# EXCHANGE REACTIONS IN DEUTEROALCOHOL

## M. S. KHARASCH, WELDON G. BROWN, AND JOHN MCNAB

Received January 30, 1937

## INTRODUCTION

It has been evident since the discovery and isolation of the hydrogen isotope that a direct method for the demonstration of the lability of hydrogen in certain types of organic compounds is now available. It consists in determining whether an exchange of light and heavy hydrogen atoms occurs when two compounds of different isotopic composition are brought together in solution at moderate temperatures. The experimental conditions may be adjusted at will from the very mildest to the most severe by a suitable choice of solvent, temperature, and catalytic agents, and the method is, therefore, not only direct but highly flexible.

It so happens that most of the work on exchange reactions which bears on the problem of hydrogen lability in organic compounds has been done with heavy water as the solvent and donor of deuterium. This is a consequence of the fact that the analytical operations are somewhat less complex for water than for other solvents which might be used. But since many of the compounds which are of interest in this connection are insoluble in water, the use of an organic solvent containing labile hydrogen can hardly be avoided in a comprehensive investigation of the exchange method.

The present work is the beginning of such an investigation and in this work we have employed heavy ethyl alcohol as the solvent and contributor of deuterium. The experiments reported at the present time are of an exploratory nature and are designed simply to provide some further orientation with regard to the types of substances which exhibit the exchange reaction.

A number of recorded observations relating to the exchange of hydrogen between water and various organic substances are summarized in Table I. The list comprises a considerable variety of compounds and it will be seen that the exchange reaction is in all cases confined to those hydrogen atoms which we know to be labile on the basis of experience with various other types of reactions, electrolytic dissociation, salt formation, condensation, prototropy, etc. Also in accord with expectations is the rapid exchange of two hydrogen atoms in cyclohexylidene acetonitrile in ethyl alcohol solution containing 0.1 N sodium ethylate, recently reported by Ingold, de Salas, and Wilson.<sup>1</sup> It is also of interest to note that the less labile hydrogens of benzene can be made to participate in exchange reactions under appropriate conditions, and that these conditions approach those under which aromatic substitution occurs. Thus it is reported by Klit and Langseth<sup>2</sup> that benzene exchanges hydrogen with hydrogen chloride in the presence of anhydrous aluminum chloride, and by Ingold, Raisin, and Wilson<sup>3</sup> that benzene exchanges hydrogen slowly with 50 per cent. sulfuric acid and more rapidly with 90 per cent. sulfuric acid.

#### EXPERIMENTAL PROCEDURE AND RESULTS

The occurrence of an exchange reaction between "heavy" alcohol and a substance of natural isotopic composition dissolved in it may be detected either by a decrease in the concentration of deuterium in the solvent or by an increase in the deuterium content of the solute. In these preliminary experiments we have relied entirely on observations of the change in composition of the solvent, and while it would be desirable to check these results by analysis of the solute, this would have necessitated the development of special analytical methods.

Analysis of ethyl alcohol for deuterium.—The analysis of ethyl alcohol for its deuterium content is accomplished by density measurements, using the temperaturefloat method,<sup>22</sup> on water obtained from the combustion of the alcohol. A 1-cc. sample of alcohol is burned in a small glass lamp containing an asbestos wick, the lamp being inserted in a chamber which is connected to a heated tube containing copper oxide, and this in turn leads to a series of traps where the water is collected. Dry air for the combustion is drawn through the system by suction. The water sample is heated under reflux for thirty minutes after adding a small quantity of potassium permanganate and sodium carbonate, and then distilled three times in high vacuum. It is collected finally in a small tube attached to the line by means of a ground joint. This tube is removed, and after introduction of the quartz float, transferred to a water-bath where the suspension temperature is determined. The movements of the float, which measures about 4 mm. in diameter and about 5 mm. in length, are observed with the aid of a low-power microscope. The temperatures were observed on two Beckmann thermometers which, together, provided a range of nearly ten degrees.

The amount of water required for the analysis is approximately 0.5 cc. This is very much less than is customary, or desirable, in density measurements by this method, but the restriction of operations to such a scale is dictated by practical considerations, such as the time required for the combustion process and the vacuum distillations. The chief difficulty lies in the purification of the water sample, as is evident from the fact that we have not been able to utilize the full sensitivity of the float method except with samples of water which, were available in quantities large enough for a preliminary purification by the usual methods. With water obtained from the combustion of alcohol, as described above, the suspension temperatures were ordinarily reproducible to within  $0.08^{\circ}$  but there were occasionally larger discrepancies apparently due to accidental contamination of the quartz surface.

<sup>&</sup>lt;sup>1</sup> INGOLD, DE SALAS, AND WILSON, J. Chem. Soc., 1936, 1328.

<sup>&</sup>lt;sup>2</sup> KLIT AND LANGSETH, Z. phys. Chem., A176, 65 (1936).

<sup>&</sup>lt;sup>3</sup> INGOLD, RAISIN, AND WILSON, J. Chem. Soc., 1936, 915; Nature, 134, 734 (1934).

In the range of deuterium concentration over which our measurements extend, namely from zero to 1.7% deuterium, the relationship between suspension temperature and density or deuterium concentration, departs only slightly from linearity, and the error introduced on assuming such a relationship is less than our experimental

COMPOUND	OBSERVATIONS	REFERENCES
Formaldehyde	No exchange.	4, 5, 6
Acetaldehyde	Slow exchange of 1 H atom, doubtful.	4, 5, 6
Acetone	Slow exchange in neutral solution; rapid in alkaline solution.	4, 5, 7, 8
Acetylacetone (2,4-Pen- tanedione)	All hydrogens exchange.	4, 5
Acetic acid	Exchange of carboxyl hydrogen only.	9
Sodium acetate	No exchange.	4, 5
Sodium formate	Slight exchange at 100°.	10
Formic acid	Exchange of carboxyl hydrogen only.	10
Monochloroacetic acid	Exchange of carboxyl hydrogen only.	10
Succinic acid	Exchange of carboxyl hydrogen only.	10, 11
Malonic acid	All hydrogens exchange rapidly.	10, 11
Ethylene glycol	Hydroxyl hydrogen atoms exchange rapidly.	12
Sucrose	Hydroxyl hydrogen atoms exchange rapidly.	13
d-Glucose	Hydroxyl hydrogen atoms exchange rapidly.	14
Cellulose	Hydroxyl hydrogen atoms exchange rapidly.	15
Hydroquinone Orcinol Resorcinol Pyrogallol	Instantaneous exchange of hydroxyl hydrogens; slow exchange of nuclear hydrogens.	16
Phloroglucinol	Rapid exchange of all hydrogens.	16

TABLE I

EXCHANGE RE.	ACTIONS BETWEEN	WATER AND	Organic (	Compounds
--------------	-----------------	-----------	-----------	-----------

<sup>4</sup> KLAR, Z. phys. Chem., B26, 335 (1934).

<sup>5</sup> BONHOEFFER AND KLAR, Naturwissenschaften, 22, 45 (1934).

<sup>6</sup> WIRTZ AND BONHOEFFER, Z. phys. Chem., B32, 108 (1936).

<sup>7</sup> Schwartz and Steiner, *ibid.*, **B25**, 153 (1934).

<sup>8</sup> ANDERSON, HALFORD, AND BATES, J. Am. Chem. Soc. 56, 491 (1934); 57, 663 (1935).

<sup>1</sup> LEWIS AND SCHUTZ, J. Am. Chem. Soc., 56, 493 (1934).

<sup>10</sup> MÜNZBERG, Z. phys. Chem., B31, 18 (1935).

<sup>11</sup> HALFORD AND ANDERSON, J. Am. Chem. Soc., 58, 736 (1936).

<sup>12</sup> Hall, Bowden, and Jones, *ibid.*, **56**, 750 (1934).

<sup>13</sup> BONHOEFFER AND BROWN, Z. phys. Chem., B23, 171 (1933).

<sup>14</sup> HAMILL AND FREUDENBERG, J. Am. Chem. Soc., 57, 1427 (1935).

<sup>15</sup> BONHOEFFER AND RUMMEL, Naturwissenschaften, 22, 45 (1934).

<sup>16</sup> MÜNZBERG, Z. phys. Chemie, **B33**, 23, 39 (1936).

### EXCHANGE REACTIONS IN DEUTEROALCOHOL

COMPOUND	OBSERVATIONS	REFERENCES
Urea	Exchange of all hydrogens.	18
Hydroxyproline	Exchange of three hydrogens.	18
Barbituric acid	Exchange of four hydrogens.	19
Strychnine	No exchange.	17
Vomicine	Exchange of two hydrogens.	17
Phenacetin	Exchange of one hydrogen.	19
Egg albumin	Exchange of amino hydrogens.	15
Methylamine hydro- chloride	Exchange of amino hydrogens.	20
Sodium vinylacetate	Exchange of one hydrogen.	21

TABLE I-Concluded

error. Moreover, since the absolute magnitude of the deuterium concentration is of no significance in the interpretation of our results, it is not essential that the observed suspension temperatures be transformed to read as actual concentrations. Nevertheless, a calibration of the float was carried out, using as reference points a number of water samples of known density, and it was thereby ascertained that the relationship between suspension temperature and concentration of deuterium was represented fairly well by the equation t = 1.62 + 3.80 N, where t is the temperature reading (arbitrary scale) and N is the concentration of deuterium in mole per cent.

Preparation of "heavy" ethyl alcohol.—Ethyl alcohol, in which a part of the hydroxyl hydrogen was replaced by deuterium, was prepared by mixing deuterium oxide with absolute alcohol, and later removing the water by means of calcium oxide. The absolute alcohol used in this preparation was first refluxed with calcium oxide and finally distilled over metallic sodium through a fractionating column, the fraction boiling at 78.3° being collected. To 194 g. of this product were added 4.2 g. of heavy water (99.5% deuterium). This mixture was allowed to stand for some time at room temperature after which it was refluxed with an excess of freshly ignited lime and finally distilled. From the combustion of samples of this product, water containing 1.52 mole per cent. deuterium was obtained. Assuming that all of this deuterium was present in the alcohol as  $C_2H_6OD$ , the concentration of this species can be given as 9.1 mole per cent. This product was used as the solvent in all of the experiments described hereafter.

Exchange experiments.—In all experiments a carefully dried and weighed sample (usually 5 g.) of the compound to be investigated was introduced into a reaction tube which had previously been connected to a vacuum line. After the opening through which the material had been introduced had been sealed, the tube was cooled in a carbon dioxide-acetone bath, and evacuated. A measured quantity (usually 5 cc.) of the solvent alcohol, contained in a vessel attached to the line through a stopcock, was then allowed to distill into the reaction tube and after a further evacuation the

<sup>&</sup>lt;sup>17</sup> ERLENMEYER, EPPRECHT, AND LOBECK, Helv. Chim. Acta, 19, 543 (1936).

<sup>&</sup>lt;sup>18</sup> WILLIAMS, J. Am. Chem. Soc., 58, 1819 (1936).

<sup>&</sup>lt;sup>19</sup> ERLENMEYER, EPPRECHT, LOBECK, AND GÄRTNER, Helv. Chim. Acta, **19**, 354 (1936).

<sup>&</sup>lt;sup>20</sup> GOLDFINGER AND LASAREFF, Compt. rend., 200, 1671 (1935).

<sup>&</sup>lt;sup>21</sup> IVES AND RYDON, J. Chem. Soc., 1935, 1735.

<sup>&</sup>lt;sup>22</sup> A discussion of this and other methods is given by UREY AND TEAL, *Rev. Mod. Phys.*, 7, 34 (1935).

COMPOUNDS	CONDITIONS	PERCENTAGE DECREASE IN DEUTERIUM OF ALC.	PERCENTAGE DECREASE IN DEUTERIUM OF ALCOHOL CALCULATED FOR THE EXCHANGE OF		
		(OBS.)	1H	2H	3H
Triphenylmethane	Room temp. for 135 days.	0	19		
Triphenylmethane	100° for 150 days	0			
Triphenylmethane	100° for 6 days	0			
-	0.02 M in NaOH.				
Diphenylmethane	Room temp. for 147 days.	0	26		
Fluorene	Room temp. for 138 days.	0	<b>26</b>	41	
Fluorene	110° for 28 days.	0			
Fluorene	110° for 8 days	35.5			
	0.02 M in NaOH.				
Fluorene	110° for 2 days	34			
	0.02 M in NaOH.				
Fluorene	110° for 2 days	0			
	$0.01 M \text{ in } H_2 SO_4.$				
Acenaphthene	110° for 36 hours.	0	28		
Dianisylphenyl-	110° for 36 hours.	0	15		
Dianisvlnhenvl-	110° for 96 hours	5.5			
methane	0.02 M in NaOH	0.0			
Ethyl acetoacetate	Boom temp for 3 days	41	31	48	58
Succinimide	110° for 25 hours.	32	36		
2-Methoxynaphthalene	110° for 22 hours.	0	26		
2-Methoxynaphthalene	110° for 22 hours	Ő			
	0.02 M in NaOH.	, , , , , , , , , , , , , , , , , , ,			
<i>a</i> -Nitrotoluene	110° for 34 hours.	16.5	33	46	60
o-Nitrotoluene	110° for 34 hours	31			
	0.02 M in NaOH.				
p-Nitrotoluene	110° for 48 hours.	Little,	30		
n-Nitrotoluene	110° for 48 hours	20			
<i>p</i> more condense	0.02 M in NaOH				
Quinaldine	110° for 60 hours	44 5	31	47	58
1.3.5-Trinitrobenzene	110° for 64 hours.	0	22	35	45
1 3 5-Trinitrobenzene	110° for 68 hours	40.5			10
1,0,0 1111100000000000	0.02 M in NaOH.	1010			
7,8-Benzoquinaldine	110° for 104 hours.	22	23	38	48
7,8-Benzoquinaldine	110° for 108 hours	40			
	0.02 M in NaOH.				
<i>m</i> -Nitrotoluene	110° for 66 hours.	6	33	46	60
m-Nitrotoluene	110° for 66 hours 0.02 <i>M</i> in NaOH.	6			
<i>m</i> -Nitrotoluene	Blank run. Alcohol re- moved immediately after mixing with <i>m</i> -nitro- toluene.	6			

# TABLE II Exchange Reactions in Deuteroalcohol

COMPOUNDS	CONDITIONS	PERCENTAGE DECREASE IN DEUTERIUM OF ALC.	PERCENTAGE DECREASE IN DEUTERIUM OF ALCOHOL CALCULATED FOR THE EXCHANGE OF			
		(OBS.)	1H	2H	3H	
Dimethylaniline	110° for 96 hours.	17.3	32	49	58	
Dimethylaniline	110° for 96 hours	14.6				
	0.02 M in NaOH.					
Dimethylaniline	110° for 96 hours.	20				
	$(P_2O_5 \text{ treatment for alc.})$					
Dimethylaniline	110° for 96 hours	(a)52.1		1		
	$0.01 M \text{ in } H_2 SO_4$	(b)54.6		1		
	$(P_2O_5 \text{ treatment of alc.})$					

TABLE II-Concluded

tube was sealed off. These reaction tubes were fitted with break-seals so that they could be re-attached to the line and opened in vacuum after they had been maintained for various lengths of time at the various temperatures noted hereafter. At the conclusion of the experiment, the reaction mixture is separated into its components by vacuum distillation, the alcohol being collected in a small tube connected to the line with a ground joint. The alcohol is then transferred to the glass lamp for the combustion.

*Experimental results.*—The experimental results are summarized in Table II, in which the extent to which the exchange reaction has taken place is indicated by the decrease in the deuterium content of the alcohol. The calculated values, corresponding in each instance to the exchange of one, two, and three hydrogen atoms, were derived on assuming a statistical distribution of the deuterium atoms determined solely by the relative molal quantities of solute and alcohol and by the number of replaceable hydrogen atoms in the solute molecule. It is well known that the equi librium constants in isotopic exchange reactions may deviate considerably from the values to be expected on the basis of a simple statistical distribution and thus that the number of replaceable hydrogen atoms in a compound cannot be determined with certainty by experiments of the type under consideration. Lack of agreement between the observed values and the calculated values may also arise from the fact that the observations now reported do not necessarily relate to equilibrium conditions.

### DISCUSSION OF RESULTS

It should be made clear at the outset that in the present study no attempt has been made to establish experimentally true exchange equilibria. Nor in the cases of compounds which did not undergo the exchange reaction can it be said that the range of experimental conditions which might conceivably give rise to exchange has been exhaustively explored. The data presented should be interpreted as implying only that under the conditions recorded exchange reactions either did not proceed at all or did take place to the extent observed. Nevertheless, certain theoretical conclusions are suggested by the facts already revealed.

The exchange reactions in which ethyl acetoacetate and succinimide

participated require no special comment. They are of the conventional type. It is of interest that ethyl acetoacetate exchanges two hydrogen atoms even in the absence of alkali.

The reaction of dimethylaniline, however, is of somewhat fresher interest, for in this compound the basic nitrogen atom carries no replaceable hydrogen atoms; exchange cannot be assumed to take place through the simple mechanism of deuteron addition and proton elimination at the basic group as with primary and secondary amines. Neither are "acidic" properties, such as are sometimes attributed to the triarylmethanes, logically ascribable to dimethylaniline. It would seem that this exchange must be related to a different kind of hydrogen lability—that which is manifested in the relatively high reactivity of this compound in nuclear substitution and in condensation reactions. It is, perhaps, significant that in the presence of a small amount of strong acid the exchange observed corresponded roughly to three hydrogen atoms. General chemical evidence supports the assumption that the labilizing effect of the dimethylamino substituent in the benzene nucleus is effective chiefly in the para and the two ortho positions.

In view of the catalytic effect of acids three possible mechanisms suggest themselves for consideration: (1) deuteron addition at the nitrogen atom, followed by simple molecular rearrangement,



(2) intermediate complex formation through a hydrogen bridge, followed by rearrangement and dissociation, or



(3) a combination of mechanisms of I and II.

We appreciate the fact that the data on hand are insufficient to evaluate

Ι

the relative probabilities of these mechanisms, and we contemplate a study of the exchange reactions of deuteroalcohol with diphenylmethylamine and triphenylamine.

Irrespective of the mechanism, however, a strikingly important fact has been demonstrated, namely, the ability of dimethylaniline to exchange a proton even in a solvent such as alcohol. In our opinion this remarkable lability of the ortho and para hydrogen atoms in dimethylaniline arises from the relatively high electronegativity<sup>23</sup> of the ortho- and para-N, Ndimethylphenyl radicals.\* In other words, the electron density in the immediate vicinity of the ortho and para carbon nuclei is greater than around the meta carbon nuclei, or the carbon nuclei of a phenyl radical. We do not suggest that this high electron density can lead to appreciable ionization even in highly polar or protophilic solvents. It might lead, however, to formation of hydrogen bridges, with the consequent labilization of the proton. We would be inclined to regard this type of hydrogendeuterium exchange as a special case of benzene-ring substitution, and to postulate as special prerequisites: (1) the presence in the ring of a substituent or substituents of the type that greatly increase the electronegativity of the phenyl radical; and (2) the presence in the medium of an acid, which can also serve as a deuteron source.

Whether or not it is an absolute prerequisite, or merely a favorable circumstance, that the benzene ring substituent may serve as a proton or deuteron acceptor, thus enabling the molecule to acquire a positive charge,

<sup>23</sup> KHARASCH AND MARKER, J. Am. Chem. Soc., **48**, 3130 (1925); KHARASCH AND REINMUTH, J. Chem. Educ., **5**, 404 (1928); **8**, 1703 (1931); KHARASCH, REINMUTH, AND MAYO, **11**, 82 (1934); KHARASCH AND FLENNER, J. Am. Chem. Soc., **54**, 674 (1932).

\* A rather attractive interpretation of the labilization by acids of the hydrogen atoms of strongly electronegative radicals and their replacement by deuterons, is given in the following highly schematic representation:



The essence of this representation is that there exists an attraction for deuterons by the o and p carbon atoms due to the high electron-density around these atoms, and that the labilization of the protons is facilitated by the approach of the deuterons. The formulae should not be looked upon as intermediates, but rather as phases of the labilization process.

is perhaps an open question. It is worthy of remark, however, that the substituent groups that we believe to be capable of increasing tremendously the electronegativity of the phenyl radical (the amino, the alkyland dialkylamino, the hydroxy and alkoxy groups) are all capable of so serving. The facts that traces of acids accelerate the exchange of the hydrogens for deuterium in dimethylaniline, while small amounts of alkali are essentially without effect, tend to support the first or third mechanisms suggested for this exchange. However, as already indicated, further experiments are necessary to test this hypothesis.

It is of interest to compare the high lability of the protons of dimethylaniline with the lack of lability of the protons of the di- and triarylmethanes in deuteroalcohol under the same conditions. Although the di- and triarylmethanes have been described as "weak acids," on the basis of their reactivity toward alkali metals,<sup>24</sup> it is fairly evident from our data that their proton ionization must be negligible.

From our standpoint, the electron density around the methyl carbon atoms in di- and triphenyl methanes would be very small, (as compared with the carbon atoms of ortho- or para-N, N-dimethylphenyl radicals), and in our notation we would define them as weakly electronegative radicals. It is possible of course for the electron density around the methyl carbon atom to decrease to a point where the proton may be readily removed by hydroxyl ions. Whether such a state is actually realized in fluorene, or whether the hydrogen atom lability should be ascribed to some peculiarity associated with the five-membered ring, the labilization of the hydrogen atoms by alkali is of considerable theoretical importance. We propose to investigate many other similar five-membered ring systems, particularly in view of the fact that acenaphthene does not undergo any exchange in deuteroalcohol.

Consistent with the interpretation that a low electron density around a carbon atom would facilitate the removal of a proton by hydroxyl ions, is the behavior of the nitrotoluenes and 1,3,5-trinitrobenzene in deuteroalcohol. Unlike the amino group, the nitro group markedly decreases the electronegativity of the phenyl radical.<sup>25</sup> These data are well in accord with observations that direct nuclear substitution proceeds more readily in aromatic hydrocarbons than in the corresponding nitro derivatives. This would imply that trinitrobenzene is a poor proton donor in acid solution. The fact that no exchange takes place when 1,3,5-trinitrobenzene is dissolved in deuteroalcohol is consistent with the view, and the

<sup>&</sup>lt;sup>24</sup> WOOSTER AND MITCHELL, J. Am. Chem. Soc., **52**, 688 (1930); CONANT AND WHE-LAND, *ibid.*, **54**, 1212 (1932); Cf. KHARASCH AND REINMUTH, J. Chem. Educ., **8**, 1740 (1931).

<sup>&</sup>lt;sup>25</sup> KHARASCH AND GRAFFLIN, J. Am. Chem. Soc., 47, 1948 (1925); KHARASCH AND GLADSTONE, unpublished work.

contrast with the behavior of dimethylaniline is marked. We would predict also that no exchange would occur in the case of trinitrobenzene in deuteroalcohol even in the presence of small quantities of acids. In alkaline solution, however, the entire relationship is changed. The exchange of dimethylaniline hydrogen atoms is unaffected, but with trinitrobenzene and the ortho and para nitrotoluenes, substances which can exist in tautomeric forms, rapid exchange takes place. It is significant that 1,3,5-trinitrobenzene exchanges all three hydrogen atoms, while in *o*-nitrotoluene the exchange is less complete. In the case of the *p*-nitrotoluene an enormous labilization of a hydrogen atom by alkali is definitely demonstrated. In the case of *m*-nitrotoluene no labilization of the hydrogen atoms can be demonstrated in the presence of alkali. It is our belief that the small exchange observed with that substance is due to some impurity.

In quinaldine and 7,8-benzoquinaldine the methyl hydrogen atoms are readily eliminated as protons. The proton labilization in an alcoholic solution of quinaldine must be considerable, and accounts for the ready condensation of the molecule with many proton acceptors (aldehydes, etc.). The increased exchange noted in alkaline solution, and the effects of traces of acids, is under investigation.

In conclusion, we should like to call attention to the fact that in the case of strongly electronegative radicals a certain liminal value in electronegativity must be reached before labilization of a hydrogen atom becomes marked in the absence of high concentration of acid. Thus, 2-methoxynaphthalene does not exchange the hydrogen atom in the 1-position, although the radical is strongly electronegative. Of course, the lack of exchange cannot be attributed entirely to the character of the radical, but is in part due to the fact that deuteroalcohol is a poor deuteron donor. With molecules which supply a large concentration of deuterons, such as sulfuric acid, the exchange would probably take place. With this in mind, the tremendous lability of the dimethylaniline hydrogen atom is most striking.

## EXPERIMENTAL DATA

Calibration of the float.—The float was calibrated with reference to normal water (laboratory distilled water) and two known samples of dilute heavy water which had been prepared by the quantitative dilution of a sample containing 12.47 mole per cent. deuterium oxide, this figure having been ascertained through pycnometric measurements of the density. The suspension temperature readings for normal water were: 1.610°, 1.625°, 1.610°, 1.650°; mean 1.625°. The readings for samples of water containing 0.87 mole per cent. deuterium oxide were 4.940°, 4.945°, 4.950°; mean 4.945°. The readings for samples containing 1.65 mole per cent. deuterium oxide were 7.925°, 7.910°, 7.895°, mean 7.910°. Analysis of stock heavy alcohol.—The suspension temperature readings for water samples obtained on the combustion of the heavy alcohol which was used as the solvent in this work were as follows: 7.380°, 7.380°, 7.485°, 7.365°, 7.375°, 7.325°, 7.425°, 7.325°; mean 7.385°.

Combustion of normal ethyl alcohol.—As a check on the method of combustion and purification a number of analyses were carried through on absolute ethyl alcohol, and the following readings were obtained: 1.605°, 1.625°, 1.655°, 1.610°, 1.620°, 1.645°; mean 1.625° (cf. value for normal water).

Exchange experiments.—Experimental data concerning the preparation of the reaction mixtures and the analyses of the alcohol samples removed from these mixtures are recorded hereafter. The figures which follow the description of the experiment are the observed suspension temperatures. The units are degrees Centigrade and the scale, though arbitrary, is consistent throughout.

Triphenylmethane.—The triphenylmethane used in the present work was carefully purified by several crystallizations from alcohol. The compound was dried thoroughly *in vacuo* to remove any traces of water and solvent of crystallization; m.p. 92°.

*Experiment 1.*—A reaction tube containing 5 g. of triphenylmethane and 5 cc. of deuteroalcohol was allowed to stand at room temperature for 133 days: 7.285°, 7.260°, 7.460°; mean 7.325°.

*Experiment 2.*—A reaction mixture identical with that of experiment 1 was maintained at a temperature of 100° for 150 days: 7.350°, 7.400°, 7.410°; mean 7.385°.

*Experiment 3.*—To a reaction mixture of 5 g. of triphenylmethane and 5 cc. deuteroalcohol 0.002 g. NaOH was added. The reaction tube was immersed in an oil bath at 100° for 6 days. The error introduced by exchange of the hydrogen in such a small quantity of alkali is of negligible magnitude: 7.470°, 7.400°; mean 7.435°.

Diphenylmethane.—This compound was purified prior to use by a series of vacuum distillations.

*Experiment 4.*—The exchange reaction solution of 5 cc. diphenylmethane in 5 cc. deuteroalcohol was allowed to stand at room temperature for 147 days: 7.355°, 7.375°; mean 7.365°.

Fluorene.—A pure sample of this compound was obtained by several crystallizations from alcohol with subsequent drying *in vacuo*; m.p. 112–114°.

Experiment 5.—A reaction tube containing 5 g. fluorene and 5 cc. deuteroalcohol stood at room temperature for 138 days: 7.410°, 7.430°, 7.425°; mean 7.420°.

Experiment 6.—A reaction tube containing 5 g. fluorene in solution in 5 cc. deuteroalcohol at 110° was allowed to stand for 28 days: (a)  $7.385^{\circ}$ ; (b)  $7.285^{\circ}$ ,  $7.325^{\circ}$ ; mean  $7.310^{\circ}$ .

Experiment 7.—A reaction mixture of 5 g. fluorene and 5 cc. deuteroalcohol containing 0.002 g. of NaOH was heated to 110° for 8 days: 5.425°, 5.255°; mean 5.340°.

*Experiment 8.*—A reaction mixture identical with that of experiment 7 was heated to a temperature of 110° for 2 days: 5.510°, 5.375°; mean 5.440°.

Experiment 9.—A reaction mixture of 5 g. fluorene and 5 cc. deuteroalcohol 0.01 molar in  $H_2SO_4$  was maintained at a temperature of 110° for 2 days: 7.395°, 7.465°; mean 7.430°.

Acenaphthene.—A pure vacuum-dried product was prepared for use in this work; m.p. 94–95°.

Experiment 10.—A 5-g. portion of acenaphthene was placed in a reaction tube with 5 cc. deuteroalcohol, and the tube was immersed in an oil bath at 110° for 36 hours: 7.430,° 7.400°; mean 7.415°.

Dianisylphenylmethane.--A quantity of this compound was purified by several

crystallizations from a mixture of chloroform and methyl alcohol; drying was effected *in vacuo*; m.p. 100-101°.

Experiment 11.—A reaction mixture of 5 g. dianisylphenylmethane and 5 cc. deuteroalcohol was maintained at a temperature of 110° for 36 hours: 7.340°, 7.370°; mean 7.355°.

Experiment 12.—A reaction mixture of dianisylphenylmethane and deuteroalcohol 0.02 molar in NaOH was heated to a temperature of 110° for 96 hours: 7.060°.

Ethyl acetoacetate.—The product used in this work was purified by several distillations in vacuo.

Experiment 13.—A reaction tube containing 5 cc. ethyl acetoacetate and 5 cc. deuteroalcohol was allowed to stand at room temperature for 3 days: 5.125°, 4.940°; mean 5.030°.

Succinimide.—A pure sample of this compound was dried for several hours in an Abderhalden desiccator at 78° prior to use in the exchange experiments; m.p. 124°.

Experiment 14.—A reaction mixture of 5 g. succinimide and 5 cc. deuteroalcohol was maintained at a temperature of  $110^{\circ}$  for a period of 25 hours:  $5.450^{\circ}$ ,  $5.640^{\circ}$ ; mean  $5.545^{\circ}$ .

2-Methoxynaphthalene.—A carefully purified sample of this compound was thoroughly dried in vacuo for use in the present work; m.p. 70°.

Experiment 15.—A tube containing 5 g. 2-methoxynaphthalene and 5 cc. deuteroalcohol was immersed in an oil bath at 110° for 22 hours: 7.435°, 7.395°; mean 7.420°.

*Experiment 16.*—A reaction mixture of 2-methoxynaphthalene and deuteroalcohol containing 0.002 g. NaOH was heated to a temperature of 110° for 22 hours: 7.425°, 7.365°; mean 7.395°.

o-Nitrotoluene.—This compound was purified by a series of vacuum distillations. Experiment 17.—A solution of 5 cc. o-nitrotoluene in 5 cc. deuteroalcohol was heated to 110° for 34 hours: 6.400°, 6.470°; mean 6.435°.

*Experiment 18.*—A reaction mixture of *o*-nitrotoluene and deuteroalcohol 0.02 molar in NaOH was maintained at a temperature of 110° for 34 hours: 5.565°, 5.615°; mean 5.590°.

p-Nitrotoluene.—A pure sample of this compound was dried thoroughly in vacuo prior to use in exchange experiments; m.p. 52°.

Experiment 19.—A reaction tube containing 5 g. p-nitrotoluene and 5 cc. deuteroalcohol was immersed in an oil bath at 110° for 48 hours: 7.290°, 7.260°; mean 7.275°.

Experiment 20.—A reaction mixture of p-nitrotoluene and deuteroalcohol 0.02 molar in NaOH was heated to 110° for 48 hours: 6.250°, 6.210°; mean 6.230°.

Quinaldine.—A quantity of this compound was purified prior to use by distillation in vacuo.

Experiment 21.—A reaction tube containing 5 cc. of quinaldine in solution in 5 cc. deuteroalcohol was heated to a temperature of 110° for a period of 80 hours: 4.795°, 4.845°; mean 4.820°.

1,3,5-Trinitrobenzene.—A pure sample of this compound was throughly dried in vacuo for use in the present investigation; m.p. 121-122°.

Experiment 22.—A reaction mixture of 5 g. 1,3,5-trinitrobenzene and 5 cc. deuteroalcohol was maintained at a temperature of 110° for 64 hours: 7.345°, 7.395°; mean 7.370°.

Experiment 23.—A reaction mixture of 1,3,5-trinitrobenzene and deuteroalcohol 0.02 molar in NaOH was heated to a temperature of 110° for a period of 68 hours: 5.075°, 5.015°; mean 5.045°.

7,8-Benzoquinaldine.-Several attempts to crystallize this compound from dilute

alcohol were unsuccessful. The compound was finally purified by distillation under very low pressure; m.p. 82°.

Experiment 24.—A reaction mixture of 5 g. 7,8-benzoquinaldine and 5 cc. deuteroalcohol was heated to a temperature of 110° for 104 hours: 6.150°, 6.090°; mean 6.120°.

Experiment 25.—A reaction mixture of 7,8-benzoquinaldine and deuteroalcohol 0.02 molar in NaOH was maintained at a temperature of 110° for 108 hours: 5.050°, 5.120°; mean 5.085°.

m-Nitrotoluene.—A quantity of this compound (Kahlbaum product) was purified by a series of vacuum distillations with subsequent drying over anhydrous Na<sub>2</sub>SO<sub>4</sub>.

Experiment 26.—A reaction tube containing 5 cc. *m*-nitrotoluene and 5 cc. deuteroalcohol was immersed in an oil bath at 110° for 66 hours: (a) 7.385°, (b) 7.045°, 7.025°; mean 7.035°.

Experiment 27.—A reaction mixture of m-nitrotoluene and deuteroalcohol 0.02 molar in NaOH was maintained at a temperature of 110° for 66 hours: 7.015°, 7.055°; mean 7.035°.

*Experiment 28.*—A control or blank run was made by mixing 5 cc. of *m*-nitrotoluene and 5 cc. deuteroalcohol and then removing the deuteroalcohol immediately by distillation *in vacuo*: 7.045°.

*Dimethylaniline*.—A quantity of this compound was purified by distillation from sodium, the distillate being allowed to stand over sodium overnight, then redistilled from sodium and a central fraction collected.

Experiment 29.—A reaction tube containing 5 cc. dimethylaniline in solution in 5 cc. deuteroalcohol was heated to 110° for a period of 96 hours:  $6.450^{\circ}$ ,  $6.325^{\circ}$ ; mean  $6.390^{\circ}$ .

Experiment 30.—A reaction mixture of 5 cc. dimethylaniline and 5 cc. deuteroalcohol 0.02 molar in NaOH was maintained at a temperature of  $110^{\circ}$  for 96 hours:  $6.595^{\circ}$ ,  $6.490^{\circ}$ ; mean  $6.545^{\circ}$ .

Experiment 31.—A reaction mixture identical with that of experiment 29 (neutral solution) was heated at 110° for 96 hours. A portion of the deuteroalcohol was distilled from the solution *in vacuo* into a receiver containing anhydrous phosphorus pentoxide. After a short period of standing a portion of this alcohol was removed by a further distillation *in vacuo*: 6.285°.

Experiment 32.—A reaction mixture of dimethylaniline and deuteroalcohol 0.01 molar in  $H_2SO_4$  was maintained at a temperature of 110° for 96 hours. The deuteroalcohol was recovered by the same technique employed in experiment 31: 4.385°.

*Experiment 33.*—Experiment 32 was duplicated with the exception that the reaction mixture stood 48 hours at room temperature after the treatment at 110° for 96 hours: 4.240°; mean of experiments 32 and 33, 4.315°.

### SUMMARY

1. The lability of hydrogen atoms in a number of organic substances has been studied with the aid of deuteroalcohol as the deuteron donor.

2. The theoretical implications of the lability of the hydrogen atoms in acid and alkaline solutions are discussed.

3. The experimental part should be consulted for the details of the analyses and the accuracy of the experimental results.

4. The work is being continued.