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Proton Chemical Shifts and Thermodynamics of the Formation of Hydrogen-Bonded Dimers and Mixed 1:1 Associates in the Ternary System Acetic Acid/Methanol/Tetrahydrofuran-d_8

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The chemical shifts of the carboxylic proton of acetic acid and of the hydroxylic proton of methanol dissolved together and separately in tetrahydrofuran-d_8 were determined as a function of the temperature and the solute concentrations. The determination of these chemical shifts was possible because in very pure samples the line positions are not affected by proton-exchange reactions. The data can only be explained by the presence of the following association reactions between hydrogen-bonded species which involve the solvent, S:

$$\mathrm{RCOOH{\cdots}S + RCOOH{\cdots}S \rightleftharpoons RCOOH{\cdots}RCOOH{\cdots}S + S}$$
$$\mathrm{RCOOH{\cdots}S + ROH{\cdots}S \rightleftharpoons RCOOH{\cdots}ROH{\cdots}S + S}$$
$$\mathrm{ROH{\cdots}S + RCOOH{\cdots}S \rightleftharpoons ROH{\cdots}RCOOH{\cdots}S + S}$$
$$\mathrm{ROH{\cdots}S + ROH{\cdots}S \rightleftharpoons ROH{\cdots}ROH{\cdots}S + S}$$

The reaction enthalpies are given by +4.2, −1.4, −3.0, and −3.3 kJ $\mathrm{mol^{-1}}$, the reaction entropies at 298 K by +10.3, −3, −9, and −16 J $\mathrm{K^{-1}\,mol^{-1}}$. These data are not very far from zero, indicating that the number of hydrogen bonds remains constant during the association. Nevertheless, the extent of association is very low, and the quasi monomers which are hydrogen bonded to the solvent dominate. This arises from the high concentration, c_S, of the free solvent. The change of c_S at higher solute concentrations has to be taken into account in the treatment of the experimental data. Similarly, hydrogen bonding between the donors and the solvent is the reason that cyclic 1:1 associates and higher associates are not observed and the reason for the slow proton exchange. It is shown that the thermodynamic data of proton donor association in different media obey linear enthalpy–entropy relationships which are typical for the functional proton donor group.

1. Introduction

The type and the degree of hydrogen bonding between proton donors such as carboxylic acids, alcohols, or similar compounds depend strongly on solute–solvent interactions.[1-11] Most spectroscopic work on hydrogen bonding of these compounds deals with association reactions in solvents where these interactions are weak.[2,5-11] The interpretation of the experimental results is often difficult because of the formation of dimers, trimers, or higher associates.[1,8]

The choice of solvents which act as hydrogen-bond acceptors or which exert other strong specific interactions on the solute has several advantages. Hydrogen bonding[12] with the solvent limits the number of different associates, and simple equilibria result. Thus, when the NMR technique is used, precise information can be obtained on solute–solvent interactions which are of the same order as the solute–solute interactions. This is very important in biological problems.[4,13]

There is another advantage of studying hydrogen bonding in noninert solvents by NMR spectroscopy. Using such solvents, it becomes possible to obtain information on mixed association between proton donors of different types because the essential condition of very slow proton exchange and noncoalesced signals is more easily fulfilled in these media. The knowledge of the thermodynamic parameters of mixed 1:1 association is, for example, of great interest for the evaluation of the mechanism of the central exchange step in cyclic two-proton exchange reactions:[14]

$$\mathrm{AH + BH^* \rightleftharpoons AH,BH^* \rightleftharpoons AH^*,BH \rightleftharpoons AH^* + BH}$$

We have recently[15] proved the existence of such a process in the system acetic acid/methanol/tetrahydrofuran-d_8. Because of a better technique for the preparation of very pure, sealed NMR samples of known composition, it was possible to study the proton-exchange kinetics by dynamic ^{1}H NMR spectroscopy in the slow proton-exchange range. The values of the proton chemical shifts in this system are reported in section 4 of this paper together with the chemical shifts of the binary systems acetic acid/tetrahydrofuran-d_8 and methanol/tetrahydrofuran-d_8. Knowledge of the thermodynamic data of proton donor self-association obtained from the binary systems is necessary in order to determine the thermodynamics of mixed proton donor association in the ternary system. The data are evaluated in terms of equations given in section 2. Because of solute–solvent hydrogen bonding the proton chemical shifts depend on the free solvent concentration, which decreases as the solute concentrations are increased. Section 2 is devoted to a quantitative treatment of this problem. Section 3 deals with experimental aspects. In section 5 the structure of the associates is discussed, and the thermodynamic results are compared with the known data of proton donor dimerization in inert media.

2. Chemical Shifts and Association in Noninert Solvents

The purpose of this section is to derive an expression for the average chemical shifts of molecules A and B as a function of the solute concentrations in the presence of solute–solute and solute–solvent association described by

$$\mathrm{A{\cdots}S}_l + \mathrm{B{\cdots}S}_m \rightleftharpoons \mathrm{A{\cdots}B{\cdots}S}_{l+m-n} + n\mathrm{S} \qquad \text{(1a)}$$

where n is the number of solvent molecules, S, which are liberated by the association of A with B. The equilibrium constant of the association is given by eq 1b, where c_S is

$$K = \frac{c_\mathrm{AB}{c_\mathrm{S}}^n}{c_\mathrm{AS}c_\mathrm{BS}} = K'{c_\mathrm{S}}^n \qquad \text{(1b)}$$

the concentration of solvent molecules which are not

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bounded by the strong solvent–solute interaction.

The average chemical shift of A is given by eq 2, where

$$\delta_A = \frac{c_{AS}}{C_A}\delta_{AS} + \frac{c_{AB}}{C_A}(\delta_{AS} + \Delta_{AB}) \qquad (2)$$

$C_A = c_{AS} + c_{AB}$ is the total concentration of A, δ_{AS} the chemical shift of A in A$\cdots$S$_l$, and Δ_{AB} the change in the chemical shift of A by association with B. As justified in section 4, we neglect, in contrast to previous studies,[11,12] the influence of the formation of true monomeric species on the concentration dependence of δ_A. By combination of eq 1b and eq 2 one obtains eq 3. This equation includes

$$y = \frac{\delta_A - \delta_{AS}}{\Delta_{AB}} = \frac{1}{2C_A}\left\{C_A + C_B + \frac{1}{K'} - \left[(C_A - C_B)^2 + \frac{2}{K'}(C_A + C_B) + \frac{1}{K'}\right]^{1/2}\right\} \qquad (3)$$

the case of self-association, A = B, if one multiplies K' by the factor 4 and sets $C_A = C_B = C/2$. For constant C_A, eq 3 represents convex curves $y = f(C_B)_{C_A=\text{const}}$. For eq 4, the

$$K'C_B \ll 1 \qquad (4)$$

curves are linear with respect to C_B and independent on C_A:

$$y_0 = \left(\frac{dy}{dC_B}\right)_0 C_B$$
$$\left(\frac{dy}{dC_B}\right)_0 = \frac{1}{\Delta_{AB}}\left(\frac{d\delta_A}{dC_B}\right)_0 = K' = Kc_S^{-n} \qquad (5)$$

Equations of this type have been derived by Mathur et al.,[16] Huggins et al.,[17] and Muller et al.[11]

However, eq 3 and 5 can be used in this form only if $n = 0$ or c_S = constant, conditions which will not be fulfilled in general. We obtain an expression for c_S as follows. The total solvent concentration, C_S, is given by

$$C_S = c_S + lc_{AS} + mc_{BS} + (l + m - n)c_{AB} = c_S + lC_A + mC_B - nc_{AB}$$

For the case that

$$nc_{AB} \ll c_S + lC_A + mC_B \qquad (6)$$

one obtains

$$c_S = C_S - lC_A - mC_B$$

By introducing the partial molar volumes $\bar{V}_i$ via

$$\sum_i C_i\bar{V}_i = 1$$

one obtains eq 7. This correction induces a more or less

$$c_S = \bar{V}_S^{-1} - C_A\left(l + \frac{\bar{V}_A}{\bar{V}_S}\right) - C_B\left(m + \frac{\bar{V}_B}{\bar{V}_S}\right) \qquad (7)$$

concave curvature into $y = f(C_B)_{C_A=\text{const}}$ in a region where these curves should already be convex. For certain values of the parameters in eq 6 the curves seem to be linear in a region where eq 4 does not hold any more.

The solute concentration range where the equations given in this section can be applied will probably be limited not by eq 6 but by the formation of higher associates between the solute molecules not taken into account in eq 1a.

3. Experimental Section

The ^{1}H NMR spectra were recorded on a Varian HA 100 MHz NMR spectrometer. The temperatures were measured with the methanol chemical shift standard.[31] A vacuum glass apparatus shown in Figure 1 was used to prepare sealed NMR samples of known composition and high purity, crucial to this work. The purified solvents were stored in glass vessels (c) over a drying agent. After degassing by the freeze–pump technique was effected, part of the liquids was transferred into graduated capillary tubes (d) by successive evaporation and condensation, permitting volume measurements before the transfer into the NMR tube (e) which was sealed off in the last stage. Only greaseless Teflon needle valve stopcocks (b)[18] were employed. Methanol and acetic acid were dried over molecular sieve (Merck, 3 Å), freshly regenerated in the vessels. THF-d_8 was dried and deoxygenized over anthracene/sodium–potassium alloy. Tetramethylsilane (1 vol %) was added to the solvent as standard before drying. The concentrations known from the volume measurements were corrected for the change with temperature. Within the margin of error of our volume measurements the densities of the solutions were found to depend in the same way on the temperature as does the density of pure tetrahydrofuran.[19]

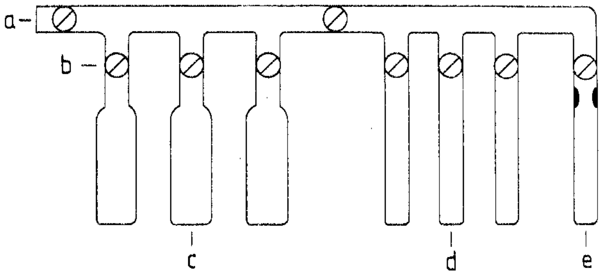


Figure 1. Vacuum glass apparatus used for the preparation of sealed NMR tubes of high purity and known composition. Explanation of symbols: (a) joint to vacuum pump, (b) greaseless Teflon needle valve stopcocks, (c) solvent storage vessels, (d) graduated capillary tubes, (e) NMR tube.

For the treatment of the experimental data a nonlinear least-squares fitting procedure of Marquardt[20] was employed.

4. Results

4.1. Self-Association of Methanol in Tetrahydrofuran-d_8. The ^{1}H NMR spectra of the binary system methanol/tetrahydrofuran-d_8 were recorded in the temperature range of 170–300 K and the concentration range of 0.06–1.6 mol L^{-1}. No broadening of the lines of the AB$_3$ spin system of methanol which could arise from intermolecular proton exchange was observed. The chemical shifts, δ, of the hydroxylic proton were calculated from the position of the multiplet lines by using equations given by Emsley et al.[21] for the AB$_3$ spin system. Figure 2 shows δ as a function of the concentration and the temperature. A nonlinear low-field shift is observed as the concentration is increased, which can be explained only by self-association of methanol in terms of eq 1a where A = B. Since methanol forms one hydrogen bond with tetrahydrofuran $l = m = 1$ in eq 1a. The calculated lines of Figure 2 were obtained by fitting the data to eq 3 by using the correction of eq 7 and setting $n = 1$ in eq 1b, which implies the formation of linear dimers ROH$\cdots$ROH$\cdots$S. The reason for the rejection of cyclic dimers with $n = 2$ will be given in section 5. Since the partial molar volumes $\bar{V}_i$ in eq 7 are not known, they were approximated by the molar volumes of the pure liquids, $\bar{V}_i°$. The error introduced by this approximation can be estimated from the densities of the system methanol/dioxane, which are known between 283 and 323 K.[22] At methanol concentrations lower than 2 mol L^{-1} the relation $\bar{V}_S = \bar{V}_S°$ holds (S = dioxane), with $\bar{V}_S°$(283

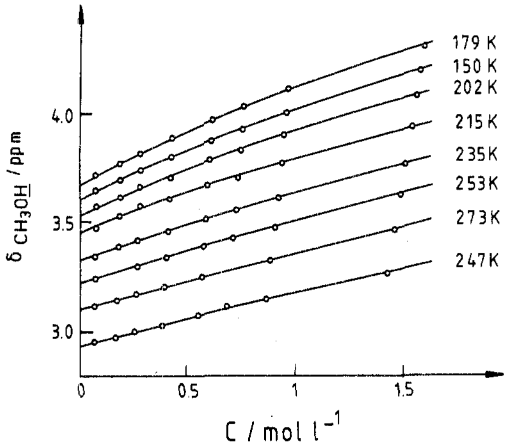


Figure 2. Experimental and calculated chemical shift dilution curves of the hydroxylic proton of methanol in tetrahydrofuran-d_8 at different temperatures.

K) = 84 mL mol^{-1} and $\bar{V}_S°(323\ K)$ = 88 mL mol^{-1}. The partial molar volumes of methanol in this concentration range are given by $\bar{V}_A(283\ K)$ = 53 mL mol^{-1} and $\bar{V}_A(323\ K)$ = 56 mL mol^{-1}, and the molar volume of pure methanol by $\bar{V}_A°(283\ K)$ = 40 mL mol^{-1} and $\bar{V}_A°(323\ K)$ = 42 mL mol^{-1}.[23] The value of the bracket, b, in eq 7 is then given exactly by $b(283\ K) = 1.64$ and $b(323\ K) = 1.63$, and in approximation by $b°(283\ K) = b°(323\ K) = 1.48$. The error introduced by using the $\bar{V}_i°$'s instead of the $\bar{V}_i$'s is then $\Delta b/b \approx 10\%$. With $\bar{V}_S°(298\ K)$ = 81.6 mL mol^{-1} (S = tetrahydrofuran)[19] this leads, according to eq 7, to a very low error in the free solvent concentration, c_S, of about 1–2% below concentrations of 2 mol L^{-1}. It was checked that in the systems acetic acid/acetone,[22] methanol/acetone,[22] and water/tetrahydrofuran[24] $\Delta b/b$ did not exceed the value of 10%. For the calculation of the curves in Figure 2, we used a value of $b° = 1.499$ at all temperatures because the change of $b°$ is smaller than 1% in this temperature range. However, the known change[19] of $\bar{V}_S^{-1}$ in eq 7 with temperature was taken into account. In a first stage of the calculations, the three parameters K, δ_{AS}, and Δ_{AA} were varied at each temperature. The values of Δ_{AA} showed no dependence on the temperature but a scattering around the value $\Delta_{AA} = 2.79 \pm 0.16$ ppm. In a second stage of the calculations, this mean value was used without variation in the whole temperature range, and only K and δ_{AS} were further varied. It was checked that no other value of Δ_{AA} minimized the total least-squares sum of all data points. Table I contains the values of K and δ_{AS} obtained by this procedure, which were used to calculate the curves of Figure 2. δ_{AS} shows a linear dependence on the temperature:

$$\delta_{AS} = (-0.633 \pm 0.003) \times 10^{-2}(T - 273) + (3.102 \pm 0.007)\ \text{ppm}$$

The neglect of the correction of eq 7 increases the least-squares sum by 40%. The van't Hoff plot of Figure 3 shows a clear linear behavior from which the enthalpy, ΔH, and the entropy, ΔS_{298K}, of the dimerization and their standard deviations are obtained:

$$\Delta H = -3.3 \pm 0.2\ \text{kJ mol}^{-1}$$

$$\Delta S_{298K} = -16.2 \pm 0.4\ \text{J K}^{-1}\ \text{mol}^{-1}$$

If one does not take into account the increase of the first term $\bar{V}_S^{-1}$ in eq 7 with falling temperature, ΔH is increased by 0.4 kJ mol^{-1} and ΔS_{298K} by 1.5 J K^{-1} mol^{-1}.

The neglect of the formation of the true methanol monomers of the concentration c_A in the treatment of the data is justified as follows. The equilibrium constant of the monomer formation is given by

$$K_m = c_A c_S / c_{AS}$$

the contribution of the monomers to δ_A by

$$\delta_m = \frac{c_A}{C_A} \Delta_a$$

Δ_a is the change in the chemical shift of A during the dissociation of AS. Since $c_{AS} \approx C_A$ and $c_S \approx \bar{V}_S°^{-1}$, one establishes that

$$\delta_m \approx K_m \bar{V}_S° \Delta_a \tag{8}$$

is independent of C_A in first-order approximation. Taking a value of $K_m = 10^{-1}$ mol L^{-1}, estimated from the data[25] of the association of methanol with tetrahydrofuran in CCl_4, and taking $|\Delta_a| \leq 3$ ppm, it follows that $|\delta_m| \leq 0.03$ ppm. The second-order change of δ_m with C_A is, therefore, a negligible contribution to the total change of δ_A in the concentration range 0–1.5 mol L^{-1}, which is about 0.5 ppm. It appears then that the change of δ_{AS} with temperature is not the result of the formation of monomers but the result of the excitation of the hydrogen-bond-stretching vibrational mode.[26]

4.2. Self-Association of Acetic Acid in Tetrahydrofuran-d_8. The ^1H NMR spectra of the binary system acetic acid/tetrahydrofuran-d_8 were recorded in the temperature

TABLE I: Equilibrium Constants K of the Dimerization Reactions $2AH\cdots S \rightleftharpoons AH\cdots AH\cdots S + S$ of Methanol and Acetic Acid in S = Tetrahydrofuran-d_8[a]

T/K	K	δ_{AS}	$\bar{V}_S° \times 10^{-3}$/L
	Methanol		
300	0.538 ± 0.013	2.491 ± 0.003	82.0
273	0.614 ± 0.01	3.100 ± 0.003	79.7
253	0.701 ± 0.003	3.223 ± 0.001	77.9
235	0.780 ± 0.008	3.330 ± 0.002	76.4
215	0.881 ± 0.028	3.463 ± 0.006	74.8
202	1.072 ± 0.026	3.542 ± 0.005	73.6
190	1.174 ± 0.011	3.617 ± 0.002	72.6
179	1.326 ± 0.018	3.684 ± 0.003	71.8
171	1.456 ± 0.042	3.729 ± 0.006	71.0
	Acetic Acid		
293	0.63 ± 0.05	10.510 ± 0.004	81.4
273	0.54 ± 0.04	10.630 ± 0.004	79.7
253	0.48 ± 0.03	10.748 ± 0.003	77.9
233	0.39 ± 0.01	10.869 ± 0.002	76.2
213	0.32 ± 0.01	10.989 ± 0.002	74.5
193	0.26 ± 0.04	11.108 ± 0.002	72.9

[a] δ_{AS} is the chemical shift of $AH\cdots S$ with respect to tetramethylsilane. $\bar{V}_S°$ is the molar volume of tetrahydrofuran taken from ref 19.

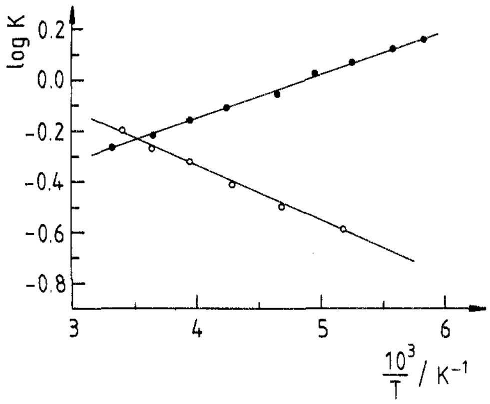


Figure 3. van't Hoff diagrams of the dimerization of acetic acid (○) and of methanol (●) in tetrahydrofuran-d_8.

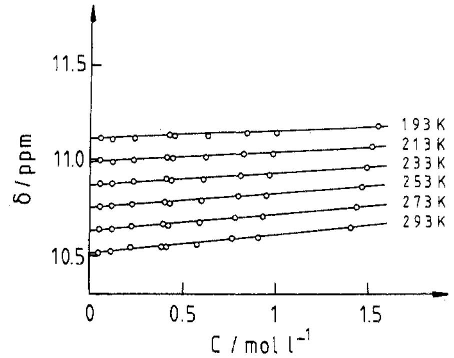


Figure 4. Experimental and calculated chemical shift dilution curves of the carboxylic proton of acetic acid in tetrahydrofuran-d_8 at different temperatures.

range 190–300 K and the concentration range 0.05–1.5 mol L^{-1}. No line broadening due to intermolecular proton exchange could be observed, and the line widths of the carboxyl and the methyl protons did not exceed the value of 1 Hz, which arises from the inhomogeneity of the magnetic field. Figure 4 shows the chemical shift of the carboxyl proton as a function of the concentration and the temperature. The curves are linear, which indicates that acetic acid forms dimers less easily than methanol. Acetic acid forms one hydrogen bond with tetrahydrofuran, and, therefore, $l = m = 1$ in eq 1. Since the curves do not show curvature, they were analyzed in a first stage in terms of eq 5, assuming the validity of eq 4. Thus the dimerization enthalpy could be determined but not the dimerization entropy, because the dimer shift Δ_{AA} cannot be obtained by the use of eq 5. However, Δ_{AA} can be estimated as follows. The value of Δ_{AA} depends on the formation of linear dimers RCOOH···RCOOH···S, where $n = 1$ in eq 1, or of cyclic dimers RCOOH–HCOOR, where $n = 2$. The relation

$$\Delta_{AA}{}^{1} = \tfrac{1}{2}\Delta_{AA}{}^{c} = \tfrac{1}{2}(\delta_{AA}{}^{c} - \delta_{AS}) \qquad (9)$$

between the linear dimer shift and the cyclic dimer shift holds in approximation if one assumes that the chemical shift of the solvent-bounded proton in the linear dimer is equal to the shift in the quasi monomer and that the shift of the acetic acid bounded proton in the linear dimer is equal to the shift of the protons in the cyclic dimer. We find by extrapolating the curves in Figure 4 to zero concentrations that δ_{AS}(THF) is given by

$$\delta_{AS}(\text{THF}) = (-0.633 \pm 0.003) \times 10^{-2}(T - 273) + (10.633 \pm 0.001)\ \text{ppm}$$

Lippert et al.[8] have found very similar relations for the chemical shift $\delta_{AA}{}^{c}$ of the cyclic dimer of acetic acid in CCl_4 and cyclohexane (CH):

$$\delta_{AA}{}^{c}(CCl_4) = -(0.614 \pm 0.036) \times 10^{-2}(T - 273) + (12.513 \pm 0.002)\ \text{ppm}$$

$$\delta_{AA}{}^{c}(\text{CH}) = -(0.60 \pm 0.06) \times 10^{-2}(T - 273) + (12.7 \pm 0.04)\ \text{ppm}$$

One then obtains temperature-independent values of $\delta_{AA}{}^{c}(CCl_4) - \delta_{AS}(\text{THF}) = 1.9$ ppm and $\delta_{AA}{}^{c}(\text{CH}) - \delta_{AS}(\text{THF}) = 2.1$ ppm, from which we estimate, by using eq 9

$$\Delta_{AA}{}^{c}(\text{THF}) = 2\Delta_{AA}{}^{1}(\text{THF}) = 2.0 \pm 0.3\ \text{ppm}$$

With this information the chemical shift dilution curves were calculated in a second stage with eq 3 and without the correction of eq 7, i.e., with $n = 0$. However, convex curves result, which is contrary to the experimental findings shown in Figure 4. Therefore, the linearity of the curves in Figure 4 at higher concentrations does not arise from the validity of eq 4 and 5 but is the consequence of the solvent participation as discussed in section 2. In consequence, the experimental data were fitted in a third stage to eq 3 by using the correction of eq 7. The value of the first parenthesized term in eq 7, $b^{\circ} = 1.706$, was calculated from the densities of the pure liquids[23] and produced, as in the case of methanol, the same error of about 1–2 % in the free solvent concentration c_S. Again, the change of $\bar{V}_S{}^{\circ -1}$ with temperature was taken into account. The data fit was carried our for $n = 1$ and $n = 2$, yielding the three parameters δ_{AS}, Δ_{AA}, and K. The values of Δ_{AA} obtained in this way did not show a dependence on the temperature but scattered about the values $\Delta_{AA}{}^{1}$ ($n = 1$) $= 1 \pm 0.2$ ppm and $\Delta_{AA}{}^{c}$ ($n = 2$) $= 0.8 \pm 0.2$ ppm. By comparing these values to the above estimates one must conclude that the chemical shift dilution curves are affected only by the formation of linear dimers of acetic acid. In a fourth stage of the calculation of the theoretical dilution curves shown in Figure 4, only K and δ_{AS} were varied, taking $n = 1$ and $\Delta_{AA} = 1$ ppm. The calculated values of K and δ_{AS} are given in Table I. The following thermodynamic data were obtained from the van't Hoff plot shown in Figure 3:

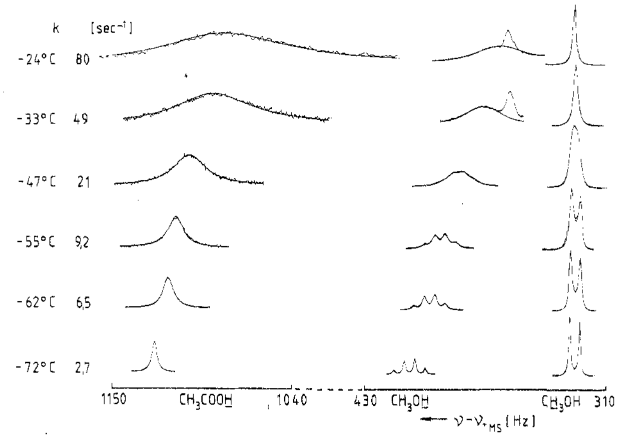


Figure 5. Superposed experimental and calculated 100-MHz ^{1}H NMR spectra of a mixture of 0.80 mol L^{-1} methanol and 0.29 mol L^{-1} acetic acid in tetrahydrofuran-d_8. The peak at $\nu - \nu_{Me_4Si} = 370$ Hz arises from solvent protons; k is the rate of proton exchange between methanol and acetic acid. (Reproduced with permission from ref 15).

$$\Delta H = +4.2 \pm 0.2\ \text{kJ mol}^{-1}$$

$$\Delta S_{298K} = +10.3 \pm 0.5\ \text{J K}^{-1}\ \text{mol}^{-1}$$

It appeared that this value of ΔH and the value obtained in the first stage of the calculation by use of eq 5 were equal within the margin of error.

The justification for neglecting the formation of true monomers in the treatment of the data is here similar to that in the case of methanol. K_m is also in the order of 10^{-1} mol L^{-1}, as estimated from the data of the association of acetic acid with dioxane.[12]

4.3. Mixed 1:1 Association of Acetic Acid with Methanol in Tetrahydrofuran-d_8. In very carefully prepared solutions of acetic acid and methanol in THF, the rates of proton exchange between the OH protons of methanol and the COOH protons of acetic acid are so slow[14,15] that the range of slow exchange is easily reached as illustrated in Figure 5. Therefore, the chemical shifts δ_{CH_3OH} and δ_{CH_3COOH} can be obtained at low concentrations and temperatures by simulation of the line shapes which, similarly, yields the rates of proton exchange.[14,15] At temperatures and concentrations higher than 230 K and 0.5–1.0 mol L^{-1}, respectively, the signals show too much broadening for the

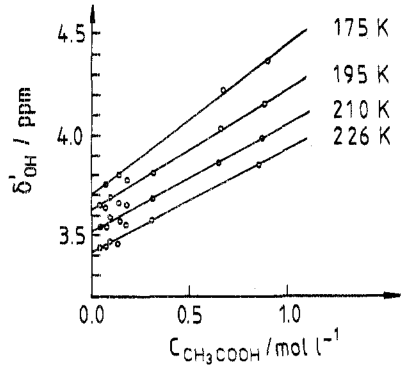


Figure 6. Chemical shifts of the hydroxylic proton of methanol corrected for self-association as a function of the concentration of acetic acid at selected temperatures in tetrahydrofuran-d_8.

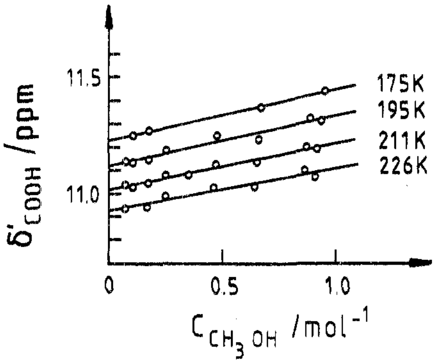


Figure 7. Chemical shifts of the carboxylic proton of acetic acid corrected for self-association as a function of the concentration of methanol for selected temperatures in tetrahydrofuran-d_8.

chemical shifts to be determined precisely enough. These chemical shifts show no correlation at first sight. However, by subtracting from these shifts the parts which arise from self-association and which are known from the experimental data of the binary systems shown in Figure 2 and 4, one obtains corrected chemical shifts δ_{OH}' and δ_{COOH}' which are affected only by mixed association. Figure 6 shows δ_{OH}' as a function of the total concentration of acetic acid, and Figure 7 shows δ_{COOH}' as a function of the total concentration of methanol. Linear curves result, as predicted by eq 5. The more pronounced scattering of the data as compared to the curves of Figures 2 and 4 arises from the greater error in the measurement of δ_{OH} and δ_{COOH}, due to the line broadening by proton exchange. The smaller experimental concentration range and the scattering of the data do not allow for the application of eq 3 and 7. However, the enthalpies of association can be obtained from the slopes of the curves in Figures 6 and 7, given in terms of eq 5 by

$$\left(\frac{d\delta_A'}{dC_B}\right)_0 = K_{AB}\Delta_{AB}(\bar{V}_S°)^n \qquad (10)$$

If one plots log $K_{AB}\Delta_{AB}$ and log $K_{BA}\Delta_{BA}$ vs. $1/T$ where CH_3COOH = A and CH_3OH = B, one obtains two curves with a different slope for both cases $n = 1$ and $n = 2$. It follows that the enthalpy of the formation of AB and of BA are different, which proves that $n = 1$. AB has then the structure RCOOH···ROH···S and BA the structure ROH···RCOOH···S. Table II contains the values of $K_{AB}\Delta_{AB}$ and $K_{BA}\Delta_{BA}$ calculated from the slopes of the curves in Figure 6 and Figure 7 with $n = 1$. Figure 8 shows the logarithms of these values as a function of $1/T$. The reaction enthalpies have the values $\Delta H_{AB} = -1.4 \pm 0.4$ kJ mol^{-1} and $\Delta H_{BA} = -3.0 \pm 0.4$ kJ mol^{-1}. The association entropies are calculated from the linear entropy–enthalpy relationships given in eq 10 of section 5. We obtain $\Delta S_{AB,298K} = -3 \pm 1$ J K^{-1} mol^{-1} and $\Delta S_{BA,\,298K} = -9$ J K^{-1} mol^{-1}. With these data we obtain the values of $\Delta_{AB} = 1.6 \pm 0.8$ ppm and $\Delta_{BA} = 4 \pm 2$ ppm, which are of the same order as the dimerization shifts Δ_{AA} of acetic acid and of methanol given in sections 4.1 and 4.2, thus proving the self-consistency of this procedure.

TABLE II: Values of $K_{AB}\Delta_{AB}$ and $K_{BA}\Delta_{BA}$ as Defined in Eq 10, Calculated from the Slope of Curves Shown in Part in Figures 6 and 7 for $n = 1$, A = CH_3COOH, B = CH_3OH[a]

T/K	$K_{AB}\Delta_{AB}$/ ppm	$K_{BA}\Delta_{BA}$/ ppm	$\bar{V}_S° \times 10^3$/ (L mol^{-1})
226	2.3 ± 0.3	6.8 ± 0.4	75.8
218	2.5 ± 0.2	7.1 ± 0.3	74.9
211	2.6 ± 0.2	7.3 ± 0.3	74.3
201	2.8 ± 0.4	8.0 ± 0.5	73.6
195	2.8 ± 0.3	8.3 ± 0.4	73.1
184	2.8 ± 0.1	9.7 ± 0.1	72.9
175	3.0 ± 0.1	10.6 ± 0.2	71.4

[a] For $\bar{V}_S°$, see Table I.

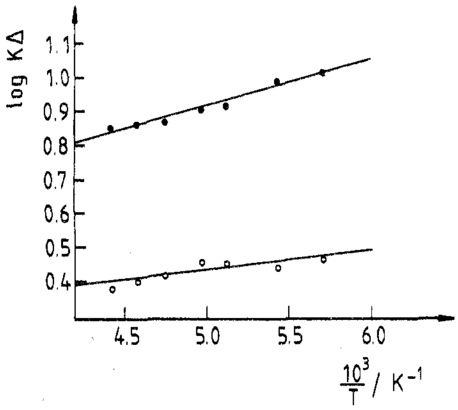
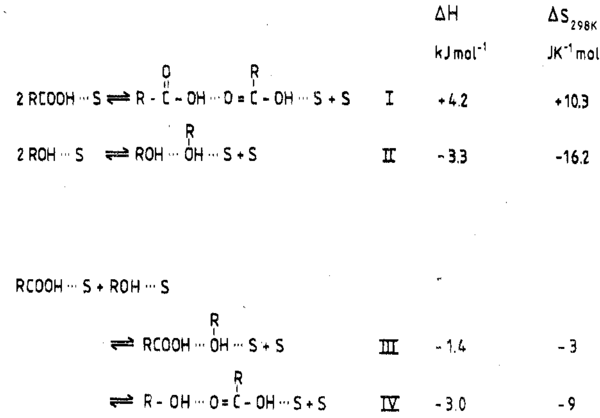


Figure 8. Logarithms of the slopes listed in Table II and defined by eq 10 as a function of $10^3/T$: (●) CH_3OH; (○) CH_3COOH.

Scheme I



5. Discussion

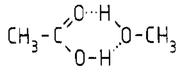
It is now possible to specify the association reactions observed in more detail as shown in Scheme I. The very small reaction enthalpies and reaction entropies which could be precisely determined show that the strength of hydrogen bonding in the solute–solute associates does not differ very much from the strength in the solute–solvent associates and that the equilibrium constants are of the order of 1. The simple association equilibria, which alone determine the chemical shifts, are the consequence of the high concentration, c_S, of free solvent molecules which prevent any observable formation of true monomers, cyclic dimers, or higher linear associates. The presence of the

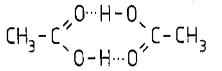
TABLE III: Standard Enthalpies, ΔH, and Entropies, ΔS_{298K}, for the Proton Donor Dimerization According to Eq 1 and 2 in Different Solvents[a]

no.	compound	medium	method	ref	m	$-\Delta H$/ kJ mol^{-1}	$-\Delta S_{298K}$/ (J K^{-1} mol^{-1})
1	acetic acid	cyclohexane	NMR	8	0	52	98
2		CCl_4	NMR	8	0	48	92
3		THF	NMR	here	1	−4.2	−10.3
4		H_2O	EMF	3	1	−2	−15[a]
5	benzoic acid	cyclohexane	IR	9	0	54	102
6		CCl_4	IR	9	0	46	89
7		benzene	IR	9	0	32	54
8	propionic acid	cyclohexane	NMR	8	0	51	93
9		CCl_4	NMR	8	0	47	87
10	methanol	gas phase		7	0	64	193
11		CCl_4	NMR, IR	6	0	39	117
12		THF	NMR	here	1	3.3	16
13	ethanol	CCl_4	NMR, IR	6	0	31	84
14	2-methyl-2-propanol		NMR, IR	6	0	19	46
15	2,6-dimethyl-2,6-hexanediol		NMR, IR	6	0	17	58

[a] Calculated from data of ref 3 with $c_{H_2O} \approx c_{H_2O}{}^{\circ} = 55$ mol L^{-1}.

solvent is equally the reason that the above equilibria are all shifted to the left, reducing the extent of association. The formation of linear solvent-bounded 1:1 associates between methanol and acetic acid of the structures III and IV was proved by finding different enthalpies of association of the hydroxylic proton of methanol and of the carboxylic proton of acetic acid. In the case of the formation of a cyclic associate of structure V, these enthalpies should have been found to be equal. However, this does not imply that there are no cyclic dimers at all. Their concentration may be estimated from eq 1b by taking $K = 1$ mol L^{-1} as an approximate value. It follows that $c_V/c_{IV} \approx c_V/c_{III} \approx Kc_S{}^{-1} \approx 0.08$, as was assumed previously[15] in discussing the mechanism of proton exchange between acetic acid and methanol in the mixed 1:1 associates.


V


VI

The situation is very similar in the case of the dimer of acetic acid, whose formation enthalpy is positive. The question of a cyclic structure VI or a linear structure I could be settled in section 4.2 in favor of structure I by a discussion of the experimental change in the proton chemical shift during the dimerization. The linear structure I of the methanol dimer follows by analogy.

The thermodynamic data listed in Scheme I cannot be explained only in terms of acceptor or donor properties of the reactants. For example, RCOOH···S and ROH···S behave very similarly to ROH···S but not to RCOOH···S. Such a finding can only be explained in terms of the properties of the product. The positive enthalpy of the formation of I can, for example, be explained by the repulsion of the components of the electric dipole moments perpendicular to the axis of hydrogen bonding. In the cyclic dimer of the structure VI, this dipole–dipole interaction is attractive and contributes to the stability of VI. Since the main component of the dipole moment of methanol lies in the axis of hydrogen bonding, this dipole–dipole interaction is absent in associates involving methanol. Weak interactions between parts of hydrogen-bonded species are normally of minor importance in association equilibria where the number of hydrogen bonds changes during the reaction.

In Table III the thermodynamic data of the dimerization of acetic acid and methanol found here for THF as solvent are compared with literature data of the dimerization of several carboxylic acids and alcohols in different media. In Figure 9 the dimerization enthalpies are plotted against the entropies. The gas-phase data[5] of acetic acid have been omitted because the entropies are very contradictory. Similarly, data which have been obtained by the partition technique[2] between water and organic solvent are not considered because they cannot be attributed to simple dimerization equilibria.[27] Figure 9 shows that linear entropy–enthalpy relationships

$$\Delta H = T_c \Delta S_{298K} \tag{11}$$

are obtained; these are typical for the two classes of proton donors with T_c(RCOOH) = 495 ± 12 K and T_c(ROH) = 335 ± 20 K. Enthalpy–entropy compensation is a well-known phenomenon and has been observed for a large number of reactions.[28] Equation 11 was used in section 4.3 to calculate the entropies of the formation of the mixed 1:1 associates III and IV in Scheme I and is, therefore, very useful for the determination of equilibrium constants in all cases where ΔS cannot be obtained because of methodic limitations. Similarly, it is possible to derive a scale of hydrogen-bond acceptor strength of different solvents[29,30] with the thermodynamic data of the substitution reactions

$$\Delta H\cdots S + S' \rightleftharpoons AH\cdots S' + S$$

calculated from Table III by neglecting in first-order approximation the contribution arising from changes in nonspecific solvation.[30]

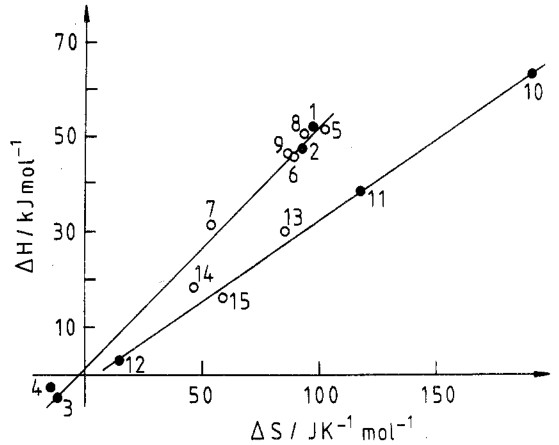


Figure 9. Enthalpy–entropy relations (see Table III) of proton donor dimerization in different media: upper curve, carboxylic acids; lower curve, alcohols. The numbering refers to Table III.

6. Conclusions

It has been shown that the study of proton donor association in noninert solvents by NMR spectroscopy has many advantages for obtaining valuable information on weak and strong solute–solvent interactions, hydrogen bonding, and proton exchange between proton donors. Knowledge of these phenomena is important for understanding many chemical and biological problems. Further experiments are possible now that the methods of obtaining the necessary information have been improved.

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Improved Canonical Variational Theory for Chemical Reaction Rates. Classical Mechanical Theory and Applications to Collinear Reactions

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We present a new variational theory of chemical reaction rates. The theory, called improved canonical variational theory (ICVT), provides a bound on the classical mechanical equilibrium reaction rate. As compared to canonical variational theory (the method of free-energy curves) it involves a more accurate treatment of the threshold region. Classically the method consists of eliminating all contributions to the generalized transition-state theory rate constant from energies below the energetic reaction threshold and then estimating the contribution from the remaining truncated canonical ensemble by variational optimization of a generalized transition state dividing surface in configuration space. The ICVT is illustrated and tested by applications to classical collinear reaction rates in several systems. We also provide tests of the unified statistical theory for two new reactions.

I. Introduction

In recent work we have applied the canonical variational theory of reactions to collinear classical reactions[1] and to collinear[2,3] and three-dimensional[4–6] reactions including effects of quantization. This theory is a generalized transition-state theory, i.e., it assumes an equilibrium distribution in phase space and that all phase points with local momentum in the product direction on a phase-space surface dividing reactants from products are direct reactive trajectories which cross the dividing surface only once. In particular the dividing surface is assumed to be a function of coordinates only and it is chosen to minimize the

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