1970 BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 48 (7), 1970—1973 (1975) [Vol. 48, No. 7

Hydrogen Bonding Interactions of Carboxylic Acids with *N,N*-Dimethylacetamide and Pyrazine as Studied by Means of NMR Dilution Shifts

Hideaki Fujiwara, Nobuyuki Yoshida, and Tsuneo Ikenoue

Chemical Research Institute of Non-Aqueous Solutions, Tohoku University, Katahira 2-1-1, Sendai 980

(Received December 9, 1974)

The NMR dilution shifts of OH proton in several carboxylic acids have been studied for mixtures with *N,N*-dimethylacetamide (DMA) or pyrazine. The acids treated were acetic, propionic isobutyric, and trifluoroacetic acids. The dilution shifts curve of OH proton in each acid–DMA system showed a characteristic ν-type curve with the minimum value at 0.65—0.75 mol fraction of the acid. The curve for the isobutyric acid–pyrazine system was linear below 0.45 mol fraction of the acid, taking the minimum at 0.75 mol fraction. These curves were explained by assuming the formation of both 1: 1 and 2 (acids): 1(base) complexes in the chemical equilibrium. The formation constants of the complexes and the shifts of OH proton in the 2: 1 complex were estimated for each system. Liability of the complex formation and the structure possible for the 2: 1 complex were discussed.

The amide-acid interaction has been of interest to many NMR investigators.[1–6)] Gillespie and Birchall[1)] studied the proton NMR spectra of several amides in FSO_3H at low temperatures and concluded that amides were protonated at the oxygen atom. It was found that the addition of trifluoroacetic acid (TFA)[3)] or dichloroacetic acid[4)] to an amide leads to the unrestricted internal rotation around the C–N bond, which was interpreted as resulting from the occurrence of *N*-protonation in the amide. The examination of the absorption spectra of amides in sulfuric acid by Goldfarb *et al.*[7)] indicates the presence of two equilibria in the mixture, one corresponding to the protonation of the amide and the other to the hydrogen bonding of the protonated amide with the solvent. Edward and Wang,[8)] however, explained the spectral data only in terms of a protonation equilibrium of the amide considering the difference in the hydration number between a protonated amide and a protonated Hammett indicator which was used to establish the H_0 scale. Thus the simultaneous interaction of the amide with two acidic protons has not been corroborated yet.

The interaction of *N,N*-dimethylacetamide (DMA) with some carboxylic acids has been studied also by measuring the density, viscosity, electric conductivity, melting point, and infrared and Raman spectra.[3,9–11)] For the acetic acid–DMA system, the formation of 1: 1 and 2 (acids): 1(DMSO) complexes has been suggested, the former from the fact that the glass formation occurred in the range 0.4—0.6 mol fraction of the acid,[10)] and the latter from the fact that the viscosity and electric conductivity became maximum in the range 0.6—0.7 mol fraction.[11)] The presence of the 1: 1 and 2: 1 complexes in the acetic acid–DMA system was also suggested by Khazova and Chesnokov[11)] as a result of the measurements of their infrared and Raman spectra, though the importance of the Fermi resonance to interpret the spectra had been pointed out by Haurie and Novak.[9)]

In a previous paper,[12)] the NMR dilution shifts for the binary systems of some carboxylic acids and dimethyl sulfoxide (DMSO) were examined and the shift curves were explained assuming the formation of both 1: 1 and 2 (acids): 1 (DMSO) complexes in the chemical equilibrium. A similar examination for the systems of some carboxylic acids in DMA has been carried out. To ascertain the participation of 2: 1 complex in such acid-base interaction, pyrazine was also chosen as a base which possesses two equivalent basic sites in a molecule. Acetic, propionic, isobutyric, and trifluoroacetic acids were used as the acid.

Experimental

All the procedures for the purification of carboxylic acids and the preparation of solutions are the same as reported previously.[12)] Commercial DMA was dried by returning the forerun through barium oxide into a still pot after the addition of toluene by 30 volume %. After drying had been accomplished, toluene was removed by distillation under reduced pressure. When methanol was mixed with the purified DMA, the NMR fine structure of OH proton was clearly observed, in particular below 0.5 mol fraction of the alcohol,[13)] showing the marked efficiency of DMA to retard the exchange rate of the OH proton.

Pyrazine was handled in a liquid state with use of a constant temperature box at about 65°C. Commercial pyrazine was purified in a similar way to that for DMA.

NMR spectra were obtained with a Hitachi R-20B high resolution NMR spectrometer (60 MHz, at 34.5 °C). The chemical shift was measured with a frequency counter, the error being within ±0.1 Hz. NMR measurements at high temperatures were carried out with a Hitachi R-20VTP prove. The sample temperatures were determined with a ethylene glycol "chemical shift thermometer". The NMR spectra for the isobutyric acid–pyrazine system at ordinary temperature were measured with a Varian V-4300B NMR spectrometer (60 MHz). The shift was determined by the side band technique with accuracy of ±0.15 Hz. The probe temperature was 33 °C.

Results

The shifts of OH proton (δ_{OH}) in the carboxylic acid–DMA systems plotted against acid mol fraction (X) are shown in Figs. 1 and 2. The dilution shift curves for isobutyric and propionic acids exhibit the ν-type pattern (Fig. 1), the curve for TFA being linear below 0.45 mol fraction of the acid (Fig. 2). These curves are similar to those obtained for the carboxylic acid–DMSO systems.[12)] The curve for acetic acid (Fig. 1) exceptionally shows no minimum in the intermediate con-

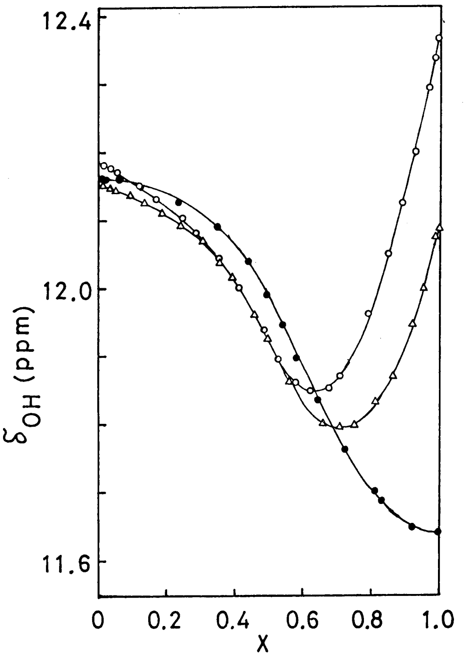


Fig. 1. Dilution shift curves observed for the acid–DMA systems.
○: Isobutyric acid. △: Propionic acid. ●: Acetic acid.

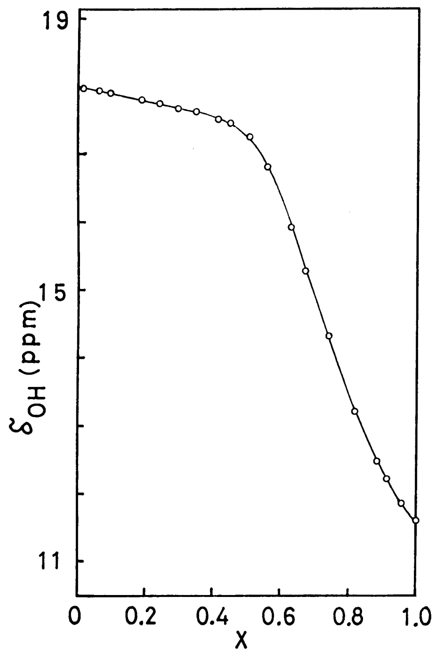


Fig. 2. A dilution shift curve observed for the TFA–DMA system.

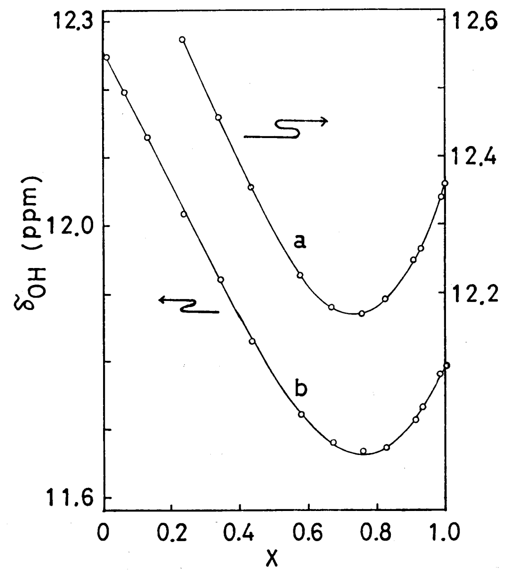


Fig. 3. Dilution shift curves observed for the isobutyric acid–pyrazine system.
a: At 33 °C. b: At 80.5 °C.

centration. This is understandable from the following facts: (1) the difference between the minimum shift and the shift for the neat solution decreases in the order of isobutyric, propionic, and acetic acids for the acid–DMSO systems, (2) the difference is smaller in the acid–DMA systems than that in the acid–DMSO systems for isobutyric and propionic acids.

The dilution shift curve for the isobutyric acid–pyrazine system at ordinary temperature (curve a, Fig. 3) also goes through the minimum at 0.75 mol fraction of the acid. The measurements for this system at two high temperatures of 80.5 °C (curve b) and 127 °C (not shown but similar to curve b in Fig. 3) revealed that the concentration corresponding to the minimum shift does not vary with temperature and the curves are practically linear below 0.45 mol fraction of the acid.

The dilution shift curve of the TFA–pyrazine system at 60 °C was similar to the curves for the TFA–DMA (Fig. 2) and TFA–DMSO[12] systems.

Two proton signals due to the two *N*-methyl groups of DMA in the TFA–DMA system coalesced into a singlet above 0.55 mol fraction of the acid.[3] The acid concentration where the coalescence occurred was temperature dependent; it decreased from 0.55 mol fraction at 34.5 °C to 0.35 mol fraction at 40.0 °C. No such coalescence was observed for the systems containing isobutyric, propionic, or acetic acid instead of TFA at 34.5 °C.

The shift of CH proton in the acid and base changed monotonously with the acid concentration. The variation of the shift was less than 1/5 of that for the OH proton.

Discussion

An acid-base interaction in solution generally produces either the ionic species such as the conjugate acid or base of the initial species, or the hydrogen bonded complex. The former is important in the case of a strong acid against a strong base, and the latter in the case of a weak acid against a weak base. Measurements of the infrared spectra on the systems of acetic acid–DMA,[14] formic acid–DMA,[15] and formic acid–DMSO[15] revealed no ionic species. Examination of the absorption spectra of pyrazine in the mixture of isobutyric acid and *n*-hexane did not show any evidence of the presence of ionic species,[16] though the dissolution of pyrazine in aqueous sulfuric acid clearly produces the ionic species such as pyrazinium ions.[17-19]

It can thus be assured that only the hydrogen bond formation is important in interpreting the NMR data for the OH protons of acetic, propionic, and isobutyric acids in DMSO, DMA, and pyrazine. Since the presence of ionic species has been reported for the systems containing TFA with DMSO,[3] DMA,[14] or pyrazine,[20] the contribution of ionic species may be unavoidable in interpreting the data for these systems.

The characteristic ν-type shift curves (Figs. 1 and 3) are interpreted by assuming that the carboxylic acid dimer produces the 2: 1 and 1: 1 complexes with a base[12] as follows:

$$A_2 + B \rightleftarrows A_2{\cdot}B \qquad K_1$$

$$A_2{\cdot}B + B \rightleftarrows 2(A{\cdot}B) \qquad K_2$$

where A_2 and B denote the carboxylic acid cyclic dimer and the base, respectively, and $A_2{\cdot}B$ and $A{\cdot}B$ the 2: 1 and 1: 1 complexes, respectively. The procedure for analysis of the ν-type shift curve is summarized below, the detailes having been given previously.[12] Under the above conditions, the shift of OH proton can be calculated in terms of the following six parameters:

δ_D=the shift of OH proton in the cyclic dimer of the acid. The value was evaluated by extrapolating the straight part of the dilution shift curve in cyclohexane to infinite dilution of the acid,

$\delta_{C\beta}$=the shift of OH proton in the 1: 1 complex. The value was substituted by the value of δ_{OH} (the shift observed) at infinite dilution of the acid in DMA or pyrazine,

$\delta_{C\alpha}$=the shift of OH proton in the 2: 1 complex,

K_1=the formation constant of the 2: 1 complex,

K_2=the formation constant of the 1: 1 complex, and

X=initial mol fraction of the acid in monomer unit.

Of these, $\delta_{C\alpha}$, K_1, and K_2 remain to be determined. δ_D, $\delta_{C\beta}$, and X were obtained experimentally. These three parameters can be determined by calculation so as to give the best fit between the calculated and observed dilution shift curves. This process of the least squares was achieved by the trial and error method, only one set of parameters being obtained for each system within an acceracy of the measurement of shifts and concentrations. Parameters obtained experimentally or by calculation for each system are summarized in Table 1, together with those for the acid–DMSO systems.[12] The shift data above 0.6 mol fraction of the acid were omitted in the calculation, since the deviation between the calculated and observed shifts never diminished in that region.

TABLE 1. PARAMETERS OBTAINED EXPERIMENTALLY OR BY CALCULATION[a] FOR CARBOXYLIC ACID–DMSO, DMA, AND PYRAZINE SYSTENMS (34.5 °C)

Base	Acid	δ_D	$\delta_{c\beta}$	K_1	K_2	$\delta_{c\alpha}$
DMSO	Acetic	13.36	11.88	100	9	11.13
	Propionic	12.49	11.89	60	9	11.00
	Isobutyric	12.64	11.92	40	9	10.87
	TFA	12.03	16.44	c	c	c
DMA	Acetic	12.36	12.162	220	10	11.70
	Propionic	12.49	12.155	60	8	11.52
	Isobutyric	12.64	12.185	90	5	11.59
	TFA	12.03	18.00	c	c	c
Pyrazine[b]	Isobutyric	12.19	12.257	20	1.7	11.353

a) δ_D and $\delta_{c\beta}$ are obtained experimentally and K_1, K_2, and $\delta_{c\beta}$ by calculation. The accuracy of calculation is $\pm 20\%$ for K_1 and K_2 and ± 0.05 ppm for $\delta_{c\alpha}$. b) The isobutyric acid–pyrazine system is investigated at 80.5 °C. c: Not fully analyzed.

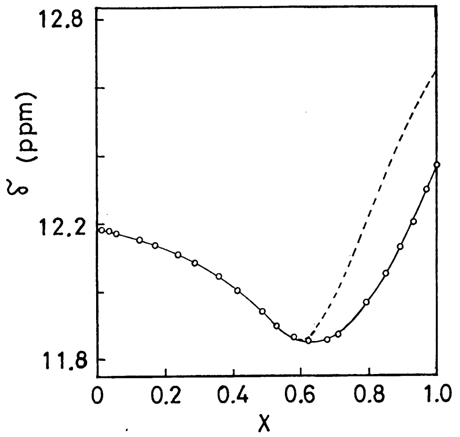


Fig. 4. A comparison of the observed and the calculated dilution shift curves for the isobutyric acid–DMA system.
——: Observed. ----: Calculated. ○: Experimental points.

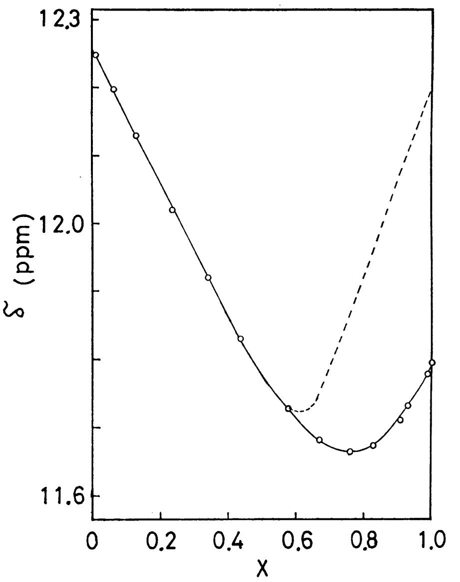


Fig. 5. A comparison of the observed and the calculated dilution shift curves for the isobutyric acid–pyrazine system (at 80.5 °C).
——: Observed. ----: Calculated. ○: Experimental points.

The deviation of δ_{calcd} (shift value calculated) from δ_{OH} (shift value observed) above 0.6 mol fraction of the acid is shown in Figs. 4 and 5. It is larger in the isobutyric acid–pyrazine system than in the isobutyric acid–DMA system. The larger deviation for the pyrazine system is presumably due to the fact that the measurement temperature was higher. Since a rise in temperature usually causes a larger contribution of the monomer and/or chain oligomer of carboxylic acid,[21] higher temperature may be responsible for the larger deviation of δ_{calcd} from δ_{OH}.

The K_1 values are always more than five times larger than the K_2 values (Table 1). The large K_1 value implies the low concentration of the cyclic dimer in solution and a remarkable tendency of the acid molecule to form complexes with the base. The Raman spectral data[9] also show a negligibly small amount of the cyclic dimer for the solutions of about 0.5 mol fraction of acetic acid in DMSO or DMA.

Although pyrazine is known to be more basic than DMSO and DMA,[22] K_1 in pyrazine is smaller than that in either DMSO or DMA. This is partly ascribed to the higher measurement temperature of pyrazine system than that of DMSO and DMA systems. The polarity of each species in a solution may also explain the small K_1 in pyrazine. Pyrazine is a non-polar solvent, while DMSO and DMA are dipolar solvents. While the cyclic dimer of carboxylic acid will be less polar, the complexes of the acid with these basic solvents may be well supposed to be polar. The polar species is stabilized in a polar medium to a larger extent than the less polar species such as the cyclic dimer, leading to the large K_1 value in a polar medium.

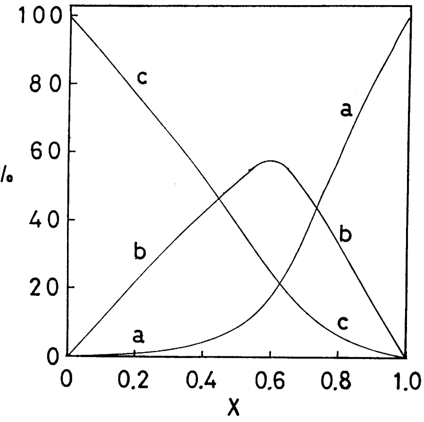
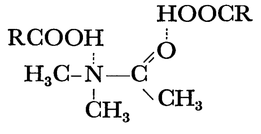


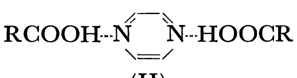
Fig. 6. A distribution curve of the acid molecule to each species in the isobutyric acid–pyrazine system.
a: Cyclic dimer. b: 2: 1 Complex. c: 1: 1 Complex.

For the isobutyric acid–pyrazine system, the dilution shift curve is linear below 0.45 mol fraction of the acid, an apparent difference from the curves for the acid-DMA systems. As seen from Fig. 6, the 1: 1 and 2: 1 complexes predominate below 0.45 mol fraction of the acid, and the shift depends almost on the K_2 value which is decisive to the ratio of 1: 1 complex to 2: 1 complex. Thus, the linearity in the dilution shift curve of the isobutyric acid–pyrazine system may be due to the smallness of the K_2 value.

It is noteworthy that $\delta_{\text{C}\alpha}$ lies in a higher field side than $\delta_{\text{C}\beta}$ and δ_{D} (Table 1). This is closely related to an appearance of the minimum in the shift curve at a higher acid concentration. The structure possible for the 2: 1 complex of the acid with DMA and pyrazine are readily given as I and II, respectively, in which two basic sites of the base interact simultaneously with the acids.



(I)



(II)

The authors are grateful to Professor Y. Ikegami and Mr. M. Kumano for their helpful discussions. They are also indebted to Mr. K. Fujieda for discussing the accuracy of NMR measurements.

References

1) R. J. Gillespie and T. Birchall, *Can. J. Chem.*, **41**, 148 (1963).
2) G. A. Olah, D. L. Brydon, and R. D. Porter, *J. Org. Chem.*, **35**, 317 (1970).
3) C. F. Nawrot and A. Veis, *J. Amer. Chem. Soc.*, **92**, 3903 (1970).
4) P. A. Temussi and R. Bellofiore, *Ric. Sci.*, **39**, 419 (1969).
5) A. R. Katritzky and R. A. Y. Jones, *Chem. Ind.*, (London), **1961**, 722.
6) R. B. Homer and C. D. Johnson in "The Chemistry of Amides," ed. by J. Zabicky, John Wiley & Sons, London (1970), Chapter 3.
7) A. R. Goldfarb, A. Mele, and N. Gutstein, *J. Amer. Chem. Soc.*, **77**, 6194 (1955).
8) J. T. Edward and I. C. Wang, *Can. J. Chem.*, **40**, 966 (1962).
9) M. Haurie and A. Novak, *J. Chim. Phys.*, **64**, 679 (1967).
10) V. F. Chesnokov and I. M. Bokhovkin, *Zh. Obshch. Khim.*, **39**, 1189 (1969).
11) I. V. Khazova and V. F. Chesnokov, *ibid.*, **40**, 7 (1970).
12) H. Fujiwara, *J. Phys. Chem.*, **78**, 1662 (1974).
13) The fine structure of OH proton had never been observed clearly in the methanol-DMA system; C.R. Kanekar, C. L. Khetrapal, K. V. Ramiah, and C. A. Indirachary, *Proc. Indian Acad. Sci., Sect. A*, **66**, 189 (1966).
14) P. Combelas, F. Cruege, J. Lascombe, C. Quivoron, and M. Rey-Lafon, *J. Chim. Phys.*, **66**, 668 (1969).
15) C. W. Chao, A. Veis, and F. Jacobs, *J. Amer. Chem. Soc.*, **89**, 2219 (1967).
16) H. Fujiwara and T. Ikenoue, *Sci. Rept. RITU.*, *A*, **25**, 145 (1975).
17) A. S. Chia and R. F. Trimble, Jr., *J. Phys. Chem.*, **65**, 863 (1961).
18) R. H. Linnell and A. Kaczmarczyk, *ibid.*, **65**, 1196 (1961).
19) M. Iwaizumi and H. Azumi, *Nippon Kagaku Zasshi*, **84**, 694 (1963).
20) H. Kamei, *J. Phys. Chem.*, **69**, 2791 (1965).
21) M. Haurie and A. Novak, *C. R. Acad. Sci., Paris, Ser. B*, **264**, 694 (1967).
22) pK_{BH^+} values of DMSO, DMA, and pyrazine are -2.8,[23] -0.19,[7] and 0.65,[17] respectively, in aqueous sulfuric acid.
23) P. Haake and R.D. Cook, *Tetrahedron Lett.*, **1968**, 428.