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Spectroscopic study of hydrogen exchange processes and structure of intermediate complexes with intermolecular hydrogen bonds

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Abstract

The kinetics of hydrogen exchange in molecular systems with H-bonds has been studied by means of kinetic IR spectroscopy and low-temperature NMR spectroscopy. The experimental values of the rate constants and activation energies for molecules capable of forming H-bonds as both proton donors and proton acceptor are collected and analyzed from the point of view of the influence of H-bond formation ability of the molecules-partners. The evidence available testifies to a molecular mechanism of the H-exchange reactions in inert solvents and in the gas phase via the formation of cyclic bimolecular intermediates. The different mechanisms and the structure of intermediate complex of molecular H-exchange process in inert media are discussed and the possible paths of experimental elucidation of reaction mechanism are offered.

Keywords: Structure of H-bonded complexes; Hydrogen isotopic exchange; IR spectra; NMR spectra

1. Introduction

The traditional approach to the investigation of hydrogen bonding (H-bonding) is the study of static characteristics of complexes, such as the geometry, spectral changes under the H-bonded complex formation, electrooptical and thermodynamic parameters. In treating some static characteristics of complexes, the question of dynamic properties of H-bonding already arises, the possible influence of fast exchange processes upon the shape of bands in optical and NMR spectra being of interest. The study of the dynamics of systems with H-bonding is interesting in itself, since H-bonds play a decisive role in kinetics of a number of processes, in particular, the processes of proton transfer and proton exchange. In the simplest case, the elementary step of hydrogen exchange (H-exchange) $RAH + R'BH^* \Leftrightarrow RAH^* + R'BH$ is cooperative proton transfer in a cyclic complex with two H-bonds [1]. Because of high rate of the reactions at room temperature, most of the problems referring to the kinetics of H-bonded systems depend, to a large extent, on the development of special techniques for the study of fast reactions.

Although, the interest in H-exchange dynamics has increased considerably in recent four decades, yet it is still not clear how to approach these problems. Besides, most results have been obtained by studying concentrated solutions and pure liquids [2,3], in cases when the interaction with the surrounding medium, which influences the mechanism of the process qualitatively, not only cannot be excluded but becomes decisive. This fact makes investigation of the dynamics of H-bonded systems expedient under conditions of minimum interaction with the surroundings, i.e. in the gas phase, or at a low concentration in inert solvents whose energy of interaction with the molecules under investigation is apparently lower than the energy of interaction between the partner molecules. The kinetic study of the H-exchange in solvents, whose molecules do not stimulate electrolytic dissociation, allows one to neglect consideration of acid–base catalysis and is of great interest for finding the mechanism of the initial interaction between the molecules concerned. Therefore, it would be desirable to carry out experiments under conditions where it is possible to separate the influence of the surrounding medium from that of the partner molecules, on the dynamics of H-bonding.

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2. Experimental

During recent decades, the kinetic IR spectroscopy and dynamic NMR spectroscopy are the most informative and wide-used experimental methods for the study of H-exchange kinetics. It is clear that using the first method, we have to study the isotopic effects and their influence on the kinetics of reaction. Studying H-exchange by NMR technique it is necessary to use the special methods for calculations of line shapes for different molecular systems and different rates of exchange (see, for example, Ref. [4]) and to compare the theoretical contour with experimental data, providing the best agreement. The line shape analysis of the NMR spectra also gives an opportunity to study the influence of the temperature and solvent polarity on the rate of H-exchange [5].

As for the kinetic IR spectroscopy, the H-exchange process is followed by measuring the time dependence of the intensity at absorption maxima of AH(AD) or/and BH(BD) stretching vibration bands, which is proportional to the component concentration. These changes correspond to the redistribution of isotopes between the functional groups of molecules-partners till the equilibrium isotope distribution. Combined with stopped-flow method [6] developed by us for the IR spectral region, it permits study of H-exchange in solutions with a half-exchange period as little as a few milliseconds. For every system, the values of specific rate of reaction (non-dependent on time) R can be determined under different relative reactants' concentrations, and the rate constants k and the orders of reaction α and β with respect to every component were obtained. The Arrhenius activation energies E_a have been determined from the $\ln k$ vs. $1/T$ dependence

$$[\mathrm{AH}]_t = [\mathrm{AH}]_\infty + ([\mathrm{AH}]_0 - [\mathrm{AH}]_\infty)\exp(-rt), \tag{1}$$

$$R = r[\mathrm{A}][\mathrm{B}]/([\mathrm{A}] + [\mathrm{B}]),$$
$$\text{where } [\mathrm{A}] = [\mathrm{AH}] + [\mathrm{AD}],\ [\mathrm{B}] = [\mathrm{BH}] + [\mathrm{BD}], \tag{2}$$

$$R = k[\mathrm{A}]^\alpha[\mathrm{B}]^\beta, \tag{3}$$

$$k = k_0 \exp(-E_a/R_0T). \tag{4}$$

3. Results and discussion

Nowadays, the information available on the kinetics of H-exchange processes embraces practically all classes of molecules capable of forming H-bonds: the carboxylic acids, alcohols, phenols, water, amines, amides and other nitrogen-containing compounds, thiols, and so on. In our review [1], we collected the values of experimentally obtained kinetic characteristics of the H-exchange processes for the main classes of molecules capable to form H-bonds. In spite of the broad variety of physical and chemical properties of the molecules studied, and the wide range of characteristic times of H-exchange (from some milliseconds to several hours), one may conclude from the available experimental data that the ability of a molecule to form a hydrogen bond determines the kinetic characteristics of the exchange process with its participation. In comparing different classes of compounds, it will be obvious that the exchange of the proton of thiohydrilic group of thiols with all the partners studied (Table 1) is accomplished much more slowly than exchange of the proton of hydroxylic group of similar alcohols. The ability of the SH group to form H-bonds as a proton donor and a proton acceptor is considerably lower than that of the OH group. Since the acidity of thiols is greater than that of alcohols, one may conclude that, in this case, H-exchange rate is determined by the ability of the molecule to form H-bonds rather than by its acidic properties.

Table 1
Rate constants k (l/mol s) for some molecular systems in CCl_4 at 293 K

Partners	CH_3OH	C_4H_9SH
CH_3COOH	4800	2.5
C_6H_5OH	240	0.1
$(C_6H_5)_2NH$	150	0.011
$CH_3CONHCH_3$	0.026	0.0033

Experimental data showed that the maximum values of the rate constants of the H-exchange with alcohols or thiols (Table 1) were found for carboxylic acids. The reaction becomes slower for phenol, still slower when water of alcohols are used, and is further retarded for secondary amines, amides, and thiols. As a rule, the sequence of decreasing proton donor ability in a series of compounds is the same. In a series of RAH molecules, the proton donor and proton acceptor abilities are changed in different directions by variation of the substituent R. Therefore, if the H-exchange takes place in cyclic complexes formed by the BH molecule with a number of partners RAH, an increase in the strength of one H-bond will have to be accompanied by a decrease in the strength of the other. That is why there are deviations from the dependence described above. For example, the k value for H-exchange in the trifluoroethanol—butanethiol system is equal to k for the reaction between methanol and butanethiol, although the proton donor ability of fluorinated alcohol is considerably greater than that of CH_3OH, since it contains strong electronegative substituents. A decrease in k was observed on the transfer from alkylanilines to diphenylamine, a still stronger proton donor. Even for carboxylic acids, we have observed a retardation of the increase of k values [7] with the rise of acidity. These facts may be considered as an indication of the influence of decrease in proton acceptor ability of the A atom in the AH group, and of the cyclic structure of H-exchange intermediates.

That is why it has been of great interest to study the situation when the molecule studied as a partner in

Table 2
Influence of the *intra*molecular H-bonding on the kinetic parameters of H-exchange

No.	Second partner	k (l/mol s)	E_a (kJ/mol)	ΔH^{intra} (kJ/mol)
(a) Methanol +				
1.	Ethyl-5-nitrosalicylate	5.1	42.0	
2.	Ethyl-3-nitrosalicylate	4.6	36.4	
3.	Salicylic aldehyde	20.0	35.6	33.5
4.	2-Nitrophenol	120.0	27	26
5.	2-Methoxyphenol	40.0	19	17.2
(b) 2-Nitrophenol +				
1.	CD_3COOH	16	22	
2.	$(CH_3)_3COH$	70	27	26
3.	$(C_6H_5)_2NH$	2.4	29	

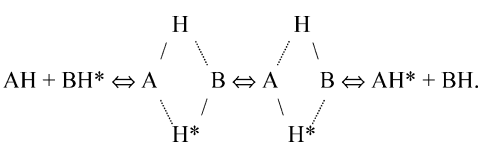
H-exchange reaction can lose its proton donor or proton acceptor ability in intermolecular interaction. The first situation can be realized by the study of the H-exchange kinetics with the participation of molecules with intramolecular H-bond where the proton of AH group is already included into a H-bond with a proton-acceptor center of the same molecule. In the H-exchange of phenol derivatives with methanol, the reaction was retarded as proton donor ability of the molecule increases. The results obtained testify to the fact (Table 2) that formation of an intramolecular H-bond by the AH group proton is accompanied by a considerable decrease in the rate of H-exchange. It would be added that the values of activation energy are close to the estimates of the intramolecular H-bond energies for the molecule under investigation. The dependence of H-exchange rate on the formation of intramolecular H-bonds by the proton donor functional AH groups can be used effectively in biochemical studies of biopolymers' structure. It has been recently showed that short strong H-bonds play an important role in the fermentative catalysis (such as in acidic and basic catalysis), and the considerable deceleration (some orders of value) of the H-exchange rate of the bridge proton with solvent in the ferment-substrate complex has been recognized as one of the criteria of such bonding [8,9].

The data above are consistent with the supposition that the process involves cooperative (or, in some papers, concerted) proton transfer in the cyclic intermediate. For such a complex to form, the A atom and the B atom must have lone pairs of electrons. We have studied the H-exchange process involving the (3-aminopropyl)dibutylborane molecule by means of kinetic IR spectroscopy [10]. This molecule possesses proton donor ability comparable with that of aliphatic alcohols, but, on account of a lone pair of the N atom involved in coordination to the boron atom, it loses its proton acceptor function completely. So (see above), we have the second situation of interest. While the k values for alcohol–alcohol and alcohol–amine systems in CCl_4 are of the order of 100–400 l/mol s, the rate constants for the H-exchange between aminoborane and methanol, or secondary amines, in the same solvent are 3–4 orders of magnitude lower. Such a result points to a cyclic rather than the linear structure for the intermediate.

The experimental data obtained confirm the conclusion that the rate of the molecular H-exchange processes of the type considered is determined by the same peculiarities of electronic structure, which control the hydrogen bonding ability of the functional groups of the molecules and the reaction takes place via cyclic intermediate complex formed by H-bonds between the functional groups of the molecules-partners. Experimental measurements of the order of reaction with respect to each component (see expression (3)) show that, in all cases of H-exchange in solution, the reaction order is close to unity. Hence, the process can be seen as bimolecular, i.e. the first step of the process takes place in the cyclic complex formed by two H-bonded molecules.

Speaking of intermediate cyclic structures, it should be clearly understood that the cyclic model of the binary complex, formed by two non-linear H-bonds between bifunctional groups AH and BH, is less expedient than the linear structures, in terms of energy and entropy. For the molecules with two different functional groups (carboxylic acids, pyrazoles, amidines, triazenes), the formation of cyclic complexes with linear H-bonds is real and has been realized for some molecular systems studied [5,7,11,12]. Although, so far there is no direct experimental evidence to support the existence of four-membered cyclic H-bonded dimers, still the results of quantum chemical calculations (see, for example, Ref. [13]) show that such a complex does possess energy, considerably exceeding the thermal energy, and is stable under the variations of geometrical parameters. Recently, some interesting quantum chemical calculations of the kinetic characteristics for the concerted mechanism of proton migration along the H-bonds in cyclic dimers and oligomers were published. The kinetic parameters of H-exchange calculated for the cyclic complex with two H-bonds formed by the acetic acid and methanol molecules [14] are in good agreement with the values obtained in experimental studies.

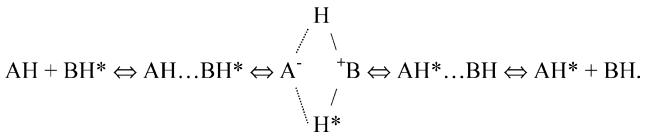
As to the possible mechanism of molecular H-exchange process, the first assumption of synchronous transfer of two protons (or proton and deuteron) in the cyclic complex was made 50 years ago [15]. The mechanism of such cooperative (or concerted) process may be represented by the scheme (5):



(5)

In solutions, other reaction mechanisms via binary complexes are possible [2]. An alternative mechanism is a sequential transfer of two protons in a linear complex, where the intermediate has to be the form of a cyclic ionic pair with

two equal H-bonds:



$$AH + BH^* \Leftrightarrow AH\ldots BH^* \Leftrightarrow A^- \quad {}^+B \Leftrightarrow AH^*\ldots BH \Leftrightarrow AH^* + BH. \tag{6}$$

Such a process would not involve the stage of breaking of the ionic pair (the electrolytic dissociation) and, therefore, could go in an inert medium.

A study of the influence of the polar properties of medium (the dielectric permeability of a solvent, for example) on the rate of H-exchange process may be a help in choosing between mechanisms (5) and (6). Our results indicated that [16] as $\varepsilon_{solv.}$ increases, the rate of H-exchange (determined by the dynamic NMR spectroscopy) in water or in alcohol–alcohol system decreases, while, for alcohol–acetic acid system, the rate of reaction rises considerably. We explained this dependence by the cooperative synchronous mechanism (5) in the former case, and by the ion-pair mechanism (6) in the latter. On formation of the transition state of mechanism (6), a great increase of the dipole moment, as compared to the initial state, must follow. Therefore, when $\varepsilon_{solv.}$ increases, the rate of exchange must be also increased. However, on formation of the transitional state of the cooperative mechanism (5), which resembles in structure the symmetrical cyclic complex, the dipole moment decreases, and this would result in the opposite effect. This very dependence has been observed experimentally. It is possible to use another way for the change of dielectric properties of the medium. The influence of strong external electric field (up to 10^7 V/m) on the rate constants of H-exchange of methanol with acetic acid, phenol and dinitro-*p*-cresol in CCl_4 by means of kinetic IR spectroscopy and stopped-flow method allowed to determine different mechanisms of the process for these molecular systems: (6) for the first system and (5) for two other ones.

The other path for the choice between the above-mentioned H-exchange mechanisms is the comparison of the kinetic characteristics of a molecular system in solution and in the gaseous phase. The results of the study of proton exchange in gaseous dimethylamine and methanol-dimethylamine system and in the solutions showed (Table 3) the decrease of the k values and the increase of the activation energies E_a for the both systems under the transition from gas to solution in deuterocyclohexane. This retardation of the reaction has been explained [1] by the stronger solvation of molecules studied in solution in comparison with the cyclic symmetric transition complex having smaller dipole moment.

At last, the study of the kinetic isotope effects (KIE) for proton exchange kinetics may be useful for this choice [17,18]. The investigation of KIE is of great importance for the determination of isotope distribution coefficients for hydrogen and deuterium. The measurement of fractionation factors using a variety of methods is an established tool of isotopic research. Especially, strong deviations from normal statistic distribution are observed for the systems with H-bonds: hydrogen has a tendency to be concentrated at the positions with the strongest H-bonds. The systematic study of the H/D exchange between the active groups of biopolymers and solvent molecules (water or water-organic mixtures) permitted to determine the main regularities which connect the values of the fractionation factor and the strength of the H-bridge formed by proton donor group [19,20]. This is an indirect criterion for the estimation of H-bond energy in the complex biological systems.

Table 3
Kinetic characteristics of H-exchange in dimethylamine and in dimethylamine-methanol system for gaseous phase and solutions in C_6H_{12}

	NH–NH		NH–OH	
	Gas	Solution	Gas	Solution
α_{NH}	1.9 ± 0.1	2.0 ± 0.1	1.0 ± 0.3	1.0 ± 0.1
β_{OH}	–	–	1.1 ± 0.2	1.1 ± 0.1
$k^{303\,K}$ (l mol^{-1} s^{-1})	87 ± 7	47 ± 6	260 ± 30	140 ± 20
E_a (kJ mol^{-1})	5.9 ± 2.5	8.4 ± 1.7	4.2 ± 1.2	7.5 ± 1.7

Fractionation factors theory constitutes the classical theory of kinetic H/D isotope effects of proton migration reactions. For example, the isotopic fractionation factors K between the acid–base complexes $AHB + Ph_3COD\cdots B \leftrightarrow ADB + Ph_3COH\cdots B$, where AH represents a variety of acids and B represents pyridine-^{15}N, were measured by NMR around 110 K, using the mixture of liquefied $CDClF_2$–CDF_3 (2:1) as solvent [21]. The low-temperature NMR technique may permit to determine K directly by integration of appropriate proton NMR signals as the slow H-bond exchange regime can be reached. Measuring the experimental fractionation factors as a function of the ^{1}H chemical shifts, the authors found that K is an almost linear function of $\delta(^1H)$ and showed that the chemical shift values can give interesting information about zero-point energy changes along the reaction pathways of proton transfer.

4. Conclusion

Summing up, one can say that there is little doubt that the ability of exchanging molecules to form H-bonds influences the kinetic characteristics of the H-exchange process. The evidence available testifies to a molecular mechanism via formation of cyclic intermediates (mostly, bimolecular ones) in an inert medium. The cooperative mechanism of proton transfer (5) is the simplest model of the reaction. Its realization in a pure form is most probable in systems with symmetrical intermediates. If the H-bond forming abilities of component molecules differ greatly, then the step-like mechanism (6) via formation of the H-bonded ion pair may

be correct. A better insight into the structure of intermediate complex of H-exchange molecular processes may be obtained by a further spectroscopic study of the cyclic complexes, determination of their lifetimes, investigation of the dynamics of successive steps of the process by various physical and chemical methods and techniques, and by high-level theoretical calculations of the potential surfaces of the interaction.

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