# On the Influence of Features of Intermolecular Interaction on the Regularities of Deuterium Exchange

1957

SovietRxiv

## Abstract

## Full Text

## PHYSICAL CHEMISTRY

**A. I. Shatenshtein and E. N. Zvyagintseva**

# On the Influence of Features of Intermolecular Interaction on the Regularities of Deuterium Exchange

*(Presented by Academician A. N. Terenin, May 24, 1957)*

The regularities of deuterium exchange depend on the features of the interaction of a substance with a solvent. Usually the isotopic exchange of hydrogen in hydrocarbons proceeds faster with protophilic and protogenic solvents than with amphoteric ones, and the faster, the stronger the protolith (acid or base) the hydrocarbon is ([1]). Turning to the consideration of hydrogen exchange in C—H bonds of nitrogen-containing organic substances, we find that exchange may also proceed differently. For example, the ortho-para hydrogen atoms of aromatic amines exchange with liquid DBr the faster, the weaker a base the amine is, since, upon energetic interaction of an amine with an acid, a deuteron is added to the free electron pair of the nitrogen atom, a positively charged ion with tetravalent nitrogen is formed, conjugation between the $p$-electrons of nitrogen and the $\pi$-electrons of the aromatic rings is disrupted, addition of deuterons to the carbon atoms of the rings is hindered, and consequently so is the exchange of the hydrogen atoms bound to them ([2]). In addition, formation of a positive charge may cause an effect of electrostatic repulsion of the deuteron in a solvent with a low dielectric constant, such as liquid DBr ($Dn_{-80} = 6$). As is shown below, the change in the valence state of the nitrogen atom in methylated heterocycles (quinaldine and $\alpha$-picoline) as a result of complex formation with alcohol can explain the higher rate of hydrogen exchange with this amphoteric solvent in comparison with protophilic liquid ammonia.

Until now there has been no direct comparison in the literature of the rate of deuterium exchange with alcohols and with liquid ammonia. In this work, in addition to the named nitrogen heterocycles, for comparison we carried out experiments with hydrocarbons (indene and fluorene) and with ketones (acetophenone and $\beta$-naphthyl methyl ketone). First of all it was shown that with both solvents the same hydrogen atoms are exchanged: in indene and fluorene the atoms of the $CH_2$- group, and in the remaining substances those of the $CH_3$-groups. Deuterium introduced into the substance by exchange with $C_2H_5OD$ was washed out upon subsequent treatment with liquid ammonia (back exchange). Incidentally it was established that in the indene molecule, with $ND_3$ and with a solution of $C_2H_5O^-$ in $C_2H_5OD$, 3 H atoms can exchange, while with a solution of DCl in $C_2H_5OD$ at 150° one H atom exchanges, but not among those that take part in reactions with bases. With a solution of DCl in $C_2H_5OD$ at 180°, a slow partial exchange of hydrogen takes place in the aromatic part of the fluorene molecule.

As is seen from Table 1, which gives the values of the rate constants ($\sec^{-1}$), hydrogen exchange in hydrocarbons and ketones occurs with liquid ammonia at a much lower temperature and considerably faster than with ethanol. For example, one H atom in fluorene exchanges with liquid ammonia in 1 hour at 25°, and with ethanol in 2000 hours at 180°. Using approximate values of the activation energy for exchange of H in acetophenone and fluorene (12 and 11 kcal), we find that the most po-

mobile H atoms in these substances exchange with liquid $ND_3$ by 4 and 6 orders of magnitude faster than with $C_2H_5OD$. Conversely, the hydrogen of the methyl groups of nitrogen heterocycles exchanges with ammonia more than an order of magnitude more slowly than with ethanol. Experiments were carried out with three preparations of quinaldine (I, II, III) and with two preparations of $\alpha$-picoline at 120°. Quinaldine with ammonia $(k \cdot 10^7 \sec^{-1})$ I: 1.0; 0.7; II: 1.0; 0.8. Picoline with ethanol $(k \cdot 10^8 \sec^{-1})$: 3; 2. For example, at a D concentration in the solvent of 25 mole %, after 230 h in the combustion water of quinaldine the D concentration was 3.5 (in the experiment with $C_2H_5OD$) and 0.6 at.% (in the experiment with $ND_3$); while in the experiment with the alcoholic solution of picoline it was 0.2 at.%, whereas with $ND_3$ no exchange of H in picoline occurred during this time.

Experiments on reverse exchange were performed with previously deuterated quinaldine. Measurements of physical constants proved that all substances remained unchanged during the experiments. Before isotopic analysis they were purified. Careful control confirmed that during isolation and purification of the substances after the experiments (for example, by precipitation as picrates and their decomposition, etc.) the isotopic composition does not change.*

Table 1

| Substance | $C_2H_5OD$ | $ND_3$ | $C_2H_5O^- +$ $C_2H_5OD$ |
|---|---|---|---|
| Indene | $10^{-6}$–$10^{-7}$ (150°) | $1 \cdot 10^{-4}$ (−10°) | 0.05 $N$ $3 \cdot 10^{-5}$ (0°) |
| Indene | – | $4 \cdot 10^{-4}$ (0°) | 1 $N$ $7 \cdot 10^{-4}$ (0°) |
| Indene | – | $9 \cdot 10^{-4}$ (10°) | – |
| Fluorene | $1 \cdot 10^{-7}$ (180°) | $2 \cdot 10^{-4}$ (25°) | 1 $N$ $6 \cdot 10^{-4}$ (25°) |
| Acetophenone | $2 \cdot 10^{-7}$ (120°) | $1.1 \cdot 10^{-5}$ (0°) | 1 $N$ $4 \cdot 10^{-5}$ (0°) |
| Acetophenone | – | $6.5 \cdot 10^{-5}$ (25°) | – |
| Acetophenone | – | $1.3 \cdot 10^{-4}$ (40°) | – |
| $\beta$-Naphthyl methyl ketone | $10^{-6}$–$10^{-7}$ (120°) | $1.5 \cdot 10^{-5}$ (0°) | – |
| Quinaldine | $2 \cdot 10^{-6}$ (120°) | $8 \cdot 10^{-8}$ (120°) | 0.1 $N$ $1 \cdot 10^{-4}$ (120°) |

| Substance | $C_2H_5OD$ | $ND_3$ | $C_2H_5O^- +$ $C_2H_5OD$ |
|---|---|---|---|
| Picoline | $3 \cdot 10^{-8}$ (120°) | – | $0.1\,N$ $1 \cdot 10^{-6}$ (120°) |
| Picoline | – | – | $1\,N$ $3 \cdot 10^{-5}$ (120°) |

**Note.** The exchange-rate constants of the first four substances with alcohol are approximate in character. Experiments with indene in alcohol are characterized by poor reproducibility, possibly because of partial polymerization of indene. Three preparations of indene gave identical values of the rate constants for exchange with liquid ammonia. The rate constants for exchange with $ND_3$ of indene, fluorene, and acetophenone were determined with greater accuracy than in work (3).

To understand the reason for the different behavior of the various groups of substances in H-exchange reactions, one must examine their acid-base properties. The substances listed below, when dissolved in liquid ammonia, behave as very weak acids, which are converted into carbanions upon addition of a base. Judging from the rate constants for hydrogen exchange in them with liquid $ND_3$ (at 120° or recalculated to this temperature), the relative strength of the acids decreases in the sequence: indene $(4 \cdot 10^{1}) >$ fluorene $(2 \cdot 10^{-2}) >$ acetophenone $(4 \cdot 10^{-3}) >$ triphenylmethane $(2 \cdot 10^{-7}) >$ quinaldine $(7 \cdot 10^{-7}) >$ diphenylmethane $(7 \cdot 10^{-9}) > \alpha$-picoline $(< 10^{-8})$.**

In alcoholic solution, indene and fluorene are extremely weak acids, and acetophenone is a very weak base, whereas the dissociation constants of quinaldine and picoline are of the order of $10^{-9}$. Measurements of infrared spectra ($^{6,7}$) show that a hydrogen bond arises between the hydrogen of the OH group of the alcohol and the nitrogen atom of the heterocycle, owing to which the valence state of the N atom changes to a certain extent; it acquires the character of $N^+$, which, in turn, favors protonation of the H atoms of the

---

* In passing, the observation was made that if solid caustic potash is present in an ammoniacal solution of quinaldine, then rapid isotopic exchange of hydrogen in the methyl group occurs in connection with formation of the potassium salt of quinaldine. Consequently, KOH in $NH_3$ metalates organic compounds (cf. 4). Absorption-spectra measurements of ammoniacal solutions, carried out by I. V. Astaf' ev, showed that by this method carbanions of indene, fluorene, tri- and diphenylmethane, and anions of aromatic amines can be obtained. The advantage of KOH compared with $KNH_2$ (2) is that measurements of the absorption spectra of ammoniacal solutions of carbanions in the ultraviolet region become possible.

** Constants are expressed in $\sec^{-1}$. Data for fluorene were obtained by Yu. P. Vyrskii and E. A. Yakovleva; for tri- and diphenylmethane, by E. A. Yakovleva.

schematic structural formulas of quinaldine complexes with ethoxide, quinaldine, DCl, and ethanol

Figure 1: schematic structural formulas of quinaldine complexes with ethoxide, quinaldine, DCl, and ethanol

$CH_3$ group. It is known that the mobility of the hydrogen of the $CH_3$ group sharply increases upon formation of the haloalkylates of quinaldine and picoline, in connection with ionization of the nitrogen ($^8$). Thus, because quinaldine and picoline interact with alcohol as bases, molecular compounds are formed whose acidity is considerably higher than the acidity of the initial substances.

Judging from the measurements of Hine and Hine ($^9$), the acidity of alcohols increases in the sequence: iso-propanol (I) $<$ ethanol (II) methanol (III) $<$ ethylene glycol (IV)*. Our experiments, carried out with thoroughly dehydrated alcohols, showed that in the same direction the rate constants for exchange with them of hydrogen in quinaldine increase (120°). I. **Iso-propanol** ($k \cdot 10^7$): 9; 9; 10; 5 (direct exchange), 11; 7; 4; 9 (reverse exchange). II. **Ethanol** ($k = 2 \cdot 10^{-6}$) (see Table 1). III. **Methanol** ($k \cdot 10^6$): 3.0; 3.0 (direct exchange), 2.6; 2.9; 2.3 (reverse exchange). IV. **Ethylene glycol** ($k \cdot 10^6$): 9.2; 9.2; 9.1; 9.1 (reverse exchange). For example, in experiments with the named alcohols ($120^\circ, 105$ hr) the deuterium concentration in the water from combustion of quinaldine was: I 4.9; II 2.2; III 2.0; IV 0.2 atom % (before the experiment, 6.3 atom % D).

Taking the above into account, it may be supposed that the rate of the exchange reaction increases with increasing polarity and concentration of the complex with the heterocycle. Indeed, addition of hydrogen chloride to an ethanolic solution of quinaldine in an amount of 0.2 mole per mole of base increases the rate of the exchange reaction by two orders of magnitude ($k_{120^\circ} = 5 \cdot 10^{-5}$ sec$^{-1}$). At a ratio of 0.5 mole/mole, $k_{120^\circ} = 7 \cdot 10^{-5}$ sec$^{-1}$, but at equimolecular ratios of acid and quinaldine $k_{120^\circ} = 4 \cdot 10^{-6}$ sec$^{-1}$ (cf. ($^{10}$)). (Control experiments established that only with an excess of DCl over the stoichiometric amount does it react with the alcohol with formation of $C_2H_5Cl$.) One should also expect more rapid deuterium exchange with quinaldine haloalkylates than with the latter.

In order for the exchange reaction to occur, the proton of the $CH_3$ group must pass to some base. As long as an excess of acid-unneutralized nitrogenous heterocycle is present in the solution, molecules of the latter (some of which may be unprotonated) perform the function of proton acceptor. Upon complete neutralization of the base by acid, the rate of the exchange reaction decreases, since solvent molecules—bases weaker than quinaldine—become the proton acceptor. Conversely, if an alcoholate—a base stronger than quinaldine—is added to a solution of quinaldine in alcohol, the reaction rate rises sharply (calculated for a $1\,N$ alcoholate solution, $k_{120^\circ} \simeq 10^{-3}$). Thus, in neutral, acidic, and alkaline solutions, complexes of different composition participate in the reaction**:

Apparently, the complex of quinaldine with alcohol is not destroyed in the presence of alcoholate. The rate of hydrogen exchange in quinaldine with a 1 *N* solution of alco-

in ethanol is at least four orders of magnitude higher than the rate of exchange with liquid ammonia, whereas in indene, fluorene, and acetophenone the corresponding rates differ only by a factor of several (see Table 1).

The presence of potassium amide in the ammonia solution (0.2 mole per mole of quinaldine) already at $-31^\circ$ causes exchange at a rate of $2 \cdot 10^{-5}$ $\sec^{-1}$, i.e., three orders of magnitude faster than at 120° in the absence of a catalyst. It should be noted that potassium amide is neutralized by quinaldine, which is converted into the potassium salt; therefore the concentration of $NH_2^-$ ions is very small.

There is a certain analogy between acid catalysis of deuterium exchange in an alcoholic solution of quinaldine and alkaline catalysis of hydrogen exchange in the aromatic ring of phenol with heavy water ([11]). In Ingold' s work, as in ours, owing to the acid-base interaction with the externally added protolyte, the reactivity of the substance in which the exchange reaction takes place is increased. The excess of unreacted substance participates in the exchange reaction, performing a protolytic function opposite to that of the catalyst.

It should also be noted that there is an analogy between the phenomena described in this article—the unequal relative rate of hydrogen exchange in hydrocarbons, ketones, and methylated heterocycles with alcohol under catalysis by $C_2H_5O^-$ and with liquid ammonia—and the change known from the literature in the ratio of ionization constants of acids of different classes on passing from one solvent to another, which has been explained by the formation of products of differing structure from the interaction of acids with solvents ([12]).

The totality of the facts presented in the article confirms that the regularities of deuterium exchange depend strongly on the specific features of intermolecular interaction in solutions.

Physical-Chemical Institute
named after L. Ya. Karpov

Received
14 V 1957

---

* In the same sequence the dielectric constants increase: 15.7; 25.7; 33.0; 37.7. The dipole moment of ethylene glycol is 2.28 D, and of the other alcohols it is approximately 1.77-1.8 D.

** In the transition reaction complexes, naturally, the solvent, which is the deuterium donor, participates.

## CITED LITERATURE

[1] A. I. Shatenshtein, *Ukr. Khim. Zhurn.*, **22**, 3 (1956).
[2] A. I. Shatenshtein, A. V. Vedeneev, Reports at the All-Union Scientific-Technical Conference on the Application of Radioactive and Stable Isotopes and Radiation in the National Economy and Science, 1957.
[3] A. I. Shatenshtein, Yu. P. Vyrskii, DAN, **70**, 1029 (1950).
[4] A. A. Morton, C. E. Klaff, H. P. Kagen, *J. Am. Chem. Soc.*, **76**, 4556 (1954).
[5] E. A. Izrailevich, D. N. Shigorin, I. V. Astaf' ev, A. I. Shatenshtein, DAN, **111**, 617 (1956).
[6] W. Gordy, S. C. Stanford, *J. Chem. Phys.*, **9**, 204 (1941).
[7] M. Tamres, S. Searles, E. M. Leighly, D. W. Mohrman, *J. Am. Chem. Soc.*, **76**, 3983 (1956).
[8] R. Elderfield, *Heterocyclic Compounds*, **4**, IL, 1955.
[9] J. Hine, M. Hine, *J. Am. Chem. Soc.*, **74**, 5266 (1952).
[10] M. S. Kharash, W. G. Brown, *J. Org. Chem.*, **2**, 36 (1937); **4**, 442 (1939).
[11] C. K. Ingold, C. G. Raisin, C. L. Wilson, *J. Chem. Soc.*, 1936, 915.
[12] N. A. Izmailov, ZhFKh, **30**, 2164 (1956).

*Note: Figure translations are in progress. See original paper for figures.*

*Source: Math-Net.Ru and CyberLeninka. Machine translation. Verify with the original.*