259. *Use of Isotopes in Chemical Reactions. Part I. The Mechanism of the Wagner–Meerwein Rearrangement. Exchange of Radioactive Chlorine and of Deuterium between Camphene Hydrochloride and Hydrogen Chloride.*

By THOMAS P. NEVELL, EDUARDO DE SALAS, and CHRISTOPHER L. WILSON.

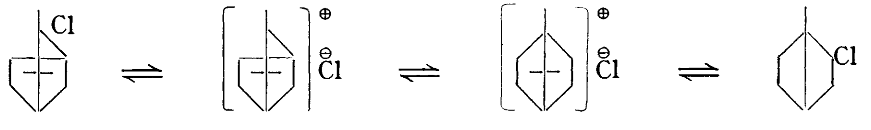
The conversion of camphene hydrochloride into *iso*bornyl chloride in chloroform solution in the presence of deuterium radio-chloride has been studied. By comparing the speeds of rearrangement of chlorine exchange and of hydrogen exchange it has been deduced that the rearrangement proceeds in two steps. The first involves the rapid establishment of an ionic equilibrium by separation of chlorine, and the second a relatively slow bimolecular reaction between the ion so produced and a molecule of hydrogen chloride.

The dissociation of camphene hydrochloride into camphene and hydrogen chloride has also been studied. This reaction has no direct bearing on the rearrangement except in so far as it supplies the hydrogen chloride necessary for the rearrangement when this has not initially been added (as in Meerwein's experiments). It follows that the rearrangement, in the absence of additional hydrogen chloride, should obey kinetics of the 1·5 order with respect to camphene hydrochloride. Bartlett and Pöckel have shown this to be the case.

Certain stereochemical aspects of the reaction have been discussed. For instance, if it is accepted that the bimolecular rate-determining step in rearrangement involves, as do all simple bimolecular nucleophilic substitutions, a Walden inversion, it may be concluded that *iso*bornyl chloride has the *exo*-configuration and is therefore related to *iso*borneol.

MEERWEIN and his collaborators studied the conversion of camphene hydrate esters into the corresponding *iso*bornyl esters (Meerwein and van Emster, *Ber.*, 1920, **53**, 1815; 1922, **55**, 2500; Meerwein and Gérard, *Annalen*, 1924, **435**, 174; Meerwein, Hammel, Serini, and Vorster, *ibid.*, 1927, **453**, 16); the process was reversible, although equilibrium strongly favoured the *iso*bornyl ester, and it was catalysed by strong acids and accelerated by solvents of high dielectric constant. Furthermore, it was shown that for a series of esters the order of velocities was: sulphonate > bromide > chloride > trichloroacetate > *m*-nitrobenzoate, which is approximately the order of the strengths of the corresponding acids. For these reasons the conclusion was drawn that the change involved the separation of ions, and for the hydrochloride this was expressed by the scheme (I) $\rightleftharpoons$ (II).

(I.)



(II.)

Meerweins's ionic hypothesis is by no means the only one which has been advanced to explain the Wagner change so frequently encountered in terpene structures. Earlier theories involved free or partial valencies or non-ionic intermediates, but as such views have been shown to be inadequate (Meerwein and van Emster, *loc. cit.*; Ingold, *Ann. Reports*, 1924, **21**, 96) we base our discussion on the scheme (I) $\rightleftharpoons$ (II). Intermediates of an ionic nature have already been postulated to account for the properties of other tertiary halides, such as *tert.*-butyl or triphenylmethyl chlorides (Hughes, J., 1935, 255); indeed, Meerwein has drawn attention to the close similarities in reactivity between the latter and camphene hydrochloride.

On the basis of the above reaction scheme it is important to determine which of the three consecutive processes is likely to control the speed of the rearrangement. Inter-conversion of ions (the second step) might be expected to be relatively rapid, since it involves only a movement of electrons, together with perhaps a slight readjustment of molecular strain. This velocity relationship is rendered more likely by the experimental observation that rearrangement is catalysed by hydrogen chloride, wherefore the slow step can hardly be inter-conversion of ions for which hydrogen chloride catalysis is rather difficult to imagine. Still more definite evidence is provided by the stereochemical relations considered later, which show that, whilst the first ion of Meerwein's scheme might be a real intermediate, the second ion (possessing the *iso*bornyl structure) can never attain kinetic freedom. Consequently, for the purposes of a discussion of kinetics we may simplify the scheme as follows:

$$\text{(I.)} \quad \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \quad \text{Ion} \quad \underset{k_{-2}}{\overset{k_2}{\leftrightharpoons}} \quad \text{(II.)}$$

Here the k's represent the individual velocity coefficients and the coefficient for rearrangement is $k_1k_{-2}/(k_{-1} + k_{-2})$. Two limiting cases can be distinguished, *viz.*, (1) that $k_{-2} \gg k_{-1}$, which implies that ionic reassociation leads preferentially to *iso*bornyl chloride (II), and that the rearrangement velocity of (I) is determined by k_1, the coefficient for ionisation; and (2) that $k_{-1} \gg k_{-2}$, in which circumstances the factor multiplying k_1 in the above expression is much less than unity, and the coefficient for rearrangement will be smaller than that for ionisation.

Exchange Experiments with Radioactive Chlorine.—If, in addition to camphene hydrochloride, the reaction medium contains radioactive chlorine ions, then every organic cation which is produced from (I) with a velocity coefficient k_1 has the chance to unite with a radioactive chlorine ion irrespective of whether (I) or (II) is produced. Under such conditions, therefore, halogen exchange is a measure of ionisation, and this test has been applied to determine which if either of the two limiting cases mentioned above is operative.

Experiments were carried out in which radio-active halogen was present as hydrogen chloride. Radioactivity was induced in hydrogen chloride in chloroform solution by irradiation with slow neutrons from a 200-mg. radium sulphate–beryllium source. According to the experiments of Szilard and Chalmers (*Nature*, 1934, **134**, 462), it would appear that each neutron capture by a chlorine atom in the chloroform results in the ejection of the halogen atom from the molecule and exchange with the dissolved hydrogen chloride, since very high activities were observed in the hydrogen chloride extracted by shaking with water. The latter was the method used to follow the change in the concentration of radioactive isotope during a rearrangement experiment. In order to hasten rearrangement an equal volume of nitrobenzene was added to the chloroform solution after irradiation.

The results were decisive. At 20°, even under conditions during which no appreciable rearrangement occurred, halogen exchange was rapid and complete. It appears, therefore, that case (2) applies, and ionisation cannot be the rate-determining step in the conversion of (I) into (II).

Dissociation of Camphene Hydrochloride.—Meerwein and van Emster (*loc. cit.*) pointed out that in solution camphene hydrochloride dissociates slightly into camphene and hydrogen chloride, and the rearrangement is then strongly catalysed by the latter. Since it has been stated (Bartlett and Pöckel, *J. Amer. Chem. Soc.*, 1937, **59**, 820; 1938, **60**, 1585) that this fission proceeds much faster than rearrangement, it was considered possible that halogen exchange was occurring by the splitting off and readdition of hydrogen chloride rather than by ionisation. However, chemical evidence tends against this supposition. For instance, camphene hydrochloride on treatment with excess of milk of lime (conditions which would preclude the re-addition of hydrogen chloride) gives camphene hydrate and not camphene (Aschan, *Annalen*, 1915, **410**, 229). By analogy with *tert.*-butyl chloride the hydrate would be the expected product of hydrolysis proceeding through ions.

In view of the uncertainty it was considered desirable to obtain, if possible, a direct measure of the speed of the addition-fission process. If halogen exchange is occurring in this way, then on introducing deuterium chloride into the reaction medium, the rate of deuterium exchange should be equal to that of halogen exchange. Using deuterium radio-chloride in chlorform solution at 0°, it was found that the speeds of the two exchange processes, that of hydrogen and that of chlorine, were equal to within the limits of experimental error. At first sight this appears to point to an addition-fission cycle as the mechanism of the hydrion and chloride-ion exchanges, but there is a difficulty about this simple interpretation. If it is assumed that exchange is due to the addition-fission cycle, then, owing to the fact that dissociation equilibrium for camphene hydrochloride corresponds to about 3% of free hydrogen chloride, the rate which determines the speed of exchange of hydrogen chloride must be that of fission. We checked this inference by following directly the dissociation of camphene hydrochloride. Meerwein showed that free acid in the reaction mixture can be titrated with alcoholic alkali if sufficient ether is first added to repress the reactivity of camphene hydrochloride. By this means, it was found possible to follow the dissociation to equilibrium, in spite of the small extent of the reaction. Under the conditions of the exchange experiments it appears that fission would occur about 20 times too slowly to account for exchange.

Actually, the kinetics of the exchanges on the one hand, and of the elimination on the other, were quite different. The exchanges were catalysed by hydrogen chloride, but the elimination was not, since, although hydrogen chloride was produced in the latter process, good first-order rate constants were obtained. The above numerical comparison of rates refers, of course, to the particular concentration (0·1M) of hydrogen chloride used for the exchange experiments : the factor would naturally be different for other concentrations.

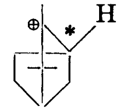
Catalysis of exchange by hydrogen chloride, with its intense positive force field, is entirely consistent with the idea that the mode of halogen exchange is ionisation, and that this is the first, and rate-determining process (Barnett, Matthews, and Cook, *Ber.*, 1927, **60**, 2353, 2366; J., 1928, 2798). This being accepted, definite restrictions are placed on what may be assumed with regard to subsequent hydrogen exchange in order to accommodate the observations already mentioned. First, the hydrogen exchange must be relatively rapid. Secondly, it must not involve the simple loss of a proton, because this, along with the preliminary chlorine ionisation, would amount to the fission reaction. The only obvious alternative is that the hydrogen exchange is a rapid bimolecular interchange of hydrogen between the organic cation and hydrogen chloride. The further consequence then follows that equality of exchange rates will obtain only if the seat of hydrogen exchange carries but one hydrogen atom; for if more than one were present, they would be exchanged rapidly and consecutively and the measured exchange rates would no longer be equal. Hydrogen exchange must, therefore, be confined to one or other of the bridge-head positions.

Rearrangement of Camphene Hydrochloride into iso*Bornyl Chloride.*—In chloroform–nitrobenzene solution at 20°, chlorine exchange is immeasurably faster than rearrangement (see p. 1190). In order to obtain an estimate of the ratio of these two velocities, experiments were carried out in pure chloroform solution at 0°. Under these conditions, rearrangement proceeded at about one-fifteenth of the speed of chlorine exchange. Like exchange, and in agreement with the findings of other authors (Meerwein, *loc. cit.*; Bartlett and Pöckel, *loc. cit.*), rearrangement was catalysed by hydrogen chloride, and this effect cannot be due to an acceleration of halogen ionisation since this is not now the slow stage. The simplest way in which dependence of hydrogen chloride can be accounted for is to assume that the slow stage is a bimolecular reaction between the organic cation and a molecule of hydrogen chloride, to give *iso*bornyl chloride.

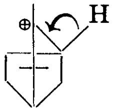
On this basis the mechanism of rearrangement is similar to that for hydrogen exchange: each process involves reaction of the organic ion with hydrogen chloride. The important difference lies in the fact that for rearrangement this process is much slower, whereas for hydrogen exchange it is much faster, than the preliminary halogen ionisation. Analogy for the behaviour of deuterium chloride either as a deuterating (exchange) or as a chlorinating (rearrangement) agent is provided by the action of deuterium sulphate, which may both deuterate and sulphonate benzene (Ingold, Raisin, and Wilson, J., 1936, 1637).

Reasons have been advanced for assuming that hydrogen exchange involves one of the bridge-head positions. The probable position is that marked with an asterisk in formula (III) (an alternative representation of the first ion of Meerwein's scheme, I $\rightleftharpoons$ II), since this hydrogen atom should be particularly vulnerable, owing to the electron-affinity of the neighbouring pole (IV) (cf. Ingold, *Ann. Reports*, 1928, **25**, 133). Like the other reactions of camphene hydrochloride examined, the elimination probably depends on halogen ionisation followed by the loss of one of the methyl hydrogen atoms to give camphene (V $\rightleftharpoons$ VI). Since the fission is a much slower process than the halogen ionisation, proton separation must be the slow step in the former. This assumption agrees with the experimental result that fission is not catalysed by hydrogen chloride, which would be expected to be but a poor catalyst for proton removal in hydrocarbon structures.

(III.)



(IV.)



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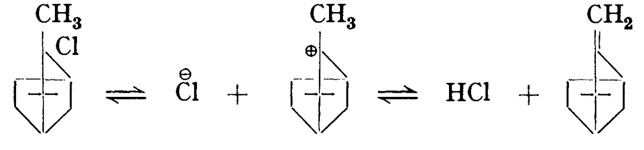


(VI.)

Table I contains the velocity constants obtained in chloroform solution at 0°. The three second-order reactions (rearrangement and exchanges) occurred in the presence of

TABLE I.

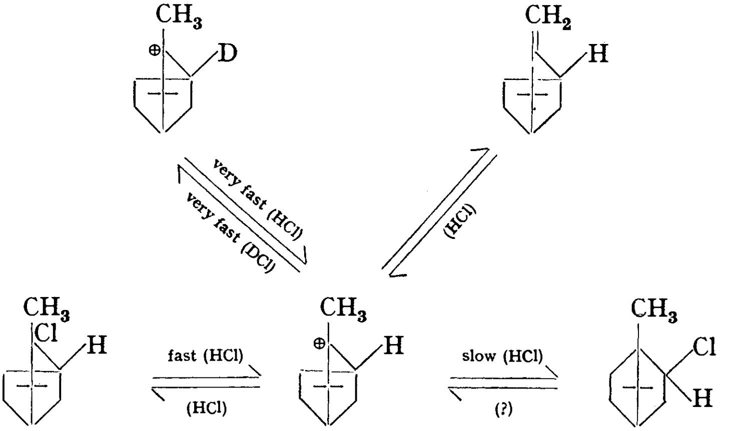
Velocity Constants of Certain Reactions of Camphene Hydrochloride (Cam.HCl) *at* 0° *in Chloroform Solution in the Presence of Hydrogen Chloride.*

Reaction.	Velocity given by	Velocity constant* × 10^5.
Rearrangement into *iso*bornyl chloride	k_2[Cam.HCl][HCl]	$k_2 = 9{\cdot}0\ (\pm 0{\cdot}2)$
Chlorine exchange	k_2[Cam.HCl][HCl]	$k_2 = 140\ (\pm 15)$
Hydrogen exchange	k_2[Cam.HCl][HCl]	$k_2 = 150\ (\pm 15)$
Fission into camphene and hydrogen chloride ...	k_2[Cam.HCl]	$k_1 = 0{\cdot}76\ (\pm 0{\cdot}02)$

* Here and throughout, k_2 is in l. g.-mol.$^{-1}$ sec.$^{-1}$, and k_1 in sec.$^{-1}$.

hydrogen chloride (*ca.* 0·1M; no appreciable difference was observed between deuterium and protium chlorides), whereas for the first-order fission process hydrogen chloride was not added initially but was developed as reaction proceeded. The probable errors are indicated in parentheses.

The completed reaction scheme is indicated in the following diagram.



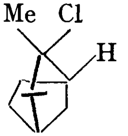
(VII.)

Although the intermediate ion is represented as having the camphene structure, it is possible that it is mesomeric between this and the corresponding *iso*bornyl structure [compare (I) $\rightleftharpoons$ (II)]. One condition (see below) would seem to be that, whatever the structure of the ion (VII), the stereochemical identity of the carbon atom marked with an asterisk must be preserved.

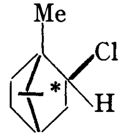
Kinetic Implications of the Proposed Reaction Mechanism.—From the constants given in Table I it is obvious that, in the presence of large amounts of hydrogen chloride, fission will be slower than rearrangement. On the other hand, under the conditions of most of Meerwein's experiments where no additional hydrogen chloride is present, the reverse will be true and dissociation equilibrium will be maintained throughout the rearrangement; this state of affairs was assumed by Bartlett and Pöckel (*loc. cit.*). However, since catalyst is being progressively removed as *iso*bornyl chloride, which is undissociated, the kinetics of the rearrangement in these circumstances should not be first order with respect to camphene hydrochloride. Meerwein's first-order constants were reasonably steady but then his measurements were limited to not more than the first two-thirds of the total reaction; however, they tend to fall, as is to be expected. That the order of the reaction should be 1·5 can be shown as follows. If K is the dissociation constant for camphene hydrochloride (concentration = c), then the concentration (h) of hydrogen chloride is given by $\sqrt{Kc}$, and the velocity of rearrangement by

$$-\mathrm{d}c/\mathrm{d}t = k_2hc = k_2K^{1/2}c^{3/2} = \text{const.}c^{3/2}.$$

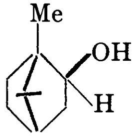
A recalculation of Meerwein's data along these lines was carried out by Bartlett and Pöckel (*loc. cit.*), who showed that an assumed order of 1·5 much improves the constants.



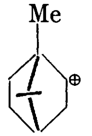
(VIII.)



(IX.)



(X.)



(XI.)

Stereochemical Considerations.—From a consideration of the probable stereochemical relation between camphene hydrochloride * (VIII) and *iso*bornyl chloride (IX) (in these

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* Two geometrically isomeric forms of camphene hydrochloride should exist. This is so for the alcohols, but each gives the same chloride. It is probable, therefore, that the latter is a mixture of forms, rapidly interconverted through ions or camphene depending on the amount of hydrogen chloride present.

formulæ the heavy lines indicate that the bonds are towards the reader), Bartlett and Pöckel concluded that the rearrangement must be kinetically of a higher reaction order than unity, with respect to camphene hydrochloride. Their argument was as follows. The configuration of *iso*borneol is almost certainly that (X) in which the *gem*-dimethyl bridge and the hydroxyl group are in the *cis*-position (*exo*-) to each other (Vavon and Peignier, *Bull. Soc. chim.*, 1926, **39**, 925; Hückel *Annalen*, 1930, **477**, 157; Asahina, Ishidate, and Sano, *Ber.*, 1936, **69**, 343; cf., however, Lipp, *Ber.*, 1935, **68**, 1029; Krestinskiĭ and Eshenko, *J. Gen. Chem. U.S.S.R.*, 1937, **7**, 415; Krestinskiĭ, Nemilov, and Bardyshev, *ibid.*, p. 423; Shavrygin, *ibid.*, p. 2754). They also consider that there is evidence for assuming a correspondence between *iso*bornyl chloride (IX) and *iso*borneol (X), and point out that consequently the rearrangement must involve a Walden inversion at the carbon atom marked with an asterisk; this is evident from the formulæ (VIII) and (IX). It is pointed out further that the process cannot involve ions of the type (XI) (the second ion of Meerwein's scheme I $\rightleftharpoons$ II; cf. Whitmore, *J. Amer. Chem. Soc.*, 1932, **54**, 3274) since these would be expected to yield a mixture of bornyl and *iso*bornyl chlorides, whereas the product is almost pure *iso*bornyl chloride. It is, of course, possible that if an ion (XI) were involved the operation of special factors might cause the preferential formation of *iso*bornyl chloride. Of the two stereoisomeric halides, *iso*bornyl chloride is the thermodynamically unstable form, being slowly converted into bornyl chloride under the same conditions as those causing rearrangement of camphene hydrochloride, and at first sight this fact, too, might be thought to disprove the intervention of an ion (XI). However, in the rearrangement of camphene hydrochloride we are dealing essentially with rates and not equilibria, and the question of the ion (XI) must be left open until more experiments have been performed, but it seems fair to conclude that the balance of evidence is against the existence of an ion (XI). Bartlett and Pöckel suggest that rearrangement involves reaction of camphene hydrochloride with a molecule of hydrogen chloride so that free ions are never formed. They argue convincingly that if hydrogen chloride thus acts as a donor of chloride ions, free chloride ions should do so much better. However, on introduction of these (as lithium chloride) into the reaction mixture in acetone as solvent, no increase in velocity was observed, and Bartlett and Pöckel confess that their theory must be incomplete. Nevertheless, this is just the result to be expected on the basis of the reaction scheme on p. 1192, since on adding chloride ions, the increase in velocity of disappearance of intermediate organic ions is just balanced by a decrease in their concentration due to a repression of the ionic equilibrium in favour of camphene hydrochloride.

We must emphasise that, although Bartlett and Pöckel relate, configuratively, *iso*borneol and *iso*bornyl halides, yet as far as we can ascertain the reagents used for the interconversion of the isomeric alcohols and halides are such as to render impossible any definite statement with regard to stereochemical relationship. The correct method of approach to this problem has been indicated by Cowdrey, Hughes, Ingold, Masterman, and Scott (J., 1937, 1252): it involves a study of reaction kinetics as well as stereochemistry.

Our experiments provide sufficient data for certain stereochemical conclusions to be drawn as to the rearrangement of camphene hydrochloride into *iso*bornyl chloride. The reaction of the intermediate ion (cf. scheme on p. 1192) with hydrogen chloride, is, as we have shown, bimolecular, and must, by analogy with all simple bimolecular nucleophilic substitutions, involve a Walden inversion. This conclusion is drawn irrespective of the above proposals regarding the configuration of *iso*bornyl chloride. It follows, therefore, that *iso*bornyl chloride has the *cis*-(*exo*-)configuration (IX), in agreement with Bartlett and Pöckel's assumption.

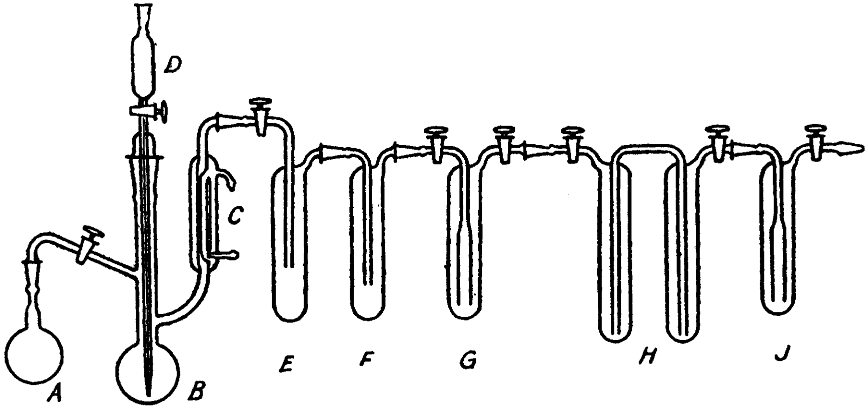
Finally, we refer to the conclusion that deuterium exchange involves one of the bridge heads. This process cannot involve a Walden inversion and therefore provides a further example in which substitution of hydrogen by deuterium proceeds with retention of configuration (cf. De Salas and Wilson, J., 1938, 319). In this connexion it is noteworthy that *trans*-decalin on nitration partly yields 9-nitro-*trans*-decalin (Hückel and Blohm, *Annalen*, 1933, **502**, 114).

EXPERIMENTAL.

1. *Materials.*—Camphene hydrochloride was prepared by a slight modification of Meerwein and van Emster's method (*loc. cit.*). Camphene (B.D.H.) was distilled from sodium under reduced pressure; the fraction (50 g.), b. p. 41—43°/1 mm., was collected, dissolved in light petroleum (b. p. 40—60°), and treated with a slow stream of hydrogen chloride at $-10°$ (ice–salt) during about 5 hours. The white precipitate (about 30 g.) was filtered off, washed with ice-cold petroleum, and freed from solvent in a vacuum over solid potassium hydroxide. Analysis (see later) showed that the product contained 85—90% of camphene hydrochloride and about 2% of free camphene, the remainder being *iso*bornyl chloride. On keeping, it slowly evolved hydrogen chloride, and the product isomerised into *iso*bornyl chloride so that after 3 weeks the camphene hydrochloride content had fallen to about 50%. Fresh samples were therefore prepared as required.

*iso*Bornyl chloride resulted by saturating a solution of camphene (300 g.) in ethyl bromide (150 g.) with hydrogen chloride at room temperature and subsequently refluxing it at 55° for six days (Meerwein and van Emster, *loc. cit.*). After removal of the solvent in a vacuum, the residue was recrystallised several times from amyl alcohol. Finally, the pure material was washed with dry methyl alcohol and dried in a vacuum. Yield 120 g., m. p. 148°. Analysis showed the purity to be 99%.

FIG. 1.



Deuterium chloride generator.

Chloroform was shaken repeatedly with water, dried first over calcium chloride and finally over phosphoric oxide, and distilled immediately.

"AnalaR" nitrobenzene was dried over phosphoric oxide and distilled under reduced pressure.

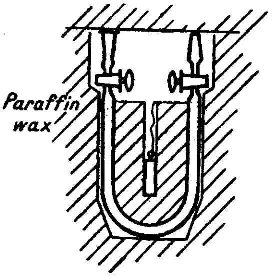
Deuterium chloride was produced by hydrolysis of thionyl chloride with deuterium oxide (99·6% D). The all-glass apparatus used is shown in Fig. 1 and is adapted from that described by Langseth and Klit (*Z. physikal. Chem.*, 1936, *A*, **176**, 65; *Danske Vidensk. Selskab.*, 1937, **15**, No. 13, 3). Purified thionyl chloride (10 g.) was heated in an oil-bath to 75° in the flask *B*, and deuterium oxide (0·5 g.) run in slowly from the funnel *D via* a capillary stem. Condenser *C* prevents the loss of thionyl chloride. Traps *E* and *F* were immersed in carbon dioxide–acetone to remove sulphur dioxide, and the residual deuterium chloride was solidified in *G* immersed in liquid air. Chloroform (50 c.c.) in the twin bubbler *H* was cooled to about $-30°$, and the deuterium chloride was passed through it three times by immersing traps *G* and *J* alternately in liquid air. On allowing the chloroform solution to warm to room temperature under atmospheric pressure, an approximately 0·1N-solution of deuterium chloride was obtained. The whole apparatus was, of course, thoroughly dried before use.

Commercial specimens of thionyl chloride gave hydrogen chloride containing only 93% of deuterium, and repeated fractionation of the starting material at ordinary pressure failed to alter this figure appreciably. This low content is undoubtedly due to the presence in thionyl chloride of light hydrogen chloride which is not removed by simple distillation. However, if ordinary thionyl chloride (15 g.) is mixed with pure quinoline (2 g.) in the bulb *A* and subsequently distilled in a high vacuum into *B*, leaving a third of the material behind, subsequent reaction with deuterium oxide gives a product containing never less than 99% of deuterium.

Langseth and Klit (*loc. cit.*) do not record having taken special precautions to purify their thionyl chloride; they used it to prepare various deuterated benzenes, and, in the absence of reliable analytical figures, these substances cannot be regarded as being of a high degree of isotopic purity.

Protium and deuterium radio-chlorides. The chloroform solution of the appropriate hydrogen chloride was transferred directly into the irradiation flask shown in Fig. 2. This consisted essentially of a soda-glass vessel, shaped like a Dewar flask and of sufficient size to contain the solution in the space between the walls. Inlet and outlet tubes carrying taps and standard joints were fixed to the rim of the vessel. The inside of the vessel was filled with paraffin wax except for a cylindrical cavity which contained the neutron source. This was 200 mg. of radium as sulphate mixed with beryllium and contained in a platinum tube. The entire glass vessel was surrounded by paraffin wax. Irradiation for 3 hours was found to be sufficient.

FIG. 2.



Neutron irradiation vessel.

2. *Estimation of Camphene Hydrochloride,* iso*Bornyl Chloride, and Hydrogen Chloride.*—The method was essentially that of Meerwein and van Emster (*loc. cit.*). Suitable portions of the reaction mixture in either chloroform or chloroform–nitrobenzene were run into dry ether (at least 3 vols.), and the free hydrogen chloride rapidly titrated with 0·02N-sodium ethoxide, lacmoid being used as indicator. Camphene hydrochloride was estimated together with free acid by running the reaction mixture into an excess of 0·2N-sodium ethoxide containing an equal volume of anhydrous methyl alcohol. After standing for one hour at 20°, the excess alkali was back titrated (lacmoid). *iso*Bornyl chloride is unaffected under these conditions but may be estimated by refluxing the reaction mixture for one hour with excess of 0·2N-aqueous-alcoholic alkali, allowance being made for the amounts of hydrogen chloride and of camphene hydrochloride present.

3. *Rearrangement of Camphene Hydrochloride.*—(a) *Experiments in chloroform–nitrobenzene solvent at* 20°. In most of the experiments described in the following sections camphene hydrochloride was approximately 5% (0·3M). In the present instance the reaction medium consisted of equal volumes of chloroform and nitrobenzene and contained initial amounts of hydrogen chloride which were varied between 0·03 and 0·10M. It was immediately obvious from the results that the speed of isomerisation was dependent on hydrogen chloride concentration. A specimen run is given below. During sampling the hydrogen chloride concentration fell slightly and the bimolecular velocity constants have been calculated from consecutive titration figures; the reaction order with respect to hydrogen chloride would appear to be greater than unity, since the constants decrease. This is supported by the data of Table II; here the results of a large number of experiments are summarised. The values of k_2 were obtained by plotting the velocity constants (k_2) against hydrogen chloride concentration for any one run and averaging the values at chosen hydrogen chloride concentrations. The figures in parentheses are the mean deviations.

Rearrangement of Camphene Hydrochloride in Chloroform–Nitrobenzene Solution at 20°.

Time (mins.)	0	60	120	170	220	270	325	387	440	500
Cam.HCl (M)	0·263	0·217	0·180	0·156	0·133	0·116	0·101	0·087	0·076	0·067
HCl (M)	0·0660	0·0587	0·0566	0·0549	0·0544	0·0539	0·0535	0·0523	0·0510	0·0500
10^4k_2	—	8·5	9·0	8·6	9·4	8·6	8·2	7·8	7·1	7·3

TABLE II.

Rearrangement of Camphene Hydrochloride in Chloroform–Nitrobenzene Solution at 20°: *Effect of varying Hydrogen Chloride Concentration.*

HCl (M)	0·030	0·040	0·050	0·060	0·070	0·090	0·100
10^4k_2	7·8 (±0·5)	8·4 (±0·7)	8·0 (±0·7)	7·6 (±1·1)	9·0 (±0·6)	9·5 (±0·9)	10·6 (±0·6)

(b) *Experiments in chloroform at* 20°. No attempt was made to calculate the chloroform–nitrobenzene data on any other than a bimolecular basis. Fortunately, strictly bimolecular kinetics were followed in pure chloroform solution. This is evident from the following table, which records the results of five separate experiments; the mean deviations are given in parentheses.

Rearrangement of Camphene Hydrochloride in Chloroform Solution at 20°.

HCl (range during run, M)	0·070—0·039	0·064—0·029	0·044—0·016	0·038—0·018	0·178—0·146
10^4k_2	1·73 (±0·08)	1·67 (±0·18)	2·01 (±0·17)	1·80 (±0·13)	1·80 (±0·17)

Mean value of 10^4k_2 = 1·80 (mean deviation, ±0·08; probable error, ±0·04).

(c) *Experiments in chloroform at* 0°. Carried out as above, these experiments gave 10^5k_2 = 9·0 (mean deviation, ±0·5; probable error ±0·2). It is obvious that the rearrangement possesses an abnormally low temperature coefficient (rate doubled for 20° rise); this agrees with the fact that rearrangement depends on the establishment of an equilibrium (see p. 1192).

4. *Chlorine Exchange.*—(a) *Method.* The chloroform solution of hydrogen radio-chloride was divided into two portions : one was used to make up the reaction mixture, the other was the radioactivity standard. After a suitable interval the reaction was stopped by shaking with water (15 c.c.). This procedure sufficed to extract the hydrogen chloride, and provided it was done quickly, the camphene hydrochloride remained unaffected. The radioactivity standard portion was treated similarly with water, and the activities of the two aqueous extracts were measured by using a Geiger–Müller counter (cf. J., 1938, 209). Chloride-ion concentrations were found by Volhard titration.

The ratio (γ) of the two activities referred to the same concentration of chloride ion and the same instant of time is a direct measure of the amount of exchange which has occurred. If the concentration of hydrogen chloride is h, then the amount of chlorine exchange is $x = h(1 - \gamma)$.

(b) *Experiments in chloroform–nitrobenzene solution at* 20°. Preliminary experiments were carried out to ascertain whether any exchange occurred with either the solvent or *iso*bornyl chloride. It was found that the activity of the hydrogen chloride extracted from the mixed solvent was always less than that from the original pure chloroform solution. Table III gives some data showing that the value of the exchange ratio (γ_0, no camphene hydrochloride present) is independent of time and has a mean value of 0·76. In view of the much greater proportion of chloroform than of hydrogen chloride, the results suggest the presence of a small amount of impurity possessing rapidly exchangeable chlorine rather than the property to remove hydrogen chloride. It is immaterial whether the chlorine of the impurity is or is not extracted by water (cf. Topley *et al.*, J., 1935, 1525). Alternatively, the anomalous behaviour could be explained by the presence of a chlorine-containing impurity which, whilst not exchanging its halogen with hydrogen chloride, does react with water to produce chloride ions, thus diluting the active with inactive chlorine. We have not pursued these experiments further, since it was found that the effect completely disappeared in the absence of nitrobenzene.

TABLE III.

Halogen Exchange between Hydrogen Radio-chloride and Chloroform–Nitrobenzene Solvent at 20°.

Reaction time (mins.)	5	5	10	10	15	15
HCl (M)	0·0868	0·0814	0·0857	0·0850	0·0887	0·0880
γ_0	0·75	0·78	0·78	0·76	0·74	0·77

Mean γ_0 = 0·76 (mean deviation, ±0·01; probable error, ±0·005).

In spite of this complication, exchange experiments with *iso*bornyl chloride and with camphene hydrochloride have been carried out in the mixed solvent. From Table IV it can

TABLE IV.

Halogen Exchange between Hydrogen Radio-chloride and iso*Bornyl Chloride in Chloroform–Nitrobenzene Solution at* 20°.

Reaction time (mins.)	5	5	10	10	15	15
*iso*Bornyl chloride (M)	0·300	0·292	0·292	0·293	0·300	0·287
HCl (M)	0·0940	0·0785	0·0785	0·0834	0·0940	0·0851
γ	0·70	0·73	0·77	0·82	0·71	0·74

Mean γ = 0·75 (mean deviation, ±0·04; probable error, ±0·01).

be seen that, allowance being made for solvent exchange, *iso*bornyl chloride is unreactive, whereas Table V clearly shows that exchange with camphene hydrochloride is virtually complete in 5 minutes, although isomerisation is almost negligible.

TABLE V.

Rearrangement and Halogen Exchange of Camphene Hydrochloride (Cam.HCl) *in the Presence of Hydrogen Radio-chloride in Chloroform–Nitrobenzene Solution at* 20°.

Reactn. time (mins.).	Cam.HCl (M).	HCl (M).		Isomerisation, %.	γ, found.	γ, corr.	Exchange, %.	
		Actual.	Apparent.				Found.	Calc. for equilm.
15	0·247	0·076	0·100	7·3	0·24	0·31	69	71
15	0·243	0·074	0·097	7·0	0·24	0·32	68	71
15	0·160	0·076	0·100	7·5	0·30	0·40	60	62
15	0·262	0·068	0·089	6·1	0·22	0·29	71	75
15	0·167	0·080	0·103	7·8	0·34	0·44	56	62
10	0·158	0·075	0·099	5·1	0·29	0·38	62	61
10	0·152	0·081	0·096	5·3	0·21	0·27	73	61
5	0·160	0·077	0·101	3·7	0·38	0·50	50	61
5	0·231	0·061	0·084	2·2	0·33	0·43	57	73

In calculating the figures of Table V allowance has been made for the impurity present in the solvent. On the assumption that this has the effect of increasing the concentration of exchangeable chlorine, it is necessary to divide the concentration of hydrogen chloride initially added by γ_0, where γ_0 measures exchange of the mixed solvent in the absence of camphene hydrochloride. In this way "apparent" values of the hydrogen chloride concentration are determined. Furthermore, the found values of γ are related to standard activity extracted from pure chloroform solution, these have now to be related to the mixed solvent, which is done by dividing by γ_0. For the purpose of these approximate calculations γ_0 has been taken from Table III and assumed to be independent of hydrogen chloride concentration. Col. 8 records the derived exchanges; the figures compare favourably with those calculated for equilibrium (col. 9).

If it is assumed that the impurity is one which, whilst not possessing exchangeable halogen, is extracted by water to give chloride ions, the found and calculated figures for exchange do not agree nearly so well as those in Table V. This is evidence against such an assumption regarding the nature of the impurity.

(c) *Experiments in chloroform solution at* 0°. Both protium and deuterium radio-chlorides have been employed as catalysts. Solid camphene hydrochloride (2·5 g.) was first evacuated to remove occluded hydrogen chloride and then dissolved rapidly in the reaction medium at 0°. Although by the very nature of the experiments the experimental error was rather large, it was obvious that speed of exchange was dependent on hydrogen chloride concentration. In Table VI, therefore, bimolecular constants have been calculated.

TABLE VI.

Halogen Exchange between (a) *Protium and* (b) *Deuterium Radio-chloride and Camphene Hydrochloride in Chloroform Solution at* 0°.

	Reaction time (mins.).	Camphene hydrochloride (M).	(a) HCl (M); (b) DCl (M).	Exchange ratio, γ.	10^3k_2.
(a)	6	0·152	0·121	0·88	2·4
	10	0·163	0·145	0·86	1·4
	10	0·151	0·114	0·80	2·6
	15	0·159	0·143	0·84	1·2
	20	0·158	0·158	0·80	1·3
	Mean 10^3k_2 = 1·8 (mean deviation, ±0·6; probable error, ±0·2).				
(b)	5	0·175	0·0916	0·88	2·0
	5	0·170	0·0500	0·93	1·3
	10	0·169	0·0716	0·79	2·3
	15	0·178	0·0355	0·82	0·9
	15	0·152	0·0780	0·83	1·3
	15	0·168	0·0550	0·76	1·7
	15	0·196	0·0208	0·83	0·5
	20	0·149	0·0833	0·79	1·2
	Mean 10^3k_2 = 1·4 (mean deviation, ±0·45; probable error, ±0·15				

A series of blank experiments showed that during the periods of time recorded in Table VI, *iso*bornyl chloride did not undergo any appreciable exchange. The data are given below:

Showing the Absence of Halogen Exchange between Protium Radio-chloride and iso*Bornyl Chloride in Chloroform Solution at* 0°.

Reaction time (mins.)	5	5	15	20
*iso*Bornyl chloride (M)	0·290	0·290	0·290	0·290
HCl (M)	0·088	0·095	0·105	0·122
Exchange ratio, γ	1·01	0·96	0·99	1·00

Mean $\gamma = 0{\cdot}99$ (mean deviation, $\pm 0{\cdot}02$; probable error, $\pm 0{\cdot}01$).

5. *Hydrogen Exchange.*—(a) *Method.* Samples of camphene hydrochloride, previously evacuated to remove free hydrogen chloride, were dissolved in the reaction medium containing deuterium chloride. Reaction was arrested by shaking with water (10—15 c.c.). The aqueous extract was shaken with carbon tetrachloride to remove chloroform or nitrobenzene (depending on the solvent used) and divided into two portions. One of these was analysed gravimetrically for chloride ion and the other was passed over red-hot copper oxide to remove organic matter (carbon tetrachloride as extraction solvent has the advantage of not containing hydrogen) and subsequently purified by vacuum distillation from silver oxide. The density of this sample was determined pyknometrically.

Hydrogen exchange is calculated as follows. If a g. (presence of dissolved carbon tetrachloride is negligible) of the aqueous extract contains b g. of chlorine and m is the deuterium concentration in the silver oxide-purified water in atoms %, then, in 100 g.-mols. of the pure water there are $10m$ g. of D_2O and $9(100 - m)$ g. of H_2O. Therefore 1 g. of the water contains $m/(900 + m)$ equiv. of deuterium; but a g. of the aqueous extract contain $b/35{\cdot}5$ equivs. of chlorine or $b/35{\cdot}5$ equivs. of $(D + H_e)$, where H_e refers to the protium which originates from camphene hydrochloride by exchange.

It is now necessary to relate the results of the two gravimetric analyses, but first, correction must be applied to allow for the fact that, in one, chlorine has been replaced by oxygen (from silver oxide) before weighing for analysis (density).

Now, $b/35{\cdot}5$ equivs. of $(D + H_e)$ are contained in a g. of extract $= a - b + 8b/35{\cdot}5$ g. of pure water, so that 1 g. contains $(b/35{\cdot}5)/(a - 27{\cdot}5b/35{\cdot}5)$ equivs. of $(D + H_e) = 1/(35{\cdot}5a/b - 27{\cdot}5)$ equivs. of $(D + H_e)$. Therefore the hydrogen exchange ratio, δ, is given by

$$\delta = D/(D + H_e) = m(35{\cdot}5a/b - 27{\cdot}5)/(900 + m)$$

and the amount of exchange by $[HCl + DCl](1 - \delta)$.

(b) *Experiments in chloroform–nitrobenzene solution at* 0°. In the absence of camphene hydrochloride it was found that analysis of the extracted hydrogen chloride by the above method gave impossible values (1·2—1·4) for δ. It would appear, therefore, that some of the chlorine of the hydrogen chloride has become non-extractable with water. We have been unable to explain the effect, but fortunately it was absent when pure chloroform was used as solvent.

(c) *Experiments in chloroform solution at* 0°. The absence of exchange with the solvent was shown by the fact that it was possible to prepare and keep for considerable periods of time solutions of deuterium chloride which on analysis gave values of δ of very nearly 0·99. This point as well as the stability of *iso*bornyl chloride under similar conditions is shown by the results of experiments in Table VII which were performed with hydrogen chloride containing 93% of deuterium.

TABLE VII.

Showing the Absence of Hydrogen Exchange between Deuterium Chloride (*containing* 93% *of* D) *and* iso*Bornyl Chloride in Chloroform Solution at* 0°.

Reaction time (mins.)	0	200	400	200	200
*iso*Bornyl chloride (M)	0	0	0	0·315	0·296
DCl (M)	0·105	0·105	0·061	0·080	0·058
Exchange ratio, δ	0·93	0·92	0·94	0·93	0·91

Exchange between camphene hydrochloride and deuterium chloride was rapid at 0°, and it was obvious from the results (Table VIII) that the speed of exchange was dependent on hydrogen chloride concentration. Bimolecular constants were therefore calculated.

Dissociation of Camphene Hydrochloride into Camphene and Hydrogen Chloride in Chloroform Solution at 0°.—Camphene hydrochloride, freed from hydrogen chloride by evacuation, was

TABLE VIII.

Hydrogen Exchange between Deuterium Chloride (containing 99% of D) *and Camphene Hydrochloride in Chloroform Solution at* 0°.

Reaction time (mins.)	5	10	15	15	15	20
Camphene hydrochloride (M)	0·175	0·169	0·171	0·152	0·168	0·149
DCl (M)	0·0916	0·0716	0·1060	0·0780	0·0550	0·0833
Exchange ratio, δ	0·92	0·79	0·76	0·90	0·82	0·71
10^3k_2	1·6	2·1	1·8	0·6	1·2	1·7

Mean 10^3k_2 = 1·5 (mean deviation, ±0·4; probable error, ±0·15).

dissolved in chloroform at 0°. Samples (20 c.c.) were run into dry ether (60 c.c.) and titrated with 0·02N-sodium ethoxide, lacmoid being used as indicator. The data of one run are given below. The only satisfactory velocity constants were those calculated on the basis of a forward unimolecular dissociation and a reverse bimolecular association :

$$\text{camphene hydrochloride} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{camphene} + \text{hydrogen chloride}$$

If a is the initial concentration of camphene hydrochloride, x the amount dissociated at time t, and x_∞ the value of x at $t = \infty$, then (cf. Bateman and Hughes, J., 1937, 1191)

$$\mathrm{d}x/\mathrm{d}t = k_1(a - x) - k_2x^2$$

or

$$k_1 = x_\infty/(2a - x_\infty)t . \ln[ax_\infty + x(a - x_\infty)]/(x_\infty - x)a$$

Dissociation of Camphene Hydrochloride into Camphene and Hydrogen Chloride in Chloroform Solution at 0° : a = 0·1192M.

t (mins.)	0	7	15	30	45	75	195	445	475
HCl (M) (10^5x)	0	43	84	134	181	257	320	320	305
10^6k_1	—	8·70	8·09	6·70	6·43	6·70	—	—	—
									Mean 7·31

The average value of the velocity constant obtained as a result of several such experiments was 10^6k_1 = 7·55 (mean deviation, ±0·77; probable error, ±0·23). The data show that the concentration of hydrogen chloride fell after equilibrium had been attained. This is to be expected, for rearrangement to *iso*bornyl chloride was becoming important.

The dissociation constant is 10^5K = 8·8 l. g.-mol.$^{-1}$, corresponding to about 3% dissociation.

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