Translated from *Uspekhi Khimii*, 48, 1600-1624 (1979) U.D.C. 541.121;541.127;541.571

Hydrogen Bonds and the Reactivity of Organic Compounds in Proton Transfer and Nucleophilic Substitution Reactions

L.M.Epshtein

Recent data on various relations between the characteristics (spectroscopic and thermodynamic) of hydrogen bonds in different classes of organic compounds and the acid-base properties of the latter are examined. The principal approaches to the study of the influence of hydrogen bonds on acid-base equilibria in various solvents are demonstrated. Fundamentally new results, obtained in combined studies of proton transfer reactions in the gas phase and in solution, are analysed and approaches to allowance for the influence of hydrogen bonds on the reactants and the transition state in nucleophilic substitution reactions as well as the role of hydrogen bonds in the alteration of the rates and modes of chemical reactions are discussed.
The bibliography includes 152 references.

CONTENTS

I. Introduction 854
II. Hydrogen bonds and acid-base properties of organic compounds 854
III. The role of hydrogen bonds in proton transfer reactions 857
IV. Hydrogen bonds in nucleophilic substitution reactions 864

I. INTRODUCTION

Increasing attention has been devoted in recent years to problems of the dependence of the reactivity of organic compounds on the medium. Among various types of interactions contributing to the solvation energy, weak specific interactions—hydrogen bonding between the solvent and the reactants—are frequently the most important.

"During the last five years there has been a revolution in the understanding of the thermodynamics of the solvation of organic ions" [1] as a result of studies on proton transfer reactions in the gas phase in combination with quantum-chemical calculations on such reactions, whose development has been strikingly rapid. The importance of this revolution is enormous, since it leads to a change in many important postulates of theoretical organic chemistry. A comparative analysis of data on acid–base equilibria in the gas phase and in solution established that solvation factors play a much more important role than had been realised previously. For many classes of organic compounds, the influence of these factors proved to exceed in magnitude the electronic effects of substituents. The nature of the influence of substituents is in many instances different from that assumed in the study of reactions in solution. In the course of investigations the role of hydrogen bonds, which in the view of many workers determine the solvation effects, was rediscovered in a new light. In the immediate future one may expect that even more valuable information will become available and that such approaches will be extended to other types of reactions, since the growing number of studies on gas-phase reactions has an avalanche-like character.

The aim of the present review is analysis of the methodology of studies designed to discover the influence of hydrogen bonds on the equilibrium position in proton transfer reactions and on the rates, mechanisms, and modes of nucleophilic substitution reactions. From the large number of studies in which hydrogen bonds are mentioned, we therefore selected only those which provide approaches to the assessment of their role in these reactions. Acid–base equilibria are analysed in greatest detail.

II. HYDROGEN BONDS AND ACID–BASE PROPERTIES OF ORGANIC COMPOUNDS

Despite many warning signals, such concepts as acidity (basicity) and proton-donating (proton-accepting) capacity in the formation of hydrogen bonds are still treated as synonymous in the literature. The roots of this kind of confusion can be understood by comparing the following equilibria:

$$AH + B \rightleftarrows AH \ldots B \quad \text{(formation of hydrogen bonds);} \qquad (1)$$

$$AH + B \rightleftarrows A^- + HB^+ \quad \text{(acid-base equilibrium).} \qquad (2)$$

The formation of hydrogen bonds is necessary for proton transfer; it can be either an intermediate stage or it can occur in a transition state, which is assumed to consist of a hydrogen-bonded complex.

There have already been many studies (see Section III) in which possible pathways of reaction (2) have been demonstrated in relation to many examples. The overall mechanism of the interaction can be represented as follows:

$$\underset{I}{AH + B} \rightleftarrows \underset{II}{AH \ldots B} \rightleftarrows \underset{III}{A^- \ldots HB^+} \rightleftarrows \underset{IV}{A^- \ldots (S) \ldots HB^+} \rightleftarrows \underset{V}{A^- + HB^+}. \qquad (2a)$$

Here stage II involves the formation of a molecular hydrogen-bonded complex, stage III the formation of an ionic hydrogen-bonded complex or an ion pair†, stage IV the formation of a solvate-separated ion pair (S is the solvent), and stage V the dissociation into ions. Fig. 1*a* illustrated schematically the potential surface of the AH + B system, which has two minima[3]. Fig. 1*b* illustrates the dependence of the potential energy on the reaction coordinate. Curves *1* and *2* correspond to cases where either a molecular complex (the equilibrium I⇌II), for example,

† One should note that the term "ion pair" is a consequence of traditional usage in the literature, since complexes of a conjugate acid with an anion differ from the ion pairs formed on ion association via electrostatic forces. According to Odinokov et al.[2], such "ion pairs" resemble molecular hydrogen-bonded complexes as regards their infrared spectroscopic properties.

in a phenol–amine system, or only an ion pair (I–III), for example, in a pentachlorophenol–amine system, is formed. Curve *3* represents the situation in which both molecular and ionic complexes are in equilibrium (I⇌II⇌III), for example, in a 2,6-dichlorophenol–amine system.

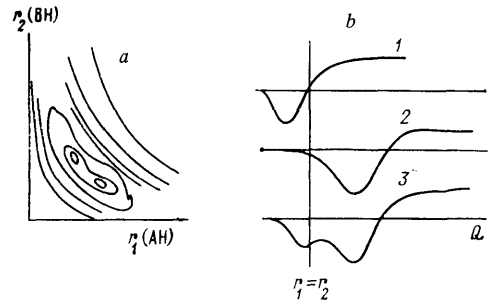


Figure 1. The potential surface of the AH + B system [3].

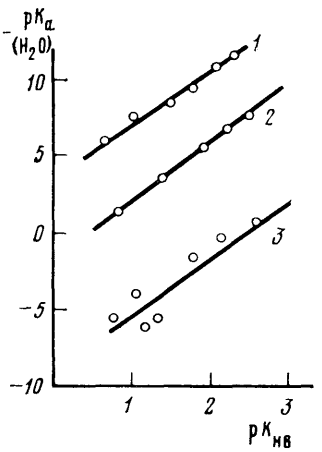


Figure 2. Relation between the free energies of protonation (pK_a) and hydrogen bond formation (pK_{HB}) reactions[10]: 1) amines; 2) pyridines; 3) carbonyl compounds.

By altering the proton-donating properties of AH, the proton-accepting properties of B, and the solvating capacity of the solvent, it is possible to drive reaction (2a) via one or other pathway. The fact that reaction (2) includes reaction (1) in some form gives rise to the idea that there is a general relation between their energetic characteristics. A relation between the linear dependence of the shifts of the stretching vibration frequencies of the AH bond [$\Delta\nu$(OH)] on formation of the hydrogen bond and the pK_a was given in an early investigation[4]. Many linear relations between frequency shifts or the hydrogen bond formation energies and the pK_a have been published in original papers[5,6] and in monographs (for example, in Ferjenson's monograph[7]). The frequency shifts $\Delta\nu$(OH) are adopted as a measure of the basicity of all solvents[8].

Convincing evidence for the absence of a single relation can be found, for example, in studies[9,10] where a thorough analysis of the relations between the free energies of reactions (1) and (2) was carried out. By analogy with pK_a, the concept of $pK_{HB} = -\lg K_{HB}$, where K_{HB} is the equilibrium constant for the formation of a hydrogen bond via reaction (1), was introduced. For all classes of compounds (aliphatic amines, pyridines, and carbonyl compounds), for which sufficient experimental data were available, three significantly linear relations, displaced along the ordinate axis (Fig. 2), were obtained. For the same capacity for the formation of hydrogen bonds (i.e. for the same pK_{HB} values), the basicity of aliphatic amines is greater by five orders of magnitude than that of substituted pyridines and by thirteen orders of magnitude that that of carbonyl compounds.

The most thorough comparative study of the hydrogen bond formation reaction (1) and the proton transfer reaction (2) was carried out by Arnett et al.[11], who analysed the ratios of the enthalpies of these reactions. The comparative analysis was based on the calorimetric method for the determination of the enthalpies of protonation (ΔH_i) in a superacid (fluorosulphonic acid) proposed previously[12]. The values of ΔH_i were compared with the calorimetric enthalpies of formation of hydrogen-bonded complexes with *p*-fluorophenol (ΔH_f). Separate linear relations are observed between ΔH_i and ΔH_f for different classes of organic compounds, similarly to data for pK_a and pK_{HB}.[10] Fig. 3 shows that the slopes of the straight lines are approximately the same.

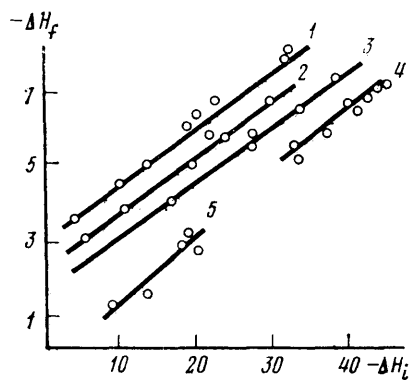


Figure 3. Relations between the enthalpies of protonation (ΔH_i) and hydrogen bond formation (ΔH_f) reactions[11]: 1) P=O; 2) S=O; 3) amides; 4) pyridines; 5) sulphides.

Studies involving such careful analyses of the relations between acid and proton donating properties of compounds of different classes have not so far been described in the literature and the amount of data permitting a comparison of the energies of different hydrogen-bonded complexes with the same base is insufficient. We therefore suggested the hydrogen-bond acidity factor (P_i), introduced[13] on the basis of the principle of the constancy of the acid and basic properties on formation of hydrogen bonds, as a characteristic of proton-donating properties.

We calculated the hydrogen-bond acidity factors from the formula

$$P_i = \Delta H_{ij}/\Delta H_{11} \cdot E_j,$$

where ΔH_{ij} is the energy of the hydrogen bond between the ith H-acid and the jth base and E_j is the basicity hydrogen-bond factor of the given base. The hydrogen-bonded complex of diethyl ether ($E_1 = 1$) and phenol ($P_1 = 1$) was chosen as the standard: $\Delta H_{11} = -5.3$ kcal mole^{-1}, i.e. the proton-donating capacity of the given acid is estimated relative to the proton-donating properties of phenol[13]. Fig. 4 clearly demonstrates the existence of different relations for different classes of compounds between the factor P_i, which we calculated from literature data[14-17], and the acidity of the compounds (alcohols, phenols, carboxylic acids, thiols). When the heteroatom in the acid AH is changed, the acid strengths of the compounds (thiols > alcohols) and their hydrogen bond proton-donating properties (thiols < alcohols) vary in opposition. The relations which obtain with retention of the heteroatom, for example, in alcohols, phenols, and carboxylic acids, can also be different (Fig. 4). Even for structurally similar "alcohols" Ph_3COH and Ph_3SiOH,[18] different relations between $\Delta\nu/\nu$ and the pK_a of the bases are observed (Fig. 5).

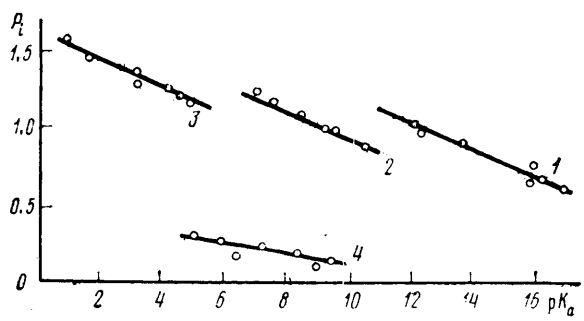


Figure 4. Relations between the acidity (pK_a) and the hydrogen bond acidity factor P_i for different groups of compounds: 1) alcohols; 2) phenols; 3) carboxylic acids; 4) thiols.

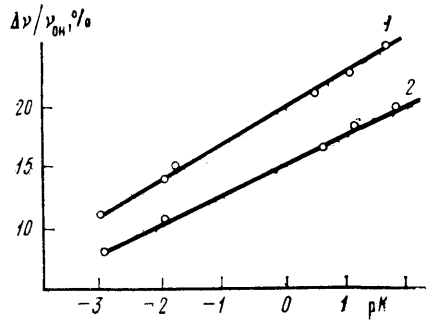


Figure 5. Relations between $\Delta\nu/\nu$ and the pK_a for Ph_3COH (line *1*) and Ph_3SiOH (line *2*).[19]

Thus, as stated correctly in the review of Gur'yanova et al.[19], linear relations between thermodynamic (spectroscopic) characteristics of hydrogen bonds and acid–base properties exist only within the limits of a single class of organic compounds. The "general" relation between ΔpK_a and ΔH_{HB}, quoted by Gordi and Stanford[5], is undoubtedly erroneous and the basicity scale for solvents based on $\Delta\nu$(OH) for phenol[18] is in fact the scale of their capacity for the formation of hydrogen bonds.

The differences between the changes in the energetics of hydrogen bond formation and protonation processes for different classes of compounds are determined by many factors. In the first place, as will be shown below, the solvation energy depends significantly on the type of compound. It plays a very important role in acid–base equilibria, which had been studied previously as a rule in strongly solvating media. On the other hand, in the study of hydrogen bonds, there is a possibility of a wide-scale employment of inert solvents and in addition the influence of solvating solvents on hydrogen-bonded complexes is much smaller than on ions. Furthermore, the energetics of acid–base reactions depends on the energy of the homolytic dissociation of AH and BH^+ bonds, on the electron affinity of the A atom, and on the ionisation potential of the B atom. Proton transfer is accompanied by a significant rearrangement of the reacting molecules. The formation of hydrogen bonds does not require the dissociation of covalent bonds and a radical rearrangement of the molecule. Quantum-chemical calculations in recent years showed (see, for example, Refs. 20–23) that the changes in electron density on formation of hydrogen bonds, which are determined by charge-transfer and polarisation effects, are not restricted to a three-atom fragment including the AH bond and a heteroatom (:)B with a lone electron pair. However, these changes are much smaller than in proton transfer. At the same time, electrostatic interactions, which make the greatest contribution to the energy of hydrogen-bonded complexes according to non-empirical calculations, depend mainly on the local polarity in the region of the hydrogen bond[22], i.e. on the charges of the B and H atoms and not on the overall polarity of the reacting molecules.

Thus, one can assume that the hydrogen bond behaves as a probe which hardly alters the given molecule during the measurement. The energy of the hydrogen bond characterises the distribution of electron density in the molecule in the ground state more adequately than does basicity or acidity.

In many instances the study of hydrogen bonds constitutes the only possibility of estimating the electron-donating properties of heteroatoms. For example, the basicity of compounds contains X–X or X–Y bonds, which are unstable when acted upon by acids (X = S, Se, or P and Y = N), cannot be determined. The study of the spectroscopic and thermodynamic characteristics of hydrogen bonds between such compounds and H-acids makes it possible to estimate their donor properties and to characterise the mutual influence of the heteroatoms[24,25]. The study of hydrogen-bonded complexes with aromatic compounds containing as a substituent a heteroatom with a lone electron pair provides a unique possibility of investigating the problem of $p-\pi$ conjugation[26]. In contrast to protonation and complex formation reactions with Lewis acids, in which the n electrons of the heteroatom

constitute the reaction centre, hydrogen bonds are also formed with the aid of the π electrons of the aromatic system; infrared spectra reveal the existence of two types of hydrogen-bonded complexes [26-28]. Comparison of the spectroscopic and thermodynamic parameters of n-complexes (with a heteroatom) with the corresponding characteristics of aliphatic compounds and comparison of the parameters of π-complexes (with a π-electron system) with the characteristics of carbon analogues makes it possible to determine the redistribution of electron density on $p-\pi$ conjugation and to estimate quantitatively the degree of $p-\pi$ conjugation for different heteroatoms [25,26].

III. THE ROLE OF HYDROGEN BONDS IN PROTON TRANSFER REACTIONS

The interaction of acids and bases leading to the dissociation of acids and the protonation of bases proceeds via the formation of hydrogen bonds and ion pairs [reaction (2a)], as stated above. However, apart from this main reaction, there are a number of side reactions associated with the formation of hydrogen bonds and ion pairs with solvent molecules and the formation of hydrogen-bonded complexes between the acid (or base) and the ionic component of the anion (or conjugate acid) formed. As a result, a change in the nature of the solvent leads to a change in the thermodynamic parameters and sometimes in the relative sequence of the acidities (basicities) of various organic compounds. For this reason, investigators have endeavoured to represent thermodynamic functions as the sum of two contributions: "internal", which is independent of the influence of the medium, and "external", which is associated with the solvation of molecules [29,30]. However, the problem of the separation of these contributions and of a quantitative estimation of the role of hydrogen bonds or other types of interaction with the medium requires the development of experimental methods for the determination of the "internal" acidity (basicity), i.e. for the measurement of acid–base equilibria in the gas phase. Such data have been obtained for a wide range of organic compounds only in the last few years as a result of the development of mass-spectrometric methods.

The principal approaches to the elucidation of the influence of hydrogen bonds, obtained in the study of acid–base equilibria in solvents of different types and also when the latter were compared with the corresponding equilibria in the gas phase, are discussed below.

1. Acid–Base Equilibria in Various Solvents

Many reviews and monographs present data for the acidity and basicity constants in various solvents and the medium effects are discussed in one way or another (see, for example, Refs. 31–36). We shall consider the approaches to the isolation of the role of hydrogen bonds in proton transfer reactions.

Studies on acid–base equilibria in various media require that side reactions associated with the formation of hydrogen bonds, which are therefore different for protic and aprotic solvents, be taken into account. In view of the amphoteric nature of protic solvents, the latter exhibit two functions—those of a proton donor and acceptor.

As a donor, the solvent interacts with
(a) the base:

$$SH + B \rightleftarrows SH \ldots B \rightleftarrows S^- \ldots BH^+ \rightleftarrows S^- + BH^+; \quad (3)$$

(b) with the anion formed:

$$SH + A^- \rightleftarrows SH \ldots A^- \rightleftarrows S^- \ldots HA \rightleftarrows S^- + HA. \quad (4)$$

As a proton acceptor the solvent interacts with
(a) the acid:

$$AH + SH \rightleftarrows AH \ldots SH \rightleftarrows A^- \ldots HSH^+ \rightleftarrows A^- + SH_2^+; \quad (5)$$

(b) with the conjugate acid formed:

$$BH^+ + SH \rightleftarrows BH^+ \ldots SH \rightleftarrows B + SH_2^+. \quad (6)$$

In media with a dielectric constant $\epsilon < 24$ there is a large number of ion pairs and hydrogen-bonded complexes; if $\epsilon > 24$, dissociated ions are also present [32].

Aprotic solvents can be divided into two groups: "inert", which hardly interact or only weakly interact with the reacting species (hydrocarbons and their halogeno-derivatives), and dipolar aprotic solvents, which can behave as proton acceptors [reactions (5a) and (6a) analogous to reactions (5) and (6)]:

$$AH + S \rightleftarrows AH \ldots S \rightleftarrows A^- \ldots HS^+ \rightleftarrows A^- + SH^+, \quad (5a)$$

$$BH^+ + S \rightleftarrows BH^+ \ldots S \rightleftarrows B \ldots HS^+ \rightleftarrows B + HS^+. \quad (6a)$$

In aprotic solvents of these two types reactions involving the formation of hydrogen bonds between the reactants assume a major role:
(a) between the acid and its anion:

$$AH + A^- \rightleftarrows AH \ldots A^-; \quad (7)$$

(b) between the conjugate acid and the base:

$$BH^+ + B \rightleftarrows BH^+ \ldots B. \quad (8)$$

Table 1. The equilibrium constants and the pK_a for substituted phenols—substituted pyridines and substituted phenols—triethylamine series [48].

Substituent in Ar	X	K	ΔpK_a
	$ArOH + XPy \rightleftarrows ArO^- \ldots HXPy^+$*		
2,6-Cl_2, 4-NO_2	2,4,6-Me_3	0.11	1.63
Cl_5	2,4,6-Me_3	0.15	2.17
2,6-Cl_2, 4-NO_2	3,5-Me_2	0.25	2.61
2,6-Cl_2, 4-NO_2	2,6-Me_2	0.85	3.21
2,6-Cl_2, 4-NO_2	2,4,5-Me_3	2.22	3.89
2,4,6-$(NO_2)_3$	2,4,5-Me_3	9.0	4.79
	$ArOH + NEt_3 \rightleftarrows ArO^- \ldots HNEt_3^+$**		
2,6-Cl_2	—	0.4	6.80
3,5-$(NO_2)_2$	—	0.5	6.70
2,4,6-Cl_3	—	0.9	7.03
2.4.6-Br_3	—	1.3	7.0
2,5-$(NO_2)_2$	—	2.8	5.31
Cl_5	—	2.7	5.26
2,4-$(N_2)_2$	—	6.7	4.07

* The relation between K and $\Delta pK_a = 0.7\Delta pK_a - 3.4$.
** The relation between K and pK_a is $K = -0.5pK_a + 3.5$.

In "inert" aprotic solvents acid dimers and hydrogen-bonded complexes of the acid and the base may be present together with associated species formed by reactions (7) and (8). The interaction of acids and bases in such media does not lead to dissociation into ions; it stops at the

stage involving the formation of ion pairs, which can associate into larger aggregates [36,37]. Thus the treatment of acid–base equilibria in solvents virtually lacking the capacity for specific interactions with the reactants proved to be fairly complex [31,36].

Studies devoted to the conversion of molecular hydrogen-bonded complexes into ion pairs have therefore acquired particular importance. Reliable spectroscopic criteria have been established for the identification of molecular (II) and ionic (III) hydrogen-bonded complexes in ultraviolet [38–40], infrared [2,41,42], and ^{1}H NMR spectra at low temperatures [43]. The study of the first stages of equilibrium (2a) in "inert" media made it possible to follow the changes in the nature of the interaction as a function of the proton-donating (for example, in series of halogeno- and nitro-phenols [3,38,39] and carboxylic acids [41–47]) and proton-accepting properties of the reactants (aliphatic and aromatic amines).

It has been shown [48] that there are linear relations between the equilibrium constants for the formation of ion pairs and the quantities $\Delta pK_a = pK_a(AH) - pK_a(BH^+)$ for certain series (see, for example, Table 1). In a number of studies the problem of the values of ΔpK_a for which ion pairs are formed (the II $\rightleftharpoons$ III equilibrium) [45,46,49,50] and of the differences between the enthalpies of formation of complexes II and III [2,38,44,51] has been discussed.

Much attention has been devoted to the investigation of the influence of the medium on the position of equilibrium (2). [38,48,52,53] It has been shown that the role of the solvent in the formation of ion pairs does not reduce the influence of the dielectric constant ϵ; the formation of hydrogen bonds with the solvent is of great importance, i.e. an enhancement of the proton-accepting properties of the medium shifts the equilibrium towards form III. [45,46,53]

In dipolar aprotic solvents the ion pairs $A^-...HB^+$ can be solvated specifically by the solvent with formation of solvate-separated ion pairs $A^-...(S)...HB^+$. Thus the solvation of a nitrophenol–amine complex has been investigated [54]; according to the authors, dimethyl sulphoxide is incorporated in the ion pair, forming a π-complex with the anion and hydrogen bonds with the cation: $A^-...(DMSO)...HB^+$. The molecular complex $\rightleftharpoons$ ion pair equilibrium has not been observed for oxygen-containing proton acceptors. It has been suggested that, with increase of the strength of hydrogen bonds, the evolution of complex formation proceeds from a molecular complex to an ion pair via a system in which the proton has a symmetrical position [55].

Reactions (7) and (8), occurring in dipolar aprotic solvents, have been studied by potentiometric titration and conductimetry in a series of investigations [56–60]. The formation of hydrogen bonds between the acid and the anion [reaction (7)] and between the conjugate acid and the base [reaction (8)] is referred to by the authors of the above investigations as homoconjugation processes. They showed that homoconjugation of type (7) plays a very important role; the formation constants of the complexes $(AHA)^-$ are much larger than K_{BHB^+}. [56,57,59] Enhancement of the proton-accepting properties of the solvent diminishes the homoconjugation constants. Thus the homoconjugation constants of benzoic acids in dimethylformamide (DMF) and in DMSO are smaller by a factor of 10 and 100 respectively than in acetonitrile [59].

In order to estimate the influence of homoconjugation on the proton transfer reaction, studies were made [56,57,59,60] of hydrogen bond formation reactions between the test acids AH and a model anion, for which the Cl^- anion was chosen [reaction (9)], and also between the test anion A^- and a model acid—*p*-bromophenol [reaction (10)] (the authors call these processes heteroconjugation):

$$AH + Cl^- \rightleftarrows AH \ldots Cl^-, \quad (9)$$

$$Br{-}C_6H_4OH + A^- \rightleftarrows BrC_6H_4OH \ldots A^-. \quad (10)$$

In this approach use is actually made of the principle of the constancy of acid-base functions in hydrogen bonds, already mentioned in Section II. [12,61] It has been shown in relation to benzoic acids and phenols that the sensitivity of the heteroconjugation reaction (the parameter ρ) to the electronic influence of substituents is smaller by a factor of approximately 4 than for the full proton transfer. The ratio ρ(phenol)/ρ(benzoic acid) $\simeq$ 1.8–2.0 remains constant for all the dipolar aprotic solvents employed [60].

The influence of solvents on acid–base reactions is determined overall by the operation of a large number of factors, namely (1) the formation of hydrogen bonds, (2) electrostatic interactions, (3) the basicity of (or acidity) the solvent, (4) van der Waals interactions, among which dispersion interactions are the most important, and (5) the structural organisation of the solvent. Allowance for the contributions of different factors is a complex problem, but certain approaches to its solution are available. Thus, in order to eliminate the role of electrostatic interactions, it has been suggested [62,63] that a pair of solvents of different types but with similar dielectric constants ϵ be used, namely methanol and DMF. The thermodynamic characteristics of acid–base equilibria in these two media differ greatly, demonstrating an important role of specific interactions.

Dispersion forces depend significantly on the shape and size of the interacting species, so that they must be taken into account in those cases where the equilibrium involves large highly delocalised and therefore readily polarisable anions. Such anions have a low capacity for the formation of hydrogen bonds and the role of dispersion interactions increases and may become decisive. For example, a whole class of CH acids such as derivatives of fluorene, diphenylmethane, and triphenylmethane exhibit a greater acidity in DMSO than in water, in contrast to OH acids [34,64]. In their analysis of the influence of the above factors the authors [64] note that, in solvents such as water and DMSO, factors (2) and (3) cancel out. Namely, as a result of the greater basicity of the solvent, the acidity of a given acid in DMSO should increase by 1.5 ± 0.5 pK_a units, while as a result of the lower dielectric constant ϵ it decreases by 1 pK_a unit compared with water. In the case of CH acids dispersion interactions are of greatest importance, while for OH acids the formation of hydrogen bonds is the decisive factor. The differences between the relative strengths of OH and CH acids in protic and dipolar aprotic solvents are determined by the operation of these factors. DMSO molecules, which have a larger dipole moment and polarisability than H_2O molecules, stabilise carbanions as a result of the operation of dispersion forces, which increases the acidity of CH acids in this solvent. The anions of OH acids are stabilised as a result of the formation of hydrogen bonds with water, so that their acidity in water is greater by 4–6 orders of magnitude than in DMSO.

It is noteworthy that in CH acids, whose negative charge is localised at the heteroatom (for example, benzoylacetone, nitromethane, and hydrogen cyanide), the decisive factor is the formation of hydrogen bonds with the solvent. As a result, the acidity in water is greater by 2–3 orders of magnitude than in DMSO, [34,64–66] as for OH acids. At the same time, an increase in the size of the anions of OH

acids combined with an increase of the degree of delocalisation of the charge leads to a decrease of the strength of hydrogen bonds with water and to an enhancement of dispersion forces. Thus, on passing from phenol to 4-nitro- and 2,6-dinitrophenols, the difference between the acidities in DMSO and water diminishes: the ΔpK_a values are 6.4, 3.8, and 1.3 respectively. In picric acid the sign of this quantity changes ($\Delta pK_a = -1.3$); this shows that the above acid is stronger in DMSO as a result of the stabilisation of the anion by dispersion forces [64]. A change of the sign of ΔpK_a (where ΔpK_a is the difference between the acidities in DMSO and MeOH) also takes place for 4-nitrophenol: $\Delta pK_a = 2.2$ for phenol and -0.8 for 4-nitrophenol [66].

Thus, apart from the acids giving rise to large anions with a highly delocalised charge, hydrogen bonding effects predominate over the dispersion forces and lead to a greater acidity in protic solvents.

The problems of the differentiating action of solvents, associated with their solvating capacity, have been examined in detail in a review [32] in relation to phenols and benzoic acids. It was shown that the differentiating effects of solvents can be estimated with the aid of three parameters:

(1) the autoprotolysis constant of the solvent (pK_S);

(2) the coefficient α in the equation

$$pK_{HA}(S) = \alpha pK_{HA}(H_2O) + \beta;$$

(3) the coefficient ρ in the Hammett equation:

$$pK_{HA}(S) = pK_0 - \rho\sigma.$$

Table 2. Parameters characterising the differentiating influence of solvents for monosubstituted benzoic acids [67] and phenols [32], and the solvent acidity factors in hydrogen bonds*.

Solvent	$\varepsilon_{25}°$	pK_S	α	ρ(b.a.)	ρ(ph.)	P_i
H_2O	78.5	14.0	1	1	—	0.55
CH_3OH	32.6	16.7	1.30	1.38	—	0.66
C_2H_5OH	24.3	19.5	1.60	1.66	—	0.63
C_3H_7OH	20.1	—	—	—	2.25	0.75
C_4H_9OH	17.1	—	—	—	2.59	—
iso-$(C_3H_7)OH$	18.3	—	—	—	3.17	0.75
iso-$(C_4H_9)OH$	17.7	—	—	—	2.67	0.44
$(CH_3)_2CO$	20	23.0	1.72	1.43	—	—
CH_3NO_2	36.0	24	1.81	1.83	—	—
DMF	36.7	29.4	1.98	2.03	—	—
CH_3CN	37.5	33.3	2.49	2.37	—	—
DMSO	46.6	33.3	2.49	2.57	—	—

*The parameters pK_S, α, and ρ(b.a.) for benzoic acids and ρ(ph.) for phenols are presented.

Table 2 shows that the values of pK_S, α, and ρ vary in parallel, demonstrating thereby the role of factor (3). At the same time the data in Table 2 indicate the absence of any parallelism in the variation of these parameters and the dielectric constant ϵ. Since the solvents belong to different classes of organic compounds, there need be no direct relation between their acid–base properties and their capacity for the formation of hydrogen bonds, as stated above. The role of hydrogen bonds is manifested by the fact that all the solvents which behave as proton donors exhibit smaller differentiating effects than aprotic solvents. However, Table 2 shows [32,67] that there is no direct relation between the hydrogen bond acidity factors P_i and the values of ρ. It may be that the absence of such a relation is due to the fact that the enthalpies of hydrogen-bonded complexes, from which the values of P_i were determined, had been obtained under the conditions leading to the formation of 1 : 1 complexes.

The relative activity coefficients have been used in some studies [58,68] in order to take into account the ability of solvents to form hydrogen bonds‡. The ability of a given solvent (S) to function as a proton acceptor in relation to a standard (S_0), for which acetonitrile (AN) was selected, was defined as $\lg {}^{AN}\gamma^{S}(H_\alpha)$ with the aid of the expression

$$\lg {}^{AN}\gamma^{S}(H_\alpha) = \lg {}^{AN}\gamma^{S}(HA) - \lg {}^{AN}\gamma^{S}(MeA),$$

where HA is the acid and MeA is its methyl ester. It was assumed that the activity coefficient of the methyl ester takes into account all types of interaction other than hydrogen bonding. The activity coefficients of the acids and their esters were determined from measurements of the solubilities s:

$$\lg {}^{AN}\gamma^{S} = \lg s^{AN} - \lg s^{S}.$$

The same activity coefficients were obtained independently from differences between the heteroconjugation constants. Thus it was concluded that the quantities $\lg {}^{AN}\gamma^{S}(H_\alpha)$ characterise the ability of the solvents to function as proton acceptors, which decreases in the following sequence:

$$DMSO\ (-1.9) > MeOH\ (-1.5) > DMF\ (-1.4).$$

The relative abilities of solvents to function as proton donors in hydrogen bonds with the anion was estimated from the values of $\lg {}^{M}\gamma^{S}_{A^-}$, methanol (M) being selected as the standard solvent. The large negative activity coefficients obtained for dipolar aprotic solvents indicate a much higher degree of solvation of anions by methanol. The quantity $\lg {}^{M}\gamma^{S}_{A^-}$ increases linearly with increasing basicity of the anion [68].

The activity coefficients obtained from studies on S_N2 reactions have been used [69] to estimate the influence of hydrogen bonds with the anion on the acid dissociation constant in protic solvents (H_2O, MeOH). However, one must bear in mind that this method is fairly approximate. The coefficients $\lg {}^{S_0}\gamma^{S}_{A^-}$ for individual ions can be determined only with the aid of non-thermodynamic postulates.

Information obtained in the study of the thermodynamic characteristics of hydrogen bonds with ions by infrared spectroscopic, ^1H NMR, conductimetric, and calorimetric methods proved to be much more accurate and reliable (see, for example, Refs. 51 and 70–72). We believe that, in analysing the influence of solvents on acid–base equilibria, one can employ widely the enormous amount of experimental data on the thermodynamic properties of hydrogen bonds of the type AH...B (see, for example, Refs. 14 and 73). The most valuable data concerning the role of hydrogen bonds have been obtained in recent years by combining the results of studies on proton transfer reactions in the gas phase and in solutions.

‡ The relative activity coefficients $-\lg {}^{S_0}\gamma^{S}$ reflect the change in the standard chemical potential of the solute on passing from an arbitrary standard solvent (S_0) to another solvent (S).

2. Comparison of the Parameters of the Acid–Base Equilibria in the Gas Phase and in Solution

The development of methods of ionic cyclotron resonance [74,75] and high-pressure mass spectrometry [76,77] permitted fairly accurate determinations of thermodynamic equilibria in the gas phase. The most important results in this field have been reviewed [78,79].

Proton transfer reactions of the following types were studied in the gas phase:

$$AH + B^- \rightleftarrows A^- + BH, \quad (11)$$

$$AH^+ + B \rightleftarrows A + BH^+. \quad (12)$$

If the acidity is defined as the free energy ΔG^0 of reaction (13), then the free energy of reaction (11) is a measure of the relative acidities of two acids AH and BH:

$$AH \rightleftarrows A^- + H^+. \quad (13)$$

The basicity in the gas phase is the term given to the corresponding free energy ΔG^0 of reaction (14) and ΔG^0 of reaction (12) is a measure of the relative basicities of the bases A and B:

$$BH^+ \rightleftarrows B + H^+ . \quad (14)$$

The enthalpies ΔH^0 of reactions (11)–(14) are believed to be approximately equal to the ΔG^0 in view of the smallness of the entropy effects. Special measurements of ΔS^0 of reaction (12) showed that these quantities are indeed very small [80]. The small contribution of entropy factors to reaction (11) is indicated by the insignificant changes in ΔG^0 when the temperature is altered by 300 K for a series of benzoic acids and phenols ($\Delta S^0 < 2-3$ e.u.). [81] The relative acidity or basicity [reactions (11) and (12)] are frequently designated by $\delta\Delta G^0$; the relative enthalpies are designated by $\delta\Delta H^0$.

In order to construct an absolute acidity scale [reaction (13)] or basicity scale [reaction (14)], it is necessary to calculate a thermodynamic cycle. The enthalpy change in reaction (13) caused by the proton affinity of the anion $PA(A^-)$ corresponds to the heterolytic dissociation energy and is defined as follows:

$$PA(A^-) = \Delta H^0 = DH^0(AH) - EA(A) + IP(H), \quad (15)$$

where DH^0(AH) is the homolytic dissociation energy, EA(A) electron affinity of the atom A, and IP(H) the ionisation potential of the hydrogen atom. The values of $PA(A^-)$ for a series of carboxylic acids have been determined with the aid of data for HCl and H_2S [82] and were then used as reference values in the study of benzoic acids and phenols [51].

The proton affinity of the base PA(B), corresponding to enthalpy of reaction (14), is defined in terms of the homolytic dissociation energy $DH^0(BH^+)$ and the ionisation potentials of the atoms B and H:

(16)

The internal correspondences in measurements of repeatedly overlapping thermodynamic cycles ensured an accuracy of the measurements to within 0.5 kcal mole^{-1}; the errors in the absolute values of $PA(A^-)$ and PA(B) are ±2 kcal mole^{-1}.

The existence of a linear relation between the acidities (or basicities) in the gas phase and the σ constants of the substituents has been demonstrated for certain classes of acids and bases. In all cases the sensitivity to the electronic effects of the substituents is much greater in the gas phase than in solution. Thus ρ in the gas phase is greater by a factor of 6.8 for phenols and by a factor of 10.6 for benzoic acids than in water [79,81]. According to other data [83–84], the values of ρ in the gas phase amount to 5.5–5.7 for carboxylic acids and 7.0–8.4 for alcohols; in protic solvents these quantities decrease to 1.7–1.8 and 2.7 respectively. The electronic influence of substituents on the basicity of pyridine in the gas phase is greater by a factor of 3.5 (Taagepera et al. [85]) (by a factor of 2.5, according to Arnett et al. [1]) than in water.

Table 3. The free energies and enthalpies of the reactions $XC_6H_4OH + C_6H_5O^- \rightleftharpoons XC_6H_4O^- + C_6H_5OH$ in the gas phase, water, and DMSO. [81]

X	$\Delta G^\circ_{gas} \approx \Delta H^\circ_{gas}$, kcal mole^{-1}	$\Delta G^\circ_{H_2O}$, kcal mole^{-1}	$\Delta H^\circ_{H_2O}$, kcal mole^{-1}	$\Delta G^\circ_{DMSO} \approx \Delta H^\circ_{DMSO}$, kcal mole^{-1}	$\delta\Delta H_{hydr}(A^-)$*, kcal mole^{-1}
p-OCH_3	−0.7	0.5	0.22	−0.6	−0.4
m-CH_3	0.4	0.18	0.02	0.1	−0.7
p-CH_3	1.3	0.42	0.02	1.7	−2.2
o-Cl	−6.3	−1.9	−1.1	−4.5	—
m-Cl	−7.9	−1.2	−0.3	−2.8	9.3
p-Cl	−6.6	−0.7	0.2	−1.5	10.9
p-NO_2	−25.8	−3.8	−0.8	−8.6	17.9

*$\delta\Delta H_{hydr}(A^-)$ corresponds to the difference between the heats of hydration of the anions $XC_6H_4O^-$ and $C_6H_5O^-$ on passing from the gas phase to an aqueous medium: $\delta\Delta H_{hydr}(A^-) = \Delta H_{hydr}(XC_6H_4O^-) - \Delta H_{hydr}(C_6H_5O^-)$.

Arnett et al. [1] and Mahon and Kebarle [81] claim that the main factor responsible for the weakening of the influence of substituents in protic solvents is the formation of hydrogen bonds with the anion for acids [81] and with the conjugate acid for bases [1]. Analysis of the hydration energies of the anion A^- in Table 3 on passing from the gas phase to an aqueous medium and the internal acidities of substituted phenols permits a semiquantitative characterisation of the contribution of hydrogen bonds to the change in the effect of substituents in water. Comparison of the acidities ($\Delta G^0_{gas} \approx \Delta H^0_{gas}$) and heats of hydration of the anions [$\delta\Delta H_{hydr}(A^-)$] shows that the enhancement of the electron-accepting properties of substituents, leading to an increase of internal acidity, is almost fully compensated by the decrease of the hydration of the anion as a result of its lower basicity and ability to form hydrogen bonds§. Thus the acidity of *p*-nitrophenol increases relative to phenol by 25.8 kcal mole^{-1} in the gas phase and solvation, which stabilises the *p*-$NO_2C_6H_4O^-$ anion with its lower capacity for the formation of hydrogen bonds, is weakened by 17.9 kcal mole^{-1}; as a result $\Delta G^0_{H_2O}$ increases by only 3.8 kcal mole^{-1}. The decrease of the strength of $A^-\ldots(HOH)_n$ hydrogen bonds leads to an increase of the degree of disorder among solvent molecules in the vicinity of the anion, which is reflected in a greater entropy change and hence in a higher value of $\Delta G^0_{H_2O}$ compared with $\Delta H^0_{H_2O}$. Dipolar aprotic solvents, which only weakly solvate anions, have

§ As will be made clear below, the differences between the electrostatic and dispersion interactions for anions of similar size are negligible and the hydrogen bonds with the base should play a smaller role than those with the anion.

higher values of ρ (this was indicated in Section II for benzoic acids). Table 3 shows that the values of ΔG DMSO are much closer to those of ΔGgas for phenols; the attenuation factor is ~2. In contrast to the values in water, the influence of substituents is manifested in DMSO mainly by a change in enthalpy (ΔG DMSO $\simeq \Delta H$ DMSO), i.e. as in the gas phase.

The smaller the ability of the anion to form hydrogen bonds, the greater the decrease of the acidity of the corresponding acid on passing from the gas phase to water (and any other protic solvent). Thus the acidities of acetic acid and phenol are similar in the gas phase, while in water they differ by six orders of magnitude[81]. The delocalisation of the negative charge owing to the resonance effect in the phenoxide anion lowers its ability to form hydrogen bonds, which makes phenol a much weaker acid in solution. In certain classes of compounds it is necessary to take into account the stabilisation of the acids themselves in addition to the hydrogen bond with the anion. Thus benzoic acid is much stronger in the gas phase than phenol, while in water its pK_a is almost the same. This has been explained[81] by the greater ability of benzoic acid, compared with phenol, to function as a proton donor in a hydrogen bond.

The role of hydrogen bonds in the attenuation of the observed electronic influence of substituents and the change in the relative sequence of acidities in solution is manifested also by the fact that these effects are absent for acids whose anions do not possess a sufficient capacity for the formation of hydrogen-bonded complexes. Indeed, it has been shown in a series of studies[85-89] that the influence of substituents in CH acids giving rise to large ions with a delocalised charge is the same in the gas phase as in solutions; the relative acidity sequence does not change. The negligible influence of water as a solvent on the energy of proton transfer has been demonstrated for a large number of CH acids[86-88]. The differences between the basicities in the gas phase and water for aryl carbonium ions with appreciable differences in structure are constant. There is a linear relation between $\delta\Delta G_i$(gas) and $\delta\Delta G_i(H_2O)$ with a slope of unity and an intercept on the ordinate axis at ~35 kcal mole^{-1}, i.e. the enthalpy of solvation does not involve a specific interaction[87]. A satisfactory linear relation (with a slope of unity and $\rho = 1$) has been obtained [86] between the acidities of a large set of CH acids in the gas phase and in DMSO.

The most detailed study of solvation effects has been made recently[1]. The authors analysed the influence of hydrogen bonds on the acid–base equilibria of substituted pyridines and showed that the apparent weakening of the effect of substituents (by a factor of 2.5) in water can be accounted for wholly on the basis of a solvation model in which hydrogen bonds play the main role. They state that the acid–base equilibria of substituted pyridines involve an optimum reaction for this solvation model, because the ions and acid molecules have similar dimensions and shapes, so that the effects of their electrostatic and dispersion interactions are similar.

Arnett et al.[1] analysed a thermodynamic cycle and isolated the contribution of the hydrogen bonds (ΔH_{HB}) to the enthalpy of solvation (ΔH_S) calculated from heats of solution and vaporisation:

$$\begin{array}{ccc} XPyH^+_{gas} + Py_{gas} & \xrightleftharpoons{\delta\Delta H_{i\,gas}} & XPy_{gas} + PyH^+_{gas} \\ \Big\downarrow \Delta H_S(BH^+) \quad \Big\downarrow \Delta H_S(Py) & & \Big\downarrow \Delta H_S(B) \quad \Big\downarrow \Delta H_S(PyH^+) \\ XPyH^+_{H_2O} + Py_{H_2O} & \xrightleftharpoons{\delta\Delta H_{i\,H_2O}} & XPy_{H_2O} + PyH^+_{H_2O} \end{array}$$

The authors follow Krishnan and Friedman[90,91] in separating the solvation energy into (1) the enthalpy of formation of hydrogen bonds, (2) the energy of van der Waals interactions, (3) the energy of formation of a "cavity", and (4) the energy of the change in solvent structure. The last three "physical" factors were determined as an overall factor[1].

Three procedures have been used to isolate the contribution of hydrogen bonds.

1. On the basis of the principle of the constancy of the acid and basic functions in hydrogen bonds[13,61], the coefficients for the transition from *p*-fluorophenol to water as a proton donor were determined and the data of Taft et al.[10] for the p-$FC_6H_4OH\ldots XPy$ system were used.

2. The difference between the heats of solvation of substituted benzenes and pyridines was attributed to hydrogen bonds.

3. A quantum-chemical calculation was carried out on the hydrogen bond formation and proton transfer reactions.

It was shown that the experimental coefficient α ($\alpha = 0.1$) in the linear relation between the energy of formation of hydrogen bonds and the energy of proton transfer in the gas phase ΔH_{HB} ($XPy\ldots H_2O$) $= \alpha\Delta H_i$ is twice as great as the calculated value ($\alpha = 0.05$), which can be accounted for by the lower strength of the 1 : 1 hydrogen-bonded complexes, assumed in the quantum-chemical calculation, compared with the real complexes $XPy\ldots(H_2O)_n$.

The hydrogen bonds formed by charged ions play the most important role; their energy exceeds approximately by a factor of five the enthalpy of formation of hydrogen-bonded complexes of substituted pyridines¶. The influence of substituents in the $XPyH^+\ldots OH_2$ hydrogen bonds leads to the opposite relation compared with the proton transfer reaction, $\Delta H_{HB}(XPyH^+\ldots OH_2) = 0.5\Delta H_i$(gas), as for the hydrogen bonds between benzoic acids and the anions. The attenuation factor for the influence of substituents in water (2.5) can be explained satisfactorily by such variations in the strength of the hydrogen bond.

The study of Arnett et al.[1] demonstrated brilliantly the fruitfulness of this approach to the analysis of the thermodynamic cycle using the following set of data: the experimental enthalpies of proton transfer in the gas phase and in solution and the enthalpies of solvation and hydrogen bond formation in combination with the results of quantum-chemical calculations. A test of the applicability of this solvation model for hydrogen bonds to other classes of acids and bases is presumably a task for the immediate future.

The possibility of using the model for the analysis of solvation effects involving aliphatic amines is of particular interest, because the problem of the preferential contribution of electrostatic interactions or of the formation of hydrogen bonds continues to remain controversial [93-97]. Measurements of the basicities of alkylamines in the gas phase established that the anomalous basicity series in water ($NH_3 < MeNH_2 < Me_2NH > Me_3N$) is related to the solvation effects[93,96]. In the gas phase the basicity varies in accordance with expectation ($NH_3 < MeNH_2 < Me_2NH < Me_3N$). There are different linear relations between the enthalpies in the gas phase and

¶ It is of interest that comparison of the influence of hydrogen bonds formed by the pyridinium ion ($C_6H_5N^+H\ldots Cl^-$) with MeOH...Py showed[92] that the effect of substituents in the first case is greater by a factor of approximately 5.

aqueous solution for primary, secondary, and tertiary amines, whose slopes decrease in this sequence (Fig. 6).[93] The basicity of amines in the gas phase is 5–6 times higher than in water.

However, the interpretations of the results by Aue et al.[94] and by Arnett and coworkers[96,97] are contradictory. Aue et al.[94] believe that the irregular basicity sequence cannot be accounted for solely by the formation of hydrogen bonds of the type $BH^+ \ldots OH_2$. They claim that hydrogen bonds of this type are responsible only for the difference between the slopes of the linear plots of proton affinity against ΔH_S for primary, secondary, and tertiary amines.

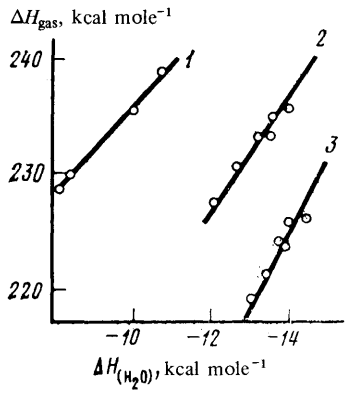


Figure 6. Relation between the enthalpies of protonation of aliphatic amines in the gas phase and water[94]: 1) tertiary amines; 2) secondary amines; 3) primary amines.

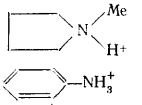
The claim by Arnett and coworkers[96,97] that hydrogen bonds are the principal differentiating factor in the solvation of ammonium ions is based on the following facts. Firstly, the solvation energy depends to a greater extent on the number of hydrogen bonds than on the size and shape of the ion. The dependences of the heat of hydration of ammonium ions on the reciprocal of the radius are different for primary, secondary, and tertiary ions, the differences increasing for large ions where the contribution of electrostatic interaction is reduced. Secondly, the average solvation energies for the three types of amines differ by 6–7 kcal mole^{-1}, which corresponds to the energies of strong $N^+H \ldots OH_2$ bonds.

Additional confirmation of the rule of hydrogen bonds was obtained on comparing the influences of substituents on the acidity of ammonium, oxonium, sulphonium, and phosphonium ions[98]. Ions of the last two types exhibit a much weaker capacity for the formation of hydrogen bonds, which means that the weakening influence of the solvent should be significantly smaller for such ions than for ammonium and oxonium ions. Indeed the influences of substituents in all four classes of compounds in the gas phase, characterised by the quantities $\Delta PA = PA(MeXH_{n-1}) - PA(XH_n)$, differ little. On the other hand, the differences between the enthalpies of protonation of methylated derivatives and hydrides in fluorosulphonic acid $[\Delta(-\Delta H)_{HSO_3F}]$ are much greater for phosphorus and sulphur derivatives than for nitrogen and oxygen derivatives. The maximum weakening of the influence of substituents in solution $[\Delta PA = 16.9$ kcal mole^{-1}; $\Delta(-\Delta H)_{HSO_3F} = 2.2$ kcal mole$^{-1}]$ is observed for oxonium ions, which corresponds to their capacity for the formation of hydrogen bonds and cannot be accounted for by electrostatic interactions. The values of ΔPA from later studies are indicated below in brackets[80,99]:

	ΔPA, kcal mole^{-1}	$\Delta(-\Delta H)_{HSO_3F}$, kcal mole^{-1}		ΔPA, kcal mole^{-1}	$\Delta(-\Delta H)_{HSO_3F}$ kcal mole^{-1}
$H_2O \rightarrow MeOH$	16,9(11,9)	2.2	$NH_3 \rightarrow MeNH_2$	11.0(9,0)	4.0
$H_2S \rightarrow MeSH$	15,0(12,0)	8.8	$PH_3 \rightarrow RPH_2$	14,4(14.4)	13.0

Comparative data on the basicities of aromatic and aliphatic amines in the gas phase and in water have been analysed in several studies[85,100–102] and several instances of the inversion of the basic strengths in solution compared with the "internal" basicity in the gas phase were noted. Thus, pyridine, which is four times less basic than ammonia in water, is eleven times more basic in the gas phase. The basicity sequence of anilines and amines in water ($Ph_3N < PhNH_2 < NH_3$) is also inverted in the gas phase: $NH_3 < PhNH_2 < Ph_3N$.[100] However, it was found that these changes are not related to the small role of resonance effects in the gas phase, but can be accounted for by the fact that the differences between the heats of solvation exceed the resonance effect in unsaturated compounds. In has been shown[85] that ΔH_S for the NH_4^+ cation is greater by 20 kcal mole^{-1} than for PyH^+, which leads to a much greater stabilisation of the ammonium ion in water. The higher heat of solvation was attributed to the greater strength of $NH_4^+ \ldots OH_2$ hydrogen bonds. However, the extent of the electrostatic interactions involving the small ion should also be greater, so that each contribution requires a special assessment.

Table 4. The heats of solution and relative acidities in the gas phase and in water of three pairs of conjugate acids differing in the degree of unsaturation[101]. The proton affinities and percentages of *s* character of the lone pair of the nitrogen atom in the corresponding amines[102].

Conjugate acid	$\Delta H_S(BH^+)$, kcal mole^{-1}	$\delta\Delta G_i$(gas), kcal mole^{-1}	$\delta\Delta G_i$(H$_2$O), kcal mole^{-1}	PA, kcal mole^{-1}	Amount of *s* character, %
	73.0	−4.3	−3.88	220.9	30
$Me_2NH_2^+$	73.0	0	0	224.6	25
	64.0	−8.3	−7.16	224.8	83
	62.0	0	0	230	25
	76.0	−9.6	−8.2	—	—
	76.0	0	0	—	—

As stated by Taft et al.[101], in order to establish the role of resonance effects one must compare the basicities of compounds with similar values of $\Delta H_S^0(BH^+)$. Such compounds are bases with the same number of acid hydrogen atoms and carbon atoms and also with a similar skeleton, differing only in the degree of unsaturation.

Under these conditions, the basicity of unsaturated compounds in the gas phase is lower than that of saturated compounds. Consequently, the resonance effect is manifested quite explicitly (Table 4) and there is no inversion in the relative basic strengths on passing from the gas phase to the solution. The changes in the basicities of unsaturated compounds are greater by 10–20% compared with saturated compounds in the gas phase relative to water, which has been explained[101] by the presence of hydrogen bonds between the bases or conjugate acids and water. The existence of a linear relation between the proton affinity and the percentage of *s* character of the lone pair orbitals of the nitrogen atom for compounds with similar values of ΔH_S has been demonstrated[102]. A greater percentage of *s* character corresponds to a lower value of *PA*, as for basicity in solution.

Marked changes on passing from the solution of the gas phase have been observed in studies devoted to the acid properties of aliphatic amines, alcohols, and thiols[103,107] (Table 5). The acidities in water decrease when the substituents are varied in the sequence Me > Et > iso-Pr > t-Bu, and there is a linear relation with the σ^* constant of the substituent. The same series, with an effective correlation between the heats of deprotonation and the σ^* constants, has been obtained in a study in DMSO.[15] However, the data in Table 5 show that in the gas phase the acidity sequence is inverted (Me < Et < iso-Pr < t-Bu), which demonstrates the lack of validity of the generally accepted relation between acidity and the inductive effect.

Table 5. The relative acidities of alcohols and thiols in the gas phase and in water ($RX^- + BuXH \rightleftharpoons BuX^- + RXH$; X = O or S).[107]

RXH	$\delta\Delta G_{gas}$, kcal mole^{-1}	$\delta\Delta G_{H_2O}$, kcal mole^{-1}	RXH	$\delta\Delta G_{gas}$, kcal mole^{-1}	$\delta\Delta G_{H_2O}$, kcal mole^{-1}
H_2O	−17.8	1.1	H_2S	1.7	5.75
MeOH	−5.6	1.7	MeSH	−4.1	1.22
EtOH	−2.7	1.0	EtSH	−1.7	0.78
iso-PrOH	−0.8	0.3	iso-PrSH	−0.8	0.49
t-BuOH	0	0	t-BuSH	0	0

The role of solvation effects has been analysed[108,109]. The enthalpies of solvation ΔH_S obtained for the anions RO^- can be arranged in the sequence $MeO^- > EtO^- >$ iso-$PrO^- >$ t-BuO^-. The values of ΔH_S then exceed the stabilisation energy of the ions in the gas phase which varies in the opposite sequence. Thus the usual ideas concerning the sign of the inductive effect, based on measurements of equilibria in solutions, are incorrect. Quantum-chemical calculations by the CNDO/2 [110] and non-empirical[111,112] methods established that, owing to its high polarisability, the alkyl group can exhibit both positive and negative inductive effects, depending on the charge on the atom to which it is linked. The calculated proton transfer energies agree with the acidities and basicities in the gas phase.

Thus measurements of the acid–base properties in the gas phase showed that solvation interactions, among which the formation of hydrogen bonds is the most important, can influence not only the magnitude but also the sequence of the properties of a series of compounds having similar structures.

We shall now consider the problem whether or not there is a general relation between acid or basic properties of organic componnds in the gas phase and the characteristics of hydrogen bonds. Strictly speaking, the comparison should be made using the characteristics of hydrogen bonds formed in the gas phase. However, the amount of data for hydrogen-bonded complexes in the gas phase is at present very small. Nevertheless, it can be shown that a general relation of this type does not exist. The lack of correspondence between the energetics of hydrogen bonds and acidity in the gas phase has been observed, for example, when the O atom in the H-acid XH was replaced by an S atom. The acidity of thiols in the gas phase is greater, as in solution, than the acidity of alcohols, while their ability to form hydrogen bonds is much weaker. This difference can be readily understood if account is taken of the fact that the energy of the acid–base equilibrium in the gas phase is an overall characteristic including the dissociation energy and the electron affinity. The lower strength of the SH bond compared with OH is the principal cause responsible for the greater acidity of thiols in the gas phase. Consequently, as one moves downwards along the Group [in the Periodic Table?] the acidity in the gas phase increases, as in solution, while the strength of hydrogen bonds with bases diminishes.

It is noteworthy that, for certain classes of compounds (aliphatic amines and pyridines), a greater similarity of the properties of hydrogen bonds and the basicities in the gas phase compared with the basicity in the solution was observed. Thus a linear relation has been obtained[113] between the energy of formation of hydrogen bonds by phenol and *p*-fluorophenol with substituted amines or pyridines and the proton affinities of these bases in the gas phase. A correlation between the basicity in the gas phase and the pK_a in water is not observed in this case, as stated previously. Studies on the frequency shifts $\Delta\nu$(OH...N) [114] and $\Delta\nu(Cl_3CH...N)$ [115] in the gas phase and the thermodynamic parameters of the $CH_3OH...N$ systems[116] in the gas phase also showed that they vary in parallel with the proton affinities in the gas phase ($Et_3N > Me_3N > Me_2NH > MeNH_2$). It is of interest to note that studies on the OH...N hydrogen bonds in solution yield other results, namely, the energies of hydrogen bonds with tertiary amines are lower than those of the bonds with secondary amines[117], i.e. there is a correlation with the basicities in solution and not in the gas phase.

Measurements on ionic equilibria of the type $(BHR^-)_{gas} \rightleftharpoons B^-_{gas} + HR_{gas}$ yielded a series corresponding to changes in the enthalpies of hydrogen bonds in parallel with the acidities of HR in the gas phase: HOH < MeOH < t-BuOH < $CHCl_3$ < PhOH < H_3CCOOH < HCOOH,[118] but it does not correspond to the energies of hydrogen bonds in solution in all respects.

We believe that there is no doubt about the importance of more extensive studies on hydrogen bonds in the gas phase and of their comparison with data for solutions and gas-phase acidities and basicities. Studies on the electron-donating and electron-accepting properties of acids and bases, extending as far as the significant rearrangement of the latter associated with the proton transfer

process, are necessary for a deeper understanding of the reactivities of compounds in acid–base reactions.

IV. HYDROGEN BONDS IN NUCLEOPHILIC SUBSTITUTION REACTIONS

The two main classes of nucleophilic substitution reactions are known to differ as regards the influence of solvents on the rate of the process:

$$Y^- + RX \begin{cases} \xrightarrow[\leftarrow]{S_{N1}} Y^- + R^+ + X^- \rightarrow YR + X^- & \text{(protic solvents accelerate the reaction),} \\ \xrightarrow[\leftarrow]{S_{N2}} [Y \overset{\delta-}{\cdots} R \cdots \overset{\delta-}{X}]^{\neq} \rightleftarrows YR + X^- & \text{(protic solvents retard the reaction, while aprotic dipolar solvents accelerate it).} \end{cases}$$

Unimolecular reactions are accelerated by protic solvents, since the formation of hydrogen bonds promotes the formation of the anion X^-.

The role of hydrogen bonds, which retard reactions of the S_N2 type, has been elucidated by Parker and coworkers (see, for example, Refs. 119–121). For the analysis of the influence of the solvent, use is made of the relative activity coefficients ${}^{M}_{\gamma}{}^{DMF}$, which make it possible to eliminate the influence of electrostatic interactions, since methanol (M) and DMF have similar dielectric constants, as stated previously. Examination of the results led Parker [120] to the conclusion that the main factor which determines the solvation properties of the medium is the hydrogen bonds between the protic solvent and the anion. The values of $\lg {}^{M}_{\gamma}{}^{DMF}_{Y^-}$ increase in a sequence which is the same as that corresponding to the ability of the anions to form hydrogen bonds: ClO_4^- (−0.4); 2,4,6-$NO_2C_6H_2O^-$ (−0.4) < SCN^- (2.7) < 4-$NO_2C_6H_4S^-$ (2.9) < $4NO_2C_6H_4O^-$ (4.1) < $C_6H_5S^-$ (4.9) < $C_6H_5O^-$ (7.7) < $CH_3CO_2^-$ (9.2). The delocalisation of the charge in the picrate and perchlorate anions leads to a higher degree of solvation by DMF, which is assumed to be due to the enhancement of dispersion interactions.

Analysis of the influence of the solvent made it possible to determine more effectively than by other methods the nature of the transition state. The "looser" the transition state, the greater the localisation of the negative charge, and the greater the capacity of the given substance to behave as a proton acceptor in the hydrogen bond. The quantity $\lg {}^{M}_{\gamma}{}^{DMF}_{[YR.X]^{\neq}}$ increases and the ratio of the logarithms of the rate constant $\lg k^{DMF}/\lg k^{M}$ decreases.

The change in the nucleophilicity sequence when the nature of the solvent is altered can be accounted for qualitatively from the standpoint of the ability of the solvents to form hydrogen bonds: we have $I^- > SCN^- \simeq CN^- > N_3^- \simeq Br^- > Cl^- > OAc^-$ in protic solvents [122] and $CN^- > OAc^- > Cl^- \simeq Br^- \simeq N_3^- > I^- > SCN^-$ in dipolar aprotic solvents [119]. Thus the ratio of the nucleophilicities of OAc^- and SCN^- decreases by a factor of 10^5 on passing from DMF to methanol, since the acetate ion is a much more effective proton acceptor [120].

Thus analysis of the influence of hydrogen bonds on the reaction rates assists in the study of the nature of the transition state and the prediction of the changes in the rate on replacement of the solvent. The influence of the formation of hydrogen-bonded complexes can be detected qualitatively by employing mixed solvents (see, for example, Refs. 123–126) or by analysing the changes in the rate constants which do not parallel the dielectric constants ϵ of different solvents (see, for example, Refs. 127 and 128).

For a quantitative estimate, one resorts to many-parameter equations relating the rate constant to different characteristics of the solvents (n and ϵ), including those which determine their ability to function as proton donors and acceptors (see, for example, Refs. 129–131). Thus the two-parameter expression for dipolar solvents includes the quantity $\Delta\nu_D$, which represents the shift of the stretching vibration frequency of deuteromethanol $\Delta\nu(CH_3OD\ldots B)$: [129,130]

$$\lg K_0 = -A + Bf(\varepsilon) - C(\Delta\nu_D).$$

Thus the above expression estimates the ability of the solvent to behave as a proton acceptor in the hydrogen bond [129].

Unfortunately it was found that, for a quantitative description of the effects of the medium, an equation with an even greater number of parameters is needed. Furthermore, in the case of strong specific solvation effects, the equations are inapplicable owing to the significant non-additivity of the contributions of interactions of different types [129,130].

The change from protic to dipolar aprotic solvents can also alter the mode of reaction. It has been shown in a review [132] devoted to ambident anions that, depending on the type of solvent, alkylation reactions lead to different products. The change from protic to dipolar aprotic solvents, which do not form hydrogen bonds with oxygen atoms, induces attack on the oxygen centre with formation of O-alkylation products.

Table 6. Synthesis of different products by a standard method and in the presence of KF. [135]

Product of synthesis	Reactants	t, °C	Yield, %	Time, h
$CH_3CH(O_2CPh)CO_2H$	$PhCO_2H/KF/CH_3CH(Cl)CO_2H$	130	90	0.5
ditto	$PhCO_2K/CH_3CH(Cl)CO_2H$	130	20	6
$PhO(CH_2)_4OPh$	$PhOH/KF/Br(CH_2)_4Br$	120	93	0.5
ditto	$PhOH/NaOH/Cl(CH_2)_4Cl$	150	49	1
$CH_4(O)_2CH_2$	$Ph(OH_2)/KF/CH_2Br_2$	120	85	1
ditto	$Ph(OH)_2/CH_2Cl_2/NaOH(H_2O)$	110	23	15–18
$PhN(Me)CH_2N(Me)Ph$	$PhN(Me)H/KF/Cl(CH_2)_2Cl$	110	92	6
ditto	$PhN(Me)H/Na_2CO_3/Br(CH_2)_2Br$	105	83	24
$MeCH(SPh)CH_2Me$	$PhSH/KF/MeCH(I)CH_2Me$	130	92	8
ditto	$PhSNa/MeCH(Br)CH_2Me$	120	45	24

During the last two years, a series of studies by Clark and coworkers [133–136] has been published under the title "Hydrogen Bonds and Organic Synthesis". The authors showed that the formation of hydrogen bonds with KF added to the solvent greatly increases the reactivity of compounds containing the OH, NH, and SH groups in alkylation reactions. All the reactions are much faster than in the absence of KF and the yields are 80–95% (instead of 23–45%). Several examples from Clark and Miller [135] are presented in Table 6. The authors showed convincingly that KF does not participate in the reaction as a catalyst. The reactions do not rule out an initial proton transfer mechanism, because neither HF nor HF_2^- appear in solution, but hydrogen bonds are formed. Clark and Emsley [137–139] investigated the strength of the hydrogen

bonds formed by infrared spectroscopy and NMR and showed that the OH...F^- bonds are very strong (with an energy of 20–30 kcal $mole^{-1}$). It is of interest that even the much weaker NH...F^- and SH...F^- bonds also accelerate the reactions extremely effectively (by a factor of 3–4) and increase the yield by a factor of 1.5–3. In the presence of protic solvents the rate of reaction naturally decreases and the yields fall. Consequently strong hydrogen bonds can "assist" in organic synthesis, permitting the elimination of competing reactions and leading to higher yields and higher rates.

It may be hoped that the development of recently initiated studies on nucleophilic substitution reactions in the gas phase[140] will permit a quantitative assessment of the role of specific solvation, particularly the role of the formation of hydrogen bonds with the solvent.

---o0o---

Thus all the facts described above show that the influence of hydrogen bonds is very great not only in proton transfer reactions but also in reactions of other types. Investigators working in the field of physical organic chemistry have sought various ways of estimating the role of hydrogen bonds, but we believe that the accumulated data on the properties and energetics of hydrogen bonds have so far been inadequately used. At the same time, within the framework of studies on hydrogen bonds, there are trends which are very important for the solution of problems associated with the reactivity of organic compounds. This concerns studies on molecular hydrogen-bonded complex–ion pair transitions, the determination of spectroscopic and energetic characteristics of ionic hydrogen bonds (between conjugate acids BH^+ and bases and between acids AH and anions), the study of the structure of the complexes $[BHB]^+$ and $[AHA]^-$, the study of hydrogen bonds in the gas phase, and the study of the influence of polar solvents on the properties of hydrogen-bonded complexes. The combination of these data is undoubtedly necessary for a deeper understanding of problems of the reactivity and structure of organic compounds.

Mention should be made of a number of studies which were published during the preparation of the manuscript for the press: on problems associated with the spectroscopic and thermodynamic characteristics of molecular hydrogen-bonded complexes and the structure of ion pairs in various solvents[141–145]; on problems concerning the elucidation of the role of hydrogen bonds by comparing the acidities and basicities in the gas phase and in solutions in different solvents[146–149]; on the problem of the influence of strong hydrogen bonds on nucleophilic substitution reactions[150–152].

REFERENCES

1. E. M. Arnett, B. Chawla, L. Bell, M. Taagepera, W. J. Hehre, and R. W. Taft, J. Amer. Chem. Soc., 99, 5729 (1977).
2. S. E. Odinokov, A. A. Mashkovsky, V. P. Glasunov, A. V. Iogansen, and B. V. Rassadin, Spectrochim. Acta, 32A, 1355 (1976).
3. G. S. Denisov and V. M. Shraiber, Dokl. Akad. Nauk SSSR, 215, 627 (1974).
4. W. Gordi and S. C. Stanford, J. Chem. Phys., 9, 204 (1941).
5. A. A. Mashkovskii and S. E. Odinokov, Dokl. Akad. Nauk SSSR, 204, 1165 (1972).
6. E. V. Titov, V. M. Belobrov, and V. I. Shurpach, Ukrain. Khim. Zhur., 42, 1044 (1976).
7. L. N. Ferjenson (Editor), "Organic Molecular Structure", Willard Grand Press, Boston, Massachusetts, 1975, p. 389.
8. I. A. Koppel' and A. I. Payu, Reakts. Sposobn. Org. Soed., 11, 121 (1974).
9. D. Gurka and R. W. Taft, J. Amer. Chem. Soc., 91, 4796 (1969).
10. R. W. Taft, D. Gurka, L. Joris, P. R. Schleyer, and J. W. Rakshys, J. Amer. Chem. Soc., 91, 4801 (1969).
11. E. M. Arnett, E. J. Mitchell, and T. S. Murty, J. Amer. Chem. Soc., 96, 3875 (1971).
12. E. M. Arnett, R. P. Quick, and J. J. Burke, J. Amer. Chem. Soc., 92, 1260 (1970).
13. A. V. Yogansen, Teor. Eksper. Khim., 7, 302 (1971).
14. M. Joesten and L. J. Schaad, "Hydrogen Bonding", Marcel Dekker, New York, 1974, p. 291.
15. E. M. Arnett and L. E. Small, J. Amer. Chem. Soc., 99, 808 (1977).
16. V. K. Pogorelyi and T. F. Divnich, Teor. Eksper. Khim., 12, 822 (1976).
17. S. F. Bureiko and G. S. Denisov, Zhur. Prikl. Spektrosk., 14, 276 (1971).
18. W. Saffioti and W. Bueno, J. Chim. Phys., 73, 731 (1976).
19. E. N. Gur'yanova, I. P. Gol'dshtein, and T. I. Perepelkova, Uspekhi Khim., 45, 1568 (1976) [Russ. Chem. Rev., No. 9 (1976)].
20. N. D. Sokolov, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 17, 299 (1972).
21. P. Schuster, G. Zundel, and C. Sandorfy (Editors), "The Hydrogen Bond", North-Holland, Amsterdam–New York, 1976, Vol. 1.
22. H. Umeyama and K. Morokuma, J. Amer. Chem. Soc., 99, 1316 (1977).
23. P. Kollman and S. Rothernberg, J. Amer. Chem. Soc., 99, 1333 (1977).
24. L. M. Epshtein, A. N. Zhdanova, Yu. A. Khozanova, M. S. Fel'dshtein, and L. A. Kazytsina, Izv. Akad. Nauk SSSR, Ser. Khim., 87 (1974).
25. A. N. Zhdanova, L. M. Epshtein, N. M. Kolosova, N. K. Magdesieva, and L. A. Kazitsina, Teor. Eksper. Khim., 14, 684 (1978).
26. L. M. Epshtein, L. D. Ashkinadze, S. O. Gorelik, N. P. Gambaryan, D. A. Bochvar, and L. A. Kazitsyna, Izv. Akad. Nauk SSSR, Ser. Khim., 65 (1974).
27. R. West, D. Powell, M. K. Lee, and L. S. Whathey, J. Amer. Chem. Soc., 86, 3227 (1964).
28. A. V. Iogansen and B. V. Rassadin, Zhur. Prikl. Spektrosk., 6, 492 (1967).
29. L. G. Hepler, J. Amer. Chem. Soc., 85, 3089 (1963).
30. P. D. Bolton and L. G. Hepler, Quart. Rev., 25, 521 (1971).
31. R. P. Bell, "The Proton in Chemistry" (Translated into Russian), Izd. Mir, Moscow, 1977, p. 60.
32. L. N. Bykova and S. I. Petrov, Uspekhi Khim., 39, 1630 (1970) [Russ. Chem. Rev., No. 9 (1970)].
33. L. N. Bykova and S. I. Petrov, Uspekhi Khim., 41, 2065 (1972) [Russ. Chem. Rev., No. 11 (1972)].
34. O. A. Reutov, K. P. Butin, and I. P. Beletskaya, Uspekhi Khim., 43, 35 (1974) [Russ. Chem. Rev., No. 1 (1974)].
35. B. G. Cox, Ann. Rep. Progr., Chem. Sect., A70, 249 (1973).
36. "The Chemistry of Non-aqueous Solvents", Acad. Press, New York–London, 1970, Vol. 3, p. 1.

37. A. Ghosh and S. R. Palit, Indian J. Chem., **12**, 383 (1974).
38. H. Baba, A. A. Matsuyama, and H. Kokobun, Spectrochim. Acta, **25A**, 1709 (1969).
39. R. A. Hudson, R. M. Scott, and S. N. Vinogradov, Spectrochim. Acta, **26A**, 337 (1970).
40. H. Romanowski and L. Sobczyk, J. Phys. Chem., **79**, 2535 (1975).
41. D. F. De Tar and R. W. Novak, J. Amer. Chem. Soc., **92**, 1361 (1970).
42. G. S. Denisov, G. V. Gusakova, and A. L. Smolyansky, J. Mol. Struct., **15**, 377 (1973).
43. N. S. Golubev, G. S. Denisov, and A. I. Kol'tsov, Dokl. Akad. Nauk SSSR, **232**, 841 (1977).
44. S. E. Odinokov, A. A. Mashkovsky, A. K. Dzizenko, and V. P. Glasunov, Spectr. Letters, **8**, 157 (1975).
45. R. Lindermann and G. Zundel, J. Chem. Soc., Faraday Trans. II, 979 (1972).
46. R. Lindermann and G. Zundel, J. Chem. Soc., Faraday Trans. II, 788 (1977).
47. V. P. Glazunov, A. A. Mashkovskii, and S. E. Odinokov, Zhur. Prikl. Spektrosk., **22**, 696 (1975).
48. F. Korler and P. Huyskens, Adv. Mol. Relax. Processes, **8**, 125 (1976).
49. A. Wojtowicz and J. Malecki, Bul. Acad. Polon. Sci., Ser. Sci. Chim., **25**, 385 (1977).
50. V. P. Glazunov, A. A. Mashkovskii, and S. E. Odinokov, Zhur. Prikl. Spektrosk., **23**, 469 (1975).
51. A. V. Iogansen, S. A. Kiselev, B. V. Rassadin, and A. A. Samoilenko, Zhur. Strukt. Khim., **17**, 629 (1976).
52. P. Huyskens, Bul. Soc. chim. belges, **85**, 617 (1976).
53. G. V. Gusakova, G. S. Denisov, and A. L. Smolyanskii, Zhur. Prikl. Spektrosk., **17**, 666 (1972).
54. T. N. Filatova and Yu. I. Khurgin, Izv. Akad. Nauk SSSR, Ser. Khim., 1011 (1976).
55. E. I. Matrosov and M. I. Kabachnik, Dokl. Akad. Nauk SSSR, **232**, 89 (1977).
56. I. M. Kolthoff and M. K. Chantooni, J. Amer. Chem. Soc., **91**, 4621 (1969).
57. I. M. Kolthoff and M. K. Chantooni, J. Amer. Chem. Soc., **92**, 7025 (1970).
58. I. M. Kolthoff, Pure Appl. Chem., **25**, 305 (1971).
59. I. M. Kolthoff and M. K. Chantooni, J. Amer. Chem. Soc., **93**, 3843 (1971).
60. M. K. Chantooni and I. M. Kolthoff, J. Phys. Chem., **80**, 1306 (1976).
61. R. Drago, G. Vogel, and I. Needman, J. Amer. Chem. Soc., **93**, 6014 (1971).
62. C. D. Ritchie and P. D. Heffley, J. Amer. Chem. Soc., **87**, 5402 (1965).
63. C. D. Ritchie and G. H. Megerle, J. Amer. Chem. Soc., **89**, 1447 (1967).
64. W. S. Matthew, J. Bares, J. Bartmess, and T. G. Bordwell, J. Amer. Chem. Soc., **97**, 7006 (1975).
65. C. D. Ritchie and R. E. Uschold, J. Amer. Chem. Soc., **90**, 2821 (1968).
66. C. D. Ritchie, J. Amer. Chem. Soc., **91**, 6749 (1969).
67. A. G. Kozachenko, E. I. Matrosov, and M. I. Kabachnik, Izv. Akad. Nauk SSSR, Ser. Khim., 2440 (1976).
68. M. K. Chantooni and I. M. Kolthoff, J. Phys. Chem., **77**, 527 (1973).
69. B. W. Clare, D. Cook, E. C. Ko, Y. C. Mac, and A. J. Parker, J. Amer. Chem. Soc., **88**, 1911 (1966).
70. S. Y. Lam, C. Louis, and R. L. Benoit, J. Amer. Chem. Soc., **98**, 1156 (1976).
71. R. R. Ryall, H. H. Strobel, and M. C. R. Symons, J. Phys. Chem., **81**, 253 (1977).
72. H. W. Aitken and W. R. Gilkerson, J. Amer. Chem. Soc., **95**, 8551 (1973).
73. P. Schuster, G. Zundel, and C. Sandorfy (Editors), "The Hydrogen Bond", North-Holland, Amsterdam–New York, 1976, Vol. 3.
74. M. T. Bowers, D. H. Aue, H. M. Webb, and R. T. McIver, J. Amer. Chem. Soc., **93**, 4314 (1971).
75. R. T. McIver, Rev. Sci. Instr., **41**, 555 (1970).
76. M. Arshadi, R. Yamdagni, and P. Kebarle, J. Phys. Chem., **74**, 1475 (1970).
77. A. J. Cunningham, J. D. Payzant, and P. Kerbarle, J. Amer. Chem. Soc., **94**, 7627 (1972).
78. C. Agami, Bul. Soc. chim. France, 869 (1974).
79. E. Caldin and V. Gold (Editors), "Proton Transfer Reactions", Chapman and Hall, London, 1975, p. 31.
80. J. F. Wolf, R. H. Staley, I. Koppel, M. Taagepera, R. T. McIver, J. L. Beauchamp, and R. W. Taft, J. Amer. Chem. Soc., **99**, 5417 (1977).
81. T. B. Mahon and P. Kebarle, J. Amer. Chem. Soc., **99**, 222 (1977).
82. R. Yamdagni and P. Kebarle, J. Amer. Chem. Soc., **95**, 4050 (1973).
83. I. Koppel and M. Karelson, Reakts. Sposobn. Org. Soed., **11**, 985 (1975).
84. I. Koppel, L. L. Maretskaya, J. Koppel, and V. Pihl, Reakts. Sposobn. Org. Soed., **14**, 86 (1977).
85. M. Taagepera, W. G. Henderson, F. T. Brownlee, J. L. Beauchamp, D. Holtz, and R. W. Taft, J. Amer. Chem. Soc., **94**, 1369 (1972).
86. T. B. McMahon and P. Kebarle, J. Amer. Chem. Soc., **96**, 5940 (1974).
87. J. F. Wolf, P. G. Harch, and R. W. Taft, J. Amer. Chem. Soc., **97**, 2904 (1975).
88. E. W. Bittner, E. M. Arnett, and M. Saunders, J. Amer. Chem. Soc., **98**, 3734 (1976).
89. F. G. Bordwell, J. E. Bartmess, G. E. Drucker, Z. Margolin, and W. Mathews, J. Amer. Chem. Soc., **97**, 3226 (1975).
90. C. V. Krishnan and H. L. Friedman, J. Phys. Chem., **74**, 3900 (1970).
91. C. V. Krishnan and H. L. Friedman, J. Phys. Chem., **75**, 388 (1971).
92. E. M. Arnett and B. Chawla, J. Amer. Chem. Soc., **100**, 214 (1978).
93. D. H. Aue, H. M. Webb, and M. T. Bowers, J. Amer. Chem. Soc., **94**, 4726 (1972).
94. D. H. Aue, H. M. Webb, and M. T. Bowers, J. Amer. Chem. Soc., **98**, 318 (1976).
95. F. M. Arnett, E. M. Jones, M. Taagepera, W. G. Henderson, J. L. Beauchamp, D. Holtz, and R. W. Taft, J. Amer. Chem. Soc., **94**, 4724 (1972).
96. E. M. Jones and E. M. Arnett, Progr. Phys. Org. Chem., **11**, 263 (1974).
97. E. Caldin and V. Gold (Editors), "Proton Transfer Reactions", Chapman and Hall, London, 1975, p. 79.
98. E. M. Arnett and J. F. Wolf, J. Amer. Chem. Soc., **95**, 978 (1973).
99. R. H. Staley and J. L. Beauchamp, J. Amer. Chem. Soc., **96**, 6252 (1974).
100. I. Dzidic, J. Amer. Chem. Soc., **94**, 8333 (1972).
101. R. W. Taft, M. Taagepera, K. D. Summerhays, and J. Mitsey, J. Amer. Chem. Soc., **95**, 3811 (1973).
102. D. H. Aue, H. M. Webb, and M. T. Bowers, J. Amer. Chem. Soc., **97**, 4137 (1975).
103. J. I. Brauman and L. K. Blair, J. Amer. Chem. Soc., **91**, 2126 (1969).

104. J.I.Brauman and L.K.Blair, J.Amer.Chem.Soc., 90, 6561 (1968).
105. J.I.Brauman and L.K.Blair, J.Amer.Chem.Soc., 92, 5986 (1970).
106. R.McIver and J.S.Miller, J.Amer.Chem.Soc., 96, 4323 (1974).
107. J.Bartmess and R.McIver, J.Amer.Chem.Soc., 99, 4163 (1977).
108. E.M.Arnett and L.E.Small, J.Amer.Chem.Soc., 96, 5638 (1974).
109. R.W.Taft, J.F.Wolf, J.L.Beauchamp, G.Scorrano, and E.M.Arnett, J.Amer.Chem.Soc., 100, 1240 (1978).
110. M.Graffenil, J.Mol.Struct., 23, 65 (1974).
111. L.Radom, Chem.Comm., 403 (1974).
112. L.Radom, Austral.J.Chem., 28, 1 (1976).
113. T.Zeegers-Huyskens, Ann.Soc.Sci.Bruxelles, 90, 263 (1976).
114. M.A.Hussein and D.J.Millen, J.Chem.Soc., Faraday Trans.II, 685 (1974).
115. M.A.Hussein and D.J.Millen, J.Chem.Soc., Faraday Trans.II, 693 (1976).
116. D.J.Millen and G.W.Mines, J.Chem.Soc., Faraday Trans.II, 692 (1974).
117. S.F.Bureiko and G.S.Denisov, Symposium, "Molekulyarnaya Spektroskopiya" (Molecular Spectroscopy), Izd.Leningrad.Gos.Univ., Leningrad, 1973, No.2, p.30.
118. R.Yamdagni and P.Kebarle, J.Amer.Chem.Soc., 93, 7139 (1971).
119. A.J.Parker, Adv.Phys.Org.Chem., 5, 173 (1967).
120. A.J.Parker, Chem.Rev., 69, 1 (1969).
121. T.J.Broxton, D.M.Muir, and A.J.Parker, J.Org.Chem., 40, 3230 (1975).
122. R.G.Pearson, H.Sobel, and J.Songstad, J.Amer.Chem.Soc., 90, 319 (1968).
123. J.Miller, "Aromatic Nucleophilic Substitution", Elsevier, Amsterdam, 1968, p.315.
124. J.H.Fendler and J.W.Larsen, J.Org.Chem., 37, 2608 (1972).
125. M.J.Blandamer, J.Burgess, and J.G.Chambers, J.Chem.Soc., Dalton Trans., 60 (1977).
126. G.Bartoll, M.Lelli, F.Ciminale, and O.Attanasi, J.Chem.Soc., Perkin Trans.II, 20 (1977).
127. D.M.Brevis, N.B.Chapman, J.S.Paine, and J.Shorter, J.Chem.Soc., Perkin Trans.II, 1802 (1974).
128. B.Ya.Aksel'rod and M.I.Siling, Zhur.Fiz.Khim., 48, 323 (1974) [Russ.J.Phys.Chem., No.2 (1974)].
129. N.Chapman and J.Shorter (Editors), "Advances in Linear Free Energy Relations", Plenum Press, London–New York, 1972, p.203.
130. V.Palm, "Osnovy Kolichestvennoi Teorii Organicheskikh Reaktsii" (Fundamentals of a Quantitative Theory of Organic Reactions), Izd.Khimiya, Leningrad, 1977, p.87.
131. N.B.Chapman, M.R.Dack, D.J.Newman, J.Shorter, and R.Wilkinson, J.Chem.Soc., Perkin Trans.II, 962 (1974).
132. O.A.Reutov and A.L.Kurts, Uspekhi Khim., 46, 1964 (1977) [Russ.Chem.Rev., No.11 (1964)].
133. J.H.Clark and J.M.Miller, Chem.Comm., 229 (1976).
134. J.H.Clark and J.M.Miller, Tetrahedron Letters, 139 (1977).
135. J.H.Clark and J.M.Miller, J.Amer.Chem.Soc., 99, 498 (1977).
136. J.H.Clark, H.L.Holland, and J.M.Miller, Tetrahedron Letters, 3361 (1976).
137. J.H.Clark and J.Emsley, J.Chem.Soc., Dalton Trans., 2154 (1973).
138. J.H.Clark and J.Emsley, J.Chem.Soc., Dalton Trans., 1125 (1974).
139. J.H.Clark and J.Emsley, J.Chem.Soc., Dalton Trans., 2129 (1975).
140. P.Ausloos (Editor), "Interaction Between Ions and Molecules", Plenum Press, New York–London, 1975, p.413.
141. I.P.Gragerov, V.K.Pogorelyi, and I.F.Franchuk, "Vodorodnaya Svyaz' i Bystryi Protonnyi Obmen" (The Hydrogen Bond and Rapid Proton Exchange), Izd.Naukova Dumka, Kiev, 1978.
142. A.A.Samoilenko, A.I.Serebryanskaya, Yu.S.Bogachev, N.N.Shapet'ko, and A.I.Shatenshtein, Dokl.Akad.Nauk SSSR, 239, 388 (1978).
143. N.B.Librovich, V.P.Sakun, and N.D.Sokolov, Teor.Eksper.Khim., 14, 435 (1978).
144. M.Leuchs and G.Zundel, J.Phys.Chem., 82, 1632 (1978).
145. L.Elegant, J.Chim.Phys., 74, 1015 (1977).
146. J.B.Cumming, T.F.Magnera, and P.Kebarle, Canad.J.Chem., 55, 3474 (1977).
147. J.B.Cumming, M.A.French, and P.Kebarle, J.Amer.Chem.Soc., 99, 6999 (1977).
148. R.W.Taft, J.Wolf, J.Beauchamp, G.G.Scorrano, and E.M.Arnett, J.Amer.Chem.Soc., 100, 1240 (1978).
149. H.P.Hopkins, C.J.Alexander, and S.Zakir Ali, J.Phys.Chem., 82, 1268 (1978).
150. J.H.Clark, J.Emsley, and O.P.Hoyte, J.Chem.Soc., Perkin Trans.I, 1091 (1977).
151. J.H.Clark, J.M.Miller, and Kwok-Hung So, J.Chem.Soc., Perkin Trans.I, 941 (1978).
152. J.Emsley, O.P.Hoyte, and E.Overill, J.Chem.Soc., Chem.Comm., 225 (1977).

Institute of Organoelemental Compounds, USSR Academy of Sciences, Moscow