				A	B	C	
Per cent deuterium in 6-posi- tion ^{e, f}	54	54	*				
Per cent <u>trans-4-</u> deuterium ^e	13 21	32		*	*		*
Per cent <u>cis-4-deu-</u> terium ^e	33 25	14		*	*		*

^fThe assumption has been made, that deuterium was either in the 4- or in the 6-position. This assumption is not valid if "shuffling" of hydrogen and deuterium occurred during catalytic hydrogenation. It is well known that catalytic deuteration of olefins gives molecules with more than the expected number of deuterium atoms. Such molecules must have lost hydrogen atoms^{84, 85}. By analogy, "shuffling" in the hydrogenation of deuterio compounds should be accompanied by a loss of deuterium. Table 3 indicates that no loss occurred in this work.

⁸⁴R. L. Burwell, Jr. and A. B. Littlewood, J. Am. Chem. Soc., 78, 4170 (1956).

⁸⁵G. A. Russell, J. Am. Chem. Soc., 79, 3871 (1957).

Table 3. Data applying to addition of deuterium bromide to cyclohexadiene at 0°

	3-Bromo- cyclo- hexene ^a	3-Acetoxy- cyclo- hexene	Cyclo- hexyl acetate	Cyclo- hexanone	Bicyclo-(2,2,2)- Δ^5 -octene- 2,3-dicarboxylic anhydride ^b
Physical constants	n ²⁰ 1.5289	b.p. 80-81° at 24 mm. n ²⁵ 1.4550	b.p. 76-77° at 26 mm.	b.p. 52- 54° at 19 mm.	m.p. 142-143°
Time of fall (sec.) Sample I		31.5 31.2 30.8	34.3 34.7 34.5	45.7 45.6 45.5	37.4 37.5 37.0
Mean		31.2 ± 0.3	34.5 ± 0.1	45.6 ± 0.1	37.3 ± 0.2
Time of fall (sec.) Sample II		31.2 31.4 31.1	35.0 35.1 35.1	46.0 45.4 46.1	
Mean		31.2 ± 0.1	35.1 ± 0.1	45.8 ± 0.3	
Time of fall (sec.) Sample III		30.4 30.7 31.0			
Mean		30.7 ± 0.2			

^aWater from 3-bromocyclohexene was not analysed. From Table 2 it is evident that no loss of deuterium accompanies the acetate displacement.

^bFrom pyrolysis of 3-acetoxycyclohexene.

Table 3. (Continued)

	3-Bromo- cyclo- hexene ^a	3-Acetoxy- cyclo- hexene	Cyclo- hexyl acetate	Cyclo- hexanone	Bicyclo-(2,2,2)- Δ^5 -octene- 2,3-dicarboxylic anhydride ^b
Weight per cent deu- terium oxide in water		5.44 5.42 5.56	4.76 4.65	3.22 3.20	5.49 ^c
Mean per cent deu- terium oxide in water		5.47 \pm .06	4.70 \pm .06	3.21 \pm .01	5.49 \pm .03
Grams atoms deuterium per mole		0.59 ₄ \pm .006	0.59 ₅ \pm .007	0.29 ₀ \pm .009	0.49 ₇ \pm .003
Per cent deuterium in 4-posi- tion ^d	51			*	
Per cent deuterium in 6-posi- tion ^d	49			*	

^cCorrected for a dilution factor. Deuterated adduct was diluted quantitatively, prior to combustion, with unlabelled adduct having m.p. 146-147°.

^dThe asterisk in the same row indicates from which analysis the result was calculated.

Table 3. (Continued)

	3-Bromo- cyclo- hexene ^a	3-Acetoxy- cyclo- hexene	Cyclo- hexyl acetate	Cyclo- hexanone	Bicyclo-(2,2,2)- Δ^5 -octene- 2,3-dicarboxylic anhydride ^b
Per cent ^d <u>trans-4-</u> deuterium	15	36			*
Per cent ^d <u>cis-4-</u> deuterium	36	15			*

DISCUSSION

Preliminary Remarks

The object of this work was to determine the geometry of addition of an unsymmetrical reagent, hydrogen bromide, to 1,3-cyclohexadiene. Deuterium-enriched hydrogen bromide was used to provide a label, thus eliminating the need for a bulky orienting substituent which might influence the steric course of the addition.

The study was complicated by the fact that the allylic product obtained could conceivably rearrange, thereby changing the first-formed addition product into one in which the relative positions of the elements of the reagent would be changed. In addition, acetate displacement on 3-bromocyclohexene could possibly occur by two different mechanisms (S_N2 and S_N2') which would give different products in the case of deuterium-labelled bromide. The S_N2' mechanism, although uncommon in systems showing little steric hindrance to the S_N2 reaction, might still compete with the S_N2 reaction to a small extent.

On the basis of the evidence gathered in this work, the extent to which the complicating factors enumerated above intervened, could be roughly estimated. Approximate values for the relative amounts of 1,2- and 1,4-addition were obtained. The stereochemistry of the additions could also be inferred.

Allylic Rearrangement of 3-Bromocyclohexene

Evidence for the thermal rearrangement of 3-bromocyclohexene was obtained from infrared spectra shown by samples of 1-deutero-3-bromocyclohexene having different histories. The spectrum of 1-deutero-3-bromocyclohexene showed a strong band at 2245 cm.^{-1} and a weak band at 2216 cm.^{-1} . The former is certainly due to carbon-deuterium vibrations arising from vinyl deuterium. The reaction of thionyl chloride with an allyl alcohol has been shown to give rearranged product from operation of the S_N1' mechanism⁸¹. By analogy the 3-bromocyclohexene produced by the action of thionyl bromide on 3-deutero-3-hydroxycyclohexene should have deuterium in the vinyl position⁸². The weak band at 2216 cm.^{-1} was not interpreted.

When 1-deutero-3-bromocyclohexene was refluxed in carbon tetrachloride solution for 16 hours, a slight change in the infrared spectrum (in the carbon-deuterium region) was produced. A weak third band appeared at 2184 cm.^{-1} and a very weak fourth band appeared at 2143 cm.^{-1} . Allylic rearrangement of 1-deutero-3-bromocyclohexene would produce 3-deutero-3-bromocyclohexene, the infrared spectrum of which should be

⁸¹H. L. Goering, T. D. Nevitt and E. F. Silversmith, J. Am. Chem. Soc., 77, 5026 (1955).

⁸²The fact that 1-deutero-3-bromocyclohexene was obtained actually proves that the mechanism of decomposition of the intermediate bromosulfite, formed from thionyl bromide and 3-hydroxycyclohexene, is S_N1' .

comparable with that of 3-deutero-3-hydroxycyclohexene except for shifts due to different substituent effects.

The spectra may be compared by reference to Figures 5 and 6. The fact that heating of the bromide produced a change in its spectrum suggests that allylic rearrangement occurred. From the intensities of the new bands, it was concluded that the rate of rearrangement under the conditions specified, is small. The possibility that rearrangement under the conditions of the deuterium bromide addition is more rapid, could not be excluded. Excess deuterium bromide in the pentane solution might complex 3-bromocyclohexene in such a manner as to facilitate allylic rearrangement.

Mechanism of Acetate Displacement on 3-Bromocyclohexene

Spectral evidence was used to infer the predominating mechanism of the reaction of tetraethylammonium acetate with 3-bromocyclohexene in anhydrous acetone. The displacement was carried out on 1-deutero-3-bromocyclohexene, the spectrum of which has already been mentioned. The 3-acetoxycyclohexene formed showed strong carbon-deuterium absorption at 2243 cm.^{-1} and a medium band at 2181 cm.^{-1} . While the former is undoubtedly due to vinyl deuterium, the latter band was not assigned to any particular carbon-deuterium vibration. Although 3-deutero-3-hydroxycyclohexene shows a medium band at the same frequency, it is not the most intense band in the

spectrum of the latter. Hence it is unlikely that the 2181 cm.^{-1} band in the ester is due to 3-deutero-3-acetoxycyclohexene. From previous work, discussed in the Historical Section, it appears that the $\text{S}_{\text{N}}2'$ reaction can compete effectively with the corresponding $\text{S}_{\text{N}}2$ reaction only when the latter is greatly retarded by steric factors⁸³. It seemed reasonable to assume that acetate displacement on 3-bromocyclohexene in acetone goes predominantly by the $\text{S}_{\text{N}}2$ mechanism.

Interpretation of Chemical Results

The chemical results tabulated in Table 2 indicate that the cyclohexanone isolated from the reaction sequence (Figure 1) had 46 per cent of its total deuterium content in the alpha positions and 54 per cent in the gamma position. This result implies either that both 1,2- and 1,4-addition to cyclohexadiene took place or that the first-formed bromide became equilibrated by rearrangement.

Data in Table 2 indicate further that the results of pyrolysis of 3-acetoxycyclohexene and of elimination from the bromide with *t*-butoxide, are in very good agreement. Pyrolysis indicated that, of the total labelled acetate, 14 per cent had cis-4-deuterium and 32 per cent had trans-4-deuterium. Elimination from the bromide with *t*-butoxide ions,

⁸³E. L. Eliel in M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, pp. 92-99 (1956).

showed that 13 per cent of the labelled material had trans-4-deuterium and 33 per cent had cis-4-deuterium. Since it is likely that acetate displacement on 3-bromocyclohexene goes predominantly by the S_N2 mechanism, with inversion, the amount of trans deuterium in the bromide should agree with the amount of cis deuterium in the acetate and vice versa.

Cis- and trans-3-bromo-4-deuterocyclohexene could, of course, have come from 1,2-cis- and 1,2-trans-addition, respectively. In view of what has been said in the Historical Section, cis-1,2-addition is unlikely. It is more likely that the 3-bromo-cis-4-deuterocyclohexene was formed by stereospecific allylic rearrangement of an isomeric bromide. The logical choice for the latter is 3-bromo-cis-6-deuterocyclohexene formed by cis-1,4-addition, since it is evident from the data that trans-1,2-addition is a minor process. Stereospecific allylic rearrangements have been demonstrated by Goering and co-workers⁸⁶ who showed that more than 26 per cent of optically active cis-5-methyl-2-cyclohexenyl chloride recovered from an incomplete acetolysis had been converted into its enantiomer without detectable geometric isomerization.

If it is assumed that all of the 3-bromo-cis-4-deutero-

⁸⁶H. L. Goering, T. D. Nevitt and E. F. Silversmith, J. Am. Chem. Soc., 77, 5026 (1955).

cyclohexene came from stereospecific allylic rearrangement, rather than from 1,2-cis-addition, then the amount of that compound (33 per cent) is a direct measure of the extent to which rearrangement of the bromide had progressed.

Pyrolysis of the deuterocyclohexyl acetate gave a value for the amount of cis-2-deuterium that is higher than the total amount of 2-deuterium calculated from analysis of the cyclohexanone. The discrepancy is almost certainly due to incomplete pyrolysis of the acetate. Calculation of the cis-2-deuterium by the method described on Page 72, depends critically on the assumption that the pyrolysis was complete. At the time the reaction was carried out, it was felt that the conditions used would assure complete pyrolysis and the acetic acid formed was not titrated to check the per cent conversion. Apparently the conditions described by Smith and Wetzel⁸⁷ for the pyrolysis of cyclohexyl acetate in high yield, were not duplicated closely enough.

Incomplete pyrolysis would leave the unconverted ester highly enriched in deuterium, because of the isotope effect. At the same time the olefin which was analysed would be low in deuterium content, making it appear as though much deuterium had been lost on pyrolysis.

Elimination from the bromide with quinoline was accompa-

⁸⁷G. G. Smith and W. H. Wetzel, J. Am. Chem. Soc., 79, 875 (1957)

nied by a larger loss of deuterium than elimination with t-butoxide or pyrolytic elimination from 3-acetoxycyclohexene. The bromide used for this particular reaction had been distilled with a maximum pot temperature of 100° while the samples used for acetate displacement and t-butoxide elimination were kept cold. It is possible, therefore, that allylic rearrangement had made more progress in the heated sample and hence that more cis-4-deuterium was present.

There is some evidence from work on alkaloids of the reserpine-type, that collidine-induced elimination of an 18- β -tosylate group has more E₁ character than elimination with t-butoxide ions⁸⁸, the conclusion being based on the fact that the former reaction gave a larger fraction of products to be expected from a carbonium ion intermediate than did the latter.

If it is assumed that the elimination with quinoline carried out in this work has some E₁ character, then the large loss of deuterium can be accounted for in another way. Less stereospecificity would be expected from an elimination reaction having carbonium-ion character than from an E₂ elimination so that both cis- and trans-deuterium could be lost. In addition, the isotope effect favoring the loss of hydrogen over the loss of deuterium should be small for

⁸⁸Private communication, Dr. E. Wenkert, Iowa State College, Ames, Iowa.

eliminations of the E₁ type.

The overall results, subject to possible errors in the assumptions, are that the addition of deuterium bromide to 1,3-cyclohexadiene in pentane at -78°, goes about 20 per cent 1,2-trans and 80 per cent 1,4-cis. These figures have been corrected for allylic rearrangement, which appears to have progressed to the extent of about 33 per cent under the conditions employed. At 0° the addition appears to give essentially the same results as at -78°. About the same fraction of deuterium was exchanged from the cyclohexanones obtained from the two runs and the results of pyrolysis of 3-acetoxycyclohexenes agree within 7 parts per hundred. Infra-red spectra of corresponding compounds from the two runs showed only trivial differences in the carbon-deuterium region. It was concluded that the mechanism of addition is probably the same at 0° and at -78°.

Assignment of Spectral Bands Due to Carbon- Deuterium Vibrations

Corey and co-workers⁸⁹ recently introduced C-D stretching vibrations as a tool for determining the stereochemistry of deuterium in substituted cyclohexanes. They were able to distinguish epimers having equatorial and axial deuterium in three widely different systems. Two of these were steroid

⁸⁹E. J. Corey, M. G. Howell, A. Boston, R. L. Young and R. A. Sneed, J. Am. Chem. Soc., 78, 5036 (1956).

systems while the third pair of epimers were cis- and trans-1-deutero-4-phenylcyclohexane. In each set of epimers Corey, et al.⁹⁰, found that the high-frequency absorption band of the isomer with equatorial deuterium occurred at a higher frequency than the high-frequency band of the isomer with axial deuterium. The simple monocyclic deuterocyclohexanes had only single C-D absorption bands. Monodeuterosteroids, however, showed doublet bands which were thought due to the presence of more than one rotational form or to vibrational interaction. The compounds 3 α -deuterocholestan-3 β -ol tosylate and 3 α -deuterocholestan-3 β -ol showed complex C-D absorption with five and three distinct bands respectively.

It seems unlikely that the spectra obtained in this study should be directly comparable to those obtained by Corey and co-workers⁹⁰. In the first place, the compounds inspected in the course of this study were mostly mixtures of stereoisomeric deuterio compounds, as the chemical evidence indicates. It is probable that in such mixtures some overlapping bands would not be resolved. In the second place, substituents in cyclohexene systems are only pseudo-axial or pseudo-equatorial. A third feature which complicates the assignment of bands to distinct C-D absorptions in some of the compounds examined, is the fact that allyl deuterium was

⁹⁰E. J. Corey, M. G. Howell, A. Boston, R. L. Young and R. A. Sneed, J. Am. Chem. Soc., 78, 5036 (1956).

present.

Table 4 lists the carbon-deuterium absorption bands in spectra obtained from this study. Assignments were made on the basis of the spectra of compounds prepared by stereospecific reactions and by analogy to the previous work discussed above. The more uncertain assignments were so labelled. Figures 5 and 6 show the carbon-deuterium region of the spectra.

Table 4. Carbon-deuterium absorption bands

Compound	Bands (cm. ⁻¹) ^a	Assignment ^b
Deutero-3-bromocyclohexene ^c	2217 (w)	not assigned
	2179 (s)	<u>4-trans</u>
	2163 (s)	<u>4-cis</u>
	2136 (w)	<u>6-trans</u> ^d
	2127 (m)	<u>6-cis</u> ^d
	2103 (w)	not assigned
Deutero-3-acetoxy-cyclohexene ^c	2250 (w)	not assigned
	2188 (m)	<u>4-trans</u>
	2180 (m)	<u>4-cis</u>
	2154 (s)	<u>6-trans</u> ^d
	2126 (m)	<u>6-cis</u> ^d
Cyclohexyl acetate ^c	2169 (s)	<u>4-trans</u> ^e
	2155 ^f	<u>4-cis</u> ^e
	2147 (s)	<u>2-cis</u>
	2120 (w)	<u>2-trans</u> ^d
Cyclohexanone ^c	2169 (s)	gamma
	2154 ^f	not assigned
	2057	not assigned

^aThe letters s, m, and w denote strong, medium and weak bands, respectively.

^bThe position and stereochemistry of deuterium.

^cDerived from the addition of deuterium bromide to cyclohexadiene at -78°.

^dTentative.

^eThis assignment is in close agreement with that for the corresponding 1-deutero-4-phenyl cyclohexane⁹¹.

^fShoulder, not well resolved.

⁹¹E. J. Corey, M. G. Howell, A. Boston, R. L. Young and R. A. Sneed, J. Am. Chem. Soc., 78, 5036 (1956).

Table 4. (Continued)

Compound	Bands (cm. ⁻¹) ^a	Assignment ^b
Cyclohexene ^c	2241 (m)	vinyl
	2193 (m)	not assigned
	2169 ^f (m)	4-pseudo equatorial ^g
	2149 (s)	4-pseudo axial ^g
	2122 (m)	3-allyl
3-Deutero-3-hydroxy- cyclohexene	2181 (m)	
	2154 (m)	
	2128 (s)	
	2099 (m)	
1-Deutero-3-bromo- cyclohexene ^h	2245 (s)	vinyl
	2216 (w)	not assigned
1-Deutero-3-acetoxy- cyclohexene ^{h, i}	2245 (s)	vinyl
	2181 (m)	not assigned
<u>Trans</u> -2-deuterocyclo- hexyl bromide ^h	2178 (s)	
	2143 (w)	
	2124 (m)	
<u>Cis</u> -2-deuterocyclo- hexyl acetate ^h	2174 (s)	
	2145 (s)	

^gThe assignment was made by analogy to Larnaudie's⁹² assignment of deuterium bands in deuterocyclohexane which has been confirmed by the work of Corey, et al⁹¹.

^hThe synthesis is described in the Experimental Section. The indicated configuration is based on the assumption that the reaction by which the compound was made in stereo-specific.

⁹²M. Larnaudie, Compt. rend., 235, 154 (1952).

Figure 5. Spectra of deuterio compounds in the C-D region

The spectra were obtained with a Perkin-Elmer Model 13 double beam spectrophotometer equipped with a high-dispersion, lithium fluoride prism and 1 mm. cells. All compounds were run in carbon tetrachloride solution at a concentration near 100 mg. per ml. Band positions are accurate to ± 2 cm^{-1} .

The scale markers were obtained by referring "pip" markers, made by the instrument, to a calibration curve. The scale, which is in cm^{-1} , indicates that the calibration was non-linear.

- deuterocyclohexene
- - - - deuterio-3-bromocyclohexene
- . . . - deuterio-3-acetoxycyclohexene
- - - - deuterocyclohexyl acetate

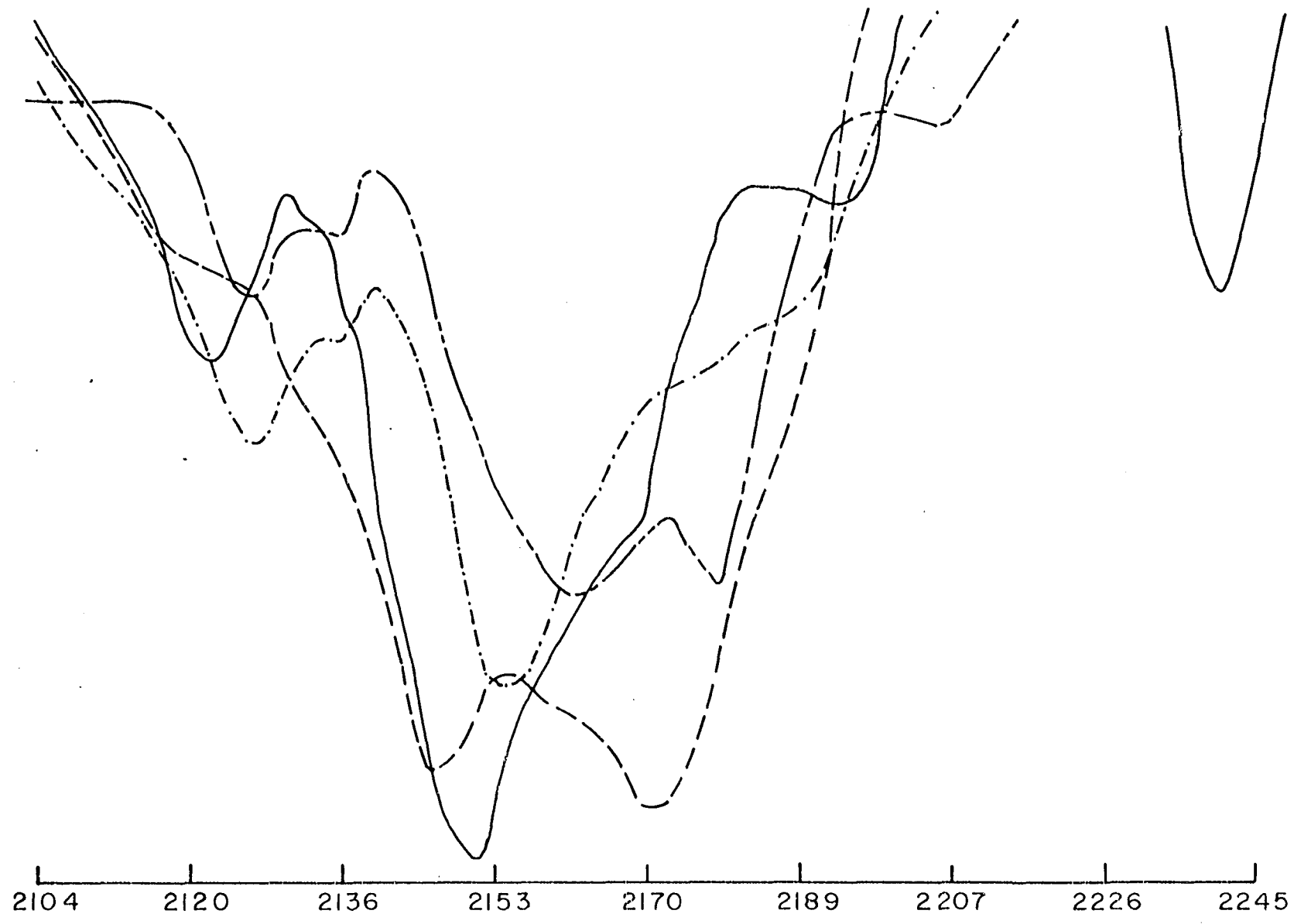
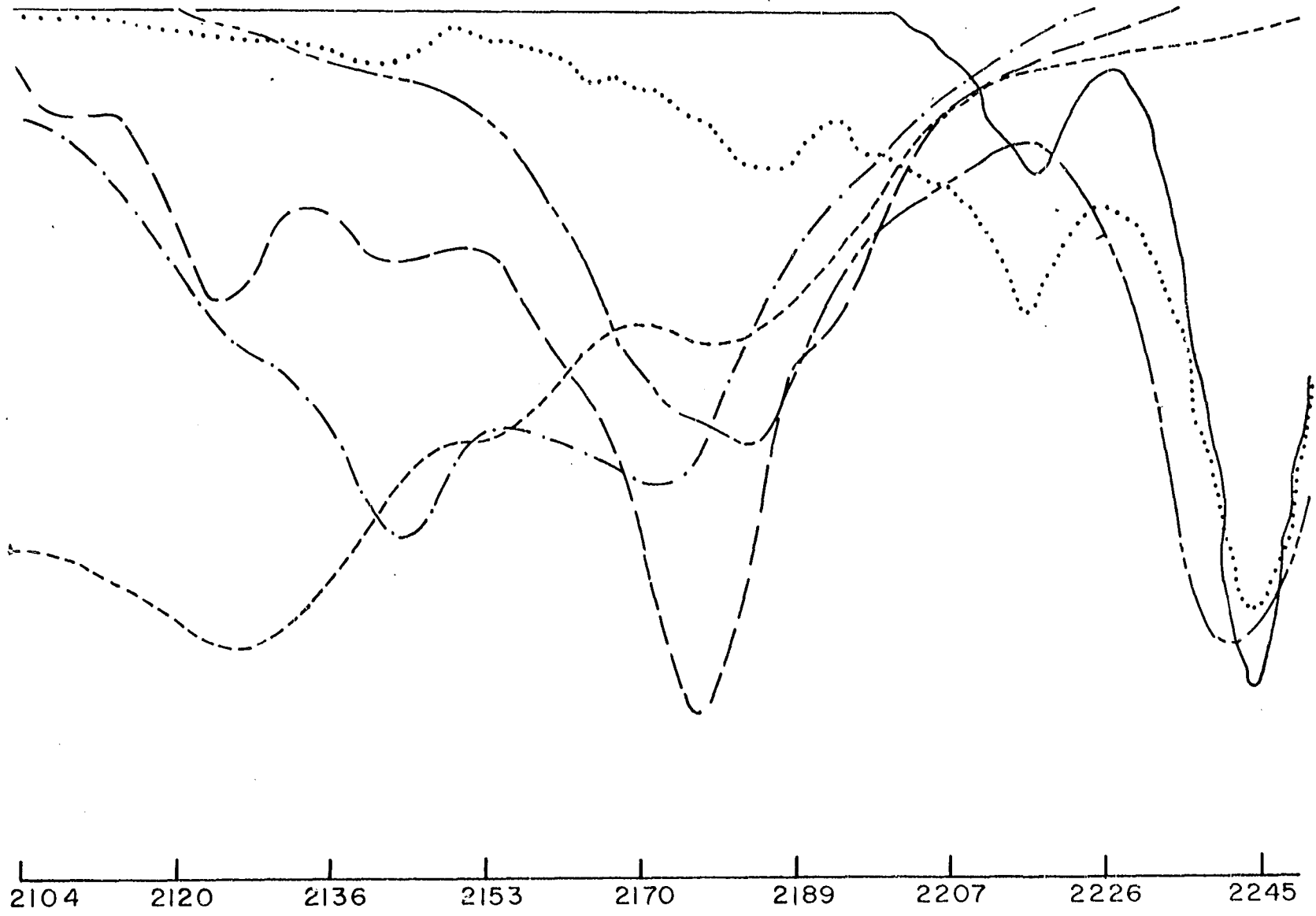


Figure 6. Spectra of deuterio compounds

Units are cm.^{-1} . Refer to the comments in Figure 5.

- 1-deutero-3-bromocyclohexene
- 1-deutero-3-bromocyclohexene (heated
in carbon tetrachloride solution)
- 1-deutero-3-acetoxycyclohexene
- — — trans-2-deuterocyclohexyl bromide
- 3-deutero-3-hydroxycyclohexene
- cis-2-deuterocyclohexyl acetate



SUMMARY

Ionic addition of deuterium bromide to 1,3-cyclohexadiene in pentane at -78° and at 0° , appears to go about 20 per cent 1,2-trans and 80 per cent, 1,4-cis. The first-formed bromide is apparently isomerized by allylic rearrangement to the extent of about 32 per cent, under the conditions employed in this work. These conclusions are based on the following observations and reasonable assumptions.

1. Acetate displacement on 3-bromocyclohexene goes predominantly by the S_N2 mechanism, as indicated by spectra obtained in this work.

2. The acetate formed by such displacement, lost about 14 per cent of its deuterium on pyrolytic elimination. The mechanism of the elimination was assumed to be 1,2-cis.

3. The bromide lost about 13 per cent of its deuterium content when treated with potassium-t-butoxide. Predominant 1,2-trans-elimination was assumed.

4. Conversion of the bromide to cyclohexanone and exchange of alpha-deuterium from the latter showed that about 46 per cent of the bromide had deuterium in the 4-position. This result implies that some 32 per cent of the bromide was 3-bromo-cis-6-deuterocyclohexene. It is proposed that the latter was formed by stereospecific allylic rearrangement, rather than by 1,2-cis-addition.

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