and those subsequently adopted[13] for carbohydrates ($J_0 = 9.3$ for $0° \leq \phi \leq 90°$ and $J_0 = 10.4$ for $90° \leq \phi \leq 180°$) were used. The two sets of angles thus obtained are shown in Table III. It is clear that the modified parameters only make significant changes for larger dihedral angles.

TABLE III

EXPERIMENTAL DIHEDRAL ANGLES FOR SHIKIMIC ACID (Deg.)

Parameters	3, 4	4, 5	5, 6a	5, 6e
Unmodified[a]	46	163	144	39
Modified[b]	48	156	141	42

[a] See ref. 11. [b] See ref. 13.

Comparison of the experimental and theoretical dihedral angles shows immediately that shikimic acid adopts a conformation which approximates most closely to the half-chair form (A) shown in Fig. 2. In terms of a "time-averaged" conformation this means that the half-chair species makes the major contribution and is hence more favored energetically than the boat form. Alternatively the difference between the calculated and experimental angles can be rationalized on a "static" basis, if it is assumed that the angle between H-4 and H-5 is *genuinely* less than 180°, which is reasonable. Then rotation about the C-3, C-4 and C-4, C-5 bonds could decrease the H-4, H-5 angle. This also would decrease the H-3, H-4, and H-5, H-6a angles which is again in accord with the experimental finding. On this basis it seems that the conformation of shikimic acid is essentially the half-chair conformation (A) shown in Fig. 2, with some deformation towards the boat conformation (B).

This work represents the first complete p.m.r. analysis of a substituted cyclohexene.[14] It also indicates that fairly accurate conformational deductions can be made from first-order coupling constants *providing* that sufficient care is taken. Although the *experimental* errors in the dihedral angles are only *ca.* ±1° due to the errors in the coupling constants, a *systematic* error of much greater magnitude is introduced by the uncertainty of the Karplus parameters. Clearly the method is generally applicable to cyclic molecules as long as suitably modified J_0 values are used.

Acknowledgment.—The author is indebted to Dr. F. A. L. Anet for the facilities used and wishes to thank the National Research Council for financial support.

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[13] R. J. Abraham, L. D. Hall, L. Hough and K. A. McLauchlan, *J. Chem. Soc.*, 3699 (1962).

[14] Since the completion of this work, E. W. Garbisch [*J. Org. Chem.*, **27**, 4249 (1962)] has published data which he considers indicative that 6-substituted 1-phenylcyclohexenes also adopt a half-chair conformation, but his investigation did not yield any complete analyses.

The Function of Base in the Catalytic Dehalogenation of Aliphatic Halides. Reduction of Dichloromethylmethylcyclohexanones in the Presence of Potassium Hydroxide and Triethylamine

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In order to elucidate the function of base in the catalytic dehalogenation of aliphatic halides, the effect of two bases of widely different character, potassium hydroxide and triethylamine, on the hydrogenolysis of 2-dichloromethyl-2-methylcyclohexanone and 4-dichloromethyl-4-methylcyclohexanone was investigated. With the 2-substituted dichloro ketone the only difference was in the time required for reduction. This difference was shown not to be due to poisoning of the catalyst and was ascribed to a basic dissimilarity in mechanism. In the case of the 4-substituted dichloro ketone, dehalogenation proceeded smoothly in the presence of hydroxide ion but led to substantial amounts of 4-dichloromethyl-4-methylcyclohexanol in the presence of triethylamine. This facile reduction of the carbonyl group of the dichloro ketone, as well as the inertness of the chlorine atoms of the dichloro alcohol to hydrogenolysis under the dehalogenation conditions, are explained in terms of intermolecular interactions, probably on the catalyst surface, involving the chlorine atoms, the oxygen function, and the amine. Possible functions of the amine in this interaction, and of bases in dehalogenations in general, are considered.

Catalytic hydrogenolysis is a useful method for the removal of halogen atoms from organic compounds under relatively mild conditions.[1] In acidic or neutral solutions aryl halides are reduced while alkyl halides are not, except certain ones activated by adjacent unsaturation.[2] In basic solutions, however, aliphatic halides are so readily and completely dehalogenated that the reaction has been used as an analytical method for the determination of halogen.[3] A similar activation of aryl halides occurs if the molecule contains a basic nitrogen atom.[2] This marked effect of base on catalytic dehalogenation often influences the selective reduction of other functional groups in the presence of halogen atoms[4-6] and is, therefore, of interest to the synthetic organic chemist.

Originally,[3] base was used in catalytic dehalogenations to prevent disintegration of the palladium-on-calcium carbonate catalyst by the halogen acid formed in the reaction. A similar reason for the necessity of base has been suggested for other catalysts,[7] including nickel[6,8] and palladium on charcoal,[9] but without supporting evidence.

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[1] W. Theilheimer, "Synthetic Methods of Organic Chemistry," Vol. I–XV, Interscience Publishers, Inc., New York, N. Y., 1947–1962, lists over eighty applications of this reaction.

[2] R. Baltzly and A. Phillips, *J. Am. Chem. Soc.*, **68**, 261 (1946).

[3] M. Busch and H. Stove, *Ber.*, **49**, 1063 (1916).

[4] M. Freifelder, W. Martin, G. Stone, and E. Coffin, *J. Org. Chem.*, **26**, 383 (1961).

[5] R. Adams and R. Miller, *J. Am. Chem. Soc.*, **58**, 787 (1936).

[6] W. Whitmore and A. Revukas, *ibid.*, **62**, 1692 (1940).

[7] K. Rosenmund and F. Zetzsche, *Ber.*, **51**, 578 (1918).

[8] C. Kelber, *ibid.*, **50**, 305 (1917).

[9] M. Mladenovic, *Bull. soc. chim. roy. Yougoslav.*, **4**, 187 (1933).

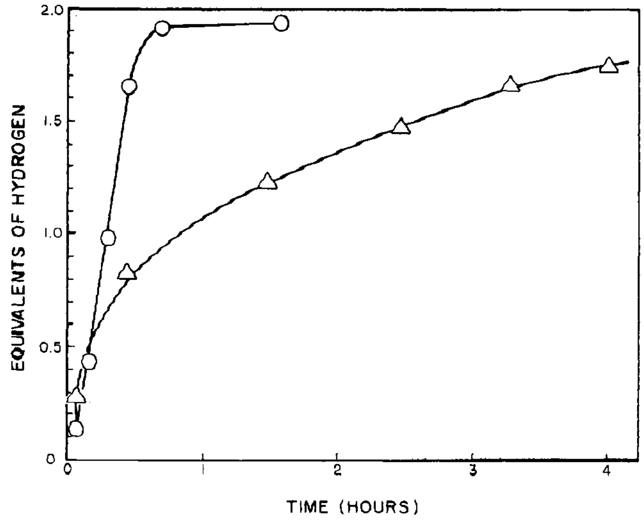


Fig. 1.—Hydrogenation of 2-dichloromethyl-2-methylcyclohexanone in the presence of triethylamine (-△-△-△-) and potassium hydroxide (-○-○-○-).

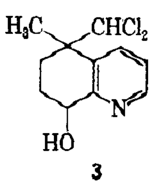
In the gas phase, inhibition of dehalogenation by halogen acids has been reported,[10] but this is not surprising since the catalysts were in the form of metallic films which are notably susceptible to poisoning.[11] In solution studies utilizing supported catalysts, only the dehalogenations of aromatic halides containing a basic nitrogen atom and certain aliphatic halides with adjacent unsaturation were impeded by acids and then merely to the extent of reducing the rates to those of compounds without such activating groups.[2]

Finally, the use of base in excess of that necessary for neutralization of the halogen acid has been found to accelerate the rate of reduction.[3,8]

These observations suggest that the sole function of base in catalytic dehalogenations is not, as has been assumed, the destruction of halogen acid, but rather that the base plays a direct role in aiding the reductive cleavage of the carbon–halogen bond.[12]

If the previous hypothesis is correct, then the ease of removal of aliphatic halogen atoms in basic solution may be related to any of a number of properties of the base such as its type (Lewis or Brønsted), nucleophilicity, ionization constant, ionization potential, etc. Considerable information on the role of base might, therefore, be obtained by comparing dehalogenations carried out in the presence of bases whose properties are quite different, as for example amines and hydroxides.

The present paper describes the results of such a study, the reduction of 2-dichloromethyl-2-methylcyclohexanone (**1**) and 4-dichloromethyl-4-methylcyclohexanone (**2**) in the presence of triethylamine and potassium hydroxide. These particular compounds were selected as substrates because, as might be expected for neopentyl-type halides, they have been reported to be quite inert to bases,[14] thus decreasing the probability of troublesome side reactions. Furthermore, Isogai recently has noted that the 4-substituted dichloro ketone (**2**) was resistant to catalytic dehalogenation in the presence of hydroxide ion, while the closely related dichloro alcohol (**3**) was readily dehalogenated under identical conditions.[15] To the extent that this difference in reactivity is due to the presence of a basic nitrogen atom in the latter compound, it was expected that dehalogenations of halides 1 and 2 in the presence of an amine or an hydroxide also would differ.[16]



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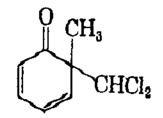

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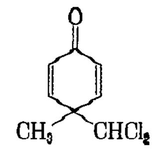

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Results and Discussion

Catalytic hydrogenation of the dienones **4** and **5** in neutral solution led to the starting dichloro ketones **1** and **2**, respectively, in good yield without any evidence of carbonyl reduction or dehalogenation. This once again[2] demonstrates the inertness of aliphatic halides to hydrogenolysis in the absence of base and also shows that the presence of the carbonyl group does not in itself promote removal of the chlorine atoms from **1** and **2**.

All dehalogenations were carried out under conditions similar to those of Isogai[15] in that a methanol solution of the halide containing at least a tenfold excess of base and half as much 10% palladium-on-charcoal catalyst as substrate was hydrogenated at ambient pressure and temperature.

The dehalogenation of 2-dichloromethyl-2-methylcyclohexanone (**1**) in the presence of triethylamine proceeded smoothly to give chiefly 2,2-dimethylcyclohexanone and a small amount of what was probably a partially dechlorinated product.

When potassium hydroxide was used as a base, however, 2,2-dimethylcyclohexanone was obtained in much lower yield and the amount of hydrogen absorbed not only was inconsistent with the expected stoichiometry but also varied from run to run. This anomalous behavior was traced to a slow reduction of the carbonyl group of 2,2-dimethylcyclohexanone[19] and to reaction of the starting dichloro ketone **1** with hydroxide ion. One of the products of this latter reaction was identified as 6-methylheptanoic acid (**6**) by comparing its infrared spectrum and retention time by v.p.c. with those of an authentic sample. This acid probably is formed during the dehalogenation by reduction of 7-chloro-6-methyl-

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[10] J. S. Cambell and C. Kemball, *Trans. Faraday Soc.*, **57**, 809 (1961).

[11] H. S. Taylor, *Discussions Faraday Soc.*, **8**, 9 (1950).

[12] A further indication that the base actively participates in the dehalogenation process is that side reactions such as Wurtz-type coupling occur only if base is present.[13] Baltzly and Phillips (ref. 2, footnote 3) also have commented on the existence of a different mechanism for dehalogenations in basic media.

[13] M. Busch and W. Schmidt, *Ber.*, **62B**, 2612 (1929), and succeeding papers; E. C. Ladd and H. Sargent, U. S. Patent 2,644,835 (1953); *Chem. Abstr.*, **48**, 5878*c* (1954).

[14] N. Kreutzkamp, H. Meerwein, and R. Stroh, "Methoden der Organischen Chemie" (Houben-Weyl), Vol. 5, part 4, Eugen Müller, Ed., Georg Theime Verlag, Stuttgart, 1960, p. 686.

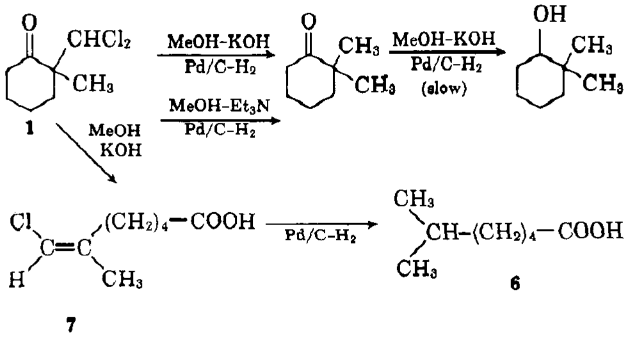
[15] K. Isogai, *Nippon Kagaku Zasshi*, **81**, 1594 (1960).

[16] Dehalogenation of the dienone precursors **4** and **5** of the dichloro ketones **1** and **2**, respectively, also have been reported to be quite sluggish when hydroxide ion was used as the base.[3] These compounds were not chosen for this study, however, because side reactions with the base were anticipated.[17,18]

[17] R. M. Dodson, J. R., Lewis, W. B. Webb, E. Wenkert, and R. D. Youssefyeh, *J. Am. Chem. Soc.*, **83**, 938 (1961).

[18] J. Leitch, *J. Org. Chem.*, **27**, 1081 (1962).

[19] The slow reduction of carbonyl groups under similar conditions has been noted previously: E. Breitner, E. Roginski, and P. N. Rylander, *ibid.*, **24**, 1855 (1959).



6-heptenoic acid (7) which has been shown to be a product of the reaction of methanolic potassium hydroxide with the dichloro ketone 1.[20]

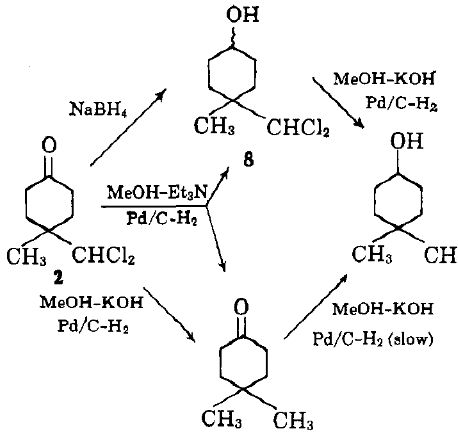
By adding the halide to the methanolic potassium hydroxide immediately before carrying out the hydrogenation under conditions which favored rapid reduction (rapid stirring, pressure, etc.), 2,2-dimethylcyclohexanone could be isolated in good yield if the reaction was stopped after two equivalents of hydrogen had been absorbed.

Except for the side reactions mentioned previously, the only difference between amine and hydroxide ion-promoted dehalogenations of the dichloro ketone 1 was that the former reaction took much longer to pick up the theoretical amount of hydrogen. As can be seen from Fig. 1, this is not due to differences in the initial rates of hydrogenation but rather to the fact that in the presence of potassium hydroxide the rate of hydrogen uptake was constant, whereas in the presence of triethylamine this rate steadily decreased as the reaction progressed. This suggests that poisoning of the catalyst by triethylamine[21] probably is not responsible for the difference in reaction time, but poisoning by one of the products could be. This possibility might seem to be eliminated by the fact that with the exception of triethylammonium ion, which would not be expected to be a catalyst poison,[21] the same products are formed in both dehalogenations. Poisoning of the catalyst by chloride ion[22] cannot be eliminated on this basis, however, since, although triethylammonium chloride is readily soluble in methanol, potassium chloride is not and might, therefore, be unable to inhibit the reduction. This hypothesis was tested and rejected, because when tetramethylammonium hydroxide was used as a base (tetramethylammonium chloride is quite soluble in methanol) the rate of hydrogenation was similar to that of the potassium hydroxide-promoted dehalogenation in that it did not decrease during the course of the reaction.

Since poisoning of the catalyst is not responsible for the differences in the rates of hydrogen uptake shown in Fig. 1, differences in the mechanism of the amine and hydroxide ion-promoted dehalogenations might be.[23] This view is substantiated by the results of the dehalogenation of 4-dichloromethyl-4-methylcyclohexanone (2) in the presence of the two bases.

In disagreement with the results of Isogai,[15] the 4-substituted dichloro ketone (2) was readily dehalogenated with potassium hydroxide as the base to give primarily 4,4-dimethylcyclohexanone. A small amount of partially dechlorinated product was once again obtained, but no side reactions with the exception of the slow reduction of the carbonyl group of the product[19] were observed. Isogai's[15] failure to observed dehalogenation under essentially identical conditions is puzzling although this may be due to the nature of the palladium-on-charcoal catalyst which was used.

Dehalogenation of the dichloro ketone 2 in the presence of triethylamine was anomalous in that in addition to 4,4-dimethylcyclohexanone and a little partially dechlorinated material, an approximately equal amount of a third product was isolated which, from the equivalents of hydrogen consumed (1.6) and chloride ion produced (1.0), as well as its broad melting point (45–60°), v.p.c. retention time, and infrared spectrum, appeared to be a mixture of the stereoisomeric 4-dichloromethyl-4-methylcyclohexanols (8). This structure assignment was shown to be correct by comparing the physical properties mentioned before with those of an authentic sample prepared from the dichloro ketone 2 by reduction with sodium borohydride.



The formation of the dichloro alcohol 8 during the hydrogenation of 2 is surprising since reduction of the carbonyl group would not be expected to occur under these conditions whereas hydrogenolysis of the chlorine atoms would. Thus, with the exception of 8, no other products of carbonyl reduction were detected from the dehalogenations of dichloro ketones 1 and 2 in the presence of triethylamine or from the attempted reduction of cyclohexanone under the same conditions. Similarly, although no systematic studies have been made, amines have been used successfully as bases in catalytic dehalogenations before,[1] and furthermore both the 2- and to some extent the 4-substituted dichloro ketone (1 and 2, respectively) were dehalogenated by this method.

The inertness of the chlorine atoms of the dichloro alcohol 8 is not due to poisoning of the catalyst by one of the other reaction products, since, on subjecting the isolated mixture of stereoisomers to the dehalogenation conditions, only a very slow uptake of hydrogen was observed. The fact that in the presence of potassium

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(20) M. G. Reinecke, *J. Org. Chem.*, **28**, 3574 (1963).

(21) G. C. Bond, "Catalysis by Metals," Academic Press, New York, N. Y., 1962, p. 99.

(22) Halide ion has been reported to inhibit dehalogenations.[2]

(23) The rate of disappearance of the dichloro ketone in the presence of triethylamine, as measured by the rate of hydrogen uptake, appears to be approximately first order. Because of the complexity of heterogeneous reactions and the wide variety of experimental factors which could effect their rate, a mechanistic interpretation of this observation would seem to be unwarranted in the absence of additional, more carefully controlled, kinetic experiments.

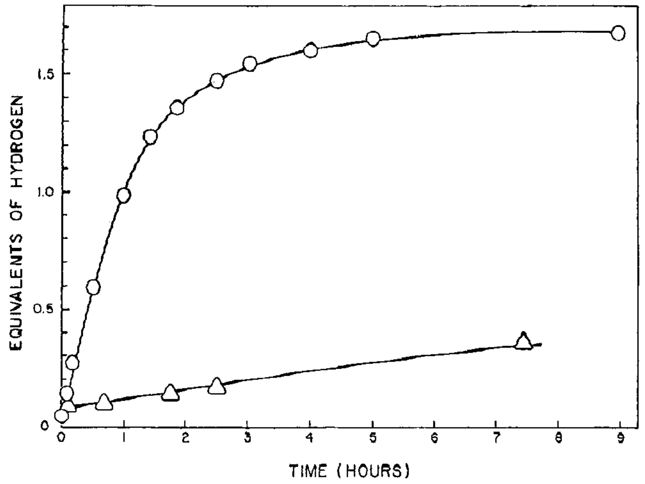


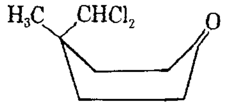
Fig. 2.—Hydrogenation of 4-dichloromethyl-4-methylcyclohexanol in the presence of triethylamine (-Δ-Δ-Δ-) and potassium hydroxide (-O-O-O-).

hydroxide the same mixture of dichloro alcohols is rapidly dehalogenated to 4,4-dimethylcyclohexanol (see Fig. 2) indicates that the inertness of these halogen atoms is dependent on the presence of triethylamine.

Triethylamine also appears to be necessary for the reduction of the carbonyl group of the dichloro ketone **2**, since, with the exception of the very slow follow up hydrogenation of 2,2- and 4,4-dimethylcyclohexanone noted previously, no such reaction was observed either in the presence of potassium hydroxide or in the absence of base altogether.

These results suggest that, during the hydrogenation of dichloro ketone **2** and the dichloro alcohol **8**, specific interactions between the chlorine atoms, the oxygen function, and triethylamine take place, probably on the catalyst surface, which are responsible for the inertness of the chlorine atoms and the lability of the carbonyl group to reduction. Although the details of these interactions are obscure, some of their general features can be discussed.

If the interactions of the chlorine and oxygen atoms are intramolecular then species such as **9** or **10** in which the cyclohexane ring is in the boat form must be involved.[24] This would predict that (1) the reduction



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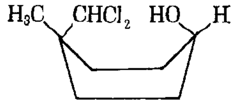

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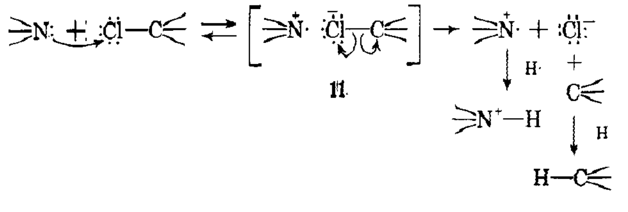
of the carbonyl group of the dichloro ketone **2** should be stereospecific, and (2) only one stereoisomer of the dichloro alcohol **8** should possess the uniquely inert chlorine atoms. Since the dichloro alcohol **8** was actually isolated as a mixture of stereoisomers, however, which after separation by fractional crystallization were shown to be equally inert to dehalogenation, it can be concluded that the chlorine–oxygen interactions are probably inter- rather than intramolecular. The possibility that the reduction of the dichloro ketone **2** was actually stereospecific but that the single stereoisomer of the dichloro alcohol **8** formed was subsequently isomerized, either in the reaction mixture or on work-up, was rejected, since, on subjecting each of the separated dichloro alcohols to the dehalogenation conditions (including the presence of 4,4-dimethylcyclohexanone which might catalyze the isomerization *via* an Oppenauer-type oxidation), the unchanged portions were recovered without any evidence of isomerization.

Additional features of the interaction responsible for the reduction of the carbonyl group of **2** are suggested by the observation that the relative amounts of dichloro alcohols **8** and 4,4-dimethylcyclohexanone formed in the dehalogenation were approximately equal whan an active catalyst was used.[25] This might simply mean that two independent reaction paths are available, one leading to normal dehalogenation and one leading to carbonyl reduction *via* the proposed intermolecular interaction. An attractive alternative is that both reaction products arise from the same intermolecular "complex" in which only the carbonyl group and chlorine atoms taking part in the interaction are reduced. If this were the case, the interaction must involve only two molecules of the dichloro ketone **2**, since a polymeric interaction in which both the carbonyl group and chlorine atoms of a molecule of **2** are involved is eliminated by the absence of the expected product of such an interaction, 4,4-dimethylcyclohexanol.

Of particular interest in terms of the original goal of this research, *i.e.*, to elucidate the function of base in catalytic dehalogenations, is the role of the triethylamine in this interaction. This role must involve primarily some other property of the amine besides its basicity, since otherwise hydroxide ion ought to produce a similar effect. One such property is the very strong tendency of amines,[26] but not hydroxides,[27] to form charge-transfer complexes. Such complexes recently have been suggested as intermediates in certain reactions of polyhalomethanes with amines which lead to homolytic cleavage of the carbon–halogen bond.[28] A similar complex (**11**), perhaps on the catalyst surface, might be responsible for the lability of carbon–halogen bonds to hydrogenolysis in the presence of amines. In the case of the dichloro ketone **2** and the dichloro alcohol **8** the oxygen function may be able to interact with this complex in some way so as to promote reduction of the carbonyl group and inhibit hydrogenolysis of the chlorine atoms, respectively.



If charge-transfer complex formation were the only way base could promote dehalogenation, then hydroxide ion ought to be much less effective than amines in this regard.[26,27] Since the opposite appears to be true,

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[24] For a recent review on boat forms of six-membered rings as reaction intermediates, see M. Balasubramanion, *Chem. Rev.*, **62**, 591 (1962).

[25] When a less active catalyst was used, the reaction time was increased and some of the dichloro alcohol was partially dehalogenated. In this case the amount of 4,4-dimethylcyclohexanone was similar to the combined amount of dichloro and what is probably monochloro alcohol.

[26] D. Booth, *Sci. Progr.* (London), **48**, 435 (1960).

[27] E. M. Kosower, *J. Am. Chem. Soc.*, **78**, 3497 (1956).

[28] D. P. Stevenson and G. M. Coppinger, *ibid.*, **84**, 149 (1962).

however, either this type of interaction is not important or hydroxide ion promotes dehalogenation by a basically different process. This latter possibility is supported by the experiments discussed in this paper which indicate that the course of catalytic dehalogenation is not the same in the presence of triethylamine and potassium hydroxide.

Experimental[29]

2-Dichloromethyl-2-methylcyclohexanone (1).—A solution of 1.91 g. of 2-dichloromethyl-2-methyl-3,5-cyclohexadien-1-one (4)[30] in 50 ml. of 95% ethanol containing 200 mg. of 10% palladium-on-charcoal catalyst[31] was hydrogenated at room temperature and atmospheric pressure. After the uptake of hydrogen had stopped (1 hr., 2.1 equiv.), the catalyst was separated by filtration and the ethanol removed with a rotary evaporator. The colorless oil which remained (1.8 g., 93% yield) was dissolved in a minimum amount of petroleum ether (b.p. 30–60°) Upon being cooled in a Dry Ice bath, this solution deposited white crystals of 1, m.p. 31.5–32.5°, lit.[32] m.p. 33°.

4-Dichloromethyl-4-methylcyclohexanone (2).—The reduction of a solution of 2.87 g. of 4-dichloromethyl-4-methyl-2,5-cyclohexadien-1-one (5)[30] in 50 ml. of 95% ethanol containing 300 mg. of 10% palladium-on-charcoal catalyst was complete (2.1 equiv. of hydrogen) in 45 min. After the catalyst and solvent were removed in the same manner as before, 2.8 g. (95%) of white crystals of 2 were obtained which after recrystallization from petroleum ether (b.p. 30–60°) melted at 46.5–47.5°, lit.[32] m.p. 47–48°.

Hydrogenation of 2-Dichloromethyl-2-methylcyclohexanone (1). A. In the Presence of Triethylamine.—A solution of 4.875 g. of 2-dichloromethyl-2-methylcyclohexanone (1) in 160 ml. of absolute methanol and 40 ml. of triethylamine containing 2.5 g. of 10% palladium-on-charcoal catalyst was hydrogenated at room temperature and atmospheric pressure. After the absorption of hydrogen had stopped (2.0 equiv., 20 hr.), the catalyst was removed by filtration and the filtrate distilled through a 40-cm. Vigreux column to remove the major portion of the methanol and triethylamine. The semisolid residue was partially dissolved in 20 ml. of water and extracted with three 20-ml. portions of ether. Neutralization of the aqueous layer with dilute nitric acid and titration with standard silver nitrate solution to a silver chromate end point indicated the presence of 1.8 equiv. of chloride ion.

The combined ether extracts were washed with two 25-ml. portions of 0.1 *M* phosphoric acid, successively dried over sodium sulfate and Drierite, and freed of ether by distillation through a micro Vigreux column to leave 2.7 g. of a colorless oil which according to a vapor phase chromatogram was a 10:1 mixture of a low- and a high-boiling substance, respectively.

The major component was obtained pure by fractional distillation and was identified as 2,2-dimethylcyclohexanone by its infrared spectrum (1702 cm.$^{-1}$), b.p. 168–169° (745 mm.), 78–79° (35 mm.), lit.[33] b.p. 168° (740 mm.); semicarbazone,[34] m.p. 199–200.5°, lit.[33] m.p. 199.6–199.8°; and oxime, m.p. 93–94°, lit.[33] m.p. 93–93.5°.

The minor, higher-boiling component had a v.p.c. retention time midway between those of the starting material (1) and 2,2-dimethylcyclohexanone. Although insufficient material was available for characterization, the infrared spectrum of this component was obtained and had peaks at 1702 cm.$^{-1}$ (C=O) and 743 cm.$^{-1}$ (C–Cl) thus suggesting that this substance was 2-chloromethyl-2-methylcyclohexanone.

B. In the Presence of Potassium Hydroxide.—A solution of 5 g. of 2-dichloromethyl-2-methylcyclohexanone (1) in 200 ml. of absolute methanol containing 2.5 g. of 10% palladium-on-charcoal catalyst and 20 g. of potassium hydroxide was hydrogenated at room temperature under atmospheric pressure. At the end of 2 hr., 1.2 equiv. of hydrogen had been absorbed, and the rate of hydrogen pickup suddenly decreased. The reduction was permitted to proceed for a total of 45 hr. (2.0 equiv. of hydrogen), the catalyst removed by filtration, the filtrate neutralized with hydrochloric acid, and most of the methanol removed by distillation through a micro Vigreux column to leave a residue which was taken up in 50 ml. of benzene. After extraction with three 30-ml. portions of 15% sodium carbonate solution, the benzene layer was dried over sodium sulfate and fractionally distilled to give 1.3 g. (40%) of a colorless oil, b.p. 89° (35 mm.), which was identified as 2,2-dimethylcyclohexanol by the melting point of its phenylurethane[35] (87.5–88.5°, lit.[36] 84–85°) and by a comparison of its infrared spectrum and v.p.c. retention time with those of an authentic sample synthesized from 2,2-dimethylcyclohexanone by reduction with sodium borohydride in methanol.[37]

The residue remaining after the above distillation contained at least three higher-boiling products (by v.p.c.) which were not identified.

The combined sodium carbonate extracts were acidified with hydrochloric acid and extracted with three 30-ml. portions of benzene which were combined and dried over sodium sulfate. The residue which remained after distillation of the benzene through a micro Vigreux column was identified as 6-methylheptanoic acid (6) by its neutralization equivalent (140 ± 3; calculated, 142), and by a comparison of its infrared spectrum and v.p.c. retention time with those of an authentic sample prepared from 1-bromo-4-methylpentane and diethyl malonate by conventional methods[38] or from 7-chloro-6-methyl-6-heptenoic acid (7) by catalytic reduction.[20]

In experiments similar to the previous in which reduction was stopped immediately after the rate of hydrogen pickup slowed down (1.6, 1.7, 1.9 equiv. of hydrogen absorbed), the chief neutral product consisted of 2,2-dimethylcyclohexanone, once again contaminated with several unidentified, higher-boiling (v.p.c.) impurities. When the reduction was run in a Parr apparatus at 60 p.s.i. immediately after mixing the reactants, 2 equiv. of hydrogen were absorbed in the first 4 min., and no further pressure drop was observed in the next 10 min. The 2,2-dimethylcyclohexanone formed in this reaction (70% yield) contained a small amount (5%) of only one higher-boiling substance.

C. In the Presence of Tetramethylammonium Hydroxide.—To 20 ml. of absolute methanol containing 0.032 mole of tetramethylammonium hydroxide (prepared from tetramethylammonium chloride and silver oxide in the absence of carbon dioxide and standardized by titration with standard acid) was added 487 mg. of 1 and 250 mg. of 10% palladium-on-charcoal catalyst, and the resulting mixture immediately hydrogenated at ambient pressure and temperature. After 45 min. (1.6 equiv. of hydrogen) the rate of hydrogenation suddenly decreased and after 80 min. (1.7 equiv. of hydrogen) the reaction was stopped, the catalyst removed by filtration, the filtrate saturated with solid potassium carbonate and extracted with three 20-ml. portions of ether. The combined ether extracts were successively dried over sodium sulfate and Drierite and the ether removed by distillation through a micro Vigreux column to leave 225 mg. (70%) of an oil which according to its v.p.c. retention time and infrared spectrum was essentially pure 2,2-dimethylcyclohexanone.

Hydrogenation of 4-Dichloromethyl-4-methylcyclohexanone (2). A. In the Presence of Potassium Hydroxide.—A freshly prepared solution of 2 g. of potassium hydroxide and 489 mg. of 4-dichloromethyl-4-methylcyclohexanone (2) in 20 ml. of absolute methanol was hydrogenated at room temperature and atmospheric pressure in the presence of 250 mg. of palladium-on-charcoal catalyst. The rate of hydrogen absorption decreased abruptly after the first hour (2.0 equiv. of hydrogen), and only 0.15 additional equivalents of hydrogen were taken up in the next half hour so the reaction was stopped and the catalyst removed by filtration and washed with methanol and water. An aliquot of this filtrate was neutralized with nitric acid and evaporated to dryness at reduced temperature and pressure. Titration of the

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[29] Melting points and boiling points are uncorrected unless otherwise stated. Infrared spectra were determined on a Perkin-Elmer Model 137 spectrophotometer, and analysis were carried out by Mr. C. F. Geiger, Ontario, Calif.

[30] K. Auwers and G. Keil, *Ber.*, **35**, 4207 (1902); *Chem. Zentr.*, **74, I**, 160 (1903).

[31] Matheson Coleman and Bell brand catalyst was used throughout this study.

[32] K. Auwers and E. Lange, *Ann.*, **401**, 303 (1913).

[33] W. S. Johnson and H. Posvic, *J. Am. Chem. Soc.*, **69**, 1365 (1947).

[34] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 218.

[35] Ref. 34, p. 211.

[36] H. Meerwein, *Ann.*, **405**, 129 (1914); *Chem. Zentr.*, **85, III**, 230 (1914).

[37] W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956).

[38] J. Cason and H. Rapoport, "Laboratory Text in Organic Chemistry,' Prentice-Hall Inc., New York, N. Y., 1950, p. 302.

aqueous solution of this residue with standard silver nitrate to a silver chromate end point indicated the presence of 1.92 equiv. of chloride ion in the original filtrate.

After the methanol was removed from the filtrate by evaporation at reduced pressure, the remaining aqueous residue was extracted with three 10-ml. portions of ether which were dried over sodium sulfate and evaporated at reduced pressure to leave 200 mg. of a colorless oil consisting of a 7:1 mixture of low- and high-boiling components, respectively, as determined by gas chromatography. The lower-boiling component of this mixture was identified as 4,4-dimethylcyclohexanone by the melting point of its semicarbazone[34] (205–207°, lit.[32] 202–204°), its infrared spectrum (1723 cm.$^{-1}$), and by conversion to 4,4-dimethylcyclohexanol on treatment with methanolic sodium borohydride.[37]

Insufficient of the higher-boiling component of the reaction mixture was available for characterization, but its v.p.c. retention time and infrared spectrum [1726 cm.$^{-1}$ (C=O) and 741 cm.$^{-1}$ (C—Cl)] suggested that this substance was probably 4-chloromethyl-4-methylcyclohexanone.

B. **In the Presence of Triethylamine.**—A solution of 489 mg. of 4-dichloromethyl-4-methylcyclohexanone (**2**) in 16 ml. of absolute methanol and 4.2 ml. of triethylamine containing 250 mg. of 10% palladium-on-charcoal catalyst was hydrogenated at ambient pressure and temperature. After the absorption of hydrogen had stopped (1.6 equiv., 9 hr.), the catalyst was removed by filtration and the major portion of the methanol and triethylamine evaporated at reduced pressure. The remaining semisolid residue was dissolved in 100 ml. of water and extracted with three 20-ml. portions of ether. Neutralization of the aqueous layer with nitric acid and titration with standard silver nitrate to a silver chromate end point indicated the presence of 1.0 equiv. of chloride ion.

The combined ether extracts were washed with three 20-ml. portions of 1 *M* nitric acid, dried successively over sodium sulfate and Drierite, and freed of ether by evaporation at reduced pressure. According to a vapor phase chromatogram, the 333 mg. of colorless oil which remained contained a trace of starting material and a mixture of three products in the ratio 4:1:4, in order of increasing retention time. From the retention times and infrared spectra of v.p.c.-collected samples, the low- and intermediate-boiling substances were identified as 4,4-dimethylcyclohexanone and the "4-chloromethyl-4-methylcyclohexanone" obtained from the hydrogenation of **2** in the presence of potassium hydroxide, respectively.

The high-boiling component had a longer retention time than the starting material **2**; a v.p.c.-collected sample was obtained as a white, crystalline solid (m.p. 45–60°) and had strong peaks in the infrared at 3200 (O–H), 1120 (C–O), and 746 cm.$^{-1}$ (C–Cl). This substance was identified as a mixture of the two stereoisomers of 4-dichloromethyl-4-methylcyclohexanol (**8**) by (1) a comparison of its v.p.c. retention time and infrared spectrum with those of an authentic sample synthesized from **2** and sodium borohydride (see following) and (2) conversion to 4,4-dimethylcyclohexanol by catalytic hydrogenolysis in the presence of potassium hydroxide (see following).

Under conditions identical with the previous hydrogenation, except for the use of a different batch of catalyst, 1.4 equiv. of hydrogen were picked up in 48 hr. and 1.2 equiv. of chloride ion produced. The ratio of products, according to the v.p.c. and in order of increasing retention time, was 5:2:3. The high- and low-boiling components were identified as **8** and 4,4-dimethylcyclohexanone, respectively, but the intermediate-boiling substance had an infrared spectrum which indicated it was probably a mixture of "4-chloromethyl-4-methylcyclohexanone" and its corresponding alcohol.

Preparation of 4-Dichloromethyl-4-methylcyclohexanol (8).—A solution of 2.00 g. of 4-dichloromethyl-4-methylcyclohexanone (**2**) and 1.75 g. of sodium borohydride in 210 ml. of absolute ethanol was stirred at room temperature for 45 min. After the ethanol had been removed on a rotary evaporator, 50 ml. of water was added to the remaining residue and the resulting mixture extracted with three 20-ml. portions of chloroform. The combined chloroform extracts were dried over magnesium sulfate and the chloroform removed on a rotary evaporator to leave 1.80 g. (89%) of **8** as a white crystalline solid, m.p. 48–74°,[39] whose v.p.c. retention time and infrared spectrum were identical (except for slight differences in the intensities of some infrared peaks) with those of the high-boiling component obtained from the hydrogenation of **2** in the presence of triethylamine.

Fractional crystallization of **8** from petroleum ether (b.p. 30–60°) gave a more soluble fraction (**8a**, prisms, m.p. 47–49°,[39] lit.[15] 49–50°) and a less soluble fraction (**8b**, needles, m.p. 82–82.5°[39]), whose v.p.c. retention times were identical but whose infrared spectra were readily distinguishable in the fingerprint region.

Anal. Calcd. for $C_8H_{14}OCl_2$ (**8b**): C, 48.75; H, 7.16. Found: C, 48.85; H, 7.23.

Hydrogenation of 4-Dichloromethyl-4-methylcyclohexanol (8). A. In the Presence of Potassium Hydroxide.—A solution of 300 mg. of **8** and 1.2 g. of potassium hydroxide in 12 ml. of absolute methanol was hydrogenated at ambient pressure and temperature in the presence of 150 mg. of 10% palladium-on-charcoal catalyst. After 9 hr. the reaction was stopped (1.7 equiv. hydrogen absorbed) and the catalyst removed by filtration and washed with methanol and water. Titration of a neutralized aliquot of the filtrate with standard silver nitrate to a silver chromate end point indicated the presence of 1.8 equiv. of chloride ion.

The remaining filtrate was saturated with potassium carbonate, extracted with three 20-ml. portions of ether and the combined ether extracts dried successively over sodium sulfate and Drierite. The residue which remained after distillation of the ether through a micro Vigreux column gave only one peak in the v.p.c. which was identified as 4,4-dimethylcyclohexanol by a comparison of its v.p.c. retention time and infrared spectrum with those of an authentic sample prepared from 4,4-dimethylcyclohexanone by reduction with methanolic sodium borohydride.[37]

B. **In the Presence of Triethylamine.**—After 67 hr. at ambient pressure and temperature, a mixture of 300 mg. of **8**, 150 mg. of 10% palladium-on-charcoal catalyst, 9.6 ml. of absolute methanol, and 2.5 ml. of triethylamine had picked up only 0.6 equiv. of hydrogen. After the catalyst was removed by filtration, the filtrate was neutralized with hydrochloric acid and the major portion of the methanol and triethylamine removed by distillation through a micro Vigreux column. The two-phase distilland was extracted with three 20-ml. portions of benzene and the combined benzene extracts dried over sodium sulfate and freed of benzene by distillation through a micro Vigreux column. A vapor phase chromatogram of the remaining residue indicated the presence of three substances in the ratio 3:1:2.5, in order of decreasing retention time, which were identified by v.p.c. retention time and infrared spectra as **8**, "4-chloromethyl-4-methylcyclohexanol," and 4,4-dimethylcyclohexanone, respectively.

The separated isomers of **8** (**8a** and **8b**) were hydrogenated under conditions identical with the previous except that 400 mg. of 4,4-dimethylcyclohexanone was added to the reaction mixture. After 33 hr., each of these isomers had absorbed about 0.5 equiv. of hydrogen. Work-up of the reaction mixtures in the previous manner gave v.p.c.-collected samples of recovered starting materials whose infrared spectra and melting points were the same as those of the pure isomers (**8a** and **8b**).

Attempted Reduction of Cyclohexanone in the Presence of Triethylamine.—A mixture of 295 mg. of cyclohexanone, 2.5 ml. of triethylamine, 10 ml. of absolute methanol, and 150 mg. of 10% palladium-on-charcoal catalyst picked up 0.05 equiv. of hydrogen in the first 2 min. of reduction at ambient pressure and temperature, but failed to pick up any additional hydrogen in the next 6 hr. The catalyst was removed by filtration and the major portion of the methanol and triethylamine distilled through a micro Vigreux column. The remaining residue had only one peak in the v.p.c. besides solvent, and the infrared spectrum of a v.p.c.-collected sample was identical with cyclohexanone.

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[39] Taken on a Kofler hot stage and corrected.